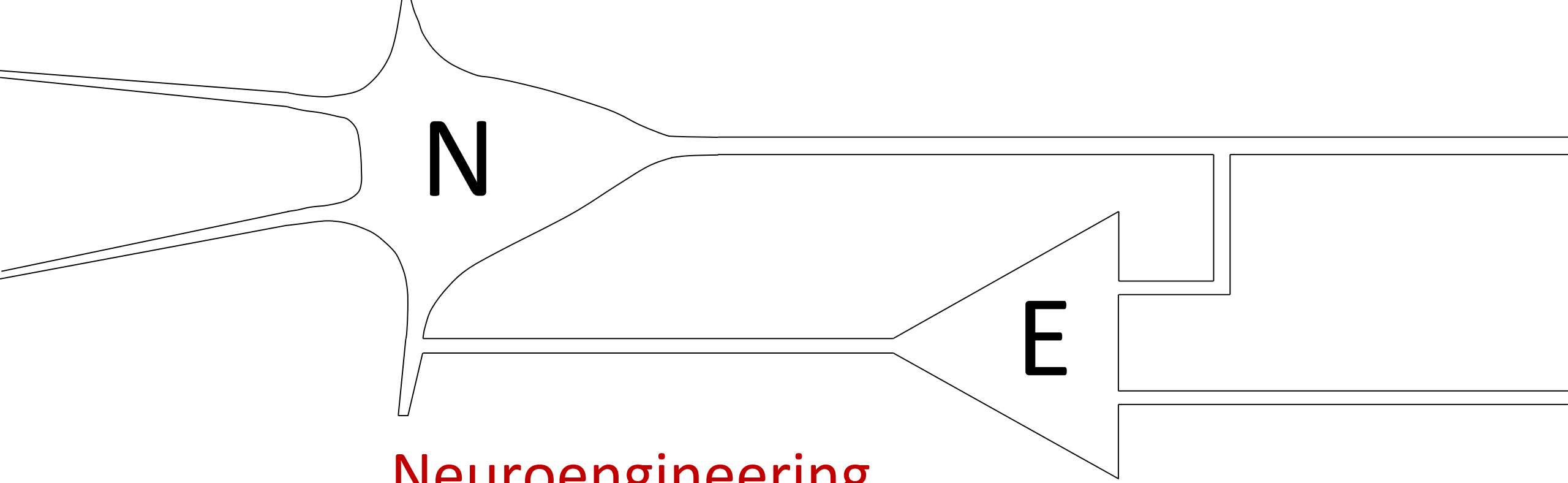


Neuroengineering the Next Decade

Dejan Marković

UCLA ECE Department

dejan@ucla.edu

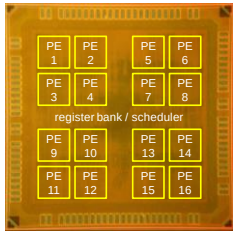
CENT

Center for **NeuroTechnology**

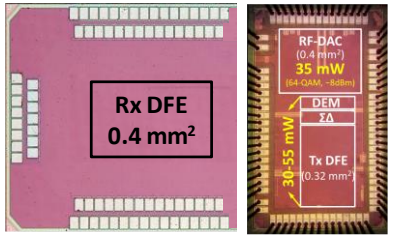
Low-Power Expertise, New Challenges

Radio

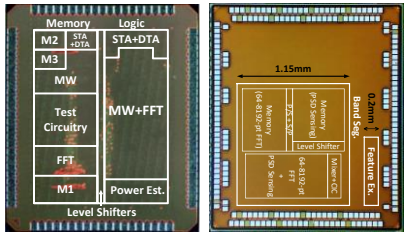
MIMO BB



SDR DFE Rx/Tx

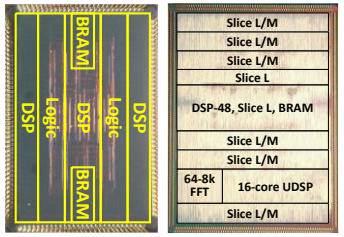


Cognitive DSP BB

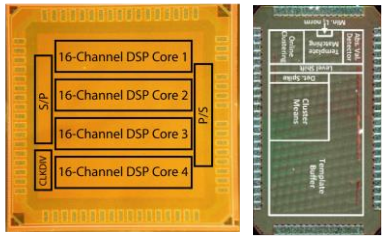


New dsp

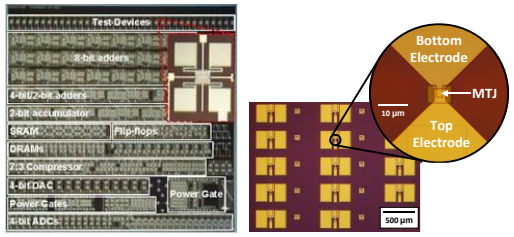
Flexible logic



Neural-spike DSP

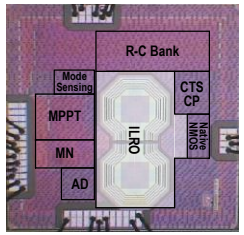


Post-CMOS

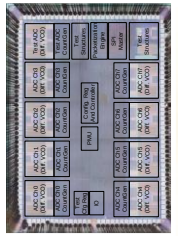


biomed

Energy harvesting



Neuroscience and therapy



Brain Disease is a Growing Problem

Socio-economic impact in US

