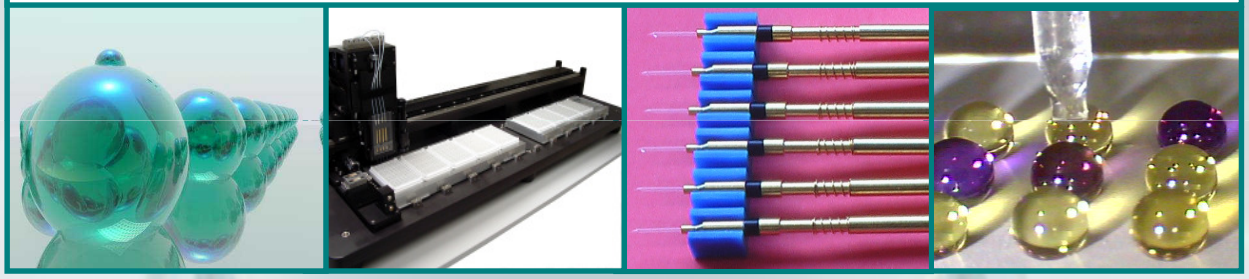
scienion
ENABLING LIFE SCIENCE



*Messung der Dispensiergenauigkeit bei der Picoliterdosierung*

Christian Wurzel

***Kleine Volumenströme in der Medizintechnik***

*Zentrum für Biomedizintechnik FH Lübeck 17.6.2009*

# Scienion operates from two locations

Distance 500 km or 3.25 hours train ride

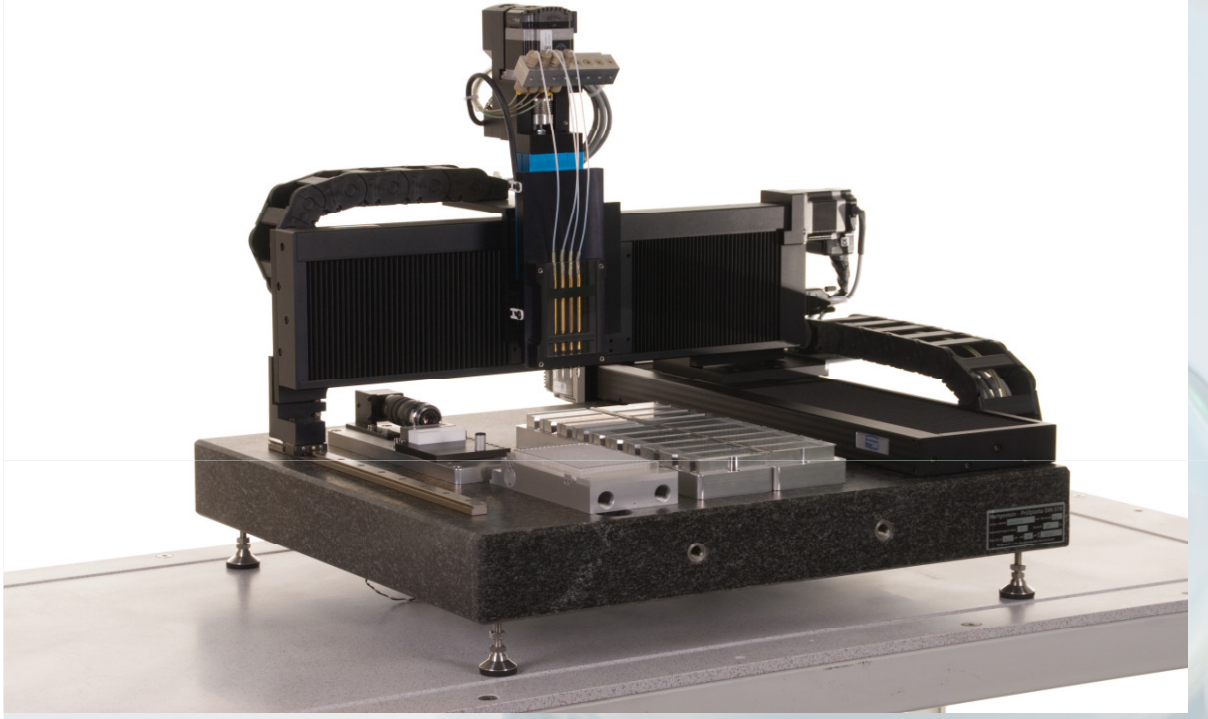
scienion

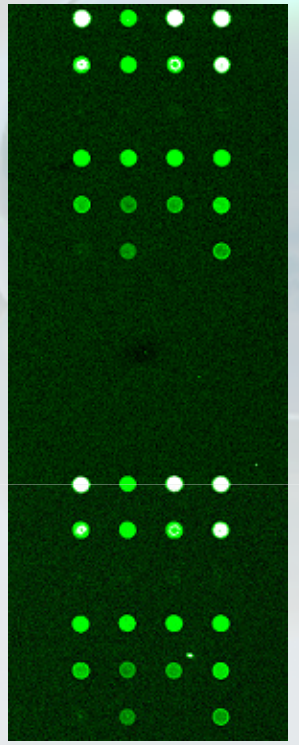

*Scienion Dortmund*
*-sciFLEXARRAYER S100*
*- sciSWIFT*
*- R&D*
*- Service*

*Scienion Berlin*
*-sciFLEXARRAYER S3, S5, S11*
*- R&D*
*- Service*
*- Administration*

# sciFLEXARRAYER – S3

scienion





Spindle stage

Up to 20 slides or 5 MTP / batch

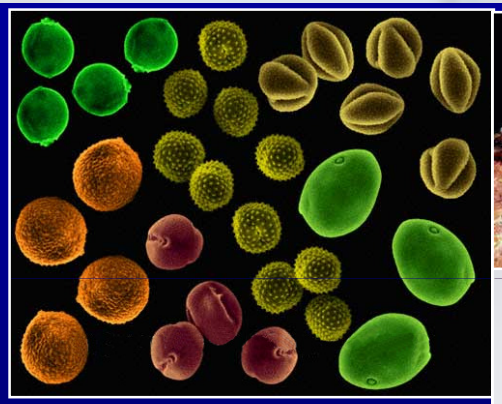
Other formats, e.g. sensors or membranes on request

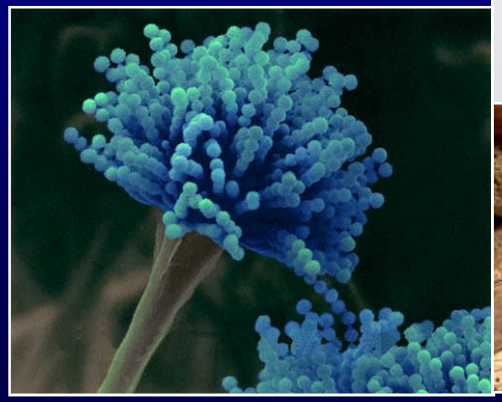
R&D

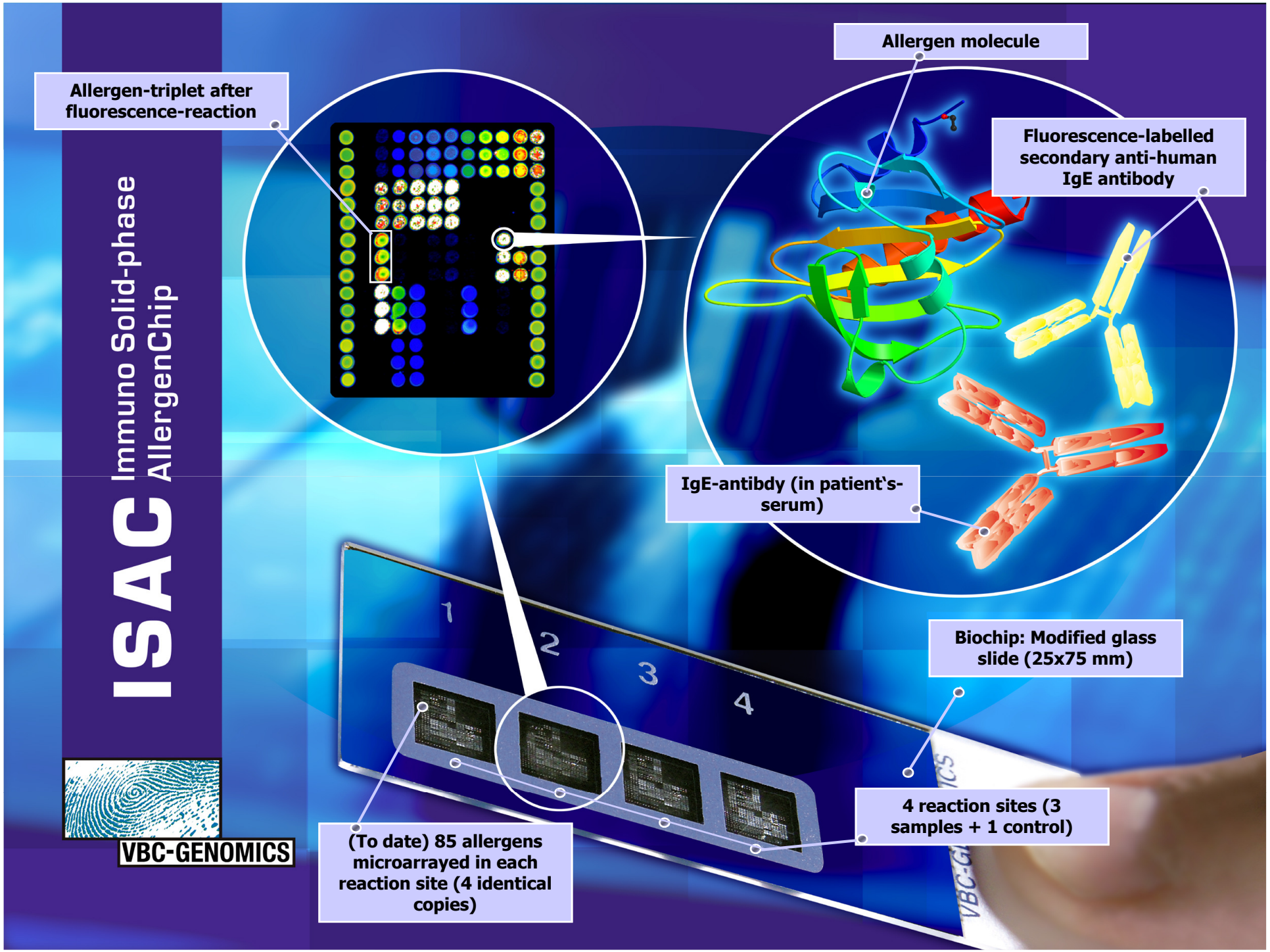
# ISAC, Immuno solid-phase Allergen Chip (CE certified), by VBC Genomics

