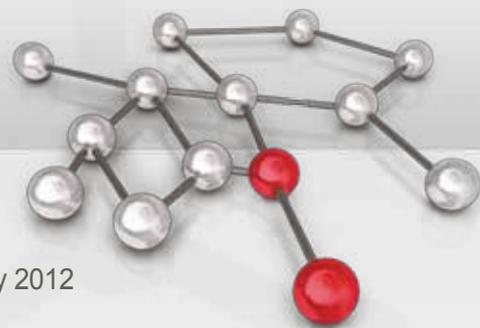


SWISS BIOINFORMATICS

A newsletter published by SIB Swiss Institute of Bioinformatics



Editorial



Swiss quality is renowned and appreciated worldwide. And not only in the field of watches and chocolate. Knowledge, accuracy and expertise are characteristic traits of the field of bioinformatics. We are also major actors on the international scene. And although bioinformatics is not nearly so popular as Switzerland's knives and watches, this discipline is one of the nation's strongest assets for the future: indeed, bioinformatics will provide essential support to face the important challenges our societies are already facing, such as healthcare for an ageing population, food security, energy diversification and environmental protection. In other words, bioinformatics contributes to the general well-being of a population.

This said, the task ahead is considerable. The quantity of data produced today with next generation sequencing is simply daunting and the trend is not showing any signs of dwindling: it has been estimated that by 2020, these new technologies will be capable of producing data one million times faster than the current rate!

If we want to unveil the many secrets all this data will harbour and pave the way to new breakthroughs, both the development of bioinformatics resources and the training of experts able to support researchers will need to keep up with this trend. SIB is already involved in many collaboration projects with the academy and the industry, and will continue not only to develop the resources which help make the difference but also to provide the expertise researchers need to help them find their way through this jungle of data.

Bioinformatics is booming and there is a growing demand for bioinformatics experts to support life science research. This explains why our institute is developing rapidly – since the beginning of this year only, eight new groups have become members. And whatever the size of our task: expertise, accuracy and quality will remain our hallmark.

Ron Appel, Executive Director

● July 2012

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News in brief

SIB welcomes eight new Group Leaders

On 27 June, our Institute welcomed eight new Group Leaders whose nomination was ratified by SIB's Foundation Council:



- Prof. Emmanouil Dermitzakis,
University of Geneva
- Prof. Jeffrey Jensen,
Federal Institute of Technology (EPFL) in Lausanne
- Prof. Petros Koumoutsakos,
Federal Institute of Technology (ETH) in Zurich
- Prof. Igor Pivkin,
Università della Svizzera Italiana, Lugano
- Prof. Mark Robinson,
University of Zurich
- Prof. Jérôme Goudet,
University of Lausanne
- Prof. Vassily Hatzimanikatis,
Federal Institute of Technology (EPFL) in Lausanne
- Dr. Michael Baudis,
University of Zurich

Felix Naef shares the 2012 Leenaards Award for the promotion of scientific research

This year, the Leenaards Foundation is assigning a total sum of 2'250'000 CHF, over a period of three years, to biomedical research carried out by young researchers working within institutions based in the Lake Geneva Region. Professor Felix Naef, SIB group leader of the Computational Systems Biology Lab at EPFL, shares an award of 750'000 CHF with two other groups from the University of Lausanne.

In a collaborative effort to grasp the ins and outs of the circadian clock which underlies our daily (24 hours) biological rhythms, the three groups – led respectively by Felix Naef (EPFL, SIB), David Gatfield (UNIL) and Frédéric Gachon (UNIL) – will combine their expertise in genomics, proteomics and bioinformatics to understand how the biological clock controls liver cell function, and how a defective one brings about a pathological state. Such knowledge is paramount for conceiving novel preventive and therapeutic approaches.

SIB and its Alumni network

SIB is in the process of creating its alumni community. In 14 years of existence, the institute has welcomed many PhD students who then moved on to continue their career in various other organisations. Former SIB members have a rich professional experience they could share with current PhD students and young SIB members. An interactive platform would not only foster such exchanges but also act as a basis for our alumni community to stay in touch and keep informed about the latest SIB news and events. We invite all former SIB members to contact us to join the SIB Alumni network (*contact: irene.perovsek@isb-sib.ch*).

Research

We can learn a lot from other species!

Life Science researchers study genes and their products to understand how the human body works and how diseases progress. This involves comparing many sets of genes to obtain analogies and differences – a mine of information for scientists!

