

High Accurate Microarray Spotting for Lab-on-Chip Applications

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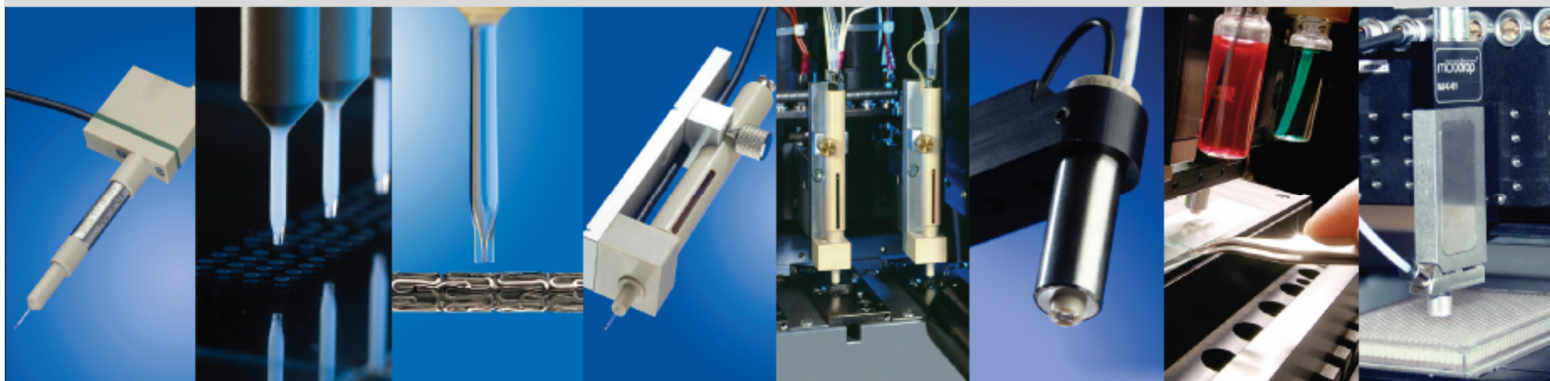
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microdrop Technologies GmbH

Products and Services for Microdispensing and Material Deposition

- Micro Technologies
- Plastic Electronics
- Life Science / Medical Technology
- Material sciences



Products - Microdrop



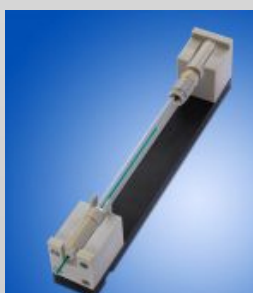
MD-E-3000



MD-K-130/-140



MD-K-801



Micropipette AD-K-901



Micropipette AD-K-501



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Products – Autodrop Platform



Autodrop Compact

200 x 200 x 100 mm³

Accuracy: $\pm 10 \mu\text{m}$



Autodrop Professional

200 x 200 x 100 mm³

Accuracy: $\pm 1 \mu\text{m}$



Autodrop Gantry

270 x 520 x 100 mm³

Accuracy: $\pm 3 \mu\text{m}$



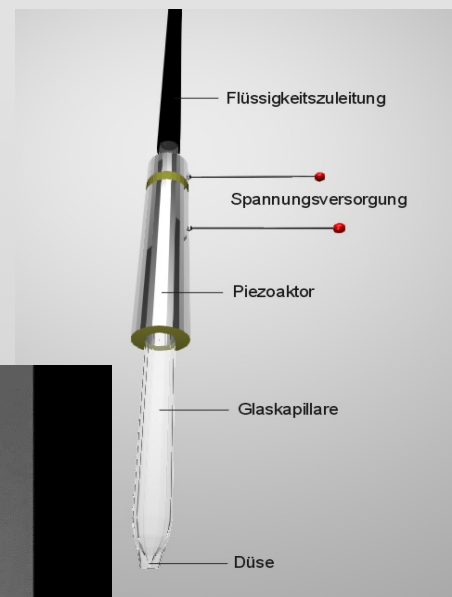
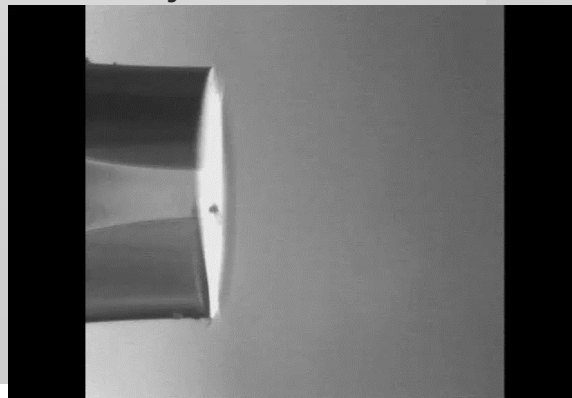
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Spotting Methode

