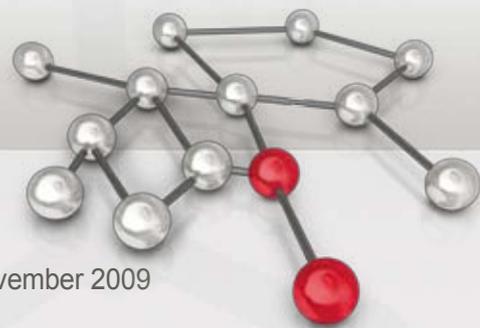


# SWISS BIOINFORMATICS

A newsletter published by SIB Swiss Institute of Bioinformatics



● November 2009

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## Editorial



The SIB Swiss Institute of Bioinformatics is a valuable part of the world life science scene. In the space of little more than a decade, the Institute has made immense contributions to help advance the understanding in the relatively young but increasingly important field of bioinformatics. Bioinformatics is the use of computer science, mathematics, and information theory to model and analyze biological systems, thus contributing to the understanding of life and improving global health.

Contributions of SIB include the UniProtKB/Swiss-Prot protein sequence database, the most widely used protein information resource in the world; SIB research teams have also helped advance knowledge of various diseases, for example breast cancer, diabetes, and Dengue fever, to name just a few.

So when the SIB was approached, following the 2006 H5N1 outbreak, by the GISAID Foundation to create a database to provide researchers with rapid access to influenza sequence data, the Institute did not hesitate to use its expertise once again for the benefit of world health.

The EpiFlu database has been an important achievement. It has brought praise for the SIB from all over the world. One reason for the database's success is the fact that it was the SIB with its world-renowned annotated databases for the life sciences, which provided competencies and substantial resources which contribute to this vital public health analysis and management tool.

The SIB was funded up to 100,000 CHF by the Confederation for the initial stage of development of the EpiFlu database. This allowed the Institute to develop the database extremely rapidly and permitted A/H1N1 data to be shared very quickly last April when the pandemic started. The rest of the funds required to keep the database operational have come out of the SIB's operating budget, as well as external funding secured by SIB.

However, there is a problem. A legal agreement has not been respected and in spite of the most dedicated efforts to keep the partnership with GISAID going, including the SIB offer to not charge GISAID for its work and find its own funding, a time comes when the SIB must step away to avoid further difficulties with this challenging partner. In the now ongoing debate on the lawsuit instituted by the GISAID Foundation, one must say that the SIB has developed this database, remains committed to the vital service, and it continues to be available to the life science community throughout the world, at no charge to users.

This represents the credo of the SIB Swiss Institute of Bioinformatics, which continues to advance the understanding of invisible structures such as proteins and to learn more about their work and function. This leads to insight into central questions of life: How do organisms work? How did life develop? How can new treatments against diseases such as cancer be developed?

At this time, it is important to continue to show our support of this world-recognized Swiss research institute.

*Peter Malama*  
National Councillor, SIB Foundation Council President

## News in brief

### Outstanding achievement – Most cited paper

A paper entitled “SWISS-MODEL and the Swiss-PdbViewer: an environment for comparative protein modelling” written by Nicolas Guex and Manuel Peitsch in 1997, has become the most cited Swiss paper in the world scientific literature for the past 10 years <http://sciencewatch.com/dr/cou/2009/09janALLPAPRS/> (Swiss-PdbViewer is also known as DeepView).

### Roundup of recent SNF grants

#### Infection Biology

The Swiss National Science Foundation (SNF) has recently awarded a research grant to an international research project containing SIB group leader Torsten Schwede (Biozentrum of the University of Basel) and headed by Biozentrum researcher Guy Cornelis. The project focuses on unravelling the atomic structure of the Yersinia injectisome (a needle type structure which helps germs carrying diseases like the plague, typhoid and food poisoning to spread) with the ultimate aim to develop new drugs to treat infections.