Epilepsy monitoring: a gateway to these indications

- Chronic pain (100M people) → **$635B / year**
- Alzheimer's (5.3M people) → **$220B / year**
- Depression (18M)
- Anxiety (3.3M)

Extremely limited or no therapy
>1,000x treatment gap

- Epilepsy (2.3M)

Limited therapy
>100x treatment gap

- Parkinson's (1M)

Effective therapy
10x treatment gap

A subset of patients (1-10%) would qualify for DBS

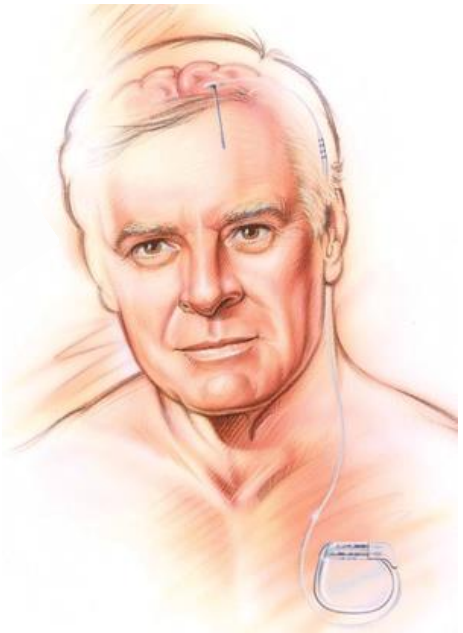
Can't treat complex network diseases with old tools

Low-Precision Tools = Large Treatment Gap

DBS leads today allow **continent-level** access

Existing DBS Device for Parkinson's Disease

- Long procedure, manual control
- Chest-based device, very bulky (**34**cc)
- Low resolution interface technology



