

The Injectrode:

a next generation probe for chronic neural interfaces



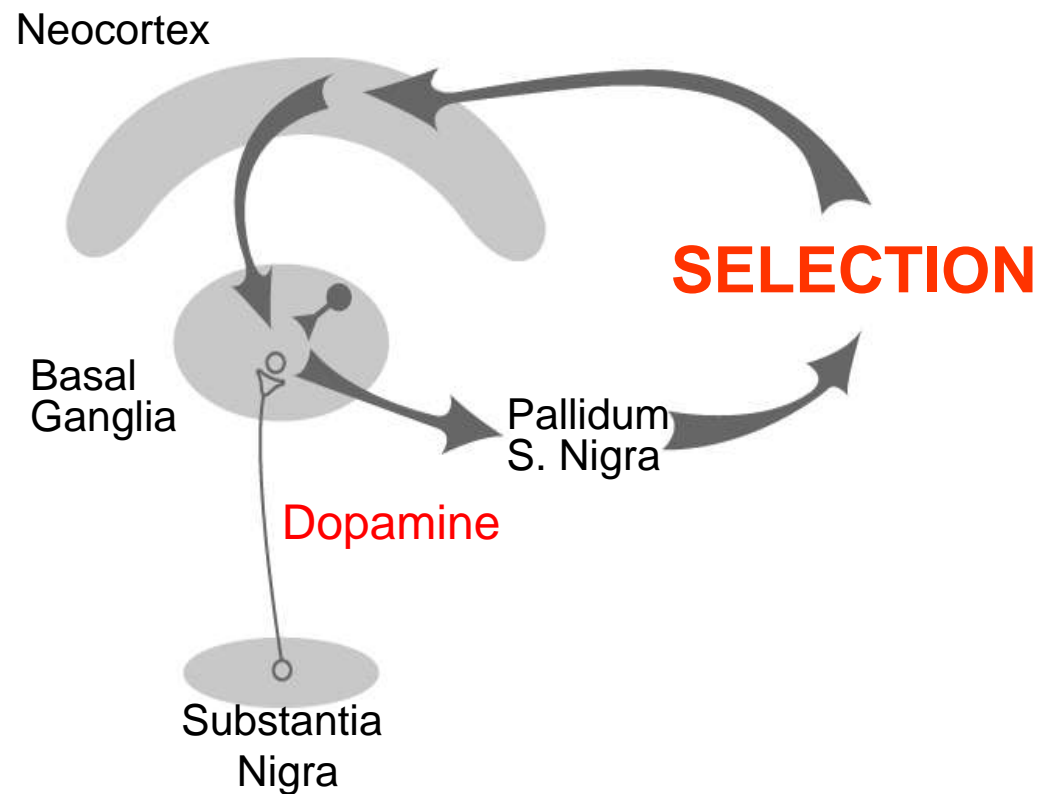
Jay C. Sy, Ph.D.



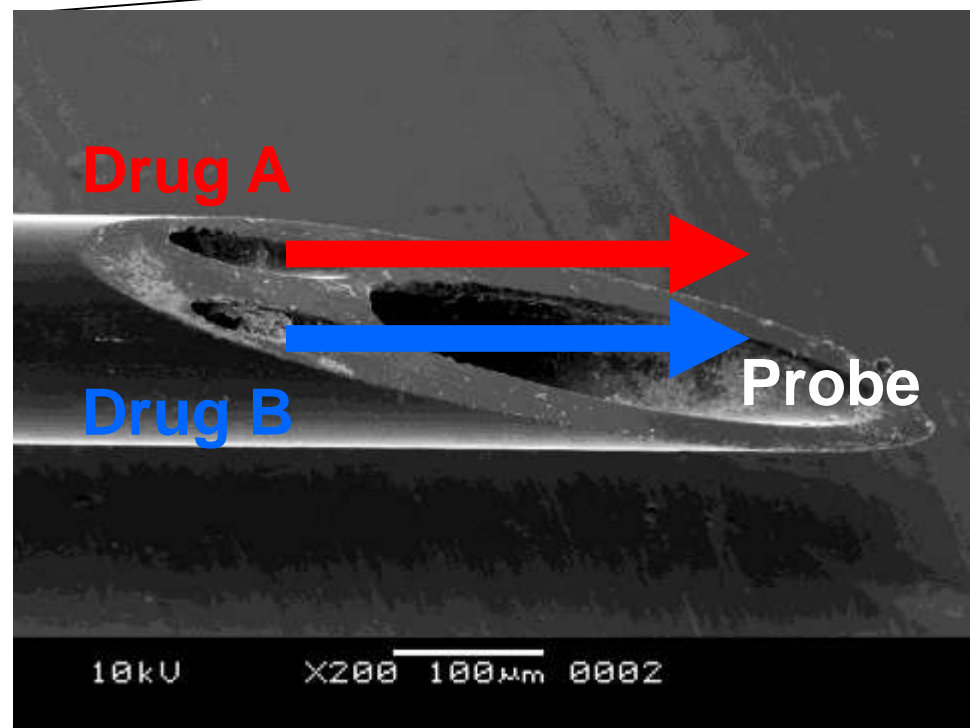
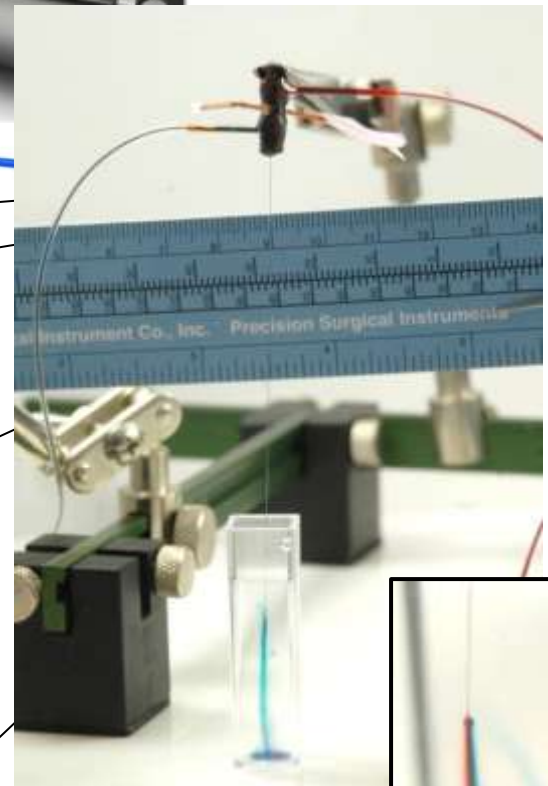
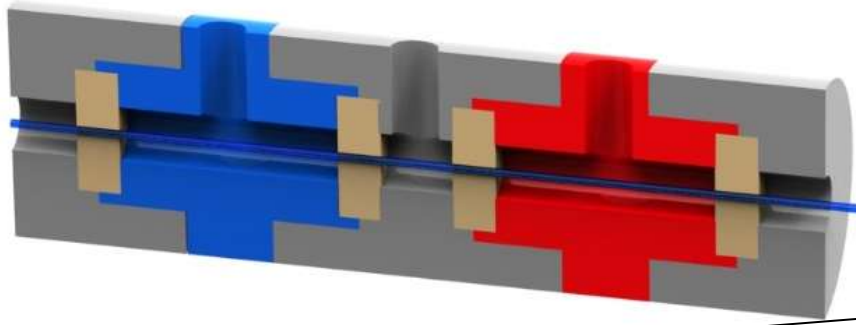
Kevin C. Spencer; Robert S. Langer, Sc.D.;
Michael J. Cima, Ph.D.

