Nano-Plotter™

Microarraying and Picolitre Pipetting

GESIM

GESIM Nano-Plotter

Microarraying and Picolitre Pipetting

Non-contact Picolitre Pipetting ensures the highest quality for both preparation of complex sample carriers with multiple biomolecules and for filling micro cavities. On a worldwide scale the Nano-Plotter™ instrument family has been proven for years in research and production.

Key Features

- **Selection of pipette types to match the sample, not vice versa**
- **No impact on sensitive surfaces through non-contact technology**
- **Homogeneous spot topology**
- **Unlimited replica spots**
- **Variation of spot volume through tuning droplet number**
- **Array layout may be arbitrary and independent of pipette head layout**
- **Combination of chilling and humidification allows dew point pipetting**
- **Alternative dispensers for larger volumes or highly viscous media available**

Flexibility and extended capability of the basic instrument configurations is possible due to open software and modularity of hardware accessories. The micro machined piezoelectric pipettes accept a wide range of liquid samples and emit drops from as little as 60 Picolitres.

Customized versions of the Nano-Plotter™, e.g. for integration into automated production lines, are available on request.

Applications

- Microarrays for research and diagnostics (DNA, Proteins, Carbohydrates, Lipids etc.)
- Spotting of cells and beads onto arbitrary targets, e.g. the bottom of 96-well plates
- Pipetting of miniaturized assays
- Loading of biosensors

System Platforms

The Nano-Plotter™ is available in two sizes with the following common features:

- 1 to 16 independent piezoelectric pipetting tips in any combination
- Sample aspiration from 96 well or 384 well micro plates
- Array density > 3000/cm^2

- Removable target tray, dust cover
- XY repetition accuracy ± 10 µm (encoder controlled), step width 2 microns
- Travel speed up to 50 cm/s
- Optical function test of each individual pipette tip after sample aspiration
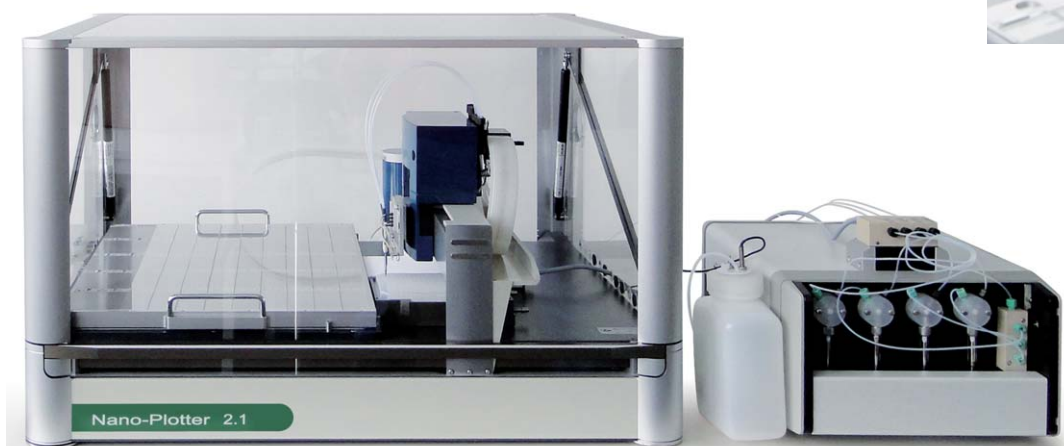
NP2.1: Platform for up to 55 standard slides

NP2.1/E: Platform for up to 120 standard slides

Technical Data	Nano-Plotter™ NP 2.1	Nano-Plotter™ NP 2.1/E
Dispensing area / slide tray (width x depth, outer dimensions)	302 x 400 mm	645 x 400 mm
Traversing range in XY-direction (widht x depth)	427 x 341 mm	777 x 341 mm
Footprint main unit	623 x 509 mm	973 x 509 mm
Height (incl. cover)	375 mm	
Weight (incl. cover)	30 kg	50 kg
Max. pipetting height	50 mm	
Pipetting channels	1...16	
Power supply	110...240 V, max. 200 W	

Piezoelectric Pipetting

The piezoelectric tips are made from silicon and glass by micromachining technology. When aspirating no more than a few Microlitres the sample only comes into contact with these materials.

