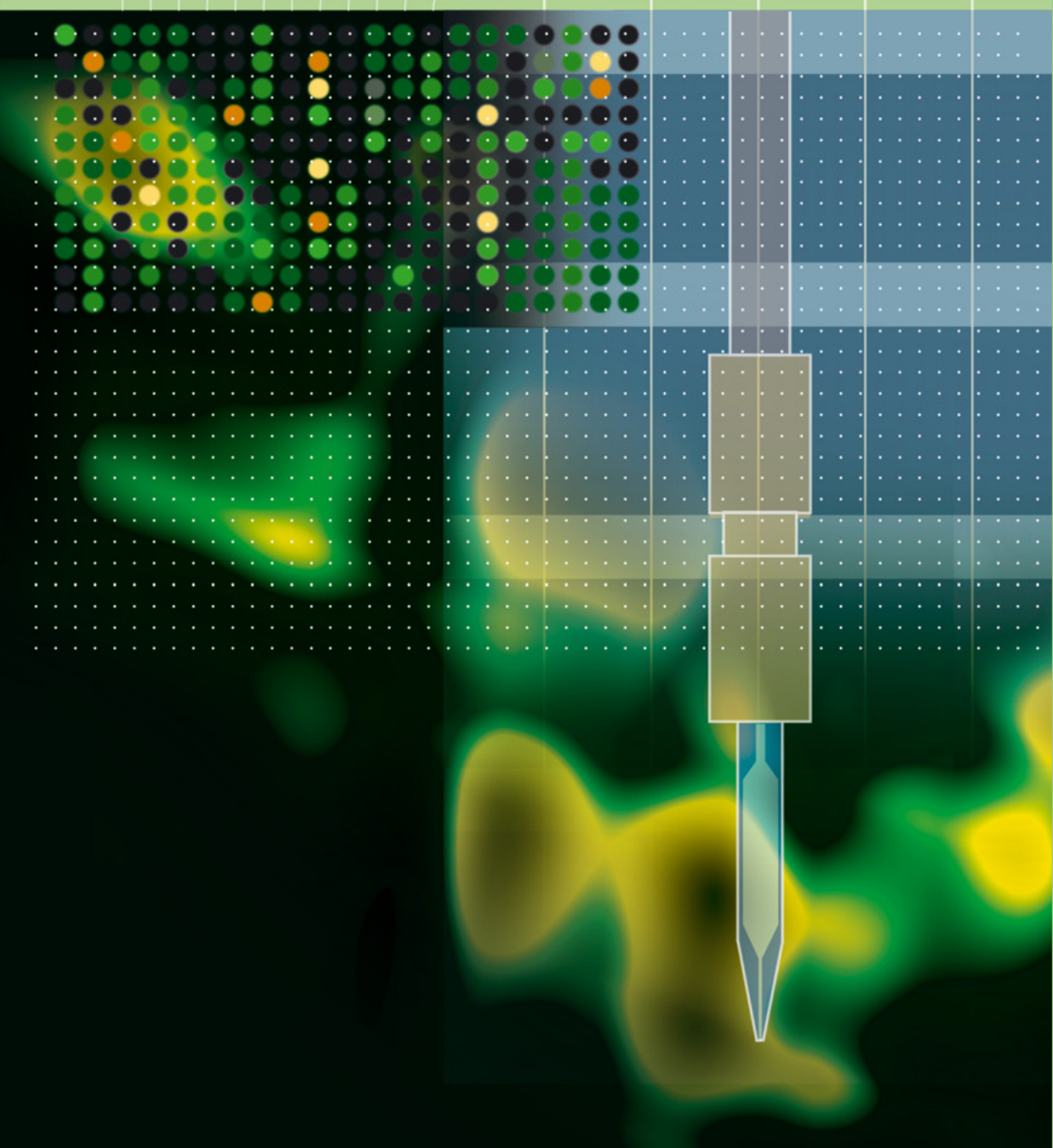


GeSiM

Gesellschaft für Silizium-Mikrosysteme mbH



Nano-Plotter

Universal Micropipetting System

www.gesim.de

Nano-Plotter™

Nano-Plotter™ is a product line of modular and flexible automatic pipetting systems for sub-microliter dispensing and arraying applications. The system features piezoelectric pipette tips that accurately dispense liquids in volumes as low as 50 picoliters, following the "drop-on-demand" principle.

Multiple pipettors can be positioned in parallel for simultaneous printing (4.5 mm and 9 mm, respectively). This non-contact printing technology allows the immobilization of extremely small spots on a variety of solid surfaces and the dosage into tiny cavities.

