EPIGRAPH

Graphene bioelectronics for epilepsy applications

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LINKÖPING UNIVERSITY

LABORATORY OF ORGANIC ELECTRONICS

The challenge:
Epilepsy & neurological disorders

6% of global population affected

Pharmaceutical solutions not satisfactory (side-effects, toxicity)

Surgical treatment highly problematic

Medtech solutions limited

The challenge:
Epilepsy & neurological disorders

An ideal theranostic (therapeutic + diagnostic) solution:

Drug delivery only where it’s needed
→ advanced drug delivery

…and only when it’s needed
→ advanced biosensing

The EPIGRAPH team

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Emmanuel Stratakis

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Organic (bio)electronics, drug delivery, biosensors, and “iontronics”

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Graphene laser-patterning, graphene-based (bio)electronics, sensors

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Neurological disorders, focus on epilepsy, electrophysiology, in vitro/vivo models

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Intellectual property management, medical device regulation, commercialization

Key questions addressed by EPIGRAPH

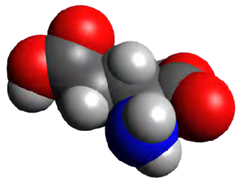
Are **graphene-based "ion pumps"** more effective at delivering relevant biomolecules?

Is metabolic activity a **predictive biomarker** for oncoming seizures?

Integrated sensing/actuation for faster and more effective therapy?

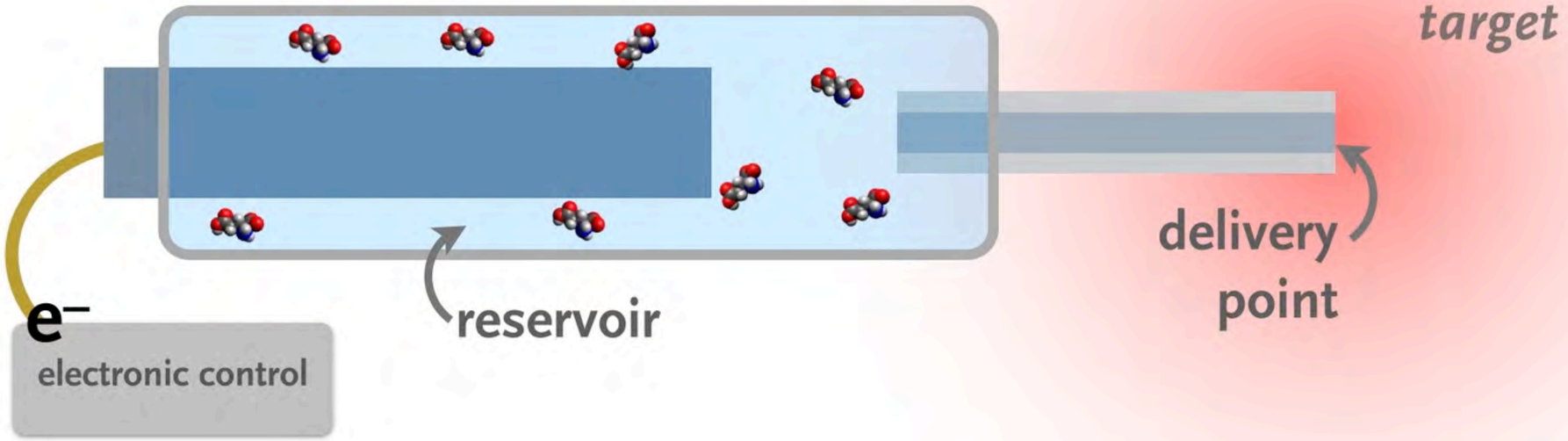
Strategies for integrating graphene-based electronics with hydrogel-based "iontronics"?