Each piezoelectric tip is controlled individually and connects to a dedicated syringe pump for aspiration and rinsing. The dead volume – additionally loaded sample – is minimised to approximately one Microlitre. Unconsumed sample can be returned to the respective well of the sample plate after pipetting.
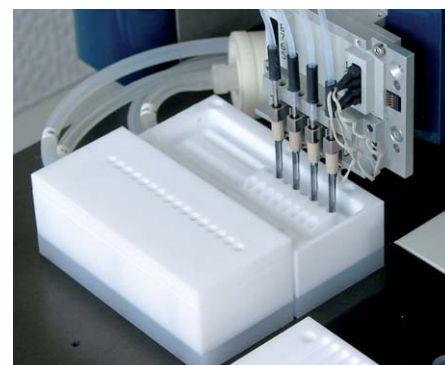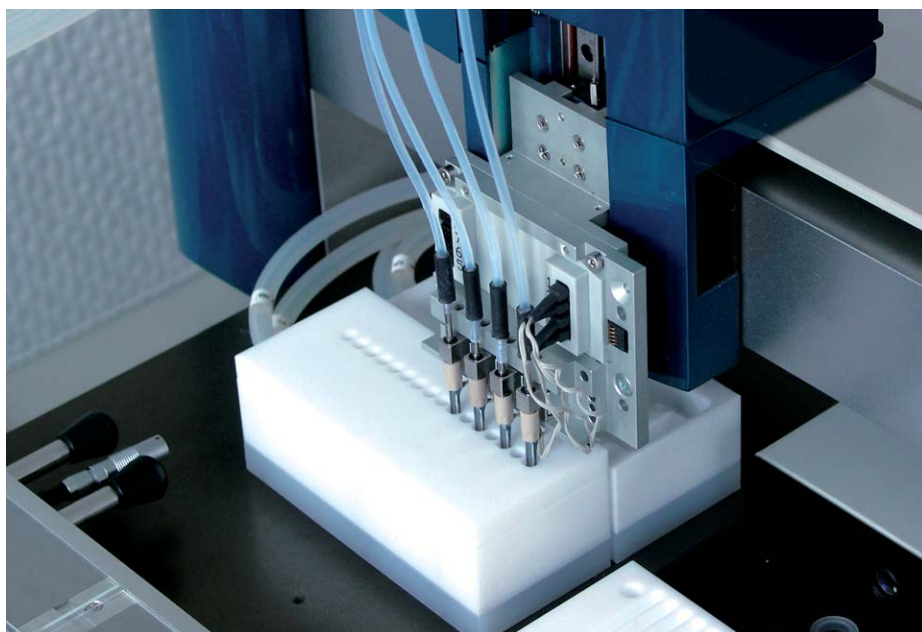
| Volume of a single droplet	
Nano-Tip J:	(0,35…0,6) nL
Nano-Tip A-J:	(0,2…0,4) nL
Pico-Tip J:	(0,05…. 0,08) nL

Special pipette tips for high viscous samples or printing into 96-well plates are available.

Highly effective washing technology prevents cross contamination between pipetting cycles. A thorough rinsing cycle washes the piezoelectric tips inside and out. For standard DNA solutions (such as oligo samples at 0.1 μg/ml), wash cycles of a few seconds are sufficient. For proteins and peptides, an additional wash step can be involved, using a dedicated wash fluid, such as a detergent, acid, or base. Alternatively the Nano-Plotter™ can be configured with a second wash bowl.