Droplet Generator

- Viscosity 1 – 150mPas
- Material resistance: glass and PTFE
- Parameter control $v_{\text{drop}} = f(U, t, T)$
- refilling: design of fluidic inlet
- results comparable with other inkjet heads
- No follow on costs

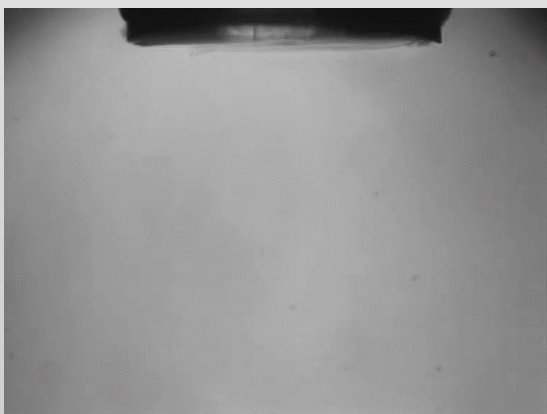
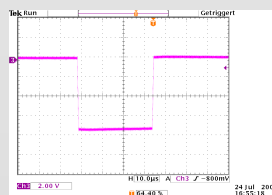


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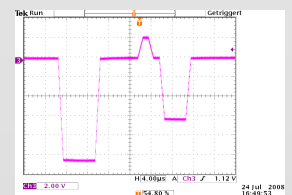
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Small Droplets from Large Nozzles

drop diameter:
80 μm



drop diameter:
30 μm



Harima Silver Nano Ink with 80 μm nozzle diameter

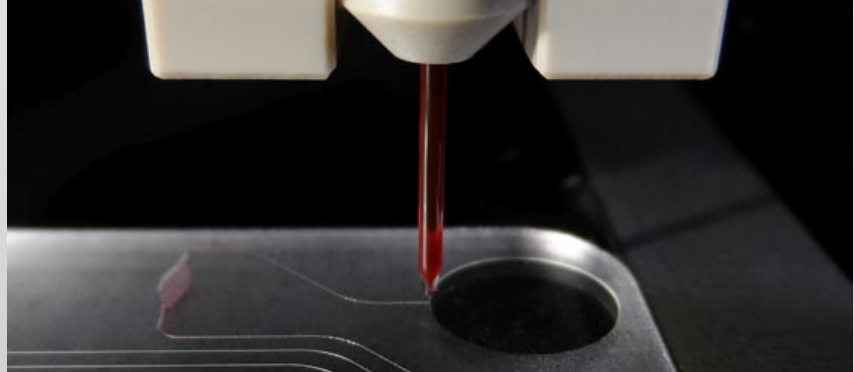


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Lab-on-Chip Devices

- Fluidic Elements
 - Channels
 - Arrays
 - Chambers
- Different substrates
 - Plastics; e. g. PC
 - Silicon
- Customized formulations
 - DNA, proteins, cells,...

