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Synthesiology

English edition

Development of high efficiency flexible solar cells

Safety assessment of high-level nuclear waste disposal in Japan from the standpoint of geology

Improvement of reliability in pressure measurements and international mutual recognition

Efficient production of active form of vitamin D_3 by microbial conversion

Synthesiology editorial board

2011

4

Synthesiology-English edition 4 2011

National Institute of Advanced Industrial Science and Technology (AIST)

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,

"*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". The views expressed in translated version are exclusively those of the Japanese authors and editors. The Japanese authors are generally consulted regarding the translation of their papers, but are not responsible for the published English version.

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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.

Synthesiology – English edition Vol.4 No.4 (Mar. 2012)

Contents

Development of high efficiency flexible solar cells

— Management of “Flexible Solar Cell Substrates Consortium” and its achievements —

Atsushi Masuda

[Translation from *Synthesiology*, Vol.4, No.4, p.193-199 (2011)]

Elemental technological challenges required for the development of flexible solar cells have been clarified and a consortium system to solve the problems has been established based on industry-academia-government collaboration. The technology to form texture on polymer base materials indispensable for high efficiency has been developed, and we have succeeded in preparation of thin-film silicon solar cells on polymer base materials whose efficiency is comparable with that of cells prepared on glass substrates. The stage has already moved from research within the consortium to practical realization research in individual enterprises. Establishment process, management policy, patent strategy and training of young researchers of the consortium are described in this paper.

Keywords **:** Flexible thin-film solar cells, consortium study, polymer base materials, texture, training of young researchers

1 Objectives for the development of flexible solar cells

Recently, the market for photovoltaics is expanding dramatically, and the growth rate is kept at about 40~50 % compared to the previous year. The annual world production volume surpassed 23 GW in 2010. This figure is equivalent to 23 nuclear power plants at peak power. The market is expected to grow steadily, and the annual production volume will reach at least 100 GW by 2030. For the diffusion and expansion of photovoltaics, the lowering of installation cost through weight reduction and the expansion of installation space are important. Since cover glass is used for the light-receiving surface in ordinary solar cell panels, in many cases, the panels cannot be installed on roofs with low withstand load, and the installation may incur considerable cost due to the additional reinforcement of the roof. On the other hand, the flexible solar cells using polymer or metal sheet as base material do not use glass, and weight reduction to about a fraction or 1/10 of the conventional solar cell panel may be possible. This also contributes to increasing the installable space. Other advantages of the flexible solar cell include: it can be applied to curved surfaces, will not break like glass and therefore is safe, has excellent productivity since the roll-to-roll process can be used in manufacturing, and it is easy to transport and store.

2 Strategy and scenario for the development of flexible solar cells

Of the various flexible solar cells, the flexible thin-film silicon solar cell is already being mass-produced in Japan, and is diffusing gradually. It is known that the thin-film silicon does not have high photoabsorption coefficient, and the photoabsorption layer cannot be thickened to suppress the decreased performance due to light irradiation. Therefore, to increase efficiency, it is important to find some way of confining the light in the photoabsorption layer. In general thin-film silicon solar cells, the sunlight is utilized efficiently by using the texture formed on the transparent conductive oxide surface for confinement. For example, in the superstrate thin-film silicon solar cell, where the layers are formed from the front side in the order of transparent conductive oxide, p-type silicon doped layer, i-type silicon photoabsorption layer, n-type silicon doped layer, transparent conductive oxide, and back-side metal electrode, the light is irradiated from the glass substrate side as shown in Fig. 1. Therefore, to achieve increased efficiency, the texture is formed on the transparent conductive oxide surface in the front side to scatter the light and confine it to the photoabsorption layer.

Asahi-U manufactured by Asahi Glass Co., Ltd. is a glass substrate on which fluorine doped tin oxide (FTO) transparent electrode is formed, and it is known that the FTO surface with texture optimal for amorphous silicon solar cells can be obtained. In Asahi-U, substrate temperature of about 500 ºC is necessary in the coating process for FTO to form the optimal texture. However, there is no general-use polymer base material with heat resistance of 500 ºC, and higher performance of the flexible thin-film silicon solar cells cannot be achieved by using the same method as in the glass substrate.

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To solve this issue, the strategy of increasing the heat resistance of the polymer base material can be considered, but in this research, we investigated the way to produce the equivalent characteristic as the texture formed on the transparent conductive oxide, by developing a new technology of forming the texture on the polymer base material itself. By doing so, the transparent conductive oxide itself does not have to be prepared at high substrate temperature necessary for the texture formation, and the film preparation condition can be eased greatly.

Such technological development could not be done by the Research Center for Photovoltaics (RCPV; currently, Research Center for Photovoltaic Technologies), AIST alone. While RCPV had abundant experiences and know-how for the fabrication of solar cells, it did not have the technology for the polymer base material or roll-to-roll apparatus necessary to fabricate the flexible solar cells. Therefore, for the smooth and quick execution of research, we conducted a joint research in the industry-academia-government collaborative consortium style, where the findings of industry, academia and government could be accumulated. This was led by the material and apparatus manufacturers that possessed the technologies.

There are roughly two objectives of the consortium style joint research. One is to accelerate the development by rapid accumulation of technologies, where multiple private companies engage in concentrated research on a topic, and this may also accelerate the transfer of the results to industry. Second is to conduct on-the-job training of the joint researchers dispatched from the private companies to AIST, and the building of human network as well as the sharing of research results can be expected through the collaborative research by multiple companies. The following account depicts the activities of the "Flexible Solar Cell Substrates Consortium" that was established to execute the R&D according to the above scenario.

The first phase of the "Flexible Solar Cell Substrates Consortium" was from June 2006 to March 2008. Eight companies participated: Ishikawajima-Harima Heavy Industries Co., Ltd. (changed its name to IHI Corporation), Ishikawa Seisakusho, Ltd., Kimoto Co., Ltd., Tsutsunaka Plastic Industry Co., Ltd. (merged with Sumitomo Bakelite and changed its name to Sumitomo Bakelite Co., Ltd.), Teijin DuPont Films Japan Ltd., The Nippon Synthetic Chemical Industry Co., Ltd., Mitsubishi Gas Chemical Company, Inc., and Reiko Co., Ltd. The Industrial Research Institute of Ishikawa and a solar cell company served as observers. Figure 2 shows the organization of the first phase of the consortium.

The second phase was from April 2008 to March 2010. Seven companies participated: Arisawa Manufacturing Co., Ltd., Kimoto Co., Ltd., Sumitomo Bakelite Co., Ltd., Teijin DuPont Films Japan Ltd., Toshiba Machine Co., Ltd., The Nippon Synthetic Chemical Industry Co., Ltd., and Mitsubishi Gas Chemical Company, Inc. The same solar cell company from the first phase participated as the observer. The third phase is in progress since April 2010, with the participation by five companies: Kimoto Co., Ltd., Teijin DuPont Films Japan Ltd., Toshiba Machine Co., Ltd., The Nippon Synthetic Chemical Industry Co., Ltd., and Mitsubishi Gas Chemical Company, Inc. Currently, the research has entered the phase of realization. Figure 3 shows the realization scenario of this consortium, limited to the content described in this paper, and indicates the members involved in this research topic and their role divisions.

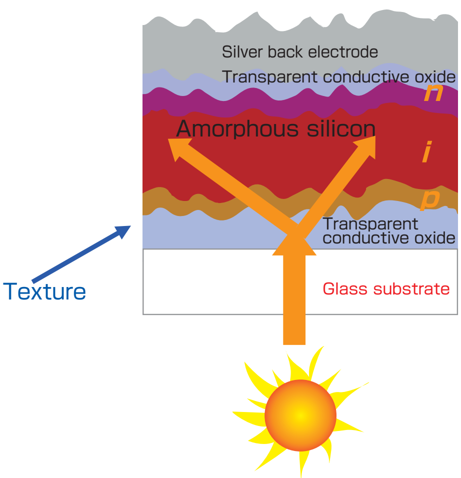

Fig. 1 Principle of light confinement in amorphous silicon solar cells

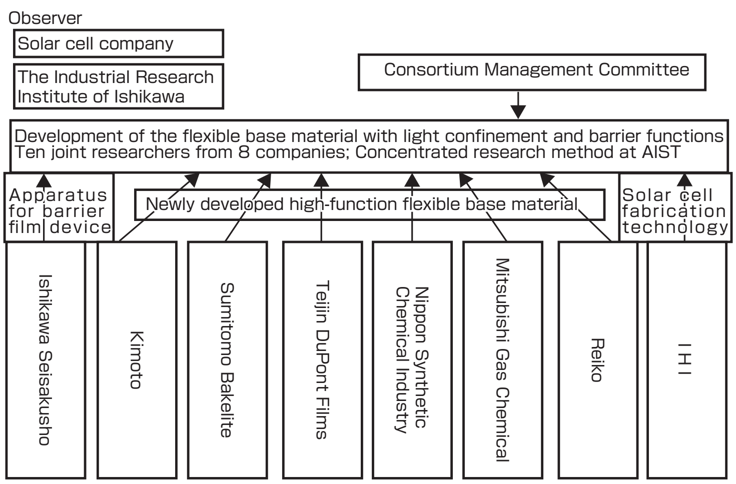

Fig. 2 Organization of the "Flexible Solar Cell Substrates Consortium" (Phase 1)

3 Elemental technology topics needed for the development of flexible solar cells

The “Flexible Solar Cell Substrates Consortium” designated the basic elemental technology to be the technology for forming the texture suitable for light confinement in the thin-film silicon solar cells, onto the polymer base material itself. By doing this, the transparent conductive oxide does not have to have the texture added, and this will ease the conditions for film preparation of the transparent conductive oxide such as the substrate temperature, and the process will be applicable to the polymer base materials with low heat resistance. The idea of forming the texture onto the polymer base material itself was not obtained for the first time in this consortium, but several prior reports had been published[1][2]. For example, the transfer method by stamp with the texture, or the method using lithography had been suggested. However, the transfer by stamping is limited to thermoplastic polymer material only, and the printed texture does not have sufficient precision or reproducibility. In the method using lithography, it is difficult to obtain the ideal texture, and the lithography apparatus is expensive. In this research, the requirements were set that the technology should be universal where any polymer base material could be used and the texture suitable for light confinement could be transferred accurately. We investigated the new method for forming the texture onto the polymer base material. As a result, we concluded that the desirable results could be achieved with the substrate laminated with UV curable acrylic resin onto which the texture had been transferred from a mold. In this paper, we present the results of the comparison of the base material to which the texture of the Asahi-U had been transferred and the base material to which the texture of the moth-eye structure, which is known as a non-reflecting structure, had been transferred.

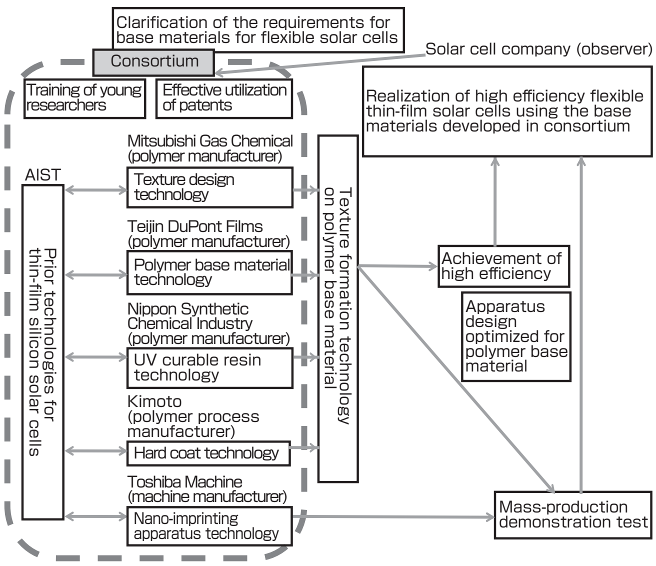

Fig. 3 Scenario for the realization of flexible thin-film silicon solar cells in a consortium style

The examples using the polyethylene naphthalate (PEN) film and polyimide (PI) film as the polymer base materials will be presented in this paper. However, the base materials that can be used in this method are not limited to those films, and the method has been shown to be effective in other polymer base materials such as polyethylene terephthalate (PET) and polycarbonate (PC). It has also been found to be usable on glass substrates.

4 Organization and management of the consortium

4.1 Role division in the consortium

While the topics of elemental technologies necessary for the development of flexible solar cells became clear, it was necessary to combine the material technologies for polymer base material and UV curable acrylic resin, process technology for laminating the layers, simulation technology for optimal texture, roll-to-roll apparatus technology needed for mass-production, and process and device technologies for thin-film silicon solar cell fabrication. The RCPV did not have all such technologies, and as mentioned in chapter 2, it was determined that the research should be carried out as a joint research in the industry-academia-government collaboration consortium. In this chapter, we present the specific management policy applied to the consortium.

In the “Flexible Solar Cell Substrates Consortium”, AIST organized the research and was in charge of the investigation of the conditions for fabricating the solar cells and the transparent conductive oxide on the polymer base material, while the participating companies were in charge of the development of the polymer base material. As shown in Fig. 3, the role division of the participating companies was as follows: Mitsubishi Gas Chemical Company, Inc. designed the texture by simulation, Teijin DuPont Films Japan Ltd. developed and supplied the PEN film (Teonex®), The Nippon Synthetic Chemical Industry Co., Ltd. developed and supplied the UV curable acrylic resin, Kimoto Co., Ltd. applied the hard coat to the polymer base material surface, and Toshiba Machine Co., Ltd. was in charge of the transfer of the texture to the acrylic resin by nano-imprinting technology using the single substrate method or the roll-to-roll method. The texture design is currently under development, and in this paper, only the results of the transfer of the moth-eye structure and the Asahi-U texture will be described. While Asahi-U uses the texture obtained by self-formation, the base material developed in this consortium has the texture formed by transfer, and the textures can be varied arbitrarily. Therefore, through the precise design of the texture, a solar cell with performance surpassing that using the Asahi-U substrate may be achieved. This implies that high efficiency solar cells can be achieved on polymer instead of the current thin-film silicon solar cells formed on a glass substrate. Therefore, the design of the texture is an extremely important research topic.

4.2 Management of the monthly research meeting

This consortium employed the concentrated research method in which the researchers were dispatched from the participating companies to AIST. A monthly research meeting in which the researchers of all companies participated was held to share the results. Through the discussions at the meetings, the setting of the collaborative topic among the participants and the review of the direction of the research topic were done flexibly. Through such activities, derivative results that were not expected at the start of the research were obtained. Therefore, comments at the monthly research meetings were considered extremely important, and the minutes of the meetings were kept carefully, since they might become evidences for recognizing a patent.

Since the companies that may be mutual competitors participated in this consortium, we set the following rules for the joint monthly research meetings. The synthesis methods and know-how that were regarded as the most important factors by the materials manufacturers that were the main members of the consortium did not have to be disclosed. The synthesis of the materials would be basically done within the participating company, and in principle, the findings should not be shared. On the other hand, the results concerning the fabrication of solar cells were considered as common knowledge among the participating companies, and in principle, disclosure was required for the characteristics of the materials that may affect the solar cell performance. Also, when combining the materials, it might be necessary to know the synthesis method for the component materials, and in such cases, separate non-disclosure agreements were signed among limited members. We believe one factor of the success of this consortium was to clearly separate the technologies that should be shared by the participants and the technologies that would be developed individually. By doing so, the advantages of consortium participation were maximized and the individual interests of the companies were protected.

4.3 Management committee and patent strategy

We set the Consortium Management Committee composed of the representatives of the participating companies and AIST to be the highest decision-making body. The Management Committee determined the handling of the results, recognized the inventor when a patent was made, and adjusted the conflicting interests. By having the participants follow its decisions, fair and transparent management of the consortium became possible and smooth management was realized. For the patents created in the consortium, the organization to which the inventor belonged became the applicant, and the share was divided according to the degree of contribution. However, participants who were not applicants may be licensed to use the patent upon payment of the appropriate licensing fee. This meant that one of the motivations to participate in the consortium was that there would be no domination by a single company. The handling of the patents became possible by setting the two basic principles: the results pertaining to solar cells were common assets of the consortium, and the findings and know-how pertaining to the materials that came from the R&D within the participating companies should not be brought into the consortium. Moreover, the results obtained at the consortium would be basically published after the patent application was filed.

4.4 Policy for training young researchers

Although this consortium was operated by private funds without public money, majority of the apparatuses used in the research were purchased by AIST's research funds before the establishment of the consortium, and much know-how applied to the research was developed by AIST. Also, AIST provided matching funds where the upper limit was the total of joint research fundings from the private companies. Considering these situations, the research results are actively published to fulfill the mission as a public research institute. In the publication of research results, we believe it was beneficial in training the young researchers dispatched from the participating companies, to do presentations at international academic conferences and to write papers in English. There were cases where the research greatly advanced from the comments provided at the academic conferences, and cases where business opportunities expanded for the participating company through newly formed human networks. Many seminars were held as part of the consortium activities for the joint researchers dispatched to AIST for the purpose of acquiring a wide-range of knowledge about solar cells, so they would be able to act as experts on solar cells at their respective companies after the completion of the joint research.

5 Results of the consortium research

The result of the consortium research was the development of the base material consisting of UV curable acrylic resin onto which the surface texture of Asahi-U, the glass with

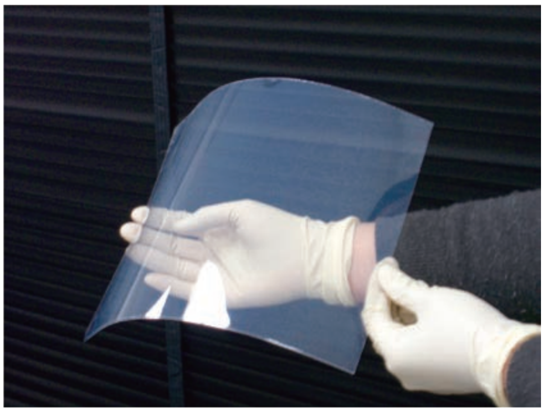

Fig. 4 Photograph of PEN film onto which the texture of Asahi-U has been transferred

transparent conductive oxide manufactured by Asahi Glass, was transferred and then laminated onto the PEN or PI films. Figure 4 shows the photograph of the developed base material. The base film of this material is PEN. The light scattering is reinforced by the transferred texture, and the film appears white to the naked eyes.

Figure 5 shows the outline of the fabrication method of the base material. Since the texture became reversed if the Asahi-U or the moth-eye structure was transferred directly, as shown in the scanning electron microscope photograph in Fig. 5, the mold to which the desired structure was initially transferred was used. The UV curable acrylic resin monomer was coated to the mold, and then the general-use PEN or PI film was laminated on top. By irradiating with ultraviolet light after laminating, the monomer changed into polymer. When the film was peeled off from the mold, the polymer material laminated with acrylic resin onto which the texture was transferred was obtained. As shown in the atomic force microscope photograph in Fig. 5, it can be seen that the texture is present on the base material surface. This method can be used not only for the single substrate method shown in Fig. 5, but it has been proven applicable to the roll-to-roll method as shown in Fig. 6, and there seems to be no barrier to mass production.

The current-density and voltage characteristics of the amorphous silicon solar cells fabricated on the PI and PEN films are shown in Fig. 7, and the quantum efficiency spectra are shown in Fig. 8. The amorphous silicon solar cell has a substrate structure with the following structure: polymer base material, acrylic resin layer with texture, gallium doped zinc oxide layer, silver back surface electrode layer, gallium doped zinc oxide layer, n-type amorphous silicon doped layer, i-type amorphous silicon photoabsorption layer, p-type amorphous silicon doped layer, indium tin oxide transparent electrode, and silver collector electrode. It is shown in Fig. 7 that sufficient light confinement is obtained on the polymer base material, and the current density increases by using the base material with the texture. From Fig. 7, it also becomes clear that there is

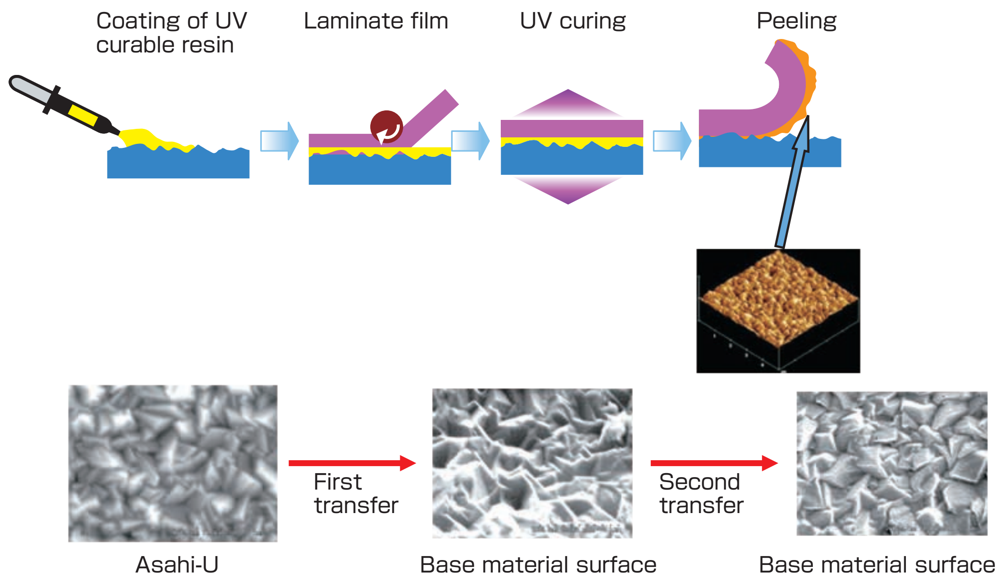

Fig. 5 Outline of the base material fabrication by single-substrate method and the microscope photograph of Asahi-U and base material surfaces

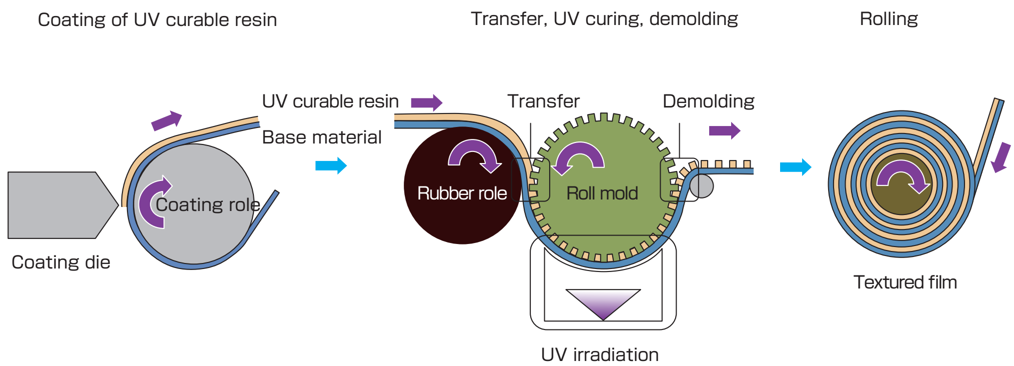

Fig. 6 Outline of base material fabrication method by roll-to-roll method

Table 1. Characteristics of the solar cells fabricated on various base materials

Base material	Short-circuit current density (mA/cm²)	Open-circuit voltage (V)	Fill factor	Efficiency (%)
Asahi-U	15.7	0.88	0.59	8.2
Asahi-U transferred PI	15.0	0.84	0.65	8.3
Non-textured PI	11.7	0.83	0.68	6.5
Asahi-U transferred PEN	15.6	0.87	0.60	8.1
Moth-eye transferred PEN	14.1	0.87	0.62	7.7

an optimal shape of the texture, and the current density of the texture of the transferred moth-eye structure does not come close to the current density of the texture of the transferred surface structure of Asahi-U. Also, from Fig. 8, when the base material on which the texture is formed is used, it is shown that the quantum efficiency in the long-wavelength region increases due to light confinement. As shown in Table 1, in the case where the polymer base material was used, solar cell properties equivalent to the one fabricated on Asahi-U were obtained. This means that we succeeded in fabricating the amorphous silicon solar cell on the polymer base material, with equivalent performance to the one fabricated on a glass substrate. With the research result from this consortium, one of the participating companies, Toshiba Machine Co., Ltd., won the Nanotech Award in the Nano-fabrication Technology Category of the 2009 International Nanotechnology Exhibition and Conference (nano tech 2009). Also, although the details will not be discussed in this paper, a participant of the consortium, Sumitomo Bakelite Co., Ltd. fabricated the amorphous silicon solar cell with superstrate structure using this transfer technology, on SUMILITE® that is its organic-inorganic hybrid film, and demonstrated its effectiveness[3].

