VIEWPOINT

Asian promise: the state and future of collaborations in neuroscience

Mu-Ming Poo, Ley Sander, Marc Fivaz and Yasunori Hayashi

Abstract | As investment in science and technology continues to grow in Asia, countries such as China, Japan and Singapore are witnessing great improvements in their neuroscience research environments; this is reflected in the opening of new research institutions and in the influx of neuroscientists trained abroad. Collaborative projects between researchers in these countries and laboratories in the United States and Europe are not only helping to shape these institutions, they are also leading to a surge in high-quality publications in both basic and translational neuroscience, resulting in increasing international recognition. Nature Reviews Neuroscience asks four neuroscientists about their collaborative experiences and the impact that such collaborations are having on neuroscience research.

What has been your own experience of collaborating with Asian researchers and institutions?

Mu-Ming Poo. In 1998, I was invited by the Chinese Academy of Science (CAS) to review the status of several neuroscience-related CAS institutes and to recommend strategies for improving neuroscience research in China. In writing my report to CAS, I found it very difficult to make any relevant recommendation for existing CAS institutes. I felt that the best way to strive for excellence was to establish a brand new institute with an infrastructure that would emphasise the quality of research and that would operate on the principle of merit-based resource allocation and promotion, with minimal administrative burden. This led to the proposal for founding an Institute of Neuroscience (ION) in Shanghai, which was soon enthusiastically approved by CAS. Since being founded in 1999, ION has grown from 7 to 24 laboratories, with research activities covering nearly all areas of neuroscience and with results being published in first-tier neuroscience journals. Substantial progress has also been made in establishing a rigorous training programme for graduate students and a merit-based system that includes regular scientific reviews of investigators. The institute is projected to expand in the next 10 years to reach the steady-state of 50 laboratories by 2020. The goal is to establish a high-quality institute that can be ranked among the best in the world.

Ley Sander. I was heavily involved with a World Health Organization (WHO) collaborative centre in neuroscience. My main research interest is in epilepsy, and in this capacity I was contacted approximately 10 years ago by the WHO, which had been approached by the Chinese Ministry of Health as they were keen to start an epilepsy programme to test the feasibility of delivering epilepsy care at the primary-care level and to understand the dynamics of epilepsy in the Chinese population. I went to Beijing and met a number of the key Chinese researchers in the field, as well as officials of the Ministry of Health. Over the next 2 years we discussed the potential project and the best ways to take it forward. This was an interesting process as it gave me a good insight into how careful and precautious our Chinese colleagues were about reaching agreements at each step. At times there were misunderstandings, of course, often owing to cultural differences, but these were usually quickly cleared up. This early interaction with Chinese colleagues helped enormously in my subsequent dealings with other Asian colleagues from Taiwan, Singapore and Hong Kong. The project was very successful, and indeed a national epilepsy programme is currently being rolled out across China.

Marc Fivaz. I started my laboratory in Singapore approximately a year ago, at DUKE–NUS, a new partnership between Duke University in the United States and the National University of Singapore. DUKE–NUS is part of an ambitious biomedical-science initiative designed to make Singapore Asia's biomedical hub and to attract researchers and health experts both into academia and into the private sector. I am part of the Neuroscience and Neurobehavioural Disorder Programme at DUKE–NUS, which consists of approximately 15 research groups that focus on various aspects of neurobiology and neurological diseases, ranging from molecular and cellular neuroscience to cognitive neuroscience and psychiatry. Start-up packages are competitive, allowing one faculty to run a laboratory of three to four people without extramural funding. One can also apply for additional grants from several different funding agencies. This allows investigators to focus on their research programme and get their laboratory off the ground quickly. My laboratory now has five people and will be expanding soon, something which would have been difficult for me to do in Europe or in the United States. Secured funding also gives us the opportunity to tackle ambitious and somewhat risky projects. Singapore is a small island and research institutes are located near one another, which also facilitates collaborations.

