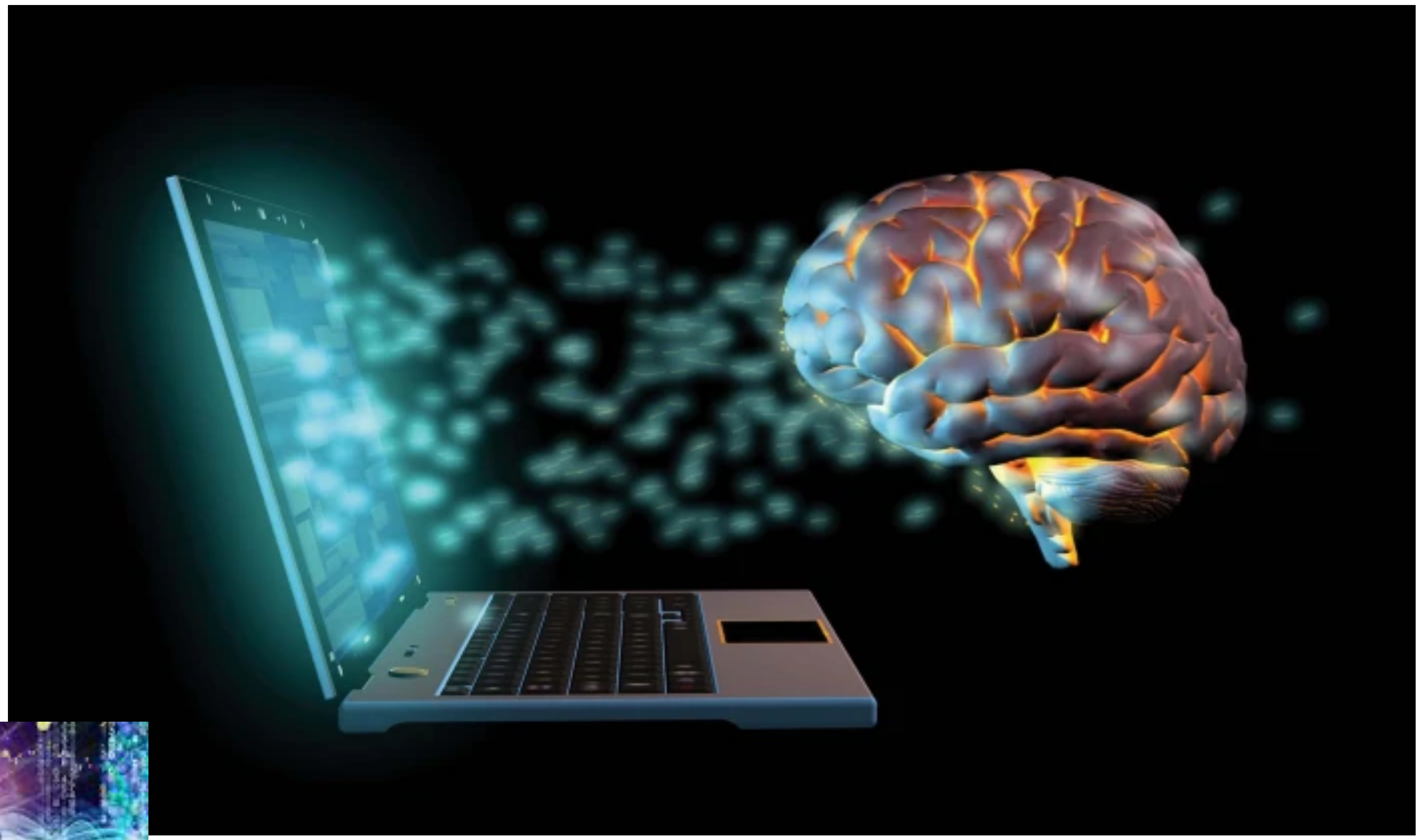
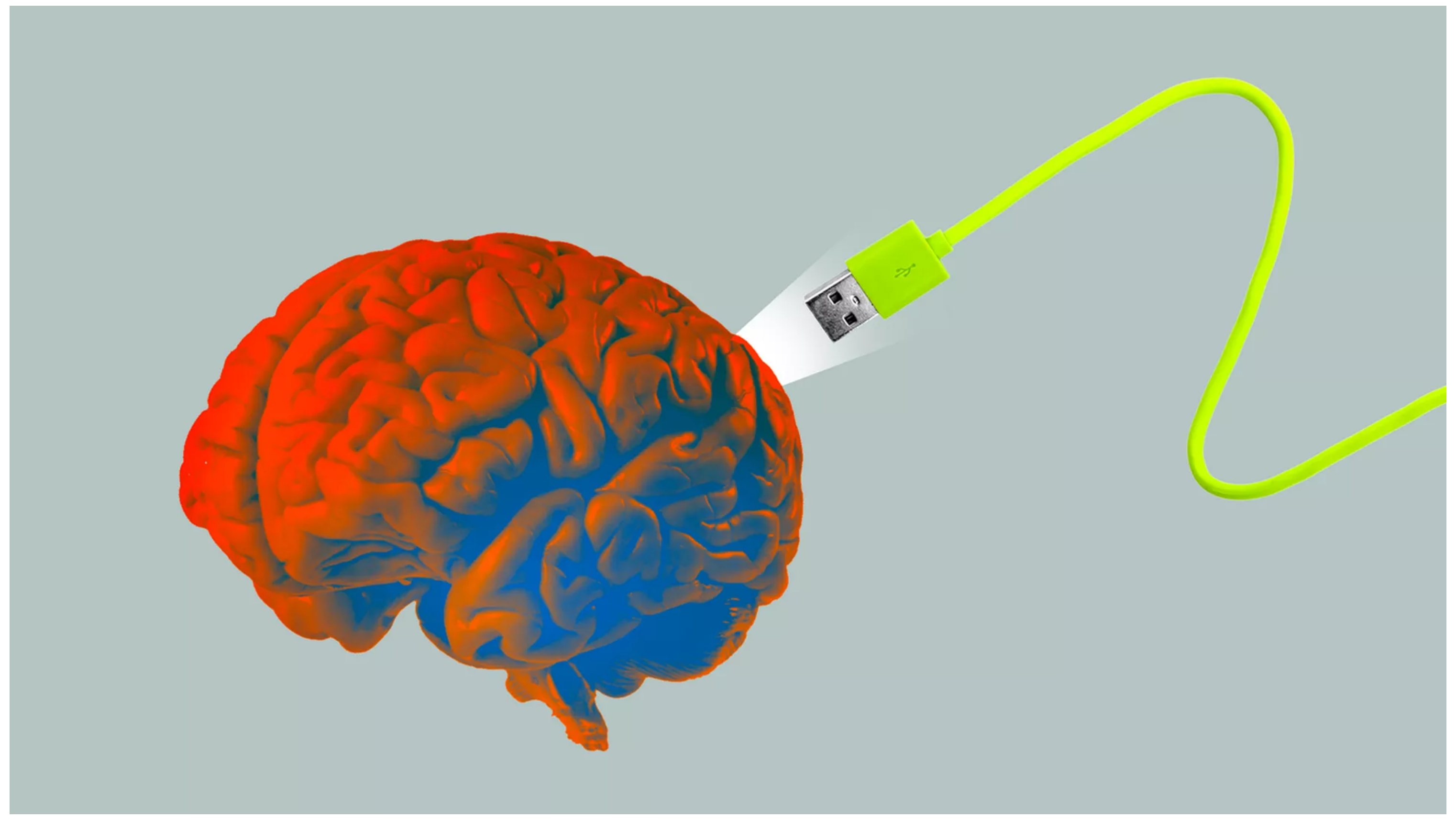
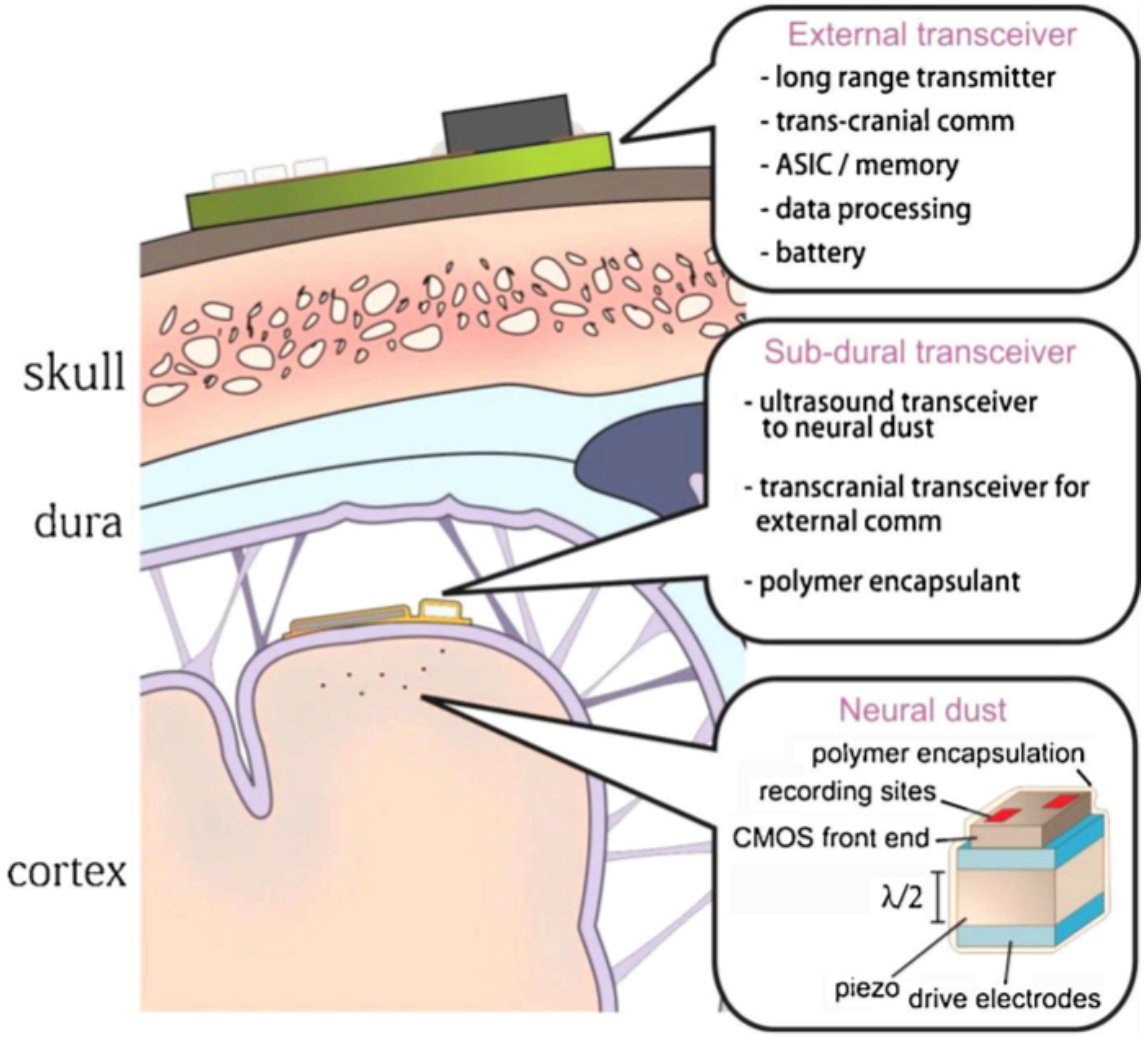
Neurotechnologies Reading Group

- Place to discuss emerging technologies for neuroscience!
- Understand fundamental principles of operation, trade-offs etc
- Big picture thinking: what problems might these technologies solve in ~10 year period?
- What are the fundamental bottlenecks with existing tools?
- Discussions + crazy ideas… collaborations?





