Microfluidics in Chemical and Biochemical Engineering Applications

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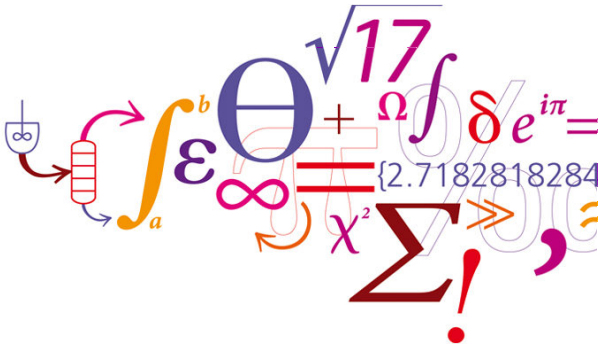


DTU Chemical Engineering
Department of Chemical and Biochemical Engineering

Ulrich Krühne

- 1987-1996 MSc. Chemical Engineering
Technical University Berlin
- 1996-2000 PhD Study
- **DTU Department of Chemical Engineering**
Stabilisation of Biological Phosphorus Removal From Municipal Wastewater (Process Control)
- 2000-2003 **Celtor Biosystems**
Researcher, since 2001 CEO (of the danish entity)
  - µ-fluidic biosensor development
  - (CFD/fabrication/test/....)
- 2003-2011 **Danish Technological Institute**
  - 2003-2007 Senior Consultant
  - 2007-2010 Team leader µ-fluidics
  - 2010-2011 Program leader µ-fluidics
- 2011-now **DTU Department of Chemical Engineering**
  - 2011-2012 Senior Researcher
  - 2012-now Assoc. Professor
  - Since 2014 Study programme leader for the BSc.E. Chemical and Biochemical Engineering

CAPEC Technical University of Denmark

CelTor Biosystems

TEKNOLOGISK INSTITUT

Technical University of Denmark

Introduction

- Why to use microfluidics
- Make the impossible possible
- What is high throughput?
- Can we use experiments of microsystems to predict on large scale processes?
- What we can calculate we do not have to measure
- Conclusions

Why to use microfluidics

- Minute amount of samples/materials
- Fast kinetics due to small diffusion distances
- Superior heat transfer – isothermal reaction conditions
- Work with toxic material becomes unproblematic
- Safety with respect to exothermic reactions
- Automation of systems
- Reaction rates can improve considerable
- Etc…

Reality is that you read news like:

Researcher from this or that … fluidic system which potentially …

And then you never hear from them again

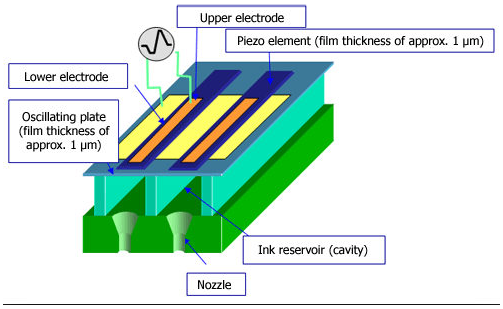
Not convinced? Please name 3 major microfluidic products, that we use in our daily life

Solution

Thermometer

Ink Jet Printer

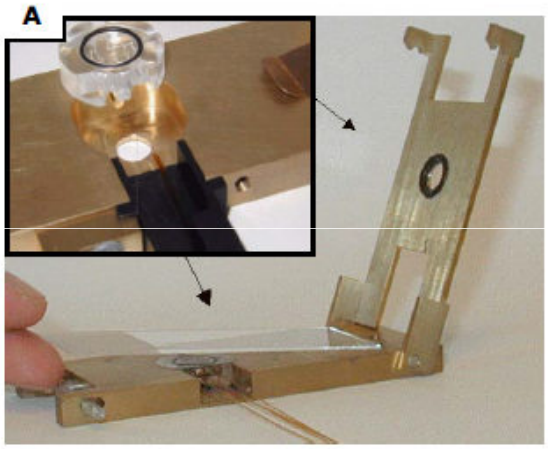
????

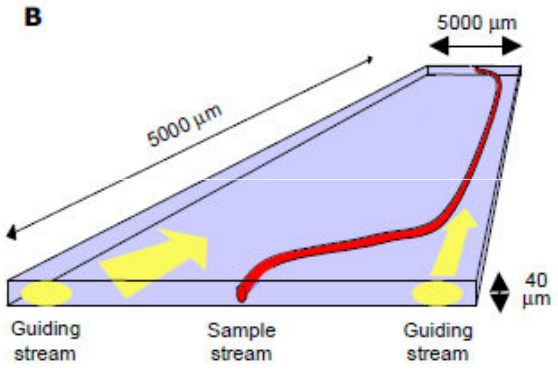


Maybe we can count a diagnostic device like HPLC, GC, Cytometer?

Make the impossible possible

Open face chip technology





Thomas Brevig, Ulrich Kruhne, Rachel A. Kahn, Thomas Ahl, Michael Beyer and Lars H. Pedersen, *Hydrodynamic guiding for addressing subsets of immobilized cells and molecules in microfluidic systems.* **BMC Biotechnology** 2003, 3:10 (July 2003).

