Contents

9. Liquid Handling

1. Well-Plate Technology
2. Conventional Pipettes
3. Inkjet Dispensers for Biofluids
4. Stream-on-Demand Technology
5. Well-Plates with Integrated Fluidics
6. Flow-Rate Dispensers

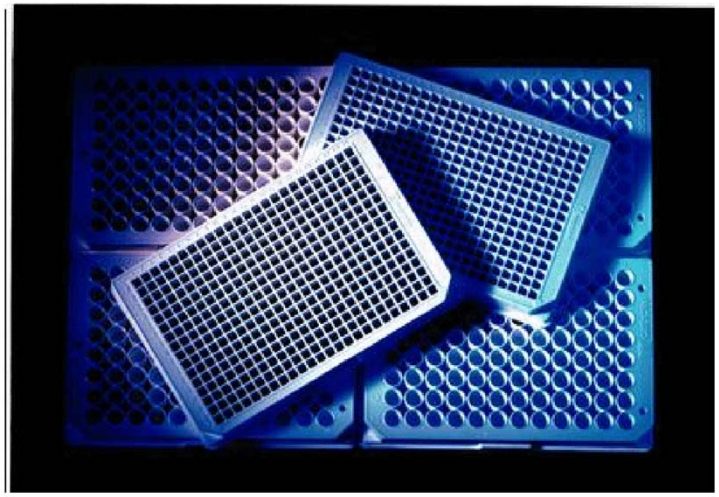
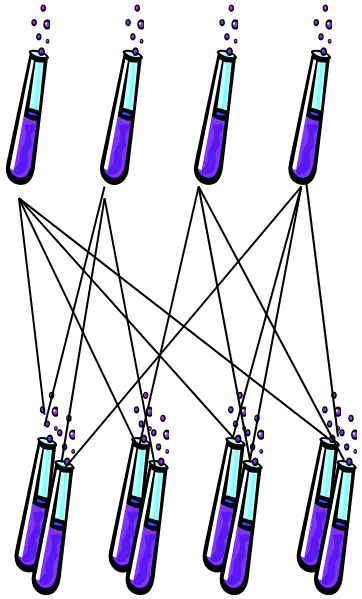
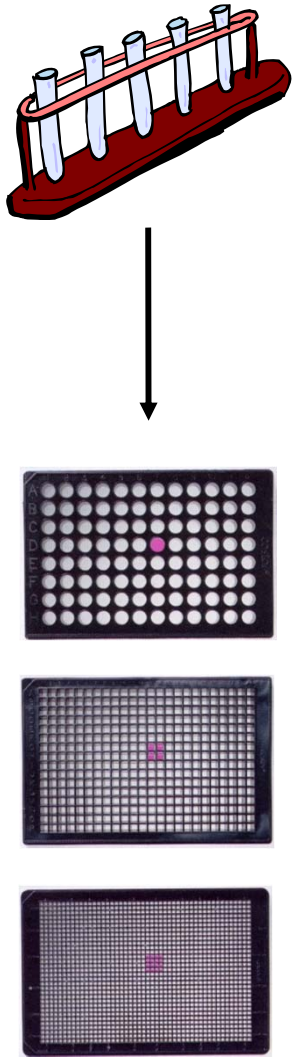


Fig. 9.1. Various 96- and 384-well microtiter plates (Corning Costar)

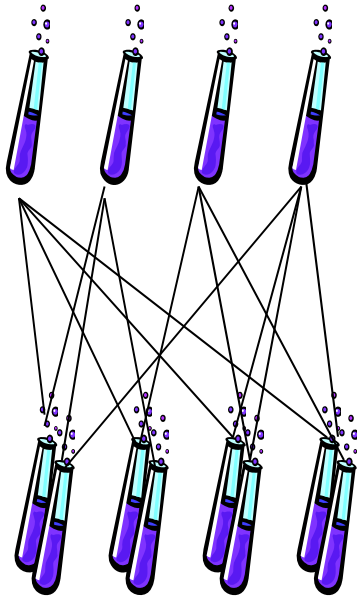
9.1. Modern Drug Discovery Process

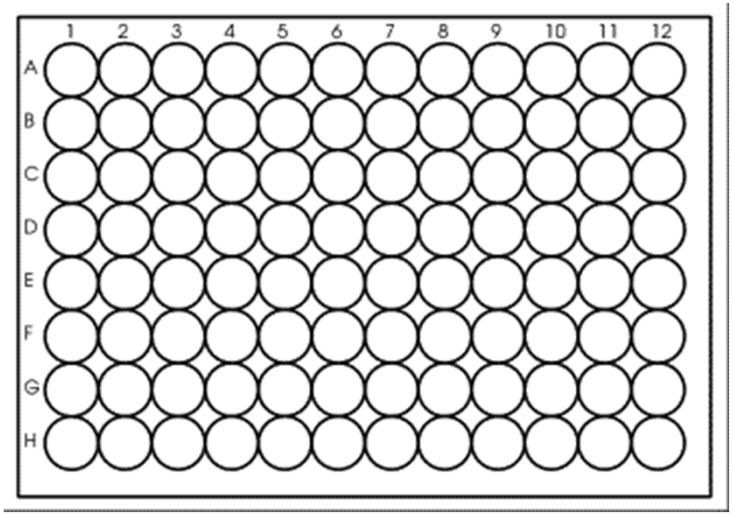




1. Combinatorial Chemisty
   - 25 educts
   - Products with 4 constituents
   - 25^4 (=390,000) products
   - Building of libraries
   - Costs of reagents are critical!

9.1. Modern Drug Discovery Process





1. <u>Combinatorial Chemisty</u>
   - 25 educts
   - Products with 4 constituents
   - 25^4 (=390,000) products
   - Building of libraries
   - Costs of reagents are critical!

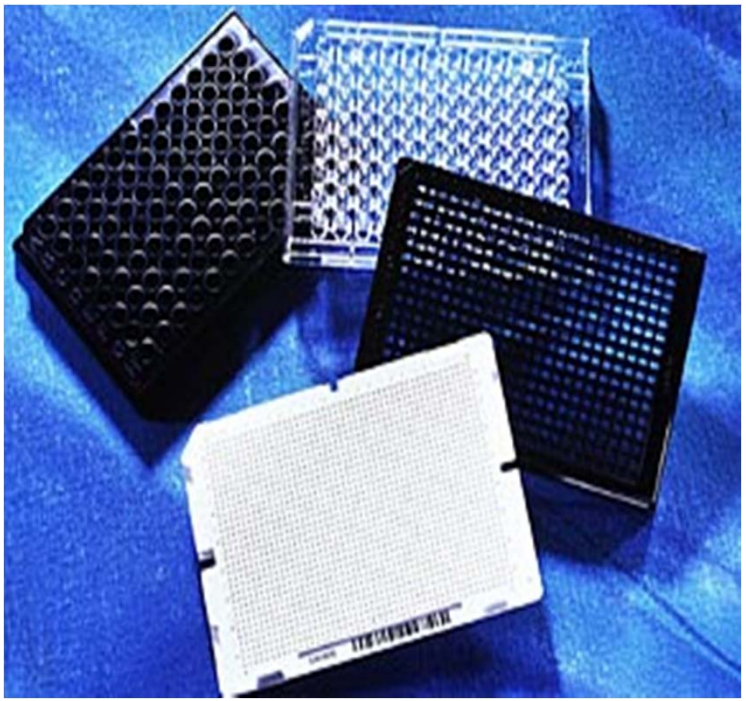
2. <u>High-Throughput-Screening</u>
   - Test of 100,000 reagents / day
   - Approx. 500 – 1,000 dosage events / min
   - Throughput is critical!

9.1. Different Types of Well Plates

96
- Pitch: 9.00 mm
- Volume: 120 µl

384
- Pitch: 4.50 mm
- Volume: 20 µl

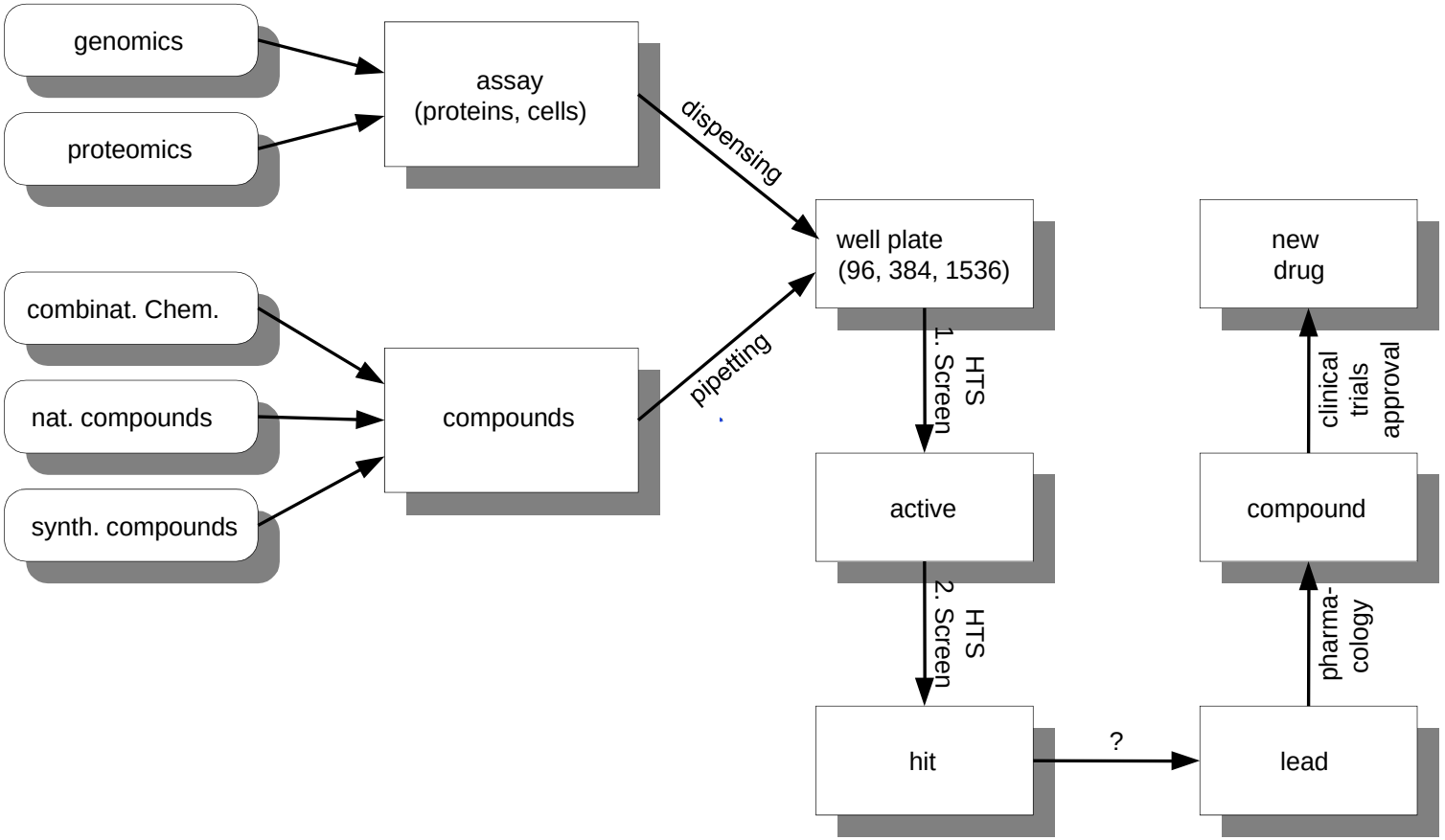
1.536
- Pitch: 2.25 mm
- Volume: 5 µl



wells / plate	volume / µl	factor
96	200	
384	50	4
1536	20	10
6144	< 0.7	> 250

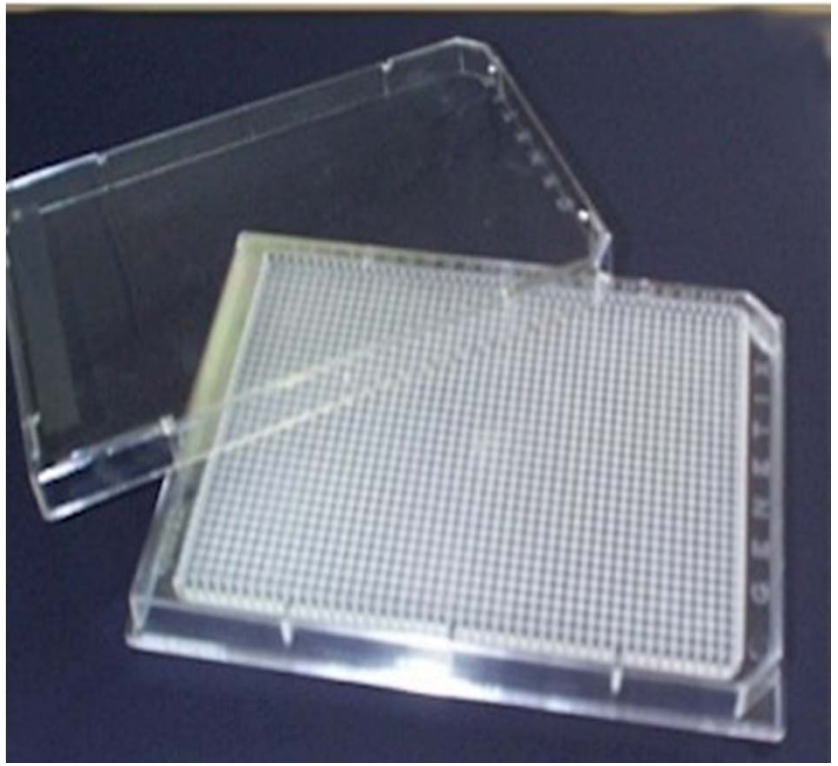
Table 9.1. Reagent savings in high-density MTP formats. With increasing well density, the assay volumes reduce significantly, e.g. by a factor of 10 by using a 1536-MTP instead of a 96-well format

9.1. Modern Drug Discovery Process



9.1. Liquid Handling Specs in Life Science

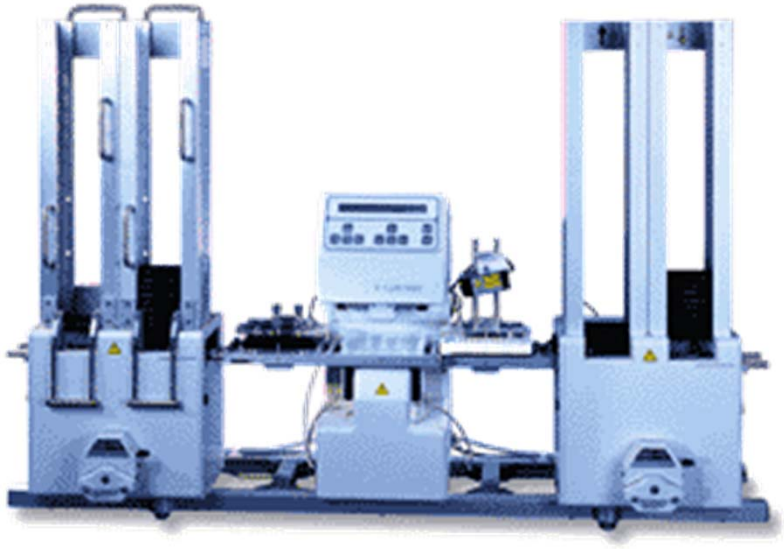
- Volume range: 50 nl – 500 nl
- Precision: typical < 5 %
- Typical liquids (DMSO, water, mixtures, ...)
- Aspiration and / or dispensation
- Throughput (highly parallel)
- Variable volumes ←→ fixed volumes



9.1. CyBio Well

<u>Performance</u>

- Equipped with 96 or 384 pipetting head
- Handling 384 or 1536 well plate format



<u>Speed:</u>

- 20 s for pipetting 384-wells

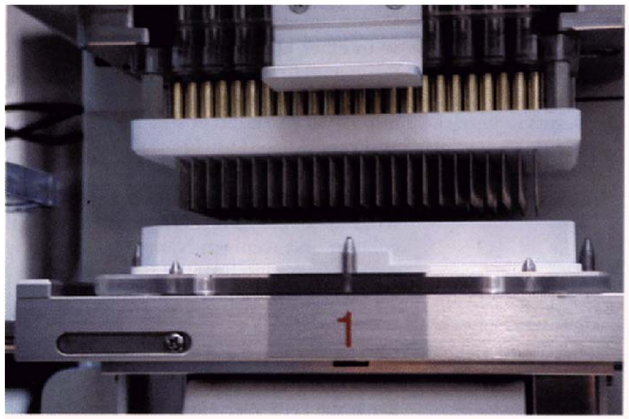


Abbildung 4: Dargestellt ist ein "Pintool" (Fa. Cybio) mit 384 Metallpins

9.1. CyBio Screen-Machine

- Pipettes
- Pumps
- Barcode readers
- Washing stations
- Incubators
- Hotels
- Computers

→ Screening of up to 300,000 compounds / day

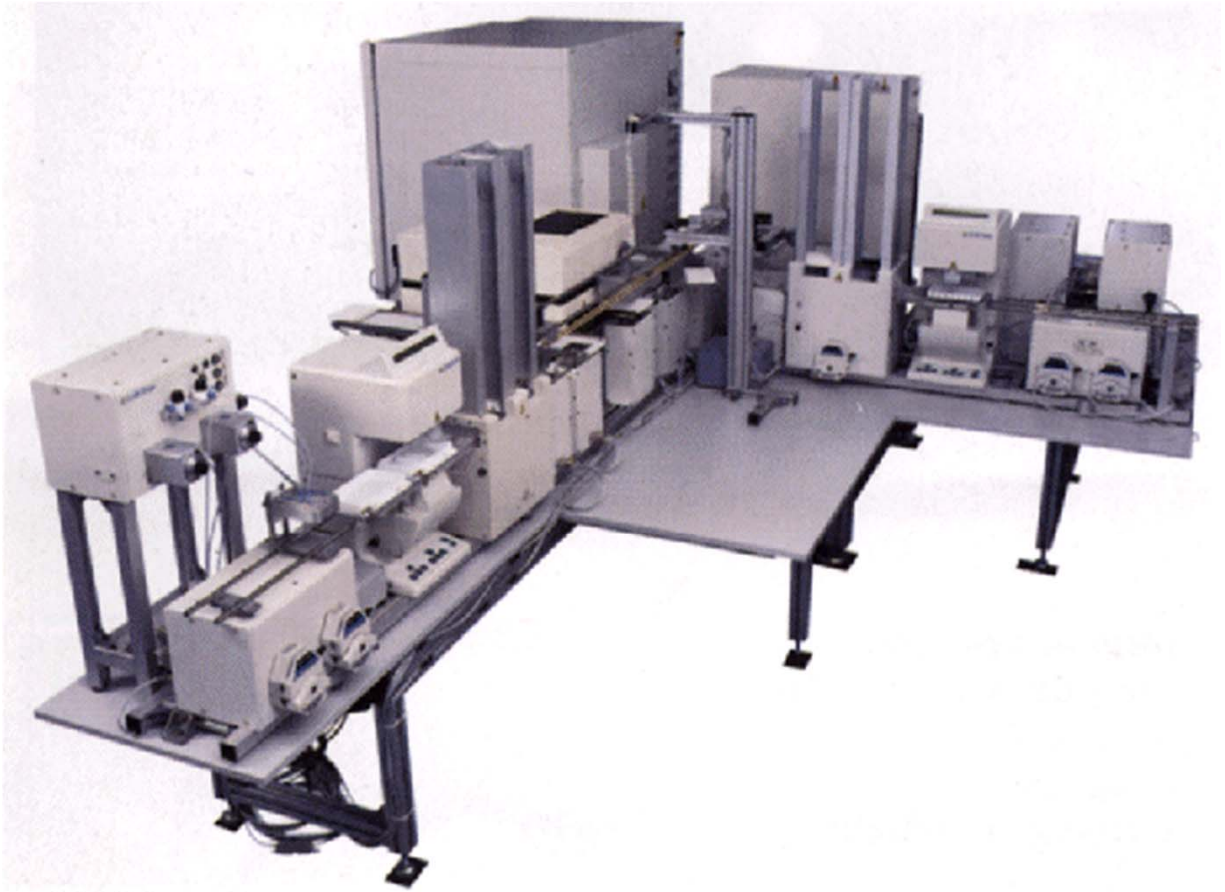


Abbildung 7:
"Cybi-Screen"- System (Cybio) mit Pipettieren, Hotel (Kendro / Heraeus), Inkubator (Kendro/Heraeus), Barcode-Reader, Spülstation

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6. Flow-Rate Dispensers

9.2. About Typical Biofluids

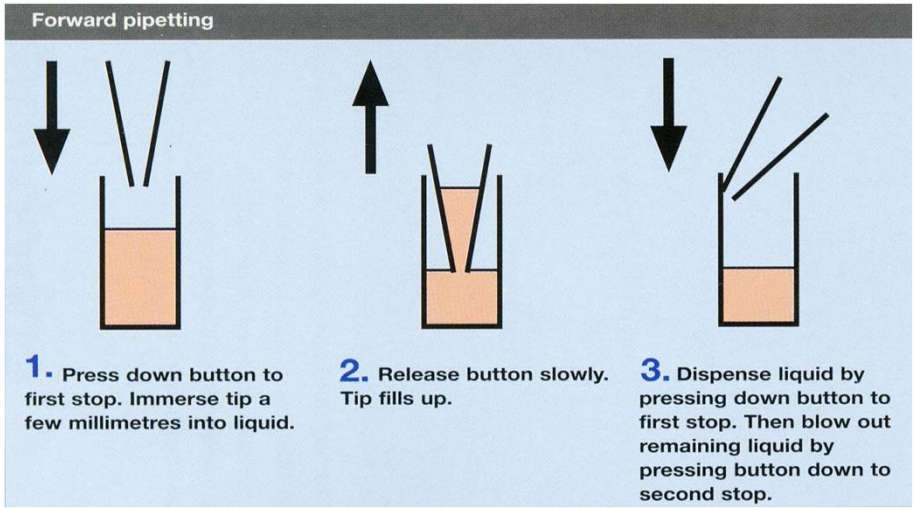
- Water based solutions
  - Small content of biological molecules (proteins, DNA, enzymes, ...)
  - Sometimes mixtures with glycerol (antifreeze)
  - Sometimes addition of surfactants (reduces surface tension or holds biological content in solution)
- DMSO (Dimethylsulfoxid)
  - Freezes at 18°C
  - Viscosity: 2.3 x water
  - Surface tension between water and alcohol (44 mN m^{-1})

9.2. Aspiration, Dispensation & Pipetting

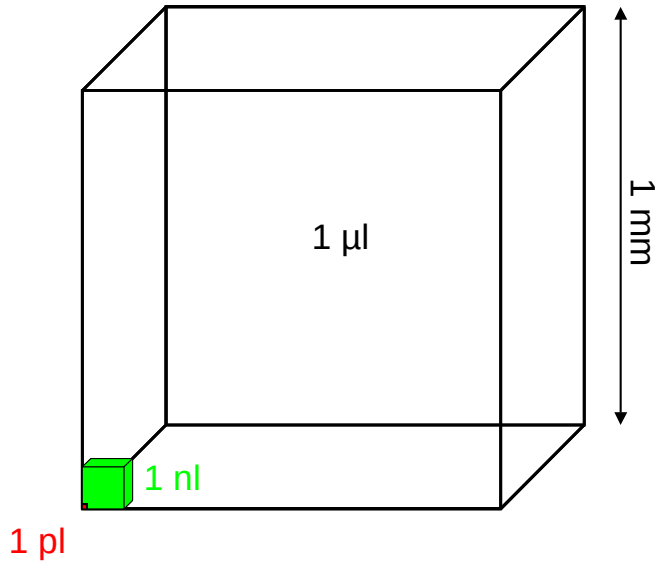
Dispensation =
delivery of defined volume of fluid