Neural Dust



Neural Dust: An Ultrasonic, Low Power Solution for Chronic Brain-Machine Interfaces

Dongjin Seo [*], **Jose M. Carmena** [*†], **Jan M. Rabaey** [*], **Elad Alon** [*‡], **and Michel M. Maharbiz** [*‡]

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[‡]Joint senior authors

Proposal: arXiv:1307.2196v1 (2013)
Validation: http://dx.doi.org/10.1016/j.jneumeth.2014.07.025 (2015)
Recording: Seo et al., *Neuron* (2016)
Stimulation: Piech et al., *Nat. Bio. Eng.* (2020)

NEUROSCIENCE

Astellas to acquire neural dust start-up Iota Biosciences $400M

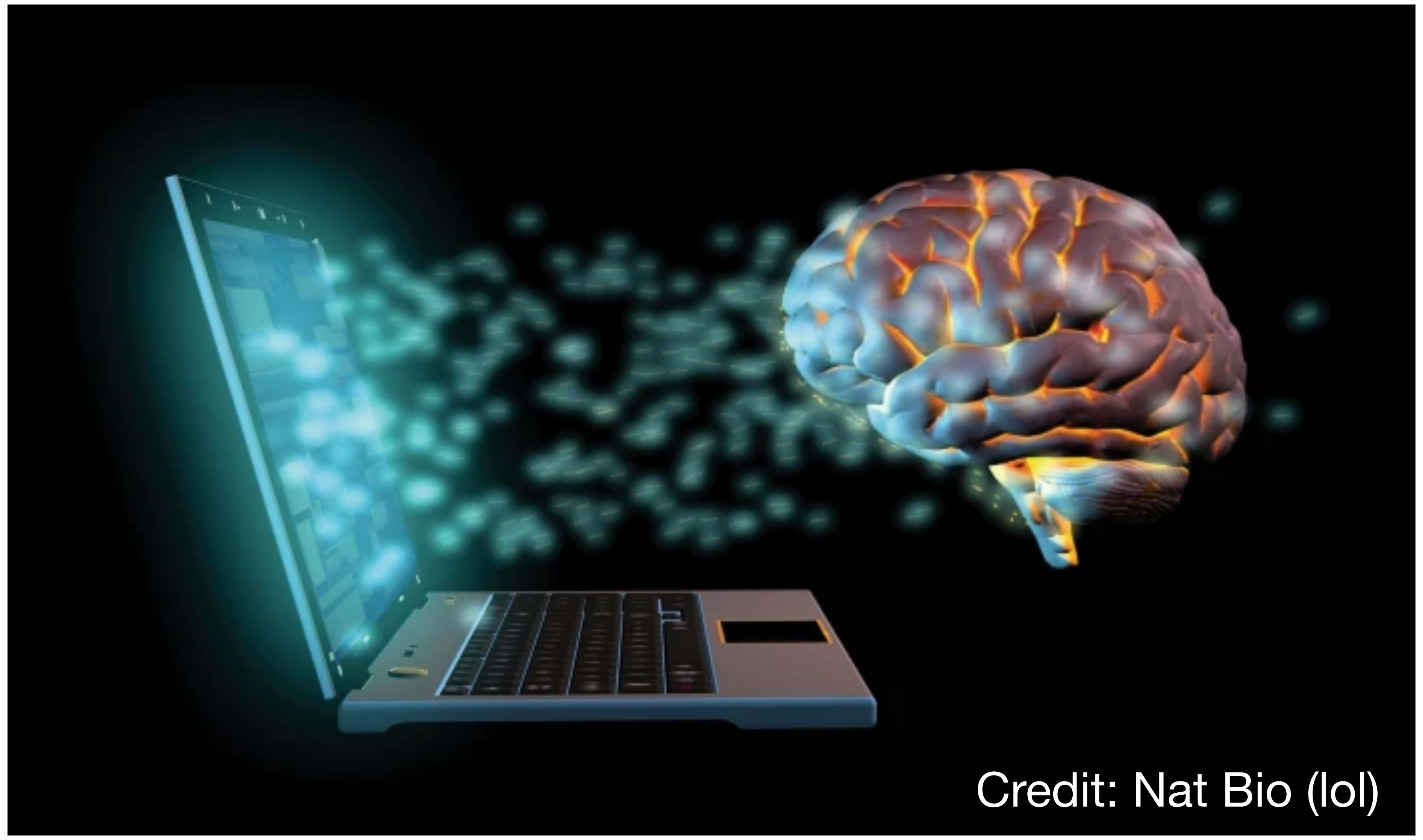
by ***Ryan Cross***

October 24, 2020 | A version of this story appeared in **Volume 98, Issue 41**

Jacques Carolan

Chronic Brain-Machine Interfaces

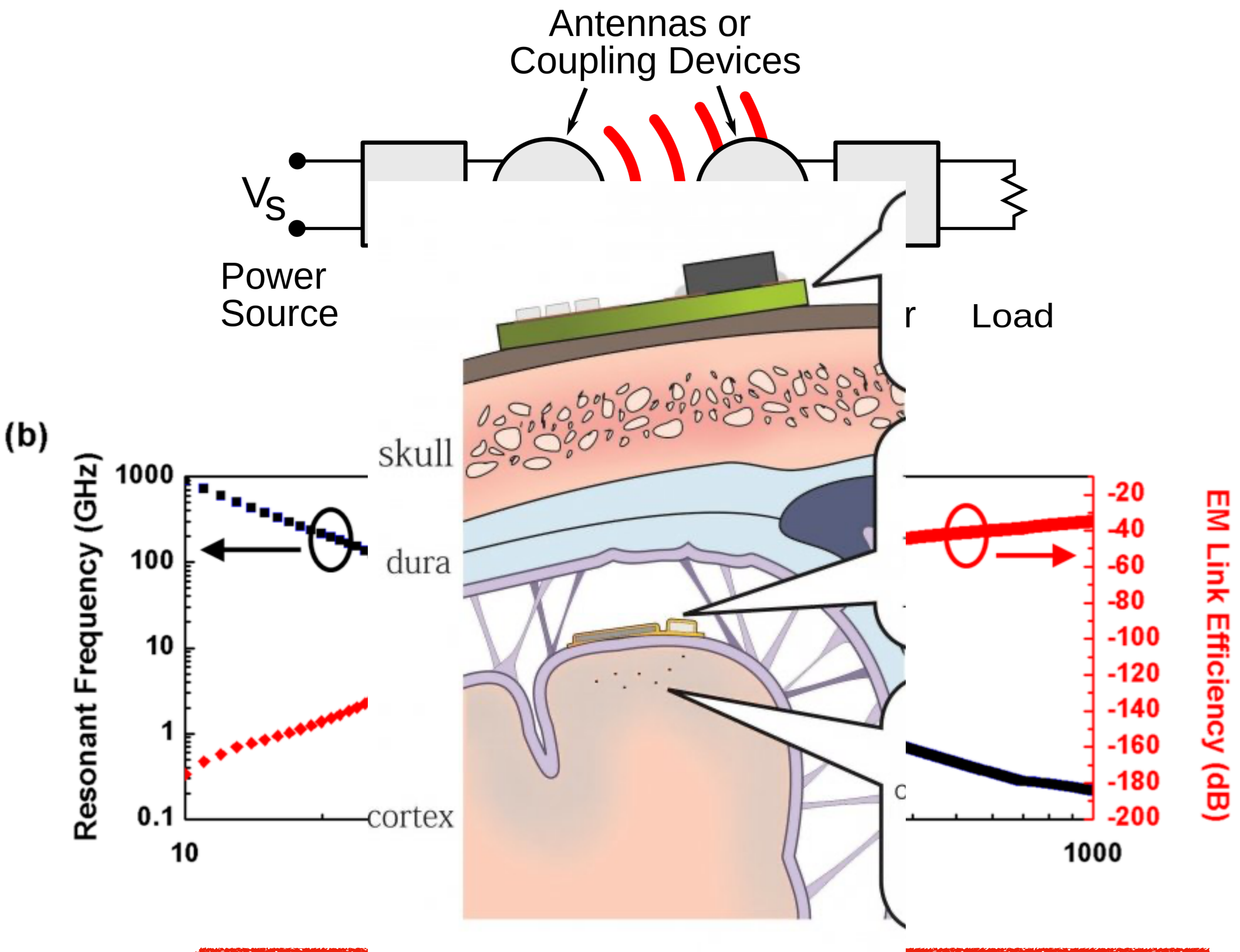
- BMI: "A device that translates neural information into commands capable of controlling external hardware of software"[1]
  - e.g. assisted living devices for individuals with motor or sensory impairments
  - Responsive neurostimulation (RNS) for drug resistant epilepsy (primitive in their sensory modalities)[2]
  - Augmented cognition (???)
- **Requirements:**
  - Wireless (c.f. N3 DARPA)
  - High-density (1000s)
  - Chronic (years)



[1] Smalley *Nature Biotechnology* (2019)
[2] Gummadavelli *Front. Neurosci.* (2018)

Implantable Devices

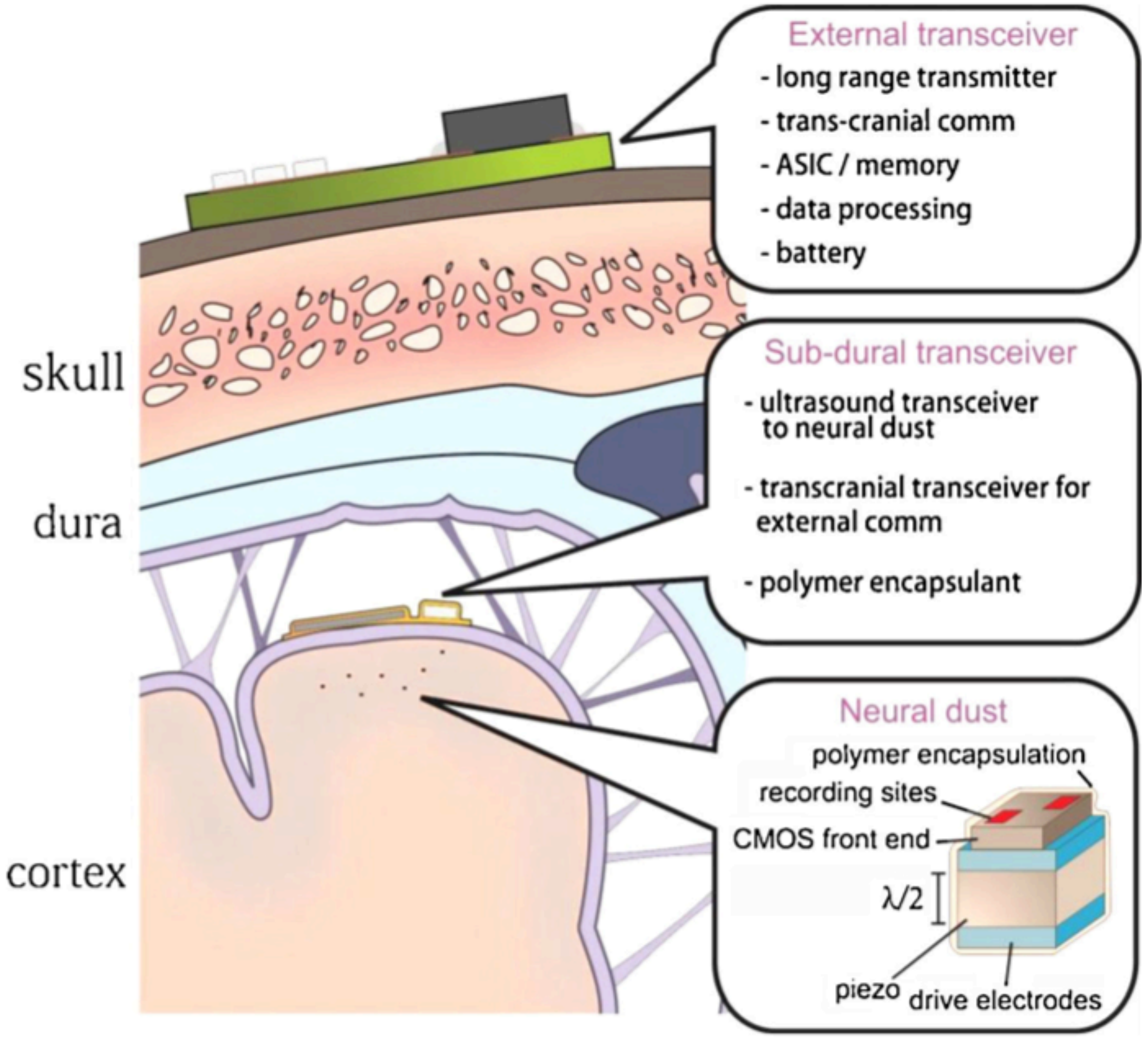
- **Size**:
  - Electrical potentials are measured differentially so small devices reduce the distance between recording electrodes (V = E*D) → decreases measured voltage (∴ poor SNR)
  - Large devices cause tissue responses (e.g. glial scarring)
- **Power**
  - With electromagnetic radiation (e.g. RF) small nodes require high frequencies (a 100 μm antenna ~ 10 GHz)
  - 10 GHz EM wave ~ 3 mm wavelength >> 100 μm
  - Loss scales exponentially with frequency!



