Neural Dust

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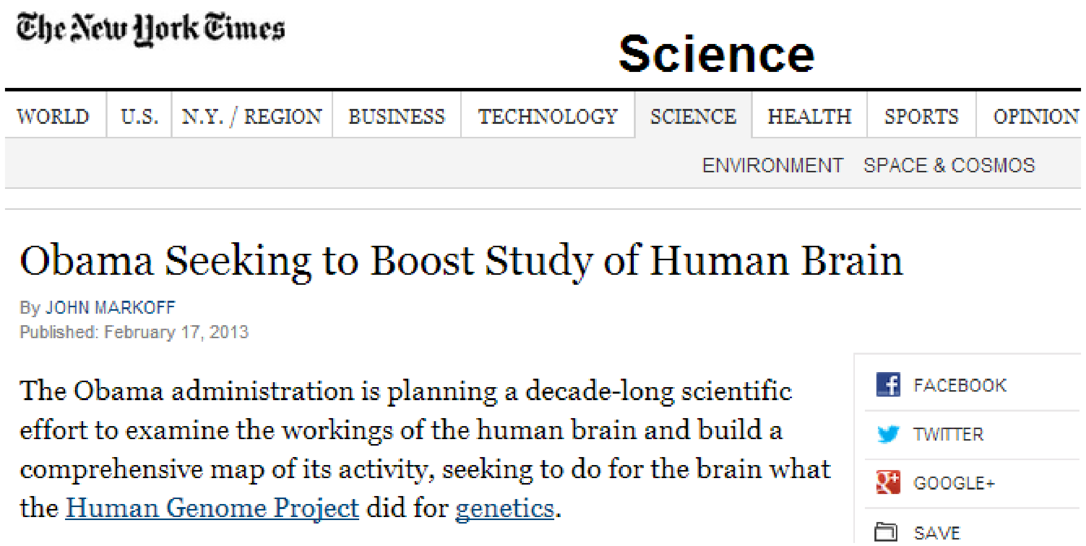
It’s a great time to build tech for the brain



Obama Seeking to Boost Study of Human Brain

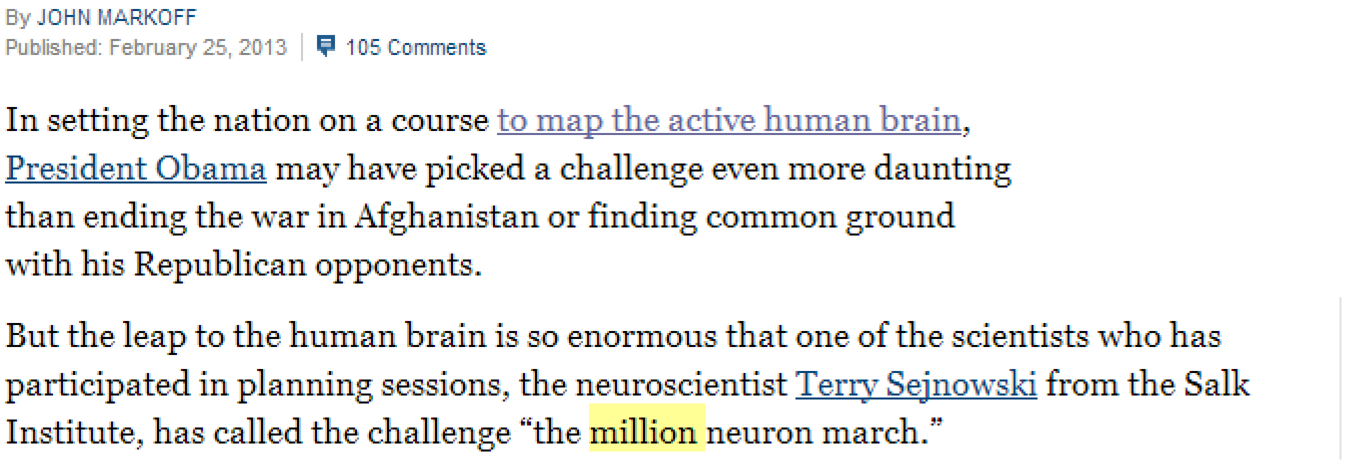
By JOHN MARKOFF
Published: February 17, 2013

The Obama administration is planning a decade-long scientific effort to examine the workings of the human brain and build a comprehensive map of its activity, seeking to do for the brain what the Human Genome Project did for genetics.

Bringing a Virtual Brain to Life

By TIM REQUARTH
Published: March 18, 2013

For months, Henry Markram and his team had been feeding data into a supercomputer, four vending-machine-size black boxes whirring quietly in the basement of the Swiss Federal Institute of Technology in Lausanne.

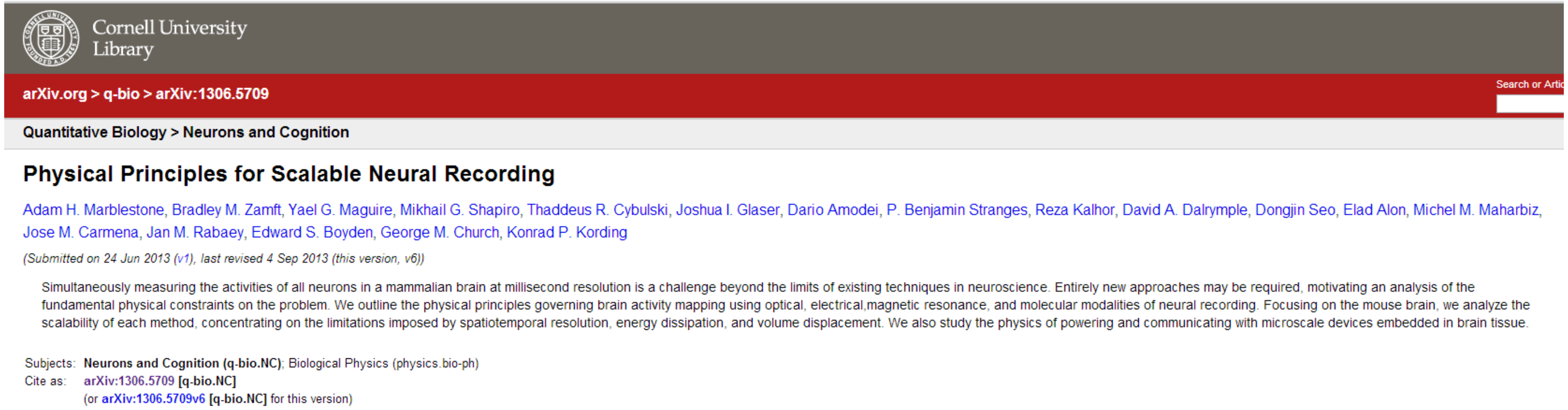


By JOHN MARKOFF
Published: February 25, 2013 | 105 Comments

In setting the nation on a course to map the active human brain, President Obama may have picked a challenge even more daunting than ending the war in Afghanistan or finding common ground with his Republican opponents.

But the leap to the human brain is so enormous that one of the scientists who has participated in planning sessions, the neuroscientist Terry Sejnowski from the Salk Institute, has called the challenge “the million neuron march.”

Can you record from every neuron in the mouse brain?



arXiv.org > q-bio > arXiv:1306.5709

Quantitative Biology > Neurons and Cognition

Physical Principles for Scalable Neural Recording

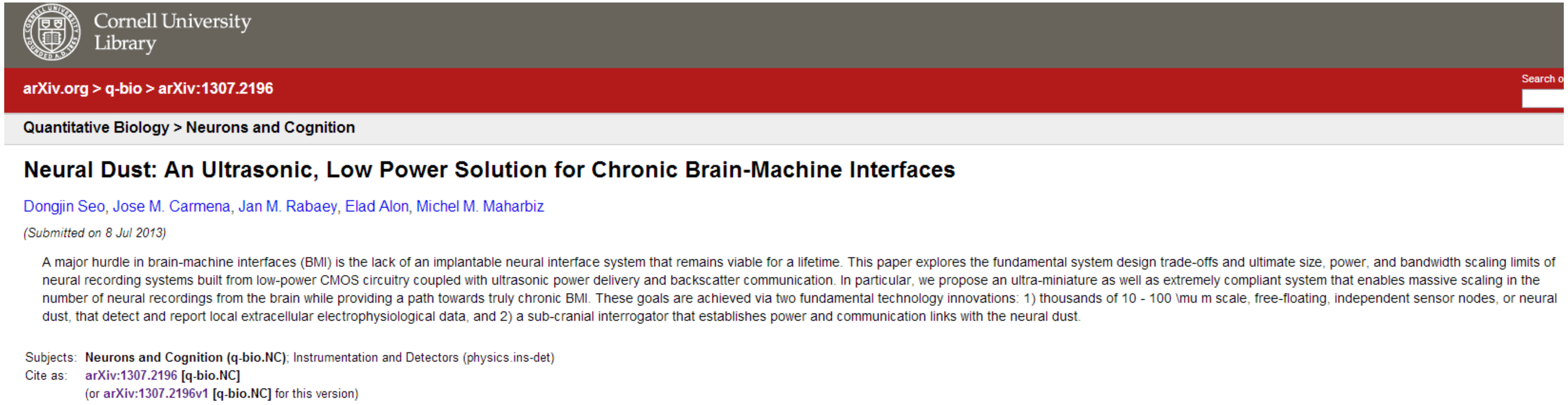
Adam H. Marblestone, Bradley M. Zamft, Yael G. Maguire, Mikhail G. Shapiro, Thaddeus R. Cybulski, Joshua I. Glaser, Dario Amodei, P. Benjamin Stranges, Reza Kalhor, David A. Dalrymple, Dongjin Seo, Elad Alon, Michel M. Maharbiz, Jose M. Carmena, Jan M. Rabaey, Edward S. Boyden, George M. Church, Konrad P. Kording

(Submitted on 24 Jun 2013 (v1), last revised 4 Sep 2013 (this version, v6))

Simultaneously measuring the activities of all neurons in a mammalian brain at millisecond resolution is a challenge beyond the limits of existing techniques in neuroscience. Entirely new approaches may be required, motivating an analysis of the fundamental physical constraints on the problem. We outline the physical principles governing brain activity mapping using optical, electrical,magnetic resonance, and molecular modalities of neural recording. Focusing on the mouse brain, we analyze the scalability of each method, concentrating on the limitations imposed by spatiotemporal resolution, energy dissipation, and volume displacement. We also study the physics of powering and communicating with microscale devices embedded in brain tissue.

Subjects: **Neurons and Cognition (q-bio.NC)**; Biological Physics (physics.bio-ph)
Cite as: arXiv:1306.5709 [q-bio.NC]
(or arXiv:1306.5709v6 [q-bio.NC] for this version)

http://arxiv.org/abs/1306.5709



arXiv.org > q-bio > arXiv:1307.2196

Quantitative Biology > Neurons and Cognition

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

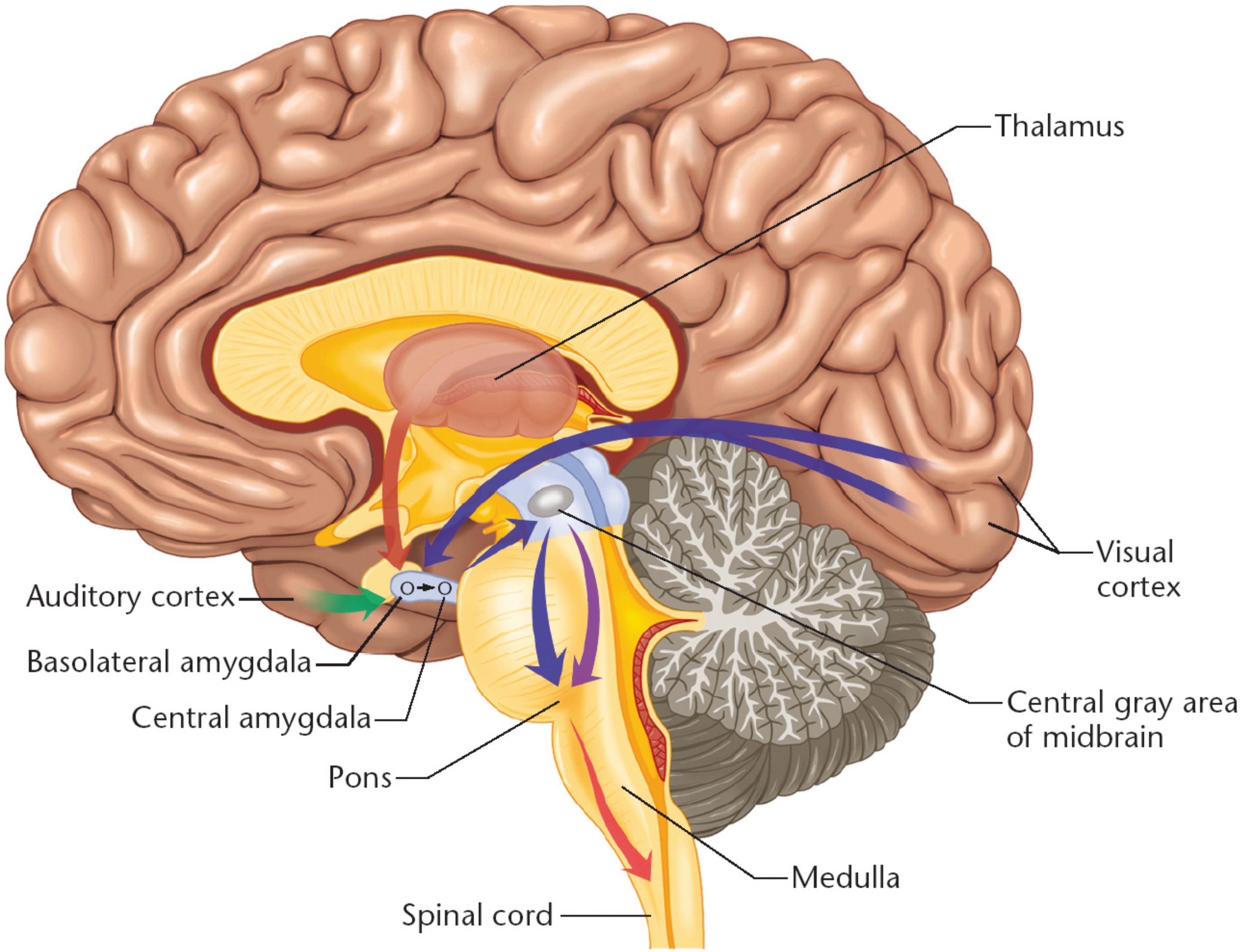
Dongjin Seo, Jose M. Carmena, Jan M. Rabaey, Elad Alon, Michel M. Maharbiz

(Submitted on 8 Jul 2013)

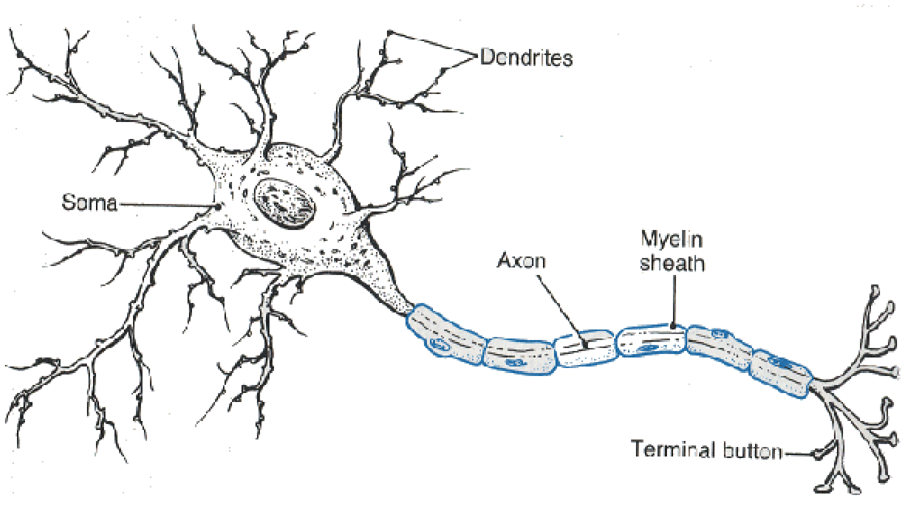
A major hurdle in brain-machine interfaces (BMI) is the lack of an implantable neural interface system that remains viable for a lifetime. This paper explores the fundamental system design trade-offs and ultimate size, power, and bandwidth scaling limits of neural recording systems built from low-power CMOS circuitry coupled with ultrasonic power delivery and backscatter communication. In particular, we propose an ultra-miniature as well as extremely compliant system that enables massive scaling in the number of neural recordings from the brain while providing a path towards truly chronic BMI. These goals are achieved via two fundamental technology innovations: 1) thousands of 10 - 100 \mu m scale, free-floating, independent sensor nodes, or neural dust, that detect and report local extracellular electrophysiological data, and 2) a sub-cranial interrogator that establishes power and communication links with the neural dust.