SUBSTANCES SUCCESSFULLY DISPENSED BY GESIM'S PIEZOELECTRIC PIPETTING TECNOLOGY: Acetic anhydride, acetone, acetonitrile, betaine (N,N,N-trimethyl-glycine, < 1 M), chloroform, cyclohexanone, dextran solutions, detergents (e. g. 2 % Triton X-100 or Tween-20), dichloromethane/trifluoroacetic acid (98:2), N,N-dimethylformamide (DMF), dimethylsulfoxide (DMSO), 1,4-dioxane, DNA (PCR products < 2 kbp, < 3 mg/ml, or plasmids < 4 kbp, < 1 mg/ml), ethanol, N-FMOC-Ile (200 mM in DMF), glycerol (< 50 % in H2O), iodine (in THF/pyridine/H2O 3:75:20:75), isopropanol, MALDI matrix (a-cyano-4-hydroxycinnamic acid in NMP, 3-HPA in 20 % acetonitrile), methanol, 1-methyl-2-pyrrolidone (NMP), 1-methylimidazole (16 % in THF), NaCl (< 3 M), phosphoramidite (T-CE in acetonitrile), polyethylene glycol 10000 (PEG, 5 %), proteins (< 1 mg/ml), silane (2-3 % in propanol), SSC (saline sodium citrate, 3x), tetrahydro-furane (THF),
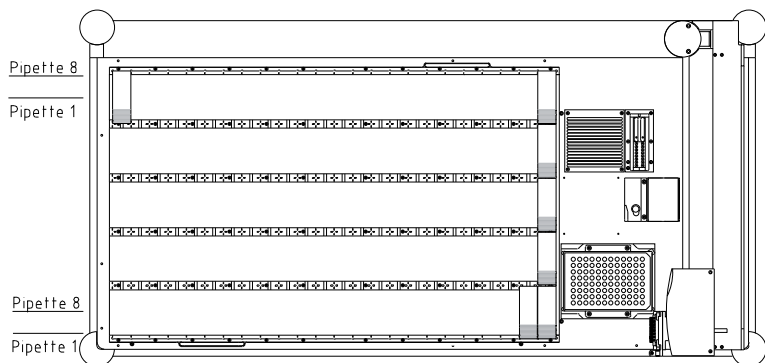
Nano-Plotter™ NP2.1

Tailor made slide trays for custom layouts are available on request for the Nano-Plotter™.
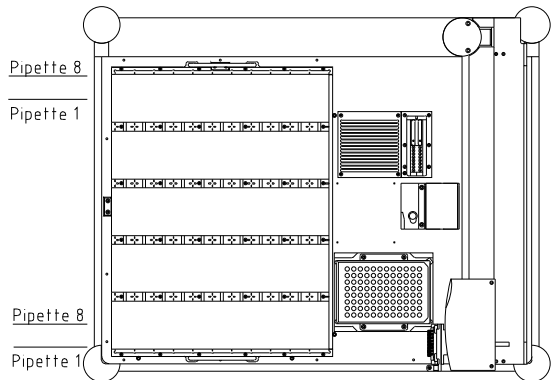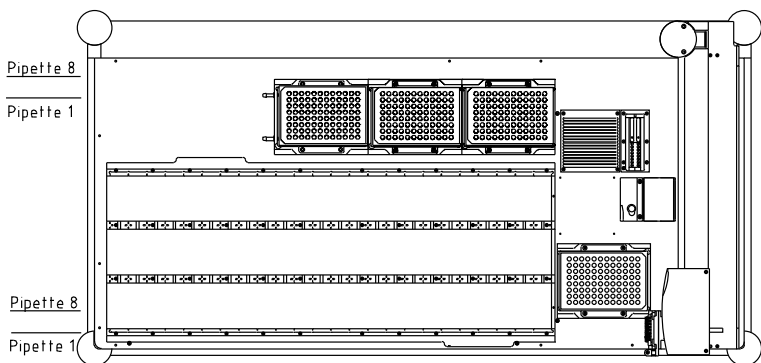

5 x 11 slides at up to 26 mm x 76 mm, one sample plate

Nano-Plotter™ NP2.1/E

5 x 23 slides bis zu 26 x 76 mm, one sample plate

3 x 23 slides bis zu 26 x 76 mm, four sample plates

A spring loaded slide fixation is optional, but usually not necessary due to the non-contact operation.

The slide trays of the Nano-Plotter™ come with hand grips and lock into the surface easily. Multiple trays with one machine allow loading and unloading while the other one is in use. An (optional) adapter plate with coolant channels and a temperature sensor allows surface temperature control, e.g. for ambient temperature compensation.

- ■ **Slides**
- ■ **Membranes**
- ■ **Micro well plates**
- ■ **Chips/slides in an arbitrary format**

The standard version of the slide tray includes fixtures for slides by locator pins as well as embedded magnets for holding membranes.

FilmArray Production

Courtesy of BioFire Diagnostics Inc.