Ranges of Application

DNA and
Protein Arrays

Cell Pipetting /
Tissue Arrays

Miniaturized
Assays

Biosensors

Key Benefits

- *No impact on sensitive surfaces through touchless technology*
- *Unlimited spot replication from each single sample aspiration*
- *Homogeneous spot topology*
- *Variation of volume dosage to as low as 0.05 nL without changing the tip*
- *Dispensing micro liter quantities through standard disposable plastic tips*
- *Array layout can be arbitrary and is independent of pipette head layout*
- *Highly effective washing and cleaning system*
- *Special humidifying and chilling technology (dew point pipetting) prevents evaporation and conserves nanoliter volumes in applications such as miniaturized assays*

GeSiM's products are highly amenable to customization. Our expert technicians will adapt hard and software components to integrate our systems into specific robotic or other automated user applications.

Nano-Plotter™ NP 2 (NP 2.1 · NP 2.1/E)

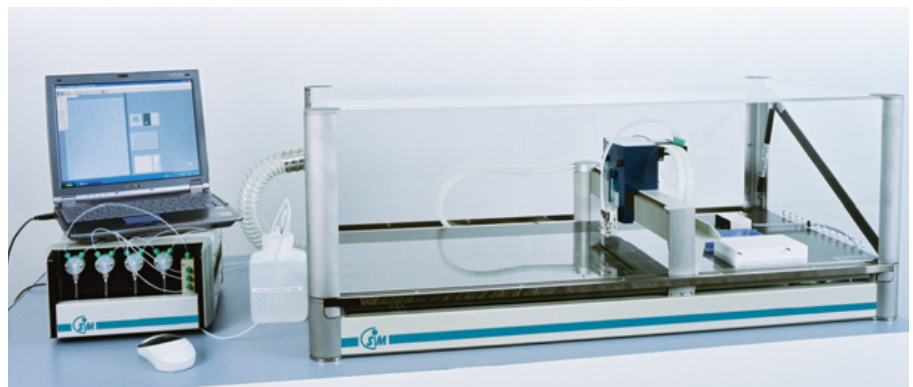
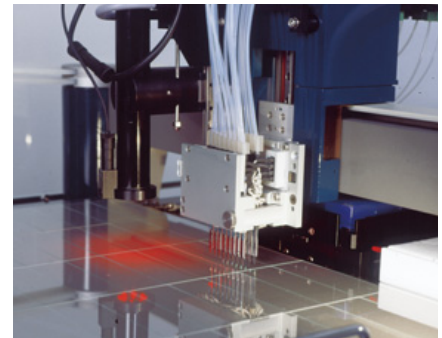
The Nano-Plotter system for high throughput production, and for high density and high precision spot positioning. The system's XYZ robotic stage is available in various sizes. (NP 2.1 bzw. NP 2.1/E).

- 1 to 16 tips (smallest drop volume 50 picoliters)
- Positioning speed up to 50 cm/sec
- Repetition accuracy up to ± 10 microns
- Array densities $> 2500 \text{ cm}^{-2}$
- Extensive line of accessories available

The XYZ stage can be configured to support a variety of dispense targets such as slides, membranes, chips and microwell plates. For convenient handling, the dispense targets can be attached to a removable tray that is positioned above the XYZ stage. To increase throughput, additional trays can be used for loading or unloading of dispense targets during the machine's run. Dispense targets can be fixated on the tray.



