

Determining total and viable cell density with in-line sensors

University Bielefeld relies on Hamilton technology



Back in 1988 Prof. Dr.-Ing. Jürgen Lehmann already realized the rapid developments in biotechnology, especially in the field of cell culture. Against this background, he founded the study group for cell culture technology at the technological faculty of the Bielefeld University. Now 30 years later, this decision has proven wise as the importance of animal cells in biotechnology increased enormously. They gained more importance not only as permanent cell lines for the production of complex recombinant proteins but also in the field of tissue engineering and stem cell biology. The study

group's aim is hence to develop an efficient procedure for the production of pharmaceutically relevant proteins using animal cell cultures. Furthermore, the research team led since 2005 by Prof. Thomas Noll, works on the further development of methods for functional genome analysis for their application in cell culture technology. 600 square meters of laboratory space as well as 150 square meters for a technical center are at the group's disposal for this purpose. Sensors of Hamilton Bonaduz AG are used for determining important parameters in order to not only allow for a sustainable research but also for

the development of cell culture technology.

Determining viable cell density

In order to gain deeper insights in the research field of cell culture technology, a significant number of organisms need to be cultivated in differently sized vessels of the University Bielefeld. “We work with animal cells, to be more precise, with CHO-cells. The bioreactors we use have working volumes between a few milliliters up to 20 liters, depending on the project, research topic as well as on the budget”,

explains Dr. Heino Büntemeyer, responsible for the study group of cell culture in the fields of fermentation, process analytics, metabolome and glyco analysis. Particularly of interest for the group and the students involved are the procedures within the CHO-cells and identifying when their productivity reached its maximum. Process insights are gained by the means of Hamilton pH and optical dissolved oxygen sensors, as well as an Incyte



sensor to measure the viable cell density. These sensors have already been used at the eight lab stations for some time. The Incyte sensor was developed especially for applications using mammalian cells, yeast, and high density

bacteria. It measures the viable cell density in-line and in real time. Due to the in-line measurement, actual information is directly available allowing the detection of process deviations immediately. Thus necessary countermeasures can be taken right away. “Monitoring viable cell density offers useful data in order to set up optimal cul-

tivation conditions and to increase the yield of the target molecule. Therefore it’s also important to know the total cell density, and how many dead cells are present”, explains the university employee.

Identifying trends with Dencytee

The persons responsible chose the Dencytee sensor of Hamilton. Because of the great experience with the Incyte sensor, standing out with stable read-

ings, durability, and an easy operation, the people in charge have also chosen Dencytee. Additionally to the easy integration in the existing measurement environment, a major reason for the purchase was a doctoral thesis, in which in-line sensors should be applied for measuring cell density. “With Dencytee measuring total cell density, we were able to follow the course of the cultivation and to receive current status values. In this way, we can identify a trend relatively fast or even at least at an early stage, and make necessary corrections”, says Dr. Büntemeyer. This was not possible prior to using the sensor, since cell density sampling had to be taken manually or semi-automatically and analyzed afterwards. The time between taking a sample was ideally twelve hours, which could not always be realized easily at the university’s everyday life. Important deviations were potentially missed, leading to cell death. With Dencytee all particles, cells, and molecules scattering light at 880 nm are detected – viable as well as dead cells.

Compatibility speaks for itself

The combination of Incyte and Dencytee allows for monitoring as well as

precise regulation of nutrients during the cell culture’s growth phase. For this purpose the sensors used for twelve days straight, have to offer continuously reliable measurements, followed by withstanding cleaning and sterilization in an autoclave. Additionally, they are used by students in internships, who do not have much experience in this matter, which makes a self-explanatory operation mandatory. “The sensors fulfill all these requirements. They run hassle-free and are totally straightforward from a technical point of view”, explains the researcher. He furthermore praised the contact to the measurement experts: “We do not need their help often, which is a good sign. But everything runs smoothly, if the sensors need an inspection at some point. I would decide on Hamilton any time again, due to the positive experience and the compatibility with the other sensors“.