COMPACT AND SOFT PROBES FOR OPTICAL BRAIN STIMULATION

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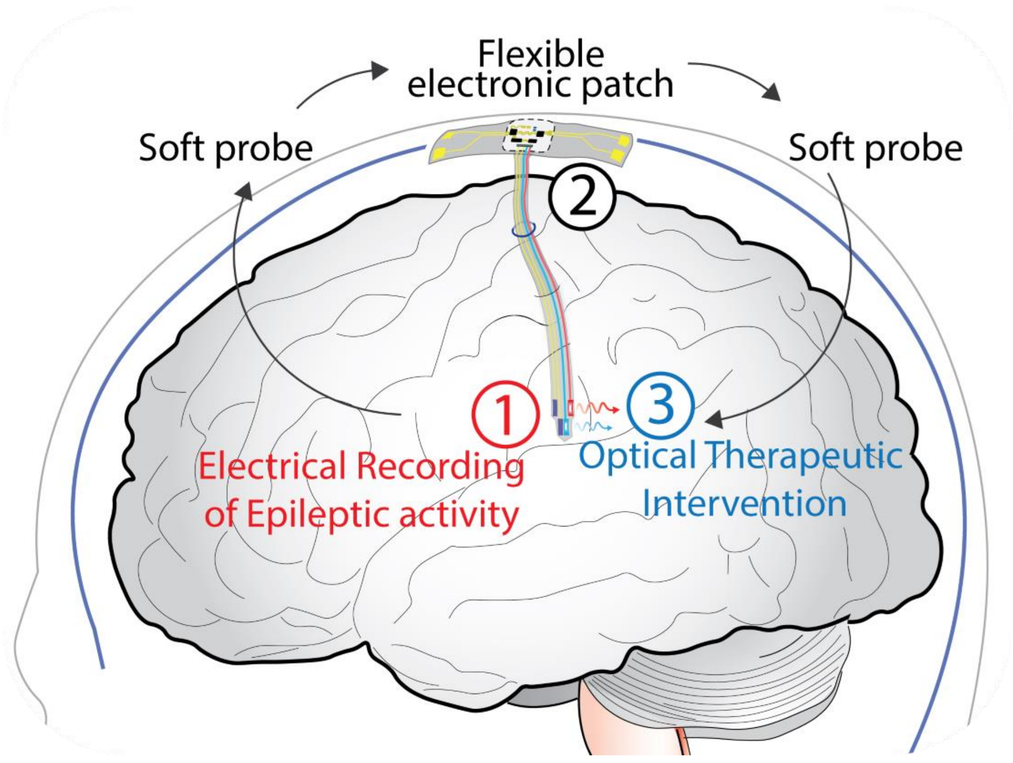
INTRODUCTION

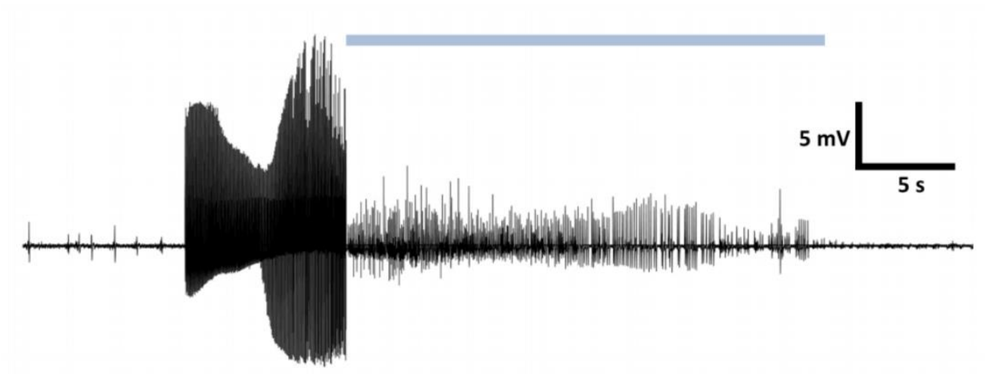
Optogenetics (OG) and optopharmacology (OP) are powerful preclinical approaches relying on the illumination of tissues:

- Study of neuron networks behavior (OG)
- Activation and inhibition of genetically modified light responsive cells (eg. Neural networks) (OG)
- Selective drug release (OP)

OG and OP principles can be employed in closed-loop therapies for epilepsy where:

1. Electrodes record the EEG
2. A microcontroller processes the EEG
3. The optical probes will activate/inhibit the involved neurons (OG) or uncage drugs (OP)