NP 2.1 for max. 55 slides



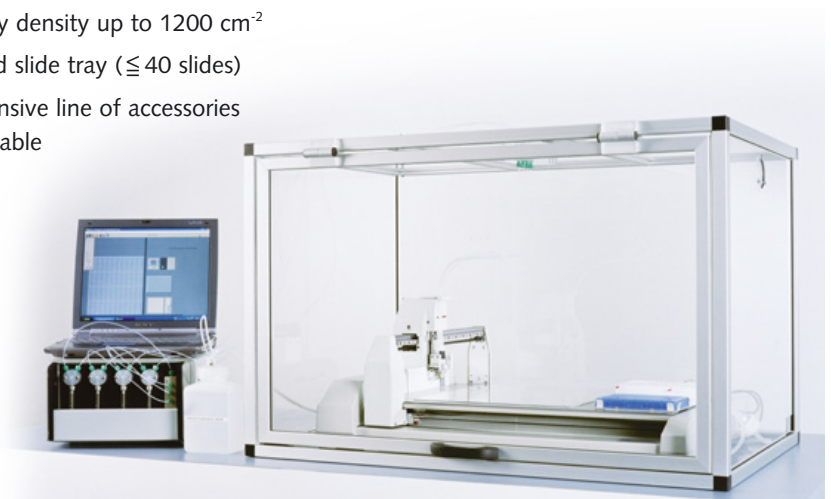
NP 2.1/E for 120 slides

Nano-Plotter™ NP 1.2

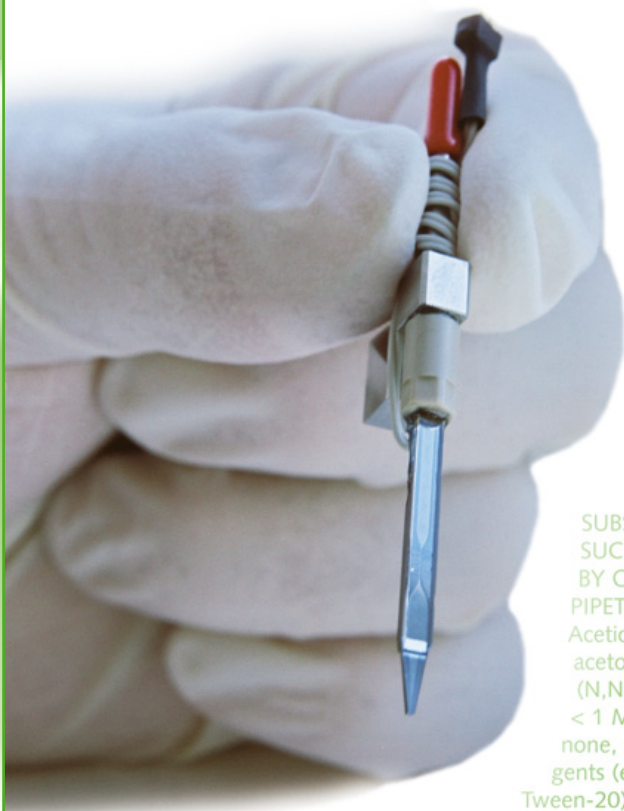
The Nano-Plotter™ system for Research and Development. It's cost effective robotic handling system will fit smaller budgets, and yet allows easy and custom specific array spotting. Both pipet tips and fluidics are identical to the larger Nano-Plotter™ 2.

- 1 to 8 Tips (smallest drop volume 50 picoliters)
- Positioning speed up to 40 cm/sec
- Repetition accuracy ± 50 microns
- Array density up to 1200 cm^{-2}
- Fixed slide tray (≤ 40 slides)
- Extensive line of accessories available

The plane surface slide deck allows mounting of (up to 40) standard slides, or customer specific targets, such as custom-fabricated membranes.



Piezoelectric Pipetting



(Standard-) Micro Pipet Nano-Tip

drop volume approx. 0.35 nL

Micro Pipet Pico-Tip

drop volume approx. 0.1 nL

Micro Pipet Pico-Tip A

drop volume approx. 0.05 nL

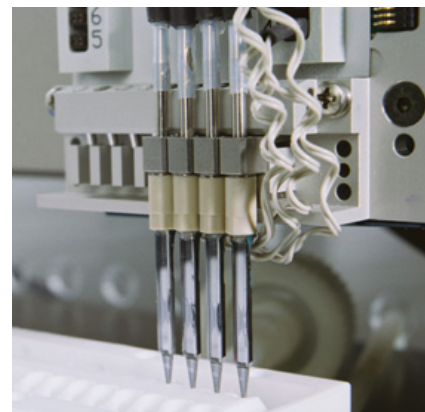
Max. dosage frequency:
approx. 1000 Hz

SUBSTANCES SUCCESSFULLY DISPENSED BY GESIM'S PIEZOELECTRIC PIPETTING TECHNOLOGY:

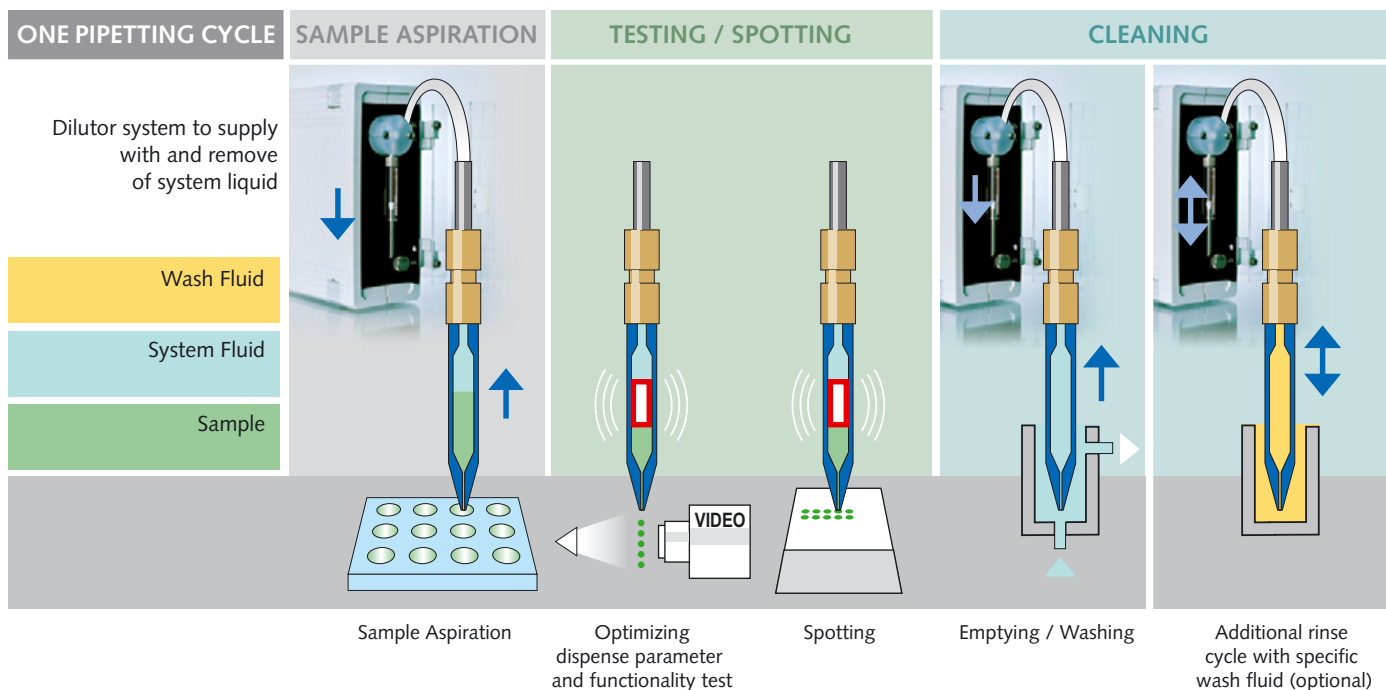
Acetic anhydride, acetone, acetonitrile, betaine (N,N,N-trimethyl-glycine, < 1 M), chloroform, cyclohexanone, dextran solutions, detergents (e. g. 2 % Triton X-100 or Tween-20), dichloromethane/trifluoroacetic acid (98:2), N,N-dimethylformamide (DMF), dimethylsulfoxide (DMSO), 1,4-dioxane, DNA (PCR products < 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 (α-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), tetrazole (in acetonitrile), toluene, urea (< 7 M), water

The Nano-Plotter™ piezoelectric pipetting tips consist of glass and silicon. They tie into the instrument's fluidic system through metal shafts. Each pipet connects to a dedicated syringe that supplies both sample and washing fluids.

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 approximately 5 seconds are sufficient. For proteins and peptides, an additional washing station can be purchased, using a dedicated wash fluid, such as a detergent, acid, or base.



