NEWSLETTER OF RIKEN Quantitative Biology Center

OBIC QBITS

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Talking With...

KATE YONEYAMA, DIRECTOR OF SALES AT THE NATURE TOKYO OFFICE

QBiTs visits Nature to discuss how the internet has changed the business model of publishing and the value Nature has for Japanese science.



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• P ao died this winter". The normally happy Junko Yoshida speaks with her chin dropped and eyes staring at the floor. She loves Pao and misses him. Pao, however, was not a friend. Nor was Pao a pet. Pao was her powder blue car, which she was as attached to as

If you want to become friends with Junko Yoshida, you better like the beach

Linus to his blanket. Anyone who saw the two together would agree that its retro style and hippy style suited someone who paints her toenails all colours of the rainbow.

With its hatchback and large rear space, Pao also was the perfect partner for a surfer, which Junko has been since eight years ago. "It's an addiction". Try inviting her out one weekend and you will inevitably be told she is busy. "I can last one week without surfing, but after a second week I get anxious. I go even when I'm sick."

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Talking with . . .

Kate Yoneyama, Director of Sales at the Nature Tokyo office, sits down with QBiTs to discuss why Nature chose Japan for one of its major offices and the future of publishing

Why did Nature decide to establish one of its first and biggest offices in Tokyo?

In the beginning we had subscriptions fulfilled through an [outsourced] company on our behalf. That was our marketing operation in Japan. Nature made a strategic decision that this is an important market for us and we need to have an operation on the ground. While Nature was a very respected publication in Japan and we had a strong subscription base considering it's an English language publication, we did also find a barrier to submitting papers to Nature because people perceived it as being too difficult. One of the key things Nature was doing from the beginning and has been part of the DNA of the company was going around universities, institutes telling people 'don't be afraid of submitting to Nature', trying to get many more Japanese authors to submit their papers. And it was obviously extremely effective. The office launched with three staff. Now we are over a 100. You can see a real big uptake in the submissions, and it is an ongoing phenomenon really. We were getting submissions, but once we launched the office that shot up. A few years back - I haven't got the most recent figures - for submissions to Nature

journals, the U.S. was #1, and Japan was #2. That may have changed in the last few years.

How is the strategy in Asia changing?

If we look back historically, Tokyo has always has been the head office of the region. We have had our own

asiapacific.com website completely independent of nature.com. The only regional brand is Nature Pacific. We haven't got Nature North America or Nature Europe. The first [Nature] website to launch was



the Japan website. It was the most profitable website in the company for years. Now the whole company and parent company has just gone through a process of redoing our branding, because the company as a whole is more complicated than it used to be. We are not just publishing Nature and the Nature journals. For example, we are investing in a number of small internet related businesses that produce useful tools that scientists can use to manage their lab for instance or manage their publication resources in a more effective way. We are actually trying to provide a much broader service to scientists. We have decided to get rid of the Asia Pacific brand. So we are now the Nature Publishing Group, but we are still going to have our Asia Pacific website. What we do is not changing, but the brand has changed.

The existing model of Nature, the print publication ... will quite likely disappear

Nature prints Nature Digest, which contains articles from Nature translated into Japanese. Is this product exclusive to Japan?

That's unique to Japan. We would like to do it in other languages or the same concept. It would be a nice thing to do in China I would think.

Why have we done it in Japan? This is given away free to our Nature subscribers in Japan. The volume of our subscription business justifies that, because it is an expense. We still have a significant number of print

subscriptions in Japan. The revenues in that justify the effort and expense in the Digest. It also started off in fact as a marketing tool, because what we found in Japan is that the way people read Nature is guite interesting. Most people read what we call the 'back half', which is the research papers. But we put in a huge amount of effort and expense into producing the news section and other parts of the journal, which we think are really important. We found a lot of Japanese people were not even looking at that. We thought this was a waste. We also thought that if more people were reading that type of content, it broadens the audience of Nature. And that's what we use in the Digest. We don't translate the papers. We translate front half content, so that readers know what's in the front half of Nature and they start reading it.

How have online subscriptions affected the front half of the journal like the News section?

Now we are not reducing our investment in news production. I don't think there is any talk of reducing it in the future. But what we may be looking at is how we package our content. The existing model of Nature, the print publication, which is front half news and back half papers, that model will quite likely disappear. That does not mean that content will not be there, but it may be packaged in a different way. One could potentially see a 'News Nature' that does not have the papers at all. Of course this is of huge significance in the science publishing business. Nature Publishing Group has a definite strategy of being ahead of the game, reading where it is going, what the needs of the scientists are going to be and having the products to meet those needs. We are trying to adapt to what is required.

