

Workshop BWAW

Mikrosystemtechnische Lösungen für die Wirkstoffsuche in der Pharmazie und für Life Sciences

Maik Müller, Head R&D

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Introduction

CyBio Solutions

Technology

MEMS - Applications

01
02
03
04

Drug Discovery / Wirkstoffsuche

Wirkstoffe:

Naturstoffe, chemische und gentechnische Wirkstoffe
ca. 500 Wirkstoffe sind heute bekannt

Kosten und Aufwand für die Entwicklung:

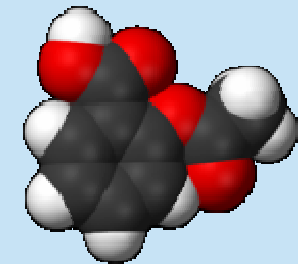
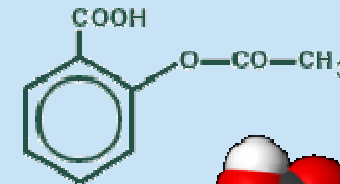
Kosten ca. 800 Mio. \$ (lt. Pharmaindustrie)

Dauer 10-12 Jahre

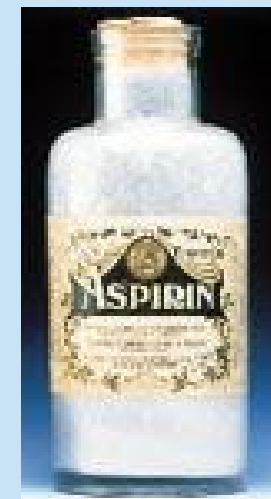
Erfolgsquote $\leq 1 : 5.000-10.000$

Entwicklungszyklus:

1. präklinische Forschung – Hochdurchsatz-Screening (HTS)
2. klinische Forschung / Tierversuche
3. Zulassung



Acetylsalicylsäure



Hochdurchsatz-Screening (HTS)

Ziel:

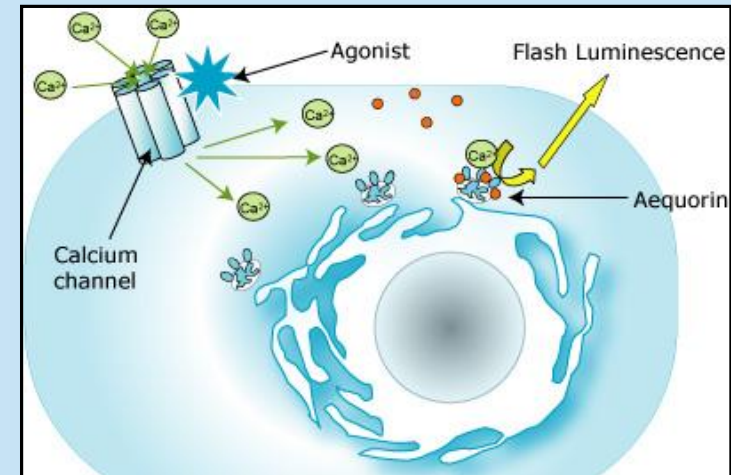
Finden von Wirkstoffen durch industriellen Test von Substanzen

Ausgangspunkt:

Target – Molekül im Körper an dem ein Wirkstoff ansetzt und den Krankheitsverlauf beeinflusst
 dazu gehören: Enzyme, Rezeptoren, Ionenkanäle und Transporter
 ist das Target nicht bekannt verlängert sich die Entwicklung um ca. 2 Jahre

Vorgehensweise (HTS) :

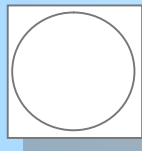
bis zu 2 Mio. Substanzen werden mit den Targets zusammen gebracht
 im HTS ca. 200.000 Tests pro Tag möglich durch Automatisierung
 Reagiert eine Substanz positiv auf ein Target, so färbt sie sich und wird „Hit“ genannt
 „Hits“ werden danach gezielt weiter untersucht, optimiert und entwickelt



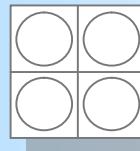
Liquid Handling in High Throughput Screening (HTS)

Highly **precise** and **parallel** pipetting and dispensing of **smallest** liquid volumes into microplates are fundamental processes in high throughput biological und chemical analysis.