T. Schwede

#### Species evolution

The speed and scope of ongoing human-generated climate change are potentially unmatched in earth's history and will affect drastically levels of biodiversity at a global scale. Some of the resulting changes will be irreversible, such as species becoming extinct. To avoid extinction, species can either move to more suitable environments



N. Salamin

and climates, or they can evolve to tolerate new conditions. Two recent projects, funded by the SNF and involving SIB group leader Nicolas Salamin from the University of Lausanne, are looking at developing methods to detect such rapid adaptive evolution events.

**Repeat proteins**

SIB senior research fellow Maria Anisimova from the ETH Zürich, has received an SNF grant to develop new models of substitution to study the evolution of proteins with tandem repeats (this describes a pattern that helps determine an individual's inherited traits) and what influences them. Such proteins are often virulence-related, confer resistance, or are related to infectious and neurodegenerative diseases. Evolutionary trends found in repeat proteins may serve to predict disease outbreaks and epidemics.



M. Anisimova

**Bacteria on leaves study receives ERC grant**

SIB group leader Christian von Mering, Institute of Molecular Biology, University of Zurich, has received a European Research Council ERC Starting Grant for his group to study bacteria in their natural habitats. Initially with collaborators from ETH Zurich, he will focus on bacteria on the surface of leaves. As more than 100 species of bacteria can be present on a single plant, with each bacterium having between 1,000 to 10,000 genes, this work will involve the collection and analysis of huge amounts of data. One hypothesis of the researchers is that plants have an interest in hosting commensal bacteria (a bacterium that exists in symbiotic relationship to its host) as they benefit from having their leaves densely populated, therefore with no place for germs to colonize.



C. Von Mering

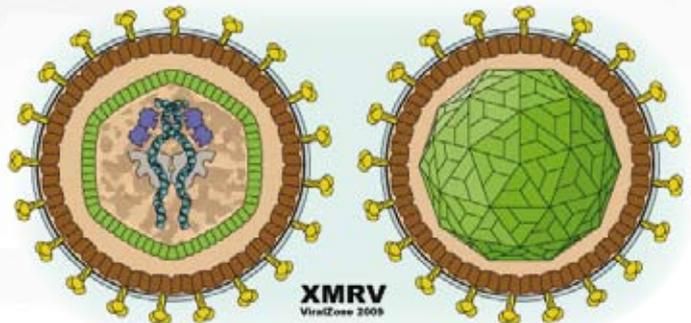


Leaf surface: more than 100 discernible microbial lineages can be found on a single plant. (Picture: Gerd Innerebner/Julia Vorholt, ETH Zurich).

**ViralZone: knowledge resource in the age of virus discovery**

ViralZone (<http://www.expasy.org/viralzone/>) is a web resource providing descriptions of all known viruses, as well as giving an easy access to protein and nucleic acids databases. Our aim is to provide a comprehensive resource linking specific viral information to genomic and proteomic databases.

Viruses are presumably the most abundant biological entities on the planet. Recent environmental studies have shown that there are millions of viruses per ml of seawater, most of them unidentified<sup>1</sup>. New technology has boosted virus discovery compared to the days when viruses had to be isolated on cell culture to be identified. This is the age of virus discovery.

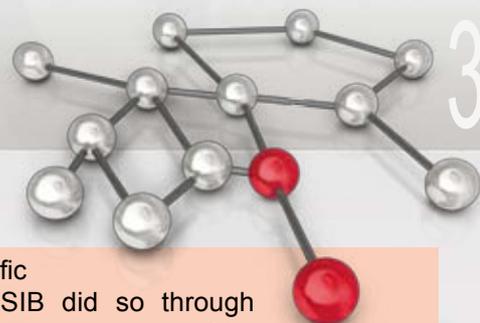


SIB's web resource ViralZone maintains the most recent virus classification, freely available to help researchers follow this ever-increasing knowledge about viruses. About 50 new description pages have been created to integrate the new viruses, raising the total number to 425 pages. New links are also discovered between viruses and diseases in humans.