scienion

## Allergy: A severe pandemic disease

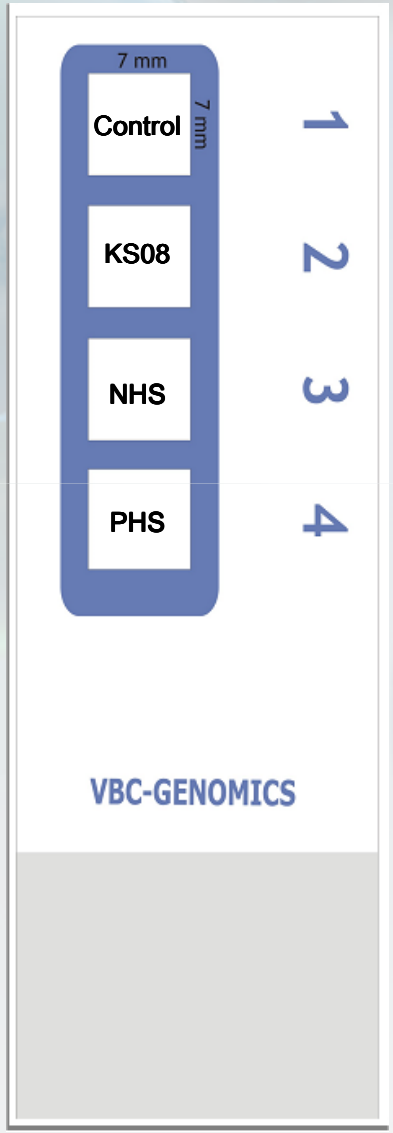



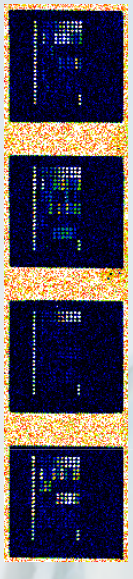



ISAC Immuno Solid-phase AllergenChip
Allergen-triplet after fluorescence-reaction
Allergen molecule
Fluorescence-labelled secondary anti-human IgE antibody
IgE-antibdy (in patient's-serum)
Biochip: Modified glass slide (25x75 mm)
4 reaction sites (3 samples + 1 control)
(To date) 85 allergens microarrayed in each reaction site (4 identical copies)
1
2
3
4
VBC-GENOMICS

# Assay scheme

scienion



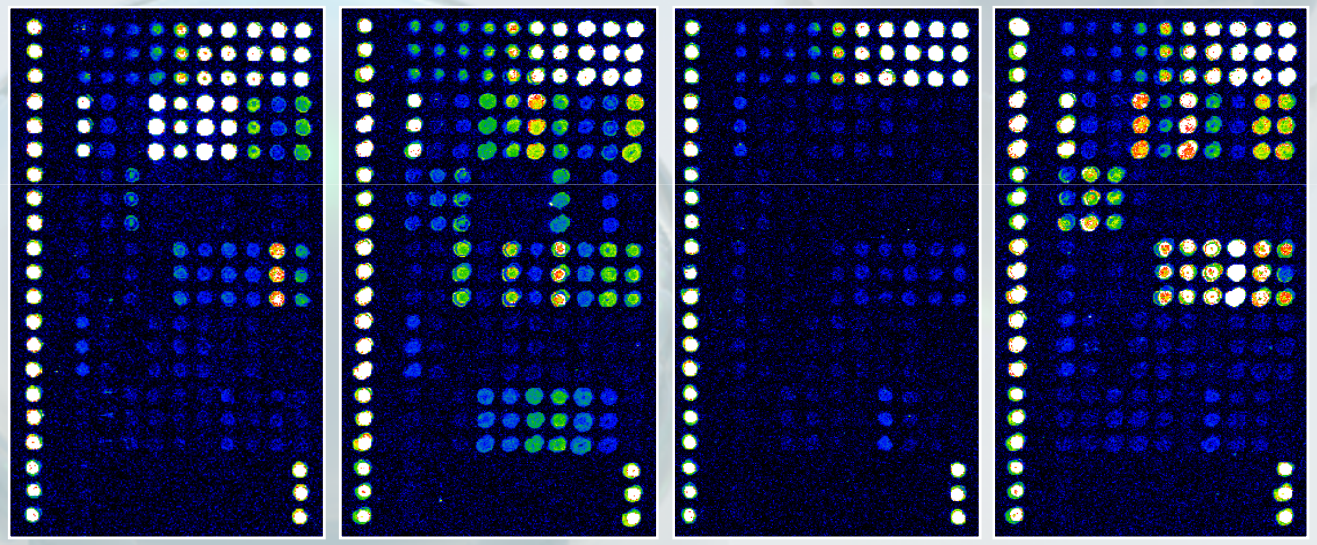



(1) **Control:** Serum used for batch quality control

(2) **KS08:** Serum used for heterologous IgE quantification

(3) **NHS:** Negative human serum

(4) **PHS:** Positive human serum (patient‘s sample)

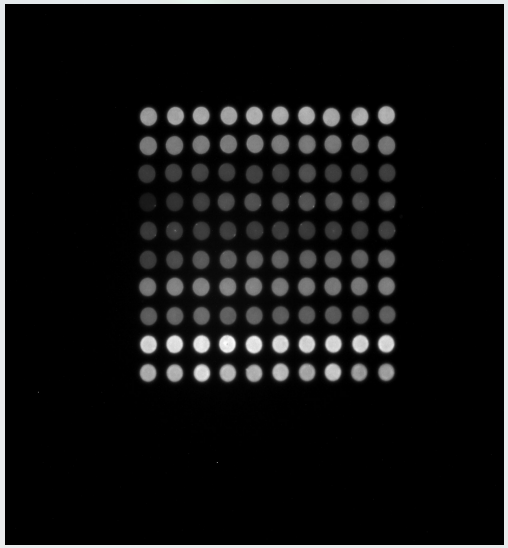


1 2 3 4

# Typical User Requirement

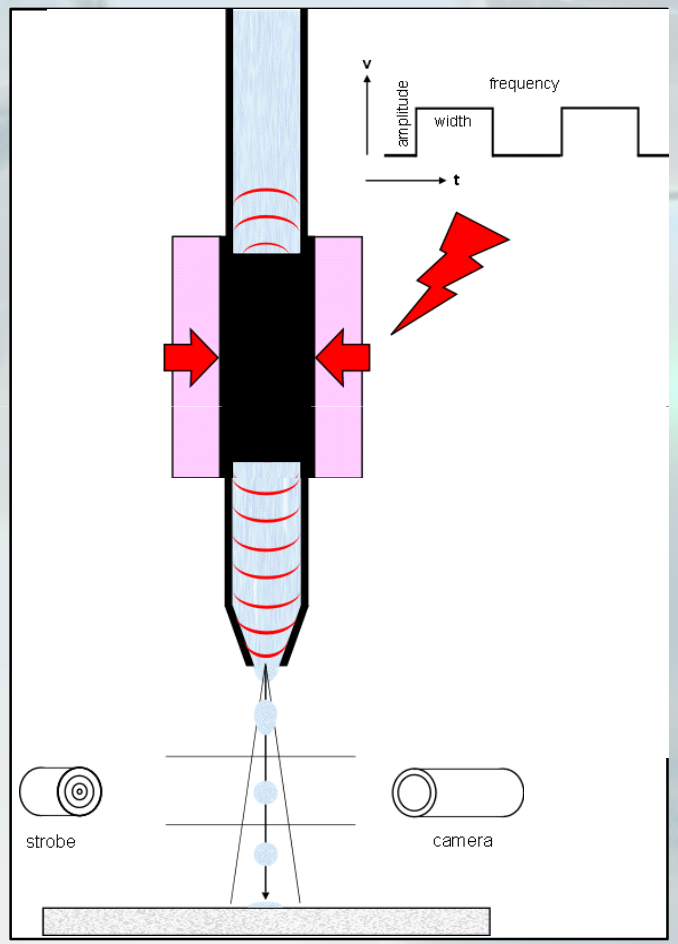
scienion

- Array 50 to 400 probes on the bottom of a MTP well
- Grid with a 200µm pitch
- Overall average deviation from the grid <10µm
- Maximum deviation from the grid < 20µm
- Inter array grid accuracy better 100µm
- Spot size 150µm → 120pl (+/- 15%)



# Piezo Pipetting - Theory

scienion




Piezo ceramic mounted around glass capillary

Piezo effect: voltage causes extension of ceramic which results in pressure onto glass

➔ Influenced by the voltage (height, length and frequency)

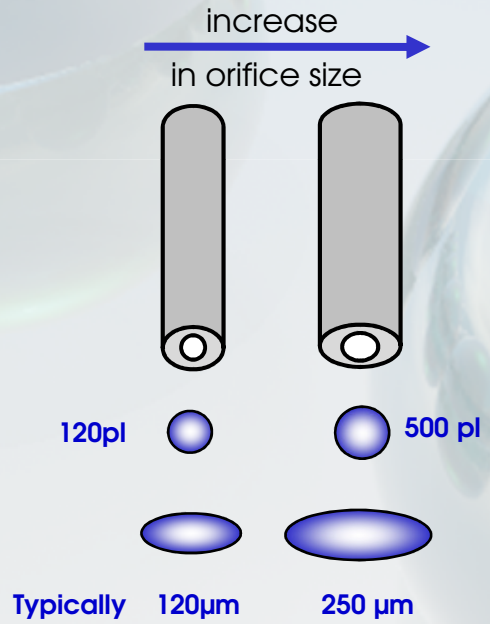
Pressure on glass results in a shock wave