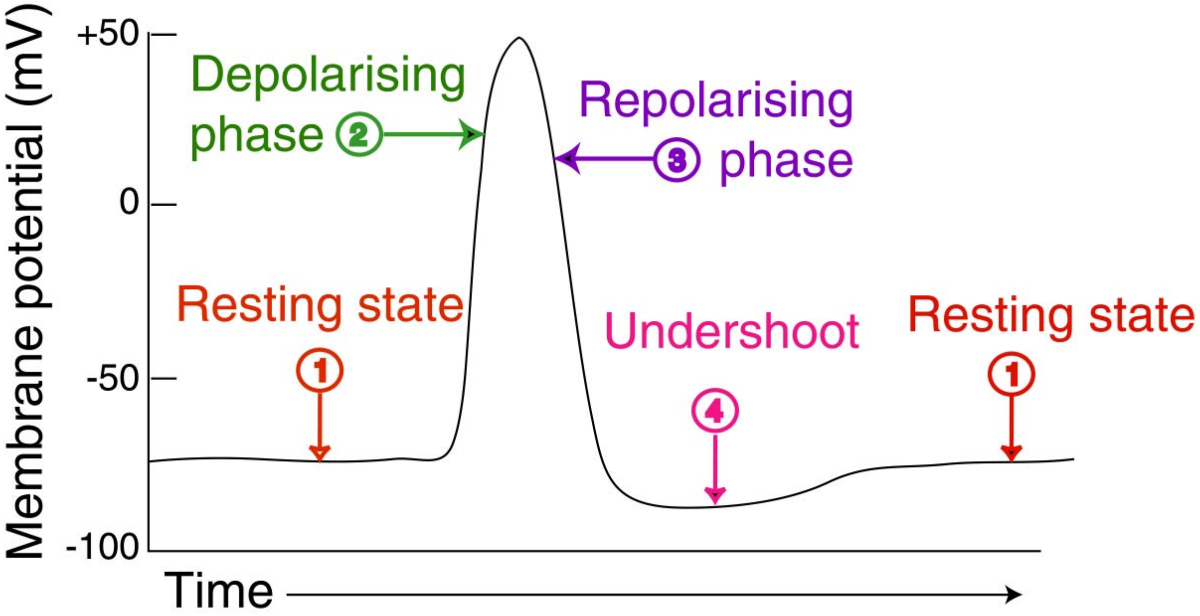
Subjects: **Neurons and Cognition (q-bio.NC)**; Instrumentation and Detectors (physics.ins-det)
Cite as: arXiv:1307.2196 [q-bio.NC]
(or arXiv:1307.2196v1 [q-bio.NC] for this version)

http://arxiv.org/abs/1307.2196

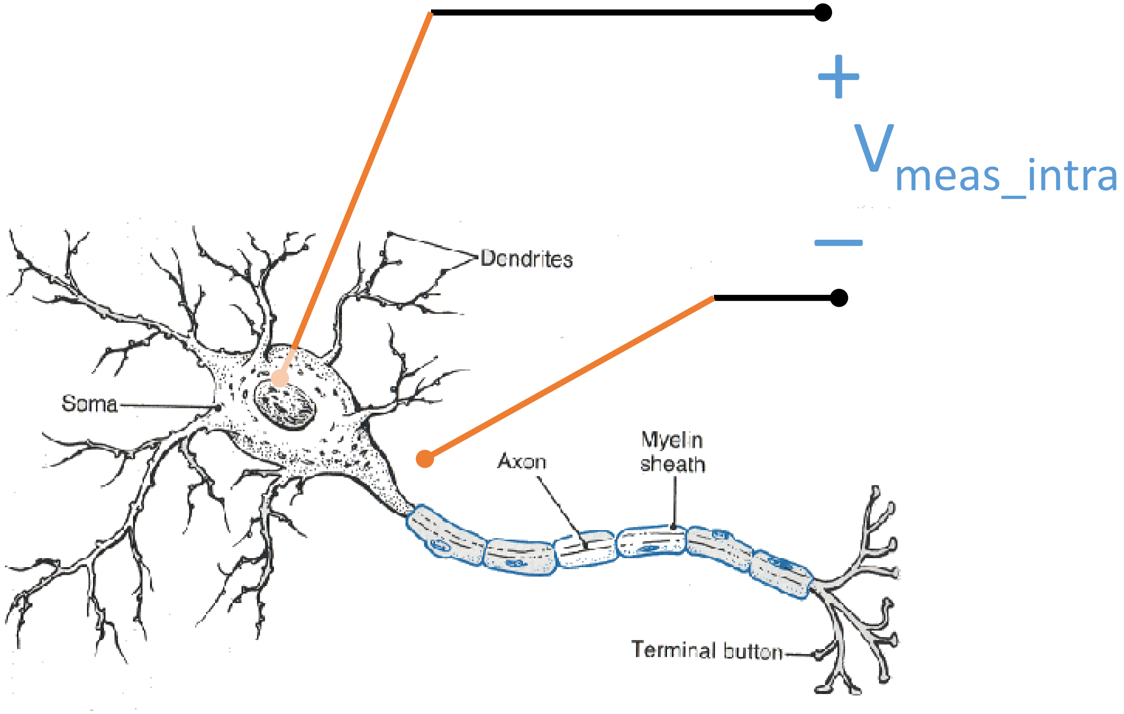

Thalamus
Visual cortex
Auditory cortex
Basolateral amygdala
Central amygdala
Pons
Central gray area of midbrain
Medulla
Spinal cord

Neurons… and action potentials

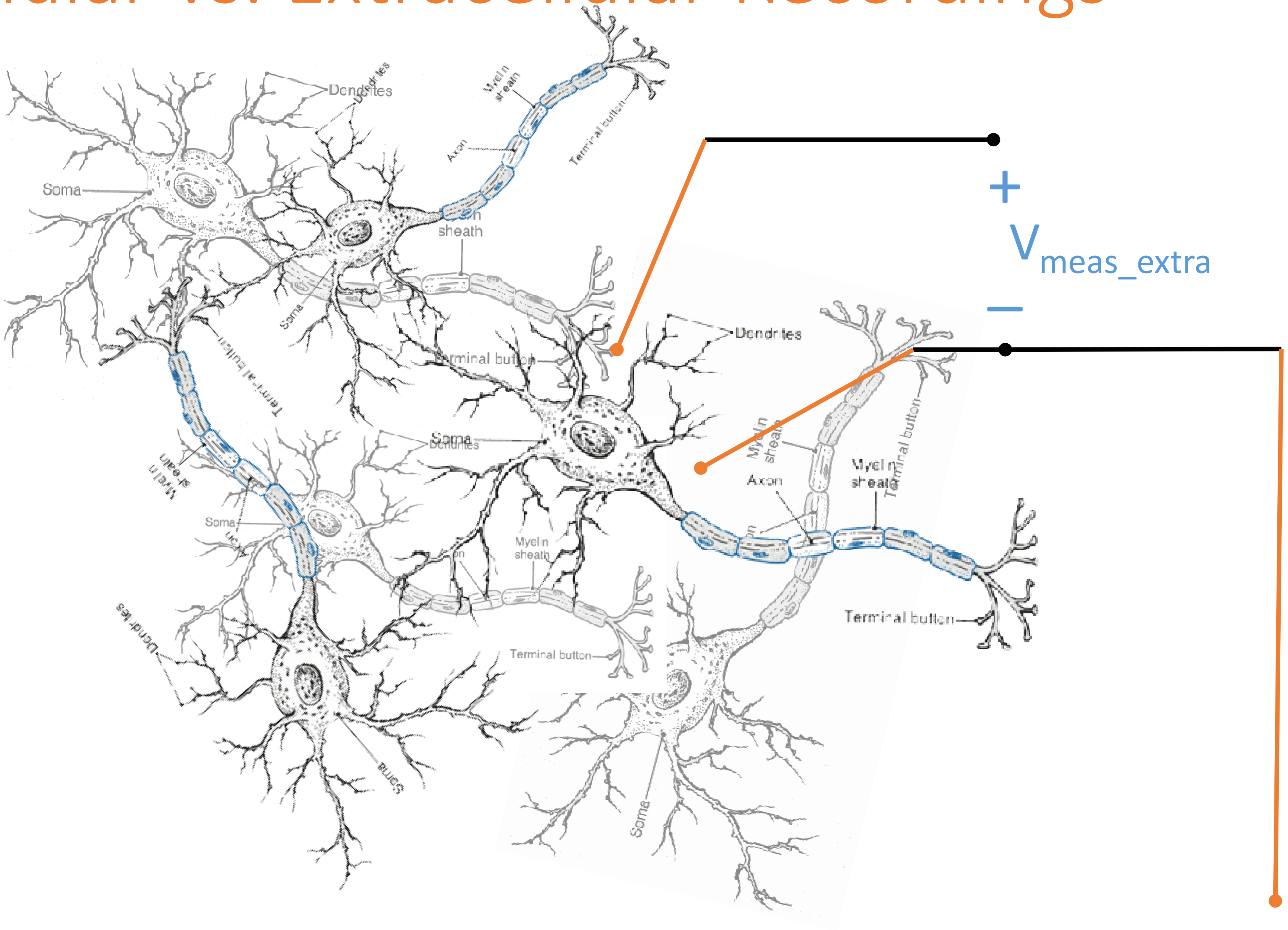




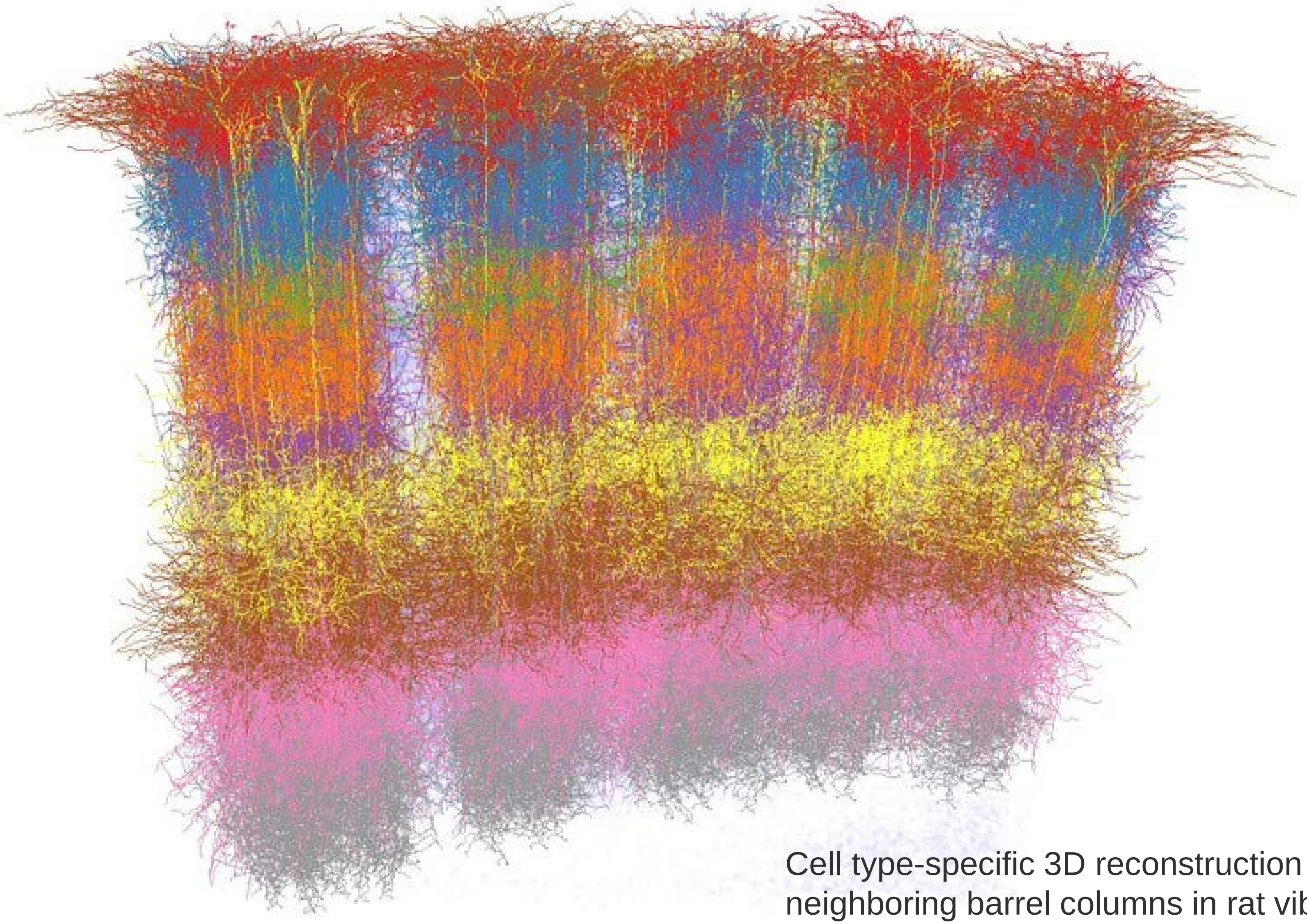
Intracellular vs. Extracellular Recordings



Intracellular vs. Extracellular Recordings



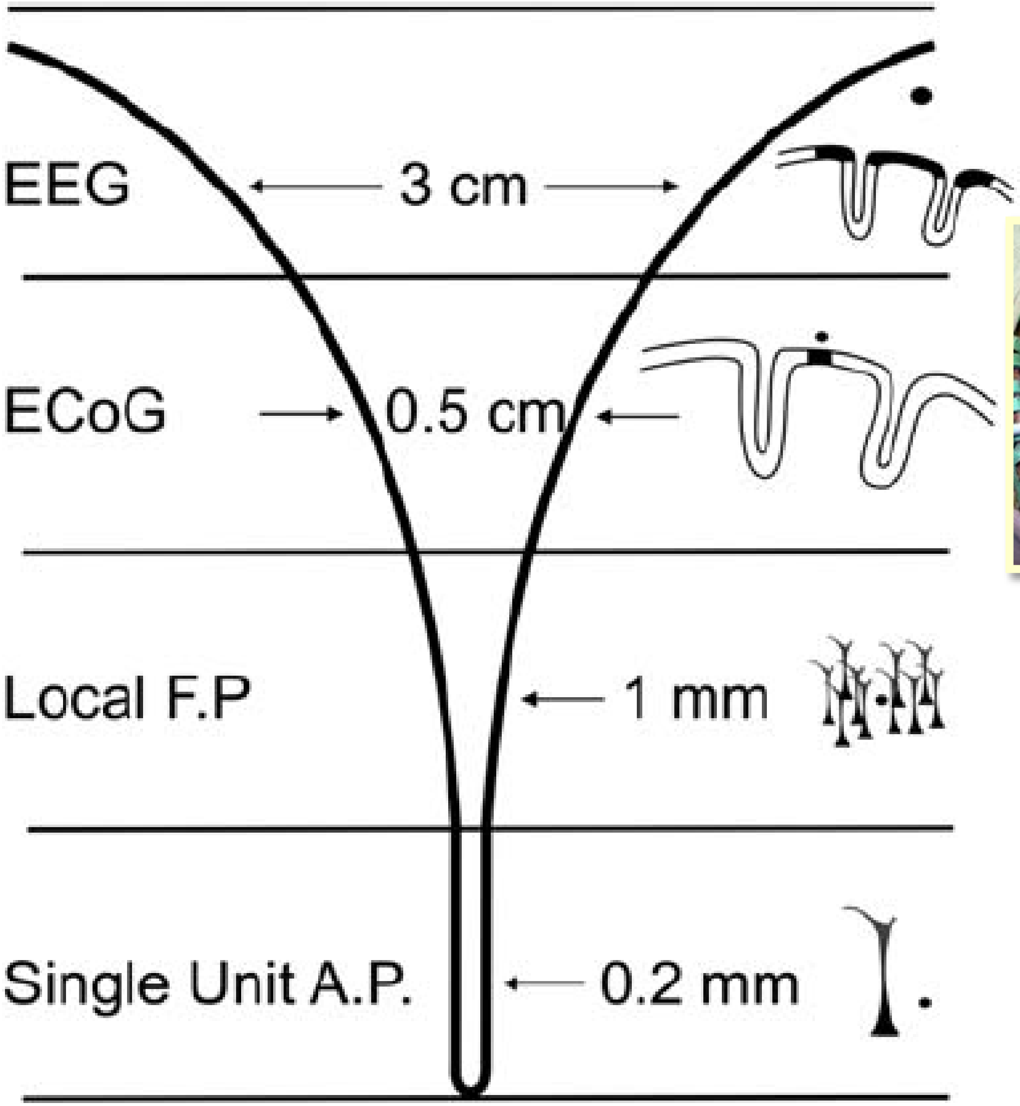
Neurons are organized in the cortex

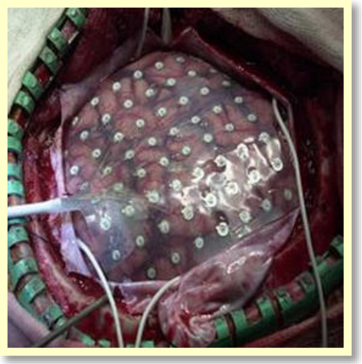


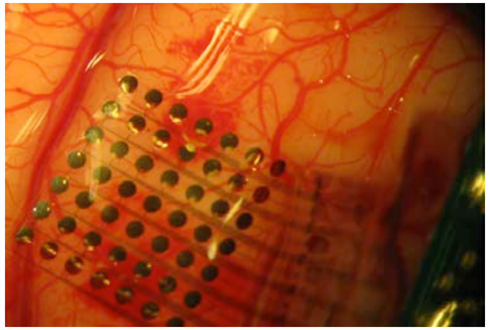
Cell type-specific 3D reconstruction of five neighboring barrel columns in rat vibrissal cortex

but debate exists: functional? anatomical? canonical?

