# Insertion and chronic performance of ultra-fine neural electrode arrays in vivo

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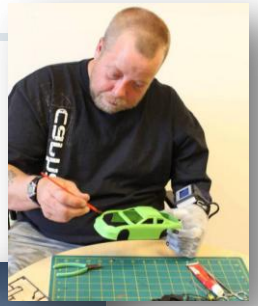
# Neurostimulation: respected family of therapies

- Deep brain stimulation (DBS)
  - Symptoms of Parkinson's disease
  - Tremors
  - Experimental: addiction, anorexia,…
- Cochlear implants
  - Nerve stimulation in the inner ear
  - For helping the profoundly deaf
    - i.e. no functioning middle or outer ear
- Pain relief

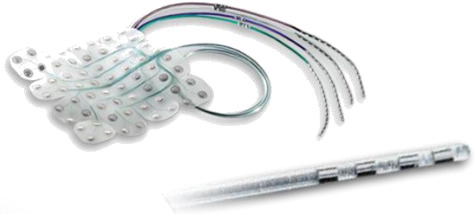
# Near future applications needing higher resolution:

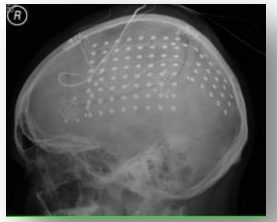
- Advanced prosthetics
- Electric medicine (‘electroceuticals’)
- Artificial eyes
- Communication with paralyzed
- Neurostimulation in pathologic brain cavity

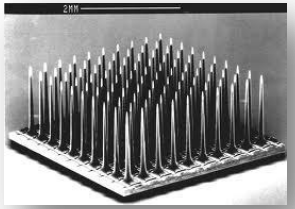


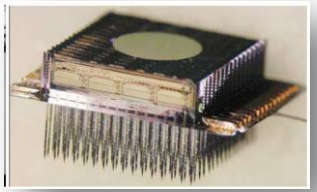

# Common high electrode count implant types

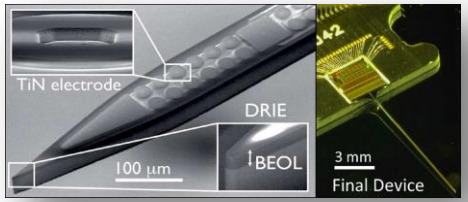
- Current clinical: silicone / PtIr
- Microwire arrays
- Silicon arrays
  - Utah style
  - Michigan style
  - Si + integrated electronics







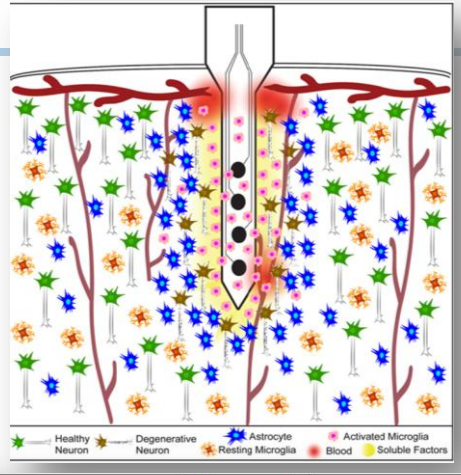



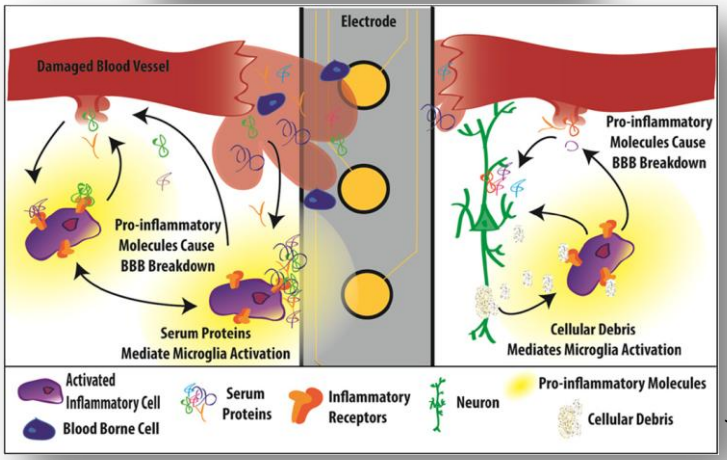


# Scar formation: issue for long-term high-res interface

Mechanisms:

- Damage by insertion / relative movement of implant
- Blood-derived proteins activate inflammatory cells and stimulate the release of pro-inflammatory and cytotoxic cytokines-> Blood-brain barrier (BBB) breakdown.
- Release of pro-inflammatory and cytotoxic soluble => neuronal apoptosis. Cellular debris => further stimulate microglia activation and BBB instability
- Chronic inflammation and astrocytic encapsulation (glial scar)

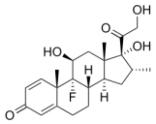


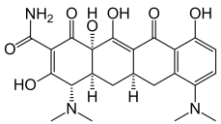




Jofi et at., JNE **12** (2015)

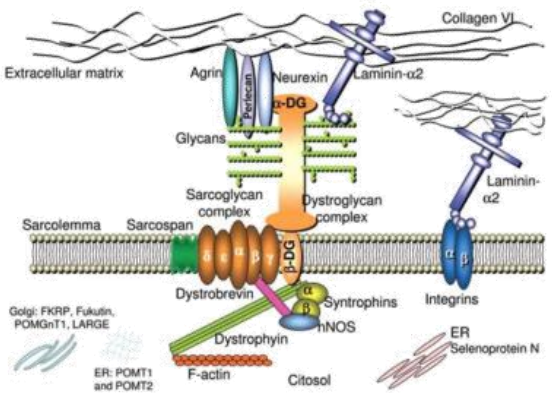
# Strategies to reduce scar tissue formation

- Anti-inflammatory drugs
  - Dexamethasone, Minocyclin,…
  - Optional: In situ drug release
  - Not a long-term strategy



