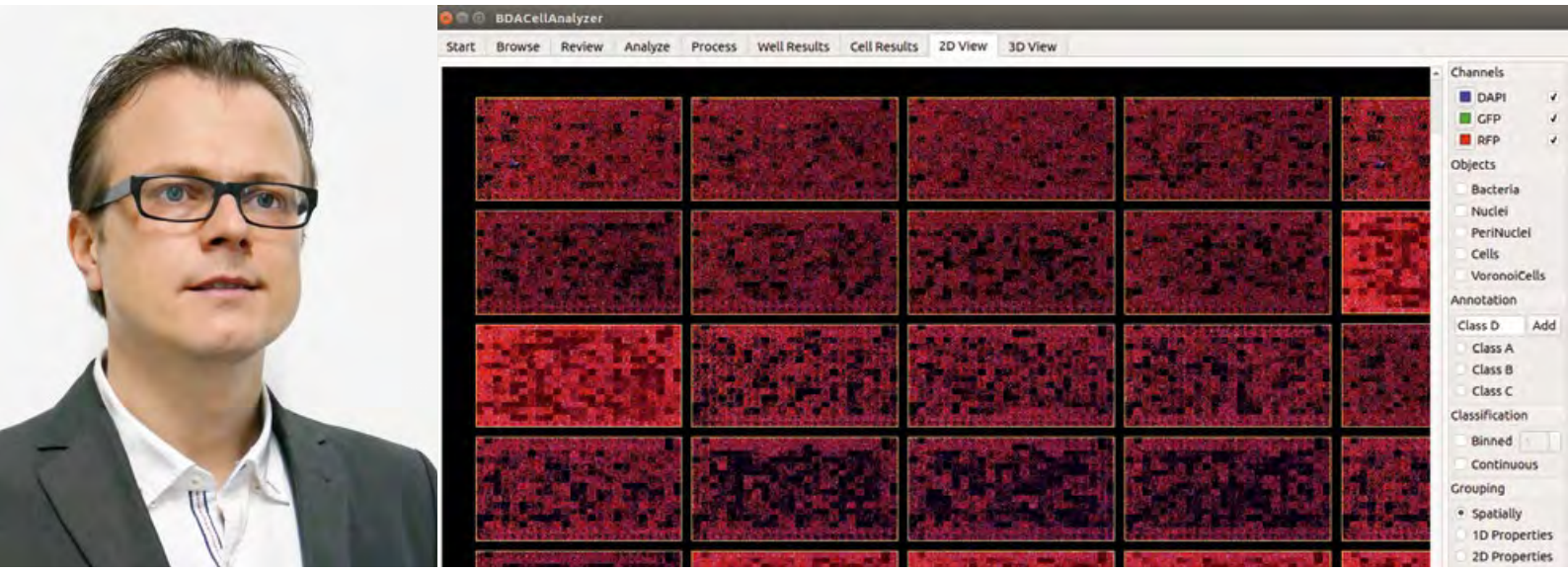
X-Letter 35

10 years of Swiss systems biology

Young entrepreneurs

From research project to startup

More than half of the roughly 2000 researchers working in SystemsX.ch projects were postdocs and PhD students. After deepening their expert knowledge in an interdisciplinary context, a number of these young researchers went on to develop promising startup ideas that now have to survive in the competitive market. Here, we present three of them.



Mario Emmenlauer wants to put the biologist in the driver's seat for image analysis. Photo: © Mario Emmenlauer

Automated image analysis and simplified image processing for biologists – this is Mario Emmenlauer's business idea in a nutshell. With this, the bioinformatician has his finger on the pulse of current biological research. Up until now, working with image analysis software was time consuming and complicated. Big data image analysis required the manual setup of a number of complex tools. Often, the analysis could only be performed with the help of an IT specialist, while the biologist could do no more than assist them from the sidelines.

Emmenlauer has experienced this first-hand. "It starts with setting the measurement parameters, which are based on highly complex algorithms," he says. As a postdoc in the Research, Technology and Development (RTD) Project InfectX, he had the task of finding new ways of analyzing millions of images generated during the project efficiently and reproducibly. "For me it was clear that such a challenge could only be overcome with a solid software solution," says the bioinformatician.

