NEWSLETTER OF RIKEN Quantitative Biology Center

OBIC OBITS Inside this issue

Talking With...

Alexander Bennett, Associate Professor at Kansai University

QBiTs talks to the 7th dan in kendō and 5th dan in naginata author of several books on the martial arts about their role in Japanese history and culture

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Interesting People



QBiC Jedi Masters- Hanae Shimo

C have heard a 3rd dan means you have the skill to kill someone". It is unclear by her tone whether Hanae Shimo, who holds a 3rd dan in kendo, is asserting or doubting the claim. She does not look like a killer, though that may make her all the more dangerous. Instead, the petit Hanae speaks with a very quiet and humble voice even though most of her colleagues describe her as very bright. Yet sometimes the simplest of questions, like "Where are you from?" will leave her stumped. You might be too if you had lived in four countries and eagerly await a chance to move to a fifth next year, all before your 24th birthday.

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Talking with . . .

Alex Bennett came to Japan wanting to learn Japanese. Instead he discovered kendo and by extension himself, leading to a career as a world scholar on the martial arts and their role in society.

- There may be nothing more synonymous with Japanese culture than the martial arts. You disagree with that perception. Why is that?

The martial arts, you could divide them into two categories. The pre-Meiji martial arts (1868), when the Tokugawa government was replaced with the imperial government. The time before that the martial arts were the domain of the samurai. Commoners did participate, but it was frowned upon. But after the Meiji period, all the class distinctions were abolished. There was no such thing as the samurai anymore. Japan embarked on its journey to create a modern nation state and the need for a national identity or nationalism. One of the motifs the Meiji government used was the connection with the samurai culture and samurai warrior as something that links all the Japanese people together as opposed to the four classes of samurai, farmer, artisan, and merchant.

The martial arts were refashioned into forms and teaching methodologies that would enable them to be taught in schools. The deeply spiritual aspects were taken out. Dangerous techniques were taken out. New ways of practicing in groups and teaching were incorporated, as well as the underlying nationalistic ideology that permeated the martial arts, 'you are doing this because it is Japanese culture'.

-Many of the martial arts today like kendō and judō were once kenjitsu and jujitsu. That transition from jitsu (art) to dō (way) indicates a significant transition in the attitude of what the martial arts represented. How did that transition arise?

From the Tokugawa period, Japan entered a period of peace. In the previous period, when the whole country was at war, the whole purpose of the martial arts was to kill someone. In the Tokugawa period, we see a massive transition. The techniques were killing techniques, but the ultimate objective was not to kill your opponent. They became a vehicle for personal growth and cultivation;



almost like a Buddhist studying towards enlightenment. Then in the Meiji period, again the martial arts evolved. They changed to suit the needs of an emerging modernnation state, in which it could teach the children the previous lessons of building a healthy body and mind, and at the same time a widespread sense of 'Japaneseness'. This snowballed into the 1930s when the martial arts were apprehended by militaristic ultra-nationalist government as a way of instilling nationalistic fervor in the youth and preparing them for war. As a result, when Japan lost the war all martial arts were banned.

After 1868 many of the old traditional schools disappeared. Gradually from around the 1870-80s, after Japan had modernized its education system, part of that new curriculum was physical education. One of the main characters was Kano Jigoro, the founder of modern judo. He created judo not as a martial art primarily for hurting people or fighting, but precisely as a form of education in schools. He studied many traditional schools of jujitsu and created something different, which he called not jujitsu, but judo. The reason being, even though in the Tokugawa period the spiritual aspect had been important, it was never called budo as it is now. He wanted to accentuate that his main objective was not fighting and hurting people, but a way of life. You are still doing hard training, building your physical strength and dexterity, but at the same time you are learning respect for your opponents and making yourself a stronger individual mentally, physically, and morally.

The ministry of education developed a form of judo or kendo that what was being taught in Tokyo would be

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the same as Fukuoka. They standardized it. That wasn't the case before. A special teacher's college to train the martial arts of any type was established and everything was referred to as dō.