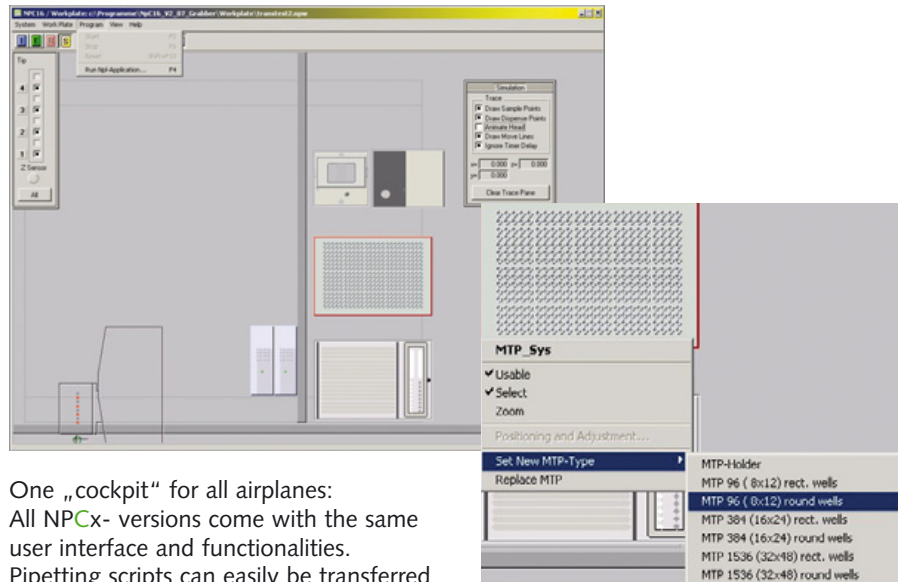
Washing station with wash wells



Micro Pipetting Software NPC8/16*

* NPC8 für Nano-Plotter NP 1.2
NPC16 für Nano-Plotter NP 2

Another flexible feature of GeSiM's non-contact dispensing technology is its ability to individually control each single pipette. Using multi-channel pipetting heads, the software allows an operator to program independent and individual spot patterns in applications such as biosensors.

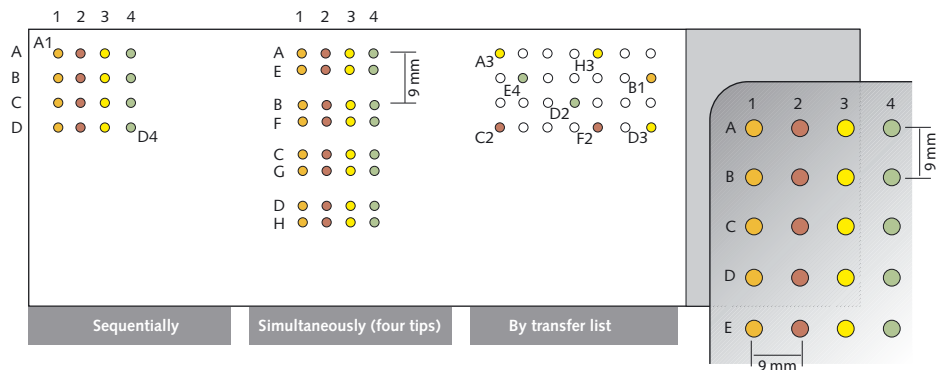


One „cockpit“ for all airplanes:
All NPCx- versions come with the same user interface and functionalities. Pipetting scripts can easily be transferred between different device platforms.

Source plate and dispense target positions can be arranged quickly and simply in the system's unique work plate editor.

Individual Application Programming versus Standard Scripts

NPC8/16 includes an application development tool similar to a high-level computer language (NPL = Nano-Plotter Language). NPL scripts offer control and feedback from current work plate settings as well as through user interface input screens. The NPCx software functions allow accessing all hardware components, including image processing system of Nano-Plotter™ 2.



NPL-Scripts

No programming effort is required for standard applications. The NPC software comes with various ready-to-use NPL-scripts for frequent pipetting procedures. GeSiM's experienced programmers will support NanoPlotter™ customers in creating NPL-scripts for any special

applications. The standard NPL scripts allow various pipette head configurations and individually check the function of each tip after sample aspiration.

Sequential pipetting:

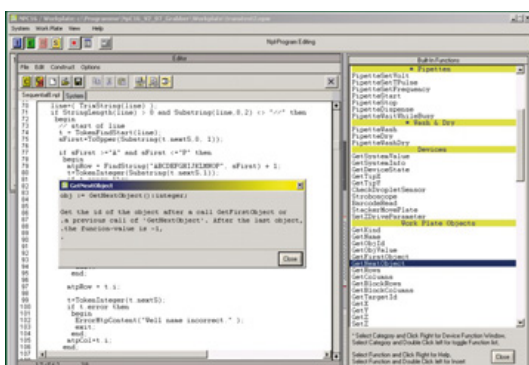
For straightforward sample tracking, a defined area of a source plate can be transferred to dispense targets, exactly copying the layout of the source plate. The user may also define replica spots for each sample.

Simultaneous pipetting:

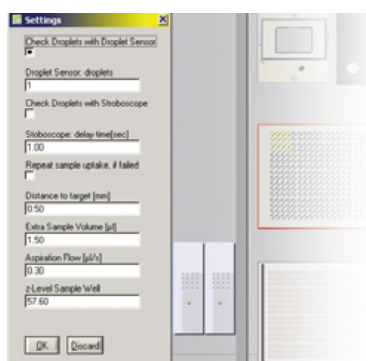
All tips dispense simultaneously and arrange spots at a distance of 4.5 mm or 9 mm, respectively. Replicas and sample spots of later cycles can be positioned in between at user-defined distances.

