

# 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.*

**CHEManager:** *How did it all start and what was there first: the idea or the company?*

**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 „prob-



Lorenz Sykora (CTO), Anja Müller (COO) and Alexander Geißler (CEO) founded Irubis in 2017.

lems“ 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.

**Which obstacles did you have to master so far during the Irubis journey?**

**A. Geißler:** As a technology-driven company, a challenge was to find the market for our technology and to understand the customer problem down to the smallest detail in order to build a great solution through a close exchange and cooperation with the biopharma industry.

**A. Müller:** We are very excited to be among the winners of the H2020 EIC Accelerator Pilot as we now have the resources to expand our team and finalize our product. The biggest challenge now is to find top-level talents.

**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

### PERSONAL PROFILES

**Alexander Geißler** (Co-founder and CEO) holds a master's degree in technology and business administration from the Technical University of Munich (2013). Before founding Irubis, he worked for 4 years for another TUM high-tech spin-off. He has vast experience in sales, marketing, and business development. He blends the needed technical and sales skills to make a high-tech company like Irubis succeed. Now he is driving all sales strategies forward and aims for the successful market launch of Monipa.

**Anja Müller** (Co-founder and COO) holds a master's degree in physics from the Technical University of Berlin (2016). Over the course of her studies, she acquired relevant knowledge and skills in the field of FTIR spectroscopy. During her master's studies, she has been awarded a scholarship for the Career Building Program at Femtec, where she acquired important management and leadership competencies. At Irubis she is responsible for funding and project management.

your needs! With Monipa, we deliver a plug-and-play device that enables continuous glucose control and monitoring.



**BUSINESS IDEA**

**Single-use Flow Cell and MIR Spectroscopy**

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 analyze 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 equip-

ment 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

■ Contact details: Irubis GmbH, Munich, Germany  
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**IRUBIS**



Monipa from Irubis connected via tubes to a bioreactor.

**ELEVATOR PITCH**

**Bioreactor Monitoring Made Easy**

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

- Development of a silicon crystal for infrared spectroscopy

**2018**

- 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



Single-use flow cell with silicon ATR crystal. It easily click-mounts to Monipa.