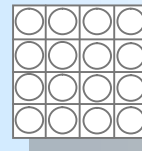
Microplate formats



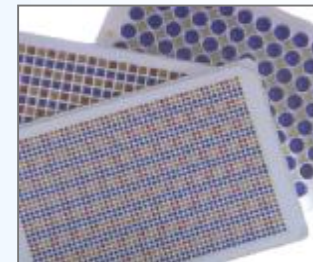
96 wells



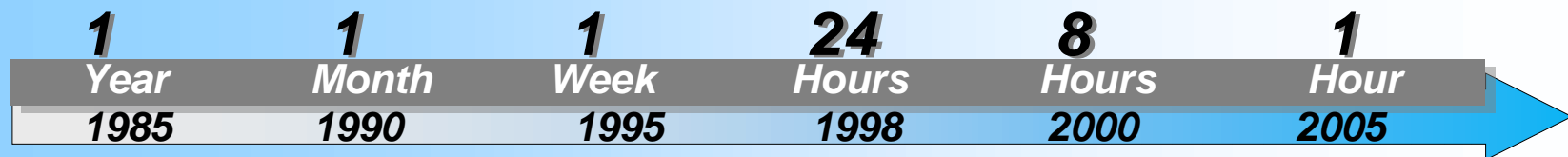
384 wells



1536 wells



10,000 biological tests need



Core Competence

more than 20 years experience in development

CyBi[®]-NanoJet



Sumal MD 96



“single-arm bandit”