Yasunori Hayashi. Shared interests and specific skills have led to fruitful collaborations between my laboratory and those of Dr Tsuyoshi Miyakawa (Fujita Health University, Japan), Dr Mitsuhiro Kawata (Kyoto Prefectural University of Medicine, Japan), Dr Masahiko Watanabe (Hokkaido University, Japan), Dr Shigeyoshi Itohara (RIKEN BSI, Japan) and Dr Atsushi Miyawaki (RIKEN BSI). Dr Miyakawa carried out state-of-the-art automated analyses of our NR3B-knockout mice, which were made together with another collaborator at RIKEN, Dr. Shigeyoshi Itohara. Drs Kawata and Watanabe carried out detailed analysis of NR3B expression in these animals, and Dr. Miyawaki helped us to set up a fluorescent resonance energy transfer (FRET) system and provided us with new green fluorescent protein (GFP)-related molecules developed in his laboratory. Many of these collaborative studies have been published already; others are still preliminary.

In your view, how have such collaborations developed over the past decade and what impact have they had on neuroscience research?

Mu-Ming Poo. Most active neuroscientists in China have ties to scientists abroad, so collaborations are often easy to establish.

At ION, I have observed three types of collaborations. First, collaborations through exchange of research materials — mostly materials provided by foreign scientists to the Chinese colleagues. This form of collaboration is highly beneficial to young Chinese scientists in that it helps them to develop their projects, and it could eventually lead to more-extensive scientific interaction between the laboratories and to collaborations on projects of mutual interest. Second, collaborations between returnee scientists and their former host laboratories abroad, often a continuation of the returnee's postdoctoral research. Although such collaborations may result in more rapid publication, they may not help the career development of the returnee in the long run. Chinese institutions and granting agencies now place an increasingly high value on the independence of the research project, and publications that have been co-authored with previous mentors are often regarded as not sufficiently independent. Third, collaborations with previously unrelated laboratories that have complementary expertise and resources. These are the most useful and most highly encouraged form of collaboration. Many neuroscience laboratories in Asia have large populations of highly motivated and well-trained students, who could perform experiments that require skill, discipline and patience (for example, making electrophysiological recordings and ultrastructural reconstructions). I can envision very fruitful collaborations with Chinese laboratories that aim to elucidate the complete neural circuitry at the cellular level in different brain regions of various species, a task that eventually has to be done if we are to elucidate the mysteries of the brain. At present, most active neuroscientists in China are young and not yet recognized by their international peers; collaboration with experienced and well-established foreign scientists will help their intellectual and career development. However, sustainable long-term collaboration of this kind is possible only when both parties in the collaboration receive their due credit and recognition in the neuroscience community. In short, the collaboration cannot be based simply on the notion that the foreign scientist provides the idea and the Chinese laboratory provides the labour. The surest way to establish a long-term win–win relationship is through the healthy development of Chinese laboratories and the careers of laboratory heads.

Ley Sander. There are a number of Asian centres of excellence in neuroscience, particularly in Japan, China and Singapore. Various collaborations have developed over the past few decades, but it is in the past 5 years that collaboration has really taken off. These collaborations not only involve these centres of excellence, they also involve upcoming institutes in India and Taiwan, which is very exciting. Many of these partnerships are in translational research, but there are also some very promising collaborations in basic science. In my experience successful collaborations usually start through personal contact, often through a department offering to host a postgraduate student or postdoctoral fellow. Collaborative work between the two institutions is often the next step. This has happened in epilepsy research, between Erlangen University (Germany) and Sichuan University (China), and in the area of bioengineering, between University College London (UCL) (UK) and several sites in China. Another example of international collaboration in neuroscience is currently being set up between my own department at the Institute of Neurology at UCL and the neurology department in the Dayanand Medical College, Ludhiana (India), after we hosted a postdoctoral fellow from this department. Many of these collaborations have not delivered much yet, but there is much excitement about their potential outcomes over the next decade or so.

Marc Fivaz. The explosion of growth and of the use of technology in Asia (Taiwan, Singapore, Hong Kong, Japan and mainland China) over the past decade has led to a remarkable increase in the number of overseas Asian scientists (Chinese in particular) returning to Asia to set up their laboratory. In fact, the migration of Chinese scientists back to Asia from the United States or Europe is in many ways comparable to the westward migration of Chinese scientists to the United States after the Second World War. Many of these returning scientists have kept strong ties with the United States, and sometimes they even keep some of their activities in the West. The increased level of funding and infrastructure in Asia gives them the ability to conduct ambitious and costly research in ways that would not be possible right now in the United States or Europe. For example, Tian Xu, a geneticist at the Howard Hughes Medical Institute and at Yale University (USA) who has embarked on a genome-wide transposon mutagenesis study in mice, has moved some of his operations to Fudan University (China), where he is currently generating tens of thousands of transgenic animals to study mammalian development and disease. Asia, and in particular Singapore, also attracts a number of Westerners. Markus Wenk, for example, started his laboratory at the National University of Singapore, where he is currently doing (among other things) large-scale lipid profiling in animal models of neurodegenerative diseases. Another example is George Augustine, a neuroscientist from Duke University in the United States, who recently joined DUKE–NUS in Singapore to study neural circuits in transgenic mice using optogenetic techniques.

