Improving gas analysis in process development laboratories

The fermentation process is pivotal to biotechnology, producing a wide range of key products in a variety of industries. Here, Jason Brown, Process Development Engineer at Thermo Fisher Scientific, discusses the importance of online gas analysis in industrial cell culture and fermentation processes and highlights a method that provides fast and accurate results.

Why is using process analytical technology (PAT) important in biotechnology processes? Can you describe the parameters you are monitoring?

It is essential to analyse the gases going into and coming out of fermenters and bioreactors to monitor the health status of any culture. This helps to identify possible contamination, as well as gain valuable information on respiration rates and the availability of nutrients. We can see if any volatile products or byproducts are being made – for example, if yeast is producing ethanol – or if the culture is consuming feed, such as methanol. Modern PAT techniques have allowed us to massively expand on the data collected by monitoring a wide range of gases, from water vapour and ammonium compounds to oxygen and carbon dioxide.

Mass spectrometry has been a preferred method for monitoring these gases for some time. What are the main benefits you see in your laboratory over other approaches?

We previously used dissolved oxygen (DO) probes to monitor cultures and evaluate vessel performance. However, both optical and polarographic probes tended to have a lag time, meaning we were essentially measuring the response time of the probe, not the actual oxygen transfer rate of the fermentation vessel or the oxygen uptake rate of the cells. We would watch for a spike in oxygen or a change in glucose concentration and start a feed, but this method was slow and cumbersome. Switching to off-gas sampling using mass spectrometry allowed us to monitor these parameters in real time to determine what was being used by the cells or absorbed into the solution more accurately. This means that we can more quickly determine, for example, if a nutrient or carbon source is depleted and start a feed before the culture becomes limited, improving the overall product quality as well as increasing yield.

Furthermore, when we performed evaluations with DO probes using the exact same parameters, we often obtained varied results, because each individual probe was slightly different or became more photobleached each day. Mass spectrometry, however, provides unparalleled repeatability every day, reducing variability to improve the quality of the data.

What is your preferred type of analyser to monitor fermentation processes?

For our lab, mass spectrometers have become an essential part of process development and monitoring, largely owing to their flexibility; their analytical capabilities are mostly defined by the software, rather than the hardware. Magnetic sector mass spectrometers are generally preferred as they offer greater accuracy and precision. They also require longer periods between calibrations, without compromising on speed. For example, the Thermo Scientific™ Prima BT™ Bench Top Process Mass Spectrometer can scan at speeds equivalent to quadrupole analysers, precisely measuring target gases coming out or going in. Additionally, these instruments are equipped with a rapid multi-stream sampler (RMS) that allows them to switch between up to 16 sample streams – and up to 60 streams with the Thermo Scientific™ Prima PRO™ Process Mass Spectrometer – without affecting the quality of the sample.

Do you need experience in mass spectrometry to use these instruments?

Just the mention of mass spectrometry can evoke fear in even the most experienced microbiologists. They often think that this method is reserved for highly trained experts. However, instruments like the Prima BT Bench Top Process Mass Spectrometer have made this powerful analytical technique accessible to all laboratories. Its easy-to-use interface and software make for simple operation and data collection without prior mass spectrometry experience.

Jason Brown

Process Development Engineer at Thermo Fisher Scientific.

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