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Synthesiology

English edition

Cyber Assist project as service science

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Establishment of compact processes

Development of an accurate and cost-effective quantitative detection method for specific gene sequences

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MESSAGES FROM THE EDITORIAL BOARD

There has been a wide gap between science and society. The last three hundred years of the history of modern science indicates to us that many research results disappeared or took a long time to become useful to society. Due to the difficulties of bridging this gap, it has been recently called the valley of death or the nightmare stage (Note 1). Rather than passively waiting, therefore, researchers and engineers who understand the potential of the research should be active.

To bridge the gap, technology integration (i.e. *Type 2 Basic Research* – Note 2) of scientific findings for utilizing them in society, in addition to analytical research, has been one of the wheels of progress (i.e. *Full Research* – Note 3). Traditional journals, have been collecting much analytical type knowledge that is factual knowledge and establishing many scientific disciplines (i.e. *Type 1 Basic Research* – Note 4). Technology integration research activities, on the other hand, have been kept as personal know-how. They have not been formalized as universal knowledge of what ought to be done.

As there must be common theories, principles, and practices in the methodologies of technology integration, we regard it as basic research. This is the reason why we have decided to publish "*Synthesiology*", a new academic journal. *Synthesiology* is a coined word combining "synthesis" and "ology". Synthesis which has its origin in Greek means integration. Ology is a suffix attached to scientific disciplines.

Each paper in this journal will present scenarios selected for their societal value, identify elemental knowledge and/or technologies to be integrated, and describe the procedures and processes to achieve this goal. Through the publishing of papers in this journal, researchers and engineers can enhance the transformation of scientific outputs into the societal prosperity and make technical contributions to sustainable development. Efforts such as this will serve to increase the significance of research activities to society.

We look forward to your active contributions of papers on technology integration to the journal.

Addendum to Synthesiology-English edition,

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Synthesiology Editorial Board

Note 1 : The period was named "nightmare stage" by Hiroyuki Yoshikawa, President of AIST, and historical scientist Joseph Hatvany. The "valley of death" was by Vernon Ehlers in 1998 when he was Vice Chairman of US Congress, Science and Technology Committee. Lewis Branscomb, Professor emeritus of Harvard University, called this gap as "Darwinian sea" where natural selection takes place.

Note 2 : *Type 2 Basic Research*
This is a research type where various known and new knowledge is combined and integrated in order to achieve the specific goal that has social value. It also includes research activities that develop common theories or principles in technology integration.

Note 3 : *Full Research*
This is a research type where the theme is placed within the scenario toward the future society, and where framework is developed in which researchers from wide range of research fields can participate in studying actual issues. This research is done continuously and concurrently from *Type 1 Basic Research* (Note 4) to *Product Realization Research* (Note 5), centered by *Type 2 Basic Research* (Note 2).

Note 4 : *Type 1 Basic Research*
This is an analytical research type where unknown phenomena are analyzed, by observation, experimentation, and theoretical calculation, to establish universal principles and theories.

Note 5 : *Product Realization Research*
This is a research where the results and knowledge from *Type 1 Basic Research* and *Type 2 Basic Research* are applied to embody use of a new technology in the society.

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Contents

Cyber Assist project as service science

— A project that began ten years too early —

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[Translation from *Synthesiology*, Vol.3, No.2, p.96-111 (2010)]

The Cyber Assist project was launched in 2000, and its R&D was conducted at the Cyber Assist Research Center at AIST from 2001 to 2005. This project was a leading activity followed by ubiquitous computing and service science in Japan as well as one of foresighted projects in the world. It should be highly evaluated even in the present time. The project had its focus on human-centered information system that provides services in the physical world.This article rebuilds the goal and activities of the research center on the basis of documents produced then, and provides future research directions.

Keywords : Cyber Assist, service science, ambient intelligence, ubiquitous computing

1 Introduction

The Cyber Assist project was conceived in 2000, and its R&D was mainly led by the Cyber Assist Research Center from 2001 to 2005. The project was one of the leading edge activities of ubiquitous computing and service science in Japan, as well as one of the foresighted activities in the world. The main point of the project is the construction of human-centered information systems and putting them into service in the real world.

In general, it takes decades for a new technology to get high recognition by society. For example, object-oriented software development, which is currently in the main stream, was first introduced in late 1970's and began spreading to society around 1990. It took another 10 years for it to become the main methodology. Compared to this, the Cyber Assist Research Center existed very briefly and therefore left many unfinished issues.

However, the goal of Cyber Assist is getting wide recognition under different research and development themes. The purpose of this article is to point out those relationships and to re-evaluate the activities of Cyber Assist as a synthetic research that establishes a new framework of research and development. In particular, we want to relate the activity to practice of "service *kogaku*" Note 1) that is getting attention recently. In the rest of this article, we first review the goal and activities of the research center based on the documents produced by the center and then evaluate them.

2 Goal of research and development and its realization method

We first describe the goal of the Cyber Assist Research Center and the structure of the center to realize the goal.

2.1 Cyber Assist project

The plan of the Cyber Assist project was first published in 1999[1], whose background situation remains valid up to now:

The concept of Cybernetics was proposed by an American mathematician Wiener in "The Control and Communication in the Animal and the Machine"[2]. He described the concept of control system with information feedback. We want to give such feedback systems (nervous systems) to cities, where central nervous systems process high-level information while peripheral nervous systems relay sensor information and communicate with human occupants.

This movement has already begun. As information infrastructure such as the Internet became available, it became rather easy for ordinary people to get hold of worldwide information. The utility of the network will increase rapidly in the near future. It is also anticipated that people will carry their own personal information processors and communicate with social information systems through them.

The Internet provides us alternative means to activities we have been doing without it, for example, buying goods and making reservations to hotels and airplanes. But the power of information processing did not stop there and opened up new possibilities that had been impossible or difficult beforehand. At the same time, as the consequent, many problems such as information screening, security and privacy issues may elicit themselves. To cope with those problems, we need personalized information processing systems. Along the line, research on personal agents has already begun. We need technologies to select necessary information out of vast flood of data and to communicate safely. Law and social framework have to be readjusted in large of course.

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But at the same time, we engineers must prepare tools and technologies for such new design of society.

The above article was written prior to the establishment of the Cyber Assist Research Center (CARC, hereafter) and covers wider topics such as digital city [3]. It conceptually covers all human daily life (potentially) related to information processing, such as transportation infrastructure and systems, which is exemplified by ITS (Intelligent Transportation Systems), for ground (and possibly air and marine) transportation, urban information systems as well as systems for city design, systems for governments and public services, telemedicine, and information infrastructure for tourism. The concept also includes providing a nervous system to a city by implanting sensors like stress gauges into structural materials of buildings and bridges, and use it for real-time sensing of damages caused by earthquakes. Since the concept is too wide-spread and vast, we later focused our attention on personal information systems and the related technologies [4]:

The aim of the Cyber Assist project is to establish a society where all people can enjoy situated support of information technology in all situations of their lives. Traditional information technology was available only through computers sitting on the users' desks. Recent spread of mobile devices increased the opportunity to use them, but still only a small portion of the people use them only in limited scenes of their lives.

The society as a whole can be animated by providing an environment for live information usable "here and now", which is accessible by anyone anytime through mobile and/or ubiquitous information technology. We want to implement technical support for not only convenient but also rich (not limited to material) life with deep human to human relationship in the physical world by providing services such as automatically buying tickets according to the user's schedule, guiding through a shopping mall, or informing that the person next to you happens to be your old-time school mate.

The widely used key phrase at the time of CARC's activity was "anytime, anywhere and anyone" (we expressed this as WWW, i.e. "whenever, wherever and whoever"). This phrase refers to accessibility and usability of information communication devices in all situations. But we were foresighted and didn't stop there. We emphasized situated service and used the phrase "here and now". Both phrases are used currently to put value on context-aware services at all times and in all situations.

In the early stage of development, the application area of information technology (IT hereafter) was limited to the digital world accessible from computers. On the other hand, activities of our lives are carried out in the physical world. Therefore, extending the IT support to all living situations of all people involves *grounding digital information to the real world*. The real world, which is meaningful to human beings, is the integral of realities of goods, individuals, and society woven together. Grounding consists of sharing meanings and situations between the digital world and the real world. The goal of Cyber Assist is to enhance ties between humans and goods by implementing grounding through information communication infrastructures for measuring physical locations and semantic structuring of information content (Fig. 1) [4].

Without tight coupling of the digital and the real world, IT cannot be effectively used. As we saw in the crash of the "net bubble" in the USA, the digital world alone cannot produce any new value. A world closed under the Internet is analogous to a world closed under finance which excludes production of goods. Information has value only because there are human beings on both sides of the information communication channel. To produce many kinds of sound IT-based business models, and to increase values in many aspects of our daily life, it is essential to use IT to integrate the digital and the real worlds.

2.2 Concrete research goals and approach toward them

To carry out the Cyber Assist project, we have to consider various supports in a wide variety of situations of human daily life including transport, medical care and emergency situations. There is no doubt that a single research center cannot handle all of this. A proper set of sub-problems must be isolated. A research organization must be managed considering both the top-down requirements described above and the bottom-up constraints of research resources including research specialization of researchers, research facilities and funding. As a result, we set the following goals (quoted from the proposal document for the establishment of the center):

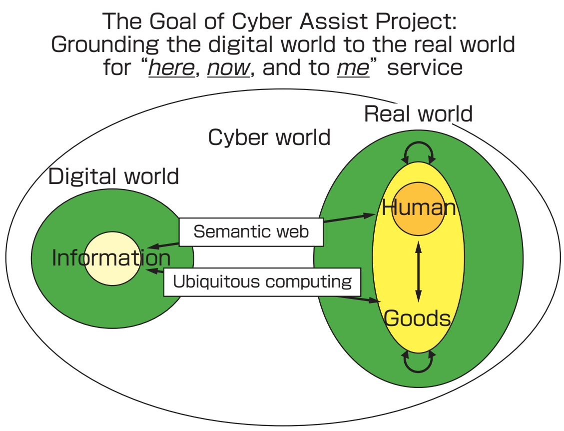

Fig. 1 The Goal of Cyber Assist Research Center

- *Goal: Personal Information Support (Technologies for information gathering, searching and presentation indexed by both location and ID)*
  1. *Situated personal agent*
  2. *Situated information search and presentation*
  3. *Structuring of content with tags*
  4. *Multimodal interface*
- *Approach: Situated communication software*
  1. *Location-based communication technology*
  2. *Gradual management of security and privacy*
  3. *Information services using physical information*
- *Media: Portable terminals and infrastructure using location-based communication*
  1. *Portable terminals*
  2. *Sensors and tags*

We held a meeting of all researchers once a week, and in the early stage of the center's activity, we concentrated on connecting each member's specialty and interest to the research goal of the center. The resulting diagram with concrete and detailed research themes is shown as Fig. 2. "Situated support" must be observed by all research themes. Everything placed under it are concrete research topics. Detailed descriptions of important research themes are given in chapter 3.

2.3 Structure and management of the research center

CARC used non-traditional organization and management to carry out research goals described in the previous section. In the current terms, it was organized to achieve Service Science, Management and Engineering.

Research and development of a system that implements a new service concept needs an organization for doing research from device to the application all together at the same place. Therefore, the research teams of CARC were organized in a ring shape as in Fig. 3, so that all the teams each of which corresponds to each technical layer can collaborate with each other toward the target of the situated support of users. The user interface team, responsible for the "interface" in Fig. 2, is given the top-level goal and collaborates with the device team, responsible for the "location-based communication" and the "devices" used for it in Fig. 2, the software team, responsible for the "communication software/infrastructure" in Fig. 2, the multiagent team, responsible for the "personal agent" in Fig. 2, and the intelligent content team, responsible for the "intelligent content", "GDA" and the "standardization" in Fig. 2. The basic concept is the same as the bazaar style of the consortium (appendix 9.3). All necessary technologies from basic to advanced levels are available in the house so that CARC can develop application systems on its own. This kind of configuration that gathers different technological areas in a single research unit is unique to AIST because of its mission to put technologies to social use. It more significantly holds for research centers that focus on the application side of research.

In the early stage of the center's activities, beside team-wise meetings, all researchers got together once every week to discuss services to be implemented so that all of them in different research areas can share the same target image. Furthermore, two or three days workshops were held annually to exchange their progress and to share application images.

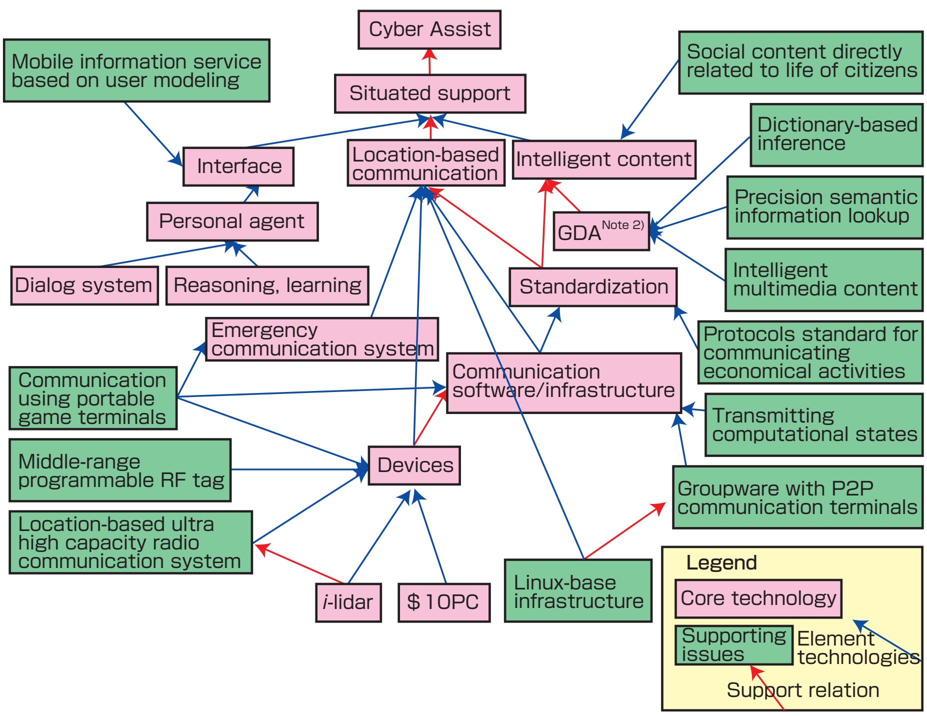

Fig. 2 Relationship among research themes of Cyber Assist (initial stage)

Since we put our stress on outcomes (applications to society), we adopted a coordinator[Note 3)] from the beginning. His activity was significant and resulted in hiring an industrial designer[Note 4)] and a head of a patent attorney office as our part-time advisor. A young patent agent attended every CARC meetings to assess patentability of our ideas. Proper management of intellectual properties is essential for joint research with private companies or establishment of venture companies. He also drafted rules for AIST consortiums because the Cyber Assist Consortium was the first one in AIST and there was no rule for it.

3 Research scenario

The Cyber Assist project has two characteristics as "ubiquitous computing" and "service science". Ubiquitous computing aims at establishing ubiquitous human assist by ubiquitous computers, and it is essential to have interfaces that do not make users aware of the existence of those computers. Vastness of the range of related basic technologies makes it difficult to focus on narrow research areas. The following research topics are therefore not consistently organized nor cover all areas of the Cyber Assist project. Moreover, the project's emphasis on practice as service science makes the list of technological issues detailed and long. It is difficult to write a traditional research paper with a clear story[Note 5)].

3.1 Location-based communication

The research area of CARC is "grounding information world to the real world". Many kinds of real-world information must be acquired and utilized to ground information content to the real world. Location is far more important and useful as information compared to others.

We proposed the concept of "location-based communication" in our early stage of research[5][6]. Location-based communication uses location of devices as the target address of communication, instead of uniquely identifiable addresses such as phone numbers or IP addresses. Use of location can hide the identity of the user for privacy protection at the same time enhancing situated (recently called "context-aware") support:

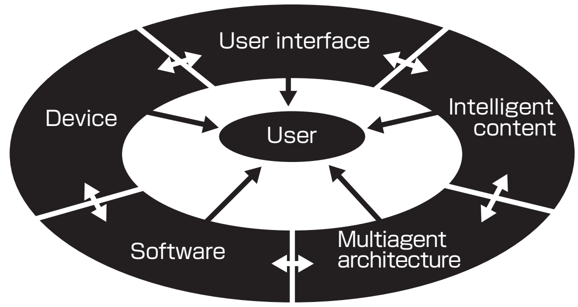

Fig. 3 Organization of Research Teams of CARC

Current information communication uses ID-based communication in the sense that communication is transmitted toward a uniquely identifiable ID of a user or a device, such as phone numbers, IP addresses, or MAC address of the hardware. To relay communication, there addresses are distributed world-wide. When the ID of an individual person is published as such, privacy cannot be protected. For example, when you pay by electrical means such as a credit card, your identity may be revealed. On the other hand, if you do not have the ID, you cannot even electronically communicate with a person in front of you and the system cannot support your every-day communication needs.

To implement useful communication systems for every-day life, while guaranteeing free societal life and economical activities, we need a communication technology that do not use personal or device ID for the target address. At the same time, we have to develop security enhancing technology to prevent malicious use of anonymity to support both privacy and security. (quoted from early CARC home page)

Location-based communication is also important for realizing situated user interface. For example, automatic gates at train stations are operated by the principle of location-based services. By physically restricting the space to allow only one person at a time, the system maps a user to payment. If a Suica[Note 6)] card is readable from 5 m distance, then the system cannot map the person to the payment, and the service breaks down. If the user's location cannot be used, then additional authentication is required and the interface of the system becomes more complicated. We claim that use of location information makes the interface simple. A similar idea is adopted in CoBIT system described later (section 4.1).

3.2 My-Button

CARC proposed a conceptual idea of an ultimate situated user interface "My-Button" [7]. It is a personal terminal with only one button (Fig. 4). This concept is rather a show model than a realistic design, to signify the target image of one-bit communication to provide "what I need, here and now", just like the communication of an old couple who is like a synchronized instrument each anticipating the other's wishes. The terminal understands and shares the situation with the user and functions properly without detailed instruction from the user. It is proposed as an ultimate image of a simple and natural interface. In practice, we need more than one button although it is still true that a small number of buttons is preferable. The concept at the same time claims that complete automation with no buttons is not good. The final authority must be left to the user.

We believe that we need this kind of idealized goal in constructive research that is neither needs-oriented nor seeds-oriented. The research scenario and the application image are constructed based on this conceptual model. Research of service science maybe composed around a new idealized service model.

3.3 Intelligent content

Content services play a large part in recent service provision. Content such as movies, news, Web pages, music, etc. must go hand in hand with mechanisms to deliver them. CARC also focused on manipulation of content provided through devices such as CoBIT (section4.1). At CARC we developed technologies for compiling and delivering structured information content, called intelligent content, as well as proposing a standard format for those structured digital data [8]. Tags annotating digital documents, movies, and so on [9] allow computer programs to process semantic structures of such content. This makes possible semantic manipulation of content, in particular semantic matching and semantic restructuring. We further developed various application technologies of intelligent content based on natural language processing and multiagent technologies. We aimed at construction of a society for sharing and reusing semantic information of content. Since information content often concerns the real-world, we can semantically reconstruct the world by grounding intelligent content to the real physical world.

Location-based communication and semantic structuring of the world are two wheels of one cart for grounding digital information. They allow computers and people to share meaning of information, which should promote a conspicuous improvement over the whole society by making it possible to realize brand-new systems, because the application domains of these technologies encompass a very large realm concerning the entire communication technologies and intelligent information processing technologies. In particular, such technologies and technologies of cellular phones, etc. are complementary to each other, so that their natural integration will enable various ubiquitous intelligent information services.

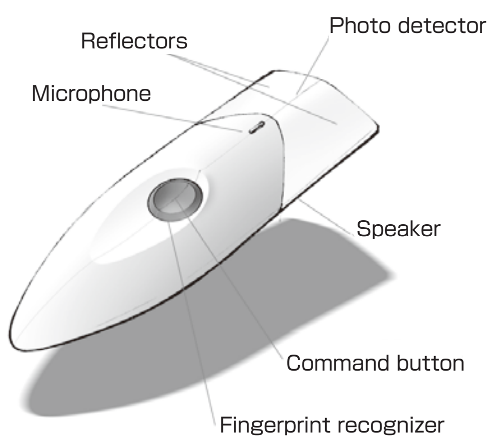

Fig. 4 Image of My-button (example)

CARC not only developed such fundamental technologies and promoted the standardization of related specifications, but also presented prototypes of representative application technologies involving major research issues, in order to provide common platforms for many applications and thereby to construct an infrastructure upon which private companies could develop various other application technologies. These research results are currently used for retrieval of movie scenes, collaborative authoring system for online comprehensive dictionary, and so forth.

CARC had also planned to use these technologies in event-space assistance system (section 5.2) and Expo 2005 Aichi Japan, to instantly reconstruct information required in the users' situations from huge annotated data and deliver it to the users' information terminals. Due to the large cost of content production and the lack of sensing equipments for extracting appropriate content, however, this plan materialized only partially.

4 Research and development projects

In this chapter, we describe research and development activities for each sub-theme at the final phase of the project. Since we covered diverse areas in our activities, the followings depict only significant results.

4.1 My-Button oriented terminals

In the early phase of the project, we were trying to implement "location-based communication" (section 3.1) using *i*-lidar-based locating and communication [11]. The *i*-lidar is a device for measuring the distance to the target by observing the resonance of frequency modulated laser beam with its reflection from the target. Combining this distance information with the direction of the laser-beam, we can measure the 3D position of the target. However, the device costs the magnitude of ten million yen for each set and it cannot be expected to become lower than one million yen even with mass-production. It is too expensive to be used in mass in the real-world applications. We therefore limited this issue for basic research only.

The concept of battery-less information terminal, CoBIT [12] was born as a deviation from *i*-lidar[Note 7] (Fig. 5). This terminal exemplifies location-based communication since it utilizes physical location to deliver information encoded as an infrared beam which also provides the power. It is the first product of CARC to realize the simple and natural interface requirement of the "My-Button" concept. By reducing the device implanted in the environment into simple LED systems, it became feasible to use the device in various applications. Many applications described in chapter 5 came up together with plans for popularization through an AIST venture company "Cyber Assist One, Inc." set up by some members of CARC.

CoBIT exemplifies location-based communication since it receives information only when it is located in front of the light source. Suica exemplifies another kind of location-based communication by its very-short range communication in the order of 10 cm while CoBIT's range is in the order of several meters. Suica must be short-ranged because it uses non-directional radio wave. CoBIT is directional, which is one of the advantages of light. Since CoBIT receives information only when it is directed toward the information source, it is possible to selectively receive one channel from multiple information sources even at the same location. As an example, consider a blind person trying to receive information of traffic light. One light is green while another light in 90 degrees difference is red. It is critical to choose information from the right direction to which the person wants to proceed.

4.2 Design and development of middleware

Traditional concept of OS that presupposes fixed configuration of devices cannot be used in ubiquitous computing where various devices are connected in an ad-hoc manner. A new layer, called middleware, must be constructed to interconnect the hardware and the software layers. The function of the middleware is to connect various devices and/or to set up a virtual hardware to be used by application programs.

The software team proposed and implemented the so called UBKit [13]. It is a set of software/hardware components to be used as modular building blocks for ubiquitous computing. They used it to implement intelligent home appliance systems.

At CARC, the device team was also developing its own middleware for CoBIT. We discussed to unify their designs in our meetings several times but did not succeed in merging them. The top priority of the center was to complete their application systems and those two middleware were based on different architecture and technologies to be merged in three years.

4.3 Applications of multiagent simulation

The multiagent team worked on various research themes including basic research on traffic simulation[14][15] and application of simulation technology for construction of standard simulators used in RoboCup [16], both in soccer and rescue, which provided the Japan originated international standard. Both soccer and rescue RoboCup's consist of real robot leagues and simulation leagues, and we participated only in simulation leagues. Our contribution to soccer leagues was initiated before CARC and carried over to CARC[Note 8], and contribution to rescue was newly added during CARC's activity. We also carried out simulation on rescue strategies and on information transfer using ad-hoc wireless connection in disaster scenes. Having a special communication system for disaster cases does not work. It is better to use the same terminal as in daily use. If we can use battery-less systems like a CoBIT, then our research themes complete a loop. Unfortunately though, we could not achieve it.

5 Abundant experiments and applications

At CARC, we emphasized not only designing a new service but also carrying out actual services and getting feedback from the applications– the practice of service engineering. The followings are typical examples.

5.1 After 5 years

When the New Marunouchi building was completed and opened for service, an exhibition named "After 5 Years" was held to present an information environment five years in the future. The original plan was to allow only silent exhibits because many booths were placed next to each other without enough separation to use any sound from speakers. We proposed to use CoBIT so that visitors can listen to the sound only when they stand in front of each exhibit, and it was successfully accepted (Fig. 6). This was our first application of location-based communication.

Using CoBIT in several exhibitions including "Doraemon" revealed the problem that LED used for the information

Fig. 5 CoBIT

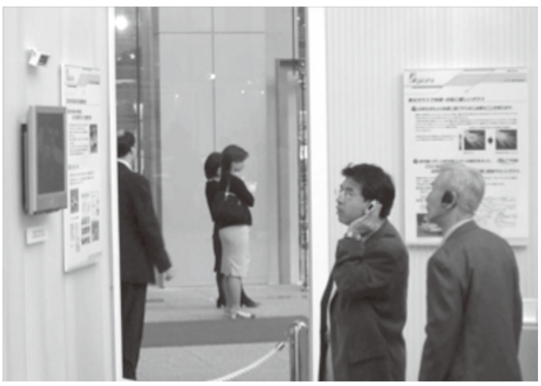

Fig. 6 Usage scenery in "After 5 Years" (The light source is located upper left)

source decays in much shorter period than their announced lifetime. We found that the cause was the periodical high voltage as the result of amplitude modulation of the source sound signal. Application of higher voltage than the design limit shortens the lifetime of LED significantly. We changed the design of the circuit to use the limiter. Laboratory tests cannot find this kind of problem.

Similar systems were used in several exhibits in many institutes including MeSci and AIST. The Aichi Exposition was the summit of them.

5.2 Event space support system

We designed a conference support system[17] and used it at the annual conference of the Japanese Society for Artificial Intelligence. As individual terminals, we used a modified version of name tags usually used for conference participants. We added an integrated system of infrared receptor, ear phone, reflector and LED light (visible at the center of the reflector) (Fig. 7 left). As information stations placed in various places of the conference site, we used a unit consisting of an infrared emitter, a camera and a display (Fig. 7 right is an experimental station using a plain PC). Besides the main function of listening to voice information from the station by the ear phone, we provided a function to keep record of the visitor who emits his/her ID using the LED, and a function to use the name tag as a mouse to give instructions to the station by tracking the movement of the reflector with the camera.

The content service of the system includes information retrieval based on the map of researcher relationships[18] automatically extracted from research papers lists on the Web [19]. This service makes use of the fact that the conferences are closed for research community only. The service also provides other contents based on conference programs. It is one of the rare applications of CARC that has intelligent contents.

This event space support system was used at consecutive annual conferences of the Japanese Society for Artificial Intelligence and also at an international conference on ubiquitous computing held in Tokyo (UbiComp 2005).

5.3 Intelligent home appliances

The software team conducted a field experiment in Yokohama to run an integrated system flexibly connecting several intelligent home appliances using UBKit[20] developed by the team. Users do not have to manipulate each appliance separately. By vocally announcing their intention, the intelligent system controlling the room accomplishes the task to fulfill their wish. For example, if you say “I want to watch NHK news”, then the system takes series of actions including turning on the TV, setting the proper channel – note that the channel settings for NHK are different by regions, closing the curtain if the room is too bright, and so forth. It is also possible to preset the timer to automatically open the curtain and turn on the air conditioner at a certain time in the morning.

The experiment was conducted at the community center. We asked volunteers from the region to come to our meeting several months prior to the experiment, to answer our questionnaires and exchange opinions on intelligent home appliances. Through the meetings we gathered precious information on how people including elderly and weak-sighted person feel about computerized appliances and fed it back to our research plans[Note 9)].

5.4 Expo 2005 Aichi Japan

The biggest application opportunity for CARC was at Expo 2005 Aichi Japan. It was an unprecedented challenge for AIST to provide a half-a-year long service in this worldwide event. CARC took part in two projects.

Global House: This was a pavilion directed by the Japanese government. It mainly featured collections supervised by Mr. ARAMATA Hiroshi, and CARC contributed technologies for audio commentaries about them. An advanced version of CoBIT equipped with ID tag was employed, named “A*i*mulet

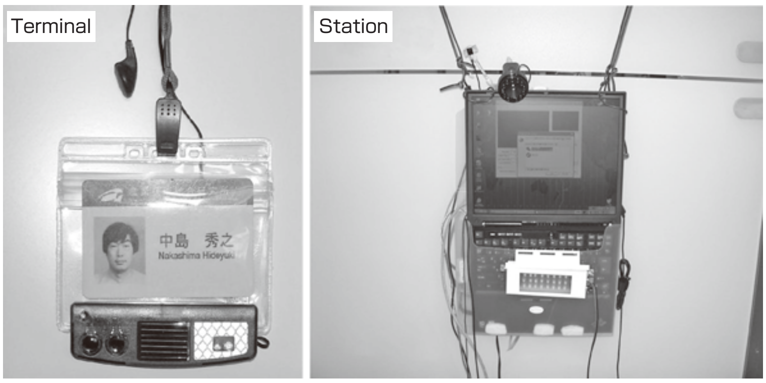

Fig. 7 The terminal (left) and the information station (right) for conference support system

Fig. 8 Field test of our intelligent home appliance system

(tm) GH” (Fig. 9). “A*i*mulet” is a neologism inserting “I” into “amulet” where “I” stands for both information and “ai” (love) in Japanese. “GH” stands for “Global House”.

A*i*mulet GH aimed at multilingualism by multiple frequency bands of infrared rays like air broadcasting. In the early planning phase of the Expo we wanted to cover five languages including Asian ones. Later experiments revealed that a sufficient bandwidth was unavailable, however, so that the actual implementation was in Japanese and English only. It is a future task of service engineering to close such a gap between theoretical possibilities and practical applications.

Besides the audio explanation provided by A*i*mulet GH, sensors on the ceiling acquired visitors’ traffic lines by detecting signals from tags embedded in A*i*mulet GH. This data will be important for later design of event sites.

Show & Walk: This was an event planned by performance artist Laurie Anderson, which provided artistic experiences to people visiting a Japanese garden installing sound sources and other artifacts (Fig. 10). Close to the principle of location-based communication, this suggested a new application field of CARC. We were responsible for the sound part only, and in the planning phase our researchers visited Laurie’s office in New York to discuss various possibilities with her staff.

Fig. 9 A*i*mulet™ GH

We first aimed at spatial localization of stereoscopic sound, but it was unsuccessful and ended up with the same audio technology as CoBIT and A*i*mulet GH.

The terminal shown in Fig. 11, named A*i*mulet (tm) LA where “LA” is the initials of “Laurie Anderson,” was manufactured inexpensively enough to distribute in place of entrance tickets. We considered that this low-price terminal should be a powerful tool, as museums and other facilities are generally having a hard time collecting without loss the rented out terminals to visitors, and the collection is even harder in an outdoor environment like a Japanese garden with many gateways. We also incorporated the notion of ecology, which was the theme of the Expo, into the frame design of A*i*mulet LA, by housing it in a bamboo sheath, which was resource-saving and inexpensive, so that the terminals needed not be collected and visitors could take them home.

Figure 11 is A*i*mulet LA viewed from the side of the photo receiver, which should face downwards when in use to avoid outdoor sunlight interference. The photo receiver uses spherical solar cells, which relax the directivity and provide a wide light-receiving area. In this connection, A*i*mulet LA was highly evaluated in terms of its usage of bamboo and solar cells, receiving a Good Design METI Minister Award for Ecology Design[Note 10] in 2006.

A*i*mulet GH and LA are beneficial also because they need no battery replacement as solar cells supply their power. Since the replacement or charge of thousands of batteries is a huge burden, maintenance-free terminals without such need would be very useful in long-term events.

6 Service engineering and ambient intelligence

As the last issue of discussion, let us re-assess Cyber Assist research in the recent research map. CARC was performing “service engineering” research to realize “ambient intelligence” in the domain of “Cyber-physical system”.

Fig. 10 A*i*mulet LA usage at Show & Walk (Left-hand side is Laulie herself)

6.1 Service engineering

Firstly, we have to clarify the meaning of "service engineering". The phrase "service kogaku (service engineering)" was first used at Research into Artifacts, Center for Engineering, the University of Tokyo ([21][22] p. 134). They define "service" as follows:

Activity of the provider to materialize the change requested by the receiver in exchange with some payment.

An English-Japanese Dictionary lists over 20 entries for "service"[Note 11] including work, religious ceremony, army, maintenance, serving a ball, and so on. This means that there is no corresponding word for "service" in Japanese.

However, it is possible to see the essence of the word: to provide something for use. The meaning differs depending on providing what. In the context of this article, service means to provide information systems for actual use. The target of service engineering is this "use" phase. Engineering in general is an academic discipline for constructing some system. Automobile engineering is for construction of automobiles, and information engineering is of information systems. In contrast to these engineering fields with vertical divisions, service engineering is a horizontal division of all of them in their "use" phase. It does not suffice to merely analyze the "use" phase objectively, as in science, but it is necessary to actually construct the phase, i.e., to provide service, and get new knowledge to feed it back to the system.

IBM is proposing a field called service science, management and engineering (SSME), and it is referred to as service science in Japanese. However, we believe that it should be called engineering rather than science if the discipline calls for actually constructing or designing a system [23]. Since service is what we should construct rather than analyze, it is proper to call it "service engineering". Japanese word "kogaku" fits much better because it has "gaku", meaning study, as in "kagaku". It is because the English word "engineering" does not fit well that the field must be called with such a long name.

Fig. 11 A*i*mulet™ LA

CARC's activity can be classified as achievement of service engineering in the sense that it is service oriented information engineering. Until the AIST research center was established, it was practically impossible to put research results into actual service unless they were turned into products of some manufacturer. This gap between research result and products is beyond the coverage of traditional public research and development funding. It was called, therefore, the "valley of death" or the "era of nightmare" [24] where neither researchers nor manufacturing companies could become involved. AIST made it possible to provide actual service by the following reasons.

1. By incorporation of AIST, it became possible to hire non-researchers with various specialties using research budget.
2. Venture assisting fund became available[Note 12).
3. In the case of Aichi Expo, running fund was given to AIST.
4. A new category of research unit, research centers, was created, whose activities were not limited to basic research.

In practice of service engineering, we believe it important to divide research units into two categories: those who primarily focus on basic research and those who primarily focus on providing services. The latter does not fit into traditional evaluation criteria of research activities.

6.2 Ambient intelligence

The research area to assist human activities through sensors and actuators located in the space of the activity is variously called as ubiquitous computing or pervasive computing. In Europe, it is often called ambient intelligence[Note 13].

Cyber Assist can be viewed as an application of artificial intelligence. In fact, many researchers at CARC including the director and deputy directors are from AI. Researchers in the US and Europe have to produce many research papers due to the strict evaluation of their research activities. They say it is difficult to aim at real application systems. Therefore, there the ambient intelligence research examples are limited to their lab and meeting room environments within their universities. CARC is unique in the activity outside the research labs, and it is why we were invited to give a talk at the International Joint Conference on AI 2007[25], whose main theme was application of AI to society.

6.3 Cyber physical system

NSF recently launched a research area called CPS (Cyber Physical System)[26]. The concept is very similar to Cyber Assist in the sense that they both deal with the feedback loop between physical and information systems where physical systems interact with information systems and information systems in turn control physical systems (although they call information systems cyber systems).

7 Self evaluation

Let us evaluate our activities.

7.1 As a research project

The Cyber Assist project was initially planned to achieve a part of "Intelligent Social Infrastructure Technology" set by the result of a pilot research program of Agency of Industrial Science and Technology, MITI. The detail is shown in the appendix. The pilot research program is conducted prior to launching a full scale national project such as the Fifth Generation Computer Program. Unfortunately, Intelligent Social Infrastructure program was never launched, partly because the plan involves many ministries and therefore it was too big to be managed by a single ministry of either MITI or METI. We were also expecting the Cyber Assist project to spread nation-wide through activities of CARC. It was a failure since we could not achieve this. We analyze the reason in the following sections.

7.2 As activity of service science

One of the roles of AIST is to go over the "valley of death" of R&D to fill the gap between the research and products. AIST has two kinds of research units: research institutes and research centers. We believe that the role of bridging the gap should be taken by research centers.

CARC tried to fulfill this role. In the IT area, the best way to fill the gap is to actually provide the service to show its effectiveness. In this sense, CARC's activity should be evaluated in the context of achievement of service science. At the same time, it can be the subject of service engineering research to establish proper research method of service engineering. This article is a review of the activity of CARC from the viewpoint of service engineering.

Services provided by CARC, e.g. event space support at conferences and exhibition guidance at Aichi Expo, can be assessed as successful when they are practically used in society. However, none of them were put into market independently. One of the reasons can be attributed to the short life span of CARC. New technologies need at least a decade before it is widely accepted by society. Three years was too short for this. If CARC remained in its form and continued on to the current Center for Service Research, some of CARC's results could have been sent out to the world.

7.3 On naming

Naming of projects, research papers, research themes and constructed systems plays a significant role in their success. Some of research themes became popular by its good naming (e.g., "Chaos") and many did not because of their bad naming. In this sense, our naming of Cyber Assist was a failure. We are proud that we have had a large influence on fellow researchers in close fields, but we could not reach further out toward manufacturing companies or planners of national projects as "ubiquitous" used by Ministry of General Affairs or "service engineering" used by Ministry of Economy, Trade and Industry.

Use of "cyber" was somewhat problematic. We used the term in the precise sense of Wiener's Cybernetics. But popular image was differently coined by the "Cyber world" of the movie "Matrix", where it is used to refer to the digitally rendered world to which people "jack in". "Cyber terrorism" is used for terrorism on the Internet. Therefore, our research may have been mistaken for activities on the Internet with no connection to the physical world. We had to repeat our definition:

Cyber = Digital + Real [27].

However, the very fact that we had to repeatedly explain it signifies our failure. What we aimed at is Cyber-physical system (section 6.3), which is recently getting attention in the US. We should have added some word that clearly designates the real world.

The second failure is that we did not use the phrase "ubiquitous". At the time of the establishment of the research center, the phrase "ubiquitous" existed but was not commonly accepted. It is reported that the prime minister at the time said it was incomprehensible and thus we could not project that it would become a common term as it is these days. It must be noted though that the current use of "ubiquitous" is along the line of Ministry of General Affairs which is in charge of communication infrastructure and hence has emphasized ubiquitous communication. It does not exactly reflect the original use by Marc Weiser. The use is limited to connectivity to the Internet "whenever, wherever and whoever". We agree that connectivity is a necessary condition but the most important part is services on top of it. It must also be noted that there are many other misuses such as "ubiquitous society".

We still think the inclusion of "assist" was a success, which puts emphasis on human support. It should be highly evaluated because it refers to the goal rather than the elemental technology or field.

If we can rename the project now, what would be the appropriate name then? Candidates are "ubiquitous assist", "cyber assist real" or "ambient intelligence".