BioFire Diagnostics Inc. - Corporate Offices
390 Wakara Way, Salt Lake City, Utah 84108, USA

"… The FilmArray integrates sample preparation, amplification, detection, and analysis all into one complete process that delivers results in about an hour.… The FDA-cleared Blood Culture Identification (BCID) Panel and Respiratory Panel (RP) are lab-ready today, and the Gastrointestinal (GI), Meningitis/ Encephalitis, and Lower Respiratory Panels are in development.…"

Production facility with multiple Nano-Plotter™ NP2.1/E for the manufacturing of clinical test substrates

Development of Biosensors

Courtesy of SESMOS Ltd.

SESMOS Ltd.
Edinburgh Technology Transfer Centre
4th Floor, Alrick Building
King's Buildings
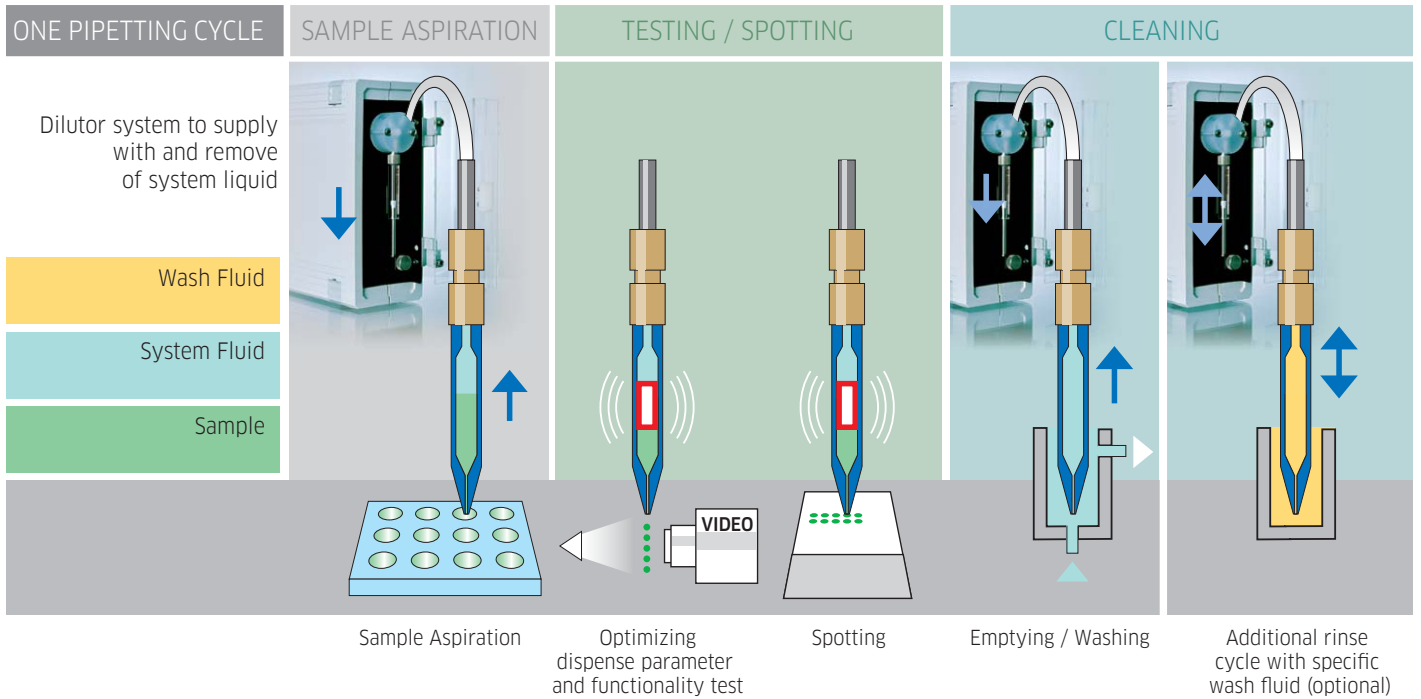University of Edinburgh
Edinburgh
EH9 3JL

"SESMOS has developed a unique discovery process, in which label-free thin film bulk acoustic resonance (FBAR) biosensor technology, miniaturised small molecule libraries and innovative screening technologies are combined. The core of this technology allows a very rapid and efficient identification of quantitative hit series against a wide range of relevant and innovative targets. In this way, SESMOS at an early stage in the drug discovery process can identify the right compound-target combinations based upon a data driven selection process."