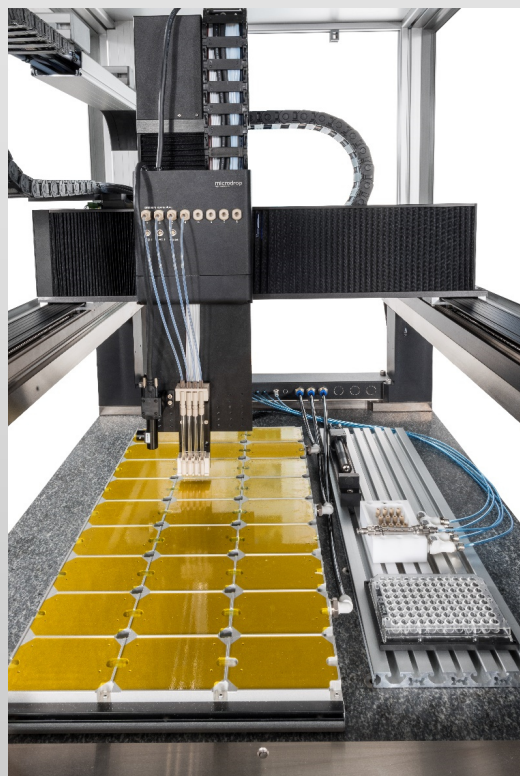


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Lab-on-Chip Devices – High Throughput

- High Throughput Requirements
 - Fast
 - High number of fluids
 - High number of chips
 - Precise
 - Pre-structured pattern
 - Volume accuracy
 - Reliable
 - High quality



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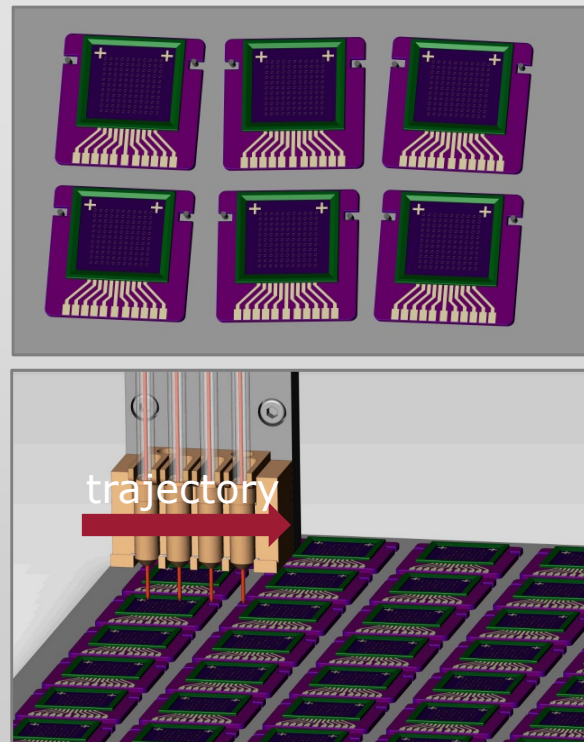
Lab-on-Chip Production - Example

Objectives

- High-throughput spotting of biochips
- Precise spotting of DNA oligos, proteins, ...
- Automated handling of different liquids

Challenges

- Chips are randomly placed $\sim 100\text{ }\mu\text{m}$
- Extremely small tolerance for positioning of droplets $\sim 5\text{ }\mu\text{m}$
- Perfect repeatability of dispensing volumes required; spot size $\sim 100\text{ }\mu\text{m}$



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Lab-on-Chip Production - Example

Data

[Load Data](#) Excel C:\Users\AT\AppData\Roaming\Autodrop\Data\Solution1_28.xlsx

Vacuum Fiducial Recognition

Dispense Table

Drag a column header here to group by that column.