For decades now, researchers have been studying genes using animal model species – such as mice for instance – to understand the roles and functions of their counterparts in humans. This is the basis of what is called the ‘ortholog conjecture’, i.e. the presumption that what we learn from a few species can be applied to many others. This has proved to be a pretty good view. However, due to the lack of available data, no one could really confirm that it was actually the best way to proceed. A study carried out by researchers at SIB and the EMBL-European Bioinformatics Institute – which was published in the open access journal *PLoS Computational Biology* in May – turned this long-held belief into a certainty. Such a study shows how the field of bioinformatics can contribute to testing fundamental principles on which the life sciences are built.

With the ever-growing field of biotechnology, which produces huge quantities of data on a daily basis, the ortholog debate can finally be settled. Using advanced computational techniques on data derived from tens of thousands of scientific articles, the researchers were able to analyse 400’000 pairs of genes from 13 different species. The results were encouraging. “We have the data to prove that studying orthologs is indeed useful, but we are only at the beginning”, says Prof. Marc Robinson-Rechavi of SIB and the University of Lausanne. This is at the heart of comparative genomics, thanks to which we extrapolate knowledge acquired from a handful of organisms and apply it to life as a whole. The team’s work also corroborates the assumption that studying the genes of mice, yeast, or even bacteria can elucidate aspects of human biology.

Link to the article “Resolving the Ortholog Conjecture: Orthologs Tend to Be Weakly, but Significantly, More Similar in Function than Paralogs”: www.ploscompbiol.org/article/info:doi/10.1371/journal.pcbi.1002514

About the ortholog conjecture
To understand the notion of ortholog, consider a wolf’s set of teeth. If we want to know more about our canines, should we refer to those of wolves? Or would it be more informative to look at human molars for instance? The answer is not so straightforward. Geneticists address a similar kind of question: Would we be better off comparing ortholog genes – i.e. matched genes found in mice and humans both of whom share a common ancestor – or to compare paralog genes, i.e. unmatched yet comparable genes which are both expressed in humans?

Statistics expertise for tailored cancer treatment

A study led by Dr Janet Shipley from The Institute of Cancer Research (ICR) in London, in collaboration with Dr Mauro Delorenzi from SIB in Lausanne, has shown that a simple genetic test could help predict the aggressiveness of rhabdomyosarcoma tumours in children. The test, which should be introduced into clinical practice, would lead to changes in treatment for many patients, allowing some children to escape potentially long-term side-effects whilst giving others the intense treatments they need to increase their chances of survival.

Until now, the PAX3/FOXO1 fusion gene only served as a classification agent for tumour histology but never as a prognostic indicator. The research team found that children who have a tumour

called rhabdomyosarcoma with this particular genetic fault have significantly poorer survival rates than other rhabdomyosarcoma patients. This fusion gene can thus be very useful in the prognosis of patient’s survival. Better still, it can provide information on how aggressively the tumour is likely to behave and thus help doctors to tailor treatment for each patient. What is more, used alongside other standard clinical measures, the fusion gene could help divide patients into one of four risk-groups, so that treatment can be fine-tuned accordingly. So far, children diagnosed with rhabdomyosarcoma were treated with a combination of chemotherapy and surgery, and sometimes also radiotherapy. These treatments have helped improve survival rates, but they can also cause serious and long-term side-effects, including the potential to develop another cancer later on in life. Which is why there is so much hope in the fusion gene.

The study required high level statistics expertise.

To analyse the data for thousands of genes from 225 rhabdomyosarcoma samples, Dr Shipley called on the expertise of the Lausanne-based SIB Bioinformatics Core Facility Group which is led by Dr. Mauro Delorenzi. This group provides statistical and analysis support for both national and international academic and private teams. Dr. Edoardo Missiaglia and Dr. Pratyaksha Wirapati performed the analysis of the data and constructed and evaluated systems to score the aggressiveness of the individual case of rhabdomyosarcoma. Their work allowed to identify a panel of 15 genes whose altered activity level could be used to predict how patients respond to treatment.

The results of their study “PAX3/FOXO1 Fusion Gene Status Is the Key Prognostic Molecular Marker in Rhabdomyosarcoma and Significantly Improves Current Risk Stratification” were published in March in the *Journal of Clinical Oncology*.
Link to the article: <http://jco.ascopubs.org/content/30/14/1670>

Internal collaboration

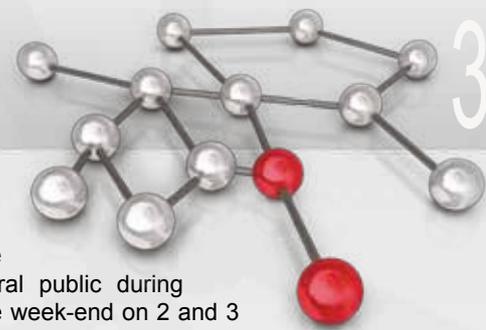
Resourceful members!