Recording electrical signals from the brain…



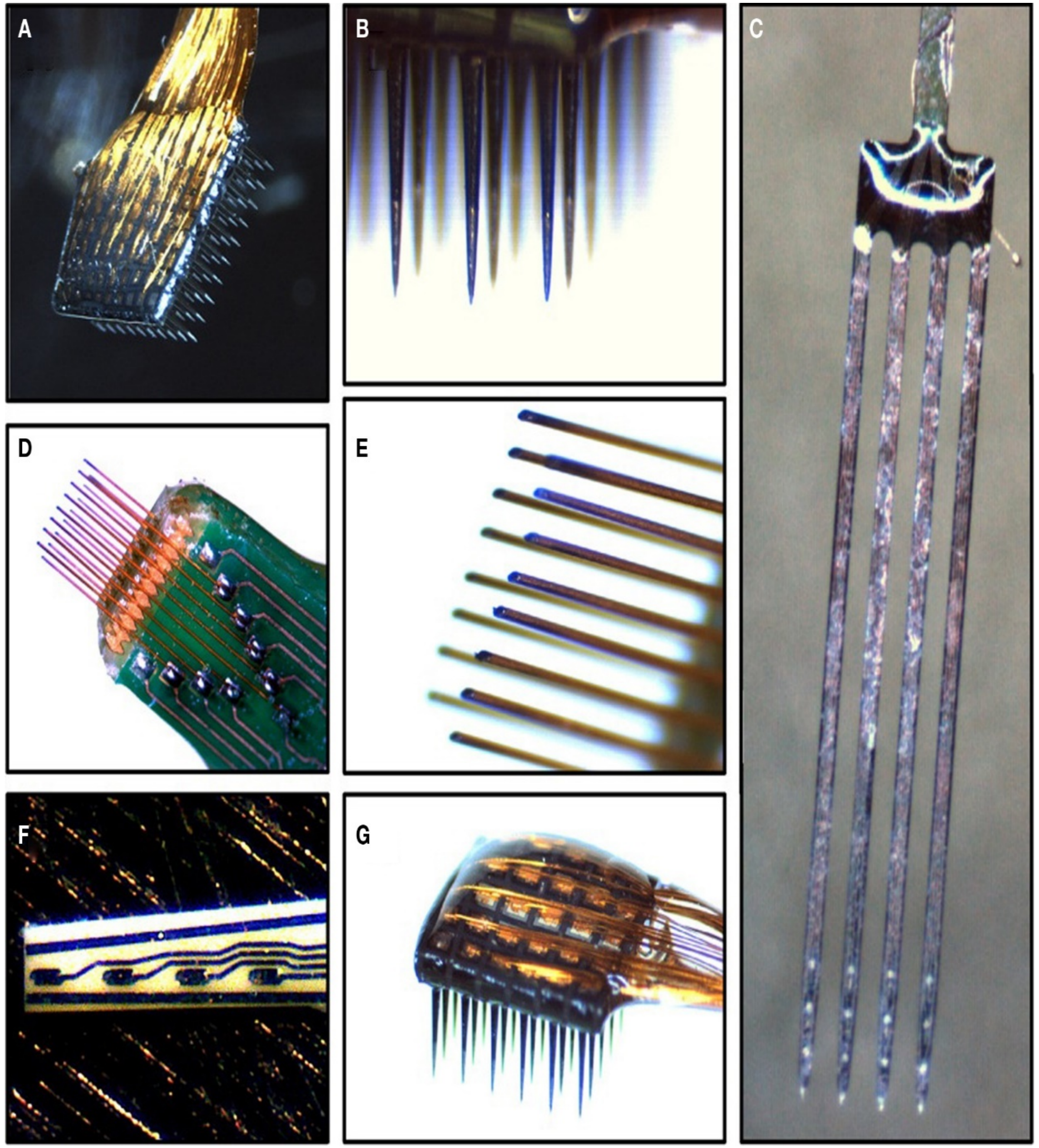


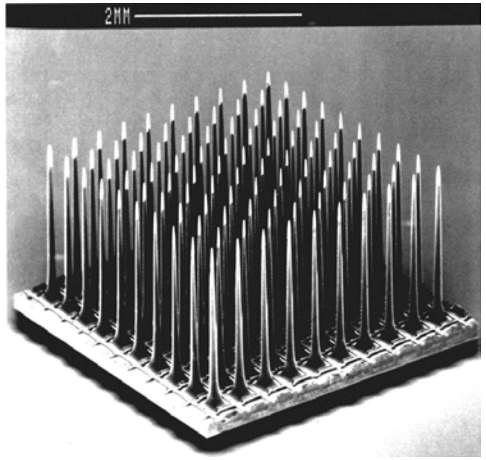


What do you need in a good technology?

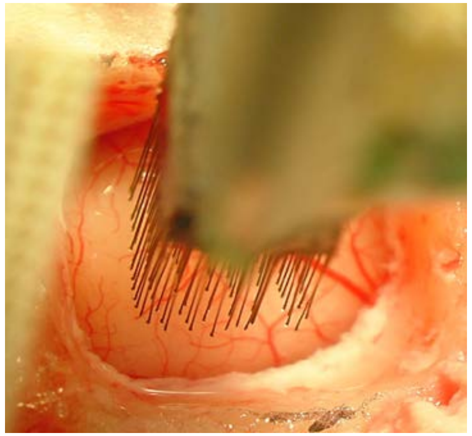
- ‘see’ the signal you want: spikes, multi-unit or LFP
- ‘see’ as many neurons as possible
- long recording lifetime
- biocompatibility
  - complex term
  - minimize the harm the brain does to the electrodes
  - minimize the harm the electrode do to the brain
- minimize chances of infection
- minimize insertion damage
- ideally, allow awake, untethered behavior

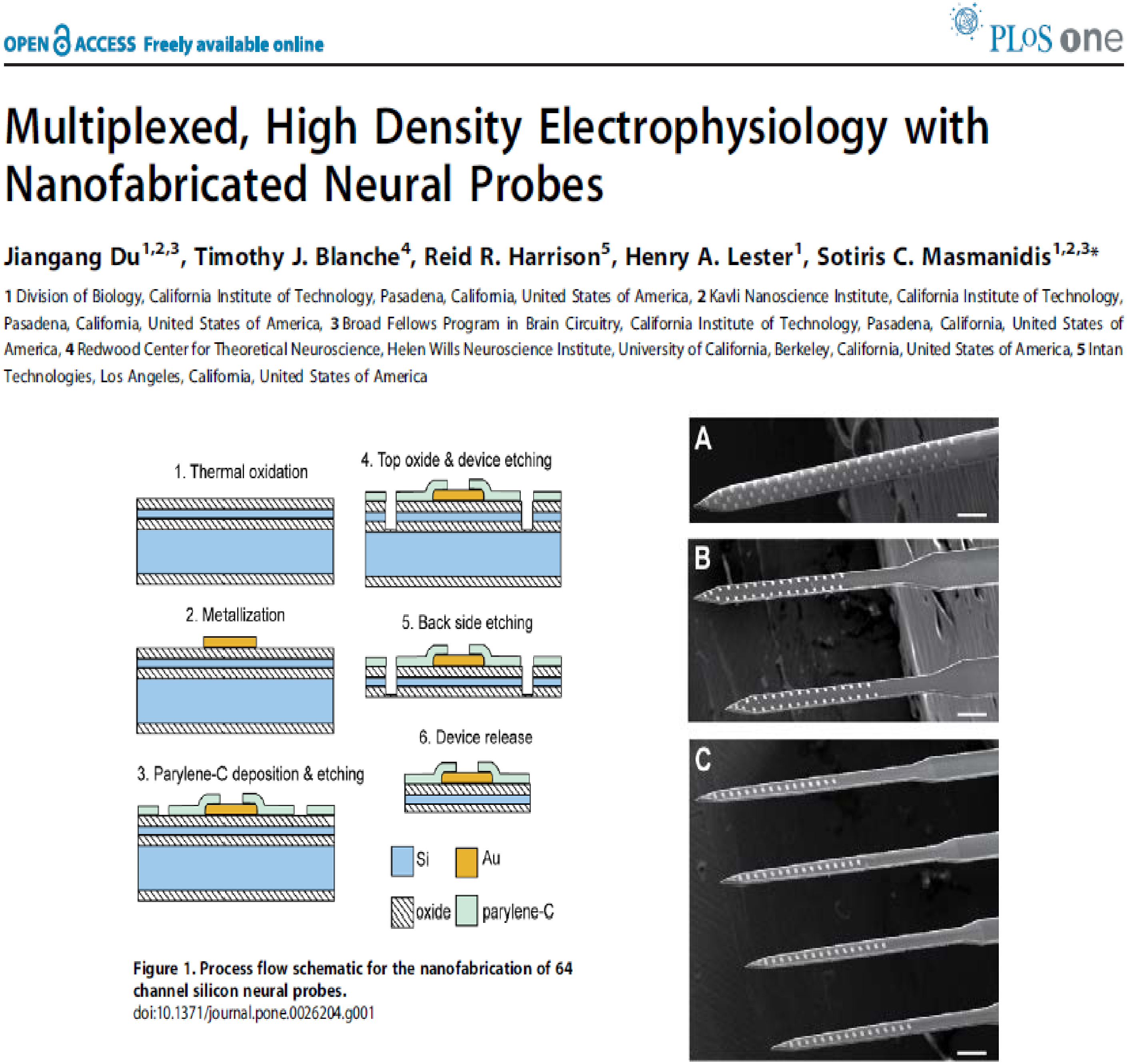
Penetrating into the cortex





(top) Utah array; (left) from Rothschild, *Front. Neuroeng.*, 15 October 2010; (bottom) Duke array





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PLoS one

Multiplexed, High Density Electrophysiology with Nanofabricated Neural Probes

Jiangang Du[1,2,3], Timothy J. Blanche[4], Reid R. Harrison[5], Henry A. Lester[1], Sotiris C. Masmanidis[1,2,3]*

1 Division of Biology, California Institute of Technology, Pasadena, California, United States of America, **2** Kavli Nanoscience Institute, California Institute of Technology, Pasadena, California, United States of America, **3** Broad Fellows Program in Brain Circuitry, California Institute of Technology, Pasadena, California, United States of America, **4** Redwood Center for Theoretical Neuroscience, Helen Wills Neuroscience Institute, University of California, Berkeley, California, United States of America, **5** Intan Technologies, Los Angeles, California, United States of America

Figure 1. Process flow schematic for the nanofabrication of 64 channel silicon neural probes.
doi:10.1371/journal.pone.0026204.g001

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Multiplexed, High Density Electrophysiology with Nanofabricated Neural Probes

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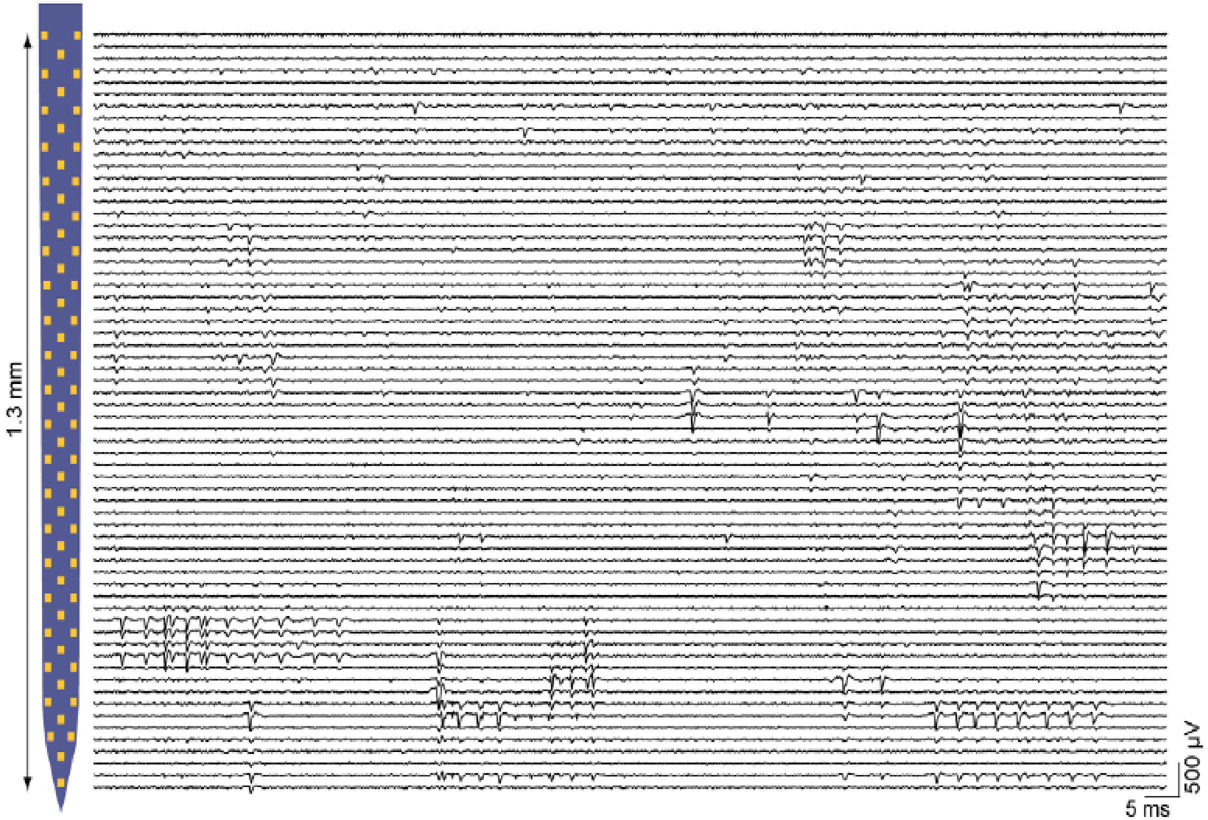
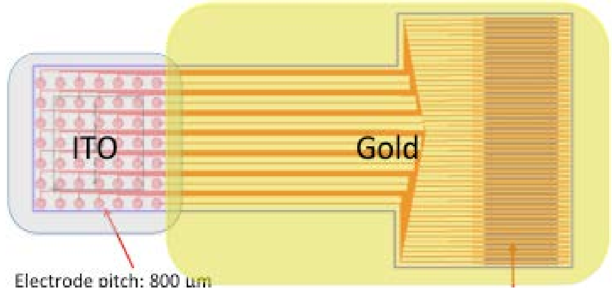


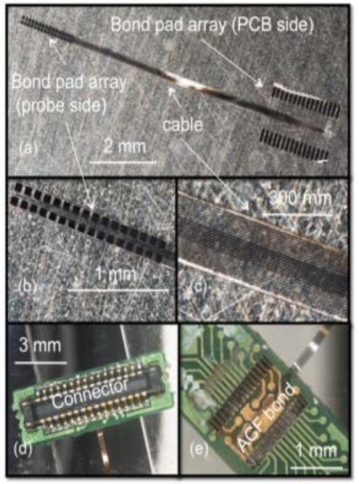
Physical Interface Platforms Across Scale and Modality



transparent ITO µECoG

Brian Pepin / Nathalie Gaudreault

Blanche / Gradinaru / Maharbiz

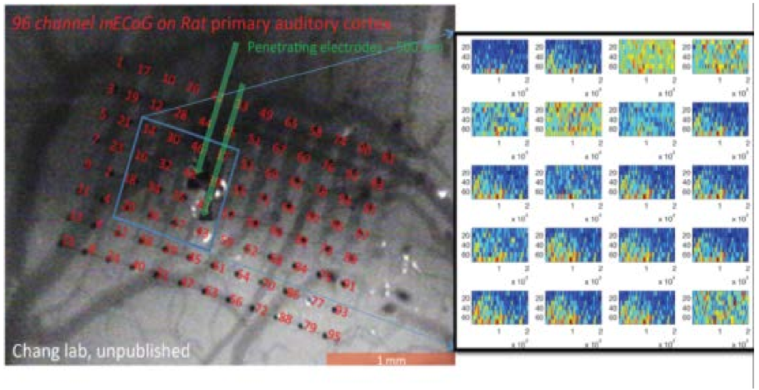


Scalable Flexible

Ultracompliant Nanocables

Peter Ledochowitsch / Raphael Tiefenauer

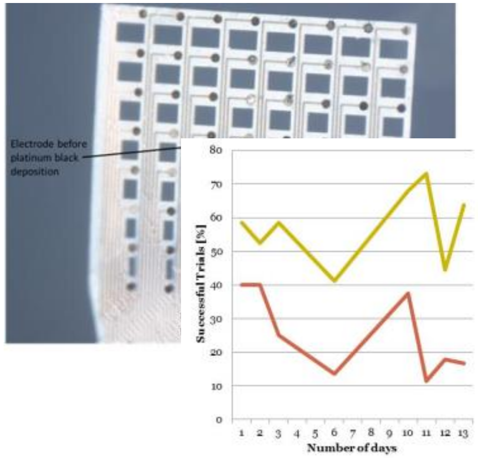
Blanche / Maharbiz



µECoG for auditory cortex

Peter Ledochowitsch

Chang / Maharbiz

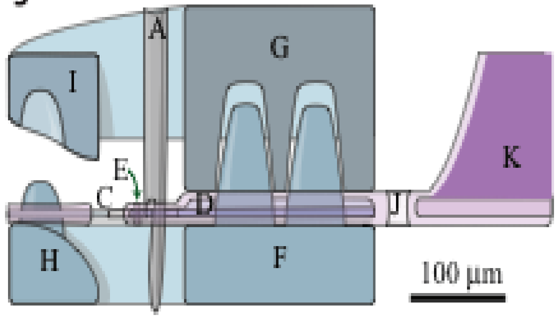


µECoG+BMI

Peter Ledochowitsch / Aaron Koralek

Carmena / Maharbiz

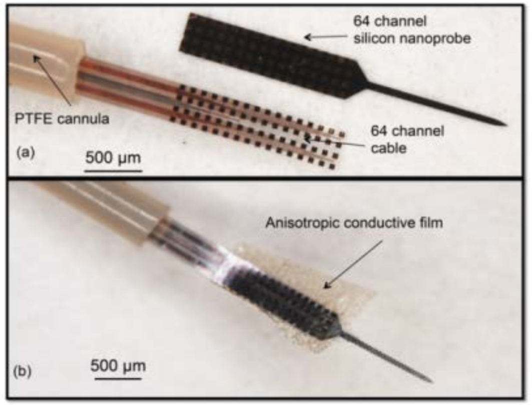
Fig 2

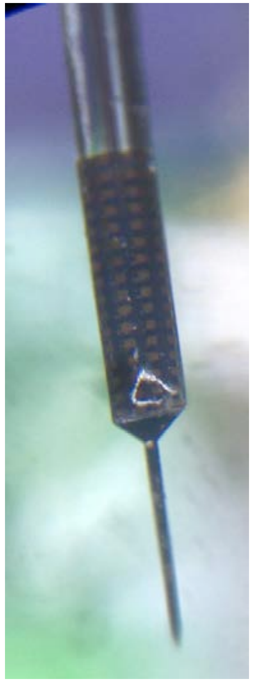


Insertion robotics for ultra-compliant electrodes

Tim Hanson

Sabes / Maharbiz





High Density Flexible Nanotrodes:

Electrical + Optical

Maysam Chamanzar

Blanche / Maharbiz

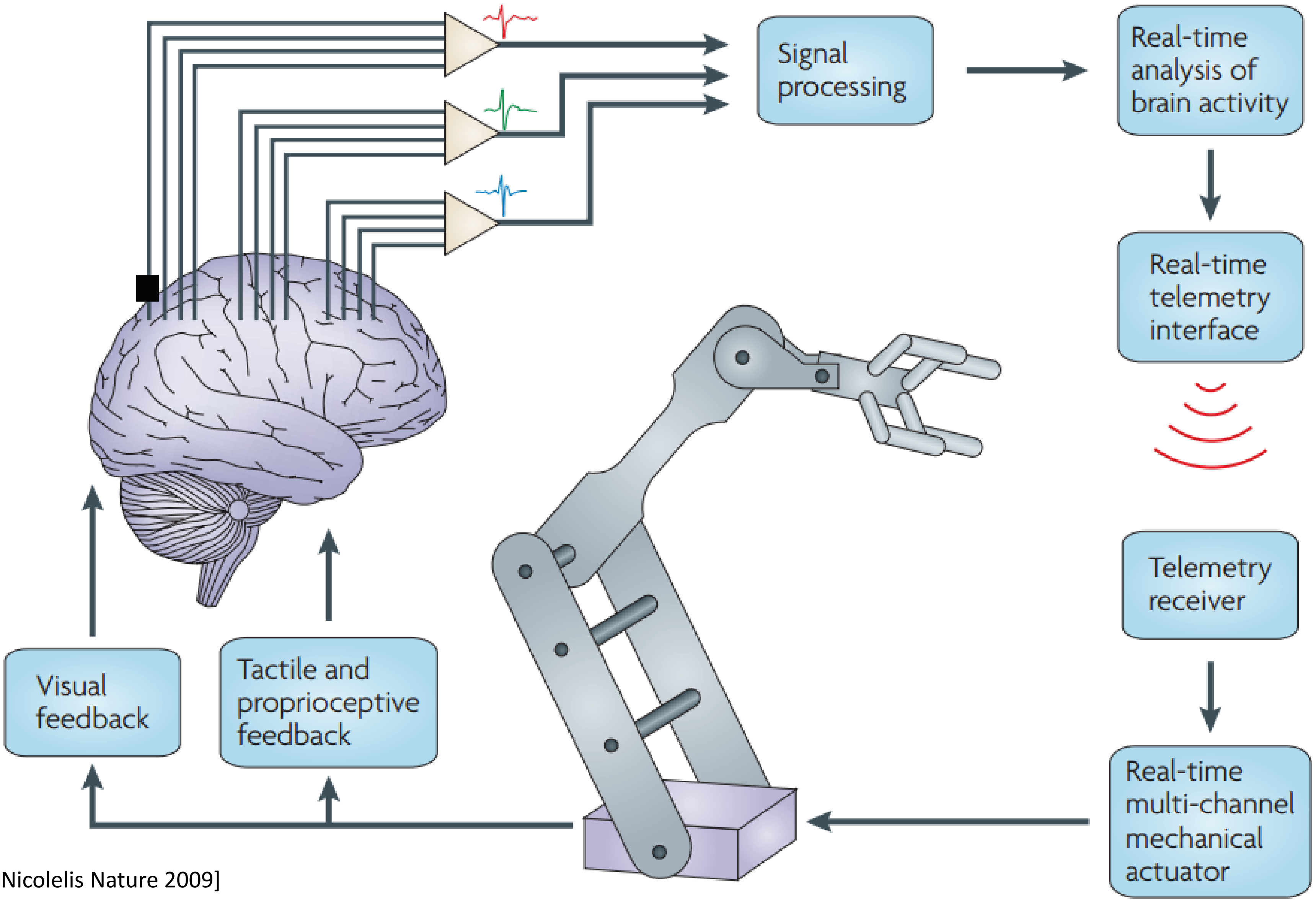
Brain-Machine Interfaces Vision

[from Scientific American]

Seamless integration between human "brain" and electronics "brain"

- **Learn about how the brain operates**
- **Assist motor control for spinal cord injuries/amputees**
  - Estimated population (US) = 200,000
  - 11,000 new cases in the US every year
- **Overall human enhancement**

Brain-Machine Interface Paradigm



Signal processing

Real-time analysis of brain activity

Real-time telemetry interface

Telemetry receiver

Real-time multi-channel mechanical actuator

Visual feedback

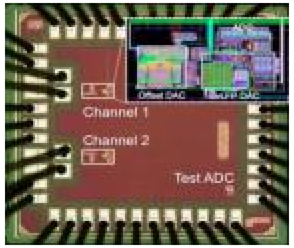
Tactile and proprioceptive feedback

[Nicolelis Nature 2009]

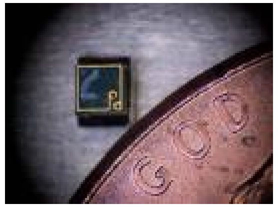
Fundamental limits in scaling

[Hochberg Nature 2006]

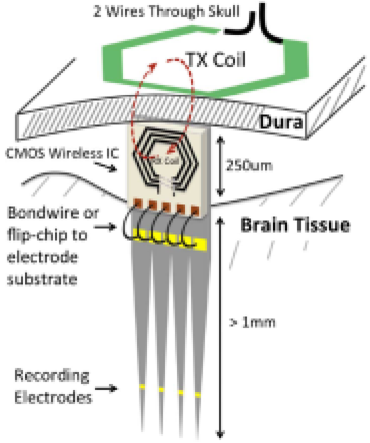
[Doerner 2010]



[Muller JSSC 2012]



[Mark VLSI 2011]



[Biederman JSSC 2013]

Today's systems

Bulky, invasive, wired, low-density

Moving towards wireless **but**

It's all about size & energy

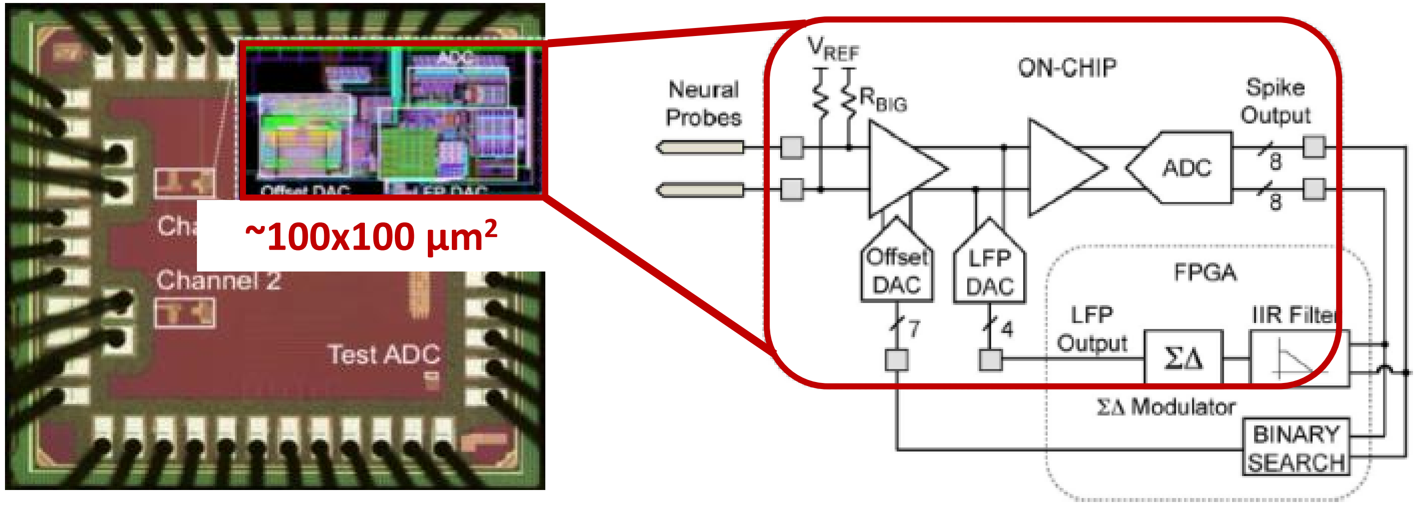
Scaling **limited** due to shank size

Smallest front end published: **250 x 450 µm^2**

Lowest Power: **2.5 µW/chan**

[Biederman 2013]

Active Implementation: CMOS Limit

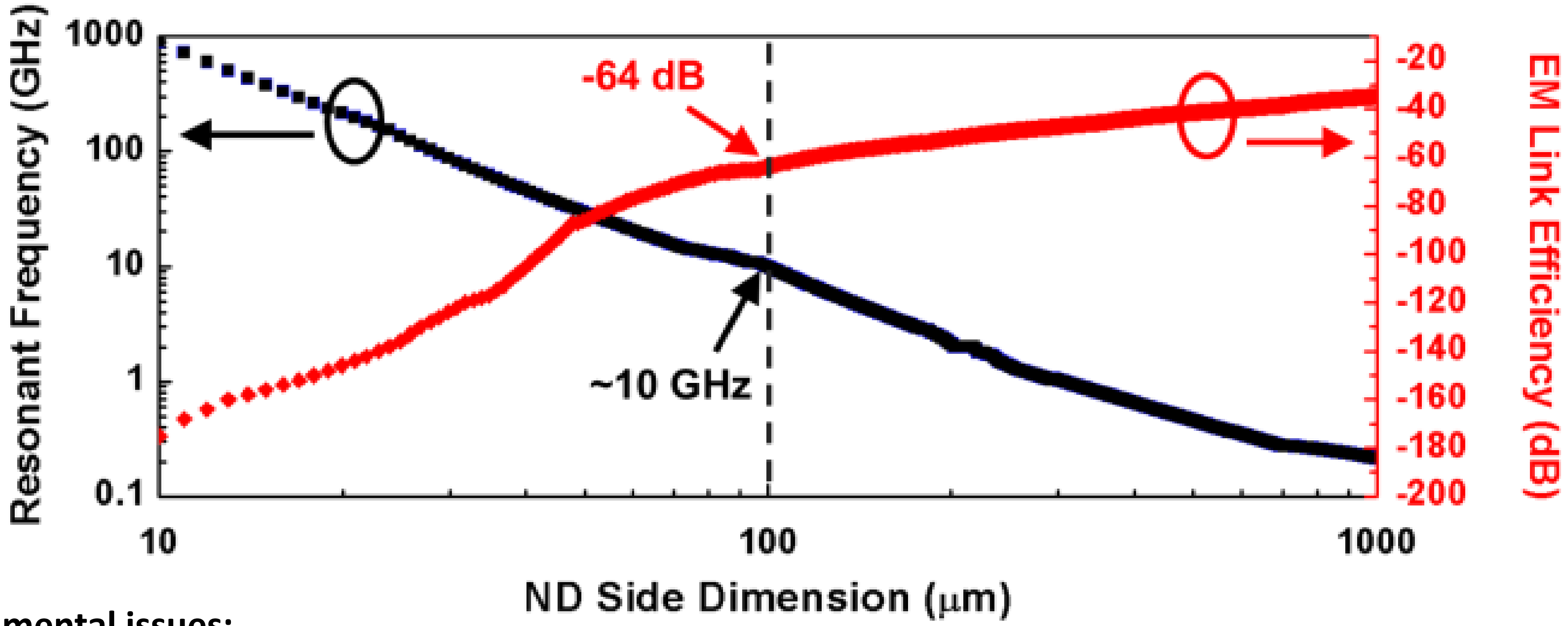


~100x100 µm^2

[Muller JSSC 2012]

- Smallest CMOS neural front-end system
  - **No** *rectifiers* and *modulators*
  - Occupies **~100 µm^2** of silicon
  - Scaling of CMOS with *same* functionality is challenging

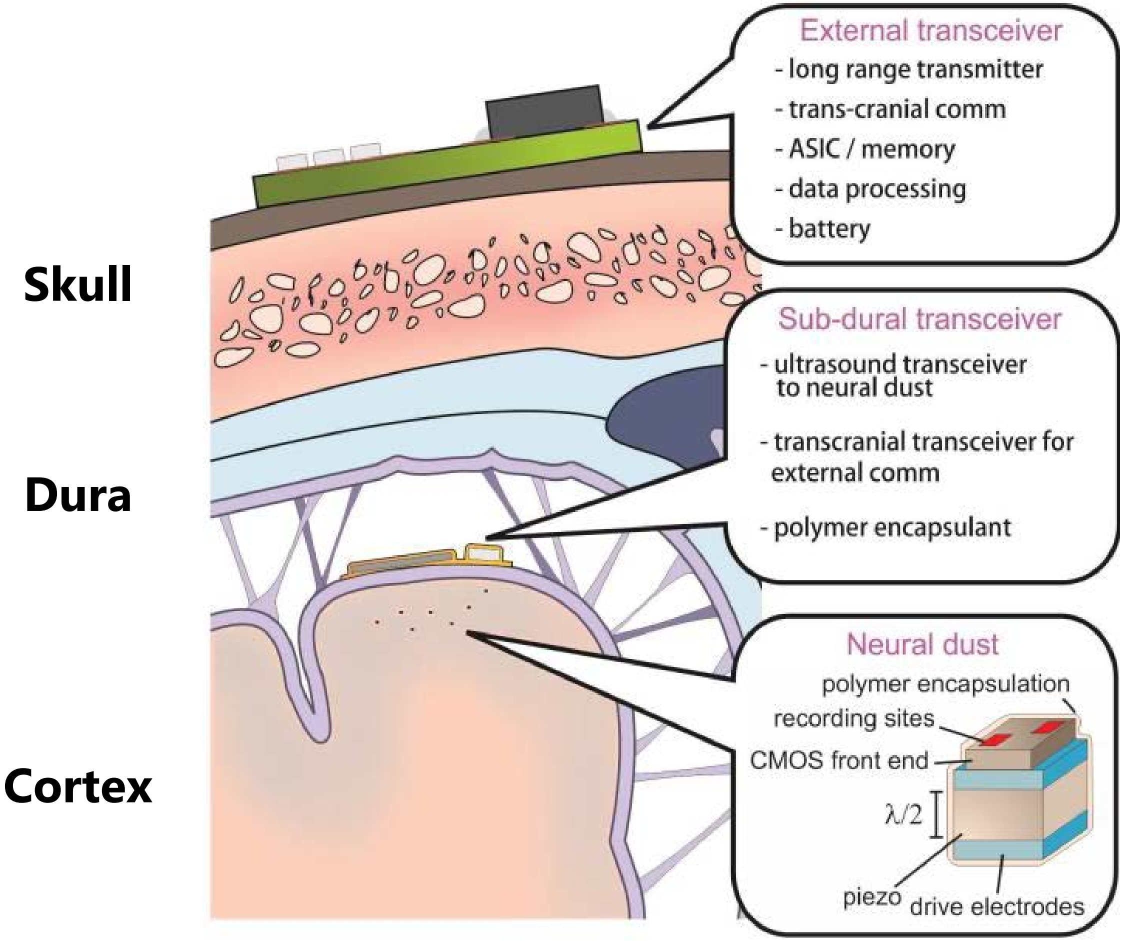
RFID to the brain?