Liquid Handling

-> high precision and robust

Laboratory Automation

-> high flexible, scalable & reliable

Reader Technology

-> high sophisticated and easy to use

CyBi[®]-Screenmachine



CyBi[®]-Lumax

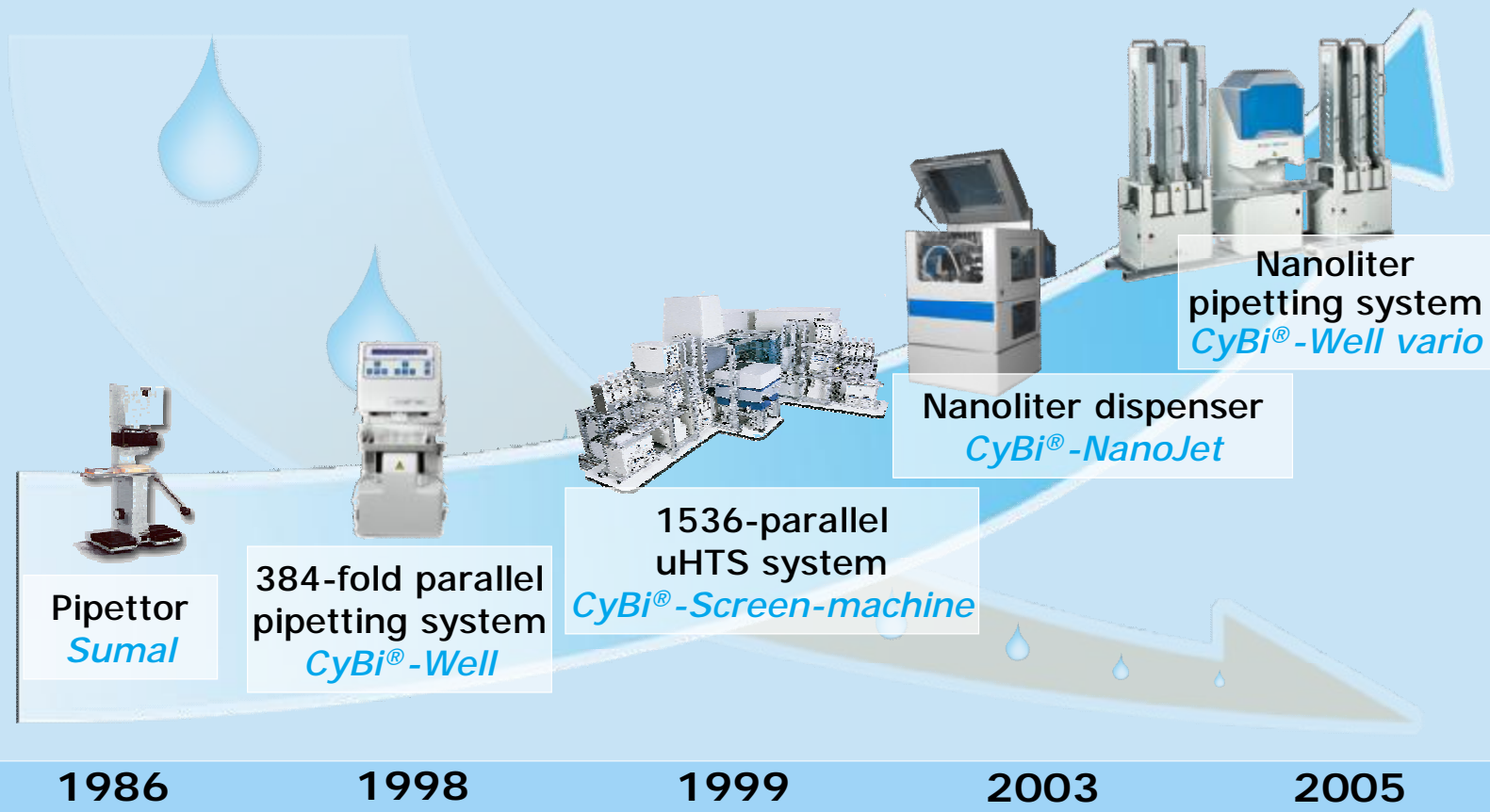


1986

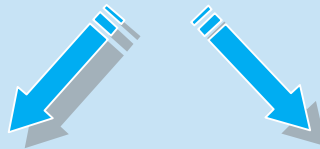
now

Miniaturization in Liquid Handling

more well per plates <- versus -> liquid volume

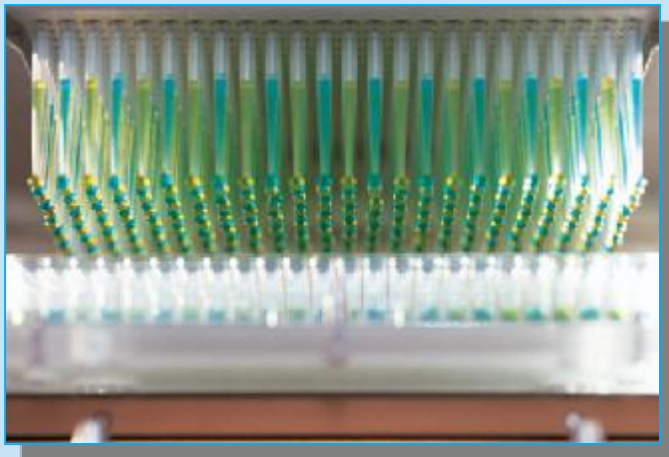


Solutions for Liquid Handling



Simultaneous pipetting:

CyBi®-DiluS^{pro}
CyBi®-Well
CyBi®-Well vario
CyBi®-Disk



Non-contact dispensing:

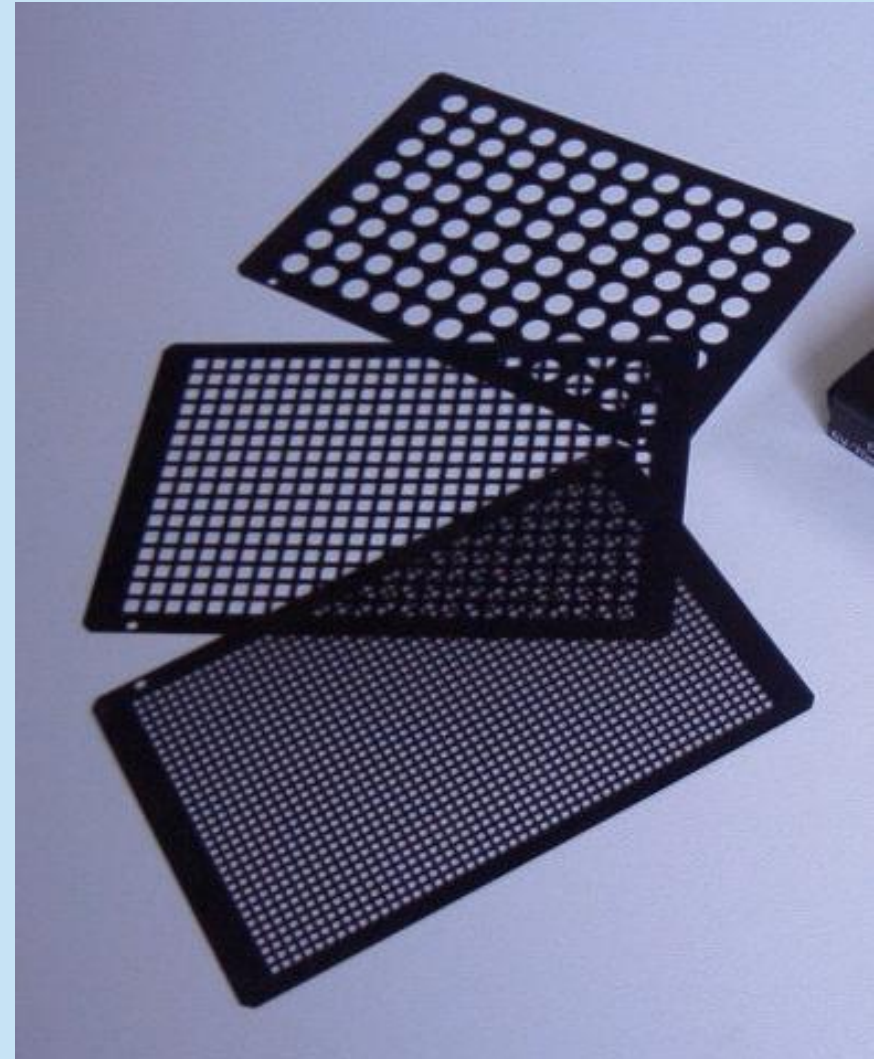
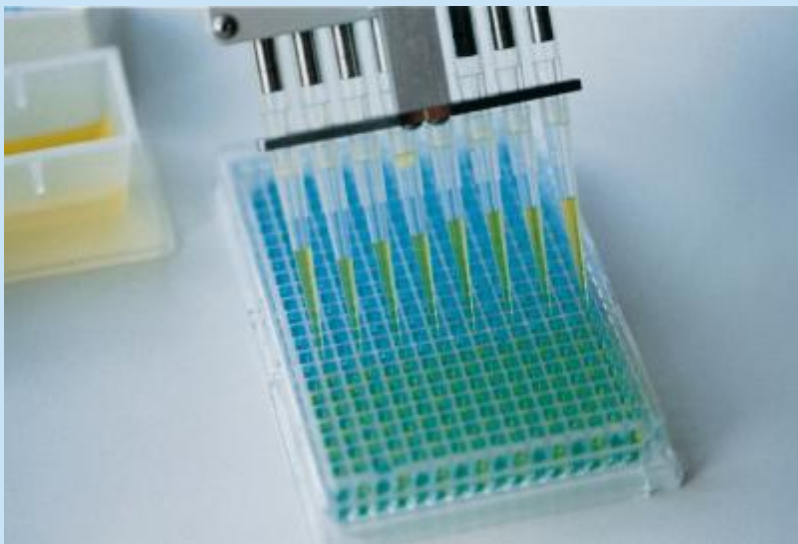
CyBi®-NanoJet
CyBi®-Drop



