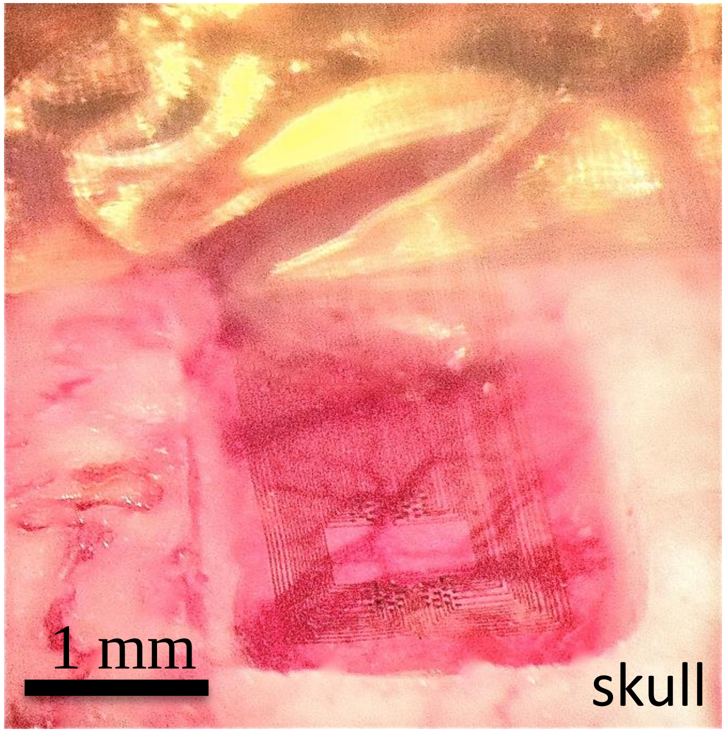
New Materials and Devices for Interfacing with the Brain



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UNIVERSITY OF CAMBRIDGE
Department of Engineering

Bioelectronics Laboratory

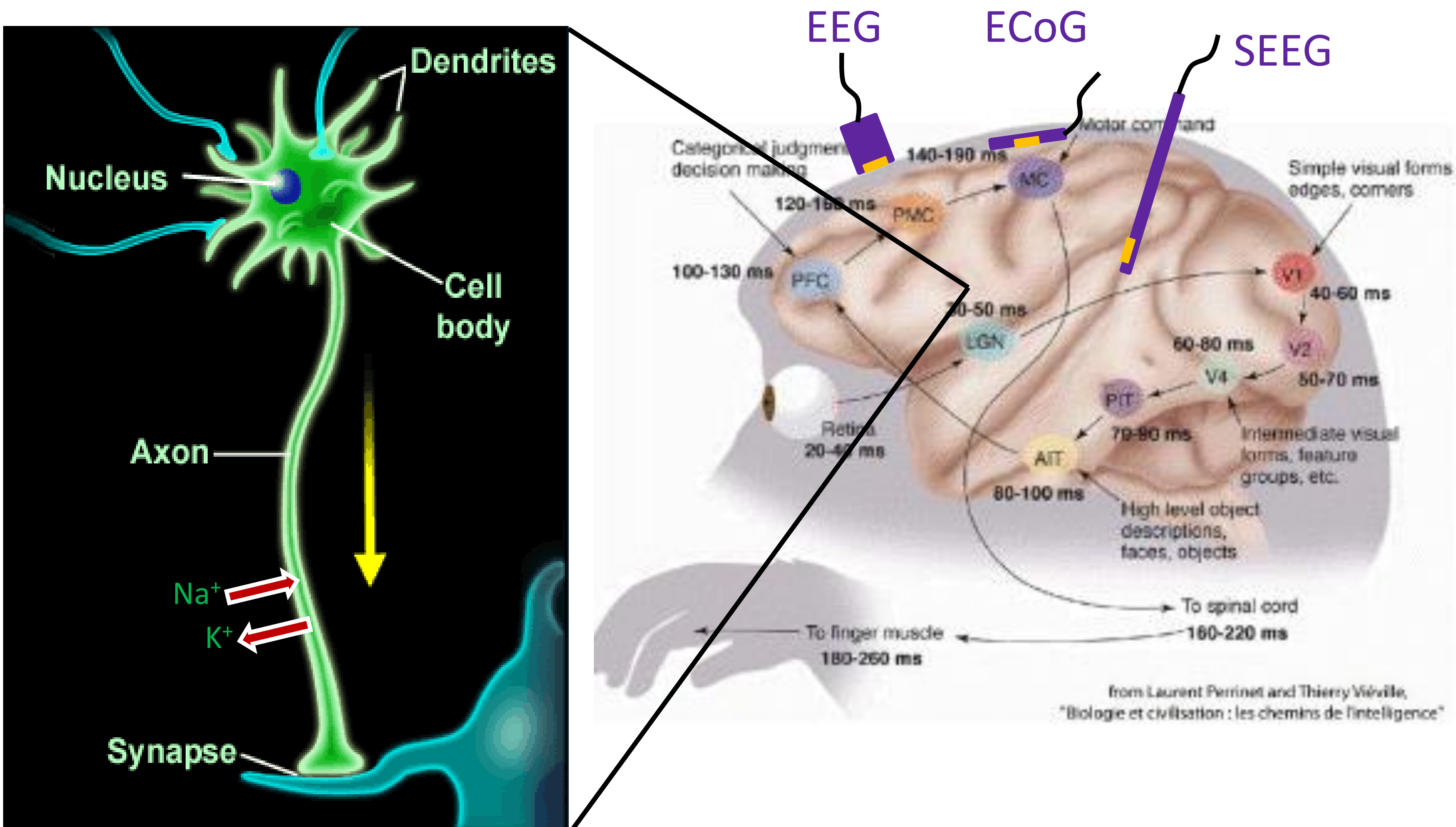
Bioelectronics: Coupling biology and electronics

Sensing
Diagnosis

Mostly soft		Hard
Complex signaling		Electrons/holes
Dynamic		Static

Actuation
Therapy

Importance of neural interfacing



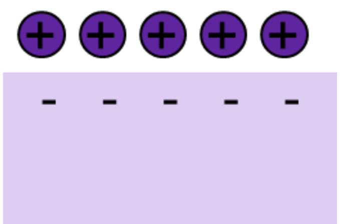
Electrical recording for epilepsy monitoring

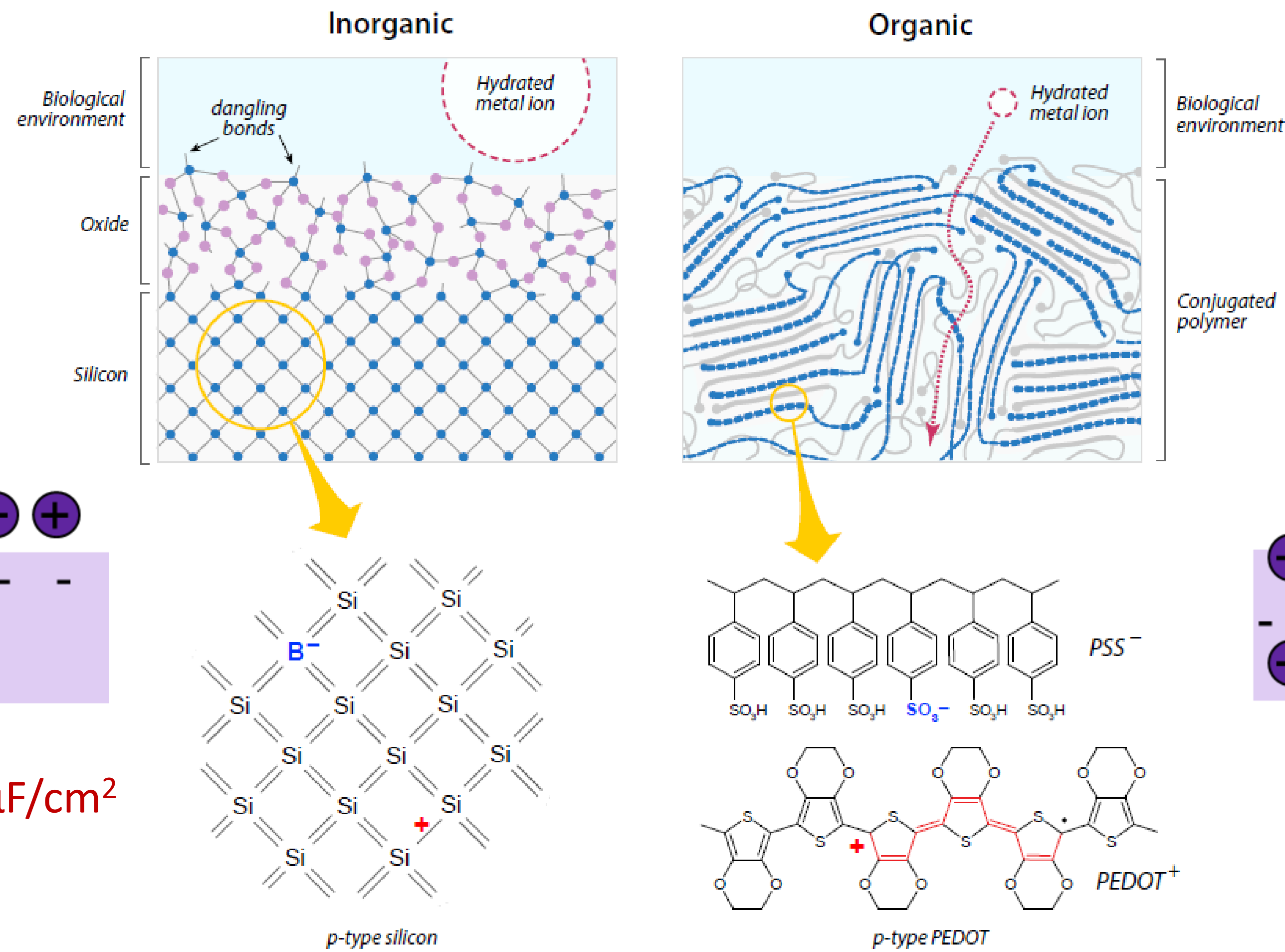
- Affects 1% of world population
- 30% of patients are drug resistant
- Resection surgery is an option

