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Single use droplet Based Microfluidics – Screening Tools for Biotechnology and Life-Sciences

Alexander Groß

Institute for Chemistry and Biotechnology, Technische Universität Ilmenau Germany, alexander.gross@tu-ilmenau.de

Jialan Cao

Institute for Chemistry and Biotechnology, Technische Universität Ilmenau Germany

Stefen Schneider

Institute for Chemistry and Biotechnology, Technische Universität Ilmenau Germany

J.M. Köhler

Institute for Chemistry and Biotechnology, Technische Universität Ilmenau Germany

Thomas Henkel

Institute for Photonic Technologie IPHT-Jena, Germany

See next page for additional authors

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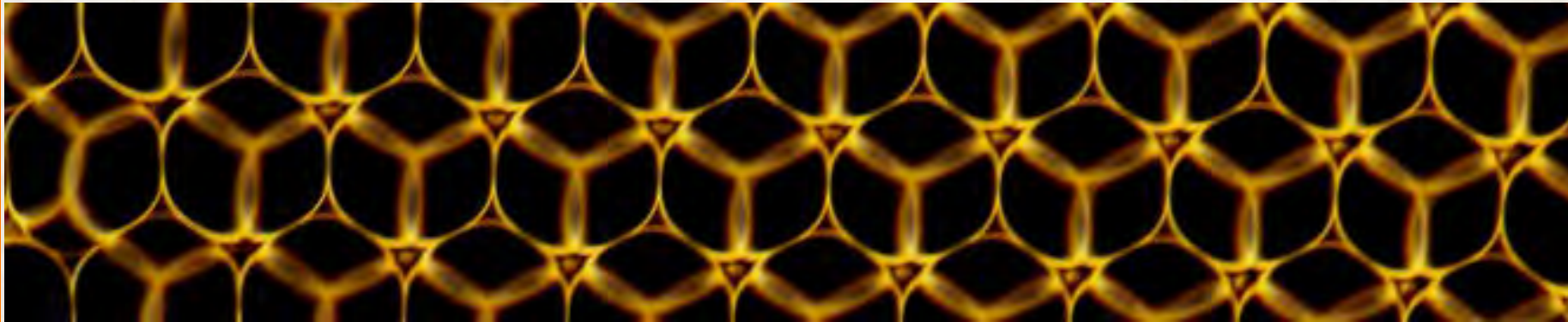
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Authors

Alexander Groß, Jialan Cao, Stefen Schneider, J.M. Köhler, Thomas Henkel, Martin Roth, Mark Kielpinsky, and Alexander Mendel

Single Use Droplet Based Microfluidics – Screening Tools for Biotechnology and Life- Sciences



Dr. Alexander Groß
Institut für Chemie und Biotechnologie
Fachgebiet für Physikalische Chemie und Mikroreaktionstechnik
Prof. Dr. J.M. Köhler
alexander.gross@tu-ilmenau.de



Goethe-Figure



Two General Principles:

Channel-Confining-Droplets
Segmented-Flow



- Droplet identity is encoded by the position within the sequence
- No drop / drop contact

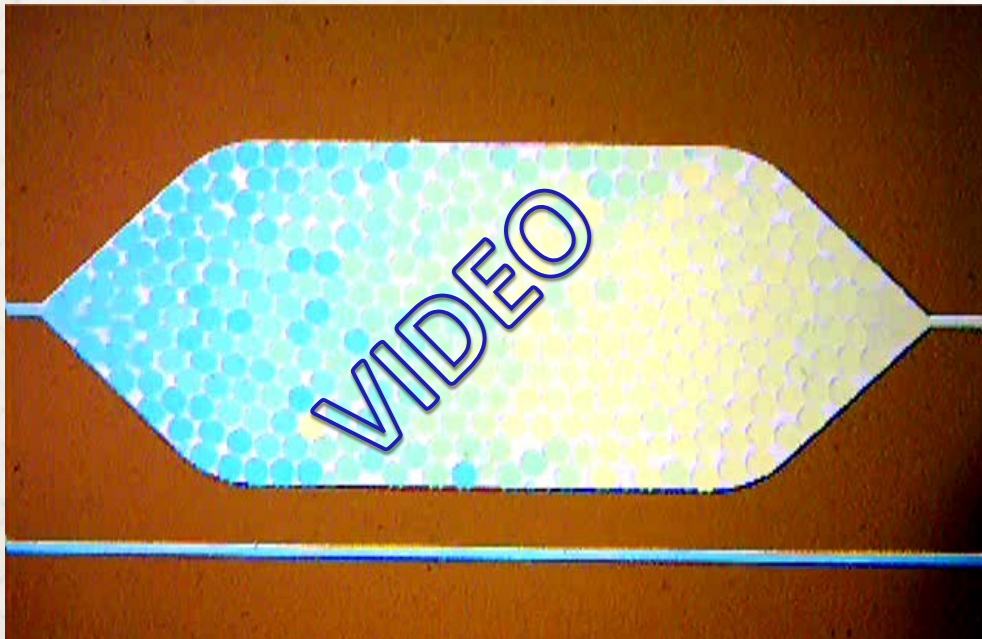
Emulsion Based Droplets



- Drop / Drop contact
- X-talk possible
- No information about the identity
- Stabilizing surfactants necessary

Droplet Based Microfluidics

Emulsion Based Processing

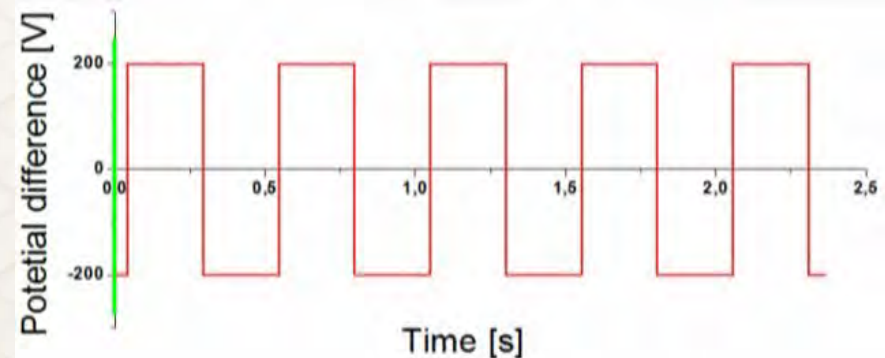


- Drop / Drop Contact
- No Drop Identity Information
- Surfactants required
- High throughput

Droplet selection

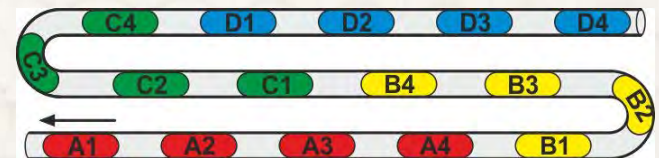
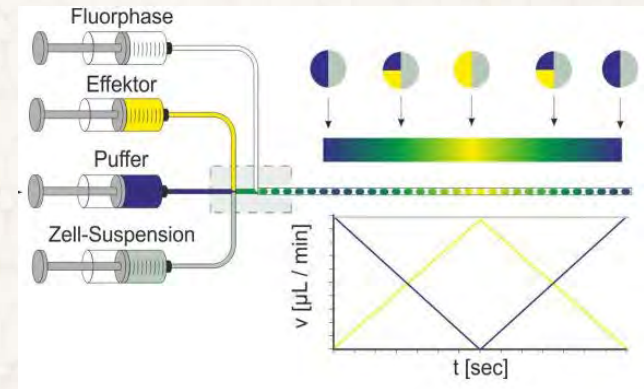


M.Budden, S.Schneider, G.A.Groß, M.Kielpinski, Th. Henkel, B.Cahill, J. M.Köhler; "Microfluidic encoding: Generation of arbitrary droplet sequences by electrical switching in microchannels" *Sen & Act A* 189 (2013) 288–297



Droplet Based Microfluidics

Channel Confined Droplets / Segmented-Flow

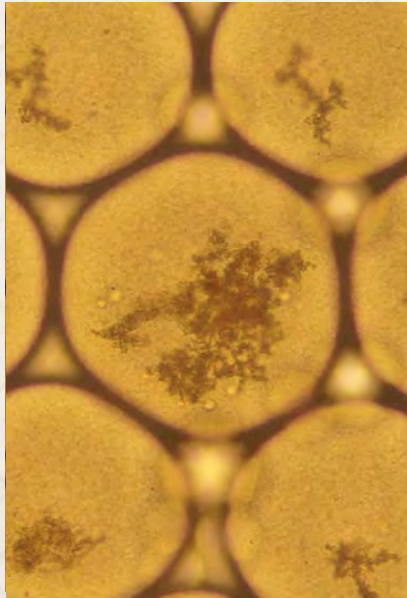


- Droplet content encoded by process history
- No Drop / Drop Contact
- Defined, Reproducible Conditions

Fluidic Screening and Analysis Platform

Multi Scale Droplet Processing

10 pL-Volume



Emulsions

5 nL-Volume



Trapped-Droplet-Array

35 nL-Volume



Chipsystems

500 nL-Volume



Droplet-Probe¹

High Throughput



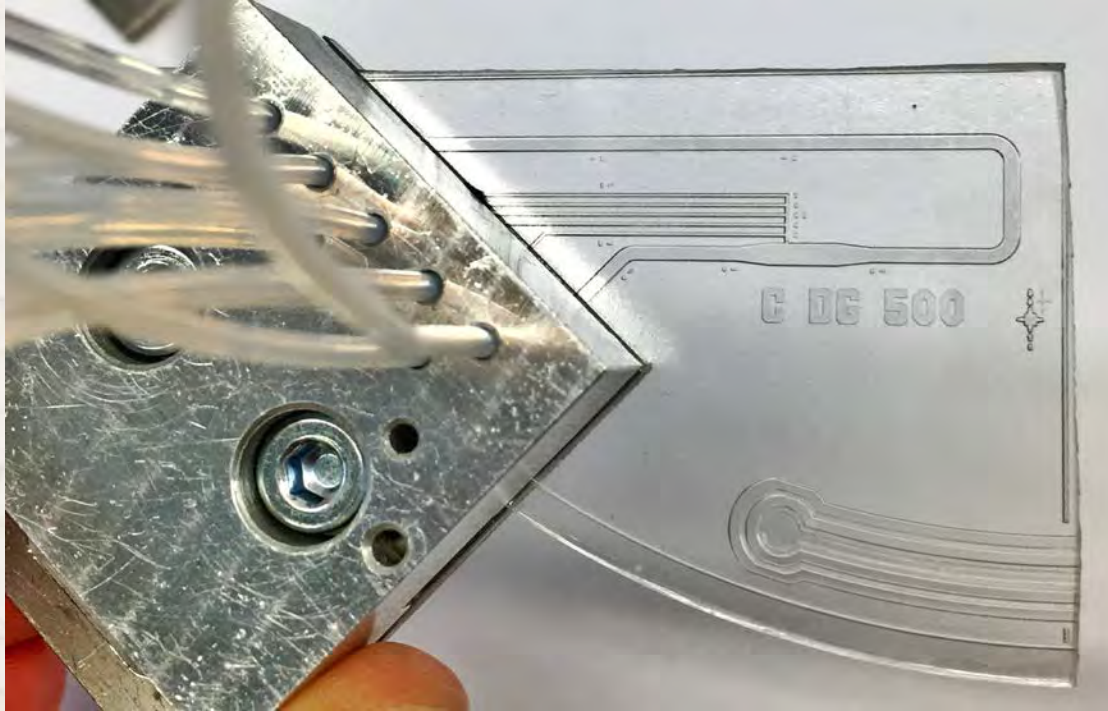
“Big” Data

¹DE 10 2009 025 007 A1 „Vorrichtung und Verfahren zur Überführung von Fluidproben in regelmäßige Probensequenzen, sowie Verfahren zur Manipulation letzterer“