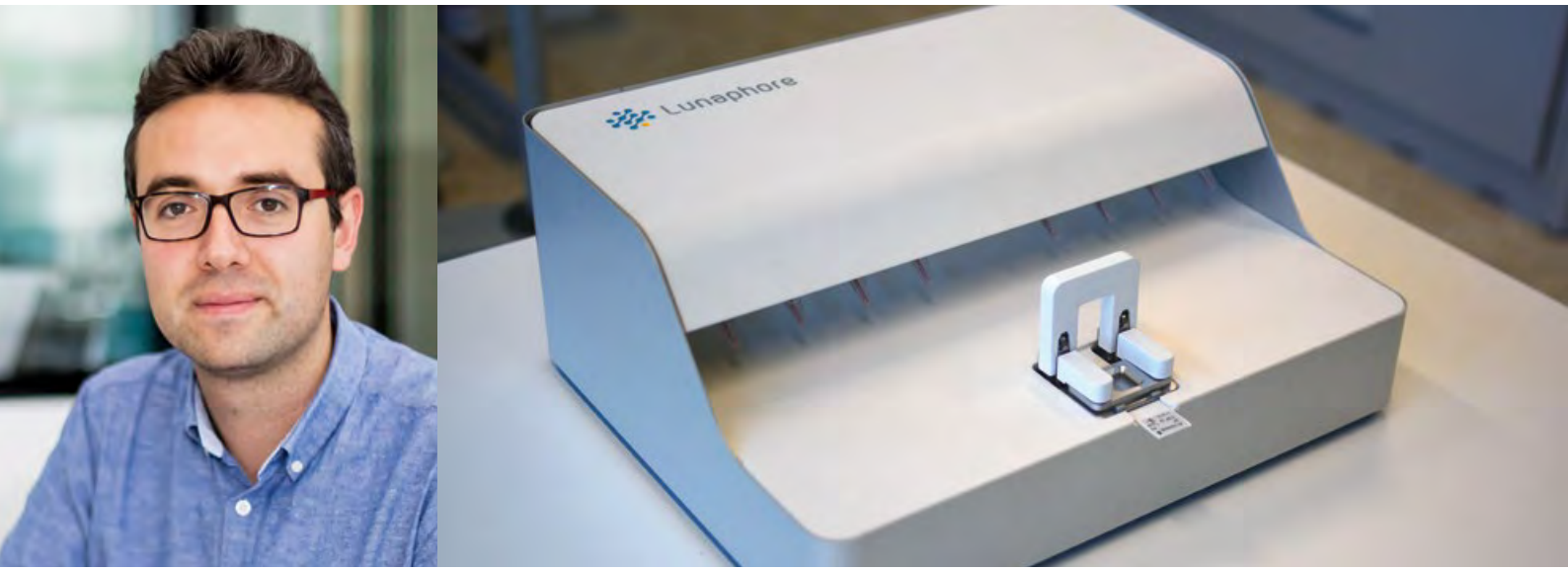
High-level image processing for non-experts

When the RTD Project InfectX came to an end in 2013, Mario Emmenlauer had already made substantial progress towards automating image analysis, and was able to seamlessly integrate his know-how into the follow-up project TargetInfectX. The conclusion of this RTD in early 2017 represented an important crossroads for Emmenlauer's career. He then went on to establish the Munich-based company BioDataAnalysis GmbH in order to make his software more widely available for biological research. Thanks to the BioDataAnalysis CellAnalyzer, biologists will soon be able to process images unaided, without requiring an IT specialist. At the same time, the software will learn how to identify cell structures independently through machine learning. The researcher initially assigns a category to each type of cell structure with a click of the mouse. "Once the software is able to recognize a cell nucleus, it looks through the data and automatically marks all of the cell nuclei it finds," explains Emmenlauer. The results then need to be verified by the researcher just once, and any errors corrected. The program records these corrections and thus avoids making the same erroneous interpretations in subsequent steps, improving accuracy. "With our CellAnalyzer, even non-experts will be able to carry out high-level image processing," remarks Emmenlauer, who is resolutely working towards the goal of his software being used at top universities worldwide within five years. "I am convinced that the BioDataAnalysis CellAnalyzer has the potential to revolutionize image analysis in biology."