7.4 On design issues

At CARC, we have been putting emphasis on design from the beginning, such as hiring an industrial designer Shunji Yamanaka as a research advisor. If we want our technology to be used in society, design is important. There are two kinds of design: design of appearance and design of functions. The latter is somehow within the ability of researchers but the former is not.

According to Yamanaka, he used to be a designer of cars, but left the field to become independent because he thought that the shape design of cars has too much freedom to realize a desired function and therefore not very interesting. His philosophy that the function determines the shape is typically exemplified in his design of the Suica reader.

Yamanaka was present at our bi-weekly meetings as well as annual off-site workshops to propose ideas of shape design that implements functions we discuss. A*i*mulet LA, which received the Good Design Award, is the best successful example we have that turned desired function into a good shape. However, we regret that the infra red communication system exemplified by A*i*mulet LA did not make it to commercial use.

7.5 Unfinished goals

We had a "digital version of a tally method" on our research agenda from the early stage of the project, but it was never realized. Tally is a method to protect information content by physically dividing a paper or a plate on which information is written into two parts so that each piece alone is meaningless. Two pieces must be together to decode information. We wanted to have a similar system on digital data for privacy protection.

> *[Example] Information storage by the tally method*
> *Gathering personal information on a server is problematic in terms of privacy protection because it is vulnerable to malicious data usage or accidental leakage. We need a security or encryption method to divide information between the server and user terminal so that information is meaningless unless both of them are present.*

We understood that this is a next to impossible goal from the beginning. Simple encryption cannot be the solution because encrypted data becomes a plain data that can be copied when it is decrypted for use. For example, an encrypted personal medical record can be copied once a doctor displays it on his terminal and the doctor can keep the copy after the patient goes home. We need a method to guarantee that the data is accessible only while the patient is present. We thought this might be an unsolvable problem within the digital world alone. We thought some physical means, location-based communication for example, must be combined and searched for the solution without success so far.

7.6 Evaluation by the Advisory Board

The following is the executive summary of the final report by the advisory board of CARC given in 2004. It matches our own evaluation of CARC.

We find that the Cyber Assist Research Center (CARC) is a unique organization that is:

- *Pursuing a powerful new vision in a field of worldwide importance;*
- *Aggressively implementing research results as prototypes in real world settings;*
- *Gaining momentum as a laboratory of international standing.*

CARC's field is ambient intelligence, an approach to pervasive computing that emphasizes the thorough integration of information technology into devices, buildings, clothing, and other artifacts to dramatically increase their capability and utility. Within this field, CARC is focusing on using information technology to help human beings in all aspects of their daily lives. CARC's unique vision is that this assistance is best achieved by making maximum use of human and physical context, leveraging relatively simple information interaction to achieve the required capability.

CARC's commitment to deploy early prototypes of its research results provides immediate feedback from the public, and also establishes the benefits of the new technology in the mind of the public. External funding has been increasing, and is now poised for significant growth based on the success of CARC's prototypes.

CARC's vision and research methodology have created a growing reputation in the international research community. CARC is seen as one of the leading information technology innovation laboratories in Japan. It has a head start in the integration of three major worldwide information technology trends: ambient intelligence, semantic web services, and multi-agent technology. To realize the benefits of this competitive advantage, CARC needs to continue as a research center in energetic pursuit of its integrative vision.

8 Acknowledgments

CARC members contributed research described in this paper. Although we do not list names of researchers here, they can be seen in the references provided below.

CARC also had many non-research staff members. Without the industrial designer Shunji Yamanaka, we could not have enjoyed the success of CoBIT and A*i*mulet. Takahiro Koshibu from Nishizawa patent office attended our weekly research meetings to find patentable ideas and then took care of all document work from writing proposals to answering claims during the check phase. Cyber Souken Co. undertook management of the Cyber Assist consortium even though it was not profitable for them. Many others contributed to the project but the list of names is too long to be listed here.

Appendix

History and management of the CARC

1) History of establishment of CARC

Primary Study report on "Intelligent Social Infrastructure," conducted under the framework of Research and Development of Industrial Science and Technology of Agency of Industrial Science and Technology (AIST), Ministry of International Trade and Industry (MITI), led by Yuichiro Anzai[28] proposed a new design of social infrastructure with IT. Proposed research area of intelligent social infrastructure technology was far beyond the coverage of MITI and did not make itself a national project. The Cyber Assist project described in this article corresponds to the software portion of the overall picture.

The name of "Cyber Assist" was coined in the committee for usability (1999)[29], which was formed as a successor of the primary research group and was also led by Yuichiro Anzai. The phrase "ubiquitous computing" was not used because it was not popular at the time.

When the Agency of Industrial Science and Technology of MITI was incorporated and reorganized as the National Institute of Advanced Industrial Science and Technology (AIST), the Cyber Assist Research Center was established as one of its research units, and literally became the center for Cyber Assist research. The following is the goal of CARC presented at its birth.

> *To realize a society in which anyone can receive sophisticated information support, we will develop and deliver the technology for information service that reflects the real world situations (situated intelligent information service) which solves information overflow, support information minority, and protects privacy. As the technological base, we will conduct research and development on the following technologies:*
>
> • *Technologies for situated communication software, location-based communication terminals and the communication infrastructure.*
> • *Technologies for semantic structuring of content and its usage.*
> • *Technologies for providing meaningful information adjusted to the user's situation.*

The following is a list of significant events during CARC's life span.

1998/3 Research report on the "Study of Intelligent Social Infrastructure technologies"
1999/3 Report of the Usability committee
2001/2 First Cyber Assist International Symposium
2001/4 Establishment of Cyber Assist Research Center (CARC) at AIST
2001/4 Establishment of Research Group on Intelligent City Information Infrastructure at Information Processing Society of Japan (till 2003/3)
2001/9 Establishment of Cyber Assist Consortium
2002/10 Second Cyber Assist International Symposium
2003/4 Establishment of Special Interest Group on Ubiquitous Computing System at Information Processing Society of Japan
2003/4 Establishment of AIST venture Cyber Assist One
2004/7 CARC joined other research institute to form Research Institute of Information Processing at AIST
2004/11 Third Cyber Assist International Symposium
2005/10 Fourth Cyber Assist (domestic) Symposium
2007/3 Termination of Cyber Assist Consortium

2) Advisory board with world top-class researchers

CARC formed its own advisory board and gathered world top-class researchers from related areas. The members are Shun'ichi Amari (Director, Riken Brain Science Institute), Yuichiro Anzai (President, Keio University), Rodney Brooks (Professor, MIT), William Mark (Vice President for AI, SRI International), Kokichi Futatsugi (Professor, Japan Advanced Institute of Science and Technology), Koji Oboshi (Advisor, NTT DoCoMo Inc.), Stanley Peters (Professor, Stanford University), Ikuo Takeuchi (Professor, The University of Electro-Communication), Yoshio Tanaka (Trustee, IBM Japan, Ltd.), Jun'ichi Tsujii (Professor, University of Tokyo), Wolfgang Wahlster (Director, DFKI GmbH – German Institute of AI), Steven Willmott (Universitat Politècnica de Catalunya), Akinori Yonezawa (Professor, The University of Tokyo) (affiliations in this list are at the time of CARC's operation).

3) Establishment of the first AIST consortium

We organized international and domestic symposiums even before CARC's establishment and held them alternatively each year since then. We used symposiums to invite companies to our consortium. The Cyber Assist Consortium was established just a half year after the launch of the center as the first consortium run by AIST – We had to draft all necessary rules for AIST.

We adopted a so called "bazaar method" where each participant brought different elements (either technology, market needs, or business plan). We allowed only one company for each particular area of specialty, and hoped that the combination of a device manufacturer and a service provider would help to bring our technology into the world.

4) Establishment of the first AIST venture company from zero

Although the director general of AIST advocated establishment of venture companies, we initially did not have a plan to do so. However, once we included application to society within our target range[Note 14)], we found it necessary to have alliance with companies to manufacture devices of our design and set them up for use. No company met our specifications. We found it best to run a company by ourselves. We gathered the minimum requirement of ten million yen for a joint-stock company and established a venture company. Half of the members were and are CARC researchers.

Our intention regarding the management of the company nonetheless did not meet the blue print of AIST venture set by AIST. The most critical obstacle was the issue of "conflict of interest". AIST excluded the venture company even from bidding to undertake CARC missions, just because there was a *possibility* of conflict of interest because some of CARC members were stakeholders and board members of the venture company. It practically nullified our intention of setting up a venture company.

There was also a mismatch on the conception of the life span of AIST venture companies. As mentioned above, we set up the company because there was none to undertake our requirements. We researchers did not intend to run it for profit. Our intention was to sell the company when it became stable in its business. However AIST claimed to retrieve the right of industrial properties back to AIST after five years. We could not sell the company. As of the righting of this article (2009), we still run the company voluntarily, but there is no future plan.

5) Activities in academic societies

The Cyber Assist project had a plan to launch special interest groups at academic societies. We established a research group called Intelligent City Information Infrastructure at Information Processing Society of Japan in 2001. Its activity was centered on social application of IT. This research group, together with another research group of intelligent home appliances, became the core of the new SIG ubiquitous computing systems of IPSJ from 2003 to date.

There was another informal research group named Ubiquitous Joho (Ubiquitous Information) formed to which the director of CARC, Nakashima, contributed actively. This research group did not belong to any society. It rather functioned to bridge those academic societies. One of the major achievements of the group is a video presentation "Small Stories 2008"[Note 15)]. At the time, there were several research promotions, or future predictions, videos by Microsoft, Hewlett Packard, NTT DoCoMo and Nokia. We authored Small Stories 2008 as a near future vision of technologies realistically achievable by participating researchers. We featured scenes with information loupe reflecting the concept of CoBIT or My-button by CARC.

Notes

Note 1) We cannot translate *kagaku* as either "science" or "engineering" here, since it narrows the definition of the word. The definition of "service *kogaku*" is not settled yet. We regard it as a study of practice. We do not use the narrow definition as science or engineering for service enterprises.

Note 2) GDA or Global Document Annotation is a set of tags for intelligent contents.

Note 3) It was just before incorporation of Agency of Industrial Science and Technology that we persuaded them to employ a non-researcher formally and the proposal was accepted.

Note 4) We were lucky to have Shunji Yamanaka who is famous in designing Nissan Q45 and the Suica reader for JR.

Note 5) If the journal of *Synthesiology* were published at the time of CARC's activity, it would have been a good target. That is why we published this paper after CARC terminated.

Note 6) Suica was put into service in November, 2001. It is later than the establishment of CARC.

Note 7) CoBIT originated from the idea to use infrared beam of *i*-lidar for communication, instead of the original purpose of positioning.

Note 8) Research themes of individual researchers usually sustain beyond the period of a project or change of organizational structure of the research institute to which the researchers belong to. At CARC, we requested each member to distribute their effort one to one for group research themes and individual research themes. They of course may not contradict each other, and many themes satisfy interest of both. RoboCup is a good example where an individual theme was carried over as a group theme.

Note 9) Although we do not have enough space for details, let us exemplify one case. We learned that even a blind person enjoys TV programs. When he encounters a scene whose details cannot be figured out only from sound information, he places a phone call to his friends for explanation. In this case, synchronization of TV channels in distant locations is useful. We implemented the function.

Note 10) Ordinary Good Design award is given to about one thousand goods, but only twenty one of them are given the name of "METI Minister Award". Ecology design award has only two slots. We are very proud of receiving this.

Note 11) In fact, the situation is the same in English dictionaries.

Note 12) The use of venture assist fund was limited to research and development within AIST. It could not directly support activities of AIST registered venture companies. Our own venture company could not succeed due to this limitation, although it was good that the venture and CARC jointly developed service providing systems with the fund.

Note 13) The European Union report, Scenarios for Ambient Intelligence in 2010. (available at ftp://ftp.cordis.lu/pub/ist/docs/istagscenarios2010.pdf)

Note 14) This was before the general director of AIST set the concept of full research.

Note 15) This video was sponsored by Ubila Project. http://www.akg.t.u-tokyo.ac.jp/ubila/video/

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Koiti Hasida

Dr. Sci. from Graduate School of Science, the University of Tokyo in 1986. Research topics concern natural language processing, cognitive science, artificial intelligence, and semantic computing. Researcher at Electrotechnical Laboratory from 1986 to 2001 and researcher at the Institute for New Generation Computing Technology from 1988 to 1992. Deputy director of CARC from 2001 to 2004 and its director in 2004. Presently, director of Social Intelligence Technology Research Laboratory, AIST, president of Japanese Cognitive Science Society, president of Association of Natural Language Processing, and a board member of Japan Society for Software Science and Technology.

Major publicatinos: Chi no Enjiniaringu: Fukuzatsusei no Chihei (Engineering of Intellect: Horizons of Complexity) (JustSystem), Gengo (Language) (Iwanami Lecture Series of Cognitive Science), Gengo no Suri (Mathematics of Language) (Iwanami Lecture Series of Linguistic Sciences), Topics in Constraint-Based Grammar of Japanese (Kluwer). For the content of this paper, he contributed to the design of the project and succeeded its execution, in particular EXPO 2005 Aichi Japan, as the second director of the center.

Discussions with Reviewers

1 Overall

Comment (Naoto Kobayashi: Center for Research Strategy, Waseda University)

I understand that this paper aims at reassessing the value of the Cyber Assist Research Center (CARC) set up at AIST in 2001 whose research strategy is still valid, or even more valid, in today's context, by looking back over its activities and comparing them with the current research trend. However, in the view that *Synthesiology* is an academic journal on *Type 2 Basic Research*, it does not suffice to merely reconstruct the research activities of CARC. To be accepted as a research paper of this journal, you should address the following issues which are essential elements of *Synthesiology*: (1) the research goal, (2) the scenario to the goal, (3) element technologies, (4) the method of synthesis of a new system by combining those elements, and (5) the conclusion.

Comment (Motoyuki Akamatsu: Human Technology Research Institute, AIST)

I understand that the theme of this paper is to describe how the Cyber Assist Research Center as a "synthesiological" research vehicle tackled the Cyber Assist project "synthesiologically", to assess the achievement and to analyze the whole process. I want you to narrow down the focus of the story, to "location-based communication" for example, and clarify the essence of your claim for the readers' easier understanding .

Answer (Hideyuki Nakashima)

I thank both of you for your objective comments. I found that issues we took for granted in designing CARC is not necessarily obvious for others. The internal structure of the center, for example, is an important one but we failed to convey the rationalization. We rewrote the overall paper to comply with your comments. However, since Cyber Assist is an activity of service engineering whose top-level goal is to support people, it is hard to focus on a narrow and coherent story. A service provider should not forget about trivial details. The whole combination of peripheral issues is meaningful more than the central device or function used for the service. This is one of the reasons that this kind of research and development was rare in the past. We also stressed the above points in our new manuscript.

2 Definition of "service engineering"

Question (Motoyuki Akamatsu)

The title of the paper claims that Cyber Assist is a kind of service engineering, and the latter is defined in your own way in the paper. In the initial manuscript, your definition of "service engineering" is unclear but there is a better description in section 6.1 of the final version. Should the definition of "service engineering" be understood as meaning, "to provide or to offer" services?

Answer (Hideyuki Nakashima)

Generally speaking, "a discipline of designing and/or constructing systems for practical use" contains as its part a phase of "providing the system for use". In this sense, "service engineering" should not be taken as its narrow meaning of engineering merely for the sake of service industries, but rather as service-providing portion of engineering, or a discipline of engineering reorganized around the phase of putting the system into practical use. We provided the description in section 6.1.

3 The subtitle

Comment (Motoyuki Akamatsu)

The subtitle states that the project is “ten years too early”, but the reason is not clear in the first manuscript. If this is an important claim, you should elaborate more on the reason why it was difficult to perform at the time, or the reason why you expect that it would do better now.

Question (Naoto Kobayashi)

Does the subtitle “a project that began ten years too early” mean that the world was premature to understand the importance of “human-centered situated information service” that is the core concept of Cyber Assist, and that the three years of activity was too short to make the concept be recognized by the world? Or, can we understand that the world has now begun to understand its importance independent of CARC’s activity?

Answer (Hideyuki Nakashima)

At the current moment, we can simply say that we are doing service engineering, for instance. However, we had to explain a lot at the time. We are proud that we were ten years ahead (our external advisory board said so). I don’t want to claim that only CARC was the exception, however. There were others and we shared the same resistance of being at the leading edge. Our activity alone did not make the world as it is. But if our center went on for ten years rather than three years, its message would have better reached out to the world.

That having been said, the most significant aspect of being too early is that we failed to provide any commercially used “practical system” to the world.

4 Technology for Cyber Assist

Comment (Motoyuki Akamatsu)

A reader expects to understand technological aspects of Cyber Assist. To be more specific, more concrete description of the process in which you considered “both the top-down requirements and the bottom-up constraint of research resources” should be provided in section “2.2. Concrete research goals and approach toward them” to comply with the scope of *Synthesiology*.

Answer (Hideyuki Nakashima)

I agree that if we could analyze and clearly describe the process of considering “both the top-down requirements and the bottom-up constraint of research resources”, it would be a very valuable document. However, our decision was made through weekly meetings, and it took very long to focus on our final shape. We cannot analyze it to make it describable. I am sorry but we could only write “We held a meeting of all researchers once a week, and in the early stage of the center’s activity, we concentrated on connecting each member’s specialty and interest to the research goal of the center. The resulting diagram with concrete and detailed research themes is shown as Fig. 2.” and add the corresponding figure.

5 The resulting technology of research and development

Comment (Motoyuki Akamatsu)

It is written that Cyber Assist aims at grounding digital information into the real world, and that the center consists of location-based communication, My-Button, intelligent content and user interface. Those are in terms of technology, not sub-goals for Cyber Assist. If possible, please explain the relationships between chapter 2 and chapter 3 using a diagram, so that readers have a better understanding of the research scenario from the view point of technological elements.

Answer (Hideyuki Nakashima)

Yes, our description was not clear on that point. We added a description and a diagram (Fig. 2) in section 2.2. Moreover, since we tried to explain all research elements and made the main story obscure, we eliminated some of them.

Since we deleted the description on a “proposal of new transportation systems” from the paper, let me briefly explain about optimum route guidance using car navigation systems here. The current navigation system is known to have a problem that the system becomes less effective as the ratio of cars using the system increases. As the current system feeds back information on traffic congestion with some time delay, undesired oscillation of the feedback system takes place. We solved the problem completely by using future projection based on multi-agent simulation. The important point is that the solution is applicable using the current technologies only. We omitted this research issue because of the shortage of space and the whole story of CARC could be told without this. Let us note that we are currently preparing to apply this technology in Hakodate area by a team of Future University Hakodate and AIST plus some others. It is an exercise of service engineering for an actual city.

6 Role of demonstration for “synthesiology”

Comment (Motoyuki Akamatsu)

I suppose that the implementation and demonstration of a system lead to the discovery of new problems or important issues and then contribute to the next phase of research, as some of the previous papers of *Synthesiology* reported. Please describe the details of findings and feedbacks to new research issues discovered from your demonstrations.

Answer (Hideyuki Nakashima)

One of the problems is that the Cyber Assist Research Center dissolved in the middle of Aichi Expo, and I could not get hold of research details after then. We nevertheless tried to cover the issue as much as possible and included Note 8).

7 Assessment of the research outcomes

Comment (Motoyuki Akamatsu)

You mention the tally method of information storing as an unfinished research agenda. From the description in section 5.2, however, I suspect that you may have chosen a goal theoretically unattainable by digital technology. If this is the case, will you describe how the impossibility became clear in the course of the research?

Answer (Hideyuki Nakashima)

We believed from the initial stage that the “tally” problem should be solved by “digital + real”. Even if the problem cannot be solved with only digital technology, it does not mean it is unsolvable. Although we could not find any effective methods, we still regard it as an interesting theme for information technology. We added some description to clarify this point.

8 Suica

Comment (Motoyuki Akamatsu)

At the end of section 2.2, there is a reference to Suica with respect to the fact that CoBIT is based on a similar concept. Suica is close to the idea of Cyber Assist in its location-based concept, user’s initiative and privacy protection. It helps the understanding of users to have detailed discussion of the relationship between them because one side is already familiar to them.

Answer (Hideyuki Nakashima)

We added a comparison with Suica at the end of CoBIT section (4.1).

9 Research institutes and research centers of AIST

Comment (Naoto Kobayashi)

In the earlier version of the manuscript, there was a statement, “In service engineering, it is important to separate two kind of research units as in AIST: basic research oriented research institutes, and service oriented research centers” (section 6.1) and "Basic and element technologies should be developed at research institutes and bridges to commercial products should be built by research centers" (section 7.2). Those are not official views of AIST. The current website of AIST (http://www.aist.go.jp/aist_j/field/index.html) states "Research Institute: Institutes continuously conduct research to achieve the missions and medium- and long-term strategies of AIST based on scenarios defined by research unit heads and research themes defined by the initiatives of researchers. Research Center: Originating from an institute or as a response to social needs, research centers intensively conduct research for a period of three to seven years under the strong leadership of research unit heads to swiftly produce technologies and knowledge to solve specific issues."

Answer (Hideyuki Nakashima)

In my personal understanding, the *Full Research* concept proposed by Yoshikawa, the president of AIST at the time, is divided into *Type 1* = "*kagaku*" (roughly but not exactly corresponding to "science"), and *Type 2* = "*kogaku*" (roughly but not exactly corresponding to "engineering"). His statement that the traditional research is *Type 1 Basic Research* matches the ordinary usage of basic research as a synonym of *kagaku* (the website mentioned above contrast them as basic and applied researches). However, since the word usage of "*kagaku*" and "*kogaku*" may differ from person to person, they must be defined here. "*Kagaku*" here refers to the analytic discipline to understand phenomena, and "*kogaku*" refers to the synthetic discipline to produce phenomena. Honestly, I do not understand the standpoint of "*Product Realization Research*", but I guess it refers to the final phase of *Type 2 Basic Research*.

According to my understanding described above, it is natural that research institutes mainly focus on *Type 1 Basic Research* and research centers on *Type 2*. Of course those two are not clearly separable. Some researchers may do both types of researches and a single research unit may have both types of researchers. However, the ideal design of units should clearly distinguish them. Defining units by time-scale as mentioned in the AIST website is subsidiary. Product realization period must necessarily be short, but not so by definition.

In any case, I managed CARC according to my understanding, and still believe it was the source of our strength that the center focused on *Type 2 Basic Research*.

Graduate education for multi-disciplinary system design and management

— Developing leaders of large-scale complex systems —

Naohiko Kohtake*, Takashi Maeno, Hidekazu Nishimura and Yoshiaki Ohkami

[Translation from *Synthesiology*, Vol.3, No.2, p.112-126 (2010)]

“System Design and Management” program, a study that integrates humanities and sciences by crossing many disciplines, is essential to foster talented persons who can lead in the development and operation of large-scale complex systems that are symbiotic, safe and secure. The subject of the new graduate school education is large-scale complex technological and social systems, with an education curriculum that provides practically oriented lectures through which students can acquire the capacity to consider systems, the faculty to design systems in line with system life cycles, and the ability for system management. By collaborating with industries and related stakeholders such as domestic and international educational research institutions, we designed an educational curriculum and recruited faculty members, developed educational facilities and research centers, recruited students, provided education, and moreover designed the method of publishing accomplishments. As for the establishment of the graduate school in April 2008, the educational curriculum was formed to provide students with opportunities to acquire must-learn capability and knowledge that were classified into six groups. The validity of the education method was confirmed based on verification of the students’ self-evaluation, evaluation by the external evaluation committee and accomplishments by students such as papers, after the first two years of graduate education.

Keywords : System design and management, large-scale complex system, multi-disciplinary

1 Introduction

The Japanese universities and graduate schools mainly provide “the education for single disciplines” and “*Type 1 Basic Research*, which is a research to strategically discover, clarify, and formulate universal knowledge by investigating an unknown phenomenon[1]”. The conventional education and research have been effective for training people with highly specialized knowledge over the years. However, the specialization and segmentation of discipline may not be appropriate for training people who can respond to issues that may stretch across different fields[2].

On the other hand, some of the recently instigated systems are producing various problems that cannot be dealt with by specialized and segmented disciplines. For example, there are difficulties in dealing with the unforeseen accidents and failures that may occur in the power generation system and aerospace system, or there are difficulties in safety design in the development of automobiles and robots. These difficulties emerge because of the increased size and complexity of the systems[3]. At the same time, the issues of earth environment, which was created as a side effect of the culture of modern science and technology, have become the most urgent issues in modern society. This means that it is difficult to design a system appropriately, if the issues of safety in the individual system and the issues of earth environment are dealt separately. To realize a system that can concurrently solve the issues of different time-space dimension, as exemplified by safety and symbiosis, it is necessary to accurately understand the complex interaction between the diverse values that have different categories and scales, such as the safety issues, environment issues, and the system and the relationship of various elements that compose the system. It is necessary to grasp the relationship among the systems, to systematize the transdisciplinary academics to design a whole system, and to provide education from the perspective of the integration of the system. However, sufficient education has not been provided in Japan on the method of problem solving across several different disciplines that may occur in the development and the operation of the diverse products in industry.

In Europe and the United States, systems engineering has played a certain role in problem solving across several different disciplines. In Japan, systems engineering is understood narrowly as engineering for the IT systems, but it is actually engineering for the analysis and synthesis of all systems including mechanical, IT, and social systems. According to the international society for systems engineering, International Council on Systems Engineering (INCOSE), systems engineering is defined as “a method and approach that stretch across several disciplines to realize a system successfully”[4]. Particularly in the United States, the education for the systems engineering defined by INCOSE is systematically practiced in 75 universities and graduate schools including the Massachusetts Institute of Technology, Stanford University, Naval Academy, and Air Force Institute of Technology[5].

In providing the education at universities and graduate schools, it is necessary to perceive the demands of the

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industrial world. According to the "Result of Questionnaire Survey on the Human Resources Wanted by the Companies"[6] of the Educational Issues Committee, Nippon Keidanren, the items shown in Table 1 are given as expectations for the human resource training at the universities and graduate schools of sciences. This is a questionnaire result of 520 companies on what they expect in terms of human resource training by the universities and graduate schools (science departments, faculties, majors) from the standpoint of engineer recruitment. The top five items with most responses are shown. In this questionnaire, each company may select up to three responses. From this result, it can be seen that the demand is for the universities and graduate schools to produce people who are capable of utilizing advanced expert knowledge, responding to the rapidly changing social situation, creating and managing the next-generation systems.

Given such a social background, the Keio University established the Graduate School of System Design and Management (SDM) in April 2008. At this graduate school, a unique, practice-oriented educational curriculum unseen in any other graduate school has been created to train people, who already are specialists or have business experience, to become capable of designing large-scale complex systems, taking in consideration the social demands such as symbiosis and safety. In other words, the people trained here will be capable of leading *Type 2 Basic Research*[1] and application research, and such human resources before could not be trained in conventional Japanese graduate schools. The large-scale complex systems include not only the technological systems such as power generation and aerospace systems, but also social systems such as the financial system, medical system, community, corporate organization, and NPO.

Our objective is to build the system design and management science (SDM science), a discipline system to creatively design and thoroughly manage the large-scale complex systems, and to provide graduate school education to train people who are capable of leading the construction and operation of large-scale complex systems. In this paper, we present the scenario for establishing the graduate school to realize our set goal, the elements selected to provide the graduate school education, and the results of the integration of the elements. We shall also present the evaluations by the students and the external evaluators, discuss the evaluations, and address the future issues.

Table 1 Expectations for universities and graduate schools from industry

Response	Companies
To have students acquire specialized knowledge	340 companies
To train the students to organize their thoughts by gathering knowledge and information	287 companies
To have the students acquire basic knowledge of other disciplines related to their specialties	231 companies
To provide education with relevancy to the real society, in addition to theories	162 companies
To have the students experience working in teams on certain topics	119 companies

2 Scenario

The Keio University established a graduate school for SDM education after a long period of deliberation. In 1996, a system design engineering department was established in the Graduate School of Science and Technology, to conduct education and research on system design engineering transcending the framework of engineering disciplines such as mechanical, electrical, information, architecture, and others. It continues to train engineers with both the abilities for basic knowledge and integrated perspectives. In 2008, the Graduate School of SDM was established independently of the Graduate School of Science and Technology for the education and research on SDM science, a discipline that fuses humanities and sciences and surpasses the framework of technology and social sciences such as science, engineering, economics, and political science.

In establishing the Graduate School of SDM, we interviewed the people involved in large-scale complex systems in Japan and abroad, on the current issues in developing and operating the large-scale complex systems, and also sought the demands of industry for graduate school education. As a result, we found that the demand for the graduate school education was almost the same as the ones described in Table 1. The format of the graduate school education was designed based on: the design method for large-scale complex systems such as automobile, robot, and plant that developed in the Japanese industry, as well as the systems engineering that developed mainly in Europe and the US; the system design methodology built by the Keio University in the 21st Century COE Program "System Design: Paradigm Shift from Intelligence to Life"[7][8]; and knowledge and methods necessary for the design and management of the social systems. The masters program was established with the educational objective of training people who can lead the construction and operation of the large-scale complex systems through a vocational graduate school type education, placing emphasis on interaction between the faculty and students or among the students themselves. The doctoral program was established with the educational objective of training specialists of SDM science with emphasis on research.

To realize our goal of the graduate school education for issues that stretch across multiple disciplines, collaborations with various interested parties (or stakeholders) are important. The relationship between the scenario set to realize the goal and the major stakeholders are shown in Fig. 1. The input and output between the stakeholders and the Graduate School of SDM are shown by arrows, and the items particularly emphasized by the School are underlined and capitalized. In this figure, society/industry, who is one of the stakeholders, represents all others except the "academia (education and research institution)" in the "industry-government-academia" and include all sorts of social organizations such as the government, local governments, and NPOs. Details of the scenario are as follows.

(1) Preparation of educational curriculum

Considering the social and industrial issues and the demands for the graduate school education, an educational curriculum is prepared by setting the abilities that the student must acquire to handle large-scale complex systems and by building the system of SDM science as a discipline system that enables nurturing such abilities. Collaboration will be done with the universities and graduate schools in Japan and abroad for the single discipline education, as necessary.

(2) Faculty recruitment

Based on the educational curriculum, the faculty members who can promote the research of SDM science and provide lectures for the courses are recruited. Particularly, faculty members with experiences in companies or overseas, as well as first-class experience in development and operation of large-scale complex systems are employed.

(3) Preparation of educational facilities

The educational facilities that promote communication and group learning by faculty members and students are prepared. To emphasize the close collaboration between society and education research, the facility should be located in a place with good access by public transportation. A communication system will be established to support discussions and conferences among students and faculty members in remote areas and with other institutions in Japan and abroad.

(4) Preparation of research center

The research center is set up to solve the social and industrial issues by application of SDM science, to utilize the obtained findings, and to further advance the SDM sciences through collaboration with other education and research institutions, international institutions, and academic societies.

(5) Recruitment of students

To enable learning based on exchange of diverse human resources, people with specialties in some disciplines of science and engineering, social sciences, or humanities are recruited (the ratio of people with specialties in so-called sciences to humanities will be 1:1, and the ratio of people with business experiences to new college graduates will be 2:1). Foreign students are actively recruited to enhance the international consciousness of the Japanese students, and to spread SDM sciences to students who are non-native speakers of Japanese.

(6) Education

The education for SDM science is executed mainly through hands-on experience and group learning of

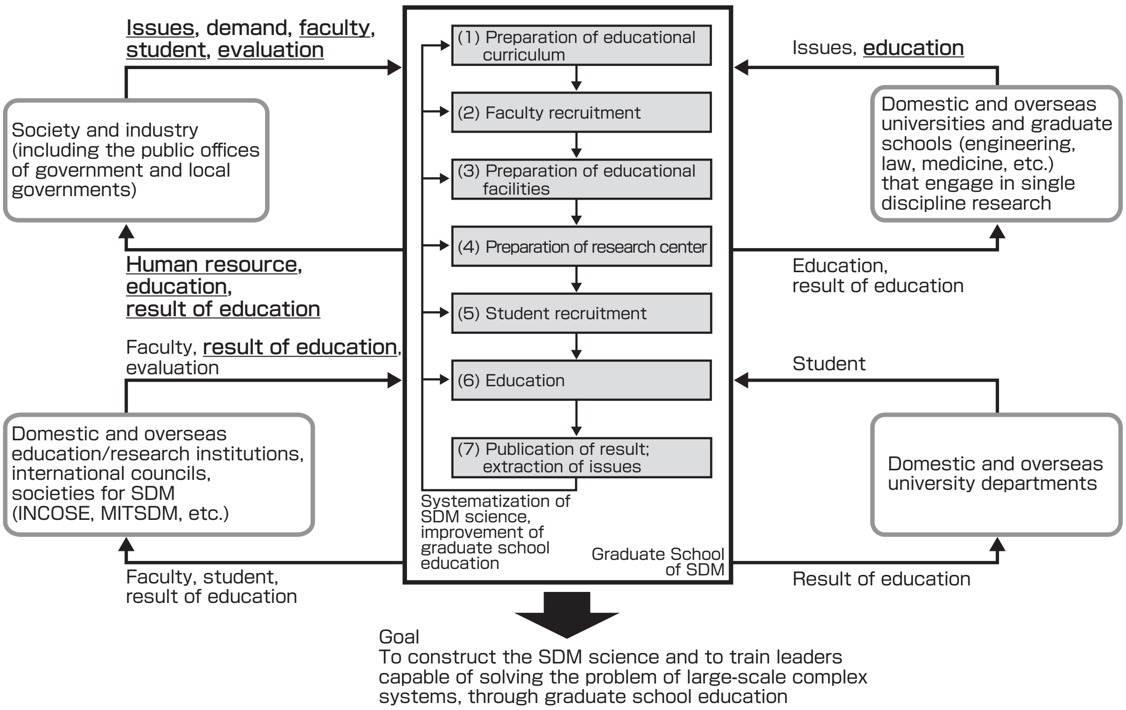

Fig. 1 Scenario for achieving the goal and the relationships with the stakeholders

unsolved issues in society. In addition, SDM seminars and lectures are actively done for business people in industry who are not participating as students, to train leaders of large-scale complex systems and to extract social issues and demands for graduate school education. Also, the opportunities for faculty development[Term 1] are regularly and frequently provided to increase the educational ability of the faculty members.

(7) Publication of results; extraction of issues
The abilities acquired by the students through the graduate school education and the findings obtained by the faculty members are presented to the stakeholders, and are evaluated. Also, evaluations will be done by students attending the Graduate School of SDM. The issues are extracted by analyzing the evaluations, and the education is improved based on the results.

The above scenario will not end in one cycle. It is a spiral-up[Term 2] scenario where the improvement of the graduate school education and further development of SDM science are conducted regularly for each steps from (1) to (6), based on the result of "(7) Publication of results; extraction of issues".

3 Establishment of the Graduate School

In opening the Graduate School of SDM, issues in industry and demands for graduate school education were extracted based on interviews with over 100 companies in Japan and abroad. As a result, the abilities and knowledge that the students must acquire to handle the large-scale complex systems were categorized into six groups as shown in Fig. 2. The horizontal axis shows the range of the related disciplines, while the vertical axis shows the scale and complexity of the system in question. This indicates that a leader who handles the large-scale complex systems must have the abilities of system design and system management, and should have the foundations for systemic thinking and communication. It also means that the students must be already versed in some

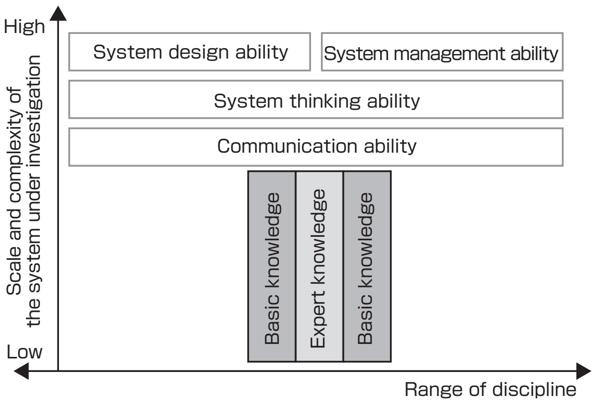

Fig. 2 Knowledge and education that should be acquired by the students

specialty and possess basic knowledge for the disciplines related to their specialty. The abilities and knowledge are defined as follows.

A) System design ability:
The ability to understand the real issues and demands of the diverse stakeholders such as user, customer, society, and environment, and to creatively suggest a solution to the issues while taking into consideration the total consistency in each lifecycle phase from conceptualization, development, operation, and disposal of the system (the design includes the proposal of concept and solutions in all designs, from technological system design, artistic design, organizational design, social design, to the grand design of management and policy)

B) System management ability:
The ability to respond to the changes in environment due to the progress of the project and the advancement of lifecycle, and to consistently carry out the system design and to manage and operate the system to fulfill the demands of the stakeholders such as the user and customer

C) System thinking ability:
The ability to capture the whole picture of the system and the essence of the issue in a transdisciplinary, birds-eye-view, and systematic perspectives, by looking at the interdependency and the interrelationship of the phenomena, as well as the independent phenomenon

D) Communication ability:
The ability to communicate one's thought to others, understand the thoughts of others, and to solve the problem by forming a team with diverse human resources

E) Expert knowledge:
Deep knowledge in certain fields of engineering or social sciences (desirable to have knowledge of multiple fields)

F) Basic knowledge:
Basic knowledge of other disciplines related to the specialty

The education at the graduate school established for the elements selected to realize the goal and the integration of these elements will be explained below.

3.1 Educational curriculum

The outline of the courses is shown in Table 2. For the abilities and knowledge that the students should acquire through education, those related to the courses are marked with ○ and those with particularly strong relations are marked with ◎ . The courses that differ according to the student's specialty are marked with △ . The individual subjects included in the recommended subject group and the elective subject group are listed in Table 3.

The basics of the four abilities that the students must learn will be taught mainly in the required subjects, and are supplemented with the recommended subjects. In the cases where the contents to be learned are different according to the student's specialty, they could be learned through the elective or recommended subjects. Since the disciplines are diverse, the students may take courses of the universities and graduate schools outside of the Graduate School of SDM to learn the expert or basic knowledge of certain fields. Particularly, the collaborations are done with the Graduate Schools of Science and Engineering and Business Administration within the Keio University, for supplementary courses to provide educational opportunities.

The credits of the courses are two credits per course for almost all courses with few exceptions. Figure 3 shows the structure of the master's program curriculum. The numbers in the parentheses indicate the credits of the courses necessary to obtain the degree. The requirement for the master's program is to complete 30 credits or more courses, including eight credits in core subjects, four credits in design project ALPS (active learning project sequence), and two credits in SDM research. The master's degree can be obtained after taking six credits or more of recommended subjects of technology, two credits or more of recommended subjects of social science, or two credits or more of recommended subjects of technology, and six credits or more of recommended subjects of social science. To allow active participation of the students, the course will be 14 sessions, 90 minutes per session, with ample opportunities for group learning, hands-on practice, and discussions. To actively accept foreign students, courses will be in English as well as Japanese mainly for required subjects.

The educational curriculum for the required subjects will be described. To teach the basic knowledge considered to be international standard, four textbooks are selected in accordance to the Certified Systems Engineering Professional (CSEP), which is an international qualification for systems engineering, and the Project Management Professional (PMP), which is an international qualification for project management. The textbooks included the one for core subjects[9], a book for the three courses except project management[4], a book for project management[10], and a book used in ALPS[11].

