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# The high-tech secret behind the traditional cheese Swissness.

## Securecell's Bioprocess Automation Platforms for efficient media development and biomass production control.

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### Swiss cheese

Cheese is Switzerland's most important agricultural-export product: around 170'000 tons of cheese are produced per year (40% of the total Swiss milk amount) with a value of around CHF 600 million.

Agroscope, a federal research institute in Liebefeld, near Bern, Switzerland, produces microbes that are necessary to manufacture and preserve the great diversity and uniqueness of Swiss cheese and make it as tasty as it is. Those microbes are used in Swiss dairy production to shape the character and the texture of the cheese and make it durable. Over 12'000 different microbial strains of 350 different species are collected and produced since the early 20th century at Agroscope. Over 90'000 liquid bacterial culture samples, in addition to 115'000 freeze-dried cultures, that can be kept for up to 2 years, are sold annually. The cultures are then propagated by the Swiss dairy manufacturers to produce Swiss quality cheese, and fermented milk products.

We had the opportunity to talk to Dr. von Ah, Head of Biotechnology Research Group at Agroscope, on how the bacterial cultures' production is supported and facilitated by Securecell's technological platforms, Numera® PAT and Lucullus® PIMS. He first got in touch with Lucullus® PIMS in 2002 during his PhD thesis at ETH; then, he followed the development of Lucullus® and Numera® in the years, applying the use of the platforms to his various projects.

Dr. von Ah supervises the federal research station for dairy technology to implement Swiss dairy including cheese production; His team ensures the production, safety, and efficiency of the starter cultures used by the Swiss cheese manufacturers. Agroscope's starter cultures are used to produce AOP cheeses such as Gruyère, Valais Raclette, Emmentaler AOP, Tête de Moine, Appenzeller and Vacherin Fribourgeois. AOP stands for "Appellation d'Origine Protégée" ("Protected Designation of Origin" (PDO) in English). This designation means that the milk from which the cheese is produced, and the location of production and maturation are the same. Only 12 different Swiss cheeses (Fig. 1) are under this designation and they are keeping alive the great passion and quality from the region in which they are produced.

Figure 1: Example of Swiss cheese produced using Agroscope's starter cultures.

## Microbial cultures production

At Agroscope, microbial cultures are produced to be used by the Swiss cheese manufacturers. For this purpose, Dr. von Ah applies Securecell's Lucullus® to increase the cultures' production performance and control the fermentation processes. In fact, operations, process control, data collection, and analysis are planned and executed automatically by Lucullus®.

**Lucullus®** is a **Process Information Management System (PIMS)** that aligns and stores all data from disparate sources of the entire bioprocess environment in one place (Fig.2). The harmonization of the different devices and data is made easy by integrated workflows and a high degree of automation. All information is centrally managed, easily accessible, and ready to be directly applied. The software provides comprehensive monitoring and control, from the initial raw material to the final product: from planning, preparation, execution to evaluation.

Production of the Agroscope's cultures starts using 6 different 0.5 l bioreactors. There, fermentation is manually initiated and successively automatically managed and controlled by Lucullus®. After the development phase into 0.5 l bioreactors, the production is automatically upscaled into 5 l bioreactors. The 5 l bioreactors are fully integrated with Lucullus®.

After fermentation and separation of the biomass in 5 l bioreactors, cryo-protective media is added to be valuated for yield and activity of the strains after freeze-drying.

During the fermentation process, sugars and acids are the main metabolites that must be taken into consideration. Sugars strongly influence the biomass production: Agroscope's goal. Sugars and acids are strong indicators of biomass production. It will be possible to plan and control the fermentation time and advancement by measuring those two parameters. For example, when glucose and lactose are completely consumed, the process could automatically stop. This automatic process control can be implemented with the help of Numera®.

**Numera®** is Securecell's automated PAT sample and sampling management system. It allows automatic sampling at set time points. At Agroscope, Numera® automatically performs sampling every 2 hours from 4 different 5 l bioreactors. Numera® helps the Agroscope team to not have to manually prepare and collect samples from the different bioreactors, real-time control the media recipe, adjust the concentration of sugars, and have better biomass production.