➔ Uniform action and drops

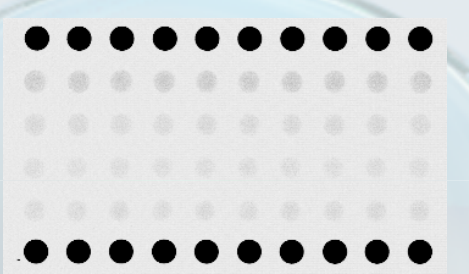
# SCIENIONS DROP ON DEMAND DISPENSING TECHNOLOGY

scienion

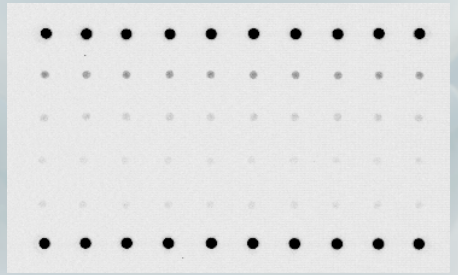
## NOZZLE ORIFICE SIZE




## TARGET SURFACE



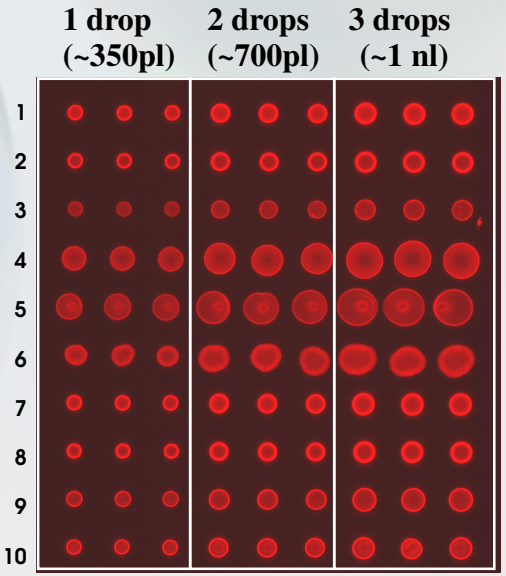
**sciCHIP epoxy**
CV = 2%, n = 240



**Schott Hydrogel**
CV = 4%, n = 240

## BUFFER

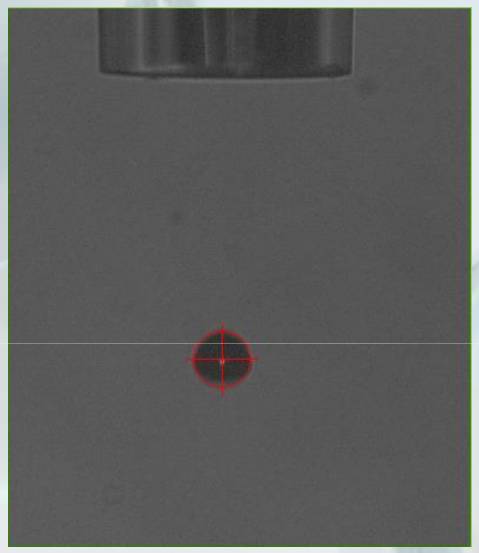
BSA 1 mg/ml
Diluted in 10 different buffers
Scanned directly after spotting



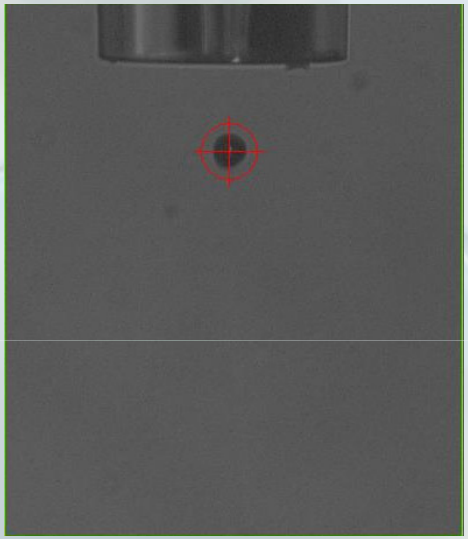
# sciSWIFTs operate reliably with DMSO solutions

scienion

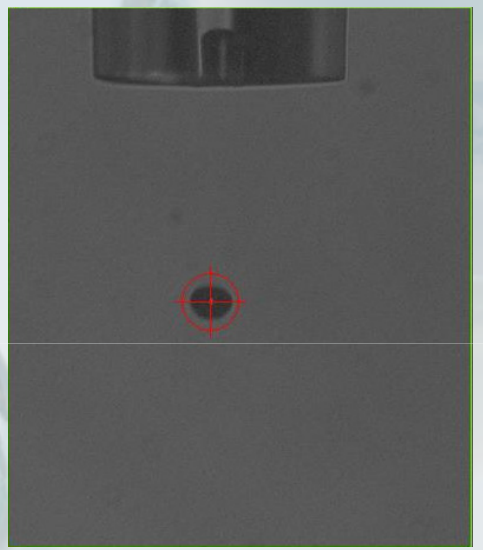
***$H_2O$ 87V 48µs***



***100% DMSO 80V 28µs***



***100% DMSO 82V 30µs***



*Auto Drop Control*

*Easy Nozzle Tuning (Voltage, Pulsewidth)*

*Automated Droplet QC*

***air buffered dispensing***

*e.g. Volumes*
*1 - 5,0 µL*

*Accuracy*
*1µl +- 5 %*
*5µl +- 2,5 %*

*Precision*
*1µl +- 5 %*
*5µl +- 1,5 %*

*Pipetting error at 0,2µl....*

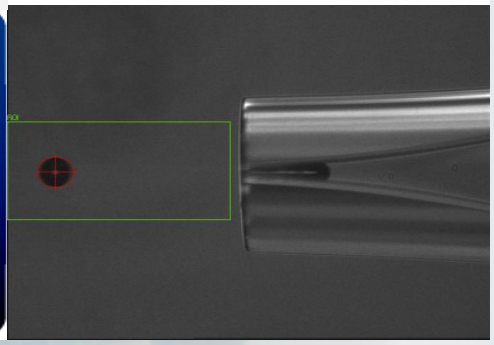
# Measurement principles

scienion

*Gravimetry*

*Fluorescence emission (cuvettes)*


*Fluorescence emission (slides)*



*Video imaging*

# Bubble sensor detects dispensing failures easily

scienion

## Pulse and reflection

*Figure 1:*

*Reflectionisnotdisturbed*

*Resulting in a proper dispensing*

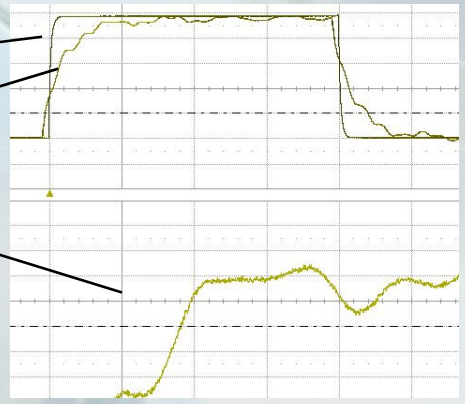
*Pulse*

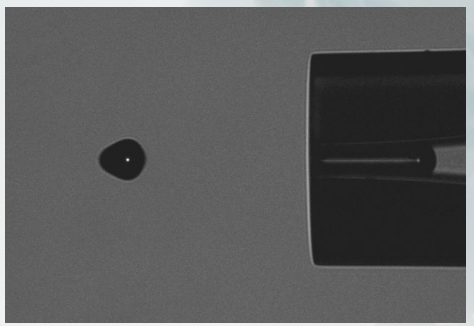
*Reflection*

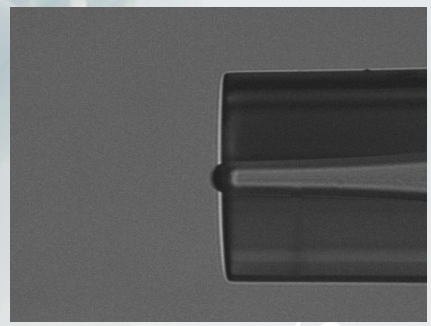
*Reflection Zoom*

*Figure 2:*
*Reflectionisdistorteddue to an airbubble in thetip*

*No drop dispensing*



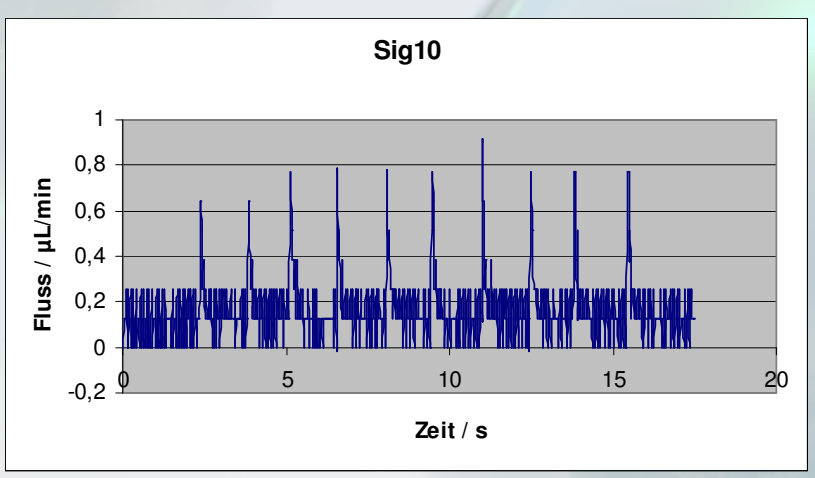




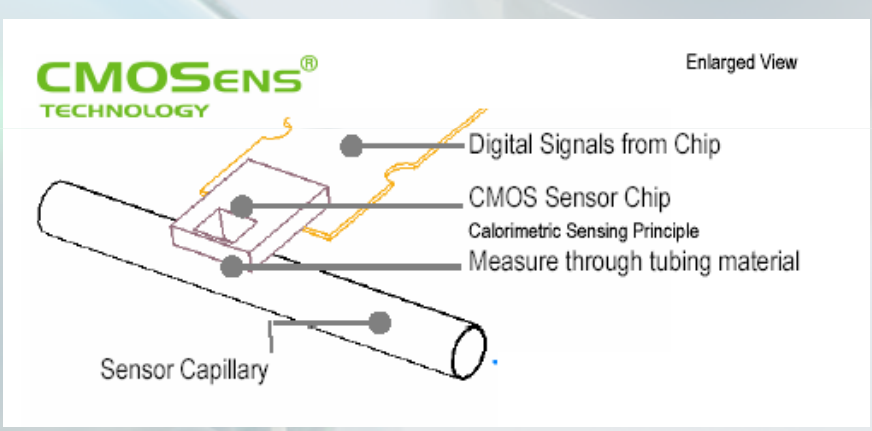
# Tropfenbestimmung mittels Flowsensor

scienion

*Düse 342*
*1.Mode*
*85 V, 12 µs*
*Volumen ca 100pl*
*Frequenz 500 Hz*
*Tropfenanzahl 10*