On 30 and 31 January this year, 373 SIB members met in Biel during the “SIB Days”. This yearly event brings our members together giving them the opportunity to get to know each other better and to collaborate if possible. Members enjoyed presentations of a few of the Group Leaders’ projects and took part in workshops on themes such as “Ortholog databases”, “Protein annotation”, or “Linking biology to chemistry”. This year, collaboration was more than ever the leitmotiv of the event with the presence of guests from the

European Bioinformatics Institute EBI. Both institutes have been collaborating for many years and are working together towards the construction of the European Life Science Infrastructure for Biological information ELIXIR, as underlined in the keynote talk given by Janet Thornton, Director of EBI.

The SIB Days program always includes a social event, during which our members can explore new ways of developing and demonstrating their creativity and innovation skills. This year,



teams were equipped with rudimentary objects such as bobbins, balloons, thread and rubber bands, and were asked to build small cars that they would race. The activity was organised by *teamworks* and allowed SIB members from our different locations to coordinate their skills and prove their various abilities in a different situation and friendly atmosphere. It was amazing how inventive some of the teams were! What had first looked like a child's game quickly revealed to be a real brain-teaser. And the results were astonishing!

www.team-works.ch/en

Education and outreach

"Les mystères de l'UNIL" – four days of science for schools and families

SIB and the Center for Integrative Genomics (CIG) entertained 300 schoolchildren (13 classes) aged 9 to 13, on the first two days of "Les mystères de l'UNIL", a science fair held on the grounds of the University of Lausanne from 31 May to 1 June 2012. During these two days, children were introduced to the Sanger method of DNA sequencing by using starting blocks and sweeping brush handles. They then led an investigation in which they were to identify two athletes – one Asian, the other non-Asian – using their respective DNA sequence and the sequence alignment tool, BLAST. This allowed the children to discover that the Asian athlete was 'naturally' more muscled than the non-Asian one. The students also had the opportunity to see a few short films on DNA and proteins.



The same activities were presented to the general public during the open house over the week-end on 2 and 3 June. According to the organisers, there were about 600 visitors and the most intrepid were able to visit the sequencing facility and test 'real' bioinformatics tools with the help of a friendly and lively team of scientists.

Some gems:

"Are there really all these letters in our body?"*A little girl*

"Thank you for these great days! Wonderfully educational, enriching and accessible."*A teacher*

Launch of SIB's new virtual exhibition: www.chromosomewalk.ch

In 2008 and amongst a host of other events spread over the year, SIB decided to mark its 10th anniversary by offering an outdoor exhibition – dubbed "Chromosome Walk" – to the layman. The exhibition was presented – for the first time – in Geneva's magnificent botanical gardens, on the lakeside. It was then taken to Lausanne, Neuchâtel and finally Divonne-les-Bains in 2010, just on the other side of the Swiss border in France. By this time, the exhibition had suffered from outdoor conditions and SIB decided that it was less costly to get rid of it.

The exhibition had been hugely successful, however. Many schools had benefited from the guided visits, and families had enjoyed strolling around the panels while learning about DNA, proteins and the world of bioinformatics. A parallel exhibition, equally appreciated, had also been thought up for younger children. Bearing this in mind, it was a shame to lose the contents of an exhibition which had been so popular. So, in 2011, SIB decided to seek for the funds it needed to design a virtual version of the exhibition.

And now, barely a year later, www.chromosomewalk.ch is online. The contents have been updated. The graphic design by Atelier Poisson has not been changed and the new website was designed by talented web designers at Ergopix. The concept remains the same: the exhibition presents the 23 different pairs of human chromosomes and, from chromosome to chromosome, the visitor learns more about genes, proteins and the importance of bioinformatics in research.



Thanks to the nature of the exhibition, the virtual version is far more interactive than the outdoor version and reaches out to many other sources of scientific interest – databanks, videos, bioinformatics tools, online magazines and other popular science sites. What is more, regular updating will be made and novelties will be added. There is also a recreational quiz for young children and a more difficult one for adolescents and, in the near future, both a German and an English version of the exhibition will be available.