The transfer list:

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



Compiler for NPL scripts

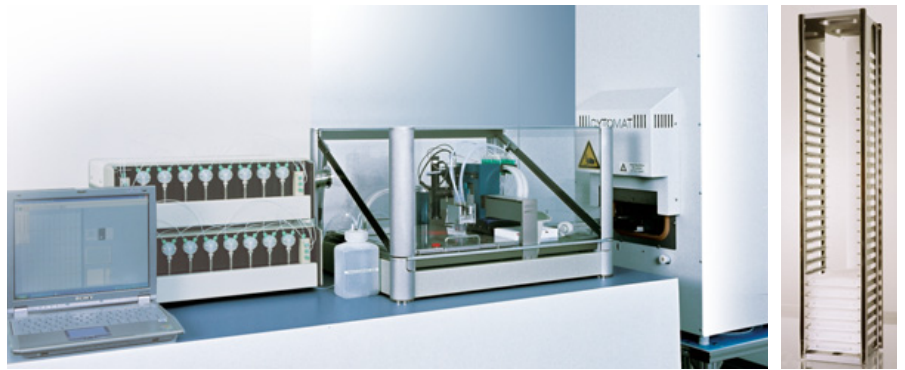


Input screen programmed in NPL

System Components and Accessories

Automatic Plate Exchange*

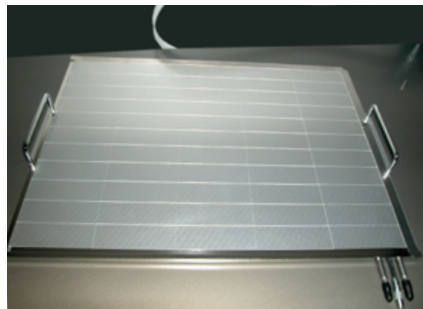
Plate handler with temperature and humidity control for up to 56 micro well plates, including rail connection to the Nano-Plotter™.



Cooling and Humidifying



Micro plate holder with refrigeration

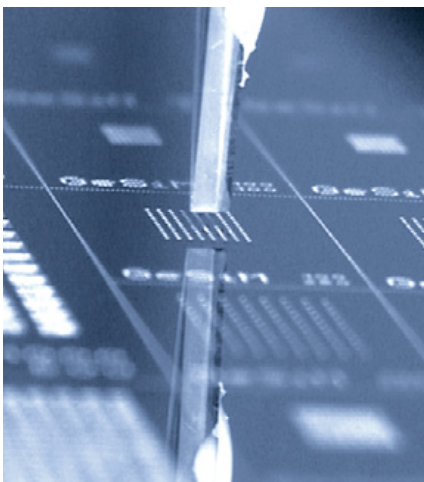


Exchangeable slide tray, suitable for refrigeration and designed to allow fixation of dispense targets*

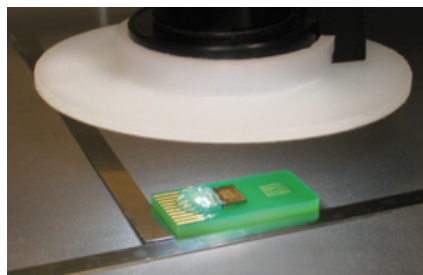


Ultrasonic humidifier system, fully adjustable humidification of up to 80 % relative humidity.

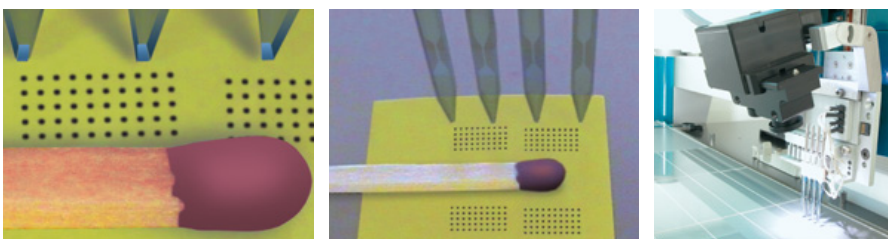
Searching and Recognizing



An integrated image processing system locates smallest objects and automatically positions pipette heads.