Aspiration =
sampling of liquid

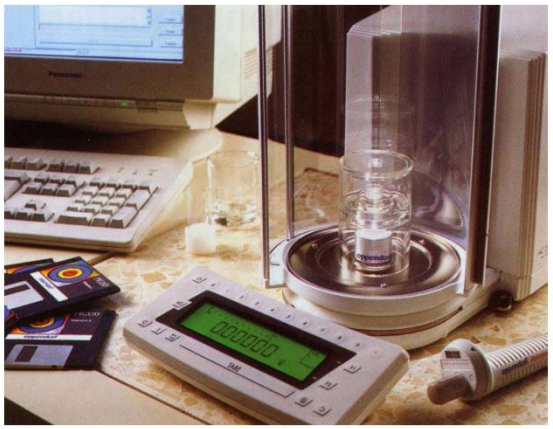
Pipetting =
aspiration & dispensation



9.2. About Volumes



9.2. How to Measure Nanoliters?

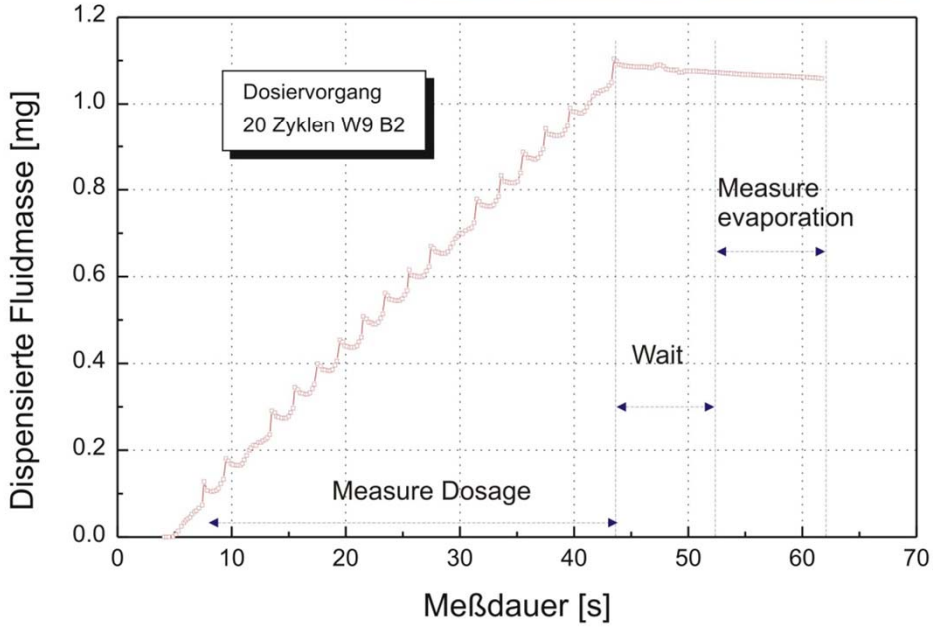


Gravimetric Measurement

- Mass corresponds to volume, for water:
  - 1 ml = 1 g
  - 1 µl = 1 mg
  - 1 nl = 1 µg

- Minimization of evaporation by high humidity atmosphere near balance

- Measurement & correction of evaporation



9.2. How to Measure Nanoliters?

Photometric Measurement

- Dispensing certain amount of fluorescent dye
- Measurement of fluorescent signal
- Number of counts proportional to dispensed amount of fluid
- Calibration of number of counts relative to larger, known volume

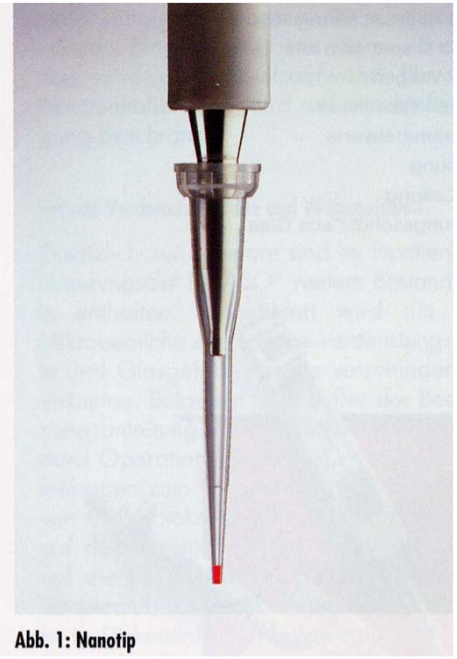
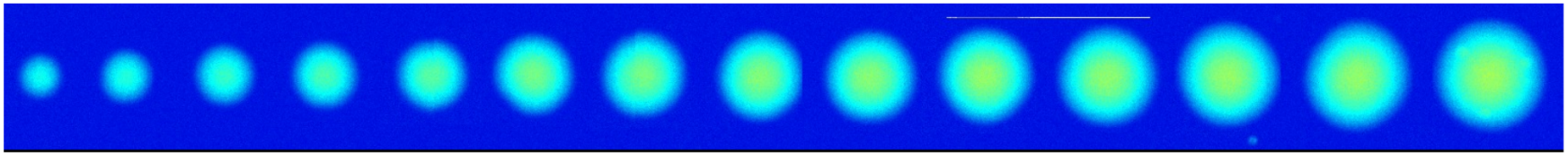
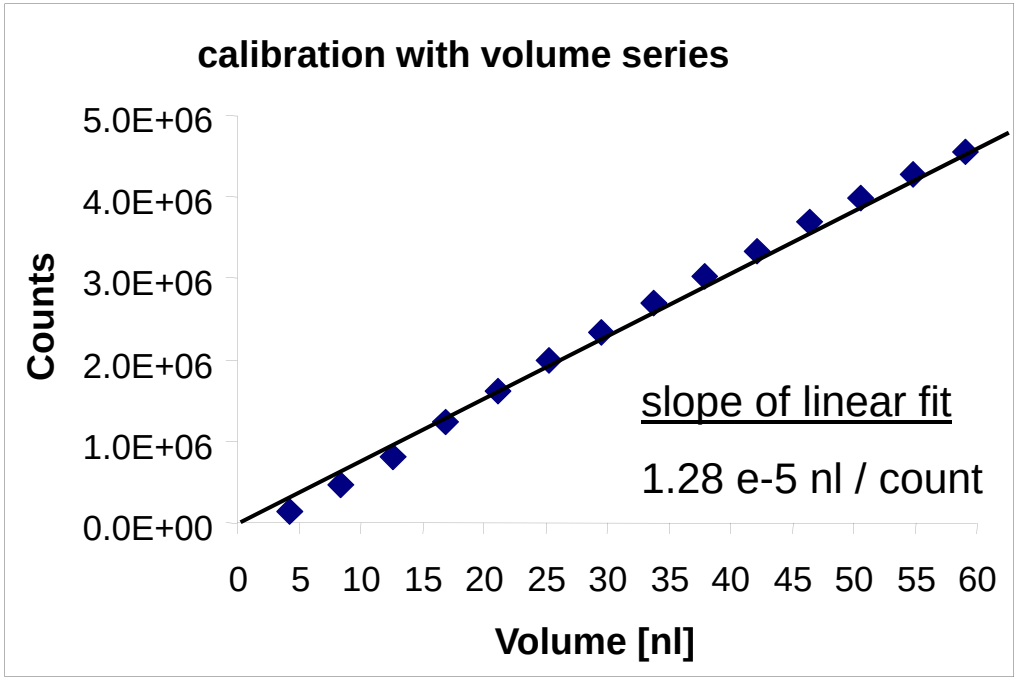


Abb. 1: Nanotip

9.2. Calibration of Photometric Measurement



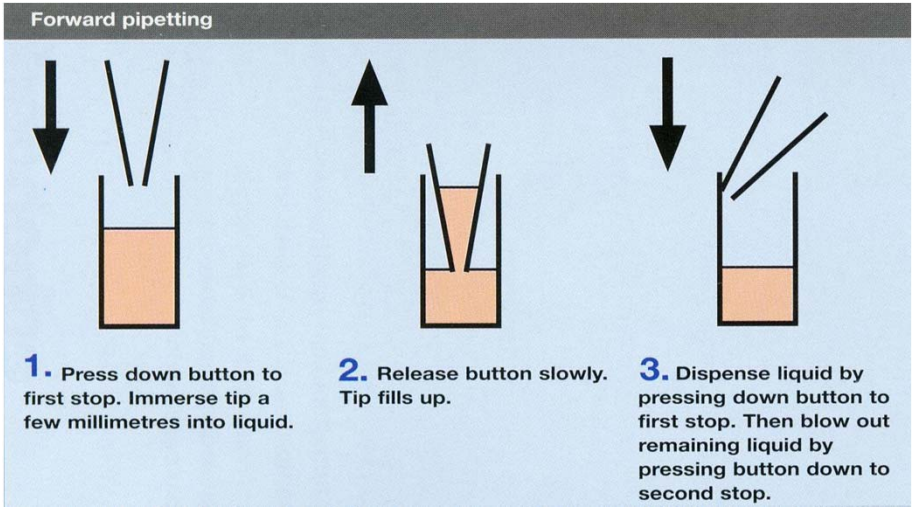


volumes dispensed with proprietary **NanoJet**-device

9.2. Manual Pipettes

Pipetting Process

- Spindle able to move between two mechanical stops
- Aspirated volume varied by moving one stop
- Pipette tip dipped into liquid
- Spindle moves back and sucks in liquid
- Tip placed above target reservoir
- Spindle pressed down to displace fluid



9.2. Manual Pipettes

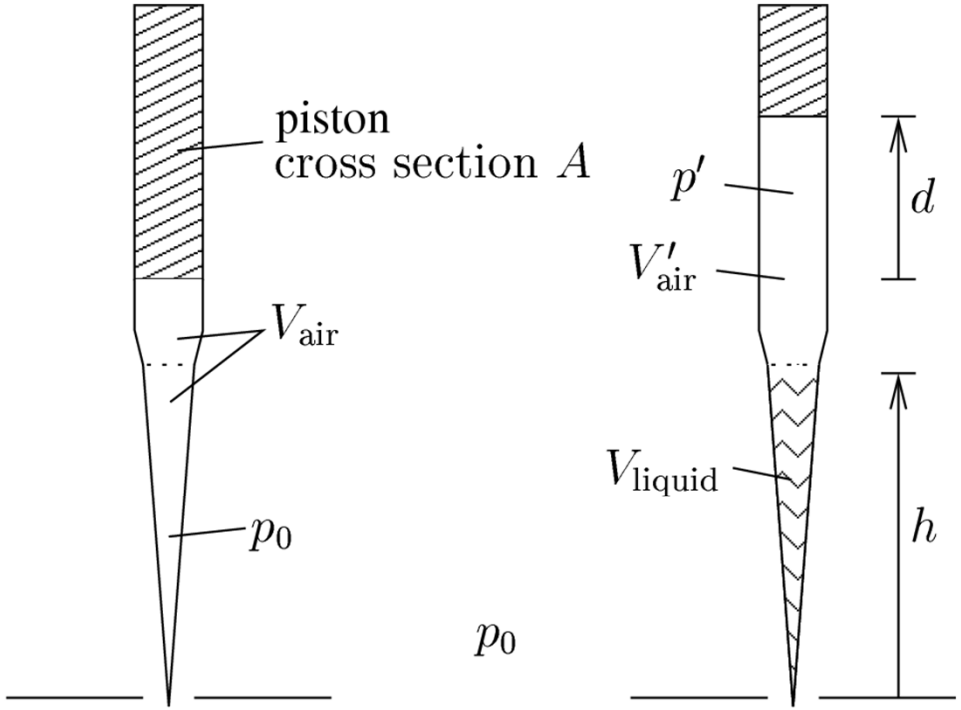
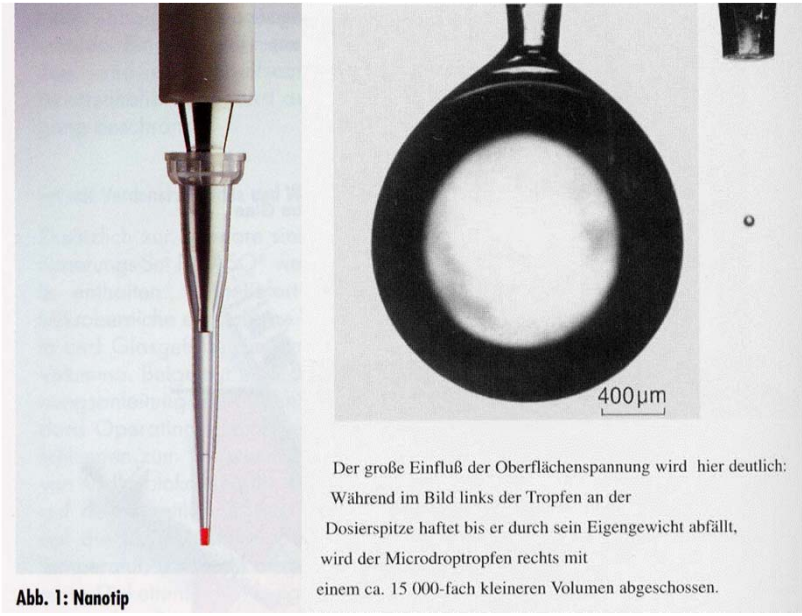


Fig. 9.4. An air displacement pipette is initially filled with an air volume V_{air} at the environmental pressure p_0. Upon withdrawal of the piston of cross-section A by a distance d, a liquid volume V_{liquid} is aspirated into the tip. After aspiration, effects like the weight of the water column of height h and capillary action exert additional pressures on the air cushion. As $p' \neq p_0$, the volume Ad displaced by the piston deviates from V_{liquid}

9.2. Manual Pipettes

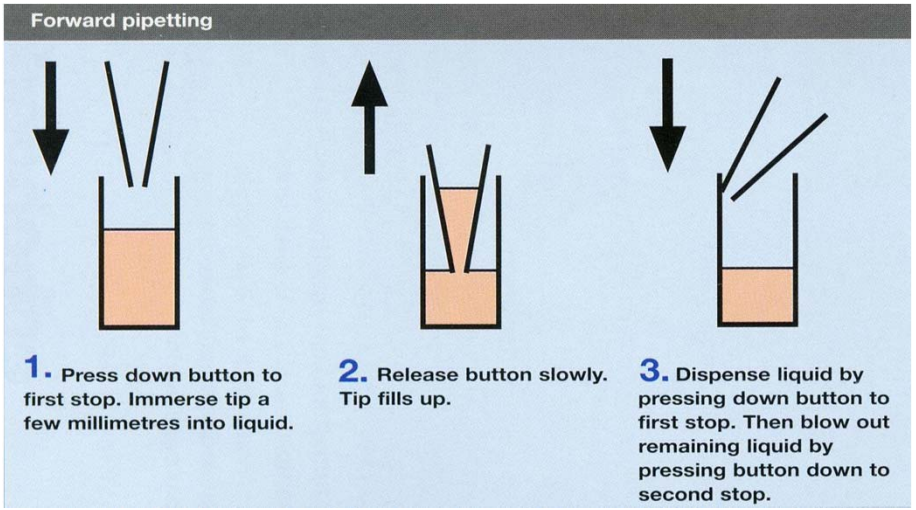
Limitations

- Capillary forces suck in more fluid than wanted
- Liquid kept back at wall of tip due to adhesive forces
- Gas volume inside tip compressible (influenced by hydrostatic pressure of liquid)



Possible improvements

- Tips containing piston reduce gas dead volume
- Physical limit:
  Volume: 200 nl
  Accuracy: 10 %



9.2. Syringe Based Systems

Process

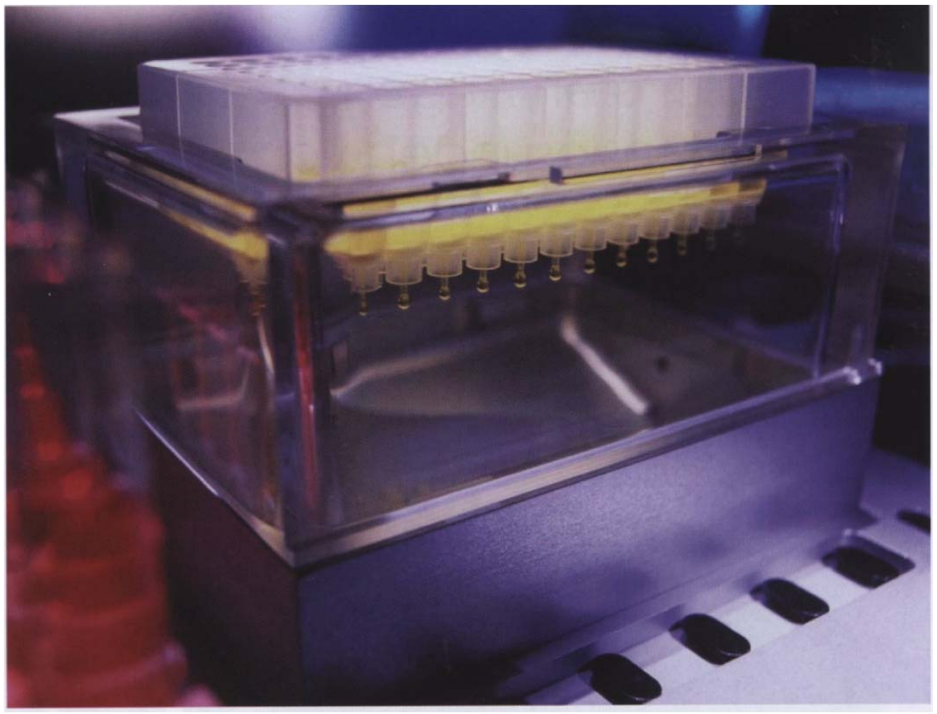
- Stainless steel plunger travels inside glass barrel actuated by stepper motor
- Syringes having variable volumes available (e.g. 2.5 to 500 µl)
- Stepper motor divides volume into up to 100,000 steps → resolution

Limitation

- Adhesive forces

9.2. Limitations of Standard Technology

- Volume range below 200 nl not accessible
  - Physics of droplet release
  - Capillary forces
  - Adhesive forces



9. Liquid Handling

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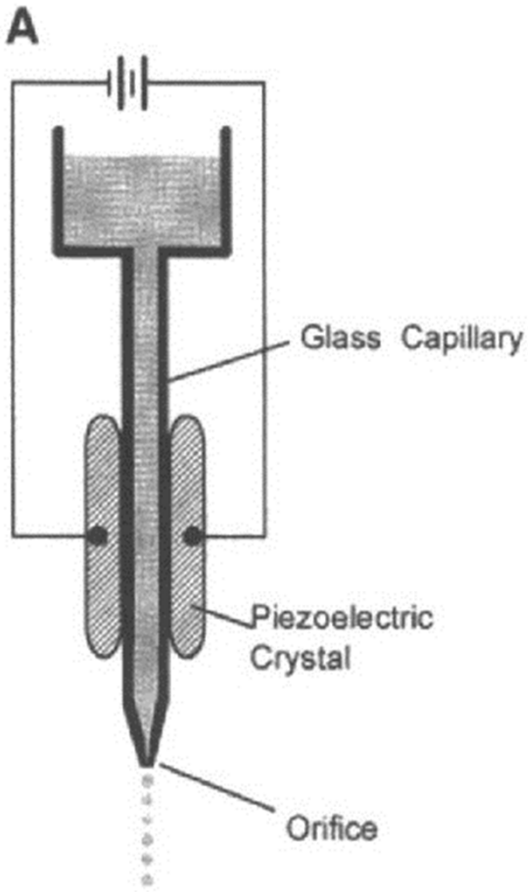
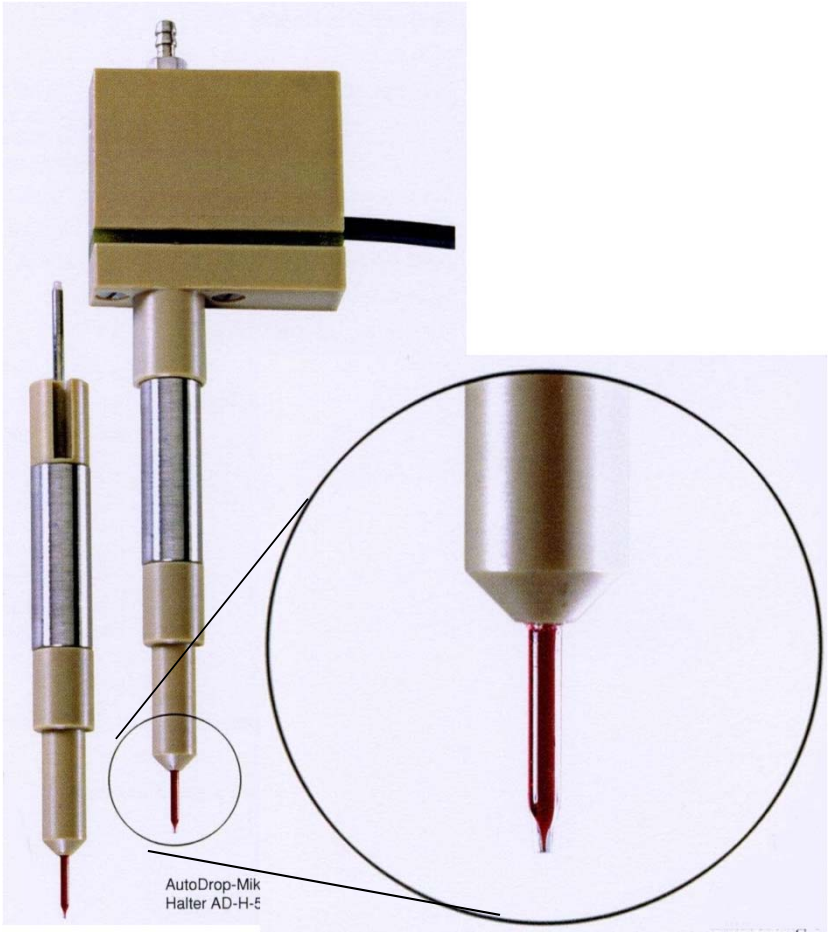
9.3. InkJet-Pipettes: Microdrop

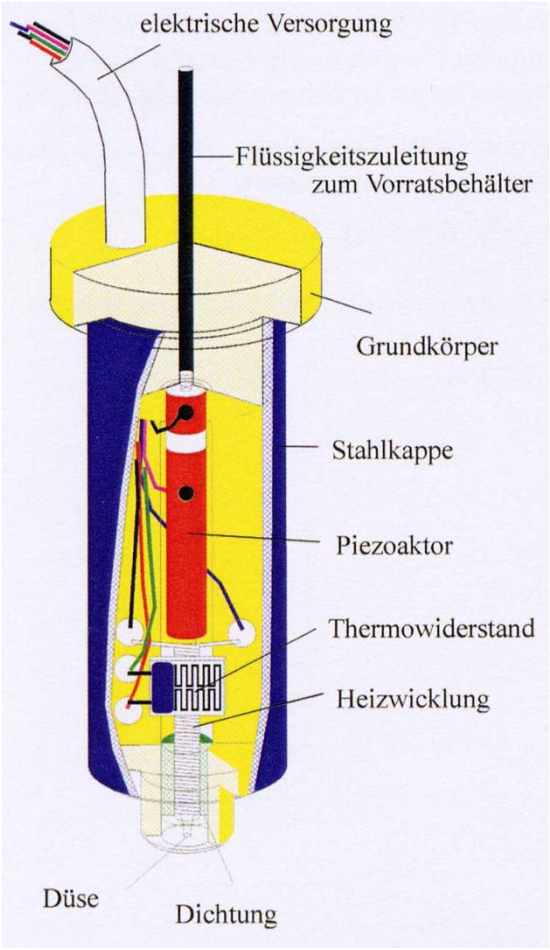
Process:

- Glass capillary enclosed by piezoelectric crystal
- Actuation generates pressure wave (acoustic wave)
- Pressure wave travels to nozzle, where high local acceleration (100,000 g) occurs ejecting droplet
- Droplet size mainly depending on nozzle size (droplet diameter ~ 1.2 times nozzle diameter)
- High reproducibility: better 0.1 %
- Sensitive to liquid properties



9.3. InkJet-Pipettes: Microdrop

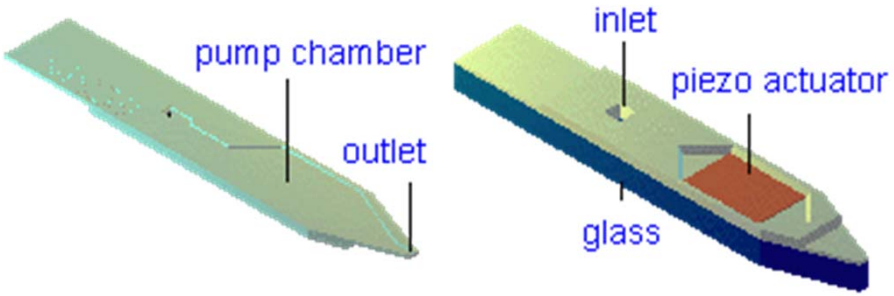




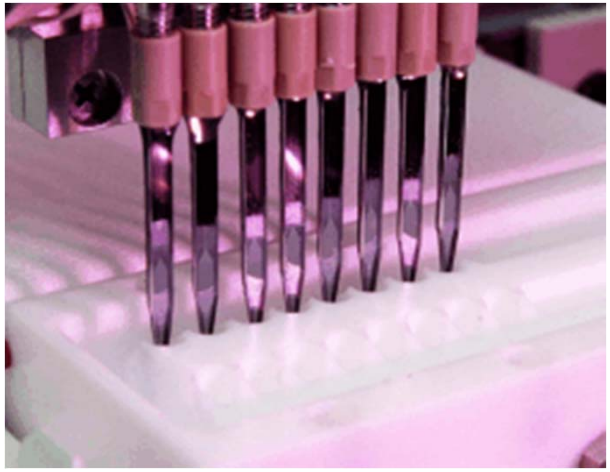
9.3. InkJet-Pipettes: GeSiM

Nanopipette

- Fabricated by silicon micromachining
  - Silicon / glass anodically bonded
  - Forming pump chamber
  - Piezodisk glued on top of diaphragm