Yasunori Hayashi. Most collaborations start from a good personal connection, especially when the work involves a large effort on both sides. Building trust is highly important. For example, it is not ideal to discover after a significant amount of work has been carried out on a collaborative project that your collaborator has lost interest in publishing it. Most of the collaborations I have been involved in originated through a past personal connection. Scientists in the United States may not need to find collaborators in Japan or other parts of Asia unless they are looking to use a very specialized technique that could open up new directions of research.

Q *What are the advantages of setting up these collaborations? Should they be further encouraged? If so, how?*

Mu-Ming Poo. China has the largest population of well-trained students in the world; they will be an important driving force for scientific and technological development in the coming decades. The stability of the government and the soundness of the economy will ensure a steady increase in research funding, which is projected to double from the present level by 2020. This offers a rather unique opportunity for young scientists wishing to pursue their research interests in China without too much diversion by fund-seeking efforts. In China, the potential for organizing big projects that involve a large number of scientists all working together to find the solution to a major scientific problem or to eradicate a major disease could yield dazzling results. However, whether this is the most fruitful way of doing neuroscience research at this time is a matter for debate. On the negative side, we may notice the lack of a tradition in basic research in most Chinese institutions. Basic research did not receive much support from the government until the 1990s. Few institutions have ongoing high-quality basic research with a history that can benefit young returnees. It takes generations of researchers to build

such a tradition, and current returnees will be key to this process. Successful international collaborations will also help to shape the future of Chinese institutions and integrate them into the international scientific community.

Ley Sander. Asia has an enormous pool of talented, ambitious young scientists who work hard and creatively. From the Western perspective, one of the advantages of setting up collaborations with centres in Asia is that they will be able to draw from this pool. Of course, interaction, cross-fertilization and exchange of knowledge are also important, as collaboration should and must be a two-way process. Some of the collaborations are focused on local neurological problems, and in our case our Asian colleagues have drawn from our experience in the area. Our own collaboration with China in the area of epilepsy, in which we are assisting in the development of a national epilepsy programme, will hopefully improve the delivery of care for people with epilepsy in China (care is currently almost non-existent in many parts of the country). Finally, we should not forget that a grant will often go much further in Asia than it would, for instance, in the UK, and so there are also economic advantages.

Marc Fivaz. I see three main advantages. First, Asia offers the resources and infrastructure for a neuroscientist to carry out large-scale and long-term studies that would probably not be funded these days in the United States or Europe. This applies to both basic and translational research. Some neuroscientists, like Yi Rao (National Institute of Biological Sciences, China), have also returned to China to start an entirely new line of research. Such bold moves may be harder to pull-off in the United States right now, considering how tight and competitive funding is there. Second, because of the strong emphasis that is placed on translational and clinical research in Asia, and in Singapore in particular, collaborative efforts between the East and West should facilitate the transition of neuroscience research from the bench to the bedside, which remains a long and very costly process. Third, several big pharmaceutical companies (GlaxoSmithKline (GSK), Novartis and Lilly) are now relocating their research activities to China and other Asian countries. GSK, for example, now has a facility in Shanghai that is dedicated to neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease and multiple sclerosis. This should facilitate collaborations between academia and the private sector and speed up the development of novel therapeutics.

Yasunori Hayashi. In my view, the shared interests between the collaborating parties make the whole experience very enjoyable and rewarding. One plus one makes three if there is good collaboration. Conferences and courses are still the best way to meet potential new collaborators. With advances in methods of communication and the increased cost of travel, attendance at web-based seminars or 'virtual' conferences may become more widespread.

