Computer simulation of wing-development of the fruit fly is a main goal of the **«WingX» project**

Prof. Hafen and his team taking a close look at wing development. Photo: msc

Matthias Scholer

When one compares the genome of any two people of the same sex, one discovers something quite remarkable: the genetic difference between the two is miniscule. Only every thousandth letter in the DNA is different. And it is this tiny difference that accounts for the variations within a species? «Yes, it really is amazing how these small deviations in the genetic structure influence our development,» says Ernst Hafen, professor of developmental biology at ETH Zurich. And he attempts a literary comparison; «If we changed every thousandth letter in Tolstoy's War and Peace, it's unlikely that anyone would notice. The same level of change in the genome, though, is at the root of the entire variety of manifestations within a species.» Exactly how this is possible is what systems biologists want to find out.

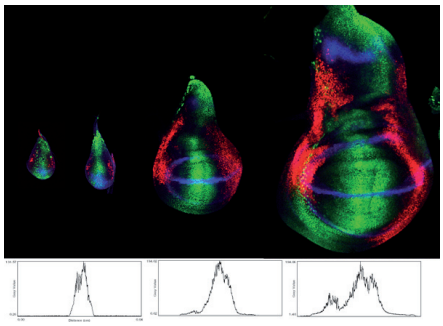
The fly as an ideal organism

Ernst Hafen and his team are investigating which genes drive the development of a living being to its form and size. The wing development of a small fruit fly, drosophila, serves as a model for their research. «We chose this organism because an awful lot is already known about it, thanks to work that has been carried out over the past 100 years. And it functions in a simpler way than a human being. Besides, the drosophila's wing develops as an autonomous body part from clearly defined embryonic cells,» explains Hafen. The embryonic cells can even be stained, which makes it easier to observe each stage of their development. It is known that, from these 20 precursor cells, within the first six days 60'000 cells develop from which the wing is formed within the following four days. But this is the view as seen from the outside. Precisely what is going on in this short space of time within and between the cells is the focus of the project entitled «WingX». «Our aim is to comprehend the single steps in development and quantify them. At the same time we want to create computer programs that can process the collected data that, in the end, will enable us to simulate the wing-growth on the computer,» is Hafen's summary of the ambitious project.

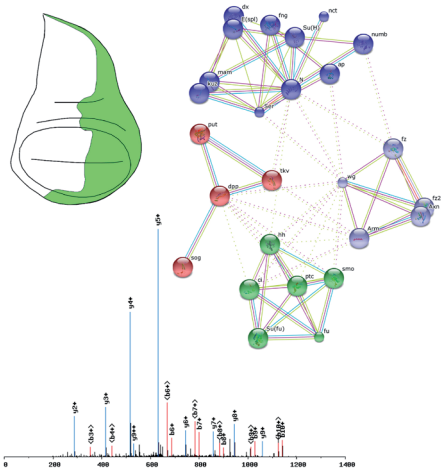
The insects used in the trials are bred at ETH Zurich. Photo: msc

Interdisciplinary team: success factor

A first step aims to measure and record the interaction between genes and their products to determine which gene is expressed in which cell of the wing and how strongly. «Only with these results will we be able to explain why, in the end, identical primary cells develop into a range of differentiated wing cells,» says Hafen. The ensuing flood of data is huge and complex. The development of models to handle this is extremely complicated and requires profound knowledge of physics and math. This is why Hafen fosters interdisciplinarity in his team. «Wherever possible we have two PhD students from different disciplines working together on the same project, for example, a biologist and a physicist. Combining the two is not only promising for the research results but it's important for the training of the young academics,» elucidates the project leader. Because, for Hafen, it's very plain that a biological system can only truly be understood if one looks at it from different perspectives. In project «WingX», moreover, great store is set on an optimal exchange of information between individual groups. «We must foster a new communications' culture among researchers. It makes no sense to remain in an ivory tower concentrating on being the first-named author of a publication. The sharing of knowledge has to be frank and as continuous as possible,» says Hafen. A requirement that the WingX team can meet thanks to an intensive use of ETH's own Wiki-platform.



