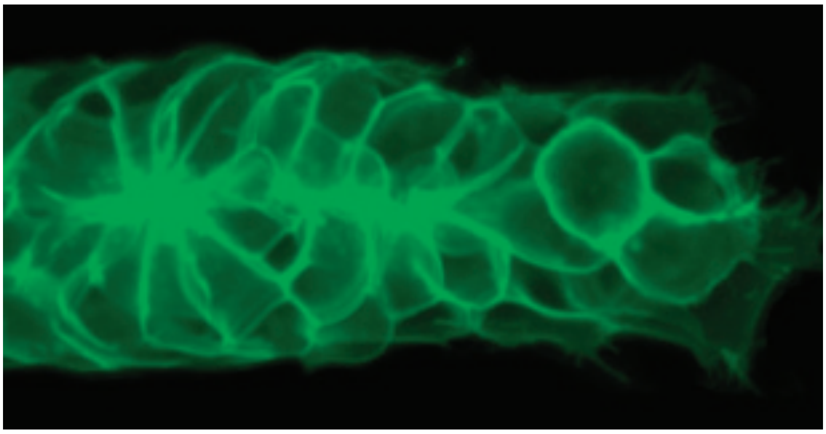
Crack the code – send the signal

BIOSS strikes new paths in synthetic biology…

Biological signals control all life processes within and between cells. And yet, not much is known about the complex rules of biological signal processing and how it is regulated. The Centre for Biological Signalling Studies (BIOSS) at the University of Freiburg provides important impetus to the research on signalling pathways, thereby helping us to learn more about the mystery of life. New ways for understanding the molecular foundations and principles of biological signalling processes are therefore in high demand.



A close up of the leading region of the posterior lateral line primordium of a 36 hour old zebrafish embryo, showing in detail the membrane protrusions in the migrating cells – the picture was taken with a 63X objective on an LSM510 confocal microscope

During embryonic development, the formation of organs often involves the migration of groups of cells. In order to better understand this process, the BIOSS research group, headed by Junior Professor Dr Virginie Lecaudy, uses the zebra fish *Danio rerio* as a model organism to reveal the mechanisms that coordinate collective cell migration, morphogenesis and differentiation during organ formation. Because zebra fish embryos are transparent and precursor cells migrate superficially under the skin, the embryos are ideally suited for live *in vivo* cell imaging.

The team uses the lateral line, which is a sensory system in aquatic vertebrates, as a model system. This system comprises mechanosensory organs called neuromasts, which are organs consisting of mechanosensory hair cells surrounded by support cells. Neuromasts are similar to our auditory sensory organs. The research group's goal is to understand the molecular and cellular mechanisms underlying the formation of these organs. More specifically, Junior Professor Lecaudy aims at determining how the different signalling pathways active in the primordium interact to control and coordinate cell fate acquisition and cell shape changes. She and her team combine molecular and cellular biology, pharmacological analysis and genetics with modern live cell imaging techniques.

From analysis to synthesis

As in the research of Junior Professor Lecaudy's team, biological signal processing can be analysed using creative methods. It can also be reconstructed and regulated. Like BIOSS's motto 'from analysis to synthesis', the goal of the researchers at BIOSS is not only to apply modern analytical procedures, but also to use new synthetic methods in the research of complex life processes.

Biologists and engineering scientists pool their talents to develop and apply new machines and methods for signal analysis. With the help of this analytic-synthetic strategy, biologists, medical scientists, chemists, physicists and engineers work to acquire a deeper understanding of the molecular processes that occur in dynamic signal processing. It is also their objective to permanently establish synthetic biology as a new area of research and field of academic study at the University of Freiburg.

BIOSS receives funding from Germany's Federal Ministry of Education and Research (BMBF) since 2007 as part of the Excellence Initiative. The four BIOSS professorial chairs are currently filled by an equal number of women and men, which is a rare accomplishment for this type of position in German universities. The research programme at BIOSS benefits from the fact that all the key model organisms for signalling studies (such as bacteria, yeast, fish, moss, rice and the human organism) are already being studied intensively in Freiburg. The interdisciplinary and cross-species research programme at BIOSS is founded on this excellent basis.

Thanks to this supportive framework, Professor V Prasad Shastri, Professor of Biofunctional Macromolecular Chemistry at BIOSS and an expert in tissue engineering, has found a way to grow tissue from the body's own cells. He and his colleagues were able to grow large pieces of cartilage in living tissue with the help of a special procedure. By combining agarose with semipermeable membranes, they were able to create regions of low oxygen content. This lack of oxygen initiates and supports the development of cartilage. Cartilage grown in this bioreactor was successfully transplanted into the knee of a rabbit, where it adapted well and did not show any signs of calcification, even after nine months.

BIOSS Toolbox and BIOSS 4D Analyser: innovative scientific platforms

BIOSS not only brings creative ideas to research at the University of Freiburg, it also makes an impact on the university's infrastructure, for example through the BIOSS Incubator and the BIOSS Toolbox. The BIOSS Incubator is a modern laboratory set-up for young researchers funded by BIOSS. The post-doc researchers working in the incubator do not answer to a particular professor and are not responsible for a junior research group. They conduct completely independent research and are provided with their own laboratory equipment and staff.

The BIOSS Toolbox is BIOSS's resource and information centre for plasmids and expression vectors relevant to signalling science. Its aim is to collect, validate, archive and distribute special plasmids that play an important role in different fields of signalling research studies. BIOSS Toolbox provides well-annotated and verified plasmids to signalling scientists and engineers at BIOSS and other non-profit research institutions worldwide.

Biologists and engineers in the BIOSS cluster have developed a unique technological platform: the BIOSS 4D Analyser. This instrument enables scientists to study cellular processes in their natural environment by combining spatially (3D) and temporally (1D) composed images with automatic and intelligent image analysis. The BIOSS 4D Analyser represents a valuable addition to the set of tools used in synthetic biology and in the analysis of signalling processes.

BIOSS created the first professorial chair in Germany for synthetic biology, a position currently held by Professor Dr Wilfried Weber. He and his team have already discovered the possibility to switch off the still dangerous tuberculosis agent's resistance to antibiotics. Professor Weber's latest research focuses on keeping the side effects of medication as low as possible by releasing chemicals from hybrid gels directly into the target tissue. In this way, a signalling molecule can be activated while at the same time protecting the surrounding tissue.

BIOSS's goal is to use these research results and the developed platforms to find new ways of understanding the molecular basis for and principles of biological signal processing. The scientists united in BIOSS can thus make fundamental contributions to biological and medical research and applications.

Interview with BIOSS Scientific Director Professor Dr Michael Reth

What makes working in the field of synthetic biology so special?

Synthetic biologists are both systems engineers and molecular designers. They start with the (admittedly) ad hoc hypothesis that biological molecules behave like parts of a machine and can therefore be functionally defined as such. But they also handle biological material in a playful, creative way. They reconstruct systems from individual biological components we call BioBricks. When these systems begin to operate like a machine, each component can be assigned a function and we can better understand how the molecules involved work together.

What potential dangers do you see in synthetic biology?

From the point of view of an expert, synthetic biology's potential to change or endanger nature has been exaggerated. Although it is a topic that will definitely play an important role in shaping how biology will be used in the future for gaining knowledge, synthetic biology is currently far from being able to create life *de novo*. And I also believe that this is not the primary goal of this science.

Professor Dr Michael Reth

I see synthetic biology rather as an opportunity to better understand life processes in order to preserve the life that is currently endangered on this planet, for example, by developing more ecological methods for the production of medications and for the extraction of resources.

Professor Dr Michael Reth
Scientific Director

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