Make the impossible possible

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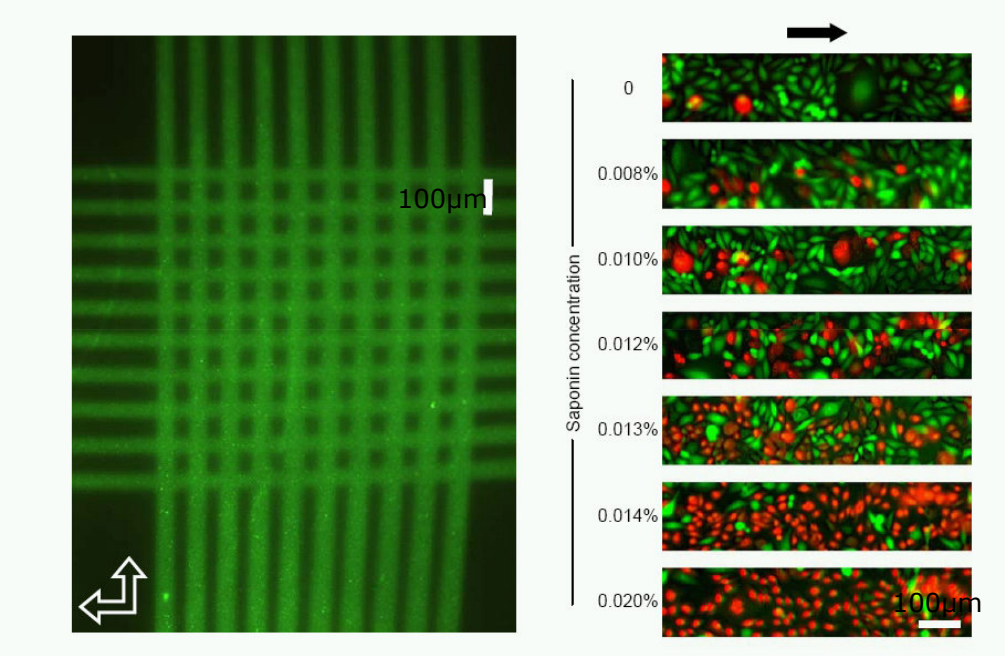

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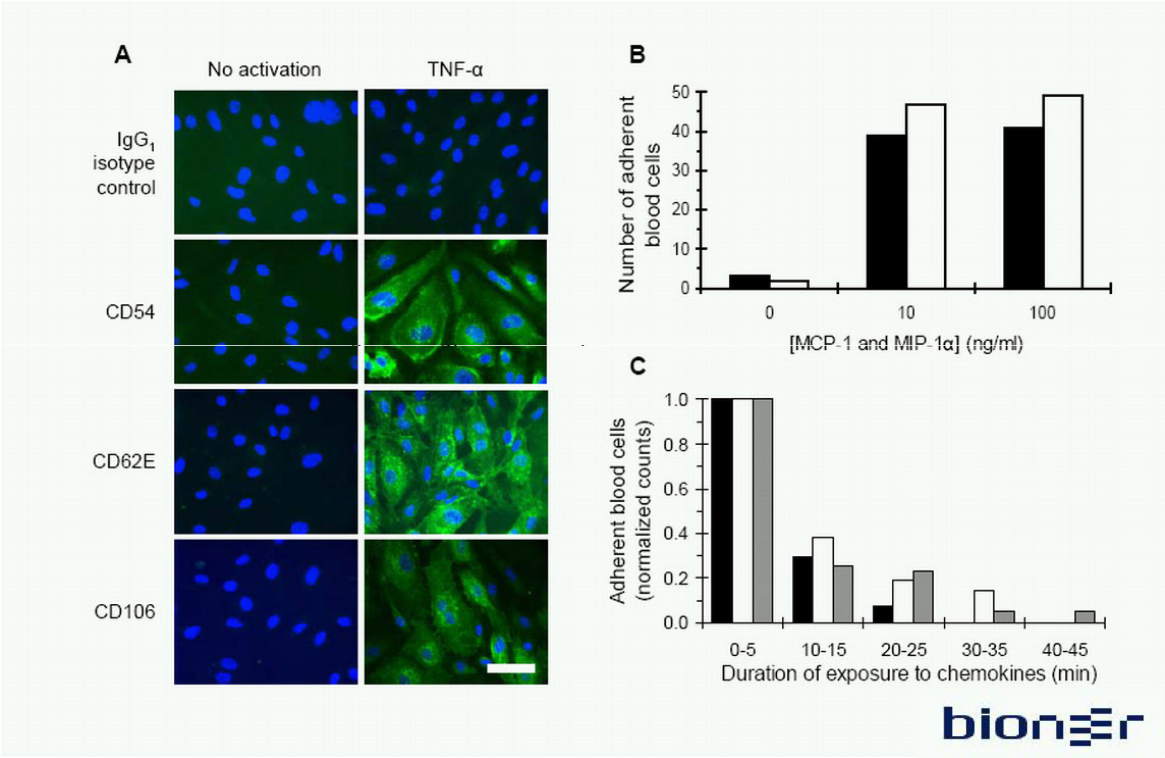
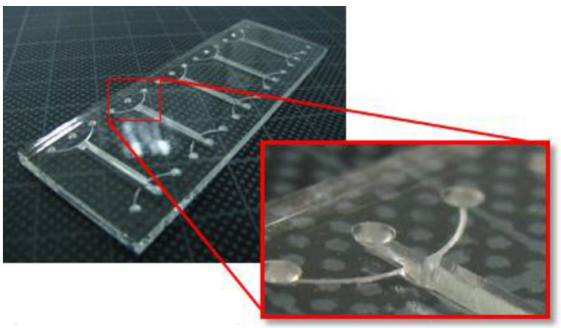
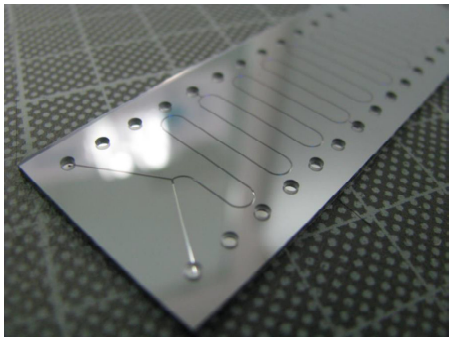


What is high throughput?