Medtronic Activa SC

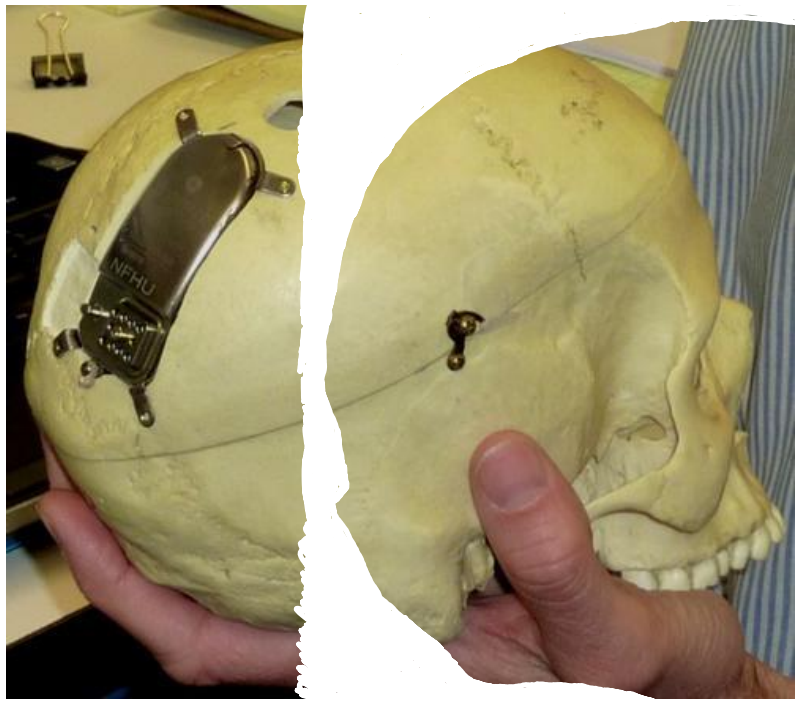
500th DBS patient @ UCLA

May 23, 2013

Courtesy: Dr. Nader Pouratian (UCLA)

Therapeutic Device for Epilepsy

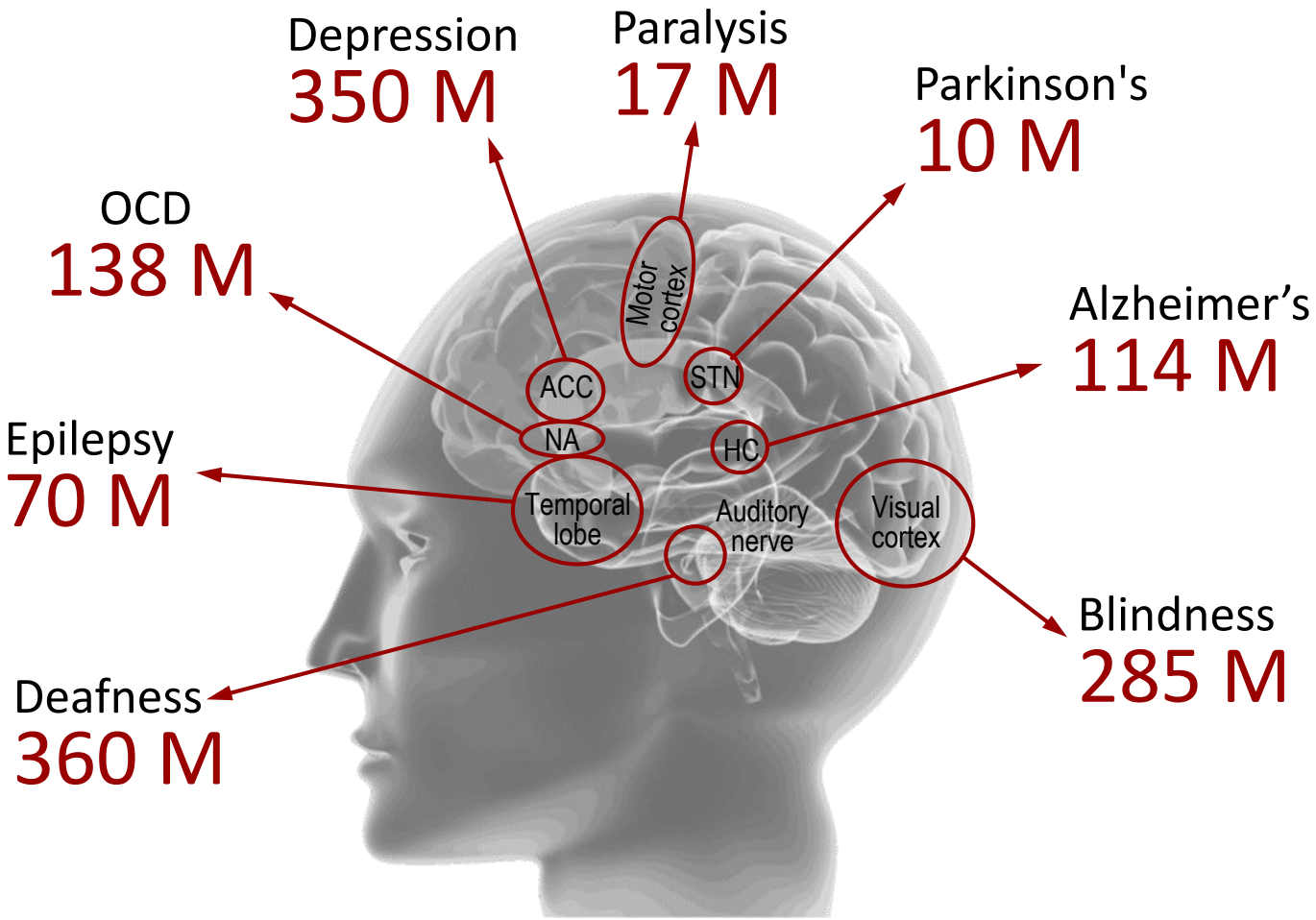
- 8 channels, record (up to 30 min)
- Rec + stim (not simultaneously)
- Replace battery (2-5 years)



