

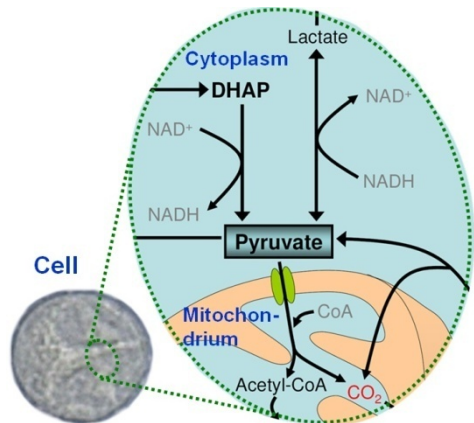
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**Project term:** 2006 – 2009  
**Financed by:** Hamburg University of Technology and BMBF



## Description:

Metabolomic analysis is an essential part of systems biology but less well developed so far. The determination of *in-vivo* metabolite concentrations in mammalian cells is of importance for both biotechnology and biomedicine. However, many problems exist, especially with respect to representative sampling under physiological conditions and processing prior to analysis (e.g. leakage of metabolites due to fragility of the cells). Further, the burden of compartmentation has to be overcome to distinguish between metabolites within the cytoplasm and inside organelles, e.g. mitochondria. Up to date, no experimental approaches have been established to properly take these issues into account. It is the aim of this project to address these problems and to generate a realistic view of metabolism in selected eucaryotic cells under physiological conditions (Fig.1).

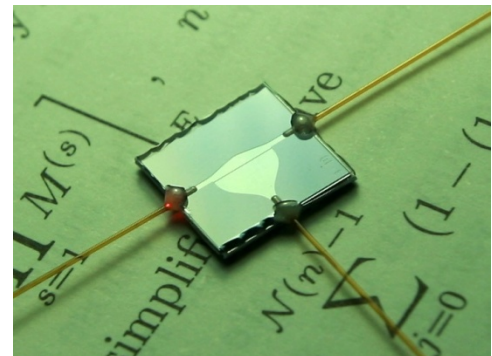
Cultivation → disturbance → rapid sampling → processing → analysis



**Fig.1.** Pyruvate metabolism as an example of compartmentation of metabolism

## Microfluidics for metabolomics

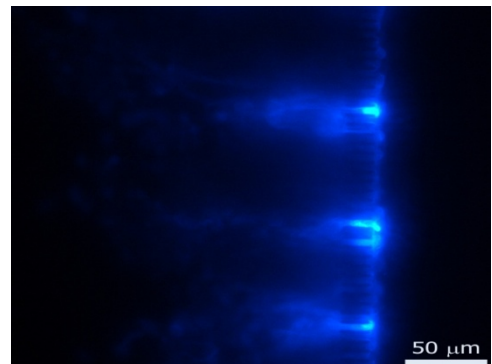
We use advanced microsystems technology for the design of our sampling systems (Fig. 2), since sample preparation plays a key role to access dynamic cellular processes under *in-vivo* conditions. Various functions, which are essential for metabolic profiling but cannot be solved in macroscale sampling systems, are integrated on-chip. Those functions are for example the rapid cooling of the sample stream, a fast disruption of cells and a separation of organelles. Following a proof-of-principle approach, our integrated systems are used for different cells in various projects, which cover questions in the fields of bioprocess engineering and biomedicine.



**Fig.2.** Microfluidic device produced at IBB

## System characterisation and application

Our systems are validated qualitatively by optical methods and quantitatively by sensor units for the detection of pressure gradients, temperature and flow profiles to enable an iterative system optimization. Biochemical analysis is used to evaluate sample quality. Our first results indicate the successful on-chip integration of essential steps for sample preparation. Recently, we demonstrated that different types of mammalian cells can be disrupted rapidly in one of our devices containing a microfabricated nanoknife sieve (Fig.3).



**Fig.3.** Cells lysed by nanoknife sieve

## References (selected)

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- A.-P. Zeng, J. Modak and W.-D. Deckwer (2002) **Nonlinear dynamics of eucaryotic pyruvate dehydrogenase multi-enzyme complex: Decarboxylation rate, oscillations and multiplicity**. *Biotechnol. Prog.* 18: 1265-1276.
- Olenberger, M. (2008) Diplomarbeit, Kultivierung einer Hybridom Zelllinie und Entwicklung von Quenching Protokollen für die Metaboliten-Analyse.

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