- BIOINTENSE

Mastering bioprocess integration and intensification across scales





SEVENTH FRAMEWORK PROGRAMME

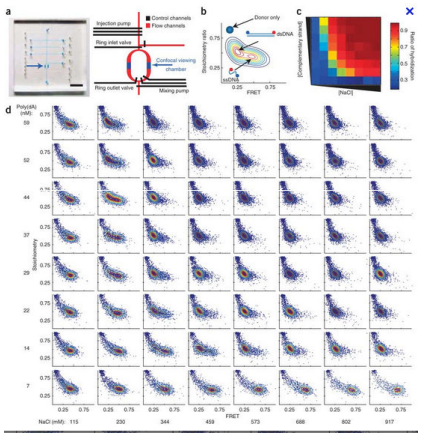
iX factory

microfluidic ChipShop

What is high throughput?

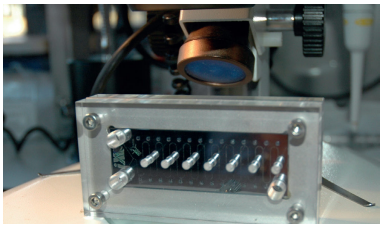
- High Content vs. Throughput?

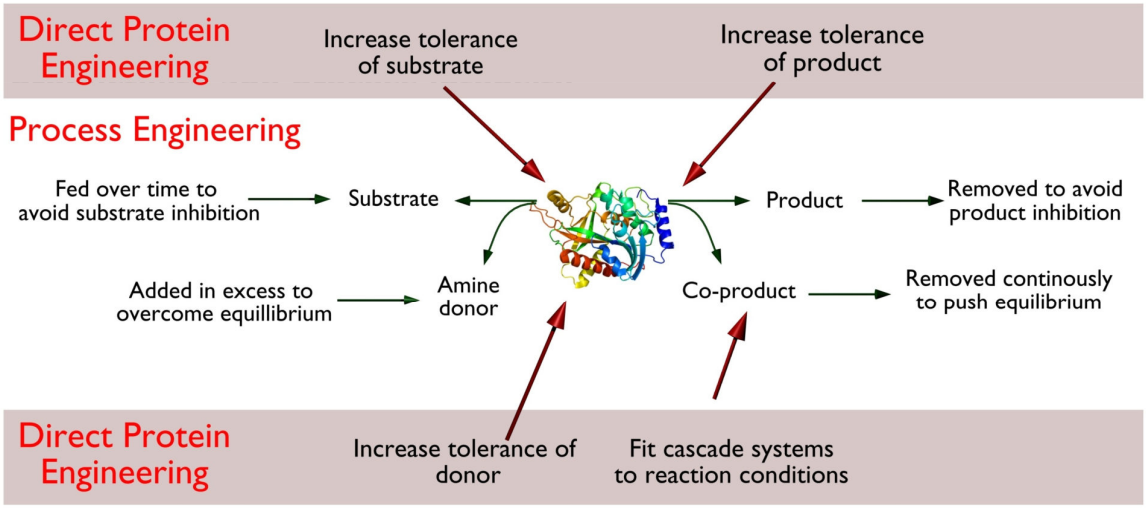
http://strangebehaviors.wordpress.com/2012/04/09/nature-isnt-simple-a-bitter-pill-part-4/



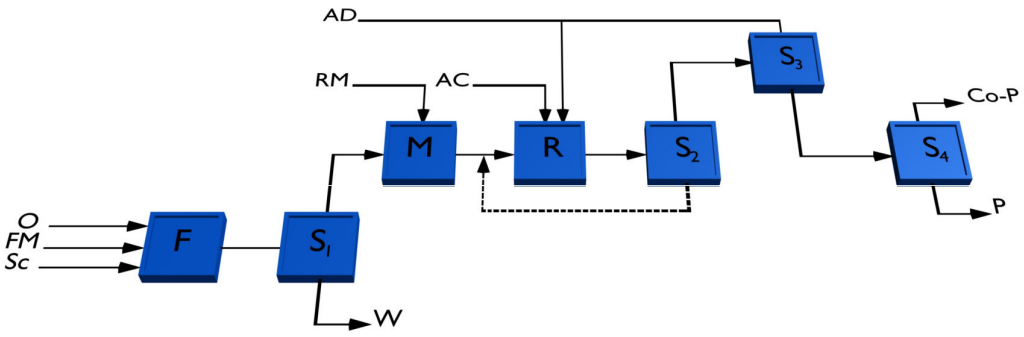
http://www.nature.com/nmeth/journal/v8/n3/fig_tab/nmeth.1569_F1.html

