Of mice and models

Alexander Löwer

Rain or shine, summer is the time for experimental and computational biologists to meet at the Berlin Summer Meeting. Initiated in 2008 by Nikolaus Rajewsky, this annual event is organized by the Berlin Institute for Medical Systems Biology and grew from a quite intimate event of selected scientists to an internationally recognized meeting with more than 250 participants last year. This year, it was time to shake things up a bit. Instead of organizing a traditional conference, Klaus and Nikolaus Rajewsky invited graduate students, postdocs and group leaders from the Max Delbrück Center as well as a number of outstanding scientists from around the world to join them for a three day retreat to Döllnsee in the beautiful Schorfheide north of Berlin.

The idea behind the retreat was to contrast two of the most promising approaches for understanding the complexity of biology: genetic dissection vs. systems biology. For decades, geneticists devised more and more sophisticated methods to modify the genomes of their favorite model organisms and used the resulting changes in phenotypes to deduce the function of the altered gene. However, this can only be done for one gene at a time, and each perturbation induces changes in the very system that is studied. The emerging field of systems biology is taking a different approach by looking at a biological system as a whole and considering all the molecular reactions that take place in a cell as part of an interconnected network. To achieve this, systems biology combines high throughput data, for example the massive information produced in modern sequencing facilities every day, with theoretical analysis and computational modeling.

Named after one of the founders of modern genetics, the MDC is renowned worldwide for its genetic analysis of mice and rats. At present, 35 of the sixty research groups work with rodents to study the causes of human diseases. At the same time, the MDC is a prominent center for systems biology in Europe. There are now four research groups and three technology platforms at the BIMSB, and more will join in the near future. The strong presence of both approaches at the MDC makes it an ideal place for thinking about the future of genetics and systems biology. Can geneticists learn something from systems biologists and visa versa and can we combine both strengths to address the questions of our time?

Maybe this can be best illustrated by a brief example. Micro-RNAs are small pieces of genetic information that do not have the capacity to produce a protein, but nonetheless have strong influence on the fate of a cell. Computer algorithms and high-throughput experiments revealed that each micro-RNA has the potential to target thousands of other molecules. Geneticists can now test how meaningful the regulation of these predicted target genes is. Often they find that only one or two of the predicted targets are relevant for a given effect of a micro-RNA on the organism. Hence, the question remains whether the other targets are relevant as well and if yes, in which context? And why are there so many to begin with?

These and other questions where discussed during the intense scientific program that featured both keynote talks from international guests such as Fabio Piano (New York University), Neal Copeland (MHR Institute Houston) or Steve Cohen (IMCB Singapore) and shorter presentations from MDC group leaders and collaborators. Although the organizers set up different sessions for systems biology and genetics, it soon became obvious that already today there are no clear boundaries between the two approaches. To give a summary of the broad spectrum of science that was presented during the three days is not an easy task, but one could condense it into four questions: What are all the molecular parts needed to make a cell work? How do these parts interact in networks to fulfill their function? How do genes and

molecular networks control the faithful development of a whole organism from a single fertilized egg? And finally, how do complex organism function in health and disease?

But excellent scientific presentations are only one side of a successful retreat. Of similar importance is the time in between, when social interactions and open discussions take place. Thanks to the perfect organization, the sun was shining every day, and during each break, scientists jumped into the lake to cool their heads, took a walk in the woods or just enjoyed the warm rays of the sun on the terrace of the hotel. There was even time for some lessons in archery where everybody could hone their skills in hitting the right target, or for an improvised football match. Football took center stage on the evening of the first day, when the auditorium was crowded for a screening of the semifinal of the European championship between Italy and Germany. The dampened mood of many participants at the end of the game was gently lifted by rounds of Grappa from our Italian friends

At the end of the retreat, everybody agreed that genetics and systems biology will have to move closer together and “marry” in order to address the complex questions still open in biology. Key to this is fostering interdisciplinarity, combining new approaches, techniques and points of view from physics, mathematics and engineering with the experience and knowledge of biologists. There are various ways to promote interdisciplinary thinking and collaboration. While personal interactions between scientists will always play an important role, education is central for laying the groundwork for effective communication and collaboration across disciplines. The MDC is in the unique position of combining strong expertise in classical fields of biology, such as mouse genetics and molecular biology, with a strong and growing initiative in systems biology. This creates the opportunity to train scientist with a broad perspective and a diverse set of skills. Education can also strengthen ties between the different areas of the MDC and bridge physical distances once the BIMSB moved to downtown Berlin.

Science moves in unpredictable ways. Sometimes it is the own son who opens up new perspectives for a well established scientist. For many others, Klaus and Nikolaus Rajewsky’s idea of a joint retreat provided inspiration and the opportunity to look beyond one’s nose and come into contact with scientist from different disciplines.