Table 2 Correspondence of educational curriculum and ability/knowledge

	Required subject group								
	Core subject								
Abilities and knowledge to be acquired by students	Introduction to systems engineering	System architecting and design	System integration	Project management	Design project ALPS	System design and management research	Recommended subject group (technology, social sciences) 12 courses	Elective subject group (technology, social sciences) 16 courses	(Subjects of other departments and other universities)
System design ability	◎	◎	◎	○	◎	◎	○		
System management ability	○	○	○	◎	◎	◎	○		
System thinking ability	◎	◎	◎	○	◎	◎	○	○	
Communication ability				◎	◎	○	◎	○	
Expert knowledge in a certain area					○	◎	△	△	◎
Basic knowledge in disciplines related to the specialty					○	○	△	△	◎

Table 3 Recommended subjects and elective subjects

Recommended subject group	Technology subjects	System environment
		Human factor
		Risk management of engineering system
		Dependable system
		System life
		Digital manufacturing system
		Model based engineering and architecting
	Social science subjects	Introduction to international affairs
		Communications
		Human relations
		System management
		Ethics for system design engineers
Elective subject group	Technology subjects	Mathematical modeling and statistics
		Mathematical technique of prediction and optimization
		Mathematical technique of dynamics analysis and control
		Database management system under network environment
		Software safety engineering and reliability
		Software engineering
	Social science subjects	Fundamental of accounting, marketing and economics
		Introduction to legal issues for engineers
		System simulation technique
		Global standardization strategy
		Methodology of creative decision making
		Business intelligence
		Design philosophy for policy and regulation
		Political economy of International systems
		Methodology and management of socio-critical system
		Special lectures on system design and management

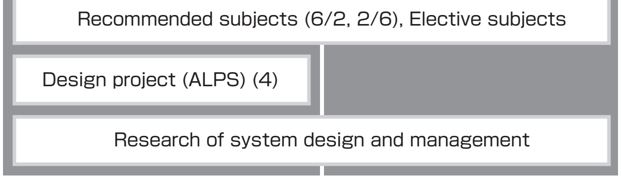

Fig. 3 Framework of master's program curriculum

Since there are many faculty members with business experience as well as knowledge and abilities in the large-scale complex systems, many courses reflect the business experiences. For example, in a core subject "System integration", the textbook is used to introduce the processes and methods that are being systematized in the field of systems engineering. Then, the faculty members who had participated in the development of the automobile and satellite introduce the actual case of problem solving, explain the gap between theory and reality, and conduct hands-on exercises using the case studies. The students learn the differences in the system integration of mass-produced automobile and custom-produced satellite, as well as the design method developed in Japan.

3.1.1 Introduction to systems engineering

The basics of strategic systems engineering according to the V-model[Term3] in the system development process is presented. Lectures and exercises are done on system thinking, requirement analysis, functional physical breakdown, and architecting[Term 4], to learn the basics of SDM which aims to meet diversified social requests. In the exercise, the students form teams to realize some specific system such as "automatic cleaning system that can be remotely operated by the user while not at home". Several faculty members will be in charge of the lectures. The students interview the faculty members who play the role of customers to extract the issues and needs, create the specification for each development process from system requirement to shipment, and develop the system along the development process. The other teams are considered to be the competitors, and all teams work to realize the system. Figure 4 shows the remote-controlled automatic cleaning system created by one of the teams. The image on the left is the service screen on the web to conduct remote control, and the photograph on the right is the cleaning system developed based on Roomba 577 of the iRobot Corporation.

3.1.2 System architecting and design

This is a course on the architecting and design of the problem-solving structure and detailed structure as well as visualization from multiple viewpoints in response to social demands. Group discussions will be held on the architecting and design of the research topics of the students.

3.1.3 System integration

This is a course on the discipline system for the process of breaking down into elements and to integrate them as a system. Lectures are given on the creation of requirement specs of a system, analysis, design, operation verification, and adequacy check of the specs. Practical group exercise will be done and discussions will follow.

3.1.4 Project management

This is a course on the basics of project management. Specifically, it will be lectures and exercises on the management of large-scale complex systems, basics and practice of logistics (personnel and procurement), and methods of cross management and project management. Figure 5 shows the exercise in tower construction using paper. The students work in teams, determine the roles including the project manager, and the preparation for tower construction is carried out according to the management process of PMP. The price of the paper and the cost of labor per student per hour are set, and the teams complete for a stable and high tower construction within a set budget and schedule. This will be followed by the evaluation of the project management of each team.

3.1.5 Design project ALPS

This is an international collaboration group project with Stanford University and the Massachusetts Institute of Technology, and the course is given in English. Under topics such as "Enhancing Senior Life in Japan" (2008) or "Sustainable Community" (2009), about four or five workshops (two days each) are conducted a year in addition to group learning between the workshops. The students join a team of five to eight members to experience the whole process of system lifecycle, and finally present a system proposal and engage in discussion[11][12]. Figure 6 shows the flow of the annual workshops and the group learning. The faculty members of the three universities adjust the lectures and methods of ALPS almost every month including through teleconferencing. This course is deeply related to the core subjects, and it is designed so the students can learn the lectures through the main course and will be able to apply the

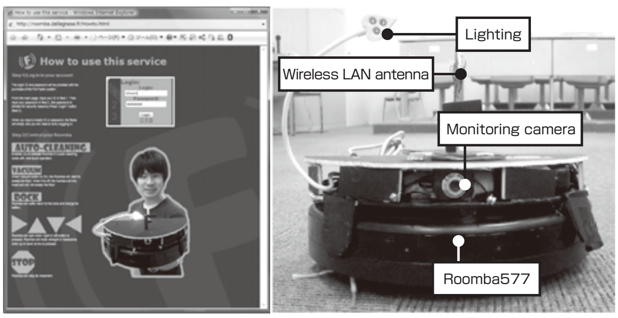

Fig. 4 Automatic cleaning system

Fig. 5 Project exercise of building tower using paper

knowledge learned in the lectures to this course. The details of the ALPS course are presented in Reference [12].

3.1.6 System design and management research

This corresponds to the research for the master's thesis. However, unlike conventional individual research, the group conducts the transdisciplinary research in project format, and the students are encouraged to engage in research that matches the social demands such as safety, symbiosis, and social coexistence. Each student writes a thesis for the part of the project that he/she is responsible.

3.2 Faculty member

Twelve full-time faculty members for the Graduate School of SDM as well as dozens of special research faculty and invited faculty members are employed. One of the characteristics is that there are many members with business experiences in industry. The faculty members employed include people with business experiences and advanced knowledge and abilities in large-scale complex systems in technological systems such as aerospace, nuclear power, automobile, information, and precision machines, as well as social systems such as finance, policy, treasury, and agriculture. The requirement for recruitment is that they must be able to give lectures in English to give courses for foreign students and to promote collaboration with educators and researchers of overseas education and research institutions.

To provide students the global trend of the academic world related to SDM science and to increase the knowledge of the faculty members as part of faculty development, about 10 lecturers are invited from abroad. These lectures are mostly on core subjects and can be heard as intensive courses or as remote conference lectures.

3.3 Preparation of educational facilities

To promote communication and group learning among students and faculty members, the classes are set up in the free seating style[Term 5], and each student is given a personal locker to store educational and experiment materials. Unlike the conventional laboratory where the spaces between the students and the faculty members are divided by partitions, there is no specific seat for any student, and the students use the rooms and seats according to their purpose such as communication and group learning. The faculty room is concentrated in a segment of the floor to enhance frequent communication among the faculty members.

An e-learning system is set up where all lectures are recorded on video by staff members, and these can be delivered online along with the lecture materials. This will enable education opportunities to students who cannot be physically present at the lectures. The teleconferencing system is introduced in several conference rooms to enable discussions and meetings with students and faculty members in remote areas and with other institutions.

To handle large-scale complex systems, it is necessary to improve the abilities in simulation and modeling technologies to support system design and system management. Therefore, the environment where the student can freely use the software for such technology through the network is offered. Also, large-scale workstation for concurrent design[Term 6] and concurrent design room composed of several high-definition displays are prepared (Fig. 7). There, the students can bring their own terminals to create designs for various systems through the network.

3.4 Research center

The SDM Research Center of the Graduate School of SDM was established as a research center to advance the SDM science by solving the diverse issues in the industrial world by application of SDM science and to accumulate the findings obtained. This center was established to solve the various issues through the collaboration of industry and academia, and the faculty members can establish a laboratory in the Center to solve some specific issues. The collaborator can obtain the information related to SDM science and may use the facilities of the Graduate School of SDM.

To solve the issues of large-scale complex systems, collaboration with education institutions transcending the framework of disciplines and international collaborations are necessary. Therefore, in collaboration with the Graduate

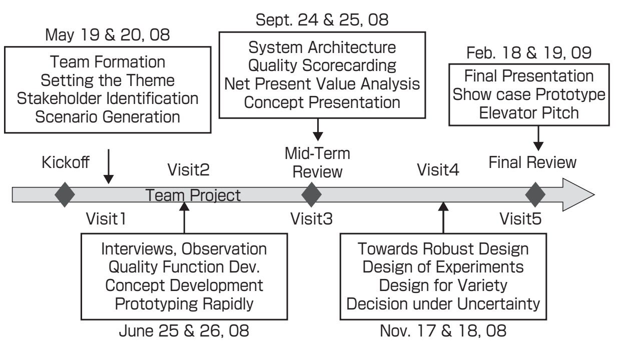

Fig. 6 Work flow of group training in the annual workshop

Fig. 7 Concurrent design room

School of Science and Technology, Keio University, the Global COE Program "Center for Education and Research of Symbiotic, Safe and Secure System Design" of the Ministry of Education, Culture, Sports, Science and Technology was started in 2008, to study the system design considering the social values such as symbiosis and safety, as well as to promote education and research of the researchers with such social values.

The following list shows some of the research topics at the Graduate School of SDM. The systems include home appliances, information, financing, insurance, human, education, and others.

- Thermal/Acoustic trade-off design for consumer electronics in a distributed design environment[13]
- A case study of the effects of platform software selection on information system maintenance cost[14]
- Transforming seamless positioning technology into a business using a system design approach[15]
- The evaluation of the alliance systems designed by "Enterprise Currencies" in Japan[16]
- Claim-payment failures of Japan's insurance companies and designing better payment architecture[17]
- A method for analyzing fundamental kinesiological motions of the human body by applying interpretive structural modeling[18]
- Capstone experience for multi-disciplinary system design and management education[12]

To be constantly aware of the global trend of academics related to SDM science and to contribute to academics through the education at the Graduate School of SDM, the School will participate in INCOSE and the Council of Engineering Systems Universities (CESUN), an international organization for systems engineering education. The faculty members will be dispatched to the meetings regularly, and the School will host the APCOSE (Asia-Pacific Conference on Systems Engineering)[19] to enhance the knowledge level of the students and the faculty.

3.5 Students

The student recruitment by the Graduate School of SDM is announced at various organizations of industry, government, and academia, and request is submitted to industry to dispatch the employees as students. As a result, after entrance examinations held three times a year, we were able to accept students almost exactly as in the set scenario. One of the characteristics is that the students are composed of wide-ranging age, diverse fields, and multiple nationalities. Students were admitted in spring and autumn semesters for the academic years (AY) of 2008 and 2009, and as of AY 2009, there were 138 students in the master's program and 46 in the doctoral program. The ages of the students varied from the 20s to 60s, and the average was 32 years old for master's students (Fig. 8) and 42 years old for doctoral students (Fig. 9). Their majors included science and engineering, law, political science, economics, literature, trade, agriculture, and physical education. Many students had business experiences, the percentages being 66 % for the master's student and 89 % for the doctoral students (Fig. 10). The occupations of those with business experiences were diverse: manufacturing, communication, consulting, information, aerospace, financing, real estate, public office, architecture, energy, system, medicine, mass communication and publishing, and law (Fig. 11). About 20 % of the students were non-Japanese including foreign students from overseas universities. As in the initial objective, it has become a place of learning based on the exchange of diverse human resources consisting of students and faculty members with diverse specialties.

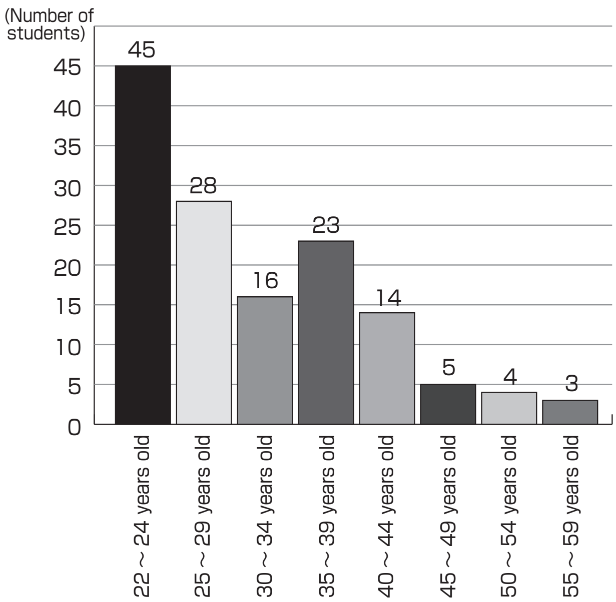

Fig. 8 Age distribution of master's students

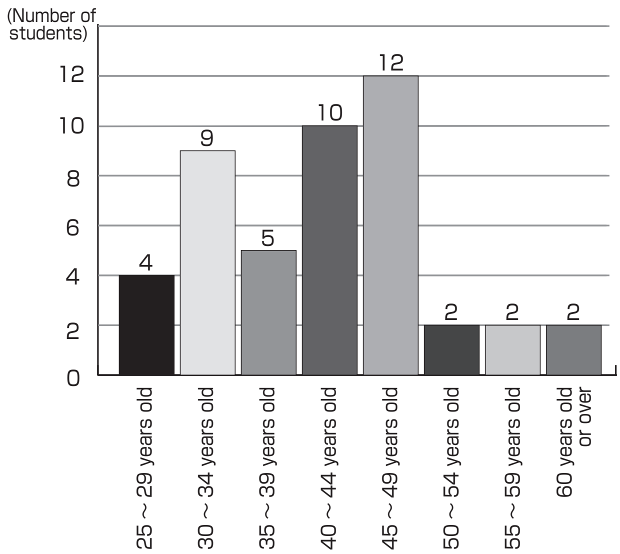

Fig. 9 Age distribution of doctoral students

3.6 Education

As mentioned earlier, since many faculty members have business experiences in large-scale complex systems, the education format is designed to reflect their experiences. Also, since there are many students who already have specialized knowledge and business experiences, there are several courses designed to seek ways to solve problems in industry or to systematize part of SDM science. For example, a faculty member with experience in the financial system may propose the topic, “What are the verification methods in the social system? What are the advantages and disadvantages of each method?” and the discussions are deepened during each session. In addition, the independence of the students is emphasized, and the students are encouraged to organize sessions where they invite students or exterior lecturers with some particular specialties as needed.

To improve the abilities and knowledge of each faculty member, opportunities for faculty development are set several times a month. The findings and issues obtained through the education experience of the faculty members are presented, and discussions are conducted regularly to share the findings and to improve education and research.

To provide learning opportunities to working students who cannot attend during office hours, the Japanese lectures of the core subjects are given on Saturdays and weekday evenings (19:00-20:30). Since most of the foreign students are full-time students who do not work, the English lectures for the core subjects are given during the weekdays. For the employees of industry who are not students, seminars and lectures for SDM science are conducted to help train the leaders of design and management of the large-scale complex systems. This is useful for the extraction of the industrial issues and the demands for graduate school education.

3.7 Publication of results; Extraction of topics

The results of the education are actively publicized, and the opportunity to be evaluated mainly by industry and the opportunity to apply the results in industry are sought. For example, in ALPS, each team proposes a service or product for a given topic in the final session. About 10 entrepreneurs, company people, and research institution people are asked to judge the proposals from the perspective of practical application in society.

For the evaluation of the courses, questionnaire survey is conducted of the students at the final session for each course. The evaluations of the course can be viewed only by the faculty members and others in charge, while the students’ evaluations on overall graduate school education are shared by all faculty members, to extract the issues and the improvements are reflected in the programs next year. Also, a system is set up where five people of industry working on the development and operation of the large-scale complex systems are asked to participate as members of the external evaluation committee, to regularly conduct external evaluation of the education at the Graduate School of SDM.

4 Results to present and future issues

Two years have passed since the opening of the Graduate School of SDM. The results and evaluation to present as the students completed the program in March 2010, and the future issues will be described below.

4.1 Result of group learning by diverse human resources

In ALPS, group projects were done by the teams over the year, and many students were able to learn the diverse ways of thinking and methods for clarifying the social demand systematically and to create and realize the ideas through experience. As a specific example, the idea and the result created by a certain team will be introduced.

The team worked on the 2009 ALPS topic “Sustainable Community” and suggested a system for hydroponic

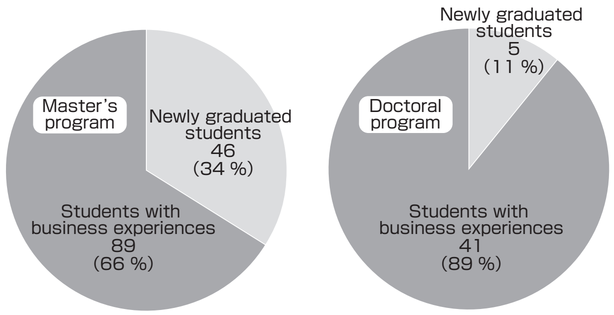

Fig. 10 Ratio of newly graduated students to those with business experiences

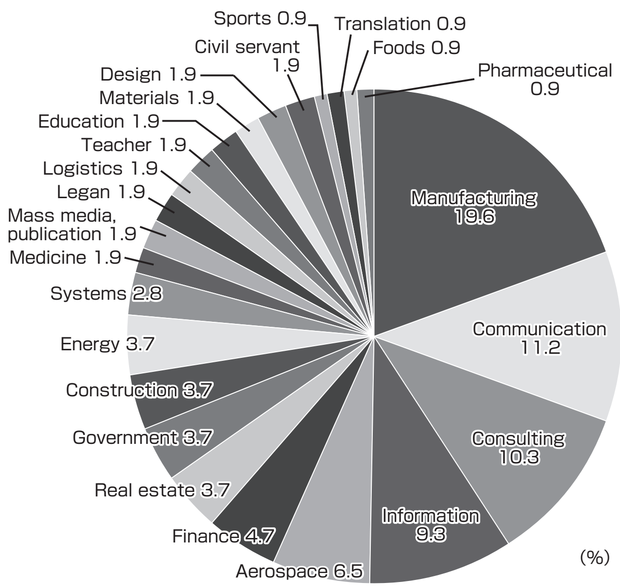

Fig. 11 Occupation distribution of students with business experiences

cultivation using the abandoned schools in the metropolitan area as a method to simultaneously solve the issues of abandoned school buildings due to low birthrate, lack of successors of agriculture, and unimproved unemployment rate of young people. Figure 12 shows part of the proposal created by this team (Roppongi Vege & Fruits). The strengths of this proposal was the construction of a sustainable business model that fulfilled the consumer demands for fresh, safe, and secure foods, as well as the demands of young people who wish to have stable income in the city. To create this proposal, the team conducted market research, questionnaire survey to the stakeholders, and interviews. Then they did a prototyping in a test plant based on the methods and knowledge learned at ALPS, and investigated the possibilities. As a result, the project won the award in the "Student Entrepreneur Championship" of the Tokyo Metropolitan Government and the Tokyo Metropolitan Small Business Center, and the Kanto Bureau of Economy, Trade and Industry Director Award in the "Campus Venture Grand Prix" organized by The Nikkan Kogyo Shimbun, Ltd. Currently, several more students have joined the team, and are considering its business development and are making adjustments with the local government and related companies. This is one example where the students acquired the ability to extract the demand from the real society and to design a system throughout its lifecycle from conceptualization, operation, to disposal, through the education at the Graduate School of SDM.

Also, it was confirmed that the concept of the Graduate School of SDM where group learning and group discussions are emphasized was effective in many courses other than ALPS. The students with diverse backgrounds understand each other's backgrounds, discuss the knowledge obtained in the course, and work together on an issue, and this results in high educational effectiveness.

4.2 Education by collaboration of multiple disciplines

The courses that transcend the framework of disciplines are realized in various forms through the collaborations of the

Fig. 12 Case study of a proposal at ALPS (Roppongi Vege & Fruits)

faculty members, and feedbacks from students are obtained. As one example, the faculty members with specialty in technology give courses in "System Simulation Method" to conduct design and verification of system using the simulation method for the "Call Triage[Term 7] Emergency System" handled by the research group consisting of the faculty members with specialty in social sciences. The analysis and investigation for improving this system in terms of technological and sociological aspects are done. For example, it has become possible to carry on a more specific and specialized discussion on the legal limitations that become issues when attempting technologically optimal solution or the limits of what can be solved technologically in the current legal limitations. It can be said that an effective education can be done through collaboration of disciplines that normally rarely come together. In "System Life Theory", education on system design method learned from the environmental adaptation of organisms is done, and lectures and exercises are given on the design theory considering the unforeseen circumstances that can not be solved with conventional systems engineering. This is one example where SDM science can be applied to social and human system design transcending the systems engineering.

4.3 Master's research and doctoral research

Unique researches on the design and management of various systems including the recommendations for design and policy of management, as well as design of services and products are being done at the master's and doctorate level. Particularly,

Table 4 Example of master's research topics for AY 2009

Research topics
Measurement of CO_2 reduction effect by battery sharing alongside solar power generation
Carbon tax design using LCA for the diffusion of clean energy vehicle
System design for symbiotic city-rural society centering on biomass energy technology
Evaluation of sustainability of copper supply with consideration for recycling in Japan
Proposal for safety management system in large-scale chemical plant
Risk management for software development project with project description language
System design of lower limb protection of passengers using semi-active knee bolster
Renewal of global maritime safety policy for the stabilization of international maritime transportation system
Survey of relationship of corporate performance and corporate customs and cultures in manufacturing
Survey of motivation of employees of local governments – For the construction of lively organizational culture
Research on the motivation of young engineers – Using the microgravity experiment project conducted jointly by multiple universities as an example
Clarification of values for social relevancy in subjective happiness
Research on the strategy to introduce ultrahigh-speed plastic optical fiber network for homes to China
Research on the future prospect of electronic books and the structural change in the print media industry
Investigation and plan for verification test for the business model for launch space vehicle using the ocean – for realization of Japanese manned spacecraft

there are many research topics on conglomerate values such as symbiosis, safety and security, and social coexistence. Table 4 shows some examples of the master's research topics conducted in AY 2009. The target systems include diverse systems from technological to social systems, but the master's researches have the common points: designing and managing a system that matches the demand of the stakeholders while considering the system lifecycle; and then to write up the verification of the result and confirmation of the efficacy as a research thesis. These are the characteristic of the research at the Graduate School of SDM. The doctoral dissertations on SDM science are also beginning to appear [20].

4.4 Collaboration with industry and overseas institutions

Seminars and lectures are regularly given to the people of industry. An agreement was concluded on SDM science with the Japan Aerospace Exploration Agency (JAXA), and collaborations in education and research are being done. As one activity, seminars on SDM science are given to the employees of JAXA, and about 93 people participated in AY 2008. Various issues occurring in the space development field were clarified, the courses systematized at the Graduate School of SDM were given, and discussions were held on the solutions of the individual issues. The result of the questionnaire survey of the participants showed high satisfaction in the seminars. Particularly, high marks were seen for the overall, comprehensive viewpoint as a system.

Collaboration with overseas institutions is actively promoted, other than the aforementioned ALPS courses and workshops with Stanford and MIT. Collaborative agreements were signed on the mutual use of educational curriculum with Delft University of Technology (The Netherlands), Stevens Institute of Technology (U.S.A.), Swiss Federal Institute of Technology Zurich (Switzerland), Institut National des Sciences Appliquées (France), and others. Master's students are exchanged with TU Delft for a successful international collaborative education. We have received request for support for the construction of SDM sciences to meet the demand of the industries of the respective countries from Khalifa University of Science, Technology and Research (Abu Dhabi, UAE), Amet University (India), and Egypt-Japan University for Science and Technology. We have become aware that there is a worldwide demand for SDM education.

4.5 Evaluation by the students

A survey was conducted to 36 second-year master's students who matriculated in spring semester, AY 2008, on the abilities that they thought improved in one year of education at the Graduate School of SDM, and the level of the satisfying experience. As a comparison, similar survey was conducted to 23 second-year master's students of the Mechanical Engineering Department, Graduate School of Science and Technology, Keio University. The survey was a six-step evaluation for each item. The t-test for each item was conducted based on the survey results of the two graduate schools. The items that showed significant difference in the evaluation with significance level 1 % are shown in Fig. 13. For each item, the graph on top shows the average values and standard deviation of the survey of the students of SDM, and the graph on bottom shows the average values and standard deviation of the survey of the students of Science and Technology.

The result shows that the education and research curriculum at the Graduate School of SDM fulfills the expectation for the universities and graduate schools of science by industry, as shown in Table 1, at the level of the self-evaluation of the students. The low self-evaluation by the SDM students on "writing ability to create the papers and reports that are logical and understandable" is an issue that must be resolved in the future. It is thought that the self-evaluation for writing ability was low since the subject of the questionnaire were master's students who just entered their second year, and since the first-year students went through the SDM education where emphasis was placed on action such as going to the site rather than creating documents. In response, we plan to strengthen the courses to improve the communication ability. For writing, in ALPS, the students experience writing a report in English as a team, and experience writing in Japanese for the master's thesis individually.

We feel that all students are capable of learning the basic thinking and method needed to solve the problems of large-scale complex systems to a certain level through required subjects. On the other hand, to be able to utilize the thinking and method in society and industry, it may be necessary to take courses other than the required ones at the Graduate School of SDM as well as at other universities and graduate schools, and the students themselves must apply them in their research and work. The effectiveness of the education depends largely on the students' strength of the consciousness for the problem, breadth of vision, and their ability to take

Fig. 13 Comparison of consciousness of SDM students (upper bar graph) and engineering students (lower bar graph)

action. Although it is difficult to solve all these issues through graduate school education only, we feel many issues can be solved by the close collaboration between the Graduate School of SDM and society and industry, the individual guidance to students by the instructors, and the further promotion of various exchanges among students composed of diverse human resources.

Since the education for enhancing deep knowledge and advanced specialty is also important, we are considering the curriculum where such abilities can be improved along with the other abilities. Another issue is the large gap in the abilities and knowledge level of the students depending on the courses since the specialties differ by students. Currently, the lectures are given for the students with higher abilities and knowledge level, and supplementary lectures are given separately.

4.6 External evaluation

As of the end of AY 2008, the external evaluation after one year of the Graduate School of SDM was conducted by the five members of the external evaluation committee. As a result, high evaluation was obtained for the new education, while the following points of improvements were indicated. These included the further collaboration with industries on the results of one year at the Graduate School of SDM, the mechanism for giving independence to students such as employing the students who have completed the program as the course mentor, and the thorough infusion of education and research concept of SDM where "both the trees and the forest are seen" or seeing the individual essence as well as maintaining a wide vision.

We are working to improve the education based on these indications. For the further collaboration with industry, we are considering and adjusting the ALPS where proposals of the team can be realized through collaboration with industry. Also, we are considering the mechanism where the issues taken up in the courses are matched with the issues in industry, and where the proposals generated in the courses are fed back to the companies that provided the topic.

5 Summary

The Graduate School of SDM was established to train people who are capable of leading the construction and operation of the diverse large-scale complex systems from technological to social systems, and the first students graduated in March 2010. From the evaluation of the students and members of the external evaluation committee, we believe the students have acquired the abilities and knowledge that they must have to handle the large-scale complex systems, as set at the inception of the graduate school. The results of the master's researches conducted by the students confirm that the students have acquired the method and thinking to clarify the social demands systematically, to create the ideas, and to realize them through the curriculum that emphasizes group learning and group discussions by diverse human resources. On the other hand, future issues include the reinforcement of the educational curriculum to improve the advanced specialties of each student, and measures to fill the gap in ability and knowledge levels of the students for each course due to the wide-ranging student background. We believe further revisions in the curriculum and further strengthening of the collaboration with society and industry, related education and research institutions, and universities and graduate schools are effective. Also, we believe this unique graduate school education can be improved by investigating and evaluating the results and issues of the graduate level education of SDM science by conducting follow-up surveys of the graduates in society and industry.

6 Acknowledgements

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Terminologies

Term 1. Faculty development: Organizational effort by which the faculty members improve and enhance the lessons and the teaching methods

Term 2. Spiral-up style: The method where a goal is achieved in a spiral form rather than in a linear form
The movement toward the goal is made by turning the PCDA (plan-do-check-action) cycle, including making a plan, executing it, verifying it, and then incorporating the improvements in the next plan.

Term 3. V-model: The framework to describe the lifecycle of system development from demand analysis, operation, to disposal
The left side of the V-shaped conceptual diagram shows that the demand drops to lower level as the demand is segmented by design, and the right side shows that the system is integrated by testing and assembly.

Term 4. Architecting: The act of realizing a concept, allotting the function to the elements, and then clarifying the relationship (interface) between the elements

Term 5. Free seating style: The style where students are assigned no specific seating
The seats and the rooms are used on first-come first-serve basis or by preliminary reservation.

Term 6. Concurrent design: The design method in system development where the people in charge of all phases of the system lifecycle from planning, operation, to disposal gather, discuss various issues, and cooperate to work simultaneously.

Term 7. Call triage: The mechanism to determine the necessity of dispatch in emergency calls, where the urgency and seriousness of the sick are determined based on the information given by the caller
The City of Yokohama started this system on October 1, 2008.

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Completed the doctoral program at the Graduate School of Science and Technology, Keio University in 1990. Doctor (Engineering). Assistant at the Chiba University, and Assistant Professor, Chiba University in 1995. Professor, Keio University in 2007. Professor, Graduate School of SDM, Keio University in 2008 to present. Studies the model-based systems engineering and system design of control for symbiosis and safety. Member of The Japan Society of Mechanical Engineers, The Society of Instrument and Control Engineers, Society of Automotive Engineers of Japan, IEEE, INCOSE, etc. For this paper, was in charge of the discussion on the education and research curriculum of technological courses.

Yoshiaki Ohkami

Completed the doctoral program at the Graduate School of Engineering, Tokyo Institute of Technology in 1968. Doctor of Engineering. Worked at the National Aerospace Laboratory of Japan, Science and Technology Agency; Department of Mechano-Aerospace Engineering, Tokyo Institute of Technology; and Professor, Department of System Design engineering, Keio University. Currently, Professor and Chairman, Graduate School of SDM, Keio University. Also worked as the Visiting Researcher at UCLA, and Research Director, Japan Aerospace Exploration Agency (JAXA). Specialty is dynamics and control of space systems. Fellow of The Japan Society of Mechanical Engineers. INCOSE Fellow. Member of The Society of Instrument and Control Engineers, The Japan Society for Aerospace and Space Sciences, IEEE, etc. Proposed the establishment of the Graduate School of SDM, and engaged in the international surveys and preparations for 10 years before the opening. For this paper, was in charge of the integration of the entire process from the creation of the scenario, execution of education, publication of results, and extraction of issues.

Discussions with Reviewers

1 Overall

Comments and Questions (Naoto Kobayashi, Center for Research Strategy, Waseda University)

This paper presents the curriculum and the basic concept and mechanism for the establishment of the Graduate School of System Design and Management (SDM) that newly opened at the Keio University in 2008. The school has unique characteristics unseen elsewhere. In this effort, multiple disciplines are integrated transcending the conventional disciplines to solve the social issues, and it is a new and attractive attempt in the practical education. The article is an extremely useful report in terms of social and education consequences.

However, looking at the first draft as a research paper, there are certain points lacking. First, I can understand the historical developments that led to the establishment of the Graduate School of SDM, but I cannot see what exactly the authors of the paper did in that process. I understand that the university itself took action to create this new school (or some preparatory organization), but I would like to know what the authors specifically did, such as designing and building the SDM as a whole, or some practical activities such as "5.2 Evaluation by the students" or "5.3.3 Collaboration with business world and overseas institutions". I also think the points that are stated in this paper should be organized and discussed.

To convert this into a *Synthesiology* research paper, (1) first clarify what the authors did in establishing the Graduate School of SDM, and (2) complete the paper by describing the research objective of this study; the scenario; the selection, synthesis, and integration of the elements; and the evaluation of results and future developments (as written in the "Instruction").

To be considered as a research paper, the following development may be taken.

[Example 1] Thinking with emphasis on the synthesis method of the new Graduate School of SDM where multiple disciplines are integrated (in this case, the authors must play central roles in the establishment of the graduate school).

1. Research objective: "To develop the synthesis method for the newly established Graduate School of SDM" etc.
2. Scenario: By discussing the synthetic method for the conventional graduate school of SDM and SDM science, describe the scenario for the construction of true SDM science and education through future curriculum revisions.
3. Selection of the elements and their synthesis and integration: Describe why the multiple disciplines (elements) needed for SDM science in establishing the Graduate School of SDM were selected, and how they were integrated as a whole.
4. Evaluation of the result and future development: Based on the above decisions, investigate whether the concept of education and research of the Graduate School of SDM for "looking at both the trees and the forest" was thoroughly achieved. If the initial goal was not achieved, suggest improvements to achieve the goals. If the goal was achieved, consider the points that will lead to further advancement.

[Example 2] Thinking with emphasis on the verification of the principles and practice of the Graduate School of SDM (In this case, the authors must play central roles in the verification and evaluation.)

Comments and Questions (Motoyuki Akamatsu, Human Technology Research Institute, AIST)

The draft gives an impression that it is an article introducing the graduate school, and the point as a thesis is not clear. Please clarify the points that you wish to communicate in terms of synthesiology, delete the parts that are unrelated to enable the readers to get to the point.

As a *Synthesiology* paper, please describe the overall effort as a scenario rather than merely listing the facts. You should describe how the whole process of curriculum creation, actual education, the effect of the education at the Graduate School of SDM was conducted with what kind of objectives or intentions, and how it was realized. Moreover, what did you think the students acquired upon seeing the actual results produced by the students? I think you can provide useful information to the readers if you state such objectives, facts, and your interpretations.

Answer (Naohiko Kohtake)

Ohkami is the proponent of the Graduate School of SDM, and had engaged in international surveys and preparations for about 10 years prior to the establishment of the School. Maeno and Nishimura are faculty members since its establishment. Maeno is in charge of the overall concept of the Graduate School of SDM and the education and research curriculum for the social skill courses, while Nishimura plays a central role in building the education and research curriculum for the technological courses. Finally, Kohtake was involved before its opening from the standpoint of industry, and became a faculty member one year after its opening. In this study, he works on the interactive courses, the international collaboration, the analysis and verification of the education results, and the discussions for the Graduate School of SDM.

To write this article as a research paper, we rewrote it according to the guideline shown in [Example 1], and the research objective, scenario, selection of elements and their synthesis and integration, evaluation of the results, and future developments were described. The newly drawn Fig. 1 represents the scenario, and the relationship between our effort and society was explained by clarifying the relationship with the stakeholders. Also, how the scenario was realized, what kind of results has been produced, what are the issues that must be solved in the future, and their interpretations are described. The presentation of the paper was substantially changed.

2 Title and subtitle

Comments and questions (Motoyuki Akamatsu)

The main title of the draft is “Graduate school education for ‘system design and management science’ transcending the disciplines”, but I think it is lacking as a title for a “synthesiology” paper. I think SDM itself is “synthesiology”, and creating the education system is “synthesiology”. Therefore, please consider a title that clearly expresses that it is a “synthesiology” paper from both perspectives, such as using the title “Graduate school education for…” with the subtitle “Developing leaders who can construct and operate large-scale complex systems”.

Answer (Naohiko Kohtake)

Thank you for your suggestion. We changed the title and the subtitle as follows to present the specific content of the paper:

> Graduate education for multi-disciplinary system design and management- Developing leaders of large-scale complex systems -

3 Objectives and points of the SDM curriculum

Comment and question (Motoyuki Akamatsu)

You wrote that you set the abilities listed from A) to C) as abilities to be acquired in response to the expectations for universities and graduate schools in Table 1, but please explain these points. Also, there is a matrix of abilities and courses in Table 2, but please state what are the points in having the students effectively acquire SDM science such as in the selection of the curriculum, points emphasized in the courses, and selection of the educational materials.

Answer (Naohiko Kohtake)

There were unclear points and redundancies in the relationships of Table 1, the list described in Items A) to C) of section 4.1, as well as in Table 2, so the relationships were clarified and revisions were made to the relationship of the abilities and knowledge the students should acquire. The abilities and knowledge the students should acquire corresponds to A) to F) of chapter 3 of the revised paper. These were determined based on the findings obtained from the interviews to more than 100 companies conducted before the opening of the Graduate School of SDM, as well as the data from the Education Issues Committee of the Nippon Keidanren described in Table 1.

We also revised the matrix of the abilities and courses in Table 2 to explain the thinking behind the curriculum setting, and the points and mechanisms of the course. A specific explanation was described in section 3.1, with particular emphasis on required subjects. The recommended subjects and the elective subjects were added in Table 3.

4 Educational method for learning SDM

Comments and questions (Motoyuki Akamatsu)

You mention the lectures, ALPS, and SDM research as ways of learning, but for synthetic research, please organize what can/cannot be learned in lectures, what can/cannot be learned in ALPS, and what can/cannot be learned in SDM research. It will also be beneficial if you address to what extent SDM can be learned through education, and what are the limits of education.

Answer (Naohiko Kohtake)

The basic set-up is to learn the theories in the lectures, to design a system in a team of about five to eight people in a set period in ALPS using the knowledge and methods learned in the lectures, and then each student engages in individual research. However, even in lectures, we emphasize interactivity where the thinking and methods are actually learned through hands-on experience. We encourage the students to attend lectures as needed during the ALPS and the research. Also, the students can invite lecturers to learn more theories, and therefore the courses are mutually supplementary. The students enhance their individual specialties through the process of research.

Since the majority of the students have business experiences, they bring their research topics from their real life experiences to the Graduate School of SDM. Therefore, it is not possible to capture every single aspect of the systems at the Graduate School of SDM. However, the faculty members and the students already have diverse specialties, and are capable of teaching their specialized knowledge to each other in the form of “semi-student semi-teacher (way in which the position of teacher and student are not set, but they learn from and teach each other)”. We believe essentially any subject can be handled using this method.

However, since the level of specialty and consciousness differ by student, we do think that what the students learn about SDM depends on the individual student’s strength of the consciousness of the problem, breadth of vision, and ability to take action. We are aware that this is an issue. Therefore, we wrote in section 4.5 as follows.

“We feel that all students are capable of learning the basic thinking and method needed to solve the problems of large-scale complex systems to a certain level through required subjects. On the other hand, to be able to utilize the thinking and method in society and industry, it may be necessary to take courses other than the required ones at the Graduate School of SDM as well as at other universities and graduate schools, and the students themselves must apply them in their research and work. The effectiveness of the education depends largely on the students’ strength of the consciousness for the problem, breadth of vision, and their ability to take action. Although it is difficult to solve all these issues through graduate school education only, we feel many issues can be solved by the close collaboration between the Graduate School of SDM and society and industry, the individual guidance to students by the instructors, and the further promotion of various exchanges among students composed of diverse human resources.”