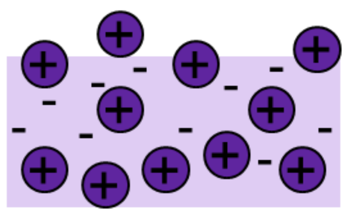
Key challenges:

- Improve electrode performance
- Make less invasive recordings

Why organics?







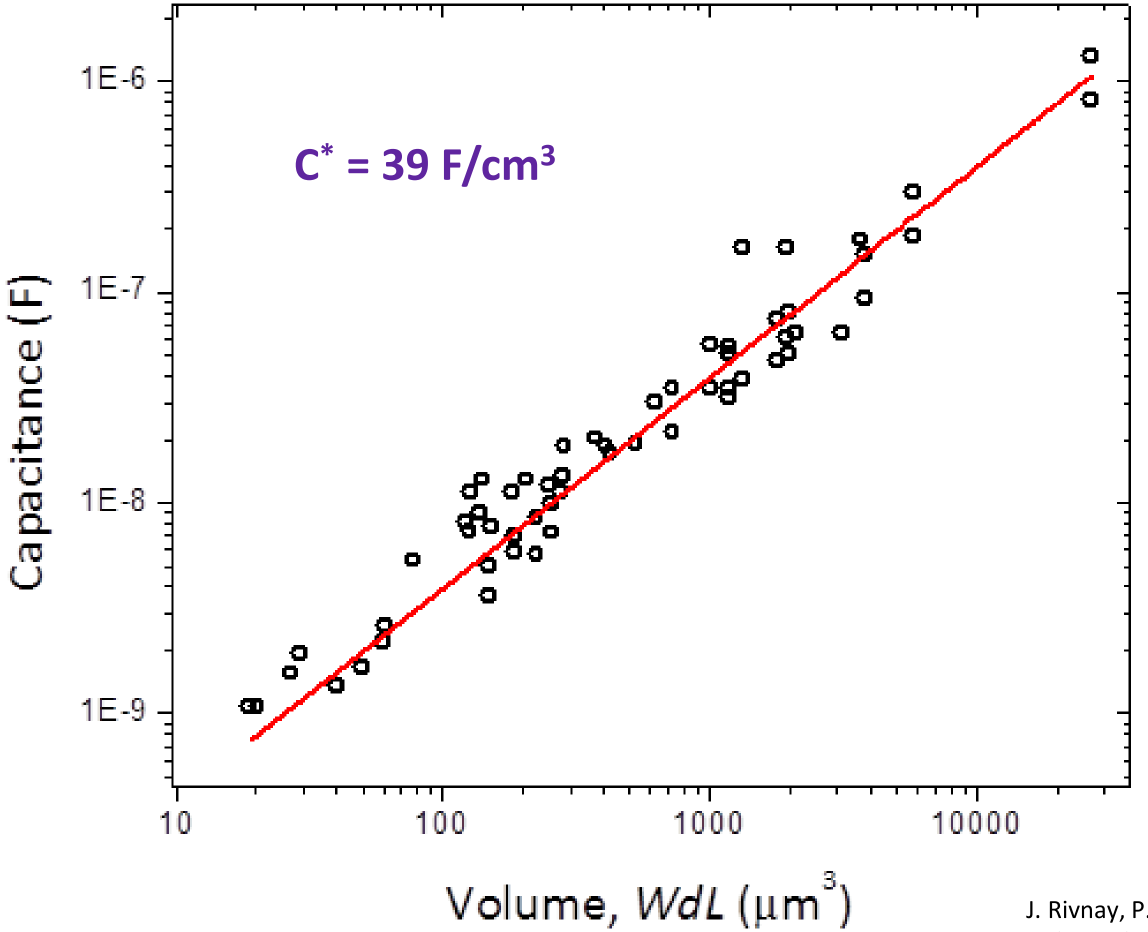
$C_{DL}' \sim 1\text{-}10\ \mu F/cm^2$

$C' >> C_{DL}'$

Mixed conductivity leads to novel/state-of-the-art devices

J. Rivnay, R.M. Owens, and G.G. Malliaras, *Chem. Mater.* 26, 679 (2014).

Volumetric ion transport in PEDOT:PSS



For d=130 nm:
$C' \sim 500\ \mu F/cm^2$

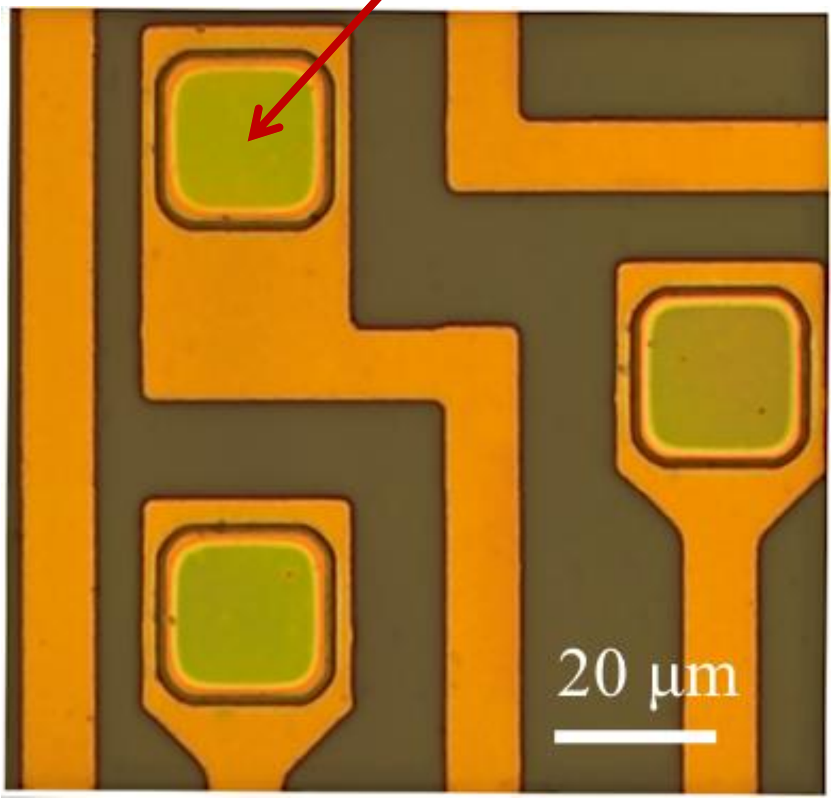
100× larger than
double layer capacitance

J. Rivnay, P. Leleux, M. Ferro, M. Sessolo, A. Williamson, D.A. Koutsouras, D. Khodagholy, M. Ramuz, X. Strakosas, R.M. Owens, C. Benar, J.-M. Badier, C. Bernard, and G.G. Malliaras, *Science Advances* 1, e1400251 (2015).