I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C		
R	0	3	17	12	0	22	28	27	8	0	8	27	28	22	12	17	13	0
R	3	9	7	18	16	12	15	5	9	14	9	5	12	16	18	7	9	3
R	27	10	12	22	4	11	8	23	10	6	10	23	8	11	4	22	12	0
R	8	14	24	5	9	28	6	7	26	21	26	7	6	28	9	5	24	14
R	0	1	2	4	0	10	20	25	13	0	13	25	20	10	4	2	1	0
R	14	5	2	19	21	15	20	17	26	17	15	11	20	15	21	19	5	14
R	2	25	13	16	23	1	2	14	18	25	18	14	2	1	23	16	13	25
R	15	21	20	17	22	6	3	26	22	24	22	26	3	6	22	17	20	21
R	24	28	1	18	25	3	21	11	25	27	25	11	21	3	25	18	1	28
R	0	11	6	8	0	5	7	4	28	0	28	4	7	5	0	8	6	11
R	22	23	16	2	24	19	12	16	1	24	1	16	12	19	24	2	16	23
R	23	17	18	3	26	17	14	12	2	25	2	12	14	17	26	3	18	23
R	21	2	3	20	10	13	1	6	11	26	11	6	1	13	10	20	3	2
R	19	19	25	13	27	21	18	19	24	27	24	19	18	21	27	13	25	19
R	0	20	26	1	0	26	19	20	3	0	3	20	19	26	0	1	26	20
R	13	10	15	9	7	23	22	8	4	6	4	8	22	23	7	9	15	10
R	7	27	5	28	12	4	24	10	5	21	5	10	24	1	12	28	5	27
R	7	16	4	11	6	8	9	17	27	14	27	17	9	8	6	11	4	16
R	0	18	23	14	0	15	16	28	7	0	7	28	16	15	0	14	23	18

Filling Table

Drag a column header here to group by that column.

ID	A	B	C	D	E	F	G	H
R12	1	13	25	0	0	0	0	0
R11	2	14	26	0	0	0	0	0
R10	3	15	27	0	0	0	0	0
R9	4	16	28	0	0	0	0	0
R8	5	17	0	0	0	0	0	0
R7	6	18	0	0	0	0	0	0
R6	7	19	0	0	0	0	0	0
R5	8	20	0	0	0	0	0	0
R4	9	21	0	0	0	0	0	0
R3	10	22	0	0	0	0	0	0
R2	11	23	0	0	0	0	0	0
R1	12	24	0	0	0	0	0	0

Fluid Nr.: 1

- ☒ Fill
- ☐ Drop Check
- ☐ Dispense
- ☐ Observe
- ☐ Wash

Sequence of operations

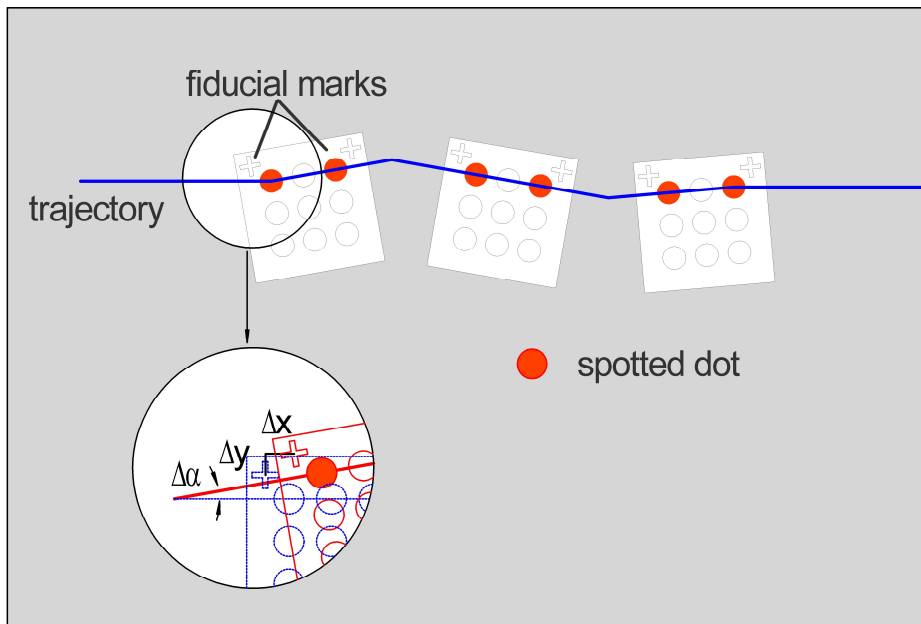
- Flexible and easy-to-use graphical user interface
- Management of individual workflow
- Process control
- Handle multiple liquids by imported data tables



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Lab-on-Chip Production – Spotting Path Compensation