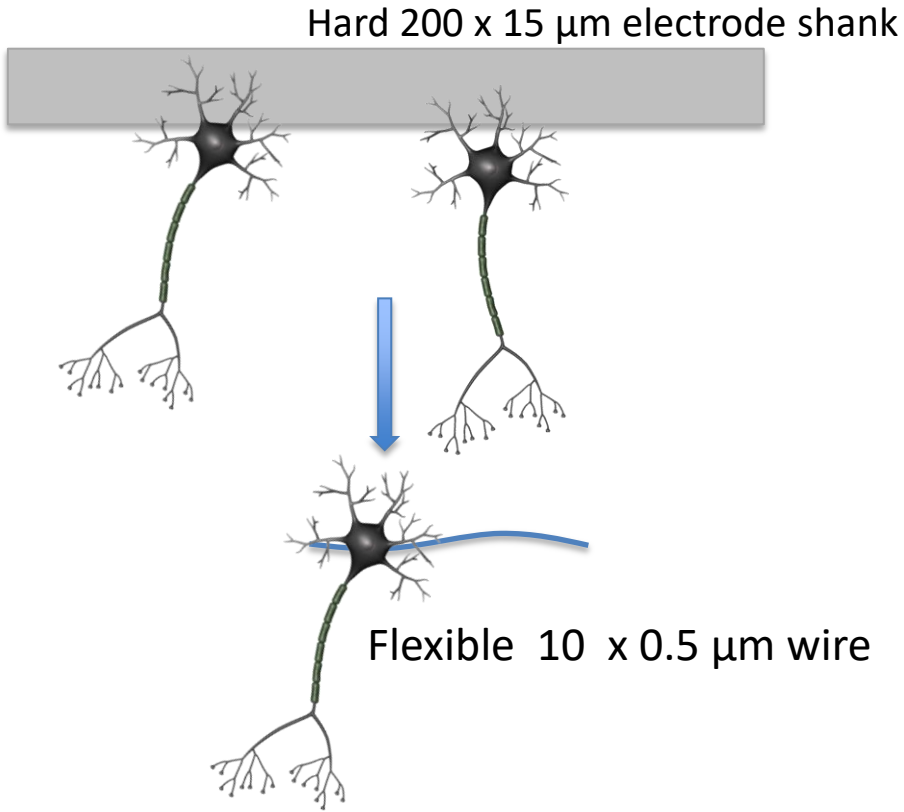


- Reducing protein adhesion
  - PLL-based coatings
- Bioactive coatings
  - Laminin, L1, IKVAV
  - Growth factor release
- Reducing mechanical damage
  - Avoiding firmly anchoring to skull
  - Reducing cross sections
  - Compliant materials
  - Resorbable materials

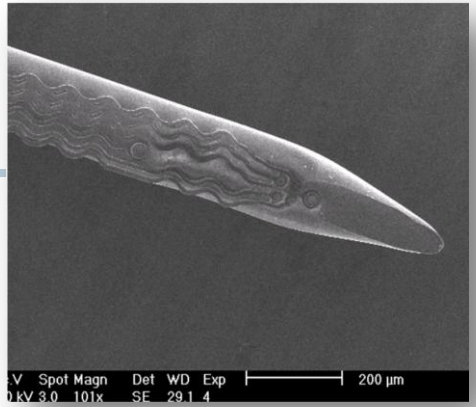


# Our approach: ultra-flexible electrode arrays

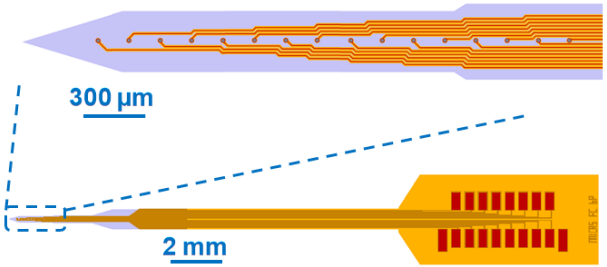
- 1 µm thick
- Need relatively stiff needle-like carrier to get into the brain
- Carrier dissolves, only bare minimum stays behind
- Total dissolution must take ≤ 4 weeks [Turner 1999]