100 μm implant @ 2 mm in cortex = - 64 dB efficiency (>10⁶)
10 mW/cm² → **40 pW** of power (record[1] ~10 μW / channel)

[1] Biederman et al., IEEE (2013)

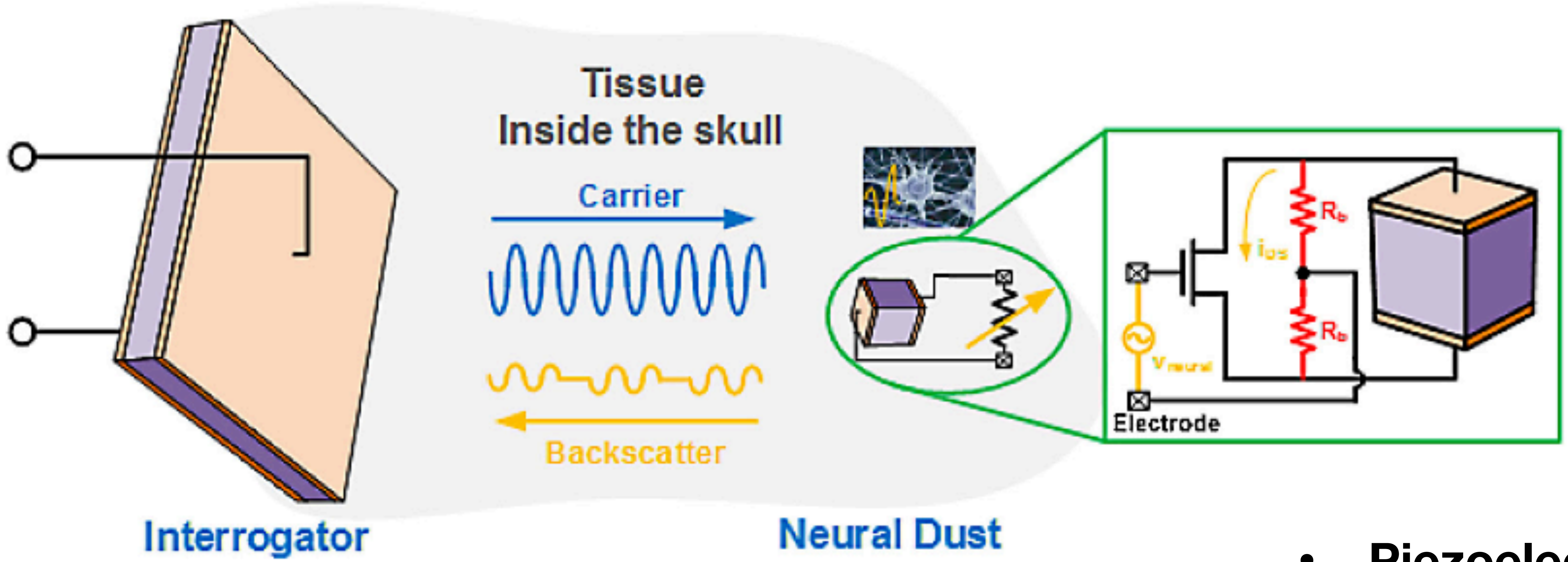
Solution: Acoustic Waves!



- **Ultrasound for power and communication**
  - Much lower loss (0.5 dB/cm/MHz)
    - 10 MHz = 1 dB loss (20%) (c.f. EM = 20 dB ~99%)
  - Higher allowed intensity (FDA) ~ 100 mW/ cm2 ~ 10x EM
  - Speed of sound is slower (~1500 m/s) ∴ wavelength is shorter!
    - 10 MHz = 150 µm

Seo et al., arXiv:1307.2196v1

Principle of Operation



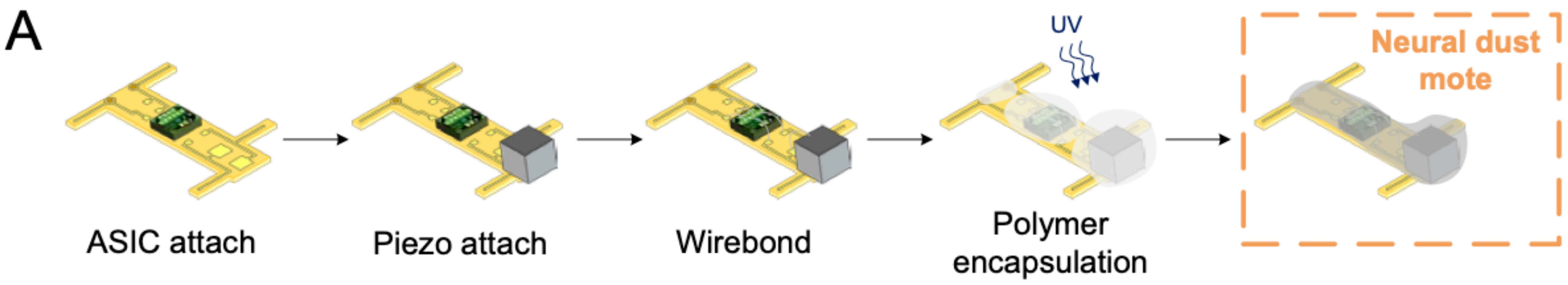
For a 100 μm dust node 2mm into the brain ~ 500 μW (10^7 > EM)

- **Piezoelectrics**
  - A material that couples mechanical properties and electrical properties
  - e.g. squeeze you can generate a voltage or apply voltage and you can squeeze
  - PZT (lead zirconate titanate 🤮) or BaTiO
- A circuit that can modulate the impedance of the PZ dependent on an action potential

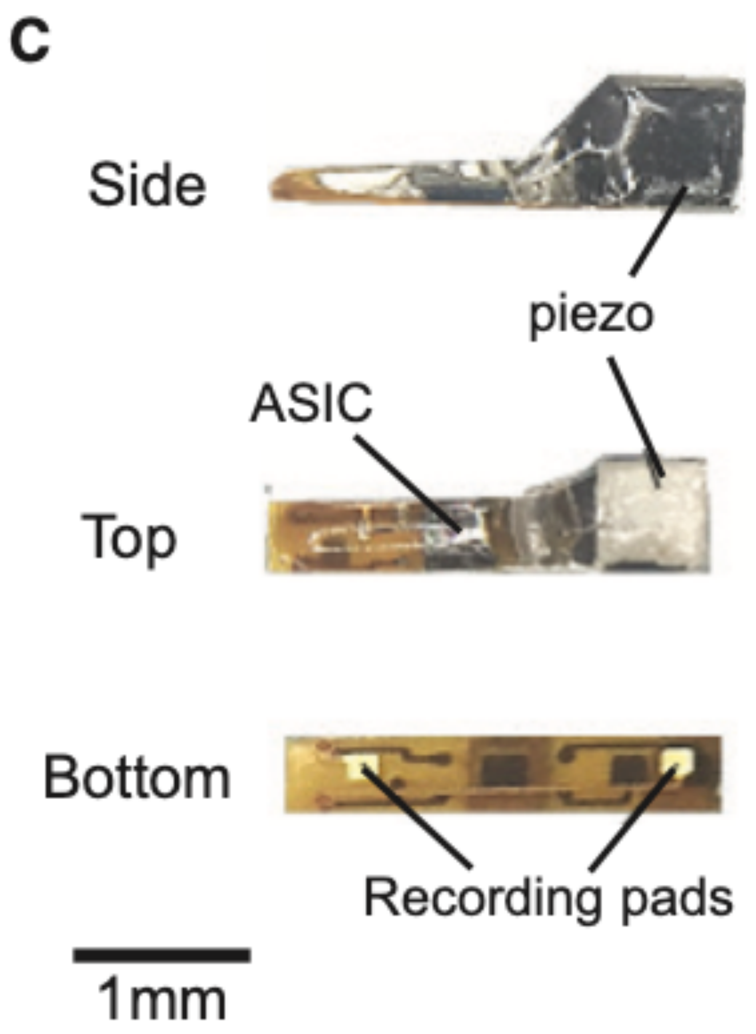
Seo et al., arXiv:1307.2196v1

Neural dust assembly

ASIC for amplification, conversion, etc



Wires for ‘ground truth data’

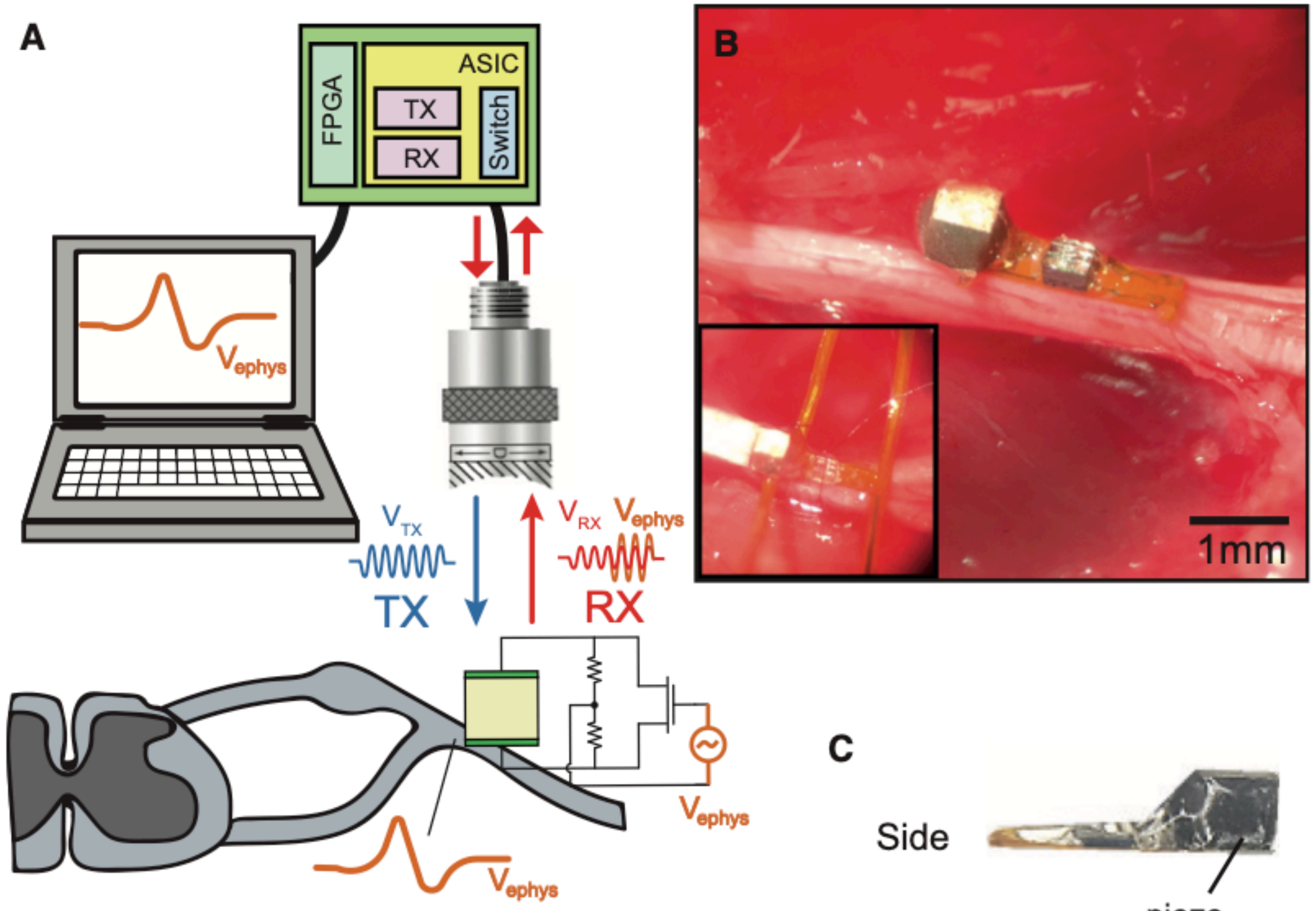


PZ: 750 µm^3
ASIC: 500 µm x 450 µm

Full device:
0.8 x 3 x 1 mm

Seo et al., *Neuron* (2016)