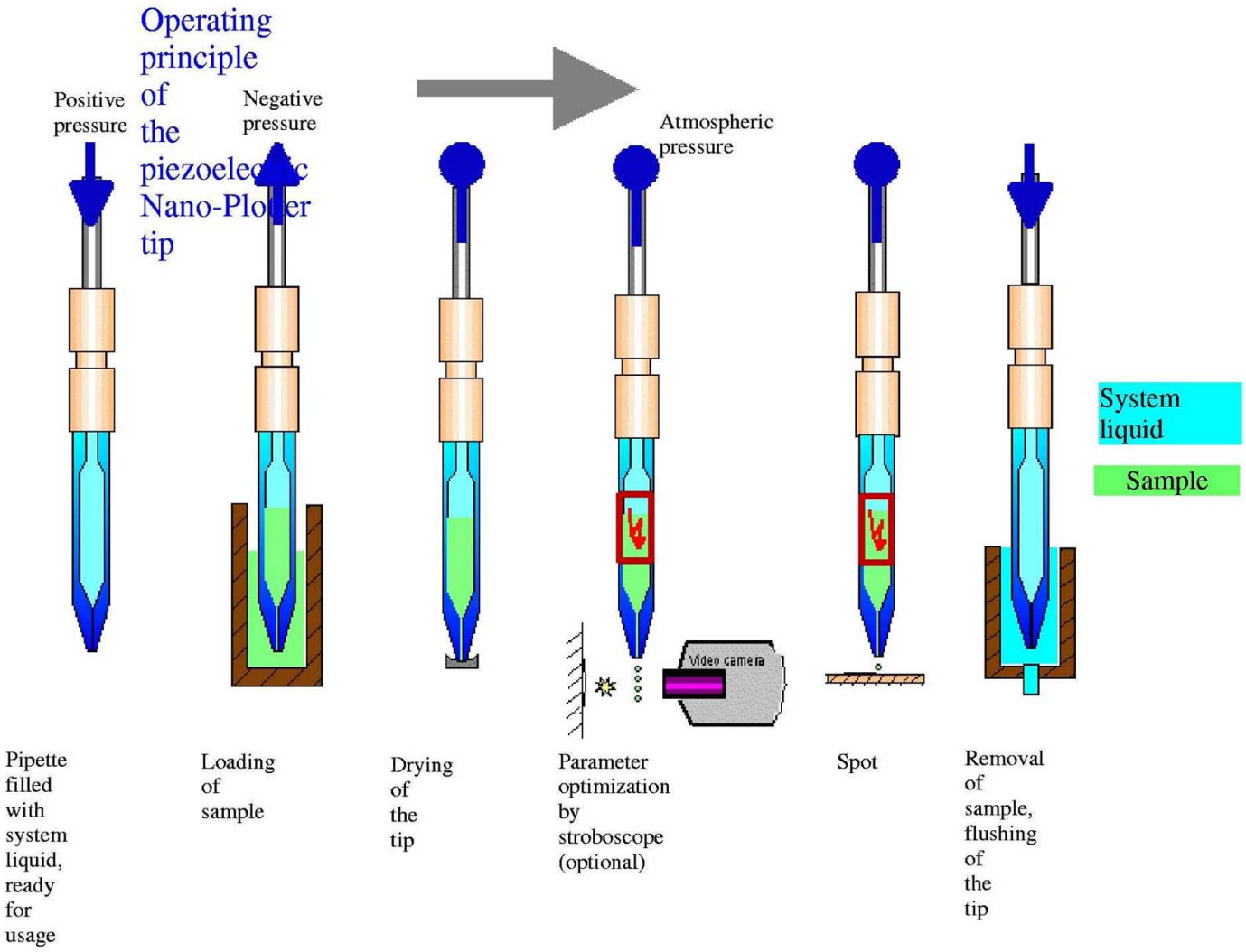


- Liquid volume variable via nozzle size between 400 pl and 1 nl



- Nanopipette to be filled with system liquid

9.3. InkJet-Pipettes: GeSiM



9.3. InkJet-Pipettes: Tecan

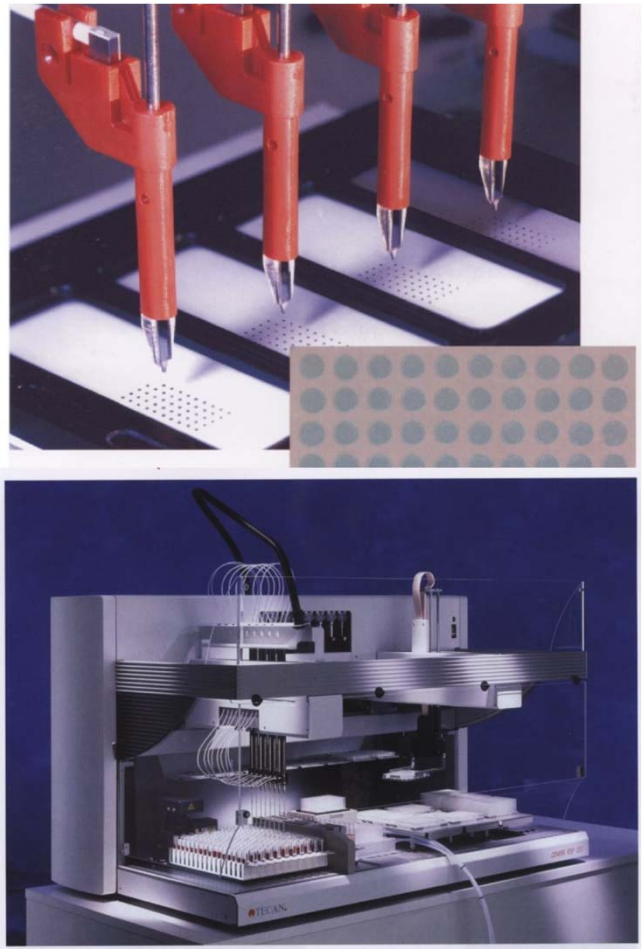
Nanopipetting option from Tecan

- Dispensing precision:
  < 5 % (single channel)
  < 10 % (multiple channel)

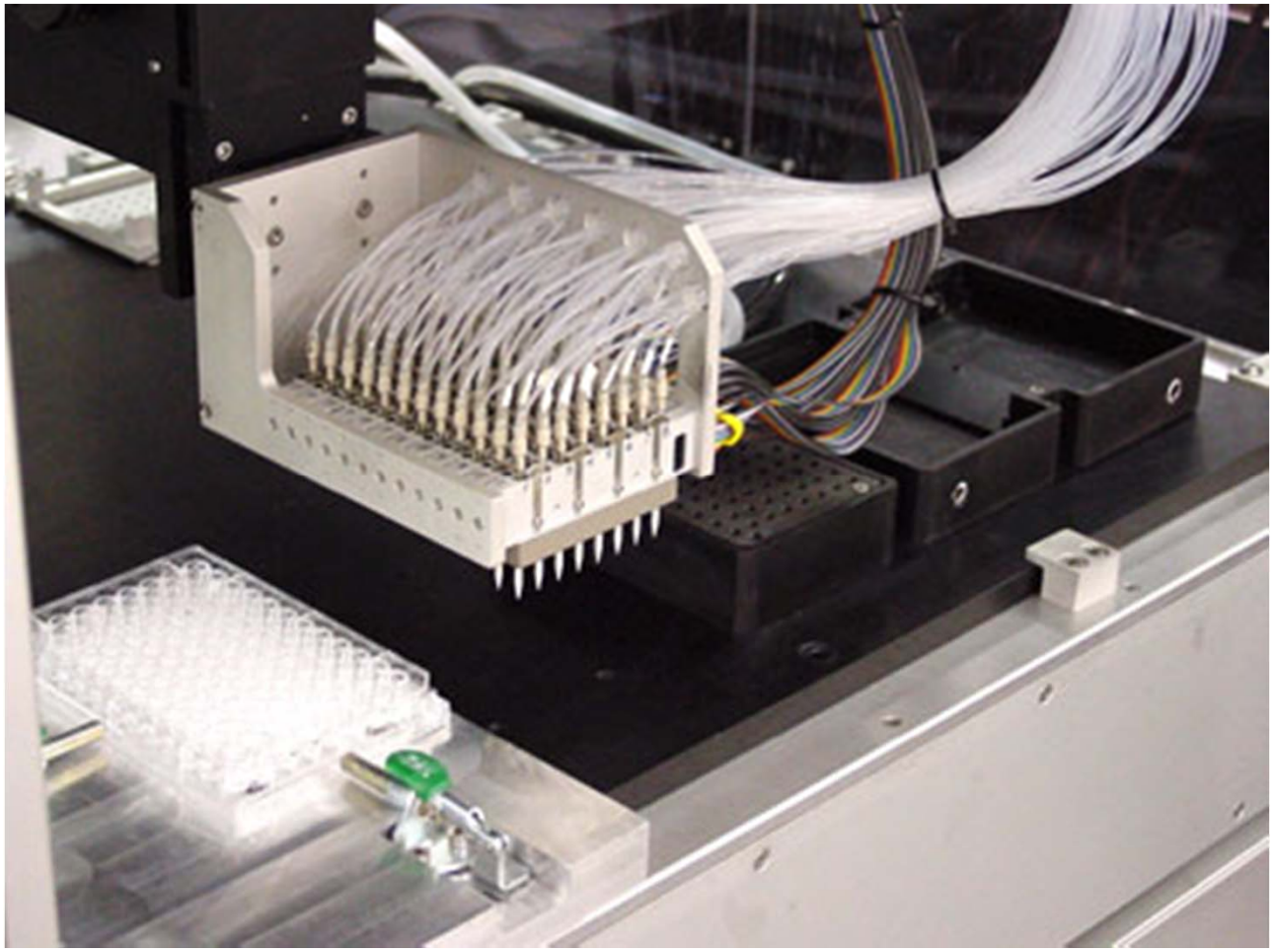
- Dispensing speed:
  0.5 µl / s

- Integrated liquid level detection

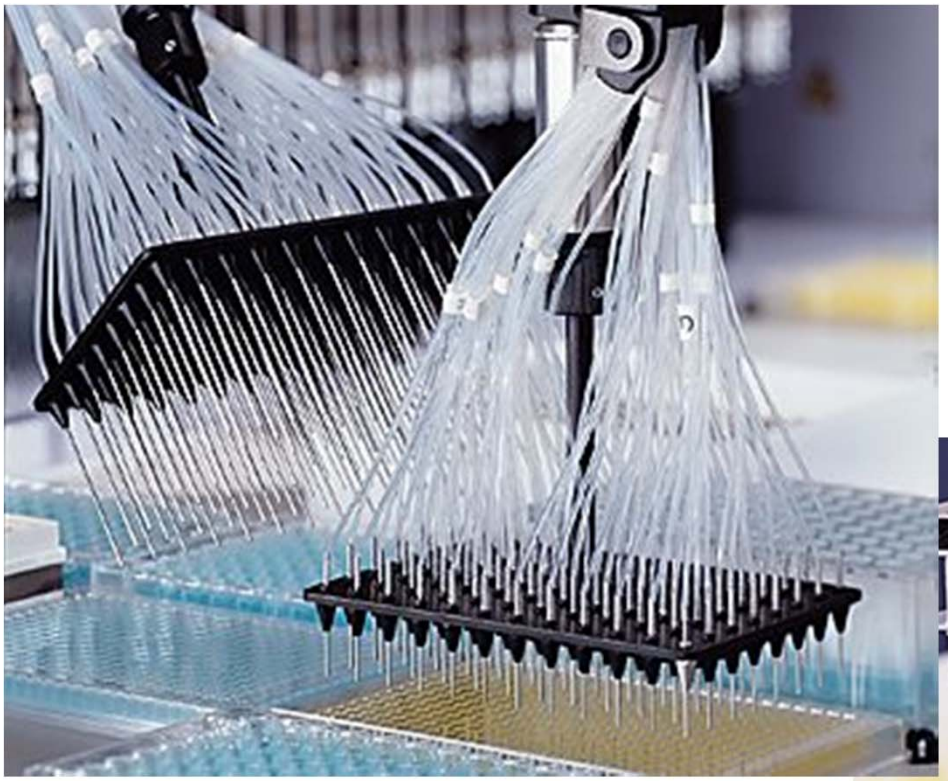
- Aspiration from 384 well plates



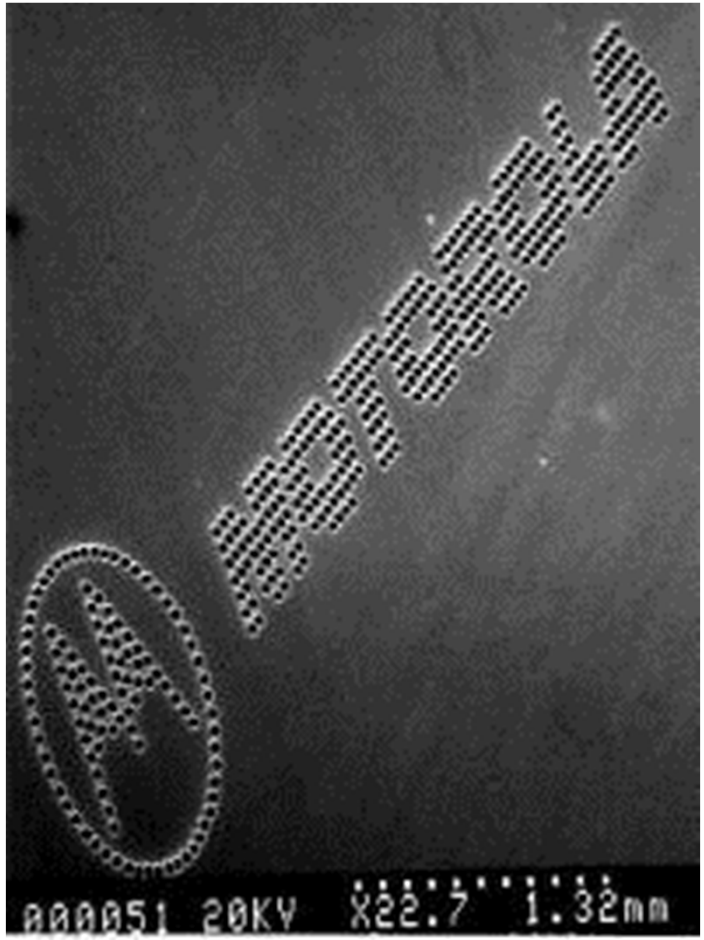
9.3. 96-Channel synQUAD Dispensing Head



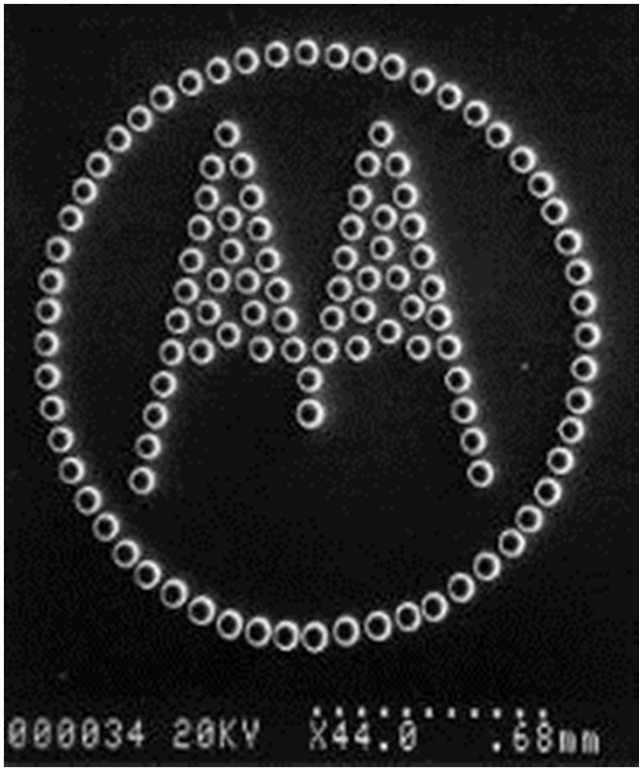
9.3. 96-Channel Pipettors from Hamilton



9.3. Printing of Solder & Adhesives



Small droplets of solder (XFab)



9.3. Femtodispenser from IMT (I)

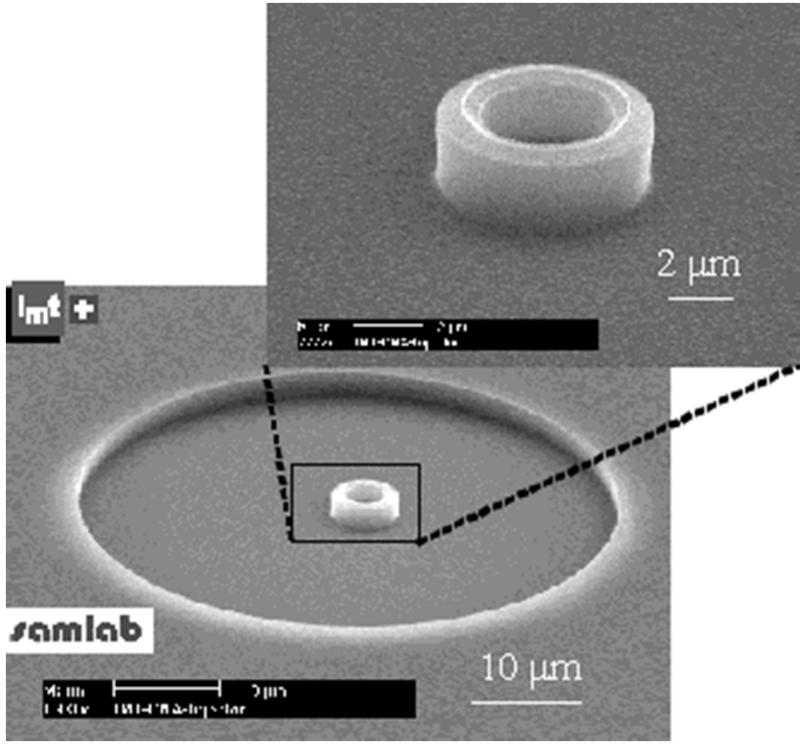
Concept

- Front-end injection device for mass spectrometer system

Principle

- Actuation at 0.5 MHz
- Size distribution centered at 3.6 fl

➢ Droplet diameter: 1.9 µm



9.3. Femtodispenser from IMT (II)

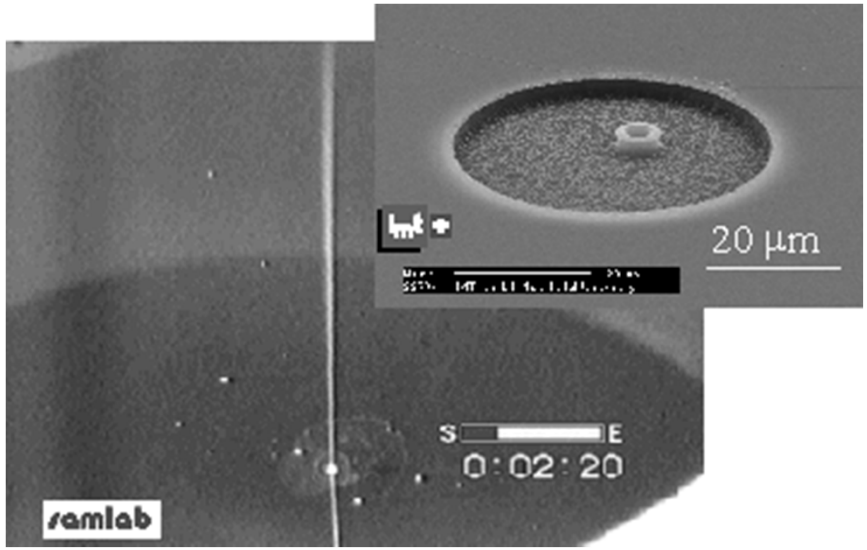
Concept

- Front-end injection device for mass spectrometer system

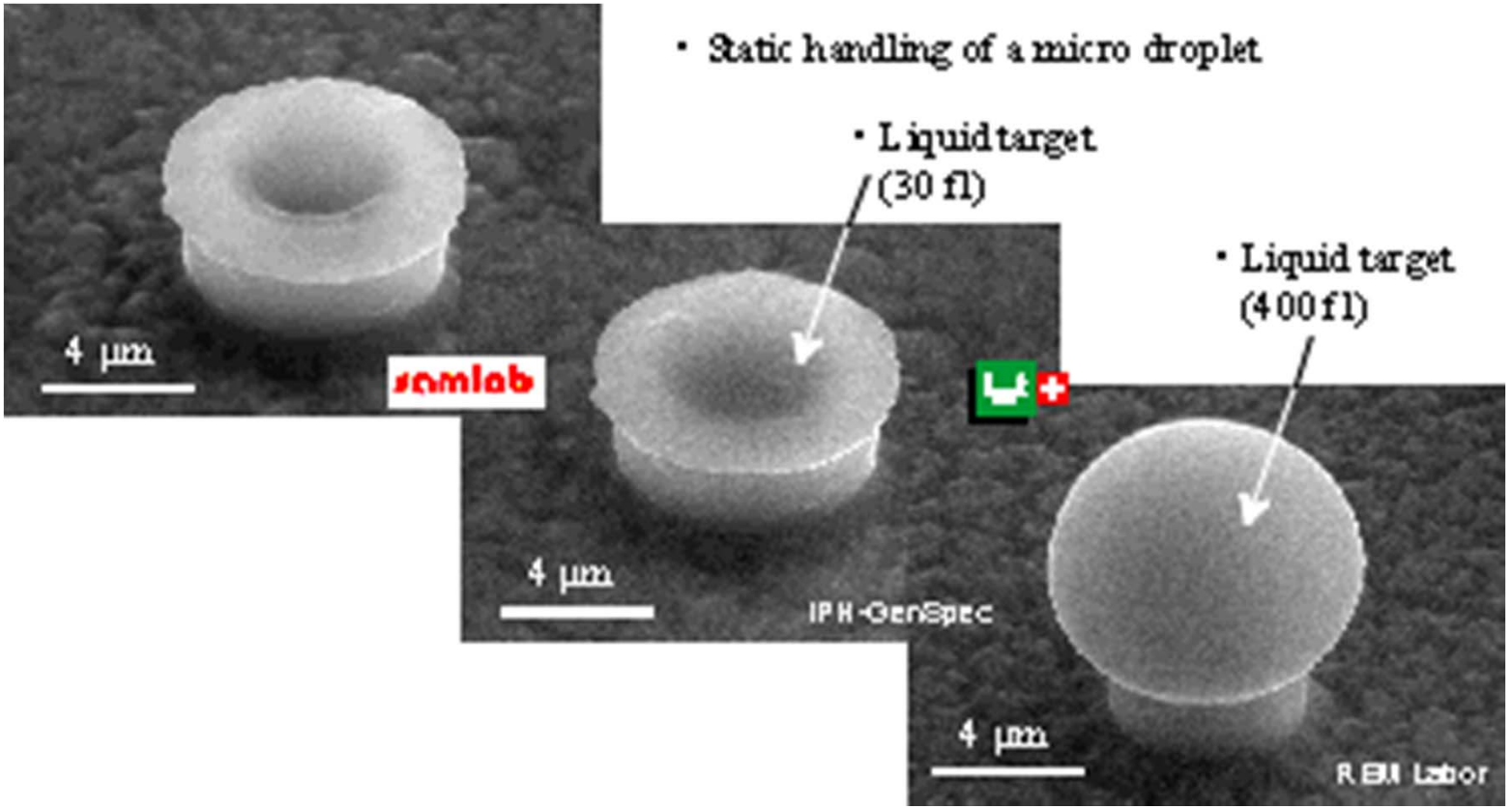
Principle

- Actuation at 0.5 MHz
- Size distribution centered at 3.6 fl

➢ Droplet diameter: 1.9 µm



9.3. Femtodispenser from IMT (III)

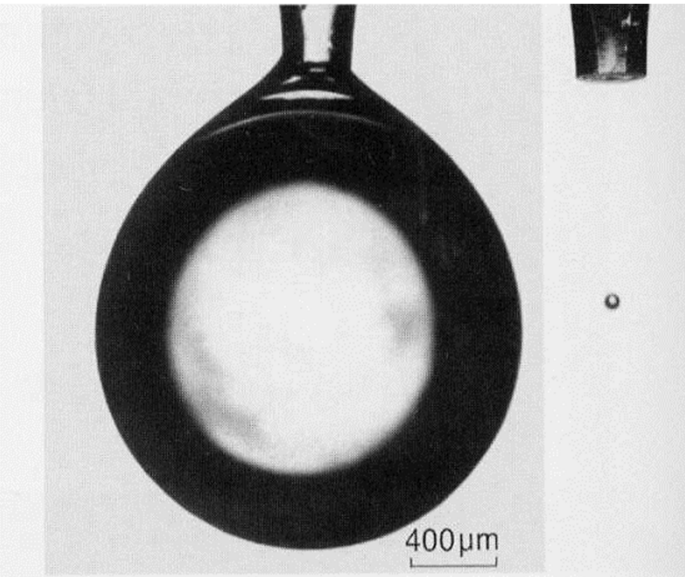


9.3. Limitations of InkJet-Dispensers

Physics of a droplet

- $E_{surface} = \sigma A = 4\pi\sigma r^2$
- $E_{kinetic} = \frac{1}{2} m v^2 = \frac{2}{3} \rho\pi v^2 r^3$

Diameter	1000 µm	100 µm
Kin. Energy	1,05 µJ	0,131µJ
Surf. Energy	0,226 µJ	0,06 µJ
Kin. / Surf. En.	4,6 →	2



Der große Einfluß der Oberflächenspannung wird hier deutlich: Während im Bild links der Tropfen an der Dosierspitze haftet bis er durch sein Eigengewicht abfällt, wird der Microdroptropfen rechts mit einem ca. 15 000-fach kleineren Volumen abgeschossen.

