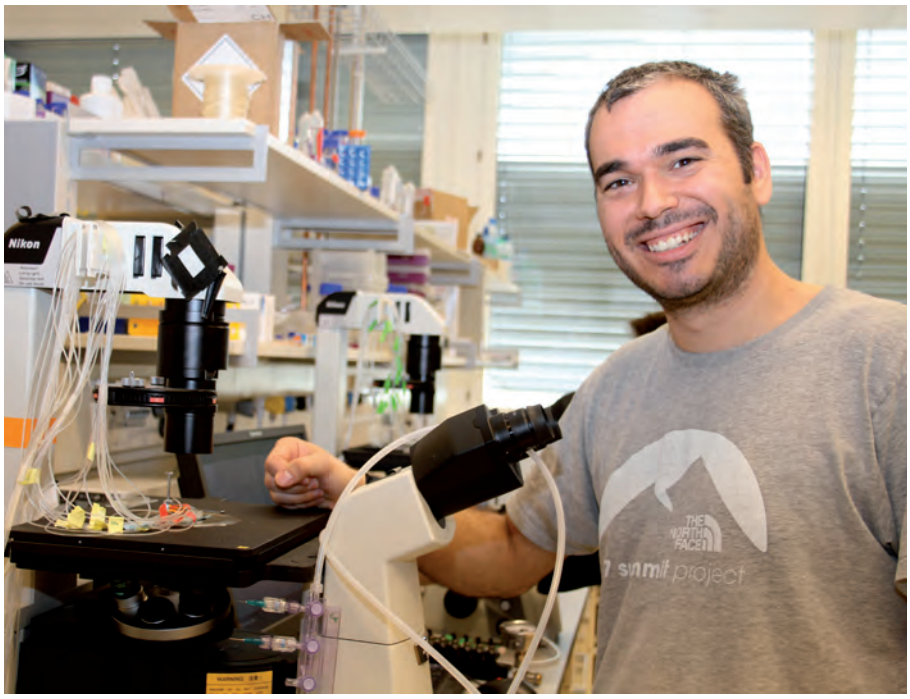
At **«DynamiX»** everything is **in flow thanks to new technologies**



Sebastian Maerkl, head of the RTD-Project «DynamiX». Photo: msc

Matthias Scholer

Something anyone who has ever made bread knows is that you can't do it without yeast. As soon as these micro-organisms come into contact with sugar and water, they are brought to life. They start by dismantling the sugar and proceed to reproduce. At a first glance, a commonplace procedure but one that is only possible thanks to a complex collaboration of various cell factors, especially proteins.

Researchers working on the RTD Project «DynamiX» are concentrating on precisely the genesis and function of these proteins. Head of project Sebastian Maerkl from EPF Lausanne explains why his team decided on yeast as the trial object. «This organism has already been the focus of a great deal of research and we were able to base our work on a large amount of already available data. What's more the number of genes and proteins in yeast is manageable and results can be applied to other organisms, like human cells.»

No research without innovation

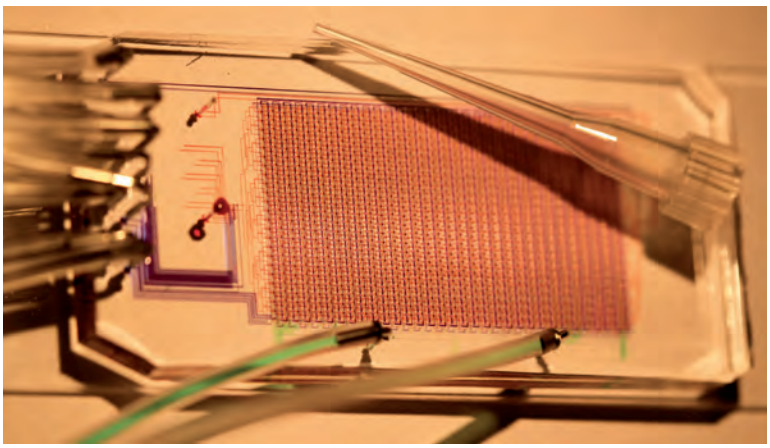
Above all Maerkl and his team are interested in the dynamics of proteins and measuring them quantitatively. «Among other things we'd like to know how much protein is produced in a cell and at what point in time, and when and how these proteins interact among themselves». The knowledge gained from the ensuing data will be used to develop computer models that can simulate the function of an organism. However, there is still a long way to go. «Biology is a science whose progress strongly depends on technological innovations. The ever more complex questions presuppose the proportionate innovation», says the scientist.

However, the DynamiX team is not waiting for appropriate technology to become available – they developed it themselves. «We've succeeded in making a tool that makes it possible for us to do a range of parallel measurements on the cell», says Maerkl.