Peripheral Nervous System

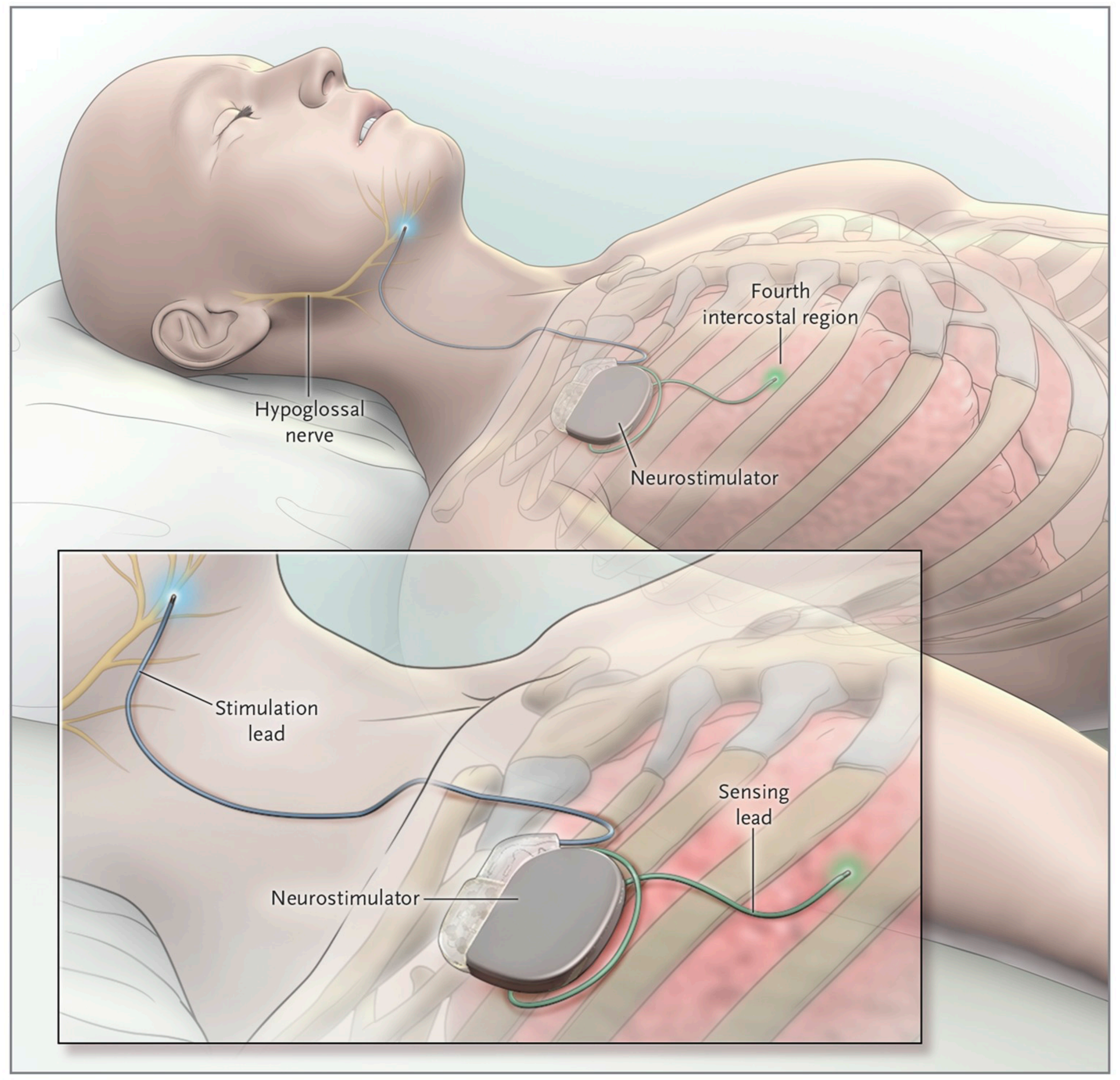


Seo et al., *Neuron* (2016)

Applications:

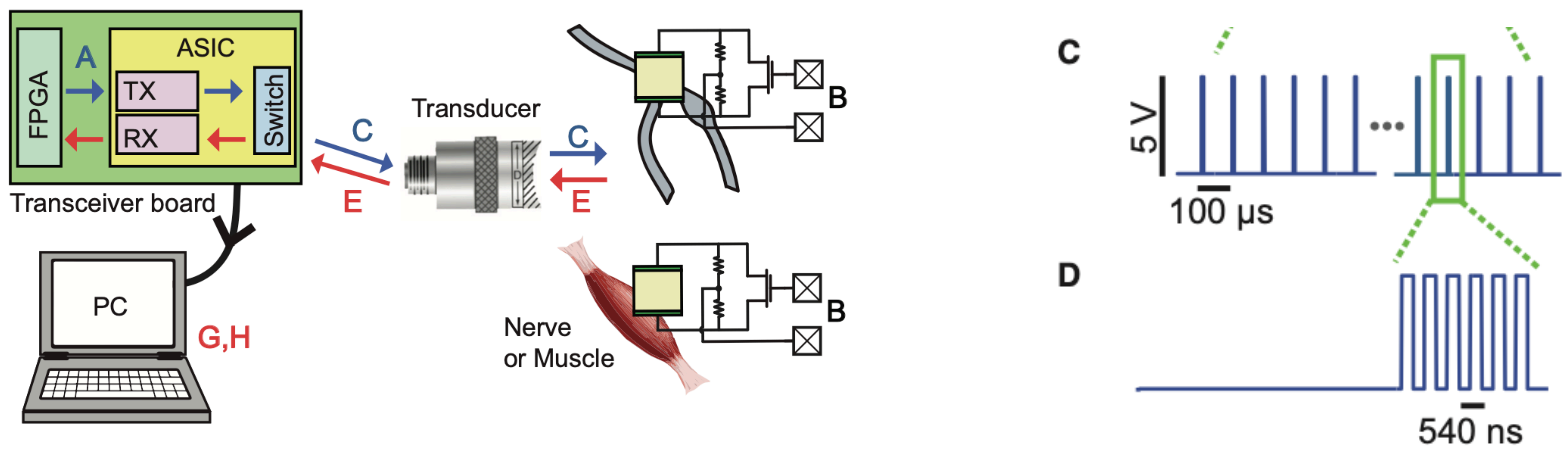
- Sleep apnea
- Control of bladder function in paraplegic patients
- Diabetes
- Rheumatoid Arthritis

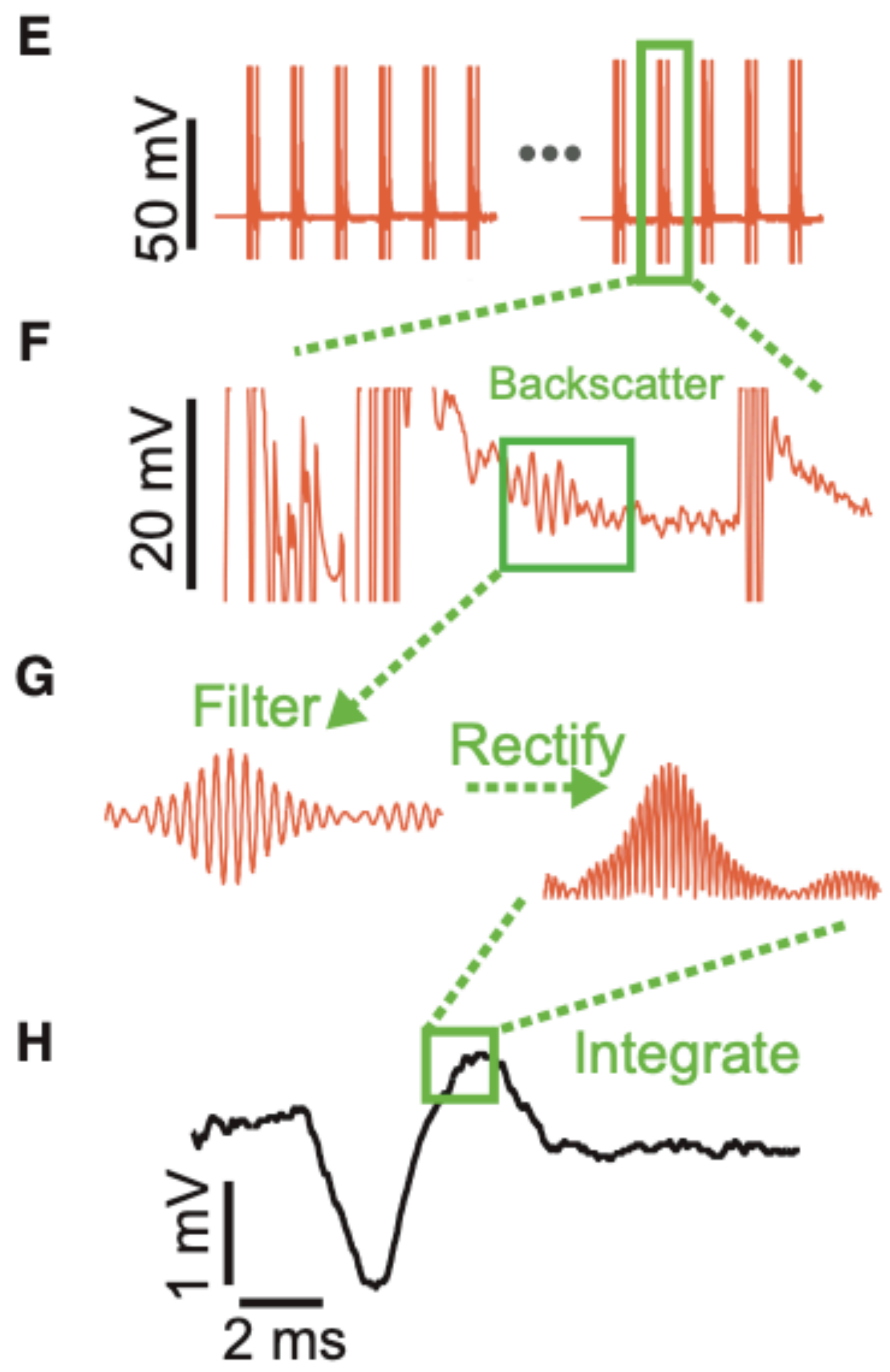
Famm et al., *Nature* (2013)



Communication

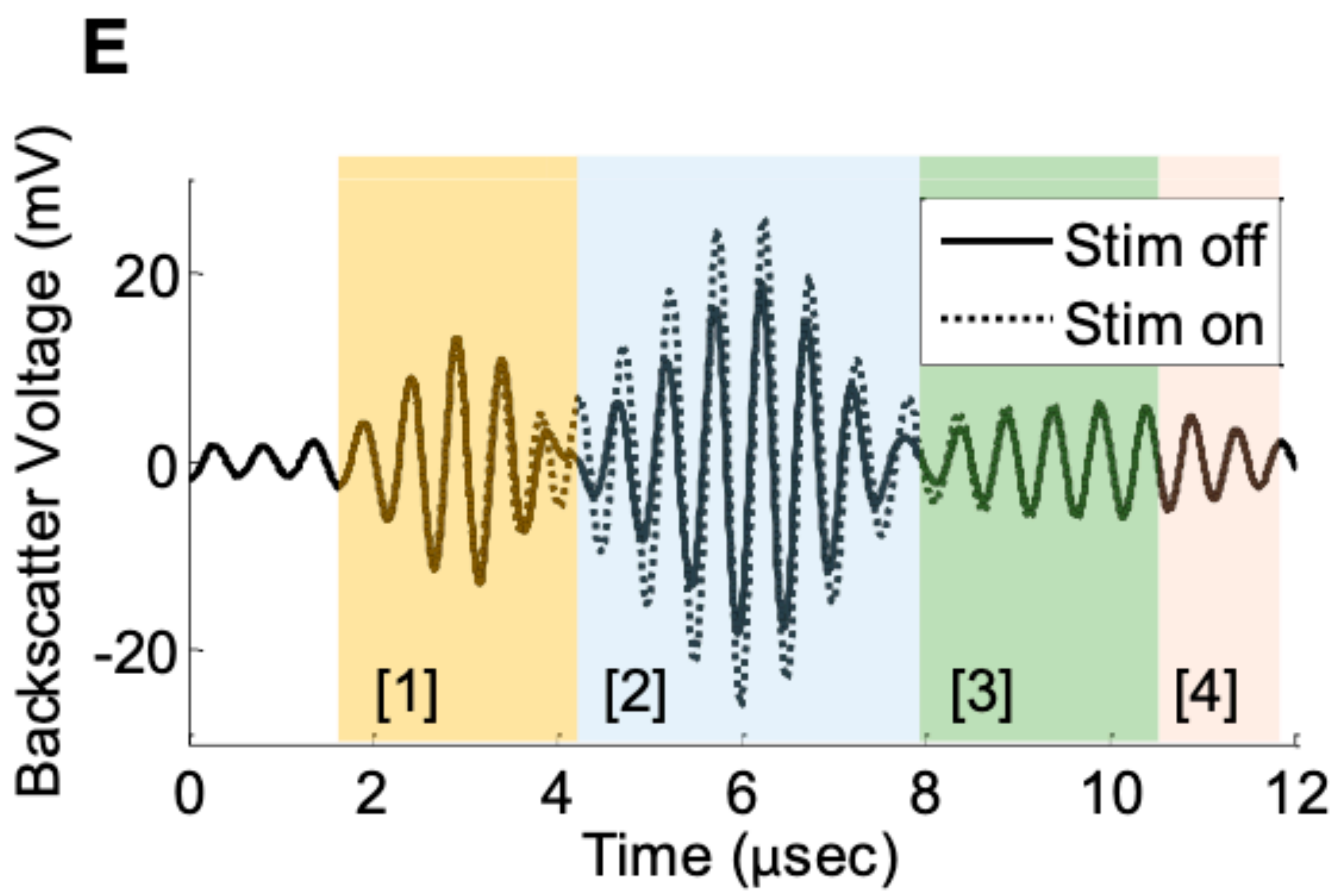
Send in pulses every 6 ns then listen!