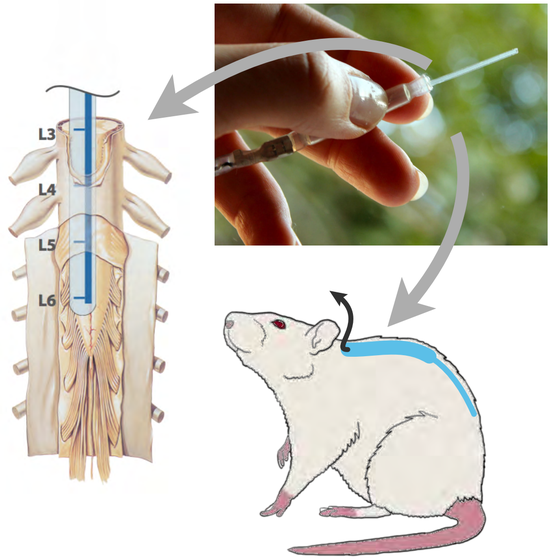
The organic electronic ion pump



therapeutic, neurotransmitter

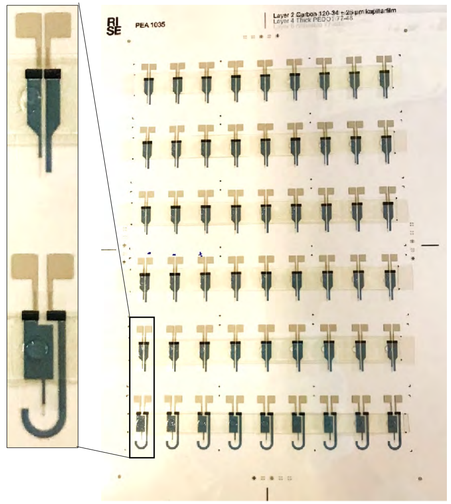
e^- electron

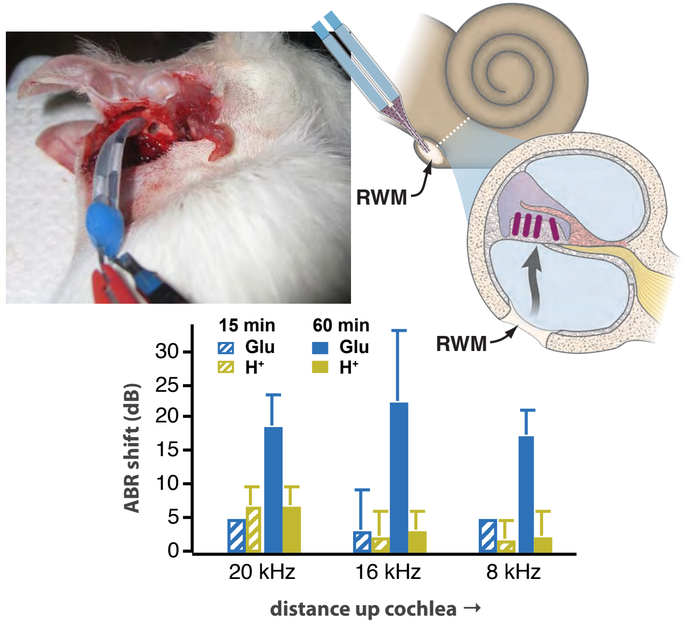




Pain therapy in awake rat[1]

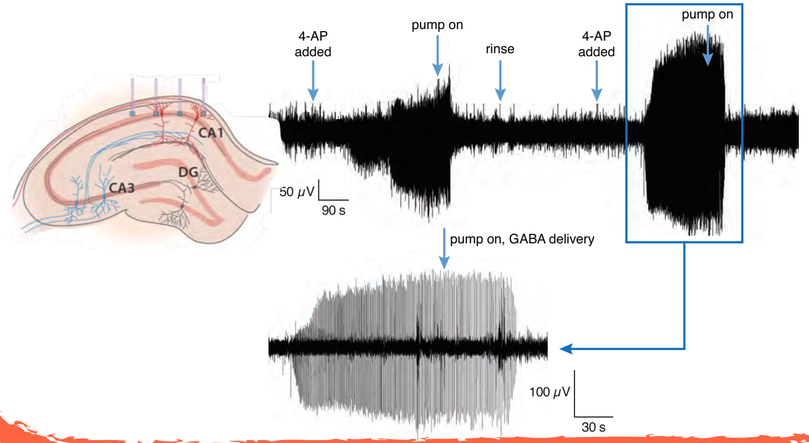
Screen-printed OEIPs[2]



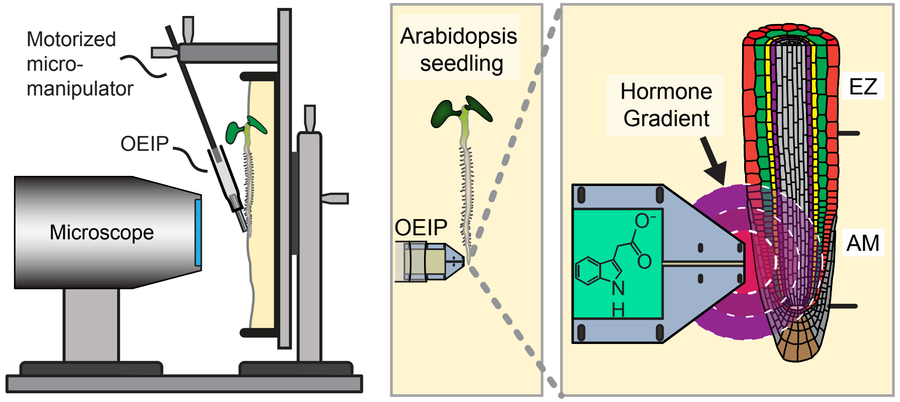


Effecting auditory func. *in vivo*[3]