Sequence of operations

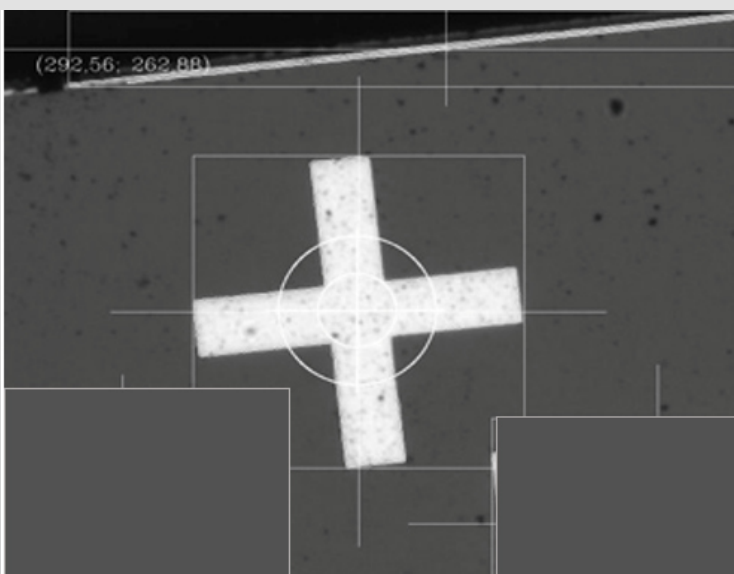
- 1) Scan alignment of chips by pattern recognition
- 2) Calculation of optimal path for high-throughput and consistently high spotting quality
- 3) Precise on-the-fly spotting



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Pattern Recognition Features