There is a slight nervousness on the impact this way of accessing information could have on science, because all this move to being interdisciplinary, you won't be able to make that great discovery unless you know what people are doing in other fields; unless your mind is open to more than just your small field. And if people working on science are doing everything online without having that broader picture, which online does not really encourage, you might find that people are much more focused – it doesn't appear to be happening – on just their own field.

Many scientists unhappy with research look at publishing as an alternative. How did you enter the profession?

I never took my science career beyond undergraduate level. I was in the U.K. and went into publishing. My career has always been in publishing. Initially it was business publishing. I was not trained in the publishing business, but my whole working life I have been in some form of the publishing business. I was never employed by Nature in London or New York. I was directly employed by the Tokyo office. The reason for me going to Nature was I liked Japan. I was employed by a British company, sent to Japan for a year, supposed to go back, but I didn't really want to. At that point I started looking for a job in Japan. Coming in as a salesperson...it was quite challenging. I was doing coldcalling in Japanese when I could barely say 'Konichiwa'. It was quite embarrassing.

Nature Rankings and RIKEN

For several years, the Tokyo office has published the Nature Publishing Index, which compares how nations and institutes perform with regards to annual publications in Nature journals. Until this year, the list was confined to just Asia Pacific nations, but is now being expanded globally. Riken has ranked in the top 5 among Asian institutes since the index was first published and in the top 10 among institutes among non-English speaking countries worldwide.

Paper Highlight

New Lab-on-Chip technology for biological studies

icrofluidics, the processing or manipulation of fluids at the picoliter scale, has become increasingly popular in the biosciences for its ability to control molecular concentrations in space and time. Microfluidics devices are normally small microchips and accordingly called lab-on-chips. These microchips are composed of a number of basic devices including a valve that is used to interrupt the flow of a solution and can therefore be used to separate mixtures. The most common material used for these valves is polydimethylsiloxane (PDMS), an elastomeric polymer that is relatively easy to bend. However, polymerbased valves often absorb or react with organic material, limiting the applicability of the microchip. Therefore, other materials are continuously being investigated as alternatives to PDMS for microchip technology.

In many ways, the ideal valve will be made of glass. Glass has a higher resistance to fluid pressure and greater detection limit than polymers along with being inert to organic substances. These properties should make for lab-on-chips applicable to a much wider range of biological studies when using valves made of glass. At the same time, glass is a vastly more difficult to handle because of its rigidity, which makes for a much more fragile valve than those made of polymers. Yo Tanaka, team leader of the Lab for Integrated Biodevices, has published a report that describes the synthesis of glass valves and demonstrates





microdevices using these valves perform equally to contemporary chips with PDMS valves. The research was stimulated by collaborations with QBiC Group Director Hiroki Ueda, who needed a device that could separate single organic molecules like DNA, and has been published in RSC Advances.



Yo's challenge was to develop a glass that was sufficiently thin so that it can bend when pressed, but sufficiently strong so that it does not break. Glass thickness and flexibility have a logarithmic relationship. Yo found that glass made to be less than 10 μ m thick using his method could bend as much as 120 μ m, more than sufficient to seal a microchannel and 5 times better than standard systems.

Although his system has not been yet applied for experiments like those requested by Hiroki Ueda, Yo is optimistic that with some more modifications, his microchip can be made even smaller and perform even better. The prospect of using glass valves should significantly expand the impact of lab-on-chips in diverse fields like mass spectroscopy, drug screening, and single molecule analysis "especially for", Yo explains, "very sensitive analysis or synthesis".

In a second publication, Yo, through an industryacademic collaboration, describes an electric-active polymer that can be used as an actuator for pushing a valve and thus sealing a channel in a lab-on-chip device. The polymer is designed to deform when stimulated with a voltage and directed to seal the channel. While piezoelectric actuators are preferred to their pneumatic counterparts because they are generally quieter, they have the disadvantaged in size, which limits their portability. Yo expects the polymer to alleviate this concern. The study is reported in *Sensors* and Actuators B.

Meet the QBiC Lab . . .

Tom Watanabe and the Laboratory for Comprehensive Imaging

ells are complex systems and have multiple states that transition between one another stochastically. One excellent example is the pluripotency of stem cells (ES and iPS cells). At some point, the cell state transitions into differentiation, and the pluripotency is lost. One of the great goals in stem cell research is to recapture the pluripotency. We are approaching this problem by investigating the dynamics of the state transitions quantitatively. The cell state is dependent on a network of transcription factors whose expressions, like the cell state, also fluctuate. Another example we investigate is the immune system, which can also be viewed as a fluctuation of states that depend on a network of regulators, as a typical immune response can be viewed as a complex network consisting of various types of T-cells, macrophages, and lymphocytes that all interact.

