Q & A

Björn Brembs

Björn Brembs was born and raised in Würzburg, a small university town in Germany. He did his undergraduate studies there and in Umeå, Sweden, before he started to work on his PhD in Würzburg. In the Department of Genetics and Neurobiology of the University, Björn worked on associative learning in the fruit fly Drosophila*, under the supervision of Martin Heisenberg. After graduating in 2000, he moved to Houston, Texas for a postdoc with Jack Byrne, studying operant learning in the sea slug* Aplysia *and learning physiological techniques to complement his training in genetics. After the postdoc, in 2004, Björn moved to Berlin to work as an independent researcher with his own lab. He completed his habilitation five years later and received a Heisenberg fellowship the same year. Ever since his first undergraduate* Drosophila *research projects in Würzburg, his main research focus has been on how brains decide which actions to generate next and how they evaluate the consequences of these actions. He maintains a website and a blog at: http://brembs.net.*

What turned you on to biology in the first place? The answers to this question often start along the lines “already as a little boy” and mine is no exception. Already as a little boy, I was riding my bike around the countryside near our home, always on the lookout for frogs in backwater, fire-bellied toads in ponds or snakes in old quarries. I soon had a terrarium with frogs and toads, and my biggest delight was to watch them forage and feed. Later, in high school, a friend recommended a science book and very soon I was reading popular books by Nobel laureates and other famous scientists and philosophers. From then on, it was clear that I wanted to become a scientist and given my inclination towards biology, I enrolled as a biology student at the University in my hometown Würzburg. From reading these books, there was only one topic I was sure would be too complicated for me to ever dare going into: neuroscience.

What turned you on to neuroscience? A lecture on the neurogenetics of *Drosophila* by Martin Heisenberg. Until this lecture, I was fascinated by developmental biology: how could a complex organism arise out of a seemingly simple and unstructured zygote? The lecture quickly grabbed my attention, however, and developmental biology was forgotten. In it, Heisenberg talked about how essential it is for every moving organism not only to respond to its environment, but to initiate actions independently of the environment, probing it and evaluating its response. This concept has far-reaching implications for how we see ourselves as agents, our freedom of choice and what genuinely special scientific objects brains are. Studying the brain of an insect also seemed a lot less intimidating than studying the human brain, and helped ease the transition into neuroscience.

What has been your biggest thrill in science, and what your biggest mistake? I can answer both questions simultaneously! A few years back, I conducted a series of experiments which proved wrong most of the initial assumptions I held when I started in *Drosophila* neurogenetics 15 years ago. Back then, I thought it would make a lot of sense if the genetic machinery for neuronal plasticity had been invented only once in evolution, and that all forms of learning then take place by using this machinery in different parts of the brain. However, I could not make any sense of my results from that perspective. I remember very heated discussions with my thesis advisor Martin Heisenberg about the direction of my experiments at the time. My mistake was that I was unable to think of a reason why evolution would invent more than one way to do the same thing: change the properties of a neuron. My biggest thrill was when the results came in which unequivocally showed not only that there are at least two fundamentally different forms of neuronal plasticity, but that these forms seem to have evolved to interact with one another. Most of these results were published here in *Current Biology* thirteen years after my first experiments addressing these questions.

What do you think are the most pressing questions in your field? In the past few decades, neuroscience has made tremendous strides studying the input–output functions of brains. Sensory physiology springs to mind, in particular vision and olfaction in my field of *Drosophila* neurogenetics, or the molecular and cellular mechanisms of classical conditioning in many model systems, including *Aplysia*, *Drosophila*, mice and man. However, brains are constantly active, even in the absence of stimuli or tasks. This has also been observed for decades, both behaviorally and with techniques varying from single electrode physiology to functional magnetic resonance imaging (fMRI): brains never rest. Until recently, the experimentally more straightforward stimulus–response experiments either reduced or averaged out this ongoing neural activity.

Today, the growing realization that this neglected activity is more than just simple noise in a complex system has led to a quest to understand its functions and mechanisms. Given that processing sensory input requires only a small part of a brain’s energy and only a tiny fraction of a brain’s synapses are carrying sensory information at any one time, these functions and mechanisms are probably diverse and complex. Despite the fascinating advances and spectacular discoveries that have been made in neuroscience, we have so far only scratched the surface of what brains do most of the time and how they do it.

In my opinion, the most low-hanging fruit in neuroscience today are also the most pressing questions: how do brains keep generating such finely balanced activity that seems to be ordered, yet probabilistic, undetermined, yet predictable? It is this fine balance between spontaneous/ongoing activity and elicited processing which defines how all brains work. The mechanisms underlying this balance are the key to understanding general brain function and thus to understanding and perhaps curing many, if not all, psychiatric disorders.