Development of label free biosensors with the Nano-Plotter™ 2.1; Photograph courtesy of Christophe Portal

Flashing and Calibration

ONE PIPETTING CYCLE	SAMPLE ASPIRATION	TESTING / SPOTTING		CLEANING	
Dilutor system to supply with and remove of system liquid					
Wash Fluid					
System Fluid					
Sample					
	Sample Aspiration	Optimizing dispense parameter and functionality test	Spotting	Emptying / Washing	Additional rinse cycle with specific wash fluid (optional)

Each piezoelectric pipetting tip is controlled individually. Both optical and microfluidic systems are available for the Nano-Plotter™ for assessing each tip automatically after sample aspiration.

8-fold flow sensor module for an 8-channel Nano-Plotter™
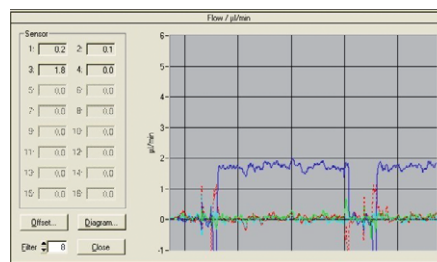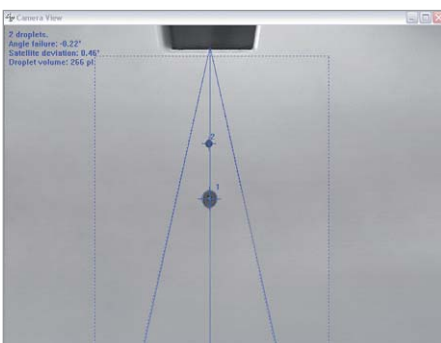
A flow rate of 1.7 µL per minute corresponds to a droplet volume of 283 Picolitres at a frequency of 100 Hz.

Stroboscopic image capture provides real-time analysis of pipette performance both before and after sample dispensing. Droplet diameter allows estimation of the dispensed volume calculated through image analysis. If, for any reason, a sample is not dispensed as instructed (e.g. empty sample well), the software logs this and allows for repetition of respective sample printing, thus ensuring completion of the task.

Naturally, the dispense behaviour of the piezo-electric tips is affected by the sample. A highly sensitive flow sensor in the system liquid path of each tip measures the compensated volume of the ejected drops. Thus an exact measurement of the droplet volume is possible.
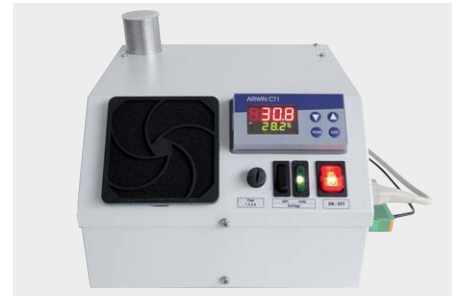
Chilling and Humidification

Coolable micro plate holders at different sizes and formats

*Removable slide tray with underlying chiller plate and temperature sensor*

*Ultrasonic humidifier, fully adjustable from 50% to 80% humidity*

Seeking and Identification

It is not possible to manually position the pipette to dispense a 50 micrometre droplet onto a similarly sized target.