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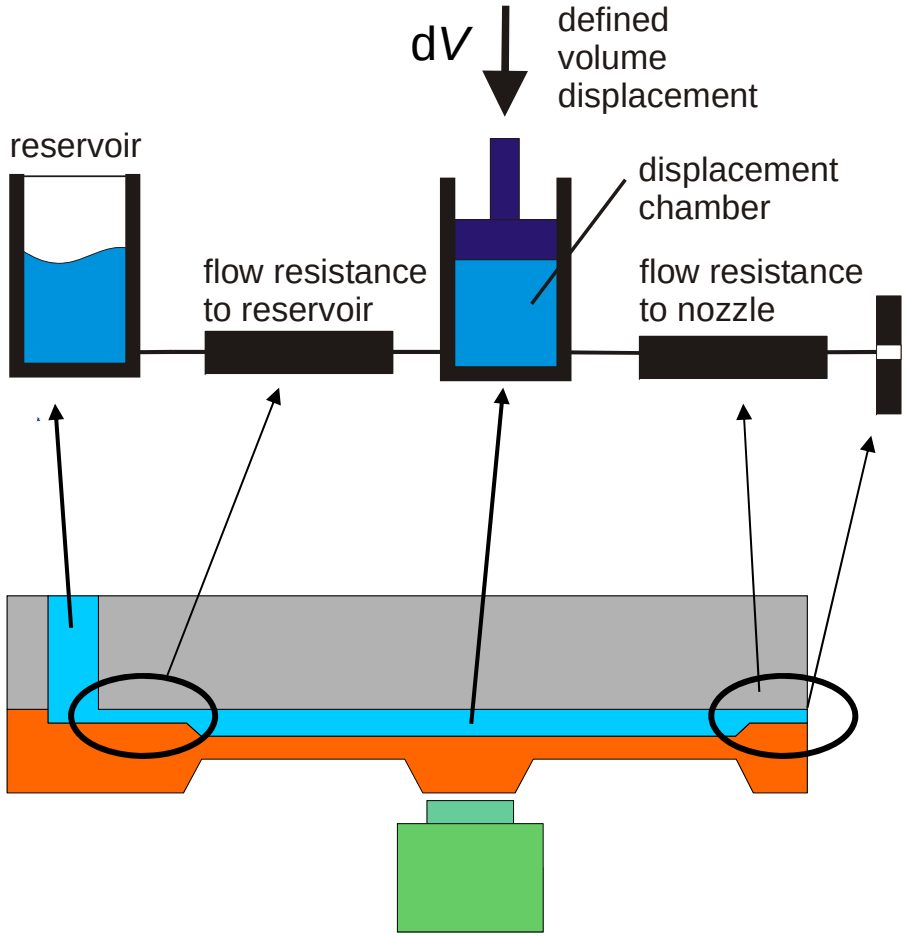
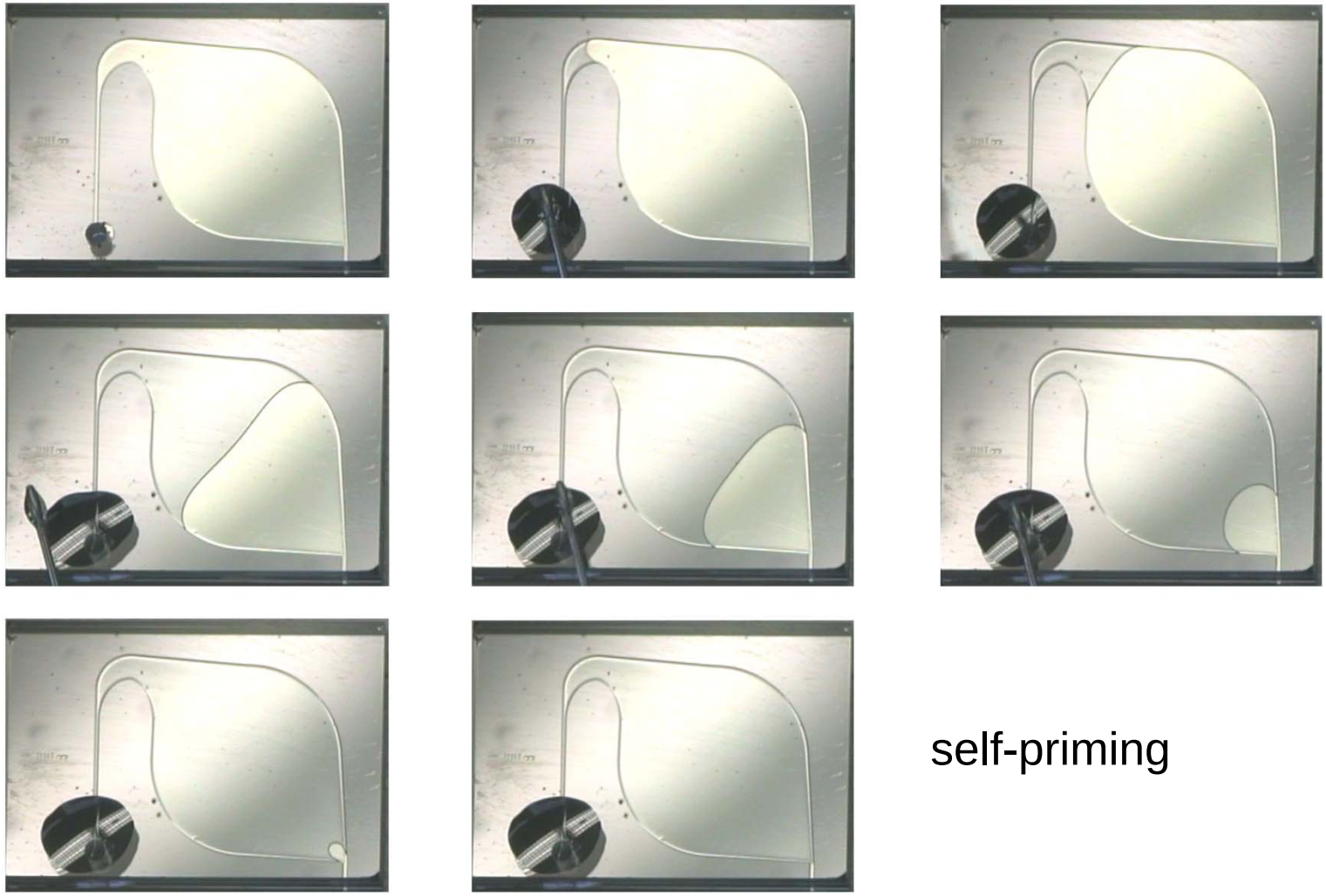
9.4. NanoJet-Dosage Technology (I)

System Configuration & Priming

- System contains
  - Reservoir
  - Displacement chamber
  - Defined flow resistances
- System is self-priming due to capillary forces



9.4. NanoJet-Dosage Technology (II)

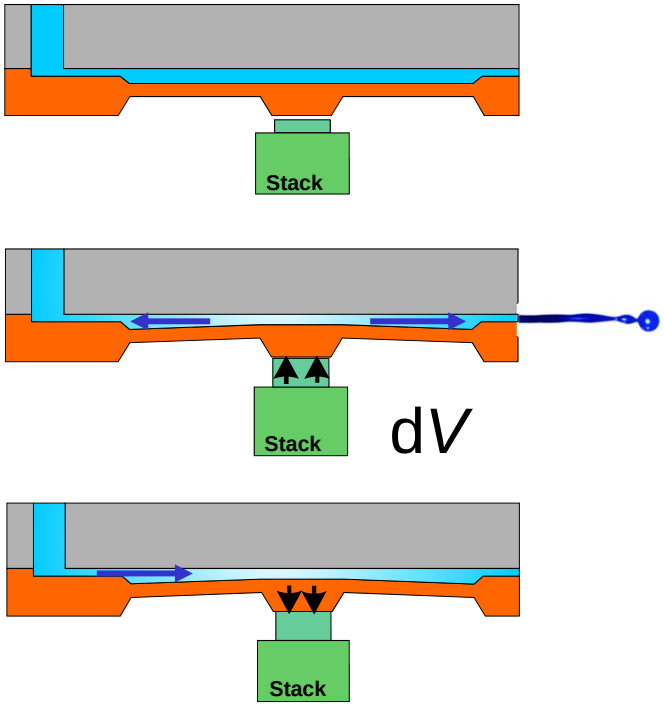


self-priming

9.4. NanoJet-Dosage Technology (III)

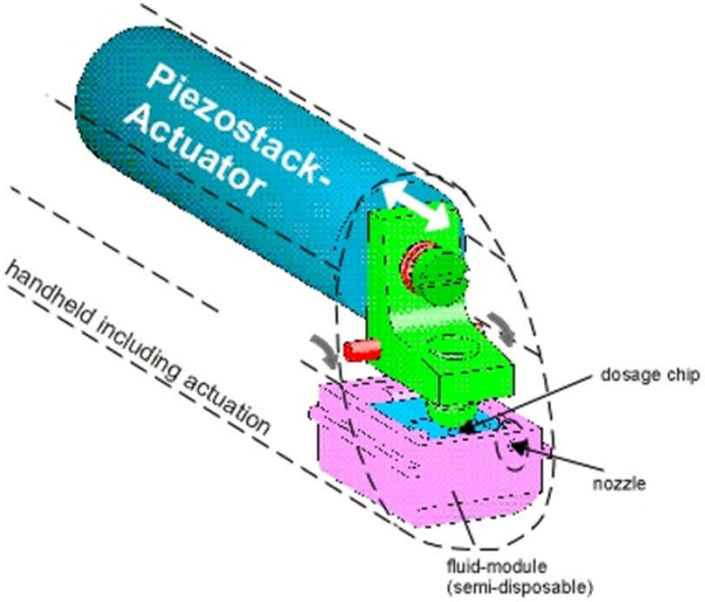
Refill & Dispensing Process

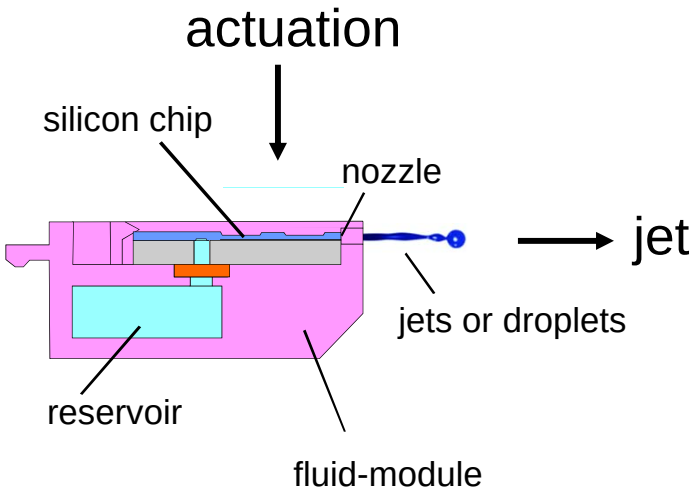
- Fluid level stays at nozzle due to capillary forces
- Fast movement of piston displaces liquid
- Slow movement of piston sucks fluid from reservoir
- Ejected volume defined by ratio of flow resistance



$$V = \frac{R_{res}}{R_{res} + R_{noz}} \, dV$$

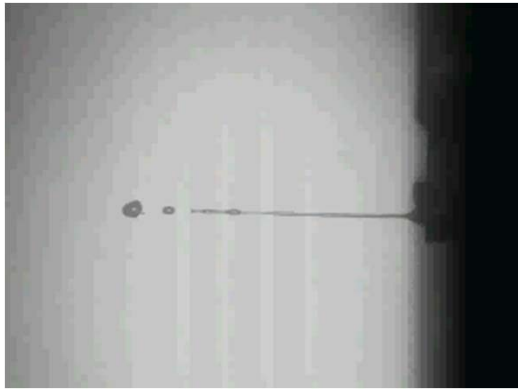
9.4. Side Shooter Configuration



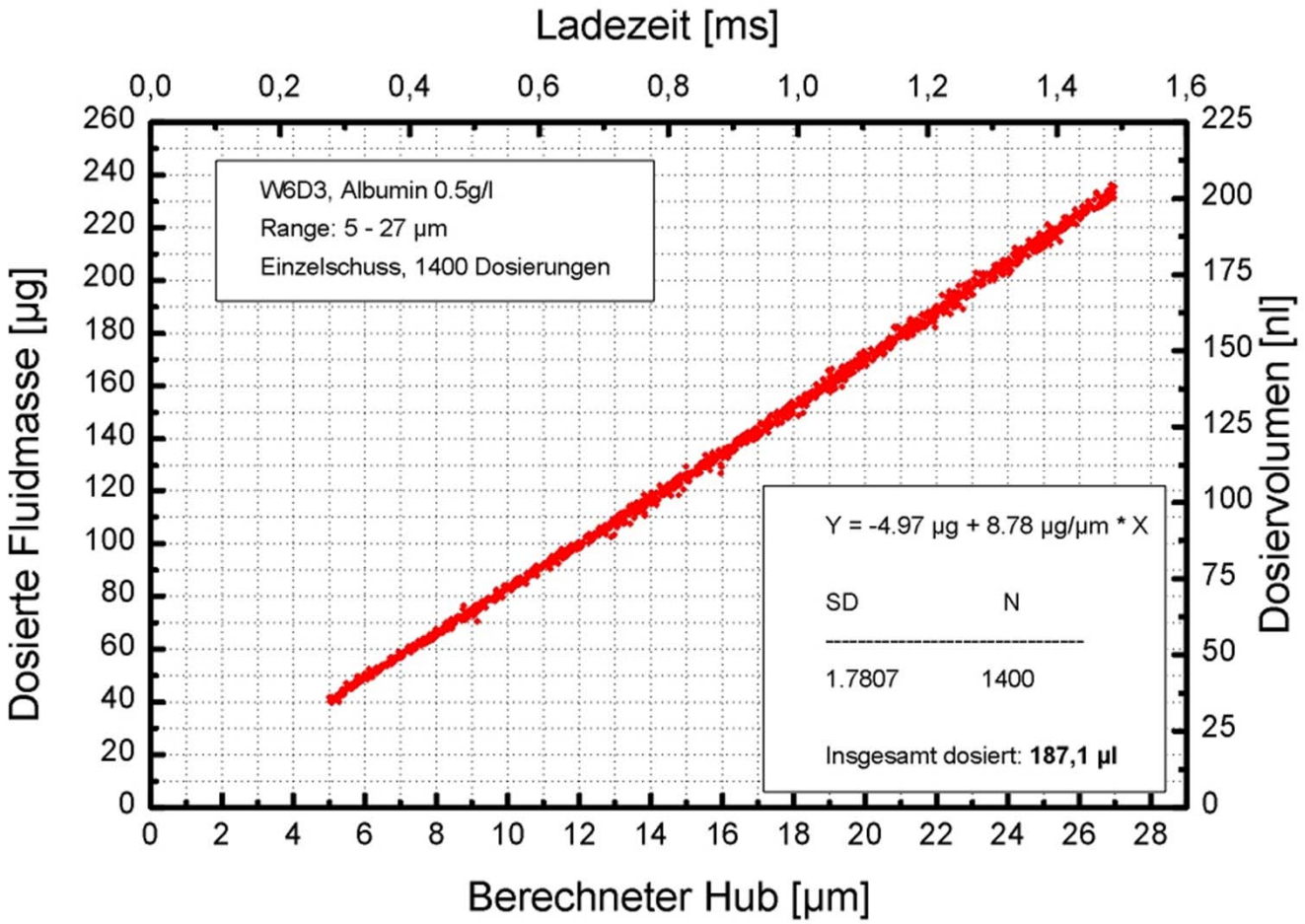


9.4. NanoZyme: Nanoliter Dispenser for Enzymes

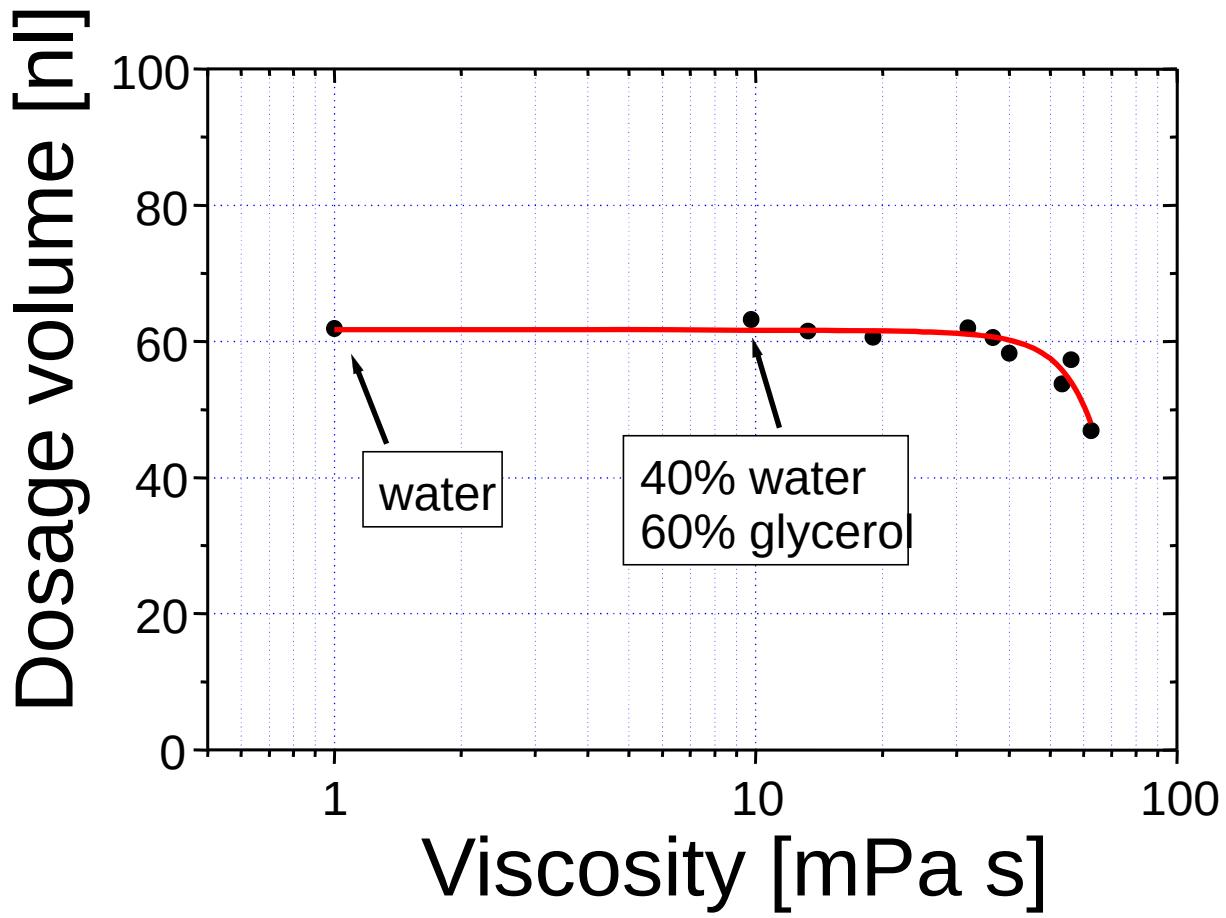
eppendorf
In touch with life



9.4. Dosage Range



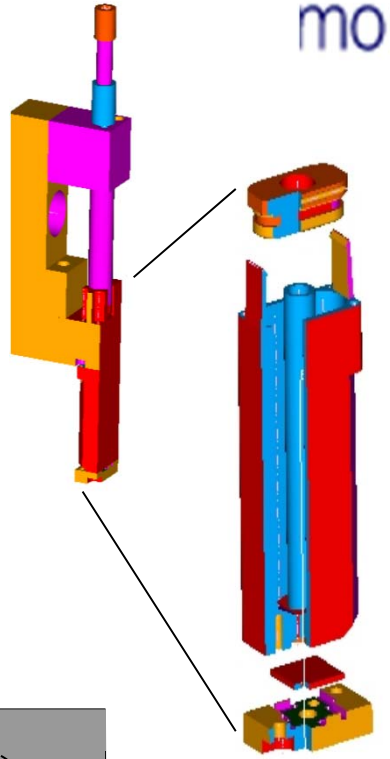
9.4. Independent of Viscosity

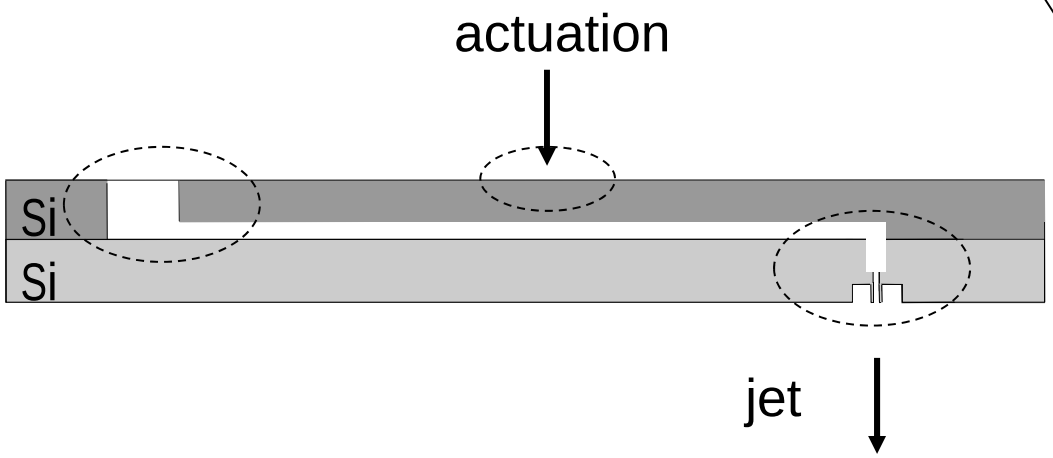


9.4. Face Shooter Configuration

Specifications

- Small footprint in pitch of well plates (9 mm)
- Dosage volume: 5 nl – 500 nl
- Fluids: DMSO, etc.
- High dosage quality and reliability

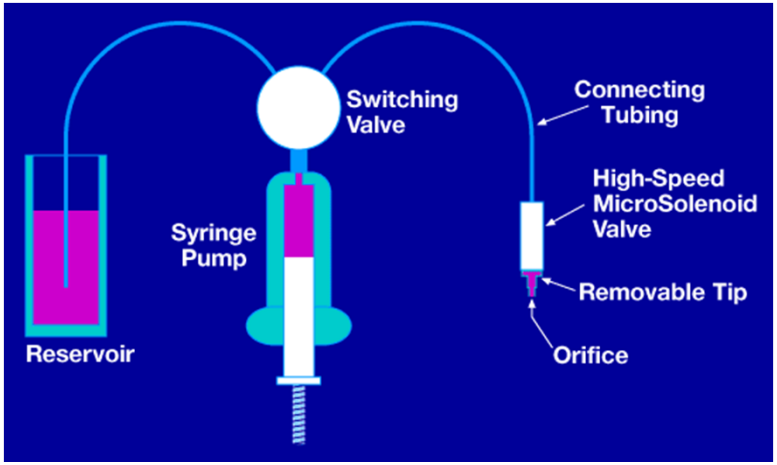


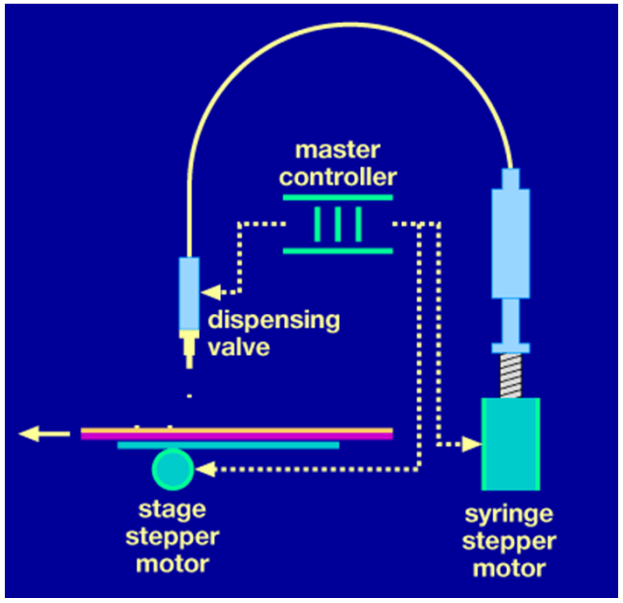


9.4. synQUAD of Cartesian

Process:

- Syringe pump displaces defined amount of fluid
- Displaced fluid creates positive pressure
- Opening of high-speed valve releases fluid as free flying jet
- The volume of dispensed liquid defined by syringe