**"All the processed data are transferred to the central hub automatically without any issue. All information is centrally managed, easily accessible, and ready to be directly applied."**

Dr. von Ah

## Media preparation

The media recipes for liquid and freeze-dried cultures media development and management are developed and controlled using **Lucullus® media tool**. The media tool offers a raw material and media database, a recipe library, sample information, and barcode support to keep track of all the samples. Moreover, it offers a complete media traceability: it is possible to track every ingredient of the recipes and have complete control over the process development of every batch of produced media. All the parameters are included and tracked in the media tool and can be shared with different groups on-site and off-site.

**"Lucullus® is a really powerful tool, it has incredibly advanced features and tools. Lucullus® implements the traceability: I can identify all the steps from the freeze-drying batch to the conserve from which I have started the process."** Dr. von Ah

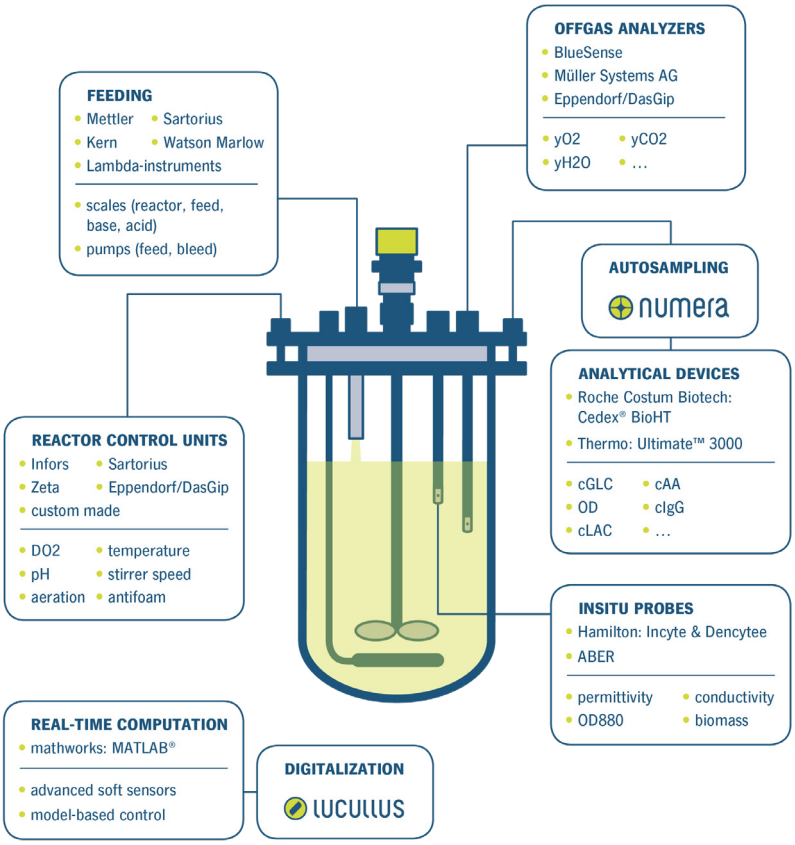


Figure 2: Example of devices and interfaces of a bioprocess development set-up integrated into Lucullus®


Figure 3: Lucullus® samples management advanced fuctionalities

## The entry of offline data into the staging area

Cell culture data are automatically imported into Lucullus® and displayed to be analyzed on-line, off-line, and even from remote. There is no accurate soft sensor that can be used to measure the biomass produced at Agroscope; this process requires off-line measurements that are successively automatically imported into Lucullus® PIMS to be automatically processed.

## Expansion plans

In 2024, Agroscope will move to Posieux (FR), Switzerland. There, the research institute will implement the production with new bioreactors that will be connected to Securecell's technological platforms, Numera®, and Lucullus®.

