July 2013 NO.8

Torrent

10^{16} Weave New Materials

Special Feature：
Furthering "Visibility" for Computational Materials Science

Achieving Increased "Visibility"

CMSI Distance Learning

MateriApps
A portal for materials science simulation

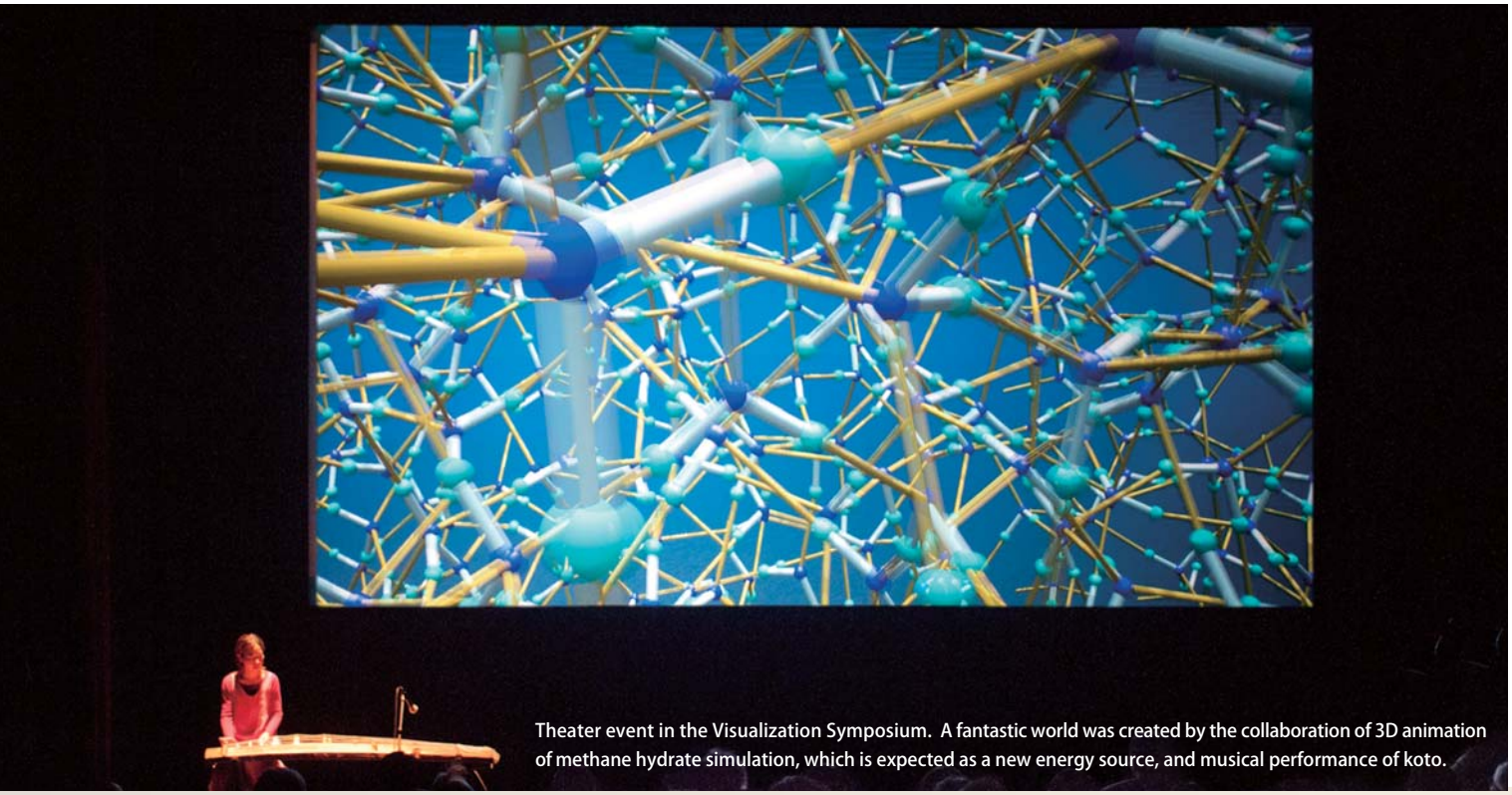
Interview with
Nobuyuki Matubayasi and
Shun Sakuraba, developers of ERmod

Torrent 【tɔ:rənt】:
The Newsletter of the Computational Materials Science Initiative (CMSI)

part 1

Special Feature | Furthering "Visibility" for Computational Materials Science

Achieving Increased "Visibility"



Theater event in the Visualization Symposium. A fantastic world was created by the collaboration of 3D animation of methane hydrate simulation, which is expected as a new energy source, and musical performance of koto.

Society has high hopes for the materials science research of CMSI, which aims at the development of next-generation electronic devices, medicines, energy conversion materials, etc. However, atoms and molecules that make up materials cannot be seen by the naked eye, and thus the computational materials science that endeavors to discover the behavior of materials through the large-scale computing is said to be too difficult to understand. How can we convert social expectation into interest? We will search for a path to "visibility" based on the discussions and proposals at the 1st Computational Materials Science Visualization Symposium in March 2013, organized jointly by Toyohashi University of Technology and CMSI.

"Increased Visibility for People" — A Primary Focus of CMSI

The move to make science more "visible" can be thought of as one part of public relations activities. Naturally communicating scientific achievements to society at large is important, but for CMSI there are other important targets as well. These include theoreticians, experimentalists, researchers in other fields and private companies, as entrances and exits of materials science research, as well as high school and undergraduate students and people in charge of hiring at companies and research institutes, as potential sources and export markets of human resources.

What kinds of things should be made "visible" in public relations activities? First and foremost are the achievements of computational materials science. Normally these are released in the form of academic papers, conference presentations and patents. For the general public and high school students, however, the publicity should include not only research outcomes but also the things that make computational materials science interesting and the views of the researchers: What they were interested in and why they conducted their research. In addition, the software programs that have been developed at CMSI and the experience and information that have been accumulated in the course of parallelization and optimization are also important CMSI assets. Publishing these assets and working to disseminate them both within the field and to other fields will also play a publicity role. Finally, public relations activities about the young researchers who are engaged in research and development within CMSI will also be essential for creating career paths and providing stimulation to the field.

CMSI is currently putting its energies into a variety of activities. The first is the establishment of a "Division Researcher" system. (This was featured in Torrent No. 3.) CMSI is a network-style community that has 14 Divisions in Japan as well as various institu-

tional participants. For this type of organization, a function is needed to gather together the experience, information and knowledge accumulated at each location, and then make it the common property of the field of computational materials science and disseminate it within that field. This is the mission of the Division Researchers. The educational activities that are conducted for the benefit of graduate students and young researchers are also taking new forms such as distance learning (Part 2 of this Special Topic).

The second effort for making computational materials science more visible is the newsletter you're reading right now. Torrent has featured special reports on major topics such as CMSI research achievements, application development, educational activities and so on. In these articles, young researchers, application developers, teachers, graduate students and other persons appear as writers or interview subjects, and the articles

Tomoyoshi Ito gave a talk on the theme of "Communicating Science Interestingly by Visualization and Scenario."

do not focus only on research achievements but also make an effort to make these people more visible. As Torrent sees it, the first step in achieving increased visibility is finding ways to get people to pick up the newsletter. For this reason, we publish it in hard copy form, and we made the cover design bright and colorful, as electrons and molecules may strike people as cold and remote.

CMSI is also working to make applications more visible. Up to now, the tendency has been to not consider application development to be research, and for this reason the face of the developers has hardly been seen. CMSI not only publishes applications but also goes out of its way to introduce the developers of those applications. CMSI is also working to form a community made up of the theoreticians, experimentalists and company people who use our applications. Currently, MateriApps, which enables these users to exchange views with one another, is also been under development (Part 3 of this Special Topic).