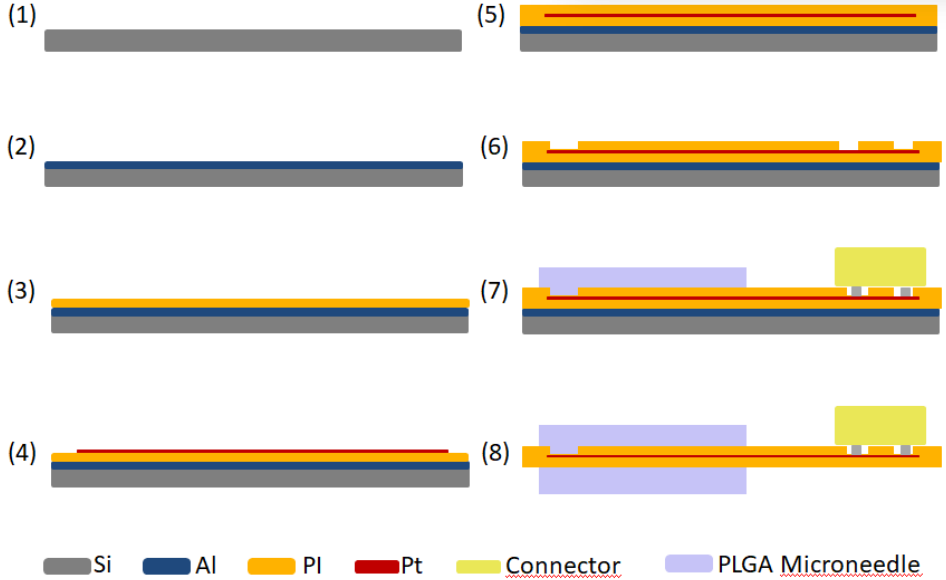


# Design & Fabrication

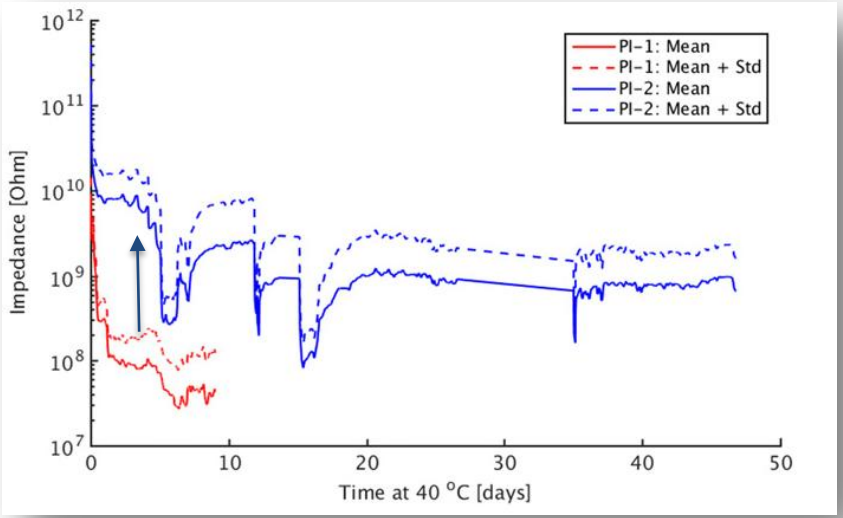



- Wafer-scale, lithography based
- Polyimide isolation
- Pt metallization
- Iridium oxide electrodes
- Dissolving PLGA microneedle as carrier