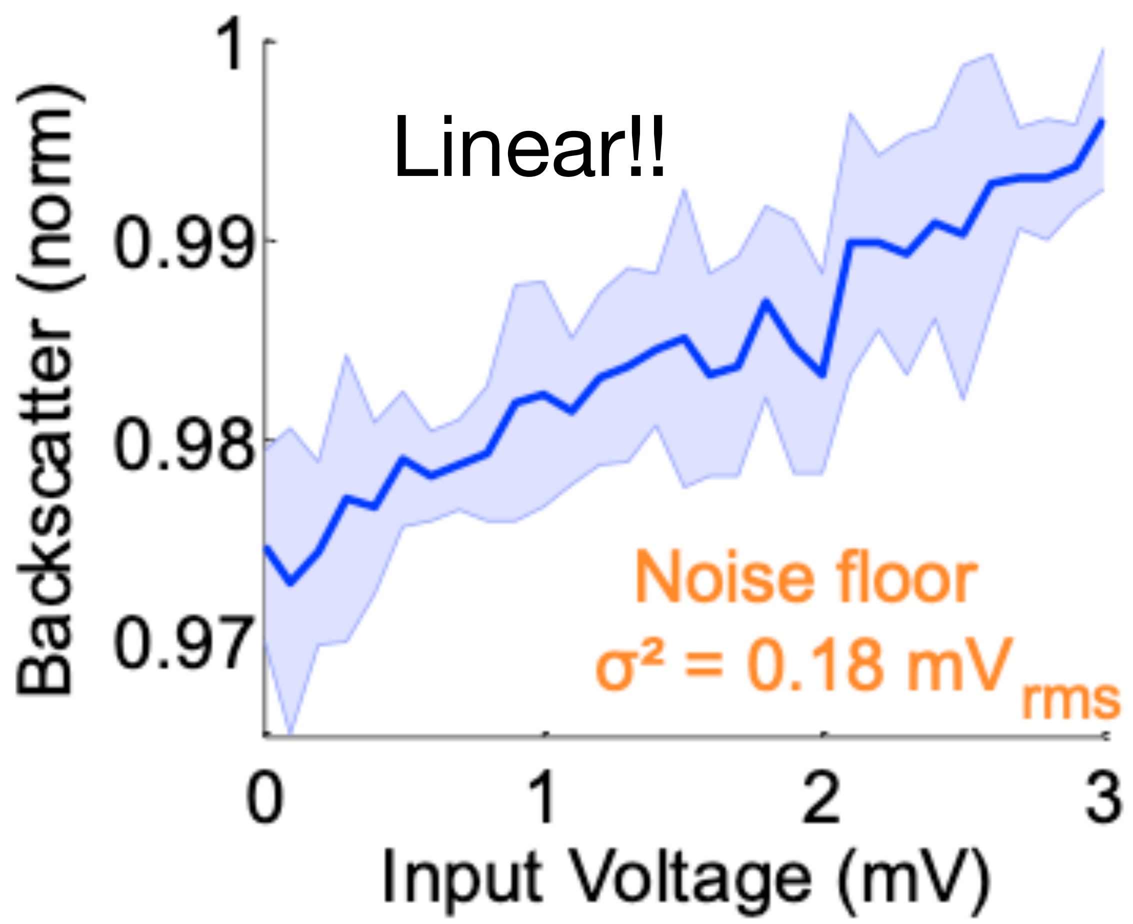


10 KHz readout!

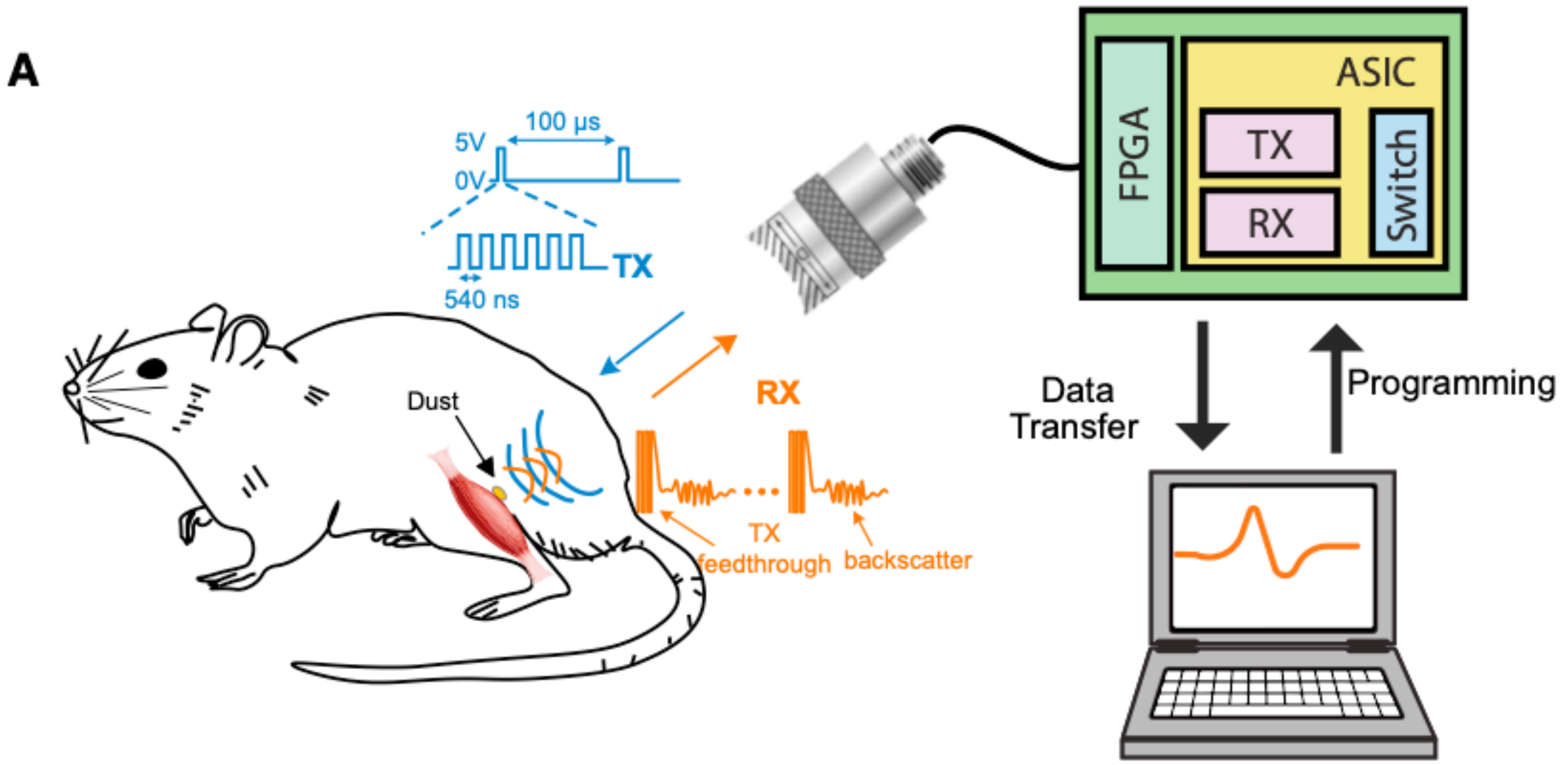
Calibration

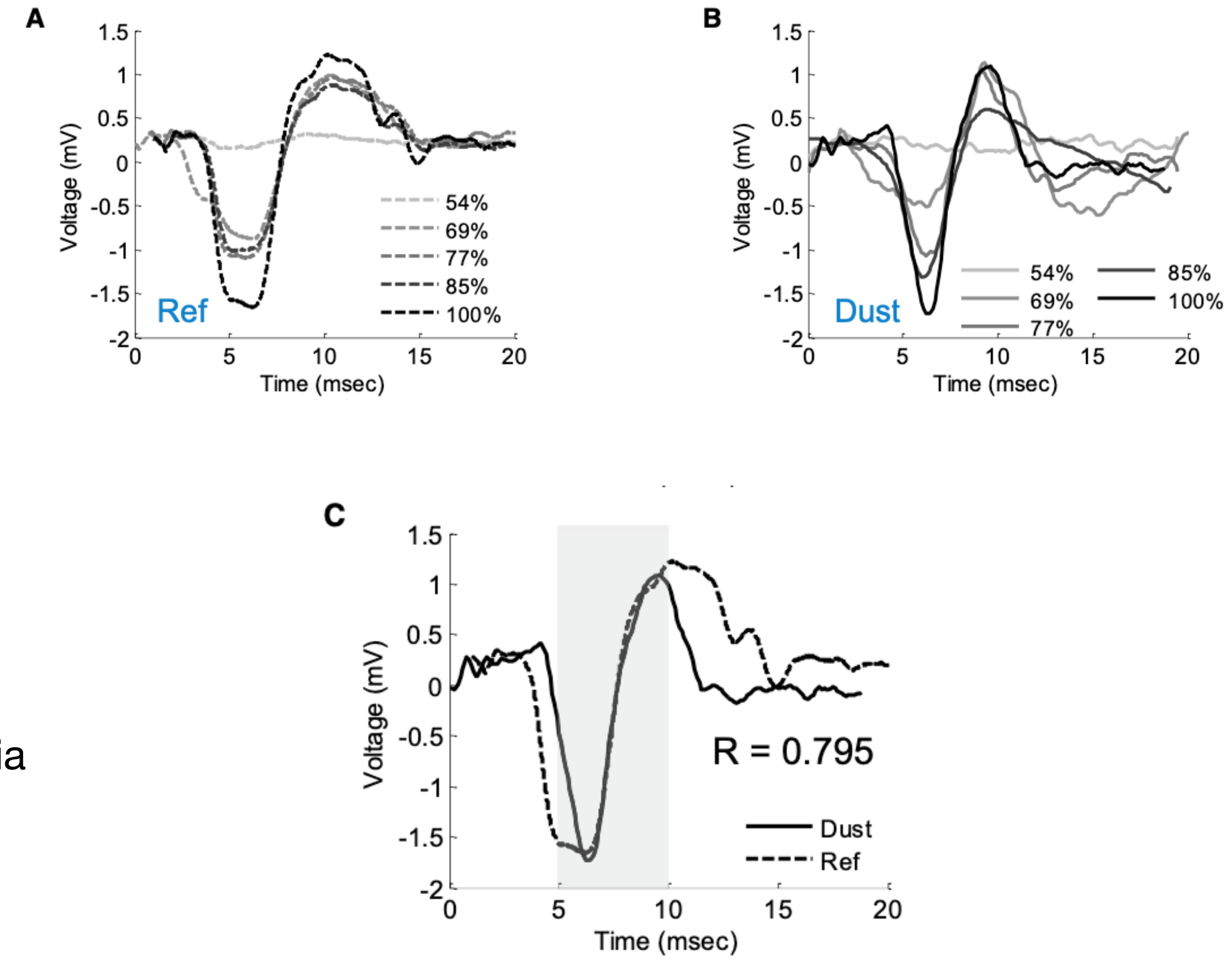


1. Water-Polymer boundary
2. Top of PZ crystal
3. Piezo-PCB boundary
