Application of Gas Analyzers in Process Automation and Production Optimization of Secondary Metabolites from Myxobacteria*

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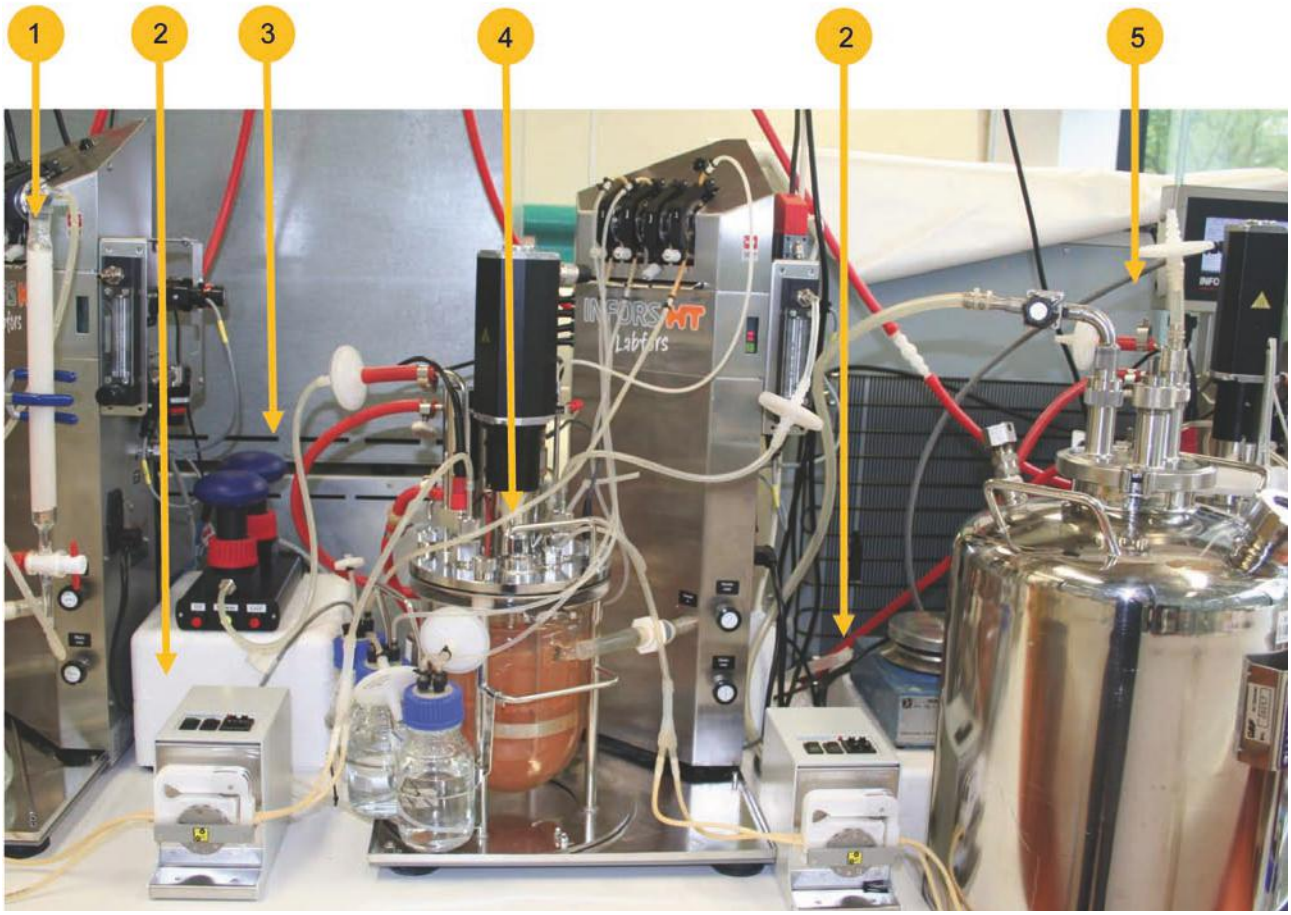
The research in the group of Prof. Rolf Müller at Saarbrücken/Germany addresses the chemistry, biosynthesis, regulation, heterologous production and mode-of-action of secondary metabolites from myxobacteria. These soil-dwelling microbes are potent microbial producers of natural products, which show strong activities as antibiotics, anti-cancer drugs or immunosuppressants, amongst others.