For quantitative study of these transitions, my lab is mainly focused on the development of microscopy techniques that can achieve increasingly better resolutions of real-time events inside live cells.



Some of the strategies we are using include Raman microscopy and second harmonic generation microscopy. To also observe these events we are developing new chemical probes, microfabrication methods, and gene engineering techniques. Therefore, our team has experts from distinct fields including physics, microscopy, biology, and systems engineering. It is an interdisciplinary group that requires any member to both teach her expertise and learn from other experts.

Newcomers at QBiC



Me: Yumi Kashihara Lab: Team Taiji Hobbies:Music, Karaoke, Watch baseball games Cheers:Yomiuri Giants

Me: Akira Sasaki Lab: Team Jin Hobbies: Snowboard, Tennis Cheers: Hokkaido Nippon Ham Fighters

Me: Chin Yin Fai Lab: Team Takahashi Hobbies: Soccer, Travelling, Music Cheers: HANSHIN TIGERS



Me: Kenneth Ho Lab: Team Onami Hobbies:Tennis, Cycling, Reading Cheers: Whoever is playing the Giants

Me: Hiroyasu Koteishi Lab: Team Ueda M Hobbies:Soccer, Music Cheers:Free Agent

Me: Shota Kawahara Lab: Team Ueda M Hobbies: Cycling, Reading Cheers: HANSHIN TIGERS

1000000000 B00000 B0 B0 B0

Me: Noritaka Fukuda Lab: Team Okada Hobbies: Research, Sake Cheers: Hokkaido Nippon Ham Fighters

Interesting People

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Junko was introduced to surfing by the film Blue Crush, not exactly a classic, but a movie that has obviously changed at least one person's life. Soon thereafter, Junko found a surf shop in Wakayama that also offered lessons and hit the waves the same weekend. "After that first class, I went back to the shop and ordered my board". Now that store sponsors her for her boards and through their contacts she has found a second sponsor for her wear. That does not mean she is always visiting Wakayama for surfing, however. Instead, every Wednesday, she visits a Japanese website that gives detailed information on the weather and expected conditions of the waves to decide her destination that weekend. As a result, even though she knows she will be surfing, usually she will have not decided where until she hops into her car Friday night for a long drive. However, more often than not she will find herself in Shikoku, especially Kochi, where "the waves are excellent and the level of the surfers is quite high".

During weekdays, Junko is "the mouse gal" at the Hiroki Ueda lab. She is responsible for injecting constructs and DNA into ES cells, identifying the positive colonies and producing the transgenic mice. She has been working in laboratories since her interest in science was sparked by an internship she did in forensics. She loved it, and her coworkers loved her, which has been the case in all the laboratories she has worked since. As happy as she is at the Ueda lab, though, her ultimate dream is a job sufficiently near the





sea so that she can begin and end each day hitting the waves.

Unintentionally, Junko has kept the science and the surfing separate, rarely spending weekends with labmates. It's not that she dislikes the idea. The problem is that none have their own surfing equipment. While some beaches have rental shops, not all do, which limits the number of beaches Junko can visit when she does go with friends. If friends did go, however, they would discover rather quickly that the carefree reputation of a surfer is not very accurate. Before each trip a lot of preparation is needed. Because there are few amenities at the beach, surfers will bring their own food, sleep in their cars, and even bring water pumps and hot water to take showers. Plus, surfers take a communal responsibility to keeping the beach clean,

> picking litter before they leave. Regardless, Junko finds surfing her meditation, as it allows her "to forget all my stresses".

> Even after a long weekend of nothing but surfing, Junko cannot escape the sea. Each time she returns home, all her surfing equipment like the boards and wetsuits bring in a little bit of her trip. It has reached the point that after all these years Junko describes her flat "as a little beach", because with each step she can hear the sound of sand crunching under her feet.

BiC has commenced an unofficial exchange program with the University of Wisconsin-Madison (UWM) this year, beginning with two undergraduates, Steve Wang and Drew Gunderson, who will be spending 10 weeks in the laboratories of Urs Frey and Yuichi Taniguchi, respectively. Both have been awarded Promega International Scientific Internship Scholarships, which will fully fund



their stays. Michelle Kern, an assistant director at UWM, has been working with QBiC staff since her days at MIT where she sustained a similar program. QBiC and UWM aim to invite students to Japan annually.

Watching Sumo

WHACK! BOOM! THUD! Whichever your favorite Adam West Batman onomatopoeia, it aptly describes the sound of two sumo wrestlers, or rikishi, crashing at the beginning of a match. To the unfamiliar, sumo may seem little more than two very fat men pushing each other in a sumo ring, or dohyo. In reality, sumo is a methodical fighting style that was used by the military. If you watch enough competitions, you will realize that the techniques and footwork require no less skill than that seen in (what was) Olympic wrestling.

