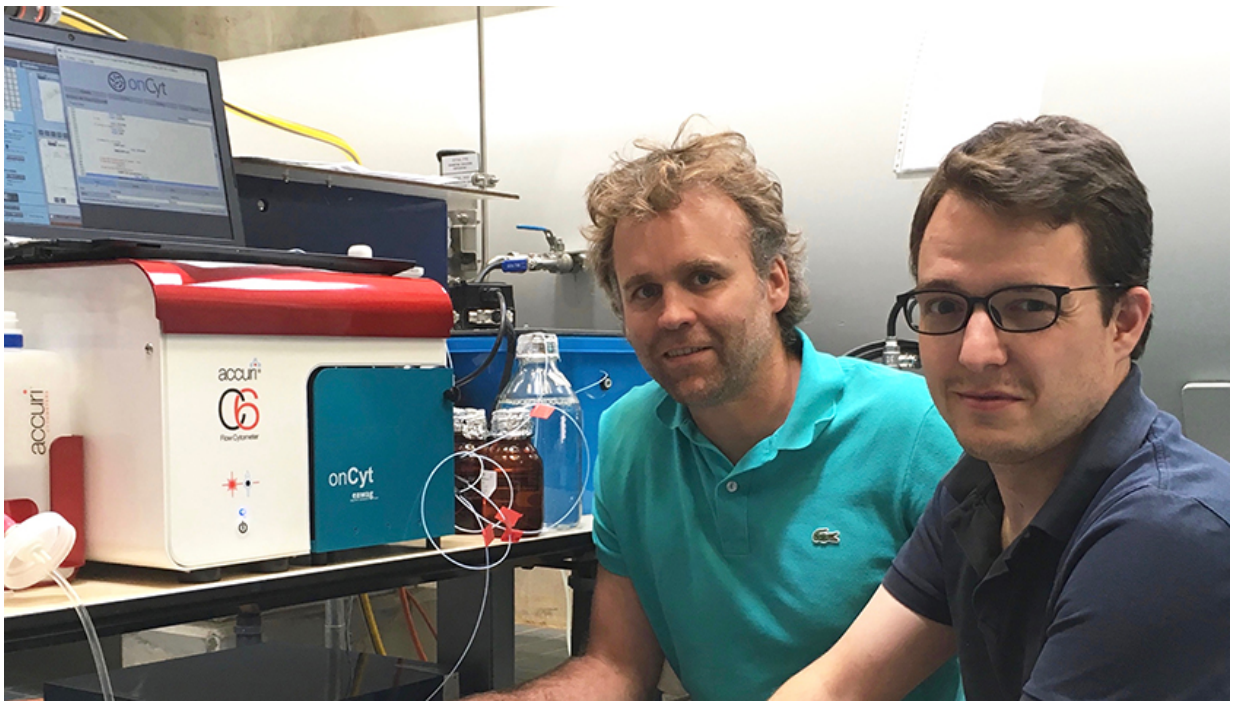

Online flow cytometry: bacterial concentration sensor

June 28, 2017 | Andri Bryner
Topics: Climate Change & Energy | Organisation & Staff | Drinking Water

Flow cytometry has revolutionised the bacteriological assessment of water quality, and with its automation the revolution is progressing even further. Following his successful basic research into this area, a researcher at Eawag has become an entrepreneur.

The bacteriological quality of water is generally still evaluated using a method that is over 100 years old, namely the cultivation of bacteria on plates containing a nutrient medium. Over the past ten years however, flow cytometry (FCM) has become established as a modern method of microbiological measurement – largely due to research undertaken at Eawag. Instead of having to wait 24 hours or more for the bacteria to grow, they can now be stained with fluorescent dyes and precisely counted by means of a laser within just a few minutes.

Automated process from staining through to sterilisation

If a researcher wants to record the microbiological dynamics of a water source over a number of hours or days, the process is still quite labour intensive, even with FCM. Every sample has to be collected from the source and then prepared and measured in the laboratory. The Drinking Water Microbiology research group therefore decided to develop an automated system for FCM measurements with high temporal resolution (Fig. 2.).

Überlandstrasse 133
CH-8600 Dübendorf
T +41 58 765 55 11
F +41 58 765 50 28
info@eawag.ch
www.eawag.ch
eawag aquatic research

Fig. 2: Fully automated online flow cytometry system containing a conventional flow cytometer (red-white) and the automation module developed by Eawag (blue). Photo: Jürg Sigrist

Instead of placing each individual sample into the flow cytometer by hand, a unit coupled to the apparatus now does everything automatically, from sampling to preparation of the sample by staining the DNA/RNA, through to sterilisation of the cytometer. The fully-automated measuring system can now be installed directly in-situ, such as at a water source or a water treatment plant. From there it can transmit temporally high-resolution data sets of the bacterial concentrations over a period of several months. This new method makes available unprecedented amounts of data – tens of thousands of measurements – on microbiological water quality.