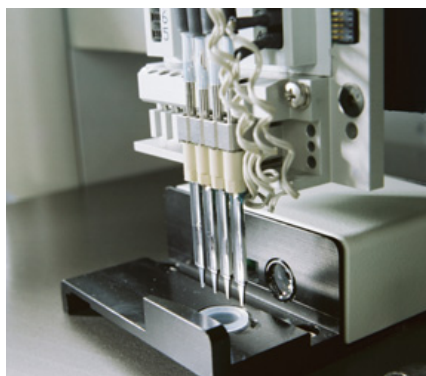
Video microscope, including light*



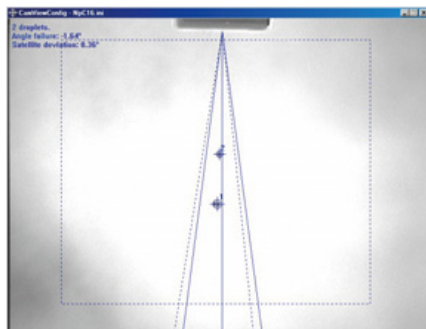
Observation camera, featuring two different magnification levels for manual teaching of XYZ positions.

Applications

Functionality Test



A stroboscope allows the operator to visualize and manually optimize dispense parameters to fit a certain sample consistency.



An image processing module of the NPC software allows automatic testing of the functionality of each piezoelectric pipette tip.

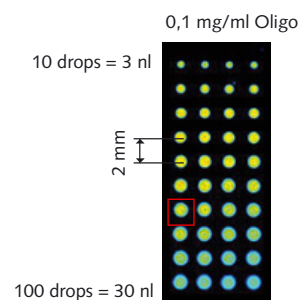
Microliter Pipetting



Adapter for standard disposable plastic tips: The Nano-Plotter's™ syringe modules can alternatively be set to dispensing following to the "displacement" principle.

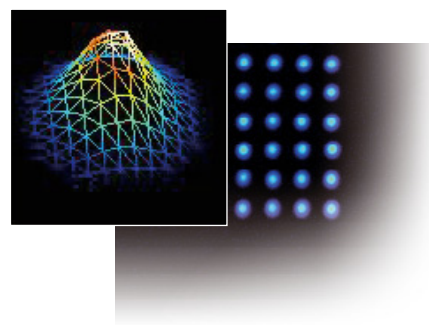
DNA and Protein Arrays**

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

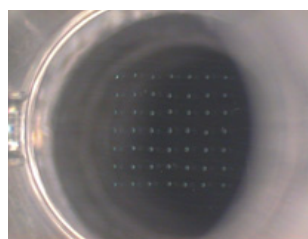


Non-contact arraying technology allows for highly consistent spots showing little or no "donut" effect.

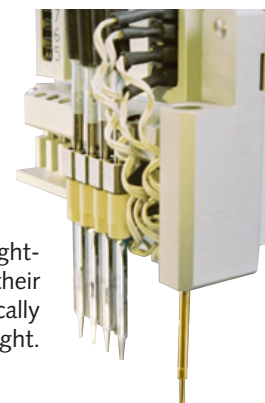
The minimum spotting distance depends on the surface structures. Hydrophobic substrates allow grid sizes down to 100 microns. Piezoelectric GeSiM tips are perfect to process all of the most common buffer solutions such as 3x SSC, PBS, Tris, but also glycerol up to a concentration of 40 %.



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.



The Nano-Plotter™ Z-height-sensor identifies their Z-position and automatically adjust spotting height.

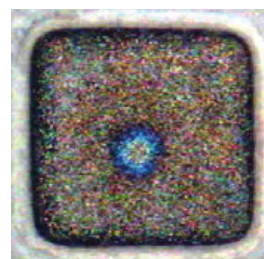


View through a microscope of a membrane with 2.5 nl spots in a 0.4 mm grid.



At a volume range of 0.1 to 50 nl, the Nano-Plotter™ is an excellent platform to tether probes onto membranes.

Microstructured substrates are well suited to center spots. Combining piezoelectric and passive dispensing technology, nano and microliter volumes can be spotted in applications such as the preparation of MALDI targets, or cryoconservation of cells.