Ultra-conformable PEDOT:PSS microelectrodes

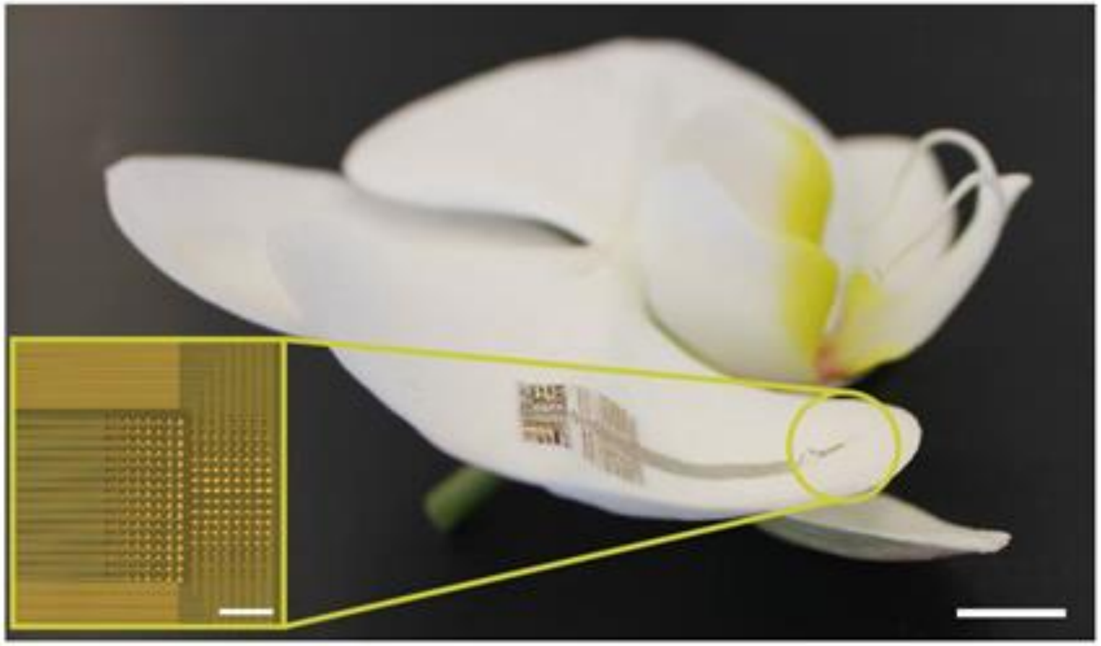
PEDOT:PSS

Parylene C – 4 µm thick

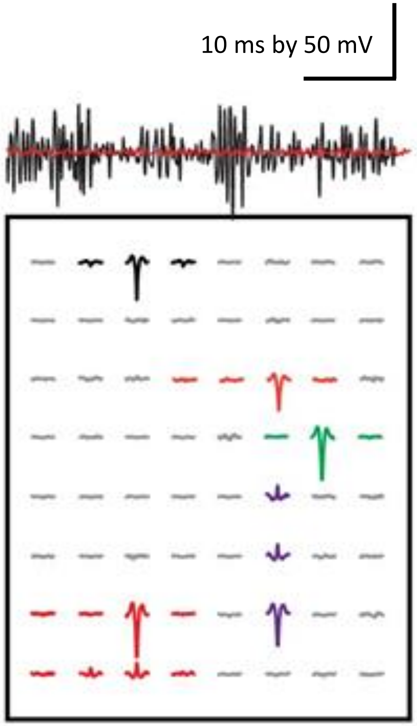


D. Khodagholy, T. Doublet, M. Gurfinkel, P. Quilichini, E. Ismailova, P. Leleux, T. Herve, S. Sanaur, C. Bernard, and G.G. Malliaras, *Adv. Mater.* 36, H268 (2011).

Recordings of single neurons from brain surface



256 electrodes, 10 x 10 μm^2 with 30 μm inter-electrode spacing

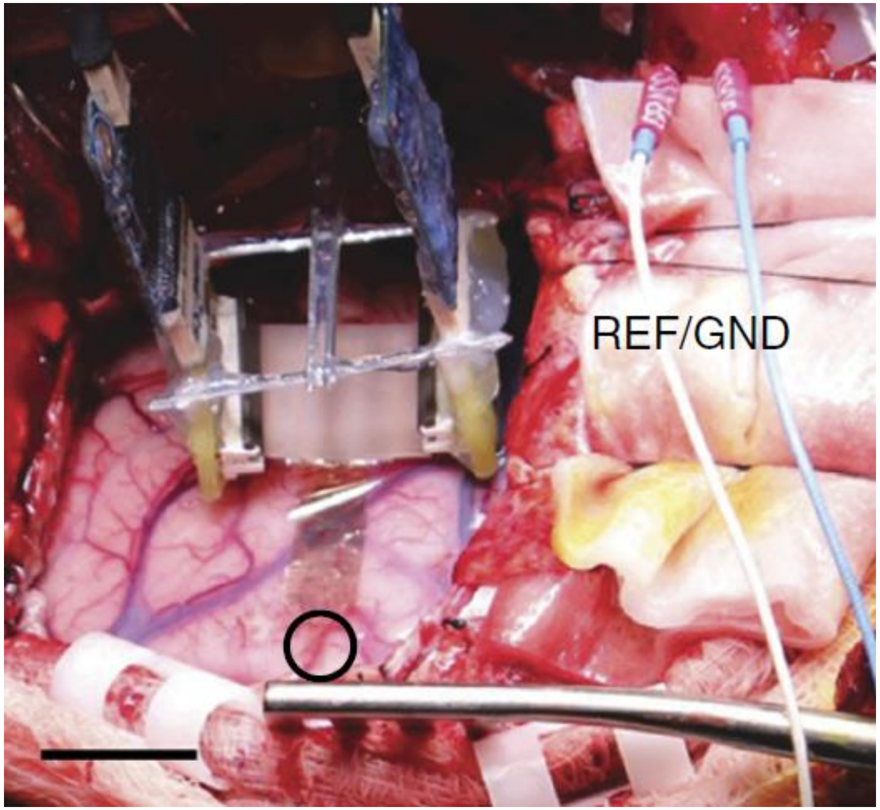


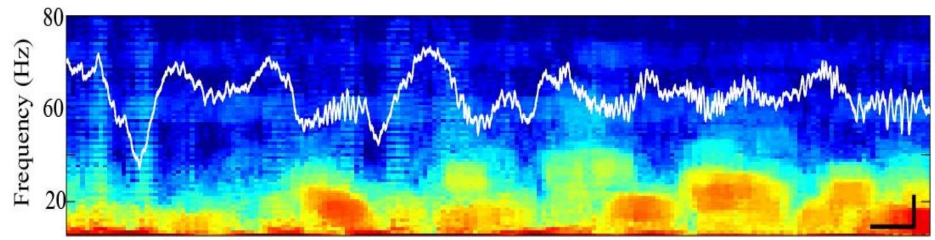
Electrocorticography in rats

w/ Dion Khodagholy, György Buzsáki (NYU)

D. Khodagholy, J.N. Gelinas, T. Thesen, W. Doyle, O. Devinsky, G.G. Malliaras and G. Buzsáki, *Nature Neurosci.* 18, 310 (2015).

Translation to the clinic





500 ms by 500 mV

20 ms by 40 mV

Intraoperative recordings in human

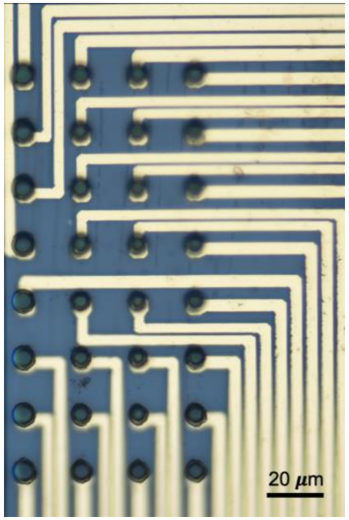
w/ Dion Khodagholy, György Buzsáki (NYU)

D. Khodagholy, J.N. Gelinas, T. Thesen, W. Doyle, O. Devinsky,
G.G. Malliaras and G. Buzsáki, *Nature Neurosci.* 18, 310 (2015).