In this consortium, the formation of the barrier film onto the polymer base material was investigated with Ishikawa Seisakusho, Ltd. and the Industrial Research Institute of Ishikawa, for the purpose of realizing a highly weather-resistant flexible solar cell. To facilitate the introduction to material companies, we set the goal of not using monosilane, a special material gas, as the raw material of the silicon nitride barrier film by chemical vapor deposition. When hexamethyldisilane

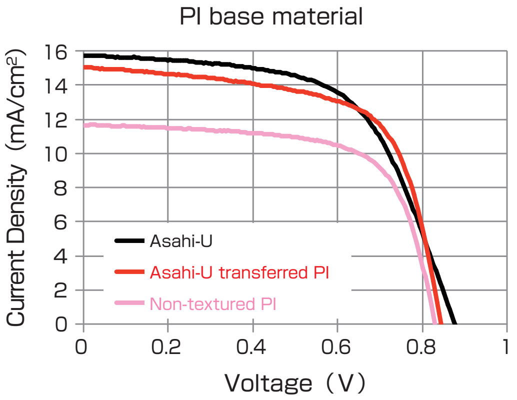

Fig. 7 Current-density – voltage characteristics of the amorphous silicon solar cells fabricated on PI and PEN films

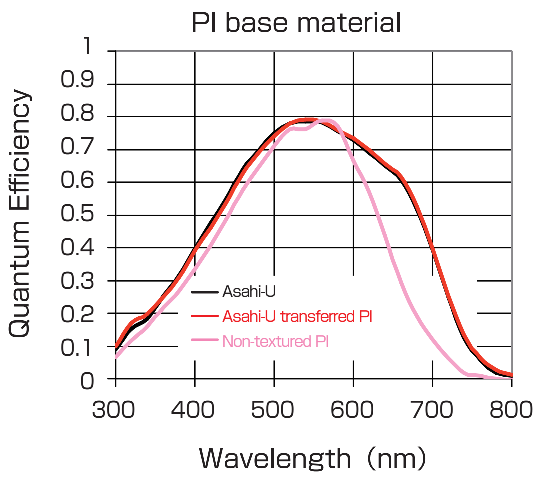

Fig. 8 Quantum efficiency spectra of the amorphous silicon solar cells fabricated on PI and PEN films

was used as raw material gas, the water vapor transmission rate of 0.02 g/m^{2}day was achieved in the barrier film formed at the deposition rate of 40 nm/min onto the PEN film.

6 Remaining issues

It has been six years since the start of the "Flexible Solar Cell Substrates Consortium", and the goals at research phases and laboratory levels were mostly achieved by accumulating the experiences and the findings of AIST and the participating companies. For product realization, the prototype fabrication at the solar cell company will become important. To replace the current base materials with the materials developed at the consortium, the design of the solar cell device structure may have to be changed, and the decisions of the solar cell company will become important. In the future, the stage will move to the development phase with actual application in view, through collaboration with the solar cell company that has participated as an observer from the initial research stage of the consortium. AIST, the participating companies, and the solar cell company started consideration for technological transfer to the solar cell company. Also, utilizing the consortium management method for the "Flexible Solar Cell Substrates Consortium", the "Consortium Study on Fabrication and Characterization of Solar Cell Modules with Long Life and High Reliability" was established with 44 organizations including 33 private companies and the Photovoltaic Power Generation Technology Research Association, starting October 1, 2009, to engage in research to reduce the cost of photovoltaics through increased lifetime and reliability of the solar cell module, as well as the development of the accurate testing method to ensure reliability. Currently, we engage in R&D with the phase II consortium with 78 organizations including the private companies.

The fusion of knowledge from wide-ranging fields from materials, processes, devices, and systems is necessary for the technological development of photovoltaics. In the field of photovoltaics, it is well known that the close industry-academia-government collaboration was done from the initial Sunshine Project that was started immediately after the First Oil Shock, and this bloomed as the current industry. Needless to say, the technological developments through the collaboration of various fields will become even more important for the further advancement of the photovoltaic industry. Moreover, as much as the technological development, for the continuous development of the industry, training of young people such as the researchers of the private companies, post-doctors, and students is important through on-the-job training in the industry-academia-government collaboration. We are working on the consortium management so the joint researches by the industry-academia-government collaboration in the consortium style conducted by the Research Center for Photovoltaic Technologies of AIST will contribute to the development of new technologies, technology transfer, and training of young researchers.

Acknowledgements

The research results of the "Flexible Solar Cell Substrates Consortium" described in this paper were obtained through the joint research with: Toshikazu Niki of Ishikawa Seisakusho, Ltd.; Joji Nobe and Susumu Kurishima of Kimoto Co., Ltd.; Yusuke Inoue and Hideo Umeda of Sumitomo Bakelite Co., Ltd.; Rei Nishio and Takashi Nakahiro of Teijin DuPont Films Japan Ltd.; Akihiko Hagiwara of Toshiba Machine Co., Ltd., Katsuhiko Katsuma and Seiichiro Hayakawa of The Nippon Synthetic Chemical Industry Co., Ltd.; Terutaka Tokumaru of Mitsubishi Gas Chemical Company, Inc.; and Yukiko Hara, Chizuko Yamamoto, Minoru Karasawa, Yoko Takeyama (currently, Tokyo Institute of Technology), and Nana Hozuki (currently, Photovoltaic Power Generation Technology Research Association) of AIST. For their valuable advice on this research, I am grateful to: Michio Kondo, director; Takashi Koida, senior researcher; and Takuya Matsui, senior researcher, Research Center for Photovoltaic Technologies, AIST.

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Discussion with Reviewers

1 Title

Comment (Yoshiro Owadano, Environment and Energy, AIST)

This is a very valuable paper as it is a report of a large-scale consortium for technological development originally planned and organized by AIST. Please modify the main title and the subtitle of the paper so they will indicate the content of the development and that it was managed in a consortium style.

Answer (Atsushi Masuda)

As you suggested, I modified the title to: Development of high efficiency flexible solar cells - Management of “Flexible Solar Cell Substrates Consortium” and its achievements.

2 Breakdown of the contents and titles for each chapter

Comment (Yoshiro Owadano)

Please use specific titles for each chapter such as shown below and break down the rather long text into paragraphs according to content, to make the paper easier to read. My suggestion is breakdown of contents as follows:

- Background and setting of themes for technological development
- Organization of the consortium and management method
- Results obtained

etc..

Answer (Atsushi Masuda)

I reorganized the structure of each chapter, and changed the chapter titles to reflect the content. For chapter 4, in response to your suggestion, I divided the text into subchapters and added some details.

Safety assessment of high-level nuclear waste disposal in Japan from the standpoint of geology

— Methodology of long-term forecast using geological history —

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Concerning the geological disposal system of high-level nuclear waste, the term subject to safety assessment of the system after closure is considered to exceed several hundred thousand years. We are faced with the major issues of how to guarantee such long-term safety and on what kind of criteria the system should be regulated. Because the Japanese islands lie in the mobile belt where earthquakes and volcanic activities often occur, a variety of geological issues required for the safety assessment have to be taken into consideration. In this paper, issues are extracted from a series of facts or scenario where incidents occur one after another provoked by one incident, and one such example is given of analysis results of the eruption history of volcanic activities. A methodology for long-term forecast addressing the causes of geological phenomena is also presented.

Keywords : High-level nuclear waste, geological disposal, seismicity, volcanism, long-term forecasting

1 Introduction

Geology is a science that studies the series of changes in the earth that occurred in the past, as described in the *Principles of Geology* by Charles Lyell, written in the early half of the 19th century. The greatest contribution of geology to humankind is the discovery of deep time, and 4.6 billion years of earth history have been unraveled from the records left in the rocks and strata. The stronghold of geology is the understanding of how a region was formed, by looking at the natural phenomenon in a time frame of several thousand to several million years. Geology was traditionally deployed in the exploration of natural resources such as oil and metals, and has recently been applied to mitigate the geological disasters such as earthquakes and volcanic eruptions.

Recently, a new issue that must be handled geologically arose due to the changes in social demand. This is the issue of geological disposal where the radioactive waste from nuclear power generation is buried underground, far away from the environment in which people live. To ensure safety of this disposal, the underground geological environment must be stable over a long term of several hundred thousand years. It is impossible to guarantee the safety over such time scale by covering the waste with an artificial structure using engineering methods. Safe disposal is possible when the underground geological environment itself functions adequately as the natural barrier against nuclear waste. Only geological knowledge can provide solutions to the issue of long-term stability assessment required for geological disposal, and geological disposal will not be realized without the safety regulation and assessment utilizing this knowledge to the maximum. Figure 1 shows the outline of the relationship of the investigation and assessment items for geological disposal site investigation and the security after closure of the site. This paper describes the extraction of the geological investigation and assessment items required for the safety assessment of geological disposal, and the methodology for long-term forecast based on the model building for the investigated geological phenomena.

2 What is geological disposal?

According to the Japanese law, various radioactive wastes must be disposed in either the category 1 or the category 2 waste disposal facility, depending on the radioactivity level. Category 1 is the so-called geological disposal, and it is a disposal method taken when the wastes must be isolated from the biosphere for a long time, and therefore is buried underground at 300 m or deeper. The wastes that must be disposed in this manner include the high-level radioactive (HLR) waste and certain low level radioactive (LLR) waste (such as the long half-life, low-heat-generating radioactive wastes). The HLR waste is the vitrified HLR waste liquid generated in the processing of the spent fuel. It is characterized as a nuclear waste with a long "lifespan" because it contains radionuclides with a long half-life. This is the reason for selecting the geological disposal method that does not require human management. The time required for the radioactivity of the HLR waste to drop to the level of original uranium ore (high concentration of 1 % grade ore) is about a hundred thousand years after power generation[1]. The category 2 waste

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disposal is a method that assumes human intervention for management, and the LLR waste other than the one mentioned above is buried in relatively shallow ground.

While the forms of radioactive waste disposal differ by the waste type, all must maintain the radiation exposure of the general public at certain value or less, and must keep it as low as reasonably achievable[2]. Considering this point as basic security, the final disposal site must be constructed from several layers of barriers consisting of the artificial barrier that includes the waste material itself and the natural barrier or the surrounding geological structures[3]. The artificial barrier plays the role of containing the radionuclides as long as possible and mitigating the release into the natural barrier. The natural barrier is expected not only to isolate the radionuclides from the biosphere, but also to provide a stable external environment to maintain the constant environment for the artificial barrier over a long period. These barriers are expected to function complementarily. The waste material itself and the multiple barriers around it are generally called the disposal system. In the case of the geological disposal, the time period that must be considered for the safety assessment of the closed disposal system must be over several hundred thousand years. The major issues are how to ensure such long-term security and what kind of standard should be set.

The geological disposal business of HLR waste in Japan is based on the "Specified Radioactive Waste Final Disposal Act" established in June 2000. This law states that the site selection is done in three stages as shown below.

(1) Selection of the preliminary investigation area (PIA): A survey of literature and other source materials (literature search) is done to select the PIA from the area that is reviewed by literature search.

(2) Selection of detailed investigation area (DIA): Land surface investigations including outcrop survey, boring, trench excavation, or physical exploration are conducted at the PIA, and the DIA is selected among the PIA candidates.

(3) Selection of the final disposal facility construction site: In addition to the detailed survey on the land, the actual facility is constructed underground, the physical and chemical properties of the strata are conducted, and the construction site for the final disposal facility is selected among the DIA candidates.

The Nuclear Waste Management Organization of Japan (NUMO) was established in October 2000 to conduct the disposal work based on the Specified Radioactive Waste Final Disposal Act. This organization has been soliciting disposal site candidates to the cities, towns, and villages throughout Japan since December 2002, but no local government has applied as of October 2011.

3 Extraction of the geological issues for the geological disposal in Japan based on FEP (feature, event, and process)

One of the major interests in the geological disposal in Japan is the point, "Is it possible to conduct sufficiently safe geological disposal in Japan where earthquakes strike frequently?" For the security of geological disposal, of course, it is necessary that the geological environment of

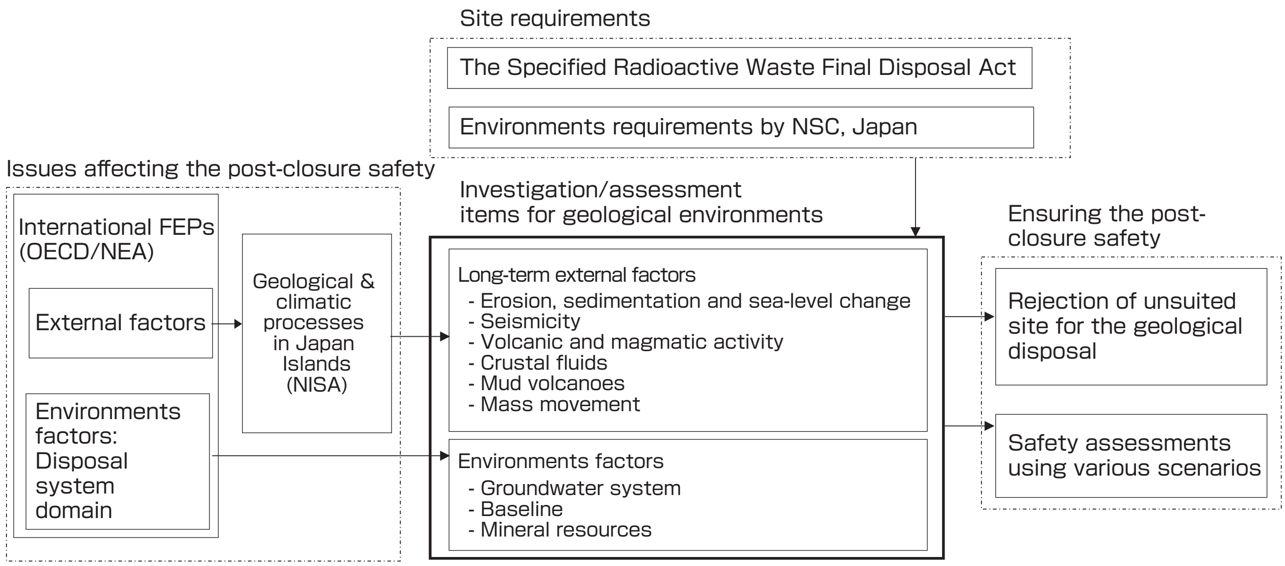

Fig. 1 Relationship between the issues affecting the site-selection survey and the post-closure safety on the geological disposal of high-level radioactive waste

the area where the disposal facility will be built is stable for a long period. The Specified Radioactive Waste Final Disposal Act requires the disposal site candidates that "there is no record of significant changes in the strata by natural phenomena such as earthquake, volcanic eruption, uplift, erosion, and others" and that "it is expected that significant change in the strata is not likely to occur due to such natural phenomena in the future". In geological disposal, it is important that the HLR waste is isolated in a stable geological environment where the effects of natural phenomena such as earthquakes will not extend. To do so, it is required to conduct a comprehensive and quantitative assessment on what kind of external impact there will be on the geological disposal system, through the long-term changes in the geological environment over a hundred thousand years. At the Research Core for Deep Geological Environments (formerly Research Center for Deep Geological Environments), AIST organized the knowledge necessary to investigate the safety regulations pertaining to the geological disposal, at the Waste Safety Subcommittee that was set under the Nuclear and Industrial Safety Subcommittee, Advisory Committee on Energy and Natural Resources, which is an advisory panel for the Minister of Economy, Trade and Industry.

Figure 2 shows the correlation diagram that identifies the phenomena that may affect the geological disposal system as external disturbances in Japan, based on the international FEP list for geological disposal created by the Nuclear Energy Agency, Organisation for Economic Co-operation and Development (OECD/NEA)[4]. The FEP is categorized into those with the geology-related FEPs that arise from the internal energy of earth "F1.2.01 Tectonic movement and orogeny", and the climate-related FEPs caused by the solar incident energy "F1.3.01 Climate change, global". In Fig. 2, these are arranged on the left and right, and the disposal system domain is shown in the lowest part. The whole process is seen as a series of phenomena (scenario) where one event undergoes a process to cause the next event (as shown by the arrows), and this in turn causes the next process and event. The FEPs in parenthesis that are not joined by the cause-effect arrows are eliminated from the investigation since their effects can be ignored in Japan.

The Research Center for Deep Geological Environments investigated the geological and climatic phenomena that may affect the aforementioned disposal system, and in 2007 publicized the "Technical Report on the Features for Preliminary Field Investigations of HLW Geological Disposals" (http://www.gsj.jp/GDB/openfile/files/no0459/0459index.html)[5]. This indicates the assessment items and investigation methods necessary for the security of the closed disposal site, in the investigations (various

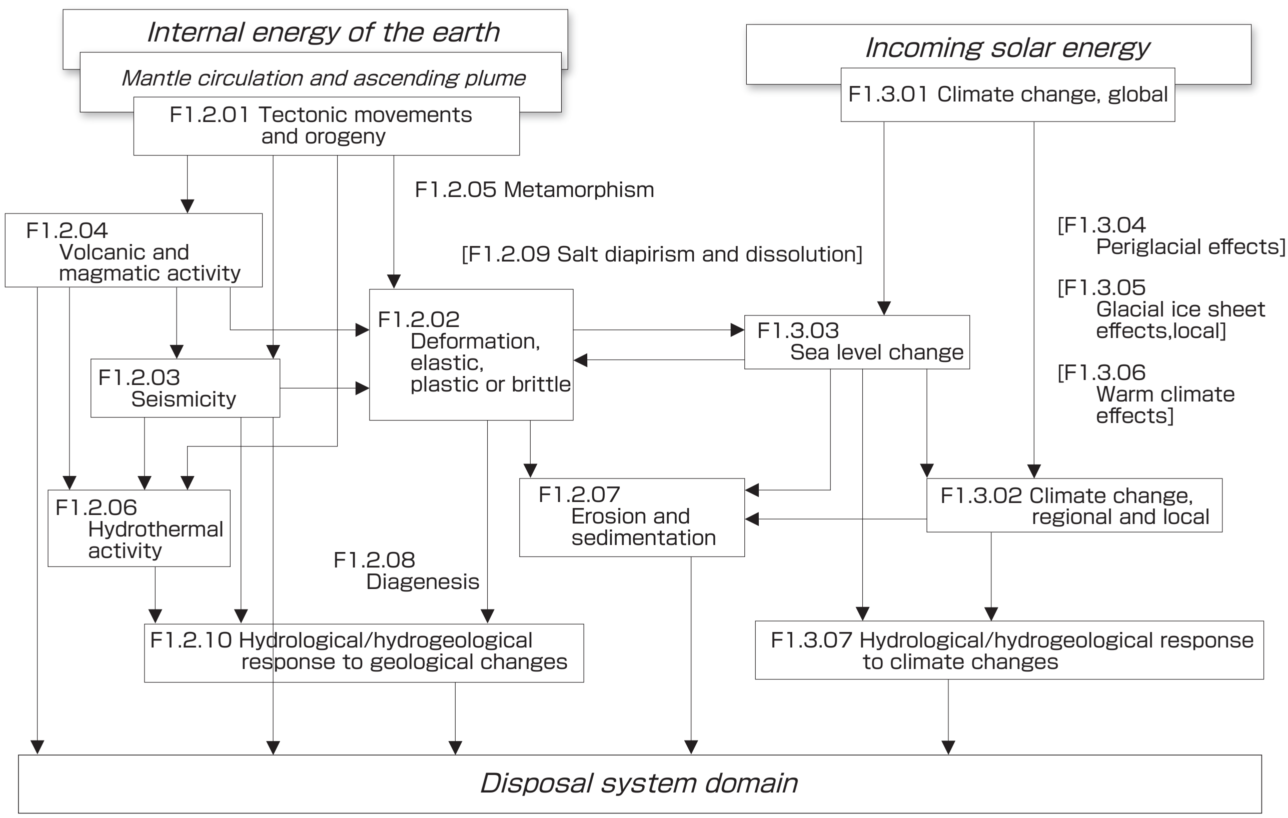

Fig. 2 Geological and climatic processes in Japan Islands using international FEPs database of OECD/NEA

Arrows indicate the effecting direction. FEPs in [ ] means ignorable ones in Japan Islands. After Yamamoto and Kodama[4] investigations from the land surface in the PIA selection phase) as designated by the Specified Radioactive Waste Final Disposal Act. The following items are extracted:

(1) Erosion, deposition, and sea level change

- It is necessary to avoid areas where the estimated erosion may become greater than the depth of burial, because the disposed material may become exposed to the surface.
- It is necessary to consider the effects of relative sea level change in the areas where the flow or quality of underground water may change and may affect the containment function of the radioactive materials in the future, due to the changes in relative sea level by uplift, subsidence, or glacial sea level change.
- It is necessary to consider the future stability of the tectonics that may affect the uplift and subsidence.

(2) Seismicity

- It is necessary to avoid the range to which the effect of the faulting may extend in areas that are found to have faults that were active in the Quaternary period, because the disposed material may be directly damaged due to the rupture along the fault.
- It is necessary to consider the range to which the effect of the rupture may extend if there is a large fault on the surface or underground, even if there was no activity in the Quaternary period, because there may be possibilities of reactivation and induced dislocation of the fault.
- It is necessary to consider the effect of the seismicity in areas where the seismicity may cause changes in the flow or quality of the groundwater that may affect the containment of the radioactive materials.
- It is necessary to consider the future stability for the tectonics that may affect the seismicity.

(3) Volcanic and magmatic activities

- It is necessary to avoid the areas that were found to have Quaternary volcanoes, because there are possibilities that the disposed materials may become directly damaged or pushed up to the surface by eruptions.
- It is necessary to avoid the areas where new volcanoes may emerge even if there are no Quaternary volcanoes, because there are possibilities that the disposed materials may become directly damaged or pushed up to the surface by eruptions.
- It is necessary to consider the effect of volcanic and magmatic activities in the areas around the Quaternary volcanoes or in the range with possibilities of large-scale eruptions, where there may be changes in the ground temperature or in the flow or water of the underground water that may affect the containment function of the radioactive substances in the future.
- It is necessary to consider the future stability of the tectonics that may affect the volcanic and magmatic activities.

(4) Crustal fluid

- It is necessary to consider the effect of the crustal fluid activities in the areas where there may be changes in the flow or quality of the underground water that may affect the containment function of the radioactive substances in the future, due to the activities of the crustal fluid.
- It is necessary to consider the future stability of the tectonics that may affect the crustal fluid activities.

(5) Mud volcano

- It is necessary to avoid the areas where there are mud volcanoes that were active in the Quaternary period, because there are possibilities that the disposed materials may become directly damaged or be pushed up to the surface by eruptions. (Mud volcano: phenomenon where the mud with abnormally high pressure gushes out to the surface with groundwater, gas, or sometimes oil.)

(6) Mass movement

- It is necessary to avoid the areas in which the effect of creep and ruptures may extend and where the signs of large-scale mass movement become apparent in the investigation, because the disposed materials may become directly damaged by the creep and fault ruptures due to slope movement. (Mass movement: general term for the movement of materials on the ground surface, and it includes landslides and debris flow.)

4 Methodology for long-term forecast

4.1 Basic thinking

As mentioned earlier, in the safety assessment of geological disposal, it is necessary to make forecasts of the geological and climatic phenomena for several hundred thousand years into the future. For example, the assessment of seismicity is divided into short-term (immediately before~about one year) and long term (about 1~100 years) according to the time scale in question, and following this categorization, the time span for the forecast for geological disposal must be called super long-term. The methodology for seismicity assessment differs by the assessment period. The main methods for short-term assessment are geophysical, geodetic, geochemical, and hydrological observations. On the other hand, the main method for long-term assessment is the statistical inference from past history. In Japan, the long-term assessment of earthquakes was done actively since the South Hyogo Prefecture Earthquake (Great Hanshin Earthquake) in 1995, and the earthquakes at the plate boundary and along the major active faults can be assessed by the recurrent rate (Headquarters for Earthquake Research Promotion, http://www.jishin.go.jp/main/p_hyoka02.htm). However, as the 2011 Earthquake off the Pacific Coast of Tohoku (M9.0) was an “unexpected phenomenon”, it cannot be said that this long-term assessment functioned sufficiently in preventing the disaster. Moreover, if the current long-term forecast is extrapolated to super long-term, the uncertainty of whether the initial conditions and reoccurrence intervals that are the basis of the long-term assessment is constant over super long-term is unknown, and we currently cannot conduct reliable assessment. Therefore, to handle the super long-term time span of a hundred thousand to million years, various geological surveys are necessary in addition to statistical inferences.

In the forecast of geological and climatic phenomena for geological disposal, the foundation will be to clarify the trends of the geological changes for the phenomena that occurred in the assessment area, and to extrapolate this into the future. If the extrapolation is done for a hundred thousand to a million years into the future, it is necessary to track back the same number of years or more into the past. If the activity history of the phenomena with sufficient quantity and quality in terms of statistical inferences can be obtained, it may become possible to conduct probabilistic assessment, as in the long-term assessment of earthquakes. However, not all histories of activities are stored geologically, and there is overwhelmingly greater number of cases where sufficient history cannot be obtained. Therefore, forecast must be done from limited data, and it is necessary to consider the fact that quantitative handling cannot necessarily be done. For example, with the plate boundary earthquakes, the activity history depends on the historical records and tsunami deposits, and there is a limit in understanding the geological marks from surface survey over a long period. Also, for major earthquakes along the active fault, the activity history of only within about 10 thousand years can be obtained depending on the relationship of the fault and the cover stratum, and many cases are expected where the amount of information will be insufficient for the assessment period. In the case where the erosion history is studied by tectonic geomorphology, the geomorphic surface index with sufficient sequence appropriate for the assessment period may not necessarily be found in the assessed area or the surrounding area. For hydrogeological phenomena, only the current value that is the sum of all past changes can be observed, and in most cases it is difficult to separate the individual history of changes.