Local treatment of seizures in slice model[4]



Regulating plant physiology *in vivo*[5]



1. *Sci. Adv.* (2015)
2. *Flex. Print. Elec.* (2019)
3. *Nat. Mater.* (2009)
4. *PNAS* (2016)
5. *PNAS* (2017)

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EPIGRAPH

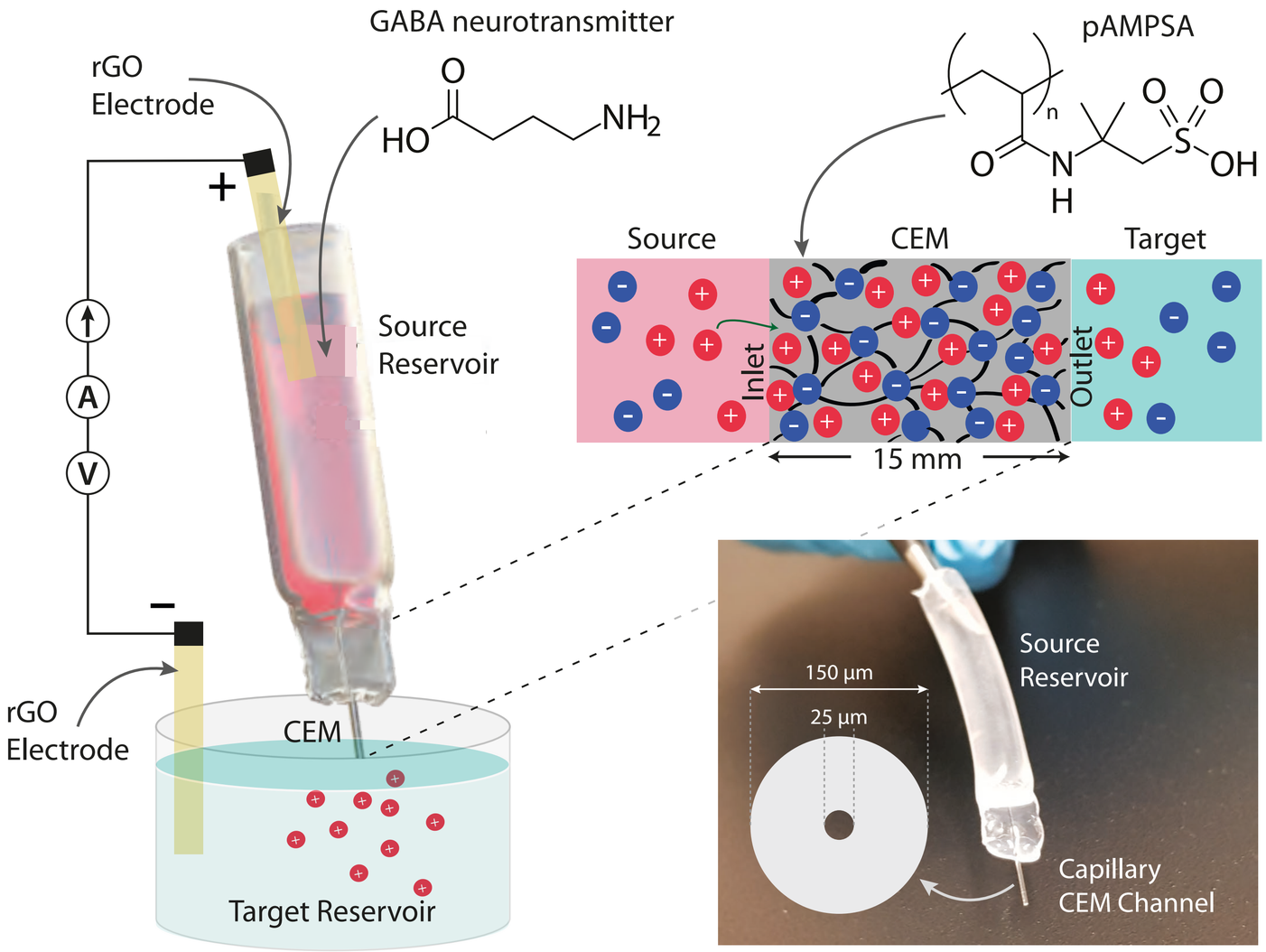
Graphene-enabled ion pumps

Laser-patterned RGO elecs on underlying PEDOT:PSS

Increased capacitance

Longer operational capacity

First integration of graphene and “iontronics”