Latest version – for chronic use in human

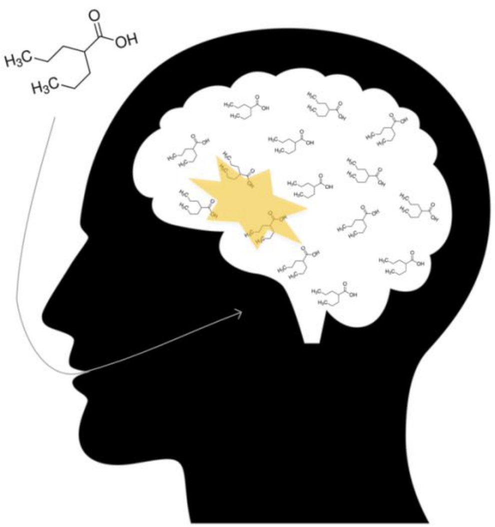
7×7 μm² sites

20 μm pitch



Options for treating epilepsy

Antiepileptic drugs



- Drug resistance
- Side effects

Resective surgery

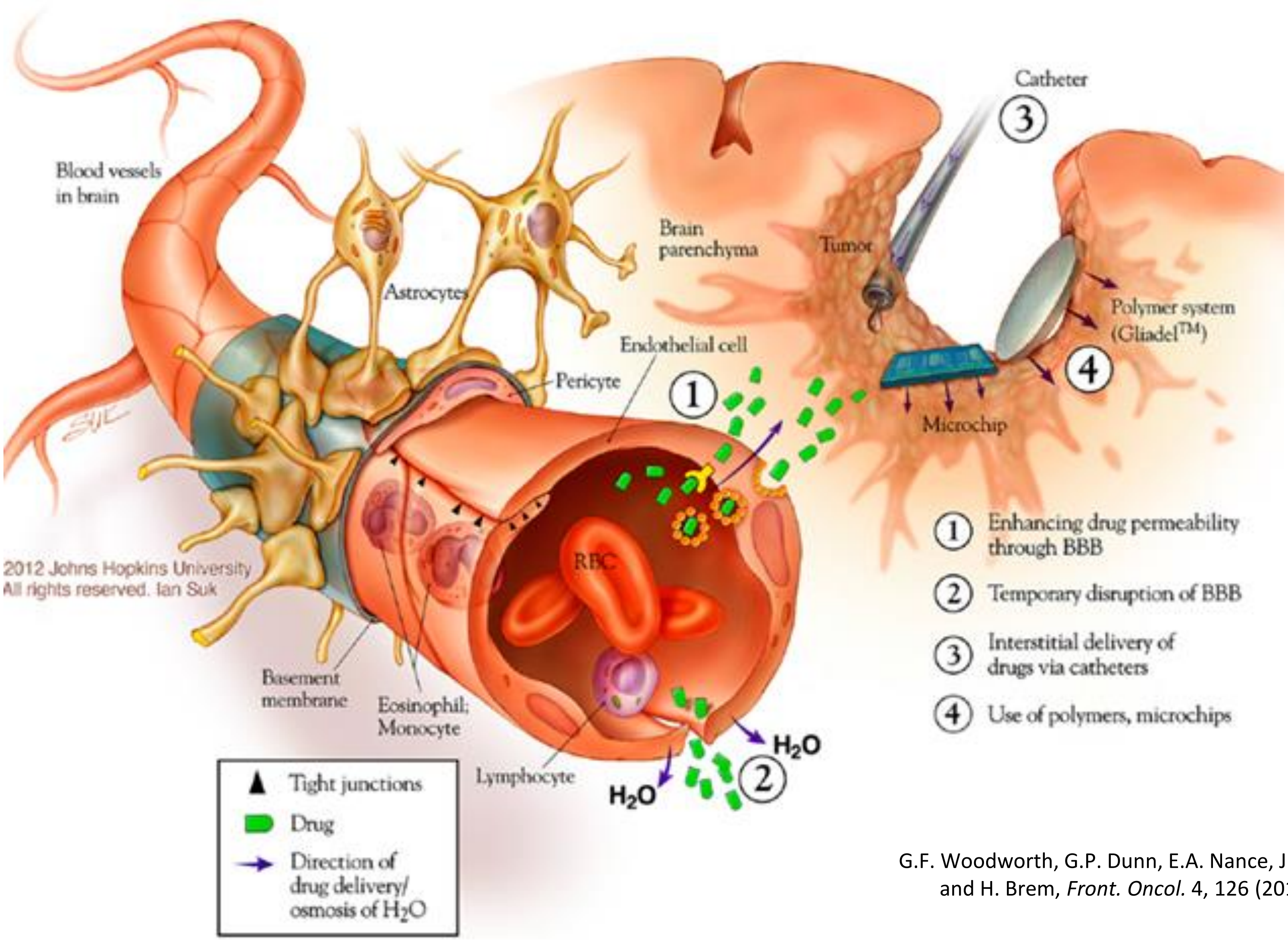
- Not always possible

Local drug delivery

- Where needed
- When needed

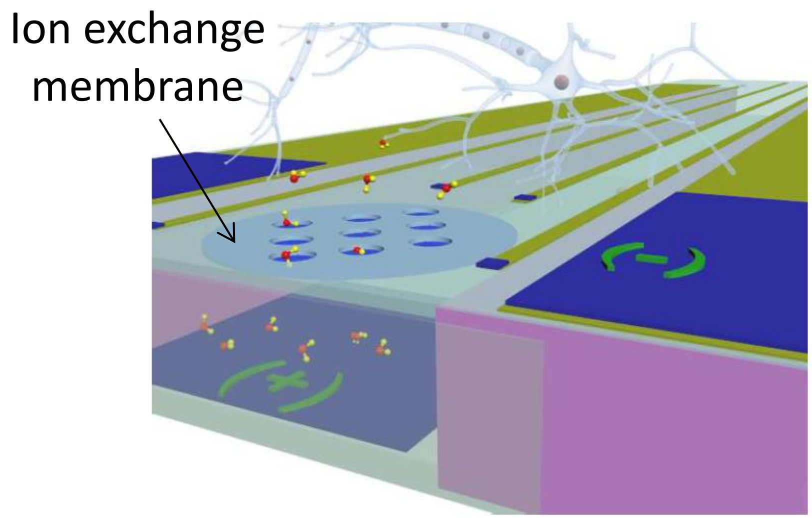
Seizure focus

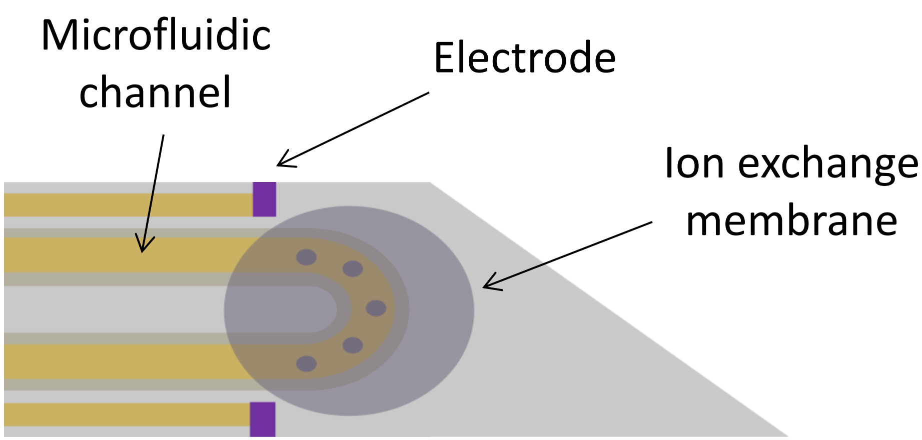
Drug delivery past the blood-brain barrier