5 Fusion of humanities and sciences; international collaboration

Comments and questions (Motoyuki Akamatsu)

There are many activities listed as the efforts of the Graduate School of SDM. I think the readers will better understand if you offer specific explanations on, for example, what is learned through human resource exchange transcending the framework of sciences and humanities, or what is the relationship between international collaboration and systems design education.

Answer (Naohiko Kohtake)

○What is learned through human resource exchange transcending the framework of sciences and humanities?

The real society is a place where sciences and humanities are fused. To design the technological or social systems, the knowledge and experience in diverse fields such as economics, political science, and engineering are necessary. Therefore, we believe the significance of the human resource exchange transcending the framework of sciences and humanities at the Graduate School of SDM is that it is possible to learn in a structure similar to the real society.

In fact, in ALPS, which is required by all first-year master's students, we take care that the teams will have diverse people not only of humanities and sciences, but also in nationality, business experience, age, and gender. The students are expected to solve a specific issue utilizing the difference in language, difference in way of thinking, and difference in specialty.

Specifically, the description in section 4.2 was revised and expanded, and specific example was given.

○What is the relationship between international collaboration and systems design education?

Using specific case studies, the descriptions in sections 4.1 to 4.4 were revised and expanded to explain the results of our efforts to present. Particularly, we explained the abilities and knowledge acquired by the students and the idea created, by presenting the activity of a team participating in ALPS.

Products and evaluation device of cosmetics for UV protection

— AIST commercialization based on regional collaboration that combines the current strategic logic, and an intermediary's experience and trial-and-error approach —

Yasumasa Takao*[1] and Mutsuo Sando[2]

[Translation from *Synthesiology*, Vol.3, No.2, p.127-136 (2010)]

We introduce a case study of UV-protective cosmetic product development. Recently, cosmetics need to solve 3 problems simultaneously: 1) UV-protective effect, 2) transparence, and 3) smooth-textured touch. However, the best recipe and usable evaluation methods are not established. This research is the result of a strategic regional cooperation of the AIST grant venture and the technical guidance that did not set a prior scenario with immediate effect of the national research institute. A new manufacturing and evaluation method has been commercialized in the forms of a highly original cosmetics and a new evaluation device. An example of the methodology is shown concerning social elements (regional cooperation), particularly. The example is illustrated by comparing 2 elements. The first is the R&D methodology that the *Synthesiology* journal advocates (the Aufheben type, breakthrough type and strategic selection type). The second is the humanities way of thinking by analogy with natural phenomena such as the evolutionary theory.

Keywords : Ceramic composite particles, UV-protective cosmetic, shearing evaluation of powder-bed, apparatus engineering, Agency of Industrial Science and Technology, AIST grant venture

1 Background of research: Issues and problems of the "UV-protective cosmetics"

The objective of this paper is to present a case study for an R&D methodology that combines a strategic scenario and the empirical trial-and-error, taking the ceramic powder technology as an example (Fig. 1).

For today's cosmetics, the technological element that is most desired is to block off the harmful ultraviolet (UV) rays, in addition to transparency and good texture. As shown in Fig. 2(a), when nanoparticles, which consist of particles of several 10 nm size for light scattering effect and titania with band gap effect for blocking the UV-B, are added to the cosmetic ceramic particles for UV protection, uneven nanoparticle aggregations occur among the ceramic particles. The nanoparticles must be added excessively to achieve the desired UV protection, and the resultant aggregate particles shield the visible light and therefore decrease transparency, and produce high friction or decrease smoothness of the texture. Yet, the UV protection effect will be insufficient when the amount of nanoparticles is decreased to prevent the decline in transparency and texture, and we are faced with a dilemma[1][2].

Therefore, in this study, we propose the composite particle[1] and the least-square (LS) approximation model[2] as the AIST-style strategic approach[3]-[7] to solve the "technological elements" of UV protection, transparency, and texture. The AIST-style strategic approach is the development and collaboration method based on short-term contract that clearly states the expected result and responsibility. The detailed scenario is described in chapter 2, and the synthesis methodology is discussed in chapter 3.

For the "social elements" including the specific idea suggestions for materials and manufacture methods, as well as the adjustments of differences in organizational interests, we propose the regional cooperation in the style of the Agency of Industrial Science and Technology[1][2], or trial-and-error based on experience (Fig. 1(b)).

The powder material for cosmetics and the evaluation device were commercialized[14]-[21], through the application of core technology for the ceramic powder unit operation[1], the establishment of evaluation technology by AIST grant venture[2], and the long-term cooperation where short-term organizational interests are temporarily suspended[8]-[13] (chapter 4). We shall investigate the process of solving the social elements as an R&D methodology by referencing the recent comparative researches[3]-[8] or the analogies to the natural phenomena[22]-[29] (chapter 5).

2 Scenario for solution

2.1 Scenario for solving the technological elements

To achieve (1) UV protection, (2) transparency, and (3) good texture in cosmetics, it is mandatory to establish a manufacturing method where the three technological elements (1) high UV blocking, (2) high visible light

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transmissivity, and (3) high lubriciousness can be achieved at the same time[1][2]. Especially, the only evaluation of lubriciousness for (3) good texture is the qualitative sensitivity test conducted mainly by questionnaire survey, as shown in Fig. 3(a). It is necessary to immediately standardize the evaluation test and device, and then provide a guideline for the powder design that may improve the lubriciousness[2].

In this study, we focused on the point that the nanoparticle segregation had never been considered in the design and mixing processes of the current cosmetics, and the most prevalent method was the simple mechanical mixing. As shown in Fig. 4, the composite particle method was created as the core technology by combining the particle packing model (solid phase method), the homogenous dispersion of nanoparticles in aquatic environment (liquid phase method), and the rapid solidification of droplets (gas phase method)[1][2][14]-[21]. The details of the synthetic methodology are discussed in chapter 3.

For the lubriciousness evaluation, we looked at the difficulty of stabilizing the sample packing density to the tools and the low reproducibility of the side-grinding force, that is, it was difficult to set the consolidation condition. As the core technology that enables evaluation in a short time and at small amounts, we devised a LS approximation model of the normal force and side-grinding force. As shown in Fig. 5(a), the powder was compacted until the packing density stabilized in the conventional method, and except for certain powder unit operation such as the silo, this evaluation method

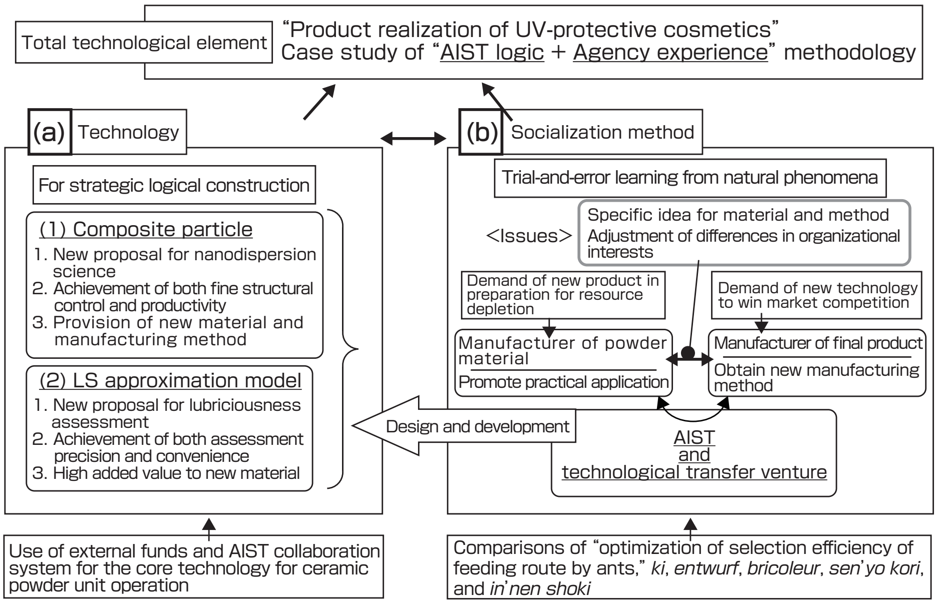

Fig. 1 Structure of the paper: Technological and social solutions to overcome the "valley of death"
(a) Solution for technological elements (logical and strategic scenario for using the powder technology)
(b) Solution for social elements (regional collaboration in the style of technical assistance during the Agency period where quick-acting scenario was not set)

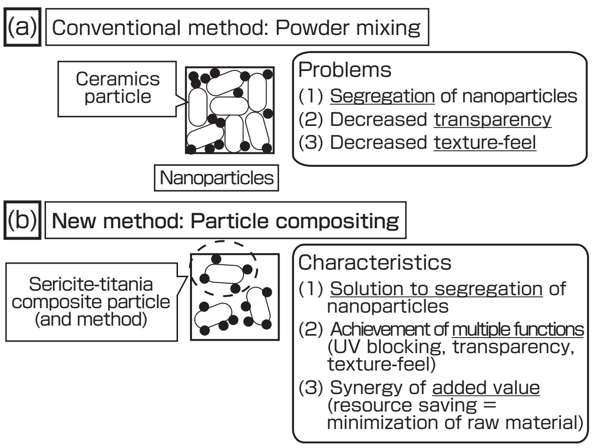

Fig. 2 Issues and problems of UV-protective cosmetics (technological point of this study)

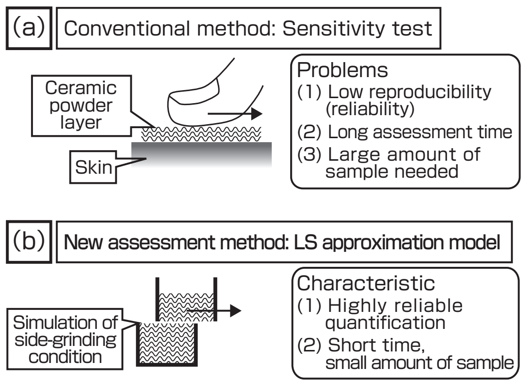

Fig. 3 Issues and problems in the texture-feel of cosmetics (technological point of this study – part 2)

did not reflect the actual ceramic manufacturing process. As shown in Fig. 5(b), the problem of consolidation condition setting in the new model was solved by continuously monitoring the normal and side-grinding forces in the transition state[1][2][14]-[21]. The details of the methodology are discussed in chapter 3.

2.2 Scenario for solving the social elements

The solution for the social elements such as the adjustment of conflicting organizational interests or the originality of idea was necessary. Before the 1990s, industry-government collaborations were conducted particularly in the regional laboratories as supportive measures that prioritized the practical application and commercialization, parallel to the R&D of science and technology[1][2]. This was followed by the practice of logical and strategic measures to build the win-win relationship between the companies and AIST based on the wide research foundation and trusting relationships[3]-[7].

As shown in Fig. 1(b), in this research, we faced the social issue of adjusting the differences in the interests of the organizations, and the realization of the development policy for the material and manufacturing method in the situation where the material manufacturer wanted a new product in preparation of resource depletion[15], and the product manufacturer wanted new technology quickly to win the market competition[17].

The solution for the social elements selected in this research is shown in Fig. 6. This shows the basic research of the ceramic powder unit operation and the history of the use of external funds and alliance system, starting with the Government Industrial Research Institute, Nagoya. The central part is the chronology, the upper part shows the material development, and the lower part shows the history of the evaluation device. Starting from the technical assistance for adding higher value to the regional specialty products in the 1990s, the pilot plant for powder synthesis was constructed using external budget in 2003, a public venture was started for the lubriciousness evaluation in 2005, a loose regional cooperation that did not require a contract was formed in 2007, and the powder material and evaluation device were realized in 2010[1][2][14]-[21]. The details of the synthesis methodology are described in chapter 3.

The following methodologies for solving the social elements were published in *Synthesiology* last year: (1) the aufheben type where a new concept is created by temporarily "sublating" the two contradicting propositions, (2) breakthrough type which is a unique "growth" model of the core technology, and (3) the strategic selection type which is an investigation of a hypothesis by a "logical" scenario[5]. This research can be considered a case where (1) aufheben thinking was applied to the social elements, in the sense that the decision for short-term organizational interests was temporarily suspended or postponed, although we were unaware of that when we were actually engaging in the research.

3 Solution (synthetic methodology)

3.1 Logical and strategic solution of the technological elements

< Ceramic powder material for cosmetics >

As shown in Fig. 4, the condition at which the nanoparticles do not segregate among the mica particles when the cosmetics is in its final form, that is, ceramic compact mixed with other ingredients such as polymers, was calculated using the DLVO

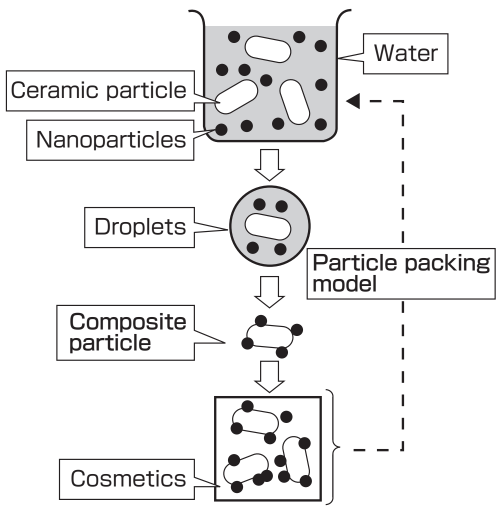

Fig. 4 Technological solution: New manufacturing method - Composite particle method with controllability and cost adjustments

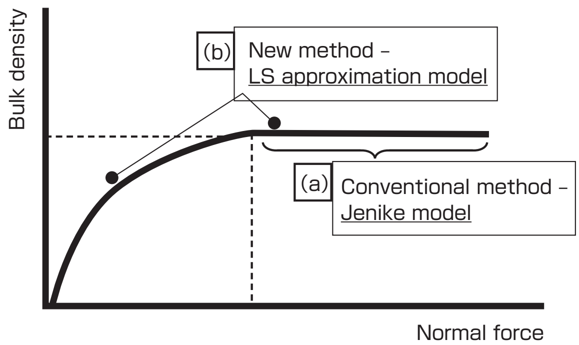

Fig. 5 Technological solution: New manufacturing method - Least-square approximation model for normal and side-grinding forces

(a) Conventional method – Jenike method: Corresponds to static friction, reproduces the consolidation condition in the hopper.

(b) New method – LS approximation model: Dynamic and static frictions are covered. Non-steady (dynamic friction) condition in the consolidation process can be quantified, as this was not possible in the conventional method, and has the following characteristics: (1) reproduces the condition in which the powder materials are actually used, and (2) has high cost performance with small amount of sample and short time.

theory (liquid phase method) for the aquatic scattering of nanoparticles and the particle packing model (solid phase method). The result was reflected in the starting composition of the raw material powder[1][21].

Figure 7 shows the structural control process of the powder including the composite particle. The slurry, which is a mixture of sericite[15] and nanoparticles, is sprayed (gas phase method), and the slurry is broken down into droplets that contain only a single or several units of sericite and nanoparticles. The droplets are continuously dried or reacted, and the composite particles (Fig. 7(a)) or granules are synthesized where the nanoparticles adhere only to the surface of the ceramic unit particle[1][2][14]-[21]. Figure 7(b)~(d) will be discussed in chapter 4.

< Evaluation device for the property of ceramic powder >

As shown in Fig. 5(a), the current lubriciousness evaluation technology requires excessive preliminary consolidation, or a state of high bulk density, to resolve the low reproducibility of the side-grinding force due to the instability of the packing density of the powder into the measuring container. This condition is not applicable to the general ceramic powder materials such as cosmetics and electronic fillers, except for some powder unit operation where over-packing may occur as in the case of the hopper[2][14][16].

Figure 8 shows the LS approximation model. As shown in Fig. 8(a)~(b), the normal and the side-grinding forces are measured sequentially from 0, whereas in the conventional method, the samples are changed for each condition from packing to consolidation. Next, the gradient, or the angle of internal friction, is calculated using the LS approximation of the normal and side-grinding forces assuming the clone powder (Fig. 8(c)). Compared to the conventional mathematical envelop approximation shown in Fig. 5(a), the new model shown in Fig. 5(b) enables the evaluation of the relationship of the normal and side-grinding forces in wider range from transition to compacting state, and it is a simple evaluation method that reflects the general ceramics process. Currently, this method is applied to the JIS standard powder as well as the materials for cosmetics, fillers, drugs, and foods, to guarantee the reproducibility and reliability as a powder evaluation method, and to confirm the adequacy as a quality control technology[1][2][14]-[21].

3.2 Empirical and trial-and-error solution of the social elements

< Basic regional industry-government alliance (former technical assistance system) >

As shown in Fig. 6, the joint work with the local mica company[15] in the form of technical assistance that suspended the short-term organizational profit was started to add high value to the specialty product (natural minerals) of Aichi Prefecture during the days of the Agency of Industrial Science and Technology in the 1990s, before the Agency became an independent administrative agency. In that process, crises in the alliance were experienced several times

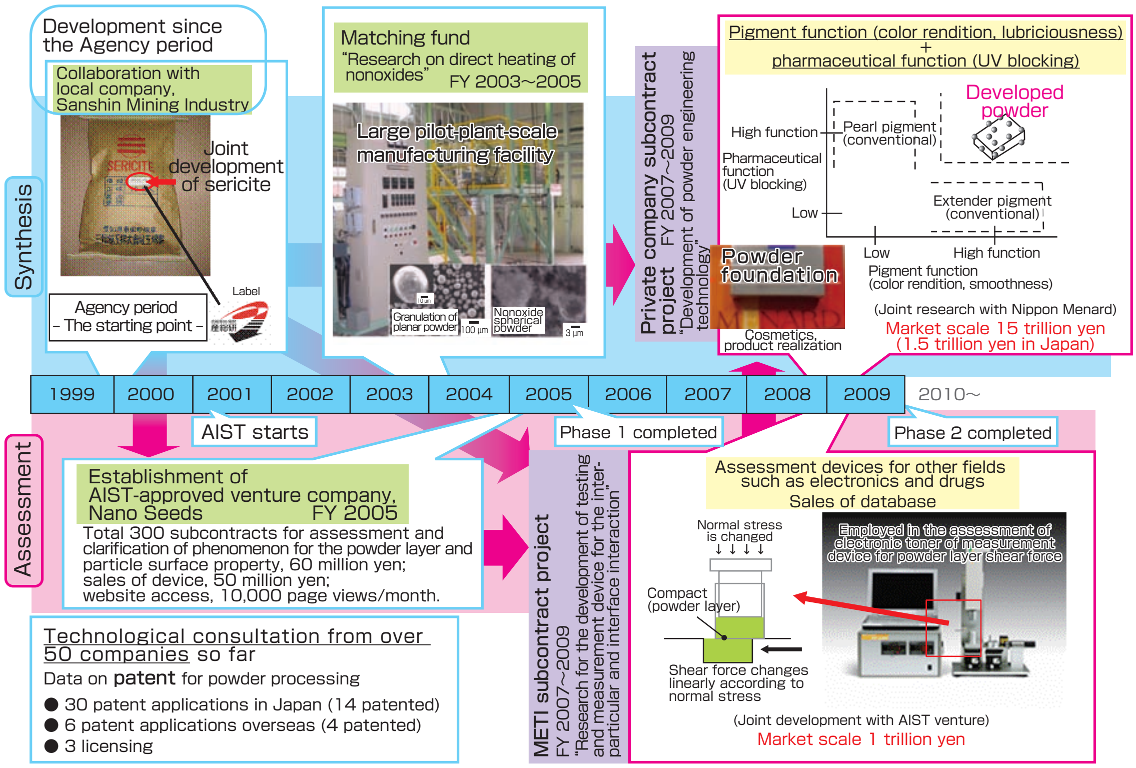

Fig. 6 Research roadmap: The chronology of the solutions for the social issues in this research

due to the different objectives of the organizations, but as a result, a trusting relationship was established for the core research of ceramic powder, including the new composite particles and morphological control[2].

< Plans for product realization of the powder materials >
While certain advancements were obtained for the ceramic powder unit operation at the level of *Type 1 Basic Research*[6][7], we were unable to realize the actual product or the implementation contract for the UV-protective cosmetics, and failed to achieve the level of *Type 2 Basic Research*. Neither the local material company[15] nor the product manufacturer[17] had much experience in signing an implementation contract. They also were hampered by intra-company barriers such as the inability to fund the project at the start, as well as the psychological barrier of whether or not to place emphasis on highly reproducible synthesis condition. From such differences in the objectives of the organizations, a crisis occurred in the collaboration and the project fell into the valley of death[3]-[7].

In general, the social elements such as the adjustment of organizational interests may not be necessarily solved by the inductive method of logic and strategy. The necessity of economic methods (such as the LCC, environmental risk science, and Pigovian tax) that internalize the technological external diseconomy is proposed, including increasing the number of elements, complicating the relationship, or temporarily suspending the project[8]-[13]. The adequacy of the synthetic methodology is discussed in chapter 5.

Based on this thinking, in 2002, we constructed a loose information provision relationship with the manufacturer by temporarily “sublating[5]” or suspending AIST’s immediate profit and system, such as the implementation contract, as shown in Fig. 1(b). Using this cooperative relationship,

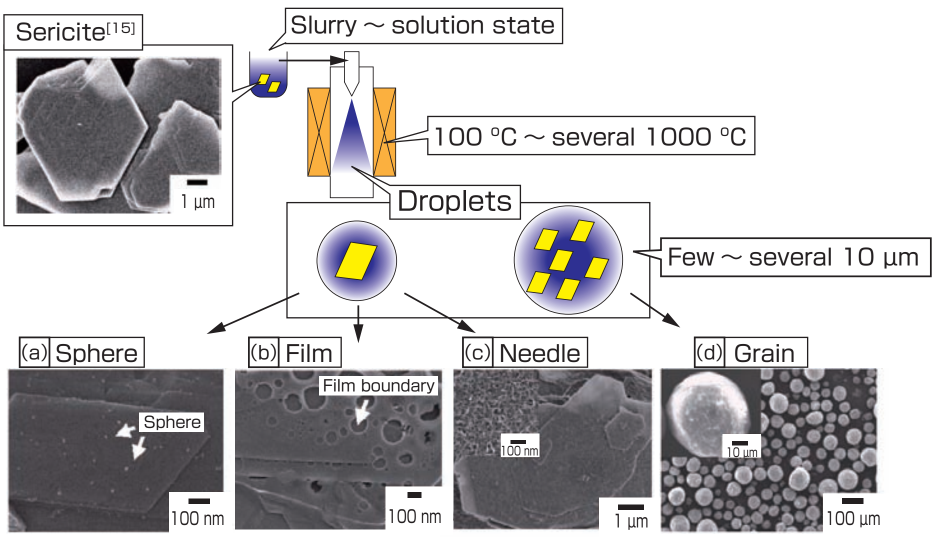

Fig. 7 Technological result: Variations in morphological control
(a) Sphere-coated composite particle: Spherical titania nanoparticles are composited evenly onto the mica surface.
(b) Film-coated composite particle: Titania film is composited evenly on the mica surface. To show the film clearly, the FESEC photo shows the area where the film has flaked off.
(c) Needle-coated composite particle: Needle-shaped titania particles are composited evenly on the mica surface.
(d) Solid mica grain: It is also possible to create hollow structure and solid/hollow titania grains.

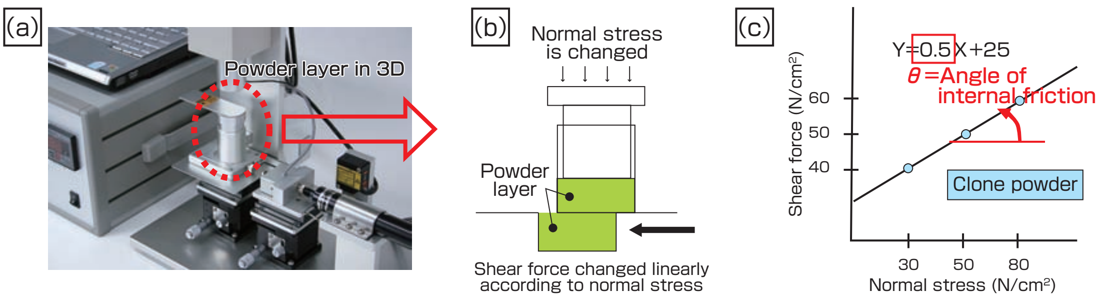

Fig. 8 Technological solution: Establishment of a simple quantification method for the angle of internal friction
(a) Central part of the assessment device that was realized as a product by the AIST-approved venture.
(b) Schematic diagram of the new least-square approximation mode.
(c) Assessment parameter: angle of internal friction

we extracted the issues such as the specific materials that do not violate the Japanese Standards of Cosmetic Ingredients (JSDI) to achieve the *Type 2 Basic Research* level. Next, the powder synthesis pilot plant was constructed at actual production level in 2003 using external budgets, and the technological element of section 3.1 was solved before the aforementioned social issues. After signing a research subcontract in 2007 with the material and product manufacturers, the relationships were adjusted for the product realization of the powder material scheduled for FY 2010[1][2][14]-[21].

< Product realization plan of powder property evaluation device >
Starting from the aforementioned material development, advancement in *Type 1 Basic Research* such as the idea for simple lubriciousness evaluation was obtained[2]. However, this was insufficient as *Type 2 Basic Research* that may provide quality control technology to other ceramic manufacturing and the design guideline for the material powder that provides high lubriciousness to the UV-protective cosmetics.

In general, the evaluation technology, like the JIS and ISO standards, should be in the form of a platform with multiple channels to pursue universality, such as subcontracting by evaluation organizations, rather than exclusive use as in the material product that demands originality and scarcity. Historically, the organizational format such as a company is like a lottery collected every time before maritime voyage, and the risk is equivalent to a modern space exploration[12]. In the current challenging social situation, the public venture theory has been developed as a way to buffer such risks[6][7].

Therefore, as shown in Fig. 6, using the AIST technology licensing organization system, we created a public venture[16] in 2005 to subcontract the lubriciousness evaluation and the development of the evaluation device. With this company as a window to the market, evaluation subcontracts were obtained routinely from several companies, and the product realization issues, such as obtaining the evaluation parameters lacking in the quality control technology, were clarified to achieve the *Type 2 Basic Research* level. As a result, among the technological elements described in section 3.1 including (1) high UV protection, (2) high visible light transmissivity, and (3) high lubriciousness, we were able to provide the design guideline to improve the lubriciousness of the material powder. At the same time, the accomplished fact that this was an evaluation method for the material design at the product realization level increased the social reliability of the evaluation device, and resulted in the adjustment of relationship where the device could be marketed widely and the orders for the device development be encouraged in the FY 2010[1][2][14]-[21].

4 Research result and discussion

4.1 Ordered mixture to resolve the nanoparticle segregation and the achievement of both UV protection and visible light transmissivity

The results of controlling the inter-particle segregation of the nanoparticles and synthesizing the composite particle (ordered mixture) where the nanoparticles are adsorbed only onto the surface of sericite[15], the cosmetic ceramic unit, are shown in the transmission electron microscope image in Fig. 9(a) and as the energy dispersive X-ray spectrometry map in Fig. 9(b)~(c). The spherical nanoparticles adhere finely and evenly on the surface of the planar sericite on both the top and edge faces of the cuboid. The nanoparticles are observed only on the unit surface, and the segregation between the particles is controlled[1].

Figures 7(a)~(c) show the results where the coating of the composite particles are morphologically controlled, and Fig. 7(d) shows the mica grains. The composite particle was created by depositing the titania on the surface of the ceramic unit particle in (a) particulate form, (b) film (the photograph shows the broken section of the film to present a clear view), and (c) needle form. The nanoparticles can be also coated in controlled uneven state on the top or edge facet only of the planar ceramic unit particle[1][2][14]-[21].

Figure 7(d) shows the solid grain of the ceramic unit (mica) particle. Other than these, different planar ceramic unit

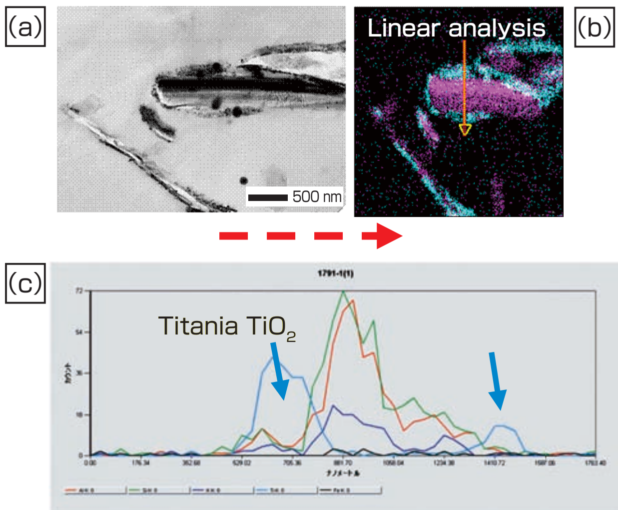

Fig. 9 Technological result: Realization of the "ordered mixture" state (resolved the issue nanoparticle segregation)
(a) TEM image: There is no titania nanoparticle that separated from the mica (embedded grinding).
(b) WDS surface analysis result: The planar particle in the center is mica, and the surrounding spherical particles are titania.
(c) EDS linear analysis result: Titania nanoparticles are composited evenly around the mica.

(boron nitride), hollow or solid grain of titania nanoparticles, and swelling grain that can include and discharge water can be fabricated[1][21].

The above morphological control can be conducted by appropriate selection of the control elements in the solid, liquid, and gas phase methods described in chapters 2 and 3, such as the parallel use of static hetero-aggregation and homo-repulsion in the solution and the particle packing model[1][2][14]-[21].

Figure 10 shows the result of achieving both the UV protection and transparency as material characteristics. In the current product shown in Fig. 10(b), the light transmissivity does not decrease in the UV range of about 400 nm or less. Not only is the blocking of UV insufficient, but also the transmissivity drops exceedingly in the visible light range of 400 nm or over, and this decreases the transparency. On the other hand, in the product developed by the composite particle method in Fig. 10(a), the decrease in low transmissivity of the UV range to achieve high blocking capability and the decrease in transmissivity in the visible light range were controlled to achieve the high transparency as shown in Fig. 10(c)[1]. For the three issues of cosmetics - (1) UV protection, (2) transparency, and (3) texture - the (1) high blocking of UV only and (2) high visible light transmissivity were achieved. One of the reasons for realizing the specific blocking of the UV range only was because the controllability of color tone improved due to the prevention of segregation between the planar ceramic unit particle (sericite) of nanoparticles, and the particles could be arranged with "controlled anisotropy" on the top or edge of the surface of the material particle[21].

4.2 Quantification of lubriciousness and good texture-feel achieved simultaneously

Figure 11 shows the graph of the normal and side-grinding forces evaluated by the LS approximation model shown in Fig. 5 and 8, for the (3) high lubriciousness, the remaining technological element of the UV-protective cosmetics. The current product shown in Fig. 11(b) has poor texture-feel due to the increased gradient of the normal and side-grinding forces, or the angle of internal friction, compared to the raw material unit shown in Fig. 11(c). In the developed product in Fig. 11(a), the internal friction angle is reduced to achieve high lubriciousness or good texture-feel.

One of the reasons for good texture-feel was the realization of the extremely small amount of sericite and nanoparticles used due to the controlled segregation of nanoparticles among the sericite, as they were deposited only on the surface of the material powder.

The effect of controlling the excessive use of the material corresponds to the reduction or resource-saving of 3R (reduce, reuse, and recycle), and presents the contribution to the mission of the Materials Research Institute for Sustainable Development: "to promote innovation and effective use of resource for the development of materials that enable sustainable development"[1][2][14]-[21].

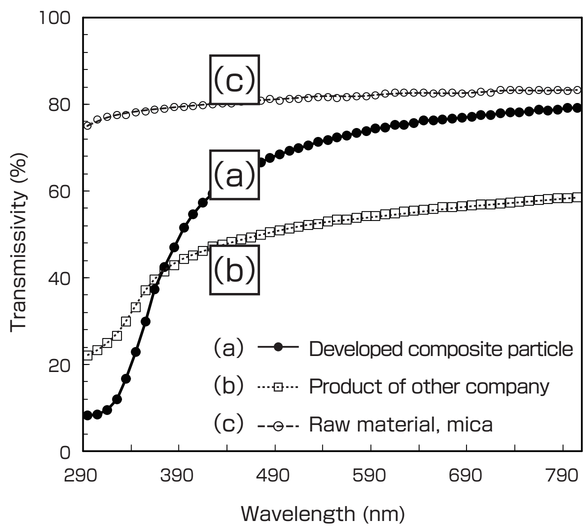

Fig. 10 Technological result: Achievement of both UV protection and visible light transmissivity

(a) Developed composite particle: Corresponds to static friction and reproduces the consolidation state in the hopper (ideal condition).
(b) Product of other company: UV protectiveness increases but transmissivity (transparency) decreases due to the aggregation of nanoparticles, and the face may look "powdery".
(c) Raw material mica powder: Transmissivity of visible light (transparency) is high but has no UV protection function.

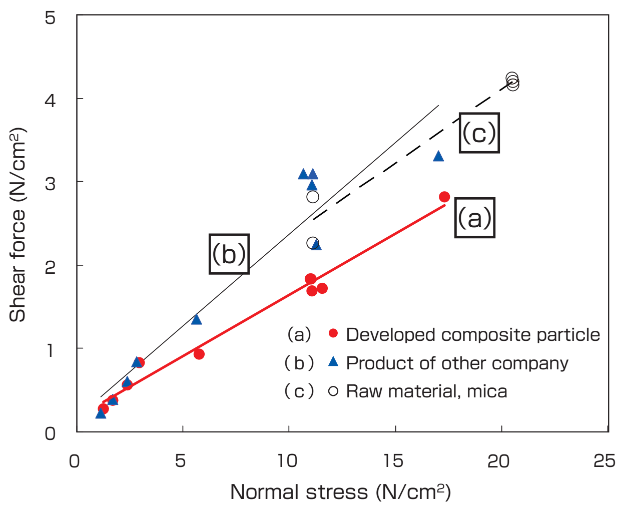

Fig. 11 Technological result: In addition to the optical property (Fig. 10), quantifications of lubriciousness and good texture-feel (skin-touch) are both achieved

(a) Developed composite particle: Angle of internal friction is minimum value.
(b) Product of other company: UV protection function increases, but lubriciousness or texture-feel decreases due to nanoparticle aggregation, and angle of internal friction increases.
(c) Angle of internal friction of the mica particle (median of the two composites).

4.3 Example of specific product

As an example of the product of the synthesis and evaluation research, (a) the cosmetic material product, (b) the evaluation device product, and (c) the public venture[16] are shown in Fig. 12(a)~(c). As discussed in section 3.2, the researches for synthesis (material) and evaluation (device) were not delineated in the preliminary scenario, to enable flexible use of any usable core technologies. As a result, the composite particle method of the material synthesis research guaranteed the wide applicability of the evaluation device, and the evaluation device research contributed to the increased function of the powder material.

The above synergy effect promoted the solution of the mutual technological elements, increased the competitiveness of the social elements, and resulted in the marketing of cosmetics with the “AIST product used” label and the evaluation device by the venture[1][2][14]-[21].

5 Verification of the R&D methodology through the analogy to natural phenomenon and summary

5.1 Verification of empirical and trial-and-error solution of the social elements

The solution of the social elements of this research will be reviewed, and the adequacy of the decision to temporarily suspend the organizational objectives and rules of AIST will be discussed.

Fig. 12 Technological and sociological result: Example of the product

(a) Material (synthesized) product: The developed powder was realized as a product by a local company[15][17] . Patent implementation contract and placement of “AIST research result used” label on the product provide high marketing value.

(b) Method (assessment) product: New assessment method was realized as an assessment device by an AIST-approved venture.

(c) AIST-approved venture[16]

Unlike the technological elements where the unification of the goal is relatively easily done as in improving the property or seeking novelty, the social elements such as the adjustment of organizational interests may not be solved by the inductive method of logic and strategy alone[8]-[13].

As methodologies for solution, *Synthesiology* states (a) the aufheben type, (b) the breakthrough type, and (c) the strategic selection type[5]. These are mainly discussed as measures to solve the technological elements. In this paper, as stated in section 2.2, the idea presented there[5] was applied to the social element in the sense that the decision of the short-term organizational profit was temporarily suspended.

Recently, the R&D methodologies include the thinking of the flow from *Type 1 Basic Research* (observation), *Synthesiology* (factual knowledge), then to *Type 2 Basic Research* (design), using the ideas of humanities such as the continuous and sustained evolution of Popper and Saussure or the cyclic hypothesis verification model[6][7]. The analogy with the natural phenomena such as the theory of evolution[3]-[7] indicates that the optimization at individual level does not necessarily lead to optimization of the whole, hence the synthesis error, as similarly reported in the adjustment of inter-organizational interests[8]-[13].

For example, the neutral theory by Motoo Kimura is a concept that dissects the natural phenomena into plant and animal individuals (logical subject) and environment (empirical object) by refining the theory of evolution, that mutations do not occur only through natural selection but also by trial-and-error at the DNA level[29]. In the selection of feeding route of ants, it is reported that the feeding efficiency of the group is higher in the presence of individuals with low feeding capacity than in a group consisting only of highly capable ants, because the probability of finding a new route increases[23][24]. The competitive society as reported[8]-[13] tends to fall into a decision-making bias where a one-way logical and strategic inductive method is only employed, and there is a heuristic cognitive tendency of becoming a red ocean on a shoestring operation that cannot survive unless it is always involved in some new activity[22][25][29]. The study of historical demography shows that there were four cycles of population increase and decrease in 10,000 years, and in the period of population decline or the period of maturation of the civilization, the concept of *sanpo yoshi* (good for three parties) or *senyo kori* (clients may go ahead and use the product, seek benefit from the product, and then pay for it afterwards) as exemplified by the ways of companies such as Toyama Medicine and Office Glico become prevalent[25]-[28]. The thinking of expanding the target range of logic to unknown clients rather than sitting on a unique logic of cause-effect can be seen in the *ki* (opportunity) of *budo* or martial arts, and *engi* (dependent arising) and *sekishu onjo* (the sound of one hand clapping) of Zen Buddhism, and *bricoleur* (do-ityourself man) of Claude Lévi-Strauss (Fig. 1(b))[11][13].

That local optimization does not equal overall optimization (synthesis error) is an assumption in the natural phenomena such as evolution. Therefore, the aforementioned analogies[3]-[7] are thought to include the solutions of the social elements where the short-term organizational interest is suspended as a cradle of the seeds for next-generation technology in the modern society, which at least is in the maturation stage. This study can be positioned as the segmentation of the aforementioned methodologies[3]-[13] into technological elements (logic and strategy of section 3.1) and social elements (suspension of short-term interest in section 3.2), as in the neutrality in the theory of evolution.

5.2 Summary and future development

This study can be categorized as an aufheben type[5] as stated by *Synthesiology*, and the logical and strategic scenario method using powder technology to solve the technological element was combined with the regional cooperation efforts in the form of technical assistance to solve the social element, although no quick-acting scenario was set. As a result, we succeeded in the development of the cosmetics using sericite[15], a regional brand product, as well as the sales of evaluation device through the public venture. Later, these led to the implementation contract and the practical application of the basic research through the "AIST research result used" product label.

Current issues are the overcoming of the valley of death upon reaching the product realization after R&D, and the market competition with the existing products, known as the Darwin's sea, for wider business development of the technology and product[3]-[7]. Since multiple manufacturing processes are combined in the composite particle method, the unit price of the product increases due to increased processes. Its use becomes limited to high-function cosmetics, and its use in general-use product with larger market scale becomes difficult. The LS approximation method is technically complex, and is not sufficiently recognized as a simple ceramic quality control technology. Although the development period was limited, we must reflect on the fact that the functional development of the materials and the consideration of cost versus effect of the manufacturing and evaluation methods were insufficient.