Two fundamental issues:

- A small form factor (volume) + speed of light → **f_{res} = 10’s GHz**
  - Significant tissue loss at such high frequency
- **Output power limit** due to safety regulations: 10 mW/cm^2
  - e.g. 1 mm^2 interrogator, 100 μm dust node, 2 mm distance → received power < 40 pW << 2.5 μW for CMOS

A Neural Dust system



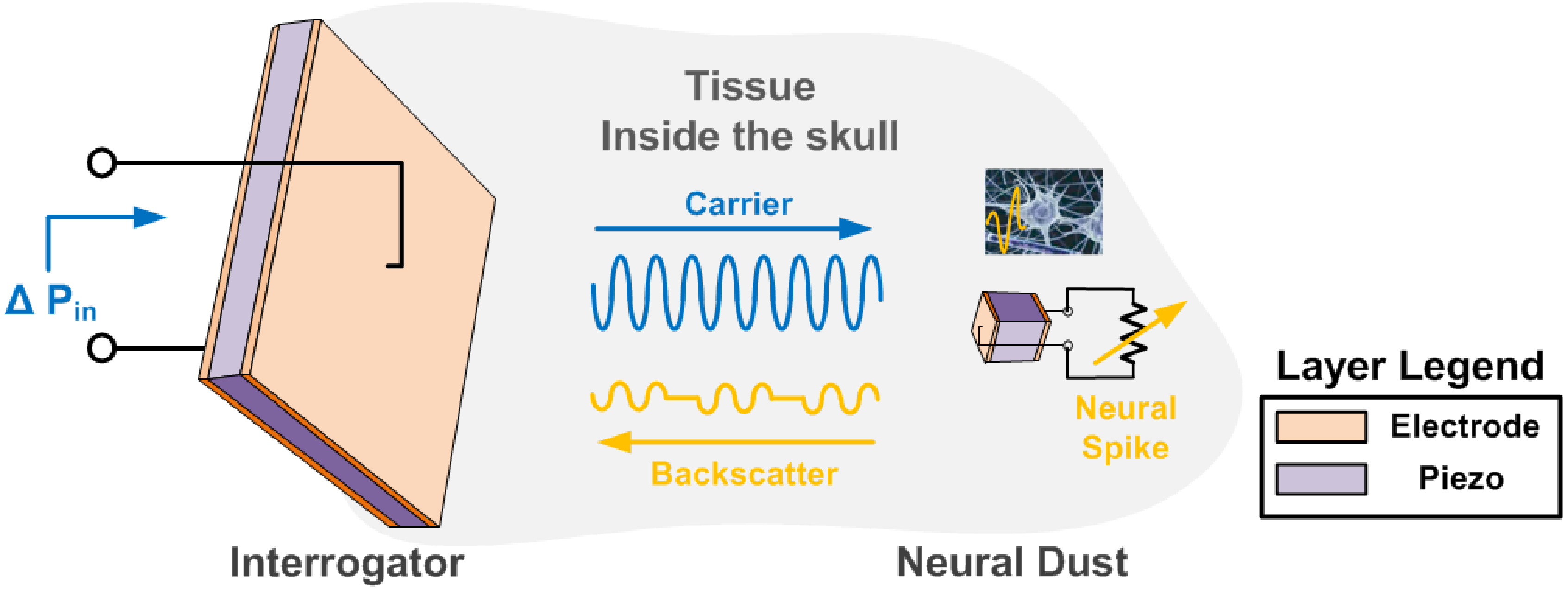
External transceiver
- long range transmitter
- trans-cranial comm
- ASIC / memory
- data processing
- battery

Sub-dural transceiver
- ultrasound transceiver to neural dust
- transcranial transceiver for external comm
- polymer encapsulant

Neural dust

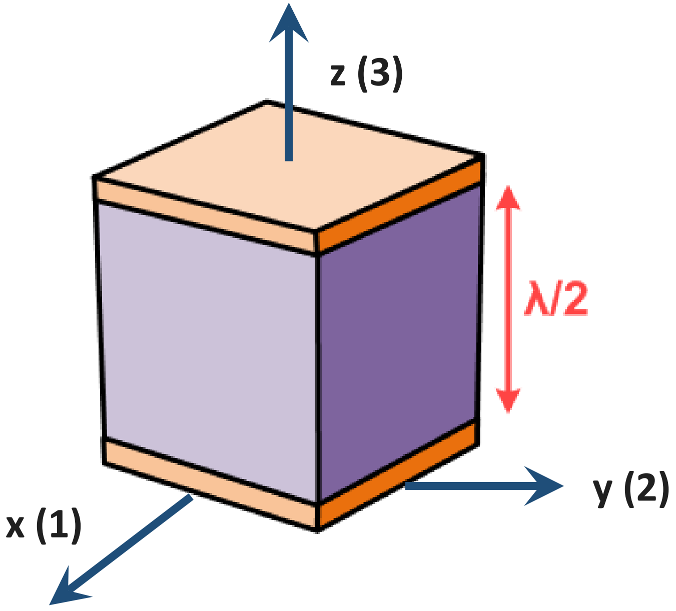
Seo D, *et al*. “Neural Dust: An Ultrasonic, Low Power Solution for Chronic Brain-Machine Interfaces,” *arXiv*, Jul. 2013
Seo D, et al. “In Vitro Characterization of Untethered, Ultrasonic Neural Dust Motes for Cortical Recording,” *submitted*

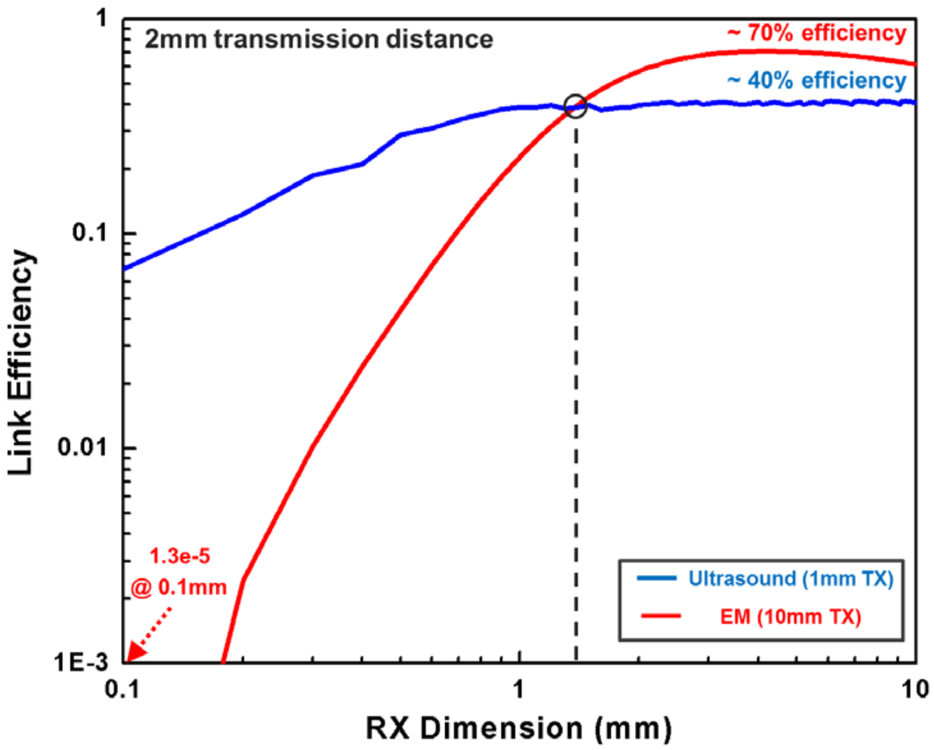
Basic neural dust operation



- the **interrogator** couples ultrasound energy to the **motes**
- the interrogator can perform both spatial and frequency discrimination with sufficient bandwidth/resolution to interrogate each mote
- each mote consists of a piezoelectric transducer, surface electrodes for electrophysiological signal acquisition, and a silicon CMOS die containing electronics for signal amplification/conversion.
- The mote reports recorded signals back to the interrogator by reflecting and modulating the amplitude, frequency, and/or phase of the impinging ultrasound wave.

Ultrasound coupling to motes

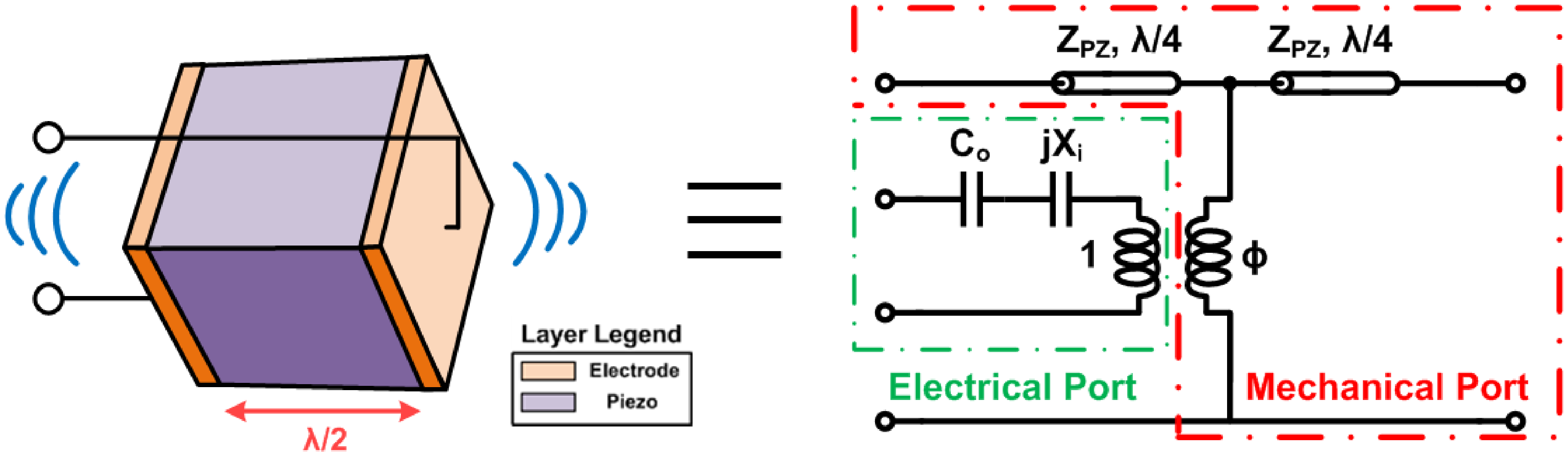




- Low acoustic velocity allows operation at a much **lower frequency**
  - e.g. λ = 150 µm @ 10 MHz **US** *vs.* λ = 5 mm @ 10 GHz **EM**
- The acoustic loss is **smaller** than EM loss
  - Safety regulation (**10 mW/cm²** for **EM** *vs.* **720 mW/cm²** for **US**)

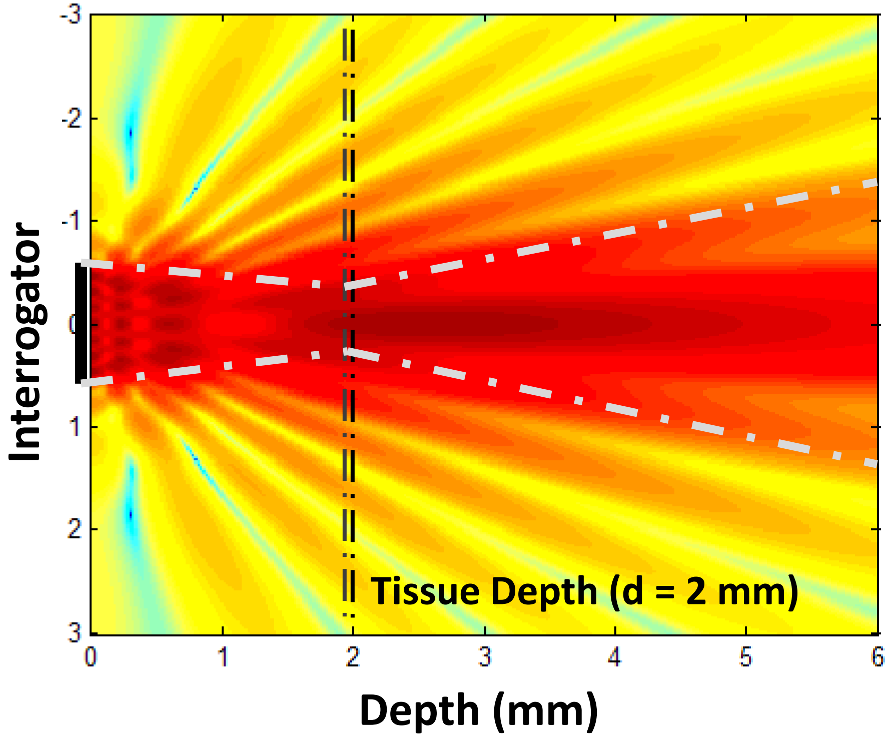
[Attenuation of ultrasound in brain is ~0.5 dB/(cmMHz) and bone is ~22 dB/(cmMHz). Peripheral tissues are somewhere in between.]

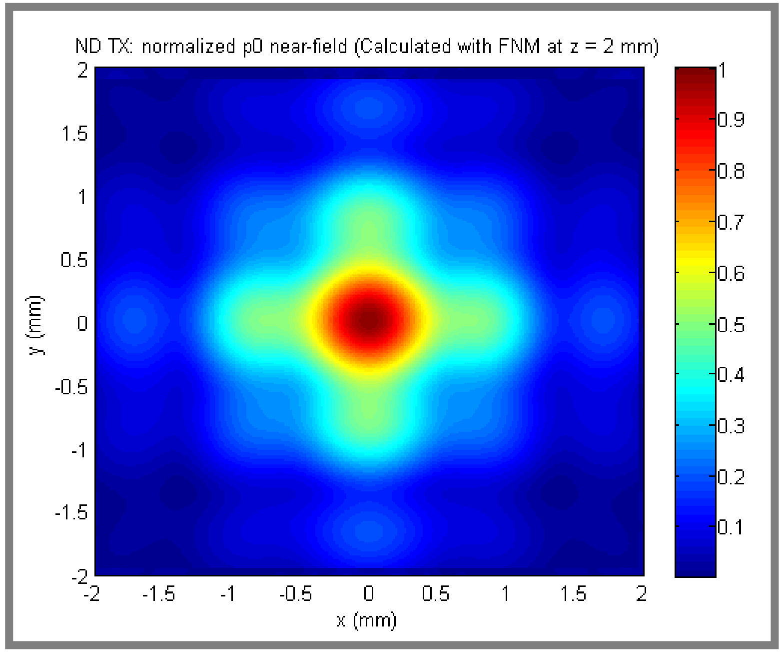
Piezoelectric XDCR



- XDCR model using 3-port network, based on KLM model (1970)
- Both electrical and mechanical resonances
  - Determined by the thickness of the XDCR
  - Aspect ratio: Interrogator (10:10:1), **neural dust (1:1:1)** for density

Model Limitation: Beam Spreading

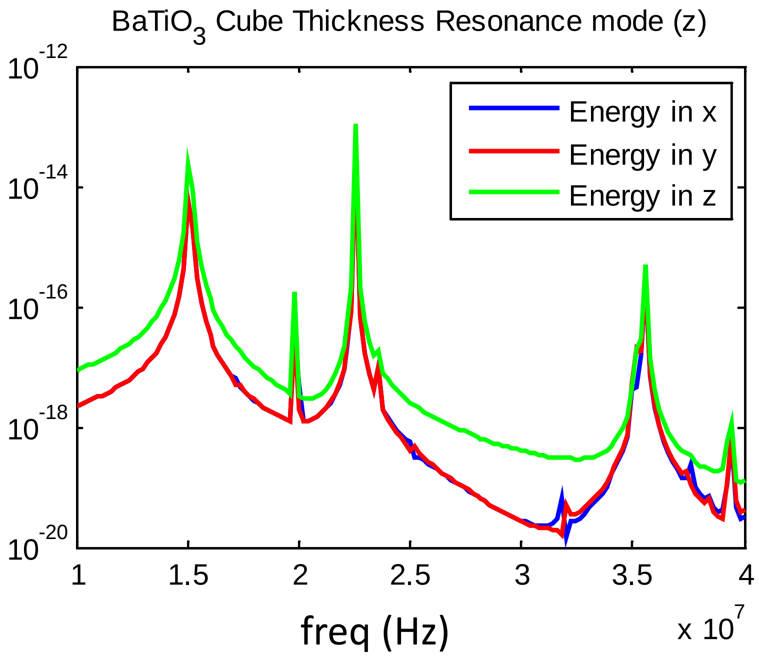




Rayleigh Distance = $\frac{D^2}{4\lambda}$

- 3D loss mechanism: beam spreading modeled as loss
- Neural dust placed at interrogator's Rayleigh distance
  - Interrogator sized **($1\ mm^2$)** to match its Rayleigh distance (natural focus) with tissue transmission distance **(d = 2 mm)** **@ 10 MHz**
- Beam steering to enable multi-node interrogation (more later)

Cube: Mode Coupling (Re-Radiation)

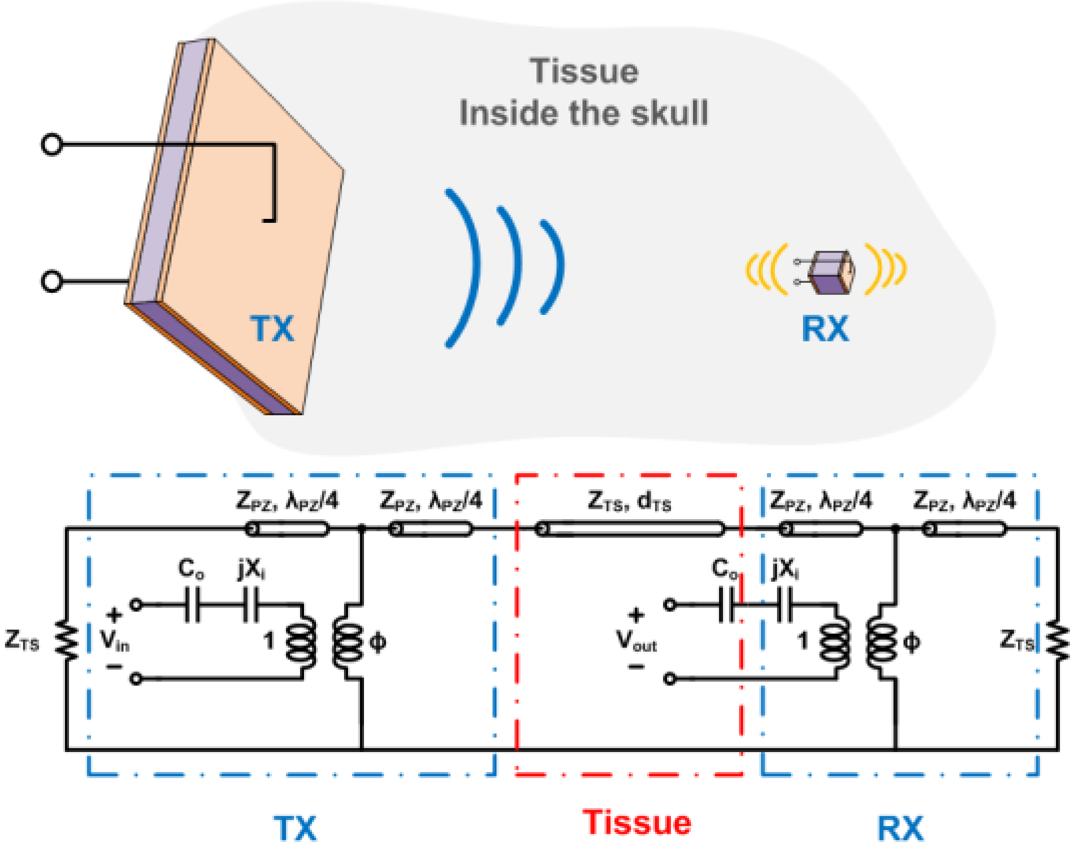


Simulation Result:

- @15MHz (1st resonance)
  E_x/E_{total} = 16.6%
  E_y/E_{total} = 16.6%
  E_z/E_{total} = 66.8%
- @22.6MHz (2nd resonance)
  E_x/E_{total} = 21.0%
  E_y/E_{total} = 20.2%
  E_z/E_{total} = 58.8%

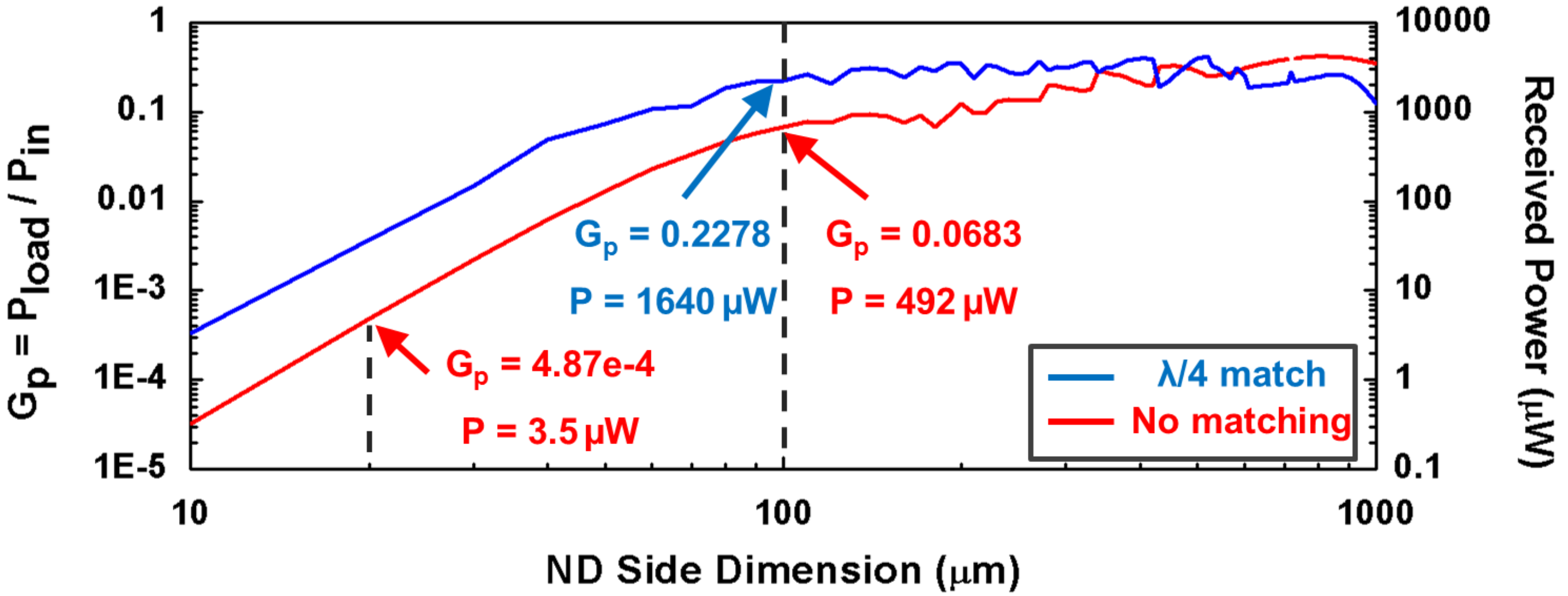
- Re-radiation along two perpendicular axes due to Poisson's ratio
  - COMSOL simulation: **>66%** of the energy kept in the main thickness resonance mode
  - Modeled as additional loss

Sub-Dural Link Model



- TX (interrogator) and RX (neural dust) modeled with KLM
  - Match resonant frequency to maximize power transfer
- 2 mm tissue as a lossy transmission line

Link power and efficiency

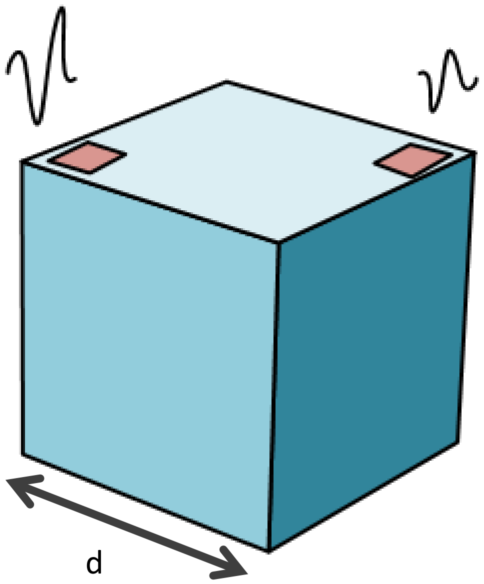


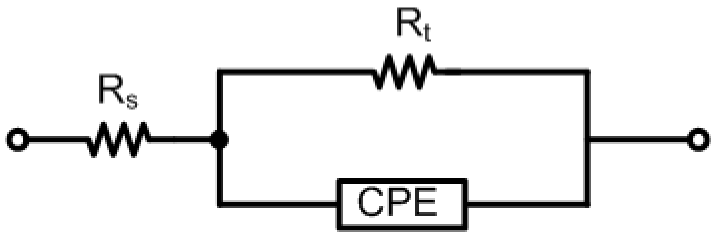
- Efficiency of **~7%** (or -11.6 dB) at 100 μm
  - Received power: **~500 μW** US vs **~40 pW** EM (1 mm^2 interrogator)

- Scaling indicates reception of 3.5 μW (> 2.5 μW) at 20 μm node

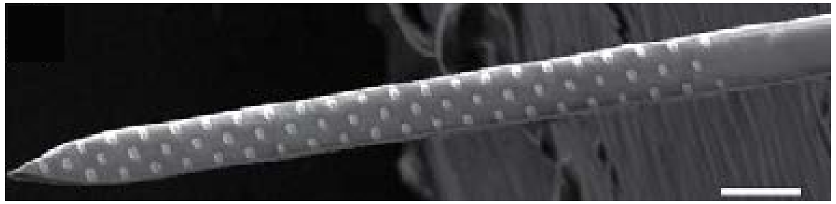
- Mechanical matching with λ/4 layer can improve efficiency
  - Attenuation of the layer (16 dB/cm·MHz) limits the improvement

Scaling: Electrode Modeling





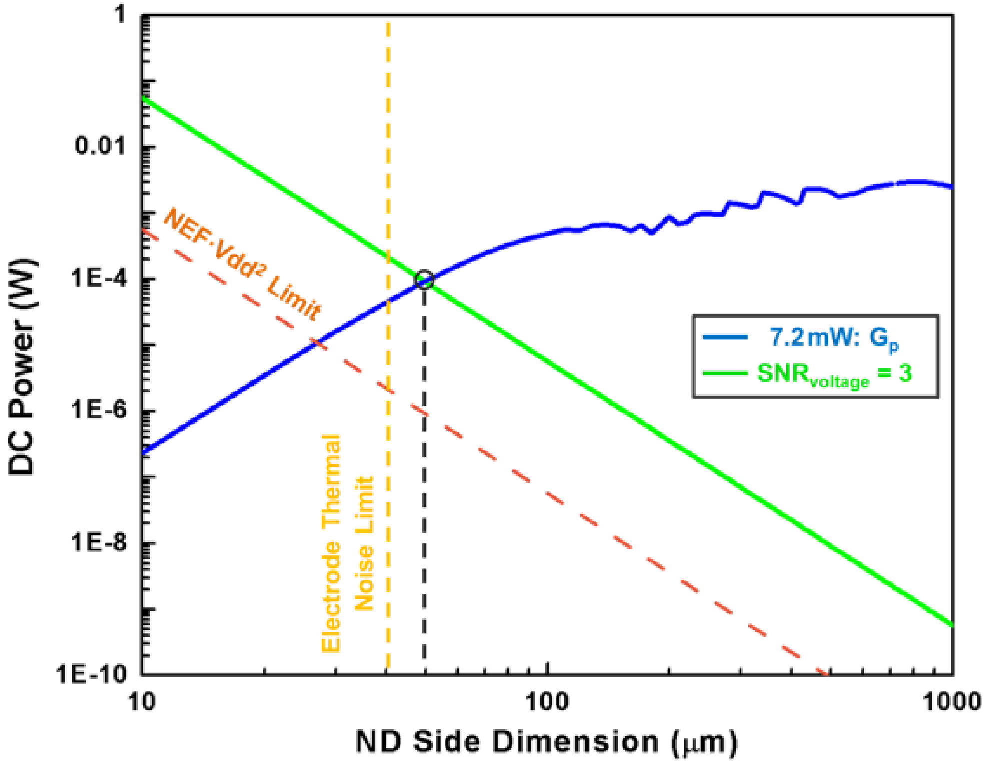
Randles Model for Electrode



[Du PLoS 2011]

- Electrode has thermal noise
  - Electrode |Z| density: $C_{dl} \sim 0.5\ \mathrm{pF}/\mu\mathrm{m}^2$, $R_s = 18.65\ \mathrm{M\Omega}\cdot\mu\mathrm{m}^2$
- Voltages are measured differentially
  - Neural dust: reference electrode on the same footprint
  - e.g., measured signal amplitude for d = 100 µm is ~10 µV [Du 2011]

Scaling of the mote



- Captured power decreases with mote size
- Extracellular recording is differential, so signal decreases with size
  - smaller motes need more power to maintain same SNR
- Fundamental electrode thermal noise

Scaling with an SNR of 10 dB shows operation down to 50 µm

Can exceed FDA safety regulation, but scaling is ultimately **limited** by electrode thermal noise

Passive Implementation Scaling

- *Area Limit*

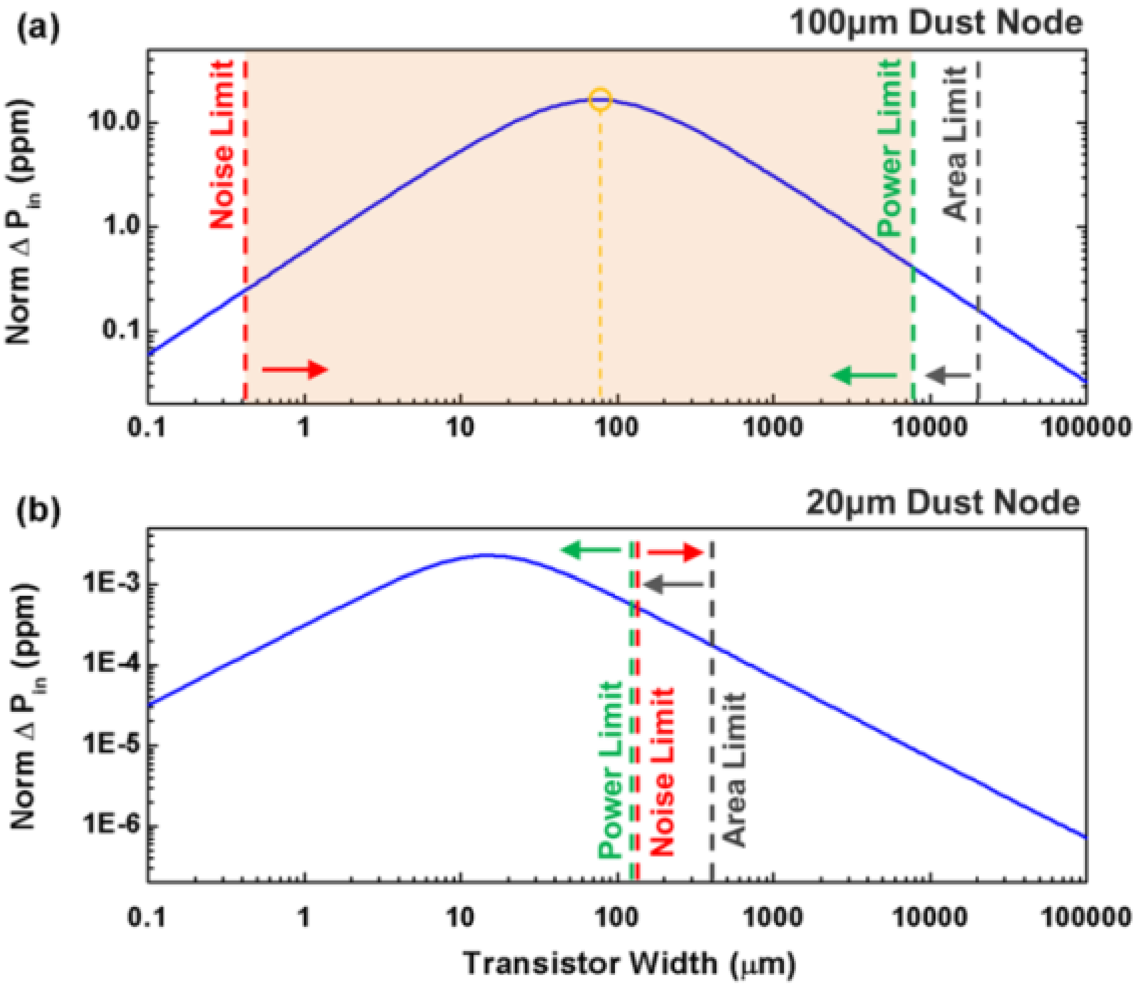
  Max. effective width of the FET on the available footprint

- *Noise Limit*

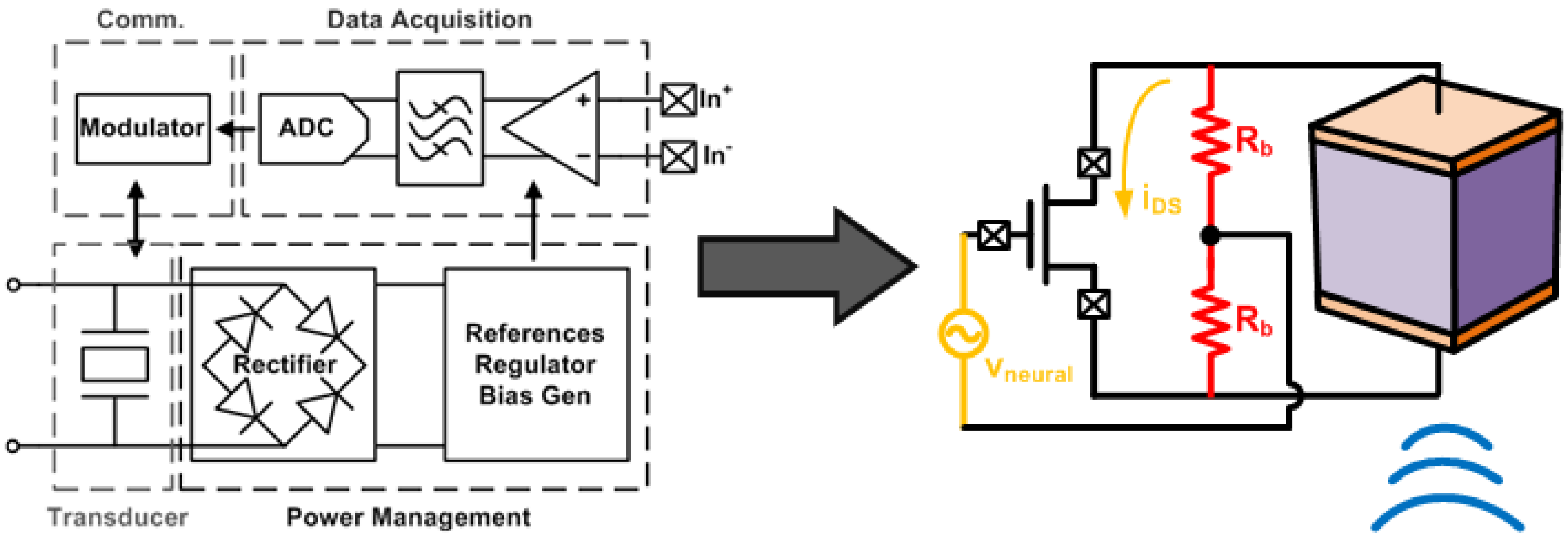
  FET width to support min. I_{DS} necessary to achieve a certain input referred voltage noise

- *Power Limit*

  Delivered power needed to operate the FET reliably (V_{DS})