4. Back of PCB



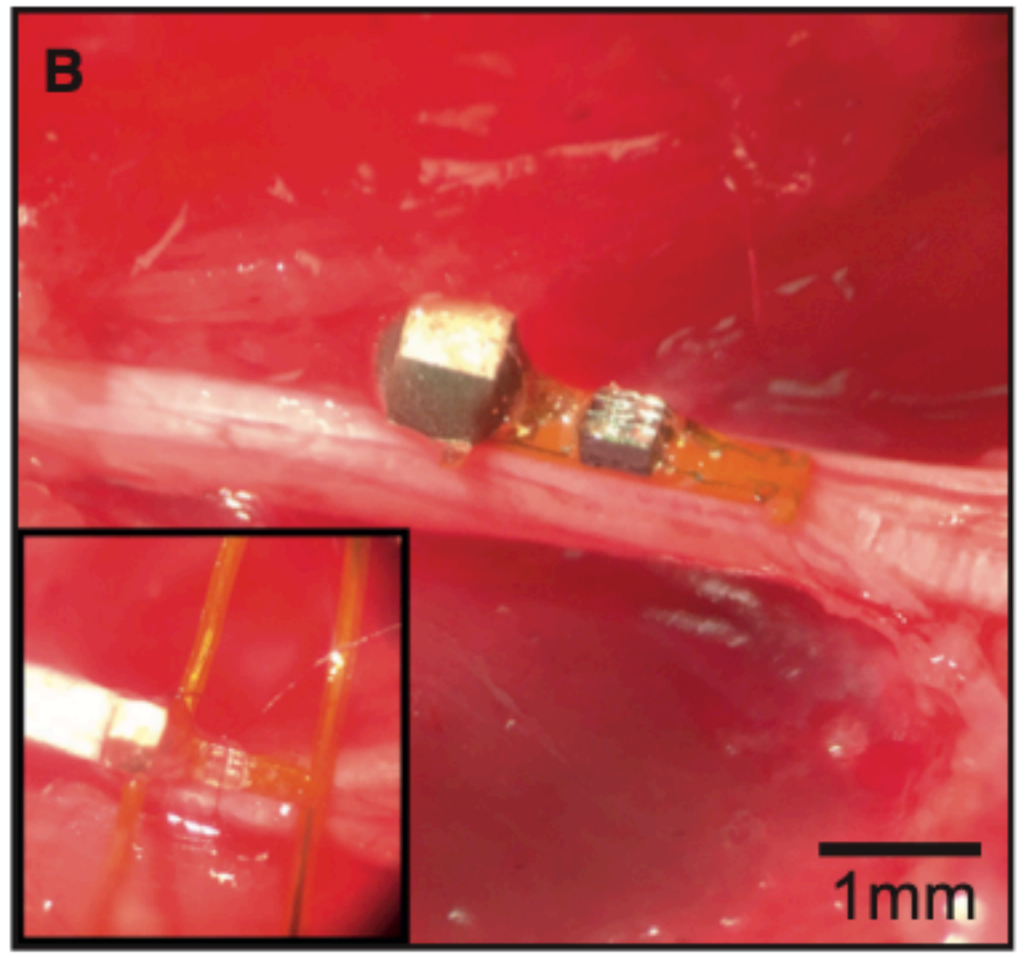
Electromyograms



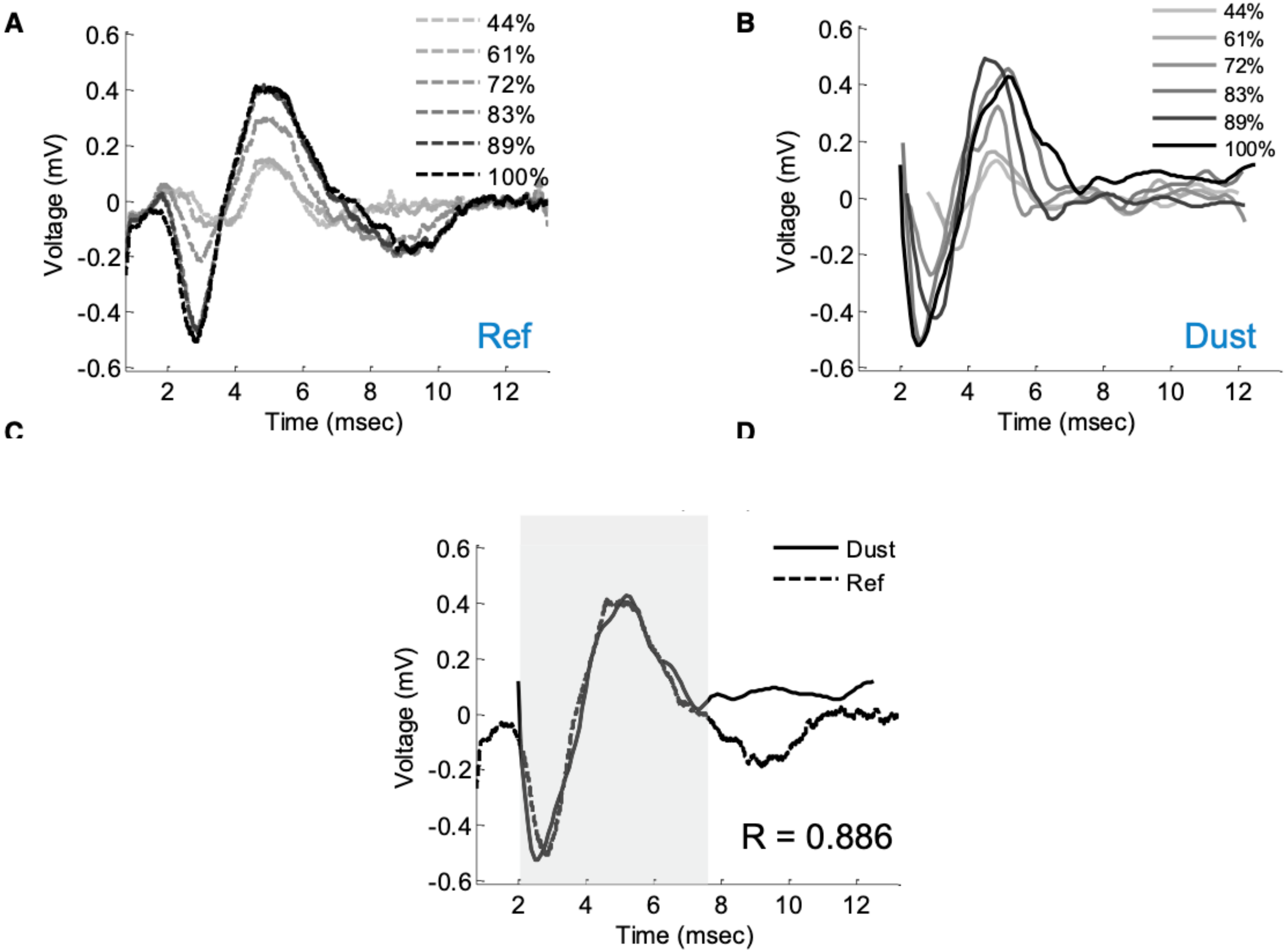


- ND on gastrocnemius muscle of rat under anesthesia
- Stimulate the muscle to invoke a response