In the future, we shall promote the wider use of the product through expansion of morphological control case studies for high-control manufacturing method, pioneer new function and use, clarify the scientific aspects of evaluation parameters, and establish the database and JIS. We shall also emphasize the "reduce" aspect of 3R, utilize the trusting relationship nurtured through the adjustment of interests through regional cooperation, and seek ways to uphold the mission of the Materials Research Institute for Sustainable Development: "to promote innovation and effective use of resource for the development of materials that enable sustainable development".

6 Acknowledgements

I am grateful to Iwao Asai, Senior Research, Sanshin Mining Industry Co., Ltd., who has been working on the development of sericite for 10 years; Yasuhiro Shimada, President, Nano Seeds Corporation, who started up the company while a post-doc at AIST; and Hiroshi Asano, Chief Researcher, Nippon Menard Cosmetic Co., Ltd. that developed the product with "AIST research result used" label; and the guidance of all people involved.

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Discussions with Reviewers

1 Technological elements and social elements

Comment (Toshimi Shimizu, Research Coordinator, AIST)

In the first draft, in categorizing the synthesis method of the technological elements, the discussion is a mixture of the so-called "technological elements" and the "social background and social elements" such as the budget allocation and support system. I think you should categorize the synthetic method by focusing on the technological elements only.

Comment (Kazuo Igarashi, Measurement Solution Research Center, AIST(current affiliation: Institute of National Colleges of Technology, Japan))

In the first draft, you write in the beginning, "We propose a method that combines the composite particle method and least-square approximation model, and the AIST-style strategic scenario and the regional collaboration of the Agency period". However in the conclusion, you state, "We reproduced the aufheben style". You must clearly describe what is the specific proposal.

Answer (Yasumasa Takao)

To clearly separate the technological elements (logical and strategic scenario) and the social elements (empirical trial-and-error), we revised the structure of the paper after the introduction and the figures of the revised draft. Also, the solution was to combine the logical strategic scenario using the powder technology as the solution for the technological element, and the technical assistance style regional collaboration of the Agency period, where no quick-acting scenario was set, as the solution of the social elements.

2 UV blocking

Question (Toshimi Shimizu)

The objective of this research is to achieve both the transparency and texture-feel of the cosmetic powder by developing a new compositing technology for the UV-blocking nanoparticles and cosmetic ceramics. However, the text states the achievement of all three issues including UV-blocking, transparency, and texture. Since UV blocking is a default for cosmetics, I think there are two issues, the achievement of transparency and texture. What is your reason for setting UV blocking as a distinctive issue?

Answer (Yasumasa Takao)

As you indicated, it is not necessary to list UV blocking because it will be consequently obtained by using the nanoparticles. Since currently there is no technology to arrange the nanoparticles appropriately on the surface of the particle, the nanoparticles must be restrained excessively to achieve both transparency and texture, and as a result, UV blocking function may be lost.

3 Issues of technological elements

Comment (Toshimi Shimizu)

In the first draft, you write that the issues of technological element are "UV blocking", "transparency", and "texture-feel". These terminologies are perceptive and non-technological expressions. From the perspective of basic physical properties, I recommend they be, for example, reworded as "high UV blocking property", "high transmissivity of visible light", and "high lubriciousness".

Answer (Yasumasa Takao)

As you indicated, I made revisions to use the appropriate terms that express the physical properties.

4 Relationship between lubriciousness evaluation device and technological issues

Question (Toshimi Shimizu)

I understand that you first developed the evaluation device for lubriciousness to qualitatively assess the texture-feel. However, you did not describe how you overcame the technological issues by setting what kind of manufacturing condition as technological issues to obtain good texture-feel, or in another word, high lubriciousness, for the UV nanoparticle-ceramics composite material. Does it mean you solved this technological problem simply by trial-and-error? I cannot quite follow the logic of how the good texture-feel was achieved by developing the evaluation device.

Answer (Yasumasa Takao)

One of the reasons for good texture-feel is the effect achieved by controlling the segregation of nanoparticles between the sericite and arranging them only on the material particle surface, and as a result, minimizing the use of sericite and nanoparticles. This point was added to the text.

5 Three types of synthesis method in *Synthesiology*

Question (Kazuo Igarashi)

In the first draft, you cite the three types of synthesis method described in *Synthesiology*, 1(2), 139-143 (2008) (*Synthesiology* English edition 1(2), 131-137 (2008)). When you are comparing them to the case reported in this paper, what exactly are you comparing? Also, you mention the integration type technological and social solutions, but what does this mean?

Answer (Yasumasa Takao)

As the methodology for solving the social elements, *Synthesiology* proposes three types of methods: (1) aufheben type, where two contradicting proposals are temporarily "sublated" to create a new concept, (2) breakthrough type, which is the unique growth model of the core technology, and (3) strategic selection type, which is the investigation of hypothesis through a logical scenario. This research can be considered a case where the (1) aufheben type idea is applied to the social elements in the sense that the short-term organizational interests are temporarily sublated or suspended.

6 Social solution

Question (Kazuo Igarashi)

Please describe what you mean when you say that the social solution will increase the product competitiveness by a combination of regional brand and original manufacturing method.

Answer (Yasumasa Takao)

The researches of synthesis (material) and evaluation (device) were not set in the preliminary scenario, to enable flexible use of the usable core technology. As a result, the composite particle from the synthesis research guaranteed the wide applicability of the evaluation device, and therefore, the device research contributed in achieving the higher function of the powder material. In another word, the researches for synthesis and evaluation contributed to the mutual solution of the technological elements and to the increased competitiveness of the social elements.

7 Feeding route selection by ants

Comment (Kazuo Igarashi)

In the first draft, you mention the "feeding route selection by ants" as a comparison to the natural phenomenon, and describe the similarity of the logical structure to that. However, the general reader does not know about the logical structure of the feeding route selection by ants. Moreover, I cannot see the relationship between the scenario of this paper and the advantage of enhancing the method by promoting the discovery of a new route.

Answer (Yasumasa Takao)

The important viewpoint of this paper is "the optimization of the individual may not necessarily be the optimization of the whole", and I added the description to clarify this point in the revised text.

Establishment of compact processes

— Integration of high-pressure micro-engineering and supercritical fluid —

Akira Suzuki*, Hajime Kawanami, Shin-ichiro Kawasaki and Kiyotaka Hatakeda

[Translation from *Synthesiology*, Vol.3, No.2, p.137-146 (2010)]

In order to realize sustainable development, it is anticipated that industrial structure, social and technical systems based on large-scale production at concentrated sites must be changed in the near future. Establishment of highly controllable compact processes with high-speed reaction is desired to realize distributed production with multi-purpose low-volume production. Integration of high-pressure microengineering and supercritical fluid has received considerable attention as a core technology for compact processes. To realize the technology, basic developments for high-pressure microengineering such as rapid heat exchange and precise temperature control were firstly needed, and then process developments on basic engineering followed. As applications of compact processes, organic synthesis under supercritical water is discussed, and inorganic synthesis and an innovative coating process using supercritical carbon dioxide are also described.

Keywords **:** Low-volume production at distributed sites, compact process, micro-reactor, supercritical fluid, rapid heat exchange

1 Background and objective of the research

The large-scale production at concentrated sites that forms the core of the chemical industry has significantly raised the modern living standard, and brought great wealth in the latter half of the 20th century. By using this method, the product cost was decreased dramatically, and excellent products became reasonably available to many people. In general, the production cost is said to increase approximately at the power of 0.6 of the production volume. According to this rule of scale-up, the production cost for 1,000 yen/kg will become 10 yen/kg at a production scale 100,000 times greater ($10^{5\times0.6} \div 10^5 = 10^{-2}$). The dramatic economic impact of the large-scale production at concentrated sites lead to the expansion (scaling up) of production scale in various fields. However, this system assumes the one-directional use of a large amount of fossil resources, it is extremely difficult to create a material cycling system since it is difficult to balance the recovery and reuse. On the flip side to mass-production, there were the issues of mass consumption (depletion) of fossil resource, immense energy consumption due to the global transportation of fossil resource, and generation of substantial wastewater and waste products. These are inducing various environmental problems such as global warming and organic pollutant contamination.

In order to realize sustainable development, it is anticipated that industrial structure, social and technical systems based on large-scale production at concentrated sites dependent on fossil resources must be changed in the near future. Specifically, it is essential to create a safe, flexible, and efficient process with low environmental load, where cycling of resource and energy can be done easily, and the use of recyclable resources such as the biomass should be set at the core. This means the realization of distributed production with multi-purpose low-volume production. To achieve this, establishment of highly controllable compact processes with high-speed reaction is desired. The compact process here means a safe, flexible, and efficient process with low environmental load, where the cycling of resource and energy can be done easily. It also must have high-speed and highly controllable performance, enabling low-volume production at distributed sites.

The microreactor is gaining attention as the core technology of the low-volume distributed production due to its compactness and the precise controllability of its reaction field[1]. In general, it is a device for conducting chemical reaction in a microspace of width from a few μm to a few hundred μm. It is categorized into the microreactor, micromixer, and micro heat exchanger according to its purpose and function. The microreactor has large surface area per unit volume (specific surface area), and therefore has extremely high heat exchange efficiency, and allows rapid temperature operation (heating and cooling) and precise temperature control. The large specific surface area of the reactor means that the reaction occurs at the interface efficiently. Also, since the micro flow channel has short diffusion distance, mixing by molecular diffusion occurs rapidly, and high-speed and efficient mixing takes place. These characteristics fulfill the conditions (high speed and high controllability) required in the compact process. However, the conventional microreactor is composed largely of materials that can be processed easily such as silicon, glass, and plastic, and cannot be used in high-temperature and/or high-pressure conditions, where the property of the

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microreactor can be taken advantage of more efficiently. Currently, the technology for a microreactor that can withstand high-temperature or high-pressure has not been established.

On the other hand, the supercritical fluid is defined as a fluid above its critical point (endpoint of saturated vapor pressure curve), and is called the fourth fluid that does not belong to the three phases of substance: solid, liquid, or gas. However, it is not very special, but is a non-condensible fluid that does not liquidize even when compressed to high density. The density of the supercritical fluid can be changed continuously and at great range from gas to liquid equivalent by changing the temperature and pressure, and the transport properties such as viscosity and diffusion coefficient, and solvent properties such as dielectric constant and ion product greatly change accordingly[2][3]. Particularly, the dielectric constant of the supercritical water, which is a state over its critical point (374 ºC, 22 MPa), is like an organic solvent, and is considered to be the only stable reaction solvent at high temperature. Also, the ion product can be increased to 10^{-10}, and the supercritical water is expected to take the role of acid or base catalyst. Such properties imply the application of the supercritical water in high-speed chemical reaction, and the technology using supercritical water is expected to become the core technology of the low-volume distributed production.

2 Integration of the microreactor and supercritical water

Until about 2002, the common knowledge was that in the chemical process using supercritical water or high-temperature and high-pressure water, the decomposition of organic compounds (by hydrolysis and pyrolysis) was possible, while synthesis was not[4]. In fact, although the acid and base properties, which were not present in regular water, were observed in the supercritical water from physicochemical or spectroscopic studies, the results always produced none or very low yield of the target substance when organic synthesis experiments under supercritical water

Table 1 Synthesis of ε-caprolactam using supercritical water (experiment result)
The yield was low in the batch reaction, but high yield was achieved in the continuous microreaction. Difference due to reaction time (including heating time) was significant.

Apparatus	Reaction temperature (°C)	Reaction pressure (MPa)	Reaction time (sec)	Yield (%)
Batch reaction	400	40	180	1.9
Continuous microreaction	400	40	0.625	83.0

condition were conducted using the batch reaction device[5]-[7]. From these results, the use of supercritical water in organic synthesis was thought to be extremely difficult, and the research for the application of supercritical water fell into stagnation (the valley of death) for a while. Research funds declined and we had no alternative but to continue to conduct reactions by self fabricating a lab-scale flow reactor using old pumps for liquid chromatography and used-up high-pressure tubes. Suddenly, we found that the yield increased. When we observed closely, we understood that the reason that the target product could not be obtained before was because the breakdown and side reactions of the raw material or the target product occurred in the heating range (cooling range) if long heating (or cooling) time was taken to achieve the reaction temperature, even though the reaction time at the reaction temperature was controlled carefully. From this moment, our research moved forward rapidly[8]. Figure 1 shows the conceptual diagram of the importance of the rapid heat exchange in this reaction. The example of the reaction that prologued the organic synthesis under supercritical water condition will be described below.

The synthesis of ε-caprolactam, a material for nylon, is conventionally done by the Beckmann rearrangement reaction of cyclohexanone oxime using concentrated sulfuric acid as an acid catalyst. However, in this synthesis, the concentrated sulfuric acid must be neutralized by ammonia, which generates large amount of ammonium sulfate, and its disposal is a major environmental and economic issue. We suggested a method of Beckmann rearrangement reaction using the acid catalyst property of the supercritical water[5][8]. The result of the

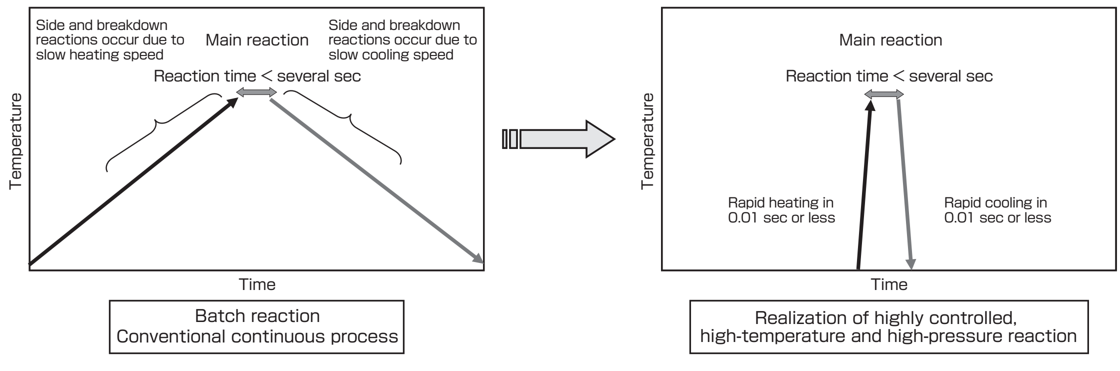

Fig. 1 Points in the development of organic synthesis using supercritical water (need of rapid heat exchange)
Since the supercritical water has high reactivity, side reactions and breakdown reactions occur and inhibit the main reaction if too much time is spent on heating or cooling. Rapid introduction and withdrawal from the reaction field is necessary.

experiment is shown in Table 1. The reaction conditions were the same at 400 °C and 40 MPa, but the yield was a few % in the batch process, while the yield increased dramatically to 80 % or more in the continuous microreaction. This difference was due to the reaction time (here, it is the time required to increase from room temperature to reaction temperature + retention time at reaction temperature). In the batch process, the heating speed was very slow, and cyclohexanone oxime was broken down to cyclohexanone in the heating process. In contrast, since the heating was done by mixing the supercritical water directly with the raw material in the continuous microreaction, the reaction temperature could be reached in an extremely short time, the Beckmann rearrangement became the predominant reaction, and the ε-caprolactam was synthesized at high yield. This showed that the effect could be achieved by combining the microreaction field and supercritical water, and would have not been achieved by each alone. This was a result of the integration of supercritical water and microreaction field in the organic synthesis reaction. Several experimental investigations were done on the ranges for high-temperature and high-pressure water below the critical point, in addition to supercritical water, and the possibilities of organic synthesis using water became realistic. The issues after this included the efficient realization of rapid introduction of raw material into the reaction field (rapid heating) and the rapid withdrawal of the product from the reaction field (rapid cooling).

3 Establishment of the high-temperature high-pressure microdevice and high-pressure microengineering

To achieve the rapid heat exchange (rapid heating and rapid cooling) discussed in the previous chapter, it was necessary to develop the direct heat exchange method employed for the ε-caprolactam synthesis or an extremely highly efficient indirect heat exchange method. In the direct heat exchange, heating to the target temperature is achieved by the direct mixing of the raw material at ordinary temperature and supercritical water, and cooling to the necessary temperature (where the reaction stops) is done by directly mixing the cooling water with the high-temperature and high-pressure reactants. The necessary temperature and mass flow of the supercritical water and the cooling water are determined by the heat balance calculation. The rate of heat exchange in the direct heat exchange is dependent on the performance of the mixer since it is determined by how the material and the supercritical water, or the high-temperature and high-pressure reactant and the cooling water are mixed to reach the equilibrium temperature. Therefore, the direct heat exchange method results in the development of the high-pressure micromixer capable of rapid mixing. On the other hand, to what extent rapid heat exchange is possible in the indirect heat exchange method will be explained later based on the heat transfer concept.

3.1 High-pressure micromixer (direct heat exchange method)

When the high-pressure micromixer is used as the heat exchange device for the supercritical water reaction, the turbulent condition with high Reynolds number can be readily applied since the supercritical water has 1/10 or smaller of viscosity coefficient compared to the ordinary temperature values, and high flow rate can be applied. In the micro device operation under the ordinary pressure condition, the flow rate must be kept low since the pressure drop cannot be large because of the reactor material (glass or plastic). However in the high-pressure micro device operation, high flow rate condition is possible since there is relatively greater allowance for pressure drop that occurs in the mixer. Therefore, the high-pressure micromixer employs the mixing method based on forced turbulence, and has different mixing method compared to the conventional micromixer where the dispersal is controlled by the laminar condition. The mixer structures include: the commercially available T-shaped mixer; swirl mixer that actively utilizes the swirl flow; and the central collision mixer where the two fluids collide in the mixing chamber. As examples of T-shaped mixers, Fig. 2 shows the standard type SS-100-3 (STD TEE) and low dead volume type SS-1F0-3GC (LDV TEE) of the Swagelok Company. Compared to the internal flow channel diameter of 1.3 mm of the STD TEE, the internal channel diameter of the LDV TEE is only 300 μm, and good mixing result based on large Reynolds number (turbulence effect) has been reported[9].

The CFD (computational fluid dynamics) simulation results of the two types of mixers are shown in Fig. 3 as the comparison and evaluation of the mixing performance. The calculation conditions were: pressure was constant at 30 MPa; supercritical water was supplied at 463 ºC, 33 g/min; raw material at 15 ºC, 12 g/min; and the temperature after mixing was 400 ºC. The property data of water at 30 MPa were used for the calculations. The Reynolds numbers of the STD (inside diameter of 1.3 mm) and LDV (inside diameter of 0.3 mm) at these conditions were 16,700 and 72,500, respectively. In Fig. 3, in the STD,

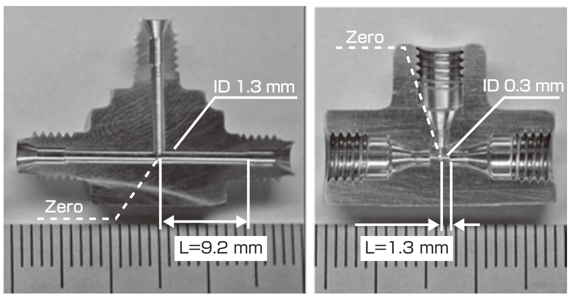

Fig. 2 T-shaped mixers (STD, LDV)
The commercially available 1/16 inch T-shaped mixer (left is the standard type, and right is the micro type of inside diameter 0.3 mm mixing flow channel).

the low-temperature fluid that flows in from the bottom part is mixed with the supercritical water that flows from the left, a temperature transition zone is formed at the bottom of the flow channel, and a temperature gradient forms within the flow channel. On the other hand, in the LDV, the homogeneous temperature fluid is formed in the micro flow channel with inside diameter of 300 μm and length of 1.3 mm, and quick fluid mixing is achieved. Figure 4 shows the plot of the maximum and minimum temperatures in the vertical cross sections from the center of the mixer to the downstream direction of the mixed fluid. It can be seen from the figure that the temperature difference is shown at the mixer exit in the STD (9.2 mm from the mixing point), while the temperature is homogenized rapidly at the mixer exit that is only 1.3 mm from the mixing point in the LDV. Estimating the average heating rate in the flow channel, the STD is 31,000 ºC/s while LDV is 270,000 ºC/s, and there is a 9 times difference. The difference in the heating rate, or the mixing rate, indicates that it is possible to precisely control the delicate synthesis reaction in which side reactions may occur.

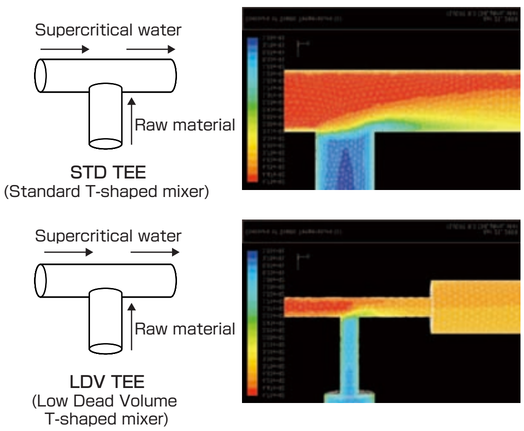

Fig. 3 Result of the CFD simulation of fluid mixing using the T-shaped mixer (temperature contour diagram)
In the STD TEE, the temperature was not even at the exit (length 9.2 mm from mixing point) of the mixer, while in the LDV TEE, mixing was almost entirely even at the exit (length 1.3 mm from mixing point) of the micro flow channel.

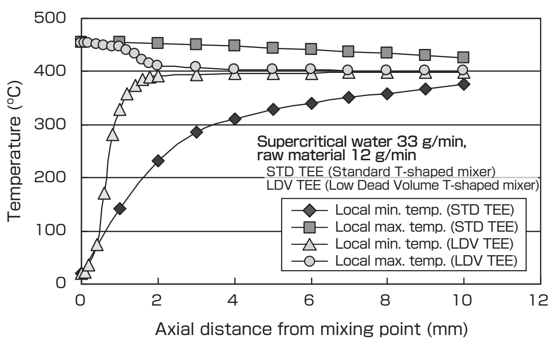

Fig. 4 Temperature profile of fluid after mixing
The temperature did not converge in the STD TEE, while it rapidly evened out in the LDV TEE.

Figure 5 shows the photograph of the micro swirl mixer that we developed and the result of the CFD simulations[10]. The raw material at ordinary temperature is supplied from the left, and supercritical water divided into two is supplied at 60° angle from the central axis. Further, the supercritical water is connected eccentrically and mutually from the center of the mixer, and the swirl flow can be generated by the divided supercritical water at the center of the mixer. The raw material is given the inertial force in the circumferential direction as well as the axial direction by the swirl flow, and it is considered to enhance the mixing performance. In the T-shaped mixer, a vortex is formed at the bend as the fluid makes a right angle turn. Since this vortex region may cause accumulation, the increase of unexpected retention time is a concern. On the other hand, in the micro swirl mixer, the accumulation region does not form in the center of the mixer since the mixed fluid is rotating and flowing out at all times. The central collision mixer shown in Fig. 6 is composed of the raw material supply channel with a needle that moves up and down in the upper part (the raw material is introduced through the thin film channel along the exterior surface of the needle) and the fluid mixing chamber with several supercritical water streams in the bottom part (central collision area), and is capable of realizing quick mixing and heating[11]. The raw material is not affected by the heat transfer from the supercritical water (due to the cooling effects by the cooling medium in the inner tube of the needle, the radiation effect by the air cooling fin, and the heat transfer limitations by a small metal seal ring), and is introduced into

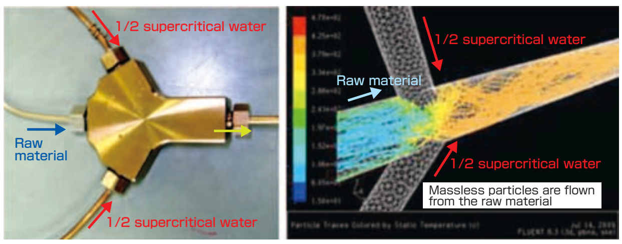

Fig. 5 Photograph of the micro swirl mixer and the result of the CFD simulation (flow line of raw material)
The supercritical water is mixed with the raw material by forming a swirl flow by dividing the supercritical water. The structure prevents the generation of vortex of the T-shaped mixing.

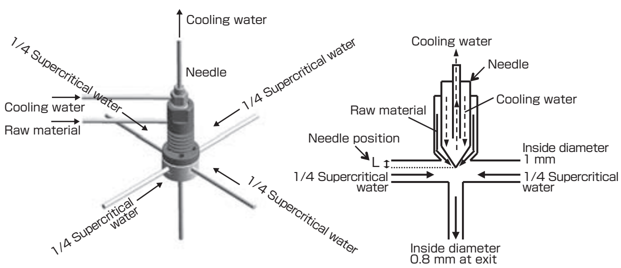

Fig. 6 Central collision mixer
The supercritical water is divided into four, and the raw material is introduced from the top into the central collision section. The needle is inserted from the top to allow adjustment of the mixing state.

the mixing field at almost the ordinary temperature without preheating. In this mixer, the needle length can be changed continuously in the fluid mixing section to control the mixing performance.

3.2 High-pressure micro heat exchanger (indirect heat exchange method)

The heat exchanger in the supercritical water reaction operation plays the role of a heater to achieve rapid temperature increase to reaction temperature, and as a cooler for rapid cooling to temperature range where the reaction stops. The high-pressure micro heat exchanger will basically use a high-pressure microtube from the perspective of pressure resistant design, and the inside of the tube will be used as the microspace. As mentioned earlier, since some degree of pressure drop is allowed in the supercritical water process, the mass flow can be set high. Therefore, the inside of the microtube will be in a severely turbulent condition (high Reynolds number), and extremely high values can be expected for the inside heat-transfer coefficient of the tube (heat receiving side, low temperature side). The issue will be how high the outside heat-transfer coefficient of the tube (heat giving side, high-temperature side) can be attained. In a general supercritical water manufacturing equipment, the convection and radiation heat transfers from the electric nichrome wire furnace are used as heating source. However, the outside heat-transfer coefficient of the tube, which is the rate at which the heat from the red-hot nichrome wire furnace transfers to the outer surface of the microtube, is extremely small, and that limits the overall rate of heat transfer (overall heat-transfer coefficient).

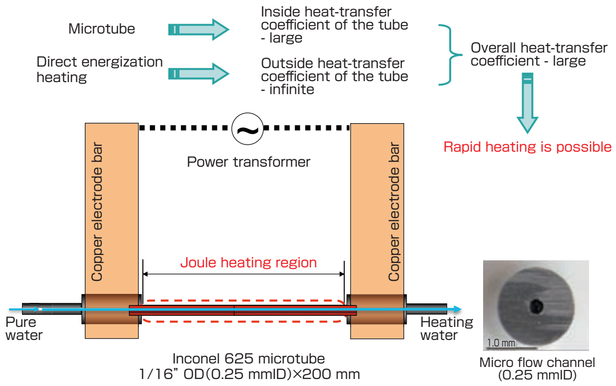

Fig. 7 Schematic diagram of the high-pressure microheater by direct energization heating
By using direct energization heating, the overall heat-transfer coefficient becomes extremely high.

We proposed a heating method for the high-pressure microheater where the joule heating is done by passing electricity through the microtube itself[12]. If this method can be employed, the outside heat-transfer coefficient of the tube can be considered apparently infinite, and the heat transfer can be determined by the metal heat transfer resistance and the inside heat-transfer coefficient of the tube. There are two methods to electrify the microtube: electromagnetic induction and direct energization method. In the electromagnetic induction method, it is necessary to install the induction coil on the exterior and is limiting in terms of downsizing, and therefore we selected the direct energization method. Figure 7 shows the schematic diagram of the high-pressure microheater using the direct energization method (tube dimensions: inside diameter of 0.25 mm, outside diameter of 1.6 mm, length of 200 mm), and Fig. 8 shows the evaluation results. The heat transfer property improved as the flow of supplied pure water increased, and this is because the inside heat-transfer coefficient of the tube increases due to the flow increase. The overall heat-transfer coefficient was maximum 10,000 $W/m^2 \cdot °C$ and the heat efficiency was 95 % or higher, and an extremely efficient heating was realized. Converting this into the rate of temperature increase, it will be maximum 150,000 °C/s. This shows that the water can be heated to critical temperature or above in a few milliseconds, and is a result that matches the temperature increase time by the direct mixing of supercritical water.

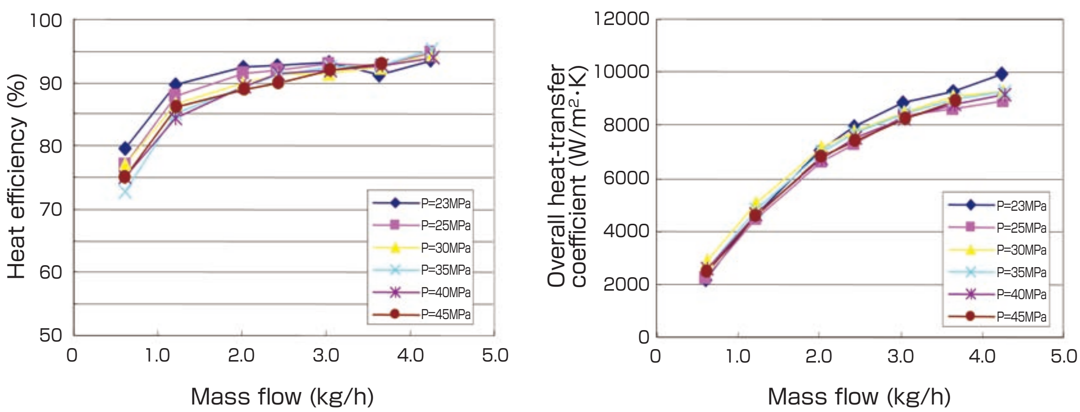

Fig. 8 Result of the evaluation of high-pressure microheater
Extremely efficient heating was achieved with maximum heat efficiency of 95 % and overall heat- transfer coefficient 10,000 $W/m^2 \cdot K$.

The description of the high-pressure microcooler will be omitted in this paper, but the high-pressure microcooler can be constructed easily by installing a cooling jacket outside the microtube. In the cooler, the outside heat-transfer coefficient of the tube can be raised by increasing the flow of cooling water. Also, during cooling, the temperature difference can be set larger than in heating, and therefore it is not difficult to achieve relatively large rate of heat transfer.

3.3 Numbering up strategy and the establishment of high-pressure microengineering

As an issue in realizing the microreactor, how to achieve the throughput increase is the major point. In the conventional chemical engineering, this is dealt by scaling up (such as increasing the size of the reaction container). In the microreactor, of course, such scaling up cannot be done because we want to utilize the advantage of being micro. Therefore, the parallelization approach (numbering up) is selected. However, an ordinary microreactor has small throughput per basic structure, and in many cases a realistic parallel number cannot be obtained. In contrast, since the high-pressure microreactor allows pressure drop to some degree, it has the advantage of raising the flow amount per basic structure. The high-pressure microheater described above can process maximum of 5 kg/h per microtube (inside diameter of 0.25 mm, outside diameter of 1.6 mm, length of 200 mm). Maintaining this high-pressure structure, the basic structure can be modularized (5 microtubes/module), and by parallelization of the module (4 modules/device), numbering up to 100 kg/h becomes possible. The concept of numbering up is shown in Fig. 9, and the photograph of the prototype numbering-up equipment is shown in Fig. 10. In this equipment, heating is done by direct energization method (12.5 kW/module × 4 modules), and cooling is done by circulating the cooling water in the jacket installed outside each module. As a result, we confirmed that the heat exchange performance

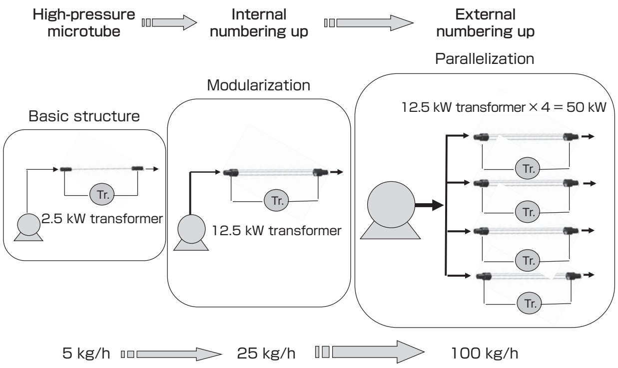

Fig. 9 Numbering up strategy
Throughput increase is accomplished by modularization of the basic structure and the parallelization of the module.

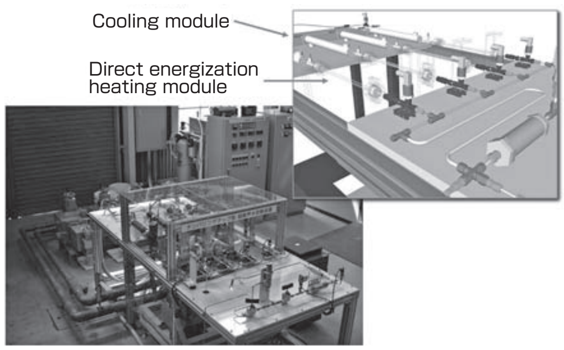

Fig. 10 100 kg/h class microreactor plant (parallel operation of four-module system)
The throughput was successfully increased while maintaining the heat exchange performance in single direct energization heating device.

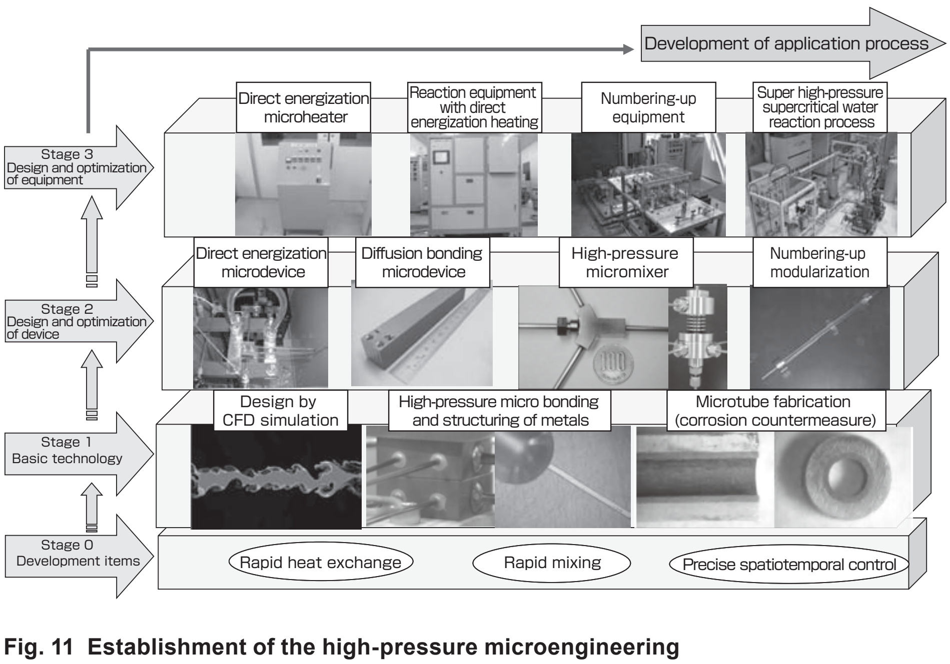

Fig. 11 Establishment of the high-pressure microengineering
From establishment of basic technology, configuration design and optimization of device and equipment, to the development of the application process.

was comparable to the basic structure, and verified that the exchange amount of heat equivalent to the substance production of several hundred tons/year could be carried out rapidly and stably through the compact process that could be installed in about 1 m × 2 m space. Comparing the capacity of the high-pressure microheater by direct energization heating used here with the conventional electric furnace heating method, the heat efficiency is estimated to be about 2 times, and the overall heat-transfer coefficient is 100 times or more. Since the difference of heat efficiency is directly related to the energy requirement, the energy cost will be one-half. Moreover, the difference of heat-transfer coefficient is thought to be almost proportional to the required heat transfer area, or the total length of the heating tube, and the heating tube will be 1/100 or less in length. As mentioned above, with 100 kg/h production capacity, the high-pressure microheater must have the total length of heating tube of 4 m (200 mm × 5 tubes/module × 4 modules/device = 4,000 mm), but the electric furnace heating method will require 400 m or more and the facility will grow large.

Figure 11 summarizes the processes of high-pressure microengineering including the items discussed above. Stage 0 (foundation) means the clarification of technical issues such as rapid heat exchange toward the integration of the microreactor technology and the supercritical fluid technology. To solve the issues, starting from the establishment of basic technologies such as micro structuring and micro bonding (Stage 1), moving on to configuration design and optimization of the high-pressure device such as mixers, and the various high-pressure equipments (Stage 2-3), we are working our way toward the developments for process applications.

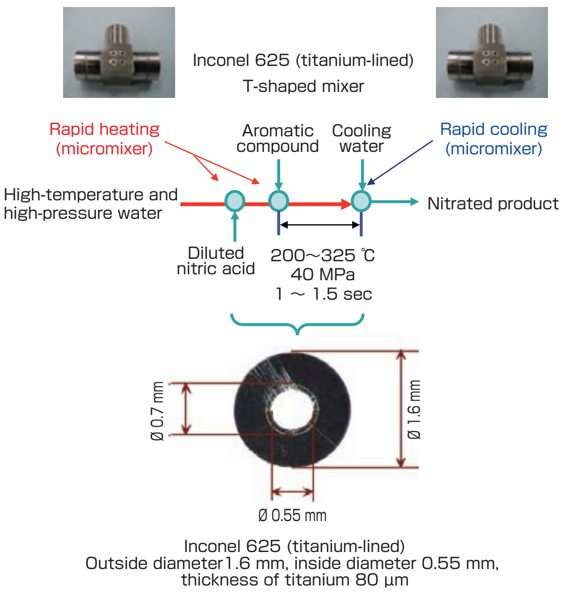

Fig. 12 Outline of non-catalyzed nitration apparatus under high-temperature high-pressure water

Inconel tubes and joints lined with titanium in the interior are used after introduction of nitric acid up to rapid cooling.

4 Establishment of the compact process through high-pressure microengineering

4.1 Organic synthesis process using supercritical water

The organic synthetic process using supercritical water and high-pressure and high-temperature water overturned the common knowledge that the supercritical water was inappropriate media as a organic synthesis field, as in the Beckmann rearrangement explained earlier, by realizing the rapid heating and cooling in the order of millisecond to microsecond by microengineering technology[8]. As another example, we describe the nitration of the aromatic derivatives. The most frequently used nitration in industry is the method using nitric-sulfuric acid, or the so called mixed acid. However, this production method has been used from the early 20th century without any change in methodology. The serial problems of the disposal of sulfuric acid waste as well as safety still remain, and the development of a new nitration technology with decreased waste has been awaited. To overcome the problems, we developed the new nitration without mixed acid by using the high-pressure and high-temperature microengineering technology, to generate nitronium ion or radical from diluted nitric acid in the high-pressure and high-temperature water. Even though the strong acids including nitric acid in high-pressure and high-temperature water create very corrosive conditions, we newly developed some microdevices, such as microtubes and joints made of titanium-lined inconel 625 and succeeded to operate these strong acids in high-temperature and high-pressure conditions using these devices. Using the high-pressure and high-temperature resistant titanium-lined devices, we conducted the nitration of aromatics, such as naphthalene, with nitric acid. The conceptual diagram of the apparatus is shown in Fig. 12, and the results are shown in Fig. 13. The reaction condition was 40 MPa and 200~325 °C. The nitration of naphthalene proceeded at 225 °C or above, and 91 % of the maximum yield of nitronaphthalene (1-nitronaphthalene 85 % and 2-nitronaphthalene 6 %) was achieved at 250 °C within only 1.3 sec reaction time. It was also found that hardly any highly explosive dinitronaphthalene and trinitronaphthalene were produced.