The official launch of www.chromosomewalk.ch took place on 7 July during the popular science fair, la Nuit de la Science, held in Geneva.

www.ville-ge.ch/mhs/nuit_science.php

Portrait: Christian Mazza



Christian Mazza, head of the Biomathematics and Computational Biology group in the Department of Mathematics at the University of Fribourg.

Ever since he can remember, Christian Mazza has been involved in solving problems related to biological issues from a statistical and probabilistic point of view. His eyes sparkle when he gets onto the subject of mathematics. "It's a language. Poetic and universal," he says. "Like music". The science of mathematics is able to depict what is happening around us. It can describe the spiral arrangement of a sunflower's florets or imagine the course of a marble on a given trajectory. "That's why we've sent mathematical formulas into space, Mazza continues, because if there is intelligent life up there, it is bound to understand". What is more, mathematics also has the power to predict. A power no other language has.

Thanks to numbers, the mechanics of Nature have been described for centuries. However, applying the theory of probability to the field of biology is recent. In this respect, Mazza has been working on a novel statistical model for food web prediction based on a theory known as the social networks theory. "A food web is a biological network built on the notion of prey and predator, he explains, which can be summed up by 'who eats who'". This may sound simplistic but it is a very difficult task to establish a web of this nature. "So complex a task that only 12 food webs have been defined so far", he notes.

Once a web has been characterised, you can build models that lend an understanding to its underlying dynamics. You can even predict what could happen to the web following, say, the extinction of one of its members or the introduction of a foreign one. Indeed, like all biological networks, a food web is not only complex but also fragile since it depends on an equilibrium that has taken millions of years to establish. Mazza and his team managed to create a model which can predict up to 73% of what is going on! To do this, they used statistical theories based on social networks to which they introduced various parameters – such as body weight, naturally, but also genetic information – as well as what Mazza terms "latent variables". "Such a variable, for example, would be the power of being a predator or the capacity of being prey", he notes. "And when I compare this model with what is actually going on in Nature, it works pretty well"! I ask him why. He smiles. "That, I am unable to answer".

A model like this can be used to understand and predict the dynamics of many networks. "Fish farms use them to know how many fish can be caught without causing irreversible damage to the food chain", says Mazza. "In the USA, such a model was used to identify a certain species of bird that had weakened the network within a reserve, and the bird was subsequently eliminated". Similar models are used to understand the mechanics which drive the spread of diseases – the basis of deciding whether a vaccine should be given or not. Christian Mazza also mentions an intriguing recent development: a model to understand the dynamics of terrorist networks. Obviously, of huge interest in our day and age.

Written by Vivienne Baillie Gerritsen, Science writer

What is bioinformatics?

Over the past 30 years new biological research techniques, along with developments in information technology, have increased both the amount and complexity of biological data. This is why scientists must often apply information technology to biological problems – a science called bioinformatics.

Life scientists use bioinformatics to store, process and analyse large amounts of data, advancing their knowledge and understanding of biological processes. This, in turn, can lead to scientific breakthroughs that enhance our quality of life in fields such as designing better medical treatments or improving crop yields.

About SIB www.isb-sib.ch

The SIB Swiss Institute of Bioinformatics is an academic not-for-profit foundation, recognised of public utility and federating bioinformatics activities throughout Switzerland. Its two-fold mission is to provide world-class core bioinformatics resources to the life science research community at both the national and international levels in key fields such as genomics, proteomics and systems biology, as well as to lead and coordinate the field of bioinformatics in Switzerland.

It has a long-standing tradition of producing state-of-the-art software for the life science research community, as well as carefully-annotated databases. The SIB includes 39 world-class research and service groups that bring together over than 540 researchers in the fields of proteomics, transcriptomics, genomics, systems biology, structural bioinformatics, evolutionary bioinformatics, modelling, imaging, biophysics and population genetics in Basel, Bern, Fribourg, Geneva, Lausanne, Lugano and Zurich. SIB expertise is widely appreciated and its infrastructure and bioinformatics resources are used by life science researchers worldwide.

Institutional members:

Swiss Federal Institute of Technology Lausanne (EPFL)
 Swiss Federal Institute of Technology Zurich (ETHZ)
 University of Basel
 University of Bern
 University of Fribourg
 University of Geneva
 University of Lausanne
 Università della Svizzera italiana
 University of Zurich
 Ludwig Institute for Cancer Research (LICR)
 Friedrich Miescher Institute for Biomedical Research (FMI)
 Geneva Bioinformatics (GeneBio) S.A.
 Hewlett Packard

*A full list of SIB research projects can be found at:
www.isb-sib.ch/research/projects.*



Swiss Institute of
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