In the case where it is difficult to extrapolate the super long-term history of change by statistical inferences, a different explanation is necessary to guarantee the stability of the geological environment of the assessed area over super long-term. For example, it is necessary to present a qualitative forecast by establishing the model of the structural development history of the assessed area, where the seismicity and uplift that accelerate erosions can be described. In hydrogeological change, qualitative forecasting will be possible only by establishing the mechanism for water quality formation that includes the chronology axis. Which kind of forecasting model is specifically necessary differs by the geological property of the area, and it is necessary to consider the forecasting theory according to the individual areas.

4.2 Example of analysis of long-term geological history for Japanese volcanic activities

To develop the analysis and assessment methods for the long-term geological history of the Japanese volcanic activities, as a typical cross-section model of the island arc, we conducted the research of the spatiotemporal distribution of the volcanic activities in the area from the Pacific Ocean side of southern

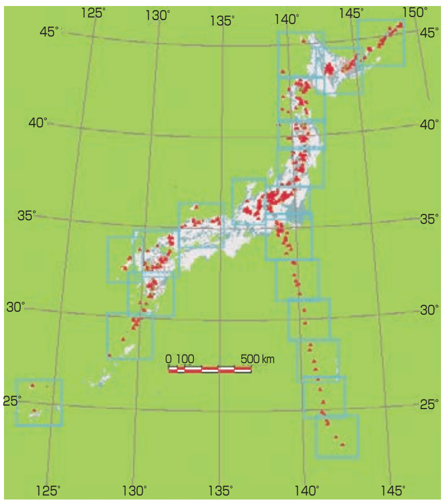

Fig. 3 Index map in "Quaternary Volcanoes in Japan, RIO-DB, AIST"
Red triangles are Quaternary volcanoes.

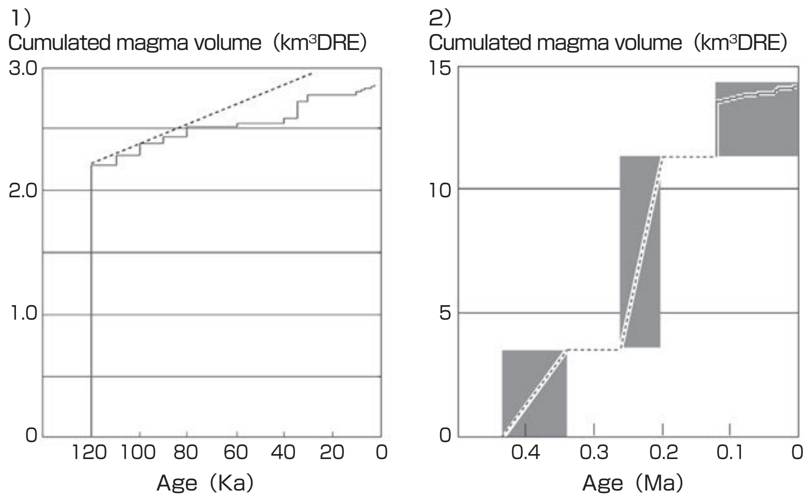

Fig. 4 Cumulated erupted magma volumes of Adatara volcano
1) and 2) diagrams are different in time scale. After Yamamoto and Sakaguchi[7]

Northeast Japan to the Japan Sea side from 2004. The example of the analysis is described below.

In Japan, there are about 100 active volcanoes (those that erupted within the last 10 thousand years or volcanoes with vigorous fumaloric activity), and over 200 volcanoes that erupted in the Quaternary period (from 1.7 million years ago to present according to the old definition) (Fig. 3). However, the volcanoes are not distributed evenly throughout the Japan Islands, and their presences are determined by the plate arrangements. This means that the Quaternary volcanoes of the Japan Islands are most densely distributed on the volcanic front located 200~300 km away from the subduction boundary of the plates toward the plates on the landside, and there is no volcano between the volcanic front and the subduction boundary (fore-arc side). Also there is a significant tendency where the volcano distribution becomes sparse in the area distant from the back-arc side or area opposite the volcanic front. In soliciting the disposal site candidates, NUMO sets the condition "the area within the circle of 15 km radius with the center at a Quaternary volcano shall not be included" for the purpose of avoiding the effect of the volcanic activity[6]. However, in thinking about the volcanic activity several hundred thousand to million years into the future, is it possible to avoid the effect with this exclusion condition only? Next, we shall consider the specific analysis of the spatiotemporal distribution of the volcanic activities.

When analyzing the eruption history of the volcanic activities, the so-called step diagram of eruptive volume is created, in which the horizontal axis represents time and the vertical axis is the cumulative eruptive magma volume. Figure 4 is an example created for the eruptive magma material of Adatara volcano, a representative active volcano in southern Northeast Japan[7]. Each magmatic eruption event is a geological instant shown as the vertical line, and during the non-eruptive state, it is shown as the horizontal line because there is no magmatic eruption. Figure 4.1 is a step diagram of the eruptive volume that goes back 120 thousand years, and as indicated by the average eruption rate shown by a dashed line, it can be seen from the step diagram that the eruptions occurred repeatedly at a certain frequency. However, when the history is extended to the time scale surpassing 120 thousand years for this volcano, as seen in Fig. 4.2, there is a major dormancy period 120 thousand to 200 thousand years ago, and the average eruption rate up to 120 thousand years ago cannot be extended into the past. There were separate magmatic activity periods 200~260 thousand year ago and 320~430 thousand years ago, but the individual average eruption rate differs by the activity period, and it is clear that the activity of Adatara volcano up to 120 thousand years ago, assuming a consistent rate, cannot be extrapolated to the past. In other words, it indicates that there is a lifespan on the magma supply that supports the individual activity periods, and for the forecast surpassing 100 thousand years, the assessment of the reactivation of the dormant volcanoes will become important rather than the currently active volcanoes.

Figure 5 shows the spatiotemporal distribution change of the volcanoes in the southern Northeast Japan including Adatara volcano, from about 1.8 million years ago or the beginning of Early Pleistocene to present[8]. The important point in the distribution pattern of the volcanoes in this period is that there is almost no change at the volcanic front while there

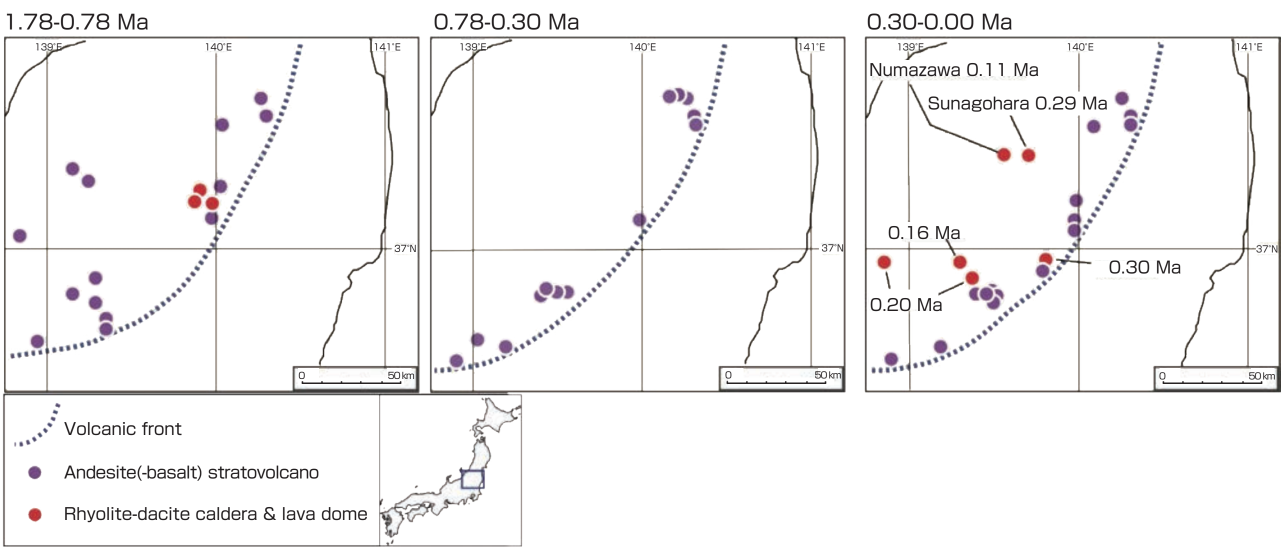

Fig. 5 Temporal change of the distribution of Quaternary volcanoes in the southern part of NE Japan arc
After Yamamoto[8]

are always volcanoes along the front. On the other hand, the distribution of the volcanoes in the back-arc region differs greatly by intervals, and the volcano that was active in the back-arc region during the Early Pleistocene became dormant in the first half of the Middle Pleistocene. 0.3 million years ago and after or the latter half of Middle Pleistocene, the new back-arc volcanic activities (Numazawa volcano, Sunagohara caldera) began, and it should be noted that they are located in the areas of volcanic activity gap. This means that if the time is set back 0.3 million years, Numazawa volcano and Sunagohara caldera appeared outside the “range within the circle of 15 km radius with the center being an existing Quaternary volcano”, and the volcanic activities cannot be eliminated based on location under this condition. To understand the spatiotemporal change of the volcanoes in southern Northeast Japan shown in Fig. 5, it is necessary to extend the time scale further and to look at the tendency of the magmatic eruption rate for the entire area. Figure 6 is the result, and the time scale of the horizontal axis is in the unit of million years, and the vertical axis is the sum total of the magmatic eruptive volume from all volcanoes in the Aizu region, from the Nasu volcano group along the volcanic front to the Numazawa volcano on the back-arc side[9]. It is clear from the ladder diagram of eruptive volume of the entire region in Fig. 6, that the long-term magmatic eruption rate shown in a dashed line for this area is dominated by the mega-eruptions where the single eruptive volume surpasses 100 km^3 and which occur at 1~2 million year intervals. The eruption site is covered with overlapping large collapse structures (caldera, shown in pink in the diagram) with diameters of over 10 km in the range of 60 km × 50 km, and the activities can be traced back to 10 million years ago[10]. The appearance of Numazawa volcano and Sunagohara caldera occurred in this volcanic activity region, and they cannot be fully positioned only by the investigation of the activity history limited to Quaternary volcanoes. The existence of the hierarchical structure of the phenomena, as presented here, shows the difficulty of forecast by simple extrapolation of the history of change. To reduce the uncertainty of the forecast for several 100 thousand to a million years into the future, it is necessary to understand the structural development history of the subject region, by tracing way beyond the assessment period, and effort must be made to minimize any “unexpected phenomenon”.

4.3 Limit of probabilistic assessment: need for a forecast that steps into the geological understanding of the phenomena

In the United States, Yucca Mountain in Nevada was determined as the HLR waste disposal site in 2002, and the safety assessment for the approval of construction was started from September 2008. However, President Obama decided to terminate the Yucca Mountain project, and the appeal to withdraw the application for approval was submitted in

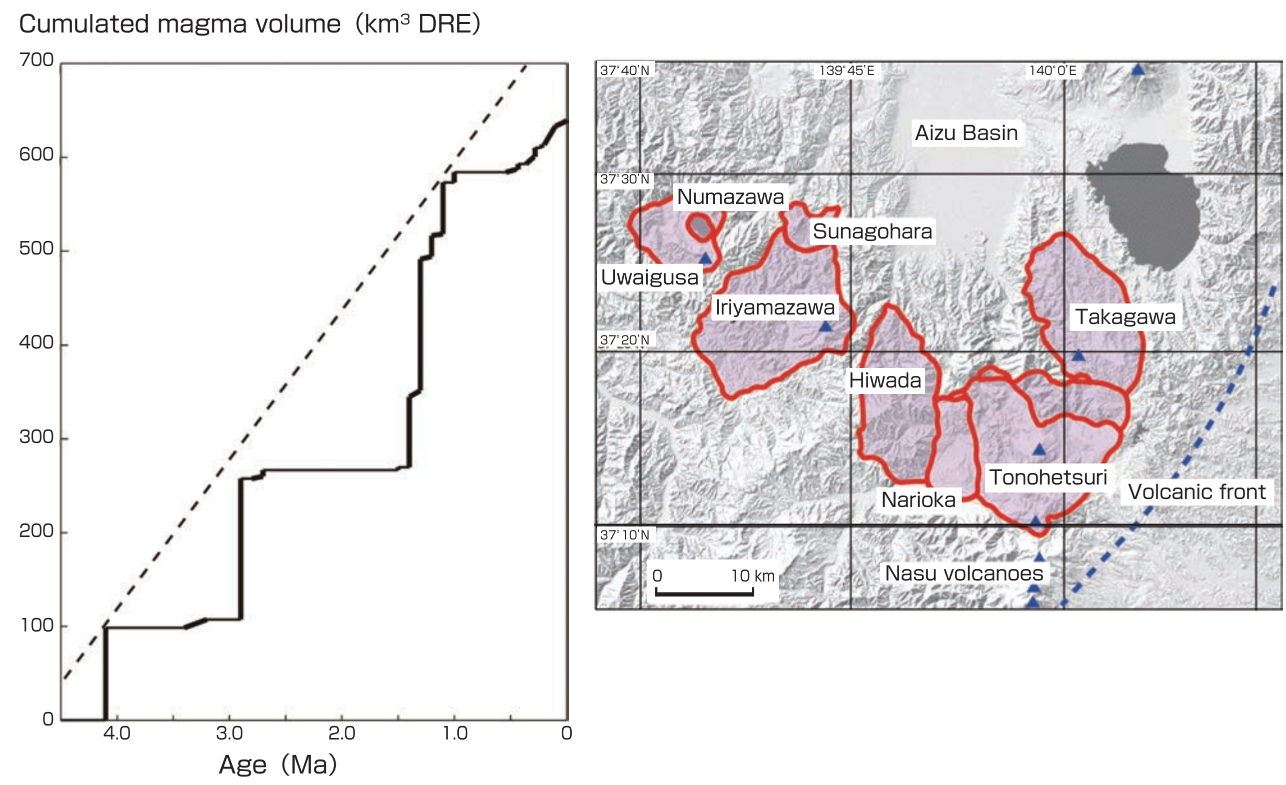

Fig. 6 Cumulative erupted magma volumes from the Aizu regions in the southern part of NE Japan arc
The average eruption rate (dotted line) is controlled by huge eruptions from caldera volcanoes (red solid lines). After Yamamoto[9][10]

March 2010. The geological disposal is essentially on hold. Aside from this course of event, reconsideration must be done for the geological disposal in Japan, as there was a major geological problem in the safety assessment for Yucca Mountain. The Yucca Mountain site was located within the basalt magma monogenetic volcano group that was active in the Quaternary period, and various assessments had to be done for the volcanic activities for the site. The US Department of Energy (DOE) that conducted the project assessed the probability of eruption at the site by calculating the average re-eruption interval from the eruption history of the past monogenetic volcanoes, assuming that a mega-eruption that may form a caldera will not occur[11]. However, the eruptive activities of monogenetic volcano groups are distributed unevenly in both time and space, and do not occur uniformly. Considering the peak of the activity and distribution state, it was inevitable that the probability shown by DOE would be considered an underestimate[12]. There is an arbitrary aspect in which the values may differ according to how the scales of time and space are set in calculating the probability, and it must be said that probabilistic forecast without scientific basis for explaining the uneven distribution of the activity frequency lacks reliability. There are some researches that apply the probabilistic assessment of the volcanic activity to Northeast Japan[13], but these are extrapolations of the distribution of the Quaternary volcanoes directly as a function of probability, and do not consider the changes in spatiotemporal distribution or magmatic eruptive volume as shown in Fig. 4 and 5 of this paper.

In evaluating the volcanic activities, it is necessary to understand the conditions of magma generation in the deep underground that is the source of volcanic activities, in accordance to the spatiotemporal changes of the activity region. Although it will not be explained in detail in this paper, the rise in partial fusibility was observed through the changes in the chemical composition of the eruptive materials in Numazawa volcano that newly appeared in the aforementioned Northeast Japan back-arc region, and it is thought that the magma was generated by the reheating of the crust[8]. In the major caldera eruption in the Aizu region in southern Northeast Japan, it was shown that the large-scale melting of the lower crust and the rearrangement in the up-down direction of the crust occurred when a large amount of magma was formed, from the geochemical property of the eruptive material. This corresponds well with the underground temperature structure shown seismologically[9]. In the forecast of the volcanic activities, the assessment that steps into the geological, geophysical, and geochemical basis as well as the magma genesis will be demanded. The probabilistic assessment that simply matches the numbers without theoretical backing not only will be questioned, but may also lead to unnecessary confusion as in the Yucca Mountain project.

5 Summary

As there is a great amount of radioactive wastes already in Japan as the product of nuclear power generation, and they continue to increase, we face a situation where the wastes must be quickly and effectively disposed. Particularly, in geological disposal, the social consensus for this project is mandatory, aside from the issue of long-term safety assessment of the geological disposal environment. While the business executer is responsible to be accountable for safety, the regulating authorities must have the ability to decide whether the application of the disposal business company is appropriate, and to disclose the information to society to obtain consensus. The Research Core for Deep Geological Environments, AIST handles the supportive research for government regulations, and its purpose is to utilize the research results and to provide technological support in the safety regulations. Particularly, the presentation of the safety thinking at a time scale that surpasses the ordinary daily perception, as in the forecast of several hundred thousand years into the future, is an issue that must be solved by the Research Core for Deep Geological Environments. The geological phenomenon may have extremely major effect on society if it happens, even if it is a rare natural phenomenon (event that occurs at extremely low frequency), and we must learn from the experience of the 2011 Earthquake off the Pacific Coast of Tohoku. This paper described the methodology of forecast and the geological issues in geological disposal. Particularly, in the assessment of the natural phenomena that may affect the disposal system, the reconstruction of the geological structure development history as the just history at the candidate site is important, and it is necessary to conduct the assessment at a time scale with sufficient likelihood to eliminate any “unexpected events”. Recently, the Nuclear Safety Commission of Japan stated that the earthquake and volcanic activities should be assessed as rare natural phenomena in the safety regulation for subsurface disposal, which is a form of category 2 waste disposal facility[14]. However, according to the current thinking of the Nuclear Safety Commission, there is arbitrariness in the way in which rare natural phenomenon is determined, and the ways of excluding the arbitrary event settings such as maintaining the low assessed dosage among the various natural phenomena have not been clarified. Moreover, in the geological disposal, which is a non-managed category 1 waste disposal facility, it is assumed that the problematic natural phenomena are eliminated in selecting the site as stated in the Specified Radioactive Waste Final Disposal Act. There is a great disparity in the fact that the earthquake and volcanic activities that were supposedly eliminated are assessed for safety as rare natural phenomena. I shall repeat that in the safety assessment of geological disposal, the basis must be the accurate geological understanding of the candidate site, and the original purpose is the maximum reduction of uncertainty through such understanding.

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Discussions with Reviewers

1 General comment

Comment (Shigeko Togashi, Evaluation Department, AIST)

In terms of synthesiology, this paper can be viewed from the perspective of the methodology for impact assessment of the natural phenomena on human activities with very long time scale.

The fact that the geological phenomena, even if it is a rare natural phenomenon, can have extremely large impact on society if it should happen, had been shown by the 2011 Earthquake off the Pacific Coast of Tohoku, and is an important issue that must be dealt with by society.

In this paper, taking the example of the geological issues required in the safety assessment of geological disposal of the HLR waste, the method of extracting the issues based on the series of events (scenario) or the process where one event will induce the next event one after the other, the limitation of the probabilistic method for the geological phenomenon investigated, and the necessity of long-term forecast based on the model of geological phenomenon genesis are described.

I think it provides an extremely important viewpoint in terms of synthesiology. In the process of review, improvements were made to clarify the characteristics as a generalized methodology.

2 Significance of the research

Comment (Akira Ono, AIST)

I think this is an excellent research that presents the methodology for assessment by integrating and synthesizing geological elemental technologies pertaining to the disposal of radioactive wastes produced by nuclear power generation.

As it became apparent from the accident at the Fukushima Daiichi Nuclear Power Plant, not only decisions by regulating authorities but wishes of people and local governments are very important in selecting the locations for nuclear power plants and waste disposal sites. I think such decisions must be made based on scientific evidences. In that sense, results of scientific researches should be shared widely by people and not only by regulating authorities. I hope this paper is read and referenced widely across the disciplines.

3 Overall processes leading to the decision of waste disposal site and the positioning of the research

Comment (Akira Ono)

I think it is easier for the readers to understand if you show the overall processes leading to the decision and where this research is positioned within the processes, because there are many people involved as disposal sites for radioactive waste are determined.

Answer (Takahiro Yamamoto)

In accordance to your comment, I added the relationship between this research and the security after closure of the geological disposal repository in Fig. 1. The ways of conducting the geological disposal business or the procedure for selecting the final disposal site are set by the Specified Radioactive Waste Final Disposal Act, and the selection of the disposal site itself is conducted by NUMO, the executive body, but the content of the safety regulation has not been established. The final goal of this research is to establish the index for selecting and deciding the investigation and assessment items for the disposal site selection investigation. For example, as described in this paper, places that may be affected by volcanic activities or places in which new volcanic activities may occur are not appropriate as disposal sites. The theme of this research is the methodology for how to establish the assessment method to determine such matters.

4 Responsibility of the current generation to the future generation

Question (Akira Ono)

In this paper it is stated that it is necessary to assess the safety of the radioactive waste disposal at a time range of several hundred thousand to a million years, and that is because this time span is required for the radiation level of the HLR waste material to decrease to a level of naturally existing radioactive substances. After this time range has elapsed, the current humanity will be in the next evolutionary stage, and it is imagined that the current civilizations, cultures, and ethnic groups will be totally gone. I think this paper is based on the thinking that the current humankind should be responsible for the earth environment and biosphere of such a distant future. What does the author think about the adequacy of this thinking?

Answer (Takahiro Yamamoto)

I think the generation that received the benefit of nuclear power should be responsible for the disposal of the waste. Since the accident at the Fukushima Daiichi Nuclear Power Plant, the public opinion is to move away from nuclear dependency, but the disposal of the existing radioactive wastes that had been produced cannot be avoided in decommissioning the plants. “No nuclear” cannot be achieved only by stopping the power generation, and our generation must be responsible for the final disposal of the nuclear waste whether we continue or discontinue nuclear power.

As for the human activities in the future, Japan is engaging in the safety assessment after closure of the geological disposal sites with this point in mind, just as in other countries. For example, it says “mineral resource” in “Investigation/assessment items for geological environment” in Fig. 1. This is because the presence of underground resource that may be mined is set as an exclusion condition, to avoid the disposed materials to come in contact with the human activities in the future.

5 Scenario for the assessment of risk occurrence in the future

Question (Akira Ono)

The risk of disposed radioactive waste to humans at a time in the future may be the product of the radiation of radioactive substances at that time and the possibility that the radioactive substances may affect humans.

The radiation level of radioactive substances can be estimated to decrease logarithmically from the nuclear physics data. On the other hand the possibility that the radioactive substances from the waste substances may affect humans is a geological issue. What scenario of geology is envisaged for the risk assessment?

Answer (Takahiro Yamamoto)

The natural barrier in geological disposal not only attempts isolation by distance. The waste materials including the artificial barrier buried deep underground will eventually lose the containment function due to corrosion. After that, the radioactive substances are expected to undergo reduction in radioactivity in the process of travelling through the natural barrier by underground water, and through delay by absorption by minerals and dilution by underground water, before it arrives to the ecological environment on the surface. The safety assessment after closure is based on such underground water transfer scenario.

Improvement of reliability in pressure measurements and international mutual recognition

— Incorporation of industrial digital pressure gauges to the national metrology system —

Tokihiko Kobata*, Momoko Kojima and Hiroaki Kajikawa

[Translation from *Synthesiology*, Vol.4, No.4, p.209-221(2011)]

Reliable pressure measurements provide the basis for all activities in society and industry, and every country shows considerable interest in them in international trade. Recently, characteristics of industrial digital pressure gauges and the short- and long-term stabilities as well as the stability under environment change and during transportation have been improved remarkably. AIST focused its attention on the technological advancement, and, after evaluating the characteristics of digital pressure gauges in detail, incorporated them to some phases in the metrology system, which are the upgrading of national pressure standards, the international comparisons of the standards and the domestic traceability system. Consequently, the reliability of pressure measurements in industrial fields has been secured through an efficient process, and the international mutual recognition has been promoted by carrying out many international comparisons.

Keywords : Pressure standard, digital pressure gauge, calibration, international comparison, metrological traceability

1 Introduction

The measurement of pressure is one of the essential measurements in people's lives, society, industry, and science and technology. The pressure measurements for safety and security include the atmospheric measurement in meteorological observation, the altitude measurement for aircrafts, the blood pressure in medicine and health management, the measurement for high-pressure gas control, and the pressure measurement in the manufacturing process of food and pharmaceutical products. The pressure measurements for energy savings include the air conditioning of buildings and the adjustment of air pressure in tires and automobile engines. Moreover, various pressure measurements are conducted at various sites such as the maintenance of clean rooms where high air purity must be maintained for the manufacture of semiconductors and precision devices, the measurement and control of pressure in various processing, and the inspection of plants. In the field of science and technology, various R&Ds using pressure control and measurements are being done.