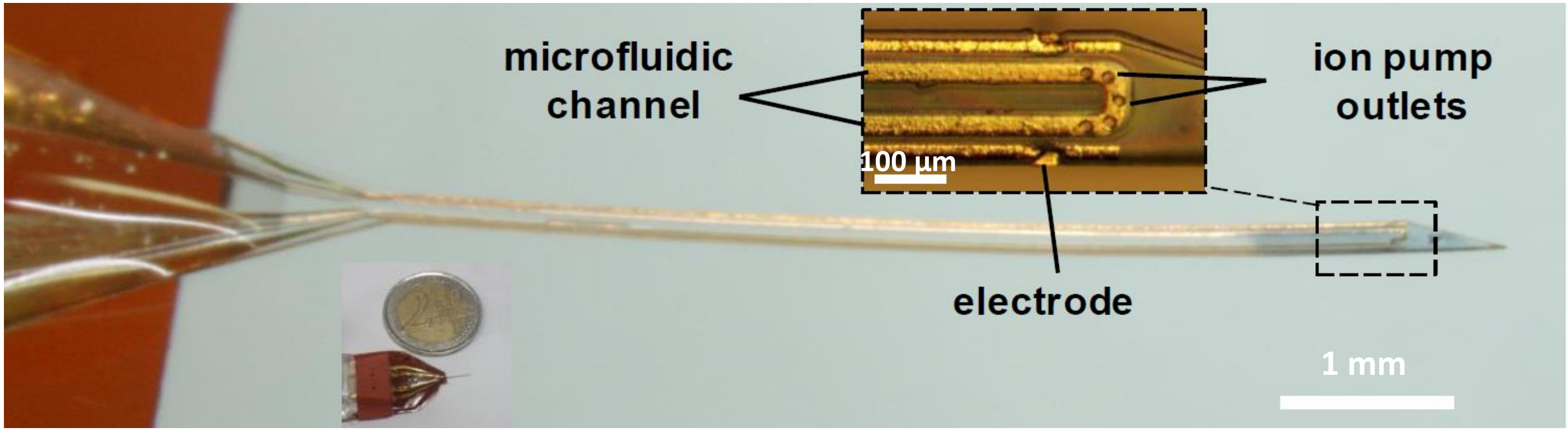


G.F. Woodworth, G.P. Dunn, E.A. Nance, J. Hanes, and H. Brem, *Front. Oncol.* 4, 126 (2014).

Electrophoretic drug delivery device



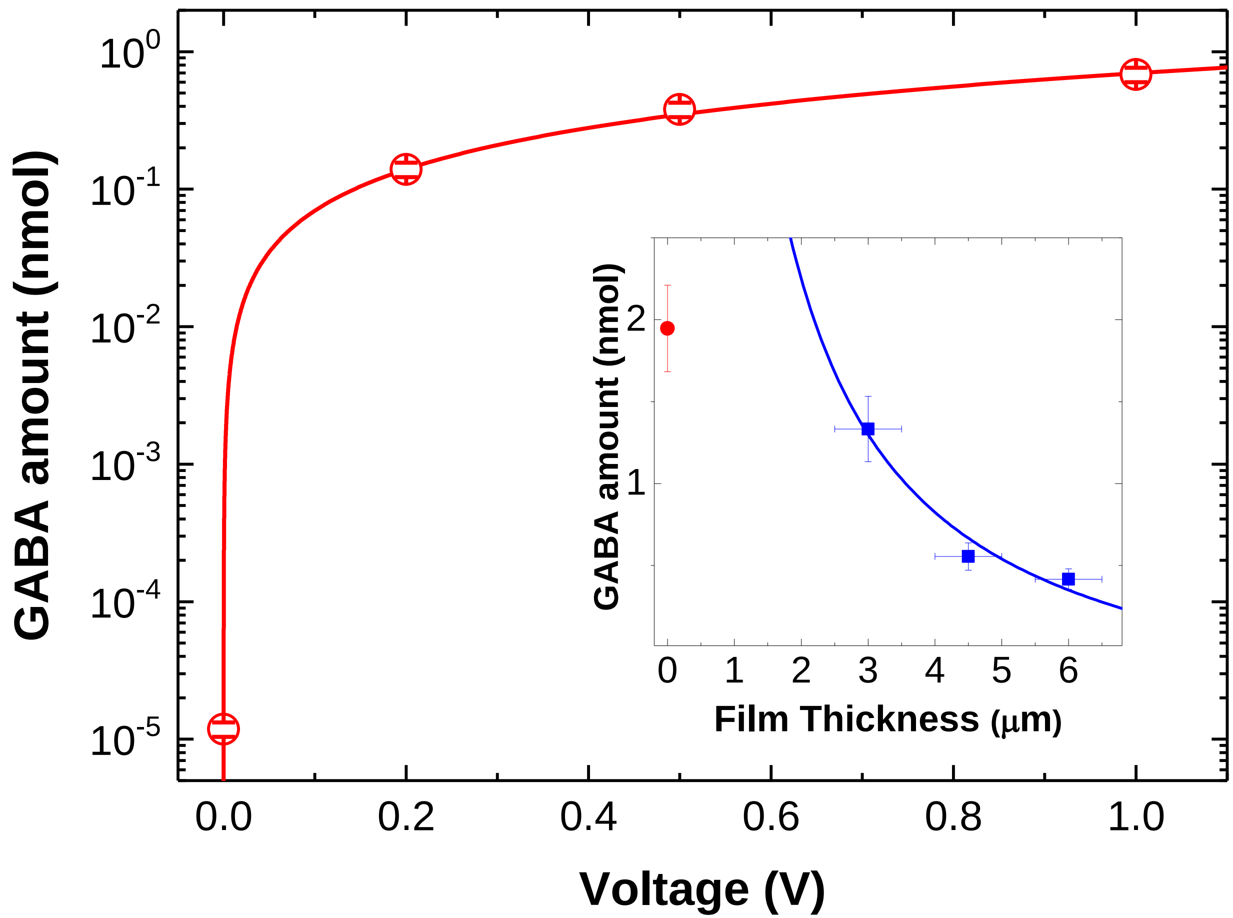




w/ Christophe Bernard (INSERM)

I. Uguz, C.M. Proctor, V.F. Curto, A.-M. Pappa, M.J. Donahue, M. Ferro, R.M. Owens, D. Khodagholy, S. Inal, and G.G. Malliaras, *Adv. Mater.* 29, 1701217 (2017).