Lab-Disk for kinetic screening operations



Disposable?
In general yes but...
Connectors are an Issue



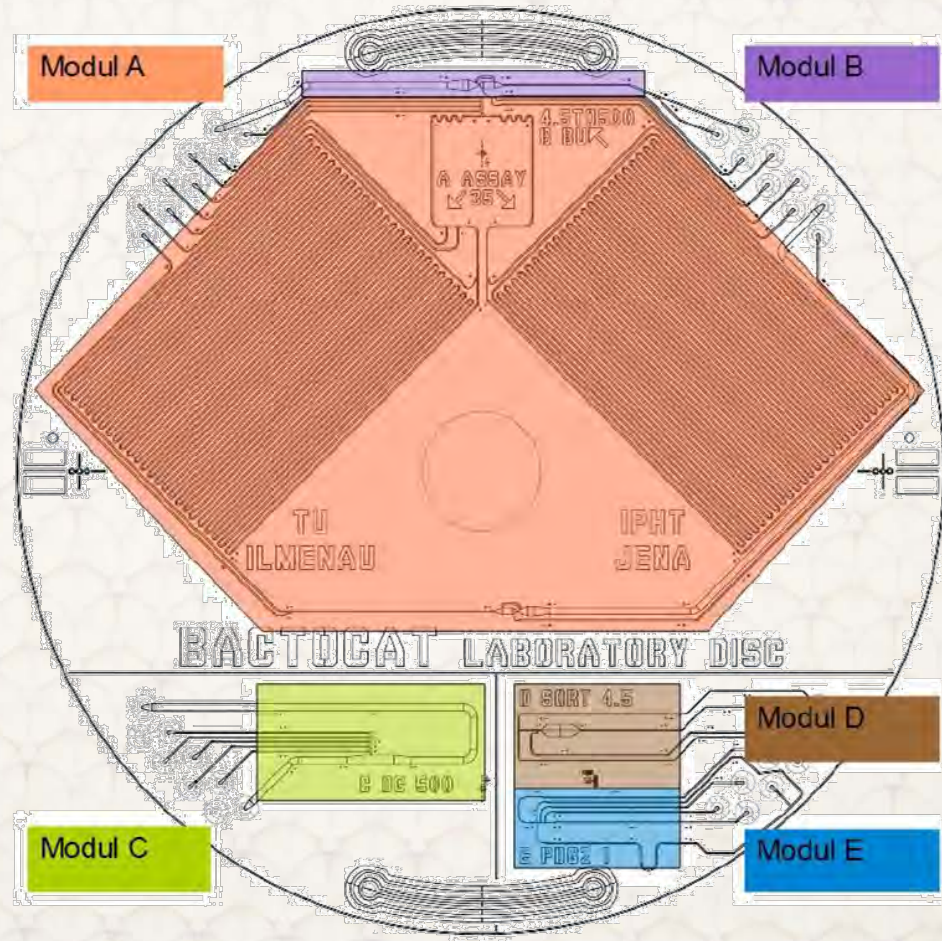
BactoCat – LabDisc

Tree Droplet volume levels:

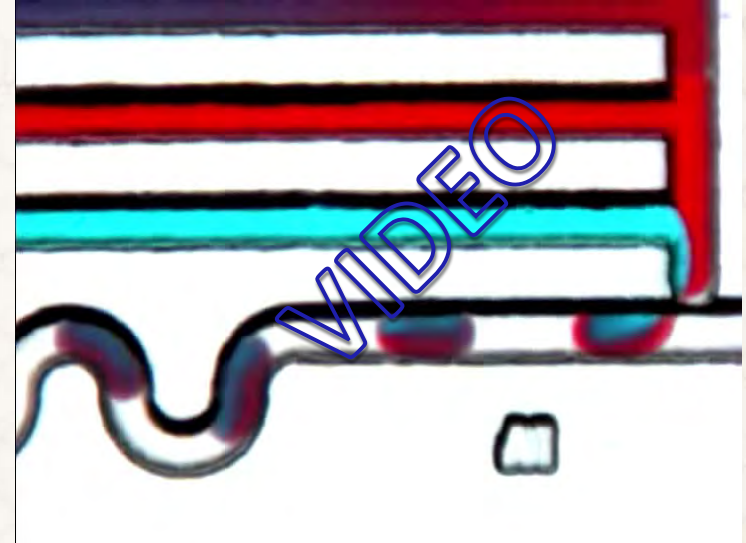
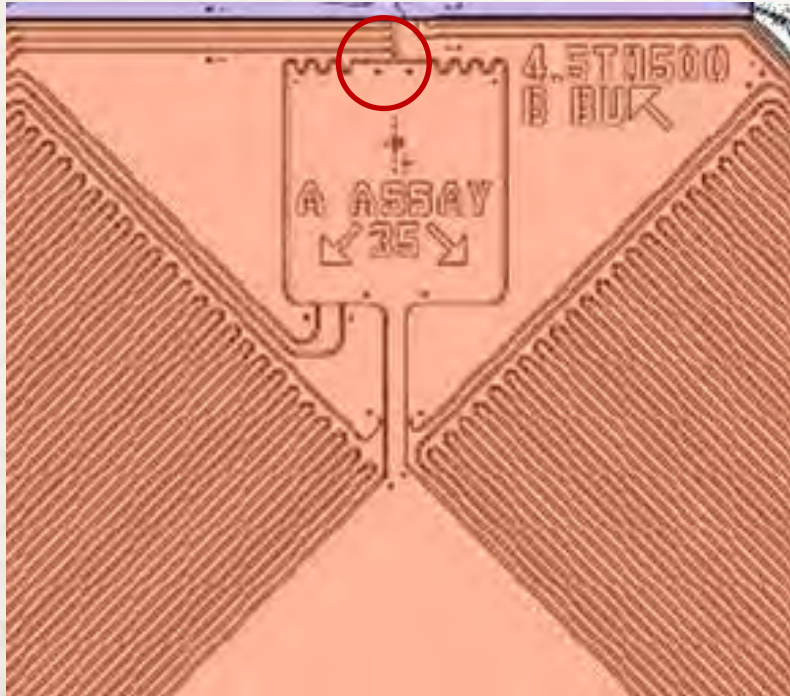
500 nL (Modul C)

35 nL (Modul A)

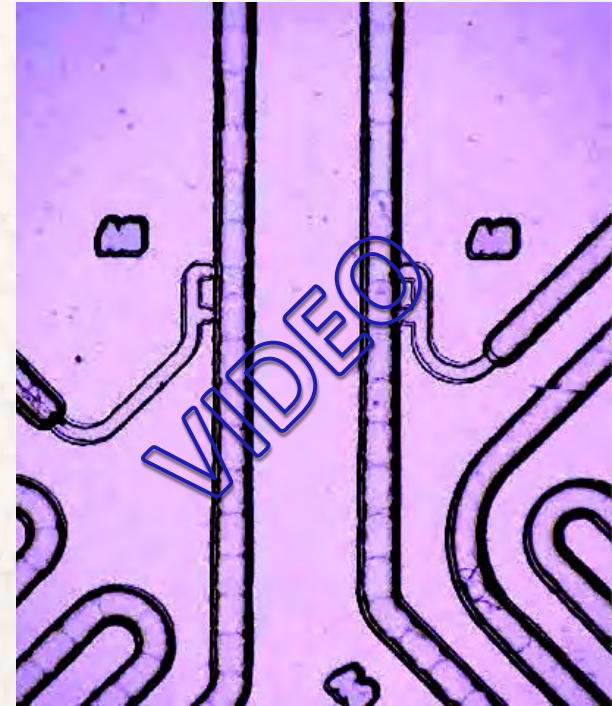
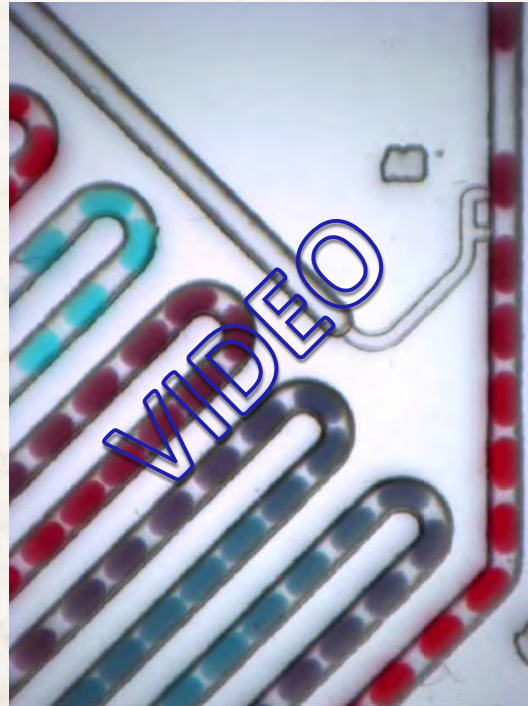
4.5 nL (Modul E)



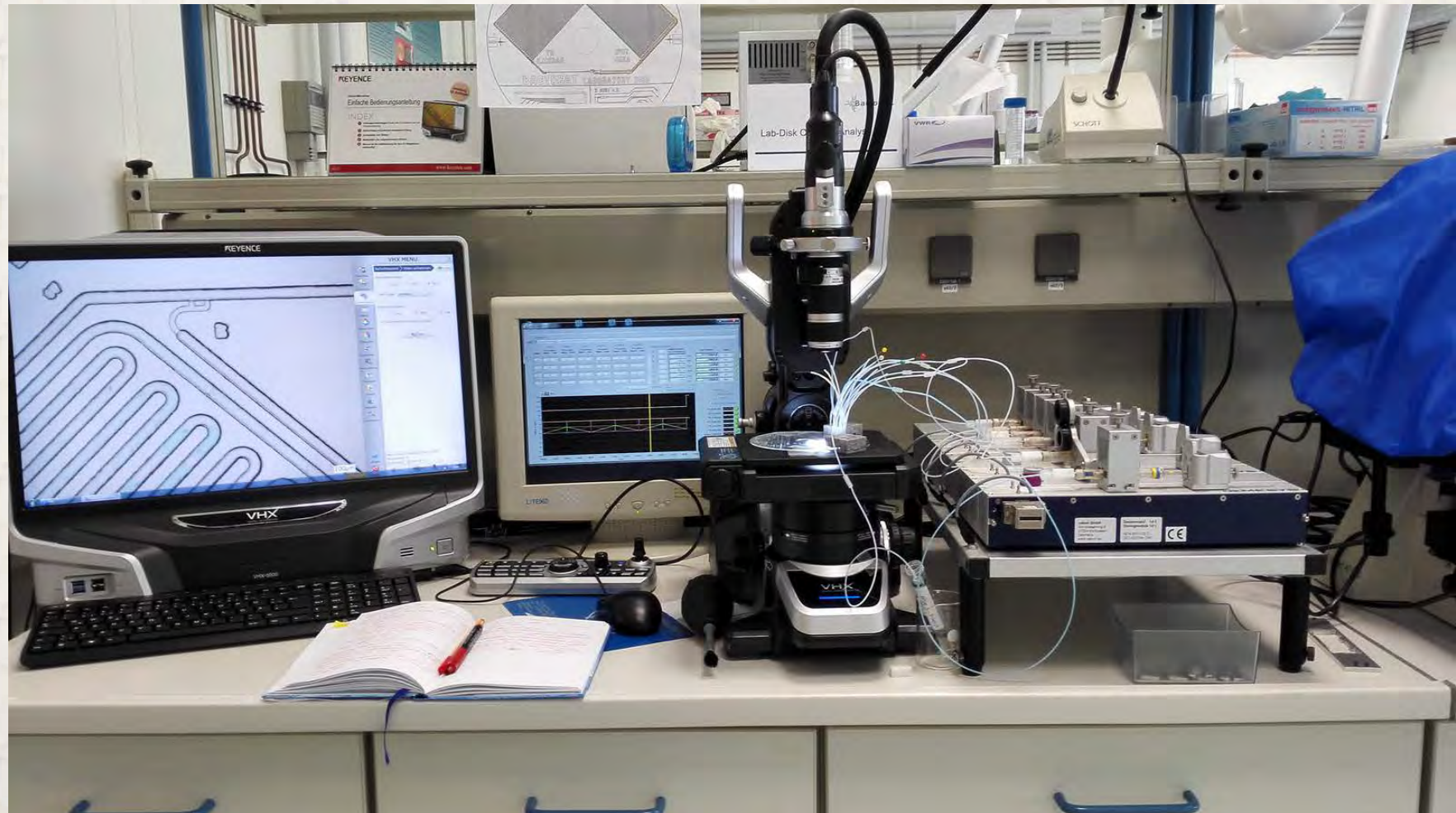
Droplet generation and storage area



Between the storage areas: drop-distance-control DDC-unit



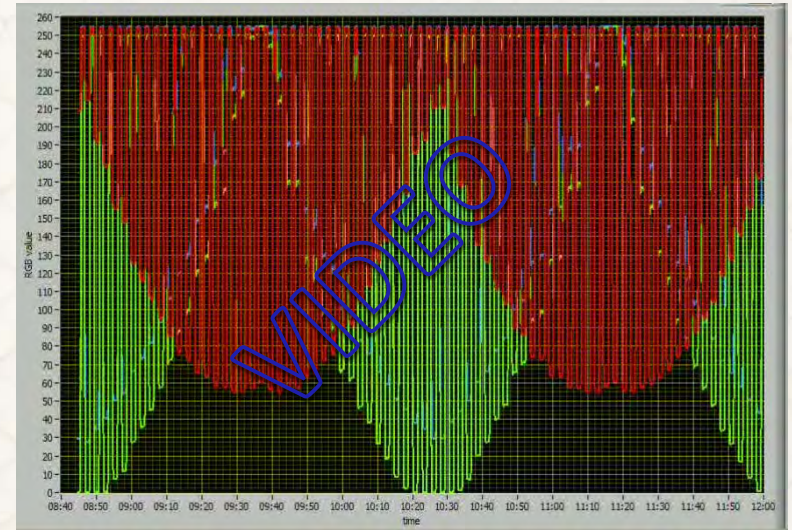
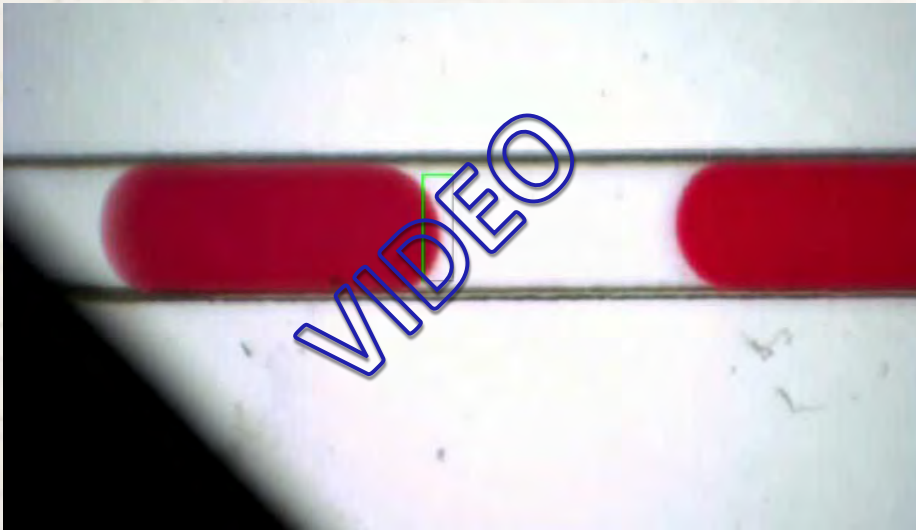
Chip in a Lab? The Chip in the Lab!