Liquid Handling - Goals

Fill liquid into wells:

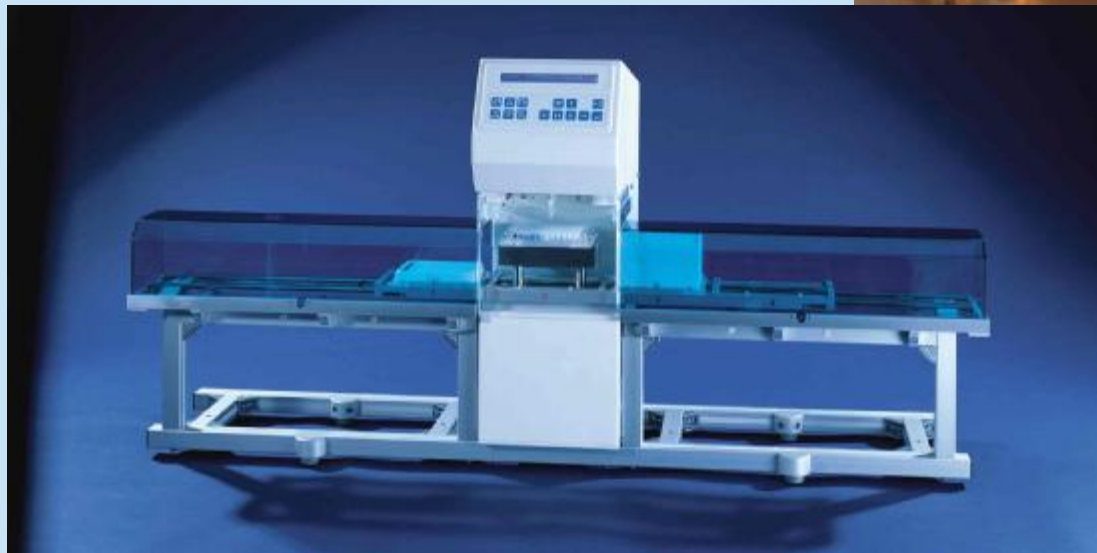
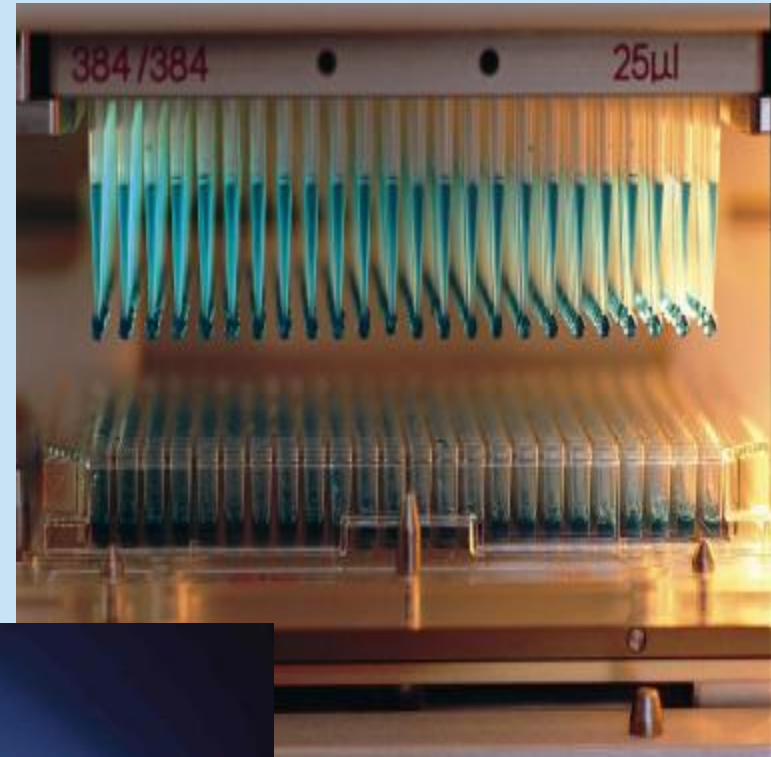
- fast and reliable
- precise und accurate
- find well in 1536 plate
- use disposable cheep tips
- etc...