Automated alignment

Accuracy < 5 μ m

Automated Head Calibration



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Lab on Chip - Application



Polystyrol chip
Channel width: 100µm

Pipette AD-K-901
Drop size: 85µm
Drop volume: 320 pl

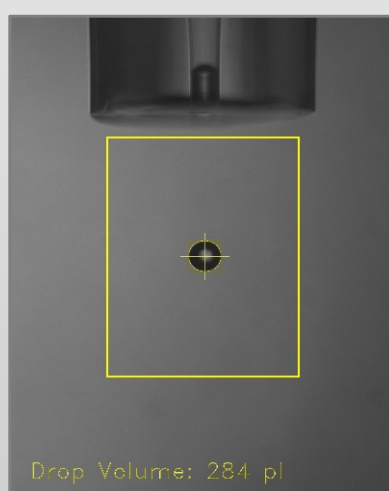


Pattern Recognition Features

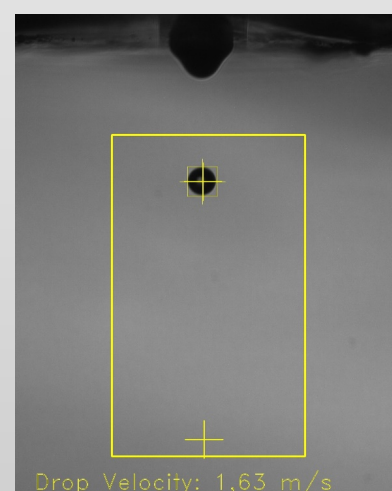
Quality of spotting process



Droplet diameter
measurement



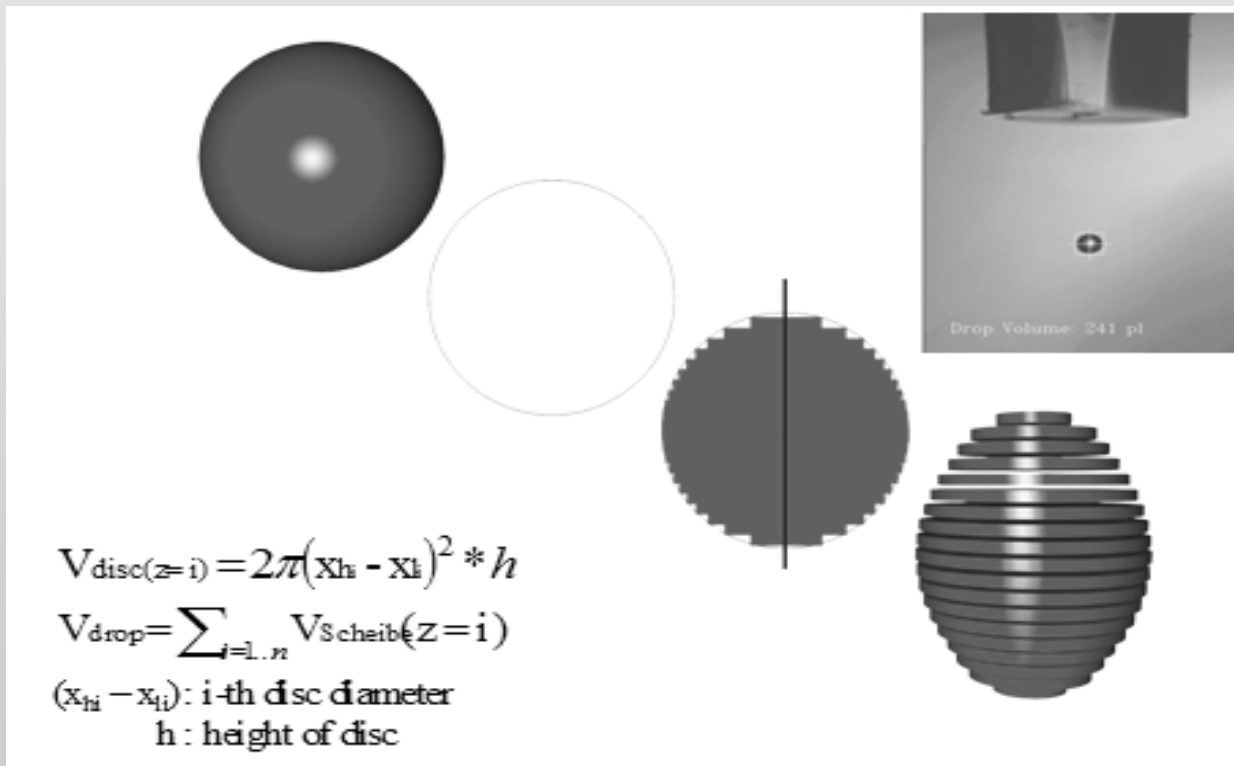
Droplet volume
measurement



Droplet speed
measurement



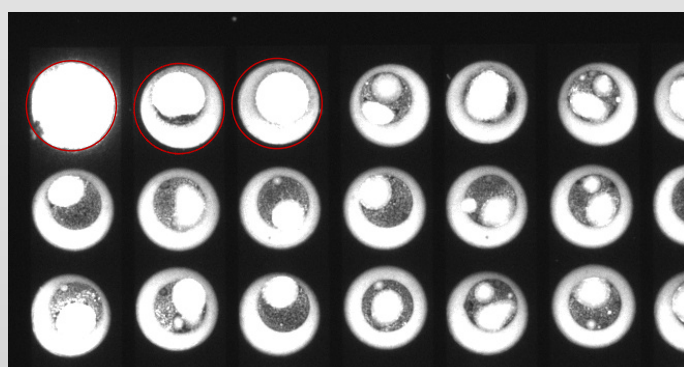
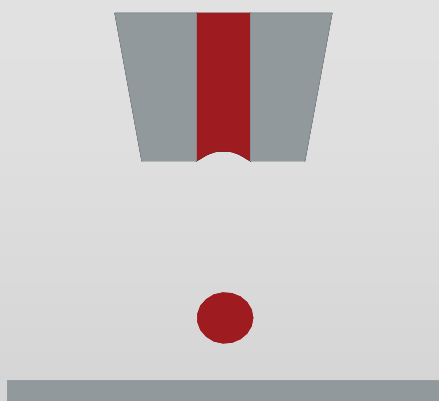
Drop Volume Measurement by Pattern Recognition



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First Drop Effect



Microarray with fluorescent marker / Spot diameter 100 μm

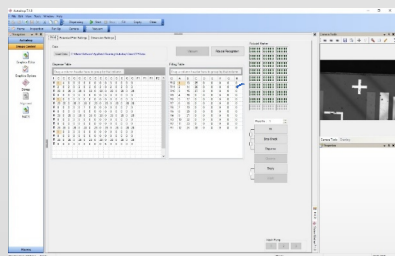
- Evaporation at nozzle front end
- Concentration of solved material increased
- Resulting spot show increased signal
- Slightly larger Spot due to wetting effects