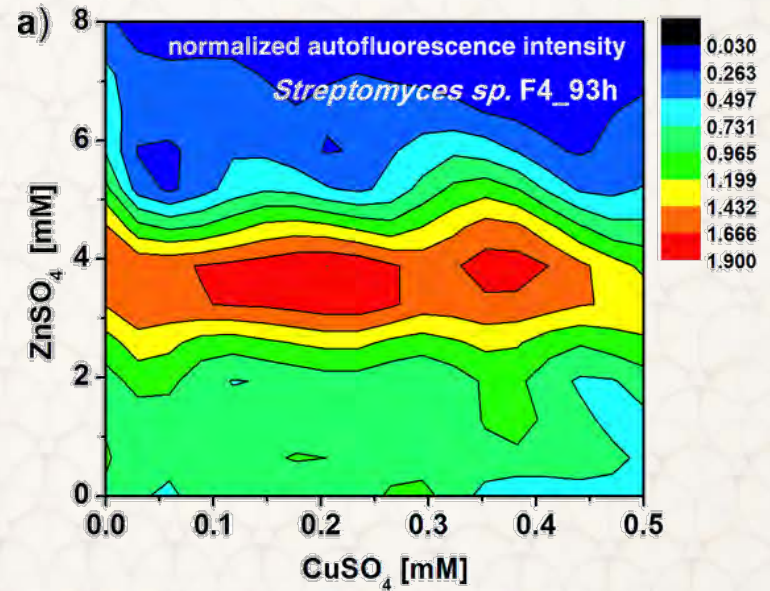
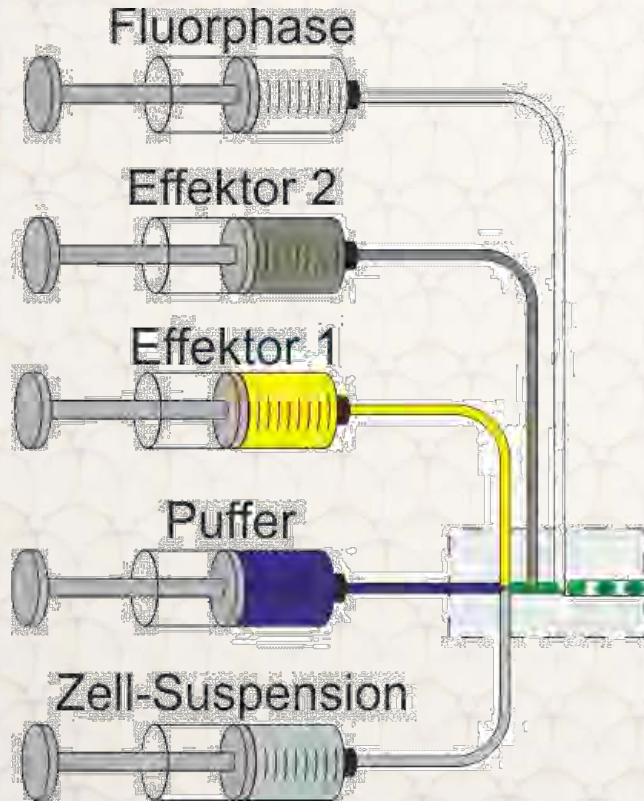
Tomar, 10 May 2017