During 1945-50, the martial arts were pretty much banned, especially in schools – books and equipment were burned. The martial arts had to be reincarnated. One of the important things had to be no central overseeing organization. If you want to do kendō, you have to create an all Japan kendō federation, or all Japan judō federation, or all Japan kyudō federation. These are all separate entities that were designed to oversee the martial arts as something that is not representative of the Japanese spirit or superiority, but purely as modern Western sport except that they are Japanese. So all the spiritual training that were very much emphasized during the war period were expunged.

-You say the spiritual was removed and yet doesn't do associate with the Buddhist way to enlightenment?

It is, totally. But the martial arts introduced to the school...for example, you cannot bow to the Japanese flag...had to purely be a physical education subject like baseball would be as opposed to what it was in the war when martial arts were physical education subjects but at the same time they had lectures on morality.

The private federations tried to maintain the culture integrity of the martial arts, while at the same time promoting a style that could not be in anyway be construed as a tool for the military. And that's how the martial arts have developed. -Back to Buddhism, many distinguish the martial arts from other sports because of its spirituality component. Is that part of the appeal? Can it act as a substitute for religion?

That is pretty much how I look at it. Practicing the martial arts is a very personal, spiritual journey. That's really been a focus of my writing on the martial arts. The martial arts I consider probably Japan's most successful export. There are 50-60 million people doing karate alone and three times more people doing judo in France than in Japan. Why do non-Japanese do martial arts? It's not just a sport or culture. The attraction is the universal aspects of the spiritual side of it. Human beings share a common thread with much of what is taught in the martial arts. I had a really interesting experience in Iran about 7 or 8 years ago. Iranians are crazy about budo. It is second only to soccer. Of course, Iranians are known for their devoutness to Islam. I got money to do research on why the Japanese martial arts? Do the martial arts not conflict with beliefs in Islam? Does the spirit of budo not conflict with Islam? And I got all these replies, 'If anything, budo makes me a stronger human being, which makes me a better Muslim'. Another person said, 'doing the martial arts are like supplements for my religion'. For me it's a substitute, for them it's a supplement. It showed me that it's not the Japanese cultural aspects that are important; it's the universal aspects that seem to transcend. That's the paradox: you are exchanging very violent techniques, but underlying that is an intrinsic and crucial respect for the person you are training with. Without it, that's not budō. 🔵

QBiC Outreach

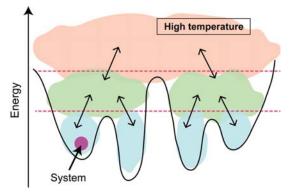


As another example of its community outreach efforts, in August, QBiC hosted a group of firstyear students from Josho Keiko High School. The event was coordinated by Unit Leader Yoshihiro Shimizu and science communicators Natsuko Izumi of Riken CDB and Takehiro Kawano of QBiC, who explained basic concepts like the Central Dogma and the importance of studying the natural sciences for those interested in biology. The 7 boys, all dressed in white collared shirts and charcoal pants, and 4 girls, dressed in grey plaid skirts and purple sweaters, looked more like they were from a family reunion than high school class. Although taciturn, their reactions to the equipment revealed a bunch mystified by the world of science.

Paper Highlight

Faster All-Pair Exchanges

The replica exchange method (REM) is a common tool in physics and biophysics for investigating the energy landscape of a system, like the multiple conformations of a protein. In 1999, QBiC Team Leader Yuji Sugita first authored a landmark paper that brought REM to molecular dynamics (REMD). The strategy of REM involves swapping the system at different replicas (normally temperature) randomly. The swapping allows conformations to escape local energy minima, which otherwise would compromise the simulation, and enables sampling at a wider range of energy configurations. To make REM more resourceful, investigators have been focusing on improving the exchange frequency of the replicas and the exchange criteria, normally by an all-pairs exchange method. Although literature has already reported several approaches, none have become universally accepted. Team Leader Makoto Taiji hopes that a recent report he co-authored with Hiroko Kondo, now at Tohoku University, and published in the Journal of Chemical Physics will change that.