For the pressure measurement conducted at the industrial sites, diverse pressure gauges are employed for wide pressure ranges, from low pressure of 1 Pa or less to high pressure of 1 GPa or more. Recently, the performance of the industrial pressure gauge increased significantly. Specifically, the performance increased in terms of expansion of measurement range, improvement in high resolution, improved short- and long-term stability, and improved stability in environment change and during transportation. AIST has focused on the improvements of the performance of such digital pressure gauge, and has spent effort on the precise evaluation of its properties. As a result, the digital pressure gauge is now utilized in the upgrading of national standard and the standard provision, and the reliability of pressure measurement at the industrial sites improved greatly. On the other hand, the international mutual recognition of the measurement results is essential in modern international trade. AIST has contributed greatly in providing technical data for the mutual recognition of the national standard, such as conducting various international comparisons using the digital pressure gauge.

In this paper, the R&D for the digital pressure gauge and its results in improving the reliability of pressure measurement at the industrial sites and the efforts on international mutual recognition to ensure free trade will be presented from the perspective of synthesiology based on the scenario.

2 Demand for the reliability of pressure measurement

2.1 Demand from the Japanese industry

To conduct highly reliable pressure measurement using the pressure gauge at the industrial site, it is necessary to correctly calibrate the pressure gauge so it will be traceable to the national standard for pressure owned by AIST. On the other hand, the main standard for pressure owned by industry is the highly precise device called the pressure balance (deadweight pressure gauge)[Note 1]. While the pressure balance

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is characterized by its excellent long-term stability, the device itself is heavy and large, and for the client receiving the calibration service, transporting this bulky device to the calibration lab is troublesome. Also, the calibration at the calibration lab may take about two months at the longest, and since the standard device cannot be used during that time, extra standard device must be kept for backup, requiring significant amount of expenditure. Therefore, industry demanded some method where calibration could be done effectively at the same precision as the conventional method, without transporting the pressure balance.

Recently, the property of the industrial digital pressure gauge improved significantly, and there is good prospect of maintaining stability during transportation and in environment change, as well as certain degree of long-term stability. Therefore, we attempted to incorporate and utilize the industrial digital pressure gauge into the standard system. Normally, the digital pressure gauge is transported to the user's site after being calibrated using the standard device at the calibration lab. Therefore, if the displayed value of the digital pressure gauge after being transported is sufficiently stable, the user will be able to maintain the calibration value that is traceable to the national standard at the same precision as before, without having to transport the heavy and large pressure balance to the calibration lab. This will ensure high efficiency of the calibration work.

To promote the use of digital pressure gauge in the standard system, the necessary conditions are: the stability of the calibration value is sufficiently maintained even when the industrial digital pressure gauge is transported anywhere in Japan, and sufficient stability is maintained until the next calibration is conducted. AIST embarked on the research to determine whether the industrial digital pressure gauge had such properties.

2.2 International demand

With the globalization of economy, production, and trade, there is rising interest in the conformity of the measurement results by various measuring equipment among different countries[1][2]. For example, at Narita and Haneda Airports, there is an increase in international business such as the maintenance of the aircrafts of foreign companies by the maintenance shops of the Japanese airline companies. Several aircraft accidents occurred in the US in the 1990s, and the US government revised the Federal Aviation Law to maintain the safety of the US citizens, and the requirements for maintaining the US-owned aircrafts demanded that the measuring devices such as the pressure gauges to be traceable to the national standard of the National Institute of Standards and Technology (NIST), the American national metrology institute. The inspectors of the Federal Aviation Administration (FAA) would conduct regular on-site inspection of the maintenance shops. The demand of the US government was applied not only to the American airline companies but also to the foreign maintenance companies that maintained the US-owned aircrafts. Japan Airlines and All Nippon Airways had to make almost all the measuring devices in their maintenance shops traceable to NIST. This became an international issue, since most of the measuring devices used at the maintenance shops of the Japanese airline companies were made in Japan, and were traceable to AIST (at that time, the laboratory for former Agency of Industrial Science and Technology). The Japanese government stated that the Japanese national standard was proven to be equivalent to the American standard, and the devices traceable to the Japanese national standard should be allowed. This claim was accepted as an individual case.

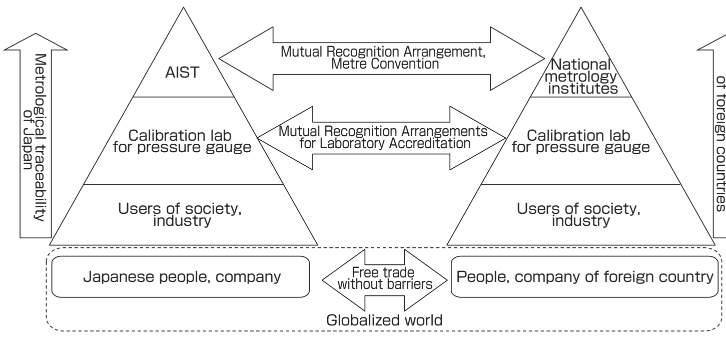

Fig. 1 Framework of the international mutual recognition for metrological standard

This issue spread to the airline companies around the world. With the background of such an issue, the Mutual Recognition Arrangement (MRA) of the Comité International des Poids et Mesures (CIPM) under the Convention du Mètre was established, to mutually recognize the equivalence of the national standards owned by the national metrology institutes around the world[3]. Figure 1 shows the framework of the international mutual recognition of the metrological standards.

In this framework, the technological requirement for mutual recognition was the actual comparison of the national standards among the countries (international comparison). The results of the international comparisons and the calibration and measurement capabilities recognized for participating institutes are registered in the Appendix B and C of the international MRA. This can be viewed on the Key Comparison Database (http://kcdb.bipm.fr/) of the Bureau International des Poids et Mesures (BIPM). The level of the national standard owned by each country can be known from this technological information.

As the Japanese metrology institute, AIST aims to establish and provide the national standard for pressure and to organize the traceability system of pressure measurement in Japan. By participating actively in the international comparisons, the international equivalence of the Japanese national standard for pressure has been demonstrated in the aforementioned Key Comparison Database. AIST is also responsible for maintaining the national interest by displaying the capabilities in calibration and measurement that are recognized by other countries.

With this background, we have been involved in advancing the national standards and in demonstrating the equivalence of the national standards with other countries, and we decided to utilize the industrial digital pressure gauge that has shown significant increase in performance.

2.3 Technological issues

The national standard for pressure[4][5] realized by AIST is for stationary fluid where hydrostatic pressure mediated by gas or liquid is established. In general, gas is used as the medium of pressure standard for low pressure, and liquid for high pressure. AIST also establishes the vacuum standard for pressure with small absolute pressure[6].

At the time of the establishment of AIST in 2001, the national standard was established for the pressure range from 5 kPa to 500 MPa using multiple pressure standard devices, and the calibration service was provided. With the advancement of science and industrial technology, various improvements such as the increased types of pressure standards, the expansion of pressure range, and the decrease of uncertainty were requested by the users at the industrial sites, according to the survey of demand for physical standards conducted in 2002[7]. Specifically, there were many requests for low-pressure standard and differential pressure standard for 10 kPa or less that were necessary for air conditioning, pharmaceuticals, medicine, and semiconductors. There were also requests for high-pressure standard surpassing 500 MPa for the development of internal combustion engines, as well as in the fields of materials, manufacturing, and machine processing.

AIST upgraded the national standards by conducting new technological development[8]-[10]. Currently, the pressure range of 1 Pa or 1/100,000 of atmospheric pressure to 1 GPa or about 10,000 times the atmospheric pressure are covered, using various pressure standard devices. To check the conformity of the generated pressure of these national standard devices, the comparative measurement among the standard devices is necessary, and efficiency and advancement were issues in managing the multiple standard devices.

At the field measurement of pressure, calibration and provision of standards that were effective yet with little burden on the user as much as possible were desired due to the increased number of devices that must be calibrated. As mentioned earlier, there have been recent new technological developments by companies in Japan and overseas, and the reliability of industrial digital pressure gauge using various pressure sensors increased. The high-precision pressure gauge with high resolution of six digits or more against full scale and with excellent long-term stability is now available. Therefore, AIST experimentally investigated whether such high-precision industrial digital pressure gauges could be used to increase the efficiency and performance of pressure standard maintenance, and whether it satisfied the requirement as standard devices.

3 Various pressure gauges

Figure 2 shows the various pressure gauges that are used at the site of pressure measurement.

The measuring device that is independently capable of conducting the absolute measurement of physical quantity without calibration by other measuring device is called the primary measuring device. Various devices are considered as primary measuring device for pressure (or primary pressure gauge), and the main ones are pressure balance[11] and liquid column manometer. Figure 3 illustrates the principles of the pressure balance and the liquid column manometer. On the other hand, the measuring device that is not independently capable of conducting the absolute measurement of physical quantity and requires calibration by primary measuring device is called the secondary measuring device. The secondary measuring device for pressure (secondary pressure gauge) includes digital pressure gauge[12] and mechanical pressure gauge (Bourdon tube pressure gauge[13]).

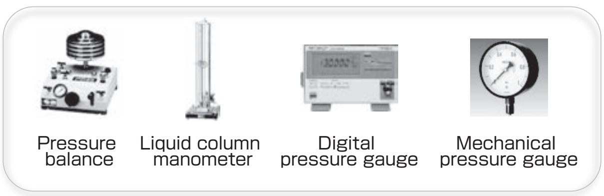

Fig. 2 Examples of various pressure gauges

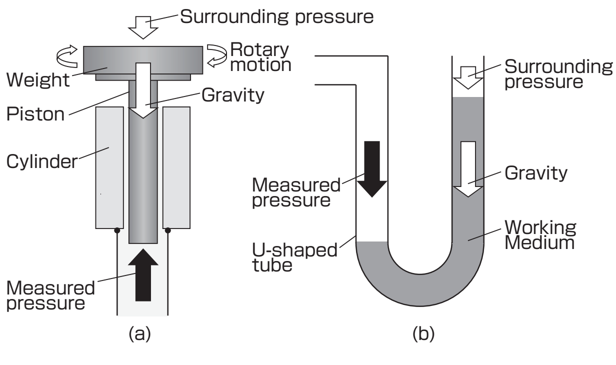

Fig. 3 Principles of pressure balance (a) and liquid column manometer (b)

Table 1. Characteristics of various pressure gauges

Types of pressure gauges	Types of measuring instrument	Maximum pressure	Size,weight, operability	Automation, systemization
Pressure balance	Primary	Over 1 GPa	Large, heavy, difficult	Difficult
Liquid column manometer	Primary	300 kPa	Large, heavy, difficult	Difficult
Digital pressure gauge	Secondary	Over 1 GPa	Small, light, easy	Easy
Mechanical pressure gauge	Secondary	Over 1 GPa	Small, light, easy	Difficult

The pressure balance is a measuring device that is capable of highly precise generation of pressure. The reliability of measurement is high, and it is used as the national standard for pressure in many countries. It is also used widely as the standard device at the industrial sites. The basic components of the pressure balance are piston, cylinder, and weights with known mass. The exterior surface of the piston and the interior surface of the cylinder are precisely machined to maintain good circularity and cylindricity. Normally, when generating pressure with the pressure balance, the piston and the weights are rotated after floating the piston, which is under downward gravity by the piston and weights, to appropriate position by upward pressure. By doing so, the mechanical contact resistance between the piston and the cylinder is reduced, and the gravity on the piston and the weights is converted accurately into pressure.

The liquid column manometer is a measuring device where the pressure is obtained from the height and density of the liquid column in the U-shaped tube that balances the measured pressure. Normally, the mercury or water with accurately known density is used as the working medium in the U-shaped tube. The foundation of the Japanese national standard for pressure is the primary interferometric standard manometer, which is a liquid column manometer using mercury as the working medium[14]. Similar pressure gauges are used as the national standard devices for pressure in the atmospheric pressure region at the national metrology institutes around the world.

The digital pressure gauge is a device that has a pressure sensor and a mechanism to output the result on a display or as digital signals[12]. There are several measurement principles of the pressure sensor, and the typical one includes the detection of change in resistance such as the strain gauge, change in capacitance of the capacitance sensor, or change in frequency of the crystal or silicon oscillator. Many are capable of consecutive external output of the measured results as analog or digital signal. With the recent rapid advances in technology, digital pressure gauges with excellent resolution and stability are becoming available.

The mechanical pressure gauge is a measuring device that measures pressure by mechanically expanding the deformation of the elastic element under pressure. The indicator with flat cross-section and bent tube with closed off ends as the elastic elements is called the Bourdon tube pressure gauge. It is used widely in society and industry due to its relatively low cost[13].

Table 1 is a summary of the characteristics and properties of the four types of pressure gauges. The pressure balance and the liquid column manometer, which are primary pressure gauges, have small uncertainly of measured pressure, excellent long-term stability, and high reliability. However, these pressure gauges, in general, require complex maneuver, are heavy and expensive. Also, the acceleration of gravity of the place of installation is necessary to obtain accurate values for generated pressure. The pressure balance, mechanical pressure gauge, and digital pressure gauge can be used in wide pressure ranges, while the liquid column manometer has limited range compared to the other gauges. The digital pressure gauge and the mechanical pressure gauge that are secondary gauges are lower in reliability compared to the pressure balance and the liquid column manometer, but are easy to handle, light, and are low in cost. Therefore, redundant installation of multiple measuring devices is done to increase the reliability. Also, while the generated pressure of the aforementioned primary gauges changes according to the acceleration of gravity, the measured values of the digital and mechanical pressure gauges are not directly affected by the acceleration of gravity. In general, the digital pressure gauge, in which the continuous measurement and transmission of measured results are easily done, is suitable for automation and systemization, and is useful in increasing the operability and efficiency.

We engaged in the development to utilize the advantages of the digital pressure gauge that are its small and lightweight portability, simple operability, and high applicability to automation and systematization.

4 R&D scenario

In this research, we set the goals as the utilization of the digital pressure gauge to confirm the equivalence of the national standard necessary for international mutual recognition and to increase the reliability of pressure measurement at the industrial sites.

The research scenario is shown in Fig. 4. The main elemental technologies for this research are the various properties of the digital pressure gauge and the evaluation and calibration technologies. The properties of the digital pressure gauge include the measurement range, resolution, weight, size, linearity, stability in environment change and during transportation, and short- and long-term stability. These properties depend heavily on the manufacturer of the measuring device. On the other hand, the evaluation of various properties and the evaluation of uncertainty of the calibration value for the digital pressure gauge are the technologies in which AIST excels, since it owns the national standard and routinely evaluates various pressure gauges.

To achieve the research objective, the aforementioned elemental technologies are integrated. First, the methods for property evaluation and the calibration methods of the digital pressure gauge are developed, to carefully evaluate the performance of the digital pressure gauge as a standard device. Particularly important are the evaluation technology for the stability of the digital pressures gauge in environment change and during transportation as well as the short- and long-term stability. Next, the use of the digital pressure gauge as the standard device is promoted to further integrate the elemental technologies, and to incorporate it into the metrological standard system including the establishment and maintenance of the national standard for pressure, international comparison of the national standards, and the standard provision in Japan. For the national standard, AIST establishes and manages the standard from 1 Pa to 1 GPa using multiple standard devices. The technological development is being done to enable efficient, high-precision calibration of the standard devices that are difficult to operate, using the digital pressure gauge effectively. For the international comparison of the national standards, the comparison will be done efficiently using the digital pressure gauge for the major pressure ranges. For provision of the standard in Japan, the standard provision method with least burden to the client will be developed. The pressure calibration service by AIST for digital pressure gauge will be expanded. The standard provision system in Japan is advanced to efficiently provide the pressure standard to society and industry, and various related technology standards will be organized.

Finally, the efficient standard provision using the digital pressure gauge will improve the reliability of pressure measurement at the industrial sites, which is one of the research objectives, in conjunction with the development of the industrial pressure gauge by the measuring device manufacturers. The international comparison using the digital pressure gauge will greatly contribute to the international mutual recognition of pressure measurement, which is the other research objective. We set such a research

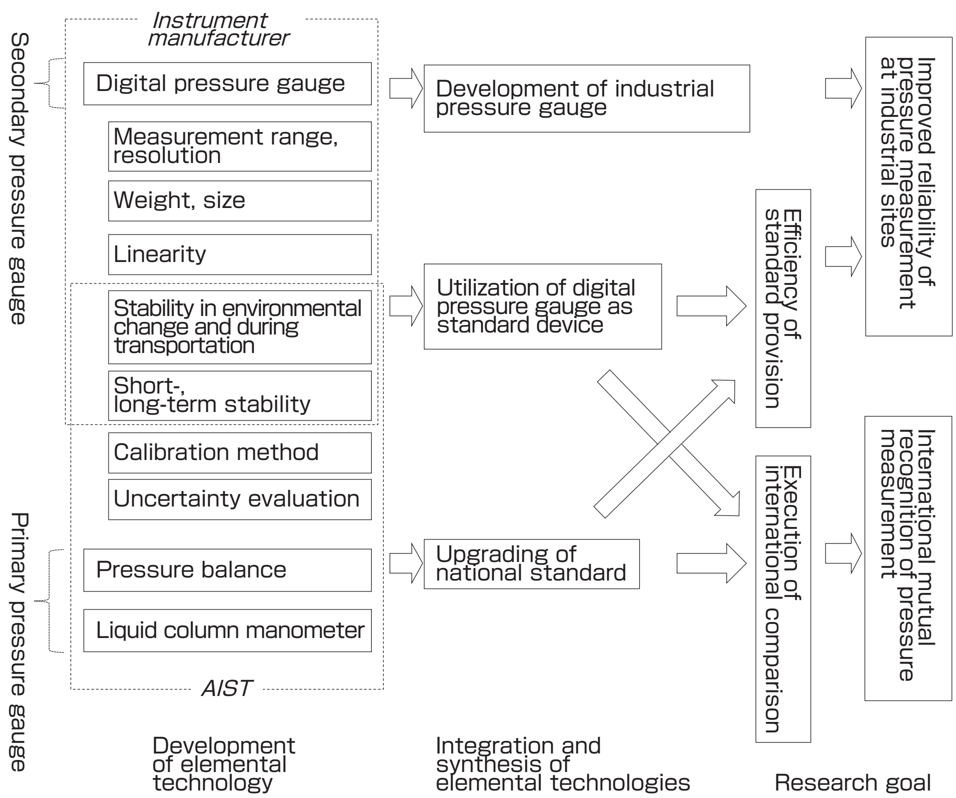

Fig. 4 Research scenario for increasing the reliability of pressure measurement and for international mutual recognition

scenario. What follows are the contents and results of the R&D that was conducted according to the scenario.

5 Evaluation of the properties of the digital pressure gauge

To build the practical and efficient standard system of pressure while maintaining reliability, the effective use of digital pressure gauge is the key. Therefore, AIST engaged in the R&D for the property evaluation and calibration method of various digital pressure gauges using the pressure standard devices[15]-[17]. The following factors can be given as the main reason for the uncertainty of the measured value displayed by the digital pressure gauge:

a) Uncertainty of the applied pressure
b) Uncertainty due to the variation in measured value
c) Uncertainty due to historical effect
d) Uncertainty due to resolution or short-term stability
e) Uncertainty arising from changes in surrounding temperature (temperature property)
f) Uncertainty arising from attitude of installment (attitude property)
g) Uncertainty due to changes in voltage of power supply
h) Uncertainty due to the linearity of input-output relation (linearity)
i) Uncertainty due to changes in line pressure (in case of differential pressure gauge)
j) Uncertainty arising from long-term stability (change over time)
k) Uncertainty arising from changes in surrounding environment (relative humidity, atmospheric pressure, vibration, impact, etc.)

In case the digital pressure gauge is used as the standard, the above property evaluation must be conducted thoroughly, and consideration is necessary on the uncertainty evaluation and correction of the calibration value according to the situation in which the device is used. Consideration must also be made in transporting the pressure gauge, since the property will be affected by the changes in surrounding environment during transportation.

Currently, various digital pressure gauges with excellent performance are available in wide pressure ranges. The two gauges, for which the evaluation of the property was mainly done in our research, were a differential pressure gauge that uses a silicon resonant sensor as the pressure sensor manufactured by a Japanese measuring instrument company, and a pressure gauge that uses the crystal oscillator as the pressure sensor manufactured by a foreign company. The stability was evaluated by conducting appropriate corrections after performing detailed property evaluation, and then regularly repeating the calibration of the digital pressure gauges using the fixed calibration method. As a result, it was found that reliability equal to the conventional pressure standard device could be obtained for the digital pressure gauge by devising the usage method. The evaluation data for the stability of each pressure gauge is illustrated in the case studies of the incorporation of the digital pressure gauge into the standard system, as will be explained later.

6 Incorporation of the digital pressure gauge into the standard system

The three case studies of the incorporation of the digital pressure gauge into the standard system for pressure are described in this chapter.

6.1 Establishment and maintenance of the national standard

The liquid column manometer and the pressure balance are positioned as the national standard of Japan or the primary standard of pressure. To use them as the primary standard, it is necessary to determine and manage the various property values. The property values of the pressure standard used at AIST are accurately measured and managed, so they are traceable to the national standards of mass, length, temperature, and others. At AIST, several pressure balances and pistons and cylinders are managed for each respective pressure range. By managing large numbers of standard devices in groups, the national standard is maintained for a wide pressure range. For the maintenance of these standard devices, comparative measurements between the standard devices are conducted regularly to check the mutual conformity. Also, from the results of the comparative measurement for various combinations, the long-term stability of the generated pressure of each standard device is evaluated. Although it depends on the pressure range, in general, the long-term stability is on the relative order of 10^{-6} per year.

Here, the case, where the digital pressure gauge was used to calibrate the pressure balance of a private calibration lab with AIST's national standard pressure balance, is described. When the pressure balance is calibrated at AIST, two pressure balances are connected directly to compare the generated pressure. In traditional calibration, the two pressure balances are operated simultaneously, the changes in the fall rate of the pistons are observed, and fine weights are added to either balance until the equilibrium is attained. However, this method involves complex maneuver, and the calibration result is highly dependent on the system configuration and the technical prowess of the calibration operator. Therefore, AIST selected and advanced the two calibration methods using the high resolution and consecutive measurement functions of the digital pressure gauge. As a result, in both methods, it was found that if the performances of the digital pressure gauge used and the pressure balance are good, the equilibrium state could be attained at the relative order of 10^{-6} or less. Currently, the calibration and maintenance of numerous pressure balances as well as the national standard devices maintained by AIST are done using the digital pressure gauge, and the process has been advanced greatly and can be conducted efficiently.

The first calibration method is the method of directly measuring the generated pressure difference of the two pressure balances using a high-resolution digital differential pressure gauge. In this method, small weights are used to adjust the pressure difference of the two pressure balances measured with the differential pressure gauge until the difference reaches zero.

The second calibration method is the comparative method where the digital pressure gauge is used as the comparator[17][18]. As shown in Fig. 5, the generated pressures of the two pressure balances are measured alternately with the digital pressure gauge by switching the constant volume valve. The advantage is that even if there is some degree of difference between the generated pressures of the two pressure balances, the difference can be obtained accurately and corrected. Moreover, this method can be applied simultaneously to three or more pressure balances. In the second calibration method, the short-term stability was utilized in addition to the high resolution and consecutive measurement functions of the digital pressure gauge.

6.2 International comparison of the national standards

Normally, in the international comparison of the national standards of pressure, the transfer device, which is a measuring device that can be transported, is circulated among the countries, and the participating national institutes obtain the calibration value for the transfer device based on their own national standards. By mutually comparing the calibration values of each country, the differences of the values of the national standard for pressure of each country can be seen. For the international comparison where the measurement of highest precision is necessary, the pressure balance that has equivalent performance as the standard was used traditionally as the transfer device.

In such a situation, AIST focused on a digital pressure gauge that was small, lightweight, and of low cost, as well as easy to handle, and engaged in the world-leading development of a transfer device for international comparison using the high-precision industrial digital pressure gauge. Using the developed transfer device, several international comparisons were actually done[19]-[23]. Multiple digital pressure gauges were used simultaneously as the transfer devices, to increase the reliability by redundancy. Through the execution period of the international comparison that normally takes over one year, the details of the long-term property changes of the digital pressure gauge was studied and the results were used to correct the calibration value. By these corrections, the lack of long-term stability of the transfer device was compensated, and sufficient comparative precision could be maintained[19]-[22][24].