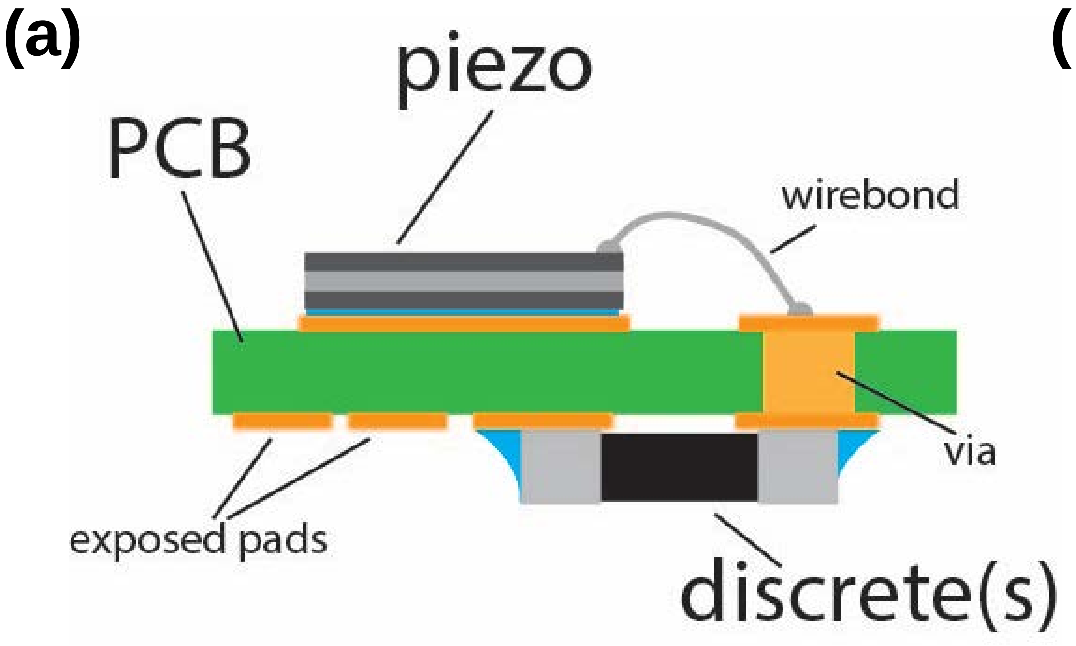


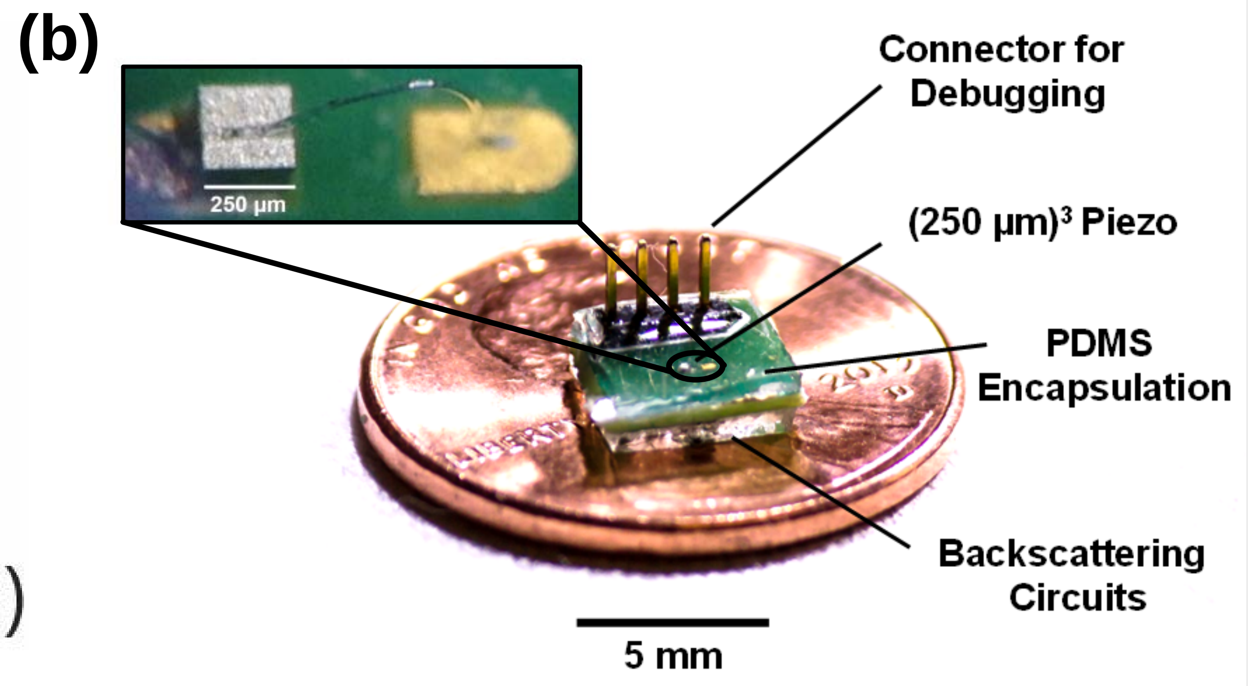
How do you build the front end?

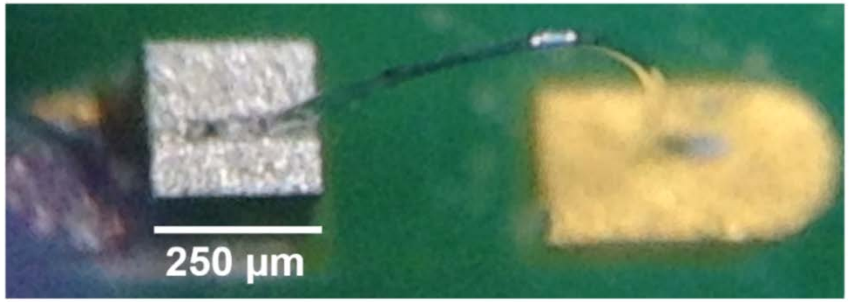


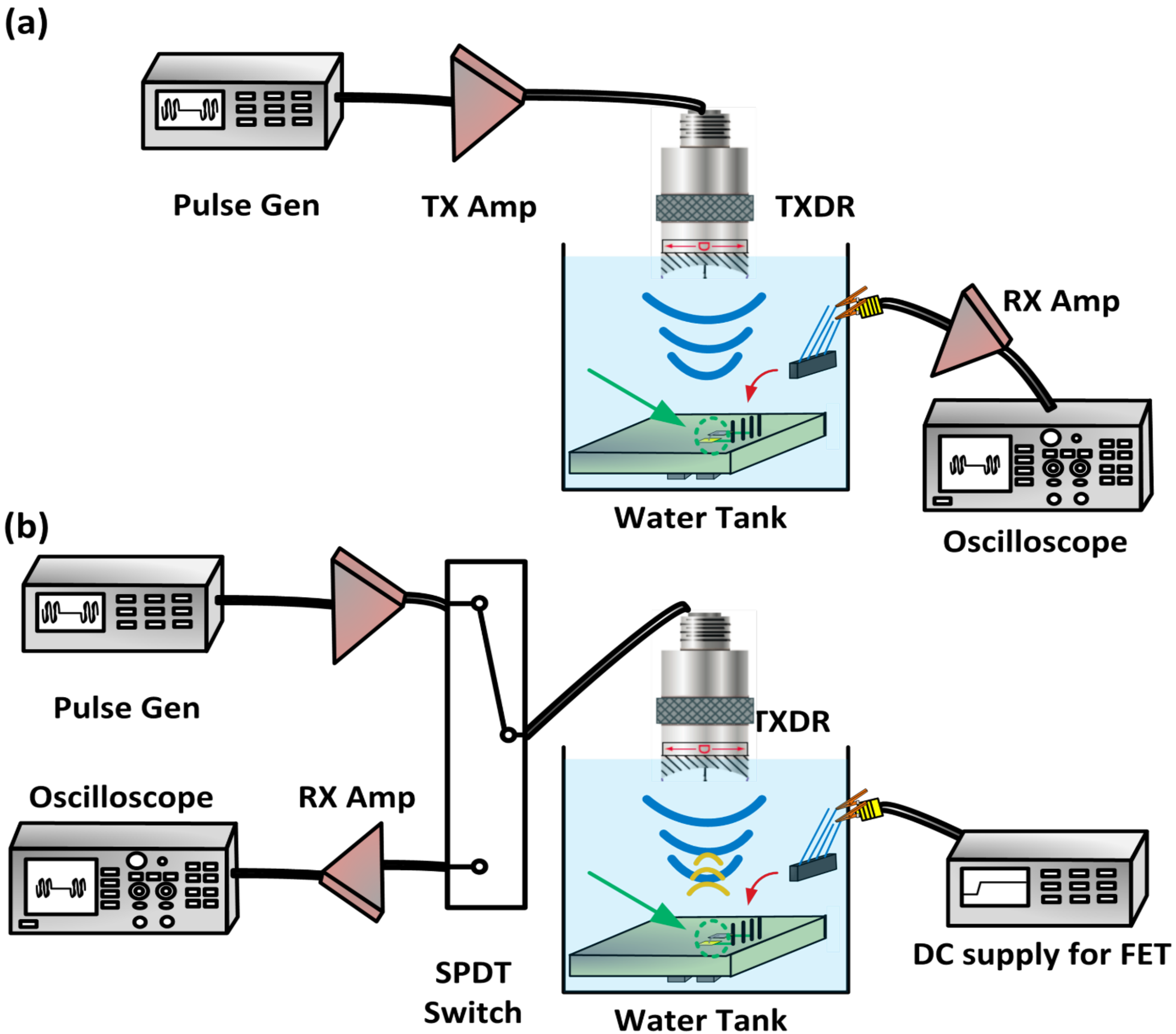
Simplified neural front-end with a single FET sensor

- Electrical load impedance (FET) varies with v_{neural}
- Instantaneous ultrasonic wave reflectivity changes
- Backscattered wave is modified


(a)
piezo
PCB
wirebond
via
exposed pads
discrete(s)

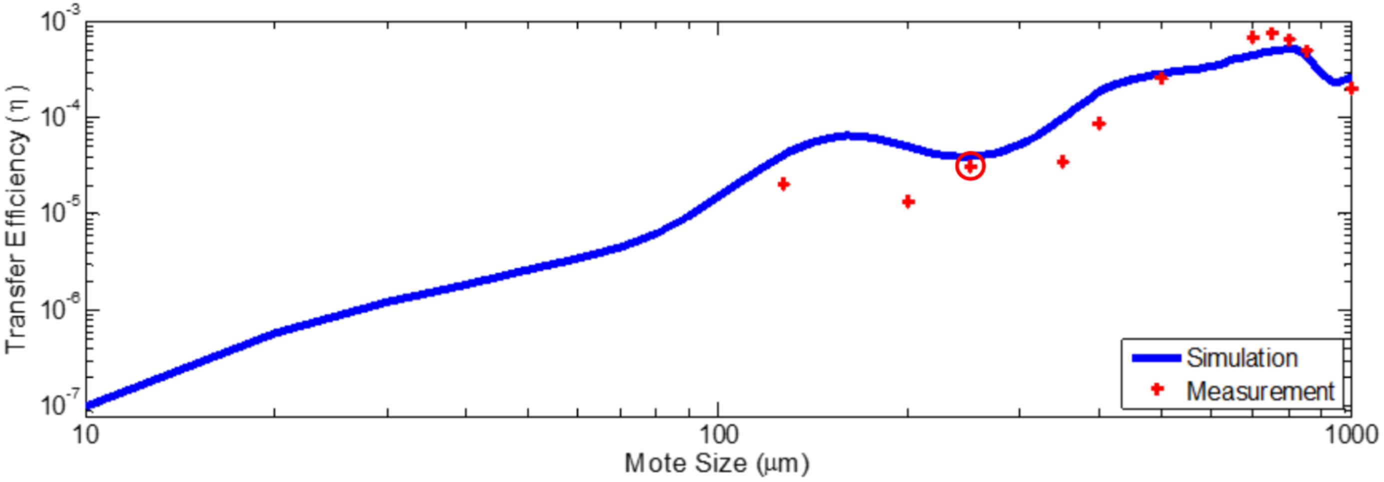

(b)
250 µm
Connector for Debugging
(250 µm)³ Piezo
PDMS Encapsulation
Backscattering Circuits
5 mm


250 µm

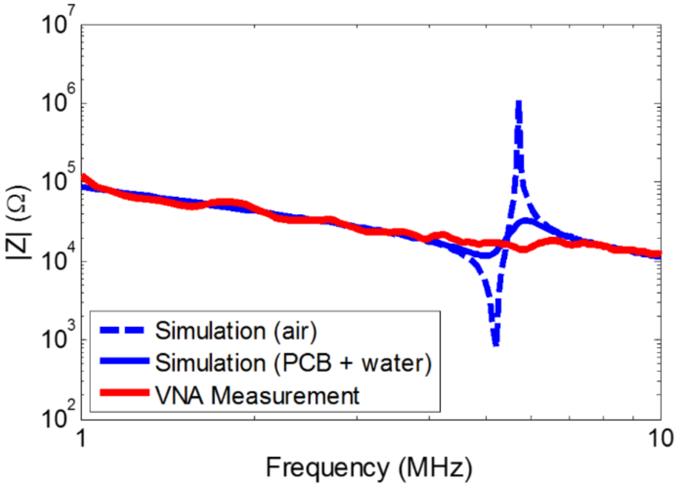

(a)
Pulse Gen
TX Amp
TXDR
RX Amp
Water Tank
Oscilloscope
(b)
Pulse Gen
TXDR
Oscilloscope
RX Amp
DC supply for FET
SPDT
Switch
Water Tank

Initial validation of power coupling

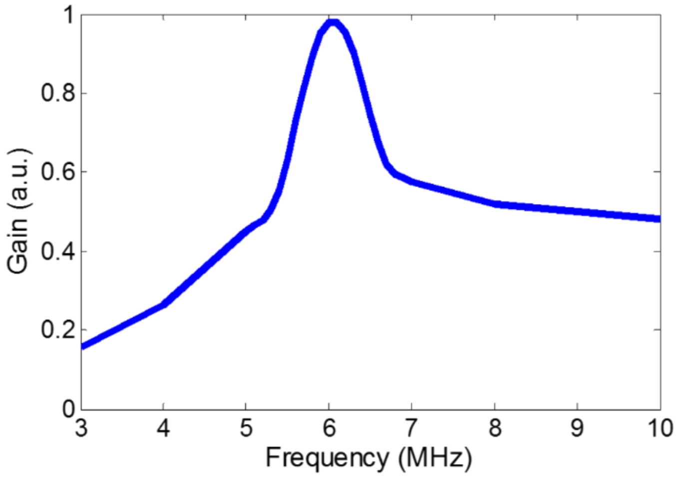
(a)



(b)



(c)

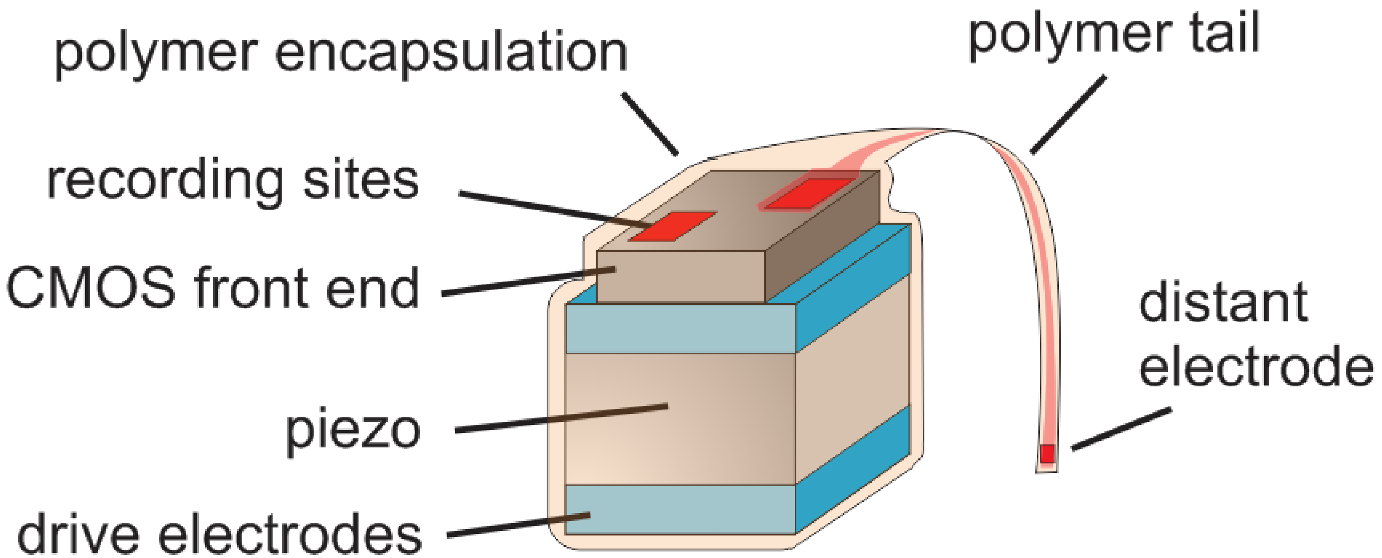


(a) Measured power transfer efficiency at various mote sizes matches simulated behavior closely.