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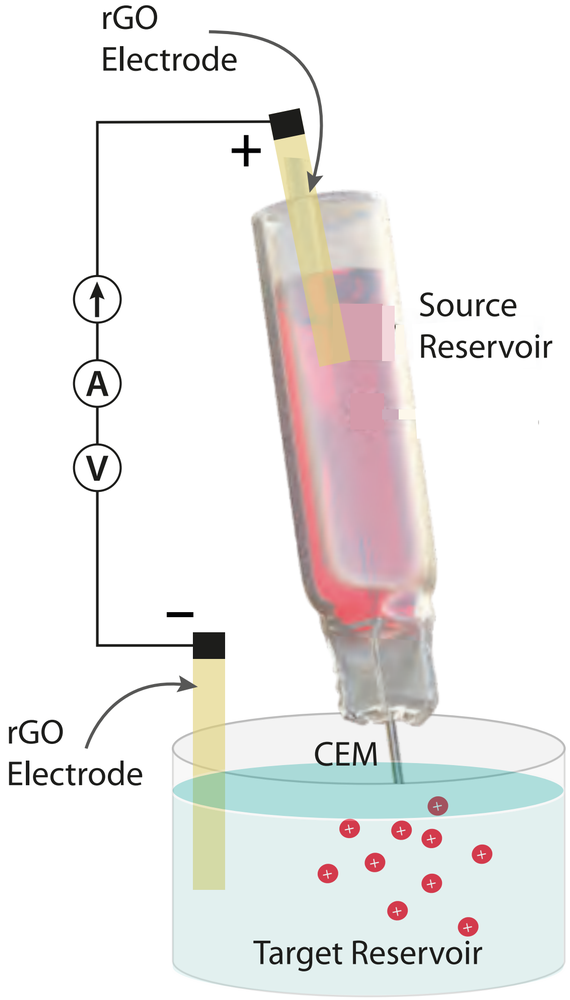