**This is the age of virus discovery**

For example, Xenotropic MuLV-related virus (XMRV) has recently been reported to be potentially associated with familial and sporadic prostate cancer<sup>2</sup> and with chronic fatigue syndrome (CFS)<sup>3</sup>. As this virus may have great public health importance, the ViralZone Gammaretrovirus page has been updated to link directly to XMRV sequences. Indeed we observed that this page is one of the most consulted by users at the end of October 2009 (Google analytics).

1. PMID: 17853907 - Nat Rev Microbiol. 2007 Oct;5(10):801-12. "Marine viruses--major players in the global ecosystem." Suttle CA.  
2. PMID: 19805305 - Proc Natl Acad Sci U S A. 2009 Sep 22;106(38):16351-6. "XMRV is present in malignant prostatic epithelium and is associated with prostate cancer, especially high-grade tumors." Schlager R, Choe DJ, Brown KR, Thaker HM, Singh IR.  
3. PMID: 19815723 - Science. 2009 Oct 8. "Detection of an Infectious Retrovirus, XMRV, in Blood Cells of Patients with Chronic Fatigue Syndrome." Lombardi VC, Ruscetti FW, Das Gupta J, Pfost MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, Mikovits JA.



## Widening horizons

The SIB PhD Training Network is a PhD program in bioinformatics offering its members summer schools, workshops and courses, to share ideas, meet their peers and expand their academic horizons. This year's highlight was the SIB Summer School "*Robustness, Stochasticity and Determinism of Biological Processes*" held in Lugano in August. The large number of participants not only extended their knowledge in bioinformatics during the lectures, but also benefited from numerous scientific discussions and new academic contacts. The PhD students formed a diverse group from all SIB partner academic institutions and its partner organizations of the Netherlands and Scotland. The organizers thank the speakers and the participants for making the first SIB Summer School such a valuable event and the Swiss National Science Foundation for the financial support.



## Interview with Ron Appel regarding the EpiFlu database

Lausanne, Switzerland, November 2009

Professor Ron Appel, Executive Director of the SIB Swiss Institute of Bioinformatics is interviewed on the subject of the EpiFlu database.

### How did the EpiFlu Database come into being?

RA: Following the 2006 H5N1 outbreak, the Global Initiative on Sharing Avian Influenza Data (GISAID) Foundation called for the creation of a database, to provide researchers with rapid access to the detailed influenza data. In the same year, GISAID approached the SIB Swiss Institute of Bioinformatics, well-known for its world-renowned annotated databases for the life sciences. The SIB developed and maintained the EpiFlu\* Database from its inception in November 2006, providing competencies and substantial resources which contribute to this public health analysis and management tool.

\* The database developed by the SIB, now called OpenFlu <http://openflu.vital-it.ch/>, continues to provide access to the scientific community at no charge to users.

### What is the problem between the SIB and GISAID?

RA: In February 2008 GISAID and SIB formalized their relationship by signing an agreement, under which substantial payments to SIB were agreed for the development and operation of EpiFlu. However, funds owed by GISAID (more than 1 million chf) were never paid to SIB. Despite this, the SIB has always avoided any interruption in access to the database to minimize inconveniences to the global scientific community.

In August 2009, GISAID brought legal proceedings in Switzerland and in the United States seeking to stop SIB from maintaining the database and making it available to

the worldwide scientific community, unless SIB did so through GISAID's web portal. This is in spite of the fact that GISAID had violated its agreement to make substantial payments to SIB to cover the costs of developing and maintaining the EpiFlu/OpenFlu Database. SIB asked the U.S Court to throw out GISAID's lawsuit and the day before the Court was scheduled to hear SIB, GISAID withdrew its case.

We no longer have an agreement with GISAID, though the arbitration in Geneva is still on-going. SIB intends to continue to maintain the OpenFlu Database to the highest scientific standards, without charge, to ensure that the global scientific community continues to have access that it needs to data and the other components of this important public health analysis and management tool.