Liquid Handling - Challenges

Use pipetting or dispensing robotic systems with the goals:

- fast and reliable
- precise und accurate
- find well in 1536 plate
- use cheap disposable tips
- etc...

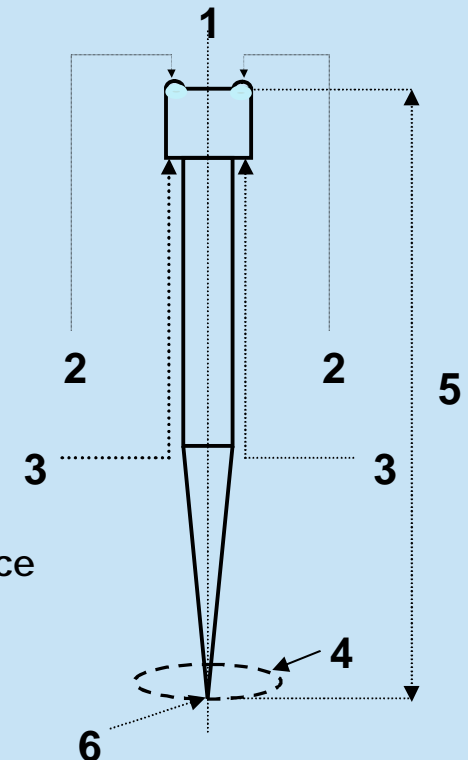
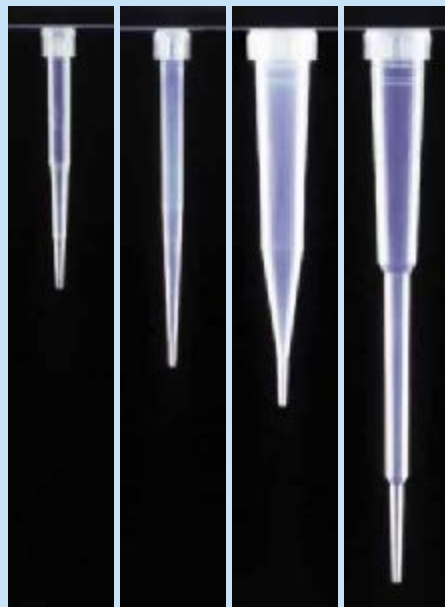


Disposable Tips

Features:

- polypropylene
- injection moulding
- cheep
- one time use

- PCR certified
RNAse, DNase and
human DNA free
- sterile
- inline filter

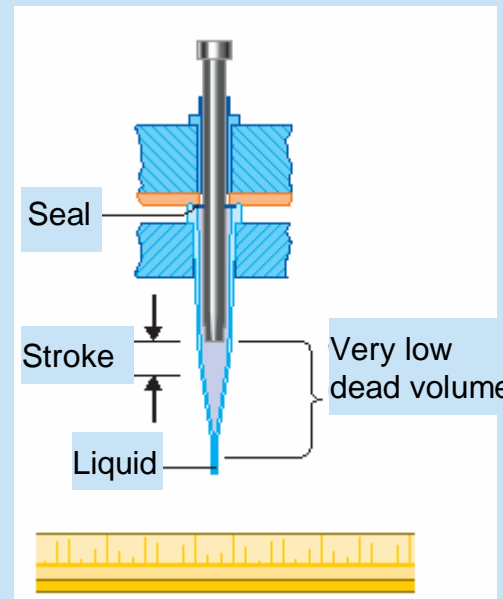


- 1: Straightness
- 2: Evenness of sealing surface
- 3: Evenness of sustaining surface
- 4: Concentricity tolerance
- 5: Length
- 6: No burrs at the outlet