Motivation





The modular concept



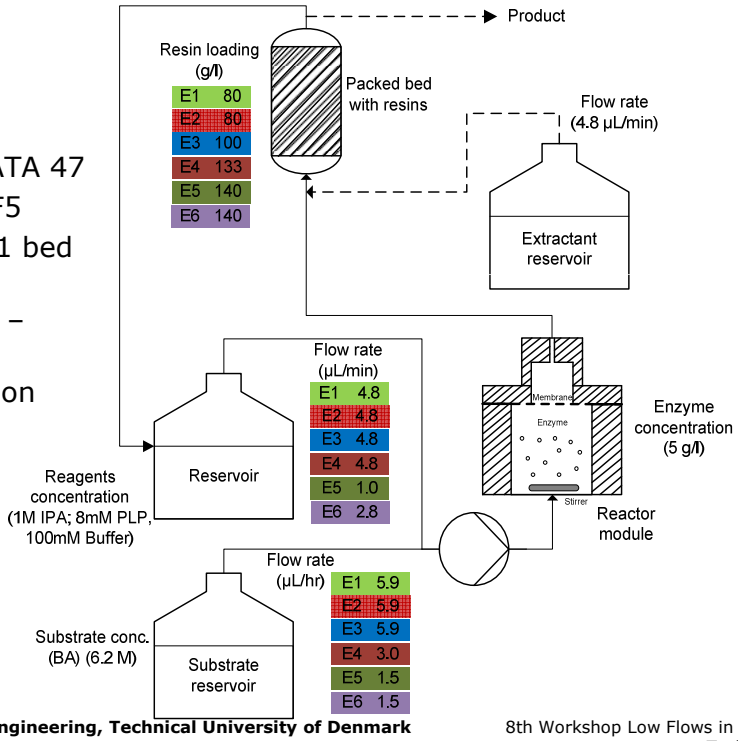
F: Fermenter
S: Separator
M: Mixer
R: Reactor

O: Oxygen
FM: Fermentation Me
Sc: Starter Culture
RM: Reaction Medium
AD: Amine donor
AC: Amine Acceptor

W: Waste
P: Product
Co-P: Co-Product
1: cell/fermentation broth S.
2: biocat./reaction m. S.
3. Amine donor/acceptor S.
4. P/co-P S.

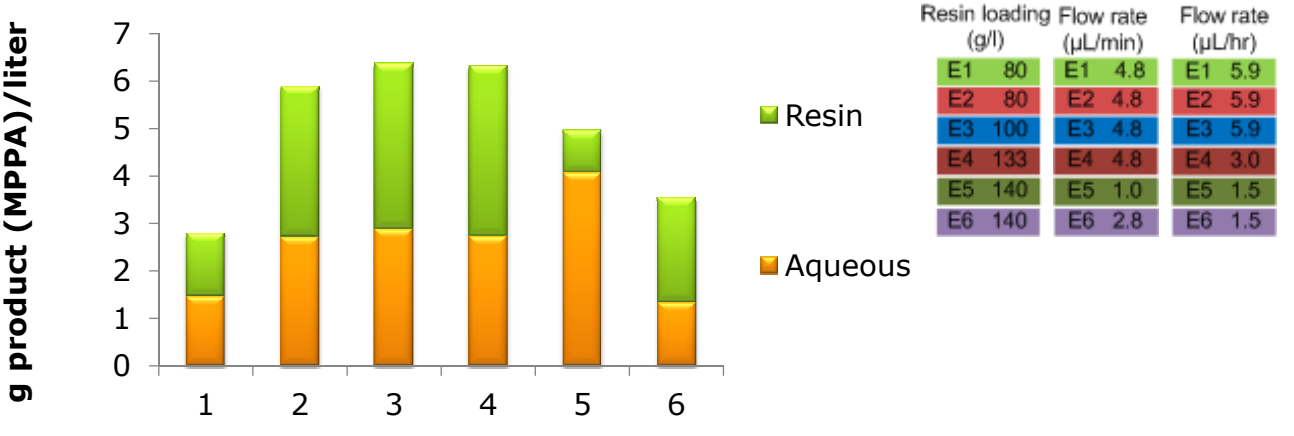
Integrated Micro Membrane packed bed reactor (IMMPBR)

- Crude Enzyme – ATA 47
- Resin – Lewatit AF5
- Extraction rate ~ 1 bed volume/hr
- Extraction solvent – Acetonitrile
- ~38 hrs of operation



Results

Experimental scenarios



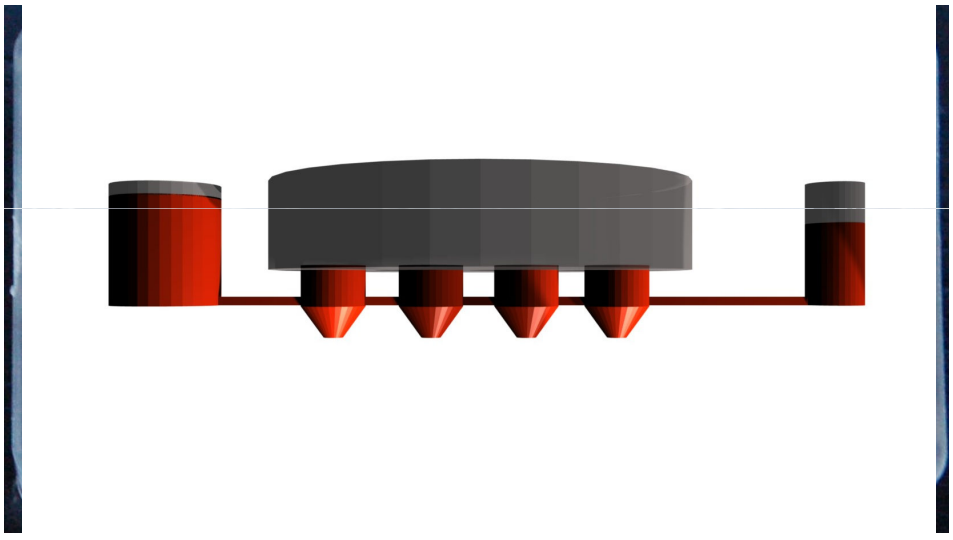
Do you know your product?