### So does the database still exist?

RA: Yes, we are still operating the database under the name OpenFlu <http://openflu.vital-it.ch/>. This contains the public data as well as many state-of-the-art analysis tools that we have developed. OpenFlu is being used by many scientists throughout the world.

### What is the SIB looking for in the courts?

RA: While it was GISAID that initiated the legal procedure when SIB was trying to find an amiable solution, SIB expects the continuing arbitration in Geneva to conclude that, while we had at all times maintained the EpiFlu Database for the benefit of the worldwide scientific community, GISAID did not respect its commitment and will have to compensate SIB for its costs and damages.

### What about GISAID's claims?

RA: GISAID's public allegations that SIB closed access to the EpiFlu Database and has somehow "undermined the usefulness of the EpiFlu Database" are completely untrue. The SIB did not close the access to EpiFlu database; however GISAID blocked all new users from accessing the database. Registered users have been able to access and continue to use the database and upload influenza data, thus ensuring that it remained an up-to-date state-of-the-art database.

### Isn't it bad that Switzerland did not keep this important database?

RA: It is certainly regrettable that efforts have been split and those scientists using the other database no longer benefit from SIB's competence and state-of-the-art tools. But we are proud to have created the database that allowed the world influenza community to rapidly access essential A/H1N1 data since the start of the pandemic. Just as the influenza database is important for approximately 1200 users worldwide, the SIB is continually developing other important health-related resources used by hundreds of thousands of users worldwide. One has to realise that we must devote our resources to other key projects rather than collaborate with unreliable partners. And we need

to remember that we developed, maintained and gave access to the database for one-and-a-half years completely free of charge, while negotiating with GISAID to try to find a reasonable solution.

*What about the image of the SIB Swiss Institute of Bioinformatics and Swiss innovation, with this issue?*

RA: Without Switzerland and SIB's competencies the EpiFlu database would have not been developed with the speed and quality with which it was. In particular, without our intervention, the A/H1N1 data would not have been accessible as early as April 2009. The worldwide influenza community would not have had the necessary data and tools to react to the outbreak as it has been able to. Switzerland should therefore be proud to have been instrumental in this.

We continue to offer the OpenFlu database to the scientific community free of charge and there are possible new future applications of the database looking at other viruses.

*How much funding did SIB receive from the Swiss government for the development of the database?*

RA: CHF 100,000 at the beginning that allowed us to immediately start developments at the end of 2006. Further developments were funded through our own means. The benefits obtained by the scientific community have largely exceeded the funds allocated by the Swiss government.

*Why did the Swiss government or the SER not intervene to keep the database in Switzerland?*

RA: GISAID is a private organisation that sub-contracted the SIB to perform work against payment. One of the parties (GISAID) did not fulfil its obligations. I do not believe this is the kind of matter where the government should intervene. Besides, SIB is working on far larger projects that bring benefits to a much larger base of users in the world scientific community, such as UniProtKB/Swiss-Prot, Swiss-Model or the STRING database, which all substantially contribute to life science research and world health. ■

## What is bioinformatics?

Over the past 30 years, new biological research techniques, combined with developments in information technology, have increased both the amount and complexity of biological data. That is why scientists 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 – for example, designing better medical treatments or improving crop yields.

## About SIB [www.isb-sib.ch](http://www.isb-sib.ch)

The SIB Swiss Institute of Bioinformatics is an academic not-for-profit foundation federating bioinformatics activities throughout Switzerland. Its two-fold mission is to provide world-class core bioinformatics resources to the national and international life science research community 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 30 world-class research and service groups, which gather more than 370 researchers, in the fields of proteomics, transcriptomics, genomics, systems biology, structural bioinformatics, evolutionary bioinformatics, modelling, imaging, biophysics, and population genetics in Geneva, Lausanne, Berne, Basel 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 Geneva  
 University of Lausanne  
 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.html](http://www.isb-sib.ch/research/projects.html)*



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