Can we make a “mechanical neuron” to treat neuropsychiatric disorders?

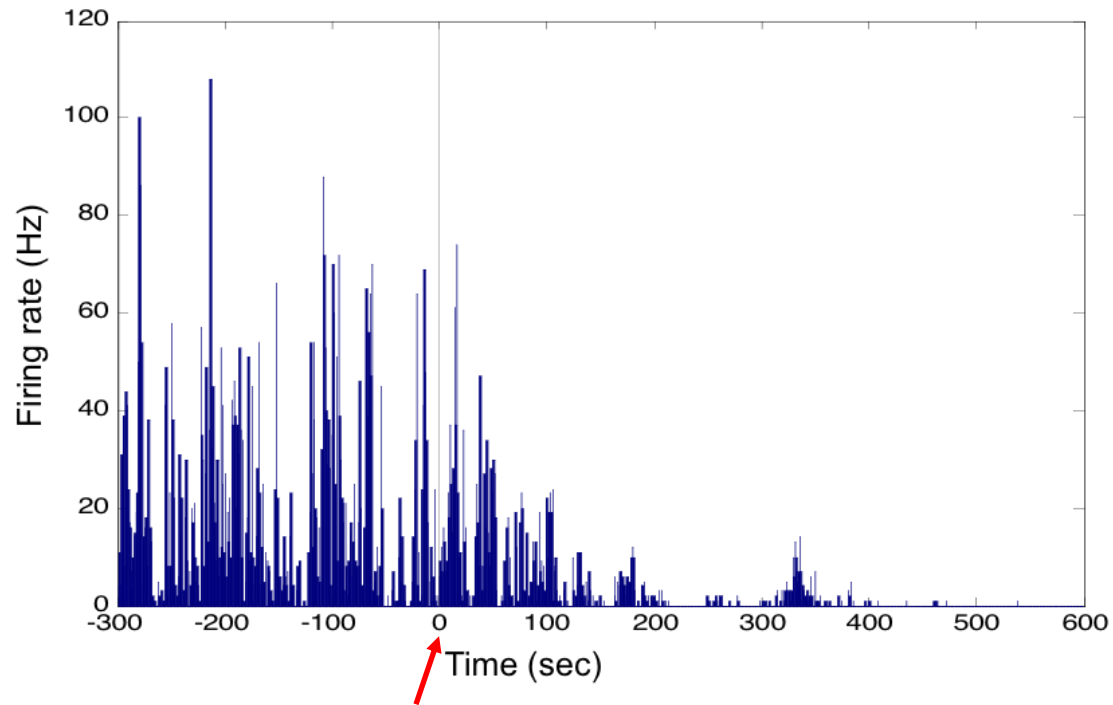
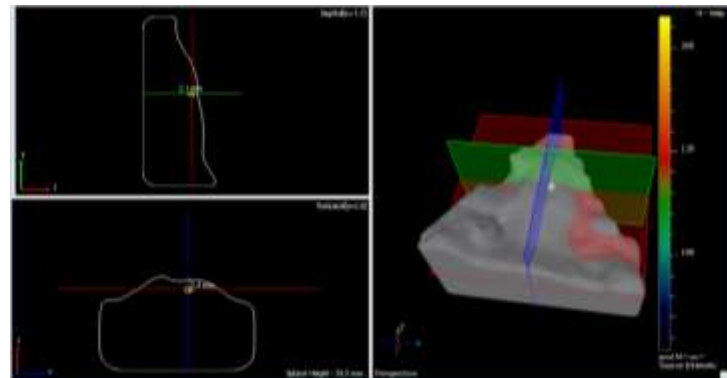
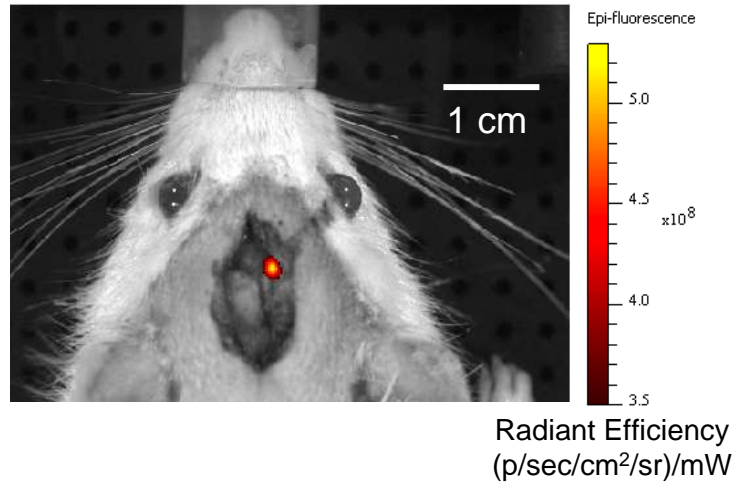
- Parkinson’s, TBI, depression, anxiety are examples of circuit disorders
- Distal anatomical sites permit multiple sites of treatment
- Is it possible to make a “mechanical neuron” to treat disorders?