The strategy depends on freeing oneself from the detailed balance condition, which requires that equilibrium must be maintained between any two microstates of a replica and imposes a number of additional demands on the simulation. Instead, Hiroko and Makoto constrain themselves to the more general balanced condition, which requires that the macrostate, which includes all microstates of a replica, be in equilibrium, but allows any two microstates to not be. This modification permits asymmetric transitions between microstates and eases the exchange criteria by reducing the rejection rate of switches between replicas. For reasons described in the manuscript, the authors call their algorithm the "heat bath like criteria" (HLC) and present it as an alternative to the commonly used Metropolis method.

They demonstrate the validity of their algorithm by investigating two standard models for REMD, an alanine dipeptide and chignolin, which is considered one of the smallest of stable



proteins, using six temperature replicas and comparing the results with alternative algorithms from the literature. The authors show that HLC provides equal or faster energy and ergodic convergence. A large reason for these better results was the higher ratio of the accepted exchange for HLC, which was twice that of the other algorithms. Moreover, these accepted exchanges included non-adjacent pairs, showing that HLC satisfies the all-paired exchange criterion. It is also effective when considering near neighbour exchange. Finally, while HLC converged to the same distribution as other methods, it had a wider sampling range that included not only folded and misfolded states, but also unstable ones, demonstrating that HLC can sample even replicas that have probability distributions with small overlap to provide a more detailed energy landscape in less time.

The algorithm is a by-product of a project the two authors expect to publish later. Hiroko realized she needed a more efficient all-pairs exchange method than current literature provided, leading her to develop the HLC. Makoto is optimistic about the potential of their algorithm and hopes to see it become standard in the field, adding, "This method can be widely used, especially for those who want to use replica exchange method with multidimensional parameters and need all-pairs exchange".



Interesting People

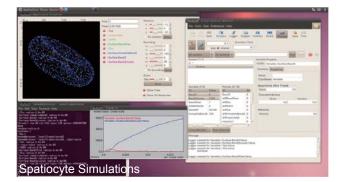
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Although born in Japan, Hanae did not begin her education here until she was 11, having first been schooled in England for three years and then four years in Germany at an American school. During high school she spent two more years abroad, this time in Taiwan at another American school, and then returned to Japan for her last year before university. "It was a very hard year for me. In the last year of high school, everyone is getting ready for their examinations. I just jumped in". Despite the challenge, she was able to matriculate at one of Japan's best private universities, Keio, where she earned her degree in bioinformatics and joined the E-cell group, from where Koiichi Takashi, Team Leader of the Laboratory for Biochemical Simulations, came. Hanae is interested in understanding how the spatial dynamics of healthy and anemic erythrocytes differ, which is why she came to QBiC to learn Spatiocyte from its founder, Satya Arjunan, a veteran member of the Takahashi team.

Having moved so much has affected her identity. Although fluent in English and Japanese, she prefers to reads novels and have casual conversations in English, but is much more comfortable discussing science in Japanese, which is somewhat surprising since many Japanese, because they read and write research papers in English, are the opposite. Moreover, though she retains very little German, Hanae has a strong grasp of Mandarin because of her time in Taiwan. She explains, "the grammar is like English and the characters are like Japanese. If you can do English and Japanese, it's easy to learn". Perhaps, but it is more likely her Spatiocyte studies will be published before her theories on linguistics are.

Kendo, which she started when she first studied in Japan, was in many ways an effort to clarify her origins. "Because I lived abroad for a very long time, I wanted something to connect me to my Japanese culture." Hanae discovered, however, that kendo's greatest asset was the bonding. "When I moved to Taiwan, I didn't have any friends. But I did kendo and I made friends there." She stopped kendo after graduating from Keio, in part because of the intensity of the practices. "During my university years, it was probably 80% kendo. We had practice 6 days a week". That does not mean kendo is purged from her life. "I still meet my kendo friends all the time", something she especially values because moving has made it hard to sustain relationships.