Hiromi Yokoyama gave a talk on the theme of "Can Visualization be the Key? — Strengths and Weaknesses of Computational Materials Science from the Viewpoint of Other Fields."

"Communicating Correctly" to Ensure "Understanding"

Many proposals were made by the invited speakers at the Computational Materials Science Visualization Symposium.

Tomoyoshi Ito (Professor of Engineering Research, Graduate School of Engineering, Chiba University) is a researcher who is studying 3D images that use holography. He noted that human vision is very severe when it comes to the quality of still images, and the low resolution of a still image bothers us. But we are very tolerant when it comes to moving images, and we will accept them as long as the content is interesting, and he proposed that moving images be used in an effort to increase visibility. However, he also pointed out that, while increasing "visibility" is certainly an effective method with respect to the general public, it may actually have the reverse effect on specialists. The essence of science is to seek things that are not well understood, so the more difficult it is to see something, the more researchers are intrigued by it and the more they want to start investigating.

Hiromi Yokoyama (Associate Director, Office of Communication, School of Science, The University of Tokyo) spoke on the question of "what is the excitement?" by introducing the words by Zeami, "It is because it is hidden that the flower is seen as beautiful; it would not be seen as beautiful if everything was revealed." She says researchers should first determine exactly what it is that they want people to understand. At some times and in some situations, they must make a choice between presenting a complete picture or ranking things in terms of what is most important, and emphasizing spatial relationships or focusing on mechanisms. Through this process, they will narrow down the content that they are communicating, enabling the listener to understand it fully.

"Understanding and Intuition" was the title of the presentation by Hideki Uematsu (Director, NHK Nagoya Broadcasting Station). He said that his motto is to get people to understand things intuitively. He said that what is needed in order to accomplish this is "déformer." He says "déformer" can make difficult topics easier to understand. As an example, he presented an NHK Hi-Vision Special entitled "People Under the Spell of Prime Numbers: The 150-year

Hideki Uematsu gave a talk on the theme of "Understanding and Intuition."

Struggle of the Geniuses Behind the Riemann Hypothesis." Mr. Uematsu said it is simply not possible to get people to understand everything about the world of abstract mathematics. So in the early part of the program, the mathematician Euler was shown single-mindedly continuing to climb stairs made of prime numbers, even in the face of fierce winds and driving rain. These stairs were modeled on a basic graph depicting how many prime numbers are distributed among the natural numbers (in other words, the prime number theorem). Mr. Uematsu said he introduced this image as a visual depiction of the hard work and enthusiasm of Euler, who calculated by hand the prime numbers up to the hundred thousand, and as something that could communicate the irregular nature of prime numbers. As Mr. Uematsu had anticipated, this scene took hold as a key image of the program, and it enabled viewers to get a sense of prime numbers. "Déformer" does not simply make difficult concepts easier to understand; it also provides depth to easy-to-understand concepts and helps to make this depth inter-

esting. This concept of "déformer" will be a major strategy for achieving visibility.

Making Science Enjoyable

One thing that the invited speakers were unanimous in emphasizing was that an effort should be made to communicate the romance, the dreams, and the fascinating aspects of science.

Once scientific achievements are put out into the world, they become mundane. But a history of the events leading up to that point exists. Surely there are passionate human dramas contained in that history. Professor Ito used holography as an example to explain that there is a century of human history that extends from Max Plank, the discoverer of quantum mechanics, to the people involved in the progress leading to the development of the electron microscope, and eventually to Akira Tonomura, who studied electron beam holography.

To Mr. Uematsu, who produces science programs, making the content interesting means everything. If viewers find the content even a little difficult or impossible to understand, they will not watch the program. So he conducts interview after interview with researchers, creates video images, and spins a narrative. In the production of the aforementioned program about prime numbers, he asked the researcher "Why are prime numbers so important?" But instead of the difficult-to-understand answer that he was expecting, he got an unexpected reply. "Prime numbers are all around us," the researcher said. "You just can't see them." From that reply, he was able to create scenes depicting numbers running through the desert and projected on the surface of the moon. Mr. Uematsu points out that, even though researchers take them for granted, there are often aspects that seem quite wondrous to the general public. So he proposed that CMSI researchers explain their research by comparing it to things in the world around them, and he also suggested that they talk about it to the people around them and watch the reaction.

Tetsuo Karaki (Director, Office for Research Communication, RIKEN AICS), who had participated as a panelist, said that it is important to speak from a recipient's perspective in order to get people to see research achievements as relevant to their lives. He said that this is important because researchers tend to talk from a "sender's" perspective, when what most people want to know is how the topic is relevant to their own lives.

Mr. Uematsu also pointed out that the reason that Japanese researchers find it difficult to communicate the romance of science is that they tend not to boast about their research. Researchers from other countries reportedly often use expressions that have a great deal of impact, such as "prime numbers are God's cyphers" and "solving this question will enable humanity to take a step forward."

The Next Step

Recently, it has begun to be necessary for researchers to talk about their research in their own words. For this to happen, a change in the awareness of the researchers themselves is needed. To communicate one's enthusiasm for research to people and get them to understand it, it is essential for the research to be seen as enjoyable, and the researchers themselves must think of ways to make their work "visible." CMSI plans to conduct a variety of activities based on the proposals made at the symposium. The achievements will be introduced at the 2nd and subsequent Computational Materials Science Visualization Symposiums.

part 2

Special Feature | Furthering "Visibility" for Computational Materials Science

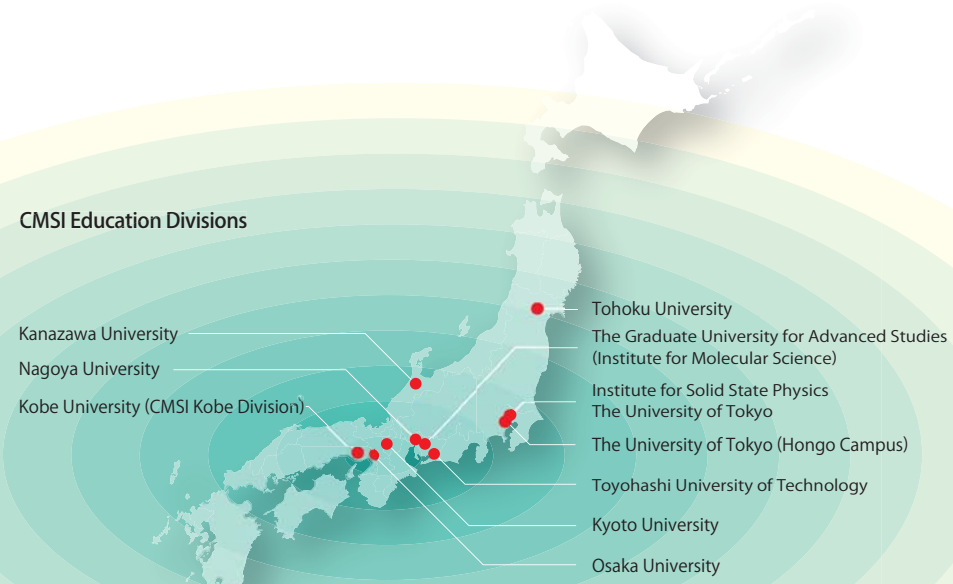
CMSI Distance Learning

Masaaki Geshi
Project Associate Professor,
Institute for NanoScience Design, Osaka University

The CMSI Personnel Development Project started in earnest from this fiscal year. Osaka University is using a video conference system to deliver the course "Advanced Computational Science A" to ten locations including key universities functioning as the CMSI Education Divisions. These lectures are recorded, and published on the CMSI website. In fiscal 2014, the course "Advanced Computational Science B" is scheduled for release. Osaka University counts the credits towards graduate school. Until now, the development of researchers

Lecture at Osaka University. CMSI Education Divisions appear on the left display.