As an example of use of the digital pressure gauge in international comparison, we describe the international comparison conducted from 2002 to 2004 to check the international equivalence of the national standard for hydraulic gauge pressure with pressure range from 10 MPa to 100 MPa (APMP.M.P-K7[19]). Figure 6 shows the transfer device used in that international comparison. The transfer device was composed of a set of two digital pressure gauges with full scale of 100 MPa, resolution of 0.1 kPa, and used the crystal oscillator as the pressure sensor. With the use of the digital pressure gauge, the total weight of the transfer device during transportation could be kept at 50 kg or less, and this was dramatic weight reduction compared to using the pressure balance (which usually weighs over 200 kg). Also, three sets of transfer devices with the same specifications were prepared and sent simultaneously to the participating institutes by

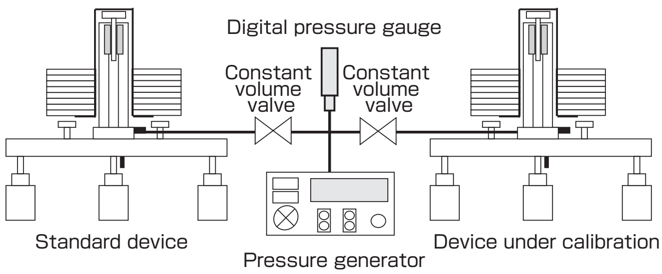

Fig. 5 Calibration by comparative method using the digital pressure gauge as the comparator

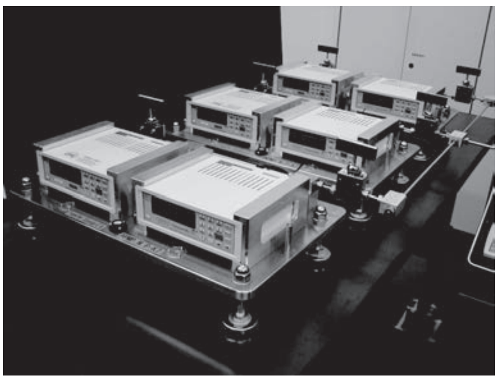

Fig. 6 Photographs of the transfer device for international comparison for hydraulic pressure using the digital pressure gauge (two pressure gauges on each transfer device, total three sets)

different circulation routes to greatly reduce the measurement period required for the international comparison.

During the measurement period, a total of six digital pressure gauges that comprised the transfer device were regularly returned to AIST that acted as the pilot institute. The stability of the transfer device was evaluated by recalibrating these digital pressures gauges using the Japanese national standard. Figure 7 shows the change per day of the calibration values of each digital pressure gauge, as the evaluation of the function of measured values. As seen in the graph, the change at the maximum measured pressure of 100 MPa was over 50 Pa per day for some pressure gauges. Since there were about 400 days for the entire measurement period of the international comparison, the measured pressure value at the maximum pressure was estimated to change 20 kPa. This corresponds to relative change of 2×10^{-4} against the measured value. On the other hand, when the pressure balance that was traditionally used as the transfer device in the international comparison was used in this pressure range, the stability was expected to be about relative 1×10^{-5}. Therefore, when the above digital pressure gauge was used without correcting the calibration value, the stability necessary for the international comparison could not be obtained. However, it was found in the evaluation that the change in each pressure was the linear function of the number of lapsed days. By correcting this and by using the average value of the calibration values obtained from the two digital pressure gauges that comprised the transfer device, ultimately, 5×10^{-6} or less for the stability of each transfer device was obtained throughout the entire measurement period[19]. We were able to obtain sufficient comparative precision that could be used in the international comparison, by understanding the details of the property of the digital pressure gauge as the transfer device and conducting appropriate corrections.

Figure 8 shows the results of the calibration values at 100 MPa of the participating institutes in the two international comparisons (CCM.P-K7[25] and APMP.M.P-K7[19]), including the aforementioned international comparisons. The horizontal axis shows the acronyms of the participating institutes and the country names, and the vertical axis shows the relative deviation from the international comparison reference value of the calibration values of each institute. The reference value was obtained by calculation of the average value of the calibration values of the participating institutes. The length of the bar for the data for each country is the uncertainty (confidence level about 95 %) of the calibration value claimed by the participating institutes. The results obtained in the same international comparison are indicated by the same markers (black or white circles). The equivalence of the national standards for pressure of the countries can be seen from Fig. 8. The Japanese national standard has almost zero deviation from the reference value, and the uncertainty is similar to the major countries. Therefore, it was confirmed that the Japanese national standard for pressure established, maintained, and supplied for the target pressure range has excellent international equivalence.

The use of digital pressure gauge as the transfer device is being done in other international comparisons. Excellent comparative precision was obtained by using the digital pressure gauge with silicon resonant sensor in the international comparison of the gas differential pressure[20]. In this manner, the efficacy of the digital pressure gauge as the transfer device was confirmed in the international comparison in various pressure ranges.

6.3 Standard provision through remote calibration

In the calibration of pressure gauges used in the industrial sites, the "carry-in calibration" is the common practice where

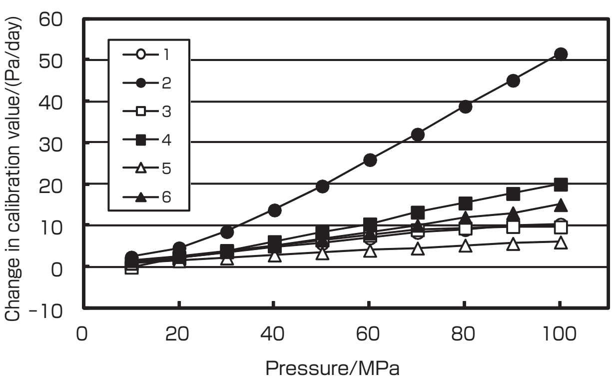

Fig. 7 Changes per day of the calibration value of the six digital pressure gauges used for the international comparison of hydraulic pressure

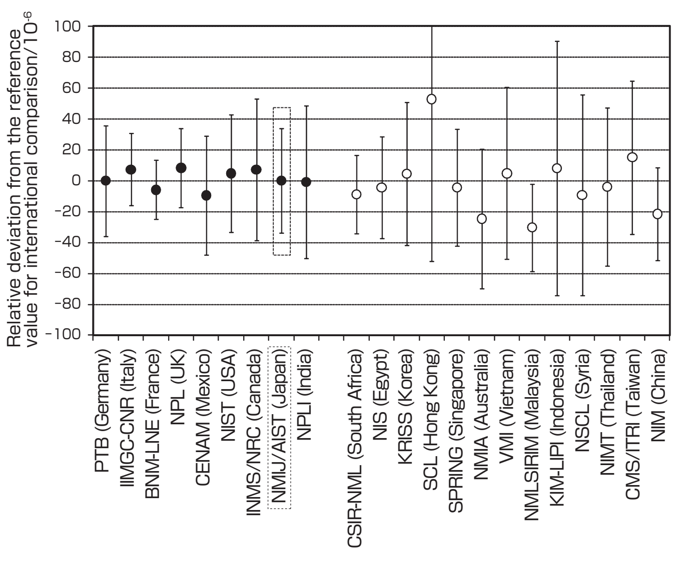

Fig. 8 Results of the two international comparisons at pressure 100 MPa
(●:CCM.P-K7, ○:APMP.M.P-K7)

Table 2. Form and characteristic of the calibration of pressure gauge

Calibration form	Carry-in calibration	Dispatch calibration (on-site calibration)	Remote calibration
Place of calibration	Calibration lab	Client-designated place	Client-designated place
Standard device	Reference standard	Transfer device (transfer standard)	Transfer device (transfer standard)
Calibration work	Lab personnel	Lab personnel	Remote operation, support personnel

the client takes the pressure gauge from the usage site to the calibration lab. However, for the pressure standard to be used in a wider range of industrial fields, it is necessary to consider a more efficient, new ways of providing the standard. In the NEDO Project "Technology Development for an 'e-trace' System", the remote calibration technology for pressure was developed to provide the pressure standard quickly, at low cost, and accurately, by utilizing the digital pressure gauge and the information technology such as the Internet[26][27]. This was a technological development that allowed the calibration of the pressure gauge at the industrial sites without moving it from the industrial site to the far away calibration lab, and was a new form of providing the pressure standard to reduce the burden on the calibration client.

Currently, when the calibration labs conduct calibration by request from the clients, the calibration can be roughly divided into three forms: carry-in calibration, dispatch calibration, and remote calibration. The major characteristics of each calibration form are shown in Table 2.

In the traditional carry-in calibration, the calibration is done as the client brings the pressure gauge to the calibration lab. In this case, the standard device of the calibration lab is used, and the work is done by the personnel of the calibration lab. When it is impractical to transport the client's pressure gauge to the lab, the calibration is done at the place where the pressure gauge is installed. The calibration done outside of the calibration lab is the dispatch (on-site) calibration. In this case, the transportable standard device (transfer device) is transported from the calibration lab to the site. The calibration work is done by the personnel of the calibration lab, as in the case of carry-in calibration.

In remote calibration, calibration is done by sending the transfer device to the place where the client's pressure gauge is being used, as in the dispatch calibration. However, the calibration lab personnel does not go to the site, and the calibration work is done by exchanging the measurement data via communication technology such as the Internet from the calibration lab. This point is different from the dispatch calibration. It is assumed that the client's pressure gauge (device under calibration) is a digital pressure gauge. The supporting personnel at the client company attends a technical seminar to do the work of installing the device under calibration and the transfer device, as this will not greatly affect the calibration result.

Figure 9 shows the procedure for remote calibration of pressure. It shows an example of the process where the client makes a request for remote calibration to the calibration lab. In this figure, the area surrounded by dashed line and marked "Internet" is the part that can be accomplished via the information network technology.

The development of the remote calibration technology was done for the two pressure ranges (gas differential pressure of 10 Pa ~ 10 kPa and hydraulic pressure of 10 MPa ~ 100 MPa) for which the performance of the digital pressure gauge has been proven in the past international comparisons, and where there was high demand for calibration from industry. Technological collaborations were obtained from Yokogawa Electric Corporation for the development of gas differential pressure, and Nagano Keiki Co., Ltd. for hydraulic pressure. The main items of development were as follows:

(1) Development of transfer device for remote calibration
(2) Development of measurement procedure applicable for remote calibration
(3) Execution of demonstration experiment in Japan and overseas

For Item (1), the portable transfer device for remote calibration was newly developed by incorporating the high-precision digital pressure gauge, pressure generator, and environmental

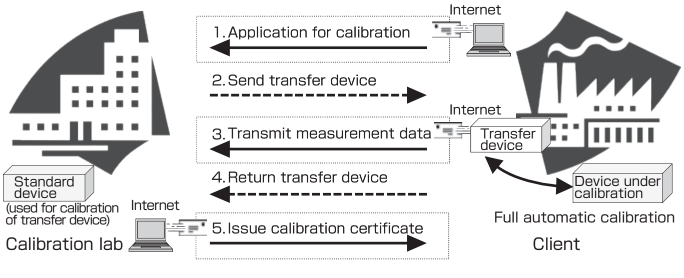

Fig. 9 Execution procedure for remote calibration for pressure

measuring device into one body to enable the fully automatic pressure generation and measurement. To increase the reliability of the transfer device, multiple high-precision digital pressure gauges were installed in each transfer device. For the gas differential transfer device, the pressure gauge with silicon resonant sensor as the pressure sensor was used, and for the hydraulic pressure transfer device, the digital pressure gauge with crystal oscillator as the pressure sensor was employed. To compensate for the lack of long-term stability of the installed digital pressures gauges, the detailed preliminary studies were done for the properties such as the stability in environment change and during transportation as well as the short- and long-term stability.

For Item (2), the program for conducting automatic calibration was created. Also, the remote calibration manuals for the personnel at the calibration lab and the supporting personnel at the client company were drafted.

For Item (3), numerous demonstration experiments for remote calibration were done in Japan and abroad using the developed transfer device. Figure 10 shows an example of the demonstration experiment for the gas differential pressure. As shown in Fig. 10(a), the remote calibration experiment was done by sending the transfer device twice to Kofu, Yamanashi Prefecture and once to Chongqing, China, with AIST as the calibration lab. Figure 10(b) shows the results of calibration of the digital pressure gauge with full scale of 10 kPa and resolution of 10 mPa, and they are shown as the deviation from the calibration value obtained in ordinary carry-in calibration. The maximum value of the deviation of each measured pressure was within 20 mPa, and this was sufficiently small at relative 2×10^{-6} or less of the full scale of calibrated pressure gauge. From this result, it was shown that the result equivalent to the carry-in calibration could be obtained by remote calibration, and that sufficient stability including the stability in environment change and during transportation could be obtained for the transfer device and calibrated digital pressure gauge.

The newly developed remote calibration technology was confirmed to be reliable from the results of the demonstration experiment, and it is currently established as the calibration service at AIST. The current uncertainties (confidence level of about 95 %) for the remote calibration service are 100 mPa or 0.01 % or less for gas differential pressure in the range from 10 Pa to 10 kPa, and 0.01 % or less for hydraulic pressure in the range from 10 MPa to 100 MPa.

7 Ripple effect to society and industry, and future issues

7.1 Increasing the reliability of pressure measurement at industrial sites

Currently, AIST establishes the national standards for the nine-digit pressure range from 1 Pa to 1 GPa, and responds to the various calibration requests from society and industry. For the maintenance and advancement of the group of pressure standard devices that comprise the national standard for pressure, the use of digital pressure gauge is promoted, as described in subchapter 6.1. Currently, we are developing the full automatic calibration technology for multiple pressure balances using the digital pressure gauge. This is expected to enhance the advancement and efficiency of the group-managed national standard devices.

For the main part of the calibration service currently conducted by AIST, the conformity assessment has been completed for ISO/IEC17025, which is the international standard that is the general requirement for the testing and calibration labs, as well as the technical assessment by the assessment personnel who are specialists invited from major overseas national metrology institutes. AIST's ability for calibration and measurement are recognized by the rest of the world.

The pressure standard provision to the industrial measuring sites and Japanese users is done mainly by the calibration labs for pressure accredited by the Japan Calibration Service

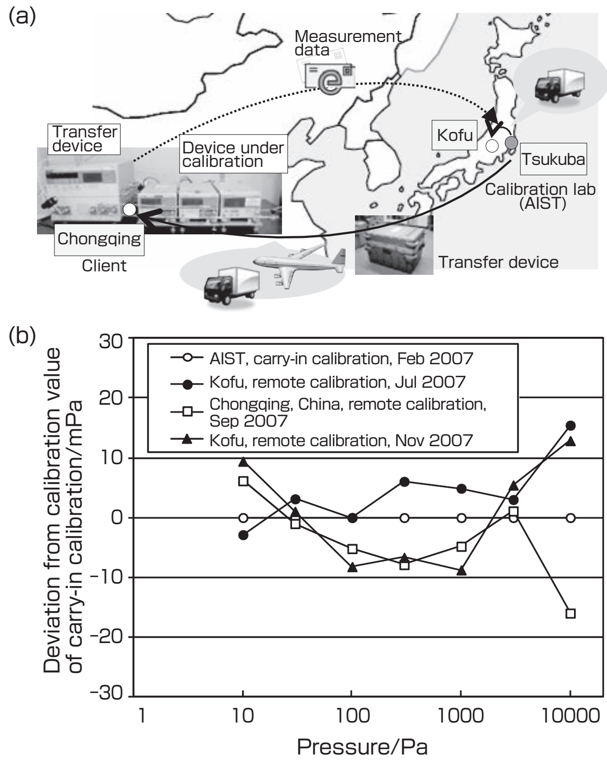

Fig. 10 (a) Circulation route of the transfer device in the demonstration experiment for the remote calibration of gas differential pressure and (b) the results (the calibration value of the remote calibration was expressed as the deviation from the calibration value of carry-in calibration)

System (JCSS) based on the Measurement Laws. Figure 11 shows the outline of this system. The values of the national standard are provided in the major pressure ranges for gas and hydraulic pressures, by AIST calibrating the pressure balances of the JCSS calibration lab. The JCSS calibration labs owns the standard device traceable to the AIST's national standard, builds the quality system through common requirements and application guideline, and are assessed by the accreditation organization. The JCSS calibration lab calibrates the various industrial pressure gauges under the JCSS using their own standard devices. AIST engages in the creation of the technical standard for pressure for JCSS, and also supports and cooperates in the accreditation assessment from the technical standpoint.

Currently, the list of accredited calibration labs and their best measurement capability can be seen under JCSS, Conformity Assessment in the website of the National Institute of Technology and Evaluation (NITE) (http://www.nite.go.jp/). As of September 2011, there are 13 calibration labs accredited in the "Pressure" section of JCSS. The number of JCSS certificates issued by the calibration labs has increased in the past three years, and about 2,300 certificates were issued in FY 2010. The number of certificates issued is expected to increase further in the future. The importance of the pressure measurement traceable to the national standard is increasing in the Japanese society and industry. The types of pressure gauge most calibrated are the digital pressure gauge and the mechanical pressure gauge. As mentioned earlier, the measured values of such pressure gauges are not directly affected by the acceleration of gravity, hence they do not have to be corrected and the traceability can be maintained easily. Also, the pressure balance that is normally used as the standard device in the high-pressure range tends to be large, and this may be a major burden on the calibration lab and the user for its installation and maintenance. However, the burden can be reduced by using the digital pressure gauge as the standard device.

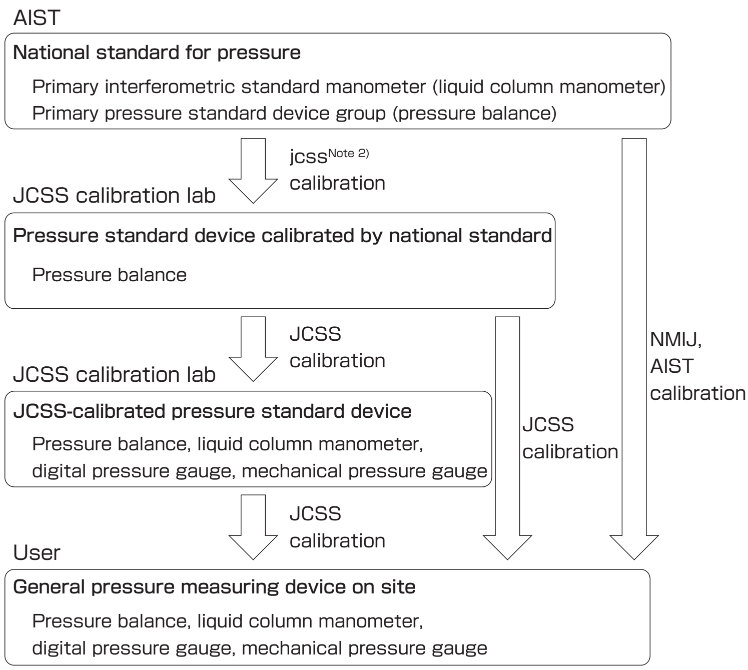

Fig. 11 Japanese standard provision system for pressure

While it is not discussed in this paper in detail, the organization of the differential pressure standard has progressed recently. There is a system where the JCSS calibration labs can set the differential pressure standard themselves using two JCSS calibrated pressure balances[8][15]. While the method using the two pressure balances ensures high precision, it is not a simple method that can be use in daily calibration work. Therefore, we developed the standard provision system using the digital differential pressure gauge to widely and efficiently disseminate the differential pressure standard. The calibration of the digital differential pressure gauge by the JCSS calibration labs has been available since 2008, and it has become possible to efficiently provide the differential pressure standard.

AIST has cooperated as the technical experts to organize various industrial standards[11]-[13] and technical standards, to enable the users of the pressure gauge and industry to utilize the technologies and findings pertaining to the property evaluation of the digital pressure gauge and the calibration method obtained by R&D. Particularly, procedures of characterization and calibration for digital pressure gauges were set in JIS B 7547[12].

The calibration method and the technology using the digital pressure gauge are improving the reliability of the pressure measurement at industrial sites through the AIST's calibration service, Japanese standard system, and various measurement and technical standards. In the development described in this paper, the main focus was on the use of relatively high precision digital pressure gauge. In the future, to maintain the reliability of pressure measurement efficiently and at low cost, it is necessary to apply the developed property evaluation and the calibration method to general industrial digital pressure gauge, and to incorporate them into the standard system.

The remote calibration is a technical development to reduce the burden on the client and to conduct the standard provision quickly, at low cost, and accurately. In this R&D, the basic technology necessary for remote calibration for pressure, or the technology to conduct calibration in a short time while maintaining reliability at the industrial site was developed. However, since the manufacturing cost of the transfer device for remote calibration is not kept low, currently the calibration cost is not lower than the carry-in calibration, and this is one factor that inhibits its wide use. Also, the framework for accrediting the calibration lab that conducts remote calibration is an issue. In the future, we would like to promote the use of

Table 3. International comparison for pressure in which AIST participated (since 2001)

Identifier	Kind	Pressure range	Year executed
APMP.M.P-K6	Gas gauge pressure	20 kPa - 105 kPa	1998-2001
APMP.M.P-K1.c	Gas gauge pressure	0.4 MPa - 4 MPa	1998-2001
APMP.M.P-K9	Gas absolute pressure	10 kPa - 110 kPa	2009-
APMP.M.P-K5*	Gas differential pressure	1 Pa - 5 kPa	2005-2006
CCM.P-K7	Hydraulic gauge pressure	10 MPa - 100 MPa	2003-2005
APMP.M.P-K7*	Hydraulic gauge pressure	10 MPa - 100 MPa	2002-2005
APMP.M.P-K7.1*	Hydraulic gauge pressure	10 MPa - 100 MPa	2007-2009
APMP.M.P-K7.TRI*	Hydraulic gauge pressure	40 MPa - 200 MPa	2001
CCM.P-K13	Hydraulic gauge pressure	50 MPa - 500 MPa	2008-2011
APMP.M.P-K13*	Hydraulic gauge pressure	50 MPa - 500 MPa	2010-
APMP.M.P-S8*	Hydraulic gauge pressure	100 MPa - 1000 MPa	2007-2010

*International comparison with AIST as the pilot institute

related technologies for the pressure gauge calibration at the industrial sites by the calibration labs.

7.2 International mutual recognition of pressure measurement

AIST participated in the international comparison of the national standards for pressure conducted by the Comité Consultatif pour la Masse et les Grandeurs Apparentées (CCM) of CIPM, as well as the Consultative Committee for Mass of the Asia Pacific Metrology Program (APMP)[19]-[23][25]. Table 3 shows the international comparisons in which AIST had participated and the ones in progress. AIST organized the international comparison as the pilot institute in the majority of the APMP international comparisons, and engaged in the creation of the execution schedule, drafting of the measurement manual, preparation of the transfer device and the property evaluation, organization of the comparison results, and the write-up of the final report[19]-[22]. In the international comparisons organized by AIST, the digital pressure gauge was used actively as the transfer device to enhance efficiency, as mentioned in subchapter 6.2.

The international equivalence of the AIST national standard was confirmed according to the results of the international comparisons of several pressure ranges[19]-[23][25]. AIST is planning to participate actively in the future international comparisons, and will continue to ensure the international equivalence of the Japanese national standards.

The results of the international comparisons conducted by AIST as the pilot institute are registered in the Appendix B of the international Mutual Recognition Arrangement, CIPM, as mentioned in subchapter 2.2. The calibration and measurement capabilities that the participating national metrology institutes claimed based on the results of the international comparison are registered in the Appendix C of the Mutual Recognition Arrangement after international recognition. By actively participating in the international comparison activities, we believe we were able to support the smooth accreditation of the calibration and measurement activities of several countries, mainly of Asia, as well as Japan.

By utilizing the digital pressure gauge, we were able to reduce the size and weight of the transfer device, hence reducing the problems during transportation. We were also able to obtain sufficient comparative precision by evaluating the long-term stability using multiple digital pressure gauges for redundancy in each transfer device. Also, the international comparison could be done in short periods by preparing multiple transfer devices and circulating them simultaneously. By using the transfer device comprised of the digital pressure gauge in the international comparison, we were able to efficiently confirm the international equivalence of the national standard necessary for international mutual recognition.

8 Conclusion

The R&D was conducted to confirm the international equivalence of the national standard for the international mutual recognition and to maintain the reliability of the pressure measurement at the industrial site, using the digital pressure gauge. As the pressure standard at the industrial site, the pressure balance and the liquid column manometer that have excellent long-term stability were traditionally used, but the use of the digital pressure gauge and various pressure generators are now increasing. The technologies for property evaluation and calibration of the digital pressure gauge described in this paper are used effectively in the pressure standard system, and the practical application of the effective standard provision system using the digital pressure gauge as the standard or transfer device is progressing. With the diffusion of JCSS, the calibration of the digital pressure gauge traceable to the national standard for pressure for a wide pressure range is now available to the general user through accredited pressure calibration labs, and this contributes to the increased reliability of on-site pressure measurement.

In the highly advanced and diversified social and industrial activities, the ensuring of reliability of pressure measurement according to usage and precision are demanded. The development of pressure calibration and standard provision that are easier, faster, and lower in cost, as well as being practical and efficient, are important, taking advantage of the operability and convenience of the digital pressure gauge in the future.

We shall engage in further R&D to maintain and improve the reliability of various pressure measurements in society and the industrial sites, by organizing and expanding the pressure standard provision system.

Acknowledgements

I am deeply grateful to Dr. Akira Ooiwa, head of Mechanical Metrology Division, National Metrology Institute of Japan, who gave us valuable advice and cooperation, and the people of the Pressure and Vacuum Standard Section.

Notes

Note 1) The deadweight pressure balance or deadweight pressure gauge is commonly called "pressure balance", "piston gauge", or "deadweight tester" in English. In this paper, it will be called the "pressure balance" which is the term generally used in the technical documents for various standards including JIS.

Note 2) In the Japan Calibration Service System under the Measurement Laws, the lower case letters "jcss" is used in the calibration certificate issued by the national metrology institute, and the upper case letters "JCSS" is used on the calibration certificate issued by the accredited calibration labs.

