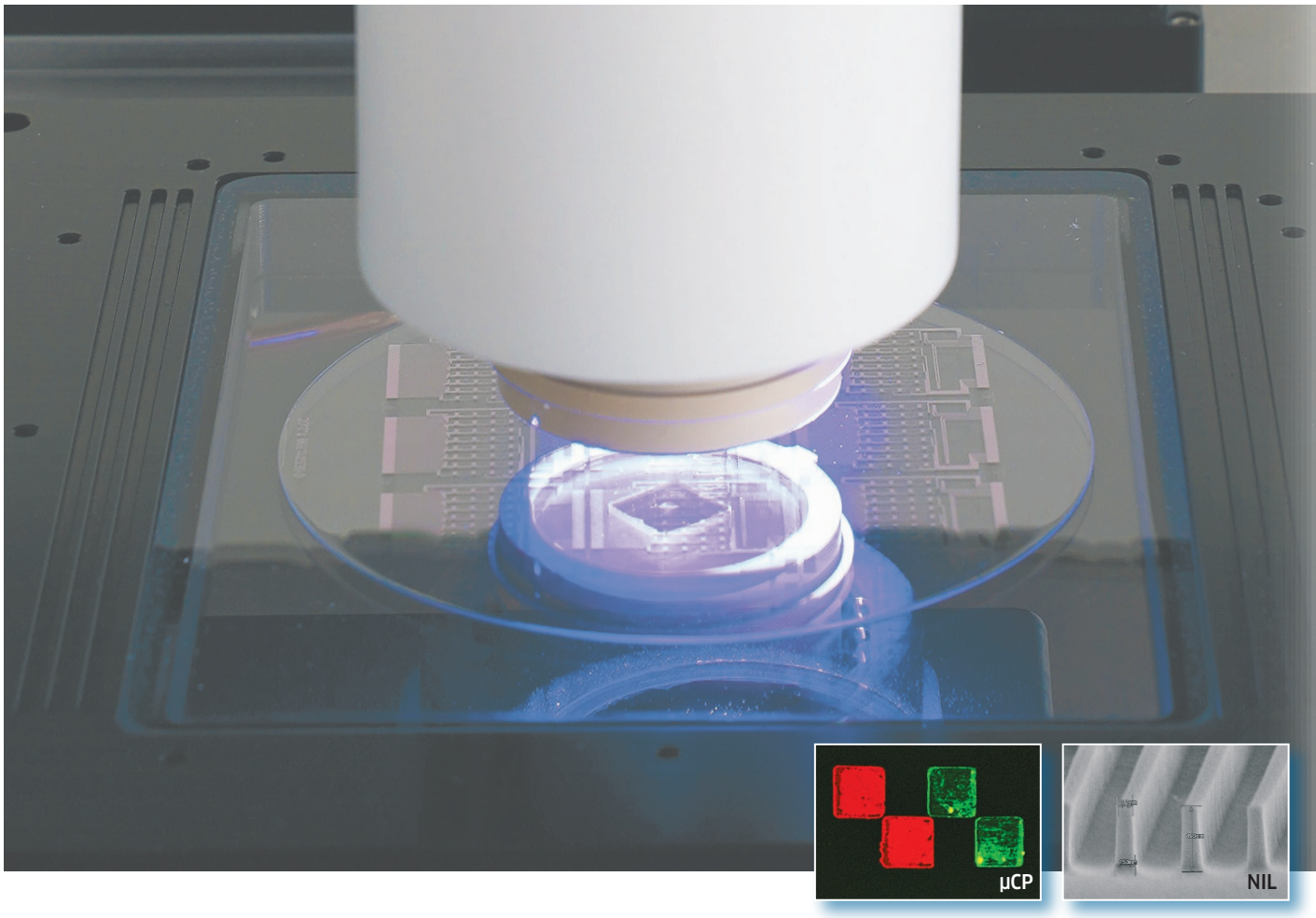
GESIM

µContact Printers

Instruments for Microcontact Printing and NIL



Create 2D and 3D Structures on the Micro- and Nanoscale

MICROCONTACT PRINTING

µCP Platforms

µCP4.1 with all items including fluidic/pneumatic control box and external UV lamp (OmniCure)

Two-level µCP6.1 with fast linear XY-motors. The lower Y-axis contains a UV collimator for precise and homogeneous irradiation especially for UV-NIL (see back page), the upper one the stamping unit. The flexible design allows easy reconfiguration.