Q *What difficulties have been encountered? How do you think these challenges could be overcome?*

Mu-Ming Poo. It has been difficult to establish a rigorous scientific review system at ION that stresses the significance and quality of the research rather than the quantity of publications. Our moderate success in this respect at ION has resulted in the surge of neuroscience papers from China that have appeared in high-tier journals. To my knowledge, ION investigators were responsible for publishing the first neuroscience papers based on work done entirely in China in *Science*, *Cell*, *Neuron*, *Nature Neuroscience* and *Nature Cell Biology*. However, by insisting on the principle of regular academic review by an international team of experts, I was on the verge of being sued by a senior investigator (a CAS academician) who claimed that academicians elected by CAS are already recognized leaders in China and thus should not be subjected to further review. In his view CAS's regulation endows academicians with a life-long right to run a laboratory.

Ley Sander. Many of the difficulties that arise when collaborating with Asian scientists are often due to misunderstandings, which are usually caused by cultural differences. Indeed, it is very important that we make a deliberate attempt to understand and engage with the local culture. Many of the misunderstandings that I came across in my early dealings with Chinese colleagues were due to cultural differences. Taking these cultural differences on board is

Box 1 | **About the contributors**

Mu-Ming Poo is the Paul Licht Distinguished Professor in Biology at the Department of Molecular and Cell Biology, University of California at Berkeley (California, USA). Before his current appointment, he held professorships at the University of California, Irvine (California, USA); Yale University (Connecticut, USA); Columbia University (New York, USA) and the University of California, San Diego (California, USA). His current interests focus on the development of neuronal polarity and the plasticity of neural circuits. Poo was born in China, received his B.Sc. from Tsinghua University (Taiwan) and received his Ph.D. from John Hopkins University (Maryland, USA). Since 1999, he has served as the founding Director of the Institute of Neuroscience in Shanghai (China), a collaborative project for which he was given the People's Republic of China International Science and Technology Cooperation Award in 2005.

Ley Sander is a professor of neurology at University College London's Institute of Neurology (UK), and a consultant neurologist with a specialist interest in epilepsy at the National Hospital for Neurology and Neurosurgery at Queen Square, London (UK). He heads the World Health Organisation Collaborative Centre for Research and Training in Neurosciences and is the Scientific Director of SEIN, the Epilepsy Institutes of the Netherlands Foundation. Sander is particularly interested in delivering epilepsy care in resource-poor settings, the epidemiology of epilepsy and patient-care issues. He was made an Ambassador for Epilepsy by the International League Against Epilepsy in 1993.

Marc Fivaz carried out his Ph.D. in the Department of Biochemistry at the University of Geneva (Switzerland) with G. van der Goot, working on the membrane trafficking of glycosylphosphatidylinositol-anchored proteins. He then joined T. Meyer's laboratory at Stanford University (California, USA) as a postdoctoral researcher, where he studied signal transduction mechanisms that underlie neuronal polarization and synaptic plasticity. Fivaz moved to Singapore in September 2007 to start his own laboratory at the DUKE–NUS Graduate Medical School. The laboratory's research focuses on understanding the fundamental signalling principles that govern cell polarization and motility in the context of axon growth, axon regeneration and synapse formation.

Yasunori Hayashi received his M.D. and his Ph.D. from Kyoto University (Japan) and carried out postdoctoral work at the University of Tokyo (Japan) and at Cold Spring Harbour (New York, USA). His laboratory at the RIKEN–MIT Neuroscience Research Center (Massachusetts, USA) examines the molecular mechanisms of synaptic plasticity. Hayashi was an active participant in the collaboration between the RIKEN Brain Science Institute in Japan and the Massachusetts Institute of Technology in the United States.

crucial: before making any assumption, one needs to attempt to see things from the perspective of one's collaborators. As an example of how things can potentially go wrong, there was an occasion when one of my European colleagues gave a very nice Swiss-made clock to the head of a department — a prospective collaborator — in China. This was a disaster from the Chinese perspective, as giving someone a clock (regardless of how nice it is) is akin to a death wish for the recipient. Another area in which difficulties might arise is to do with the budget of any joint project. To avoid misunderstandings, this needs a lot of attention and clarification early on, so that all parties involved know exactly what to expect.