Therefore a microscope camera is employed for target recognition and piezoelectric tip alignment.
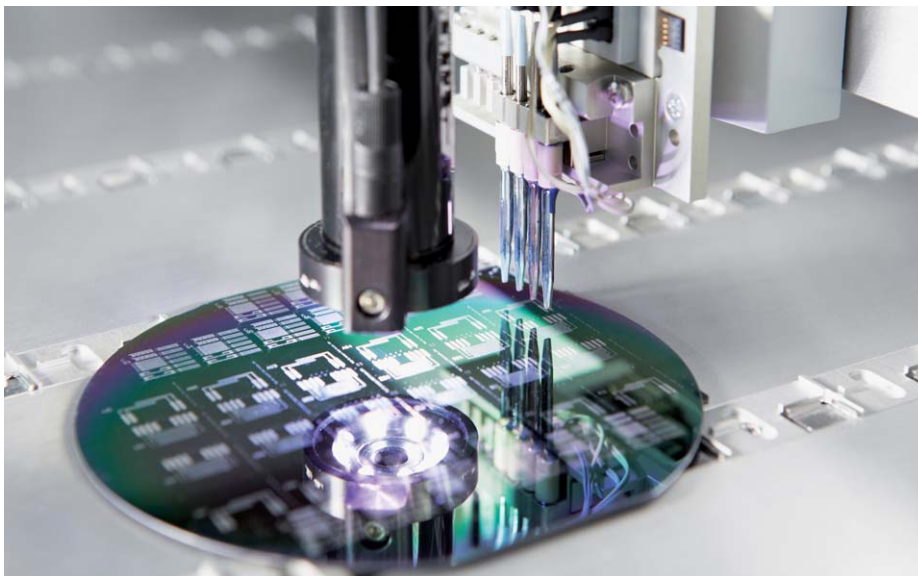
The automatic pattern recognition works for 2 and 3-dimensional targets, e.g. microfluidic chips.
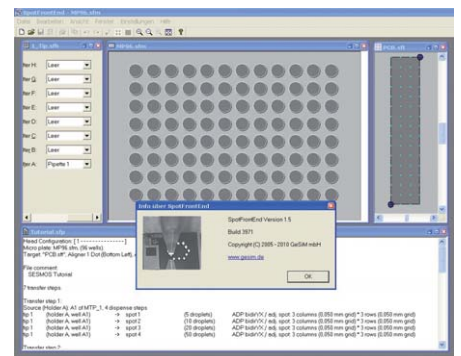
*A software extension allows the unlimited definition of dispense positions relative to marker patterns.*

Replacing and Storing

All Nano-Plotter™ variants can be used in conjunction with plate hotels of a third-party manufacturer. This allows automatic replacement of up to 56 384-well micro plates.
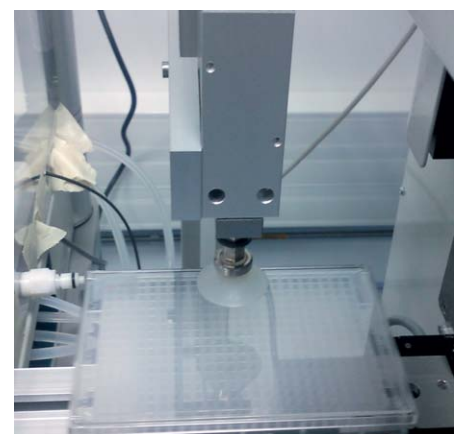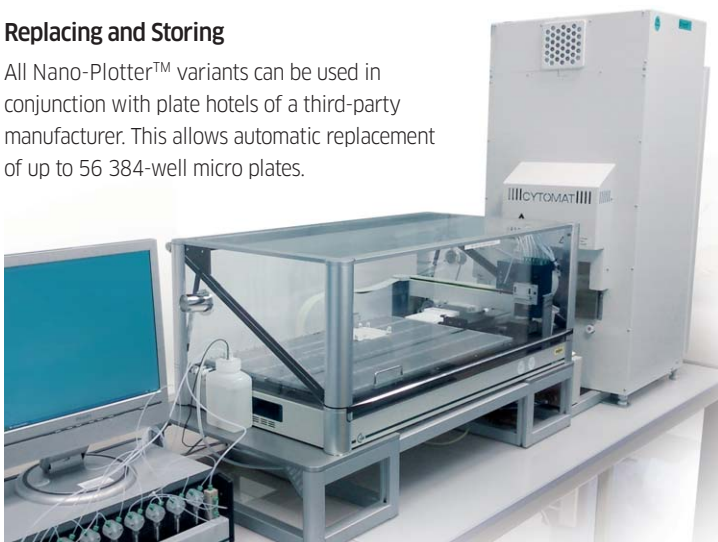
The plate hotel includes temperature control. A lid handler supports covered sample plates (e.g. in case of non-aqueous samples).

Components and Accessories

Observation and Magnification
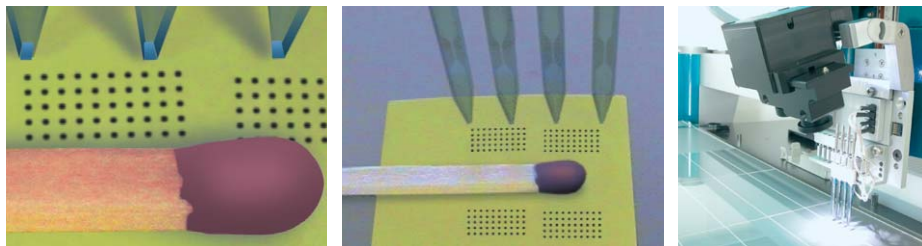
The observation camera without software support allows two different magnifications and offers the manual teach-in of XYZ positions.