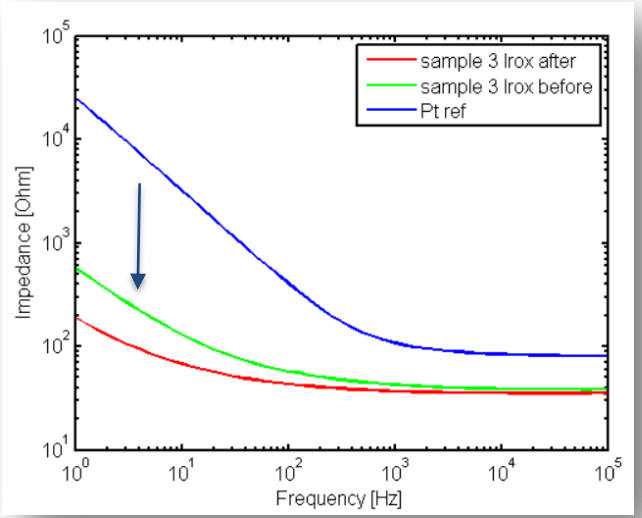


# Implemented process improvements

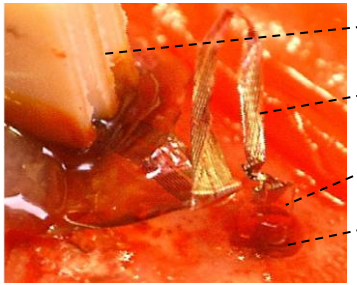


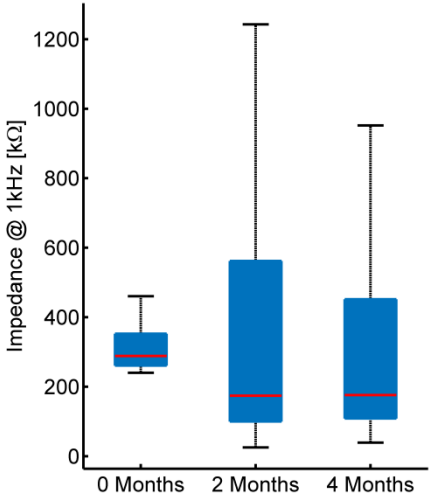

- Improved leak impedance of isolation

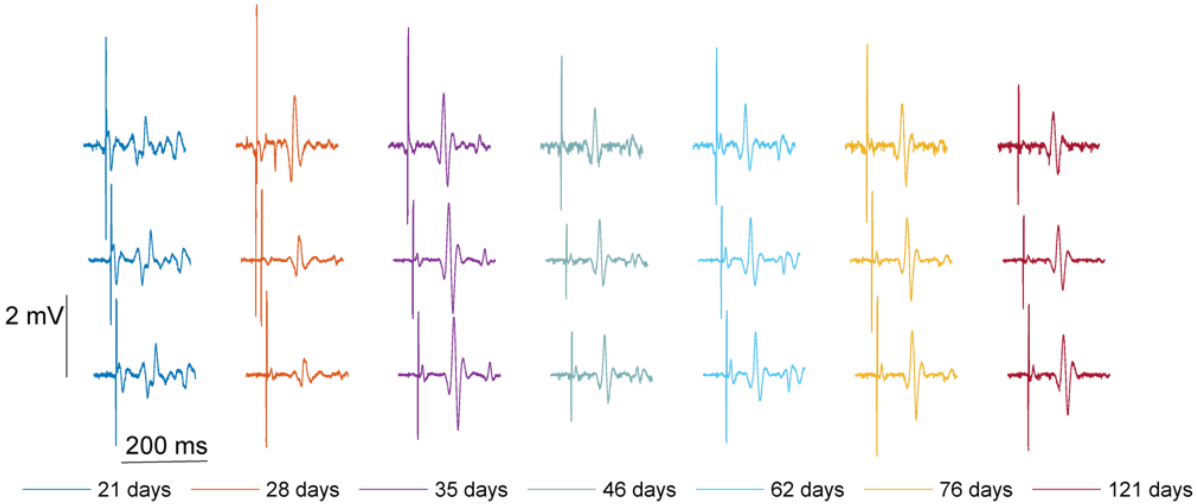



- Reduced electrode impedance

# In vivo tests in rats (4 months)



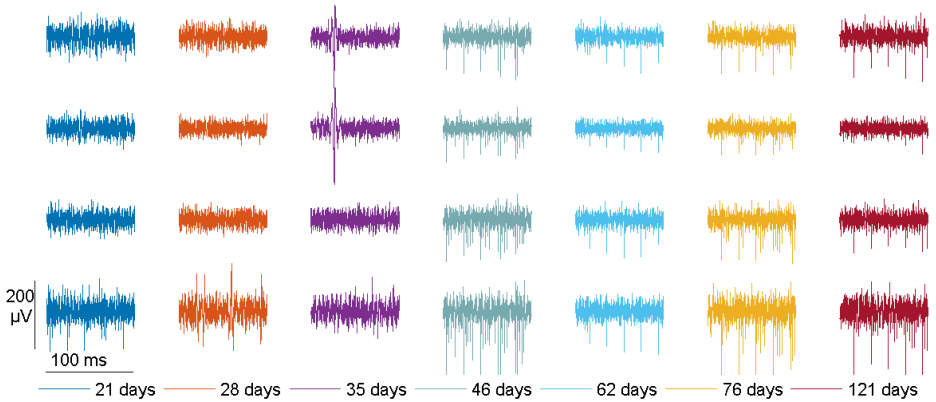



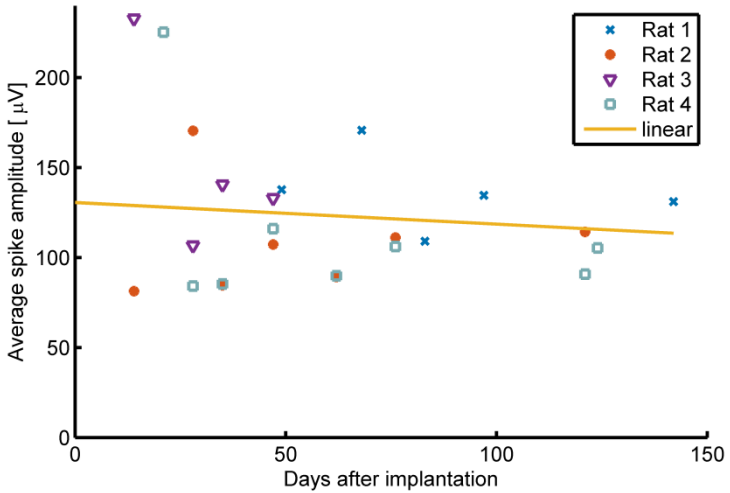




- Stable impedance
- Stable evoked potential recording (representative signals from 3 electrodes)