** We are not licensed under any patents owned by Oxford Gene Technology Limited (OGT) or related companies and cannot pass any such license to our customers. A license under OGT's patents may be necessary to manufacture or use oligonucleotide arrays. GeSiM mbH

Applications

Loading of Samples into Microfluidic Systems

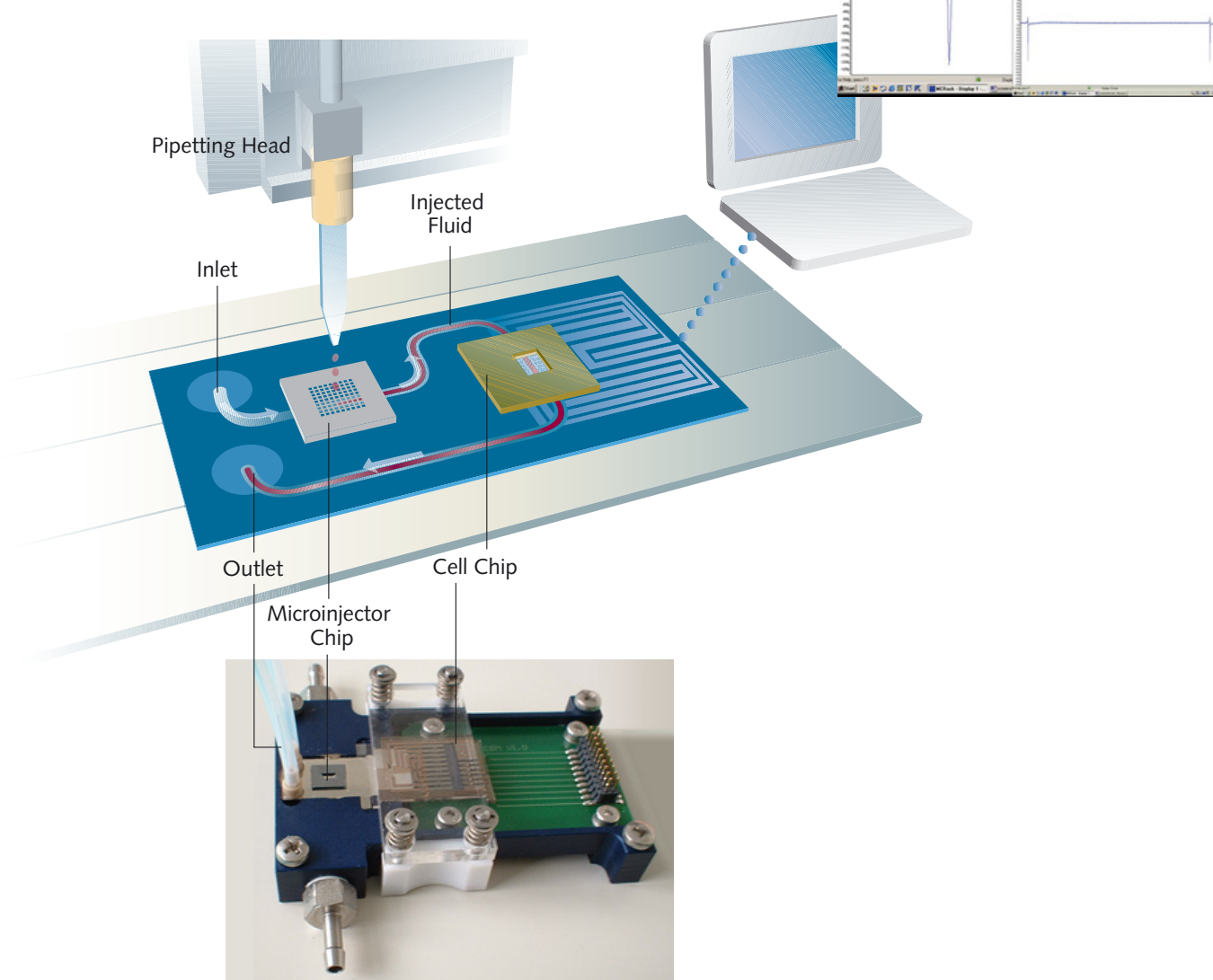
Dispensing sub-microliter volumes bridges the gap between conventional substance libraries (96 and 384 well format) and microfluidic flowthrough cells (Lab-on-a-Chip).

Microfluidic system for vitality measurements on cardiovascular and neurological cells

A microinjector chip developed by GeSiM, interacting with the Nano-Plotter™, allows the injection of nano-liter volumes into the flowthrough system. Cells immobilized inside the cell chip can be subjected to different drug components successively. Cell chips can be designed to feature microelectrodes or fluorescent signal detectors.

Electro-physiological activity of cardiovascular cells

A joint project of GeSiM mbH and MPI for Polymer Physics in Mainz, Germany



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Subject to changes