LabDisc: Video Based Read-Out

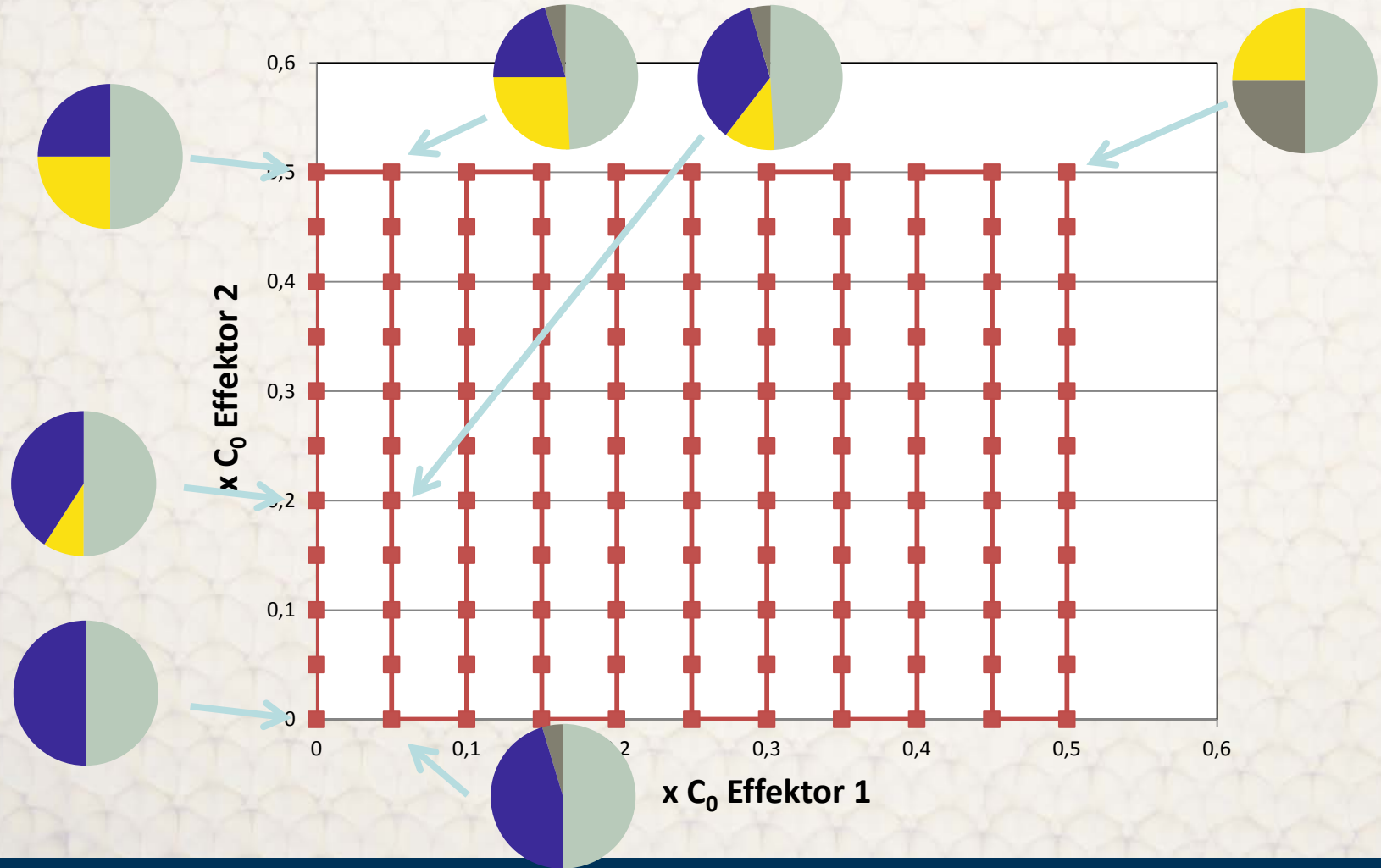


Combined effects of two noxes



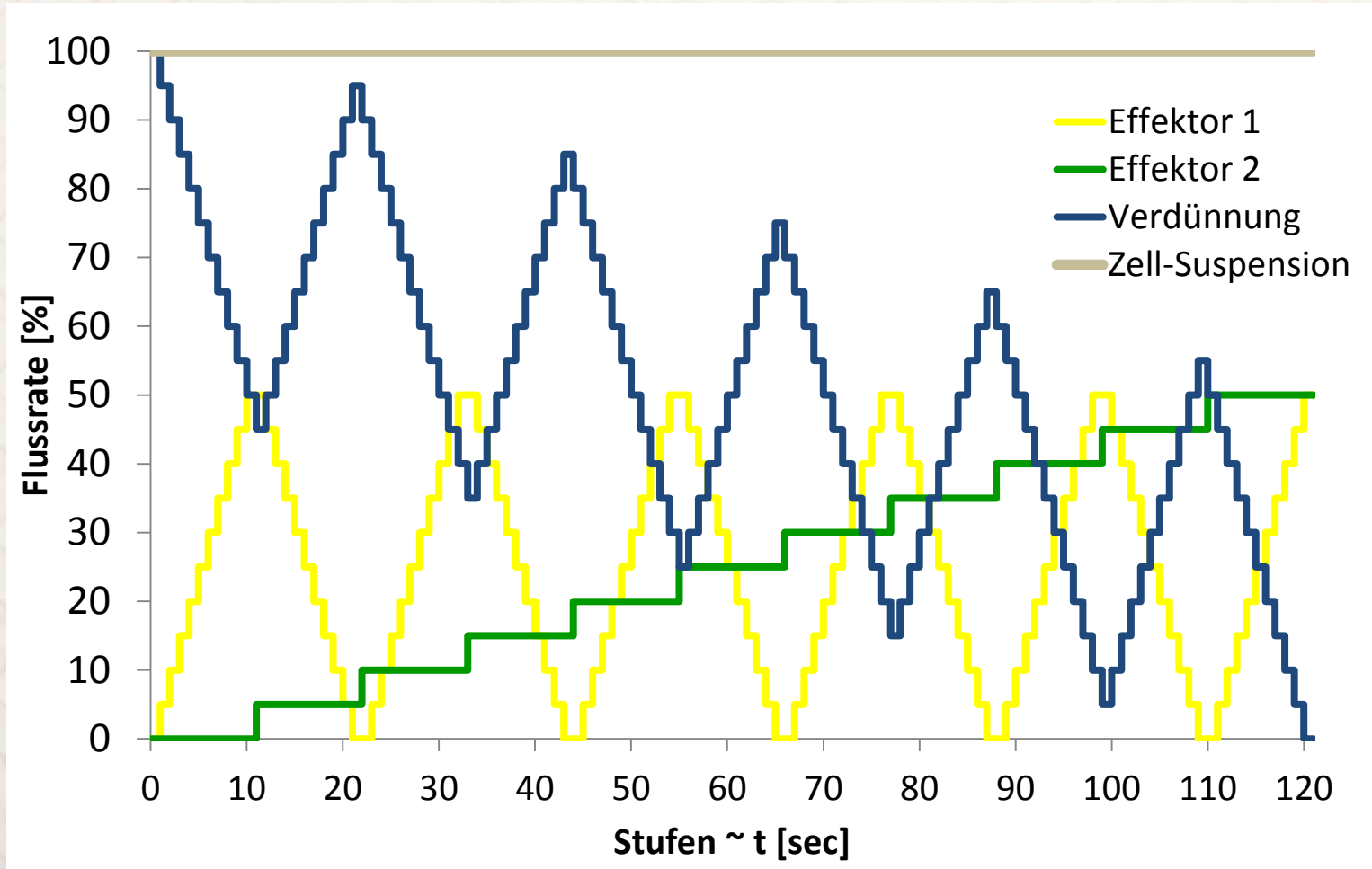
2D – Dosis / Response

Combined effects of two noxes



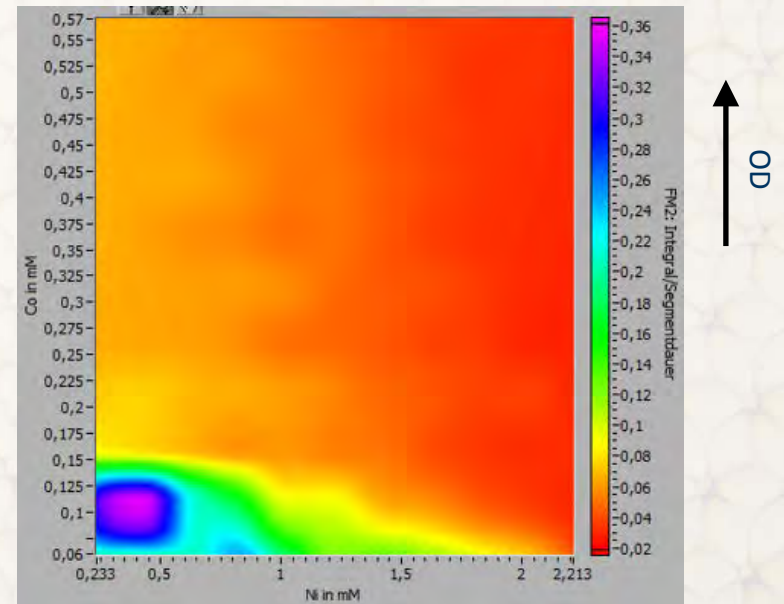
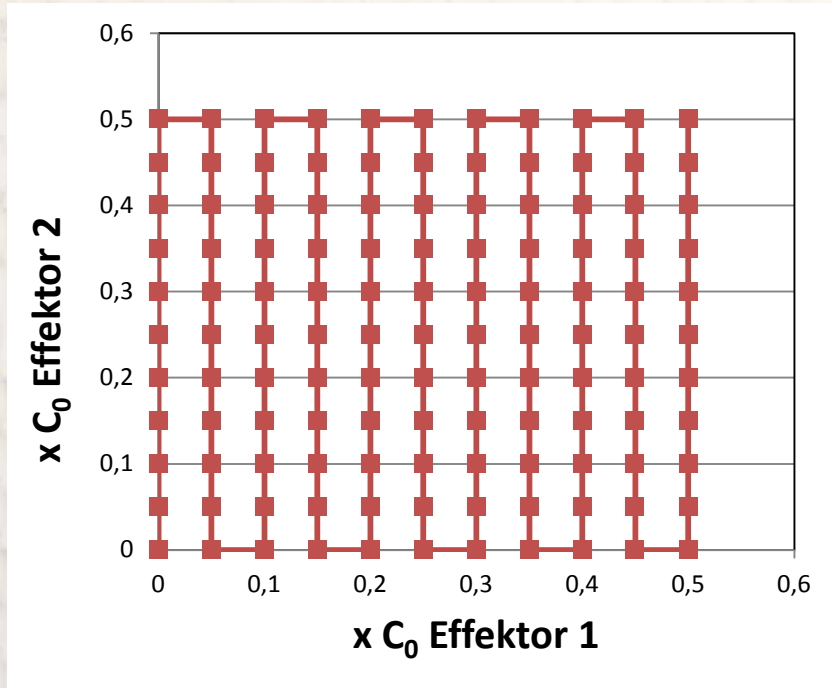
2D – Dosis / Response

Combined effects of two noxes

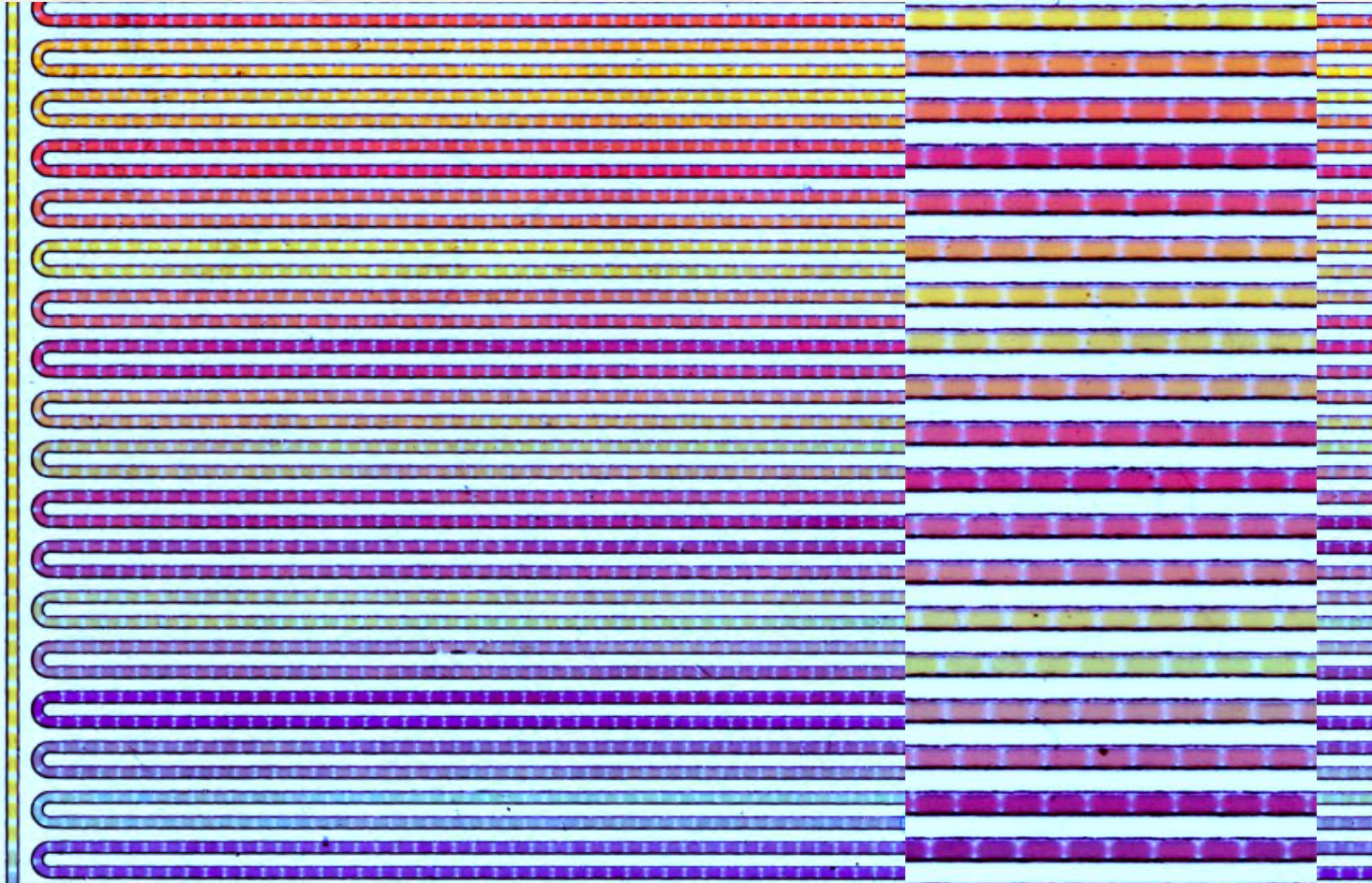


2D – Dosis / Response

Combined effects of two noxes

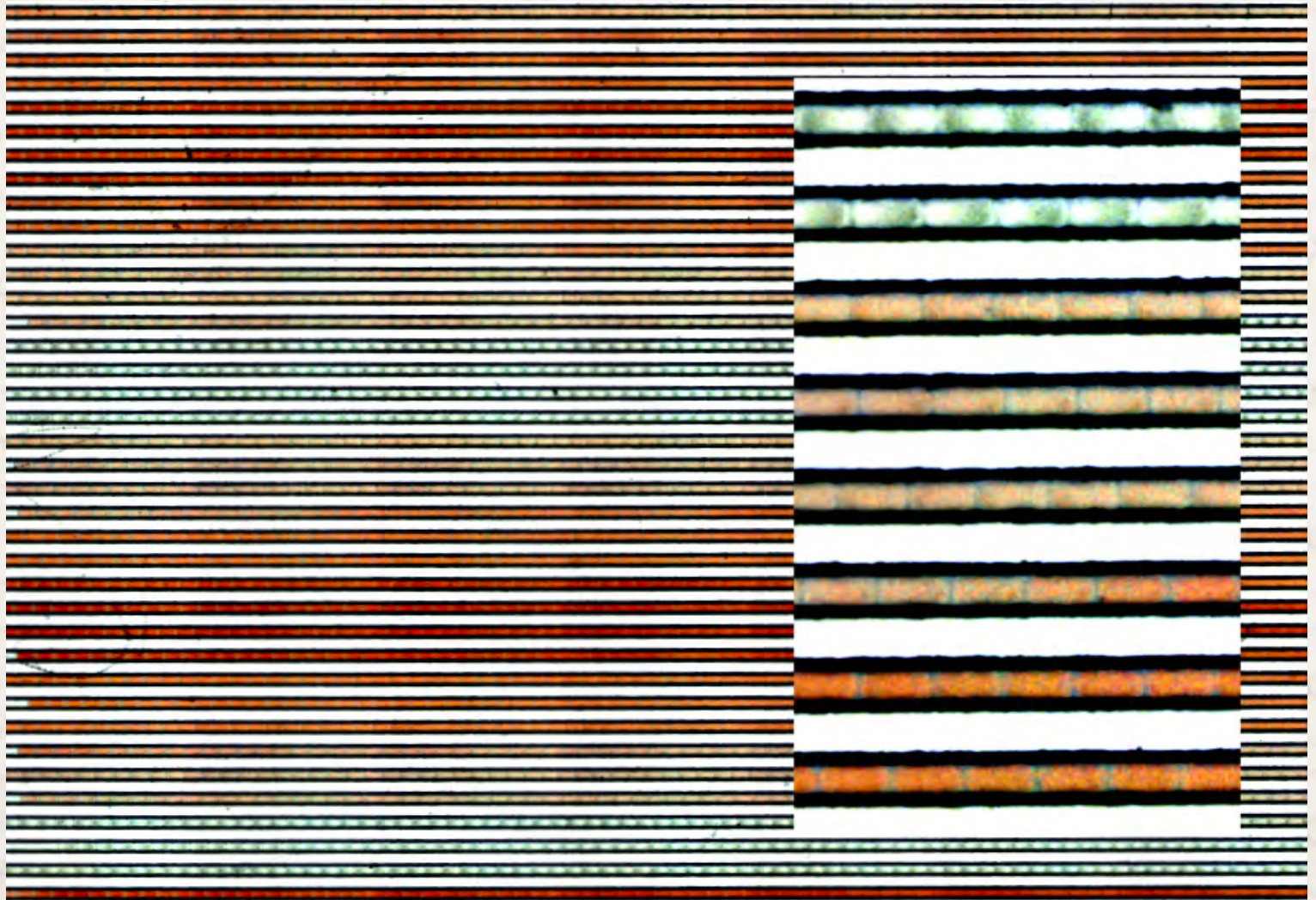


Storage array with about 5000 droplets

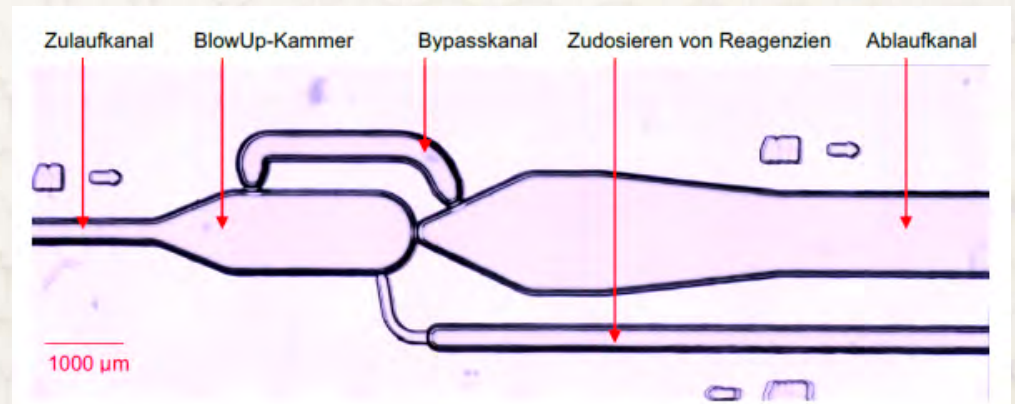
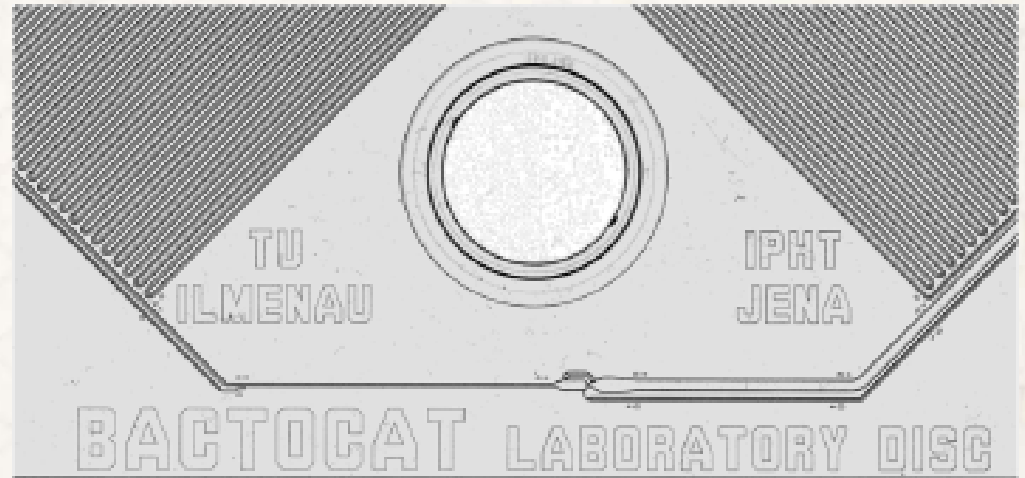
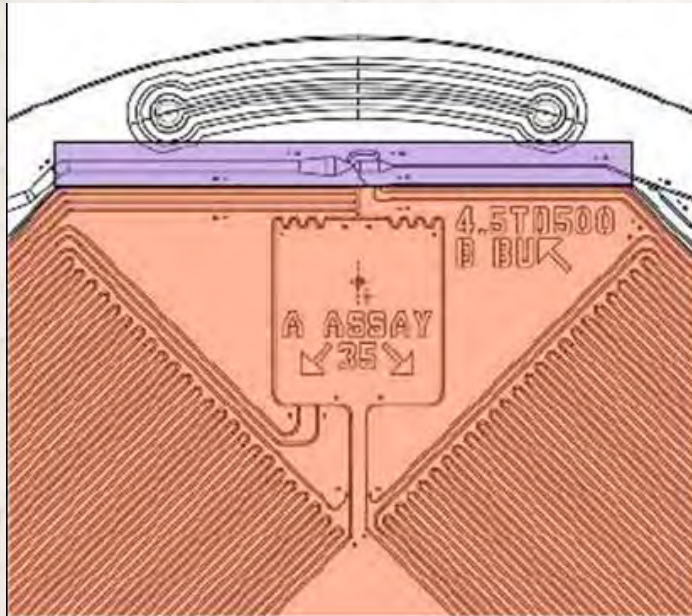