The Injectrode: a multifunctional interface with neural circuits

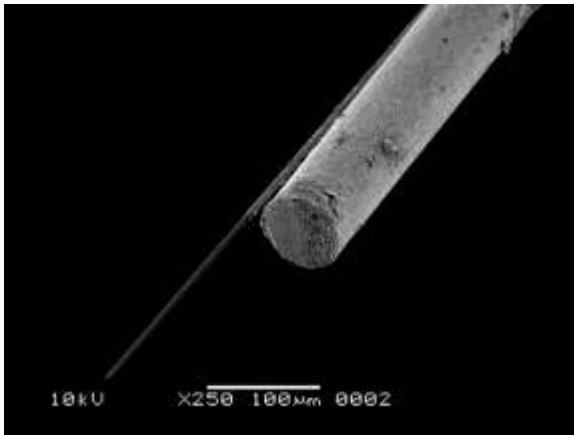


Recording and pharmacological modulation of neural activity

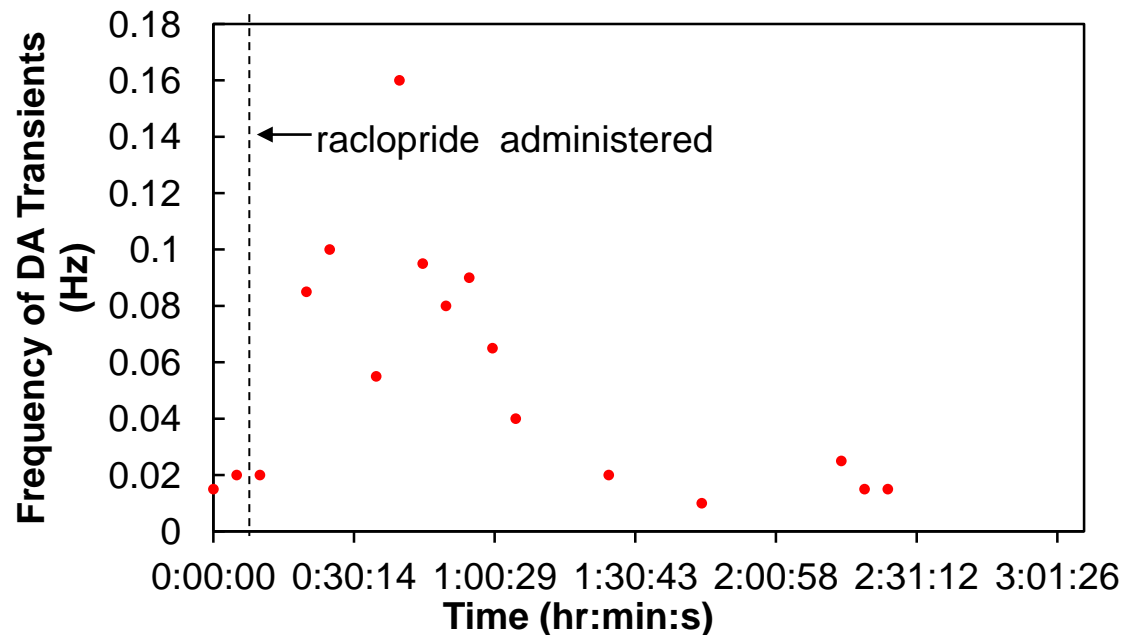
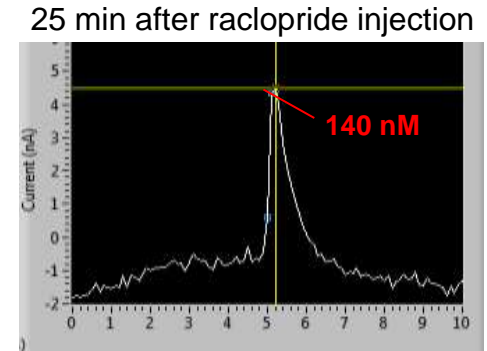
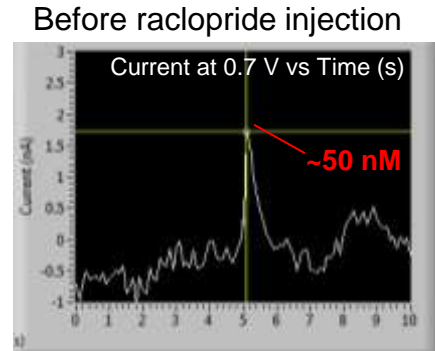


200 nL muscimol
(GABA agonist) at
time 0 infused into
striatum

Carbon fiber probes can be used to measure dopamine *in vivo*



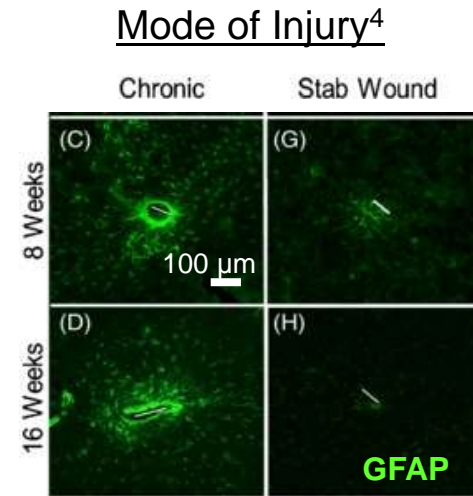
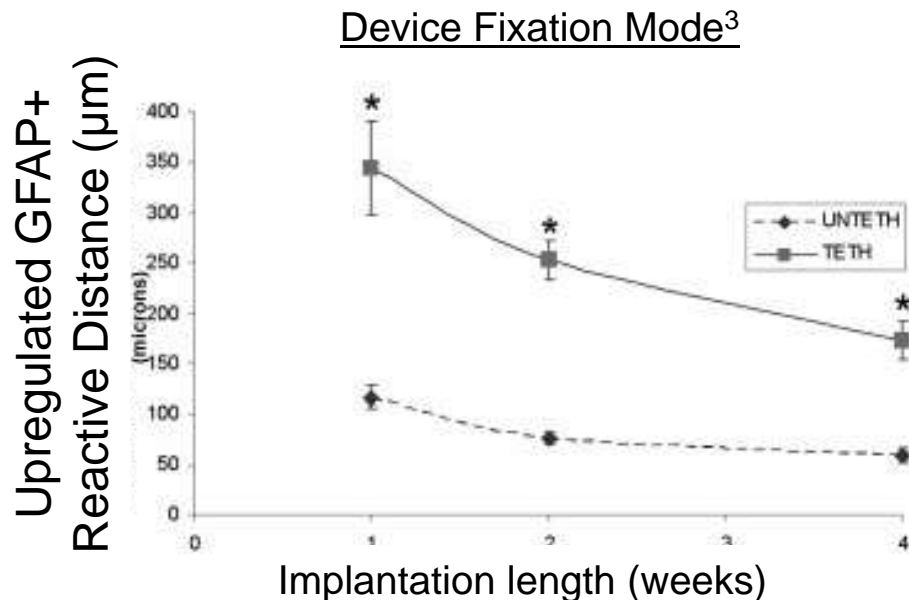
Raclopride (D2 receptor antagonist, increases DA release) administered IM to observe changes in stimulation evoked DA current



Mechanical mismatch and brain micromotion in gliosis

- Brain tissue undergoes displacements
- Difference in mechanical properties ($E_{\text{Device}} \approx 100 \text{ GPa}$ vs. $E_{\text{brain}} = 6 \text{ KPa}$) leads to constant inflammation

