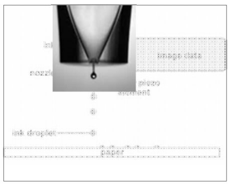
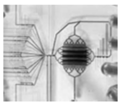
LOSCHMIDT LABORATORIES

6. Microfluidics – „Lab on a Chip“

Microfluidics

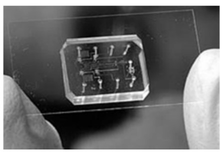
- developed in the 1980s (IBM)
- **multidisciplinary field**
  (engineering, physics, chemistry, material science, nanotechnology)
- **integrate processes on chip**
  - miniaturization
  - full automation
  - high throughput
  - low energy consumption
  - low sample consumption
  - less waste production



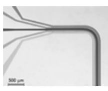


Microfluidics

- **narrow channels**
  (mm, μm)
- **extremely small volumes**
  (nL, pL, fL)



- **micro domain** differs greatly from macroscopic fluids:
  - surface tension
  - capillary forces
  - fluidic resistance
  - fast thermal relaxation
  - laminar flow
  - diffusion

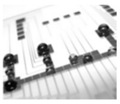


Microfluidic designes

- **continuous-flow microfluidics**
  manipulation of continuous liquid flow through microfabricated channels

- **droplet-based microfluidics**
  manipulating discrete volumes of fluids in immiscible phases

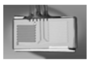
- **digital microfluidics**
  droplets manipulated on a substrate using electrowetting



Lab on a Chip (LOC)

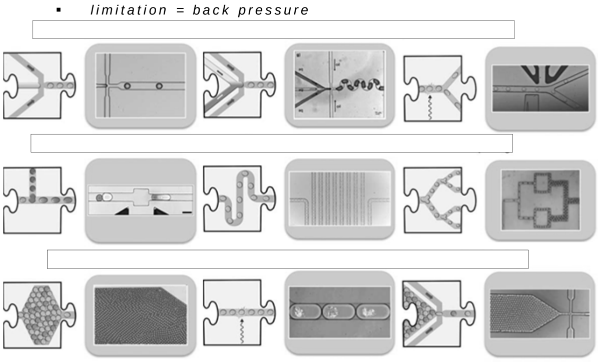
- **integration of laboratory assays on a chip**
  - sample preparation
  - sample treatment
  - detection

- **life science applications**
  - molecular biology
  - diagnostics
  - sequencing
  - DNA analysis
  - proteomics
  - clinical studies



Lab on a Chip (LOC)

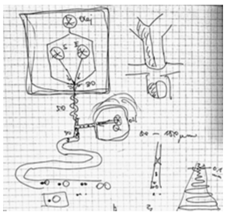
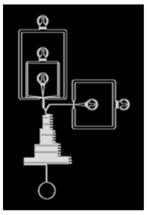
- **large variability** of designs in LOC toolbox
  - *limitation = back pressure*



Chip design and manufacturing

DESIGN

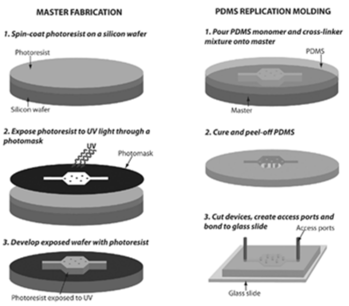
- **design** softwares (e.g., AutoCAD, DraftSight)
- printing the **mask**

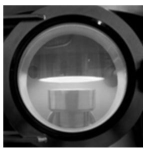
Chip design and manufacturing

FABRICATION

- soft photolithography



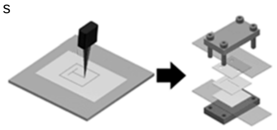


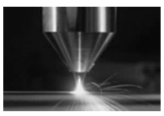
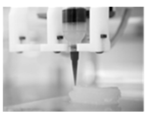
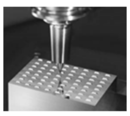


Chip design and manufacturing

FABRICATION

- direct fabrication methods
  - laser cutting
  - 3D printing
  - CNC micro-milling