Since she is expecting to graduate next year with her masters degree, she is now considering where to study for her Ph.D. Switzerland, a rare country she has not visited, is tops on that list, because of its reputed education and strength in systems biology. After that it will probably be another country. "I like change. If I'm at one place for too long I get used to it. I'm scared of that".



Bon Voyage, Simon



Simon Leclerc returned to the University of Strasbourg last month after a 6-month stay in the Laboratory for Single Cell Gene Dynamics as an International Research Associate (IPA). Simon came to QBiC shortly after finishing his exams in February and is now returning for his final set before receiving his master's degree. A component of his studies required an internship. Although he looked at a number of institutes, QBiC was his number one choice. "High resolution microscopy and a high interest in biology? For me it was a complete match". He plans to continue to the Ph.D. program at Strasbourg, but do all his research at QBiC, an option because of the IPA agreement. The project has him seeking new strategies for the double labeling of proteins and for the fabrication of microchips to separate the proteins. Simon expects to be back before Christmas and looks forward to his future three years at QBiC, "even if the summer is very hot".

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Meet the QBiC Lab . . .

Toshio Yanagida and The Laboratory for Cell Dynamics Observation

Biomolecules can be viewed as nanomachines that convert chemical energy into mechanical work. Additionally, because of their size, biomolecules are susceptible to thermal vibrations, or noise. Our studies indicate that rather than suppressing this noise, biomolecules exploit them to conduct their function, which reduces their energy demands and makes them a potential paradigm for energy-efficient motors. We aim to clarify the fundamental mechanism driving this energy transduction, with special interest in noise. Our strategy is heavy in single molecule techniques, beginning with total internal fluorescence microscopy. Historically the lab has used myosin as its model molecule, although we are expanding our studies to other motors like RNA polymerase. The group also collaborates closely

Sweating the Summer

How hot was it in Osaka-Kobe this August? The summer temperature kept the institute in such a lethargic funk that one QBiC member fled the heat by taking a one-week trip to Bangkok. Which is why QBiC decided to have a small ceremony the end of the month for cooler weather. Dozens of virgin beers were sacrificed by the more than 40 participants. The gods were appeased, as September 1st saw the daily high dip below 28 °C for the first time since June.



with the Immunology Frontier Research Center at Osaka University, where we are investigating how these mechanisms can be used for more accurate drug targeting, and the Center for Information and Neural Networks, where the mechanisms are being employed as design principles for robotics and communication networks, providing a rich environment of both basic and translational research.



Briefs



The Laboratory for Nano-Bio Probes has published a report in *Chemical Communications* and first authored by Yuko Nakane on new quantum dots (QD) for non-invasive imaging in the highinfrared 2nd near-infrared (NIR) biological window (1000-1400 nm). Probes that emit at wavelengths

farther from the visible light range are less susceptible to scattering and other noises caused by the tissue, making

their development a key focus in non-invasive imaging techniques. The authors show the applicability of their probe for both in vitro and in vivo imaging of cancer cells in mice.

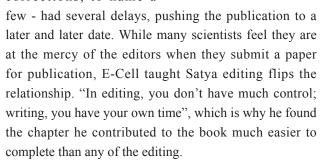
While sphingosine-1-phosphate (S1P), a lipid mediator, is known to have roles in several biological processes, details in how it regulates development are limited. First author Yu Hisano (photo) and other members of the Laboratory for Cardiovascular Molecular Dynamics use double mutant zebrafish to show that S1P signaling and fibronectin cooperatively regulate myocardial migration and low jaw formation. The report can be seen in *Biology Open*.

