Glucose Control of Bioprocesses
Online Monitoring and Control of Bioreactors by Mid-Infrared Spectroscopy

Irubis is a biotechnology start-up based in Munich, Germany. It was founded in 2017 with the aim to make online monitoring and control of bioreactors by mid-infrared spectroscopy to become standard. Biopharmaceuticals are predominantly expressed by mammalian cells in so-called bioreactors. A major challenge is to ensure the optimal nutrient concentration for the cells. Currently, in most bioreactors samples are taken manually once per day to measure the nutrient concentration in a separate analytical device. Irubis enables continuous monitoring and control of the nutrient concentration with a novel mid-infrared spectroscopy system and a machine-learning evaluation software.

Alexander Geißler: It all started with a cost-effective silicon crystal that serves as a sample carrier for mid-infrared spectroscopy. The master’s thesis of our co-founder Lorenz Sykora was about this silicon crystal. This sensor component, which is up to 100 times cheaper than conventional crystals, laid the foundation for the company. The big question was for which market and for which application.

How did you find your market in the biopharmaceutical industry?

A. Geißler: We did a lot of market research, read dozens of publications and spoke to many people from different industries. After digging deeper and deeper into the various „problems“ of the customers, the application has finally revealed itself to us, as several experts from the biopharma industry asked: “Why don’t you use your single-use technology to monitor bioreactors?”

Why didn’t other companies monitor bioreactors with spectroscopy? What makes Irubis’ technology different?

A. Geißler: With existing spectroscopic methods, a time-consuming calibration of up to three months is required to monitor cell culture processes. Instead, we will initially focus on glucose control. Our analytical device Monipa requires only a starting value and then keeps this value constant based on a relative measurement.

Anja Müller: The relative measurement is achieved by our mid-infrared spectroscopy system combined with our software that evaluates the spectra, controls feeding pumps and thus creates a closed loop system for glucose. We realized a plug-and-play solution without the need of a calibration. The bioreactor is connected to our device by disposable flow-cells that contain the silicon crystal.

Where does the device name “Monipa” come from?

A. Müller: Monipa is the combination of “Monitoring” and “PAT”. PAT stands for process analytical technology, a term defined by the FDA for the control of important process parameters in manufacturing of pharmaceuticals.

What will be the next steps to develop Monipa?

A. Müller: The next steps for Monipa are to complete a certified small series in 2021 and to share the message to all biopharma companies around the world: We have the solution for your needs! With Monipa, we deliver a plug-and-play device that enables continuous glucose control and monitoring.
Biopharmaceuticals are produced mainly by mammalian cells in vessels, so-called bioreactors. Production and process development of biopharmaceuticals require a precise monitoring and control of key parameters such as nutrients and metabolites. Currently, nutrients and metabolites of most bioprocesses are measured by offline analytical technologies. Offline measurement means taking the samples from the bioreactor and analyzing them in a separate device. This manual process needs to be performed by the lab technicians once a day and also at weekends. Thus, a continuous regulation is not possible, leading to suboptimal product yields and an increased risk of cross contamination. By online monitoring, which means a 24/7 control of the process, a higher product quality and yield can be achieved.

The high potential of mid-infrared (MIR) spectroscopy for online monitoring of glucose and lactate in mammalian cell cultures was already demonstrated in several publications. Translating this technology into bioprocessing has been an issue because of high equipment costs and low robustness of the probes used so far. Irubis developed Monipa, an innovative MIR spectrometer system that enables efficient and robust online control of glucose concentration in up to four bioreactors simultaneously. It uses a qualitative measurement method, thus eliminating the time-consuming need of generating calibration models. Monipa can be easily integrated into the bioprocess by connecting its single-use flow cell via a loop to the bioreactor. The external flow cell results in a higher robustness than an inline alternative. Monipa allows the use of infrared spectroscopy in bioprocessing, which leads to a high product yield and product quality.

Features of Irubis’ Technology:
- 24/7 online control of glucose by closed loop
- No contamination due to sterile single-use flow cells
- High robustness compared to other spectroscopic methods
- No calibration model necessary, thus very high transferability (scale-up, cell lines, media, etc.) possible

Irubis was founded in 2017 by Lorenz Sykora (CTO), Alexander Geißler (CEO) and Anja Müller (COO). The three young professionals started their business with a cost-effective silicon crystal for infrared spectroscopy. While other sample carriers for infrared spectroscopy are usually made of diamond, zinc selenide or germanium, the Irubis crystals are fabricated from silicon wafers. They therefore only cost a fraction of the price while maintaining the same high quality. The Irubis microstructured silicon crystal is an innovative sample carrier for ATR infrared spectroscopy. ATR stands for attenuated total reflection and is the method of choice for almost all routine analyses of fluids and solids. In 2018, the founders started building an online monitoring system for bioreactors and to test it in the biopharma environment at three big biopharma companies. In 2020, Irubis began expanding the team and completing product development.

Milestones
2017
- Winner of the Medical Valley Award
- Foundation of Irubis

2018
- Development of a silicon crystal for infrared spectroscopy
- Technological proof of concept: online monitoring of glucose with Irubis silicon crystal and mid-infrared spectrometer
- Prototype with higher sensitivity of the system

2019
- Validation of Monipa prototype at three biopharma companies

2020
- One of the winners of the H2020 EIC Accelerator Pilot
- Additional projects and validation of Monipa prototype in the biopharma industry

Roadmap
2021
- Certification of Monipa
- Market entry in Europe

2022
- US market entry