Do you have a favorite paper? That changes whenever the next big breakthrough is announced. In my field of research, I’m currently very excited about a whole set of papers over the last couple of years from Marcus Raichle's group on the so-called 'default-mode network' — the brain networks in the human brain that are active when the person is resting and not involved in any specific tasks. I find it amazing how analogous the results being found in humans are to those we are obtaining with flies, at least at an abstract level.

Outside of my field of research, my current favourite is a systems biology paper and based on genome research in bacteria. In 2008, Isalan *et al*. — 'Evolvability and hierarchy in rewired bacterial gene networks' (Nature *452*, 840-845) — showed that one can short-circuit arbitrary nodes of the genetic network of *Escherichia coli* without wreaking the sort of havoc such actions would wreak in networks engineered by humans.

Both this paper and the discovery of the default-mode network (together with other papers in the preceding five or six years) have hammered home how idiosyncratically evolution works and how nothing in evolution is designed or engineered. Biological organisms are evolved and that entails robustness, degeneracy and sub-optimal solutions which are endlessly tinkered with.

Are the -omics approaches that are currently popular in other areas of biology relevant to modern neuroscience? Perhaps not surprisingly, neuroscientists are trying to copy the popular -omics approach with connectomes, neuromes and so forth. Of course, it makes a lot of sense to use the increasing computing power to try and look at everything one could possibly look at and ask questions later. Such big-science, no-risk research projects have rightfully been very popular with funders all over the world, and there can be no doubt that these approaches will transform neuroscience. We can already see the impact neuroscience can have when it joins forces with informatics, evolutionary theory and paleontology/archeology: as a trained neurogeneticist and evolutionary biologist, I find it extremely exciting to experience our growing understanding of how the genes that are the basis for all brain development and function have changed over evolutionary history and make us who we are. The unfolding story of the *FoxP2* gene and language is a great example of the sort of neuroscience that comes from incorporating informatics and evolutionary biology.

Speaking of computers — what do you think about the 'electronic revolution' in publishing? I don't see a revolution coming any time soon, but we may need one if we want to be able to handle further growth of the scientific community. Compared to our increasingly creative use of computers for gathering, storing and analysing data, our use of computers for disseminating those data is lagging behind dramatically. Despite the technological advances, the principles of our publishing system haven't changed much in 400 years. We still write stories which are circulated among our peers via specialized journals. Only the scale has changed: together, the sciences now churn out 2.5 million publications per year and the number of journals has increased to 24,000. Sure, you can get your publication from the web instead of the mailman, but the underlying organization remains largely unchanged, notwithstanding current debates about who should pay the bills.

Scientists today are in desperate need of sophisticated computational assistance in filtering and sorting the deluge of information. The semantic, social and computational technology is already sufficiently developed to provide us with a flexible, trainable service which would be able to very effectively screen out irrelevant information and provide a ranked list of relevant pieces of information (according to the criteria of importance and quality specified by the individual scientist, rather than an editor's idea of what is good enough for their particular journal). What is keeping scientists from this service are political developments which seem to require a revolution: in order to filter and rank effectively, we need full-text access to all the scientific literature (and data) at the time it is made public. Obviously, this would automatically entail the eventual demolition of the current journal rank system and the development of a modern, multi-faceted reputation system in which what is published is again more important than where it is published.

Those are some pretty radical ideas — what about the idea of reducing the number of publications instead? I agree that a reduction in the number of traditional papers would be desirable. But given the annual increase of the global number of scientists of about 3%, I don't see how this should be possible, short of imposing a maximum number of papers per scientist. Instead, I suggest using the power of social networking technology, not only for our search and rank services, but also to disseminate research findings. There are many possible ways of implementing social technology being discussed right now, and I like most of them. The scenarios keep changing with the technology and new initiatives, but right now I favor one in which colleagues in the same research area contribute non-reviewed data and discuss it. The circle of scientists would entail the same individuals who would usually review each other's data anyway and who would know the results of their colleagues either from this review work or from posters and conferences long before they would be officially published. Similar to a wiki, these groups of collaborating labs would post data to a central platform where the contribution of each person, be it an idea, data, analysis or technique, is attributed such that every participant can build a reputation within the group according to their talents and efforts. Once the significance and amount of scientific insights have accumulated enough to be communicated to people outside of the particular field, the contributors to this field would draft a more conventional manuscript for outside peer-review and eventual dissemination beyond the close circle of specialists.

This system differs only on the technical level from the way scientific information is currently transmitted. The principles behind the communication — informal review within the field, formal review outside of the field — remain largely the same. Social technology would greatly facilitate the informal review, reducing the number of 'traditional' papers and providing all collaborators with a fair attribution of their contributions to each field.

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