GESIM

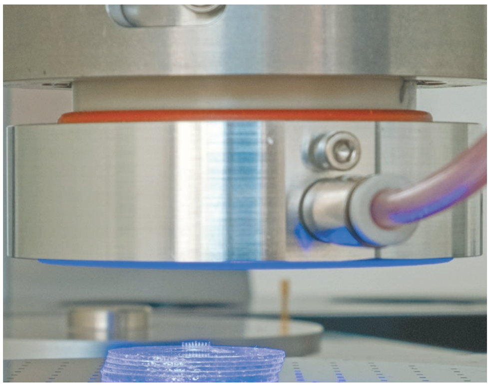
µContactPrinters Application Note

Manufacturing of Micro-Needle Arrays by Nanoimprinting

Why micro-needle arrays?

Micro-needles (MN) in the range of 1 mm or less of various types (solid, coated, dissolving, hollow) are gaining increasing interest for the subcutaneous delivery of drugs or vaccines, as they painlessly breach the outer skin layer. By allowing self-administration, this makes them an attractive alternative to injection.

Different approaches have been used to deliver drugs by micro-needle arrays: bioresorbable polymers blended with deliverables, non-soluble needles with reservoirs for or just coated with active ingredients.



Vacuum stamp of a µContactPrinter µCP4.x after NIL and UV exposition. Please read the brochure on GeSiM µContactPrinters for general information.

Many ways exist to produce MN arrays. For research, 3D SLA (stereolithography) printers are available at affordable costs, but they work only with special UV-curable resins at limited spatial resolution. Micromachining technologies allow smaller feature sizes, but at high costs due to the need of well-equipped cleanrooms. Injection moulding requires expensive machinery and pays off for mass production only.

Nanoimprint lithography (NIL)

The GeSiM solution featuring NIL combines the benefits of other methods:

- Affordable instrumentation
- Low operational costs
- Small design features as low as 1 µm that aid drug delivery,
- Quick process (ca. 5 min per MN array)
- Wider range of printable materials

Technically, an elastomeric stamp is used along with a UV-curable or thermomelting material. Well-proven piezoelectric nanolitre pipetting can be used to tether biomolecules to the needle surfaces after the NIL process is finished.

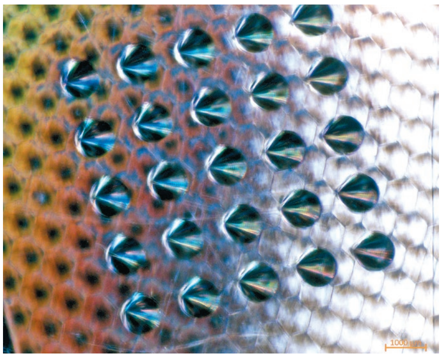
Micro-needle arrays – An application for the µCP4.x

The µCP4.x can automatically handle up to five soft polymer (usually PDMS) stamps, i.e. up to five MN array designs can be printed at once without rearranging the instrument during a print run.

General procedure:

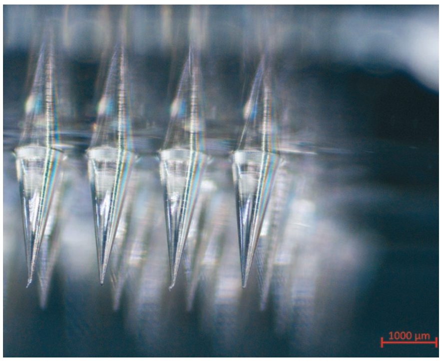
1. Provide your MN array design(s) to GeSiM.
   → GeSiM delivers stamp masters for each design. (Several masters fit on one wafer.)
2. Mould your stamps with the included casting station, which results in elastomeric stamps in their stamp frames.
3. Mount the stamps on the µCP4.x in the stamp rack of the instrument and fill dispenser(s) with the proper polymer for NIL.

Consumed stamps are easy to renew.



Micro-needle master, manufactured by 2-photon-lithography on top of a silicon substrate. This is a service provided for our µCP customers.

PDMS stamp, bottom view. This disposable print tool is made at your lab bench.