Morphogen distribution during wing growth. Graphic: E. Brunner

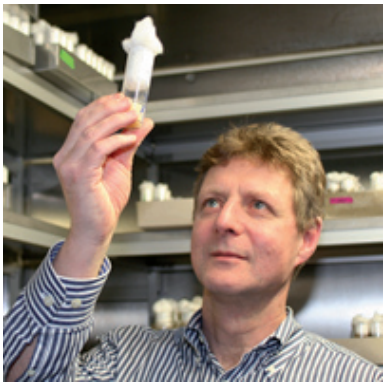


Proteomanalysis of slices of wing enables images of the protein network to be captured. Graphic: E. Brunner

Exciting future prospects

Efforts to create the best possible working atmosphere are bearing fruit. The WingX project is on course. First promising results have emerged and the individual working groups are beginning to coalesce. Yet what benefits can we expect from the project and the knowledge it delivers? Hafen answers, «WingX's main goal is to be able to model the biological system – or, rather, a part of it to start with – of wing development, in order to be able to simulate the process of development, any errors that occur, as well as the consequences of such errors.»

However, this is only the beginning. Once the biological system of a simple model organism is understood, one can transpose this knowledge onto a human organism. Because, «the syntax of the genetic language between flies and human beings is similar. After all, all the important genetic functions – ours and the fly's – were already in existence 600 million years ago, before our evolutionary paths diverged.» It is therefore conceivable that in the foreseeable future system biologists will be able to test a model that shows how an organism reacts to a given pharmaceutical substance or determine the most effective combination of medication for a certain patient. Exciting future prospects that could also awaken the interest of the pharma-industry. Before that, though, a few generations of flies will have to sacrifice their wings to scientific research.



Ernst Hafen - Lord of the Flies. Photo: msc

WingX – Individual groups and their project goals

Proteomics

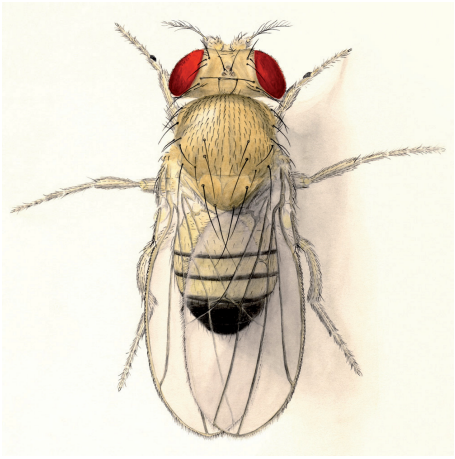
This project aims to identify and measure the proteins that develop during the wing-development process.

Modeling

In this project, existing data is being processed with newly ascertained data to enable a step-by-step simulation of wing development on the computer.

Imaging

This deals with the creation of a method to visualize the entire wing-development process, including gene expression and protein activity.



The fruit fly «Drosophila». Illustration: WingX

Epigenomics

Measurements of which areas of the genome are turned on (or off) during wing development.

In vitro Culture

Developing micro-culture chambers that allow scientists to observe the development of the wing outside the larva. This means that the development can be observed under the microscope, which simplifies the physical, chemical and genetic processes. msc

«WingX – Systems Biology of the Drosophila Wing» at a glance

WingX
Systems Biology
of the Drosophila Wing

Principal Investigator	Prof. Ernst Hafen
Involved research groups	ETH Zurich: R. Aebersold, D. Iber, P. Koumoutsakos, I. Sbalzarini, H. Stocker, B. Wollscheid, R. Paro; University of Zurich: C. Aegerter, C. Lehner, S. Luschnig, C. von Mering, E. Brunner, K. Basler, T. Aegerter; EPF Lausanne: D. Floreano, P. Renaud, H. van Lintel; University of Lausanne: S. Bergmann; University of Basel: M. Affolter.
Number of research groups	14
Researchers : Administration	42 : 0.5
Biologists : Non-biologists	1 : 2
Total budget (2008-2011)	13'816'830, thereof 5'150'000 CHF from SystemsX.ch