The making of micro- and nanostructures in 2D…

Few affordable techniques exist to produce micro-patterns on a surface. Microarray spotting (e.g. with the GeSiM Nano-Plotter) generates resolutions around 100 µm. **Microcontact printing (µCP)**, on the other hand, can work on the nanoscale: a stamp of an elastomeric polymer like PDMS (silicone), cast on a micro- or nanostructured master, transfers molecules to an even surface. Chemicals, self-assembling monolayers (SAMs), biomolecules, nanoparticles, beads and cells can be printed with unlimited complexity, which is why µCP is getting increasingly popular in the life sciences, e.g. to study the influence of matrix proteins or growth factors on growth, differentiation and movement of cells.

…and 3D

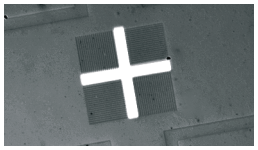
Nanoimprint lithography (NIL) has become a hot topic in microelectronics and cell biology. Here the 3D stamp structure is replicated in a polymer at elevated temperature and fixed by cooling or UV cross-linking.

Both µCP *and* NIL can be performed on the automatic GeSiM µContactPrinters or the semi-automatic µCP Core, making both methods completely reproducible. The printed structures can be tiled together to a larger one via step & repeat, especially when doing UV-NIL with a silicon mask in the stamp to exactly define the area that is cured ('double-side patterning'). For higher throughput and more exactly defined UV curing using a collimator on the lower level, the µCP6.1 exists. The systems speak G-code and their repeating accuracy in X/Y is better than 5 µm.

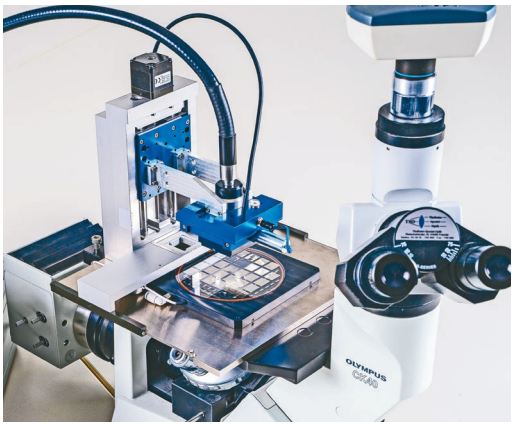
Stamps

Shipment includes a casting station that lets you manufacture your own stamps at reasonable costs. Customized, teflonised silicon masters with structure sizes as small as 100 nm can be ordered from GeSiM. Stamps are usually made of PDMS, except for NIL structures < 500 nm with high aspect ratio that require stiffer materials such as PFPE.

Stamps are picked up from a rack, allowing to combine different stamps during a run, e.g. when inked with different proteins. The accurate pneumatic actuation of the stamp (for NIL: high overpressure while stamp is down and de-tooling using vacuum pulses while lifting up; GeSiM specialty!) is fundamental for reproducible prints across the entire area.



An integrated microscope and the rotating print head help to accurately align stamp and substrate (picture), either manually or via image processing.



µCP Core, here with large stamp and UV optical fibre, on an inverted microscope (control box, temperature control, UV lamp and tubes for compressed air/vacuum not shown)

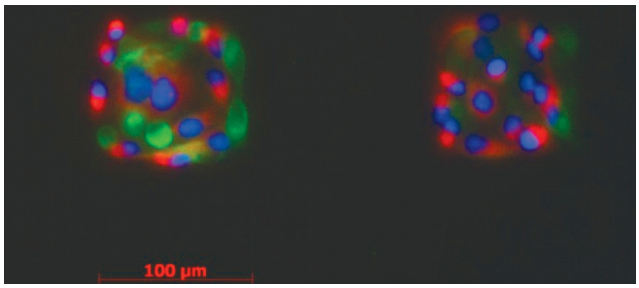
Platforms

All GeSiM µContact Printers feature a proprietary stamping technology based on an accurate Z-drive and pneumatic actuation during printing. It is precise and reproducible and does not need expensive granite beds and vibration damping tables.