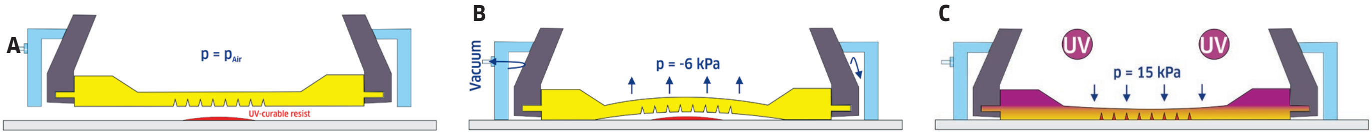


Printed MN array made from NOA63 photoresist (upside down) ; height 1.2 mm, bottom diameter 0.4 mm

µContact Printers
Micro-Needle Arrays

2022

Automatic stamping of micro-needle arrays with the µCP4.x



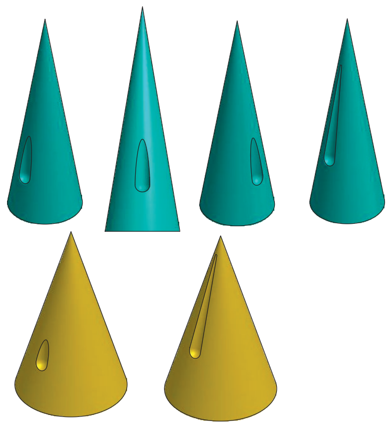
UV-NIL stamping procedure for MN arrays. A, the dispensed UV-curable resist is being heated. B, the print head contacts the surface, but the stamp is not yet contacting the substrate. The volume outside the stamp is evacuated. C, the stamp is pressed onto the substrate by applying overpressure. Conditions must be optimised experimentally.

1. A defined volume of NOA63 resin (Norland Products, Inc.) is dispensed onto the heated substrate by a heatable cartridge dispenser.
2. An adapter with sealing O-ring (an extra feature) is attached to the stamp print head such that a vacuum chamber is formed at the outside. This allows to remove the air from the interface between stamp and surface.
3. The stamp is moved all the way down towards the resin (**A**).
4. At the same time, a controlled vacuum ('negative pressure' compared to atmospheric pressure) is applied to the stamp head, which retracts the PDMS membrane so that it does not contact the resin during the following step.
5. Now vacuum is applied to the outside chamber (**B**). This avoids that air bubbles are trapped inside the mould and so facilitates the flow of resin into the fine features of the mould.
6. NIL proceeds by applying overpressure to the stamp, which bulges out towards the substrate, with a contact time of about five minutes.
7. NOA63 resist is cured by UV exposition for about 20 seconds (**C**).
8. Both outside vacuum and (inside) stamp overpressure are switched off.
9. Gentle demoulding is achieved by slowly lifting the stamp while a pulsating vacuum is applied to the stamp membrane..

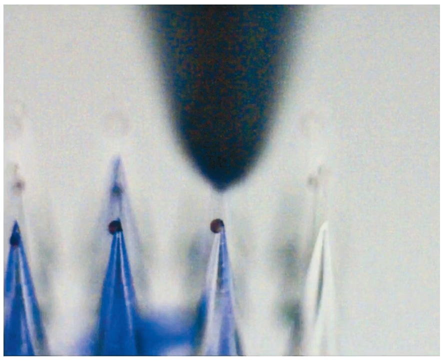
Specialties

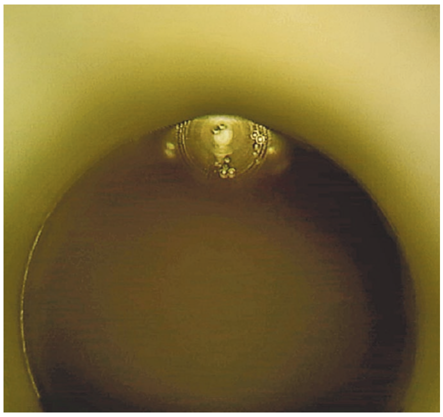
The outstanding spatial resolution of GeSiM's NIL technology enables the fabrication of micro-needle arrays with special design features such as grooves, indentations and channels for subsequent drug deposition.

GeSiM's proprietary non-contact piezoelectric pipettes can transfer liquid amounts as small as 0.05 nl, in a controlled manner. For this purpose the µCP4.x is available with one piezoelectric tip on board. Alternatively, e.g. to dispose larger sample sets onto MN arrays, GeSiM offers its microarray spotter, **Nano-Plotter**, with automatic target recognition (see separate app note).



Needles with grooves (volumes about 1 nl). They have either a height of 1.2 mm and a base diameter of 0.4 mm (top) or a height of 1 mm and a base diameter of 0.6 mm (bottom).





Needle viewed from the top. In the lateral groove, tiny (8 µm) beads were entrapped after liquid deposition by a piezo pipette. Top picture: GeSiM piezo tip above a micro-needle array during printing.

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