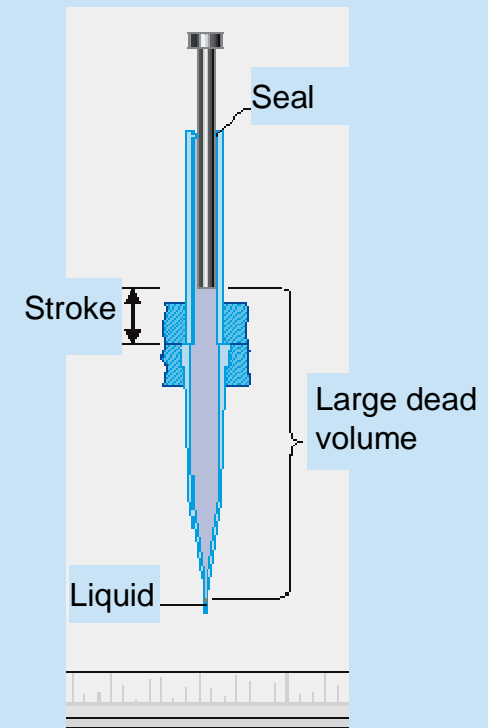
Disposable Tips - Principles

Minimized dead volume between piston and liquid.

- Minimized volume of compressible air combined
- Extremely precise movement of the piston



CyBi®- Well technology



Large dead volumes reduce precision

nl-Pipetting – High End Liquid Handling

Nanoliter Pipetting Head: 96/nl head
384/nl head

Volume range: 25 nl – 2500 nl in 1 nl increments

Precision:* 2500 – 500 nl < 3%
500 – 250 nl < 5%
250 – 100 nl < 7%

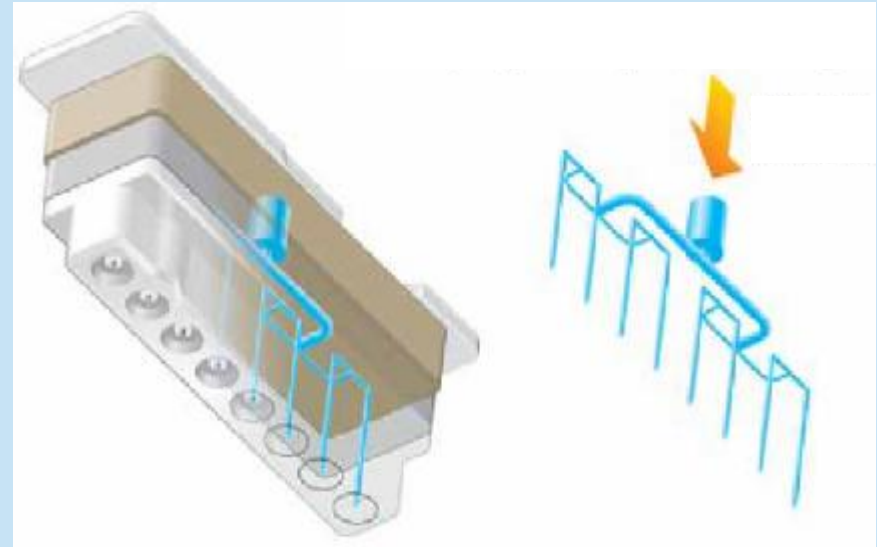
* percentage of standard deviation from the arithmetic mean

Using special ceramic tips



Dispensing Comb

Patented liquid distribution system within the dispensing heads ensures maximum precision and reproducibility

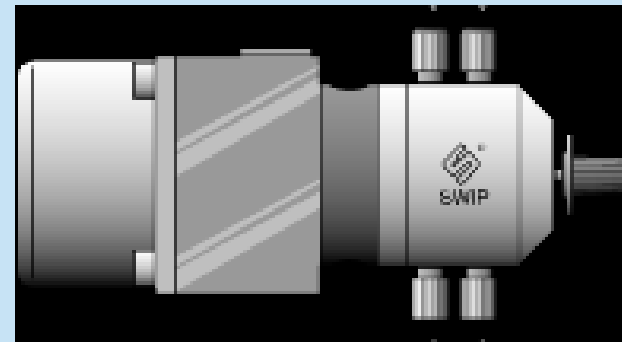
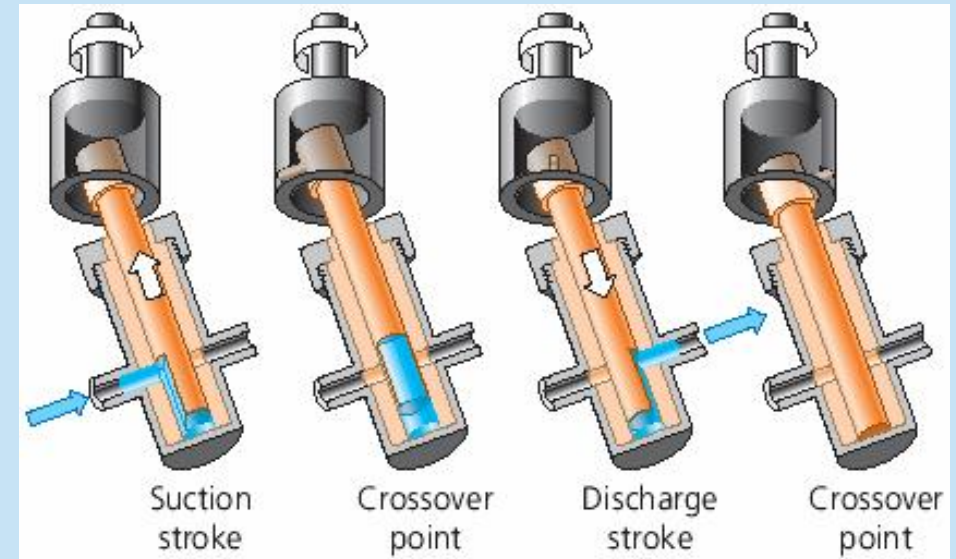