Attending the lecture at CMSI Kobe Division.



in computational science depended on individual laboratories scattered across the country, and in most cases, numeric calculation technologies have only been studied and learned to the extent required for the respective research according to need. However, the mainstream of computers is moving from vector computers to massively parallel types, and hardware configurations are also becoming more complex. Gaining the knowledge to program on them to exploit their performance is largely beyond the capability of a single laboratory or individual. In the past, people thought, "First let's make it serially, and if we have problems with speed, we' ll make it parallel." But now, if it is clear from the start that the software being developed is large scale with long computing times, they realize that they should be starting development by creating parallel algorithms from the beginning. In other words, it is necessary to know about parallelization such as HPC from the start of development. Most of the globally renowned computational science software comes from America and Europe. In order to compete with this, instead of individual laboratories continuing to work on development, it is necessary to establish a common curriculum with the goal of training young staff across Japan as a whole.

Since the personnel who need to be developed by CMSI are scattered around the country, it would be efficient to use teleconferencing to provide lectures simultaneously. In this way, even if the teaching staff are busy and cannot teach the students from zero, it will be possible to reduce their burden by distributing the minimum knowledge on the Web, with each teacher providing additional guidance in accordance with the themes of their respective laboratories.

The personnel required for the future of computational science can be broadly divided into two — people who can develop software, and people who will use the software for research (users). The former will be essential to progress in computational science. In addition to scientific ability, they will need to have knowledge of numerical analysis and architecture, and the ability to collaborate with specialists in those fields. As for the latter, the number of experimentalists can be expected to increase further, with computational science increasingly being used as an experimental tool. In the curriculum for the former, the technologies and knowledge common to all fields will be provided as common subjects, with the technologies specific to the various techniques being provided as specialized subjects (Figure 1). For user training, lectures will be given outlining the basic theory of the respective techniques and various methods, with examples of applications (Figure 2). The most important lectures will involve practical work, with hands-on training in actual use of the software. Curricula must be developed in this way to match the needs of developer training and user training, establishing a system for training the community as a whole.

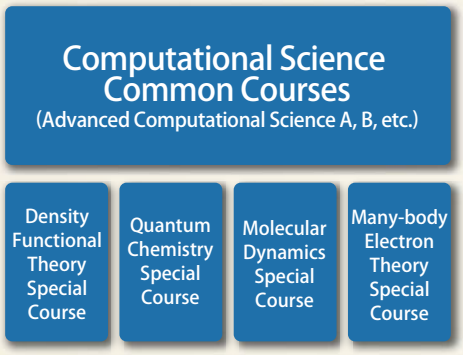


Figure1. Developer training curriculum

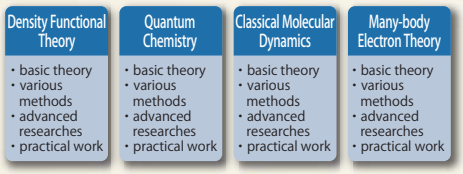


Figure 2. User training curriculum

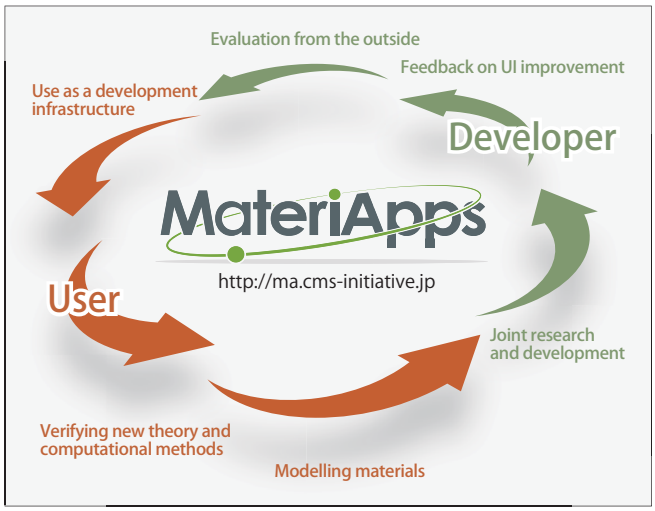
Personnel development has an inseparable relationship with making the hardware for a supercomputer. Today when planning for the next exaflops-class supercomputer after the K computer has started, we must now focus on training personnel who can make use of it as soon as it goes into operation. In addition, it is essential to obtain highly capable personnel and so another issue of the highest priority is undertaking public awareness among the generation who will be active in ten years' time. These lectures are being conducted with know-how implemented by Osaka University in educating adults and graduate students for the last ten years, and this approach will become a model case for the future of graduate school education.

MateriApps
A portal for materials science simulation

Ryo Igarashi
CMSI Condensed Matter Physics Division Researcher
Institute for Solid State Physics, The University of Tokyo

Even an evolutionary advance in the computing performance of computers is not by itself sufficient to promote next-generation materials science research using the K Computer and other state-of-the-art supercomputers. The development of techniques for efficiently solving equations that describe materials and phenomena — in other words, algorithms — also plays a crucial role. In the real-world research settings where state-of-the-art materials science simulations are conducted, new algorithms are proposed on a daily basis, and there are spirited debates regarding their application.

Meanwhile, software is becoming increasingly complex as a result of parallelization and the increasing scale of computers, and the cost of optimization, upgrading and maintenance in software development is increasing. Moreover, releasing software and actively promoting the use of that software require a great deal of time and effort, in terms of preparing documentation, providing operational support and so on. For this reason, the developers who actively strive to release software are still a minority. The result is that, despite the development of many software programs that include state-of-the-art algorithms which are both very sophisticated and highly precise, some of these programs remain unreleased or have inadequate documentation, and experimentalists, company researchers and other users remain unaware of their existence. For this reason, algorithm development and the software and its developers do not receive proper recognition. Under the present circumstances, most users rely primarily on published software and commercial software programs that have been developed overseas, for which there is a great deal of information available.



CMSI is working to promote materials science simulation software, and also to increase the visibility of the developers of this software, through a portal site called MateriApps. On the site, the developers themselves speak in their own words about the benefits of the software, as well as its future and applicability. The site also introduces the features and characteristics of various materials science simulation programs that have been developed both at home and abroad. CMSI also provides assistance to the developers of published software for the preparation of fully-developed manuals and tutorials and so on, in order to provide an environment that will make it easy for users to try out the software.

MateriApps also enables users to perform multidimensional searches for things that they are interested in doing or learning about, such as calculation methods, target materials, interesting phenomena, physical quantities and so on. Forums have also been set up for each software program, in order to encourage communication between users and developers and enable information-sharing, exchanges of views and so on.

Future development of materials science simulations will require not only an evolu-

English version of MateriApps is due to be released in August 2013.

tion in the computing performance of computers and progress in algorithms but also the nurturing of community codes (software applications developed and used by the field as a whole). In the materials science field, development up to now has been conducted primarily by individuals or within small groups. But as the community grows larger, it will also become necessary to introduce source code management systems and other joint development environments (such as GitHub).

On the MateriApps site, support is provided for introducing GitHub for software development, preparing documents, holding software seminars and so on. By encouraging the sharing of information between developers and users and linking this to the effort to form communities for published software, CMSI is working to support developers who want to release their software. CMSI is also working to encourage standardization and integration of input and output formats for applications with similar features, as well as creating animations depicting the results of simulation and otherwise presenting them in visual form. These activities will provide information from a user's perspective and help to create a community that will be useful to both users and developers.