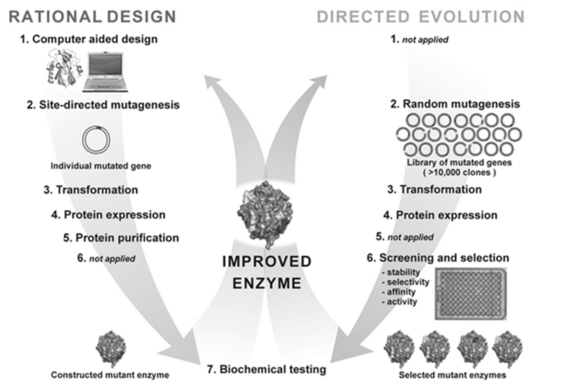




Example of LOC application

1. **DIRECTED EVOLUTION IN μDROPLETS**
2. **DRUG SCREENING IN CAPILLARY**
3. **TRANSIENT KINETICS ON CHIP**

- **small volume** → low sample consumption
- **small design** → low demand for lab space
- **fast operation** → high throughput, fast kinetics

1. Evolution in μDroplets

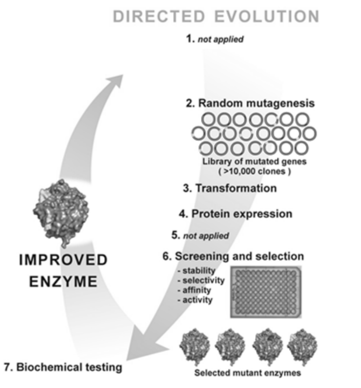


1. Evolution in μDroplets

volume: 10´ mL
assays/day: 10´

volume: 100´ μL
assays/day: 1000´

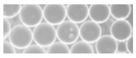
volume: 10´ pL
assays/day: 1 000 000´

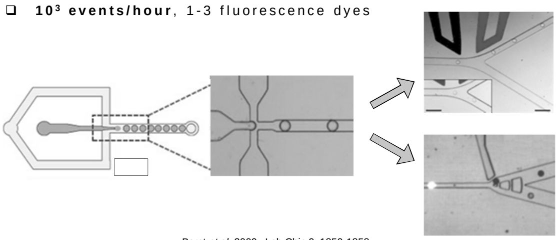


1. Evolution in μDroplets

- **monodisperse emulsion**

  (50 pL, 10^7 droplets/hour)
- **on-chip fluorescence-activated droplet sorting** (FADS)
- dielectrophoresis, membrane valves, laser manipulation
- **10^3 events/hour**, 1-3 fluorescence dyes



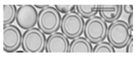


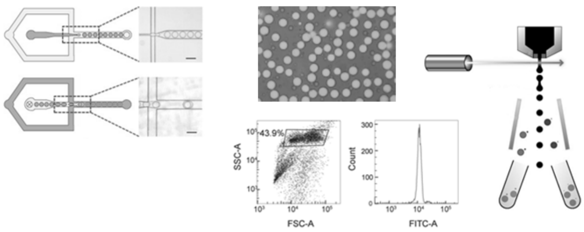
Baret *et al.* 2009. Lab Chip 9: 1850-1858
Abate *et al.* 2010. Appl. Phys. Lett. 96: 203509

1. Evolution in μDroplets

- **monodisperse double emulsion**

  (2 pL, 10^7 droplets/hour)
- **off-chip fluorescence-activated cell sorting** (FACS)
- **10^8 events/hour**, 8-12 fluorescence dyes

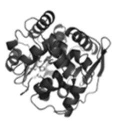


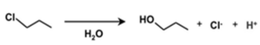


Lim *et al.* 2013. Lab Chip: Advance Article

1. Evolution in μDroplets

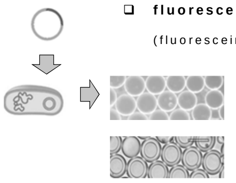
- **engineering of dehalogenase activity**

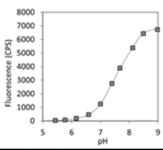


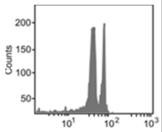


- large library (>10^6) in **double emulsion**
  - **fluorescence based activity assay**

    (fluorescein, rhodamine)