NeuroPace RNS-300

The Burden of Neurological Disease

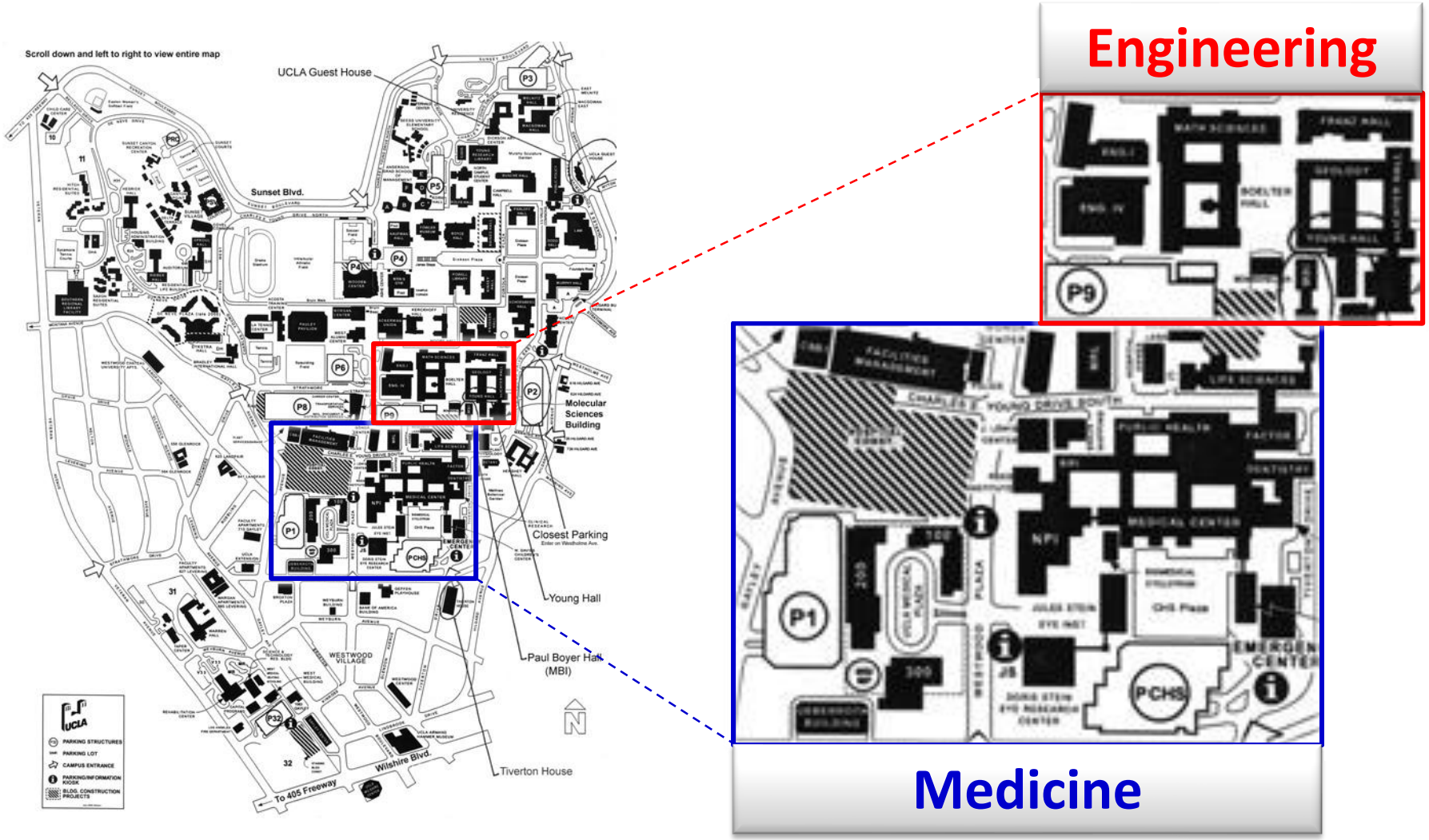
- Pharmacological therapies are limited
- Surgical therapies are even more limited
- Existing surgical therapies
  <10% market penetration