Smart Biosystems A/S vs. DTI

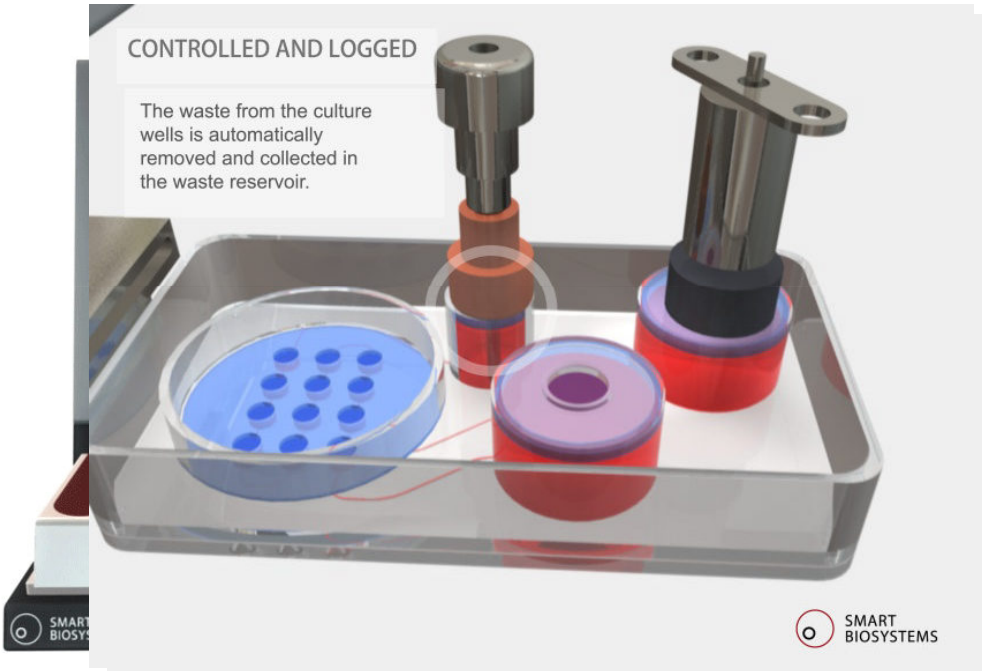
Always expect the unexpected….

I want to revolutionize the in vitro fertilisation industry
I do not have any money….
My idea is to automate the process….
But I do not know how….
The only thing I know is the knowledge I have about IVF….

Concept

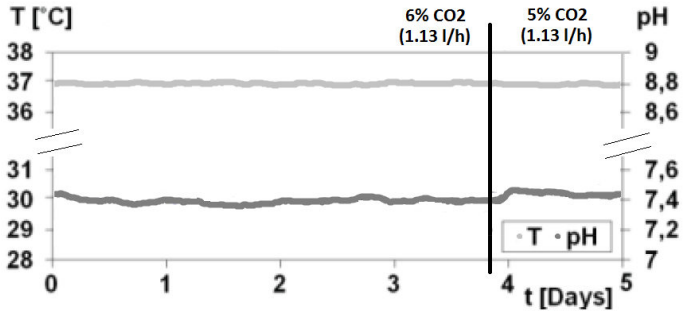


Concept

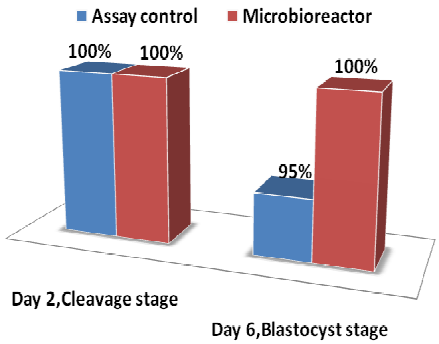


IVF chip

Experimental Results



pH and T measurements



Cytotoxicity tests

Can we use experiments of microsystems to predict on large scale processes?

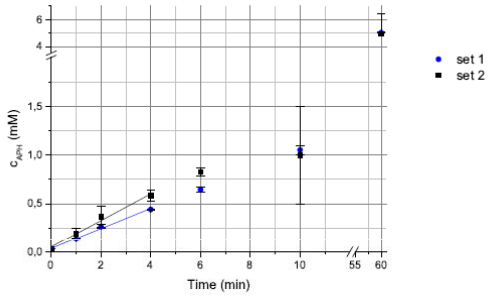


Figure 4.1: Variation of c_{APH} over time in the batch system for activity measurement.

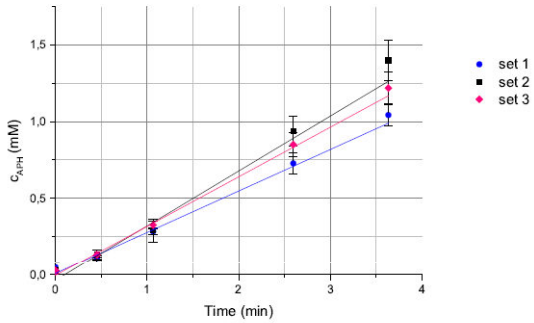
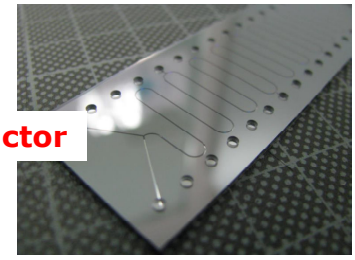


Figure 4.2: Variation of c_{APH} over time in the microreactor for activity measurement.