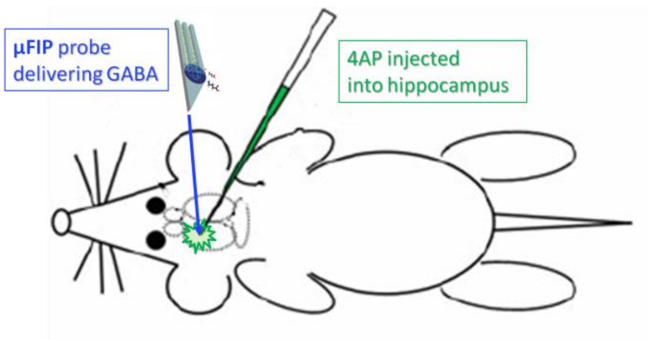
GABA delivery in vitro

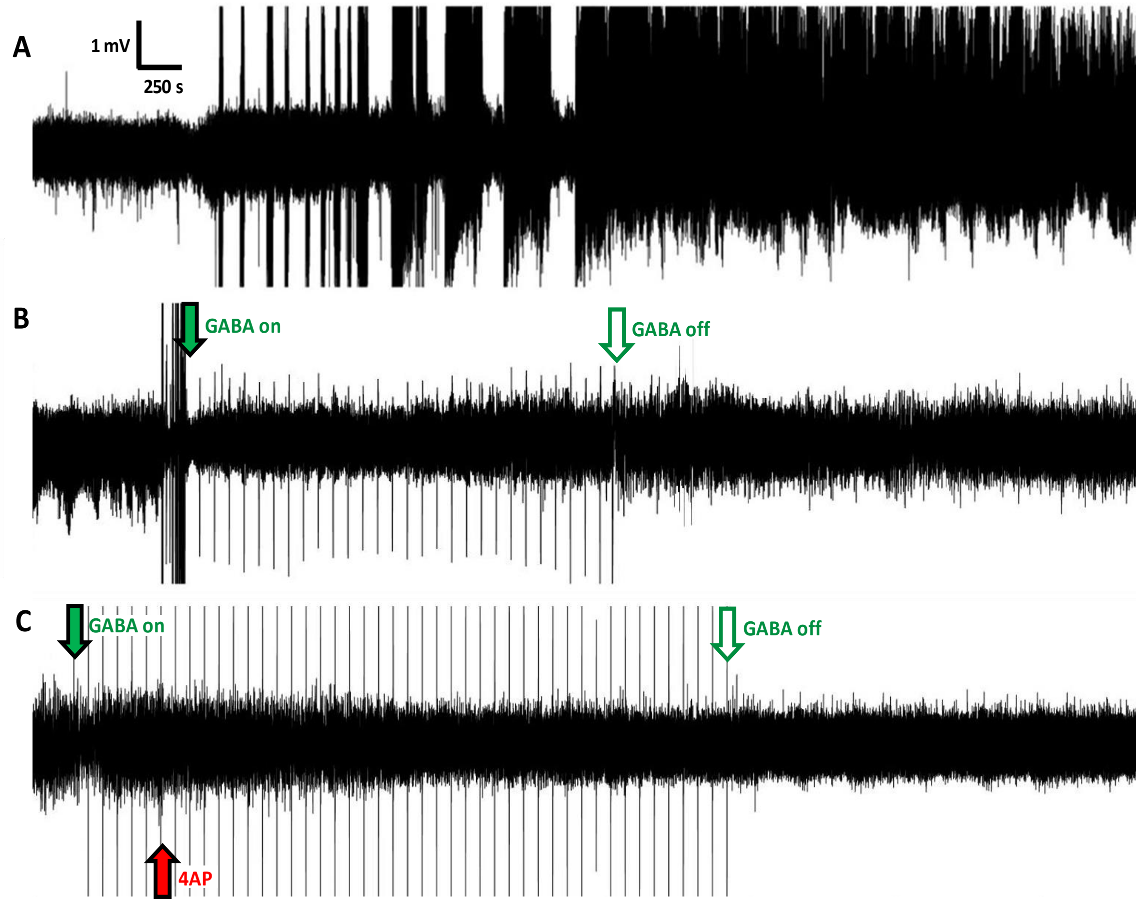


I. Uguz, C.M. Proctor, V.F. Curto, A.-M. Pappa, M.J. Donahue, M. Ferro, R.M. Owens, D. Khodagholy, S. Inal, and G.G. Malliaras, *Adv. Mater.* 29, 1701217 (2017).

Low voltage operation, high ON/OFF ratio

Implantable device stops/prevents seizures

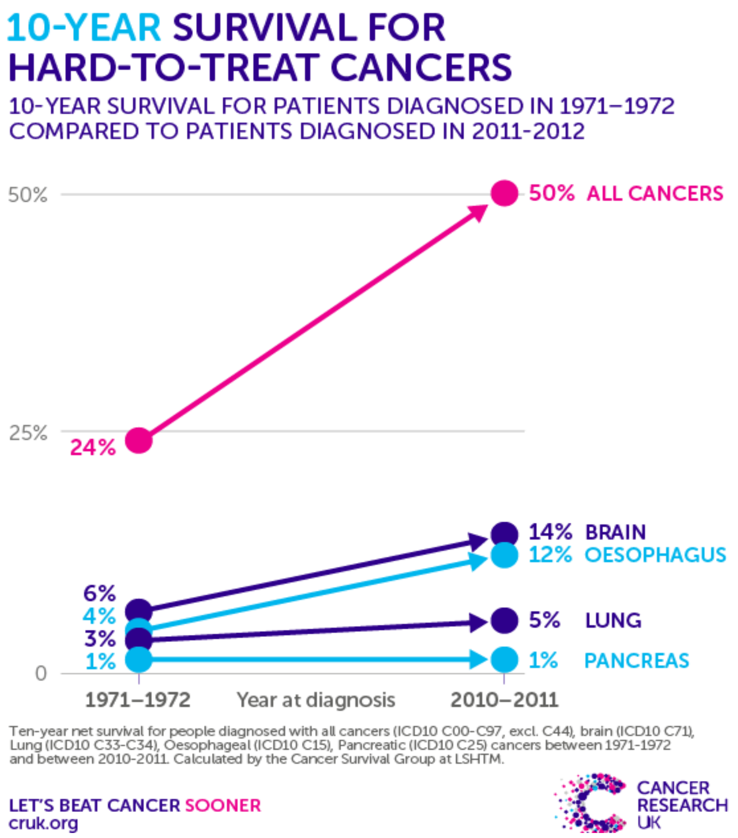




w/ Christophe Bernard (INSERM)

C.M. Proctor, A. Slézia, A. Kaszas, A. Ghestem, I. Del Agua, A.M. Pappa, C. Bernard, A. Williamson, and G.G. Malliaras, *Science Advances* 4, eaau1291 (2018).

Brain tumours



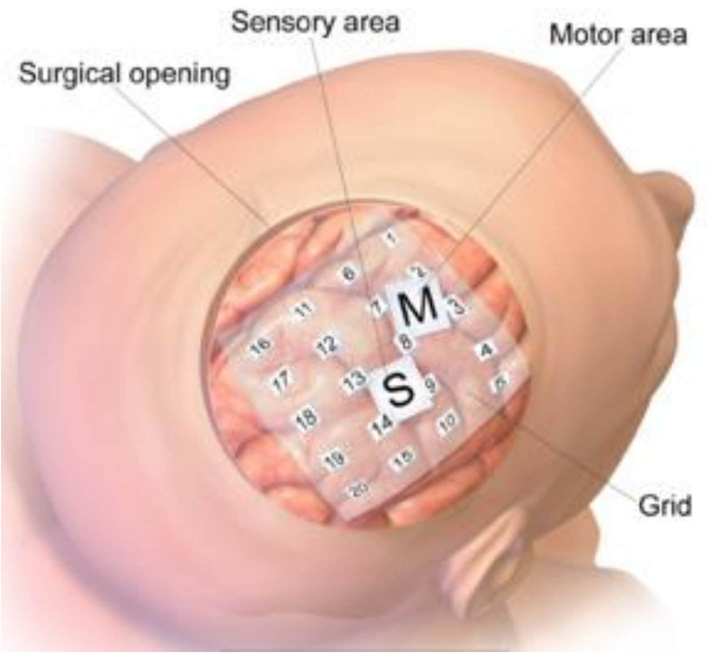
Main challenges: late presentation, bioavailability of drug

EPSRC IRC Targeted Delivery for Hard-to-Treat Cancers

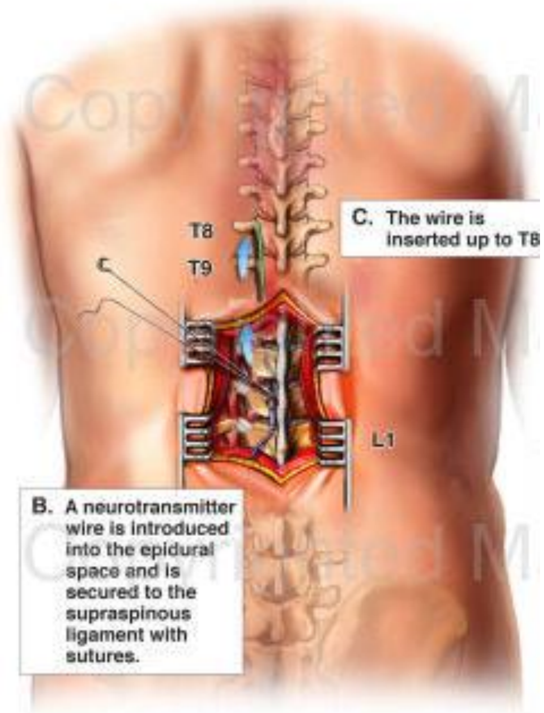
EPSRC Engineering and Physical Sciences Research Council