Problems: Why Did Other Indications Fail?

- Same probe design in nearly all DBS applications, despite morphological and anatomical differences in target nuclei
- Mostly open-loop stimulation (on 1 or 2 contacts)
  - Continuous 130-Hz stimulation (amplitude, pulse changes)
- Limited sensing (no sensing, or blank during stimulation)
  - Limited understanding of stimulation tissue response
- Limited wireless data (kbps) and power
  - Limited understanding of deep-brain activity
- Bulky devices, long surgeries

UCLA Medicine and Engineering



A Challenge: Understand Memory

- Alzheimer's disease (age 65+)
  - Cost of care in 2015: **$221B** [1]
  - Apple 2015 revenue: **$233B**

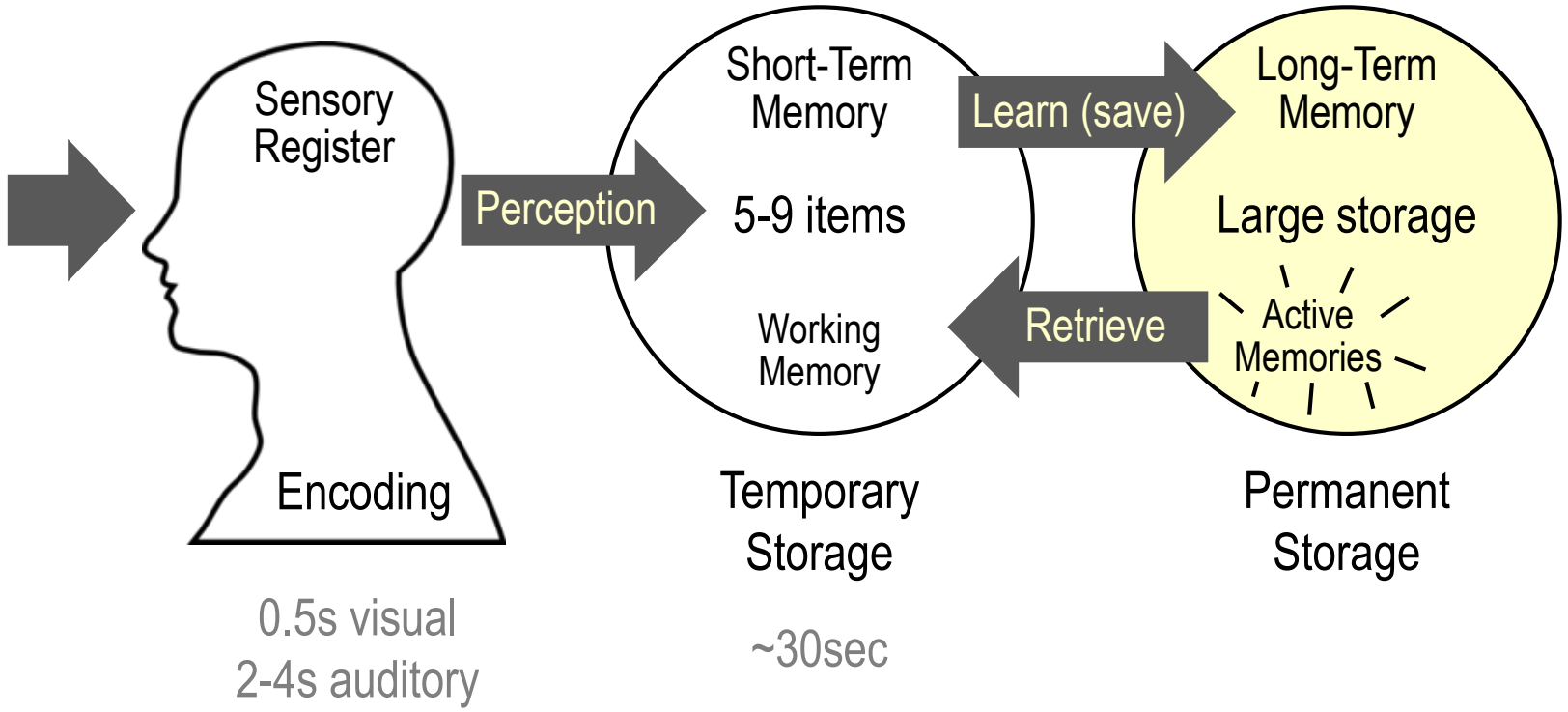
- Younger population (0-14), US
  - Epilepsy: **5 children per day** [2]
  - TBI: **1 ER visit per minute** [3]