Take Me to the Other Side

Satya Arjunan explains what it is like being an editor for a book

he invited review. It is an opportunity to share your views of where a field is headed, but also and an intrusion on your research. Frequent messages from editors about upcoming (or missed) deadlines and complaints about unscientific matters like the formatting and image quality make it almost inevitable you wonder why you ever agreed. Yet how often have you considered the editor's side? Satya Arjunan of the Takahashi team took that journey when he edited E-Cell System: Basic Concepts and Applications, a book released this year, with Pawan Khar and Masaru Tomita. Satya began the project by making a mailing list of potential authors who he calls, "the usual suspects. Those we thought would be using E-Cell". The 11-chapter book received, according to Satya, much interest, but because of the book's specificity, he had to be very selective in who qualified. That left Satya with just enough authors and required he be extra patient with missed deadlines, since he could illafford to lose any of the needed chapters.

All the communications for the book, including those to the authors and publishers, were done by e-mail. In fact, although editors are corresponding with a large number of people on a daily basis, there is very little direct interaction. Once the e-mails were sent, Satya could do nothing but wait. "Some of them just don't respond. This is the problem faced by the editor". Each stage of the book - and there are many, including the acceptance of the invitation, submission of the first draft, and corrections, to name a



Cell System

cpts and Applications

Somewhat like writing a review, Satya found editing a book gives a feeling of regret during the process, but satisfaction when the final product appeared. "When I showed this to my father, he was very happy". As nice as it was to give joy to his father, Satya is terse when asked if he wants to edit another book sometime soon. "Not really", he says and walks away.

A major breakthrough in single molecule tracking has been the ability to follow a labeled molecule's Cartesian trajectory inside a cell. However, absent in this information is the angular orientation of the molecule. A collaboration involving the laboratories of Tom Watanabe (first author), Takashi Jin, and Toshio Yanagida has led to a new report in *Biophysical Journal* that describes the synthesis of rod-shape quantum dots for this purpose. The authors demonstrate the application of these qrods by attaching them to membrane receptors in living cells.

A report in *Computational Chemistry* describes a new strategy for reducing the computational demands of pairwise nonbonded interactions during MD simulations. The Laboratory for Biomolecular Function Simulation proposes defining the energy and gradient as a linear function of the inverse of the square of the distance when investigating short-range interactions using the particlemesh Erwald method. The result is new lookup table that outperforms other tables both in accuracy and speed when table densities are large. The work was first authored by

Jaewoon Jung.



Retreat



QBiC had its 3rd annual retreat the end of June on Awaji Island, the same location as the previous year. Because QBiC is divided into multiple locations, with the bulk of labs being in Osaka and Kobe, the retreat offers the rare opportunity for all members to meet. The retreat this year was organized to highlight collaborations. To showcase this point, each talk had multiple speakers describe their respective roles on a particular project . The retreat lasted 3 days and 2 nights and included 143 participants, a good number of whom found time for fishing on the second day. ●

New Faces (and new babies)

Yukiko Onishi (left) of the Laboratory for Cell Signaling Dynamics will soon be saying goodbye to her QBiC colleagues and hello to her second child. Taking advantage of Riken family benefits, she will be taking maternity leave. The program allows her to have 6 months post-birth, but also up to two months pre-birth. Group Director Masehiro Ueda has hired Mayu Hata (right) for this period. Mayu is an avid volleyball player, preferring it to the national pastime, baseball. She does admit, however, that her husband is a diehard HANSHIN TIGERS fan, making her one as well.



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THE CHOW DOWN Carnivorous Oatmeal Crunch

Ingredients

300 g of any meat (pork, beef, chicken, etc.)200 g of zucchini and/or peppers

100 g oatmeal (even better if mixed with dried fruits)

3 tablespoons olive oil

2 tablespoons white wine

(sauce)

- 2 tablespoons mustard
- 4 tablespoons rice vinegar
- 1 tablespoon honey



Rub both sides of the meat with salt and pepper and let rest for 5 min

Wipe away any liquid from the meat and then rub with the wine

Rub again the meat with salt and then oatmeal until it sticks

Add the olive oil to a pan and at medium heat fry the meat until its surface browns (about 5 min)

Add the vegetables and continue cooking on low heat (10-15 min)

During this time, mix the sauce ingredients

When finished frying, put the meat and vegetables on a plate and pour the sauce over



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