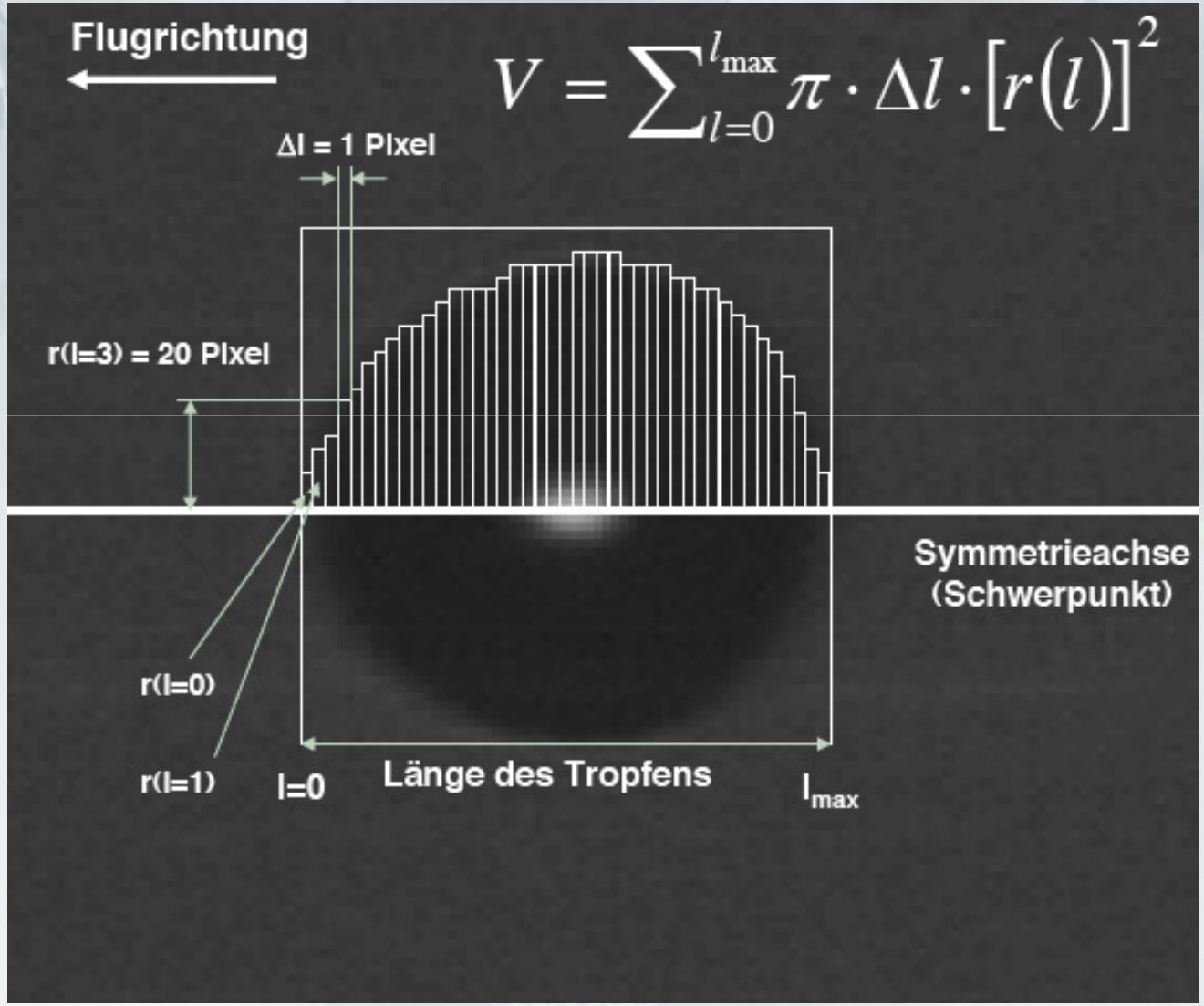



*Sensirion SLG 1430 - 420*



# *Online drop volume analysis allows for accurate results*

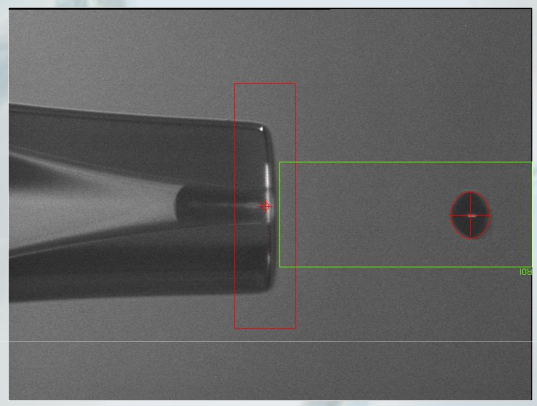
scienion



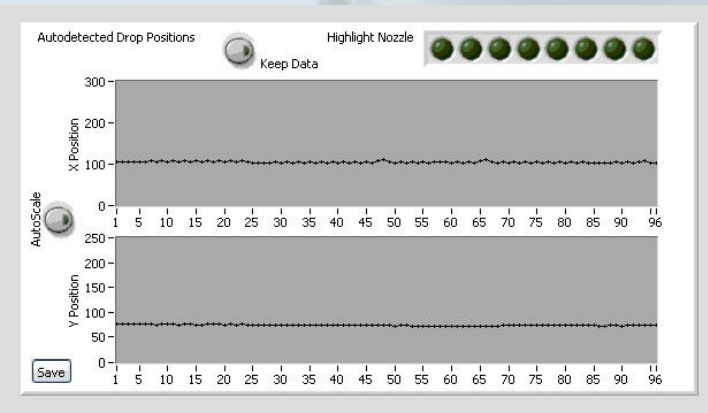
# AutoDrop Control

scienion

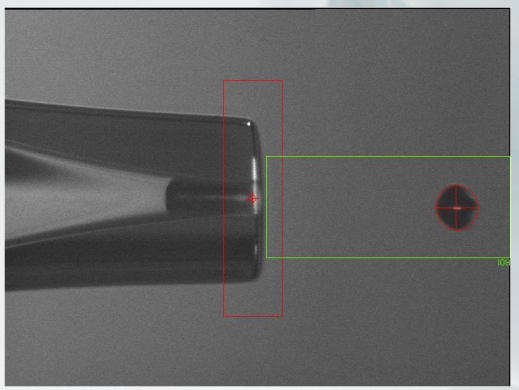
## Prespot



## Dropgraph




## Postspot

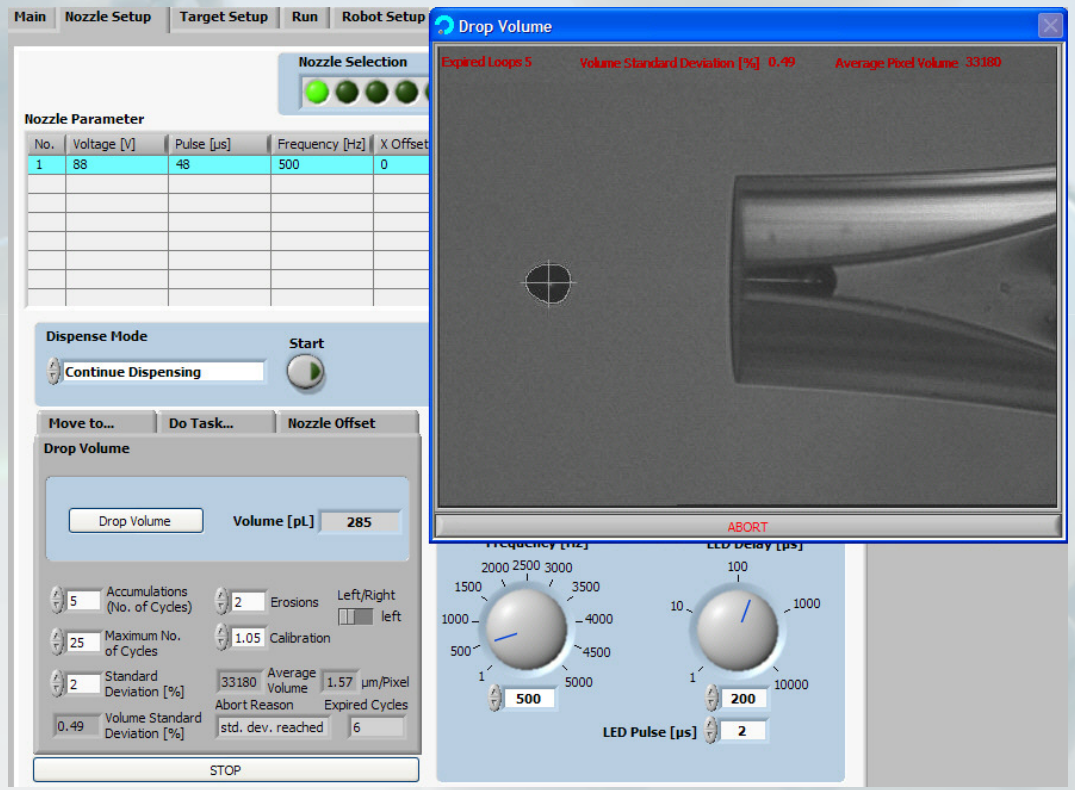


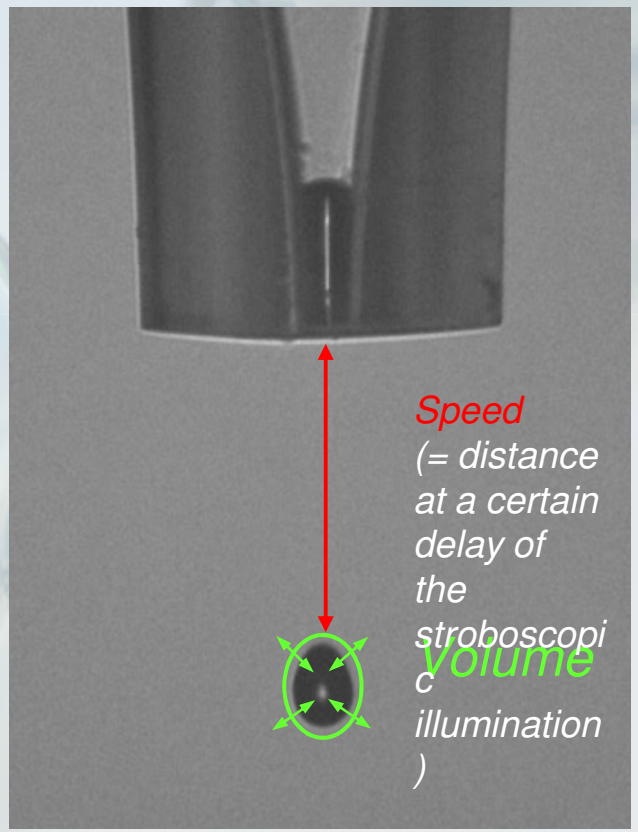
***Stability of spot formation can be tracked***