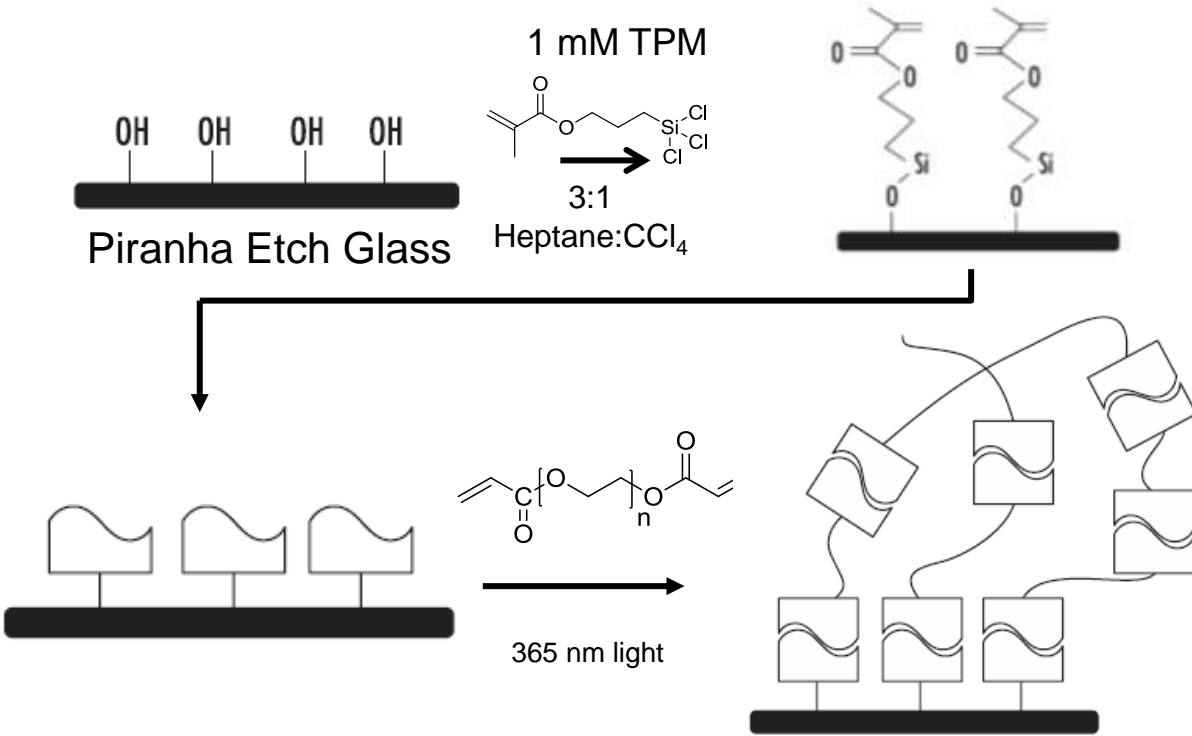
Motion Source	Magnitude (μm)	Frequency (Hz)
Mild acceleration ¹	40	N/A
Respiration ²	10-30	2
Vascular pulse ²	2-4	4-7






1. Fee, M. S. (2000). Neuron.
2. Aaron, G. and M. Jit (2006). J of Neural Eng
3. Biran, R, et al. (2007 J of Bio Mat Res
4. Kelsey, A. et al. (2012). J of Neural Eng.

PEG hydrogels act as shock absorbers

Molecular View



Macroscopic View

-  Surface treatment
-  Polymer coating
-  Hydrogel formation

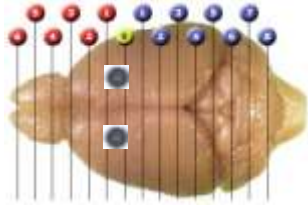


$$E_{\text{hydrogel}} = 11.6 \text{ kPa}$$

Histological analysis at acute and chronic time points

Implant devices in rat brain

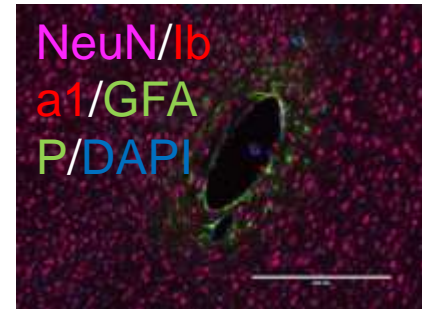
Bregma +0.5 mm, 3mm over



Section brains for histology

- Acute (7 days)
- Chronic (4 week, 8 week)

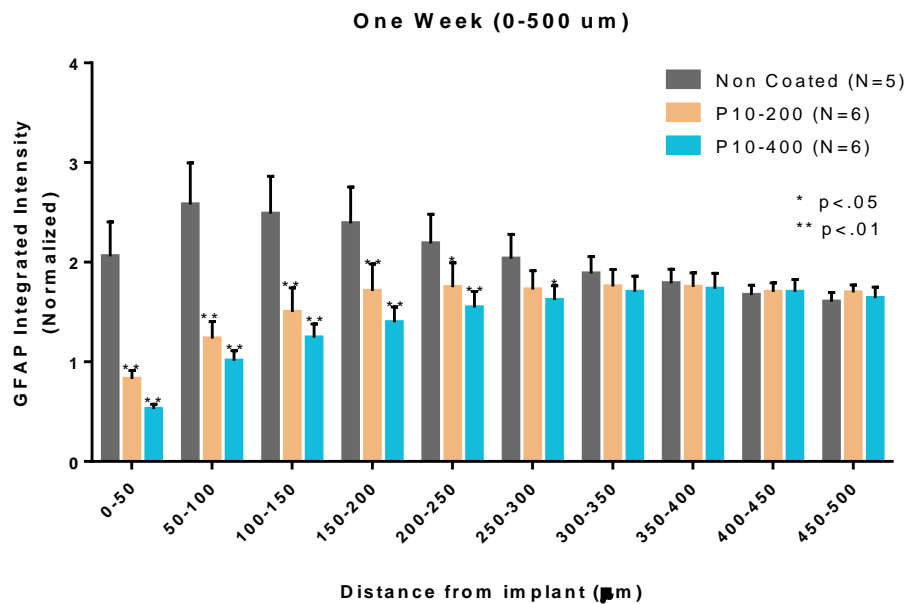
Analyze with IHC



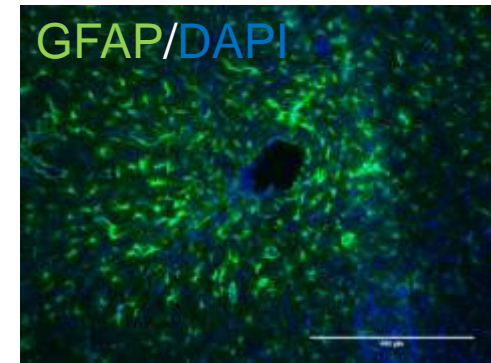
Device Name	Modulus	Diameter
Non Coated	63 Gpa	150 μ m
PEG 10-200 (10% w/v, $E \approx 40$ kPa)	40 kPa	200 μ m
PEG 10-400 (10% w/v, $E \approx 40$ kPa)	40 kPa	400 μ m
Sham	N/A	N/A

Cell /Protein	Marker
Astrocytes	GFAP
Microglia	CD-68/ED1
Neural Nuclei	NeuN
BBB Permeability	IgG

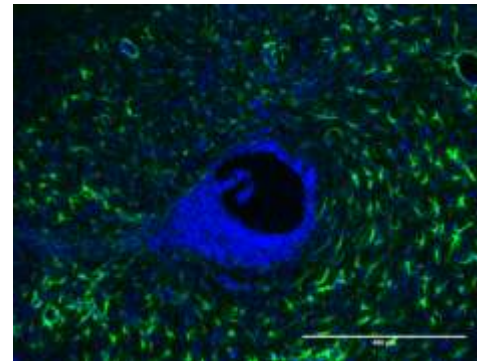
Hydrogel coatings reduce GFAP values around the device at one week



