THE AUTHOR FILE

Uwe Sauer

How to make cells spill their metabolic guts in high-throughput, and why work does not feel like work.

It's a simple pleasure to achieve something in the lab that others have not thought to try, says Uwe Sauer, professor of systems biology at ETH Zurich. In his latest work, he and his colleagues have automated the identification of around 300 cellular metabolites in *Escherichia coli*, yeast and hybridoma cells over an extended time period and at 15-second resolution.

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This automated, high-throughput approach can be used to track changes in the metabolome over time. Unlike traditional metabolomics, the process involves the rather unthinkable task of rapidly injecting entire cells into a mass spectrometer. As they leave the cultivation chamber and enter the instrument bathed in a solvent, the cells die and their innards are released, which makes it possible to measure their metabolites and secreted compounds.

As Sauer explains, his approach helps researchers generate molecular hypotheses from complex data that defy intuitive interpretation. "The great challenge was to make sense of the data and figure actual mechanisms out," he says. That data integration took 80% of the project's time, with discussions that kept sending the team back to the drawing board.

Sauer and his group used the method to characterize metabolic adaptation in *E. coli* that were starved for two hours and then allowed to resume growth in glucose-enriched media. The metabolites that amassed during starvation—amino acids that are costly to make—turned out to be the materials used first for protein synthesis when growth resumed. Saving costly metabolites during famine instead of burning through them to generate energy gives "a kick-start advantage" when conditions permit, he says.

Following metabolic dynamics with more traditional approaches would have taken much sample prep and mass spec measurement time. "It would have been painful to generate all the data manually, and from our data we see that there are long phases when not much happens," says Sauer. His high-throughput metabolomics approach lets researchers fast-scan a metabolic network over an extended period and zoom in on a particular metabolic phase and subnetwork that matter to them, he says.

"The writing is on the wall that metabolomics will and already is pushing metabolic research to another level," he says. Metabolomics needs automation, scale and throughput for research and for the efficient processing of large numbers of clinical samples.

Sauer did the work for his PhD in microbiology at the University of Göttingen. He was headed to a postdoctoral fellowship at the University of California, Berkeley, when an ad for a position at the new institute for biochemistry at ETH caught his eye. "I applied mostly for the fun of it, but after I had seen the place I knew this is where I wanted to be," he says. What ensued has been the rest of his career: a postdoctoral fellowship, a group-leader position and a full professorship, all at ETH.

Beyond the lab, Sauer enjoys being with family, which includes two young adult daughters, and spending time in the gym, biking or skiing. In the past, he explored industrial microbiology and advised several biofuel companies through a firm he founded as a postdoctoral fellow. "I learned so much from these advisory roles about scientific and engineering problems as well as career issues that it was worth the time spent," he says. In some instances he was paid for his advice, but he mainly did it for the fun of it.

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Sauer fosters creativity and out-of-the-box thinking in the researchers he supervises. "I think I could not have envisioned a better mentor," says Matthias Heinemann, a systems biologist at the University of Groningen. Heinemann was doing an ETH postdoctoral fellowship across campus and met Sauer at a conference. They stayed in touch, and Sauer offered Heinemann a junior group-leader position with start-up funding to build his own group within Sauer's research unit. "I could even publish without him," says Heinemann. "I think that was really great."

Heinemann entered Sauer's lab an engineer and mutated into a systems biologist. He enjoyed that Sauer always took time to speak with people in his lab and says discussions with his mentor were rigorous. "What is this good for?" Sauer would always ask. These interactions, says Heinemann, sharpened his thinking and helped him find his way as an independent scientist.

To Sauer, being in the lab does not feel like work. "In fact I am often happy that they pay me a salary for doing what I would probably also do without payment," he says. "If I am proud of anything, it is the lab."

Vivien Marx

Link, H., Fuhrer, T., Gerosa, L., Zamboni, N. & Sauer, U. Real-time metabolome profiling of the metabolic switch between starvation and growth. *Nat. Methods* **12**, 1091–1097 (2015).