Dose-Response

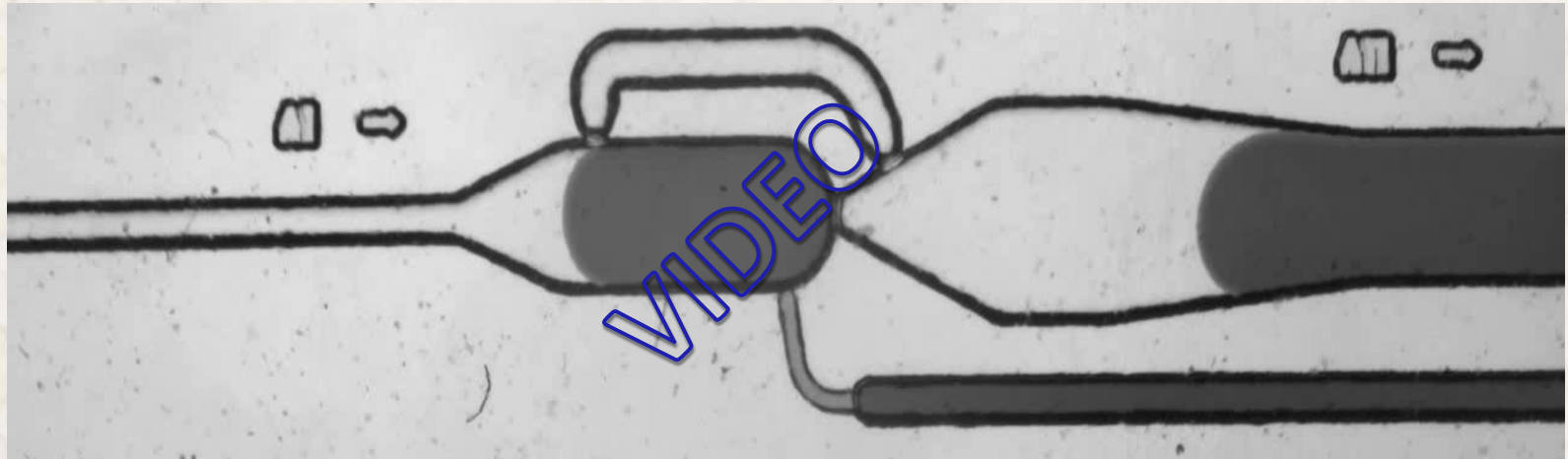
Single Droplet Dose-Response Screening (characterization of the copper tolerance of a soil bacterium (FSU Jena), S. Schneider, J. Cao et al. 2016)



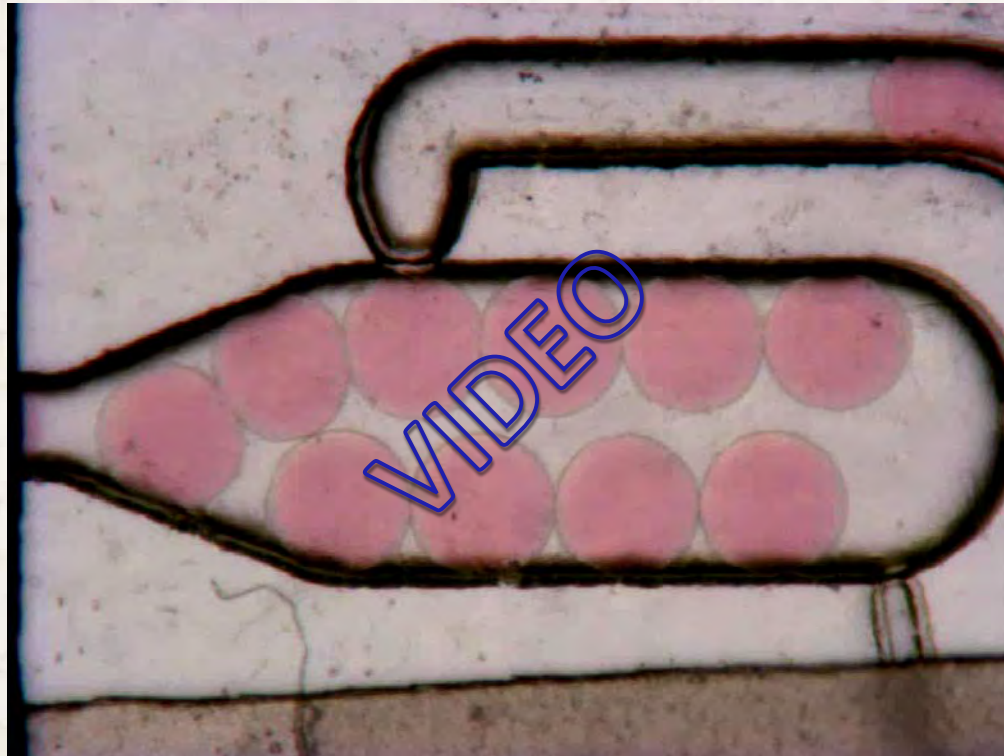
LabDisc: Blow-Up Unit



LabDisc: Blow-Up Unit Droplet generation mode

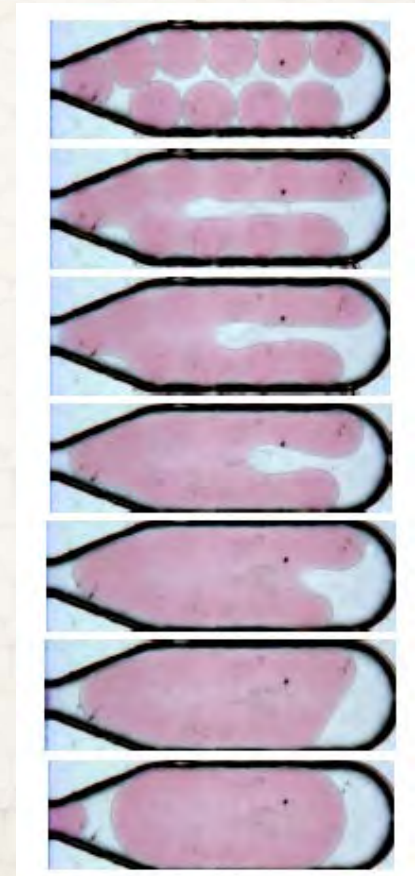
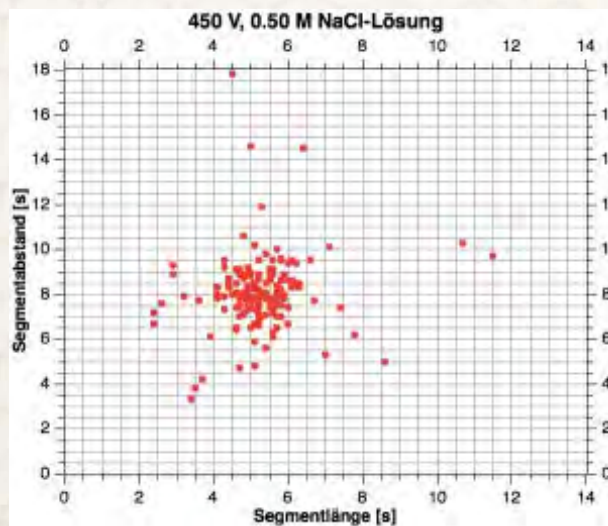
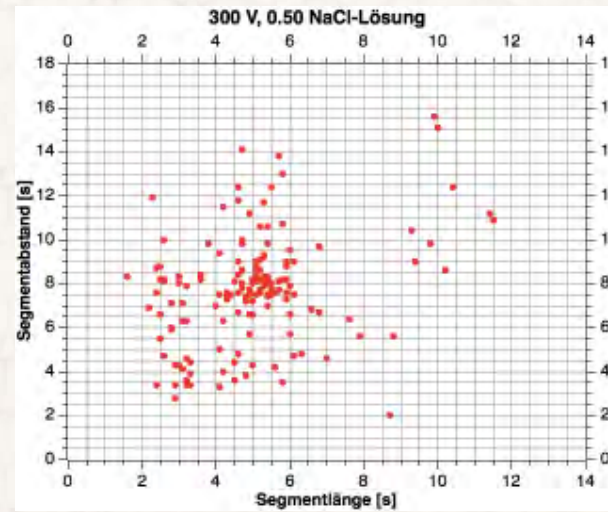
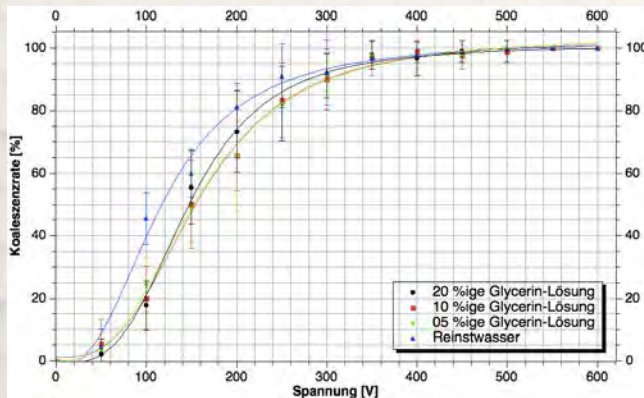
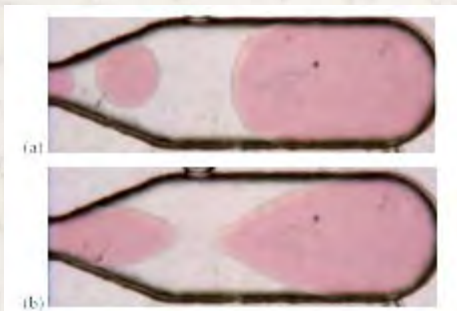