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Discussions with Reviewers

1 General

Comment (Akira Ono, AIST)

This paper describes an excellent research to improve the reliability in pressure measurements at industrial environments and to promote the international mutual recognition of pressure measurement results, by adeptly incorporating industrial digital pressure gauges with increased precision into the national standards system. Processes to identify elemental technologies by looking at the overall standards system for pressure measurements, and then creating a new pressure standards system by integrating the elemental technologies are well described. I think it is an appropriate *Synthesiology* paper.

2 Cause of time-dependent change of digital pressure gauge

Question (Akira Ono)

Figure 7 in the text shows change with time in the calibration results of digital pressure gauges used for the international comparison. While it may be difficult, since the degree of time-dependent change differs for individual pressure gauges, do you have any idea of what caused the time-dependent change?

Answer (Tokihiko Kobata)

The degrees of time-dependent change of the calibration value of the pressure gauge differ according to the types of gauges, the pressure range in which it is used, and the way it is used. In general, the time-dependent change of the calibration value of the pressure gauge is large in the gauge for high pressure, and small in the one for low pressure. In some cases, time-dependent change may not be so apparent. Also, as shown in Fig. 7, the amount of time-dependent change may be the function of applied pressure within a pressure gauge.

Therefore, while I cannot generalize, one factor for time-dependent change of the calibration value is the effect of plastic deformation of the pressure receiver. If the pressure receiver undergoes complete elastic deformation, it deforms according to the amount of pressure applied, and returns to the original form when the pressure becomes zero. However, in actual pressure gauges, when the pressure is applied, the pressure receiver may undergo slight plastic deformation. Even though the deformation may be slight, it will not return to the original shape completely when the pressure is back to zero. When the process of applying pressure then returning to zero is repeated, the receiver shows larger deformation with the same pressure. In the example of Fig. 7, the calibration values of the six pressure gauges all change as the deformation of the receiver increases with time, even at the same applied pressure. The time-dependent change of these calibration values contains the effect of the plastic deformation as described.

However, such changes are very small compared to the specified precision stated by the manufacturers, and it is hardly a problem in general use. However, in international comparison, the change must be corrected since a high level of measurement precision is demanded.

3 Quantitative comparison of the conventional method and the new method

Question (Jun Hama, Energy Technology Research Institute, AIST)

The calibration technology, where the high-precision digital pressure gauge is used as the transfer device, greatly contributes in reducing the works for the on-site pressure calibration, as a means to guarantee data reliability in product development and R&D.

Please indicate the actual cases where there were reductions of number of days or cost of calibration compared to the conventional method, due to the easier, more efficient, and lower cost of on-site calibration.

Answer (Tokihiko Kobata)

As the actual case of efficiency, normally one to two weeks of calibration period is needed, including the transportation of the device under calibration, in the carry-in calibration for the digital pressure gauge, while in the various demonstration experiments conducted in Japan, the calibration could be done in two days by remote calibration in most cases. Also, in remote calibration, the duty hours of the person in charge of the calibration can be reduced, so the cost of labor can be reduced. However, currently, the cost of remote calibration is not sufficiently low compared to carry-in calibration. The main reason is because the cost of the multi-function, high-performance transfer device used for remote calibration is high. To diffuse remote calibration, it is necessary to decrease the cost of the transfer device by narrowing down the functions according to the required uncertainty.

4 Region where the digital pressure gauge can be used as transfer device

Question (Jun Hama)

Please describe the specific work on the development of the simple, fast, and low cost method for calibration and standard provision for pressure using the digital pressure gauge, as much as you can disclose. Particularly, the advancement of remote calibration method at the industrial sites is an important key word. What is your assumed region of coverage in Japan and abroad? Are there some regions that are limited due to the uncertainty factors of the digital pressure gauge?

Answer (Tokihiko Kobata)

The specific developments were added in subchapter 6.3 for the remote calibration of pressure. I think it will become important to provide the realized values of the national standard for pressure widely and smoothly to the industrial sites. In the future, to further increase the reliability of pressure measurement, I think it is necessary to not only guarantee the results of calibration done at intervals but also to guarantee the reliability of the displayed values of the pressure gauge used in the industrial sites consecutively during regular use.

For the region covered by remote calibration, basically if it is a place where the transfer device can be sent safely, installed stably, and where the information network such as the Internet can be used, I don’t think there is any particular limitation, regardless of whether it is in Japan or abroad. However, in regions that may require a long time to send the transfer device, quick calibration that is the merit of remote calibration may be lost. Also, as you indicated, since the digital pressure gauge is used as the transfer device in remote calibration, the uncertainty factors shown in chapter 5 must be considered according to the environment where the calibration is done. For example, if the air conditioning is not sufficient, the uncertainty of calibration may increase due to the changes in the surrounding temperature.

5 Trends of foreign countries in using the digital pressure gauge

Question (Akira Ono)

Is there a trend toward incorporation of high-precision digital pressure gauges as a transfer device in foreign countries as well? Or is it a trend only in Japan?

Answer (Tokihiko Kobata)

In this paper, the establishment and maintenance of the national standard for pressure, international comparison of the national standard, and the cases for incorporating the digital pressure gauge into the Japanese national standard were described. I shall explain the situations.

First, on the use of digital pressure gauge in the comparative measurement of the pressure balance used for the establishment and maintenance of the national standard for pressure, the method of using the digital differential pressure gauge or the first calibration method described in subchapter 6.1 is used in other countries particularly for the calibration of gas pressure. However, the comparative method, the second calibration method, includes an elemental technology developed originally by AIST, and currently only AIST applies this method to the calibration in a wide range of pressure from low to 1 GPa. These two methods upgraded by AIST are recognized to conform sufficiently to the calibration results of the traditional methods, and are suitable for automation. In fact, they are being employed by Japanese calibration labs, and I believe it will eventually be used widely in other countries also.

Next, the use of the digital pressure gauge in the international comparison of the national standards is expanding. Particularly, in the low-pressure range of 1 kPa or less that normally cannot be generated with a pressure balance, it is common practice to use multiple high-precision digital pressure gauges as the transfer device. Also, in the international comparison that involves transportation in vast areas such as the Asia Pacific, United States, or Africa, there is greater transportation merit in using the small and lightweight digital pressure gauge as the transfer device, rather than the large and heavy pressure balance, as mentioned in subchapter 6.2.

For the remote calibration indicated as an example of incorporating the digital pressure gauge into the Japanese national standard, several similar technological developments have been reported around the world. However, currently, the remote calibration service for pressure gauge is established only at AIST. Several national metrology institutes around the world are interested in this remote calibration technology, and if the issues such as the reduction of calibration cost and the building of the framework for the calibration lab accreditation can be solved, as mentioned in subchapter 7.1, its use is expected to expand overseas as well as in Japan.

6 Development of remote calibration technology for quantities other than pressure

Question (Akira Ono)

I think the description in this paper is an example where increased performance of the transfer device had a major effect on the entire standards system. Are there any examples for quantities other than pressure?

Also, can you please briefly describe what approaches were taken for quantities other than pressure in the NEDO project for the remote calibration mentioned in subchapter 6.3?

Answer (Tokihiko Kobata)

Recently there have been various efforts to increase the performance of the transfer device (transfer standard) for various quantities, and the effect of the transfer device on the respective standard system is increasing. For quantities other than pressure, an example where the increased performance of the transfer device had great effect on the standard system is in the temperature measurement as described in *Synthesiology* [Vol. 3, No. 1, pp. 26-42 (Jul. 2010)]. In that paper, Arai *et al.* built the standard system for high temperature, and effectively utilized the newly developed thermocouple as the transfer device to maintain the reliability of the measurement.

In NEDO’s e-trace Project, the development of the remote calibration technology was done to efficiently provide various measurement standards. The various measurement standards that were studied in the e-trace project can be roughly categorized into two groups. One is the standard for the remote calibration using the international positioning system (GPS) and the optical fiber network, and the other is the standard using the portable transfer device. The former includes the standards for time (frequency), length (wavelength and optical fiber application), and electricity (direct current voltage), while the latter includes the standards for electricity (AC voltage, low frequency impedance), radiation, three-dimensional coordinate measurement, vibration and acceleration, pressure, and temperature. In the time (frequency) standard that is a typical example of the former, the remote calibration technology for frequency was developed using the method mediated by the GPS satellite. For the latter, we developed the technology for conducting the remote calibration by sending the transfer device to the client-designated place and then using the Internet to do the calibration, in the same way as in the pressure standard described in subchapter 6.3.

Efficient production of active form of vitamin D_3 by microbial conversion

— Comprehensive approach from the molecular to the cellular level —

Yoshiaki YASUTAKE and Tomohiro TAMURA *

[Translation from *Synthesiology*, Vol.4, No.4, p.222-229 (2011)]

Conversion processes of organic compounds using biocatalyst generally have high regio- and stereo-selectivity, and are becoming increasingly important for efficient production of chemicals. In addition, biocatalysis is less hazardous, less polluting and less energy-consuming than the conventional chemical method. We report the highly efficient bioconversion system using actinomycete *Rhodococcus erythropolis* to produce active form of vitamin D_3 currently used as a pharmaceutical. The improvement of performance of the enzyme used for the bioconversion has been achieved by the combination of evolutionary engineering and structure-based methods. Accordingly, the practical production efficiency of active form of vitamin D_3 has been substantially increased. In addition, we have succeeded in significant improvement of cellular permeability of vitamin D_3 by using nisin-treated cells, and have developed a new platform for vitamin D_3 hydroxylation process.

Keywords : Cytochrome P450, vitamin D_3, bioconversion, nisin, structural biology, protein engineering

1 Introduction

Vitamin D_3 (VD_3) is a fat-soluble secosteroid hormone involved in various important physiological functions in the human body[1]. Humans take in most of the VD_3 from food, and the ingested VD_3 is converted into active forms of VD_3 (25-hydroxyvitamin D_3 ($25(OH)VD_3$) and 1α,25-dihydroxyvitamin D_3 ($1\alpha,25(OH)_2VD_3$)) in the liver and kidneys. These active forms of VD_3 are deeply involved in maintenance of calcium and phosphate homeostasis, cell reproduction and differentiation, immunity adjustment, and other functions in the human body. The deficiency of active forms of VD_3 due to genetic or environmental factors is known to cause diseases such as osteoporosis, rachitis, psoriasis, and hyperparathyroidism, and in fact, active forms of VD_3 are used as the treatment drug for such diseases[1].

Currently, the $1\alpha,25(OH)_2VD_3$ mainly used as drugs is manufactured by a chemical synthesis method, and it can be synthesized in approximately 20 reaction steps with cholesterol as the starting substance (Fig. 1A). However, the yield is only about 1 %[2]. It is commercially manufactured despite such low production efficiency, since the active form of VD_3 shows pharmacological effect at very low dose (0.5~several μg/day or less), but the price is extremely high. While the price of VD_3 sold as general-use reagent is about 7 yen per 1 mg, the price of $1\alpha,25(OH)_2VD_3$ is about 130,000 yen/mg, according to the catalog of Company S. To mass-produce such fine chemicals, the manufacture method becomes complex due to low reaction efficiency in the aforementioned chemical synthesis, and high cost must be paid to manufacture highly pure product that can be used as pharmaceuticals. Also, in the chemical synthesis method, it is difficult to conduct regio-selective hydroxylation for the steroid skeleton, and it is not a suitable method for manufacturing active form of VD_3 and its derivatives that may be pharmacologically effective.

As an alternative to this chemical synthesis method, the manufacture of $1\alpha,25(OH)_2VD_3$ using the microbial conversion capability has been realized[3][4]. The actinomycete *Pseudonocardia autotrophica* that conducts this microbial conversion has the capacity to convert the VD_3 added to the culture into $1\alpha,25(OH)_2VD_3$. Moreover, the reaction intermediate $25(OH)VD_3$ produced in this microbial conversion process is a valuable medical intermediate with the pharmacological effect equivalent to $1\alpha,25(OH)_2VD_3$, and the $25(OH)VD_3$ can be obtained in the same process. The price of $25(OH)VD_3$ sold as general-use reagent is about 40,000 yen per 1 mg, according to the catalog of Company S (Fig. 1B).

The biocatalytic conversion using the enzymes of organisms, in general, shows high regio-selectivity and stereoselectivity, and has major impact on the synthesis of chemical substances. Also, the biocatalytic conversion is a safe method compared to the conventional organic synthesis, in that it has very low emission of pollutants under mild reaction condition (ordinary temperature and pressure), and involves low energy consumption. The term "green chemistry" is used for the biocatalytic conversion technology with the aforementioned characteristics, as it is known as an environment-friendly synthesis. The production of active forms of VD_3 by *P. autotrophica* is an environment-friendly production method with all of

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these characteristics. However, the productivity has not been maximized since there are various issues that will be explained later. In this paper, the issues and the development goals of the microbial conversion that has been currently realized are presented. Then, the research methods used to solve the issues, how the methods were combined, and the ideas that turned out to be useful are explained to illustrate the construction of a highly efficient and high performing recombinant microbial conversion system.

Please note that, in this paper, the information pertaining to the VD_3 hydroxide production, which is currently being done commercially by pharmaceutical companies, cannot be disclosed, and we cannot present the actual figures for how much the developed technology contributed in increasing the efficiency of the production.

2 Issues that must be overcome and the development goal

The advantages of the activated VD_3 production technology by microbial conversion are as stated above. Currently, the companies employ the method of culturing the breeding strain of *P. autotrophica* that has high VD_3 hydroxylation capacity, adding the VD_3 and cyclodextrin (CD) that increases the solubility of VD_3, and accumulating the hydroxylated VD_3 while growing the microorganisms (Fig. 1B). In the early research, the wild strain *P. autotrophica* was used, and 200 μg/ml VD_3 was added two days after culturing, and accumulation of 45 μg/ml 25(OH)VD_3 was observed after three days of culture[4]. Currently, the breeding strains are used for production, and the production efficiency is thought to have increased significantly.

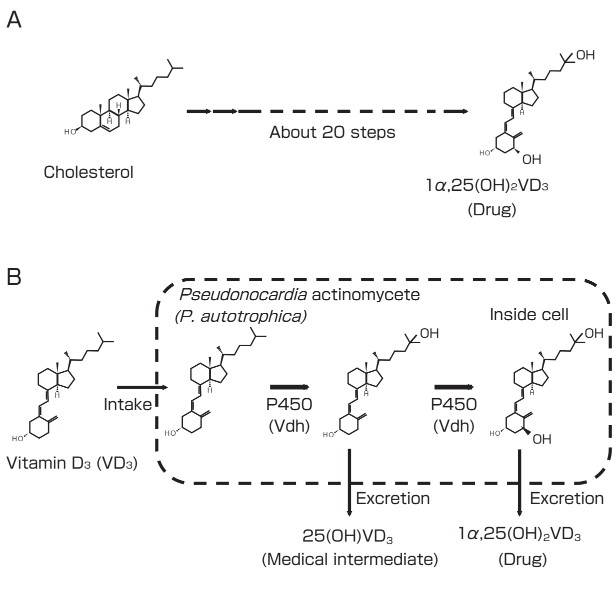

Fig. 1 Production method for active form of vitamin D3
Organic synthesis method (A) and microbial conversion method using *P. autotrophica* (B).

However, there are issues that must be improved in this method, and achievement of microbial conversion with dramatically increased performance can be expected by solving the issues. The issues and the expected causes are analyzed and summarized as a solution guideline as follows.

(1) Conversion efficiency: In the current microbial conversion, not all VD_3 added to the culture are converted, and there are remnant unreacted substrates. In the laboratory level analysis, over 30 % of unreacted substances are observed. Since the convertible amount may be dependent on the absolute amount of intracellular enzymes, the technology to stably express and accumulate a large amount of enzymes in the cell is necessary. By doing so, it may become possible to construct a conversion system where the majority of the added VD_3 can be converted into the active form.

(2) Conversion rate: In the currently conducted microbial conversion, over 100 hours is necessary for one conversion reaction. The main reasons are because the growth rate of the microorganisms is slow and because the enzyme reaction rate is slow since the VD_3 is a nonnative substrate for the enzyme. It is thought that the active forms of VD_3 of the same amount can be obtained in a shorter time by creating a variant enzyme with higher activity, and conducting the reaction in the microbial cell with a fast reproductive rate.

(3) Presence of the product of side reaction: The greatest issue in the microbial conversion is a production of side reaction products where the carbon-26 is hydroxylated. This 26-hydroxyvitamin D_3 (26(OH)VD_3) is eluted as a proximal or overlapping peak of the 25(OH)VD_3 in high-performance liquid chromatography. Therefore, to produce pharmaceutical quality 25(OH)VD_3, it is necessary to remove the 26(OH)VD_3 completely. This is a factor that reduces the yield of 25(OH)VD_3. This is caused by the low regio-selectivity of the enzyme reaction, and it is necessary to create a variant enzyme with improved regio-selectivity to control the 26-hydroxylation.

(4) Issue of cell membrane permeation: VD_3 is a fat-soluble vitamin with poor water solubility. Therefore, as mentioned above, cyclodextrin (CD) is added to the conversion culture along with VD_3, and VD_3 is dissolved by trapping it in the cyclic structure of the CD. Since the CD-VD_3 complex with relatively high molecular weight cannot permeate the cell membrane, it is necessary to devise a way where only the VD_3 separated from CD can permeate the membrane, or is made to permeate along with the CD. The rate of cell membrane permeation is the rate-limiting factor of this microbial conversion, and if the issue of membrane permeation is improved, both

the reaction efficiency (1) and the apparent reaction rate (2) can be expected to increase.

Of the above issues that must be solved, issues (1) to (3) pertain to the performance of the enzyme that is actually involved in the conversion reaction. Therefore, characterization of the enzyme and improvement by introduction of the mutation, as well as the mass accumulation technology of the enzyme in the cell are necessary. As it will be explained later, this enzyme is one of the enzyme group called cytochrome P450. Cytochrome P450 is the name of the enzyme group that holds the heme in the molecule and has the ability to insert the hydroxyl group into the hydrocarbon chain of various substances by receiving external electrons. It requires appropriate electron-supplying protein to be active. Therefore, it is necessary to look for a redox partner gene that allows the efficient transfer of electrons to this enzyme, and this gene must be coexpressed along with the enzyme. Issue (4) is related to the structure of the cell membrane itself, or the function of the transporter protein that allows a substance to permeate the membrane, and the cell that can obtain such information is desired.

To solve the above issues, we gathered data using the conversion host, which is a microorganism without the VD_3 hydroxylation capacity, is capable of mass recombinant expression, is easy to culture, reproduces quickly, and whose genome information can be utilized. This information was fed back to the *P. autotrophica* system. As an organic species that fulfilled this condition, we decided to use the *Rhodococcus* erythropolis host-vector system[5] that belonged to the same actinomycetes as *P. autotrophica* (Fig. 2).

3 Road to results

3.1 Isolation of the enzyme and identification of the gene

It was about 20 years ago when it was found that *P. autotrophica*, a rare actinomycete, possessed the ability to convert VD_3 to $1\alpha,25(OH)_2VD_3$. Due to the characteristic where it catalyzed the hydroxylation to the steroid skeleton, the enzyme that catalyzed this reaction was predicted to be a cytochrome P450, but the identification of the enzyme was not done successfully for a long time. Therefore, we started by searching the gene that encoded this enzyme. Since the genome sequence analysis had not been done for *P. autotrophica*, we attempted the purification of the enzyme directly from the cell extract using the VD_3 hydroxylation activity as the index. In general, the VD_3 hydroxylation activity could be detected by the coexistence of electron transferring protein that was needed for P450 to be active, and the target enzyme was confirmed as a P450 as predicted. However, purification was difficult due to the occurrence of the phenomenon where the VD_3 hydroxylation activity became undetectable during the purification process. After much trial and error, we found that salt (NaCl and others) had to be present in the reaction solution for this enzyme to be active, and it was possible to follow the activity to the final step of purification[6]. After identifying the N-terminal and internal amino acid sequences from the purified enzyme, we succeeded in cloning the gene that encoded this enzyme.

3.2 Reproduction of the VD_3 hydroxylation reaction in vitro

It was possible to produce the enzyme that showed VD_3 hydroxylation activity, by using the general overexpression system of the *E. coli*. However, it was necessary to add 5-aminolevulinic acid, a heme precursor, to the culture media to obtain the heme-containing holo enzyme. This is a method commonly used for the mass production of P450 enzyme using *E. coli* as a host cell. On the other hand, this enzyme could be obtained using *R. erythropolis* without adding 5-aminolevulinic acid to the culture. This was thought to be because the actinomycetes possess many P450 genes, the heme biosynthesis pathway functioned stably, and the level of intracellular heme could be maintained without depletion. Since 5-aminolevulinic acid is an expensive reagent, the microbial conversion using *R. erythropolis* as a host cell is advantageous when conducting the recombinant expression.

Next, the function of the enzyme was analyzed by *in vitro* reconstitution experiment. P450 required two electrons for one catalytic turnover of hydroxylation, and it was necessary to add the redox partner protein that supplied the electron to the assay system. Here, we used the commercially available redox partner proteins from spinach used widely for P450 assays. As a result, it was clarified that this enzyme continuously catalyzed the two-step hydroxylation from VD_3 to $25(OH)VD_3$ and from $25(OH)VD_3$ to $1\alpha,25(OH)_2VD_3$. Since $1\alpha(OH)VD_3$ was not detected, it was found that this

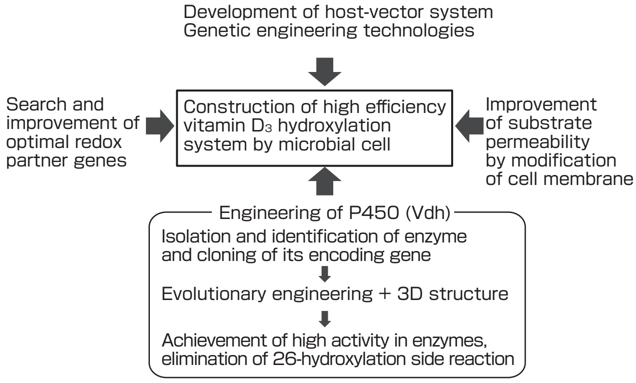

Fig. 2 Outline of R&D

enzyme first hydroxylated the carbon-25 of VD_3 and then hydroxylated the carbon-1 of 25(OH)VD_3. Also, a small amount of 26(OH)VD_3 was detected, and these substances matched the results detected in the cellular VD_3 conversion by *P. autotrophica*. We determined that this P450 was the enzyme actually responsible for microbial conversion, and named it vitamin D_3 hydroxylase (Vdh). The P450 will be called Vdh hereafter.

3.3 Intracellular conversion using the recombinant expression

Next we constructed the microbial conversion system that accomplished the VD_3 hydroxylation, using the recombinant cell of *R. erythropolis*. The VD_3 hydroxylation activity was very low with a single expression of Vdh, and it was necessary to coexpress some kind of redox partner protein. Therefore, we constructed a thiostrepton-inducible expression vector that contained genes encoding the Vdh and redox partner proteins (ferredoxin and ferredoxin reductase) derived from *R. erythropolis*. Then, co-expression was conducted in the *R. erythropolis* cell, and VD_3 was added to the culture. As a result, it was confirmed that the active forms of VD_3 were produced when the *R. erythropolis* cell was used. It has been reported that the redox partner that is capable of most efficiently supplying the electrons to P450 is not necessarily the protein with which P450 couples in the cell of the original organism[7]. This is thought to be because the electron transfer efficiency is affected drastically by the slight difference in the intracellular environment or the intracellular expression level of the gene. Therefore, we conducted the conversion tests by inserting various electron transfer protein genes to the aforementioned co-expression vectors, and looked for the redox partner that showed high VD_3 hydroxylation activity. As a result, it was found that the proteins called AciB and AciC from *Acinetobacter* were the most compatible partner to Vdh.

3.4 Two different approaches to enzyme improvement

In general, the enzymes produced by organisms are catalysts that specifically respond to certain substrates and are exclusive to some specific reaction. However, since VD_3 is not found in the soil where the *P. autotrophica* exists, it is thought that Vdh is not an enzyme that evolved for (is specific to) the hydroxylation and metabolism of VD_3. In fact, the VD_3 hydroxylation activity of the isolated and purified enzyme is fairly lower than the activity of the P450 with the specific function involved in the biosynthesis of some substance. Therefore, the VD_3 hydroxylation activity of Vdh is not at all optimized as an enzyme, and we believe it can be improved further.

There are two completely different approaches when introducing variations to improve the enzyme. One is the rational design where the 3D structure of the protein is analyzed and the mutation is introduced based on this structural information. While this is a powerful method in the case where the correlation of the structural functions is clear, since the 3D structure of the protein is a complex system composed of multiple parameters, there may be no simple correlation between the amino acid residue and the function. The other approach is the evolutionary engineering (directed evolution) where the genetic variation library to which the random mutation is introduced is created to screen the variants with improved performance. While much effort will be required to create the library and to verify the variations by assay, this may enable extracting the variations that may improve the enzyme function at any part of the sequence. In our research, we conducted improvement of enzymes using both methods, without choosing one of the two approaches (Fig. 2). As a result, the advantages of both the strategy of variation introduction based on structure and the strategy based on evolutionary engineering could be utilized, and we were successful in creating a useful variant.