Marc Fivaz. Despite booming economies and large investments in research, the impact of neuroscience in Asia still lags behind that of neuroscience in the United States (as measured by the number of papers that are indexed by Thomson Scientific). This is partly due to the fact that Asia has only been on the map of neuroscience research for approximately a decade. Recent studies indicate that Asia is in fact quickly catching up with the United States and Europe and predict that article output (in terms of number of papers per capita and impact factor) will match that of the United States in the next 10 years or so. The impact of neuroscience in Asia will also depend on the commitment of governments and research institutes to appoint researchers and fund their research on the basis of merit. Competitive funding and merit-based systems are in place in many Asian countries already, including Singapore, Japan and Taiwan, and are now being implemented in mainland China.

Yasunori Hayashi. It is difficult to easily access information about Asian researchers online. Often their web pages introduce laboratories as, for example, the Department of Neurophysiology or the Research Team of Synaptic Plasticity, in detriment of the visibility of the researcher's name. This contrasts with web pages in the United States, which centre on the researchers, not on a department or laboratory. Sometimes web pages are only in the local language, and even if an English version is provided, it is often not as extensive as the version in the local language.

Q *What lessons have been learnt? Where do you foresee these types of collaboration going?*

Mu-Ming Poo. There are now more Chinese scientists returning to China after receiving years of training abroad. Armed with good training, the latest technologies and abundant resources, these scientists will become the main driving force in Chinese neuroscience research. The returnees will face some difficulties, however. Few of them have had extensive experience as independent scientists abroad, and most Chinese institutions lack experienced senior investigators (of the generation that was hit by the Cultural Revolution) who could serve as their mentors. Furthermore, the environment of many institutions is not conducive to high-quality research. This is exemplified by the lack of a tradition of rigorous scientific interaction among colleagues, the seniority-based rather than merit-based promotion and resource allocation, and the excessive and inefficient administrative structure. The tradition of an authoritarian top-down approach in scientific administration still permeates most institutions, discouraging individual research projects that are based simply on scientific curiosity and passion. Nevertheless, research support has been increasing steadily for all laboratories of reasonable quality. Some excellent science is bound to be done in China in the future. Although we have not seen truly ground-breaking discoveries in neuroscience from China so far, the situation may change in the coming decades as the number and quality of the laboratories continue to increase. In some sense, the absence of existing scientific traditions may prove to be a positive in the long run — new returnees are pioneers in a virgin land who have the opportunity to flourish in their own ways, distinct from the mainstream science of the West, and hence are in the position to make a more unique contribution.

Ley Sander. I think that there is a very good outlook for these collaborations. Indeed, my feeling is that as many of these collaborations mature and we start to see the results, more collaborative efforts will be set up and this will create a momentum of its own. With time, I would not be surprised to see Asian neuroscientists taking the driving seat and the Western partners becoming the juniors in the relationship. There is such potential in Asia, and this will really start to be fulfilled once intra-Asian collaborations take off. Can you imagine combining Indian creativity with Chinese tenacity or Japanese technical prowess? Indeed, I think we have not seen anything yet.

Marc Fivaz. Having been in Singapore for one year and having been exposed to research in other Asian countries by attending conferences, I have little doubt that Asia will be a major player in neuroscience research in the years to come. The quality and breadth of research presented by scientists from China, South Korea, Taiwan, Singapore and Japan at the recent Molecular and Cellular Neurobiology Gordon Conference in Hong Kong is a clear sign that Asia is fast becoming a major hub of neuroscience research. Building strong collaborations between the West and Asia is part of a global and multidisciplinary approach that the neuroscience community needs to take in order to make significant advances in our understanding of brain function and disease.

Yasunori Hayashi. In addition to collaborations at a personal level, institutes such as the RIKEN–MIT Neuroscience Center greatly facilitate international collaborations. The RIKEN–MIT Neuroscience Center is based at the Massachusetts Institute of Technology but is funded by money from RIKEN in Japan. There has been criticism in Japan of giving research budget to MIT, which is quite understandable. However, I strongly believe that this effort displays the quality of Japanese neuroscience to the world in the long run. I understand that similar collaborative projects are underway between the United States and several Asian countries, including Singapore. Setting up such initiatives requires strong leadership from the heads of the institutes, as well as support from their immediate peers.

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FURTHER INFORMATION
ION: http://www.ion.ac.cn/
National epilepsy programme of China: http://www.who.int/bulletin/volumes/86/07-047050.pdf
DUKE–NUS: http://www.duke-nus.edu.sg/
RIKEN–MIT Neuroscience Center: http://web.mit.edu/picower/about/rikenmit.html

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