- Dispensing of:
- liquids
 - cell suspension
 - bead suspension

Dispensing Pump

Ceramic rotating piston pump:

- inert
- precise
- robust



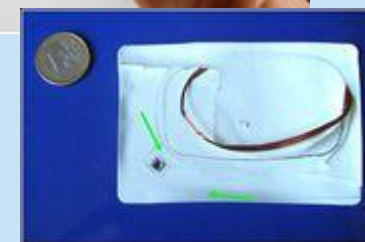
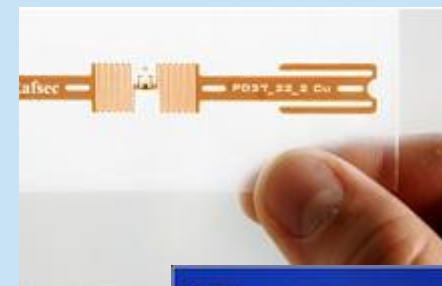
Identification

- Identification and tracking of micro plates for
- compound management in automated storage systems
 - interpret assay plates

today : bar code



future: RFID

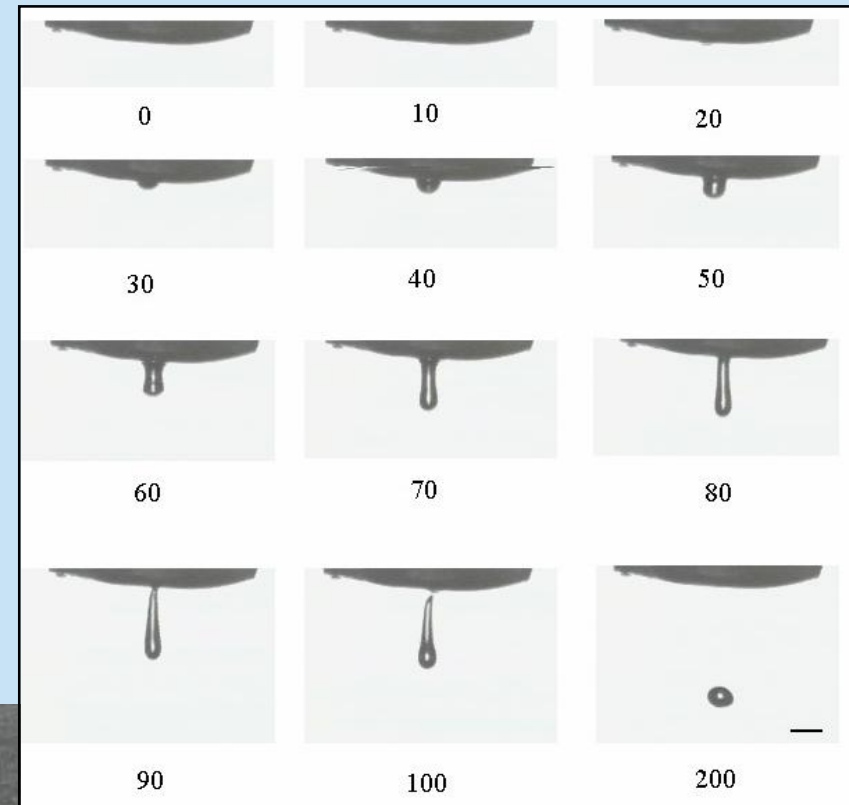
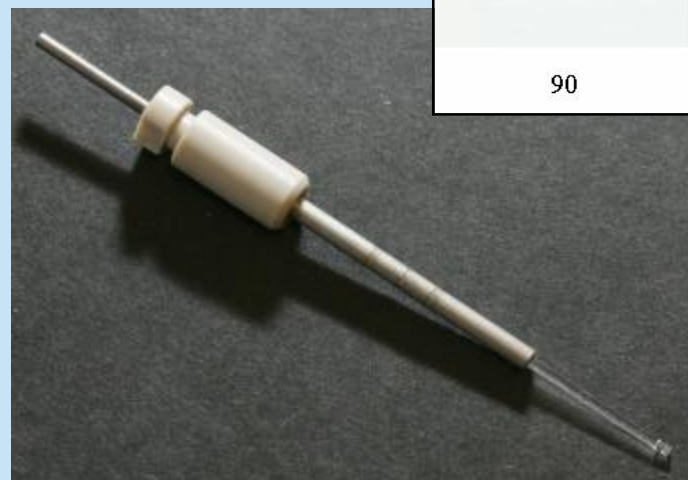
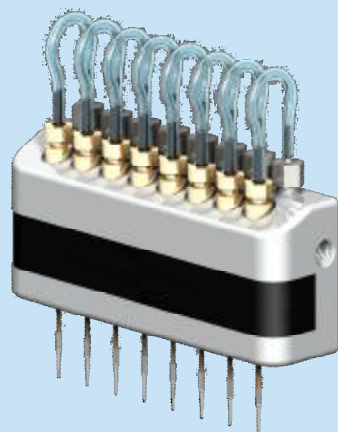