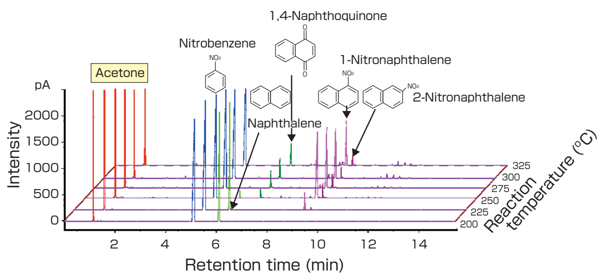

Fig. 13 Result of nitration experiment of naphthalene

Nitration progressed at 225 °C or over, and maximum yield of 91 % was achieved at 250 °C.

We further developed a process for conducting safer nitration using highly active acetyl nitrate as a nitration agent under the high-pressure conditions in microreactor for the precise reaction control of reaction time, reaction temperature and reaction point. In this method, the acetyl nitrate was generated instantly in the micromixer by exothermic reaction with acetic anhydride and nitric acid, while the mixing temperature was maintained at desired temperature of 40 ºC ± 0.2 ºC. The nitration of phenol was achieved of the yield of 96 % with the selectivity of almost 100 % at reaction temperature of 40 ºC and the reaction time of 1.8 sec. Since the reaction was conducted at low temperature of 40 ºC, corrosion of reaction system hardly occurred and as the unreacted acetyl nitrate in reaction residue easily hydrolyzed in water after the reaction, we can safely and easily handle these reactions outside of the system. This reaction system can realize efficient low temperature nitration in high-pressure condition, and can be applied to the various aromatic compounds having substituent groups, particularly for the nitration using medical and agrochemical intermediates. We also realized ultrafast and highly efficient organic reaction in water for piancol rearrangement, Claisen rearrangement, and estirification by our reaction methodology with precise control by rapid heating, and rapid cooling in high-pressure and high-temperature micromixer[13]-[15]. At present, we further achieved the high yield, high selectivity synthesis of useful compounds from sugars derived from biomass, such as 5-hydroxymethylfurfural for which physiological activity such as blood pressure decrease has been reported[16].

4.2 Metal oxide fine particle synthesis process using supercritical water

The supercritical hydrothermal synthesis is a method for obtaining fine nano-level particles by reducing the solubility of the metal oxides produced in the hydrolysis and dehydration reactions by heating the metal salt water solution rapidly to a supercritical state[17][18]. In the subcritical condition (200~300 ºC), the reaction rate of the hydrothermal synthesis is low, the dielectric constant of water is high at about 30, and the produced crystals tend to grow large. On the other hand, in the supercritical condition (representative condition is 400 ºC, 30 MPa), the reaction rate increases, the dielectric constant falls to a single digit, and the produced crystals do not grow. Therefore, the point of this method is how to increase the temperature rapidly to supercritical condition, and this rapid heating can be realized by the direct mixing of the metal salt water solution and the supercritical water. Figure 14 shows the particle size distribution of the product obtained by using different mixers for the synthesis of boehmite by supercritical hydrothermal synthesis using aluminum nitrate as raw material. The mixers used were 1/16 inch STD TEE described above, swirl mixer, and central collision mixer (adjustable needle of fluid channel space is applied). The reaction condition was 400 ºC, 30 MPa, and 2 sec. From the figure, both the swirl mixer and the central collision mixer produced microscopic particles and showed narrow distribution compared to the standard T-shaped mixer (STD TEE: flow channel diameter 1.3 mm). In the central collision mixer, the fluid mixing performance is higher when the needle position is L = 1 mm (see Fig. 6) with narrower flow channel clearance, and as a result, fine particles were synthesized by rapid mixing. The efficacy of this technology was shown in the synthesis of compound oxides as well as single oxides, and is expected to be applied in various usages such as fluorescent substances, ferromagnetic substances, transparent electrodes, cell electrode materials, and catalysts.

4.3 Innovative painting process by supercritical carbon dioxide

The total amount of volatile organic compounds (VOC) emitted from all industries in Japan is about 1.5 million tons (FY 2000), of which 33 % or 500,000 tons is the emission from the paint industry. The paint industry is the largest VOC emitter among all industries. The VOC is a cause substance of photochemical oxidants and suspended particulate matter, and their reduction is demanded immediately. We aimed to develop a painting method to significantly reduce the VOC emission by changing the thinner solvent (major VOC material) used abundantly in spray coating of conventional organic solvent paints, with extremely small amount of carbon dioxide, while maintaining the finish quality equivalent to the one achieved by organic solvent paints. The basic principle of this technology was developed as a new painting process[19] principally by the Union Carbide Corporation of the U.S.A., but in this process conventional static mixer was mainly used for mixing paint and carbon dioxide based on the fluid multi-stage segmentation theory, and quick mixing was difficult. For this reason, the paint

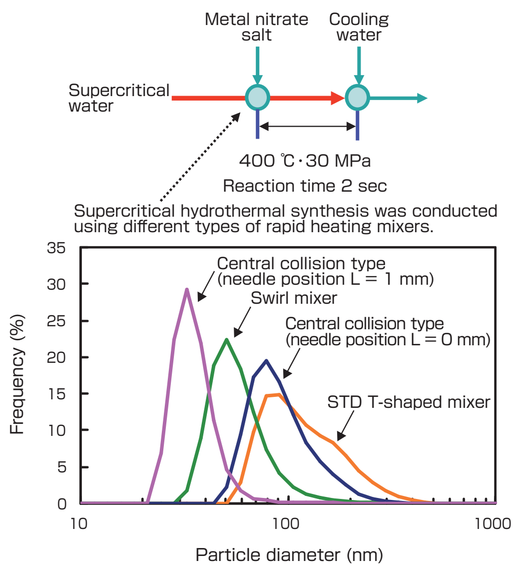

Fig. 14 Particle size distribution of the fine particles from Beohmite synthesis by the micromixer

Large difference in the particle size distribution can be seen depending on the type of the high-pressure micromixer (difference in quick mixing property).

that could be used was limited due to the problem of line clogging. In contrast, the carbon dioxide painting process that we developed uses the high-pressure micromixer based on the turbulence mixing theory, and enables extremely fast mixing and allows stable painting regardless of the type of paint. The conceptual flow diagram of the carbon dioxide painting technology is shown in Fig. 15. The paint and carbon dioxide are mixed instantly in the mixer, and the carbon dioxide dissolves completely in the paint. As a result, the viscosity decreases and spraying is enabled. The mixer was a version of the central collision micromixer modified for painting, and it was originally developed to realize the rapid heat exchange in the supercritical water reaction. As a result of evaluation by a third party of the painted sample using this method (mixer condition: 40 ºC, 10 MPa), it was confirmed that the paint film quality was of practical level[20]. Therefore, the VOC from the thinner solvent can be basically reduced, and seen from the amount of thinner solvent used currently (several hundred-thousand tons per year), the effect of reduction is thought to be significant.

5 Summary and future development

The organic and inorganic synthesis reactions using high-temperature and high-pressure water have the potential of greatly changing the conventional process of the large-scale production at concentrated sites. In this reaction field, an efficient and ideal substance synthesis is possible through rapid and precise temperature, pressure, and spatiotemporal control. As a result, fine chemical synthesis and creation of high value-added substance by natural product conversion in addition to bulk chemical synthesis is strongly expected.

For example, the ε-caprolactam that was described as the prologue in the organic synthesis using supercritical water is produced at about 100,000-ton scale per year per factory. It consumes the same amount of sulfuric acid and about half of ammonia, and discards about 1.5 times the amount of ammonium nitrate as waste product. If this is done as low-volume distributed production using the supercritical water organic synthesis of 10,000-ton scale per year, production is possible without using sulfuric acid or ammonia. Though further advancement in high-pressure microengineering is necessary to increase the processing amount at a basic unit (structure), to achieve this, a compact process of 10,000-ton scale per year can be realized.

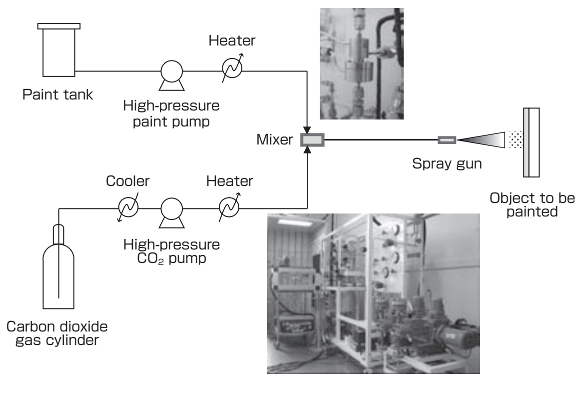

Fig. 15 Schematic diagram of carbon dioxide painting technology
Central collision type micromixer developed for painting was employed as the mixer.

On the other hand, the quick diffusion of carbon dioxide painting is demanded as the key technology for reducing VOC. The objective of this technology is not simply to reduce VOC, but also to save energy by reducing the energy for the drying process etc, and can be considered as the key technology in reducing carbon dioxide. The atomization using carbon dioxide can also be applied to wide ranging areas such as the technologies for painting, printing, adhesion, and application (film coating) of functional films, as well as particle technologies for drugs, polymers, and functional substances.

The establishment of high-pressure microengineering to realize the integration of the microreactor technology and the supercritical fluid technology will help to realize the low-volume distributed production (compact process) and contribute greatly to a sustainable society.

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Authors

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Completed the master's program at the Department of Chemical Engineering, Graduate School of Engineering, Tokyo Institute of Technology in March 1978. Doctor of Engineering in 1990 (Tokyo Institute of Technology). Joined a water treatment engineering company in April 1978. Engaged in the research and development for supercritical water oxidation process and succeeded in its practical application for the first time in the world. Joined AIST in April 2003. Has been working on R&D mainly for supercritical fluid engineering, and currently aims to establish a new process from the perspective of concert of supercritical technology and micro technology. In this paper, was involved in all aspects, but was particularly in charge of the establishment of high-pressure microengineering and the development of innovative painting device.

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Shin-ichiro Kawasaki

Completed the master's program at the Department of Mechanical Engineering, Graduate School of Science and Engineering, Kagoshima University in March 1996. Joined a water treatment engineering company in April 1996, and engaged in research for the practical application of supercritical water oxidation (SCWO) process for the complete decomposition of persistent hazardous waste (such as polychlorinated biphenyl and dioxin). Completed the doctorate program for Environmental Chemistry and Ecoengineering at the Graduate School of Environmental Studies, Tohoku University in March 2006. Doctor (Environmental Studies). Joined AIST in April 2006, and engages in engineering research for the technology of using supercritical water and supercritical carbon dioxide. Particularly specializes in the development of the micromixer, and studies the metal oxide fine particle synthesis by supercritical hydrothermal process as the core research for fluid mixing devices. In this paper, was in charge of the development of the micromixer and the development of the metal oxide fine particle synthesis using supercritical water.

Kiyotaka Hatakeda

Completed the doctorate program at the Graduate School of Environmental Studies, Tohoku University in March 2005. Doctor (Environmental Studies). Joined the National Industrial Arts Research Institute in 1966. Worked at the Government Industrial Research Institute, Tohoku, Tohoku National Industrial Research Institute, and then at AIST. Experimentally clarified the synthesis of ε-caprolactam that initiated the research of organic synthesis using supercritical water. In this paper, was essentially in charge of the continuous synthetic system of the nitro compounds under high-pressure and high-temperature water conditions.

Discussions with Reviewers

1 Overall

Comment (Koh Harada, AIST Tohoku)

Please explain why you used both words of “integration” and “concert” in the subtitle.

Answer (Akira Suzuki)

The subtitle “Integration and concert of high-pressure microengineering and supercritical fluid”, expresses the point that these integrations are not merely “1+1=2”, but the property of supercritical fluid may become 3 or 4 or anything by using microengineering. Recently, in the world of chemistry, the phrase, “concerted reaction field”, comes into use. The word “integration” does contain the element that it is more than simply getting together, and therefore to enhance the reader’s understanding, I deleted “concert”, and the subtitle shall be “Integration of high-pressure microengineering and supercritical fluid”.

Comment (Yoshiro Owadano, Research Coordinator, AIST)

For non-specialist readers, I think you should write clearly to which category the compact process described in this paper belongs:

1) Makes possible the synthesis that was conventionally impossible

2) Achieves lower environmental load or higher yield compared to the conventional method

If 2) is the case, please indicate as much as possible, what the volume of production (possibility) or rate of energy saving is in quantitative terms, or what are the figures set as the goal. For example, I think you should describe a more specific future image, such as what manufacturing method and in which industry this will be used in the sections, “Numbering up strategy” and “Future development”.

Answer (Akira Suzuki)

The compact process described in this paper is a high-speed, highly controllable process to convert the bulk chemicals that were produced conventionally by large-scale concentrated production to low-volume distributed production for producing the necessary amount at the necessary place. Therefore, it is not a process for synthesizing products that were conventionally impossible, but is a process that has low environmental load and realizes high yield compared to the conventional processes. In this paper, two reactions (Beckmann rearrangement and nitration) are given as examples of organic synthesis. While both reactions conventionally use concentrated sulfuric acid as the acid catalyst, in the compact process, high-temperature and high-pressure water plays the role of concentrated sulfuric acid, and it is now possible to establish a process that uses no catalyst (no sulfuric acid → low environmental load) and has high speed (microreaction → high yield).

To clarify the above discussion, we described the superiority of the micro heat exchange compared to the conventional technology in the “Numbering up strategy”. We described the possibility of increasing the production volume using the example of ε-caprolactam synthesis in the “Future development”.

Comment (Koh Harada)

I think that the phrase “compact process” used in this paper has a narrower meaning that is used specifically in the chemical industry, compared to the general usage. Please define what is the “compact process” for non-specialist readers.

Answer (Akira Suzuki)

In the text, we added: “The compact process here means a safe, flexible, and efficient process with low environmental load, where the cycling of resource and energy can be done easily. It also is high-speed and has highly controllable performance, and enables low-volume distributed production”.

2 Balance in establishing a circulating system

Question (Koh Harada)

In the discussion of “1 Background and objective of the research”, you state the “balance or recovery and reuse” are important. Is this a requirement to establish the circulating system?

Answer (Akira Suzuki)

In the large-scale concentrated production method, the amount handled is extremely high. Although reuse in other processes or at other plants may be done through the recovery of the byproduct or recycling of waste products produced in certain processes, I don’t think they provided realistic solutions due to the balance of supply and demand and the problem of transportation. The establishment of the circulating system was difficult in the large-scale concentrated production method.

3 Comparison with conventional method

Question (Koh Harada)

You would be better to mention about a comparison of your method with the conventional method at the beginning of the discussion of “2 Integration and concert of microreactor and supercritical water”.

Answer (Akira Suzuki)

The caprolactam synthesis by Beckmann rearrangement using concentrated sulfuric acid is a high-yield process of 98 %. On the other hand, the yield by high-temperature and high-pressure water described in Table 1 is 83 %, and is inferior in terms of numbers, but is superior in the fact that it does not use concentrated sulfuric acid at all. Here, to emphasize that the yield can be dramatically increased using supercritical water alone by precisely controlling the reaction time, we intentionally did not mention the yield of the conventional method.

4 Advantage of electromagnetic induction

Question (Koh Harada)

In “3.2 High-pressure micro heat exchanger”, what is the advantage of the electromagnetic induction method? It was written that it was not employed due to its size, but in what case would it be more advantageous?

Answer (Akira Suzuki)

Compared to direct energization application, the advantage of the electromagnetic induction may be that there is no need to take measures against electric leaks, and the heating intensity can be changed by how the induction coil is wound. Which is better is a case-by-case consideration, but I think for a microdevice, direct energization application is better because it does not require the induction coil.

Development of an accurate and cost-effective quantitative detection method for specific gene sequences

— Development of a quantitative detection method for specific gene sequences using fluorescence quenching phenomenon —

Naohiro Noda

[Translation from *Synthesiology*, Vol.3, No.2, p.147-157 (2010)]

DNA and RNA quantifications are essential in various fields such as biomedicine, agriculture, fishery, environment, and food. We have developed an accurate and cost-effective method for the quantification of specific nucleic acid sequences; the method involves the use of the fluorescent quenching phenomenon via an electron transfer between the dye and a guanine base at a particular position. This paper describes the elemental key technologies and their synthesis for the development of such a gene quantification method. Furthermore, based on the findings of a collaborative research project with a private company, we report the scenario for the industrialization and the practical use of the developed method.

Keywords : Gene quantification, fluorescence quenching, life science, fluorescent probe

1 Introduction

The genetic analysis technology is used in the wide-ranging socioeconomic activities including medicine, agriculture, fisheries, environment, and foods. Its use in clinical genetic testing is particularly increasing. Specifically, the test kits for hepatitis C virus and tuberculosis bacterium are already commercially available, and the genetic analysis technology is applied to hepatitis B virus, HIV, and sepsis pathogen. The venture businesses are beginning to provide subcontract service for genetic analysis for lifestyle-related diseases. In fields other than clinical tests, genetic analysis technology is used for DNA typing in the forensic investigation, detection of the food poisoning pathogens, quantification of the contents of genetically recombined foods, breed identification, as well as in bioterrorism countermeasures and environmental measurements. It is certain that the genetic analysis technology will be applied further, and the technology to detect and quantify certain genes is one of the most basic and important genetic analysis technologies.

There are eight items of quantitative analysis including the gene quantification technology: (1) specificity, (2) trueness, (3) precision, (4) detection limit, (5) linearity, (6) range, (7) robustness, and (8) commutability. Specificity is the ability to accurately measure only the molecule to be investigated amongst the coexisting similar molecules, and the point in nucleic acid detection is whether the target nucleic acid molecule and those with other sequences can be properly identified. Trueness is the degree of match between the measurement result and the true value of the measured subject. Precision is the degree of (smallness of) variations in the results when the measurements are repeated. Detection limit is the minimum amount by which the measured molecules can be detected, and the quantification limit means the minimum amount of measured molecule that can be quantified with sufficient trueness and precision. Linearity is the degree of the ability by which the measurement result and the amount of substance of the measured molecule within a certain range can be expressed as a linear relationship. Range is the upper and lower limits of the concentration of the measured molecule that give appropriate trueness, precision, and linearity. Robustness is the degree in which the measurement value is unaffected when the measurement condition shifts, and for example, in gene quantification, the inclusion of inhibitors may affect this factor. Commutability is the equivalence of the obtained measurement value, when the obtained value is compared with the one obtained by measuring the same sample using another (standard) method. Other than these indices for quantification, convenience of use, cost performance, throughput, and speed are important factors from the perspective of realizing the measurements. Considering the development of a practical gene quantification technology, the technology must have a certain level or higher of specificity, trueness, precision, and detection limit. Furthermore, for the technology to become diffused widely, it must have high robustness (accurate quantification must be possible even in the presence of inhibitors), be easy to use, and have excellent cost performance.

In the quantification of a specific gene, it must be kept in mind that the target gene within the sample may be extremely minute in amount. Therefore, to quantify a specific gene, it

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is necessary to amplify only the gene to be quantified among the various nucleic acid mixtures. There have been various methods developed for the amplification of the target gene, and the one most frequently used is the polymerase chain reaction (PCR) method. The PCR method was developed in 1984 by Kary Mullis, an American researcher who won the Nobel Prize in Chemistry. In this method, the target gene can be amplified exponentially using a simple method where the temperature is changed cyclically using reagents such as heat-resistant polymerase or short DNA fragments (primers) that act as the originators of the reaction. However, since the amount of the final amplified product by PCR does not necessarily reflect the amount of the target gene in the initial reaction solution, the amount of the initial target gene cannot be directly quantified from the amount of the final amplified product. Therefore, to quantify the target gene using PCR (quantitative PCR), it is necessary to find a way to measure the amount of the target gene in the initial reaction solution.

In the quantitative PCR, there are several methods with different measurement principles such as the real time[1], the competitive[2], and the most probable number (MPN)[3] methods. The real time PCR (RT-PCR) method is most commonly used. In the RT-PCR, the amount of amplified product is measured at each cycle of PCR, and the number of cycles required for the reaction product to reach a certain amount (or cycle of threshold: Ct) is calculated in the region where exponential amplification reaction is occurring. The relationship between the Ct and the amount of genes in the initial reaction solution is plotted to obtain the standard curve, and the amount of the target gene in the initial reaction solution can be calculated from this standard curve based on the Ct for the unknown sample.

In the RT-PCR, it is necessary to measure the amount of the amplified product at each cycle. The method used is to label and quantify the amount of amplified product with fluorescence. The major methods are the method using intercalator such as the SYBR Green[4] or the one using fluorescent probe such as the TaqMan probe[5]. SYBR Green is a special fluorescent dye (intercalator) that emits fluorescence when incorporated into the double-stranded DNA. When the SYBR Green is added to the PCR solution, the SYBR Green intercalates into the double-stranded DNA amplified by PCR and the fluorescence increases. The amount of PCR product can be measured by measuring the intensity of the fluorescence. This method allows using the same reagent for the target genes of any sequence, and it is used widely because of its low cost and convenience. On the other hand, since fluorescence increases with nonspecific amplified product such as primer dimer, there is a disadvantage that the fluorescence intensity and the amount of PCR product may not necessarily correspond. As shown in Fig. 1, the TaqMan probe method is a method using the TaqMan probe, in which one terminal of the oligonucleotide corresponding to the base sequence of the segment of the amplified region of the target gene is labeled with a reporter (fluorescent dye), and the other end is labeled with a quencher to turn off the fluorescence of the reporter. When the TaqMan probe is added to the PCR solution, the TaqMan probe that bonded to the amplified product is broken down by the elongation reaction by the 5’→3’ exonuclease activity of DNA polymerase. When the probe is broken down, the reporter fluorescent dye begins to emit its original fluorescence by separating from the quencher. The amount of PCR product can be measured by measuring the fluorescence intensity. Since the TaqMan probe bonds specifically only to the amplified product, it is not affected by any nonspecific amplified product such as the primer dimer, and allows highly specific quantification. While this method is widely used, it requires labeling by two fluorescent dyes.

RT-PCR has advantages that it can measure the amount of target gene in a short period (30 min to 2 h), and there is very little contamination of the laboratory with the PCR product since gel electrophoresis is unnecessary. It also has excellent trueness and precision. Also, the detection limit is low due to gene amplification, and the measurement range reaches 10^5~10^8 copies. However, it has the following disadvantages: 1) since it is necessary to measure the fluorescence per cycle of PCR to measure the amount of the amplified product, it is necessary to install an expensive RT-PCR device that embodies the fluorescence measurement device and the PCR thermal cycler (problem of initial cost); 2) while the specificity may increase in the fluorescent probe method, it is necessary to design and synthesize the fluorescent probe for each target gene to measure the amount of amplified product (problem of running cost performance); and 3) the amount of the target gene may be undervalued or may produce pseudo-negativeness in the case the measured sample contains a substance that inhibits PCR (problem of robustness). Considering the use of the gene quantification technology

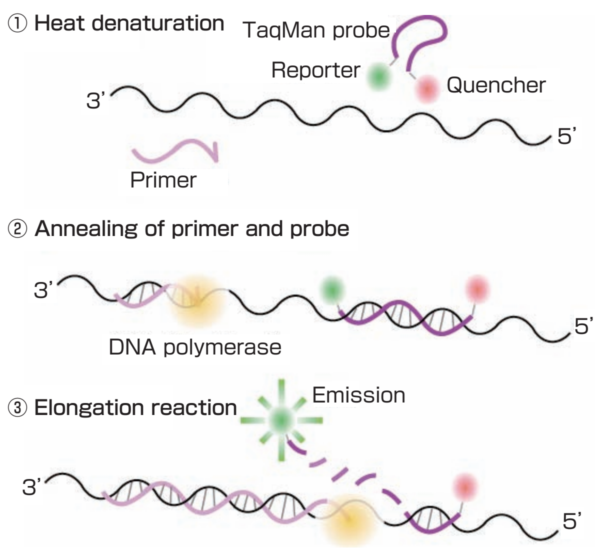

Fig. 1 TaqMan probe method

for multiple samples on site, it is necessary to concentrate on robustness, convenience, and cost performance, while maintaining an equivalent level as the current RT-PCR technology.

In this paper, the two quantitative PCR methods developed as new technologies to solve the problem inherent in the current RT-PCR are described, and the cooperation with companies for the practical application of the developed technology will be presented.

2 Scenario for the development of gene quantification technology with excellent accuracy and cost performance

2.1 Core technology for technology development: quenching phenomenon by the guanine base

To solve the problem inherent in the current RT-PCR, we developed a new quantitative PCR to overcome the two issues: 1) quantification can be done using only one type of fluorescent probe for different target genes (cost reduction by general-use fluorescent probe), and 2) accurate quantification is possible even with the presence of PCR inhibitors. The core technology in this technological development is the "quenching phenomenon by the guanine base." Fluorescence means the emission of light as the fluorescent molecule absorbs light, transforms into an excited-state molecule, and then returns to the original ground-state molecule. The difference in energy between the excited and ground states of the molecules is released as the fluorescence energy. When the molecule transforms from the excited state to the ground state, if there is another molecule with high electron density nearby, this molecule acts as an electron donor and gives away electron to the fluorescent molecule. At this moment, the electron excited by the original fluorescent molecule cannot return to the ground state, becomes unable to emit fluorescence, and the fluorescence disappears. This phenomenon is called the photo-induced electron transfer (PET), and is known to occur within and between molecules[6]. Among the bases that comprise the nucleic acid, guanine has the highest electron density, and therefore, tends to cause quenching through this PET reaction. However, not all fluorescent dyes cause quenching, and it is known that some fluorescent dyes such as BODIPY FL and TAMRA are more likely to cause quenching by the guanine base[7].

Since the quenching phenomenon by the guanine base is a reversible reaction, it can be used conveniently as a tool to detect and quantify nucleic acids. Completely complementary DNA is prepared for a fluorescent probe of about 20 bases, in which the cytosine base of the terminal is labeled with BODIPY FL. When the temperature and other conditions are adjusted to induce annealing (hybridization) in the same reaction solution, the fluorescence of the BODIPY FL is quenched. Then when the hybridization is broken by raising the temperature or other conditions, the BODIPY FL begins to emit fluorescence again. By controlling the hybridization and separation, the on/off of the fluorescence can be controlled. By measuring the degree of quenching, it becomes possible to estimate the amount of complementary strand of the fluorescent probe. The quantitative PCR method using this phenomenon was developed and put on the market as the quenching probe (QProbe) PCR method through joint research with Dr. Shinya Kurata *et al.* of the J-Bio 21 Corporation, an AIST venture that spun off from the Institute for Biological Resources and Functions[8]. The author formed the joint research structure with Dr. Kurata's group, as well as the group of Dr. Satoshi Tsuneda, School of Advanced Science and Engineering, Waseda University, to develop a new technology that extends the QProbe PCR method.

2.2 Development of the universal QProbe method that achieves cost reduction through general-use fluorescent probe

While it is necessary to label the probe with two fluorescent dyes (reporter and quencher dyes) in the TaqMan probe method, which is a method used most frequently as a RT-PCR using the fluorescent probe, only one fluorescent dye is necessary in the QProbe PCR method, which is also a RT-PCR, because it uses the guanine base as the quencher. Moreover, in the QProbe PCR, the adequacy of the amplified product can be checked by a melting curve analysis where the melting temperature of the fluorescent probe that hybridized to the amplified product is measured by raising the temperature gradually from around 40 ºC after the completion of the reaction. This cannot be done in the TaqMan probe method. Although the QProbe PCR has such advantages, it is the same as other fluorescent probe methods in that the fluorescent probes must be designed and synthesized according to the target gene. In the fluorescent probe method, although the specificity of the detection and quantification increases since a fluorescent probe specific to the amplified product is used, the cost increases since the fluorescent probe must be designed and synthesized

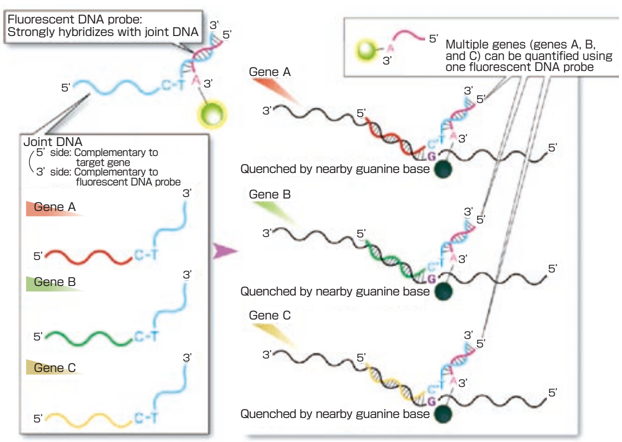

Fig. 2 Universal QProbe method

in addition to the PCR primer. While the synthetic oligonucleotide DNA without the fluorescent label can be prepared at about 2,000 yen per target gene, the probe labeled with fluorescence costs over 20,000 yen. In case there are several target genes, the fluorescent probe much be designed and synthesized for each target gene, and the cost becomes high. If it is possible to quantify any target gene with one fluorescent probe regardless of the sequence, a new gene quantification method with excellent cost performance may be established, having the advantage of mass-synthesized fluorescent probe.

The universal QProbe method was developed based on this thinking (Fig. 2)[9]. While maximizing the principle of the QProbe method that uses the quenching phenomenon by guanine base and realizing the concept of quantifying all types of target genes with one fluorescent probe (the universal QProbe) regardless of the sequence, in the universal QProbe method, we added the idea of the joint DNA that binds both the target gene and the fluorescent probe. The joint DNA is a single-stranded oligo DNA that has a complementary sequence of target gene on the 5' side and a complementary sequence of fluorescent DNA probe on the 3' side, and the two sequences are joined with cytosine and thymine. The fluorescent probe is labeled with a dye whose fluorescence is quenched by the guanine base nearby. The joint DNA bonds to both the target gene and the fluorescent probe, and the fluorescence of the fluorescent probe is quenched when the fluorescent probe approaches the guanine base in the target gene. Therefore, it is possible to measure the amount of the target gene by measuring the degree of quenching as in the QProbe method. The fluorescent probe in this method has the adenine base on the 3' terminal labeled with the fluorescent dye. It is designed so the quenching occurs when the guanine base approaches the fluorescent dye, because this adenine base is positioned across the thymine base of the cytosine-thymine sequence within the joint DNA strand, and the guanine base of the target DNA is positioned across the neighboring cytosine base.

The joint DNA must be designed and synthesized for each target gene, but the cost and time of synthesis can be reduced greatly since it is not labeled with the fluorescent dye. This method will enable the quantification using only one type of fluorescent DNA probe, even if the genes under investigation have different sequences.

2.3 Development of the alternately binding probe competitive (ABC) PCR that is resistant to PCR inhibitors

In the RT-PCR method, it is known that the quantification result may be undervalued or show pseudo-negativeness if the sample to be measured contains a substance that inhibits PCR. While such issues are negligible in samples that contain very little inhibitors or samples that are highly purified, amplification inhibitors are thought to be present in blood samples and soil samples that contain decomposed materials, and inhibition of amplification may be an issue. Although the competitive PCR method is a classical method, it solved the issue of such amplification inhibitors. In the competitive PCR, amplification is done using the same primer as the target gene, but uses an internal standard gene with different amplified base length than the target gene. Specifically, the internal standard gene that is shorter or longer than the target gene is created by removing part of the internal sequence of the target gene or by adding extra base. The internal standard gene of known concentration is added to the sample, and PCR is conducted competitively with the target gene. Since the lengths of the strands differ between the target gene and the internal standard gene, the target gene and the internal standard gene are separated by electrophoresis after PCR, the gradation of the bands of the target gene and the internal standard gene are compared quantitatively, and then the amount of the target gene can be measured from the known amount of the internal standard gene. Using this method, even if the PCR inhibitor is present in the sample, accurate quantification is possible since the inhibition equally affects both the target gene and the internal standard gene. While this method allows accurate quantification even in the presence of the PCR inhibitor, it is no longer used recently since it requires labor-intensive and time-consuming post-PCR procedures for the separation of the PCR products by gel electrophoresis.

By utilizing the advantage of the competitive PCR that can avoid the issue of PCR inhibitors, and by using the quenching phenomenon by the guanine base, we developed the alternately binding probe competitive (ABC) PCR method as a convenient gene quantification method that eliminates the electrophoresis that was a problem in competitive PCR (Fig. 3)[10]. In the ABC-PCR, internal standard gene

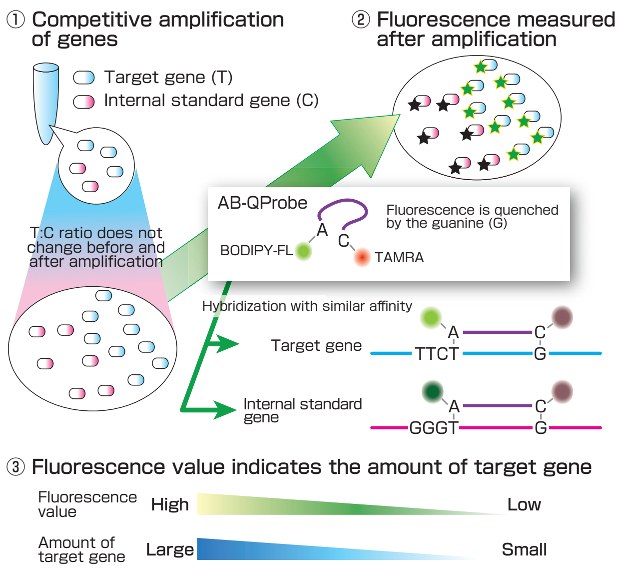

Fig. 3 ABC-PCR method

has the same strand length as the target gene, and also is amplified by the same primer and the fluorescent alternately binding probe (AB-Probe). One terminal of the AB-Probe is labeled with the green fluorescent dye (BODIPY FL) where the fluorescence is quenched with the nearby guanine base, and the other end is labeled with the red fluorescent dye (TAMRA) that is quenched by the guanine base. The sequence of the AB-Probe is designed to be complementary to the common sequence of the target gene and the internal standard gene, and it hybridizes with the same affinity to both genes. In the internal standard gene, the three exterior bases on the green fluorescent dye that hybridize with the AB-Probe are replaced with the guanine base (the bases in the target gene are those other than guanine). Therefore, the AB-Probe binds competitively to the amplified product derived from the target gene and that from the internal standard gene with the same affinity, and green fluorescence is emitted when it binds with the target gene, but does not emit fluorescence when it binds with the internal standard gene since the fluorescent dye is quenched by the guanine base. The green fluorescence becomes stronger as there are more target genes than the internal standard genes, while the green fluorescence becomes weaker as there are less target genes than the internal standard genes. The amount of the target gene can be calculated since the amount of the internal standard gene is known. TAMRA, the red fluorescent dye, is quenched in the same manner when the AB-Probe is bonded either to the target gene or the internal standard gene. The presence of amplification can be checked since the degree of quenching of TAMRA changes according to the amount of amplified product derived from the target gene and the internal standard gene.

The ABC-PCR can be considered as a method where the electrophoresis step that was mandatory in the competitive PCR method is replaced with the fluorescent probe using the quenching phenomenon by guanine. Since it is a competitive method, it not only allows accurate quantification in the presence of the PCR inhibitors, but is also an endpoint quantification method where the degree of quenching can be measured after the completion of PCR. Therefore, the expensive device needed in the RT-PCR is not necessary, and the target gene can be quantified with an inexpensive thermal cycler and a fluorescence measurement device.

3 Results of the development

3.1 Universal QProbe PCR method

We conducted an experiment to verify the principle of the universal QProbe PCR by using the β-actin, albumin, and β -globin genes as target genes. The most important point is the stability of the joint DNA and the fluorescent probe. It is desirable that the hybridization between the joint DNA and the fluorescent probe does not dissociate but remain stable during the PCR reaction. Therefore, we used a synthetic oligonucleotide where the nucleic acid of the fluorescent probe was replaced by locked nucleic acid (LNA). The LNA is an analog of the nucleic acid that has two cyclic structures in the molecule, and it is known that the oligonucleotides including LNA show dramatic heat stability against the complementary DNA and RNA[11]. A fluorescent probe labeled with BODIPY FL composed of LNA of 13 base length was synthesized, and the *Tm* of the complementary sequence of this fluorescent probe and the joint DNA was calculated using the Exiqon Tm prediction tool (http://lna-tm.com). The result was 102 ºC. Since the highest temperature encountered in PCR was 95 ºC at heat denaturation, it was thought that the complex of the fluorescent probe and joint DNA would be prevented from dissociation during the PCR cycle.

Using the designed fluorescent probe and the joint DNA, the quantification of the target gene was conducted using the universal QProbe PCR. The fluorescent quenching rate was calculated from the fluorescence value at denaturation step (state where the probe and target genes are dissociated) and the fluorescence value during annealing step (state where the probe and target genes are bonded). Figure 4 shows

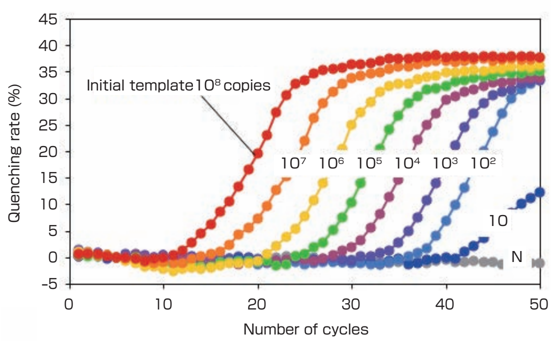

Fig. 4 Relationship between the number of cycles and quenching rate in the universal QProbe method

This shows the quenching rate when the β-actin gene is amplified from 10 to 10^8 copies. The calculation of quenching rate was done according to Reference [8].

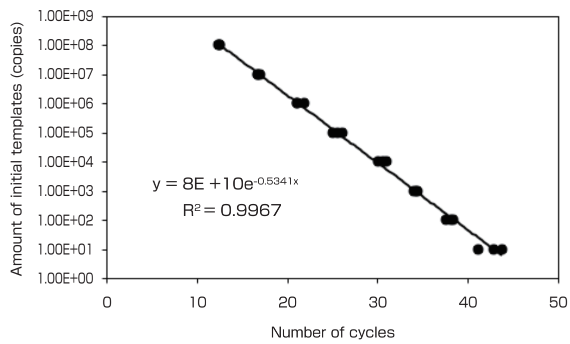

Fig. 5 Standard curve in the universal QProbe method

This shows the relationship between the number of cycles required for the reaction product to reach a certain amount and the amount of initial templates, calculated from the relationship between the number of cycles and quenching rate of Fig. 4.

the relationship of the number of cycles and fluorescent quenching rate when the β-actin gene was quantified. The fluorescent quenching rate was about 30~40 %, or about the same as the QProbe PCR. Figure 5 shows the standard curve created by calculating *Ct* from Fig. 4. The lower limit of quantification was 10 copies, and the correlation coefficient R^2 of the standard curve was 0.9967. Both the lower limit of quantification and the correlation coefficient were about the same as the QProbe PCR. The amplified product can be checked by conducting the melting curve analysis where the temperature at which the complex of the fluorescent probe and joint DNA dissociates from the amplified product is measured by gradually raising the temperature from around 40 °C after PCR. Results with equivalent quantification precision were obtained for the albumin and β-globin genes as well as the β-actin gene. Our initial objective of developing the quantification of multiple target gene sequences using one fluorescent DNA probe while maintaining the same quantitative quality as the QProbe PCR was achieved with this universal QProbe PCR [9].