- *Software detects drop (red spot)*
- *x- and y-coordinates are logged*
- *each sample (with image) is logged*
- *enables quick spotting development and in-process QC*

# Software features
# sciDROPVOLUME and sciAUTOTUNE

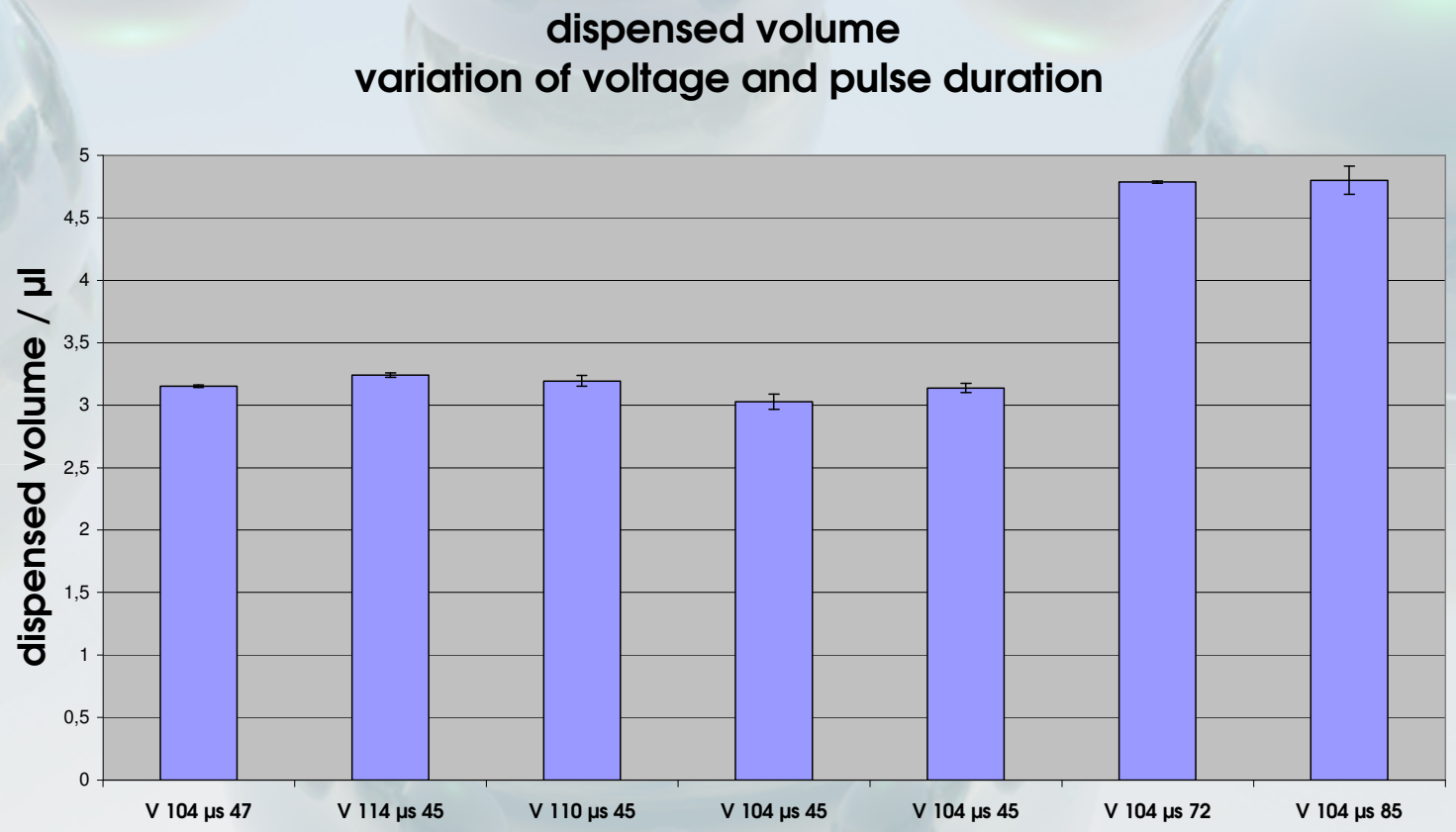
scienion



# Outstanding accuracy of dispensing volume

scienion

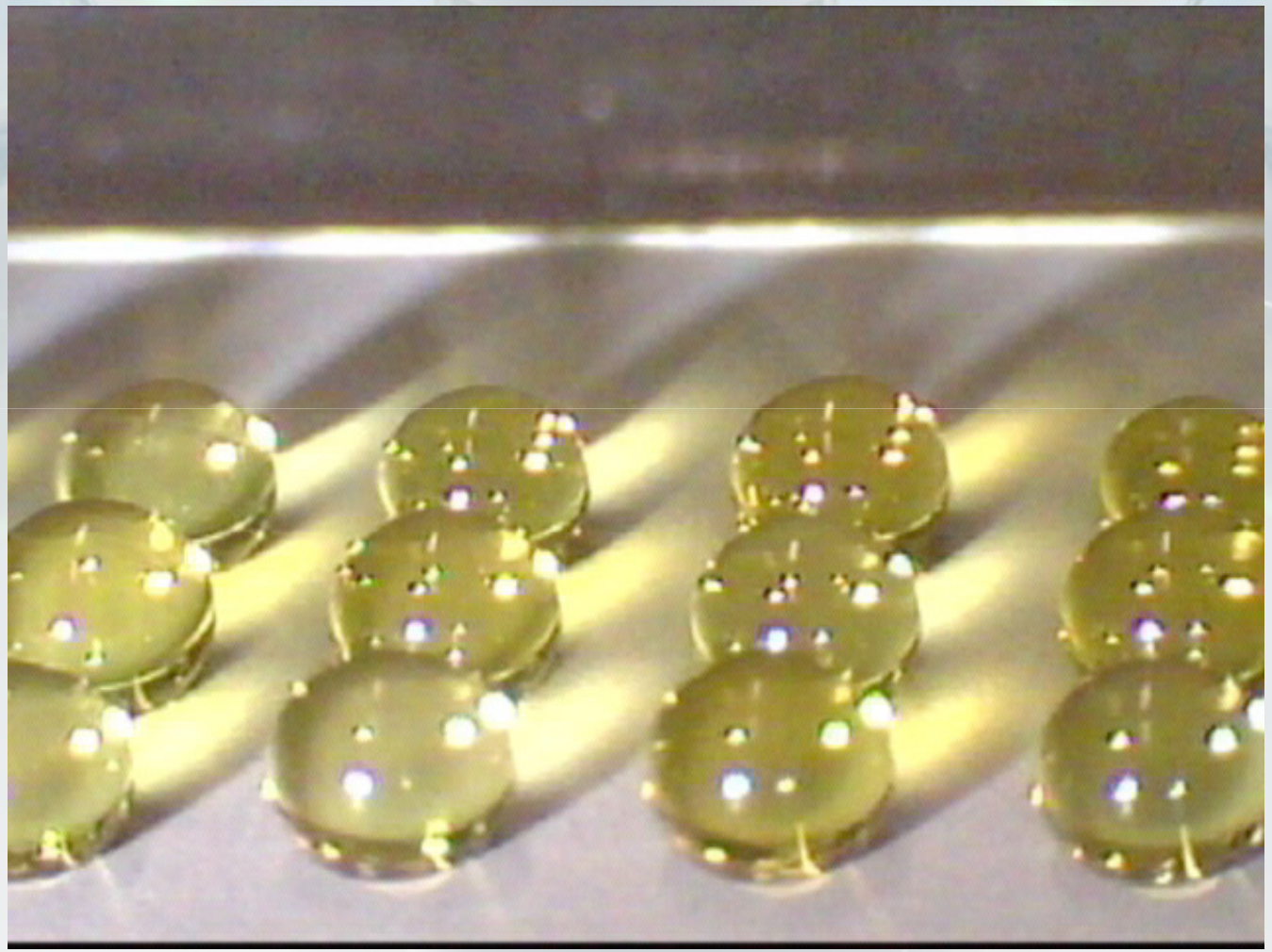



***Measurement: Gravimetrically***
*calculations: mean value*
*error bars: standard deviation*
*repetitions: n=10*

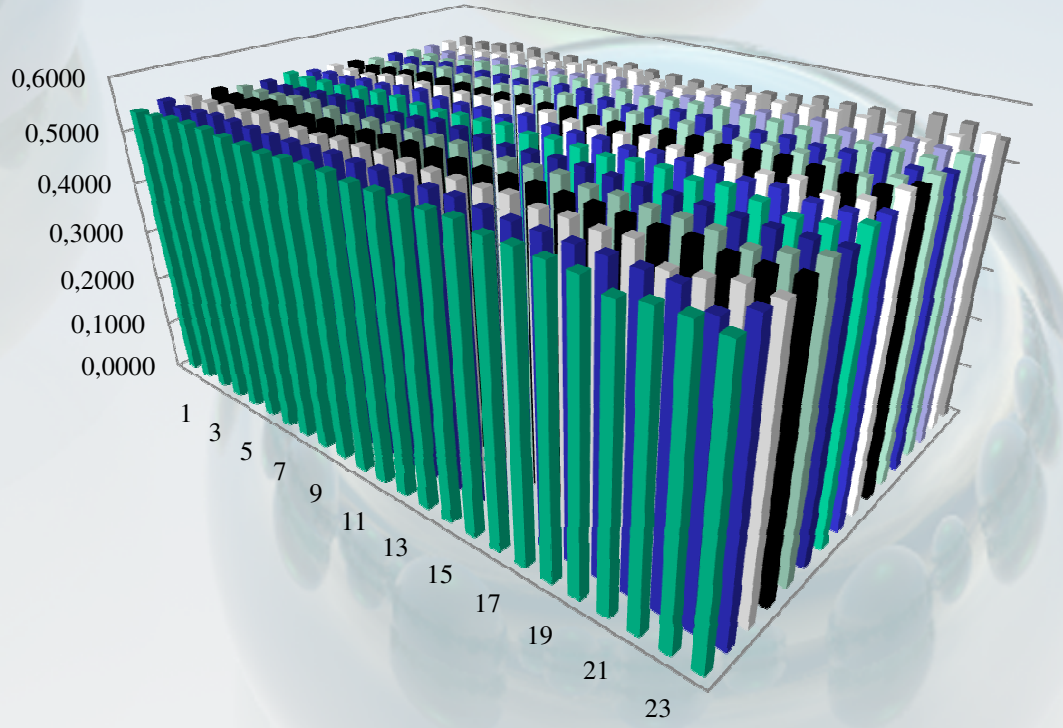
***Conditions:***
*dispensed liquid: water*
*mode: spotting 10,000 drops @ 500 Hz*