Electroneurograms

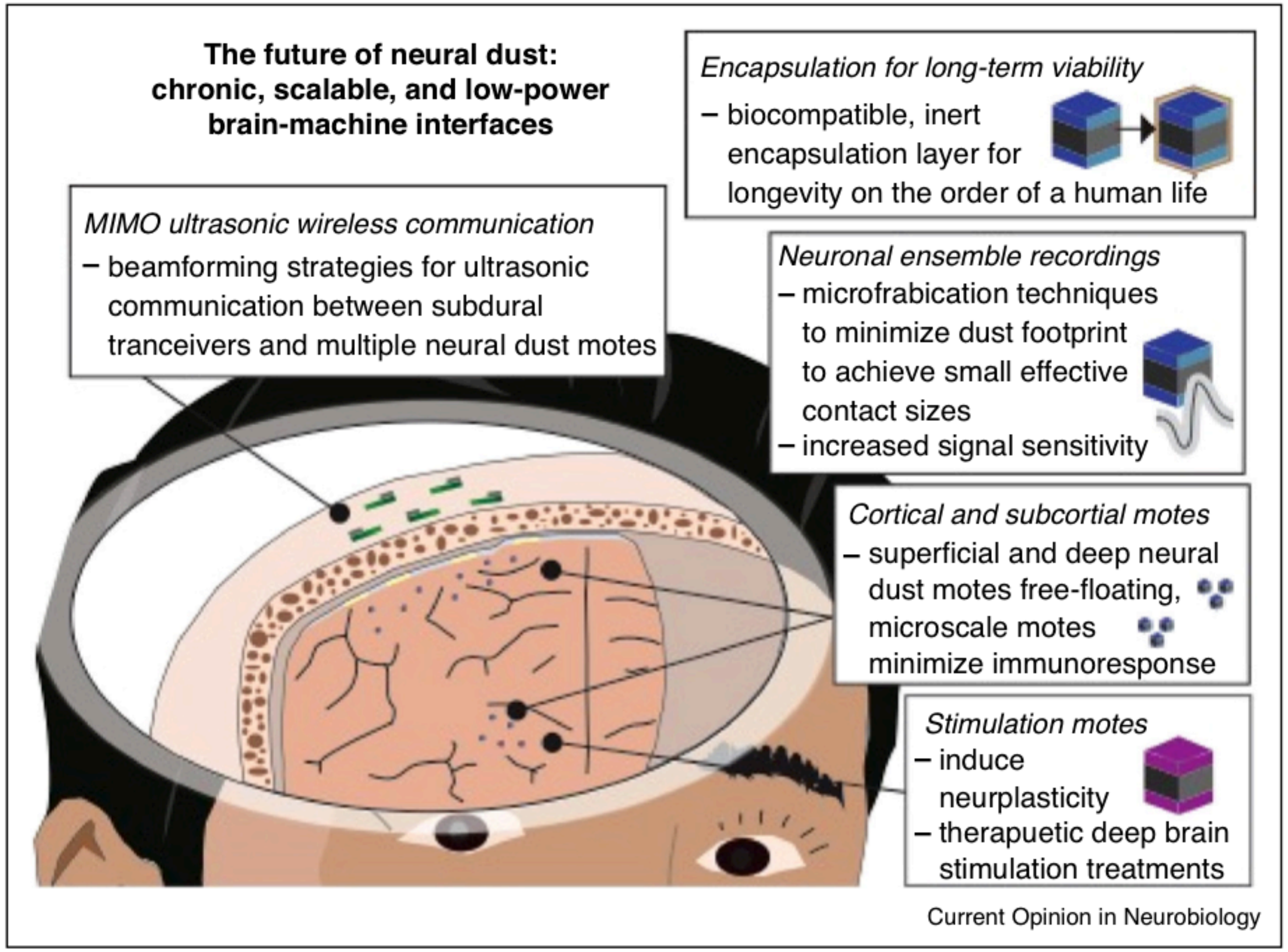


Neural Dust on sciatic nerve



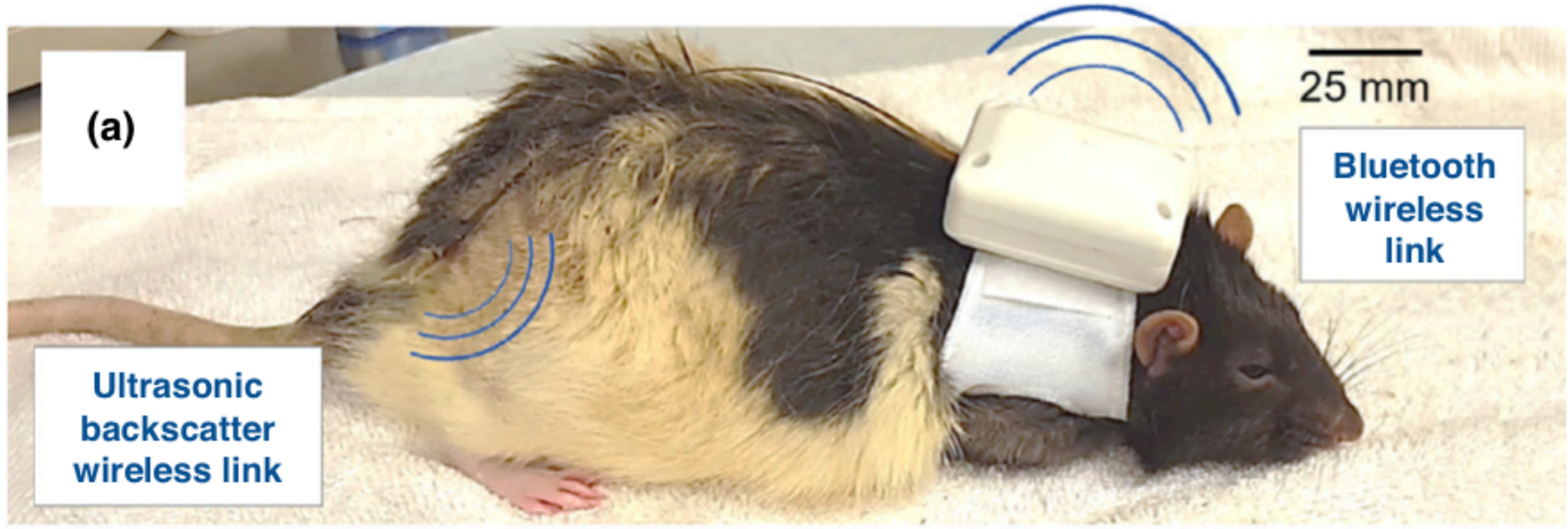
Technical Challenges

- Reducing size down is hard!!
  - Smaller piezoelectrics → worse SNR → more stringent CMOS
- Biocompatability
  - Move away from PZT (but lower piezoelectric effect)
  - Polymers permeable to water vapor ∴ new encapsulation materials (SiC)
- Packaging
- Alignment and online motion correction

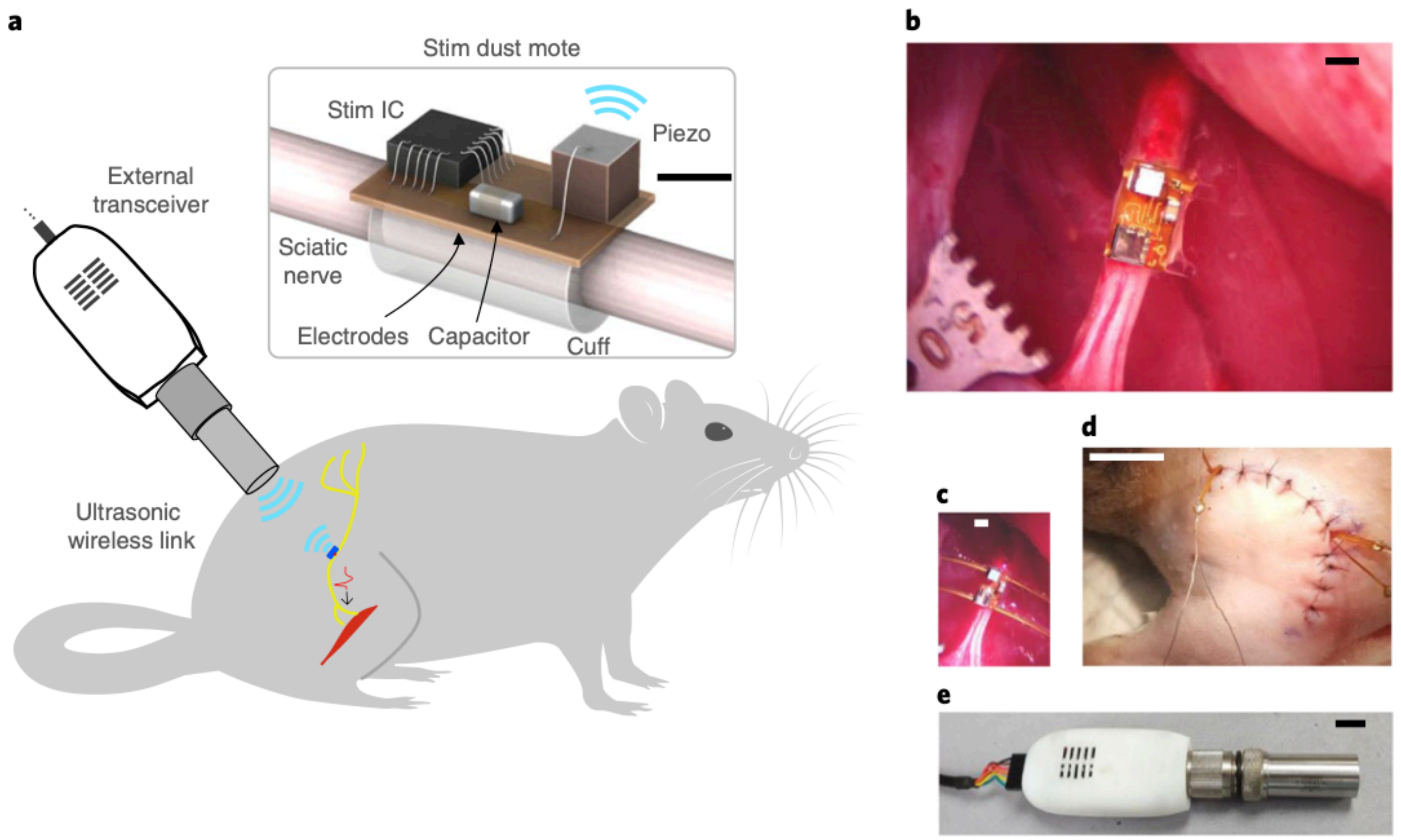


Where can this go?

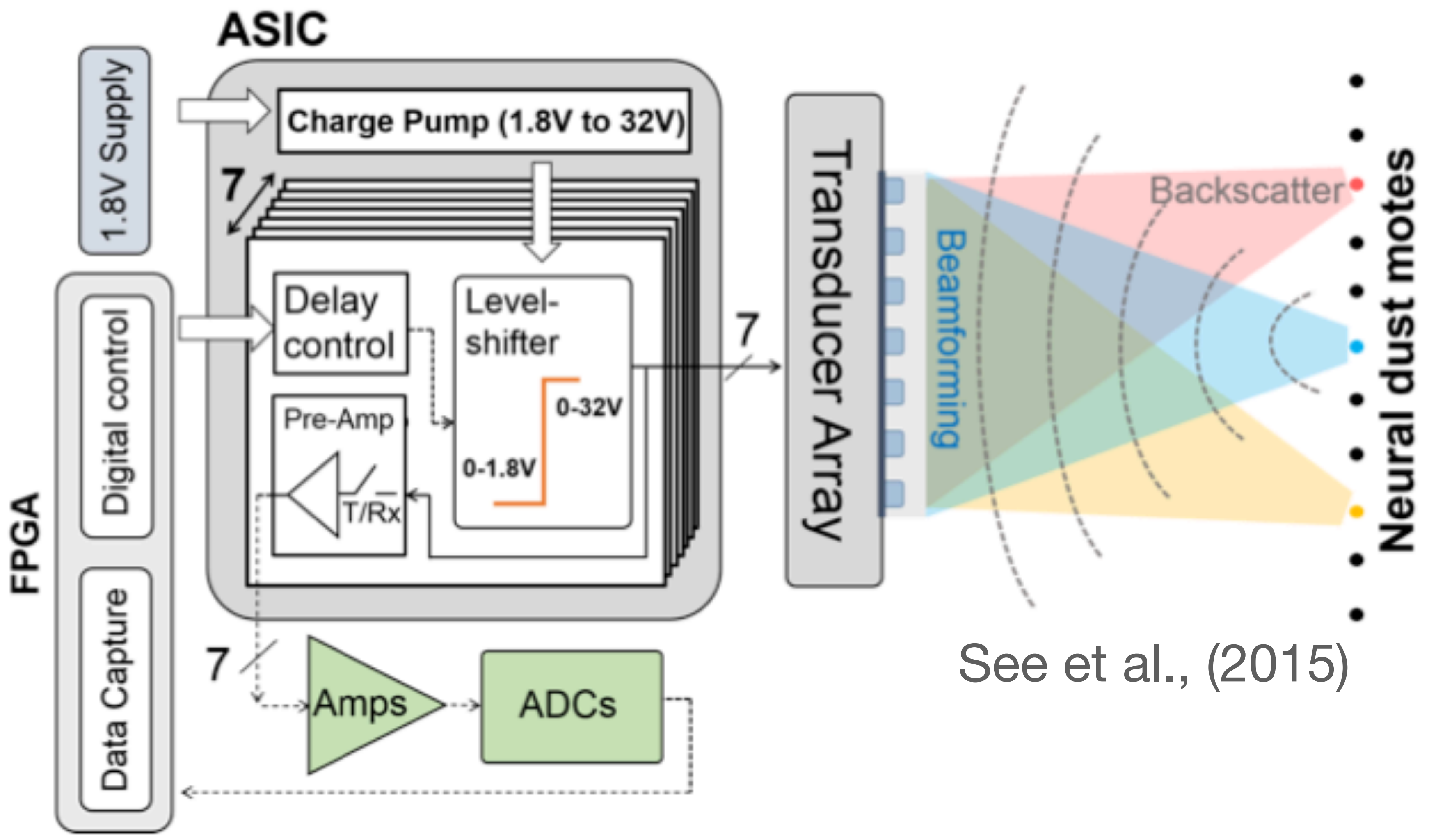
- Wearable ultrasound transducer with bluetooth link
- Transducer arrays for beam steering to interrogate multiple neural dusts motes + correct misalignment
- StimDust!



Piech et al., IEEE (2017)

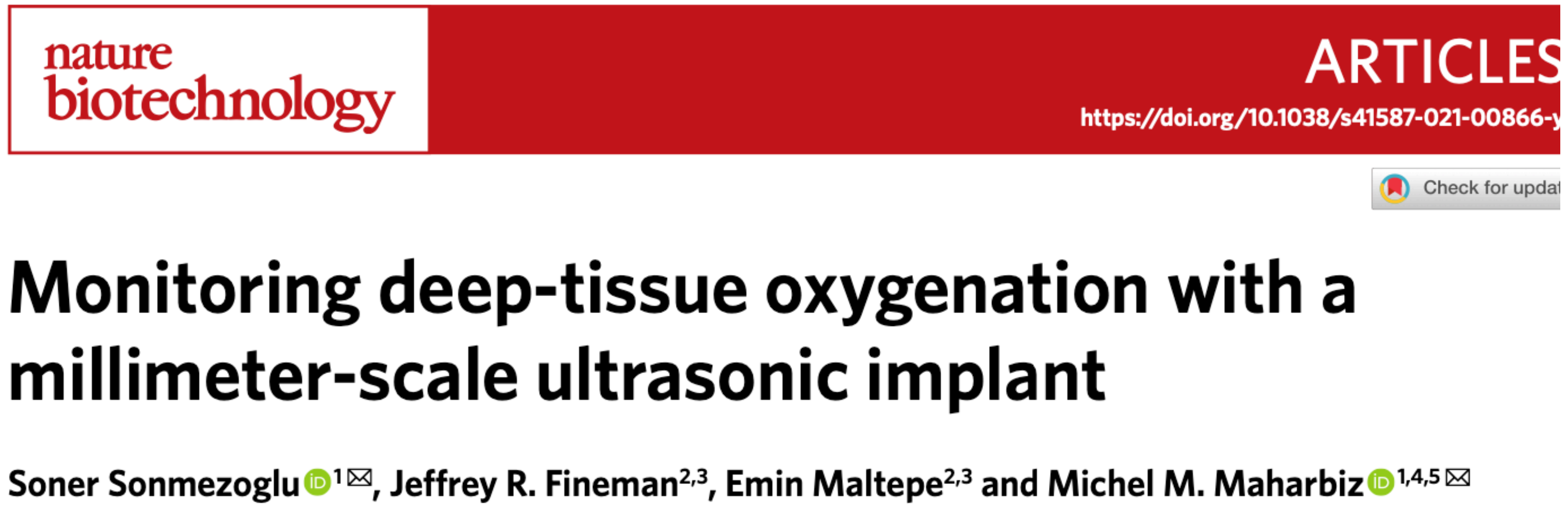


Piech et al., Nat Bio Eng (2020)