Controlling and Programming

The instrument software, NPC16, comes with an intuitive user interface and supports quick setup of the Nano-Plotter™ for all arraying tasks. Service routines avoid the "drying up" of the piezoelectric tips during short breaks and monitor test results and images of the on-board cameras for quality documentation on request.

Furthermore, NPC16 comes with an embedded programming tool for the development of specific procedures (NPL programs) for research projects. The flexible hardware of the Nano-Plotter™ is completely accessible for the programming tool.

Standard Procedures

No programming is required for standard applications. The NPC16 software comes with a couple of "ready-to-use" NPL programs for frequent pipetting procedures. Changes of the pipette head configuration as well as working with different targets do not require any program code modification.

GESIM's experienced programmers will support customers in creating NPL programs for any special application.

| Sequentially | Simultaneously (four tips) | By transfer list |
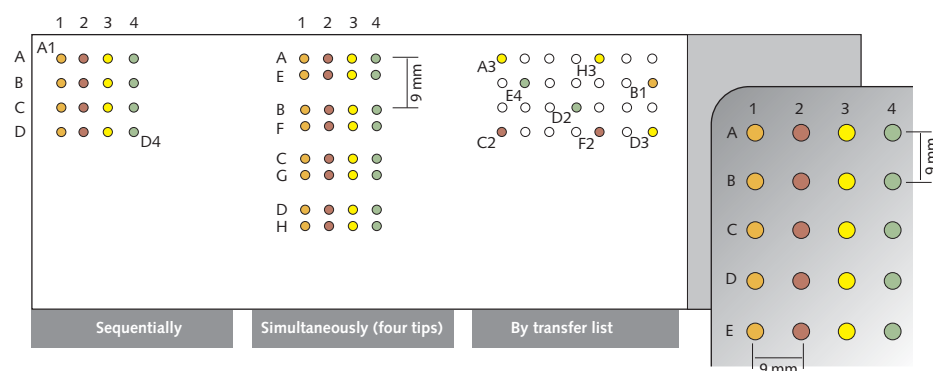
Sequential pipetting:
For straightforward sample tracking, a defined area of a source plate can be transferred to dispense targets, exactly copying the layout of the source plate. The user may also define replica spots for each sample.

Simultaneous pipetting:
All tips dispense simultaneously and arrange spots at a distance of 4.5 mm or 9 mm, respectively. Replicas and sample spots of later cycles can be positioned in between at user-defined distances.

The transfer list:
The user arbitrarily assigns sample wells to target spots by defining a simple transfer list.

Viscous Samples and Large Volumes

All Nano-Plotter™ are customizable with other dispense heads, even from third party manufacturers.
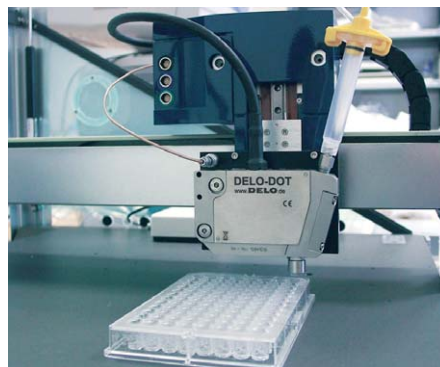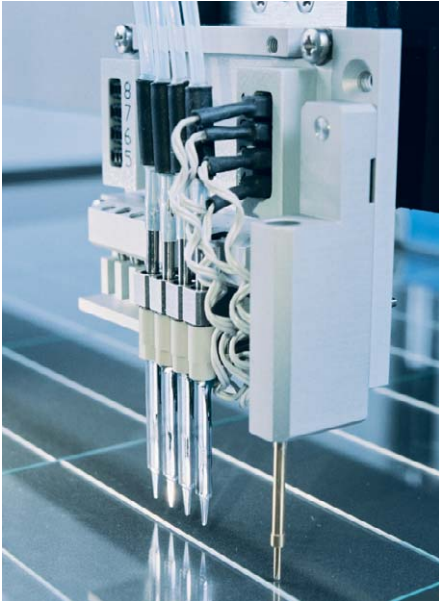

*Temperature controlled dispense heads from DELO eject 3 Nanolitre drops and accept viscosities of up to 20.000 mPa*s.*

For bulk dispensing of a larger number of smallest drops (from 10 Pikolitres) a reservoir (3 Millilitres) is available for the piezoelectric tips.