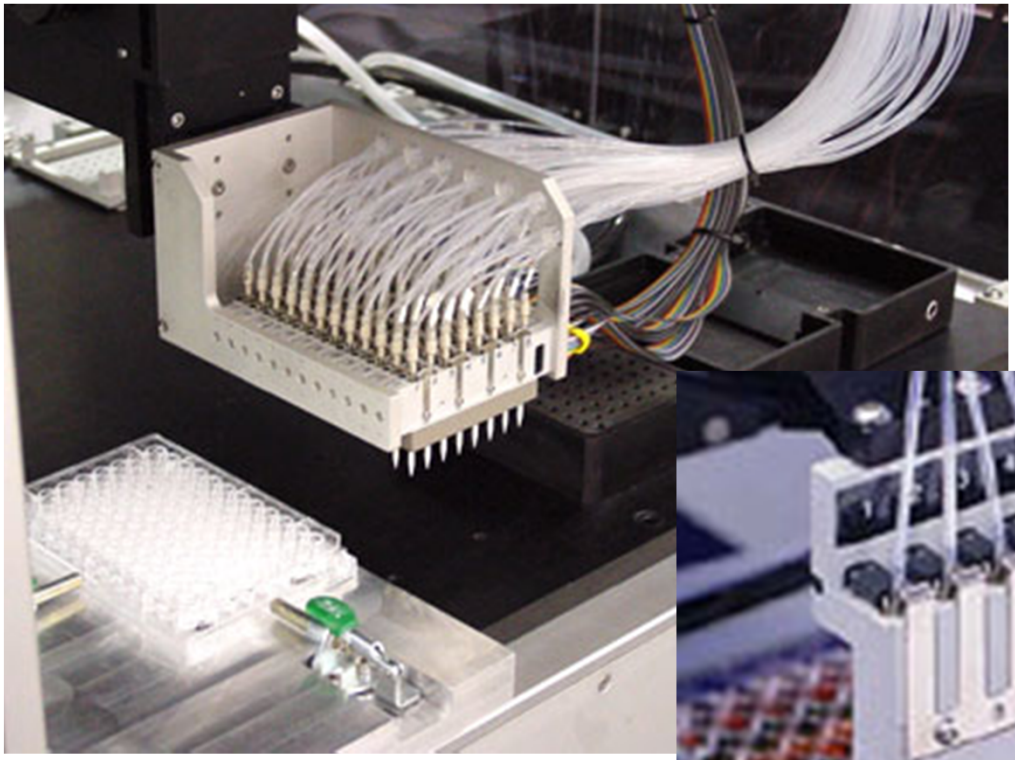




Features

- 100 µl syringe with 24,000 stepper motor provides resolution of 4.2 nl
- Volume range: 50 nl to 8 µl

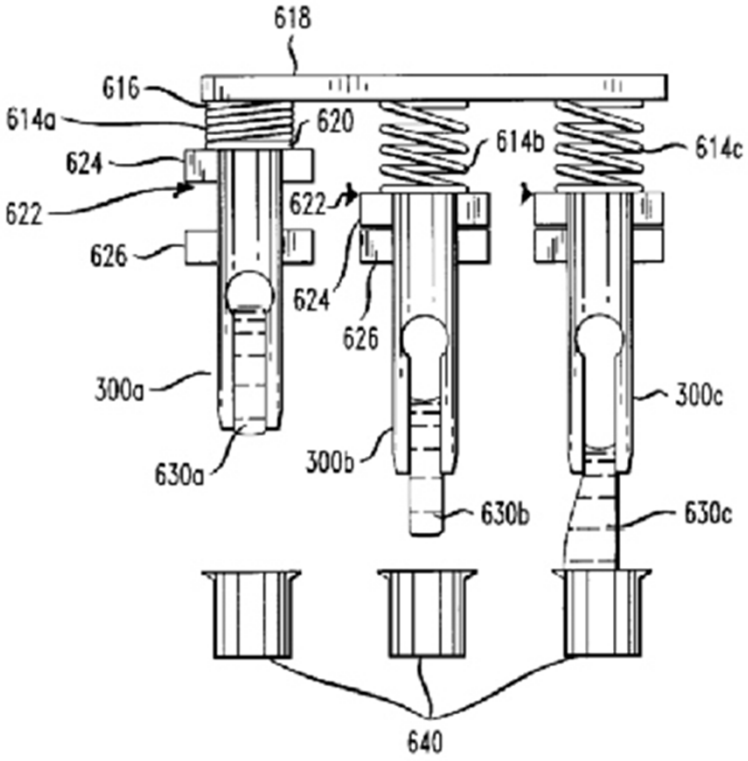
9.4. synQUAD by Cartesian



96 channel
dispense head

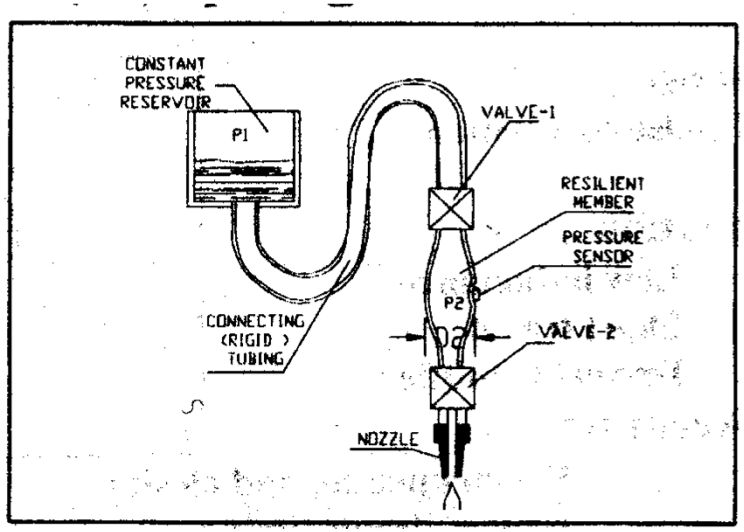
8 channel
dispense head

9.4. Dispensers from Pharmacopeia



Process:

- Liquid held by capillary forces
- Cavity accelerated and stopped
- Liquid escapes due to inertia



Process:

- Constant pressure inside reservoir
- Liquid released by opening valve (similar to synQUAD)

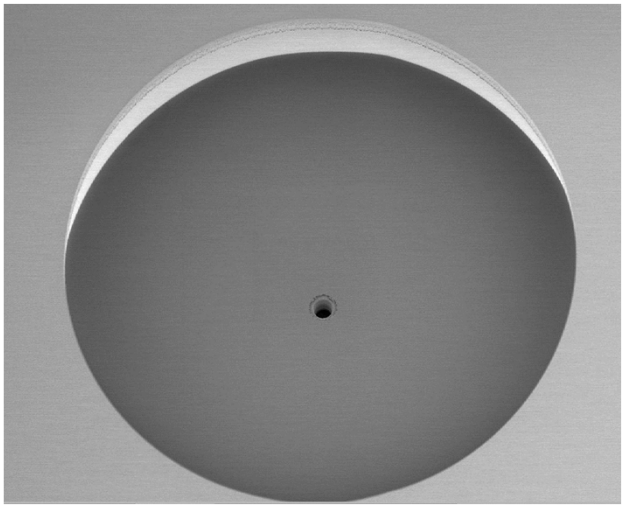
9. Liquid Handling

1. Well-Plate Technology
2. Conventional Pipettes
3. Inkjet Dispensers for Biofluids
4. Stream-on-Demand Technology
5. Well-Plates with Integrated Fluidics
6. Flow-Rate Dispensers

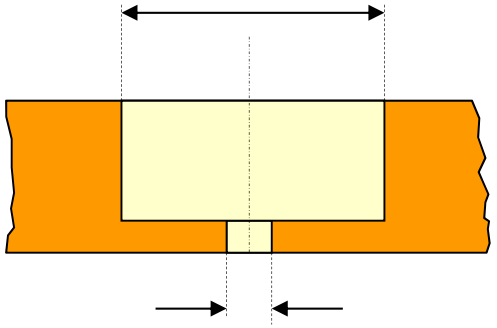
9.5. Hole in Reservoir

What would be the easiest way

to dispense highly parallel?



- Drill hole in every well
- Apply pneumatic pressure to whole plate
- Control time and amplitude applied pressure

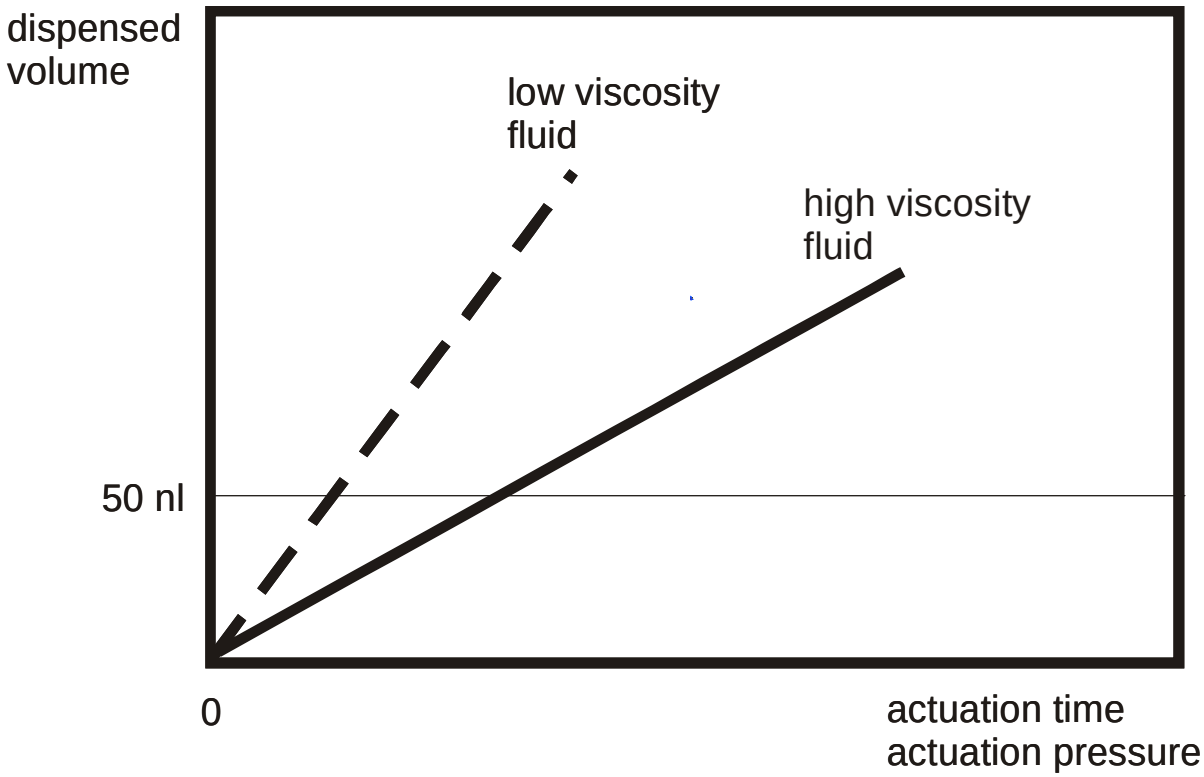


?

Problem:

- Dispensed volume depends on viscosity, switching time, pressure amplitude, etc.

9.5. Hole in Reservoir

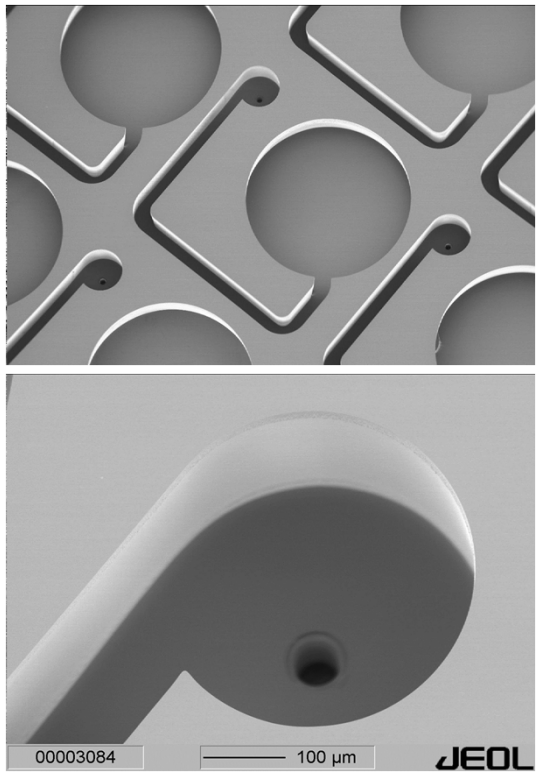


9.5. Dispensing Well Plate (DWP)

What would be a better

solution for that?

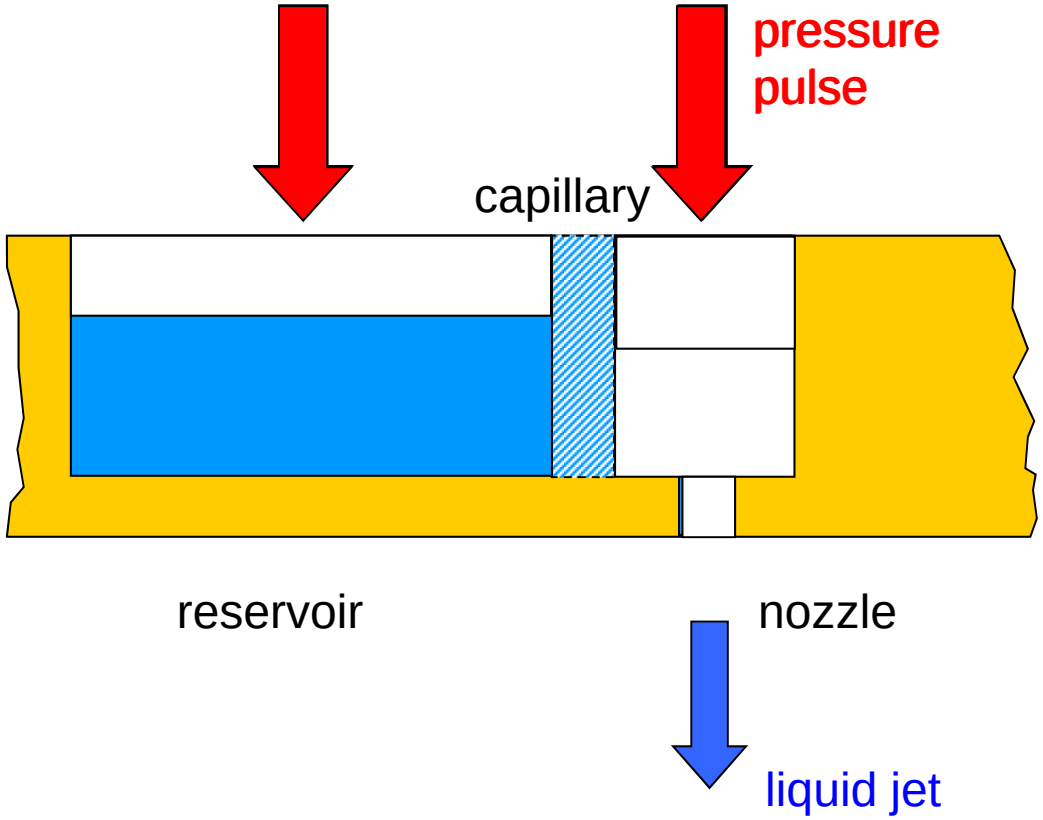
- Separate hole and reservoir
- Define liquid volume by volume of hole and attached chamber
- Dispense entire chamber volume

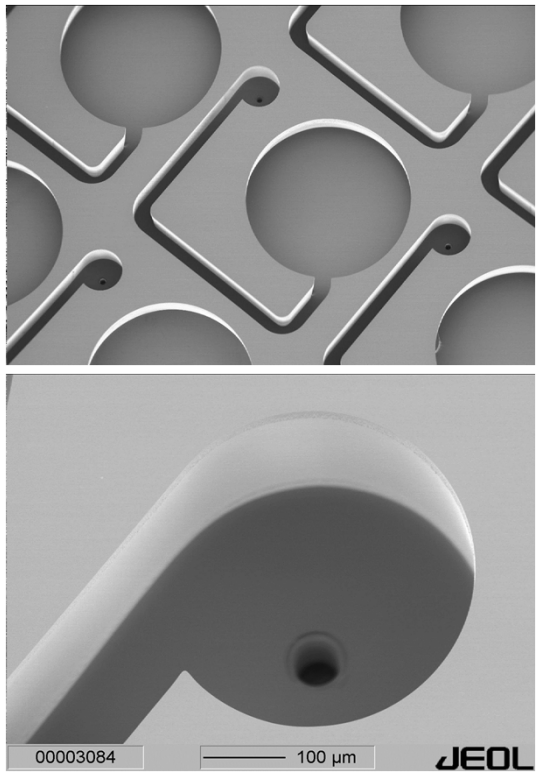


Advantage:

- Process nearly independent of time & amplitude of pneumatic pressure
- Process independent of liquid properties

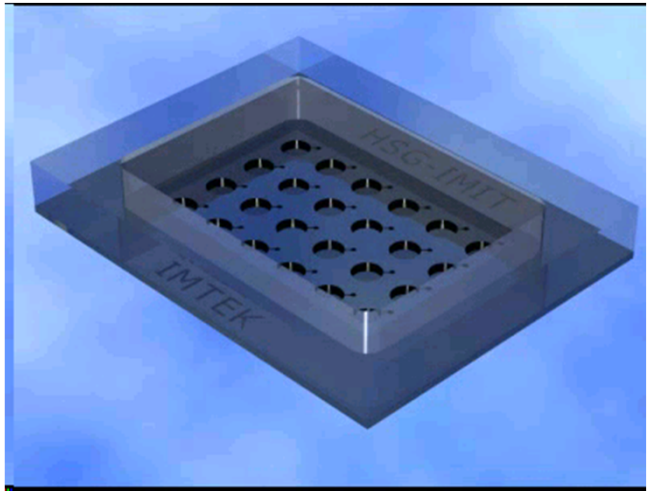
9.5. DWP Principle





9.5. Dispensing Well Plate

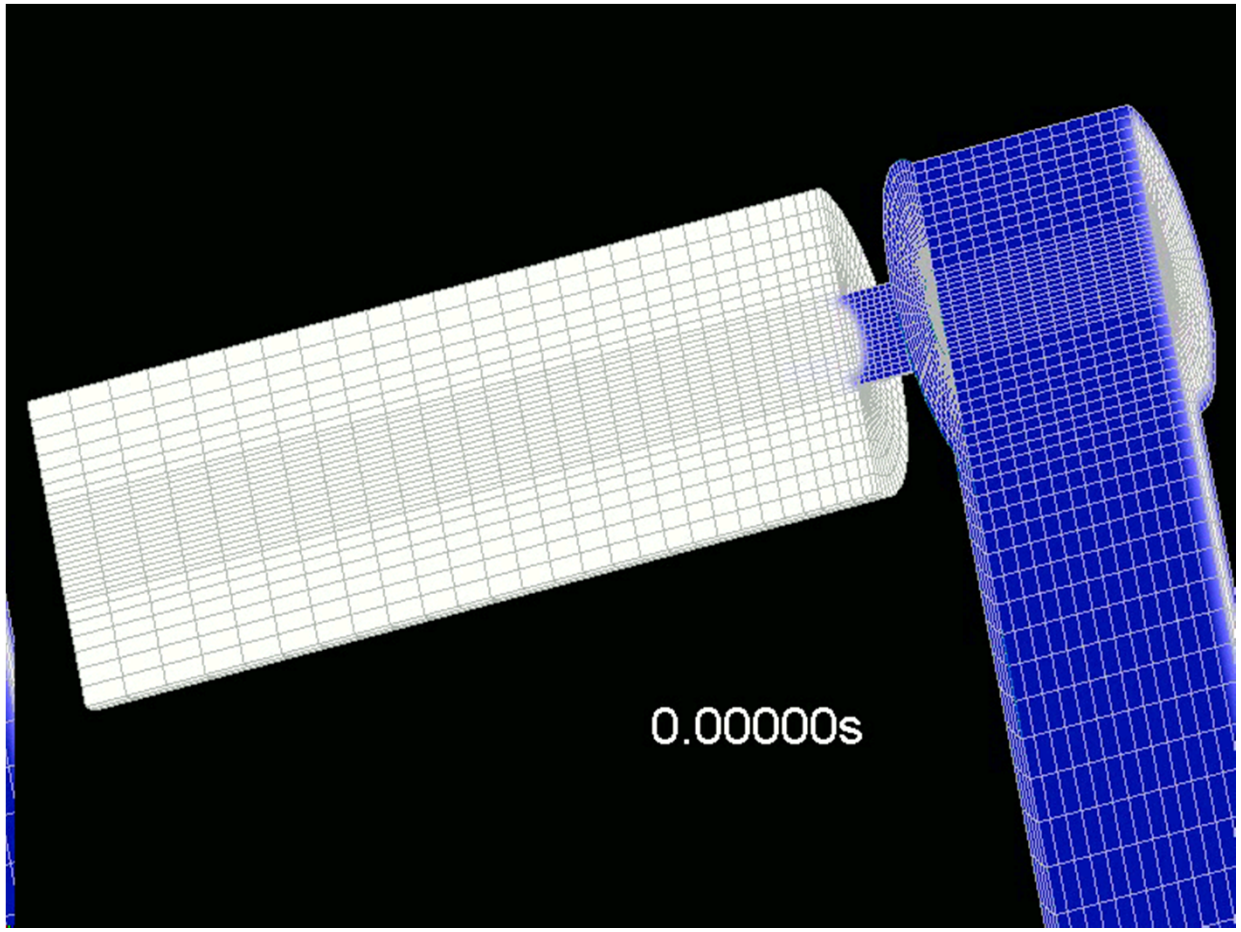
Fixed volume dispenser (e.g. 50 nl) for
simultaneous dispensation into (up to) 1536-wells



<u>Dispenser requirements:</u>

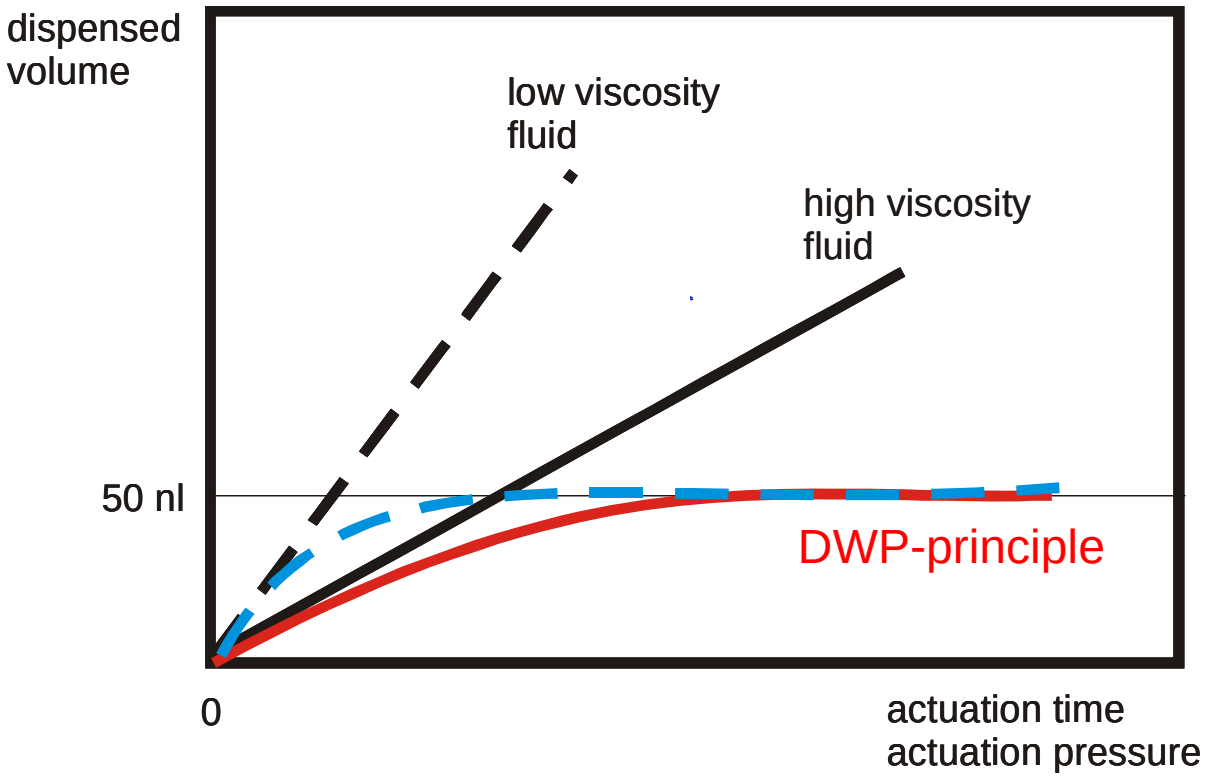
- Disposable device
- Parallel dispensing
- Media: DMSO & water
- CV better than 10%
- Low cost !