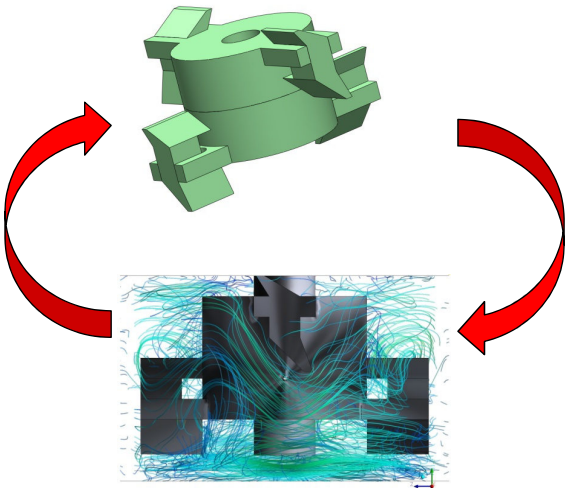
3 fold activity in a microreactor



Can we use experiments of microsystems to predict on large scale processes?

- Continuous culture microreactors PhD project Andrijana Bolic

Stirred NOT Shaken



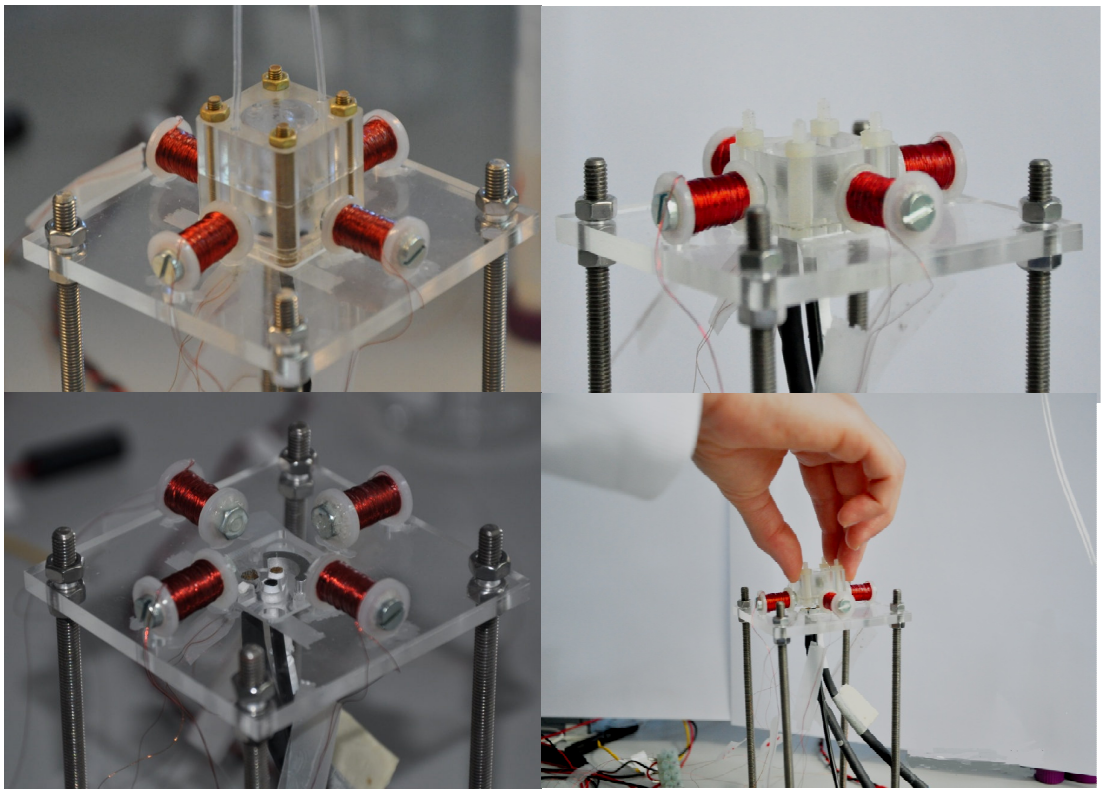
Main challenges:

Transfer the microbioreactor platform from 100 microliter to 1 mL scale

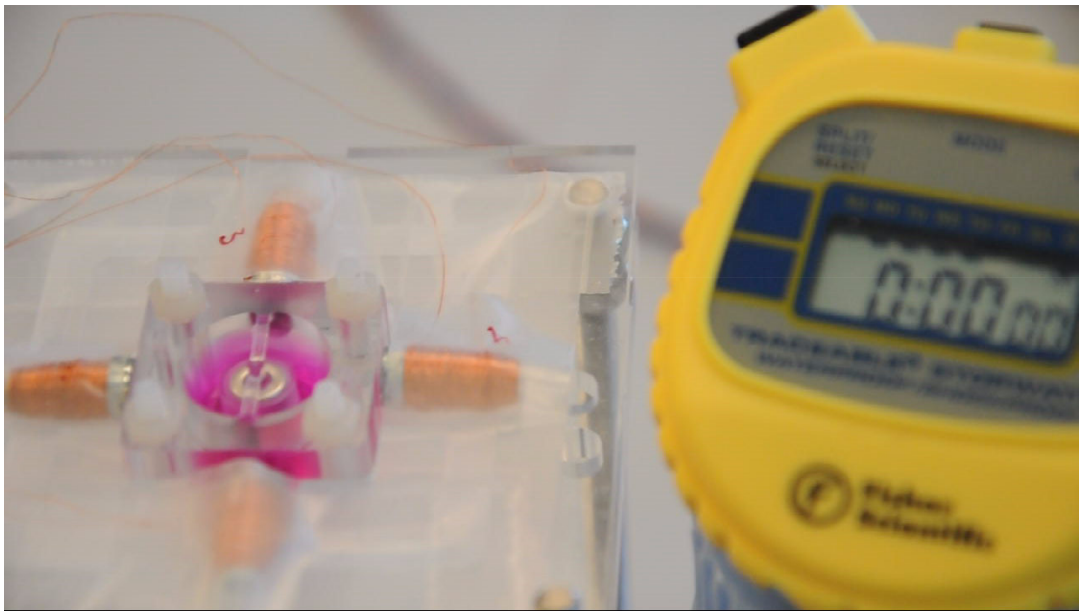
Integrate spectroscopy (e.g. NIR) in the microbioreactor platform

Demonstrate scalability of results

µ-Bioreactors at work



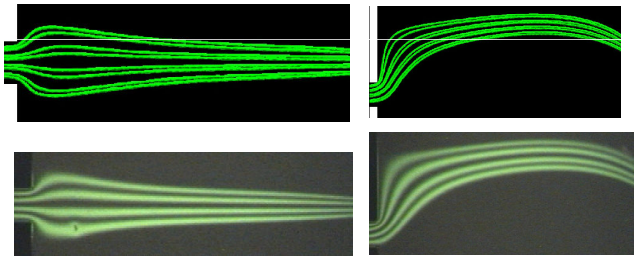
μ-Bioreactors at work



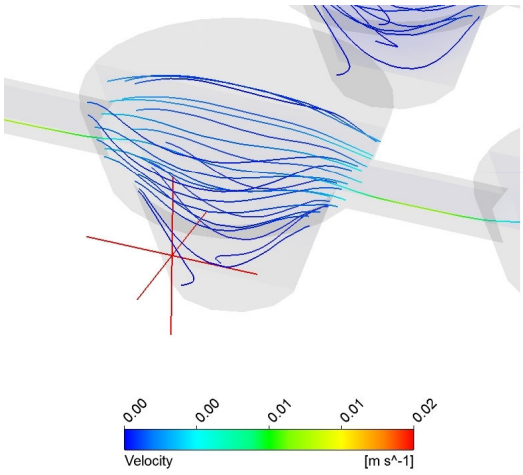
What you can calculate you do not have to measure

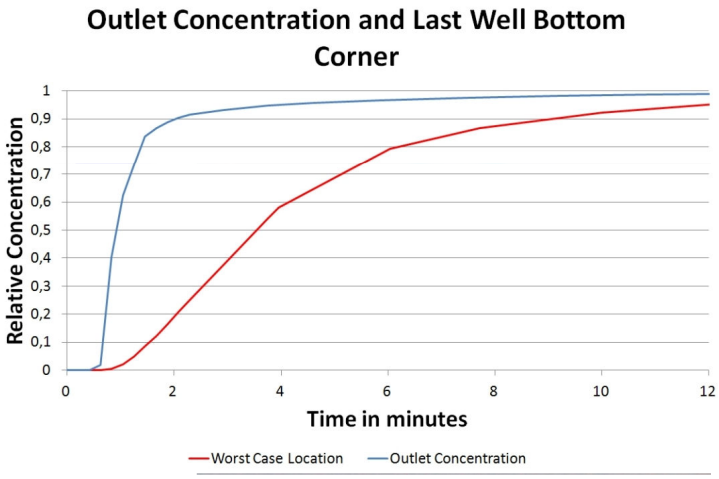
An essential advantage is that you can actually very well calculate with Computational Fluid Dynamics what is happening in the microreator.