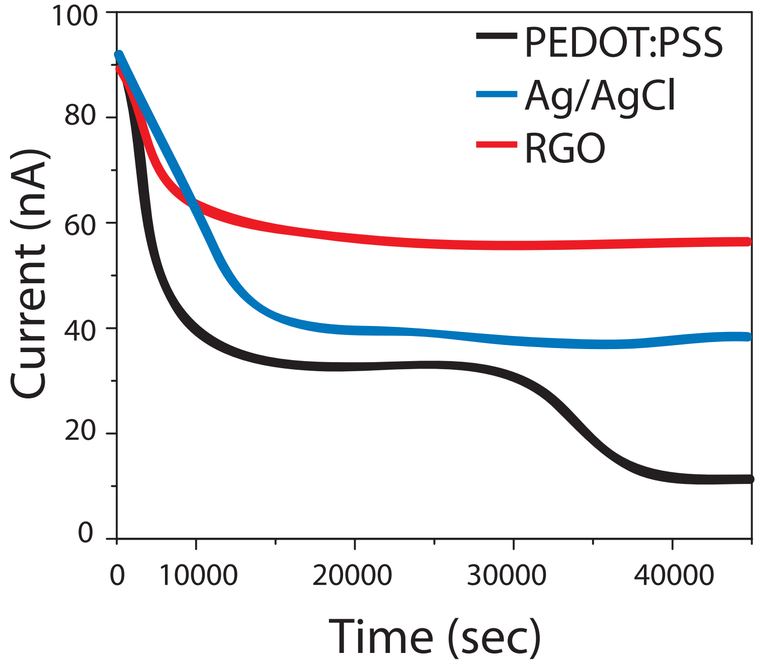
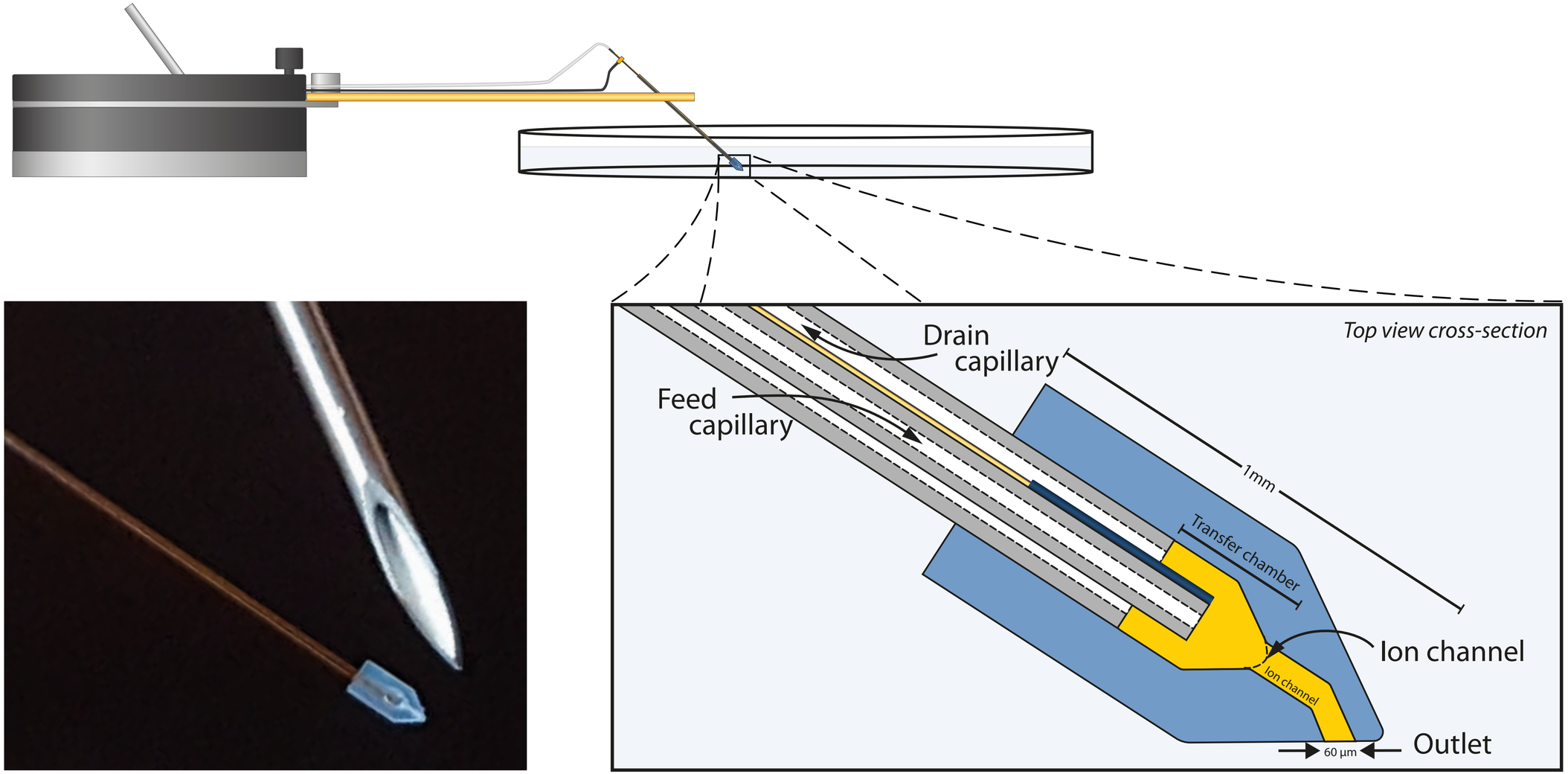