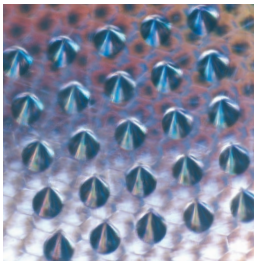
- **µCP4.x:** The smallest platform with XYZ stage, with camera, stamp holder and UV lens head on a single level. Max. stamp size 20 mm × 20 mm.
- **µCP6.x:** A µCP with linear motors. A UV source with collimator and photo mask on the lower level irradiates the transparent substrate on the upper level. The alignment of the exposition frame with the stamping area allows 'chessboard'-like multiple imprints on one target (up to 6" = 152 mm large) with zero spacing in between.
- **µCP6.x/E:** Like µCP6.x, with twice the work area
- **µCP Core:** Semi-automatic, budget µCP device consisting of µCP Z-drive and adjustable substrate holder. It provides the same stamping technology as the other instruments, but is placed on an inverted microscope (not included).

Patterns for cell growth

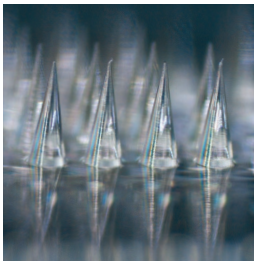
One can modulate cell growth and hence differentiation by µ-contact printing of patches of extracellular matrix proteins. Here, 100 µm large squares of fibronectin were microcontact-printed with a PDMS stamp onto a cell-repellent, plasma-polymerized polyethylene glycol (PEG), and human umbilical cord blood neural stem cells (HUCB-NSCs) were grown on these squares to study the influence of cell motility on differentiation, as cells adhere only to the fibronectin squares. After culturing, cells were fixed and immunostained. Courtesy of EC Joint Research Centre, Nanobiosciences Unit, Ispra, Italy (Dora Mehn)



HUCB-NSC cells on 100 µm fibronectin squares, fluorescence image. Green: beta-tubulin-II neuronal marker; red: GFAP; blue: cell nuclei.



Master structure for stamp casting, made by 2-photon lithography using a stiff material.



Micro-needle array from Norland NOA63 optical adhesive, printed using a PDMS stamp.

Micro-needle arrays

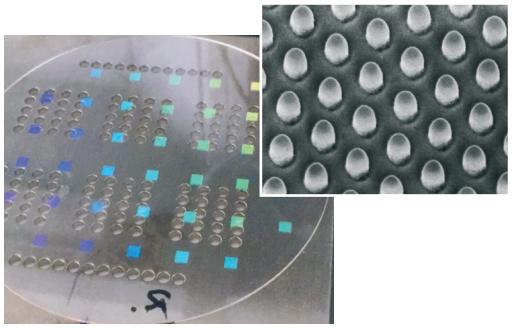
Micro-needle arrays are gaining interest for non-invasive, convenient transdermal drug delivery. Micro-needles consist of bioresorbable polymers blended with deliverables or of solid material (with reservoirs or coated with active ingredients). NIL allows better spatial resolution than 3D-SLA, at low operational costs and sizes ≤ 1 mm, thus allowing quick processes using a wide range of materials. GeSiM's NIL technology enables micro-needles with grooves, indentations and channels. Subsequent drug deposition onto them can be done with GeSiM piezo pipettes, either directly in the µCP or on a GeSiM Nano-Plotter.

High aspect ratios (here: height 1.2 mm, radius 0.2 mm) are achieved by evacuating the space around the PDMS stamp while it is in contact with the surface.