Profile of CMSI Division Researchers

Ryo Igarashi

Condensed Matter Physics Division Researcher
Institute for Solid State Physics, The University of Tokyo

Majored in solid state physics at the Graduate School of Science, The University of Tokyo. After receiving his Doctorate of Science, conducted simulations using the parallel DMRG method at the Japan Atomic Energy Agency.

Motivation for applying for the position

While working on my own to pursue research and development of open source applications for large-scale computing on the K Computer and other supercomputers, I wanted to be involved in operating MateriApps to promote the release of applications, with the goal of aiding the development of computational materials science.

Mission / Role

I want to manage CMSI computing resources, operate MateriApps and develop and study published applications, in order to help disseminate and further the development of materials science simulations.

Towards Design of Functional Polymer Membranes Using ERmod

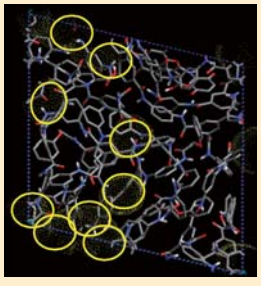
Isamu Shigemoto
Research Associate
Advanced Materials Research Laboratories, Toray Industries Inc.

Toray is implementing Green Innovation Business as a group-wide project in order to bring leading edge technologies to bear on global environmental problems. This project is widely expected to achieve polymer membranes as advanced materials essential for ameliorating and solving global environmental problems, whether as polyelectrolyte membranes for the fuel cells that are expected to be the next generation energy source, or reverse osmosis membranes for seawater desalination considered as a means for ensuring water resources in arid areas. To this end, our Computational Chemistry Group is working to develop and apply techniques for the analysis of permeability using molecular modeling, with the target of designing polymer membranes with advanced selective permeability.

There are two factors that determine the permeability of a substance, diffusivity and solubility. The approach which we considered initially for the former was to find the diffusion coefficient using molecular dynamics simulations, and for the latter, to calculate the free energy of solvation. However, free energy is a physical quantity with one of the highest calculation loads in molecular modeling, and there was no way to calculate the solvation free energy of a small molecule in polymer within a reasonable simulation time and work load involved.

In 2007, I and Professor Matubayasi were both invited by chance to a lecture on the subject. The lecture about methods of energy representation was the opportunity for asking Professor Matubayasi to undertake joint research with us. The original program was not envisaged as applying to giant molecules like polymers, and so under Professor Matubayasi's guidance, we undertook research into methods of calculating the interaction energy of polymers and small molecules, improving energy functionals and so on. As a result, we succeeded in building techniques for calculating free energy of solvation with realistic calculation times and accuracy. At the end of last year, we published an article authored jointly with Professor Matubayasi in J.Chem.Phys. Now, it is beginning to bear fruit in the form of polymer electrolytes and separation membranes using this technology, and it is also highly regarded within the company too.

In this way we arrived at ERmod by a stroke of luck, but when the company researchers want to try leading edge simulations that are impossible with general-purpose software, it is not easy to find software that matches the company's needs. For this reason, I think that the gradual establishment of MateriApps will be beneficial for future academic-industrial matching. In particular, if there are extensive tutorials and article summaries, it will be easy to see how they can be used for actual research, which will be very helpful.



A molecular model of a reverse osmosis membrane. Yellow circles indicate free volumes in the membrane.

From the Front Lines of Application Development 6th

Interview with Nobuyuki Matubayasi and

N. Matubayasi (front left) and S. Sakuraba (front right), explaining ERmod to S. Yonezawa (back right) and Tomoko Mizuguchi (back left, the author of the article on p.16).

Inteviewees:

Nobuyuki Matubayasi
Associate Professor,
Institute for Chemical Research,
Kyoto University

Shun Sakuraba
Postdoctoral Fellow,
Japan Atomic Energy Agency

Interviewer:

Shingo Yonezawa
Assistant Professor,
Graduate School of Science,
Kyoto University

Materials are all around us, and we use various functions of these materials. For example, polymers that are used in diapers have the function of adsorbing and releasing water molecules. The positive and negative electrodes of a battery have the function of drawing in and releasing electrons. Then, is it possible to calculate such various functions of materials within a single framework and even to predict unknown functions? In this section, we will introduce the software application ERmod (prouounced "eee-arr-mahd") that has been developed to address this question.
http://ma.cms-initiative.jp/en/listapps/ermod

Shun Sakuraba, developers of ERmod

"Dissolving" and "Mixing": Material Functions From a Chemical Approach

The original developer of ERmod, Nobuyuki Matubayasi, had an idea: if we expand the concepts of "dissolving" and "mixing," it may be possible to achieve a unified understanding of material functions. In the example of the water-absorbing polymer, if we view the water molecules as a "solute" and the polymer—the environment that takes in these water molecules—as a "solvent," then the phenomenon of water molecules being taken in by the polymer can be thought of as a "solute" (water molecules) being dissolved in a "solvent" (polymer). Similarly, in chemical reactions (reduction reactions) in which electrons are taken in, we can think of the electrons as being "dissolved" into the molecules. This approach is not just paraphrasing; it gives rise to tremendous advantages. The "solution theory," which links these macroscopic "dissolving" and "mixing" phenomena to microscopic molecular-level dynamics, makes it possible to conduct high-speed calculations that are difficult simply by tracking movements of individual particles. From this bold shift in perception was born the software program ERmod.

The Birth of ERmod

Matubayasi was originally an experimental chemist who was studying liquids. "I wanted to combine experiments with calculations in order to pursue research both safely and efficiently," he thought. So he began to conduct simulations using the molecular dynamics (MD) method. The MD method is a calculation technique that tracks movements of individual atoms and molecules over time. However, with this method, it was often difficult to obtain results that were truly useful for experiments. Matubayasi wanted to develop a calculation method that could not only reproduce experimental results but also predict unknown facts. This desire was the starting point for the development of ERmod.

The gold-standard way to compare experiments and calculations is to calculate the quantity called "free energy." The free energy is an indicator of the overall stability of aggregations of molecules or atoms. The free energy is fundamentally important because it determines how the aggregations experience various changes, such as dissolution and chemical reactions. However, it takes an extremely long time to calculate the free energy using only the MD method. As shown in the upper half of Fig. 1, this is because to do this it is necessary to calculate not just the state before the change occurs (initial state) and the state after the change is completed (final state) but also numerous intermediate states.

Matubayasi hit on the idea of using the solution theory by which we can obtain the free energy from the molecular-level information of the system. According to the solution theory, it is possible to construct a function that takes a histogram of molecules on a certain parameter (such histograms are known as a distribution function) as an argument. Because this function is a function of a function, it is called a "functional." From this functional, the free energy can be calculated. In other words, by using the MD method only to calculate histograms at the initial and final states and entering these histograms into an appropriate functional, we obtain the change in free energy. Thus, one can avoid all the time-consuming calculations for the intermediate states and calculate the free energy change in a short period of time (the bottom half of Fig.1).