Implants often require highly invasive surgery

Electrocorticography



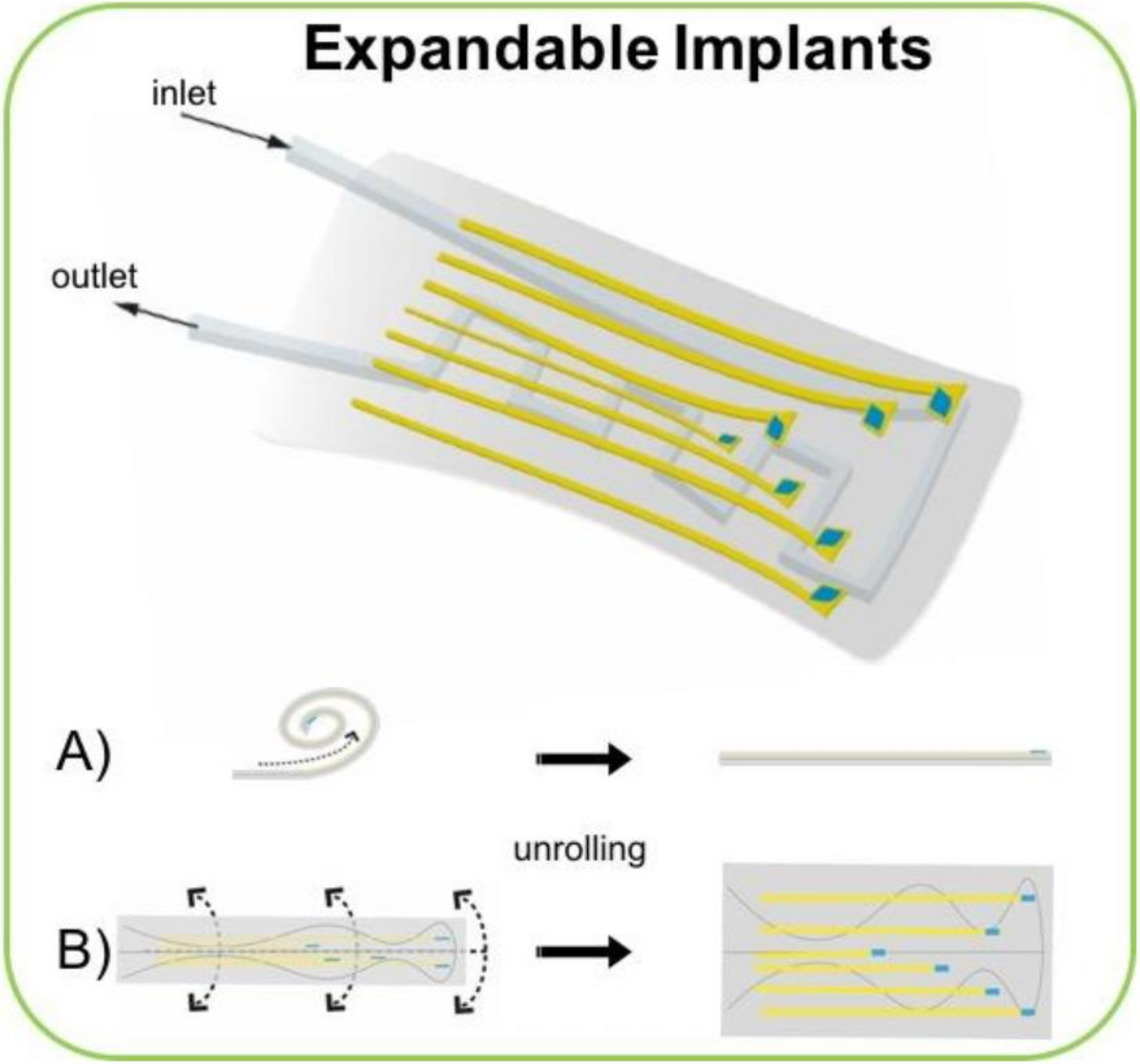
Spinal Cord Stimulation



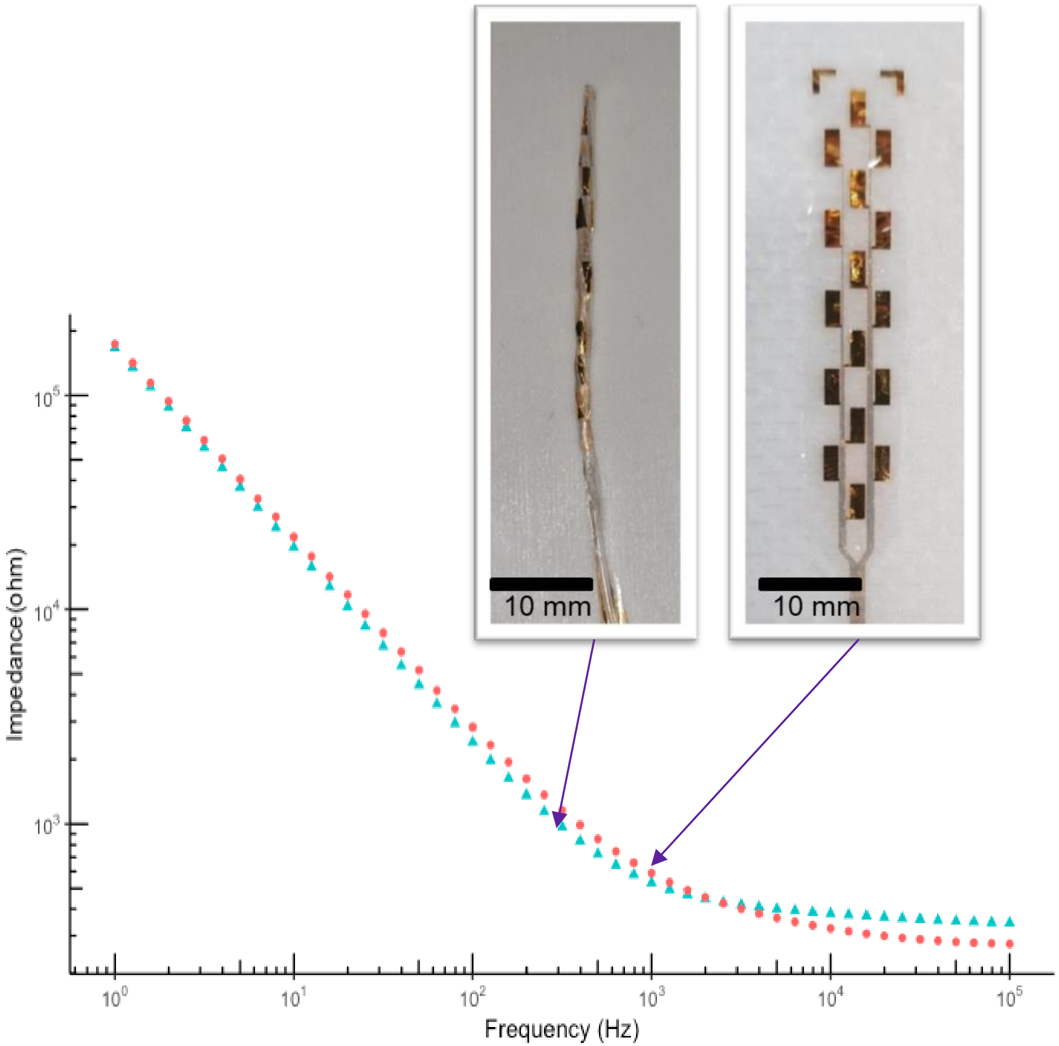
Pneumatically-activated soft robotics

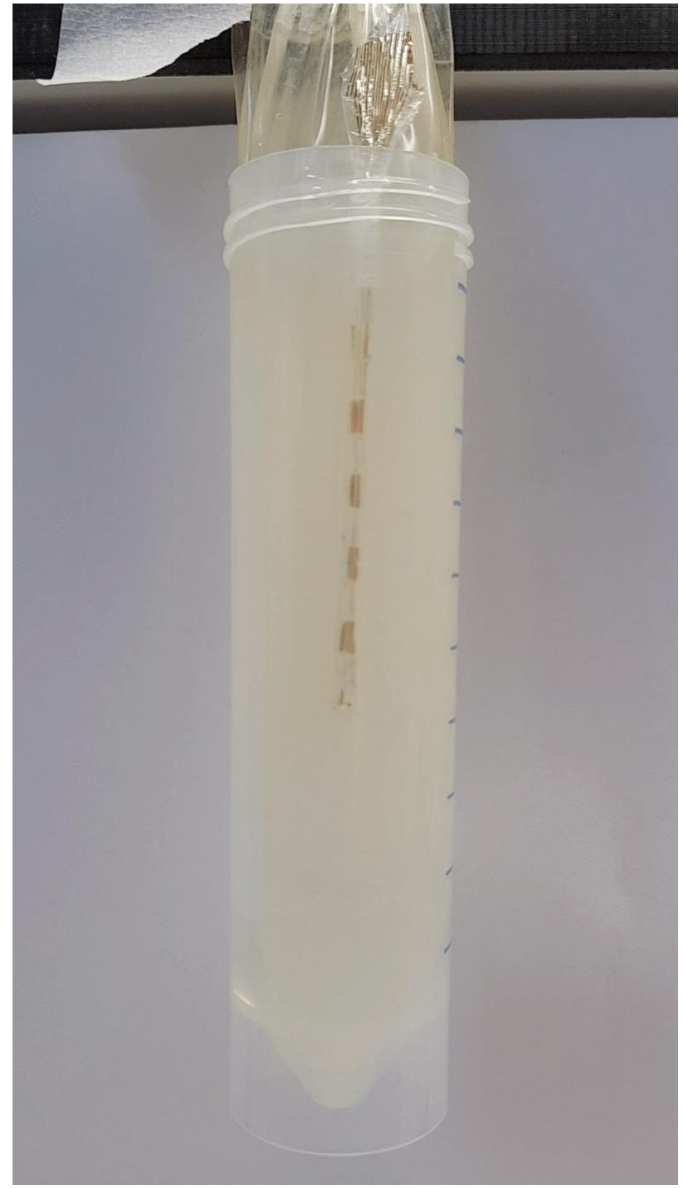
From: R.F. Shepherd, F. Ilievski, W. Choi, S.A. Morin, A.A. Stokes, A.D. Mazzeo, X. Chen, M. Wang, and G.M. Whitesides, *PNAS* 108, 20400 (2011).