See et al., (2015)

Oxygen Sensor!



nature biotechnology

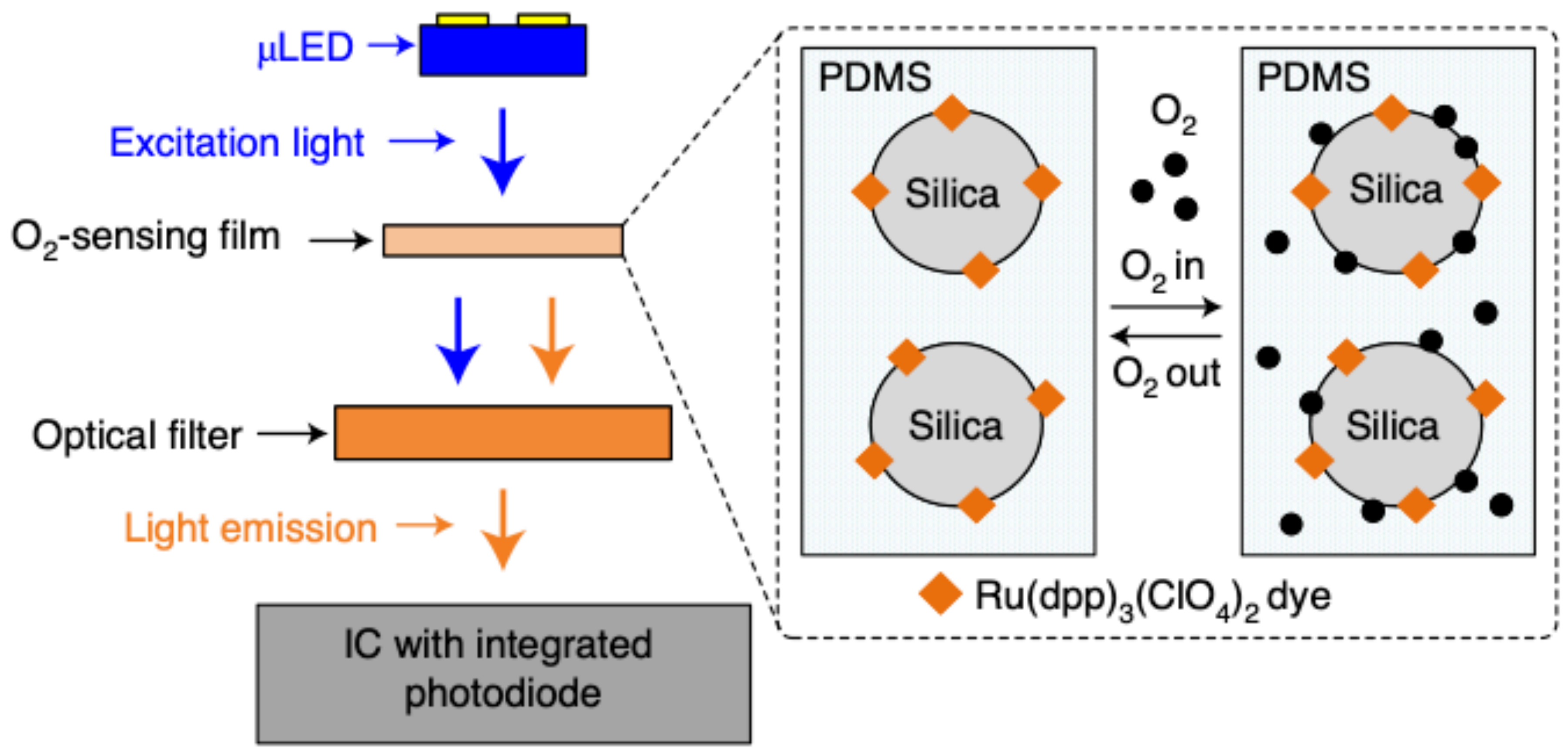
ARTICLES

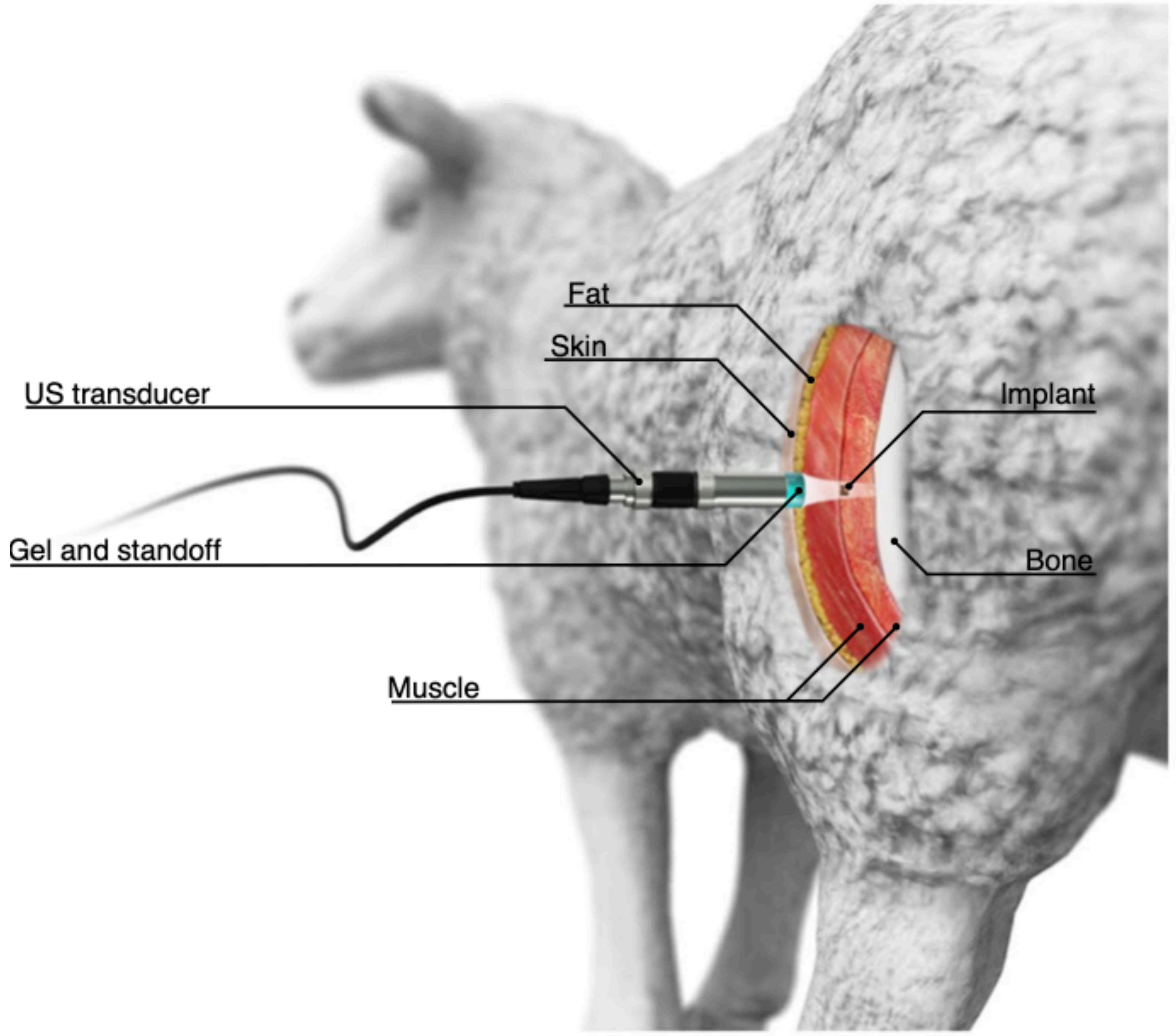
https://doi.org/10.1038/s41587-021-00866-y

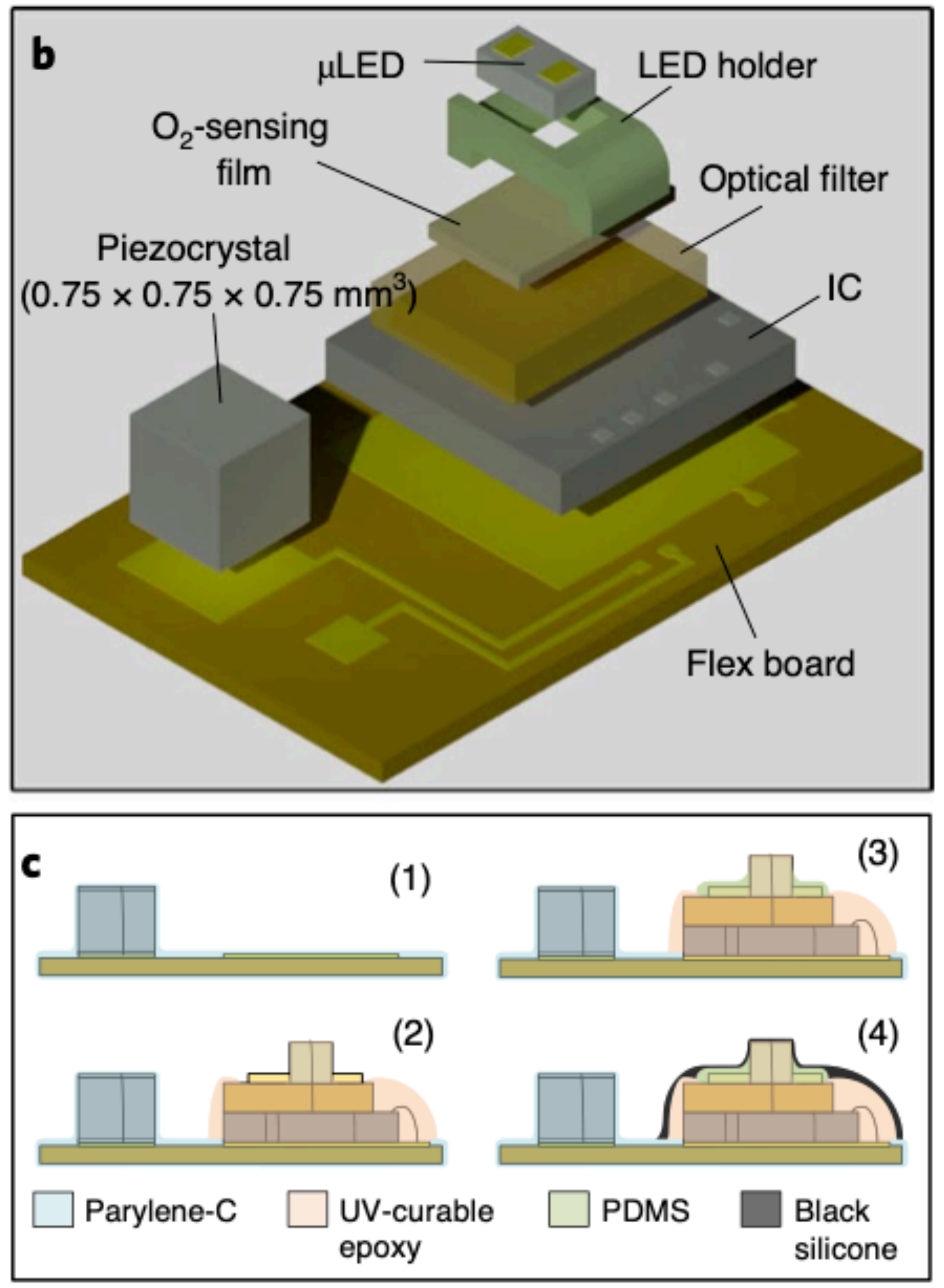
Check for updat

Monitoring deep-tissue oxygenation with a millimeter-scale ultrasonic implant

Soner Sonmezoglu[1]✉, Jeffrey R. Fineman[2,3], Emin Maltepe[2,3] and Michel M. Maharbiz[1,4,5]✉







Questions

- Neuroscience: What could we learn from chronic, high-density recordings?
    - What are the critical parameters: High density (how high?), distinct brain regions, time-scales?
    - Compare with e.g. miniscope (1200 cells over months)
- Other modalities? Pressure, pH, temperature?
- Single unit AP vs LFPs?
- Clinical: Is non (or minimally) invasive really a pre-requisite for practical BMIs?
    - Can people envisage BMIs in healthy humans?