9.5. Dispensing Well Plate



9.5. DWP-Principle

dispensing well plate concept is based
on a limitation of the dispensed volume
corresponding to the volume of the nozzle



9.5. Prototype

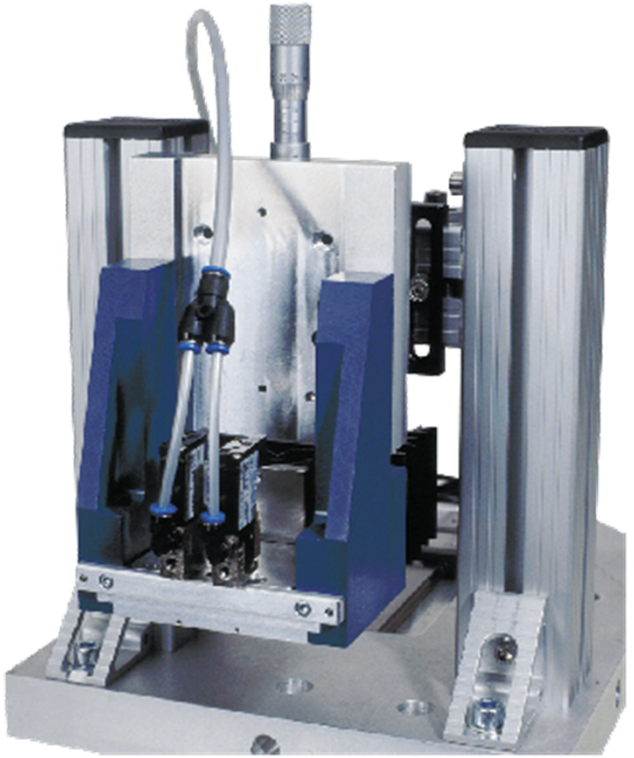
DWP in Silicon / Pyrex:

- 96 or 24 channels with pitch of 2.25 mm
- Reservoir volume < 0.7 µL

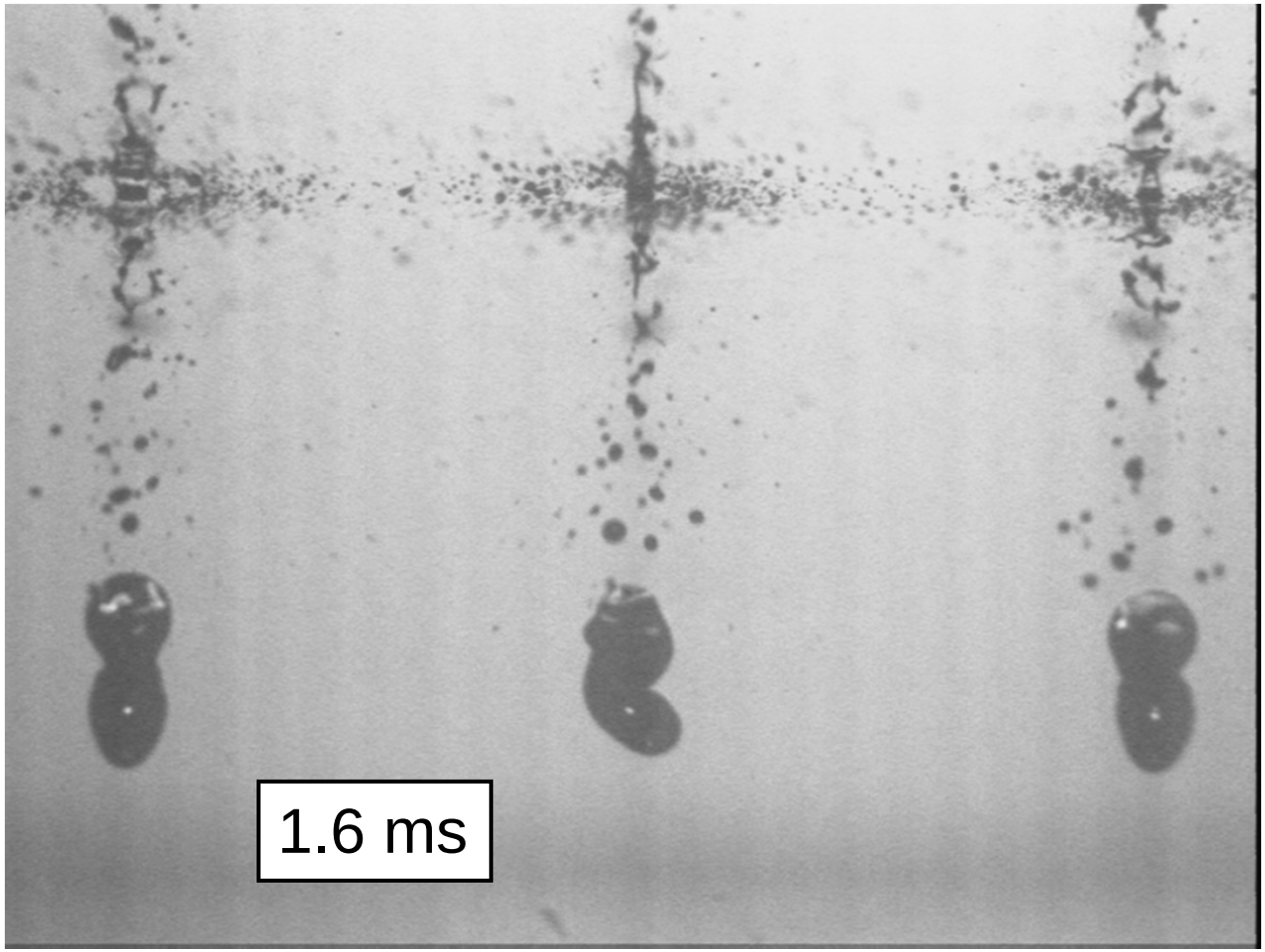
Manufactured by silicon dry-etching and fusion bonding

Actuation unit:

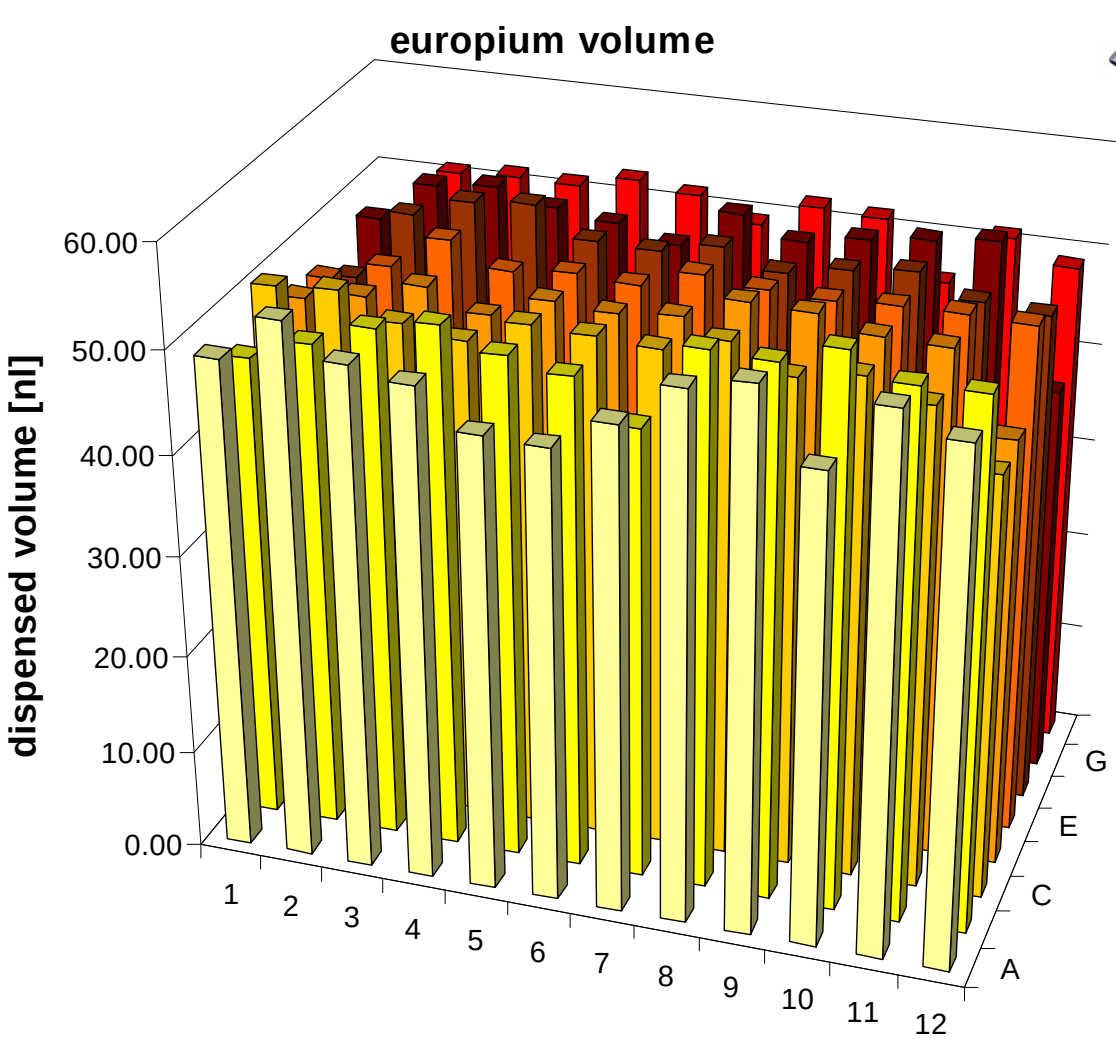
- Pressure chamber
- Two pneumatic valves



9.5. Stroboscopic Video



9.5. Measurement Based on Plate Reader



96 channels
dispensed in plate

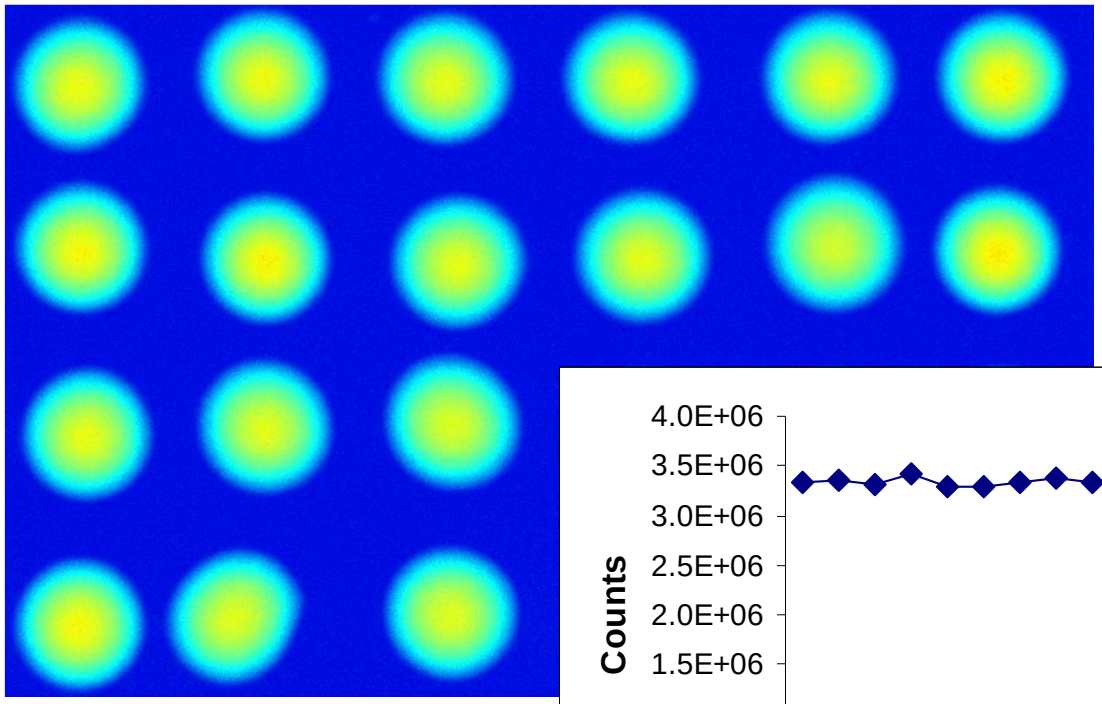
mean: 50 nL
CV = 5.4% *

Accuracy limited by:

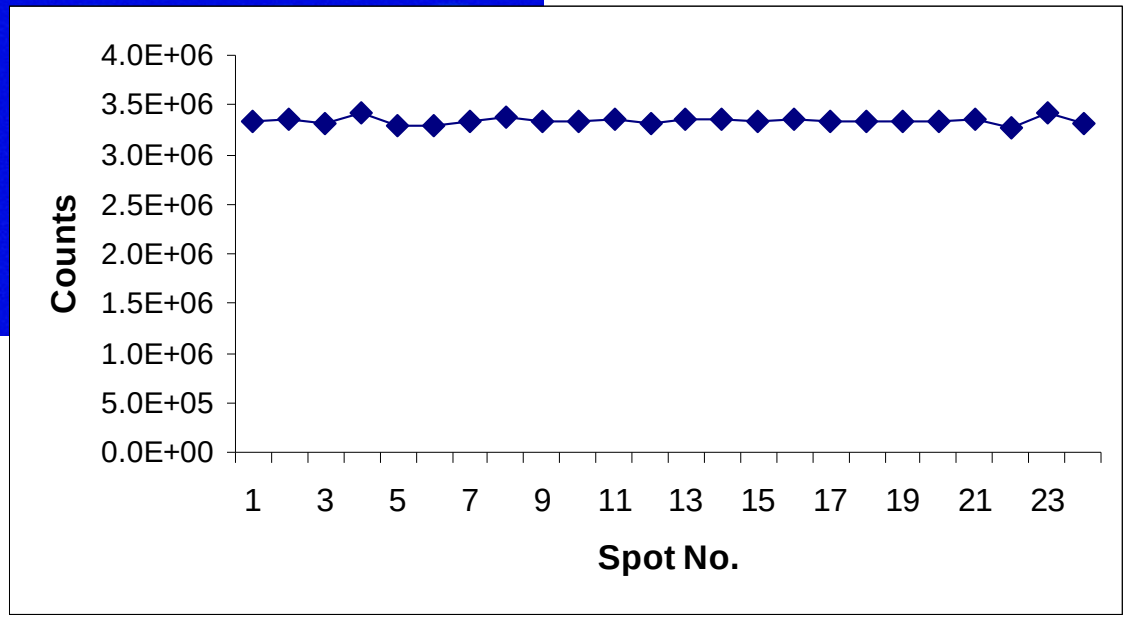
- Complicated calibration method
- Large CV of pre-dispensed volume

9.5. Measurement Based on Chip Reader

24 channels
dispensed on slide



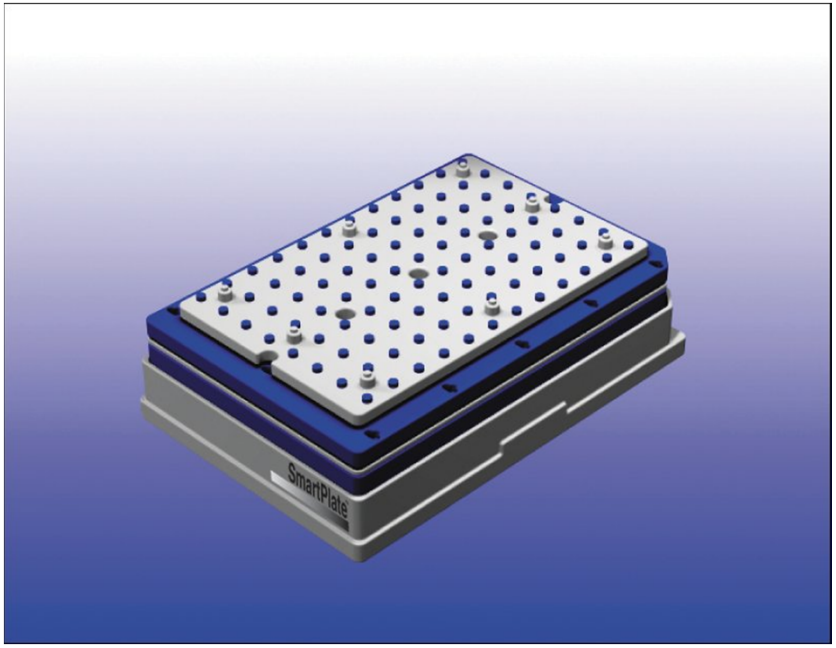
Mean: 43 nL
CV = 1%

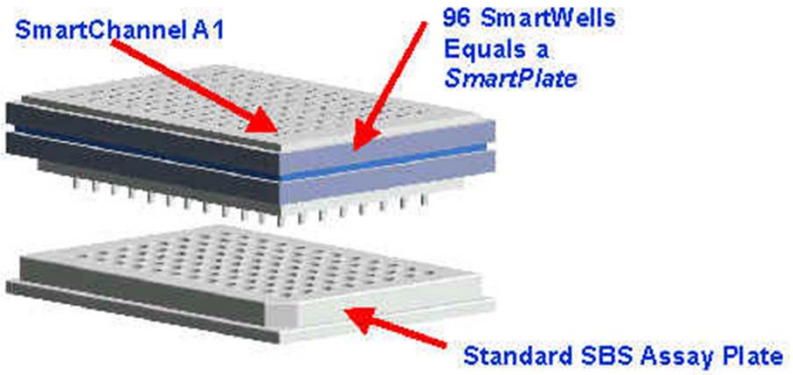


9.5. Smart Plate (Boston Innovation)

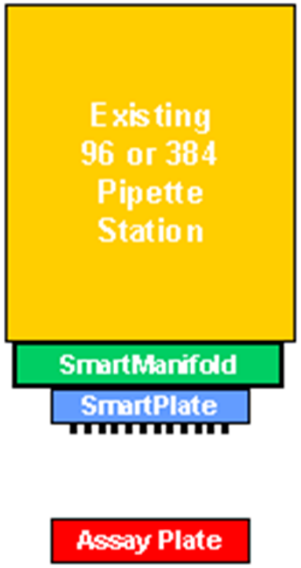
Smart Plate Concept

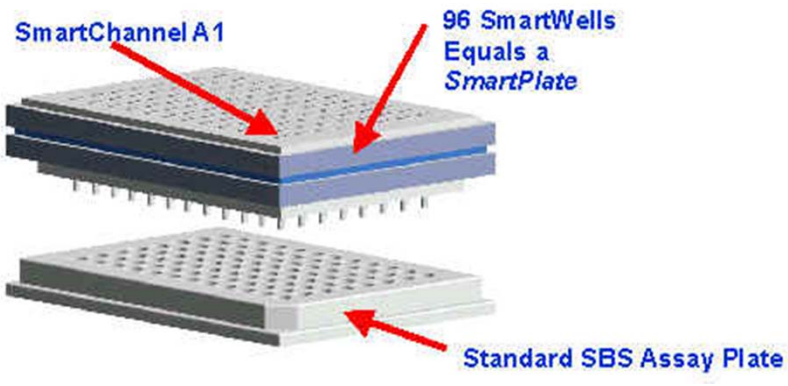
- Well plate with completely sealed, integrated storage capability (10 – 100 µl)
- Samples of nl volume taken from internal storage
- Samples diluted with system liquid
- Samples dispensed into standard well plate
- 8-channel prototype available

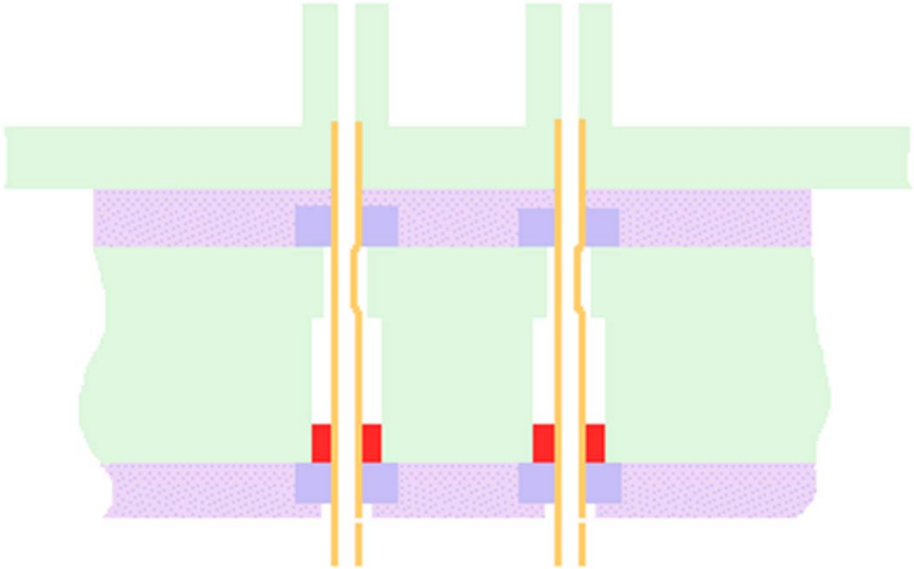




9.5. Smart Plate (Boston Innovation)



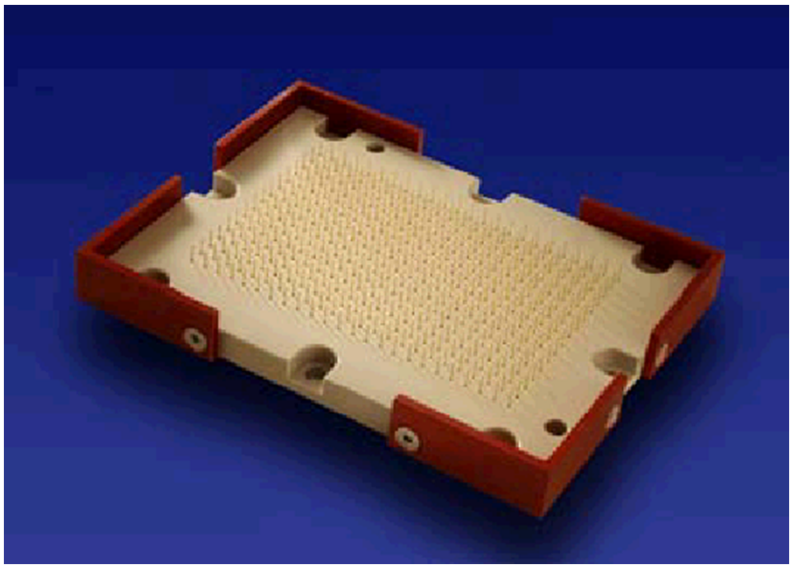




9.5. Humming Bird (Cartesian)

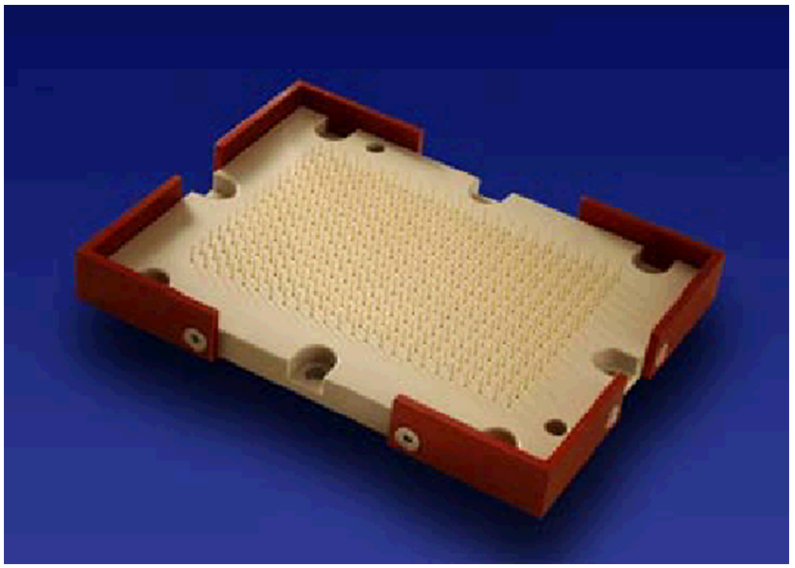
Concept

- Dosage head with integrated capillaries made of steel (96, 384 or 1536 capillaries)
- Volume of each capillary well defined
- Aspiration by capillary forces
- Dispensation by pneumatic pressure
- Fixed volume pipette
  - 50 nl; 100 nl; 250 nl
  - CV: < 10 %
  - 35 seconds for plate transfer



HUMMINGBIRD™ TECHNOLOGY

9.5. Humming Bird (Cartesian)



HUMMINGBIRD™
TECHNOLOGY

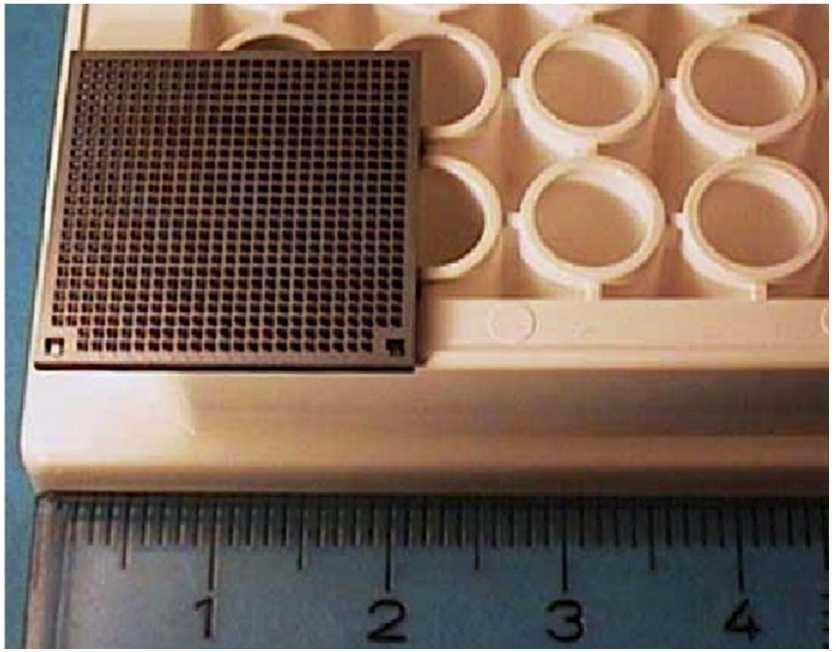
9.5. Well Plate Technology

- Introduction
- Standard Technology
- Improvements by MEMS
- NanoPlates
  - NanoPlate
  - Lilliput System

9.5. NanoPlate

Concept

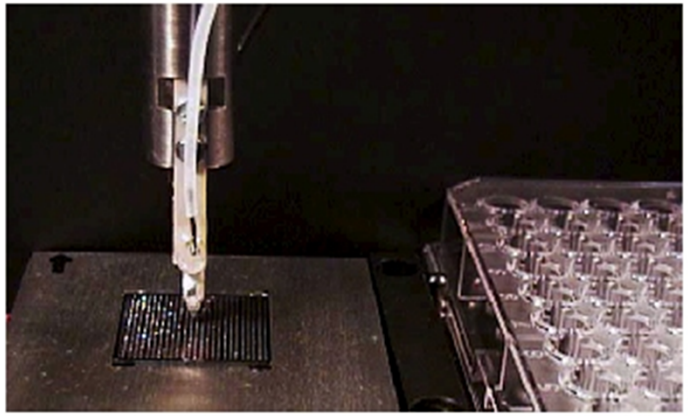
- Further reduction of assay volume
- Miniaturization of assay successfully demonstrated at University of Tübingen, Germany
- Pitch: 750 µm
- Volume: ...