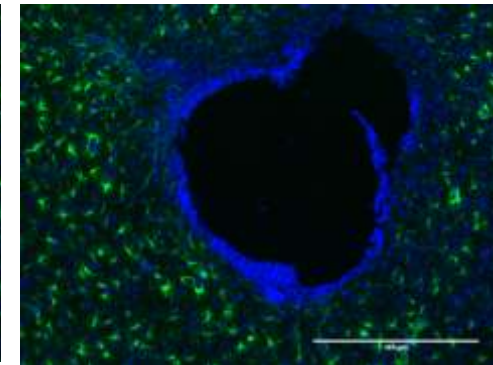
Non-Coated



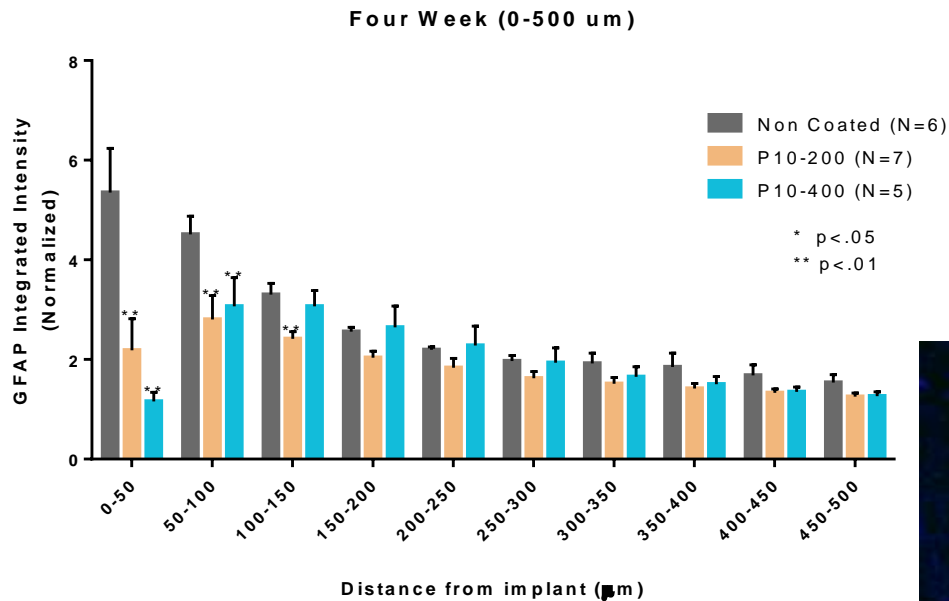
P10-200



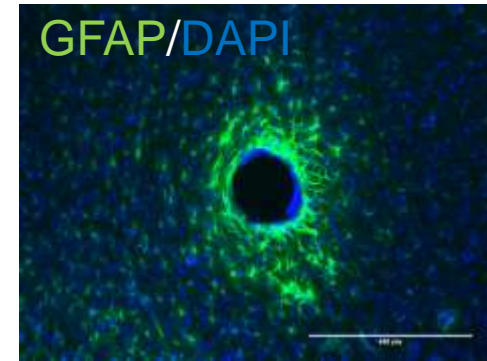
P10-400



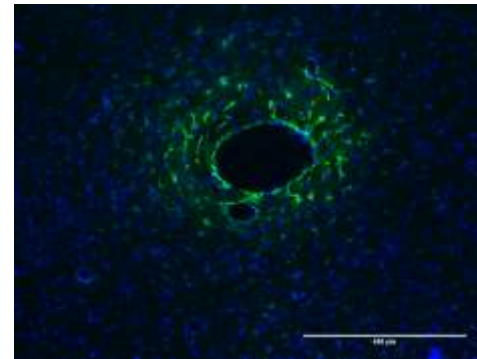
Hydrogels reduce GFAP expression at four weeks



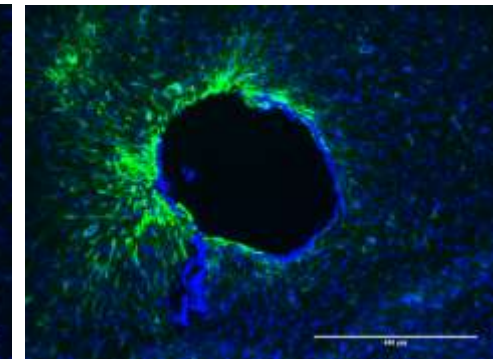
Non-Coated



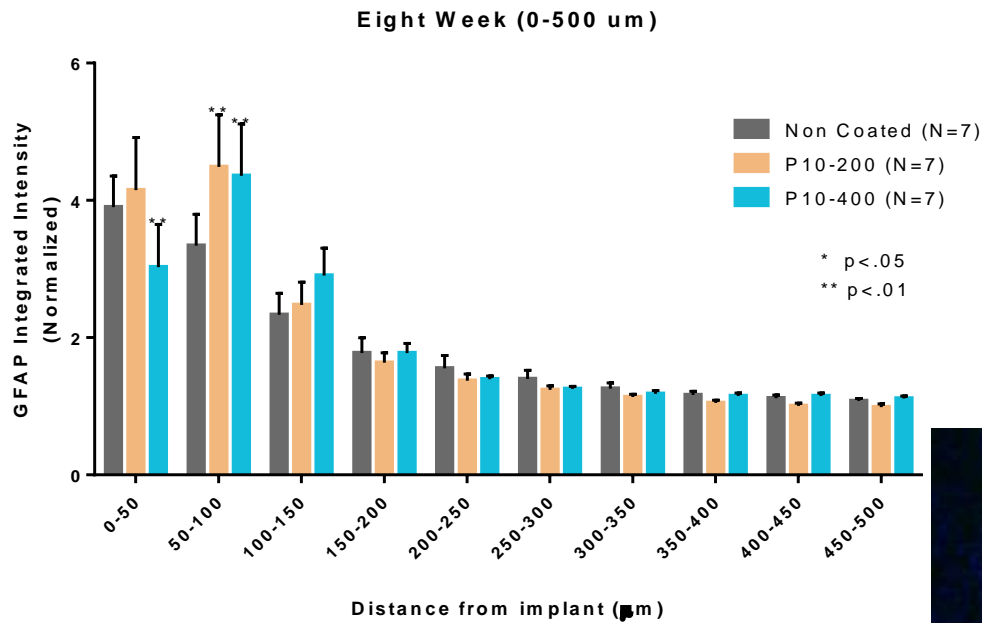
P10-200



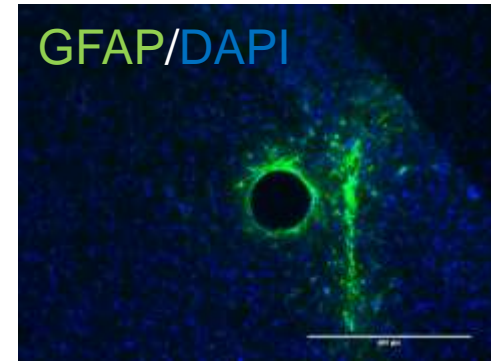
P10-400



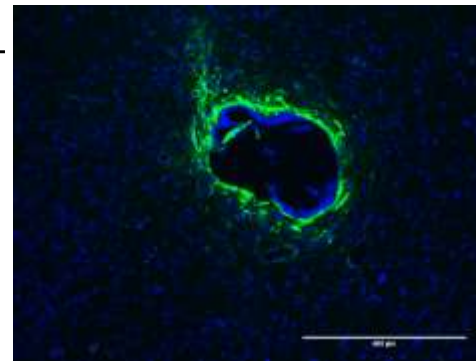
Differences observed within 100 μm of implant at eight weeks