BioDataAnalysis GmbH
Intuitive image analysis and data mining

More information can be found at: **www.biodataanalysis.de**

Matthias Scholer



The microfluidic device, developed by Ata Tuna Ciftlik, makes tumor sample diagnostics faster and more accurate. Photo: © Ata Tuna Ciftlik

Eighteen employees with an average age of 30, nine languages, two interns and a diverse range of specialisms mixed with dynamics and passion – this is how the Lunaphore team looks today. The Lausanne-based Lunaphore Technologies SA is undoubtedly the most advanced of all the startups in which SystemsX.ch has played a vital part. The success story started with the funding of Ata Tuna Ciftlik's Interdisciplinary PhD Project (IPhD) through the initiative. "Thanks to my IPhD, I was able to lay the foundations of our business accomplishments," recalls Ciftlik, the company's founder and CEO. During his time at EPF Lausanne, the engineer and mathematician, who had previously never worked in biological research, developed a microfluidic device.

Harnessing microfluidics

The core technology of the device is a microfluidic chip. This is traversed by a number of microcapillaries with a diameter of a thousandth of a millimeter. "There is an inlet on one side of the chip through which the capillaries can be filled with liquid. On the other side is an outlet through which the liquid is sucked out again," explains Ciftlik. In the center there is a chamber, the real core of the device. Here, samples can be examined by means of immunohistochemistry (IHC), a method widely used in medicine and biology for visualizing cellular components. To do this, specific antibodies that bind to the components of interest in the sample material are added to a liquid reagent. With the help of different dyes, the bound antibodies can then be localized and quantified.

The novel aspect of Ciftlik's technology, which goes by the name of Fast Fluidic Exchange Technology, or FFeX for short, is the fast delivery and high flux of the antibodies to the tissue sample relative to other available methods. Additionally, not only does the microsystem allow the tissue sample to be brought into contact with the reagent for a precisely defined time period, but the arrangement of the capillaries also ensures a uniform distribution of the liquid over the entire sample. These are all factors that increase the accuracy of the measured results. Ciftlik summarizes the advantages of the microfluidic device: "fast and precise!"