The next question is what kind of histogram (distribution function) should be used. The first that comes to mind is the distribution function on positional information. However, it is not evident which real-space parameter should be used among the enormous quantity of positional information (even for the simplest case, for a system of N molecules, there are $3N$ parameters). One day Matubayasi, who had been wrestling with this question, came up with the idea of using the distribution function for the interaction energy between molecules. It was an exciting moment. "I had just awakened from sleep when the idea popped into my head, and then it was just a matter of writing down the equations." Furthermore, he realized that the use of the energy distribution function provides several advantages, such as the ability to handle nonuniform systems and systems with degrees of freedom within molecules. This "Columbus' egg" type of inspiration (something that looks easy only after it has been achieved) was greeted with astonishment. The comment of a certain famous professor is still fresh in

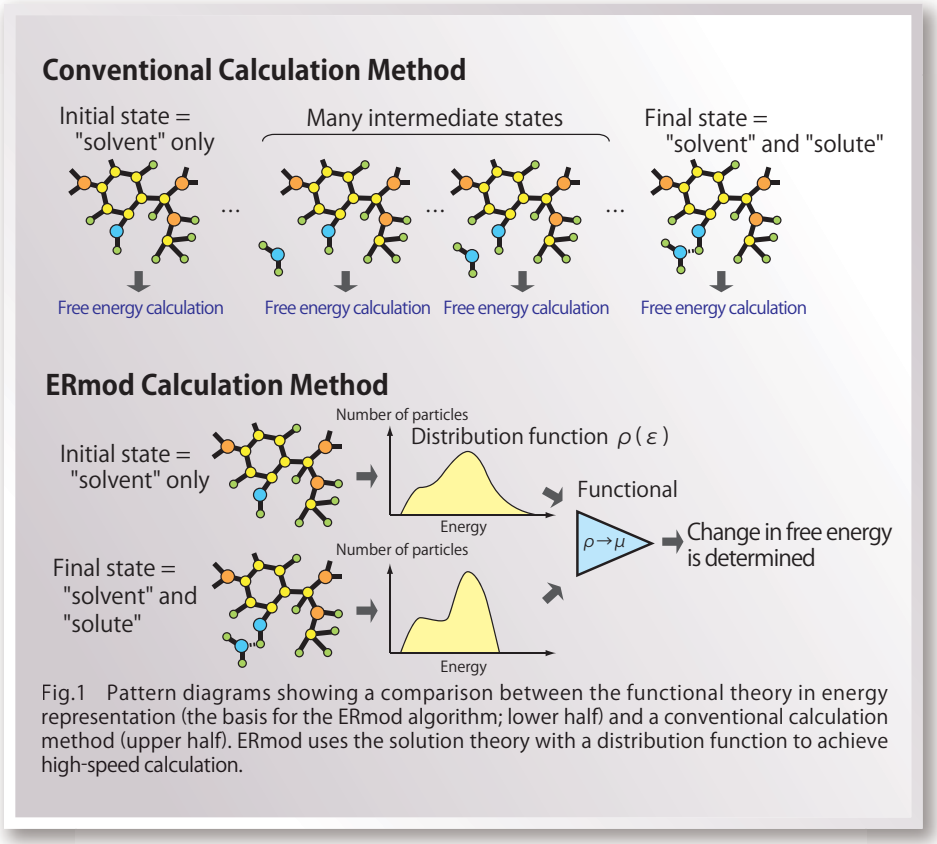


Fig.1 Pattern diagrams showing a comparison between the functional theory in energy representation (the basis for the ERmod algorithm; lower half) and a conventional calculation method (upper half). ERmod uses the solution theory with a distribution function to achieve high-speed calculation.

Matubayasi's mind. "Was it really you who came up with this idea?" he asked in surprise.

ERmod represents this idea turned into an actual program. By the end of the 2000s, ERmod had been incorporated into various MD calculation programs as a module. The name "ERmod" is a combination of the initials for "Energy Representation" and "mod," meaning module. So it retains a vestige of its early days as a module.

Development as a Standalone Program

The major turning point for ERmod came when Shun Sakuraba became involved in its development. Sakuraba was a software developer who had previously worked at an IT venture firm, and he was also a theoretical chemist who had previously performed calculations for biomacromolecules. "I realized that, with the rapid diversification of computers and MD calculation methods in recent years, it was going to be difficult for ERmod to continue to be developed as a module in MD software programs," he says. So Sakuraba took on the major task of converting ERmod from a module into a standalone program. First of all, the program, originally written only in Fortran, was modified using C and Python to strengthen its cooperability with other MD programs. Parallelization and other improvements were also added to the core computing portion of the program. As a result, the calculation speed increased by thousand times. He also upgraded the documentation, improved error messages, and made it possible to run the program easily in a variety of environments. In this way, a great deal of effort was paid to such behind-the-scenes works that are designed to make the program more convenient for users. Moreover, in order to expand the user base, they published the entire program including the source code on the Internet. The program is now being downloaded by users around the world.

"Almost all of my proposals were accepted by Prof. Matubayasi—in fact, to a worrying degree," says Sakuraba. Matubayasi also says that his policy is to begin a joint research project with trusting the partner by 100%. I felt that their relationship of

Nobuyuki Matubayasi

After receiving his Ph.D from Rutgers University, he joined the Institute for Chemical Research, Kyoto University, where he is currently Associate Professor. Originally he conducted experimental research into supercritical water, but shifted his focus to theoretical research. He has received many awards, including the Young Researcher's Award from the Minister of Education, Culture, Sports, Science and Technology, for the formulation of a functional theory in energy representation (the basis for ERmod). He is also a proud father who decorates his laboratory with many creations made by his beloved daughters in kindergarten and elementary school.

Shun Sakuraba

He received his doctorate in computational biology from the University of Tokyo Graduate School of Frontier Science. He conducted research into protein simulation. He is a skilled programmer who was involved in a venture firm (established by a classmate while they were studying at the University of Tokyo) and worked on the development of a compiler. He is currently pursuing research as a postdoctoral fellow at the Japan Atomic Energy Agency, and is also playing a leading role in ERmod development.

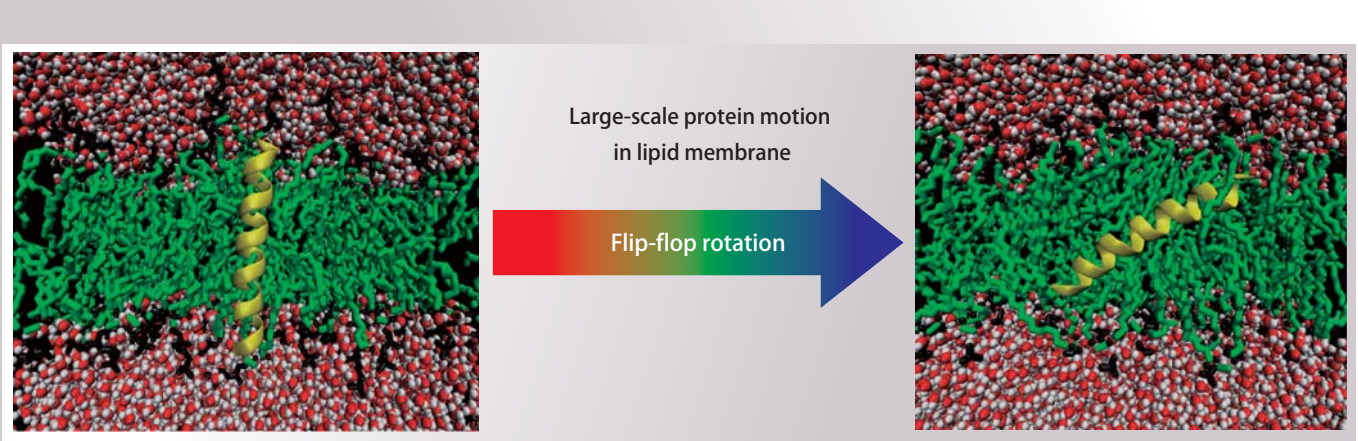


Fig. 2 Example of ERmod application. Pathway of large-scale protein motion in lipid membrane. In addition to this example, ERmod has been applied to a variety of systems.

trust was the driving force for the great leap of ERmod.