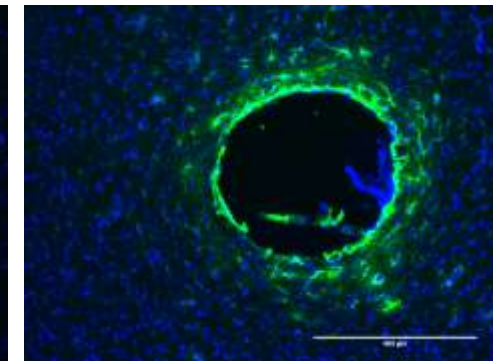
Non-Coated



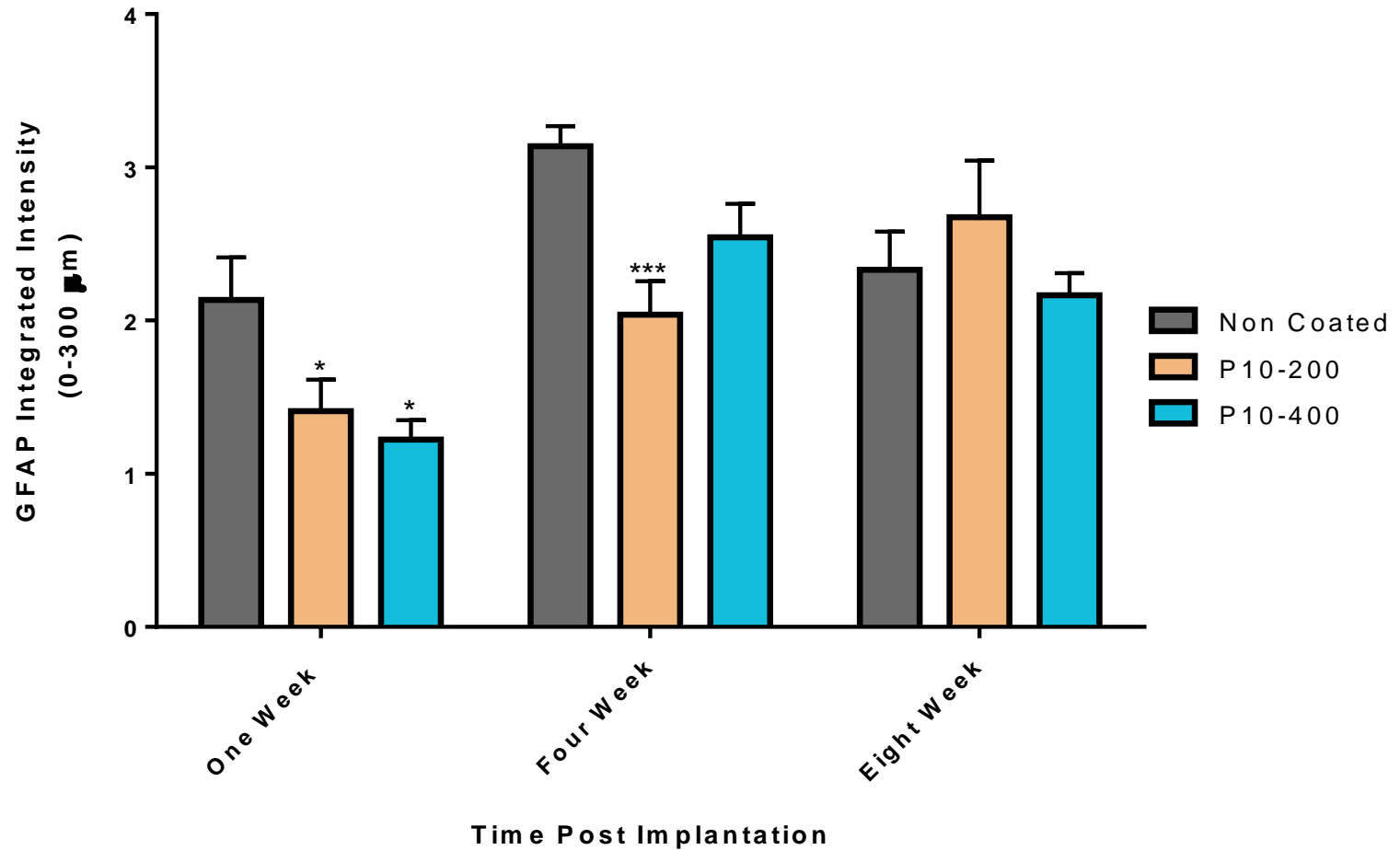
P10-200



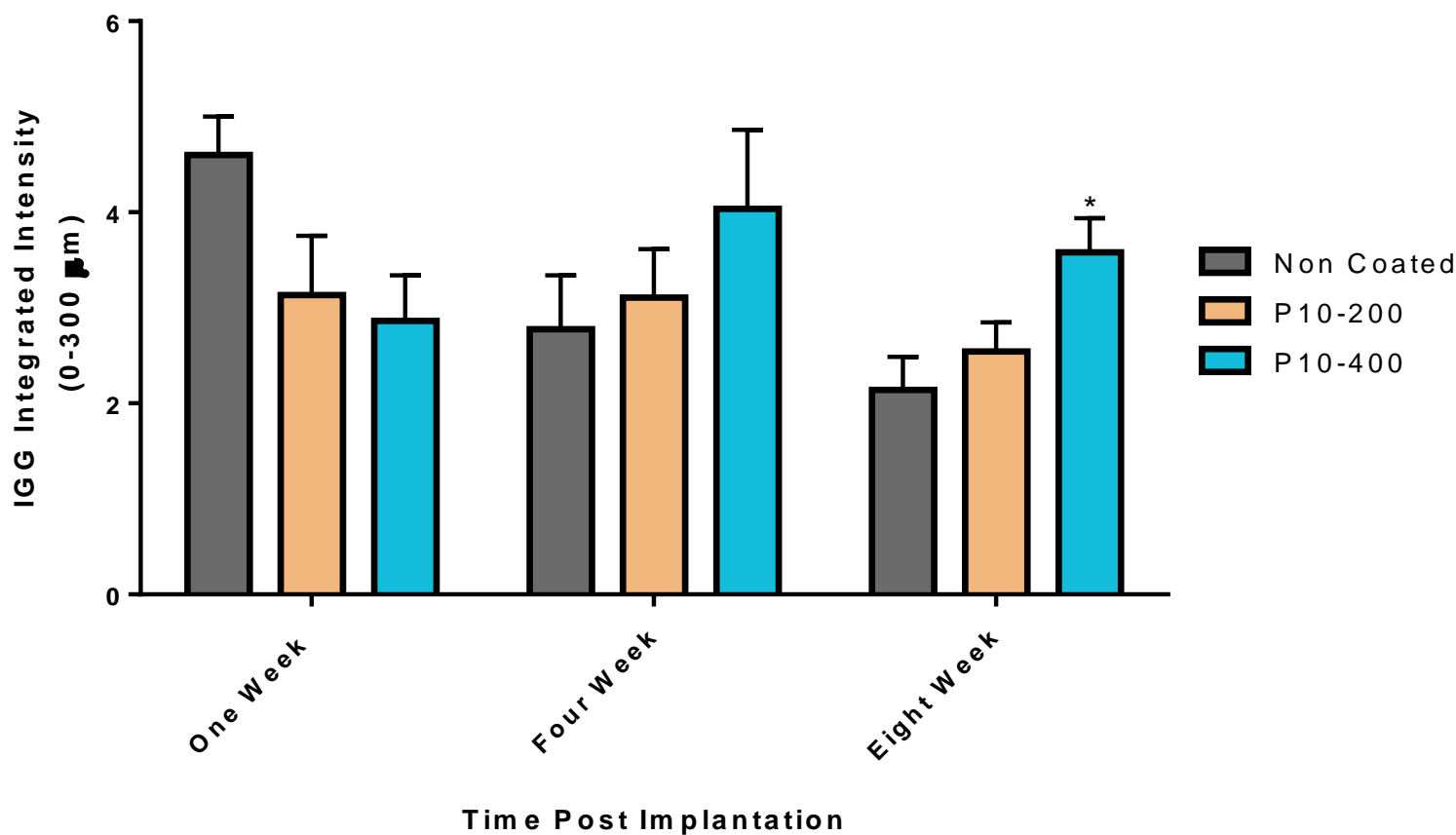