Identifying risk periods

Applications for the automated FCM system have been comprehensively tested in both natural and technical systems. Most of the tests were carried out by Michael Besmer in the context of his doctoral thesis at Eawag and the “Basel-Landschaft 21 Regional Water Supply” project. Many of the water supply systems in the Jura Arc source their water from karst springs. Rain and surface water – along with any contamination – can flow very quickly into the groundwater through the fissures and caves that are typical features of karst geology. As a result, maintaining water quality is particularly challenging in such areas. Up to now, reductions in quality have been monitored using measurements of attributes such as conductivity, turbidity, pH etc. so that any contaminated water sources can be isolated rapidly from the water mains network. In the project, karst springs were monitored over several weeks, with measurements being taken fully automatically every 15 minutes. In dry weather, the bacterial concentrations were very low and stable, whereas after rainfall, significant contamination peaks occurred within just a few hours and took several days to abate. These findings assist the relevant water suppliers to better identify periods in which the risks are heightened, and to take targeted measures to safeguard water quality. Besmer sums it up: “We now know where, when and how we have to look more closely”. Some of the processes in natural ecosystems as well as in technical systems such as water treatment can now be understood more clearly and optimised in a more targeted way.

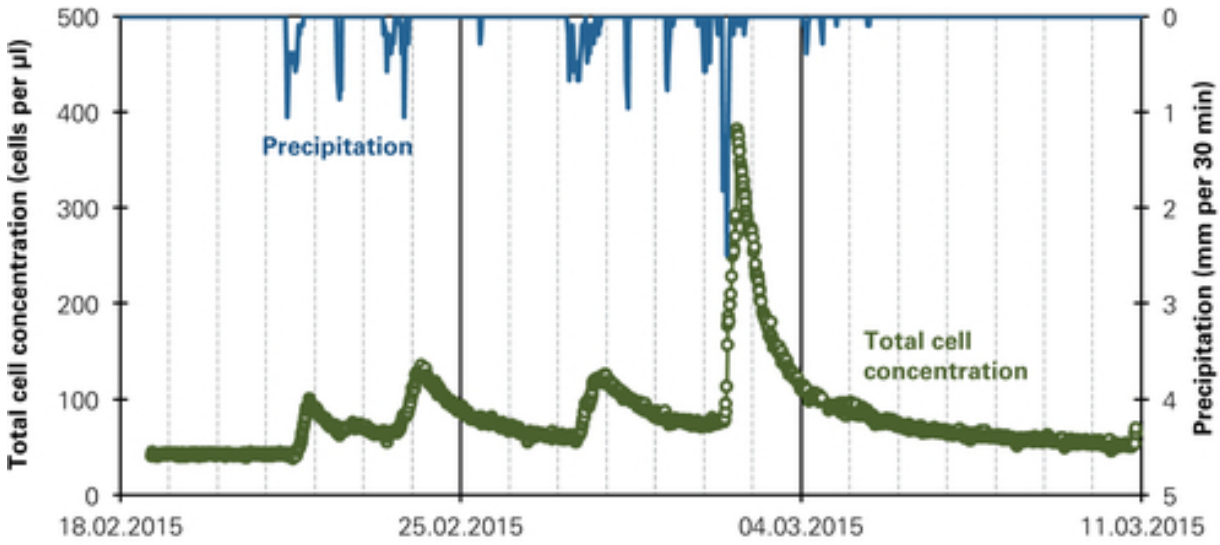

Fig. 3: Continuous online measurement of the total cell concentration (green) in springwater every 15 minutes during 3 weeks; regional precipitation (blue).

From research to industry

Even while he was undertaking his thesis research, Michael Besmer realised that there was a significant amount of interest in the technology from both academia and industry. This knowledge prompted him to establish a spin-off company together with colleagues. The spin-off relies on the newly-developed instruments with two patent registrations, plus knowledge gained on microbiological dynamics. As this is still a young market, many clients value highly the expert knowledge and advice that is provided along with the sale of the instruments. Thanks to wide-ranging and successful collaborations with practitioners in Switzerland, as well as with international research groups and industry partners, Besmer has access to all of these. In terms of technology, Eawag and the spin-off are focusing on the aforementioned automation unit, which can basically be used in conjunction with every flow cytometer generally available on the market. Its advantages lie in the ultra-flexibility that allows it to meet a wide variety of client requirements. Also not to be underestimated, says Besmer, is a high level of credibility anchored in scientific articles in peer-reviewed journals.