Combining bioelectronics with soft robotics



Dynamic control of device shape

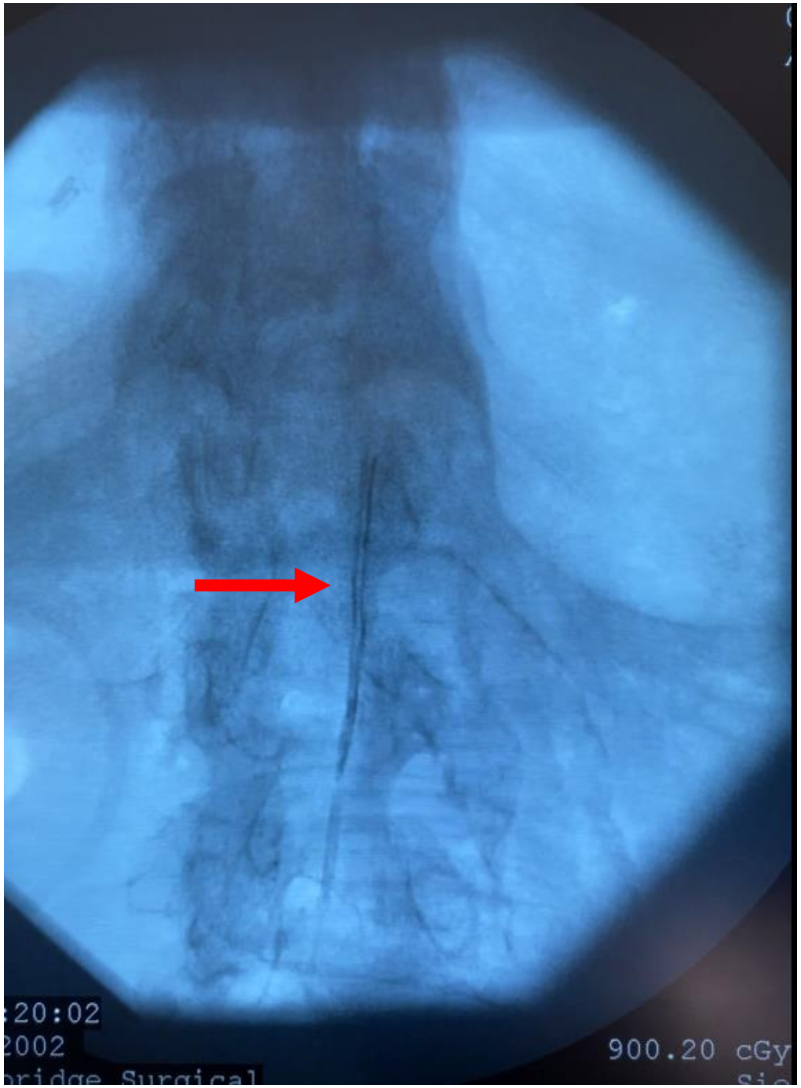




C. Proctor, V. Curto, B. Woodington, D. Barone, et al., unpublished.

Deployment in cadavers

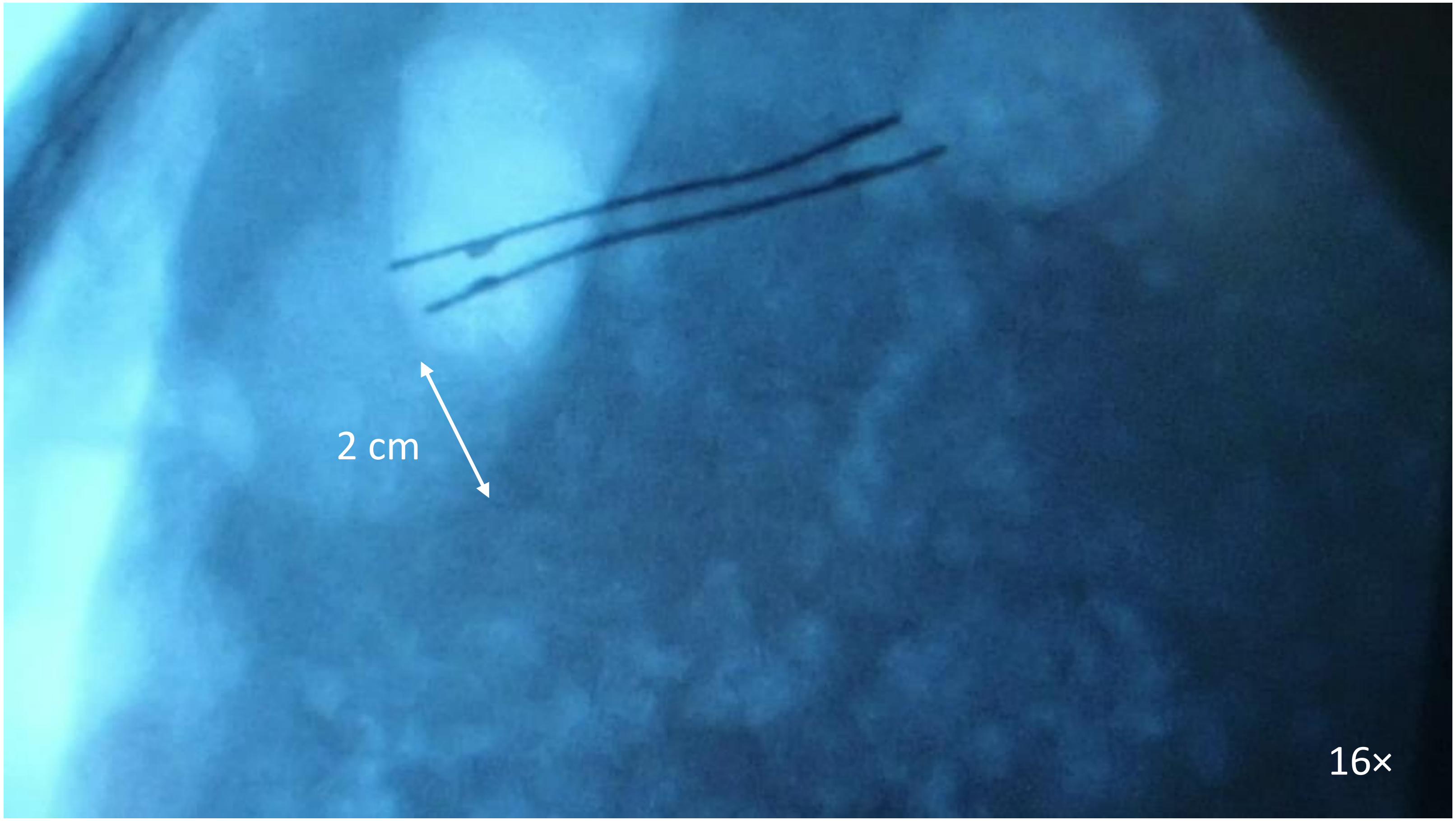
Rolled



Unrolled

C. Proctor, V. Curto, B. Woodington, D. Barone, et al., unpublished.

Deploying implant on the brain



C.M. Proctor, V.F. Curto, B. Woodington, D. Barone et al., unpublished.

Conclusions

- Implantable electronics hold considerable promise for understanding the brain and addressing its pathologies.
- Conducting polymer microgrids record single neurons without penetrating the brain. They are used in the clinic.
- Electrophoretic devices can deliver the drug without the solvent, with excellent spatiotemporal resolution. They stop/prevent seizures in an animal model.
- Microfluidics allow expandable implants that minimise invasiveness of surgery.

Bioelectronics Laboratory

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