P10-400



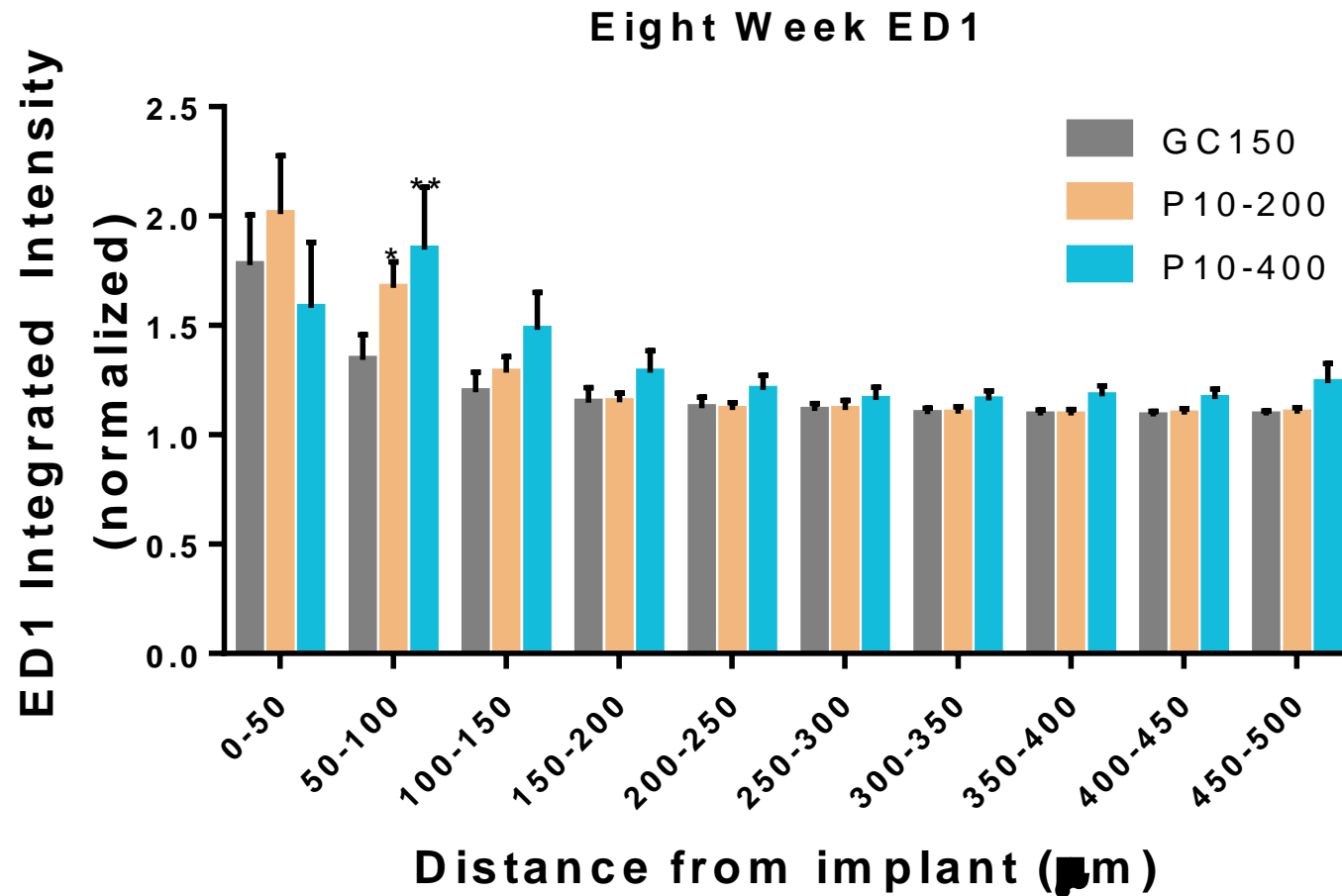
Integrated GFAP values are reduced at one and four weeks