Each year there are six annual tournaments in Japan, with one in Osaka every March. The Osaka tournament is held in a fairly modest auditorium where in the halls rikishi can be found clubbing walls in preparation of their bout, or torikumi. Before the mathe the rikishi will approach the dohyo stoically. There they walk to their respective corners (the 4:00 and 8:00 positions) and undertake an elaborate ritual that involves clapping to the Gods and purifying the dirt of the dohyo with salt. The two rikishi then position themselves across one another, squat and lean forward on their fists while they wait for the referee, or gyoji, to commence the torikumi. It is not uncommon during this wait, or shikiri, for one of the rikishi to stand and return to his corner much like how a batter steps out of the batting box in a baseball game. There, the rikishi repeats his rituals. This can happen several times and, depending on their patience, can exasperate the audience. Considering that many rikishi weigh over 200 kg, this bending and standing can take a larger toll on the knees and back than the actual rumble and is certainly to the advantage of a smaller rikishi, who can be half the size of his opponent, because, unlike similar sports, sumo does not separate its rikishi by weight class.

When the gyoji does start the match, most often the two rikishi collide like two swift gazelle. Normally, one rikishi gains quick advantage and victory, making the match slightly longer than a blink. Sometimes, neither rikishi gains an edge, which brings a roar from the spectators. The rikishi battle like two heavyweight boxers, leaning on the other while at the same time reaching for his opponent's mawashi, the massive belts that are the only thing on the rikishi's body and prevents a riskishi from being completely naked. (Looking at the girth of many of the rikishi, I have concluded it also prevents their bellies from touching the ground and thus immediate defeat). In extraordinary moments, the rikishi will leverage his grip on the mawashi to lift his elephantine adversary and throw him to the ground.

The Osaka tournament lasts 15 days, with all rikishi



having one match on each. The days begin in the morning, when the lower-class rakishi battle, and end in early evening with the sekitori, the most talented class of rikishi. While it is likely you have never done sumo, when the day is over and you finally stretch your legs from your cramped seating, you will know what it's like to live like one.

Briefs

Cell Adaptation

BiC Team Leader Chikara Furusawa, in collaboration with Kunihiko Kaneko, has demonstrated in silico that epigenetic feedback regulation (EFR), the feedback between epigenetics and gene expression, is responsible for a cell's robustness. By looking at different relationships between the cell growth rate and the epigenetics, EFR, they show, is especially advantageous when the cell cannot detect signals from the environment, as otherwise the cell risks having a low growth rate and in turn low fitness should it not adapt to the new conditions. Applying EFR, the cell can stochastically select a gene expression pattern that results in a high growth rate to efficiently adapt to environmental change. Experimental evidence has already shown that phenomena like DNA methylation and DNA supercoiling may be two mechanisms that facilitate EFR. The report can be read in *PLOS ONE*.

> Want to join QBiC ? Please see our website http://www.qbic.riken.jp for the latest job opportunities

THE CHOW DOWN celery Dumplings

Ingredients for 20 pieces

Celery 1-2 stalks Mince Pork 200g Oyster sauce 1 tsp Chicken stock 1 tsp Soy Sauce a drop Sesame oil a 1/2 tsp Store bought Dumpling Skins (20)

> Have a recipe you want to share, contact us at: qbits@riken.jp

Ah, Venice

Nano technology global challenges 2013



kihito Komatsuzaki of the Laboratory for Nano-Bio Probes may forever be disappointed with future academic conferences after attending the Global Challenges: Opportunities for Nanotechnology. He was one of over 70 young researchers, but the only one from Japan invited to attend the 4-day event in April for discussion on how nanotechnology can be used to solve the great challenges of the future like energy conservation, climate change, and food and water availability. The event itself was essentially a number of brainstorming sessions where Akihito and others drew ideas on how to apply their research outside of the laboratory. What made the event exceptional, though, was that it was held in Venice. Akihito remains silent about how much time he spent at the actual meeting and how much he spent exploring the historic city. 🔵

Chop the celery, put in a bowl, ad salt and mix. After 5 minutes squeeze out any water.

Mix the pork, oyster sauce, chicken stock and soy sauce in a separate bowl. Add the celery and then the sesame oil. Place in the refrigerator for 30-60 minutes.



Put some filling onto a dumpling skin and wrap. Using high heat, add sesame oil to the frying pan and the wrapped dumplings, being sure they do not burn. Add 50-60 cc of hot water and cover.

Once the filling is cooked, remove the cover to let the water evaporate. Then pour more sesame oil along the side of the pan so that it reaches only the bottom of the dumplings and continue to simmer. For the sauce, mix vinegar and sesame oil or balsamico.



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