The Effect of "Selection and Focus" in ERmod

ERmod's distinctive feature can be described in a single phrase: "selection and focus." In a sense, it ignores all the vast information in the real space and focuses on high-speed calculation of the free energy, which is critical for experiments. This is a reflection of the development philosophy that Matubayasi has had since the very beginning: the desire to create a program that is useful for experiments. The program is also characteristic for its use of other MD programs to calculate the distribution functions. Naturally, there are also other ways to calculate distribution functions independently, repeating the process over and over again until the error converges. But ERmod outsources this distribution-function calculation to an existing MD calculation program, and concentrates on achieving more advanced functions. Importantly, there is a theoretical background ensuring that this way does not matter: Due to the variational principle, errors in MD calculations are not heavily reflected in the result of the free energy calculations.

The effect of "selection and focus" in ERmod is evident in the actual calculation results. For example, when calculating the change in the free energy before and after a solute is dissolved in a solvent, the required time for calculation is less by several dozen times as compared to the amount of time required for the ordinary method (rigorous calculation), with a degree of accuracy that is by no means inferior. ERmod is currently being used in joint research with Toray Industries, Inc., for example, to design water-absorbing polymers (Read p.7 for more details on this joint project). The program has also achieved a wide variety of applications as exemplified in Fig.2.

Evaluation for Behind-the-Scenes Work

"The lack of detailed documentation is one of the major reasons that Japanese academic software applications do not often become world-famous," says Sakuraba. He also displays a professional's perspective in saying that error messages are not only important for users. "From a long-term perspective, improving error messages also eases the burden on the developers." However, no methods have been established to provide proper evaluation of such tasks. Matubayasi and Sakuraba are united in saying that this is a problem.

I myself also have experiences to develop programs for my experiments. Thus, I understand that it is very annoying to compile documentation explaining the program and provide a complete array of error messages. And yet despite this annoyance, such efforts are not often evaluated properly. Similar types of work for experimental laboratories are arranging shelves or processing wastes. How should this type of behind-the-scenes works be evaluated properly as an important part of a researcher's job? How should we avoid a case of "the earnest man makes a fool of himself?" I get a feeling that this is becoming a serious issue not only in academic software application development but in various other fields of research as well.

The Future of ERmod

How will ERmod be developed in the future? The first objective is to extend its use to large-scale computers. For example, the way to use ERmod on the K computer has been comprehensively introduced in the ERmod website. The developers also intend that the program be installed on large-scale computers so that users can use it without compiling and installing by themselves. If this is realized, users who are not familiar with theoretical chemistry can more easily access ERmod, leading to applications in a wider range of systems such as biological materials and batteries.

Moreover, progresses in the underlying theories will also be indispensable for further development of ERmod. For example, if time evolution of a system can be calculated, the range of applications will become even wider. It will be possible to determine the lifetime of the association state of a certain molecule, and to calculate electrical conductivity. Matubayasi is also planning to incorporate the "coarse graining" technique in order to perform calculations for even larger targets. The “coarse graining” is a technique to increase the speed of calculation by, for example, considering a polymer of 100 monomers as a group of 10 clusters, each consisting of 10 monomers. Such progress would undoubtedly further expand the range of applications for ERmod.

ERmod has been progressed through the harmony of Matubayasi's insight and Sakuraba's software development expertise. I am looking forward to see further developments and success in the future.

◆Interviewer's Postscript

Shingo Yonezawa

I am an experimental physicist mainly studying superconductivity, and thus I am not an expert of theoretical chemistry. In this interview, however, both Prof. Matubayasi and Dr. Sakuraba explained their study in great depth and spoke passionately about the subject. So I came to understand their subject very clearly, and the scheduled interview time was up before I knew it. I feel that Prof. Matubayasi, who seems very easygoing, and Dr. Sakuraba, who seems very earnest, make an excellent team with a very good harmony of their personalities.

3 Visiting Our Graduates

Michiko Tawada

Pharmaceutical Research Division
Takeda Pharmaceutical Company Limited

Majored in physical chemistry and quantum chemistry at the Graduate School of Arts and Sciences, The University of Tokyo, and conducted research into theoretical calculation techniques for noting the dynamics of electrons in chemical reaction processes. After receiving her master's degree, joined Takeda Pharmaceutical Company Limited.

On the Front Lines of Drug Discovery Using the Computational Chemistry Approach

For the third in our series "Visiting Our Graduates," in which we talk to computational materials science graduates who are currently employed in the industry, CMSI Division Researcher Takehiro Yonehara visited Michiko Tawada, who is working to develop new pharmaceuticals at Takeda Pharmaceutical Company Limited. He interviewed her to hear about her graduate school research, the path that led her to her work in drug discovery, and the role of computers in drug discovery.

Takehiro Yonehara

CMSI Molecular Science Division Researcher
Graduate School of Arts and Sciences,
The University of Tokyo

Aspiring to Create Products that Help People

Yonehara : What motivated you to choose to work in the area of drug discovery?

Tawada : At university, I learned about all aspects of chemistry: organic chemistry, physical chemistry, inorganic chemistry and biochemistry. I became interested in the use of basic physical principles to explain the mechanism of life. In graduate school, I worked on the development of theoretical calculation methods, and in the course of doing that, I realized I wanted to work on creating products that would help people. So in looking for a job that would enable me to put into practice the research I had done in graduate school, I learned about the world of drug discovery, and that led me to join this research center.

Yonehara : How do you go about developing new medicines?

Tawada : First we determine the target protein that holds the key to the occurrence of the disease (the target for drug discovery). There are many different kinds of target proteins, and when one of these is related to the cause of the disease, you can treat the disease by inhibiting the functions of the target protein. Next, you search the compound library to find the compounds that bind to the target protein. These are the "seed compounds" from which the drug candidates will be derived.

Starting from these seed compounds, we transform their structure so that they will bind more tightly to the target protein. This process is known as "optimization of the lead compound." Then we evaluate efficacy and stability and select the compound that will be the most desirable as a medicine. From that point, we pursue research into that compound with the goal of developing it as an industrial product.

Yonehara : What part of this process are you in charge of?

Tawada : I'm in the computational chemistry group. Our main tasks are the discovery of seed or lead compounds and the optimization of lead compounds. The discovery of seed or lead compounds is to conduct both actual screening by means of experiments and virtual screening by means of computation. We're in charge of the virtual screening. To optimize lead compounds, we design compounds that have sufficient binding affinities, based on structural information on the lead compounds and the target protein.

Contribution of Computational Chemistry in the Area of Drug Discovery

Yonehara : What is the scale of the calculations you perform during the virtual screening?

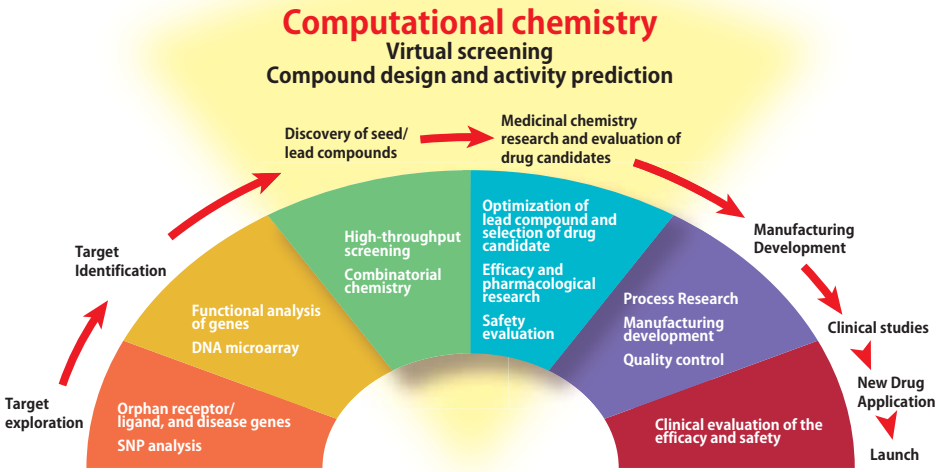
Tawada : We use mainly cluster PCs for computation, and we have them running for several weeks.