LabDisc: Blow-Up Unit Droplet coalescence Mode

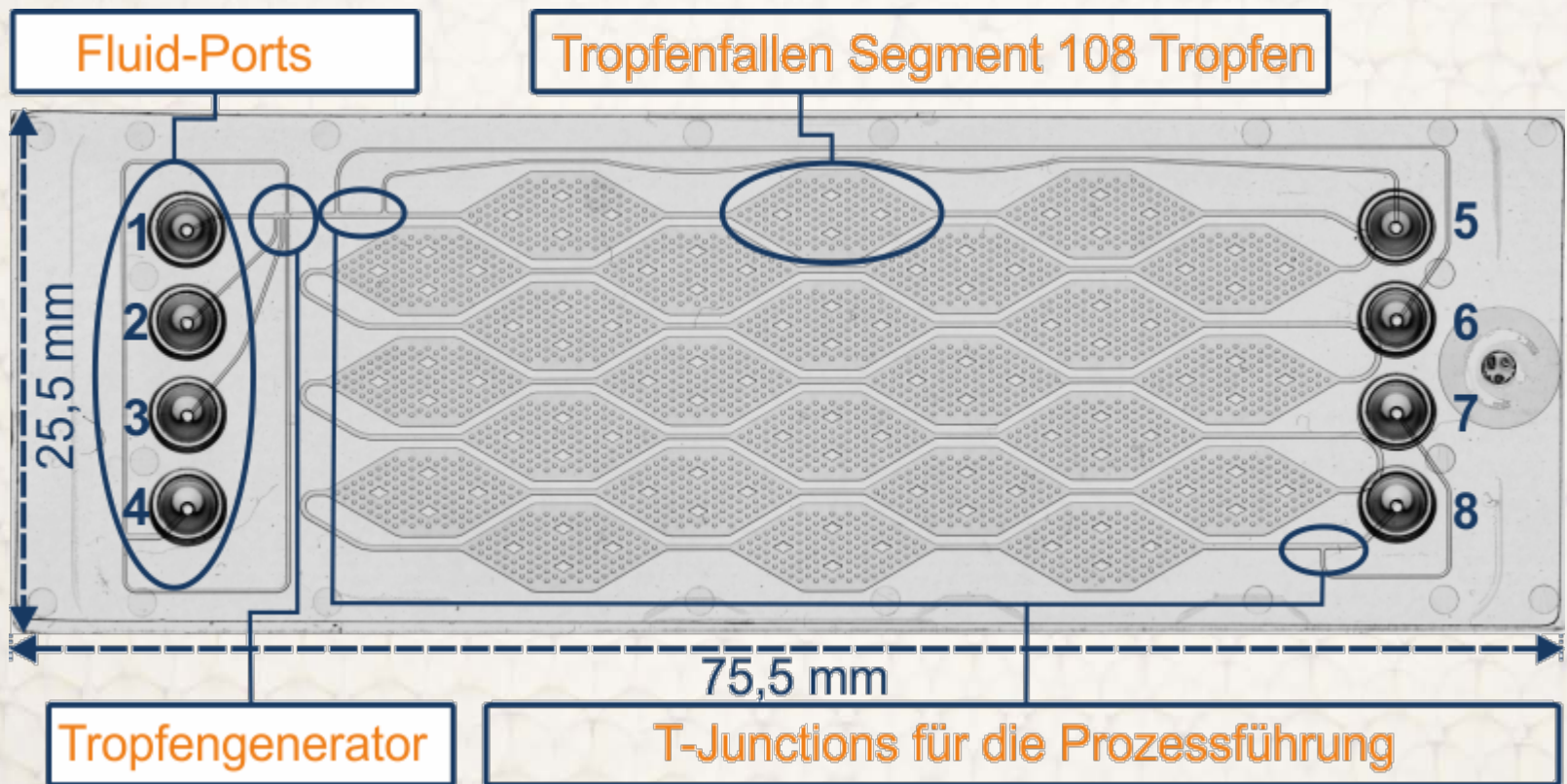


LabDisc: Droplet fusion

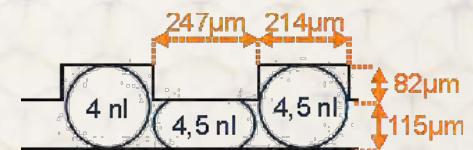
(design by M. Kielpinski,
fusion experiments by O. Walther, 2016;
Time interval (right): 500 ms)



Droplet-Trap-Array for 4.5 nL Droplets

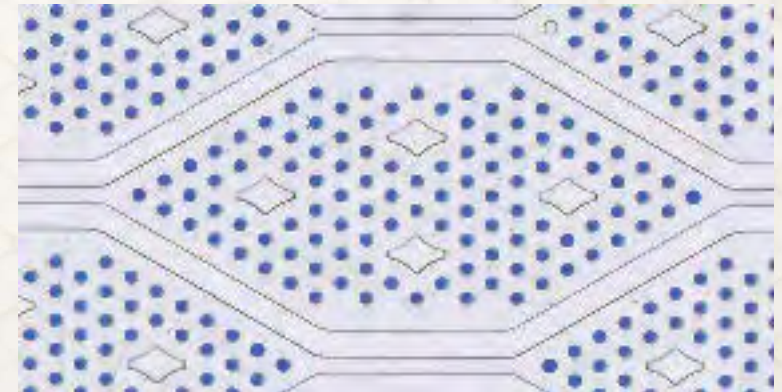
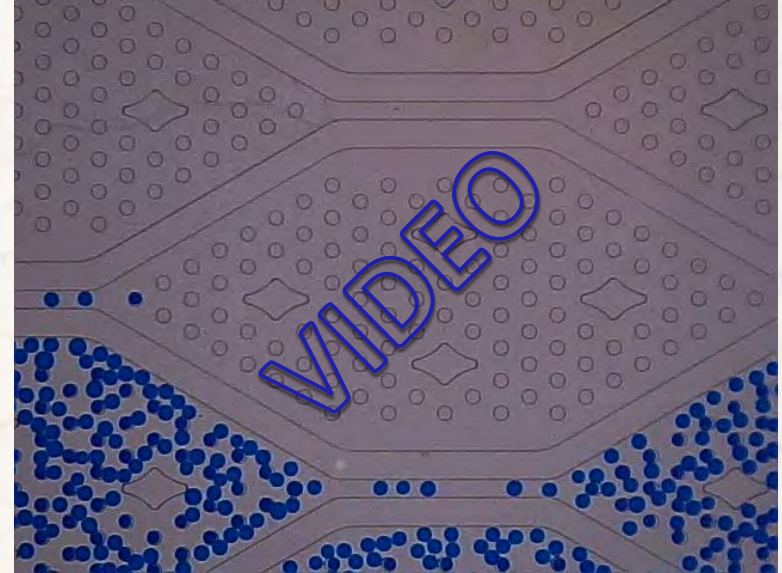
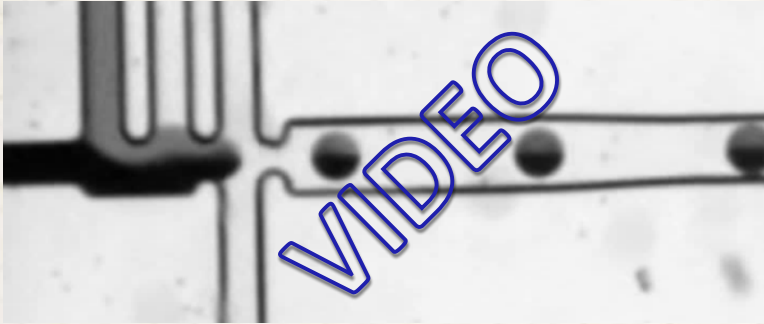


M.Kielpinski, K.Bergmann, C.Gärtner, A.Groß, J.M. Köhler, Th. Henkel, Proc. 4th Eur. Conf. on Microfluidics - Microfluidics 2014 - Limerick, December 10-12, 2014, μ Flu-14-61



Droplet Storage Array

Droplet generator

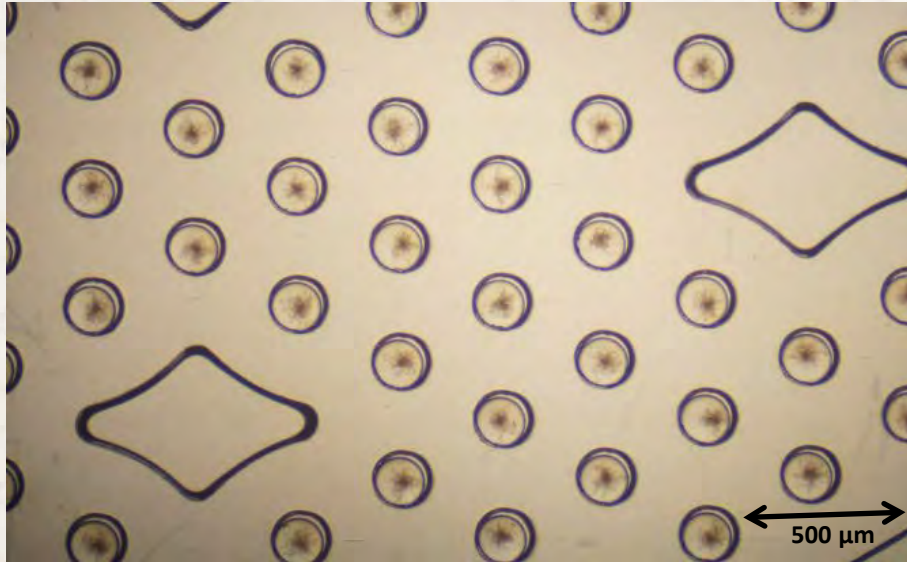


Applications:

- Stochastic pre-screening for optimized „Hit-Rates“
- Profiles for e.g. co-cultures
- Long-term incubation
- Morphology

Droplet Storage Array

Co-Kultivierung

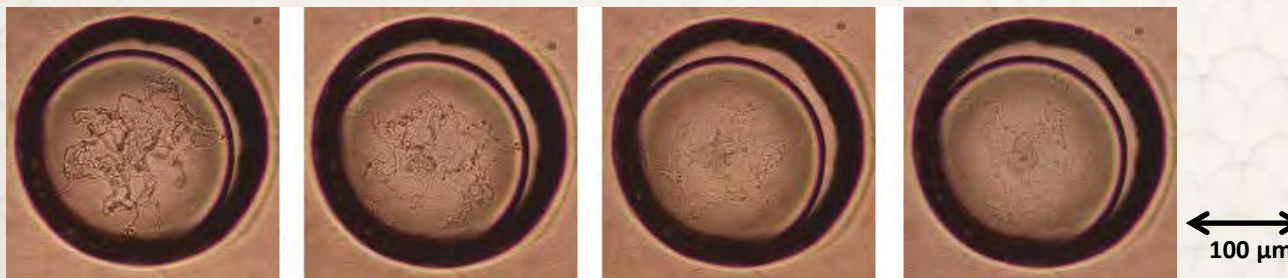


Readout Image-Analyse:

- Auflicht- / Durchlicht- / Dunkelfeld-Mikroskopie
- Fluoreszenz-Imaging

Ergebnisse:

- Langzeitkultivierung
- Co-Kultivierung
- Stressinduzierte Morphologie-Studien
- Statistische Analysen von Bodenproben



4 Tage

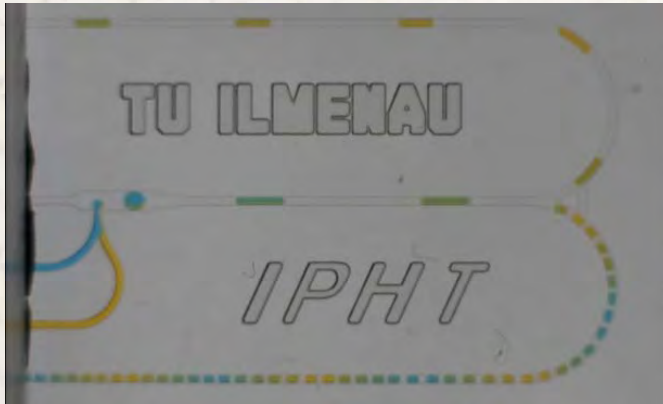
7 Tage

21 Tage

56 Tage

New Technology based on Compartmentalized Processing

**Droplet Based
Screening / Optimization
Process Development**



**Compartmentalized
Production**

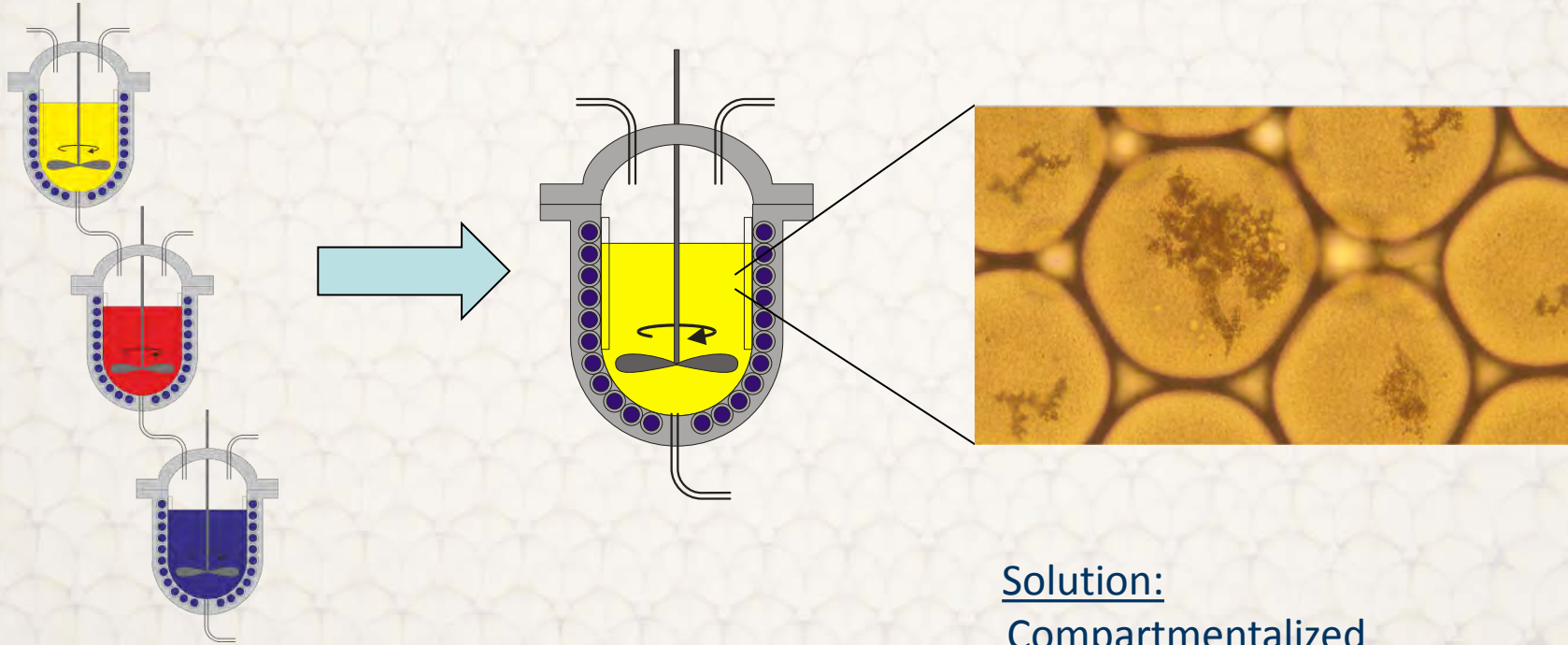


Drop to Production?