storage room with thousands of compounds

Dispensing Technology

Piezo Dispenser

- 500pl drops (depends on diameter and piezo force)
- 1nl - 100µl dispensing volume with multi drop
- very fast, very accurate
- needs calibration for every channel
- sometimes unexplainable dropouts



Thermal Measurement

Goal:

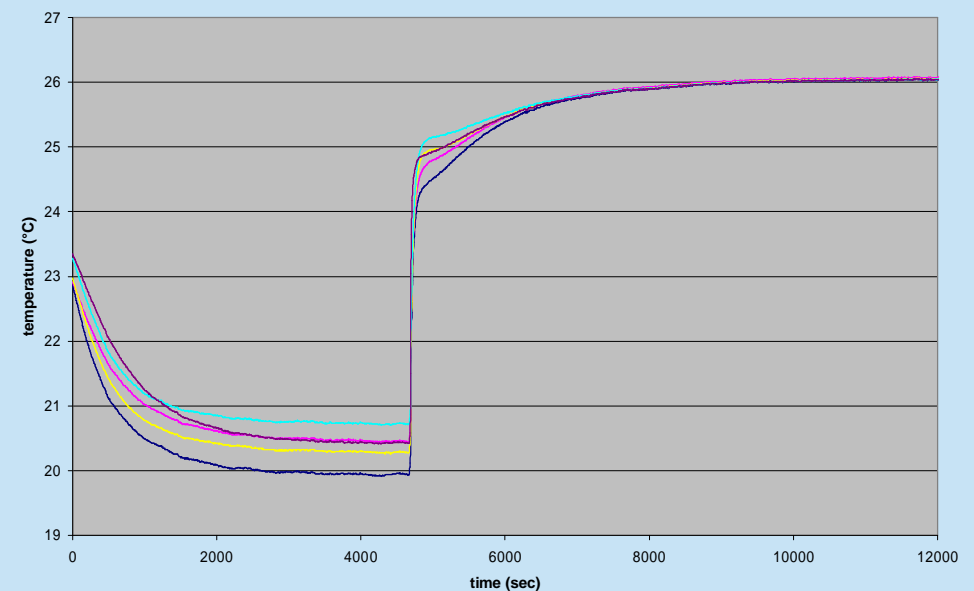
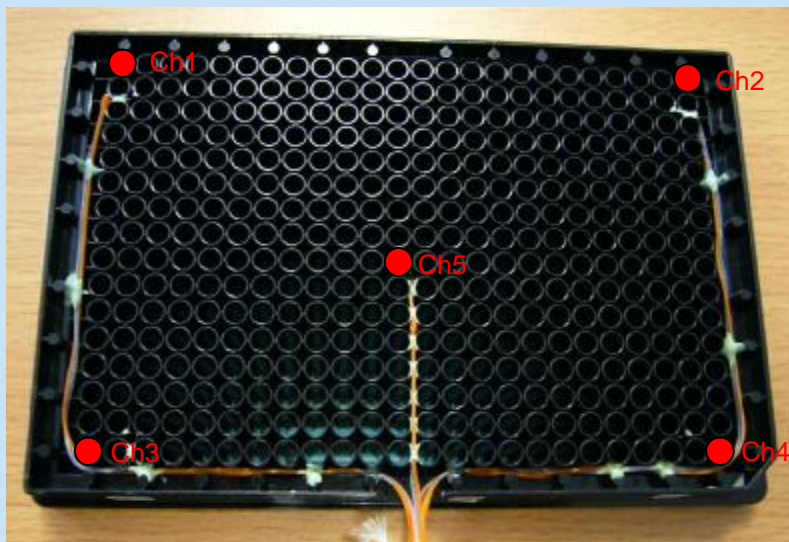
- measurement of gradient in plate
- measurement of equilibration time

Needs:

- fast response
- precise calibrated sensors
- very low thermal capacity
- exactly replaceable



cooling down and equilibration on carousel level 5



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Maik Müller
CyBio AG
Head R&D