INHIBITION OF EPILEPTIFORM AFTERDISCHARGES IN RAT BY BLUE LIGHT ILLUMINATION. BLUE LINE REPRESENTS THE ILLUMINATION ON [1]

IMPLANTABILITY & BIOCOMPATIBILITY

Hydrogel (HG) biomaterials may be used as multifunctional coating:

- Soft and biocompatible coating
- Mechanical support during implantation

High stiffness is required to allow the probe penetration through tissues but foreign body reaction is limited by low stiffness probes. Some HG (e.g PAAm-Alg, Acrylamide-Alginate) have swollen stiffness (kPa range) much lower than dehydrated state stiffness (Mpa range).

- Transition Time ~10'
- Demonstrated in agarose phantom brain

CHALLENGES

Chronic implantations of optical probes need to meet a number of requirements to guarantee a successful operation of the device.

1.Foreign body reaction (FBR) minimization
   - Shank Dimensions (<100µm)
   - Low stiffness
2.Optical Requirements
   - Low optical losses (<0.5dB/cm)
   - Irradiance up to 200mW/mm^2
3.Surgical protocols compatibility
4.Limited heating of tissues during stimulation
5.Light source Integration

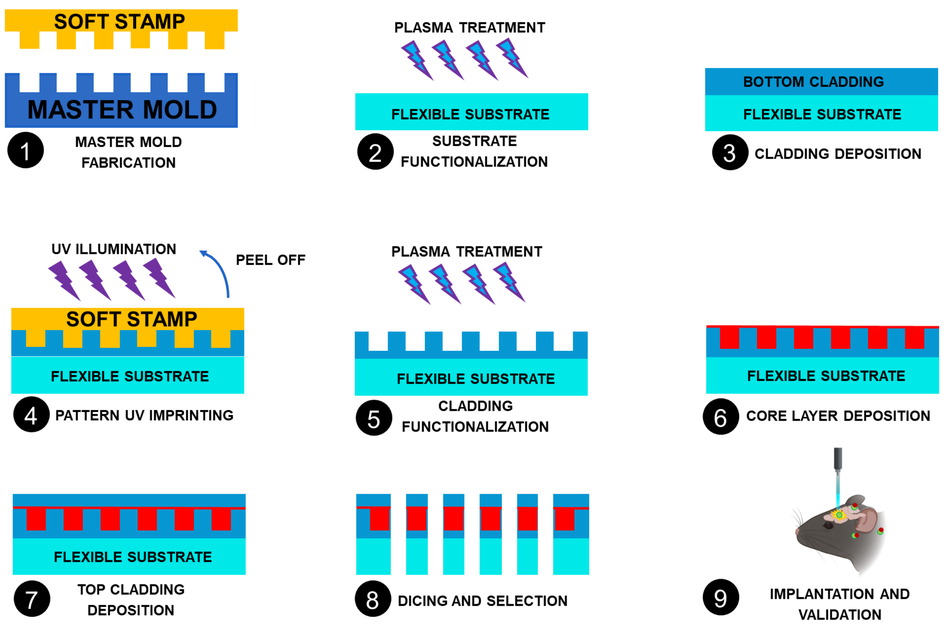
FABRICATION

Nano Imprinting Lithography **(NIL)**

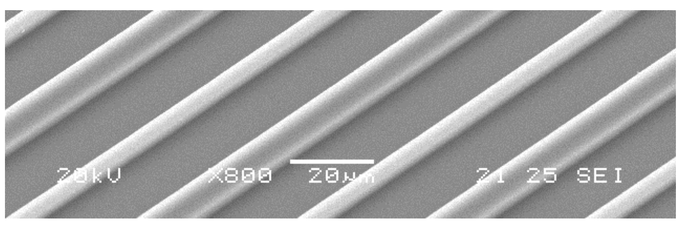
- Pattern replication via Molding
- Inexpensive
- Fast prototyping

Process overview:

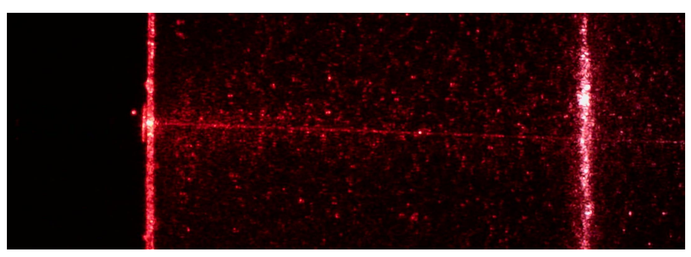
- Master Mold fabrication
- Imprint the pattern on Soft Stamp
  - Better control during imprinting
  - Lower probability to damage the master mold
- On working substrate (PET foil)
  - Deposition of the optical material
  - Pattering via soft stamp imprinting
  - UV polymerizarion of the optical material



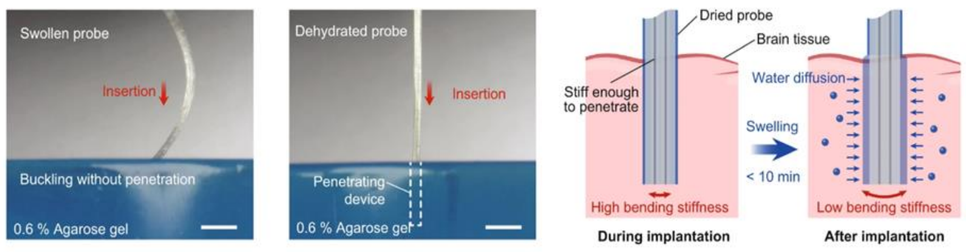
NANOIMPRINTING LITHOGRAPHY PROCESS FLOW



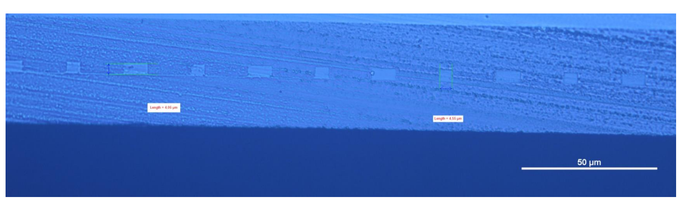
SEM MICROGRAPH OF SOFT STAMPS



FABRICATED WAVEGUIDES TRANSMITTING LIGHT



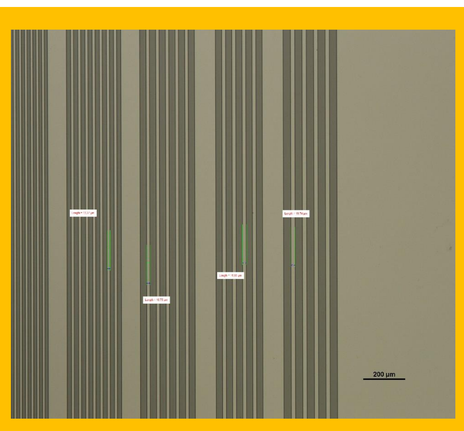
HGs BENDING STIFFNESS VARIATION [2]



CROSS SECTION OF THE NIL FABRICATED WAVEGUIDES

CONCLUSIONS

- NIL technique is capable to produce flexible waveguides with overall dimension (thickness and width) smaller than 100µm
- Optical measurements reported more than 60% of light is transmitted (for WGs wider than 5µm)
  - An efficient coupling will lead to lower losses
- Microscope images show low surface roughness of the side walls
  - Surface roughness is one main responsable for optical losses
- Biomaterial coating is currently under development



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Contact

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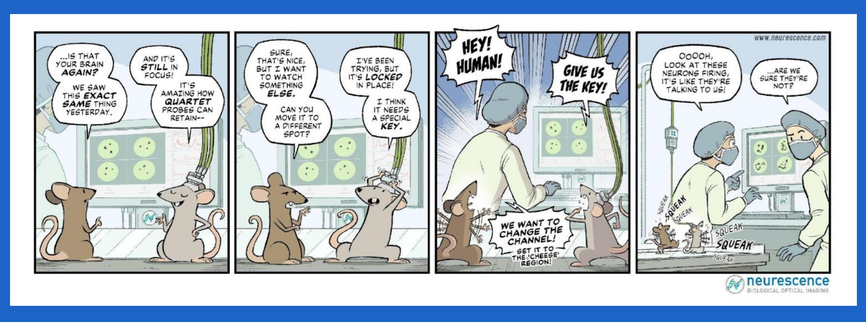

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References

[1]Acharya, AR et al. *CNS Neurosci Ther*. 2023; 29: 907-916. doi: 10.1111/cns.14029

[2] Park, S. *et al. Nat Commun* 12, 3435 (2021). https://doi.org/10.1038/s41467-021-23802-9