Yonehara : How many searches do you run?

Tawada : It varies depending on the case, but anywhere from several hundred thousand to several million. From there, we narrow it down to several dozen and then hand it off to the experiment department.

Yonehara : What sort of data do you look

Drug discovery processes and computational chemistry



at when you're studying compounds?

Tawada : For example, we check for affinity based on the difference in energy when the lead compound and the target protein are separated and when they are linked. As there are limits to the accuracy of the models that are used, the score and the actual activity do not always match. So we try various things.

Yonehara : So am I correct in thinking that, in investigating the binding characteristics, there is no particular need to rely on approaches that, in principle, can provide more detailed information on the binding process than energy evaluation — for example, dynamics computations that track the behavior of molecules over time and so on?

Tawada : No, that's not it. The only reason that we don't use those methods is that there are limits to the power of our computers.

Takeda is accumulating technologies in preparation for the time that screening using dynamics computations will become possible.

Yonehara : I understand that you occupy a midlevel position in the computational chemistry group. The computer environment must have changed tremendously compared to when you joined the company.

Tawada : Yes. It's not just that it's now possible to conduct large-scale computing. The biggest change is that we're now able to obtain many X-ray crystal structures of proteins. By conducting computations based on this information, we're now able to obtain highly reliable results.

Yonehara : Can you give an example in which information on a protein structure was used in actual drug development?

Tawada : This is an example from an overseas research base, but a diabetes medication known as the DPP-IV inhibitor* was quickly turned into a commercial product through compound optimization based on information on protein structures.

Yonehara : What computing tools would you like to be able to use in a drug discovery setting?

Tawada : I think it would be great to have a tool that could predict whether a compound could bind tightly with a protein based on an energy evaluation. I'd also like to have a tool that could estimate the stability of a manufactured pharmaceutical compound. And I'd like to have a tool that could investigate the ratio of absorption into the body. Moreover, you don't want there to be side effects, so it would be great if we had software that could investigate the effect on other proteins. I have high hopes that CMSI research will provide such tools.

The Qualities Needed to Become a Company Researcher

Yonehara : Have any of the drugs you've been working on been turned into actual products?

Tawada : During a researcher's entire career, he/she may only have the opportunity to experience his/her work actually becoming a product once or twice. It takes that long for a drug under development to become a product. I haven't yet had the experience of a drug I've been working on becoming an actual product. But it makes me very happy when my results prove to be useful during the drug development process that's being conducted by someone else, and to have them feel gratitude toward me. That encourages me. For me, it makes what I do meaningful.

Yonehara : I guess you need to have many different types of knowledge to do the work that you do.

Tawada : I learned everything I know about drug discovery from scratch, starting when I joined the research center. In addition to specialist knowledge, what you need in particular in a drug development setting is the ability to use that knowledge in a flexible, off-the-cuff manner. Also, you need a wide-ranging knowledge of chemistry as a whole including computational chemistry. But whether you're at a university or at a company, you learn what you need as you go along.

Yonehara : Are there any opportunities for you to share the basic knowledge you've learned in the process of drug discovery with people who work at other pharmaceutical companies?

Tawada : We get together at academic society meetings and so on. For example, there are academic groups such as the Biophysical Society of Japan and the Pharmaceutical Society of Japan. And there are corporate groups such as the Medicinal Chemistry Symposium. It's also possible to do this through software user groups. General development techniques come up as a topic of conversation in settings like these.

Yonehara : Can you say a few words about the type of person who aspires to do corporate research, and the difference between a company setting and a university setting?

Tawada : In my case, when I was at a university, there was virtually no need to think about the effect that the results of my research would have. But in a company research center, your own work and your own research have a major impact on the people around you. From that standpoint, you become very careful about prioritizing the tasks that's been assigned to you. Also, in a corporate setting, I think the desire to help people and the desire to all work together toward a single objective in pursuing a project leads to good work. So I think the type of person who is naturally able to feel gratitude toward the people that she's working with is well-suited to doing corporate research.

Yonehara : I feel as if you've helped me to see the origins of product development in a group setting. We'll be looking forward to seeing the results of your activities in the future.

(May 27, 2013 At Shonan Research Center, Takeda Pharmaceutical Company Limited)

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* Dipeptidyl peptidase-4 (DPP-IV) inhibitor : Diabetes is a metabolic disorder in which there is a decrease in the quantity of insulin that is secreted, or the insulin itself does not function properly, leading to a chronic state of high blood sugar. DPP-IV is an enzyme that degrades a hormone known as incretin that promotes the secretion of insulin. The inhibitor is able to selectively inhibit DDP-IV.

Institute for Materials Research, Tohoku University

Yayoi Terada
Associate Professor, Institute for Materials Research, Tohoku University

In this issue, Torrent features a new section introducing each of the CMSI Divisions and the supercomputer center in those divisions. For this first installment, we will take a look at the Computational Materials Research Initiative and the Center for Computational Materials Science, which is in charge of the operation and maintenance of the supercomputing systems installed at the Institute for Materials Research. Our guide will be CMSI Associate Professor Yayoi Terada.

Division Established within the Historic Institute for Materials Research

The Computational Materials Research Initiative (CMRI) is located within the Institute for Materials Research at Tohoku University. The Institute for Materials Research (IMR) was founded nearly 100 years ago, in 1916, as the 2nd Division of the Provisional Institute of Physics and Chemistry Research of Tohoku Imperial University. As is well known, its first director was Kotaro Honda, who invented KS (magnetic) steel. The Institute has produced many research achievements, primarily in the field of metals and alloys. Currently we have been expanding our target to a wide range of substances and materials, from basic properties to application, with the aim of creating new materials that will be useful to society.

In 1993, the IMR introduced a supercomputer that began operating in 1994. Since that time, it has been very active as a research center for materials science by means of large-scale simulations and numerical calculations using computers — said to be the "third" major research technique in addition to experimental and theoretical studies. Under the Computational Materials Science Initiative (CMSI) established in 2010, the CMRI was set up at the IMR in 2011 to be in charge of promoting fields relating to computational materials science, development of research, training of personnel and so on. 20% of the resources of the supercomputer (which was just upgraded in April of last year) at the Center for Computational Materials Science in the IMR are provided within the CMSI framework, and since November of last year reciprocal access from other Divisions has also become available. I was appointed in January of this year to be an Associate Professor, the IMR in charge of the CMRI personnel training and education. In April, the CMRI Division Project Leader Tetsuo Mohri assumed the position of Head of the Center for Computational Materials Science. In this way, the Division structure of CMRI is gradually taking shape.

"Listen to the Voices of Users and Work to Make Supercomputers More User-Friendly"

The technical staff members who operate the supercomputer play an important role in supporting the diverse activities of the CMRI. We spoke to Nobuaki Igarashi, who has worked at the Center for Computational Materials Science for 13 years, and who assists users by giving advice on program and job execution and so on. We asked him to talk briefly about the Center, the rewarding aspects of his work and so on.

Nobuaki Igarashi

I majored in computer systems science at the University of Aizu and received my Master's degree from that university. I visited several departments within Tohoku University during job hunting and I chose this office, where the supercomputer was scheduled to be upgraded in February 2001. Starting from this fiscal year, I've been working as the coordinator of the supercomputer system. I'm very aware of the important responsibility with which I have been entrusted.

"The Center for Computational Materials Science is a Collaboration Research Center that provides various services for more than 100 users per year. In the last fiscal year, 36 of those users were from overseas, so it is quite an international environment.