But does CFD work? Example Hydrodynamic focussing

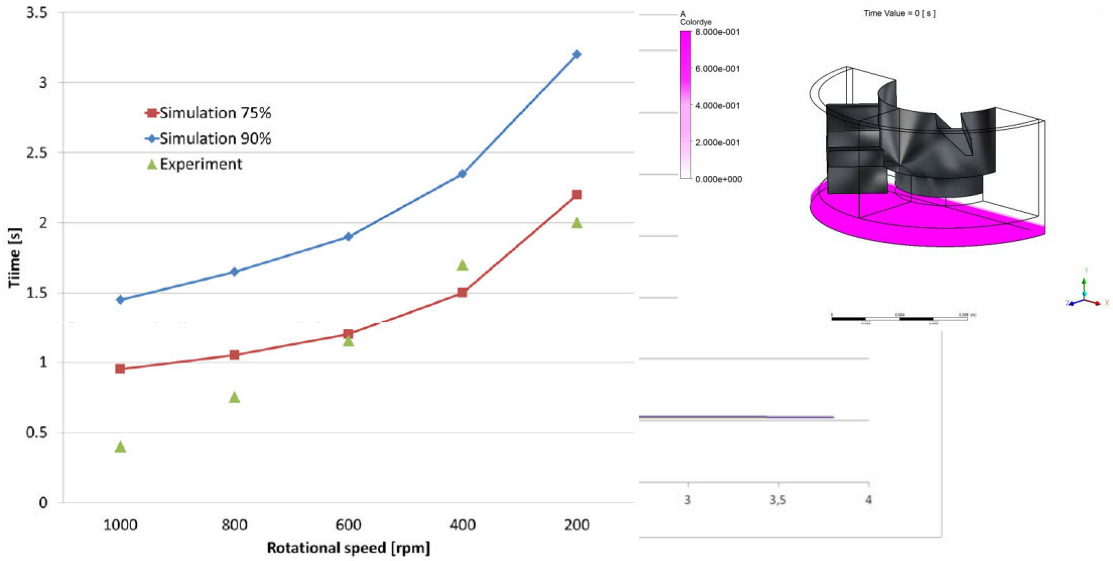


CFD helps to design



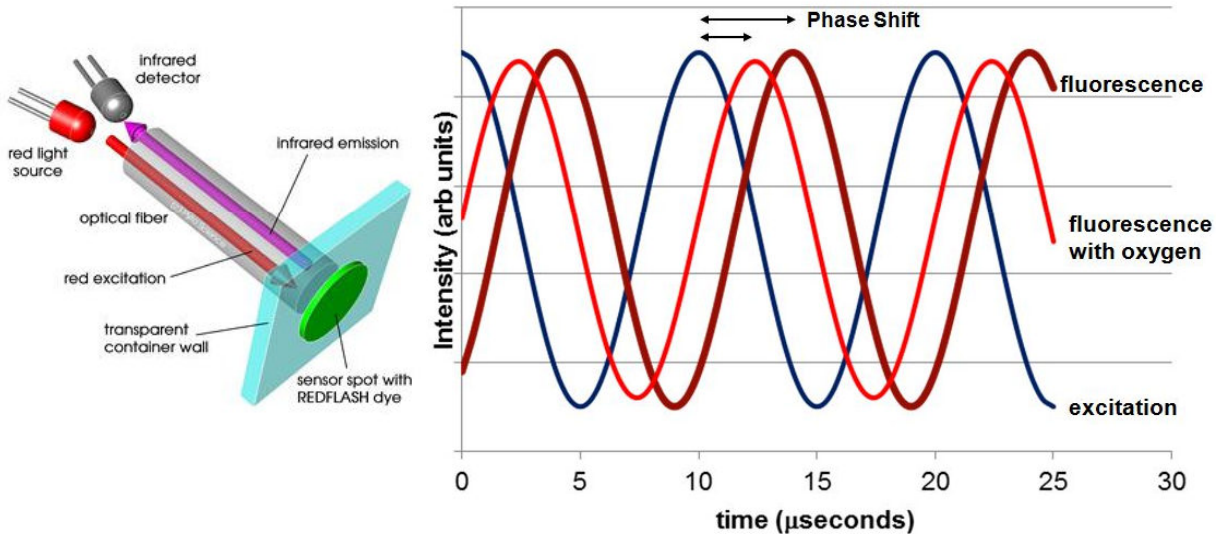


µ-Bioreactors at work



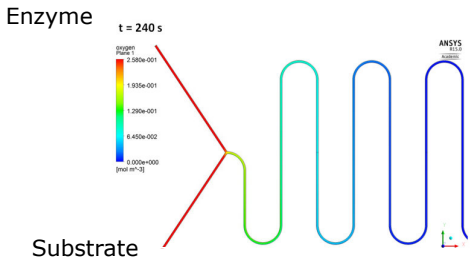
Experimental: 200rpm is 2s and 1000rpm is 0.4s.

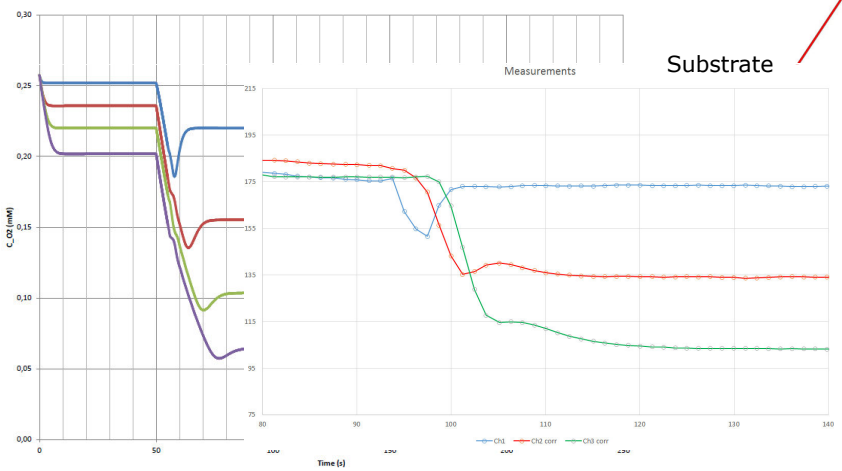
Measurements of Oxygen



Experimental data vs. simulation

O_2+substrate $\xrightarrow{\text{Enzyme}}$ Product





Conclusions

- Microsystems have a considerable advantage with respect to automation, safety and reaction conditions (throughput)
- But we should not take the advantages of microfluidic systems as given
- They are powerful tools but they still have to prove that you can use them across scales
- Very often it takes a PhD to operate a microsystem
- But you can do experiments that are sometimes not otherwise possible
- You can well simulate the fluidic conditions in the system and have therewith a good knowledge of mass transfer conditions
- Even if mass produced it is questionable if they will ever replace existing large scale technology

Acknowledgement

Danish Research Council for Technology and Production and the FTP project (no. 10-082388)

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Thank You for your attention

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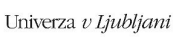



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