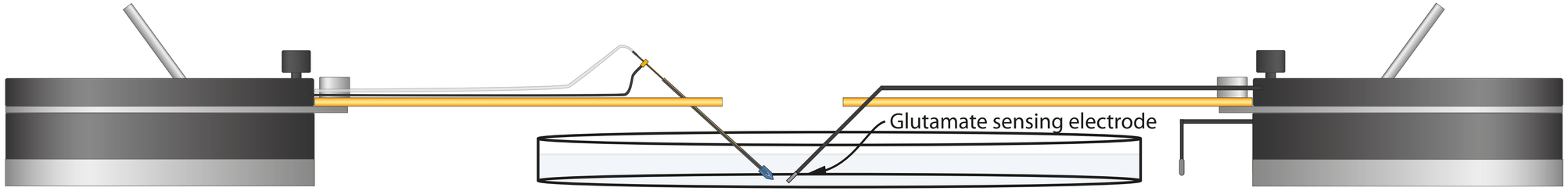


Next-gen fluidic ion pump probes



Arbring Sjöström et al. *Adv. Mater. Technol.* **5**, 1900750 (2020)

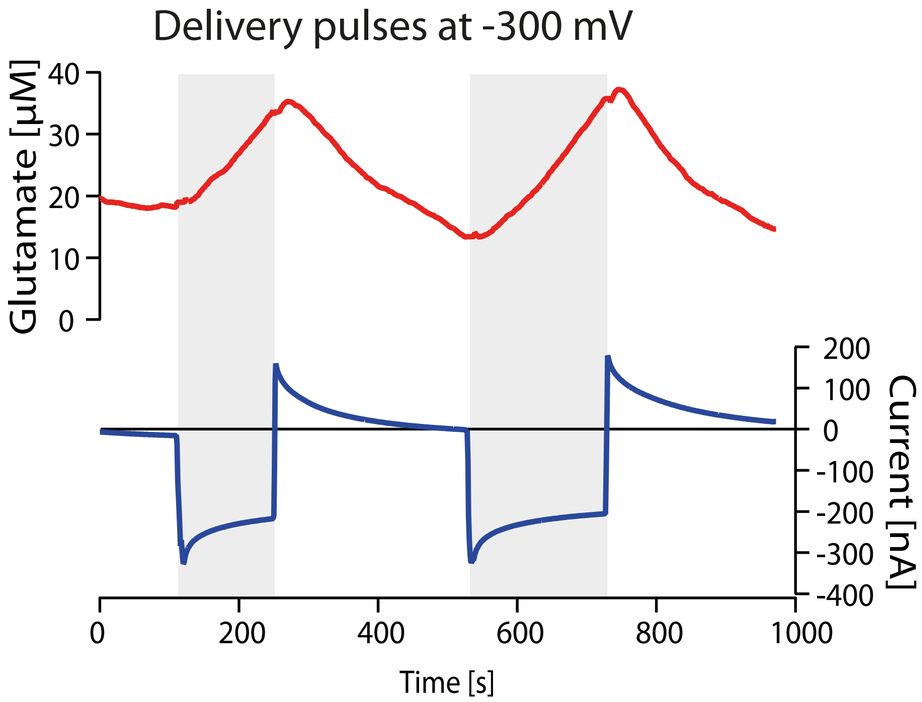
Next-gen fluidic ion pump probes



Local delivery and (bio)sensing

Excitatory neurotransmitter glutamate

Precedent to brain-slice models of epilepsy…



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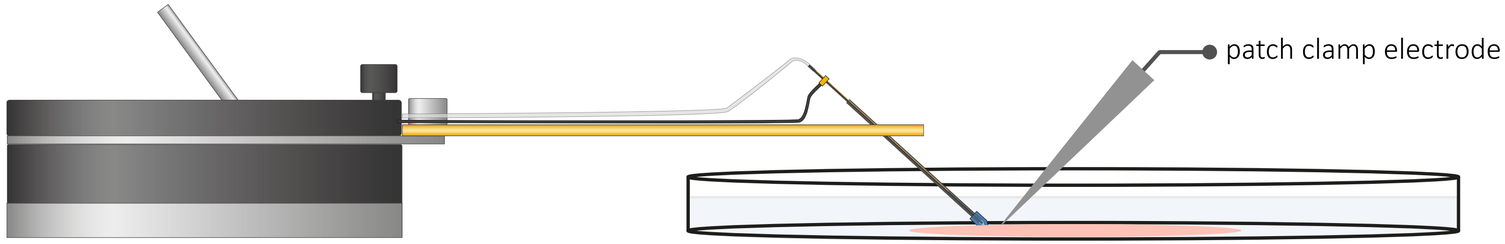
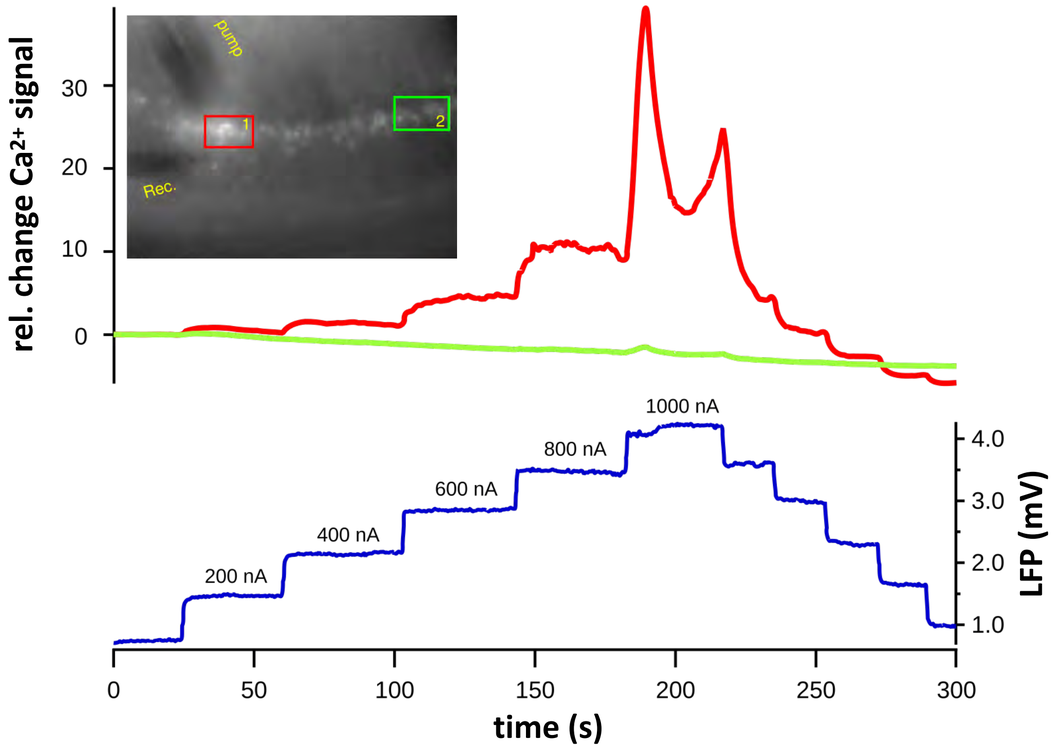
Next-gen fluidic ion pump probes