The Center provides a lot of applications software including freeware in order to respond to diverse requests from users. We also support the installation of freeware upon the request. This way, we are well prepared to provide versatile software services and technical supports to our users, and supercomputer becomes more user-friendly. Since supercomputers are also evolving on a daily basis, we

also upgrade the supercomputer every few years to enable it to always take on cutting-edge challenges. I feel great satisfaction in doing this.

Many of the users within the CMSI framework, who began use starting from the previous fiscal year, are engaged in large-scale computing with code that they have developed by themselves. So we increased the number of queues that use a large number of nodes and took other steps to make it easy for them to use the supercomputer. Since the most important thing is to enable people to produce research achievements using the supercomputer at our center, we want to encourage people to feel free to give us their opinions and requests. Overseas users feel free to ask questions by email and so on. I think this kind of response from users will help to create a more user-friendly supercomputing system."

The Center for Computational Materials Science has five technicians (including Mr. Igarashi) and two resident system engineers (SE), all of whom are charged with the operation of the supercomputer. In my area of personnel training and education as well, the help of the technical staff is indispensable. In order for computational materials science researchers and engineers to be able to handle the K computer and future supercomputers, they need not only specialist knowledge in the fields of engineering and science but also computer science knowledge. In providing that type of education, I've been helped many times by the accumulated experience and knowledge of our technical staffs.

In this way, those of us who are engaged in the CMRI activities are supported by the technical staffs. At the CMRI, the technical staffs, the researchers, and the teaching staffs who provide next-generation personnel training and education will maintain close communication with one another while continuing to fulfill their respective roles, in order to achieve more well-developed activities.

CMRI and Center for Computational Materials Science staffs: (From left to right in the back) Kazuhiro Satoh (technician), Taiga Ohtaki (technician), Hiroshi Mizuseki (concurrent Associate Professor), Nobuaki Igarashi (technician), Kohta Tanno (technician), and Akie Kato. (From left to right in the front) Tetsuo Mohri (CMRI Division Project Leader), Kyoko Ichinoseki (technician), Yayoi Terada (concurrent position) and Nozomi Kadowaki. The background of the photograph is a cross-sectional test specimen of the 400-ton Mn-Mo-Ni low-alloy steel ingot fabricated in 1969 by Japan Steel Works, Ltd., at the time the world's largest, which was donated by the Metals Museum.

Message from Tetsuo Mohri, the CMRI Division Project Leader and Head of the Center for Computational Materials Science

On April 1 of this year, I started a new position at the Institute for Materials Research and have been appointed Head of the Center for Computational Materials Science. I will strive to do my best in activities at both the Center and at the CMRI, and to work for the further development of the field of computational materials science. At the university where I was previously, I was surrounded by students only, and now I'm surrounded by faculty only, so I feel like I'm now in the adult world. Considering the fact that the young technicians are no different in age from the undergraduate and graduate students that I've been teaching up to now, I've been amazed at the fact that the same young people can become so incredibly grounded in response to this environment. The staffs at both the Center and the CMRI Division are all in high sprit. We would like as many people as possible to use the supercomputer, and at the same time we hope people will participate in CMRI activities.

CMSI Calendar

For more information, see the CMSI website
http://cms-initiative.jp

●CMRI Workshop (Study about Special Support Research Topics)
Date: July 30, 2013
Venue: Institute for Materials Research, Tohoku University

●1st Research Field Summer School 2013 "Considering Energy Issues"
Date: August 12 - 16, 2013
Venue: Hotel Jurin (Zao)

●The 20th Anniversary of TOMBO and Russian Megagrant Opening International Conference
Date: August 21 - 22, 2013
Venue: Katahira Campus, Tohoku Univ.
※22th: Study about Special Support Research Topics

●17th Molecular Simulation Summer School
Date: September 2 - 4, 2013
Venue: New Otani Yuzawa (Niigata Pref.)

●CMD®23
Date: September 2 - 6, 2013
Venue: Graduate School of Engineering, Osaka University

●TCCI 4th Workshop
Date: September 10 - 11, 2013
Venue: Okazaki Conference Center, National Institutes of Natural Sciences

●CMSI International Workshops
Date(Venue) : October 16 - 18, 2013
(The RIKEN Advanced Institute for Computational Science),
October17–19 (The University of Tokyo (Hongo), Nagoya University)

●CMSI International Symposium 2013 "The New Materials Science Made Possible by Massively Parallel Computing"
Date: October 21 - 22, 2013
Venue: Ito International Research Center, The University of Tokyo

●TCCI Winter College (Molecular Simulation)
Date: October 23 - 25, 2013
Venue: Okazaki Conference Center, National Institutes of Natural Sciences

●TCCI 3rd Symposium for collaboration with Experimental Chemistry
Date: November 5 - 6, 2013
Venue: Fukui Institute for Fundamental Chemistry, Kyoto University

●4th CMSI Workshop
Date: December 11-13, 2013
Venue: Institute for Solid State Physics, The University of Tokyo

Hydration (solvation)

The keyword for ERmod, the application featured in this issue, is "hydration (solvation)." This is a phenomenon that has tremendous significance.

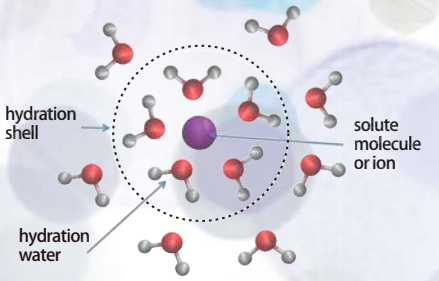

Figure1. A schematic illustration of hydration. Water molecules are attracted to a solute molecule and form a hydration shell around it. Water molecules which locate far away from a solute move independently from the solute molecule. On the other hand, the movement of hydration water molecules is constrained by the solute.

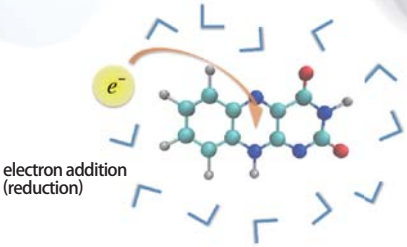

Figure2. Electron addition to an oxidant in water. One can consider water and the oxidant as a mixed solvent, and added electrons as a solute, in order to view the reduction reaction from the perspective of solvation.

What is hydration?

When a substance dissolves in water, the dissolved substance (a solute) is stabilized by being surrounded with water molecules. This process is called "hydration." When we say that a certain substance is exceptionally soluble, we mean that it is hydrated well. When hydration occurs, the properties of the solute molecules change. In addition, the reactive properties and stability of the water molecules around the solute also change as compared to when the solute is not present (and as compared to water molecules located far away from the solute). The phenomenon of hydration plays a crucial role in a variety of situations such as the manifestation of protein functions.

Solute molecules do not dissolve only in water. In general, when a substance (solute) dissolves in other molecular assembly systems (solvent), the interaction between the solute and the solvent produces changes in the properties of both solute and solvent. This is known as solvation, and in particular when the solvent is water, it is called hydration.

Expanding the concept of solvation

The concept of solvation can be expanded to consider phenomena other than so-called "dissolution." For example, heterogeneous miscible systems that are made up of water + biological membranes can be seen as solvents, and proteins can be seen as solutes, in order to consider the bonding of proteins to membranes from the standpoint of solvation. Additionally, in reduction reactions, the electrons that are added can be seen as solutes, and the substances that receive the electrons and the surrounding medium can be collectively seen as a solvent, in order to enable the concept of solvation to be introduced.

In this way, the concept of "solvation" is expected to enable a unified understanding of various phenomena relating to dissolution, bonding, absorption and so on.

Torrent No.8 July 2013

Cover：Next bubbles, their next bubbles, further next bubbles—small bubbles are getting together to form a big bubble. Also in the network of CMSI, plenty of small ideas are coming into contact with to develop into a big science.

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