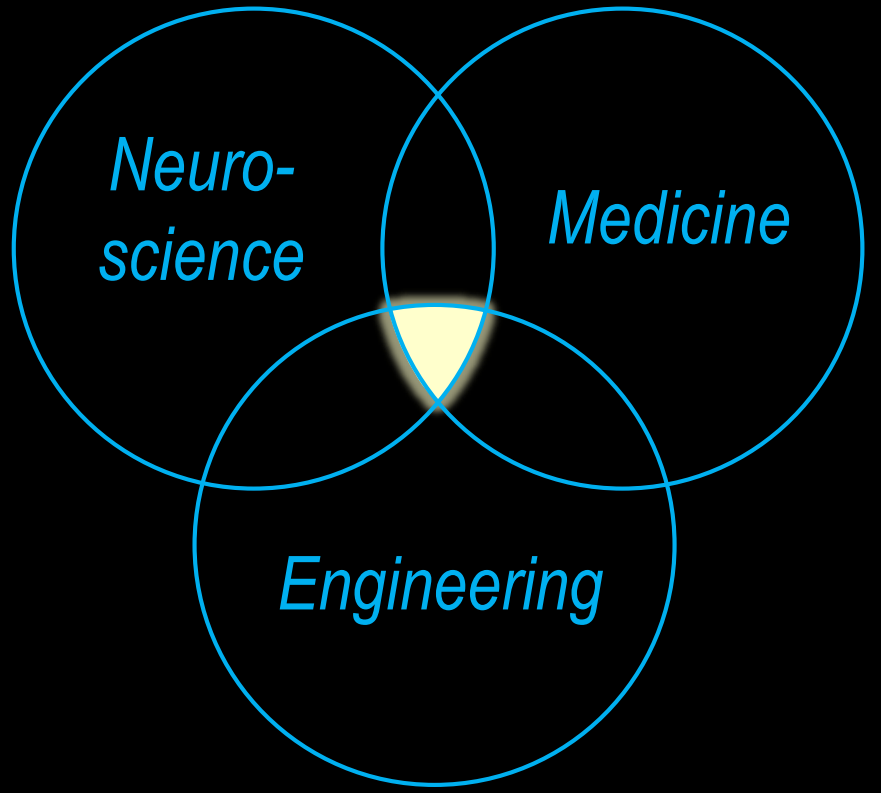
Negative effects on declarative memory

[1] www.alz.org [2] www.epilepsyfoundation.org [3] www.cdc.gov

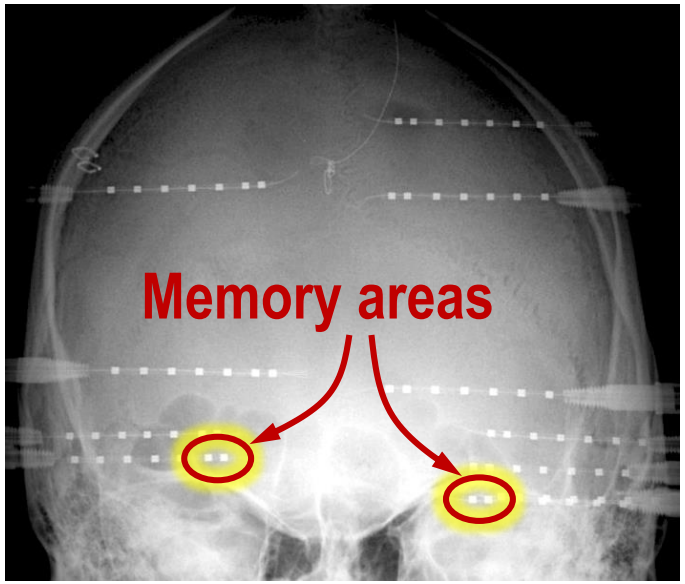
Perception and Memory Model