IgG staining scales with implant size at chronic time points

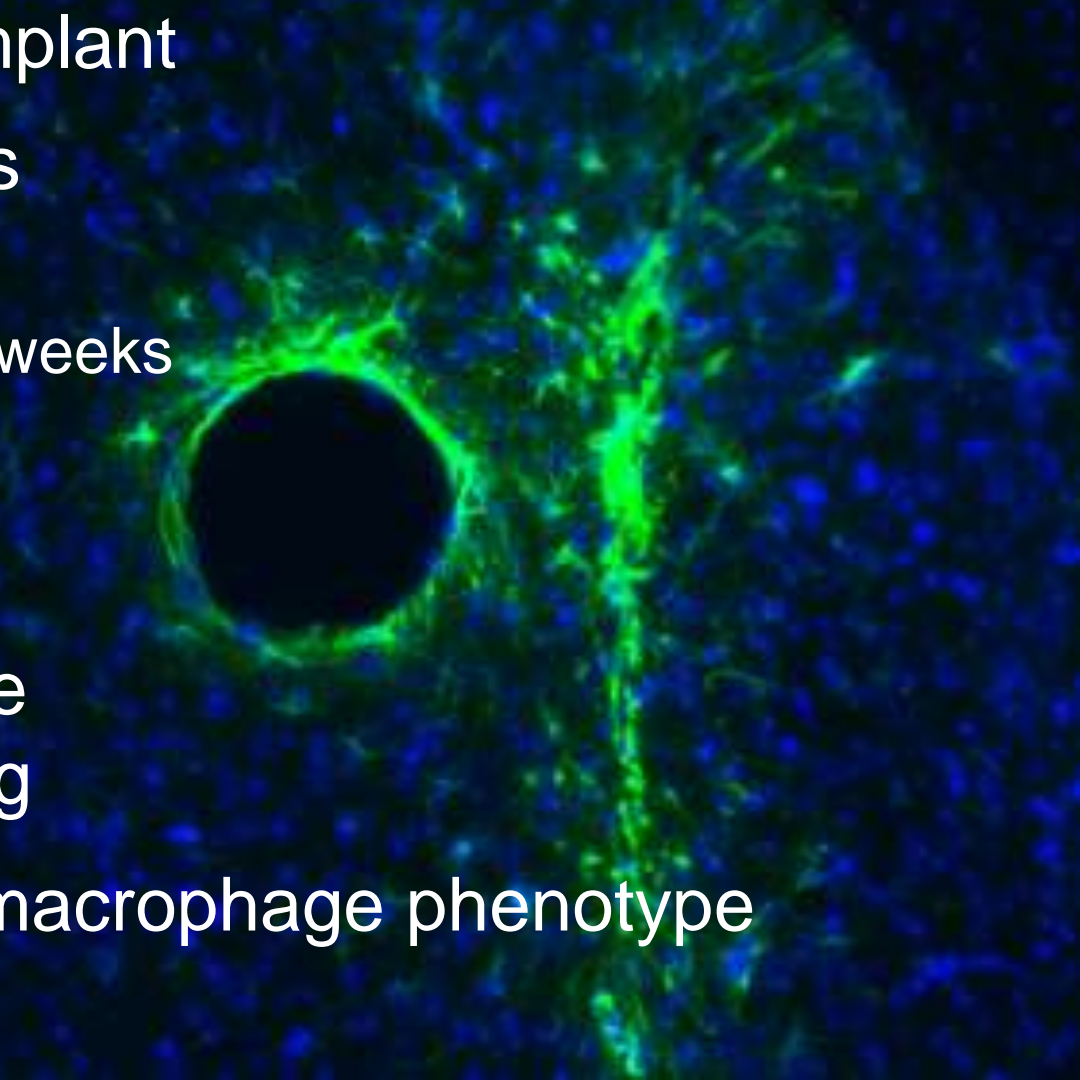


Coated implants have prolonged macrophage response

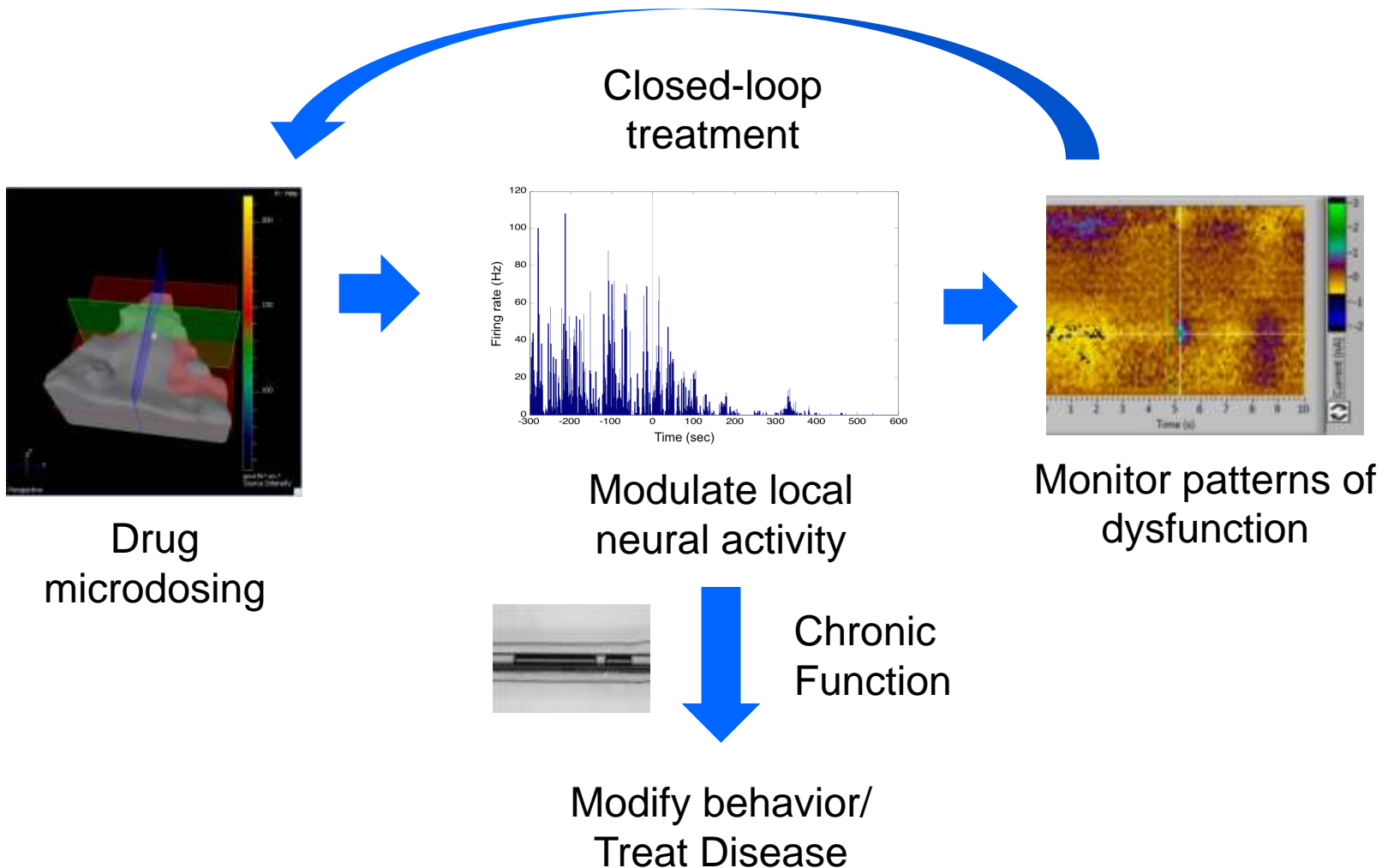


Conclusions

- PEG coatings have tunable moduli and reduce strain fields around implant
- GFAP ↓ with coatings at one and 4 weeks
 - No difference at eight weeks
- IgG ↑ with coatings at chronic time points
- Macrophage response prolonged with coating
- Currently examining macrophage phenotype



The Injectrode: a device for chronic treatment of circuit disorders



Acknowledgements



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