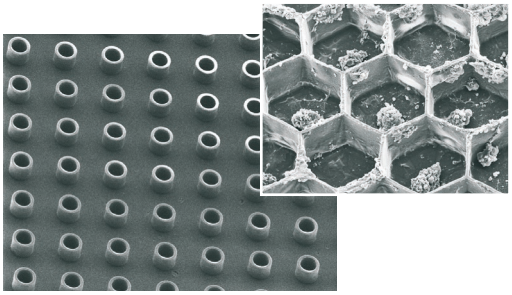
Nanoplasmonic sensors

Surface plasmon resonance (SPR) sensors enable the label-free real-time quantification of biomolecules. Classical SPR utilizes a gold film on a prism. To scale this down, a nanostructured gold layer was used to excite plasmons without bulky optics. The resulting sensor was used to measure pollutants in wastewater. Central to this method was the reproducible fabrication of nanostructures by UV-NIL using a GeSiM µCP 4.1 and a UV-cross-linkable photo-resist, followed by gold coating. *Ref.: Steinke, N. et al., Sens. Act. B 254, 2018, 749–754*

Similarly, ethanol formation during fermentation can be measured with an ethanol-sensitive hydrogel with nanoplasmonic surface.
Ref.: Kroh, C. et al., J. Sens. Sens. Syst. 7, 2018, 51–55



Nano-patterns repeatedly printed on a glass wafer. Small picture: REM image of the nano-pillars; the pitch is 450 nm.



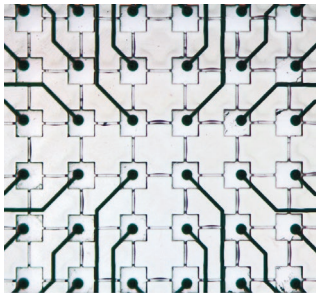
Picowells, 25 µm diameter (large picture), and spheroids in 250 µm wide honeycomb wells, both formed via NIL

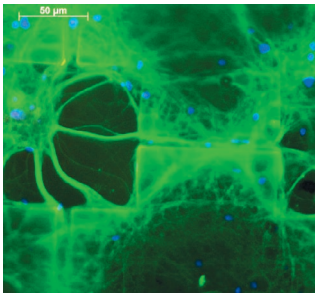
Picolitre wells for cell biology

In cooperation with M. Deutsch's lab from Bar-Ilan University and others, pico-well arrays were printed by UV-NIL in UV-curable adhesives such as NOA81 to measuring the activity of individual cells e.g. via multi-parametric enzymatic assays. One application was toxicology testing of nanoparticles that the GeSiM Nano-Plotter had spotted into the picowells, another the formation and study of organoids from cancer cells in honeycomb structures, with and without electrodes. Courtesy of Motti Deutsch, Bar-Ilan University.
Ref. (selection): Afrimson, E. et al., BMC Cell Biology 11, 2010, 83
Markovitz-Bishitz, Y. et al., Biomaterials 31, 2010, 8436–8444
Zurgil, N. et al., Lab Chip 14, 2014, 2226–2239

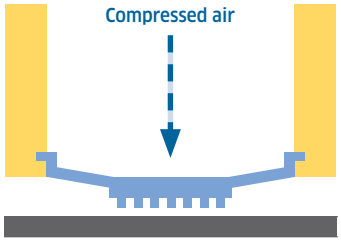
In vitro neurotoxicity assay development

To direct neuronal growth to certain sites, 100 µm wells above microelectrodes and channels between the wells were formed by UV-NIL. The stamp was aligned with the electrodes and a PEG-based hydrogel polymerized by 60 s UV exposition (left picture). The right picture shows rat neurons grown in such wells/channels (green: β-tubulin III neuronal marker, white bar 50 µm). Courtesy of EC Joint Research Centre, Nanobiosciences Unit, Ispra, Italy (Dora Mehn, Jakub Nowak).



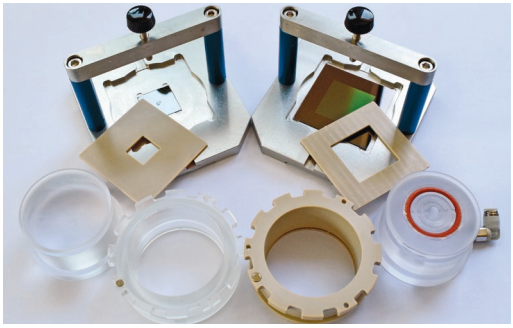


The revolutionary stamping technology of the GeSiM µContactPrinters



GeSiM µCP stamping principle: the stamp membrane is bulged out while contacting the surface, resulting in defined pressure and even transfer. Demoulding after NIL utilizes controlled pulses of vacuum while moving up; this ensures that structures with high aspect ratios don't get destroyed.