# *Drop Dispensing on the fly*

scienion



# sciSWIFTfordispensingassays in 384 MTPs



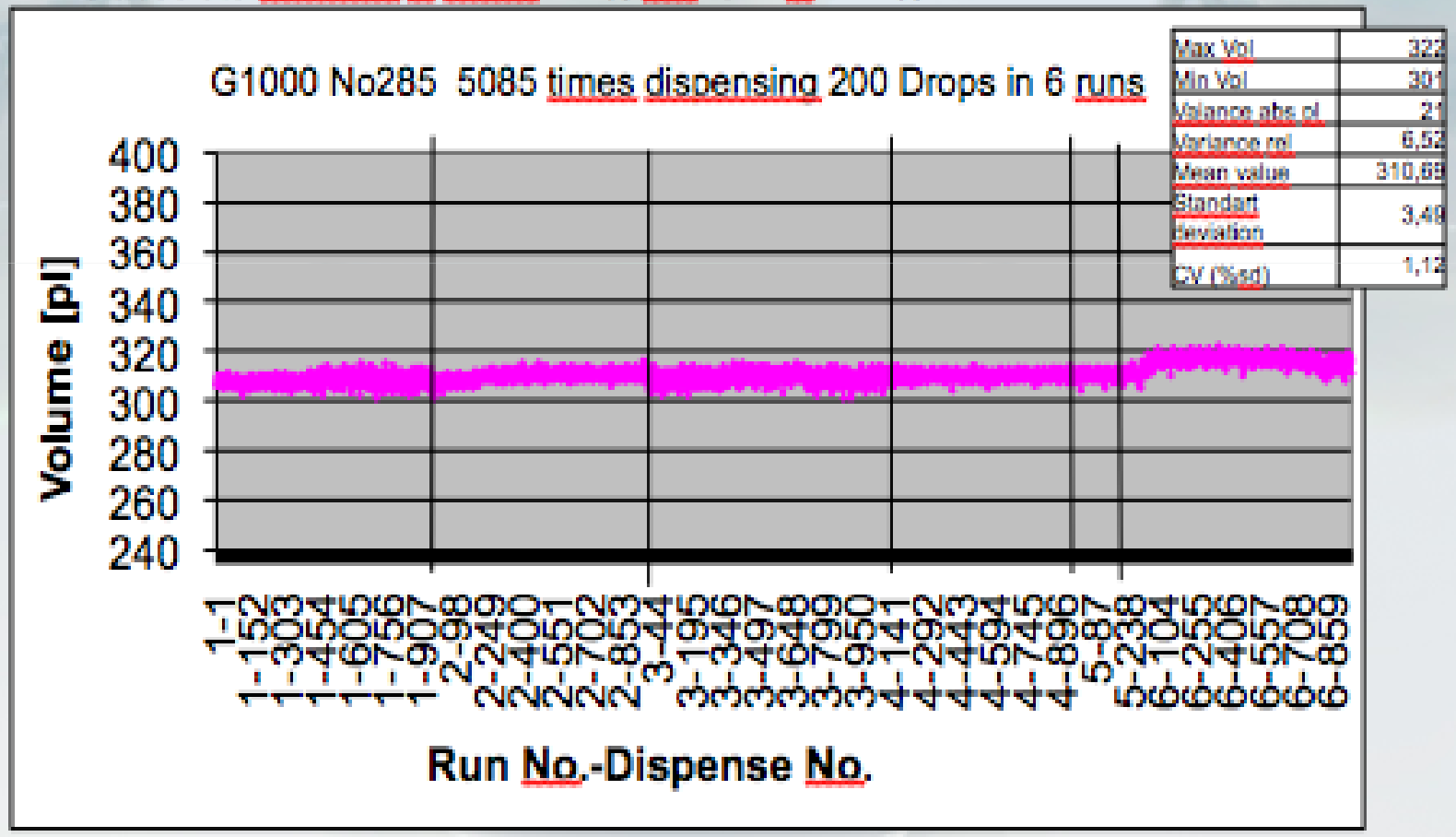

*Fillingoneplatewith 520 nL*

*CV < 1,5%*

# SWIFTER: Dropvolumeaccuracy and repeatability

*Sixruns, filling 960 wells of each 1536 well plate,, 62 nL per well, online drop control*

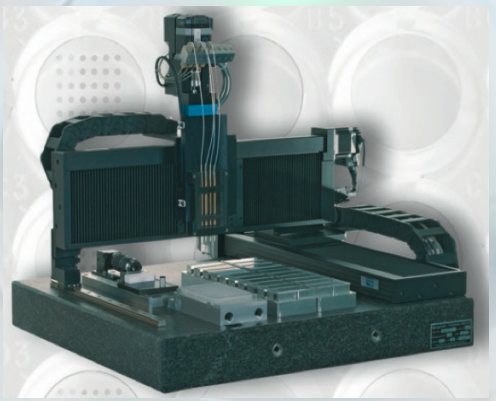
*The absolute varianceisbelow +-4% the CV is 1.12%*



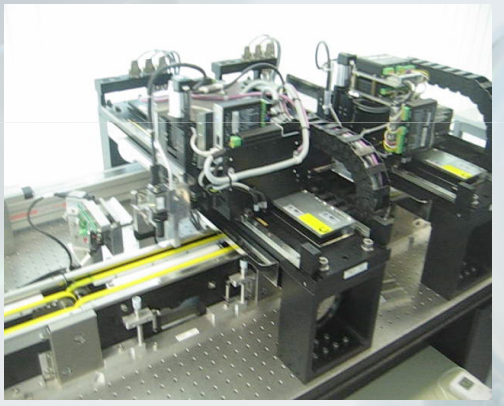
# Scienion : One technology from R&D to Production

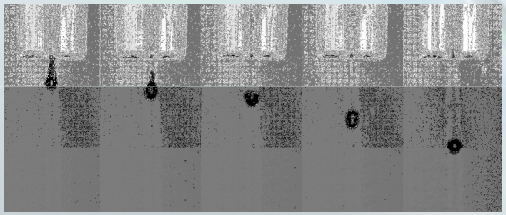
scienion

*sciFLEXARRAYER DW*

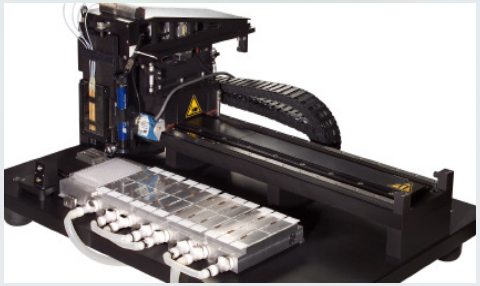


*sciFLEXARRAYER S3*



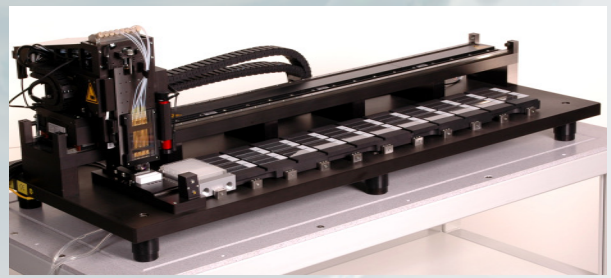


sciDROP & sciSWIFT Technology



*sciFLEXARRAYER S5*

*sciFLEXARRAYER S100*



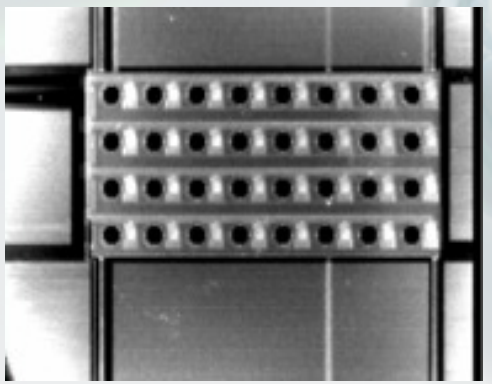
*sciFLEXARRAYER S11*

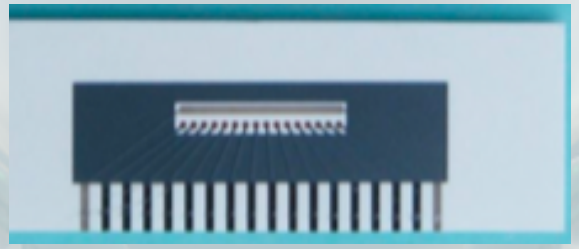
# Scienion is a specialist in Biosensor production

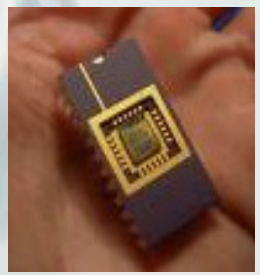
scienion

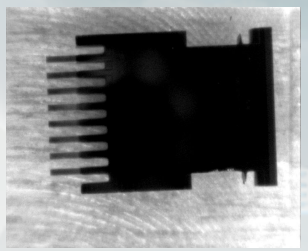
*A Biosensor is a sensor device for detecting and measuring very small quantities or changes in a biochemical or chemical substance, in which a microelectronic component registers reactions related to the substance and translates them into data.*

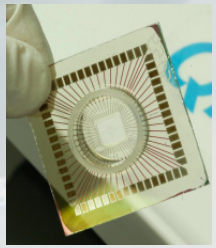
*Scienion has established multiple Biosensor/Biochip production sites*