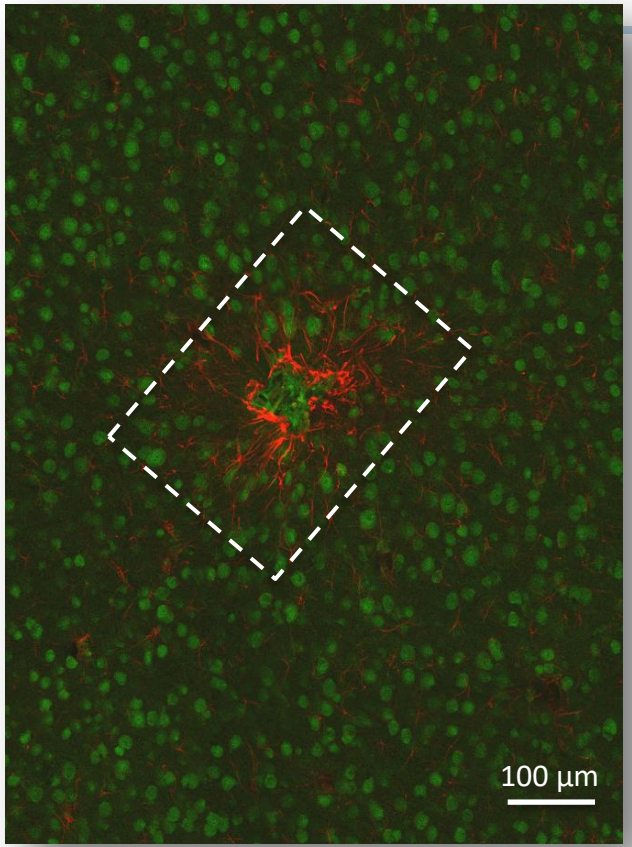
# In vivo tests, part II

- Long term action potential recording possible (<> Si needles)
- After a 1 month incubation (needle dissolution)

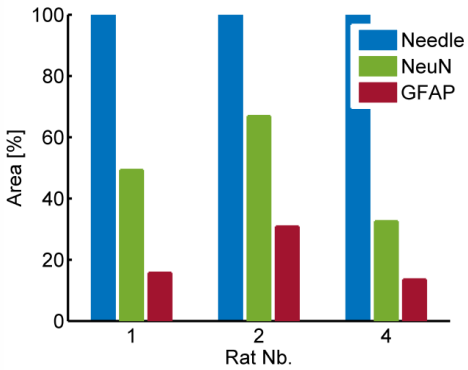


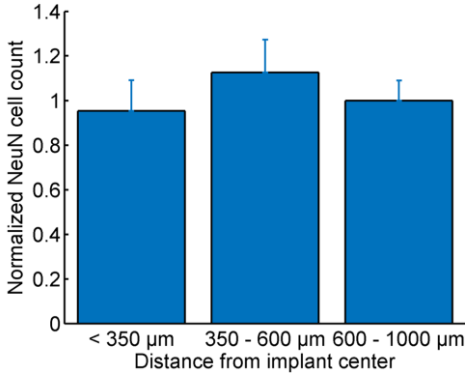



# Histology




- NeuN stain (green=viable neuron)
- GFAP stain (red = astrocytes)
- Scar only 20% of original needle
- Neurons grown into area formerly occupied by dissolving needle



# Thanks!

- Special thanks to my co-authors:

  *Marta Bovet Carmona, Dries Kil, Marjolijn Deprez, Ester Tooten, Bart Nuttin, Aya Takeoka, Detlef Balschun, Michael Kraft, Robert Puers*

- And of course our sponsors: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