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Demonstration of Workflow



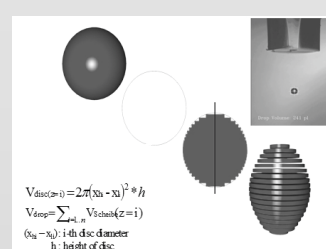
Process Initialisation



Chip Localisation



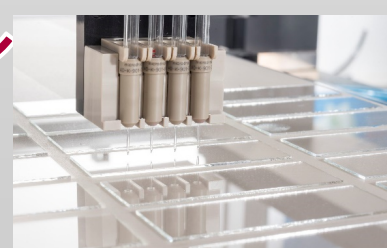
Liquid Aspiration



Drop Detection



Tip Washing



Array Spotting Process & Path Compensation

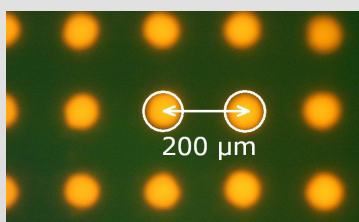


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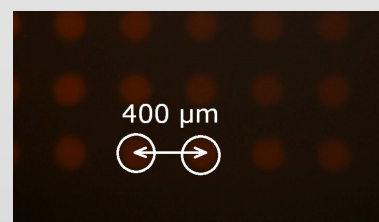
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Spotting of Microarrays

- Printing of fluorescently labelled DNA oligo / silicone substrate

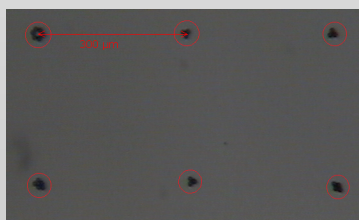


droplet volume < 50pl

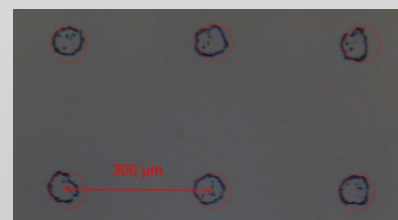


droplet volume ca. 500pl

- Dispensing of PMMA beads onto functionalized surface



Bead diameter: 10.53µm



Bead diameter: 2µm

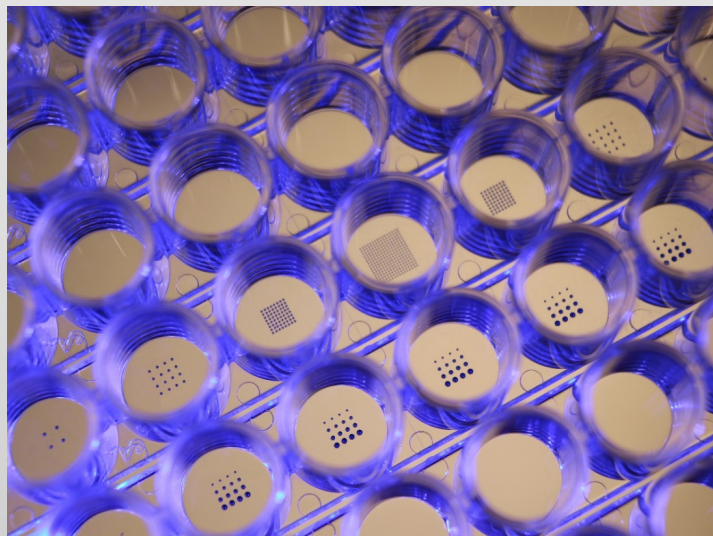


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Conclusions

- Utilization of inkjet spotting enables high throughput chip production
 - Highly automated workflow by use of pattern recognition & printing path compensation
 - High precision
 - Spot location within 5 μm
 - Volume 1% CV
- Throughput numbers? – **Well, it depends!**
 - Number of fluids?
 - Chip geometry & Pattern?
 - Individual process!



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