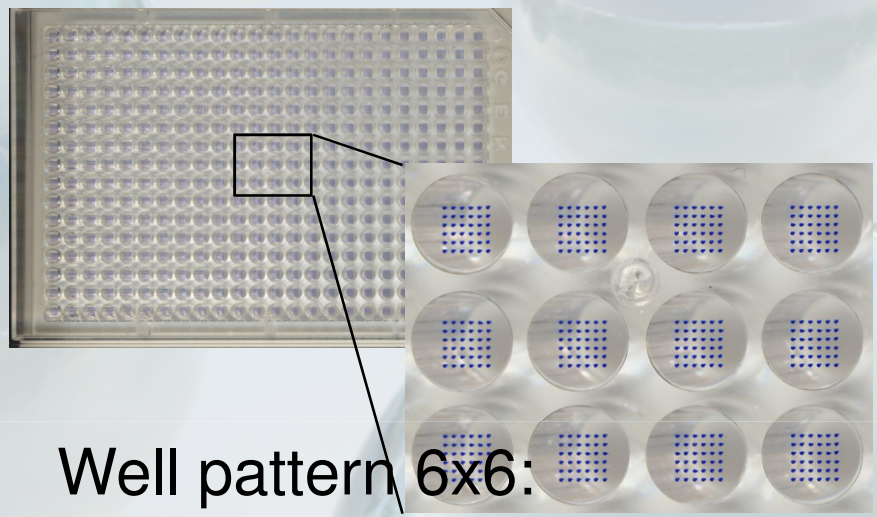




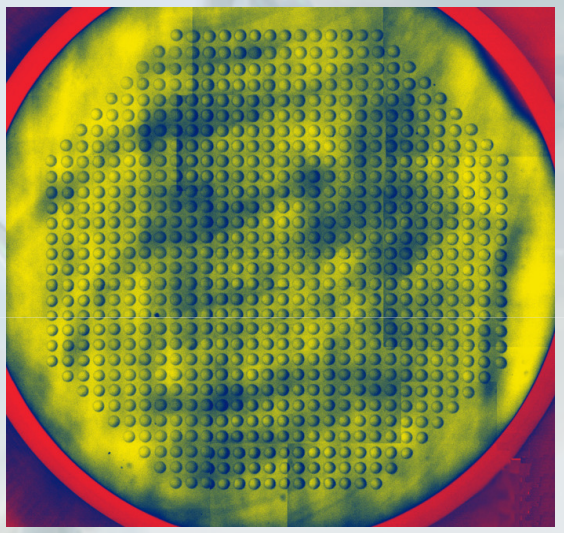


# Arrays in Microplates

scienion



Well pattern 6x6:



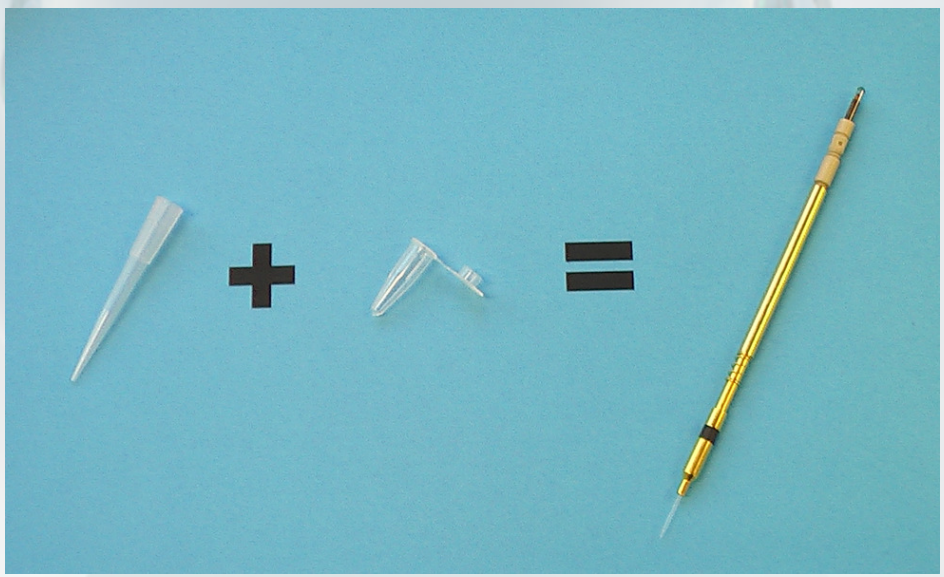
756 Spots

# sciSWIFT Dispensing Pens

scienion

**sciSWIFT**
(Scienion Washfree Identifyable Fluid Technology)

sciSWIFT Dispensing Pens are
integrated **storage AND dispensing** devices
for
ultra-low volume liquid handling



# Multiple challenges of today's systems

scienion

| Challenge | Implications |
| --- | --- |
| • Water condensation | • Wrong concentrations |
| • Precipitation | • Difficult to handle |
| • Washing and aspiration required | • Dilution & cross-contamination |
| | • Suboptimal speed |
| | • Complicated liquid handling systems |
| • Restricted dispensing volume flexibility | • Too much valuable reagent might be used |
| • Tracking of probes | • Loss or mixing up of probes |
| • Retesting, new assay testing | • Reagents must be recreated or at least filled into the system again |
| • mixing small volumes | • key to miniaturization |

# sciSWIFT – Core Characteristics and Benefits

scienion

- Valve
- RFID tag
- Liquid storage
- Piezo pump
- Sealing

- Simplified workflow through elimination of process steps
- Full traceability and high process reliability through RFID tag
- Sealed and sterile long-term sample storage
- Reduced loss of substance through washfree setup and high-precision dispensing
- No water condensation and less precipitation
- Sonicator included
- Elimination of contamination
- Convenient exchange between operational sites

**Significant cost savings possible through combination of efficient substance use and reduced operational risk (lower process variability, six sigma)**

Source: Scienion

# Advantages of the sciSWIFT

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*sciSWIFT g1000*

- *Aliquot preparation*
- *Precision in dose response tests*
- *Dilution series*
- *Cross contamination*
- *Ultra low quantities*
- *Handling errors*
- *Labels on vials*
- *Array generation / throughput*
- *etc…*

- *Ready to use*
- ***Disposable** product – no contamination*
- *Picoliters to Microliters @ highest accuracy*
- *No Handling errors*
- *RFID label (others possible)*
- *Highthroughput / Speed*
- *Sterile filling*
- *Flexible storage volumes*
- *etc…*

# P30 drops from 200 pl to 1.8 nl

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# Piezo Dispense Capillaries and sciSWIFTs operate reliably over a wide parameter range

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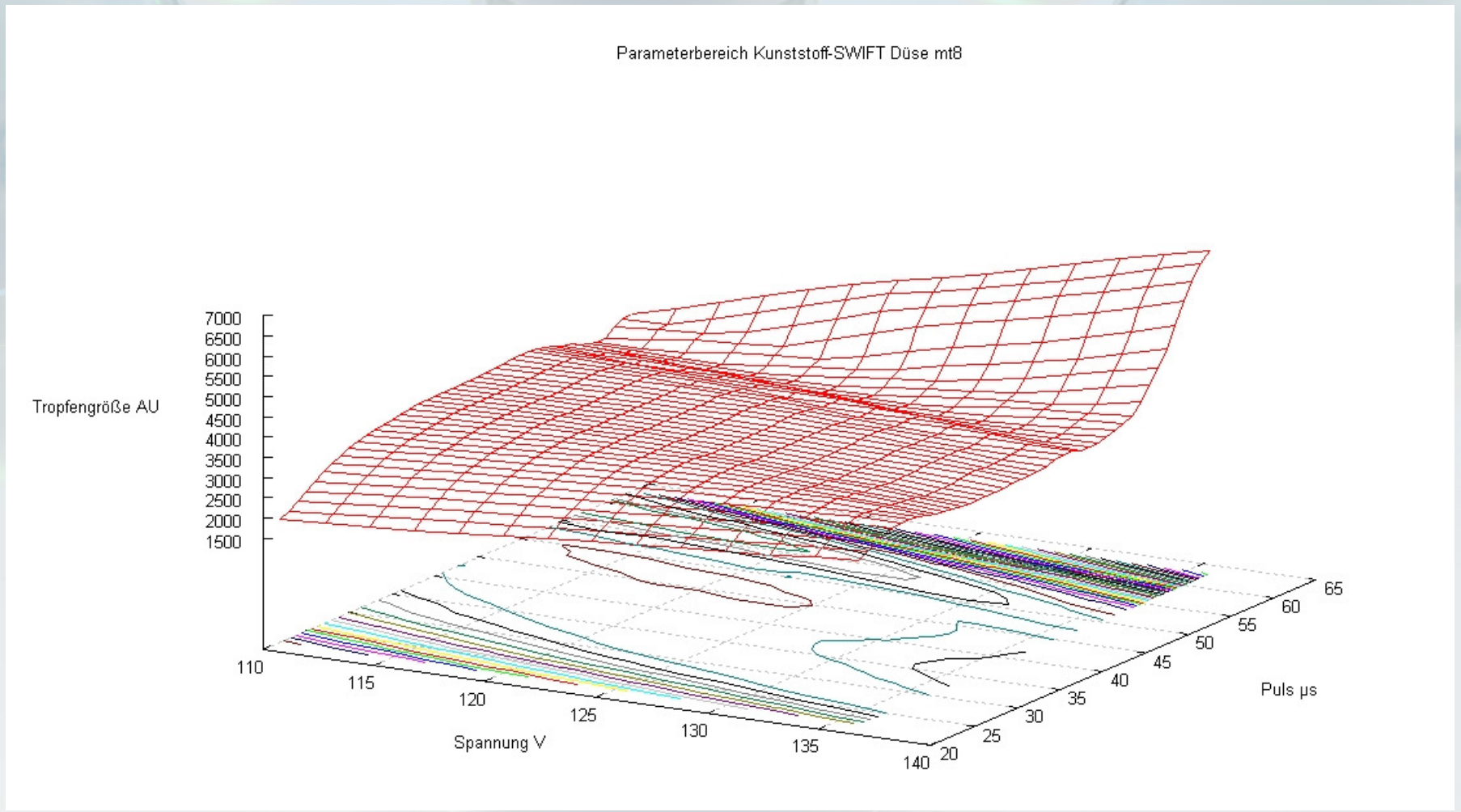