Hi-tech under the microscope

The hi-tech instrument, known as the «microfluidic device», looks remarkably unspectacular. A little bigger than a postage stamp, it's made of a transparent synthetic material and contains a inner field of geometrically ordered lines. «These linear structures are the core of our development. They enable us to control the flow of a medium», says Maerkl, centering a plate under the microscope. Indeed, only with this magnification does the complexity of the structure become apparent. A host of small chambers stand in rank and file next to, above and below one another. «To start the experiment these chambers are smeared with a layer of yeast cells. The micro-organisms then live in them under controlled conditions». They are provided with constant nutrition by a medium that flows through the chambers.

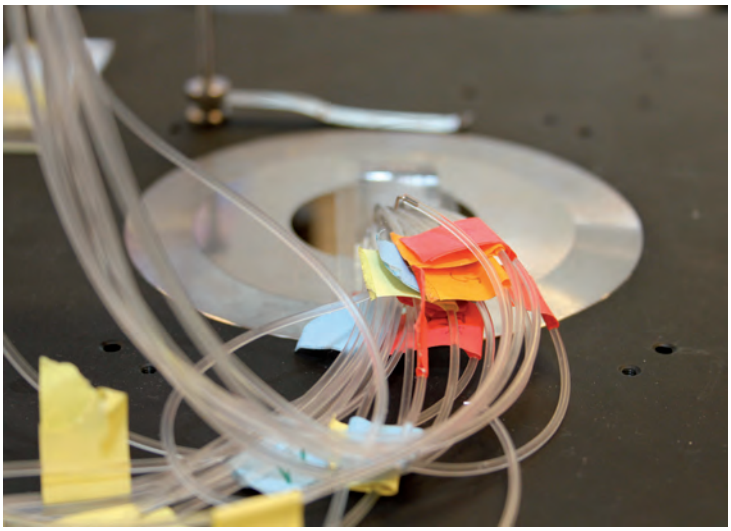
As soon as the cells are fed, their metabolism kicks in and they begin to repro-



The «Microfluidic Device» with its ingenuous chamber arrangement. Photo: Maerkl

duce. They migrate upwards in the chamber and once they reach the edge they are rinsed out by the medium. In this way, a constant population of cells establishes itself in each «incubator».

These conditions allow the team to examine, in detail, the life cycles of each individual yeast cell. «Thanks to the chamber arrangement we can run complex biological experiments in parallel. And rapidly and precisely into the bargain», is how Maerkl sums up the advantages of the method.



Complex experiments thanks to High-Tech Photo: msc

Measuring protein activity

For the main part, the DynamiX team uses the plates in two areas of research: on the one hand, to carry out quantitative measurements of the protein and, on the other, to examine the interactions of the protein among themselves and with the DNA.

In order to obtain the necessary data, the researchers allocate yeast cells that have been loaded with a fluorescent marker to each chamber. This marking allows them to optically follow the development of the protein over a defined period of time. «For the duration of a second we record, on film, each and every chamber. So, in a quarter of an hour we can record the activity in each chamber. We can repeat this procedure any number of times and in the end we have obtained enough film to investigate and measure the dynamics of the proteins», explains Maerkl.

It is not only the protein activity under normal conditions that interests the biologists, however. They also carry out a targeted stressing of the cells. For instance, by adding a stressor agent to the medium, which damages the genetic substance of the trial cells. Interestingly, this activates specific proteins in the cell to repair the damaged DNA. These repair jobs are extraordinarily complex and one stage of the process triggers or initiates the next. «We learn a lot of new facts from such trials about the function of the individual proteins», adds Maerkl.

Looking into the future

But what advantage can be gained in the long run from knowledge about the dynamics of proteins? «Trial arrangements already exist to analyse the reaction of pathogens to the deactivation of specific genes. Subsequently, we can observe whether and how the reaction patterns of the proteins change when antibiotics are added», says Maerkl, referring to a possible interface with human medical research. So perhaps further down the line certain medical diseases and disorders can be treated more efficiently and more effectively thanks to yeast research. Perhaps something to ponder on next time while we're kneading the bread dough.

DynamiX is teamwork

The RTD project «DynamiX» includes five project heads, each with a different area of responsibility:

Davis Shore
- The transcriptional regulation of the ribosomal biogenesis
- The regulation of cell growth

Jacques Rougemont
- Bioinformatics and biostatistics

Michael Unser
- Development of imaging techniques
- Processing biomedical recordings

Felix Naef
- Computer-based modeling of cell-cycle regulation and its temporal sequence

Sebastian Maerkl
- Development of «microfluid techniques»
- Systems Biology

«DynamiX – Yeast Protein Network Dynamics» at a glance

DynamiX
Yeast Protein
Network Dynamics

Principal Investigator	Sebastian Maerkl
Involved research groups	Prof. Sebastian Maerkl, EPF Lausanne; Prof. Michael Unser, EPFL; Prof. Davis Shore, University of Geneva; Prof. Felix Naef, EPFL; Dr. JacquesRougemont, EPFL
Number of research groups	5
Researchers : Administration	12 : 0
Biologists : Non-biologists	7 : 5
Total budget (2008-2011)	4'790'000, thereof 2'296'000 CHF from SystemsX.ch