3.4.1 High activation of the enzyme

The mutant that significantly improved the VD_3 hydroxylation activity was constructed by combining mutations generated by directed evolution. The quadruple mutant (Vdh-K1) that had the highest improvement showed about 12 times increase of 25-hydroxylase activity and about 25 times increase of 1α-hydroxylase activity compared to the wild type Vdh (Vdh-WT)[6][8]. Interestingly, the four mutations were located far from the active site, and it is difficult to find such mutations by rational design. The discovery of Vdh-K1 was the result of the maximization of the benefits of evolutionary engineering unfettered by structural information. On the other hand, we were able to infer why such variations brought about major activity improvement through the analysis of the 3D structure. Major structural change was observed between the Vdh-WT and Vdh-K1, and three of the four mutations might have induced such structural changes. This suggested that the activity increase of Vdh was not caused by an optimization of the substrate binding pocket, but by the orchestration of the conformational equilibrium between open and closed forms (Fig. 3)[8]. P450 is an enzyme involved in the detoxification and the biosynthesis of the secondary metabolites and various substances in nature, and there are many molecular species of the enzyme with wide substrate specificity. The conformational shift by introduction of a few mutations observed in our research may be a mechanism that allows in nature to adapt P450 to ever-emerging new conditions and substrates. Through the results obtained, the possibility of significantly improving the production efficiency of hydroxylated VD_3 was found. However, due to the issues in membrane permeability of the substrate that will be described later, major increase in the production efficiency of hydroxylated VD_3 had not been achieved simply by increasing the enzyme performance.

3.4.2 Completely eliminating the enzymatic side reaction

In the active form of VD_3 production by *P. autotrophica*, side reaction product, in which the carbon-26 is hydroxylated, was also produced at the rate of about 10 %. This was clearly an issue of the substrate recognition of the enzyme, and it was thought necessary to either fabricate the enzyme that tightly recognized the VD_3, or to fine-adjust the bonding orientation of the substrate in the substrate binding pocket. Therefore, we attempted to determine the crystal structure of Vdh in complex with VD_3, and based on the structural information, we introduced the mutations to the substrate-binding pocket. Vdh-WT had low substrate binding affinity, and substrate complex crystal could not be obtained. However, high activity mutant Vdh-K1 was successfully crystallized as the complex with VD_3, and we were able to clarify how the enzyme recognized VD_3 (Fig. 4)[8]. Of the amino acid residues that formed the substrate binding pocket, we focused on the amino acid residue positioned in proximity to the carbon-24 to -27 of VD_3, and the variant (I88V) with lowered percentage of side reaction was obtained by saturated mutagenesis for those residues[9]. The quintuple variant of Vdh-K1+I88V decreased the side reaction rate to about 1 % in the bioconversion test by *P. autotrophica*, and the 26(OH)VD_3 decreased to below detection limit in case of the single I88V variant. While this result was based on the structures, it was not entirely a rational design. It is extremely difficult to logically estimate which variation of what amino acid residue will reduce the side reaction. We succeeded in selecting the mutant that achieved the side reaction reduction by selecting the amino acid residues based on the 3D structure, and then by taking the strategy of saturated mutagenesis for the selected amino acid residues. Through this research result, we succeeded in increasing the production efficiency of the 25(OH)VD_3, and the development for practical application is currently in progress.

3.5 Processing the cell

In producing the active form of VD_3 by R. erythropolis with recombinant expression of Vdh, the final major issue was the cell membrane permeability. This is not a unique problem of *R. erythropolis* but a similar issue was observed also for *P. autotrophica*. In *R. erythropolis*, no correlation was recognized in the conversion rate of hydroxylated VD_3 and the amount of intracellular enzyme. Even if the expression level of Vdh was changed, the conversion rate was fixed at a certain rate[10]. Even the Vdh-K1 (see section 3.4.1) in which dramatic high activity was confirmed using the *in vitro* reconstitution system did not show much significant difference from the wild type when the conversion was done in the *P. autotrophica* cell. This meant that the performance of the enzyme inside the cell was not utilized, and it was estimated that the cell membrane permeation of substrate VD_3 acted as the rate limiting factor. The VD_3 is a fat-soluble steroid and solubility in the water is extremely low. Therefore, in the current microbial conversion, the solubility is increased by adding CD to the culture to trap the VD_3 in the cyclic structure of the CD. In fact, the VD_3 hydroxylation of Vdh increases dramatically by the addition of CD to the solution both *in vivo* and in vitro experiments. However, the permeation of the high molecular weight CD-VD_3 complex through the cell membrane is difficult,

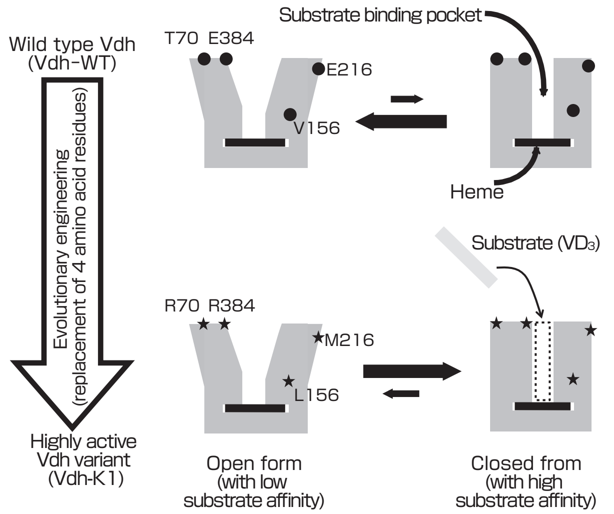

Fig. 3 Structural mechanism of activity enhancement of P450 Vdh

In general, P450 is in equilibrium of open and closed structures, and the substrate is likely to bind with the closed structure. The equilibrium between these structures shift greatly according to the variation selected by evolutionary engineering. The population in closed form increased and the activity was enhanced.

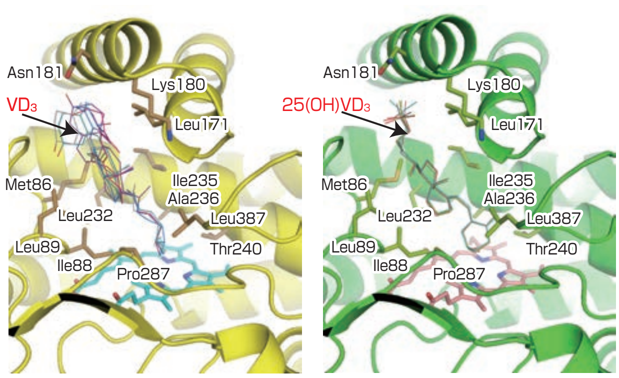

Fig. 4 Recognition mechanism of substrate in an anti-parallel orientation by P450 Vdh

The VD_3 (left) and 25(OH)VD_3 (right) can bond to the enzyme in an anti-parallel orientation, and that gives them the capacity for two-step hydroxylation to 1α,25$(OH)_2VD_3$. The amino acids that were candidates for variations to eliminate the side reaction were selected from the detailed structural information of the substrate binding site.

and the VD_3 is thought to enter the cell diffusely after it breaks off from CD. However, the actual mechanism of the intake of VD_3 into the cell is completely unknown (Fig. 5). Therefore, considering the possibility that the VD_3 may be transported by some kind of membrane protein (transporter), we attempted the identification of a gene that might increase the VD_3 conversion activity, by conducting the random gene destruction experiment using transposon and by using the *R. erythropolis* genome information. However, we have not been able to find such genes.

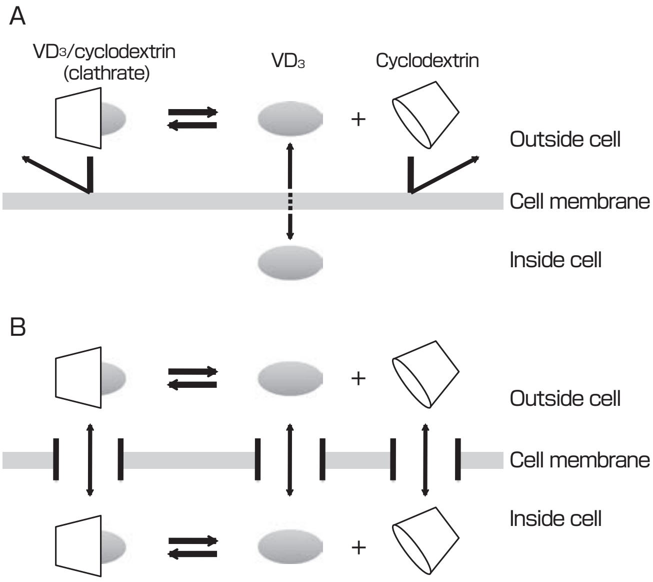

Fig. 5 Conceptual diagram of the permeability of cell membrane

In the cell membrane in an ordinary state (A), only VD_3 may permeate the membrane by natural diffusion. In the cell membrane with pores created by nisin-treatment (B), the low molecular weight substance including cyclodextrin can move through freely.

Therefore, we changed our way of thinking and investigated whether the CD-VD_3 complex could be delivered directly to the intracellular enzyme by physically making a hole in the cell. We focused on the antibacterial substance called nisin[11]. Nisin is an antibacterial peptide composed of 34 amino acids derived from *Lactococcus lactis*, and is approved as food additive. The action mechanism of nisin has been studied thoroughly, and it shows antibacterial activity by creating pores with diameters of about 2-2.5 nm in the membrane of the gram-positive bacteria, and the intracellular low molecular substances leak outside of the cell through the pores[12]. Although excessive addition of nisin will cause bacteriolysis, the *R. erythropolis* cell is characterized by bacteriolysis resistance compared to other bacteria. Therefore, by adjusting the amount of nisin added, it is possible to create a unique situation where pores will be formed while the cell structure is maintained without bacteriolysis. In theory, proteins such as ferredoxin and P450 cannot leave the cell, so such a cell can be used as a reaction vessel packed with high concentration of enzymes. To experimentally investigate whether CD and VD_3 could freely enter and leave the cell through the pores, green chemiluminescence CD was added to the nisin-treated cell, to observe the intracellular intake of the substances. As a result, it was confirmed that the luminescence level from the cell increased depending on the nisin concentration and treatment time, and the pores could be used as the passage of CD.

Next, the nisin-treated cell was used to conduct the VD_3 hydroxylation experiment under various conditions, and we found that the hydroxylation capacity increased depending on the amount of enzyme present in the nisin-treated cell, unlike the untreated cells. Moreover, it was found that it was important to have a NADH regeneration system in the

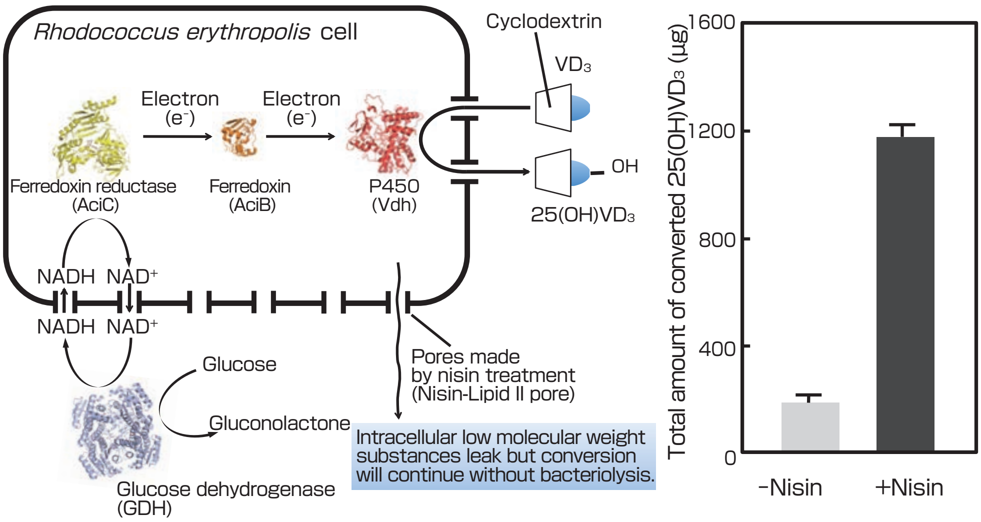

Fig. 6 Conceptual diagram of the hydroxylated VD_3 production using the nisin-treated *R. erythropolis* cell

reaction system and to have a stable redox partner in the cell[10]. Glucose dehydroxylase (GDH) was used as the NADH regenerator, and the reaction system using the wild-type Vdh, in which the AciB and AciC derived from *Acinetobacter* were co-expressed, was constructed as a highly stable redox partner (Fig. 6). The hydroxylated VD_3 productivity of the nisin-treated cell was observed using this system. As a result, it was confirmed that hydroxylation efficiency was several times higher in the nisin-treated cells, compared to that of the untreated cells. It was also found that when the reaction, where one cycle consisted of a 16-hour reaction, was repeated in the nisin-treated cell, the VD_3 hydroxylation rate per cycle increased to maximum 90 % (less than 50 % in untreated cells), and the total yield of 25(OH)VD_3 after four reaction cycles was about six times higher compared to the untreated cell[10]. The conversion reaction system using nisin could convert 90 % of the VD_3 in a short time, and significantly increased the production efficiency of the 25(OH)VD_3. Moreover, since the nisin-treated cell used the buffer system as the reaction solution instead of culture media, the amount of foreign substances could be reduced. Also, the cells could be recovered and reused, and this is an effective method in the case where the productivity must be raised by increasing the number of reactions using the substrate with low solubility. If this technology could be used in *P. autotrophica*, we believe we can create a production system where highly active enzyme Vdh-K1 can be maximized.

4 Future developments and issues

This R&D was conducted to find an efficient production method of active form of VD_3 by microbial conversion and to construct an excellent conversion system in terms of efficiency and cost by overcoming the issues of conversion by wild-type strains that are currently done by the companies. The conversion system of *R. erythropolis* cell treated with nisin that was constructed in this research may realize a production efficiency that surpasses the system using *P. autotrophica*. Currently, we are engaging in the investigation of whether further efficiency can be achieved in the electron transfer between the redox partner and P450. Since the structural stability of the highly active mutant (Vdh-K1) is reduced, we think it is necessary to construct a system that promotes activity while maintaining the thermostability. There are already reports that the electron transfer efficiency has been increased in P450 and the activity is increased[13], and the introduction of the mutation on the ferredoxin binding region is expected to increase the conversion performance. On the other hand, the substance conversion technology that combines CD and the formation of pores by nisin treatment can be applied widely to the conversion system of substances where the highly hydrophobic, poorly soluble substances and CD are used as carriers. In general, the achievement of high efficiency in the microbial conversion of fat-soluble substance is very difficult, and we think there is high value in such usage. In the future, we would like to evaluate the usage value of nisin and CD in other microbial conversion systems.

Acknowledgements

This research was conducted jointly with the Pharmaceutical Chemical Division, Mercian Corporation (currently, this division is part of Micro Biopharm Japan Co., Ltd.), with the support of research funds from the NEDO Project "Development of Basic Technologies for Advanced Production Methods Using Microorganism Functions". We express our sincere gratitude.

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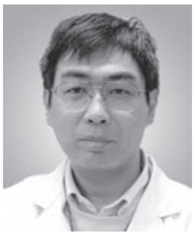
Completed the doctorate course at the Graduate School of Science, Hokkaido University in 2004. Industry-academia-government collaboration researcher, Graduate School of Science, Hokkaido University. Doctor (Science). Researcher, Research Institute of Genome-based Biofactory, AIST in April 2005. Researcher, Bioproduction Research Institute, AIST in April 2010. Currently engages in the researches for the VD_3 hydroxylation reaction described in this paper, as well as the biosynthesis enzyme of new antibiotic material and the structural function analysis and achievement of high function for useful function proteins such as the medical diagnostic enzymes. In this paper, was in charge of the structural research, functional analysis, and functional alteration of the proteins involved in microbial conversion.

Tomohiro TAMURA



Completed the courses at the Faculty of Medicine, The University of Tokushima in 1993. Research Fellow of the Japan Society for the Promotion of Science. Doctor (Medicine). Post-doctorate at the Research Unit for Molecular Structural Biology, Max Planck Institute of Biochemistry in 1994. Joined the Hokkaido National Industrial Research Institute, Agency of Industrial Science and Technology (currently, AIST) in 2000. Professor of the Graduate School of Agriculture, Hokkaido University in 2002. Leader of Proteolysis and Protein Turnover Research Group, Bioproduction Research Institute, AIST in 2011. Visiting professor of the Graduate School of Agriculture, Hokkaido University. Currently engages in the development of expression platform that allows the use of the *Rhodococcus* actinomycetes for diverse purposes. In this paper, planned and summarized the research for overall VD_3 hydroxylation reaction.

Discussion with Reviewers

1 Overall comment

Comment (Kazunori Nakamura, Biomedical Research Institute, AIST)

Overall, the specific reaction system is not clearly stated in the paper. Also, since you do not state the specific figures for the cost and efficiency of the conventional method, it is difficult to determine quantitatively how much increased productivity and cost reduction were achieved in this research.

Answer (Yoshiaki Yasutake, Tomohiro Tamura)

I added the explanation pertaining to the reaction system as you indicated. However, this reaction system is a technology that is currently being used in production, and is a corporate secret. Therefore, I cannot disclose any specific information including the production efficiency. I added and modified the descriptions to the extent that I can disclose at this point.

2 Description of specific production method

Comment (Kazunori Nakamura)

In the description relating to bioconversion rate, you say that the issues are the slow rate of growth of the microorganisms and the reaction speed of the enzymes, but it is difficult to know which phase is a more serious problem since you do not describe the specific production method. For example, do you convert using non-growing cells after culturing the microorganisms, or using growing microorganisms? Please describe the specific production method in detail.

Answer (Yoshiaki Yasutake, Tomohiro Tamura)

As mentioned in Discussion 1, the various information relating to the current hydroxylated VD3 production system cannot be disclosed. Therefore, please understand that I cannot provide comparisons using actual figures. I added and modified the descriptions to the extent that I can disclose at this point.

3 Future issues in realization

Question (Motoyuki Akamatsu, Human Technology Research Institute, AIST)

You write that you developed a production method with extremely high production efficiency in this research, and you aim for further efficiency of electron transfer in "4. Future developments and issues". Why do you need further efficiency? Pertaining to this, you mention that this is a joint research with Micro Biopharm Japan Co., Ltd. Do you need further R&D for actual production? Is the electron transfer efficiency the barrier for the production? Please describe any other barriers, if any, to clarify the positioning of the results.

Answer (Yoshiaki Yasutake, Tomohiro Tamura)

This R&D is an effort to enhance the efficiency and refinement of the production method using *P. autotrophica* that has already been realized. The productivity has greatly improved through the modification of the enzymes based on evolutionary engineering and 3D structure, as well as changes in the organic species. However, the thermostability of the enzyme with increased activity by the introduction of variation is low, and the issue that the enzyme cannot be accumulated in large amounts in the cell became apparent. Therefore, as a method for increasing activity while maintaining enzyme stability, we think the increased efficiency of electron transfer for P450 is necessary, and we infer that there are rooms for improvement in the Vdh, AciB, and C systems. By advancing the electron transfer efficiency, I think it is possible to go beyond the current production efficiency. On the other hand, the barrier in using the reaction system by *R. erythropolis* in actual production is not a matter of production efficiency, but is the problem of using recombinant bacteria. Currently, the company uses the breeding strain and does not engage in production by recombinant bacteria. To change the bacteria type and to start up the production system using the recombinant bacteria, various procedures including safety tests will become necessary, as well as additional facility investment to build such a plant. The market for active form of VD_3 is expected to grow further, and I expect the production using the technology we developed will be in demand in the future. I modified the paper according to your comment.

4 Significance of high activation of enzyme in the production process

Comment (Kazunori Nakamura)

You describe the increase of the activity of the enzyme itself in achieving high activation. I think you need to provide some description on how effective this activity increase is in the actual production process. I think it will be better if the reader can image how much cost reduction can be ultimately achieved by such a process.

Answer (Yoshiaki Yasutake, Tomohiro Tamura)

In the laboratory level analysis, high enzyme activation or the increased intracellular accumulation of enzymes were achieved, yet these have not led to the dramatic improvement of the production volume of 25(OH)VD_3. This may be because VD_3 is a fat-soluble substance, and transfer into and out of the cell is limited greatly compared to water-soluble molecules. The conversion rate was improved significantly by increasing the solubility by trapping the VD_3 in cyclodextrin, but the improvement of activity dependent on the accumulation volume of the intracellular enzyme was not confirmed. As described in the paper, we obtained the result that the conversion activity could be increased by removing the barrier of VD_3 cell membrane permeability by using the antibacterial substance nisin. However, when the nisin-treated cell was used, the production volume of the hydroxylated VD_3 increased according to the accumulation volume of the intracellular enzyme. I predict that similar effect will be obtained if highly active enzymes are used. In the near future, if we could use the system, in which the membrane permeability is improved using nisin, in actual production, I think the highly active enzyme can exert its potential sufficiently.

Systems and synthesiology

[Translation from *Synthesiology*, Vol.4, No.4, p.230-237 (2011)]

Editor-in-Chief Ono and Senior Editor Akamatsu of *Synthesiology* visited Mr. Hiroshi Kuwahara, Senior Corporate Adviser of Hitachi-Maxell, Ltd., former Vice-Chairman of Hitachi, Ltd., and former member of the Council for Science and Technology Policy. Mr. Kuwahara is also a member of the Systems Science and Technology Committee headed by Senior Fellow Hidenori Kimura, Japan Science and Technology Agency (JST). Mr. Kuwahara has spearheaded several proposals at the Committee based on his abundant experience in various systems developments. We held a roundtable discussion under the keywords, systems and synthesiology.

Synthesiology Editorial Board

Participants of the roundtable discussion

Hiroshi Kuwahara	Senior Adviser Emeritus, Hitachi, Ltd.; Senior Corporate Adviser, Hitachi-Maxell, Ltd.
Akira Ono	Senior Vice-President, AIST (Editor-in-Chief, *Synthesiology*)
Motoyuki Akamatsu	AIST (Senior Editor, *Synthesiology*)

Akamatsu

AIST promotes the *Type 2 Basic Research*, because we feel that the research results cannot be utilized fully in society with analytical research alone, and we need to establish a methodology for the science of manufacturing "things" or the synthetic research.

Mr. Kuwahara emphasizes the importance of systems building. Manufacturing "things" leads to enhancement of the system, and in terms of how to build without falling into reductionism, I feel that the aim of systems is similar to the aim of synthesiology, although the terminologies may be slightly different. This is why we wanted to hear from Mr. Kuwahara.

Based on your experiences, Dr. Ono, please introduce AIST's synthesiology. Then we would like to ask Mr. Kuwahara to discuss systems building.

Synthetic research and analytic research

Ono

I was a student of the Department of Physics, Faculty of Science in my university days. After graduation I studied temperature measurements and standards at the former National Research Laboratory of Metrology, Agency of Industrial Science and Technology. The Laboratory was reorganized into AIST in 2001. Then I was greatly influenced by Prof. Yoshikawa, the first president of AIST in terms of *Type 2 Basic Research* proposed by him

When I worked on measurements and standards, I had experiences where original papers of our research results would not be accepted in a straightforward way by the academic societies. Our mission was to create highly accurate national measurement standards and to calibrate measuring instruments at the highest accuracy. Since the calibration work extended to business in the private sector, we worked not only on raising the accuracy of the standards, but also on making the calibration work as simple as possible and even on considering cost performance to establish a national traceability system in Japan. Yet, results obtained in these research efforts were not very easy to be accepted as original research papers by the academic societies. We were often asked by the reviewers, "What are the novelty and originality of your work?"

We envisaged a scenario for the national traceability system that best fits the Japanese society. For example, we designed a traceability system by thinking which private calibration labs had sufficient levels of technology, what equipment they had, and how many engineers they had. However, such stories were said not to be appropriate as original research papers. Then we had to write papers only about new elemental technologies that were introduced to the national standards system.

Although it may be more or less different in different disciplines, the Japanese academic societies are mainly for "academia" itself and are not for "engineers" as in the United States, and therefore, it tends to pursue academic novelty.

I’ve always felt that such pursuit may lose good contact with society, and that’s not healthy. When I create something valuable to society, I want to write about it in my original research paper, and I hope it is accepted. But the academic society does not often have such a mind to do so.

However, Prof. Yoshikawa said, “There is *Type 2 Basic Research*.” He stated that not only conventional research for elemental technologies but also processes of integrating elemental technologies and manufacturing things are important, and that it was a new kind of basic research. Although such researches were taken lightly in the traditional scientific academy and were considered to be at lower levels, he said that that was not true. When I heard him say so I thought that this is exactly what I wanted. I thought that points of contact with society should be described in research papers, and now I have become the editor-in-chief of *Synthesiology* to realize this.

Today’s science was established over a long period of time. Various kinds of factual knowledge were acquired by observing nature and entities, hierarchizing, and analyzing through reduction to elements. Although this method has been greatly successful in science, looking at the current environmental issues and the nuclear power plant accident, the current science that rests upon reductionism and analysis is insufficient in facing the reality of solving such complex issues. Perhaps, there may also be a problem in the current scientific academies that function only within their finely segmented discipline.