Real-time bacterial sensors soon to be a reality?

Group Leader Frederik Hammes, who supervised Besmer's dissertation, has confidence in the potential of online FCM. He is particularly excited about the newly developed product's rapid transfer to practical application in the Basel-Landschaft project. The additional funds granted by the Eawag directorate to purchase new equipment have thus more than proved their worth. While Besmer is concentrating on further developing the instrument in his new company, "onCyt", Hammes is forging ahead with plans for other applications for the technology in fundamental and applied research. One version that is already a reality is one with an even higher temporal resolution, whereby the online flow cytometer also acts simultaneously as a bacteria sensor. If, for example, the apparatus were mounted on a boat, it would be possible to sail along the coastline and monitor continuously to ascertain where the

bacterial concentrations in the water are changing – for example due to effluent.

Microbiological dynamics become visible
Thanks to automated flow cytometry, microbiological dynamics can now be tracked promptly and in detail. To give one example: the total cell counts in a running tap in a large building were measured at 15-minute intervals, which allowed a typical 24 hours to be documented, with increased bacterial concentrations seen during the night, and a sudden drop in the morning, once water was being used again in other parts of the building. In a stream, the automated FCM revealed a diurnal cycle that was determined by photosynthesis, as well as a rise in cell counts after rainfall. It was also exciting to see the technology being deployed in a larger-scale drinking water plant, where evidence of microbiological patterns following the water treatment process and the filling of the reservoirs will now enable the operators to optimise their processes.

Interview

Going it alone doesn't work

Interview with Michael Besmer, CEO of onCyt Microbiology AG

Why did you decide to set up a company?
It wasn't my lifelong dream to become an entrepreneur, but I was fortunate to be able to base my doctoral thesis around the very practically-oriented "Basel-Landschaft 21 Regional Water Supply" project. The spin-off offered a huge opportunity to continue this exciting work and to remain in this particular field. I am very confident of the potential that our method holds, both from a substantive as well as a business perspective. For example, by deploying automated flow cytometry in the water supply sector, we are doing something worthwhile, which is important to me in my work.

Are the tills already ringing?
We started in March. I haven't actually paid myself any salary yet, just to safeguard the liquidity of the new company. But the first orders are beginning to come in now, and I will at least be able to earn what I did when I was working on my thesis. We are already planning to take someone else on, and by the end of the year at the latest, I should be earning a post-doc-level salary. The support given to us by Eawag is invaluable, of course. A well-equipped laboratory and the use of expensive equipment would barely be affordable for a start-up company otherwise.

And now? Are you waiting for the best take-over bid, or are you afraid that someone else will copy your idea?
No, certainly not, but we are of course looking for partnerships, and we're keeping an open mind. But anyway, we will only be an attractive takeover proposition if we are doing our work well. In spite of having registered patents, our technology can nevertheless be imitated. However, we see our strengths as being our all-round competence. This will allow us to offer a very different service to our clients, and to advise them on where the use of our equipment can create real added value. That is clearly much more difficult to copy. Apart from that, we are also working on further developments and new ideas that we want to implement as quickly as possible – not least thanks to our close connection to research.

Have there been any crises on the road to developing the company?
Last year I worked extremely hard, and very long hours. At the same time as finishing my thesis and the extensive project report, I was also working on the formalities and preparations for the spin-off. For six months over the summer I was working seven days a week, and family and friends were very much neglected. But the results have been very rewarding from a research point of view as well as on the business side. These successes have only been possible with the fantastic support from mentors and colleagues, and indeed from Eawag as an institution, as well as from my family and friends.

What advice do you have for other researchers with a start-up idea?
Find partners who will help you as well as act as critical sparring partners. Going it alone doesn't work, which will already be very clear to anyone involved in research, actually. In contrast to research though, a good technological idea doesn't necessarily always make it in the market. That is why support from organizations such as the KTI Start-up Coaching are so helpful. To avoid nasty surprises, the potential can and should be well explored beforehand. Admittedly, there comes a point when you have to make that leap of faith – when first setting up, as well as repeatedly thereafter. I think, also, that one shouldn't work for nothing or for rock-bottom wages for an extended period of time. If the company is not generating a reasonable salary, then it won't last long anyway.

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Article in Aqua&Gas 7/2016: Online-Durchflusszytometrie in der Praxis (Online Flow Cytometry in Practice) [pdf, 633 KB]

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On the finalisation of the project “Basel-Landschaft 21 Regional Water Supply”

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Dr. Michael Besmer
PhD Candidate
Tel. +41 44 552 38 80
Send Mail

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