

BIOANALYTICS

AutoMATically Well Sampled

BaychroMAT combines sterile sampling with operationally excellent analytics. This special technology offers online process analysis for biotechnology applications. With the new BaychroMAT Lab there is now a version specifically designed for development projects.

People who move from one job to another can often offer a very unique perspective to new challenges. One case in point is Dr. Martin Gerlach. For many years, the German chemist worked on analysis systems for medical diagnostics in the Bayer Group. When he then changed to Process Analyzer Technology (PAT), one thing attracted his attention almost immediately: “There were plenty of online analysis systems for classical chemical production, but only a few for biotechnological processes.” It could not have been for a lack of appropriate instruments. From his previous work, Gerlach knew of many systems capable of recording the relevant biochemical parameters.

Gerlach could not get this incongruity out of his mind. When he transferred to PAT Sales in 2004, he asked his customers whether they might be interested in an online process analysis system for biotechnological applications. They were. The U.S. Food and Drug Administration (FDA) had only just started an initiative to encourage producers of biopharmaceuticals to rely more and more on process analysis technologies.

This discovery gave new significance to the BaychroMAT process analysis platform already introduced in the 1980s. Until then, this system for online process analysis was primarily used in polymer synthesis, where it combined automated sampling with chromatographic determination of the degree of polymerization. The subsequent feeding of analysis results into process monitoring also takes place automatically. So, experts at PAT asked the question, why not use this same approach of automatic sampling with subsequent analysis and linkage to process engineering in the booming biotechnology sector? Working in collaboration with colleagues from Processing Technology and Biotechnology Process Engineering, they designed an applicable system.

The key part is a sampling valve, developed and patented by Bayer Technology Services, which can be directly flange-mounted onto a fermenter. The crucial feature here is that before the valve opens for sampling, its interior is sterilized for 20 minutes with steam heated to 121° Celsius. While it cools down, it is also scoured with sterilized air. The actual sampling only takes place after this sterilization procedure. “Depending on the customer’s specifications, very different systems can be integrated into the platform for subsequent analytics – ranging from cell counting and chromatography to classical medium determination or determining the metabolic parameters of glucose or lactate,” says Dr. Stefan Steigmiller, who is responsible for the development of BaychroMAT at PAT.

The resulting system for biotechnology applications has been available since 2008. Companies that produce, for example, therapeutic antibodies, insulin, vaccines or other protein substances in fermenters can now monitor important production parameters fully automatically. Customers typically use the BaychroMAT system in combination with devices to assess cell concentration or to measure sub-

Growing Importance

The number of “biologicals” is constantly growing. More and more new therapeutic approaches are based on active ingredients stemming from living organisms or modeled on such substances. As their production is complex and thus expensive, producers are very enthusiastic about every possible process improvement.



“By taking measurements as frequently as you want, you can learn a lot about the process.”

Professor Frank Gudermann, Technical University Bielefeld

Someone who wants to check the state of cells in a fermenter (here mice cells), can combine sampling and analytics with the BaychromAT system.

you want, you can also learn a lot more about the process and intervene far more selectively.” In addition, his students use the data collected for computer modeling. For Bayer expert Steigmiller this amount of data offers “the possibility to gain ideas for process improvements and, consequently, for higher yields”. Many customers would also like to use BaychromAT to ensure reliable glucose controls.

The handy BaychromAT Lab system was introduced this year

for development work. “With this new version, product development can also make use of automated process analysis,” says Steigmiller. For example, it can help determine the suitable conditions and the optimal medium for the subsequent production of a new antibody. As Steigmiller says, BaychromAT thus offers support for all phases from lab development and the first pilot plant right up to the actual production fermenter. The system is equally suitable for stainless steel, glass and disposable fermenters. And Dr. Martin Gerlach, who is now Head of PAT, is particularly pleased that such a successful product has developed from his insistence on following up on an initial idea.

stances that permit conclusions regarding the actual metabolism of the cells.

For Steigmiller, the advantages for customers are self evident: “Until now, the samples had to be taken by hand, carried to the laboratory and analyzed there, whereas now BaychromAT does all these tasks automatically.” And it is more precise and more sterile. This method also frees up lab personnel to perform other tasks. Professor Frank Gudermann, who is Head of Analytical Instrumentation in Biotechnology at the Technical University Bielefeld and who also uses a BaychromAT system, sees a further advantage: “As you can take measurements as frequently as