- Liquid handling by inkjet dispenser
- Control of evaporation is critical!

9.5. NanoPlate

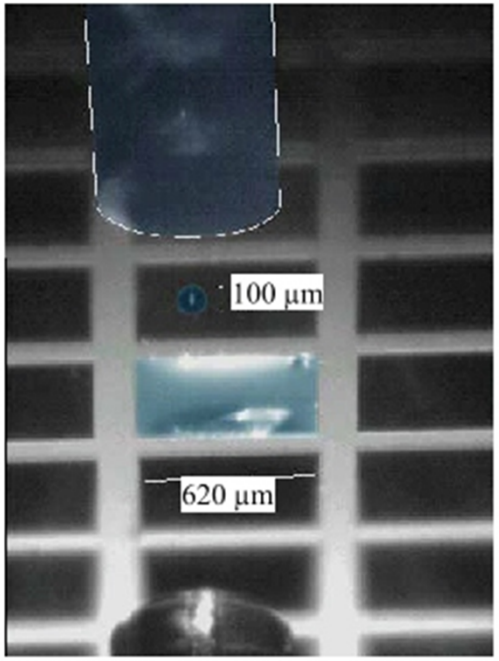
Probenhandhabung



Mikropumpe über einer Nanotiterplatte

Piezoelektrische Dosiersysteme:

- Tropfenvolumen: 0.5 - 2 nl
- rel. Dosierfehler: < 2%
- x,y Positionierung: 1 µm



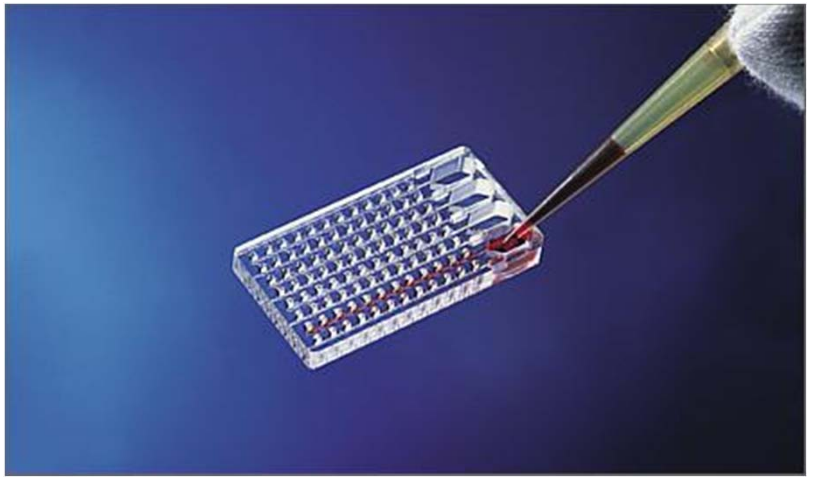
Befüllung einer Kavität der Nanoiterplatte.

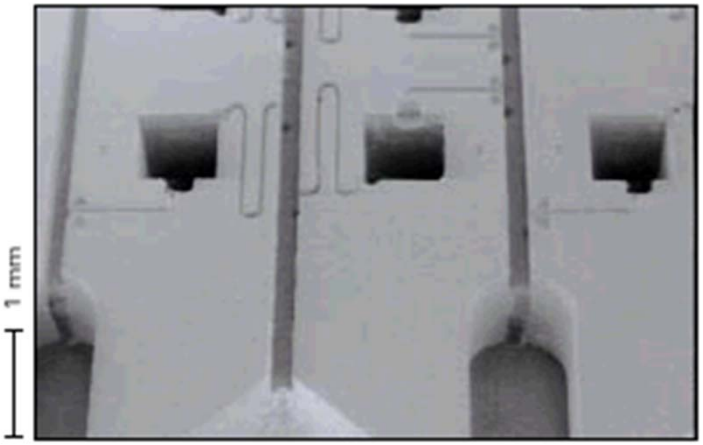
9.5. Lilliput System

Concept

- Miniaturized plastic carrier with 96 wells divided into 4 segments
- 24 different biological reagents immobilized on every segment
- All wells of segment accessible by dispensed liquid (cell suspension) on right hand side
- Liquid transport by capillary forces
- Screen 4 different samples for 24 different reagents
- Size: 20 x 38 x 3 mm^3

Merlin Diagnostika, Bornheim
In cooperation with Microparts





9. Liquid Handling

1. Well-Plate Technology
2. Conventional Pipettes
3. Inkjet Dispensers for Biofluids
4. Stream-on-Demand Technology
5. Well-Plates with Integrated Fluidics
6. Flow-Rate Dispensers

9.6. Objectives - Area of Application

- Local, intermittent long-term treatment of chronic diseases

- Examples
  - Tinnitus therapy
    - Local application of medicaments of the middle and inner ear are invasive and unpleasant for the patient
  - Insulin delivery

- Traditional drug delivery systems
  - Pills
  - Hypodermic injection

9.6. Objectives & Engineering Concepts

- Delivery of drugs in liquid phase from reservoir to tissue / blood stream
- Small size for carry-on (e.g. watch) or implantable device
  - Microfabrication
- Subcutaneous deployment
  - Reduced risk of infection
  - Invisible
- Small power consumption for long-term usage
  - Micro-actuators
- Flow-on-demand
  - Integrated flow control
- Accurate flow rate / accumulated flow volume
  - High precision inherent to microfabrication
- Emergency shutdown
  - Active flow control and / or normally-closed valving
- Biocompatibility, e.g. to prevent thrombus formation
  - Choice of materials
- Refilling

9.6. Overview

1. **Pressure-Driven Transport**
   - **Pressure source**
   - **Capillary throttle**
   - **Active valve for interruption of flow**
2. Micro Displacement Pumps
   - Pump chamber
   - Actuator with energy supply
   - Passive valves
3. Other Pumping Concepts

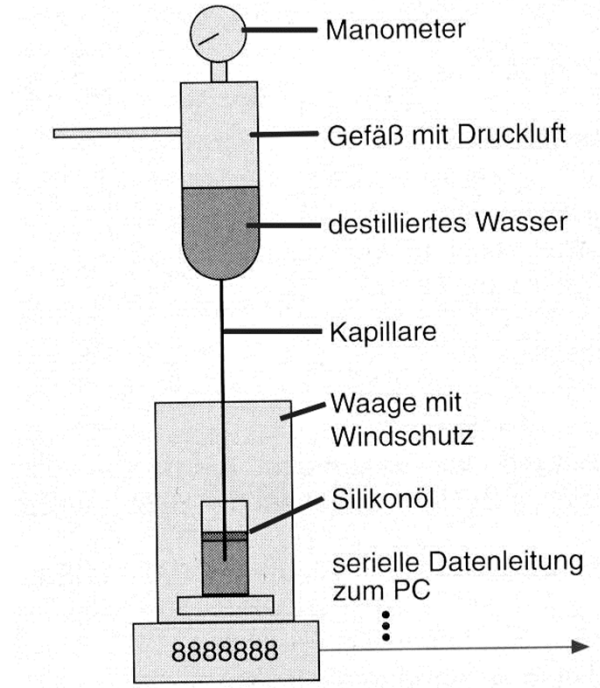
9.6. Pressure-Driven Microdelivery

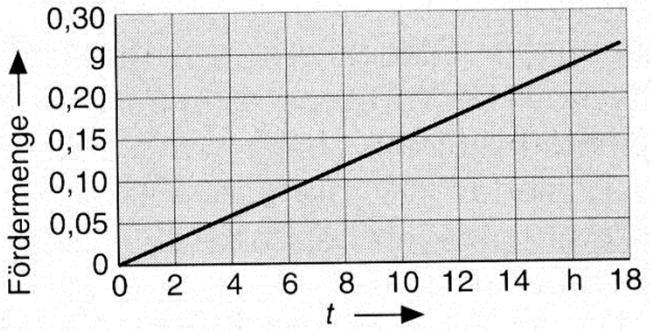
Working Principle

- Pressurized liquid tank
- Throttle
  - Glass capillary
  - Tiny channels on Si chip
- Adaptation of flow resistance by length/diameter of capillary
- Constant, non-adjustable delivery rate

Optional

- Active microvalve to interrupt flow





9.6. Implantable Drug Delivery System

Applications

- Pain therapy
- ...

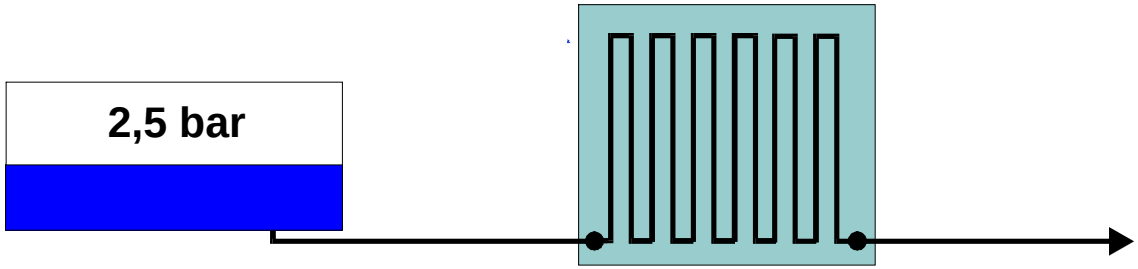
Specifications

- Flow : ~ µl / min
- Low power consumption
- Small size
- Well defined flow rate
- High reliability

9.6. Implantable Drug Delivery System

Concept

- **Constant pressure is transformed in a ..**
- **... constant flow of drug**
- **... by a well defined flow resistance**



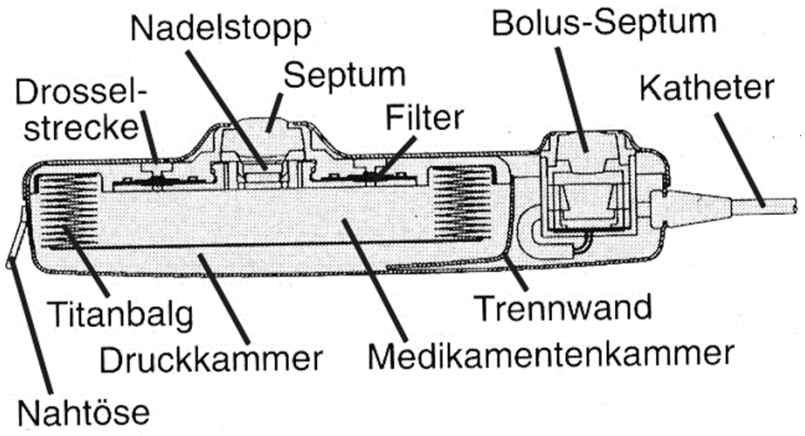
reservoir

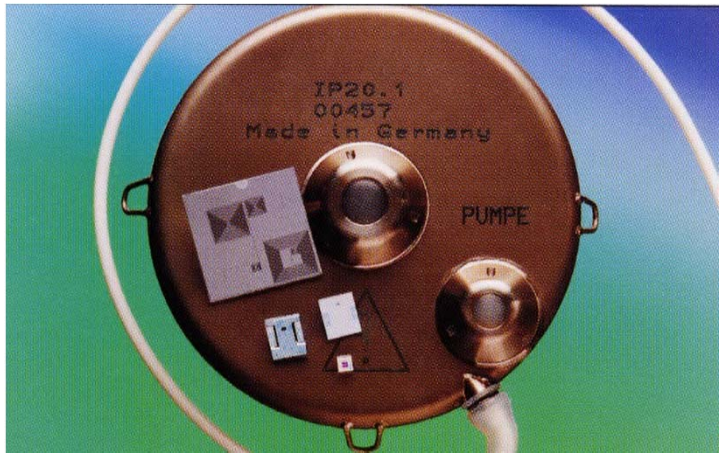
capillary transforms constant pressure in constant flow

9.6. Implantable Drug Delivery System

Realization

- **Pressure generation by two phase fluid (vapour pressure)**
- **Flow resistance by small capillary in a silicon chip**

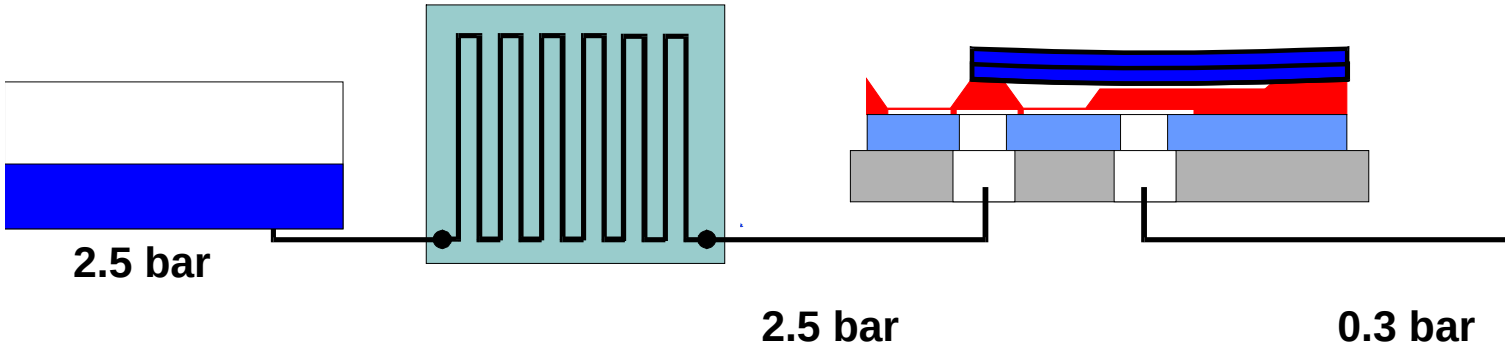




9.6. Implantable Drug Delivery System

Concept of controllable drug delivery system

- Usage of cut-off valve (normally closed)



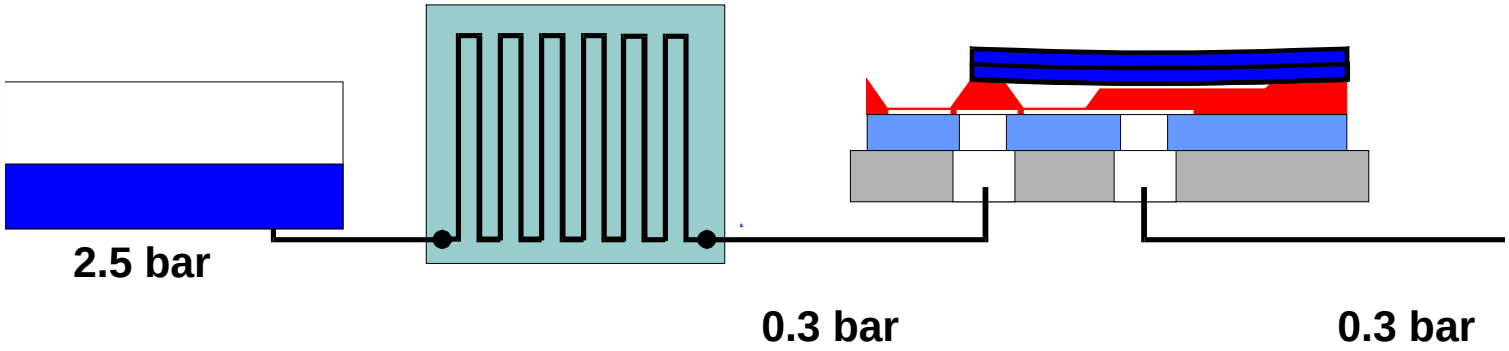
Additional specifications

- Filtered fluids (0.2 µm)
- Leakage rate < nl / min
- Small energy consumption (battery life time > 7 years)
- Small size

9.6. Implantable Drug Delivery System

Concept of controllable drug delivery system

- Usage of cut-off valve (normally closed)



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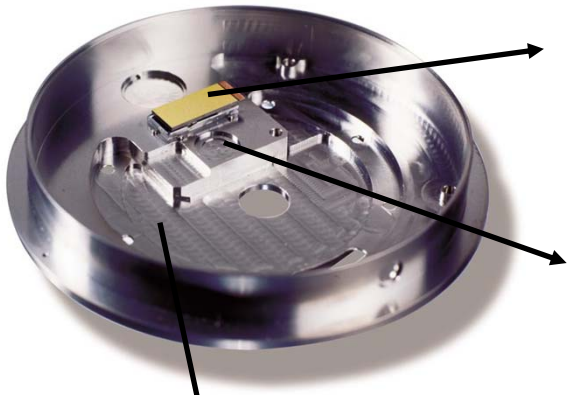
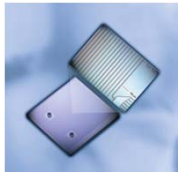
- Small size

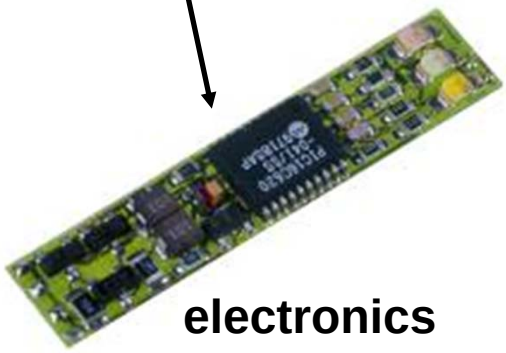
9.6. Implantable Drug Delivery System



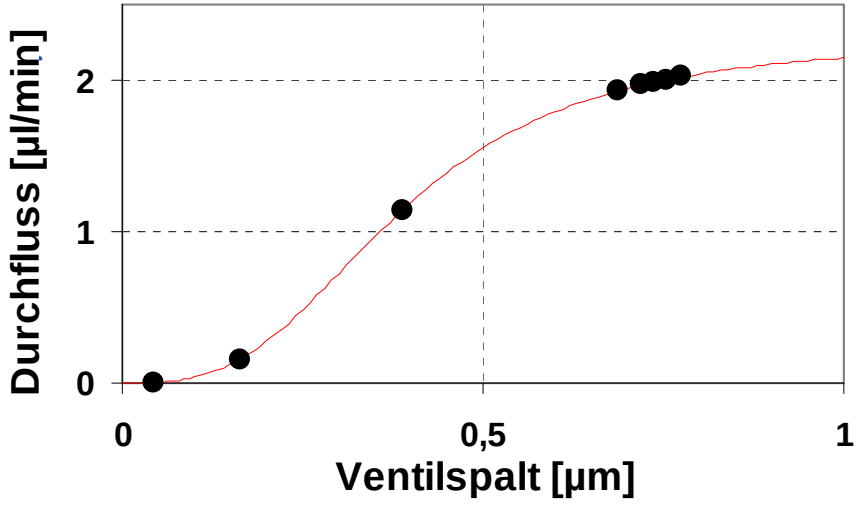
valve



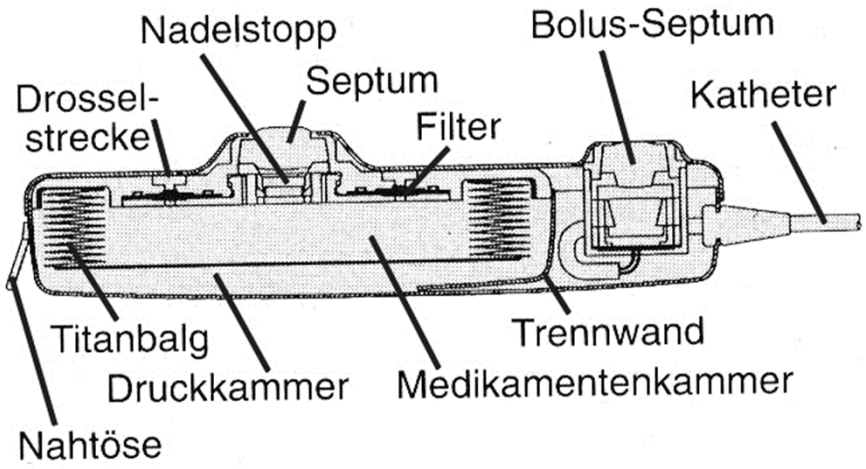
flow resistance

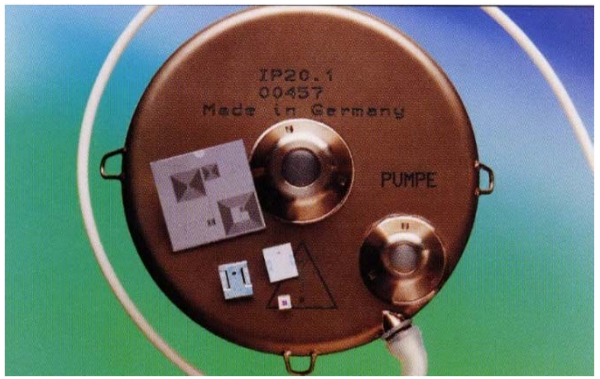


electronics



9.6. Implantable Drug Delivery System





<u>Company Tricumed (Kiel, Germany)</u>

- Pressure generation by
  - Spring
  - High-vapor pressure liquid like fluorocarbon
  - combination
- Capillary throttle realized in Si

9.6. Extra-Corporal Drug Delivery System

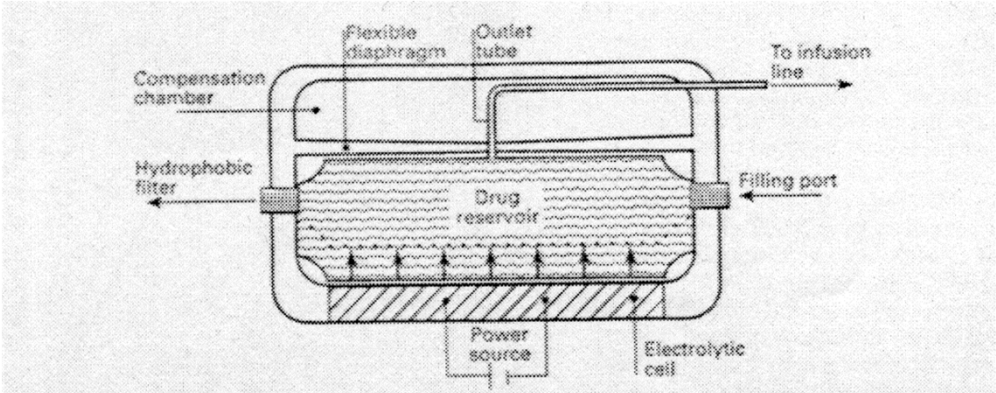


Figure 1 Schematic diagram of the pump cartridge, illustrating the operating principle. A battery supplies current to an electrolyte-containing membrane and produces gas which compresses a reservoir which contains medication. A compensation chamber corrects for fluctuations in ambient temperature and pressure. The filling port and hydrophobic filter are placed as shown.

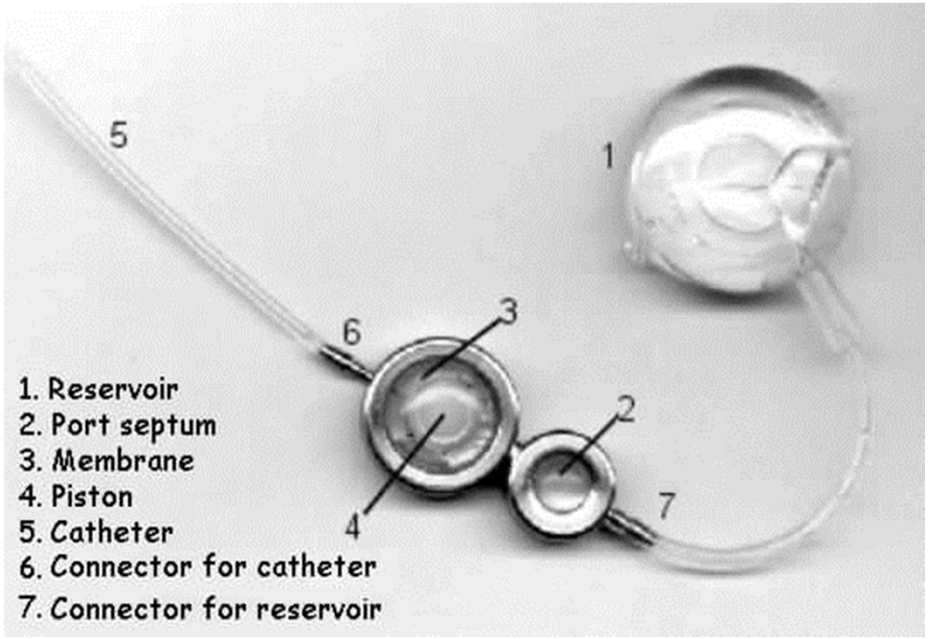
Figure 2 The infusion pump showing the pump cartridge removed from the electronic control unit. There is a filter in the infusion line.