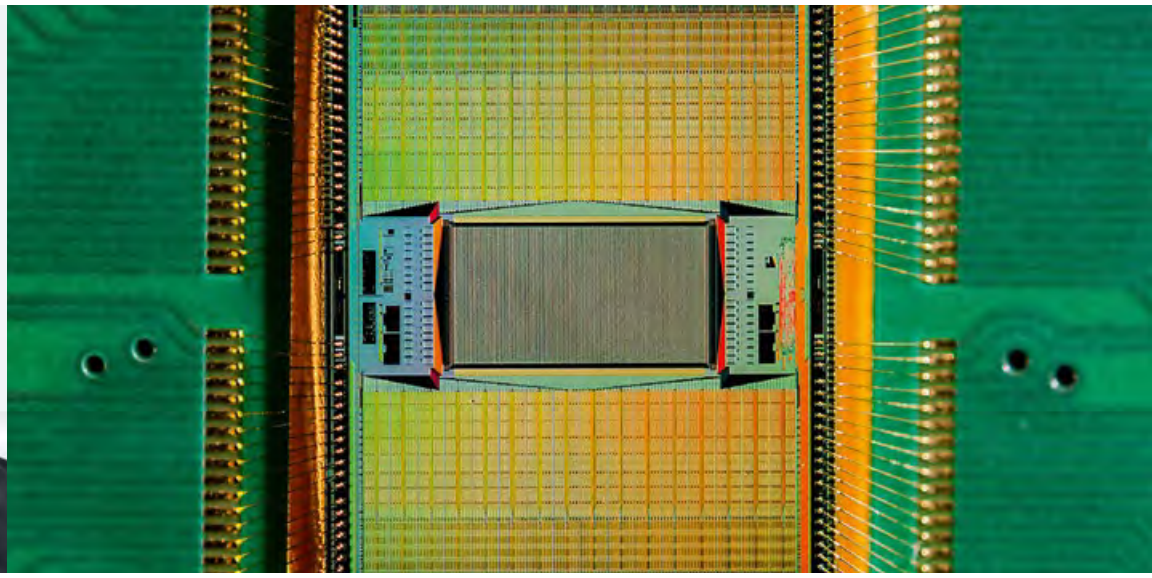
Top-ten finish

Ciftlik and his team envisage that their technology will be mainly used in diagnostic laboratories, where essential information about tissue samples can be passed on to surgeons during time-critical operations to help optimally inform decision-making. "With conventional devices, IHC staining takes several hours. FFeX delivers a result in as little as 12 minutes," emphasizes Ciftlik. Furthermore, the device can also be operated by laboratory personnel without any prior experience with microfluidics – yet another advantage for Lunaphore, which aims to make a name for itself in the diagnosis of breast and lung cancer worldwide. The chances are high that the young entrepreneurs will succeed in their goal. An indication of this is given by the numerous prizes that have been awarded to the company over the past couple of years, not least a top-ten place in the past three years' Top 100 Swiss Startup Awards. In addition, Lunaphore Technologies SA was one of 18 young companies selected to present their business idea to 200 investors and CEOs at the 2017 World Economic Forum's Annual Meeting of the New Champions.

The company is also making progress in its global expansion. Ciftlik and his team have already been able to demonstrate their device at several hospitals and laboratories at home and abroad, where it is being tested by experts. Despite the success, Ciftlik has managed to remain grounded. "Good products need time to grow and constantly develop," he says sagely.

Lunaphore Technologies SA
The power of tissue diagnostics

More information can be found at: **www.lunaphore.ch**



According to Michele Fiscella, the MaxWell technology is an ideal tool for basic research, enabling the long-term monitoring of single-cell activity as well as network dynamics. Photo microchip: Jan Müller et al., Lab Chip, 2015, 15, 2767–2780.

The company MaxWell Biosystems AG was founded in 2016 in Basel. The founding scientists themselves are not the only ones enthusiastic about the enterprise and its business idea. “Last year we received 130,000 Swiss francs from the startup promoter Venture Kick,” says Michele Fiscella with pride. Fiscella is one of the four founders of this startup, which develops microchip platforms. The company currently offers two products, the MaxOne Single-Well and the MaxTwo Multi-Well platforms.

The MaxOne was the first product to be developed, and the main motive behind the establishment of the company. “Two of my business partners, Urs Frey and Jan Müller, developed MaxOne during their PhD studies at ETH Zurich. As part of my SystemsX.ch Interdisciplinary PhD Project (IPhD), I developed methods to make the device compatible with electrophysiological investigations of nerve cells.” At the core of MaxOne is a microchip that measures the functionality of nerve cells. During his IPhD, Michele Fiscella studied the activity of ganglion cells in the mouse retina. “Thanks to the methods I developed, by the end of the project we were able to investigate how different classes of ganglion cells encode a visual stimulus into electrical signals and send them to the brain for further processing,” explains the biotechnologist. With MaxOne, scientists are thus not only able to use the microelectronic platform to measure the function of single neurons, but also for the study of whole neural networks.

Fast and yet exceptionally precise

This is a remarkable achievement in itself, but for Fiscella and his business partners, this was only just the start. Their next step was to apply their technology to the study of human eye disorders. To this end, the team first examined 30 mice which possessed a gene mutation that also occurs in humans. The scientists, however, did not know what effect the specific mutations had on eyesight. They therefore studied the properties of the neurons in the eye tissue of the rodents with MaxOne. They were able to identify a gene mutation that causes comparable vision deficits in mice and humans. “This mouse strain now serves as a model for the investigation of certain eye disorders in humans,” says Fiscella. It took the MaxWell team less than two weeks to determine this. “Using conventional methods, it would have taken several months,” notes the researcher. The MaxWell technology is not only notable for its speed, but also for its high accuracy. This is no wonder, as MaxOne has 26,400 measurement points as compared to its competitors’ 64. “Thanks to its speed and accuracy, MaxOne is the ideal tool for basic research,” says Fiscella.

No time to rest on one’s laurels

But this young startup does not want to stop there. The scientific and pharmaceutical industries are making increasing use of induced pluripotent stem (iPS) cells in their research. These are obtained through the manipulation of human skin or blood cells and are then transformed into different tissues such as neural or heart tissue. These newly manufactured cells can be used in place of animal experiments to test drug safety by measuring the activity of the iPS cells upon exposure to a substance. “This recent development has opened up a completely new market for us,” enthuses Fiscella. In order to stay ahead in this new domain, the MaxWell team developed MaxTwo, a platform which can carry out several electrophysiology measurements in different wells simultaneously. With these innovative products, the team’s interdisciplinary expertise and their pioneering spirit, it seems like we will be hearing even more from MaxWell Biosystems AG in the future.