Reduced Time to Market?

New Processes using Compartmentalized Technology?

Multiple Step / Multiple Strain Processing?



Issues:

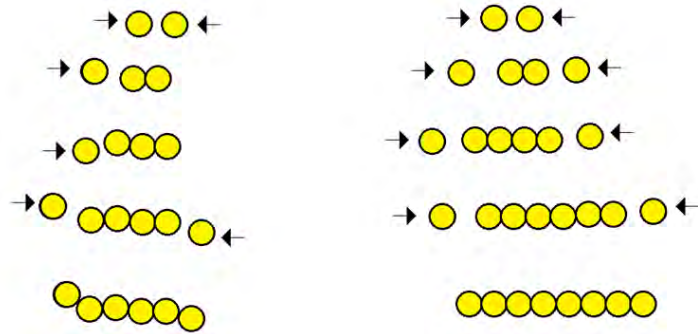
- Process Control ??
- Media ??
- Reproducibility ??

Solution:

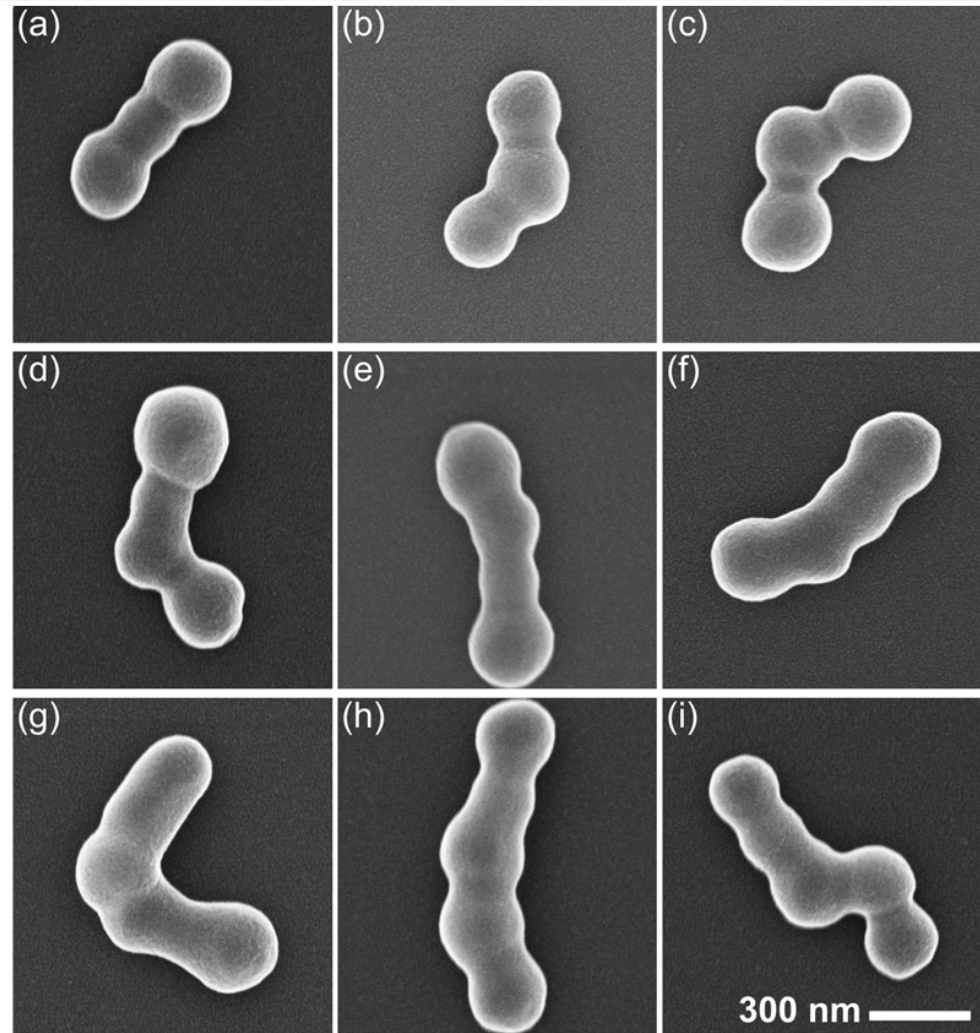
Compartmentalized Reaction Containers:

- Emulsions
- Capsules
- Solid Carrier Partikels

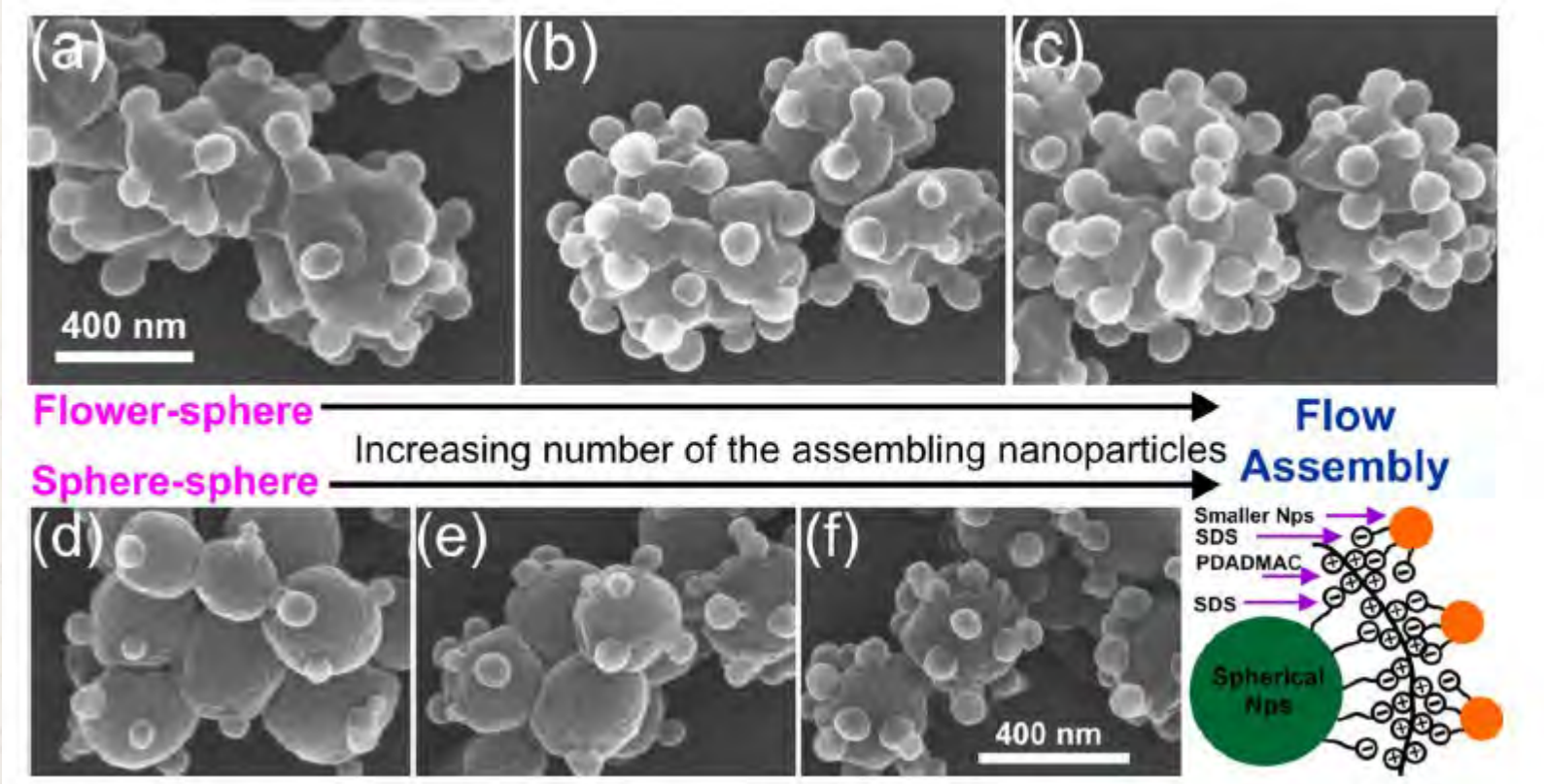
Microfluidics Particle Formation / Aggregation



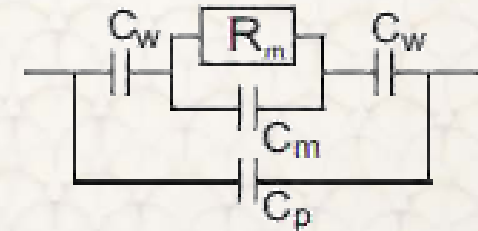
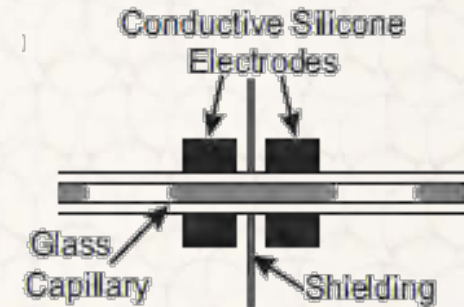
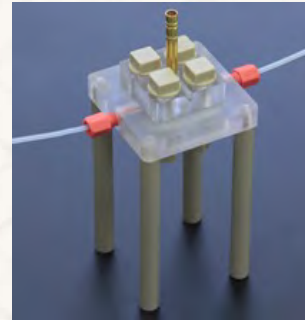
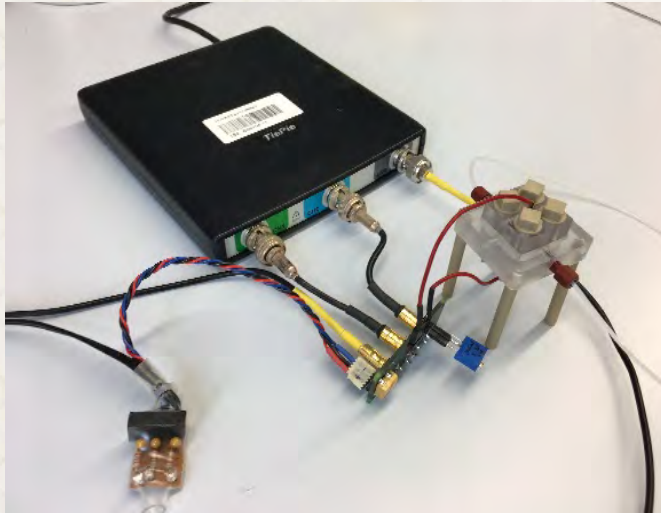
Concept of guiding spherical particles to the ends of a rod-like or necklaces-like assembly for linear growth of the nano necklaces interpreted by the model of "limited polarizability" caused by adsorbed polyelectrolyte molecules.



