GESIM

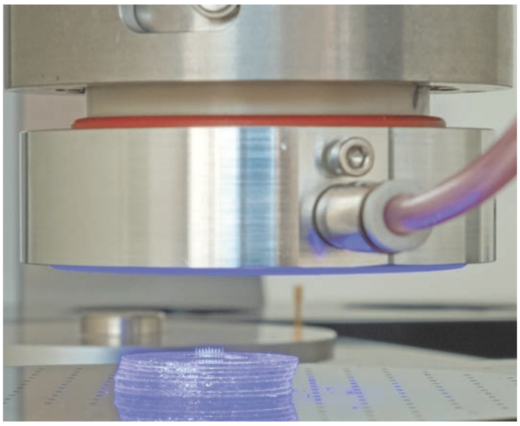
µContactPrinters Application Note

Manufacturing of Micro-Needle Arrays by Nanoimprinting

Why use micro-needle arrays (MNAs)?

Micro-needles in the range of ≤ 1 mm 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. This makes them an attractive alternative to injection and allows self-administration.

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



µContactPrinter µCP4.1 with vacuum stamp after NIL proces and UV exposition. Please read the brochure on GeSiM µContactPrinters for general information.

Many ways exist to produce MNAs from different materials. For research, 3D SLA printers are available at affordable costs, but they work only with special UV-curable resins at limited spatial resolution. MEMS 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 and low operational costs
- Special design features to improve drug delivery, down to 1 µm
- Quick process (approx. 5 min per MNA)
- Wider range of printable materials

Technically, a PDMS 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.

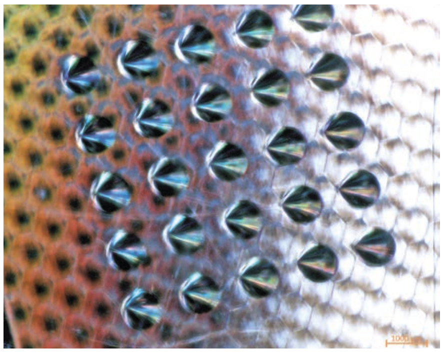
MNAs – An application for the µCP4.1

The µCP4.1 can automatically handle up to five soft polymer (usually PDMS) stamps, This means that up to five MNA designs can be printed at once without reorganizing the instrument during a print run.

General procedure:

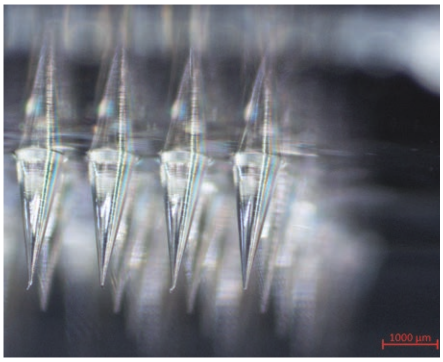
1. Provide your MNA design(s) to GeSiM.
   → GeSiM delivers stamp masters for each design. (Several masters fit on one wafer!)
2. Mould your stamps with the included casting station, which results in elastomeric stamps in their stamp frames.
3. Mount the stamps on the µCP4.1 in the stamp rack of the 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 master. This is a service provided for our µCP customers.

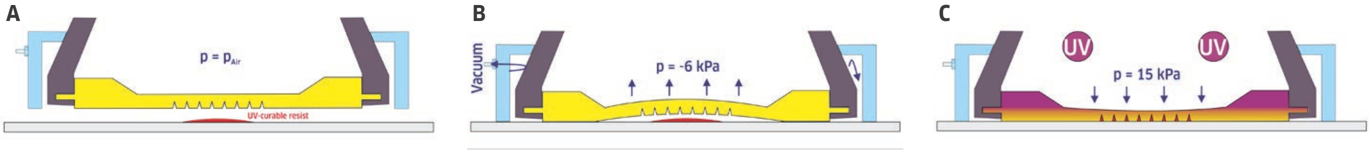
PDMS stamp, bottom view. This disposable print tool is made at your lab bench.



Printed MNA made from NOA63 photoresist; height 1.2 mm, bottom diameter 0.4 mm

µContact Printers
Micro-Needle Arrays

Automatic stamping of micro-needle arrays with the µCP4.1



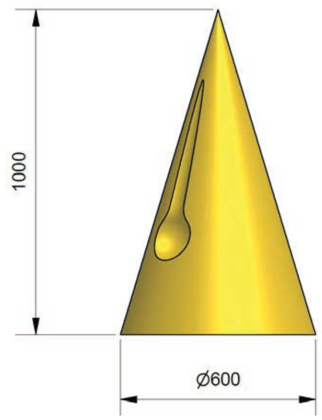
UV-NIL stamping procedure for micro-needle arrays. A, the UV-curable resist has been dispensed and is being heated. B, the print head contacts the surface, but the stamp does not yet contact the substrate. The volume outside the stamp is evacuated. C, the stamp is pressed onto the substrate by applying overpressure. The ideal conditions must be tested experimentally.

1. A defined volume of NOA63 resin (Norland Products, Inc.) is dispensed onto the heated substrate by a heatable cartridge dispenser.
2. The stamp print head is equipped with an adapter with sealing O-ring (an extra feature). 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..

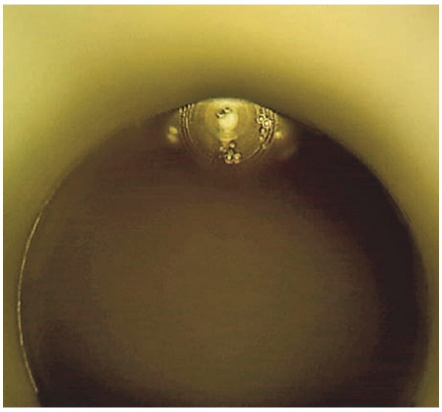
Specialties

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

The proprietary piezoelectric GeSiM pipettes can transfer liquid amounts around 0.1 nl in a controlled manner. The µCP4.1 is available with one piezoelectric tip on board. Alternatively, e.g. to dispose larger sample sets onto MNAs, GeSiM offers its microarray spotter, Nano-Plotter NP2.1, with automatic target recognition.



Needle design with spherical groove (diameter 80 µm), volume about one nanolitre. This needle has a height of 1 mm and a diameter of 300 µm.



Single needle viewed from the top. The lateral groove shows 8 µm large beads that were entrapped after fluid deposition by a piezoelectric pipette.

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