Electrochemical Pressure generation

- Gas released in electrochemical reaction
- No capillary throttle required

9.6. Manually Driven DDS

- Mikro Infusions Systme GmbH, Austria
- Totally implantable
- Manual pressure generation
  - No power source required
- Biocompatible materials
  - Pure Ti
  - Pure silicone



9.6. Manually Driven DDS

- **"Bolus-on-demand"**
  - The patient can release a **preset quantity (bolus)** of **5 µl or 10 µl** of the drug by **finger pressure** as required. A larger quantity of the drug can be delivered by **repeated operation**. Unlike conventional drug pumps, the TI-DDS user can act independently of preset pump intervals and volumes.

•Pump rate volume5 µl or 10 µl

•+/- 10% per single pump action)

•Finger pressure force

•approx. 5 N

•Drug reservoir volume

•2.5 ml

•System weight (filled)

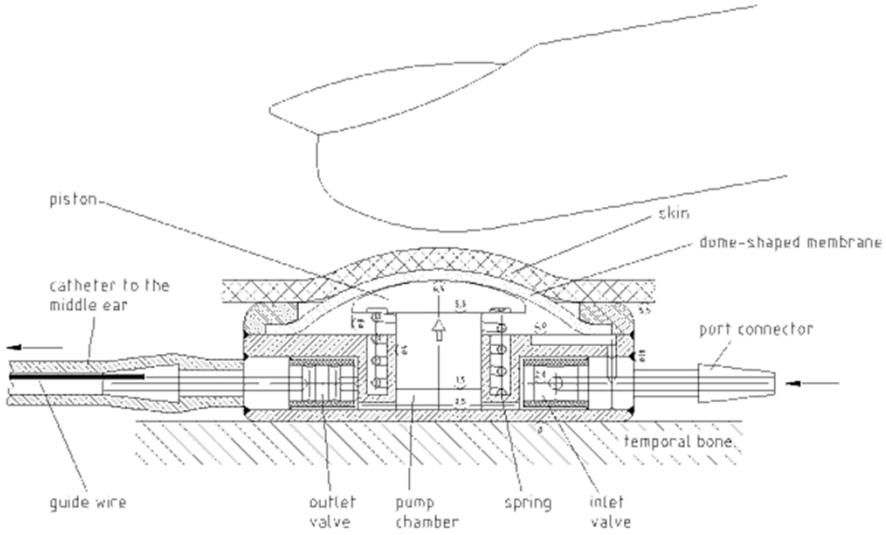
•12 g

•Number of septum punctions

•max 1000

•Integrated particle filter

•max. particle size 20 µm



9.6. Responsive Drug Delivery System

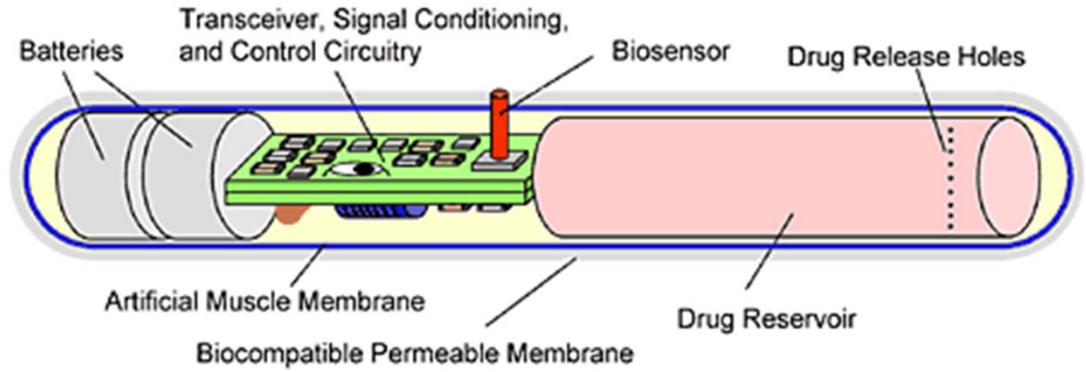
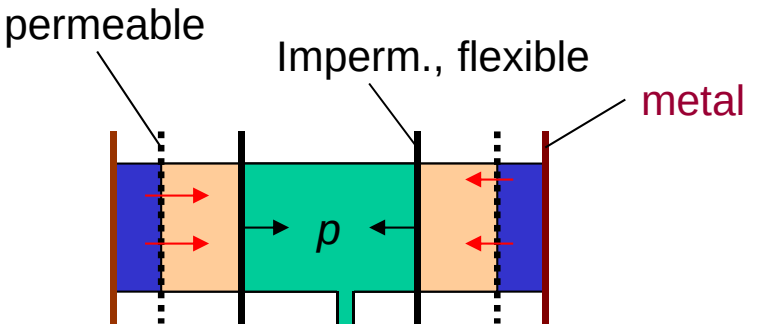


Diagram of a Responsive Drug Delivery System

- Development at NASA
- Controlled drug delivery (or controlled release)
- Diseases such as diabetes, heart disease, hormonal disorders, and cancer
  - Require drug administration either at a life-threatening moment or repeatedly at a certain critical time of day
- Smart metallic and polymeric reversible valves (artificial muscle) in flexible non-Si substrates
  - Different types of drug delivery implants
  - In conjunction with selective sensors

9.6. Osmotic Delivery System

- Setup
  - Osmotic pressure to release drug at constant rate
  - Drug contained in impermeable diaphragm
  - Osmotic agent surrounds diaphragm
  - Semipermeable membrane contains osmotic agent
  - Entire pump housed in immovable metal casing
- Mechanism
  - Diffusion of water through semipermeable membrane squeezes diaphragm holding drug, forcing drug into bloodstream



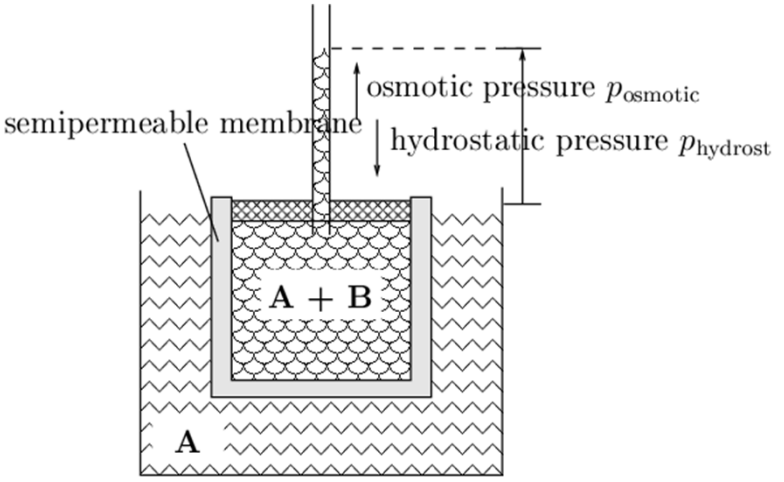
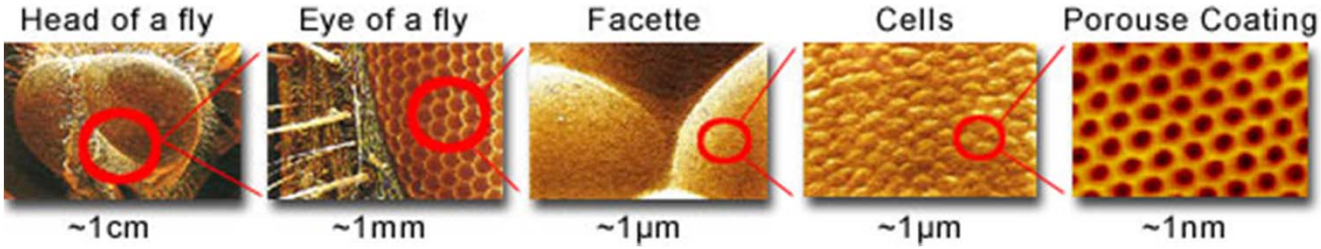
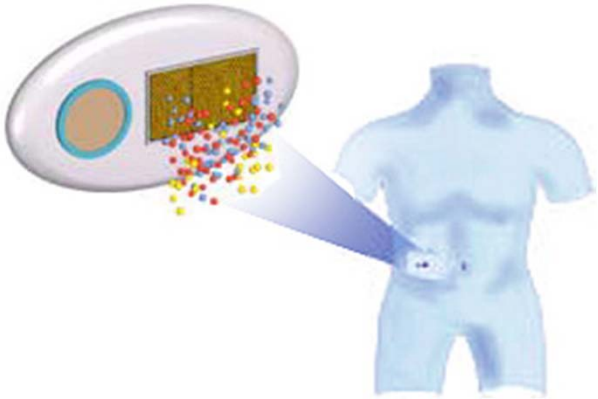


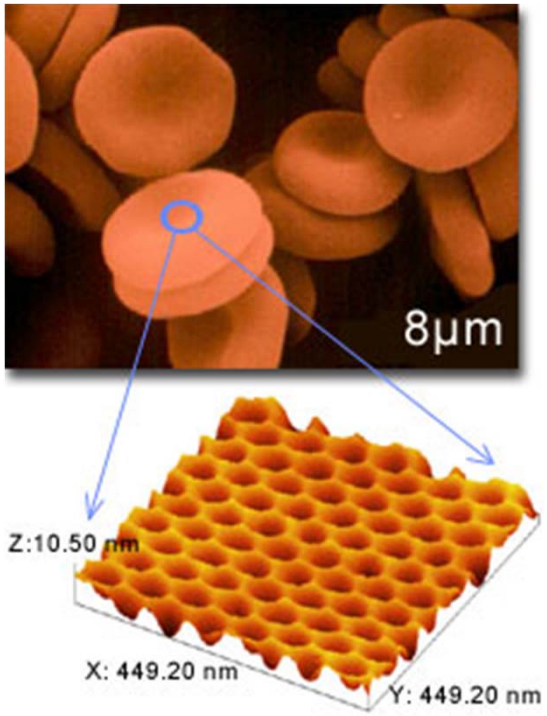
Fig. . Pfeffer cell. The semipermeable lets A pass in either direction while constituent B is kept in the inner vessel. The osmotic pressure $p_{osmotic}$ is equivalent to the hydrostatic pressure in the column

9.6. Debiotech: Osmotic DDS



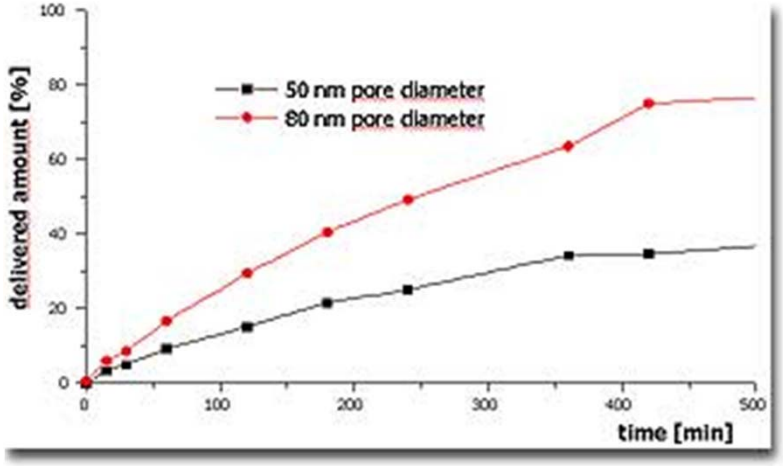
- Implantable drug delivery technology for sustained delivery of pharmaceutical compounds
- Delivery through nanopores

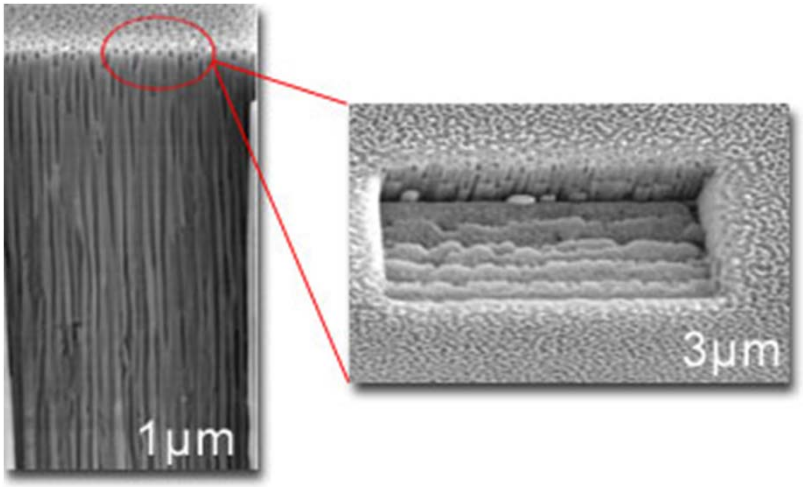


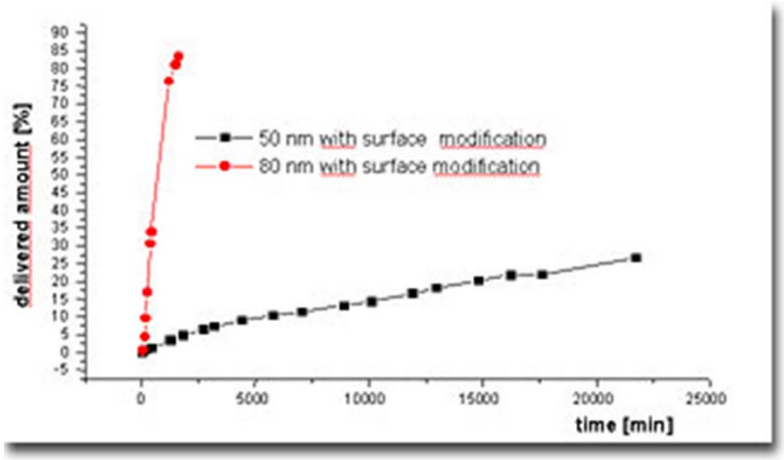


9.6. Debiotech: Osmotic DDS

- Nanopores
  - Accurately controlled fabrication scheme
  - Running parallel through layer
  - Length can be less than 50 nm and more than 150 µm







9.6. Overview

1. Pressure-Driven Transport
   - Pressure source
   - Capillary throttle
   - Active valve for interruption of flow
2. **Micro Displacement Pumps**
   - **Pump chamber**
   - **Actuator with energy supply**
   - **Passive valves**
3. Other Pumping Concepts

9.6. Micro-Displacement Pump with Fixed Stroke

Debiotech; Switzerland; 1998

- Based on pump design by Harald van Lintel
- Integrated particle lfilter
- For implantable DDS
- Expensive!

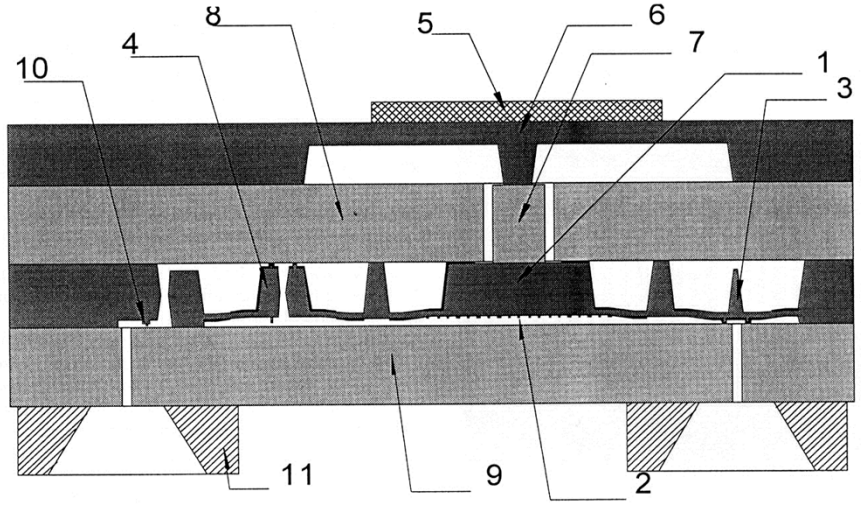
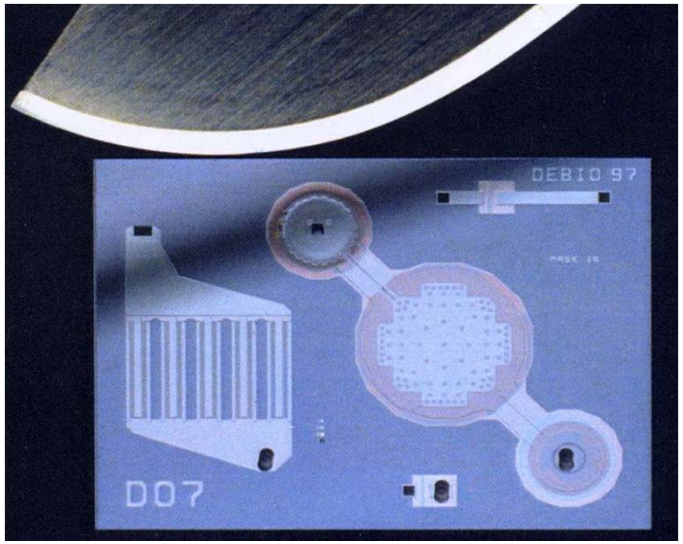
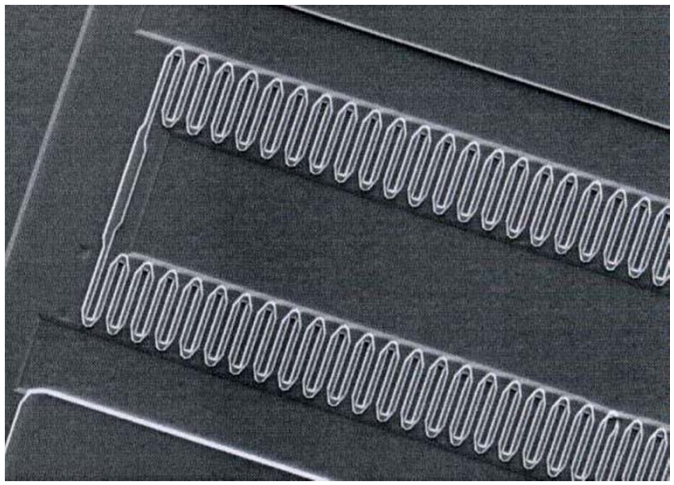


Figure 2: Schematic cross section of the pump (not to scale)

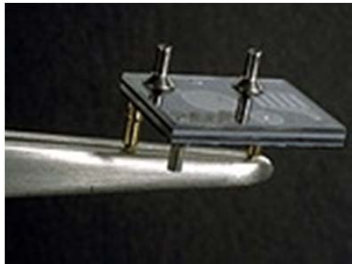


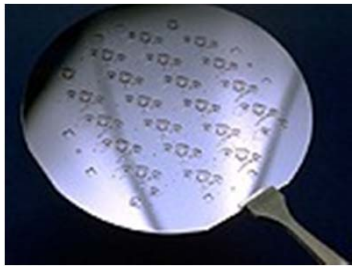


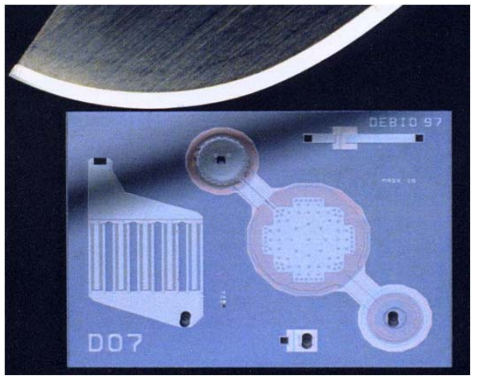
9.6. Micro-Displacement Pump with Fixed Stroke

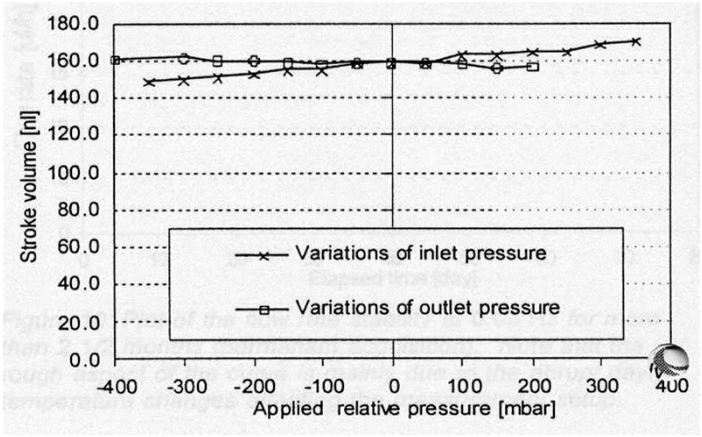
Debiotech; Switzerland; 1998

- Membrane deflects between two mechanical stops
- Fixed pump volume
- Pump rate analogous macropump
  - Set by frequency
  - Independent of back pressure









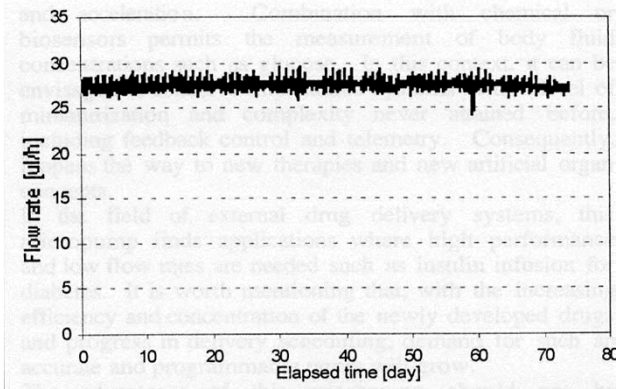


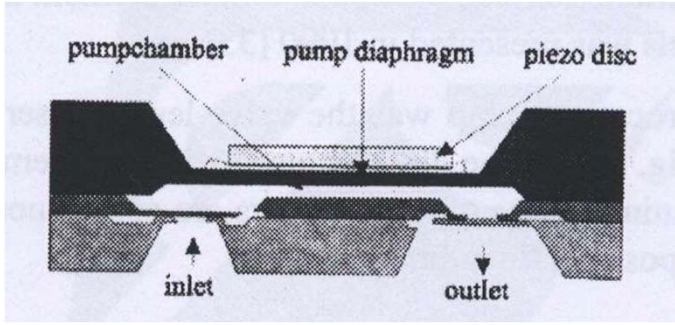
Figure 10: Plot of the flow rate stability at 0.05 Hz for more than 2 1/2 months (permanent acquisition). Note that the rough aspect of the curve is mainly due to the abrupt daily temperature changes affecting the measurement setup.

9.6. Micro-Displacement Pump with Fixed Stroke

Main performance specifications

- Flow rate 0 to 100 µl/h
  - Linear range, stroke volume constant and flow rate proportional to frequency (Frequency range 0-0.2Hz)
- Priming rate 250 µl/h
  - Maximum flow rate in uncontrolled range (frequency 2Hz)
- Stroke volume
  - 150 nl
  - Minimum dosage unit
- Leakage
  - Non measurable < 0.05 ml / h
  - Forward and backward leak with 150 mbar overpressure applied on inlet respectively on outlet
- Accuracy ± 5%
  - Overall accuracy of stroke volume within nominal conditions
- Inlet pressure
  - -350 to +350 mbar
- Outlet pressure
  - -400 to +200 mbar
- Viscosity 0-10 mPa s
  -
- Actuation voltage -40V/ +110V
  - Voltage applied to piezo
- Compression ratio
  - $E = \Delta V / V_0 = 1.15$
- The pump is self priming and tolerant to small air bubbles.
- Reliability
  - $1.8\ 10^8$ strokes
  - 67 days
  - Equivalent to 25 years of use
- Chip dimensions
  - 16x12x1.86mm

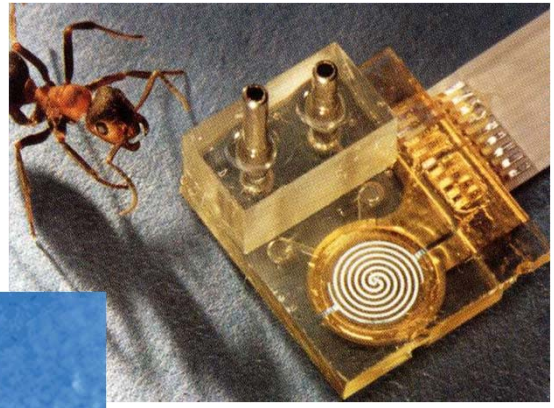
9.6. Micro-Displacement Pumps with Check Valves



FhG-IFT: 1996

Common Problems and Solutions

- Failure due to gas bubbles
  - Minimize chamber volume
  - Maximize compression
  - Gas trap
- Leakage
  - Integrated particle filtering
  - Prefiltering
- Expensive manufacturing
- Low production numbers



IMM-Mainz

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