# Nanoliter Cell Based Screening. Workflow

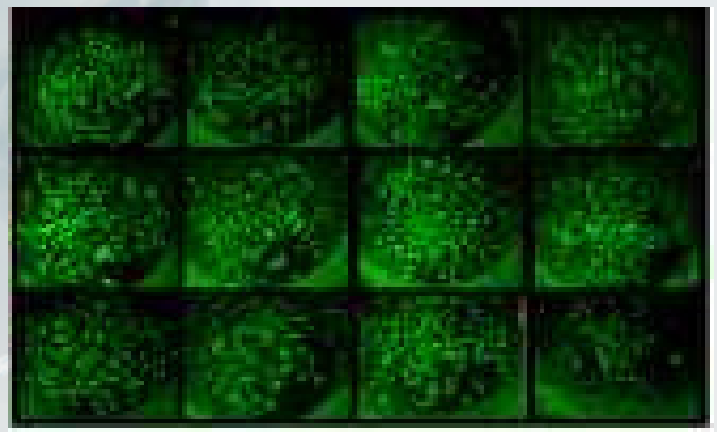
Courtesy of CEA

Array Generation with sciFLEXARRAYER

Local Transfection or adding chemicals on arrays utilising sciFLEXARRAYER

Courtesy of CEA

Read Out:
Any detector



Courtesy of CEA

# Cell based assays: Vessel free reaction set-up

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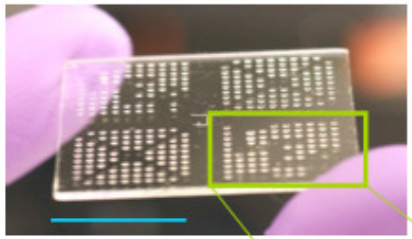
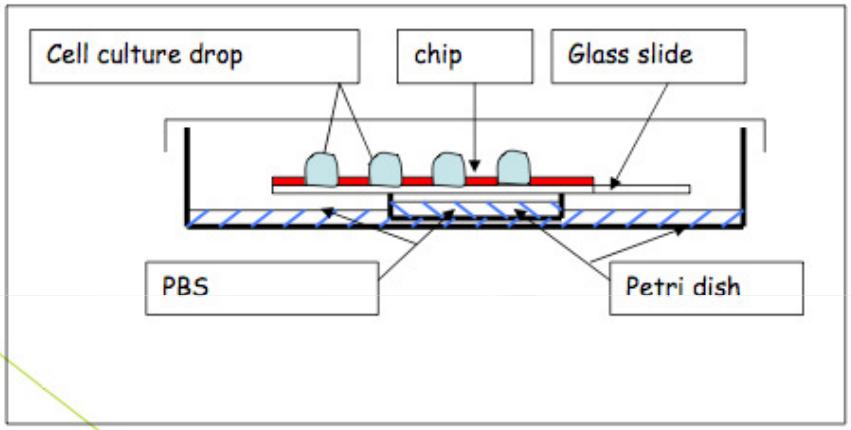
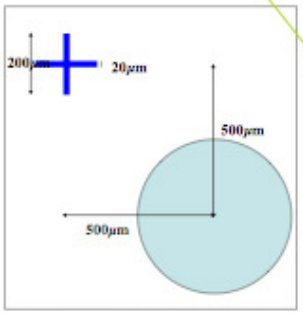
## Cellchip for 400 cell based assays

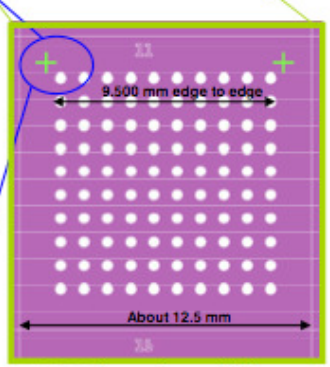


1 cm

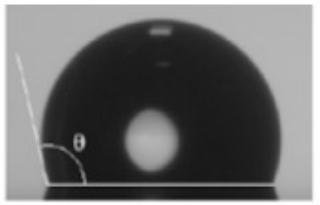







100 hydrophilic spot per cm2




*Courtesy of CEA, Grenoble, France*

# Cellbasedassays: Protocols

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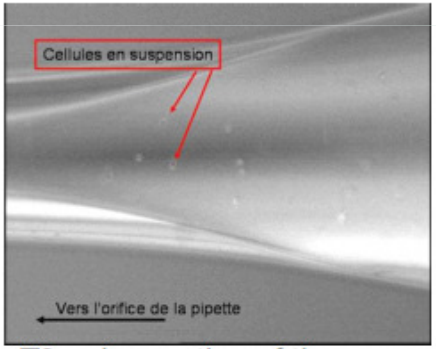
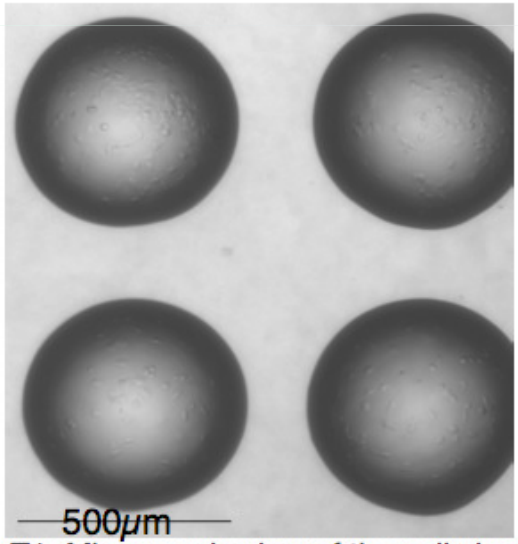
## protocols

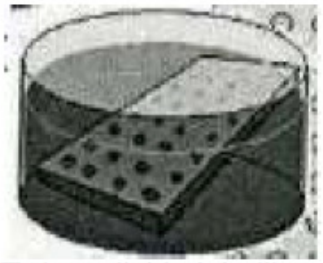
- T0: cell spotting (200 drops)
- T1: drug spotting (20 drops)
- T4 or T5: fixation of the cells, labelling and microscopic observations




*T0 : observation of the nozzle during the cell spotting*




*T1: Microscopic view of the cells in drops*



*T4/5: cellchip labelling*

*Courtesy of CEA, Grenoble, France*

# Cellbasedassays: IC 50 set-up

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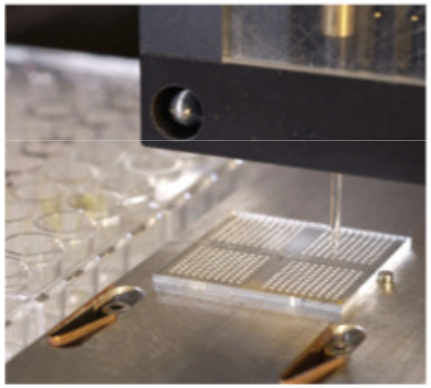
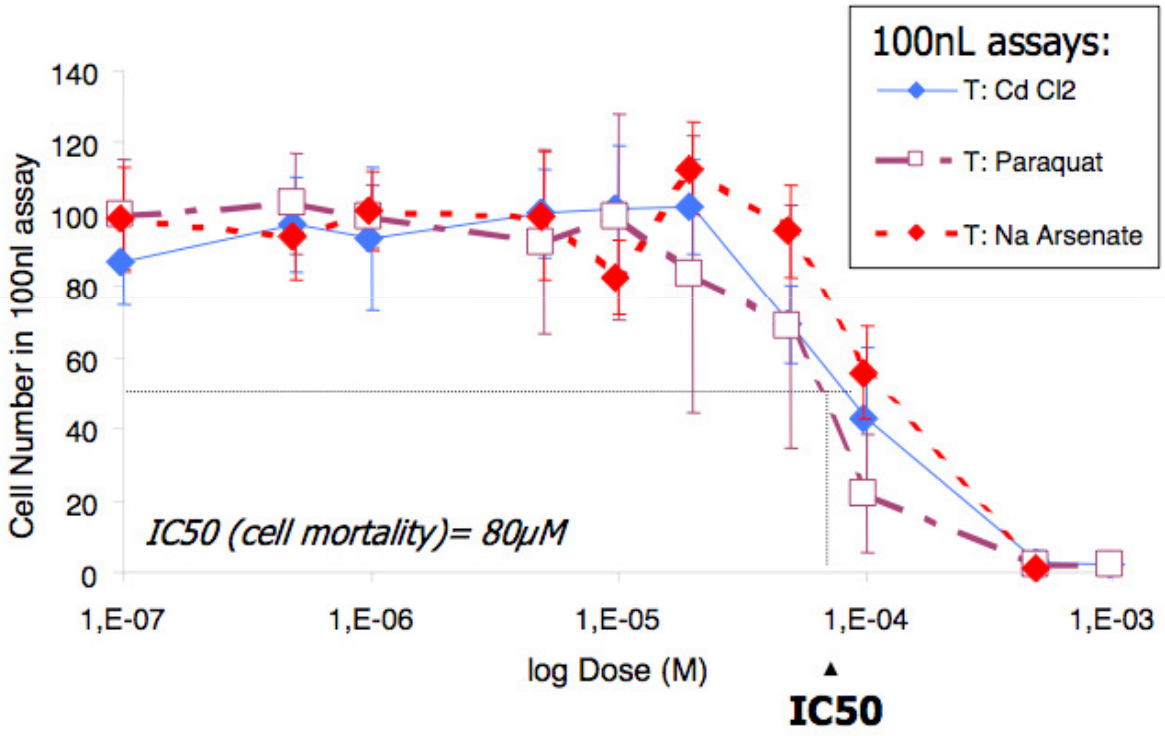
*Quintuplicate assays, 10 toxic doses, 3 toxics, 2 cell lines, 2 independent experiments*



- massively parallel processing
- cyto-Tox activity assays: eg. cell mortality
- strong standard operating protocol (SOP)




*Courtesy of CEA, Grenoble, France*

# Thank You for Your Interest

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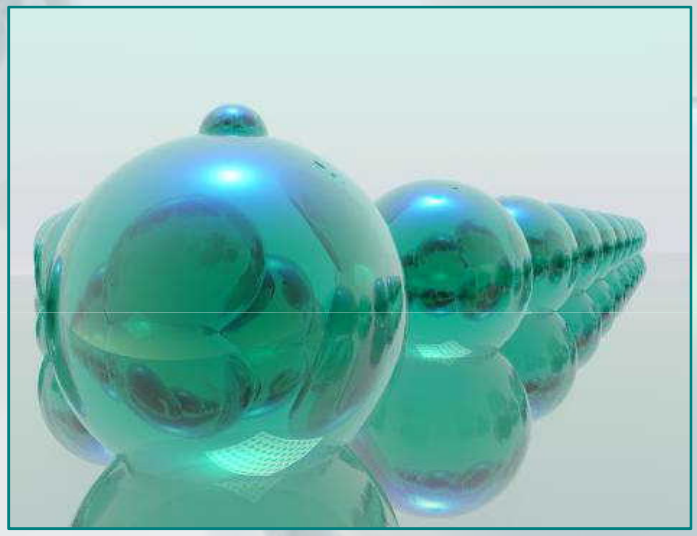

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