Delivery of K^+ to brain slice
(ex vivo seizure model)

Cells near outlet (red) respond

Distant cells (green, ~1 mm away)
non-responsive

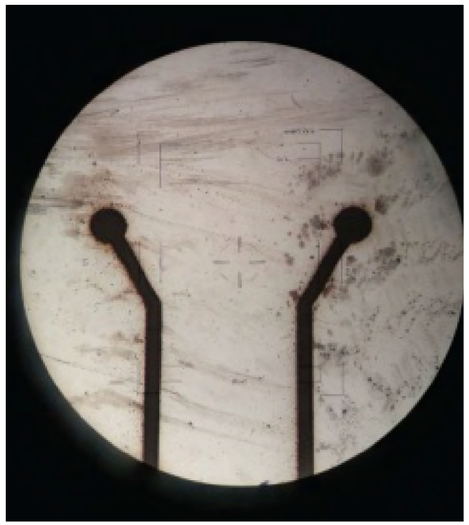


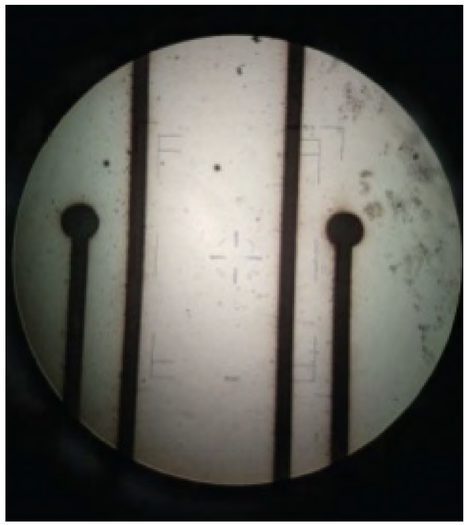
Next steps: integrated sensors and iontronics