We applied the universal QProbe PCR method to the genetic analysis of single nucleotide polymorphisms (SNP) in the human gene. SNP is a single base DNA variation occurring in the genome, and is defined as a mutation seen at 1 % or higher frequency in a certain group. Recently, through the advancement in human genome and genetic analysis research, SNP is drawing attention as one of the causes of the individual differences such as susceptibility to disease or reactivity to drugs. SNP is said to occur on average in one place among 1000 bases, and there are over 3 million SNPs in the 3 billion base pairs on a human genome. We differentiated these SNP gene types through the melting curve analysis using the universal QProbe PCR. The joint DNA was designed to be completely complementary to one allele, and had one base mismatch on the other allele. After annealing the fluorescent probe and joint DNA complex with the PCR amplified product by decreasing the temperature, the SNP was analyzed by obtaining the melting curve from the fluorescence emitted by the quenched probe as the temperature was raised. The fluorescence is emitted as the dissociation occurs at low temperature if there is a mismatch, while the fluorescence is emitted at higher temperature if there is a perfect match (Fig. 6). Figure 7 shows the result of the analysis of the three gene types for SNP: wild homo, mutant homo, and hetero types. Separation was easy since the positions of the peak of emission differ for the wild and mutant types. Both peaks were observed in the hetero type where the wild and mutant types were mixed. Since the universal QProbe PCR allows quantifying multiple target genes with one fluorescent probe, it is expected to be an effective tool in genotyping the SNP, since it is said that 3 million SNPs exist in the human genome.

3.2 Alternately binding probe competitive (ABC) PCR method

We investigated the quantitative property in the ABC-PCR method using the *gfp* gene, which is the famous green fluorescent protein, as the target gene. The internal standard gene was created based on the sequence of the *gfp* gene, and the verification of ABC-PCR was conducted. The quenching rate calculated from the fluorescence values after the PCR that was corrected by several background fluorescence values was set as the relative fluorescence intensity. Figure 8 shows the graph of the relationship between this relative fluorescence intensity and the amount of the target gene in the initial template. Using this method, the standard curve could be regressed to a sigmoid curve just as in the standard curve obtained by other general competitive measurement methods such as the competitive ELISA. According to Fig. 8, the correlation coefficient of the standard curve was 0.9997. The lower limit of quantification was 10^3 copies. Since this method is competitive, the quantifiable range using one standard curve is in the order of 2~3, but the quantifiable range can be adjusted by changing the concentration of the internal standard gene. It is also possible to calculate

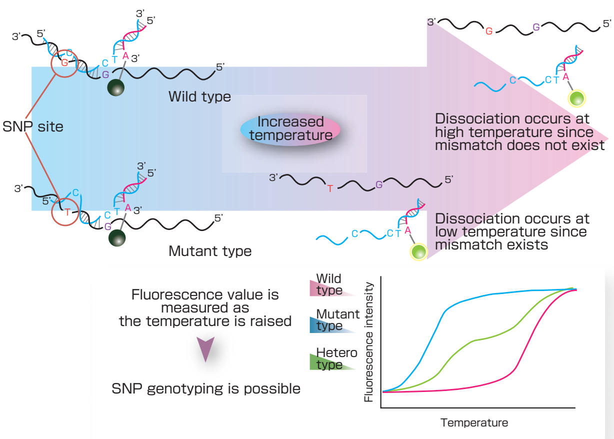

Fig. 6 Principle of SNP typing by the universal QProbe method

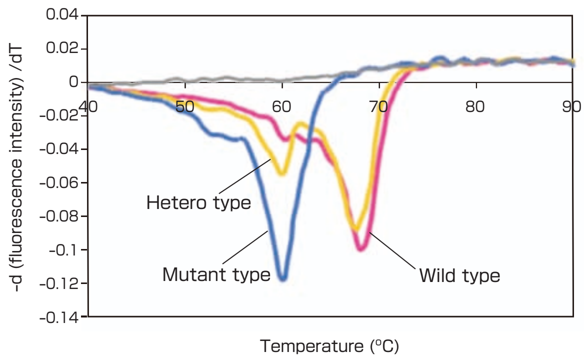

Fig. 7 Result of SNP genotyping by the universal QProbe method

SNP genotyping is conducted from the analysis of dissociation curve where the fluorescence values are measured as the temperature is gradually raised from 40 °C to 90 °C. The vertical axis shows the value obtained by the primary derivation of fluorescent value by time.

the amount of the standard gene from the diluted sample within the quantifiable range by conducting measurement by creating a dilution series of the unknown sample. This method can be also used as genotyping to identify the SNP as in the universal QProbe as well as for gene quantification[10].

We evaluated the effect on the quantification value in the ABC-PCR and RT-PCR methods by adding humic acid that is found in the soil and is known as a DNA amplification inhibitor. As a result, in the RT-PCR, the quantification value turned out to be lower than the true value as the concentration of the humic acid increased, while in the ABC-PCR, the quantification value was almost the same as the true value even in the presence of humic acid[10]. In the experiment using urea and Triton X-100 as the DNA amplification inhibitor, it was found that the ABC-PCR was capable of highly accurate quantification compared to the RT-PCR[12].

The ABC method not only is capable of accurate quantification in the presence of the DNA amplification inhibitor, but also is capable of quantifying the target gene by measuring the fluorescence after the gene amplification reaction. This means that the target gene can be quantified in a similar manner whether the gene amplification reaction is PCR or some other technique. Recently, methods such as the loop-mediated isothermal amplification (LAMP) and helicase-dependent amplification (HDA) have been developed as the isothermal gene amplification, as alternative to the PCR. By combining such isothermal gene amplification methods with the ABC method, similar quantification as the ABC-PCR can be done. The ABC method is not only accurate, but is also highly universal from the perspective of combining with the gene amplification methods.

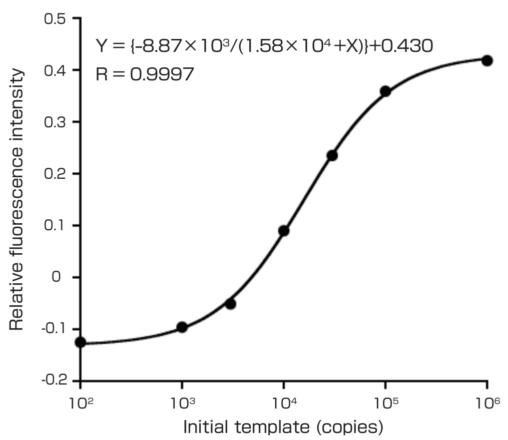

Fig. 8 Standard curve in the ABC-PCR method
This is the relationship between the amount of target genes in the initial template and the relative fluorescence intensity. The relative fluorescence intensity is the value where the fluorescence value obtained after the completion of PCR is corrected by some background fluorescence values[9]. The plot obtained is regressed by equilateral hyperbola. R is the correlation coefficient.

4 Evaluation of the development technology and scenario for realization

The advantages and the disadvantages of the two newly-developed gene quantification technologies, universal QProbe PCR and ABC-PCR methods, will be compared to the current technologies, and the scenario for their realization to maximize the advantages of each technology will be discussed (Fig. 9). Table 1 shows the comparison of the properties of the current technologies (TaqMan probe, QProbe, intercalator, competitive methods) and the universal QProbe and ABC-PCR methods. Since the technologies have their advantages and disadvantages, it is necessary to consider the ways to realize them by thoroughly understanding the properties of the technologies. The business for the realization of the universal QProbe PCR and the ABC-PCR is currently undertaken by the J-Bio 21 Corporation, the partner of the joint research.

Table 2 shows the comparison of the characteristics of the universal QProbe PCR with the conventional RT-PCR (fluorescent probe and intercalator methods). As it can be seen from Table 2, the universal QProbe PCR is a technology that takes the advantages of the fluorescent probe and the intercalator methods. Although this paper does not refer to multicolor detection, four different colors can be used as dyes where the fluorescence is quenched by guanine, and this method can be used in the multicolor detection and quantification. Since the universal QProbe PCR is a RT-PCR, the thermal cycler for RT-PCR is necessary. However, thinking alternatively, this method can be used immediately if there is a thermal cycler for RT-PCR available. Therefore, the prime strength in realizing this technology is that we can recommend it to users who are already using the RT-PCR method. In the conventional RT-PCR, the reagent kits are commercially available for the detection and quantification of specific genes (such as pathogenic bacteria, virus, or certain SNP). However, such pre-marketing method is not compatible for the universal QProbe PCR. One of the advantages of the reagent kit is the cost merit of mass synthesizing the fluorescent probe to detect a specific gene. However, since only one type of fluorescent probe is necessary for various gene sequences in the universal QProbe PCR, there is hardly any cost advantage in providing the reagent kit. Therefore, as business plans to optimize the advantage of this method, the joint DNA and fluorescent probe according to the client's target gene sequence can be provided, or the genetic analysis service can be subcontracted to detect and quantify the client's target gene sequence. In these business plans, the low cost of the fluorescent probe and the short time for the preparation of the fluorescent probe synthesis that are the characteristics of this method can be optimized fully, to provide a low-cost, quick-delivery gene analysis service. One of the clients who may benefit from the low cost and quick delivery may be a company in the field of

Table 1 Comparison of the characteristics of quantitative PCR methods

	Real time method				Internal standard method	
	TaqMan probe method	QProbe method	Intercalator method	Universal QProbe method	Competitive method	ABC method
Fluorescent probe	Needed for each target gene (label with 2 colors)	Needed for each target gene (label with 1 color)	Not necessary	Can deal with all target genes with one fluorescent probe (label with 1 color)	Not necessary	Needed for each target gene (label with 2 colors)
Internal standard gene	Not necessary	Not necessary	Not necessary	Not necessary	Necessary	Necessary
Electrophoresis	Not necessary	Not necessary	Not necessary	Not necessary	Necessary	Not necessary
Check amplified product by melting curve analysis	Impossible	Possible	Possible	Possible	Impossible	Possible
Real time PCR device	Necessary	Necessary	Necessary	Necessary	Not necessary	Not necessary
Resistance to inhibitors	No	No	No	No	Yes	Yes

Table 2 Comparison of the universal QProbe method and the conventional RT-PCR method

	Conventional method		Universal QProbe method
	Fluorescent probe method	Intercalator method	
Specificity	○ (Non specific product is not detected)	× (Non specific product is also detected)	○ (Non specific product is not detected)
Cost* (probe, primer)	× (1 gene: 20,000 yen or higher)	◎ (1 gene: about 2,000 yen)	○ (1 gene: about 6,000 yen)
Time needed for preparation*	× (1～2 weeks)	○ (Minimum next day)	○ (Minimum next day)
SNP genotyping	○	×	○
Multicolor detection	○	×	○

*Based on estimates by J-Bio 21 Corporation.

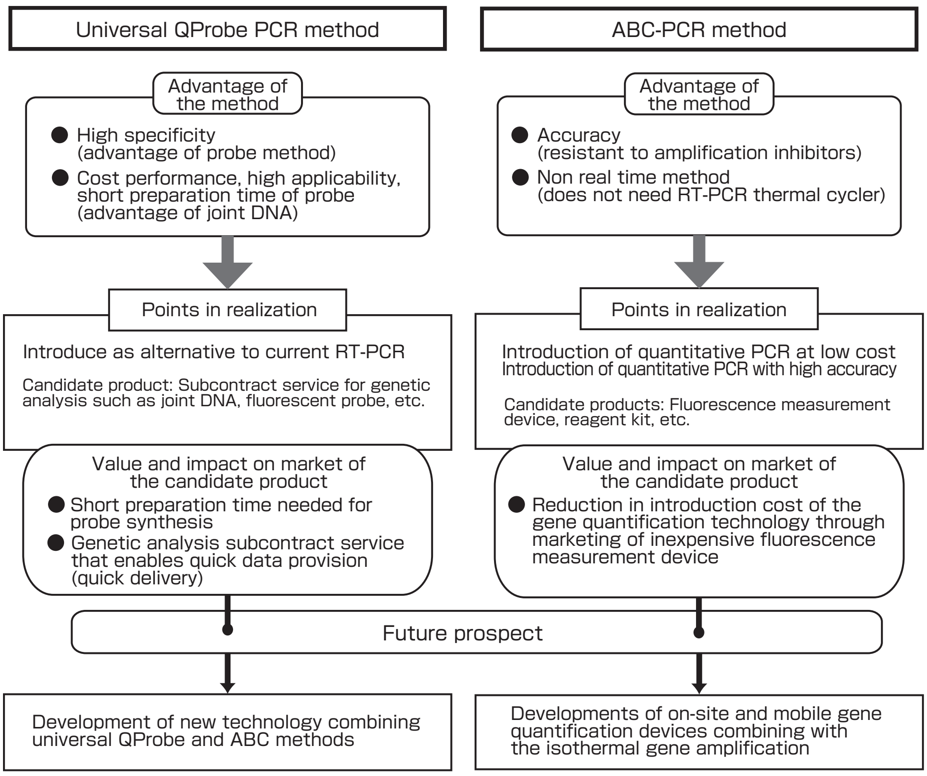

Fig. 9 Scenario for the realization of the universal QProbe PCR and ABC-PCR methods

environmental cleaning using bacteria. As covered in the newspapers and other media, the “brownfield” with soil contamination has become an issue. For cleaning such soil contamination, bioremediation using bacteria is thought to be effective in terms of cost. However, when cleaning up the contaminant by introducing the bacteria in the environment, the bioremediation guideline states that it is necessary to assess not only the introduced bacteria, but also the effect on the microbial community that originally exists in the soil. The method using the genetic information is effective for the assessment of the microbial community, and the gene quantification technology is drawing attention in this field. There is a diversity of microbes in the environment, and the microbes to be investigated change for each soil type. Therefore the universal QProbe PCR method that allows quantifying various gene sequences using one type of fluorescent probe is extremely effective in the detection and quantification of the various environmental microbes. Therefore, one of the ways of practical use for the universal QProbe PCR is the subcontracted analysis business in the field of environmental cleaning business where the various microbial community can be detected and quantified at low cost and in a short time.

Since the ABC-PCR method has different advantages and disadvantages from the universal QProbe PCR, the scenario for its realization differs. The advantages of ABC-PCR are that accurate quantification is possible without the effect of the gene amplification inhibitor, and the target gene can be quantified by simply measuring the fluorescence after the gene amplification reaction. For the former, the users who are already using the RT-PCR but are facing the problem of amplification inhibitors will probably see merit in introducing this method. Moreover, in this method, the target gene can be quantified by simply measuring the fluorescence after the gene amplification reaction, and the expensive thermal cycler for RT-PCR is not necessary. Instead, the fluorescence measurement device for measuring the fluorescence after the gene amplification reaction is necessary. The marketing of the fluorescence measurement device (named EGBox) is in progress at the joint researcher J-Bio 21 Corporation (Fig. 10). This device is specialized to measure fluorescence in the ABC method. The specifications are: one fluorescence measurement area; depth 18 cm × width 30 cm × height 15 cm; 3.5 kg; LED light source; and three excitation wavelengths. The fluorescence value can be measured simply by inserting the PCR tube into the sample port. J-Bio 21 Corporation is trying to keep the retail price below 1 million yen. By offering such inexpensive fluorescence measurement device and reagent kit, we believe we can do business with people who wish to be involved in the gene quantification technology but are hampered by the facility cost. The ABC-PCR is extremely appropriate for cases that wish to introduce the gene quantification technology at low cost such as in developing countries. To realize such a scenario, the issues are downsizing to portable size, and energy-saving configuration where the device can be powered by batteries. As the technologies to achieve downsizing and energy saving, the micro total analysis system (μ-TAS), where reaction, separation, and detection are done in microspace, by forming the flow channels and circuits on a silicon or glass substrate using the microfabrication technology, was developed and is being used in the analysis of biomolecules such as nucleic acids and proteins. Downsizing and energy saving will be achieved by fusing the μ-TAS technology and the ABC method. The ABC method can be used in combination with the gene amplification methods other than the PCR. For example, if it is combined with the isothermal gene amplification method, quantification can be done with a simple and inexpensive device consisting only of an isothermal device with low energy use instead of a thermal cycler. To develop these technologies, there are many issues that must be solved such as the selection of gene amplification technologies (development of a new isothermal gene amplification method if necessary) as well as the development of simple nucleic acid extraction technologies. However, if these issues are overcome, it is expected that a gene quantification technology that is simpler and less expensive than the one currently used widely can be achieved.

The dream of the author is the diffusion of the gene detection and quantification technologies based on the universal QProbe and the ABC methods, in pursuit of convenience and cost performance. We also aim for the development of the new technology combining the universal QProbe and the ABC methods in the future. Specifically, this involves the replacement of the fluorescent probe used in the ABC method with the universal QProbe, but there are several difficult problems because it is necessary to advance the idea on the joint DNA. However, the technology in which the universal QProbe and ABC methods are integrated will have both the accuracy of the ABC method and the flexibility of the universal QProbe method, and is expected to have great social impact due to its cost performance and the reduced preparation time for probe synthesis.

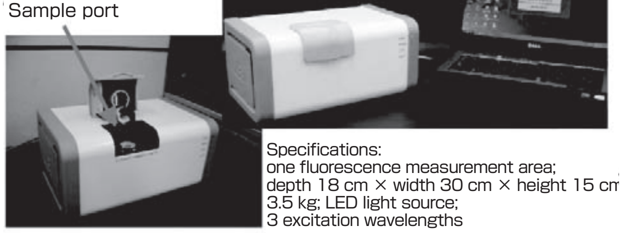

Fig. 10 Prototype of simple fluorescence measurement device (EGBox) (made by J-Bio 21 Corporation)

The Japanese market in 2009 for RT-PCR was estimated to be 6.8 billion yen for devices (0.3 billion yen increase compared to the previous year), and 4.5 billion yen for reagents (0.5 billion yen increase compared to the previous year)[13]. The demand for the quantification of gene expression such as the detailed expression analysis of human genes is increasing, and the market for RT-PCR is expected to increase further in the future. It is expected that the use will expand in the facilities and the developing countries that were reluctant to introduce gene tests due to their cost, and we believe a system that can be introduced at low cost is important. The universal QProbe PCR and ABC-PCR have excellent cost performance and universal applicability, and are expected to be the next-generation gene quantification technology in such social situations.

5 Conclusion

In this paper, for the two gene quantification technologies, universal QProbe PCR and ABC-PCR methods, the elemental technologies in the development phase and the scenario for the realization after their development were discussed from a synthesiological perspective. Although the diagram of the principle of the developed technology seems to be simple, we encountered various problems and engaged in trial-and-error in the processes from the selection of elemental technologies to their integration. Over 10 researchers combined ideas, repeated discussions, and completed the technology under the tri-party joint research of AIST, Waseda University, and J-Bio 21 Corporation. The technologies that resulted were the universal QProbe PCR and the ABC-PCR methods, and these were accomplished by repeating the work of filling each piece as if completing an extremely difficult puzzle. The core elemental technology of these technologies is the quenching phenomenon of the fluorescent dye that occurs between the guanine bases, but there were infinite quenching patterns of the fluorescent probe due to the bonding force and other factors of the probe and the amplified product as well as the positions of the fluorescent dye and guanine base. It was necessary to do trial-and-error to determine which one would quench most efficiently and stably and was appropriate for gene quantification. Since not all quenching patterns could be predicted by knowledge and experience, the work of trying out each unknown possibilities was like walking in the dark with no signs of the goal ahead. We fortunately were able to complete the technology this time, but this could not have been possible with just one or two persons. It is work accomplished by the cooperation of several researchers involved, even with them engaging in vicious discussions at times.

In the advancement of *Type 2 Basic Research*, the process of generating a practical technology by reviewing the phenomena discovered in *Type 1 Basic Research* from multiple angles is important. To advance *Type 2 Basic Research* in an effective manner, it is important not only to push forward the ideas and viewpoints of a small number of people, but the R&D must be carried out by building trusting relationships among the people of industry-academia-government, and by respecting each other's values.

6 Acknowledgements

The development of the universal QProbe PCR method was accomplished through the cooperation of: Shinya Kurata, Kohei Ichikawa, *et al.* of the J-Bio 21 Corporation; Professor Satoshi Tsuneda, Hidenori Tani (currently at the Radioisotope Center, The University of Tokyo), *et al.* of the Center for Advanced Biomedical Sciences, Waseda University; and Kazunori Nakamura, Yuji Sekiguchi, *et al.* of AIST. The development of the ABC-PCR method was accomplished through the cooperation of: Shinya Kurata *et al.* of the J-Bio 21 Corporation; Professor Satoshi Tsuneda, Hidenori Tani (currently at the Radioisotope Center, The University of Tokyo), *et al.* of the Center for Advanced Biomedical Sciences, Waseda University; Takahiro Kanagawa of Kyoto Gakuen University; and Kazunori Nakamura, Yuji Sekiguchi, *et al.* of AIST. The development of the ABC-PCR method was supported by the Grant for Industrial Technology Research, New Energy and Industrial Technology Development Organization (NEDO).

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Discussions with Reviewer

1 Specific assumed client and scenario development

Comments (Yoshifumi Jigami, Evaluation Division (current affiliation: Research Center for Medical Glycoscience), AIST)

I think you need to analyze the issues and problems that must be overcome to make this business successful. For example, you should consider the attributes of those whom you specifically assume to be your clients that can take advantage of “the low cost and quick delivery”, and then present the scenario to develop the business.

Answer (Naohiro Noda)

The assumed clients that can take advantage of “the low cost and quick delivery” include the environment companies that must monitor diverse environmental microbes in bioremediation, and the genetic testing companies that must analyze innumerable gene types. We used the example of the environment companies for monitoring the environmental microbes because their market is expected to expand in the future, and revised the manuscript accordingly.

2 Issues and points for the diffusion

Comments (Yoshifumi Jigami)

The sales plan for the inexpensive fluorescence measurement device (less than 1 million yen) with accompanying reagent kit is discussed, and its diffusion as a tool for the quantification and analysis of genes at low cost in the developing countries and others is suggested as a probable business development. While this is a very interesting suggestion, you did not give the issues and points that must be overcome to realize this.

Answer (Naohiro Noda)

As the issues and problems that must be overcome to realize the diffusion to developing countries, downsizing and energy saving of the developed technology are necessary. To achieve these, I think the development of the biochip that combines the micro total analysis system (μ-TAS), which is advancing dramatically recently, is important in the future scenario. This point was described in the revised manuscript.

3 Value and social impact on the market

Comments (Yoshifumi Jigami)

Figure 9 shows the points for realization and the corresponding candidate products. I think it will be easier to understand if you describe the value and social impact of these products on the market.

Answer (Naohiro Noda)

“Value and social impact of the products on the market” was added to the product candidate in Fig. 9.

4 Problems in technological development and scenario for solution

Comments (Yoshifumi Jigami)

As future prospects, you describe “the development of the new technology combining the universal QProbe and the ABC methods” and “the development of the on-site or mobile gene quantification device combined with the isothermal gene amplification method”. While these are important in looking at the “researcher’s dream” or the “link between the research objective and the society (social values)”, you should discuss the issues that must be overcome to achieve such technological developments, scenario to solve the issues, and the impact on the market when they are realized.

Answer (Naohiro Noda)

For “the development of the new technology combining the universal QProbe and the ABC methods”, it is necessary to generate ideas about joint DNA that is compatible with the ABC method by advancing the concept of current joint DNA. (The details of the idea will be omitted here since the development is in progress.) For “the development of the on-site or mobile gene quantification device combined with the isothermal gene amplification method”, selection of isothermal amplification technologies (development of new technology if necessary) and simplified nucleic acid extraction technology are needed. The issues that must be overcome for technological development and the impact on the market when they are realized are described in the revised manuscript.

Synthesiology: Knowledge for interdisciplinary consilience

[Translation from *Synthesiology*, Vol.3, No.2, p.158-163 (2010)]

The 3rd Conference organized by the Transdisciplinary Federation of Science and Technology (TFST) was held at the Tohoku University in December 2009. The special session entitled "Synthesiology: Knowledge for Interdisciplinary Consilience" included a lecture and a general discussion. The outlines of the general discussion and the paper read of the lecture are presented here with the permission of TFST.

***Synthesiology* Editorial Board**

[Opening address]

Hisatoshi Suzuki (Vice-Chairman, TFST; University of Tsukuba)

The Transdisciplinary Federation of Science and Technology (TFST) is an organization that was formed for the development and promotion of core sciences, which are the foundation of technology, different from natural sciences. It is a federation of the academic associations of various specialties, across humanities and sciences. In January 2008, an academic journal *Synthesiology* was launched by AIST. I think the objectives of the journal, "to establish a discipline to synthesize things that are beneficial to society by integrating the scientific findings and technologies in addition to the traditional science for obtaining the knowledge on nature", as well as the methodologies presented in the papers published in the journal share close semblance to the thinking of TFST.

A joint workshop was held by TFST, the Institute of Statistical Mathematics (ISM), and AIST with the objective of promoting this field in January 2009. This effort was extremely significant, and led to this special session of the 3rd TFST Conference.

Dr. Akira Ono, the Vice-President of AIST, will lecture on the essence of the AIST method of synthetic research to "utilize the results of the basic research in society". Then we shall have a general discussion with Dr. Motoyuki Akamatsu as the coordinator.

[Lecture]

Akira Ono (Editor in Chief, *Synthesiology*; AIST)

[Refer to the paper, "Synthesiology: The method and description of synthetic researches" on pages 179~183 in this issue.]

[General discussion]

Motoyuki Akamatsu (Executive Editor, *Synthesiology*; AIST)

I believe one of the aims of TFST is "integration of knowledge", and the synthetic research addressed in *Synthesiology* is "integration" in many ways, and I think we are aiming for common grounds. Therefore, in this general discussion, we shall have a three-way discussion with TFST, AIST, and ISM which is a supporter of TFST.

Synthesiology publishes papers of varying fields. To avoid the discussion from becoming too abstract, we will have Dr. Atsuo Kishimoto of AIST explain his paper "Strategic approach for comparing different types of health risks" that was published in Volume 1 Issue 1, as a specific example of synthetic research.

Next, we shall hear from Dr. Tatsuji Hara on which direction the synthetic research should go from the standpoint of TFST, and then from Dr. Yoshiyasu Tamura from the standpoint of ISM. Dr. Naoto Kobayashi will explain the types of "synthesiology" scenarios. Finally, we shall engage in discussion.

[Strategic approach for comparing different types of health risks]

Atsuo Kishimoto (AIST)

Rather than getting into the content, I shall focus on the "way of thinking" presented in this paper. While I am not certain whether my research represents a typical AIST style, because I was given an opportunity to write for *Synthesiology*, during the writing process, I think I was able to organize my way of thinking at the time I was doing research, and I caught myself saying, “Oh, so that’s what I was thinking!”

My research is risk assessment of chemical substances. I had to think of a way to rank the risk reduction measures in Japan according to priority for about 100 thousand industrial chemical substances. To do so, I had to compare the magnitude of the risks of various chemical substances.

Risk can be expressed by multiplying the level of exposure and the strength of toxicity. Combining the two data for the distribution of exposure level for all Japanese, and how much increase there is in the incidence rate when the exposure level increases, and then looking at the size of risk of each chemical substance, these become the “necessary information”. However, it was found that the “available information” amongst the “necessary information” were way insufficient.

For exposure level, there are several examples of people exposed to extremely high concentrations. For example, there are many examples of extremely high measurements of formaldehyde concentration in a newly built house and short-term daily average values. However, there was hardly any data on long-term annual average values that we wanted to obtain, nor was there data showing the seasonal changes. For toxicity, there were data for no-observed-adverse-effect level of “concentration below which no adverse effect will occur”, but there was no data for dose response function showing “this much incidence rate will occur if there is this much exposure”. Therefore, the current elemental technologies could not be used, and we had to on our own develop and modify the elemental technology.

The “existing elemental technologies” that we determined to be “useless”, while they include the ones I recognized after I wrote the paper, were the ones for the risk assessment of chemical substances reflecting the initial demands in society. These elemental technologies were selected when conducting a chemical substance screening, which involved the elimination of no-risk substances amongst the milliard chemical substances. Therefore, the method to achieve that objective was pursued. The elemental technology was developed to find the level that was safe for high concentration exposure, and it was optimized for the work of saying “if this substance is okay at high concentration, then it is safe at ordinary concentration”.

The elemental technology thus developed was established by repeated practice. Guidelines and manuals were written, became routine, and the methodology for the initial risk assessment for chemical substances was established.

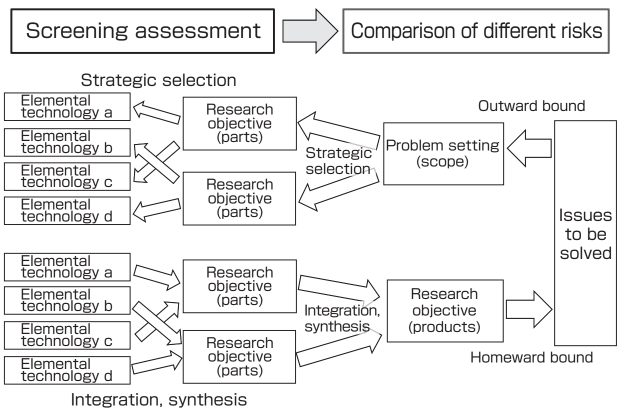
However, what we were trying to do was “risk comparison for several types of chemical substances”, and in a sense, it was a new social demand. The existing elemental technology was inappropriate for this purpose. The existing elemental technology was for a different social demand, because it was a part of the set of elemental technologies optimized for screening assessment. Therefore, we became aware of the gap where we could not use the risk assessment technology for the new demand.

We returned to the origin, and started looking at the methodology of which elemental technology was necessary to enable the “comparison of different types of risks” that was the new social demand. This is called “re-synthesis” in “synthesiology”. Rather than measuring only the people with high exposure concentration, we looked at the distribution of annual average values of the individual exposure estimate and the distribution of the environmental concentration estimates in Japan. Rather than looking at one value where anything below it is safe, we looked at the whole picture, and saw that there were various elemental technologies that must be optimized. Development of these elemental technologies is the “strategic development of elemental technologies”. Next, the elemental technologies developed are integrated and synthesized. Then, we enter the phase of “integration and synthesis of various elemental technologies” where we establish the new methodology and put them in practice.

The essence of the paper written for *Synthesiology* was to develop a new methodology and to conduct risk assessment to compare the various types of risks.

When I was doing this, I thought about “the trap of the fields of specialty”. It may be extravagant, but the currently existing specialty and research topics were always derived from some past social demands. The “fields of specialties” that were formed became divorced from their origins and went through their unique evolution. For example, they generated academic societies, specialists, guidelines, journals, courses, and textbooks, and became autonomous. However, social demands and societal values are ever changing. In modern society where changes occur dramatically, the specialties fall into autotelism, and I

Changes in issues to be solved by risk assessment of chemical substances



painfully realized that they might have become so distant from social demands. Of course, it isn't that the existing elemental technology is useless. It is useful for screening chemical substances, but it is not directly useful for any other purposes.

I think there are outward and homeward passages to solve an issue. In "synthesiology", the main passage is homeward bound from integration and synthesis to the goal (product). To do so, there is a strategic selection of reviewing all elemental technologies, and I think I walked outward when I thought about how to combine the established technologies. When the social issue that one wishes to solve changes, this cyclic path is traveled again, and when another issue that must be solved arises, you must walk through the cycle yet again.

[New academic system]

Tatsuji Hara (The University of Tokyo)

I was the chief editor of the journal called the *Okan* or the Journal of TFST for two years, and currently, I am a senior member of the Knowledge Integration Subcommittee, Integrated Engineering Committee, Science Council of Japan, under Chairman Tachi. I would like to present my thoughts, along with the activities of TFST.

When Dr. Yoshikawa was the chairman at the Science Council of Japan, the framework of science for recognition and science for design were created for the "new academic system". While conventional "science" corresponds to science for recognition, it is academics for science, and is the "pursuit of what is" On the other hand, science for design is what is conventionally called "technology", and this is academics for society, and is "the pursuit of what should be". Both academics based on intellectual curiosity and academics focusing on values and objectives are equally important, and this is the new system of academics.

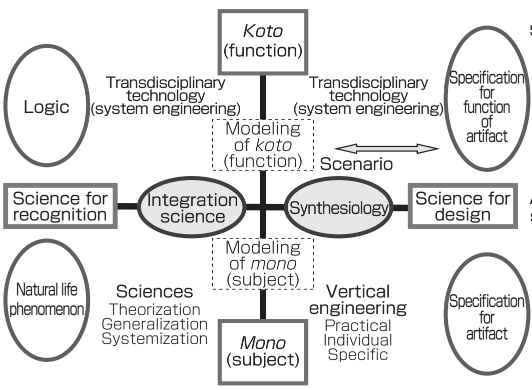
I considered along the two axes: one of science for recognition and science for design, and the other of *mono* and *koto* proposed by TFST.

What we called science for recognition and science for design at the Science Council might correspond to the way of thinking focusing on *mono* (subject). Science for recognition is roughly considered "science" where the subject is nature, life, and phenomenon, and aims at theorization, generalization, and systematization. In contrast, science for design is an artifact system, or designing and realizing the artifact. It is characterized by keywords of practical, individual, and specific. I think it corresponds to the conventional vertical engineering based on the vertical disciplines such as mechanics and electrics. These more or less look only at the *mono*. However, to actually create an artifact system that is useful to society, both *mono* (subject) and *koto* (function) are necessary. Science and vertical engineering are firmly established as disciplines for accurately understanding the "subject". However, for system engineering and system theory that are transdisciplinary technologies to be valid, it is necessary to define what corresponds to the specification of the "function" for "subject".

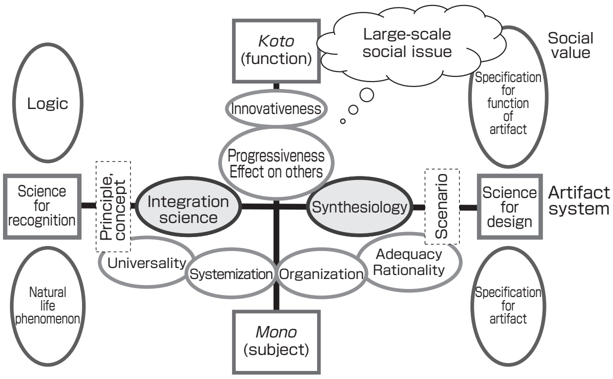
When we think "what is 'synthesiology'", it is not just "subject" and it is not just "function", but it probably aims right in between. As a contraposition to "synthesiology", I shall set "integration science" since the other keyword of TFST is "knowledge integration". If this integration science and "synthesiology" correspond to the new science for recognition and science for design that deal with "subject" and "function", I think that is one way of drawing the picture.

I think "scenario" will be the major keyword for "synthesiology", which is a "scenario-driven research". When we look at the "subject", to conduct an academic study, one standard way of science and technology is to create a model for the subject, and then conduct research based on this model. However, I don't think "modeling of function" has been sufficiently done. Therefore, when we say "subject" and "function" are two wheels of a vehicle, it is necessary to define function modeling. Considering these and then thinking what a scenario is, I think the scenario is to connect the model and the specification for the function of artifacts. It is to consistently and rationally link these two.

"Transdisciplinary science and technology" + "synthesiology"



Evaluation in "integration science" and "synthesiology"



For evaluation, what should be assessed in "synthesiology" and integration science? The integration science is to create new principles and concepts for integration, to pursue universality based on those principles, and to systematize. In "synthesiology", consistency and rationality are important. Consistency is to bind the separate items into one, and it is also to establish a single scenario, and these are different from the logical consistency. Perhaps "rationality" should be called "adequacy". In Dr. Kishimoto's example, the methodology can be used in other places, not only for solving the risk comparison. It will become universal by systematization and generalization. When it is possible to define "consistency in this sense" as a new evaluation standard, I think evaluation is possible. Whichever it is, it will be based on a scenario.

Another point is, since our subjects are large-scale, complex social issues, we must question "whether it is innovative, or progressive, and whether there are effects on others" in our evaluation. To prevent systematization and universalization from anchoring the subject in that field, it is important to accurately evaluate the progressiveness and effect on others.

The transformative research, for which support is considered by NSF, is an attempt to transform science through revolutionary developments. In the United States, unexpected developments, effect on multiple fields, and creation of new research disciplines are expected. The European-type fusion is where a team is created to conduct the fusion research to arrive at an innovation, and is an attempt to gain something through fusion.

In Japan, the fusion research is not necessarily going well. The reason is because, when an area of concentration is determined, the research activities go straight to the center, the objective will be solving the problem and whether one gets a result or not. It is even doubtful whether the fusion research is really being conducted.

In such situations, I think I would like to see a proper academic approach to the social issues through "synthesiology" and integration science, and that may produce progress and effect on others.

[ISM and synthetic research]

Yoshiyasu Tamura (ISM)

Because of the term "statistical data analysis", many people may think statistics is analysis, but it is in fact the opposite, and I feel there are many "synthesiological" factors. In the past, a research on cement was conducted by Dr. Akaike at ISM. To operate the cement kiln stably, no conventional method worked, so a new statistical control method was considered, and this turned out to be successful.

I'll talk about studies done by graduate students. The first research by a student who got his doctorate in March was a study on "where the respiratory center was located in the rat brain". He really loved mathematics and wrote all these mathematical models, and was scolded by the physician. Why was he scolded? Because he neglected physiology. The physician pointed out, "That kind of research is no good", but the graduate student was so shocked he quit the research. Another graduate student had been working at a control system company, and was a very experienced 60 years old. His data was dyed slices of the brain that he looked through a microscope, but he grasped the heart of the research. While using mathematical techniques and statistics, he was able to match the physiology and the model because he had hands-on experience in problem solving and did not get entangled in virtual mathematics. The student who failed with the rat brain went on to analyze the shape of the rat jawbone. The quantification of shape could not be done with existing techniques. So, he used the data from the Institute of Genetics, and now seems to be successful.

It is often said that "fusion research was never successful", but the fusion research between the National Institute of Genetics (NIG) and ISM is going fairly well. That is because genetics and statistics share the same roots, and the geneticists and statisticians seem to get along very well.

At ISM, there are many students who come from the financing world, and their objective is "how to prevent the company from suffering losses". They think about what scenarios to write and how to gain most profit by using quite difficult differential equations for probability. Various elemental technologies are combined. Since the scenario model for what to select to get the best is the most important point in statistics, I think statistics has always blended well with the "synthesiological" way of thinking. What we call analysis is the analyzing done at the final level, but "what kind of analysis should be done" must be carefully integrated and synthesized.