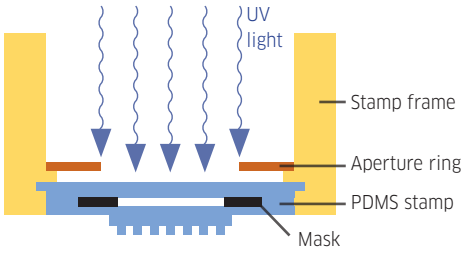
Stamp casting



Casting stations for small and large stamps. Max. stamp size is 20×20 (mm×mm).

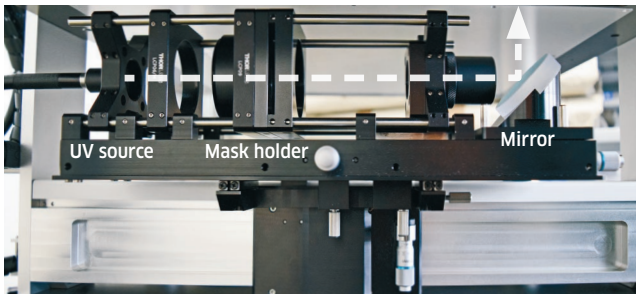
'Double side patterning' / 'chessboard-like' UV-NIL

The cured region in UV-NIL is normally larger than the stamp region. Placing a silicon mask in the stamp, however, restricts the cross-linked (cured) area to the mask area; this allows to exactly place NIL structures side by side in a chequerboard-like manner:



Double-side patterning with the µCP4.x. The silicon mask limits the size of the cross-linked area under the stamp.

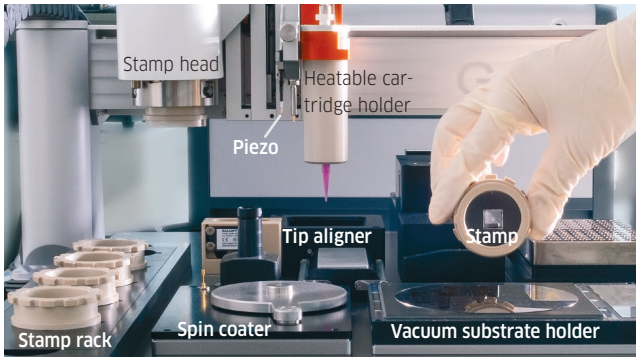
In the µCP6.x, a **collimator** on the lower level produces parallel UV light beams that shine through a photo mask before they reach the transparent substrate on the upper level. Not only is the cross-linked area more exactly defined, you can also insert a *patterned* mask to use two structuring methods at once, namely photolithography and stamping. This can generate quite complex designs, e.g. a nanostructure in a microfluidic channel, in a single step.



UV collimator (cover removed) on the lower Y-axis of a µCP6.1. It allows to mount a photo mask and very precise adjustment via micrometre screws.

Tools on the work deck and on the multi-Z tool head

The stamping unit is assisted by other tools. A typical configuration of the µCP4.x is shown here:



Work deck tools: stamp rack, spin coater (e.g. for semi-dry inking, with stamp height sensor), heatable/coolable (up to 100 °C) holder for 4-inch substrates. In the rear, hidden: wash/dry stations, tip aligner, stroboscope. Tools on the print head: stamping unit, piezo pipette and substrate height sensor (on same Z-axis), heatable cartridge holder for pastes/glues, especially for NIL.

Select from a plethora of accessories, also from other GeSiM Robotics systems, i.e. BioScaffolder (3D bioprinter) or the BSyS (pipetting machine for chemical synthesis), so please see their brochures for details:

- Integrated dust-protecting lid, making you independent of biological safety cabinets
- Work plate: coolable/heatable microtitre plate holders, 'double-side patterning' stamps (see left, with casting station), holders for slides, glass vials and microcentrifuge tubes
- Print head: various dispensers, e.g. cartridge cooler (5…100 °C), piezo-driven powder dispensers for µg quantities, pipettors with disposable plastic tips, pH titration tip, plasma pen etc.

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