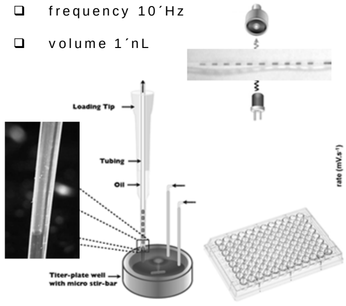


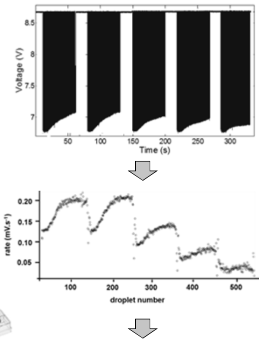




2. Drug screening in capillary

- **high throughput** generatio of droplets (**10^3 assay/day**)
- combinatorial measurements
- concentration gradients
- frequency 10´Hz
- volume 1´nL





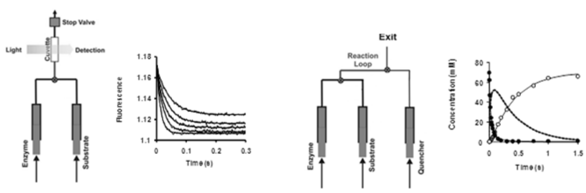
K_m, k_{cat}, K_i

3. Kinetics on chip

- **RAPID MIXING TECHNIQUES**

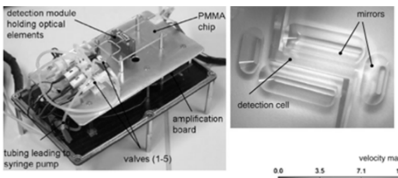
STOPPED-FLOW

RAPID-QUENCH

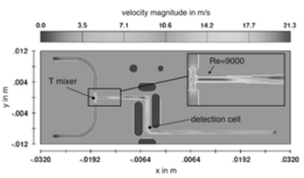


3. Kinetics on chip

- **continuous-flow microfluidics**



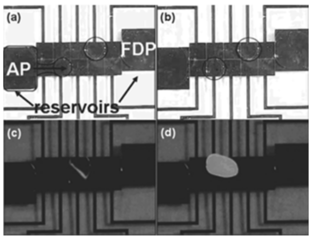
- **dead time 8-9 ms (turbulence)**
- **volume of reactants 20 μL**
- poly-(methyl methacrylate) (PMMA; Plexiglas® 7N) – UV transparent
- LED (Trp fluorescence, 280 nm)



Bleul *et al.* 2011 Anal. Bioanal. Chem. 399:1117–1125

3. Kinetics on chip

- digital microfluidics

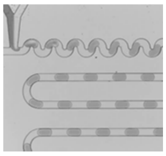


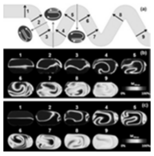
- **dead time 15 s (difusion)**
- **volume of reactants 0.07 μL**

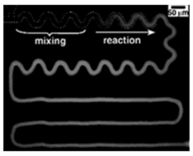
Miller *et al*. 2008 Anal. Chem. 80, 1614-1619

3. Kinetics on chip

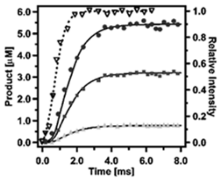
- droplet-based microfluidics







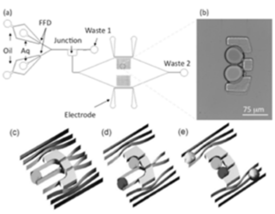
- **dead time < 1 ms (chaotic advection)**
- **volume of reactants 0.15 μL**
- poly-(dimethylsiloxane) – PDMS and glass
- CCD camera and microskop

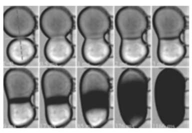


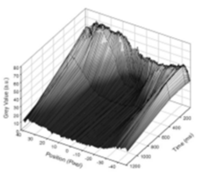
Song *et al*. 2003 J Am. Chem. Soc.125:14613-14619

3. Kinetics on chip

- droplet-based microfluidics





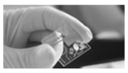


- **dead time 0.1 ms (difusion)**
- **volume of reactants pL´**
- poly-(dimethylsiloxane) – PDMS and glass
- CCD camera and microscope

Huebner *et al*. 2011 Anal. Chem. 83: 1462-1468

Microfluidics

- **new field** of development
- exponentialy **growing area**
- large space for applications
- number of **scientific journals**
- **commercial companies** arrises



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