The search for new lead compounds in drug development is pursued in two ways: the (biological) activity and the (microbiological) genome driven approaches, combined with advanced physico-biological analysis, production optimisation and scale-up.

Members of the interdisciplinary research group employ a broad spectrum of techniques, including microbiology, cell biology, genetics, molecular biology, protein chemistry, enzymology and analytical chemistry and small scale process engineering.



1: Adsorber Resin Packed Column
2: Feed-, and Removal-Pump
3: Off-Gas-Analysis
4: Bioreactor
5: Feed-Tank

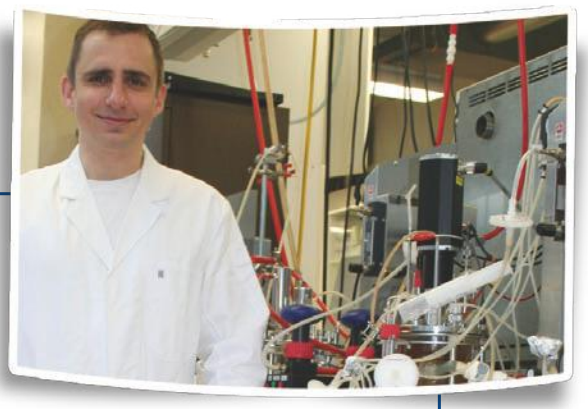
***=Note by BlueSens:**

The complete scientific survey will be published soon. Find here a short abstract of the project report. Visit BlueSens.com for the bibliographic reference soon.

To improve yields and production processes for secondary metabolites alternatives to the established batch or fed-batch processes are needed. The gas analyzer project aims at the optimization of bioprocesses involving myxobacteria as natural product producers. Myxobacteria are growing very slowly on complex substrates like whole cell yeast or methanobacter media. Usual parameters like oxygen transfer rates, carbon dioxide evolution rate and respiratory quotient are not significant enough to monitor the culture status. Therefore we were looking for more meaningful indicators that could be used as triggers for process automation.

The applied gas sensors allowed the full automation of the production process with data from the respiratory activity exclusively measured via off-gas analysis. The gas monitoring approach dimishes problems associated with the contamination of media components during downstream processing and increases the productivity for several known compounds compared to standard conditions. By periodic exchange of cultivation media and capturing of secondary metabolites through an adsorber resin, the fermentation can now be run in a semi-continuous process.

The results indicate that the developed method is a significant improvement of process monitoring and control, including dilution or feeding rates in fed-batch, chemostat or perfusion processes. Furthermore, it is shown that the composition of the gas phase has direct effect on the yield of several secondary metabolites. Thus, off-gas analysis is a valuable tool to create defined fermentation environments for the enhancement of the productivity of specific natural products even with ambitious microorganisms. Results are in preparation for publication.



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Research in the Müller group

The main part of the work addresses the genetics and mechanistic enzymology of natural product biosynthesis in myxobacteria and actinomycetes. One aspect is to rationally modify the product structures by genetic engineering. Further, we identify new myxobacterial strains from locations worldwide, using a set of efficient purification techniques. The strains are analyzed for the production of novel, bioactive compounds using (bioassay-guided) LC-MS coupled to high-resolution mass spectrometry and advanced statistical approaches. Natural products are evaluated against whole cells. We investigate the mode-of-action of promising compounds using a range of cell biology techniques. ***www.helmholtz-hzi.de/hips***

The Project Team

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Literature

The results are currently prepared for publication.