For each mote dimension, both **(b)** the impedance spectroscopy and

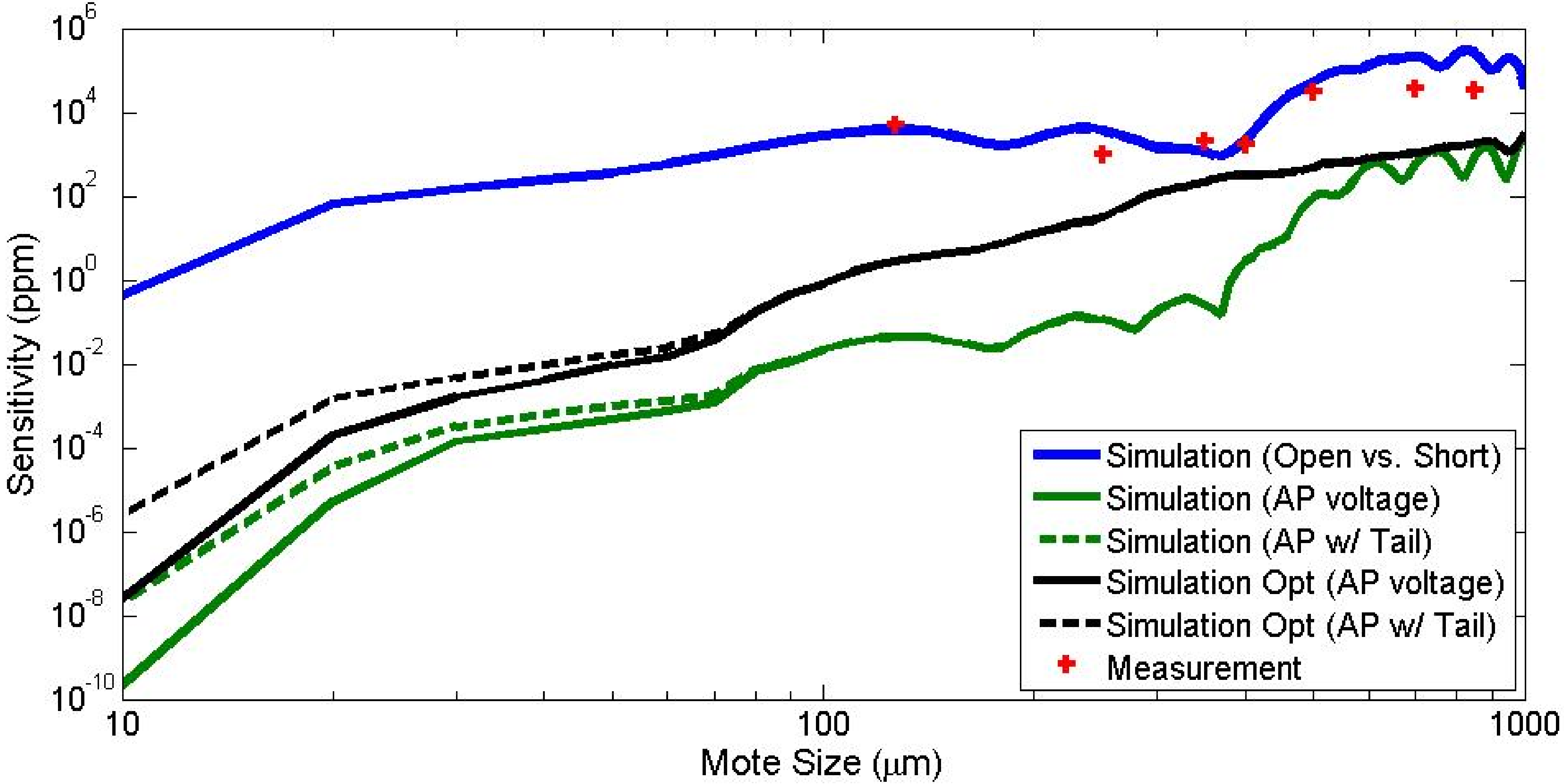
(c) frequency response of harvested power on the PZT reinforces the reliability of the simulation framework.

Re-design of Neural Dust: Tail



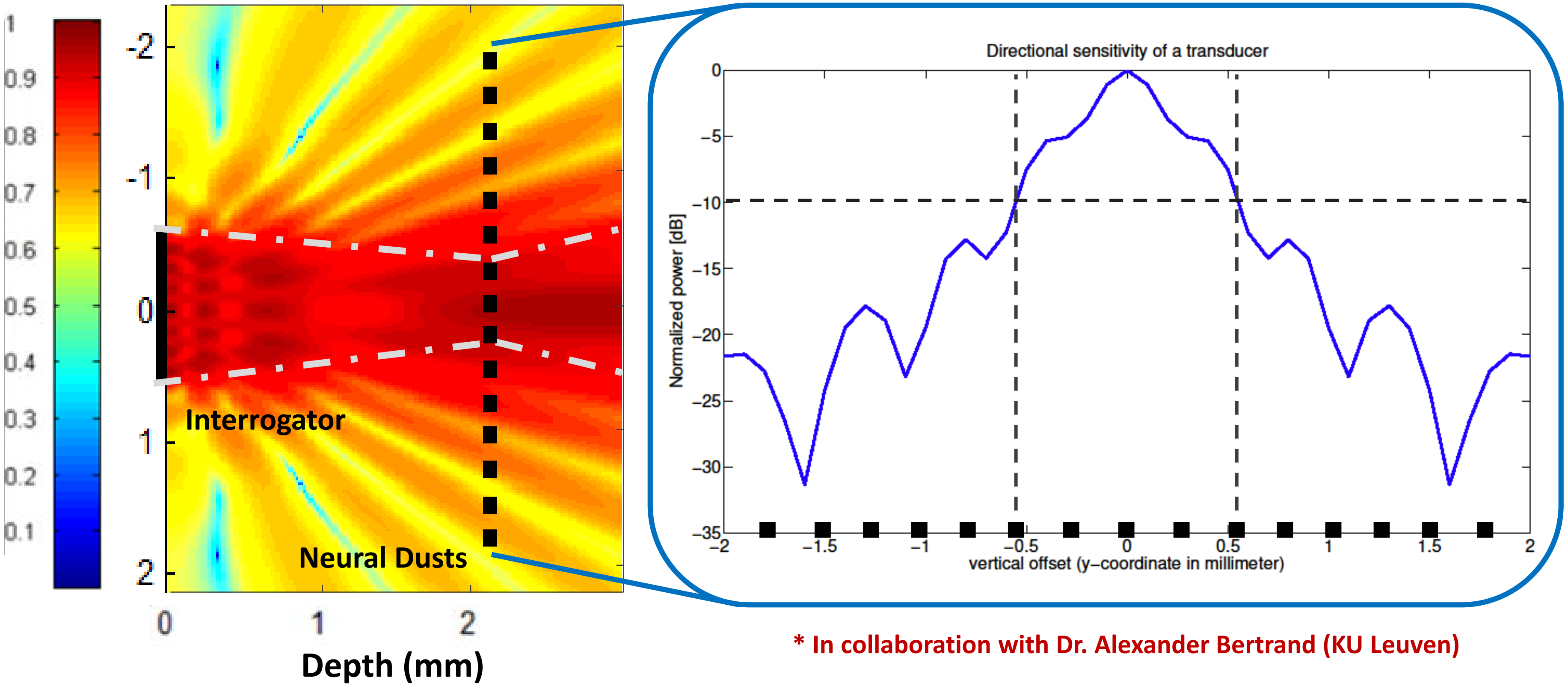
- Scaling of both *active* and *passive* limited by the <u>noise requirement</u>
  - ~1 – 5 µm wide "*tails*" placing ref electrode(s) ~100 µm from the base
  - Flexible and ultra-compliant substrate
  - Decoupling the interplay between size of the implant and the achievable input SNR

Initial validation of power coupling



Simulated backscatter sensitivity scaling plot for various impedance levels.

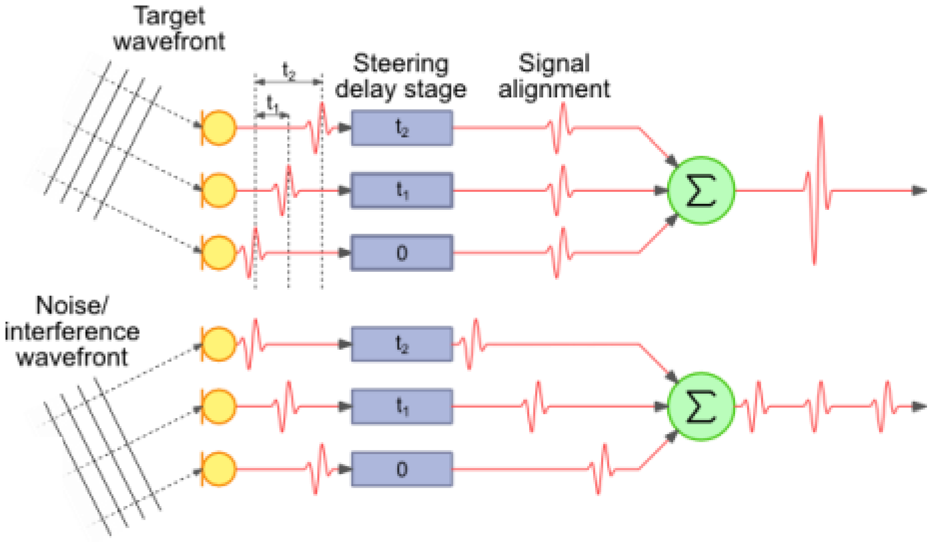
Interrogating Multiple Neural Dusts?



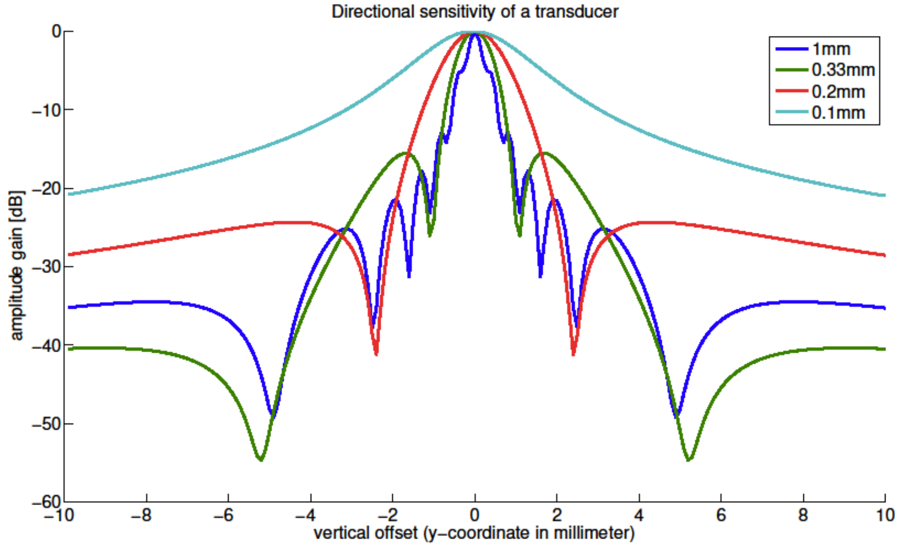
*** In collaboration with Dr. Alexander Bertrand (KU Leuven)**

- Single transducer interrogator (1 mm) is quite directive
  - Signal reception at neural dust nodes is unequal
  - Want to maximize **power transfer** & **reflectivity** at each neural dust

Interrogating Many NDs



* from www.labbookpages.co.uk



- <u>Beamform</u> to maximize power transfer to every node
  - If the total aperture is 1mm, then same Rayleigh distance ($d = D^2/4\lambda$)
  - e.g., 10 x 0.1mm transducers <u>**in total**</u> distributed over a 1mm interrogator
- Simulations under 2D simplification & assume sequential interrogation

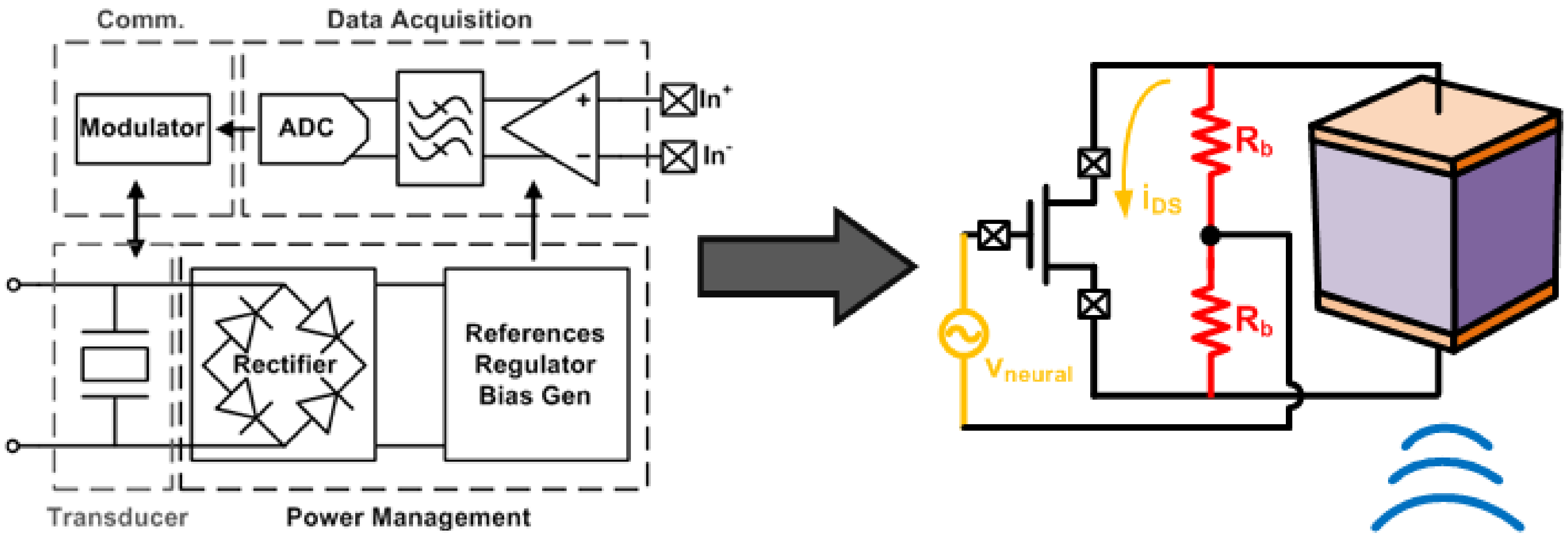
Looking forward

- Many opportunities and challenges as we miniaturize hardware and move into organisms!
- “Extreme” miniaturization / ultra-low power / new sensors will create entire new opportunities in neural applications
- Exciting times!

Thanks!

Questions?

Passive Implementation



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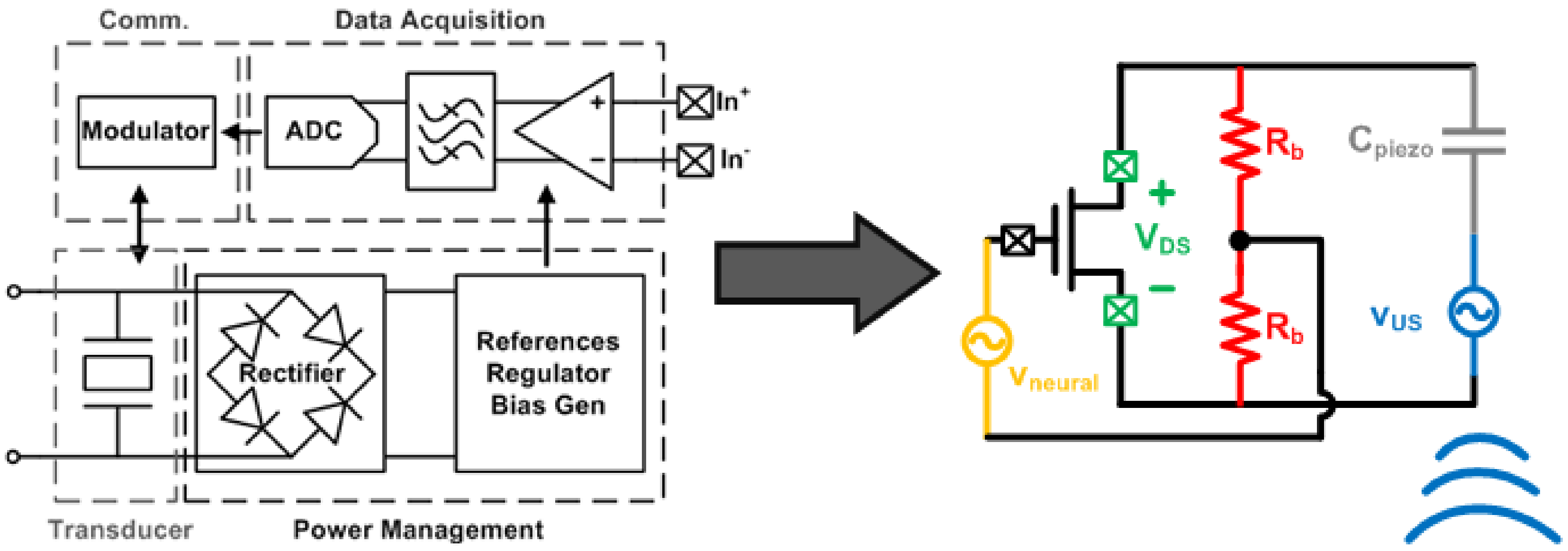
Passive Implementation



- Harvested V_{DS} of the FET swings both positive and negative
  - Careful **not** to forward-bias source/drain to body diodes

- Design considerations:
  - R_b & C_{piezo} filtering: $f_{LP} > 10$kHz (BW of v_{neural}), $f_{HP} < 10$ MHz (v_{US})
  - FET sized to maximize reflectivity