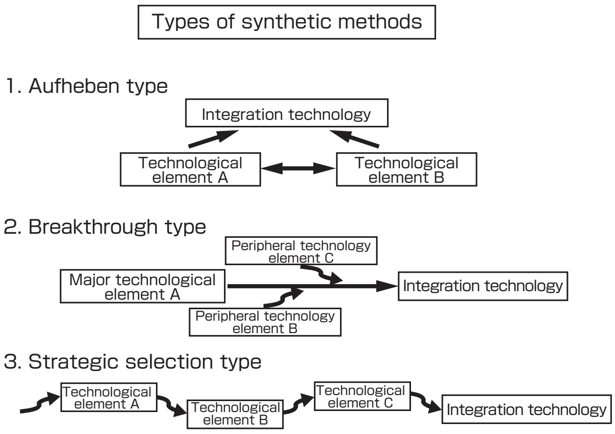
Right now, the people of statistics and information science like to use the word "data-driven", and they say the fourth science is the "science of data". Modeling of data may sound strange, but what is most important is how to model the system that generates the data, and I think it mixes well with synthetic research.

[Categorization of synthetic method]

Naoto Kobayashi (Waseda University)

Since my specialty is physics, I tend to think analytically even when talking about synthesis. Therefore, I shall look at the synthesis method in an analytical manner. This figure was presented when I had a discussion with Prof. Richard Lester of MIT in *Synthesiology* Volume

1 Issue 2. As I read the published papers and talked to the authors, I saw there were different synthesis methods in the papers, and I categorized them into three groups.



First is the “aufheben style” borrowed from the Hegelian dialectics. This is a type where different theses such as technology factor A and technology factor B are integrated, and some new concept is created.

Second is the “breakthrough type”. The scientists and engineers are fairly good at this. It is a type where one’s elemental technology generates a technology that will become a key, and when the peripheral elements are bound to that technology, an integrated technology is formed and then there is a breakthrough. Actually, things are not that simple, but there are some successful cases.

Third is the “strategic selection type”. Dr. Kishimoto mentioned outward and homeward passages, and when I read Dr. Kishimoto’s paper, I thought it might be this type. The exit is set first, and various elemental technologies are selected and synthesized to get there. In this case, the importance of the individual elemental technologies is similar, but a strategy is needed to select and synthesize them.

Of course, there are other types, and combinations of the three types. I also think it is rather difficult to have a clean-cut categorization. What is more important is the essential leading principle when synthesizing these elemental technologies.

We’ve been going around asking people to understand the objectives for launching *Synthesiology* and to write papers, but I don’t think we have arrived at a methodology of synthesis yet. When I do the reviews and explain the importance of scenario and synthesis of elemental technologies to the authors, I ask, “You mean this, right?” and they say, “Oh, you may be right. But I wasn’t thinking about that at all”. I think this part is similar to the argument by Dr. Hara that “‘synthesiology’ is a scenario-driven research, and the definition for function modeling is necessary”. It is perhaps very similar to the argument for innovation. Although the road may be long, perhaps we may be able to reach a methodology for the integration of knowledge.

[Question and Answer]

Akamatsu

Does any of you in the audience have questions or comments for the four speakers?

[Does the “artifact” include company?]

Audience

This may be a simplistic question, but is it okay to include something like a company among the artifacts? Dr. Kishimoto talked about risk. There is a way of thinking that avoiding risk will be beneficial to the citizens, and a company too faces several risks such as management issues and earthquakes. I have surveyed the standard for risk management, and the direction emphasized in the risk management standard by the companies based in Australia and New Zealand is “risk is chance”. Rather than avoiding risks, the companies can create innovations using the risk as a chance, and raise its new corporate value. As this method spreads to other companies and become commonplace, not only does the immediate corporate value increases, but the benefit is returned to the entire society. When investigated from the company’s standpoint, it isn’t entirely mathematical because the business models or somewhat incomprehensible elements enter, but can these be included in the artifacts?

Kishimoto

I spoke about citizens when I talked about the entire Japan, in the sense that we engage in researches as public institutions. We do consider “a risk is a chance”. To capture what may be the risk in the future, to develop a method, and then to standardize the method—this will lead to the competitiveness of Japan. To do so, it is necessary to specify “for whom”. If it is specified “for the company”, the strategy for companies will be created, and we can apply the “synthesiological” framework.

Hara

I wrote “artifact system” in the figure, and that was proposed at the Science Council. When we considered *koto* or subject, it includes the social systems and the human endeavors, and I think it should be taken as a very wide-ranging concept.

[Organization of knowledge integration]

Audience

When we talk about “knowledge integration” and “synthesis”, I think we should organize the different domains of the structure of “knowledge” that are considered as a subject.

First, there is the domain that can be investigated by the natural providence such as nature and the physical world. Next, there is the logical world or thinking world, and in this there may be mathematics and models. The problem is the type that deals with the so-called human society, and this includes intentions, meanings, values, and includes ourselves who are trying to do the investigation. Moreover society includes nature and engineering. I think the knowledge integration should be organized by three dimensions. The integration that links those three may be ambitious, or there may be a new type of movement called the ad hoc integration for some problem solving.

Akamatsu

When there was a discussion on why launch another journal when there are already millions of journals in this world, I thought unless we accumulate case studies, theorization alone will be unusable, and we must collect the data of successful cases of research and learn from them. Therefore, in *Synthesiology*, there are papers on various researches that the editors and the authors consider to have synthetic approaches. As presented by Dr. Kobayashi, we are trying to categorize research by trial-and-error, and I think the categorization suggested by the audience just now is also possible. Since we just started collecting case studies, I think we shouldn't hurry, and we can take time categorizing as more cases are accumulated.

Audience

Dr. Hara's figure ("Transdisciplinary science and technology" and "synthesiology") is very interesting, but I would like to ask one point. While the natural phenomenon is a subject, what is the positioning of the social phenomenon? Does it belong to a different world? Can the social phenomenon be expressed in this figure just like a natural phenomenon? Is society somewhere outside, and is the knowledge accumulated and the logic built here given some sort of meaning in a separate society?

In my thinking, it is assumed that "science is also a social phenomenon". Society is moving and science is moving. I think what is challenging and interesting is the interaction between the two, and if you express this in this context, you may appreciate the advantage of TFST.

Another point,—you use the word "synthesis" to mean the lump held together by multiple logics and how they will be made into one story. "Integration" is to become one through combinations in a deeper way. Until now, various fusions of different fields were attempted, but they are difficult. I think synthesis is more practical in reality. Ultimately, I think some kind of fusion will take place, a new discipline is born, and that will go into a cycle to become something new.

Akamatsu

What we target in *Synthesiology* is the "activities of the researchers". We suppose there is a social background that moved the researchers. Dr. Kishimoto's research is a research done through the interaction with society. You become aware when reading the papers of *Synthesiology* that there are several researches conducted with the background of the interaction among the researchers of a research organization or the interaction between the researcher and industry. Rather than targeting only the completed product, what is important is the process where the researcher interacts with society, defines the goal, and thinks what must be combined together to achieve the goal. One of the objectives of *Synthesiology* is to describe this process as papers, whereas such things were done before without much thought given to them. Therefore we chose not to use the word "integration", but decided to use the word "synthesis" to express the process of gradually building something.

Today, we were able to discuss many points, and I hope we will all continue to work hard. Thank you very much.

[Closing Address]

Hidenori Kimura (Chairman, TFST; Riken)

About two years ago, I heard about the launching of *Synthesiology*, and I honestly thought, "Wow, they got there before us". They were doing exactly what we were thinking, and the results are impressive too.

Dr. Yoshikawa stated that the discipline is necessary for the field to develop, and even said that it is a necessary evil. He believes that the passion of the researcher will always overcome the evil and solve the problem. Dr. Kishimoto who spoke today has first-handedly experienced the limit of the discipline, has overcome that, and yielded wonderful results. However, the academic societies are set up by disciplines, and if we call that necessary evil, we will end up with a contradiction that academic federations cannot exist. Therefore, we must strike a balance, acknowledge their existence, and seek the passion for overcoming them. I think this is the direction that must be taken for the academics to advance in the future.

AIST that harbors several thousand excellent researchers started this activity, and we would like to pay attention to their activities in the future. We would also like to provide as much support as possible as academicians.

Synthesiology: The method and description of synthetic researches

A. Ono and M. Akamatsu (National Institute of Advanced Industrial Science and Technology)

[Translation from *Synthesiology*, Vol.3, No.2, p.164-168 (2010)]

Abstract - A new method and processes are provided for synthetic researches integrating elemental technologies to realize societal values. The synthetic researches are characterized in comparison to the analytical researches and are modeled in the cycling processes among society, researchers and academic communities. A new description framework is given to writing original scientific papers of the synthetic researches. It is now demonstrated by the publication of a new scientific journal, *Synthesiology*, for the synthetic researches.

Index terms - Synthetic research, method, description, type two basic research, synthesiology

1 Introduction

The science has a great history that it advanced dramatically since the 17th century using the method of reductionism. It has been recognized, however, in the 21st century that this method alone will not be able to address the complex issues such as the global environments. In the 20th century, the technology has greatly advanced through the backup of the science while it is clear that the technology did not advance on reductionism alone.

While the opposing relationships such as science for recognition vs. science for design, analytical method vs. synthetic or integrating method, or science vs. engineering are being discussed, we are witnessing recent pursuits of new sciences that are different from reductionism.

In this lecture, we will focus on the role of synthetic or integrating method, comparing with analytical method, in the basic research of science and technology. The importance of synthetic method is indicated in the process of basic research to create societal values, and a methodology of such synthetic research is discussed. Also, a new form of writing an original research paper is presented to describe the processes and contents of such synthetic research. The methodology of synthetic research presented here has been discussed in the practice of *Full Research* or *Type 2 Basic Research* at AIST since 2001[1]. The new form for papers has been actually deployed in *Synthesiology*, a new scientific journal launched by AIST in 2008[2].

2 New methodology for basic research

Researches are often categorized into the basic research, the application research, and the development research. Here, we categorize them into the following three types.

- *Type 1 Basic Research*: This is a research whose subject is nature. Unknown phenomena are analyzed by observations, experiments, and theoretical calculations, factual knowledge is accumulated, and then universal laws and theories are built. It corresponds to the pure basic research. The researches are normally conducted within one discipline; it is rare that it stretches across several different disciplines. The researches are driven by researcher's academic curiosity.

- *Type 2 Basic Research*: This is a research where societal value is sought by synthesizing and integrating knowledge from multiple disciplines. Knowledge of what research should be done is accumulated and the methodology is built. It is a similar type with the objective basic research and application research. The researches are driven by the researcher's desire to realize some societal values.

- *Product Realization Research*: This is a research to actually put a new technology in use in society by utilizing results and knowledge obtained from the above two types of researches and actual experiences. This type of research corresponds to the developmental research. The researches are driven by the will of researcher who wishes to actualize research results in society.

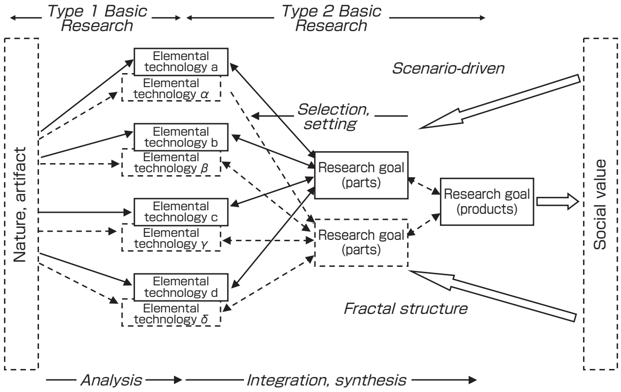


Fig. 1 Method of Type Two Basic Research

This paper is a draft of the lecture presented at the special session of the 3rd Conference of the Transdisciplinary Federation of Technology and Science on December 4, 2009. It is reproduced with the permission of TFST.

- *Full Research*: This is a research where the activities are conducted continuously and concurrently from *Type 1 Basic Research* to *Product Realization Research* with emphasis on the above *Type 2 Basic Research*. It is conducted often by a group or an organization. Individual researcher is normally in charge of some part of the *Full Research* series. Seen chronologically, a researcher may shift from *Type 2* to *Type 1 Basic Research*, or from *Type 2* to *Product Realization Research*, or he may be in charge of several types of researches concurrently.

Figure 1 shows the method of *Type 2 Basic Research* and also the relationship to *Type 1 Basic Research*. In *Type 2 Basic Research*, first, a research goal with societal value is set. Whether the research goal is close or not to the exit to society, its relationship to the societal value is stated clearly. Second, the research goal is broken down into research items expressed in the terms of science and technology, and then a scenario to address the items is set. After the setting of the scenario, what elemental technologies are selected for addressing the items is important. The selected elemental technologies may lie across several different disciplines. Third, the elemental technologies are combined, synthesized and integrated for the research goal to be achieved.

It should be noted here that there may be more than one scenario in such synthetic research to achieve the research goal. Several different scenarios may exist. It is also reasonable that the best scenario may vary depending on the researchers. It may be usual that researchers take into account several scenarios and, after comparing them, he/she chooses the best one. If the scenario is different, the elemental technologies selected will be different depending on the researcher.

The elemental technologies selected by the researcher are usually based on the results or conclusions already obtained in *Type 1 Basic Researches*. When trying to achieve a complex research goal, it is rare that necessary elemental technologies fall in one discipline. Rather, the elemental technologies are normally selected from multiple disciplines. While in some cases the existing elemental technologies can be applied to *Type 2 Basic Research* in its original form, in other cases the existing elemental technologies will be modified or improved. Also, if there is no appropriate elemental technology to fit the scenario, the researcher or the research group may return to *Type 1 Basic Researches* to obtain new elemental technologies necessary to achieve the research goal.

Table 1 Characteristics of Type One and Type Two Basic Researches

	Type 1 Basic Research	*Type 2 Basic Research*
Method	Analysis	Synthesis, integration
Action	Discovery, clarification	Invention, creation
Range of subject	Single discipline	Multiple disciplines
Uniqueness of solution	Exclusive solution	Multiple viable solutions
Drive power	Academic curiosity	Realization of social value
Important property	Adequacy of logic	Usefulness of solution
Originality	Dramatic advancement of solution	Uniqueness of method
Novelty	Novelty of solution	Novelty of method
Evaluation method Viewpoint of evaluation	Peer review Consistency, dramatic advancement	Merit review Usefulness, uniqueness

When a certain result is obtained by conducting *Type 2 Basic Research*, one cycle is completed upon evaluating how much the initially set research goal has been achieved. *Type 2 Basic Research* will continue to progress toward the exit to society as it repeats the cycles. Then the conclusions obtained in the previous cycle are carried over to the next cycle. The *Type 2 Basic Research* follows the above cycles in all cases, and is thought to have a fractal structure whether the research goal is big or not. Various characteristics of *Type 2 Basic Research* described above are shown in Table 1 in comparison with *Type 1 Basic Research*.

3 Returning the research result to society

Figure 2 shows the process by which results of basic researches are returned to society. In the modern society public funds are provided to basic researches of science and technology. The public funds are entrusted to research institutions reflecting the sponsor's will, and researches are made by the researchers under contract. The research results are written up as original research papers by the researchers and submitted to an academic society of the discipline. The paper undergoes a peer review or a process of anonymous evaluation by researchers of the same field. If it is accepted, it is published in an academic journal and contribution of the researchers to the academia and knowledge is recognized.

In reality, modern science and technology are finely segmented into many disciplines. Usually an academic society is organized for one segmented discipline, and the society has its own academic journal. The more

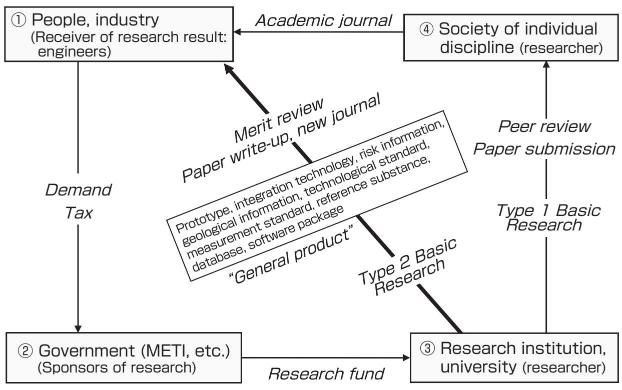


Fig. 2 Cyclical process of research in the society

the disciplines are segmented, special terminology and knowledge are necessary to be able to read and understand the papers. So it can no longer be easily understood by other people of the general society who may wish to utilize the research results. It is also often difficult for researchers of other disciplines.

Since publication of original research papers in an academic journal is the most basic requirement to a researcher, the researcher works full force to write such papers. Particularly, since a paper will not be published in an academic journal unless the research result is deemed valuable by peer reviewers or researchers of the same discipline, the author of a paper often writes primarily to get assent of researchers of his/her own discipline. The more the researcher engages in such efforts, the papers become more incomprehensible to researchers of other disciplines and general engineers. Many recent academic journals have been published worldwide and the number of papers being published is skyrocketing. But there is no change in the situation where the results of the basic research done by public funding are not returned directly to the sponsors.

There are some researchers, however, who provide the results directly to society and industry without going through the academic societies of the individual discipline. For example, when developing a prototype of products in a joint research, this will be an excellent opportunity for the research institute and the company to share the research results. Also patent, risk information, geological information, document standards, measurement standards, reference materials, and software package may be delivered directly to the users without going through the academic society.

These results are representative of the *Type 2 Basic Research* being highly valuable from the point that they contribute directly to society. However, these activities are apt to be taken lightly as mere sideline work of the main research activity. Moreover, there is no established methodology or medium to describe the results of *Type 2 Basic Research* as an original research paper. We believe there is great significance in evaluating the processes and results of the *Type 2 Basic Research* as valuable, in developing a new form of original research papers, and in issuing a new academic journal as a place for publication.

4 Development of a new form of research papers

It is commonly accepted today that writing an academic paper on the process and content of the research conducted and contributing it to an academic journal is something done routinely by researchers. A researcher who does not write any papers is unthinkable, and such a person is not evaluated as a researcher proper. However, one may realize that the research papers of science and technology that we are used to write have an extremely limited form.

The origin of modern science arose in 17th century Europe, and the method of science thereafter incorporated positivism to investigate whether a certain phenomenon is true or not. When a researcher writes a research paper, sufficient information must be described to enable other researchers to do a follow-up test to investigate whether they can obtain the same result described in the paper. Then the researchers investigate the logical relationship among the phenomena confirmed to be true and establish laws and theories.

In the modern research papers of science and technology, items unrelated to the “objective” phenomenon such as why the author started the research, what motivation and intention the author had, or why the author made a certain decision are not included. Even if such items are described a little bit in a paper, they are not subjects interesting in the peer review. The reason is because, in *Type 1 Basic Research* whose priority is the accumulation of factual knowledge, the descriptions of “objective” phenomenon are important, and those alone are sufficient. On the other hand, in *Type 2 Basic Research* where a selection is made among several equivalent scenarios with the research motivation being the realization of a societal value, the most vital part of the research cannot be expressed just by describing the “objective” phenomena.

A table of typical content of *Type 2 Basic Research* paper is shown in Table 2. The processes of *Type 2 Basic Research* methods shown in Fig. 1 are arranged in the order of research conducted. The originality of paper is represented by the uniqueness of the set scenario and the novelty of the integration and synthesis process of elemental technologies. Even if the same research goal is given, researchers will set different scenarios. They also take different processes of synthesis and integration if different elemental technologies are selected. Thus these are unique to individual researcher, and they represent the researcher’s “originality”.

It is not necessary to repeatedly describe details of the elemental technologies in a *Type 2 Basic Research* paper.

Table 2 Contents and features of *Synthesiology* papers

Structure of paper

1	Setting of research goal
2	Social value of research objective
3	*Proposal of scenario and selection of elements*
4	*Relationships between elements, and their integration and synthesis*
5	Evaluation of results and future developments

Characteristic of papers

Originality	・Set scenario ・Selected elements and methods of integration and synthesis
References	・Results of *Type 1 Basic Research* should be included in references

Since it is supposed that details are already published as the result of *Type 1 Basic Research*, they can be listed in References and only the conclusions need to be described.

5 Publication of a new academic journal *Synthesiology*

A new form of original research papers and instructions for authors were set, and then a new academic journal *Synthesiology*[3),4)] was launched in 2008. The titles of research papers published in Volume 1, Issue 1 are listed below.

- Mass preparation and technological development of an antifreeze protein
- Development and standardization of accessible design technologies that address the needs of senior citizens
- A challenge to the low-cost production of highly functional optical elements
- A strategic approach for comparing different types of health risks
- Technologies for the design and retail service of well-fitting eyeglass frames
- Improving the reliability of temperature measurements taken with clinical infrared ear thermometers

The keywords such as mass preparation, standardization, low-cost production, assessment strategy, design and retail service technology, and reliability improvement found in the titles were seldom used in conventional academic papers. The typical characteristics of *Type 2 Basic Research* is represented well.

The review of papers of *Synthesiology* is not a peer review that is done by researchers of the same discipline with the authors, but is a merit review that is done by a researcher of roughly similar field to the author's one and another from a totally different field. The merit review is done from the viewpoints shown in Table 1.

As one of the features of *Synthesiology*, discussion between the authors and the reviewers appears after the text of paper. The names of reviewers are also disclosed. Since the form of paper for *Type 2 Basic Research* is not finalized as of now, we decided, in solidifying the form, that it would be useful to publicize the discussions between the authors and the reviewers. We receive many comments from the readers that this discussion is very new and interesting.

It has been almost two years since the launch of *Synthesiology*, and we have noticed several points after publication. First, many authors commented that they were able to write the things that could not be written in conventional academic journals even if the authors had wanted to do so. Researchers seem to hope that the background and reason of research and the scenarios they employed in executing their research are publicized. They also have positive attitudes toward communicating more about that with other researchers.

Next, the reviewers commented that the originality of research become manifest in their scenarios most easily. On the other hand, the ways of synthesis and integration of elemental technologies are diverse. It is difficult to settle upon some uniform style at this point, but it is expected that some categorization of scenarios will eventually emerge. The point most reviewers found surprising was that they were not only able to understand the content of an original research paper written by researchers of different disciplines, but were able to give comments to the authors at a certain level of quality. This is a major characteristic of *Synthesiology* that would have never occurred in current academic journals dealing with *Type 1 Basic Research*. Thus there is a possibility that the journal would be accepted by a wide-ranging readership.

The readers have sent us many comments pointing out the advantages and usefulness in understanding and knowing about researches in fields outside of their own disciplines.

In this modern times when many complex issues such as global environments emerge and new industry-government-academia collaborations such as open innovation are suggested, we believe the methodology of synthetic research will play an important role along with *Synthesiology* that is a medium for its expression and a place of information exchange.

6 For further discussion in the symposium

Usefulness in the society is emphasized in the synthetic researches. However, the science was already expected to be useful at the beginning. The philosophy of natural science research in which we currently engage started with Francis Bacon, who stated that the humankind will become happy by studying nature and making discoveries and inventions[5)]. At the same time, the natural science took the route of positivism, and academic journals were established as their method. Then the emphasis was placed on the investigation of factual knowledge. On the other hand, the research community has never worked on the investigation method for usefulness that was expected by Bacon. However, the society expects "major discoveries" and "great inventions" by science and technology. One of the criteria evaluating such values is certainly usefulness, however the evaluation of usefulness is not simple. From the perspective of impact on society, one can evaluate a research result in terms of how much effect it has on the market. But the market dynamics is often moved by factors different from those of science and technology, such as protection of vested interests and industries, trendiness, and price competition. Due to these factors, the evaluation in the market cannot be fixed without the test of time. Therefore, measuring usefulness according to the impact on the market is not necessarily appropriate.

When the result is sent out to society by conducting synthetic research, there may be some cases where the elemental technologies are put together without a definite aim, and there may be other cases where the elemental technologies are synthesized with thorough think-through. The ones that are synthesized without a definite aim might sometimes work very well, but most of them will probably not yield good results. A good think-through is mandatory to produce usefulness and other values. The way or process on which research is done is called "scenario" in *Synthesiology*, which we ask the authors to describe in the papers. However, how to consider usefulness or what the scenario should be to realize such usefulness has not yet been very clear to us.

As a joint project of the Transdisciplinary Federation of Science and Technology, the Institute of Statistical Mathematics, and the National Institute of Advanced Industrial Science and Technology, we invited Dr. Yoshiyasu Tamura (ISM), Dr. Tatsuji Hara (The University of Tokyo), Dr. Atsuo Kishimoto (AIST), and Dr. Naoto Kobayashi (Waseda University) as panel members to have a general discussion on this subject. First, Dr. Kishimoto will explain the risk assessment of chemical substances as a specific example of synthetic research, to introduce to the audience and panel members a *Synthesiology* paper. Dr. Hara will speak on "synthesiology" from the perspective of knowledge integration. Next, we discuss about what the usefulness of research is and how usefulness is described, and how to evaluate the scenario to link scientific research to societal values. Dr. Tamura will speak about the modeling and simulation technology as tools for scenario building and usefulness evaluation. Dr. Kobayashi will propose an idea on what types of scenarios were put to practice with the papers published in *Synthesiology*, and the categorization of scenarios will be discussed. Based on these discussions, the meaning of describing interdisciplinary integration of knowledge as activities of researchers, and the future direction of the activities for giving values to research in society will be investigated.

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1) H. Yoshikawa and K. Naito: *Sangyo Kagaku Gijutsu No Tetsugaku (The Philosophy of Industrial Science and Technology)*, The University of Tokyo Press (2005) (in Japanese).
2) http://www.aist.go.jp/synthesiology/
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4) *Synthesiology*, 1 (1) (2008).
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Editorial Policy

Synthesiology Editorial Board

Objective of the journal

The objective of *Synthesiology* is to publish papers that address the integration of scientific knowledge or how to combine individual elemental technologies and scientific findings to enable the utilization in society of research and development efforts. The authors of the papers are researchers and engineers, and the papers are documents that describe, using "scientific words", the process and the product of research which tries to introduce the results of research to society. In conventional academic journals, papers describe scientific findings and technological results as facts (i.e. factual knowledge), but in *Synthesiology*, papers are the description of "the knowledge of what ought to be done" to make use of the findings and results for society. Our aim is to establish methodology for utilizing scientific research result and to seek general principles for this activity by accumulating this knowledge in a journal form. Also, we hope that the readers of *Synthesiology* will obtain ways and directions to transfer their research results to society.

Content of paper

The content of the research paper should be the description of the result and the process of research and development aimed to be delivered to society. The paper should state the goal of research, and what values the goal will create for society (Items 1 and 2, described in the Table). Then, the process (the scenario) of how to select the elemental technologies, necessary to achieve the goal, how to integrate them, should be described. There should also be a description of what new elemental technologies are required to solve a certain social issue, and how these technologies are selected and integrated (Item 3). We expect that the contents will reveal specific knowledge only available to researchers actually involved in the research. That is, rather than describing the combination of elemental technologies as consequences, the description should include the reasons why the elemental technologies are selected, and the reasons why new methods are introduced (Item 4). For example, the reasons may be: because the manufacturing method in the laboratory was insufficient for industrial application; applicability was not broad enough to stimulate sufficient user demand rather than improved accuracy; or because there are limits due to current regulations. The academic details of the individual elemental technology should be provided by citing published papers, and only the important points can be described. There should be description of how these elemental technologies are related to each other, what are the problems that must be resolved in the integration process, and how they are solved (Item 5). Finally, there should be descriptions of how closely the goals are achieved by the products and the results obtained in research and development, and what subjects are left to be accomplished in the future (Item 6).

Subject of research and development

Since the journal aims to seek methodology for utilizing the products of research and development, there are no limitations on the field of research and development. Rather, the aim is to discover general principles regardless of field, by gathering papers on wide-ranging fields of science and technology. Therefore, it is necessary for authors to offer description that can be understood by researchers who are not specialists, but the content should be of sufficient quality that is acceptable to fellow researchers.

Research and development are not limited to those areas for which the products have already been introduced into society, but research and development conducted for the purpose of future delivery to society should also be included.

For innovations that have been introduced to society, commercial success is not a requirement. Notwithstanding there should be descriptions of the process of how the technologies are integrated taking into account the introduction to society, rather than describing merely the practical realization process.

Peer review

There shall be a peer review process for *Synthesiology*, as in other conventional academic journals. However, peer review process of *Synthesiology* is different from other journals. While conventional academic journals emphasize evidential matters such as correctness of proof or the reproducibility of results, this journal emphasizes the rationality of integration of elemental technologies, the clarity of criteria for selecting elemental technologies, and overall efficacy and adequacy (peer review criteria is described in the Table).

In general, the quality of papers published in academic journals is determined by a peer review process. The peer review of this journal evaluates whether the process and rationale necessary for introducing the product of research and development to society are described sufficiently well.

In other words, the role of the peer reviewers is to see whether the facts necessary to be known to understand the process of introducing the research finding to society are written out; peer reviewers will judge the adequacy of the description of what readers want to know as reader representatives.

In ordinary academic journals, peer reviewers are anonymous for reasons of fairness and the process is kept secret. That is because fairness is considered important in maintaining the quality in established academic journals that describe factual knowledge. On the other hand, the format, content, manner of text, and criteria have not been established for papers that describe the knowledge of “what ought to be done.” Therefore, the peer review process for this journal will not be kept secret but will be open. Important discussions pertaining to the content of a paper, may arise in the process of exchanges with the peer reviewers and they will also be published. Moreover, the vision or desires of the author that cannot be included in the main text will be presented in the exchanges. The quality of the journal will be guaranteed by making the peer review process transparent and by disclosing the review process that leads to publication.

Disclosure of the peer review process is expected to indicate what points authors should focus upon when they contribute to this journal. The names of peer reviewers will be published since the papers are completed by the joint effort of the authors and reviewers in the establishment of the new paper format for *Synthesiology*.

References

As mentioned before, the description of individual elemental technology should be presented as citation of papers published in other academic journals. Also, for elemental technologies that are comprehensively combined, papers that describe advantages and disadvantages of each elemental technology can be used as references. After many papers are accumulated through this journal, authors are recommended to cite papers published in this journal that present similar procedure about the selection of elemental technologies and the introduction to society. This will contribute in establishing a general principle of methodology.

Types of articles published

Synthesiology should be composed of general overviews such as opening statements, research papers, and editorials. The Editorial Board, in principle, should commission overviews. Research papers are description of content and the process of research and development conducted by the researchers themselves, and will be published after the peer review process is complete. Editorials are expository articles for science and technology that aim to increase utilization by society, and can be any content that will be useful to readers of *Synthesiology*. Overviews and editorials will be examined by the Editorial Board as to whether their content is suitable for the journal. Entries of research papers and editorials are accepted from Japan and overseas. Manuscripts may be written in Japanese or English.

Required items and peer review criteria (January 2008)

	Item	Requirement	Peer Review Criteria
1	Research goal	Describe research goal (“product” or researcher's vision).	Research goal is described clearly.
2	Relationship of research goal and the society	Describe relationship of research goal and the society, or its value for the society.	Relationship of research goal and the society is rationally described.
3	Scenario	Describe the scenario or hypothesis to achieve research goal with “scientific words” .	Scenario or hypothesis is rationally described.
4	Selection of elemental technology(ies)	Describe the elemental technology(ies) selected to achieve the research goal. Also describe why the particular elemental technology(ies) was/were selected.	Elemental technology(ies) is/are clearly described. Reason for selecting the elemental technology(ies) is rationally described.
5	Relationship and integration of elemental technologies	Describe how the selected elemental technologies are related to each other, and how the research goal was achieved by composing and integrating the elements, with “scientific words” .	Mutual relationship and integration of elemental technologies are rationally described with “scientific words” .
6	Evaluation of result and future development	Provide self-evaluation on the degree of achievement of research goal. Indicate future research development based on the presented research.	Degree of achievement of research goal and future research direction are objectively and rationally described.
7	Originality	Do not describe the same content published previously in other research papers.	There is no description of the same content published in other research papers.

Instructions for Authors

Synthesiology Editorial Board
Established December 26, 2007
Revised June 18, 2008
Revised October 24, 2008
Revised March 23, 2009

1 Types of contributions

Research papers or editorials and manuscripts to the "Readers' Forum" should be submitted to the Editorial Board.

2 Qualification of contributors

There are no limitations regarding author affiliation or discipline as long as the content of the submitted article meets the editorial policy of *Synthesiology*, except authorship should be clearly stated. (It should be clearly stated that all authors have made essential contributions to the paper.)

3 Manuscripts

3.1 General

3.1.1 Articles may be submitted in Japanese or English.
Accepted articles will be published in *Synthesiology* (ISSN 1882-6229) in the language they were submitted. All articles will also be published in *Synthesiology - English edition* (ISSN 1883-0978). The English edition will be distributed throughout the world approximately four months after the original *Synthesiology* issue is published. Articles written in English will be published in English in both the original *Synthesiology* as well as the English edition. Authors who write articles for *Synthesiology* in Japanese will be asked to provide English translations for the English edition of the journal within 2 months after the original edition is published.
3.1.2 Research papers should comply with the structure and format stated below, and editorials should also comply with the same structure and format except subtitles and abstracts are unnecessary. Manuscripts for "Readers' Forum" shall be comments on or impressions of articles in *Synthesiology*, or beneficial information for the readers, and should be written in a free style of no more than 1,200 words. Editorials and manuscripts for "Readers' Forum" will be reviewed by the Editorial Board prior to being approved for publication.
3.1.3 Research papers should only be original papers (new literary work).
3.1.4 Research papers should comply with various guidelines of research ethics.

3.2 Structure

3.2.1 The manuscript should include a title (including subtitle), abstract, the name(s) of author(s), institution/contact, main text, and keywords (about 5 words).
3.2.2 Title, abstract, name of author(s), keywords, and institution/contact shall be provided in Japanese and English.
3.2.3 The manuscript shall be prepared using word processors or similar devices, and printed on A4-size portrait (vertical) sheets of paper. The length of the manuscript shall be, about 6 printed pages including figures, tables, and photographs.
3.2.4 Research papers and editorials shall have front covers and the category of the articles (research paper or editorial) shall be stated clearly on the cover sheets.
3.2.5 The title should be about 10-20 Japanese characters (5-10 English words), and readily understandable for a diverse readership background. Research papers shall have subtitles of about 15-25 Japanese characters (7-15 English words) to help recognition by specialists.
3.2.6 The abstract should include the thoughts behind the integration of technological elements and the reason for their selection as well as the scenario for utilizing the research results in society.
3.2.7 The abstract should be 300 Japanese characters or less (125 English words). The Japanese abstract may be omitted in the English edition.
3.2.8 The main text should be about 9,000 Japanese characters (3,400 English words).
3.2.9 The article submitted should be accompanied by profiles of all authors, of about 200 Japanese characters (75 English words) for each author. The essential contribution of each author to the paper should also be included. Confirm that all persons who have made essential contributions to the paper are included.
3.2.10 Discussion with reviewers regarding the research paper content shall be done openly with names of reviewers disclosed, and the Editorial Board will edit the highlights of the review process to about 3,000 Japanese characters (1,200 English words) or a maximum of 2 pages. The edited discussion will be attached to the main body of the paper as part of the article.
3.2.11 If there are reprinted figures, graphs or citations from other papers, prior permission for citation must be obtained and should be clearly stated in the paper, and the sources should be listed in the reference list. A copy of the permission should be sent to the Publishing Secretariat. All verbatim

quotations should be placed in quotation marks or marked clearly within the paper.

3.3 Format

3.3.1 The headings for chapters should be 1, 2, 3…, for subchapters, 1.1, 1.2, 1.3…, for sections, 1.1.1, 1.1.2, 1.1.3.
3.3.2 The text should be in formal style. The chapters, subchapters, and sections should be enumerated. There should be one line space before each paragraph.
3.3.3 Figures, tables, and photographs should be enumerated. They should each have a title and an explanation (about 20-40 Japanese characters or 10-20 English words), and their positions in the text should be clearly indicated.
3.3.4 For figures, clear originals that can be used for printing or image files (resolution 350 dpi or higher) should be submitted. In principle, the final print will be 15 cm × 15 cm or smaller, in black and white.
3.3.5 For photographs, clear prints (color accepted) or image files should be submitted. Image files should specify file types: tiff, jpeg, pdf, etc. explicitly (resolution 350 dpi or higher) . In principle, the final print will be 7.2 cm × 7.2 cm or smaller, in black and white.
3.3.6 References should be listed in order of citation in the main text.

Journal – [No.] Author(s): Title of article, *Title of journal* (italic), Volume(Issue), Starting page-Ending page (Year of publication).
Book – [No.] Author(s): *Title of book* (italic), Starting page-Ending page, Publisher, Place of Publication (Year of publication).

4 Submission

One printed copy or electronic file of manuscript with a checklist attached should be submitted to the following address:

Synthesiology Editorial Board
c/o Publication Office, Public Relations Department, National Institute of Advanced Industrial Science and Technology (AIST)
Tsukuba Central 2, 1-1-1 Umezono, Tsukuba 305-8568
E-mail: synthesiology@m.aist.go.jp

The submitted article will not be returned.

5 Proofreading

Proofreading by author(s) of articles after typesetting is complete will be done once. In principle, only correction of printing errors are allowed in the proofreading stage.

6 Responsibility

The author(s) will be solely responsible for the content of the contributed article.

7 Copyright

The copyright of the articles published in "*Synthesiology*" and "*Synthesiology English edition*" shall belong to the National Institute of Advanced Industrial Science and Technology (AIST).

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Letter from the editor

Synthesiology Volume 3 Issue 2 has now been published with the efforts of the authors and the reviewers.

In this issue, we have an article on the general discussion held in a special session called "Synthesiology: knowledge for interdisciplinary consilience" organized by the Transdisciplinary Federation of Science and Technology. The article describes the discussions on the synthesis and combination of knowledge and the scenario, to match and link the "knowledge" generated from scientific and technological researches to the social demands and values that are continuously changing. The discussions remind us that it is mandatory for the research and the researchers to interact with society.

Five papers were published in this issue, and there are two papers that are different from the ones that had been published so far. One is a paper on human resource training. It describes the efforts of the Graduate School of System Design and Management (SDM), Keio University that was established to educate the SDM specialists. The individual elements of the graduate school education are described very specifically, and the synthesis and integration of each elements as well as the scenario are discussed in terms of the education of desired human resources. In Japan today, there seems to be multitudes of training programs, and I hope such programs are able to meet the social demands. The second paper is a reflection on the Cyber Assist Project. The activities of the Cyber Assist Research Center (CARC) that started with the establishment of AIST are the precursors of the current service engineering, and the results of the *Type 2 Basic Research* are discussed. The strong feeling that "if it was continued for 10 years" is expressed, but the findings of the Cyber Assist Project have been integrated as components of the current service engineering research, and I hope it will eventually come to full bloom as a major contribution of AIST.

In April 2010, AIST endeavored on the five-year Third Mid-term Plan. In the Third Period, the plan is to engage in R&D with focus on "solving the issues of the 21st century" and "strengthening the open innovation hub function", in synch with the new growth strategy set forth by the government. To achieve the objectives of the Third Mid-term Plan, AIST will promote *Full Research*, or the continuous research starting from basic research with known exit and ending with product realization. This is expected to link the results of basic research to product realization conducted by private companies, to contribute to the innovations in Japan. I hope the results born from the scenarios "in society, for society" will be published in this journal with submissions from both inside and outside of AIST, and that *Synthesiology* will play the role of linking "knowledge" and "society". Please give us your support in our third year.

Senior Executive Editor
Masahiro Seto

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-English edition

Messages from the editorial board

Research papers

Report

Editorial policy
Instructions for authors

"Synthesiology-English edition" is a translated version of "Synthesiology" which is published quarterly, ISSN 1882-6229, by AIST. Papers or articles published in "Synthesiology-English edition" appear approximately four months after the publication of the original "Synthesiology".

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