The Nano-Plotter™ Z-height-sensor identifies the target Z-position and automatically adjusts spotting height.

Powder Dispensing

A pneumatically actuated powder pipet allows to pick up and deposit Micrograms of granular material.

Microliter Pipetting

The syringe unit of the Nano-Plotter™ allows displacement dispensing. Passive tips or adapters for passive tips are available on request.

DNA-, Protein Arrays **

Piezoelectric technology allows different spot sizes by varying the number of drops per spot without changing the tip itself.

Non-contact arraying technology allows for highly consistent spots showing little or no „donut" effect.

The minimum spotting distance depends on the surface structures. Hydrophobic substrates allow grid sizes down to 100 microns. Piezoelectric GESIM tips are perfect to process all of the most common buffer solutions such as 3x SSC, PBS, Tris, but also glycerol up to a concentration of 40 %.
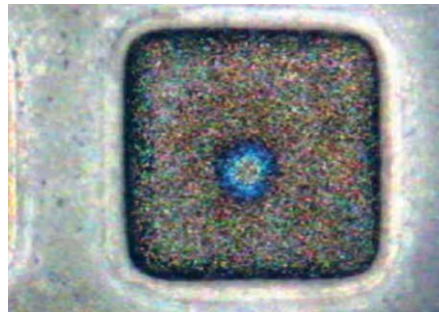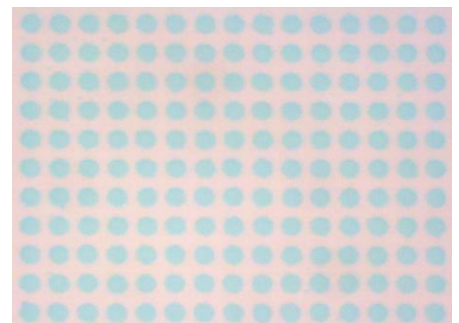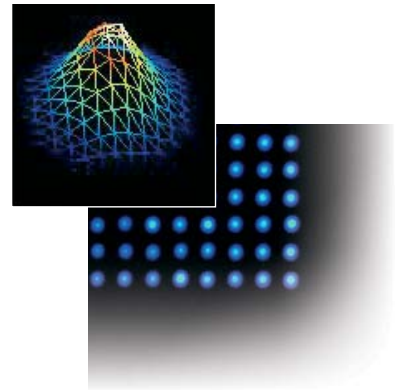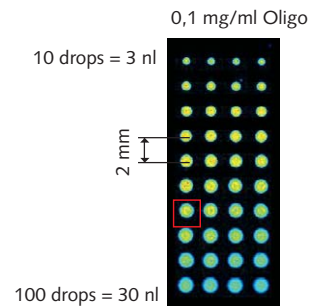

Microstructured substrates are well suited to center spots. Combining piezoelectric and passive dispensing technology, Nanolitre and Microlitre volumes can be spotted in applications such as the preparation of MALDI targets (Picture), or cryoconservation of cells.
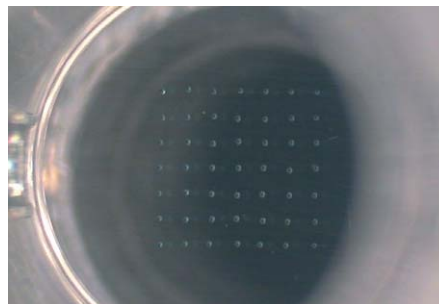
Microarrays also can be generated onto or inside 3-dimensional objects like well bottoms of micro plate wells.
The picture shows spots of about 1 nl volume in a 0.4 mm grid.

0,1 mg/ml Oligo

10 drops = 3 nl

2 mm

100 drops = 30 nl

View through a microscope of a membrane with 2.5 nl spots in a 0.4 mm grid.
At a volume range of 1 to 50 nl, the Nano-Plotter™ is an excellent platform to tether probes onto membranes.

More details as well as scientific customer publications are available on www.gesim.de

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