**"After moving to Posieux, we will for sure keep using Lucullus® and Numera®, even more extensively. Since we started using microtiter plates for the screenings and pipetting robots, we will probably extend the control of Lucullus® to those systems."** Dr. Von Ah

## Lucullus® PIMS and Numera® PAT

Lucullus® acts as a central data hub communicating with a vast range of devices to design and automate your experiments with ease. All data, including those from sample analytics and media preparation, can be automatically aligned. This way, Lucullus forms a central interface to monitor and control all aspects of your bioprocesses efficiently (Fig.4). The ever-increasing amount of data generated by high-throughput parallel bioprocessing and a growing range of novel sensors is neatly brought together with tracked and guided user activities as well as context information. Lucullus® covers the whole process workflow from the design of experiments, setup and media preparation, sample analytics, process execution and, built on that, efficient evaluation, and batch reporting.

Numera® is Securecell's automated sample-based PAT solution, it addresses the shortcomings of manual and partly automated bioprocess development approaches. Numera® allows automated high-frequency sampling at the lowest volume possible. It allows conducting a faster, safer, and easier drawing and processing of samples and real-time monitoring ensuring data integrity through automation and digitalization. Numera® in combination with Lucullus® and its centralized data management capabilities allows us to automate the workflow, to have real-time analytical results, and to always access and control the bioprocess, even from remote sites (Fig.5).

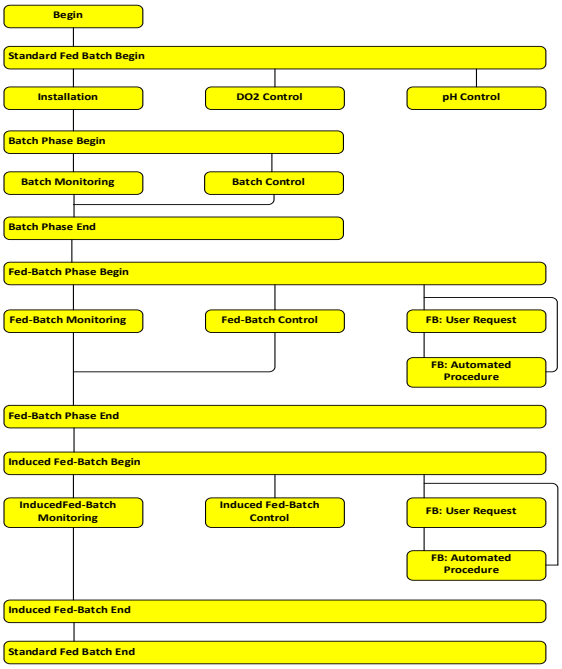


Figure 4: Step chain for a whole bioprocess including initialization, process overarching DO2 & pH control and the three process phases: batch, fed-batch and induced fed-batch. All monitoring, control and handmade actions are coordinated, controlled and documented by Lucullus® PIMS.

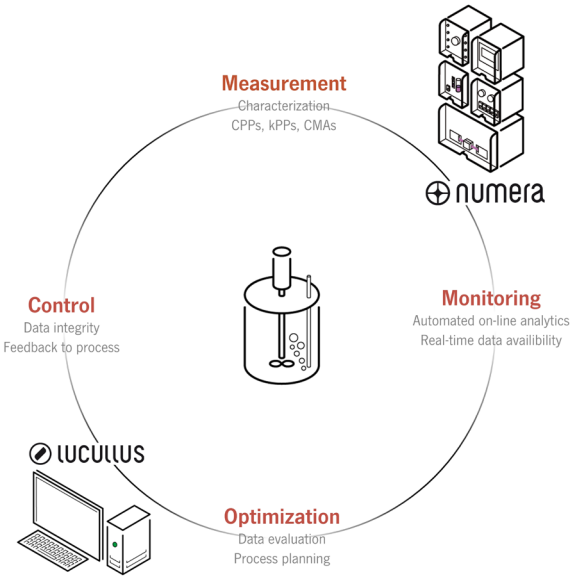


Figure 5: Science-based process design can be achieved by following the presented loop. Within the loop, the process must be characterized for critical process parameters, key process parameters and critical material attributes; and be monitored, optimized and controlled.

CONTACT

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