Microfluidics Particle Formation / Assemblies



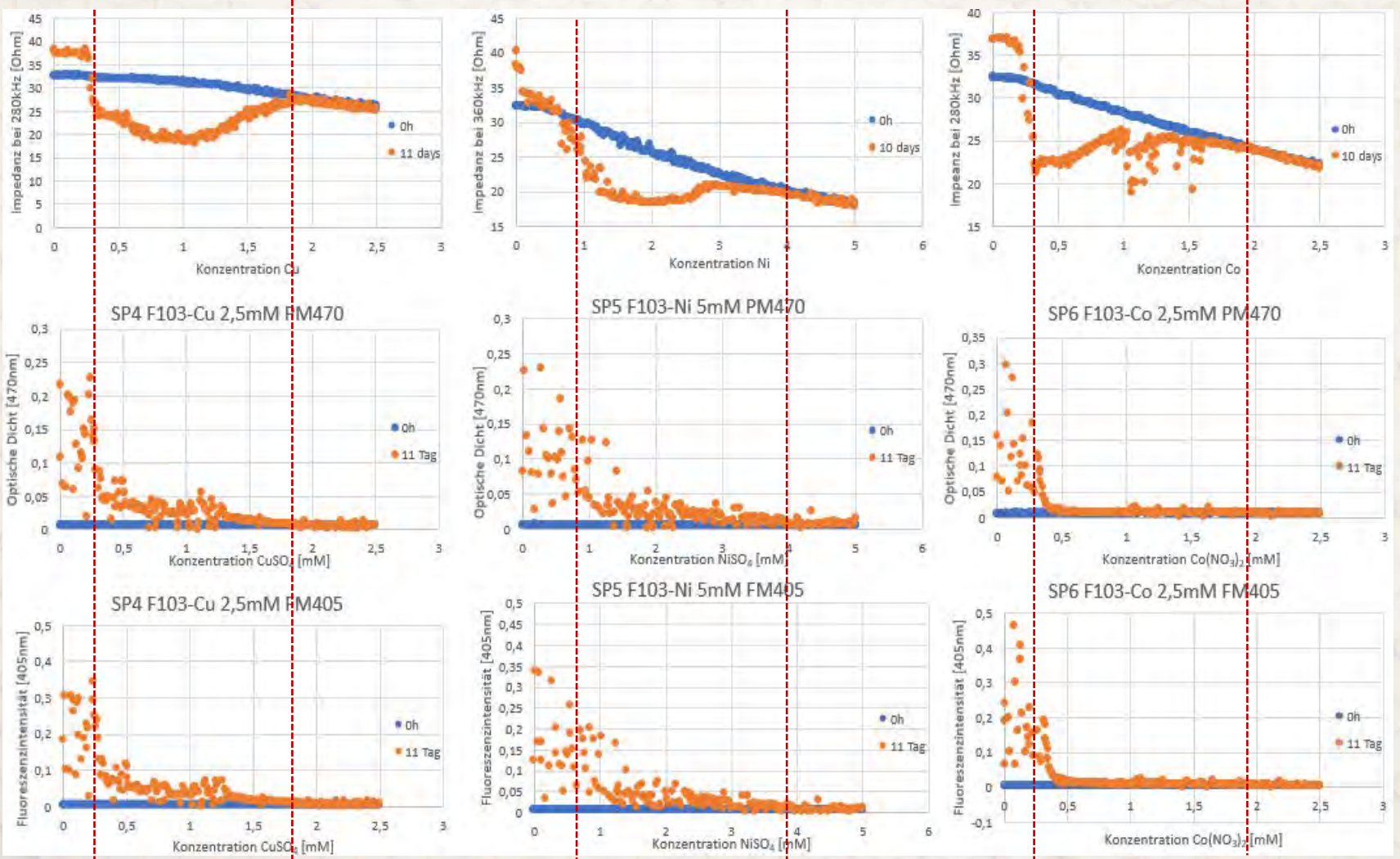
Impedance Sensor

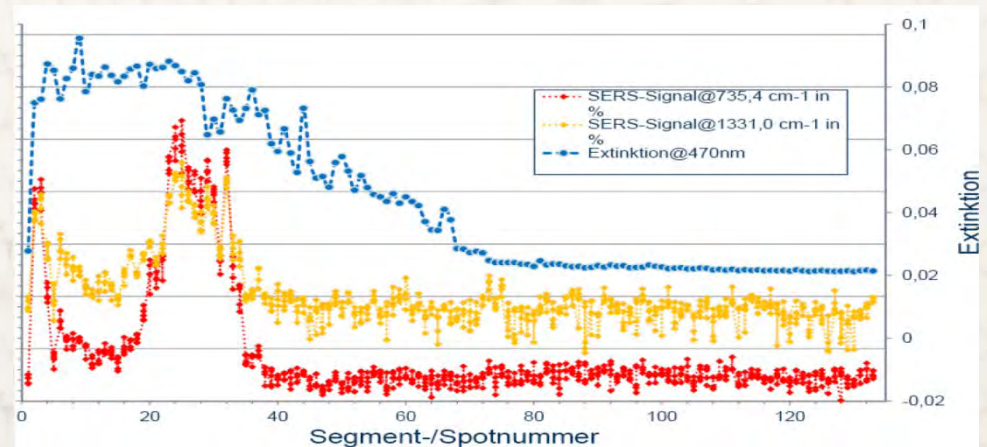
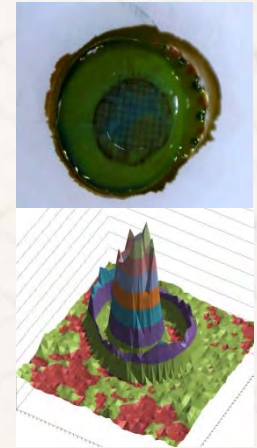


$$Z(\omega) = \frac{2 + j\omega R_m(C_w + 2C_m)}{j\omega(C_w + 2C_p - \omega^2 R_m(C_m C_w + C_p C_w + 2C_p C_m))}$$

- Z: Impedanz aufgrund der Frequenz
- j: Die imaginäre Einheit aufgrund der Phasenwinkel
- w: Kreisfrequenz
- C_m: Kondensator des Medium
- C_w: Kondensator von Glaskapillare-Wand (Isolate)
- C_p: Begleitende Kondensator von Kabel und elektroden
- R_m: Widerstand des Mediums

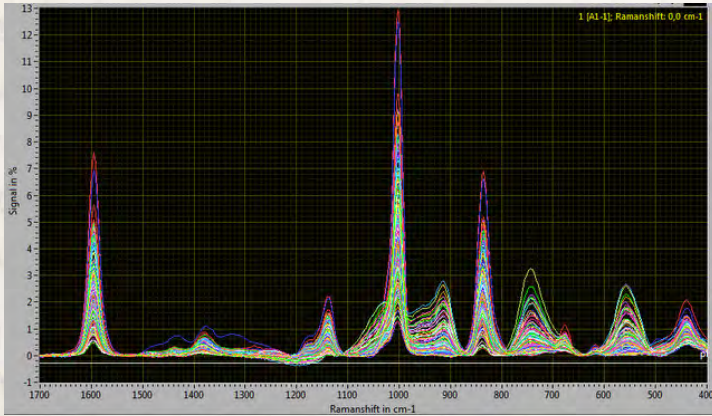




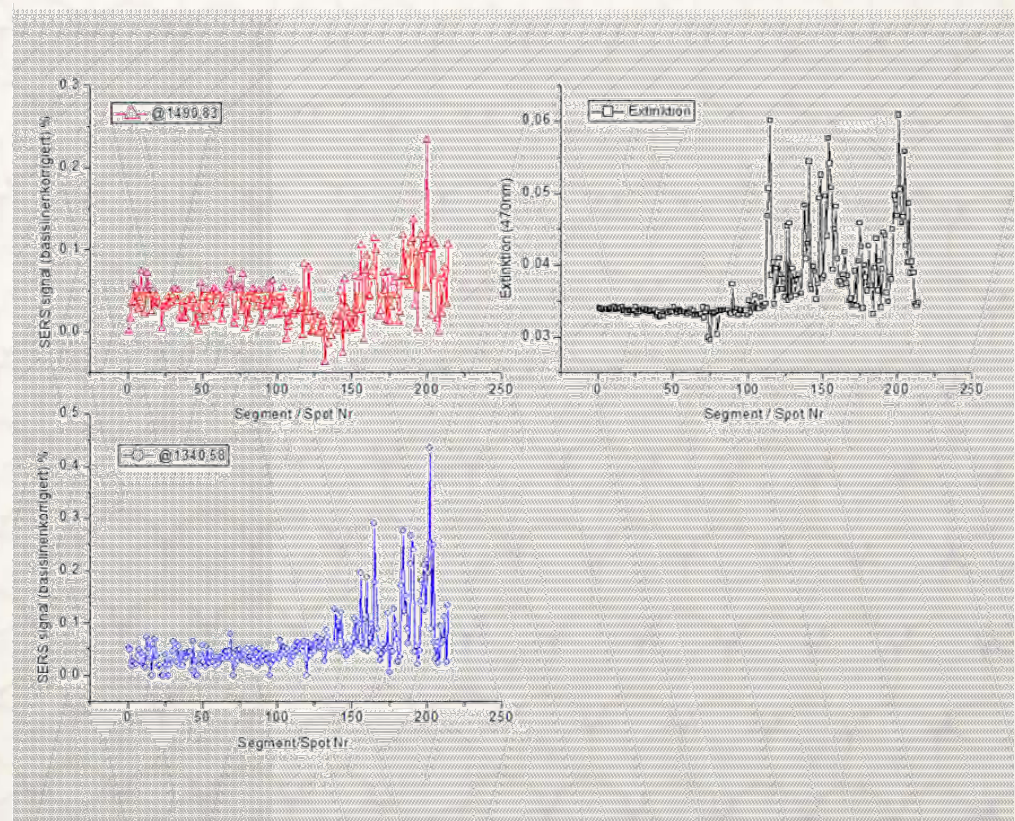


SERS-Messung: Riboflavin

Bacillus subtilis: 28 Tage

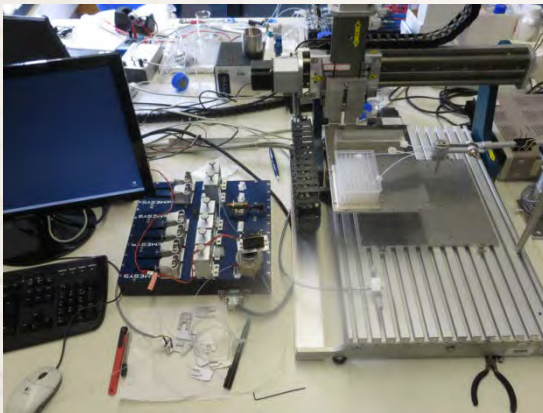


Ramanspektren einer Sequenz aus 214 Segmente



Droplet Aspiration Tool – The missing link

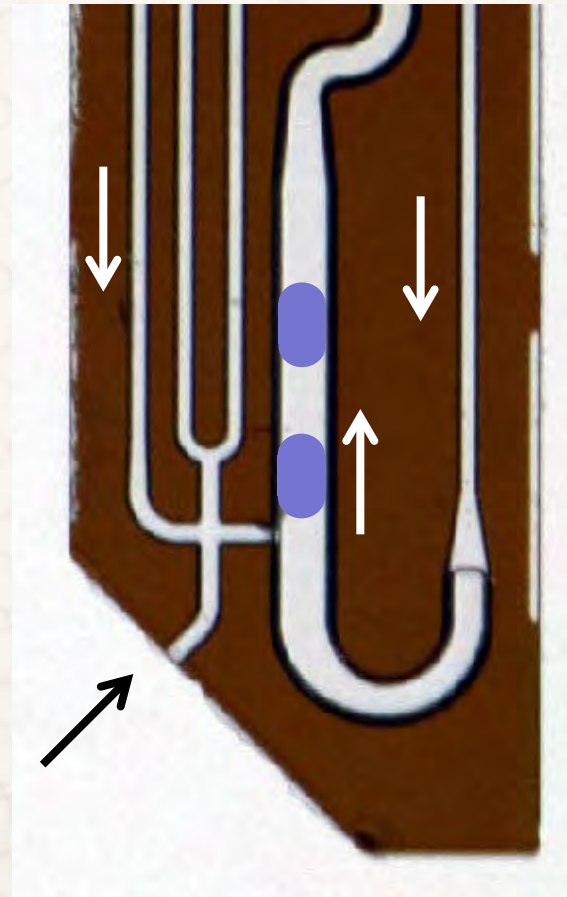
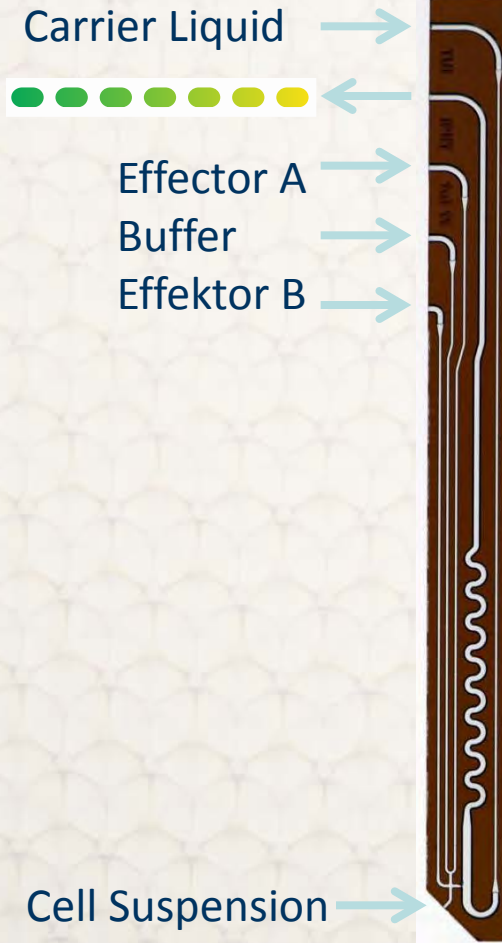
Interface between MTP & Droplet Based Processing



Example: 2D-Droplet Take-up

Droplet Aspiration Tool

Loop-System



TUI_13



TUI_11

Acknowledgments



FKZ: 031A161A



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ILMENAU

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Andrea Knauer
Christian Bock
Oliver Walter
Lin Yang



Dr. Thomas Henkel
Mark Kielpinski



Gunter Gastrock
Brian Cahill



Dr. Steffan Loebecke
Dr. Dusan Boskovich
Alexander Mendl



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