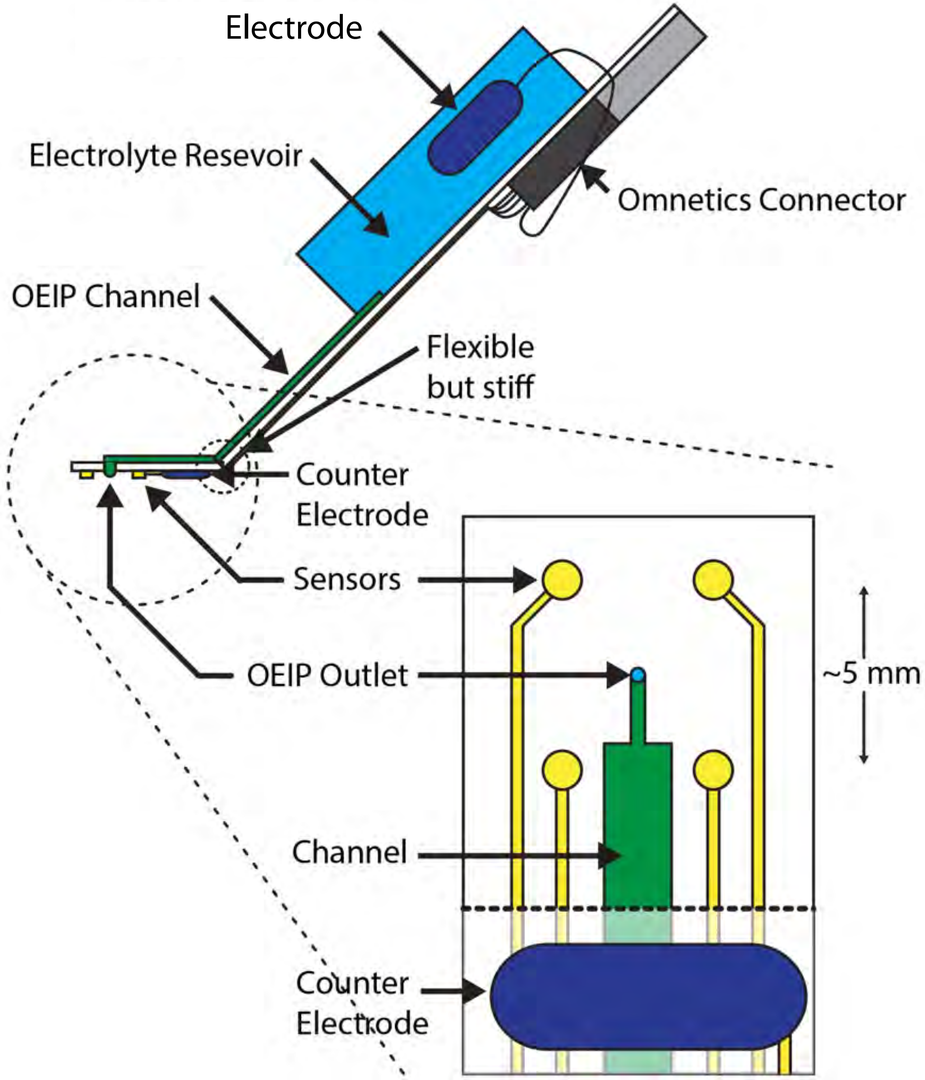
Integrate graphene sensing electrodes…

And ion pump on single substrate

Status: laser-patterned RGO on parlylene-C



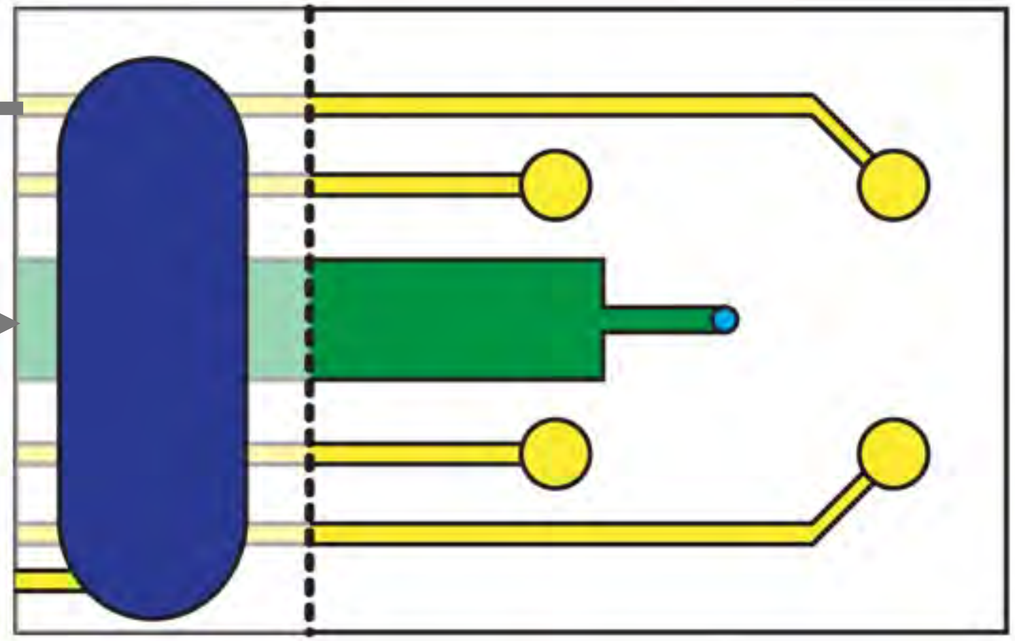




Next steps: closed-loop sensing and actuating

sensor signal

on-demand drug delivery



Sensor (glucose, etc.) and ion pump…

With closed-loop software/hardware control

Status: demonstrating RGO-enabled glucose OECT sensors, developing software control

WPs and timeline ...extended to end of 2021

WP1: Gr-based biosensor via laser processing, targeting seizure occurrence (FORTH, M1-M24)

WP2: Gr-based ion pumps (LiU, M1-M24)

WP3: Integration into EPIGRAPH-device, evaluation *ex vivo* (AMU, M13-M36)

WP4: EPIGRAPH-device *in vivo* (FORTH, M13-M36)

WP5: Management (LiU, OBOE IPR, etc.)

Responsible Research and Innovation (RRI) topics

1. **Medical implant ethics.** How should we design and plan to adhere to regulations?

2. **Animal studies.** How can we implement the “Three Rs”: replace, reduce, refine?

3. **Open science.** How to balance open-access vs publication fees, etc?

Acknowledgements

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FLAG-ERA