In fact, private companies are engaging enthusiastically in “synthesis” and “systems,” but the current science has failed to reach that stage. I thought science should extend to include synthesis and systems. It would be science of designing systems and science of integration and synthesis. These are called *Type 2 Basic Research*. If AIST works harder in this field, I feel communications with industry people will go more smoothly. I hope a synthetic approach will be recognized as a method of R&D in contrast with an analytic approach.

Although development and commercialization that are done by private companies are similar to *Type 2 Basic Research* in terms of synthetic activity, public research institutes such as AIST and private companies may have different positions even though the objectives are the same. We are trying our approach while hoping to firmly position the processes of creating systems and products in research.

Systemic thinking for achieving the objective

Kuwahara

I agree with your comments overall. I come from a background of electricity. I joined the company to work somewhere between electricity and mechanics. When I entered the company, the word “systems” was not a general term, but I worked on all sorts of systems including chemical plants, batch control of chemical and food products, sequence control, thermal power plants, nuclear power plants, nuclear plant operation training simulators, and production management systems for automobiles, tires, and building materials.

For the thermal power plant, the United States was ahead in systems, and Japan was a licensee of the US. Our customer made a request that they wanted to automatize the operation. To learn the technology from the US that was engaging in the challenges in this field, I studied in the US for a year, but things were not that great as expected. What I studied hard was their “failures”. I learned carefully what kind of failures there were in the past, used that experience to automate the Japanese plants, and as a result, Japan became number one in the world in the automation of thermal power plants.

The problem was what do you do when the plant undergoes unexpected failure. It can not be fixed by computers and it has to be done by persons. If we all depend upon automation only, we overlook training our operators for such cases. To control the plant during emergency, the basic policy is “stopping” it, but it has to be stopped safely. Accurate decision can not be made if the operators are not trained for such non-computer-controlled emergencies. We learned that the emergency training must be done separately while working on automation.

Dr. Akira Ono

Mr. Hiroshi Kuwahara

Also, the Japanese iron and steel making technology became number one in the world in only 30 years after WWII because of the advanced control technology. It was the issue of systems of how to control the process. In the US, the method used was to gather and analyze voluminous data and control the plant by a simple feedback method, while in Japan the original approach for a control system was developed by seeking a theoretical solution by computer. The objectives were the improvement of operation efficiency and of product quality.

Needless to say, systematic thinking and system technology are essential in R&D. The outlet of science and technology for society is the "system" as a complex body of various fields of science and technology. Systematic thinking is not about just creating systems and products, but about obtaining a solution when a certain objective is set. Since the "objective" is clearly set ahead of proposing, planning, and hypothesis formation, everything will be processed smoothly if one creates a competitive scenario to achieve the objective. I believe the key point here is that the challenger must take vigorous actions at this point, but what is the situation now? I think it is really pessimistic.

I know the importance and the value of academic papers, but the Okochi Award is given to the achievements in R&D for production engineering and production technology as well as the actual execution of advanced production method, so this is an award for the world of practice. As Dr. Ono states, heavy emphasis is placed on the papers in traditional academic societies, and the issue is how *Type 2 Basic Research* can gain acceptance as a research discipline, including giving positive evaluation to researchers active in this field.

However, I should say, the term Type 2 "Basic Research" gives us a feeling of a kind of uncertainty. Of course, I fully understand its importance, but the word, "basic research," implies that "it is not an applied research". Yet, I think we need to have the perception that there is *Type 2 Basic Research* together with applied research. The acceptance must be achieved as such . In Japan there are over 750 societies for natural science, and I think you should engage in a strong movement for creating a "systems society" and awarding the researches in this field.

Ono

Certainly, it is difficult in the traditional, segmented academic societies.

Akamatsu

How do you think one can learn such systemic thinking or systems synthesis ability, and what do you think are the qualities necessary?

Kuwahara

What is most important is the "spirit of never-give-up" shared among researchers and designers trying to accomplish competitive systems. It means that what is important is the state of mind for the "spirit of never-give-up", that one will never compromise until he/she achieves fully the objective. If the person has that spirit, whether he/she succeeds or not depends on the ability to create the system. The person with the ability should think of something totally unimaginable and come up with some new competitive system. Therefore, it is necessary to keep "training people" toward that direction by giving them actual hard work for a while ("a while" means until an academic system methodology is established). Excellent system designers have plenty of past experiences and wide-ranging knowledge, and draw them out according to the objective to create the scenario. I have been wondering whether it is possible to theorize such thinking process soon, and we must try to realize this. Other abilities include the ability to cooperate with other people to gain other's help, the ability to organize the total process, and the ability to make appropriate compromises.

Akamatsu

For researchers, it is important to maintain the goal without wavering in executing the research. When one feels, "Well, this will do", it is usually when the goal becomes fuzzy and self-evaluation loosens.

Kuwahara

In industry, easy compromise will always lead to failure. If one looses, one will know for sure. It is a very severe and cold finding.

Ono

It means that the criterion of evaluation is very clear in companies, but it may not be so clear in academia. Objective self-evaluation is important.

Systems building and scenario

Akamatsu

Earlier, Mr. Kuwahara said, "If we have a clear objective, once the scenario is written everything will be easy thereafter." As the editorial policy of *Synthesiology*, we ask the authors to "write your scenarios", but this is rather difficult.

Dr. Motoyuki Akamatsu

Ono
We tell the authors that a *Synthesiology* paper is requested to describe two things, i.e. a scenario to reach the goal and elemental technologies to be integrated. The scenario includes why the authors wanted to do the research and what the authors thought at the beginning of the research. The elemental technologies include materials and parts for the authors to select to do the research. However, since most researchers are just familiar with *Type 1 Basic Research*, they have a hard time writing. Even though they are the ones who actually did the research, they often say, "I don't recall how I came up with my own scenario."

Kuwahara
That's the point. They've got the answer, and they must think about how they arrived at the answer. I have experiences where I come up with a hint for a system when I am hanging out with people unrelated to my work, or in my leisure time. I think various input lay behind scenario building.

Ono
I think so, too. It may seem to be a flash thought, but even a flash thought will not come to you unless there is a base. So, I ask the authors to write what their bases are. That is quite difficult, but I wish to gradually systematize this process.

Kuwahara
Were the papers of *Synthesiology* about this?

Ono
The point might not have been clear. I guess that insufficient communication between the editor and the author is the excuse.

Kuwahara
Before going on to the scenario, it may be useful to do a breakdown of "what knowledge you have, and which other knowledge you poured in to achieve the objectives" Such efforts are important for system generation, and I support such efforts.

Another thought I had was that the researchers are almost always evaluated by their papers, but perhaps that may not lead to an outlet emphasizing policy. *Type 2 Basic Research* is fine as is, but the assets of systems are the discoveries that result into patents. I think additional value should be placed there.

Ono
Conventional papers were of analysis and breakdowns, weren't they? One wrote about taking a watch apart and described what came out. We didn't have a paper that described the act of assembling the parts to make a watch.

Kuwahara
Yet, when we ask the researchers to do *Type 2 Basic Research*, they will do it if it is the development of the *Type 1 Basic Research* in which they were involved. The researchers will never do it from someone else's *Type 1*. Japan will not be able to achieve innovation in this way. To break this is my primary request to AIST.

Ono
That is the best part about AIST's *Type 2 Basic Research*. At AIST, we encourage the researchers to get out of the "octopus hole" or of the compartmentalized way of thinking to transcend the framework of segmented scientific academies and to look at things with a bird's eye view.

Mr. Kuwahara mentioned, "Systemic thinking does not always create outlets, but systemic thinking is essential to obtain a solution for objectives." I totally agree. I think it is the same for joint researches. The point is that doing joint research is not of value itself, but that we have to do research jointly because one cannot realize societal values alone. Therefore, we must consider the scenario for a system.

While the levels of the systemic thinking and scenarios may differ in corporate minds and with those of the AIST researchers, I think good joint research will evolve by sharing common factors. I think we had not been enthusiastic about sharing a scenario until now because our attention was paid to details of technology. If corporate people would discuss scenarios a bit more, I think we can talk about what are different in the scenarios, what are the same, and what we can share. I expect such talks will take off from there. What do you think?

Kuwahara
As one example, there is the seawater desalination system. Currently, the seawater is filtered through the reverse osmosis film. When I hear the explanation on its principles, I am surprised that there are many things that are done without knowing the exact basic principles about water, salt and others. The researchers should clarify and understand basic principles first, and then try out what would happen if this or that film is used or if some biological treatment is applied, or if certain intermediary treatment to the sea water is applied. Various options should be studied for achieving competitive systems. This is currently being done as a JST project. We are working to make this Japanese desalinization process technology overwhelmingly competitive in three, or if not, five years.

We do not have organized thoughts about the principles or laws, and many people in the academia do not know about systems or synthesiology. To find common grounds for our respective fields, I think it is important for us all to study "what system generation is". We are starting a study session for systems technology in a project of the Center for Research and Development Strategy. I hope people of AIST will join us. Basically, joint work will be the best solution.

Akamatsu
Until about 1965, I think the university professors and company people worked closely together to solve various issues. After 1965 and well into the 70s, the companies gained force, and the companies became leaders in system generation and the professors were left behind. I feel that the situation is still continuing. We must do something about this.

Kuwahara
I was the chairman of the Japan Society for Technology of Plasticity. If one has a firm objective of "I want to make this hardware by Plasticity", studies could be completed and the solution could be obtained using the plasticity technology only. However, if safe and secure society and environment are involved, IT comes in, police system enters, and various services become relevant. This cannot be dealt with by segmented, vertically divided academic societies alone.

Today, our government is promoting the export of Japanese systems overseas and national budget is allocated here and there. Now is the chance. Japan has advanced technology for water, environment, food, and others, and considering the export industry, I think major contributions can be made if the points discussed herein are brought together for system generation.

Effective industry-academia-government collaboration

Akamatsu
AIST is spending effort to promote the collaboration among industry, universities, and public research institutions. I think the industry-academia-government collaborations will become more important in the future.

Ono
Actually, I don't think the industry-academia-government collaboration is going very well in Japan currently. The reasons are due to the budget and the organizations. Yet, besides that, I think there may be a gap in the consciousness of researchers and engineers. If we understand each other more clearly on what our objectives are, what our differences are, and what can be shared as a common goal, I think industry-academia-government collaboration may be pursued more smoothly.

In AIST, research group leaders have their own scenarios in pursuing their research. We can present these scenarios to obtain better understanding of corporate people, and we are able to communicate with each other at scenario levels. Can we expect such efforts from the corporate side? Are there any barriers such as the issue of corporate secrets?

Kuwahara
That barrier is not small. We must sign a non-disclosure agreement, we must set limits on paper writing and the publication at academic societies must be done after patents are filed, or the researcher must never talk about what they are doing in the project. All of these are for protecting against unnecessary disclosure of corporate strategy. The researchers are itching to publish as soon as possible, and I don't have a good general solution on that aspect. For now, we must go case by case, and some good solution must be provided for each individual project and I think we can do it.

Akamatsu
Dr. Ono mentioned that the industry-academia-government collaboration is not going very well. What should we consider to do an effective collaboration?

Kuwahara
To strengthen the industry-academia collaboration and for the science and technology to make contributions to the development of society, the Council of Science and Technology Policy must acknowledge *Type 2 Basic Research*, and the government must provide budget to this field. It must gain general acceptance in the academic arena. And then there must also be an unspoken perception that the traditional basic research will not be eliminated.

Ono
AIST is recently encouraging the consortium method where collaborations are done with multiple companies, and this is being done for solar cell projects. AIST and each company sign separate agreements to ensure that information does not flow directly from company to company while the objectives and information for the basic parts are shared among the participants.

Expectation for AIST on systems research

Akamatsu
You talked about the importance of systemic thinking. There is a scenario before the system is created, and I believe the methodology of the scenario for creating the system is synthesiology.

Kuwahara
I have no objections to your comment. The 20th century was called the age of systems, but in Japan, thermal power, nuclear power and chemical plants are almost entirely copied from others. The systems that were created originally in Japan are quite small in number and they are iron-steel manufacturing and railroad train control.

Therefore, I would like AIST to engage in systems research in the 21st century. One example is solar power generation. If you want to do it as *Type 2 Basic Research*, I hope you do at least about one-third of the system, hopefully the kernel of the system. That way, the rest can be an opportunity for system engineers at AIST to learn and grow in the actual project.

Akamatsu
I think it is the matter of how to create "the ability to think systems" rather than the "thing". In traditional science and technology, the scholarship was considered to be the manufacturing of "things". What is truly important is how to "think about things", and it is necessary to position this as part of the discipline. The "ability" part of the discovery ability is important.

Ono
We would like to advance friendly competition of discovery ability with private corporation researchers.

Kuwahara
That will be great. My proposal is for us to cooperate and set a path to summarize "how it is actually done", and to consider together what must be further enhanced and what the academic positioning is in the future.

Akamatsu
We would like to work on that. Thank you very much for today.

(This roundtable discussion was held at Hitachi Maxell, Ltd. in Chiyoda-ku, Tokyo on May 9, 2011.)

Article contribution after the roundtable discussion

The Editorial Board asked the participants to contribute articles on subjects that could not be covered in the roundtable discussion and they are as follows.

Hiroshi Kuwahara:
Speeding up the development of systems technology

It is commendable that the stance of placing importance on the relationship of science and technology and society, such as the returning the results of science and technology R&D to society and promoting R&D with consideration for the outlet, is gaining acceptance.

The contact points of science and technology with society is all systems in the field of industry. They include extremely wide ranges from simple systems (such as home appliances) to large-scale complex systems (nuclear power plants, various smart systems, etc.). However, it is regretful that not much effort has been spent on R&D in this field, and it is an urgent issue considering the progress of Japan.

Then we must ask, "what a system is" and "what the system building technology is". Although these are important basic understandings that are essential to the future systems related R&D, their analyses are almost untouched, and it must be done immediately. When people understand these points correctly, only then can we move to the next step. At this moment, it is reckless to start theoretical building right from the initial stage.

As someone who has somewhat deeper experience in systems building, I shall attempt to set a bold hypothesis as follows. I would like to see a discussion.

Typical procedure for systems building

Step 1: Clearly define the objective of the system.

Step 2: Seek the essence of the system. Investigate what principles are expected to be processed and how they are applied in terms of physical, chemical, or social sciences, for the system.

Step 3: Widely gather the findings, knowledge, and research results that may be necessary for building the system based on Step 2.

Step 4: Extract the necessary items, or if some item is missing, assume new technology that is desired and is realizable. Then design several system building plans.

Step 5: Evaluate them quantitatively according to the objective, and the related parties convene to evaluate and discuss them. Make any additions if necessary, and determine the final plan. In this case, price and realizable time scale must be raised as important evaluation items.

I think many people, including researchers, have gone through similar experiences in the past. As people bring their experiences to the discussion, I hope the form of what we are pursuing will take shape. I fear that unless the discussions start from actual experiences, it will end up as a hollow theory.

I had a valuable opportunity to engage in discussions with the people of AIST, and it was extremely significant. However, I also felt that both parties will be hardened into their own ideas and the investigations will go off into different directions if they are left as they are.

There is a momentum now where various activities are starting up, such as the investigations of systems technology at CRDS, at AIST, and at the Transdisciplinary Science and Technology Research Group (Federation and Committee), as well as the emphasis on systems at the Council for Science and Technology Policy, consideration of systems at the Council on Competitiveness Nippon (COCN), and others.

The mutual collaborations of these activities and the activities that may arise in the future are important and significant, and I hope the industry-academia collaboration will bring about wonderful results.

Profile

Hiroshi KUWAHARA
Graduated from the Department of Electrical Engineering, School of Engineering, The University of Tokyo in 1960. Director of Omika Works, general manager of Electric Systems Business Section, managing director, senior managing director, vice-president, and vice-chairman of Hitachi, Ltd. Former member of the Council for Science and Technology Policy, Cabinet Office. Chairman of Hitachi-Maxell, Ltd., Hitachi Cable, Ltd., and Hitachi Kokusai Electric Inc., Special consultant of Hitachi, Ltd. Former president of Global Water Recycle and Reuse System Association. Former vice-chairman of Japan Federation of Engineering Societies. Currently, Senior Adviser Emeritus of Hitachi, Ltd. and Senior Corporate Adviser of Hitachi Maxell, Ltd.

Akira Ono: Future of systems and synthesiology

I have spent all of my working time in the government and the academia. Before the meeting, I was a little bit concerned about how much common ground I could have with Mr. Kuwahara, who had worked as a member of the Council of Science and Technology Policy, and is the opinion leader of R&D in the private sector. Yet, when the roundtable discussion was finished, I saw commonality in several points with him, and I am grateful to him for our sharing this precious opportunity.

I was able to reaffirm that the essence of “scenario” and “integrated and synthetic research” emphasized in *Synthesiology* was deeply related to systems research and systemic thought. I feel that I now see the path and issues for good collaboration among researchers of universities and public research institutes like AIST and researchers and engineers of private companies.

Science was born in 17th century Europe, and reductionism has been very successful. Scientists have conducted researches using analysis as a main tool under the belief that it was important to understand to the lowest layers by breaking down and hierarchizing various phenomena. This approach has been firmly established in the time span of three hundred years, and it is still greatly effective. Yet looking at the environmental issues and the nuclear power plant accident in Fukushima, we can see that reductionism alone is insufficient in dealing with the systems and complex problems. The current science cannot respond to such social demands. Also, as a result of thorough practice of reductionism, the scientific academy has become extremely segmented, and the members have become content with studying narrowly within their own disciplines.

Figure a is a comparison of processes in the analytic approach and in the synthetic one. Processes in the current science (*Type 1 Basic Research*) that are mainly of the analytic approach are illustrated in the upper part of the figure. In contrast, processes in the synthetic approach (*Type 2 Basic Research*) are shown in the lower part of the figure. The current science starts from nature and entities, where human beings are one of the entities, on the right-hand

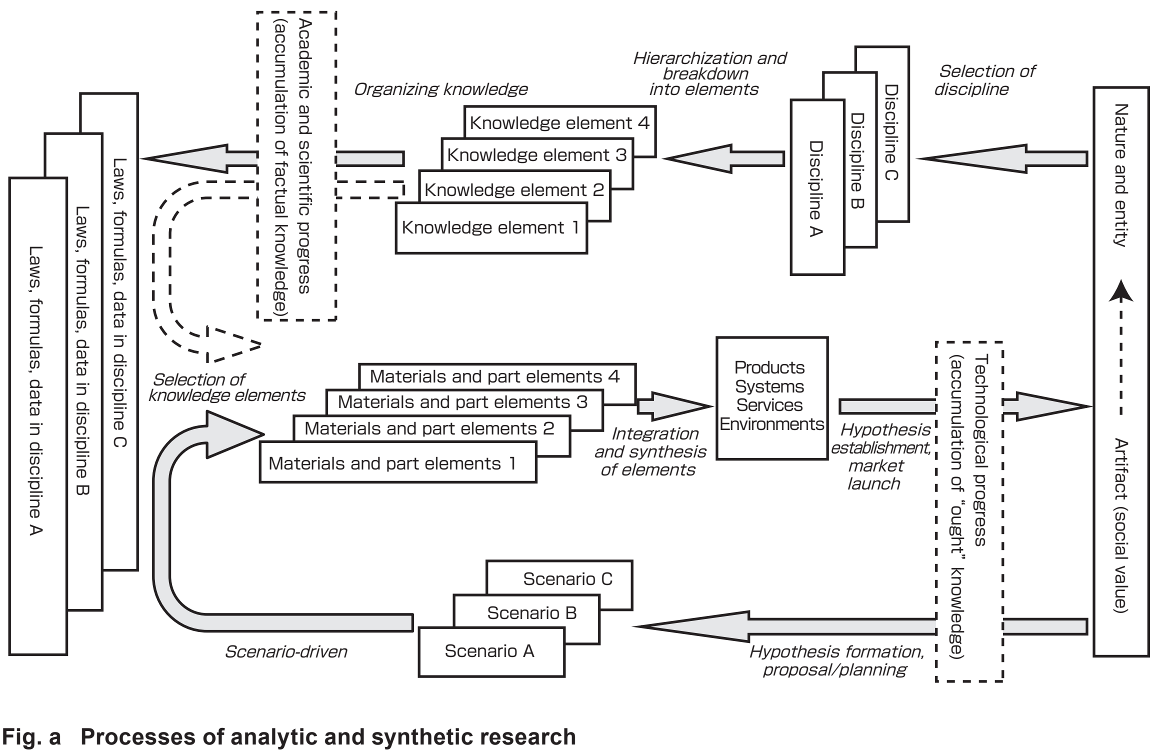


Fig. a Processes of analytic and synthetic research

side, and these are analyzed from viewpoints of individual disciplines. For example, there are physics, chemistry, biology, mechanical engineering, electrical engineering, and others. Nature and entities are observed from individual viewpoints, ranked into hierarchy, broken down into elements, and knowledge elements are organized to enable logical understanding within individual disciplines. For example, in Discipline A, laws, formulas, and data in physics are organized, while in Discipline B, those of mechanical engineering are organized.

On the other hand, human beings have manipulated nature and entities, or have used technology to create “artifacts” that are socially valuable. In solving current complex issues, the final goal of making “artifacts” on the right-hand side in Fig. a, or social values, cannot be attained unless scientific results transcending various disciplines are used. The lower part of Fig. a shows what processes are taken for synthetic R&D. If there is an artifact that one wishes to create, one must make a scenario for realization. In a company, it may be proposals and planning, but in general, it may be “hypothesis formation”. The hypothesis for creating a target artifact is considered by researchers and engineers, and various scenarios are made. Researchers and engineers engage in scenario-driven R&D based on the scenario that they consider best. Optimal items are employed amongst the knowledge elements accumulated in the individual disciplines to create materials and part elements. Then products, systems, services, and environments are created as “artifacts”.

Created artifacts are put into the market, undergoes evaluation, and returns to the proposal, planning, and hypothesis formation, to enter the loop of evolution. If the created artifact is recognized as an “entity”, it will be incorporated into the above loop and becomes the subject of scientific (*Type 1 Basic Research*) analysis.

Current research papers mostly describe the upper processes in Fig. a. The academia highly evaluates the act of organizing knowledge elements such as how an important knowledge element was discovered or how important laws or formulas were found. On the other hand, the lower processes are also an advanced intellectual activity, and I wish to consider it as an extension of science. To do so, it is necessary to separately define the originality and novelty of the lower processes. This is a challenge of *Synthesiology*.

Mr. Kuwahara indicated that it is important to consider how to set up a scenario when the artifact that one wishes to create is determined. This is also another challenge of *Synthesiology*. I think that a person who completed good R&D valuable to society must have had a good scenario. I want him to reconstruct and describe his own scenario in retrospect. When the industry, academia, and government share such scenarios, I hope it will greatly promote mutual understanding and further collaborations.

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
Revised August 5, 2010

1 Types of contributions

Research papers or editorials and manuscripts to the "Readers' Forum" should be submitted to the Editorial Board. After receiving the manuscript, if the editorial board judges it necessary, the reviewers may give an interview to the author(s) in person or by phone to clarify points in addition to the exchange of the reviewers' reports.

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:

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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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Vol.4 table of contents (2011)

Vol.4 No.1

Research papers

Round-table Talk

Report

Vol.4 No.2

Research papers

Round-table Talks

Vol.4 No.3

Research papers

Round-table Talks

Vol.4 No.4

Research papers

Round-table Talks

Letter from the editor

This issue contains the roundtable discussion with Mr. Hiroshi Kuwahara, former vice-chairman of Hitachi, Ltd. and current honorary advisor of Hitachi Maxell, Ltd., and Editor-in-Chief Ono and Senior Editor Akamatsu of the *Synthesiology* Editorial Board.

Mr. Kuwahara indicates the importance of the “systems” in R&D as the complex of science and technology in all situations, not just the “systemic thinking and systems technology”. Mr. Kuwahara, a former member of the Council for Science and Technology Policy, states it is necessary for the Council to acknowledge *Type 2 Basic Research* so it would gain wide acceptance.

In the article contribution after the roundtable discussion, Mr. Kuwahara addresses the importance of gathering the findings and knowledge that may be important for systems building, of establishing the hypothesis for new technology if it is lacking, and of designing and evaluating the proposals. Also in the contributed article, Editor-in-Chief Ono indicates that proposing and planning through multiple scenarios are necessary to realize an artifact that one wishes to create. The two authors both point out that it is necessary to formulate and verify a systemic hypothesis to create an artifact that is valuable to society. That is the essence of “systems and synthesiology”.

As I wrote in the “Letter from the Editor” in the previous issue, an artifact operates and exerts its function in the environment of a real society, is traded on the market, and fulfills individual utility. Unless those conditions are met, an object is merely an artificial thing that may not generate value. I also wrote that the value is not simply market diffusion, but also includes social acceptance and cultural ripple effect, and the value is social because its essence is “spread”. The four papers published in this issue are strongly related to market diffusion and social acceptance, and are written in anticipation of generating social value.

One question arises here. That is, can “social value” be a subject of synthesiology? The synthesized artifact is an output into society, while the real society that receives the input is full of imperfect information. The value cannot be determined beforehand, but the value is synthesized socially. As the network externality spreads further in society today, perhaps the “synthesis of value” may be the challenge for *Synthesiology*.

Editor
Kanji UEDA

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