- **Conscious recollection:** uniquely human
  - Episodic (events), semantic (facts)




Neuro-
science
Medicine
Engineering

Studies of Human Memory Today



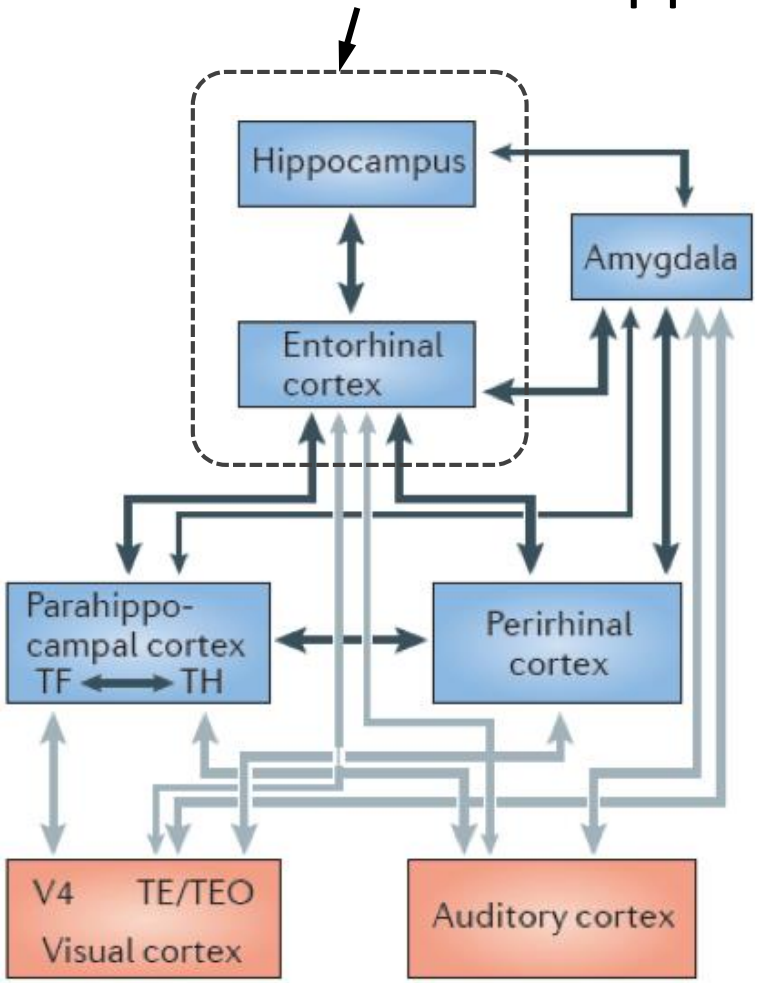
Courtesy: R. Staba (UCLA)

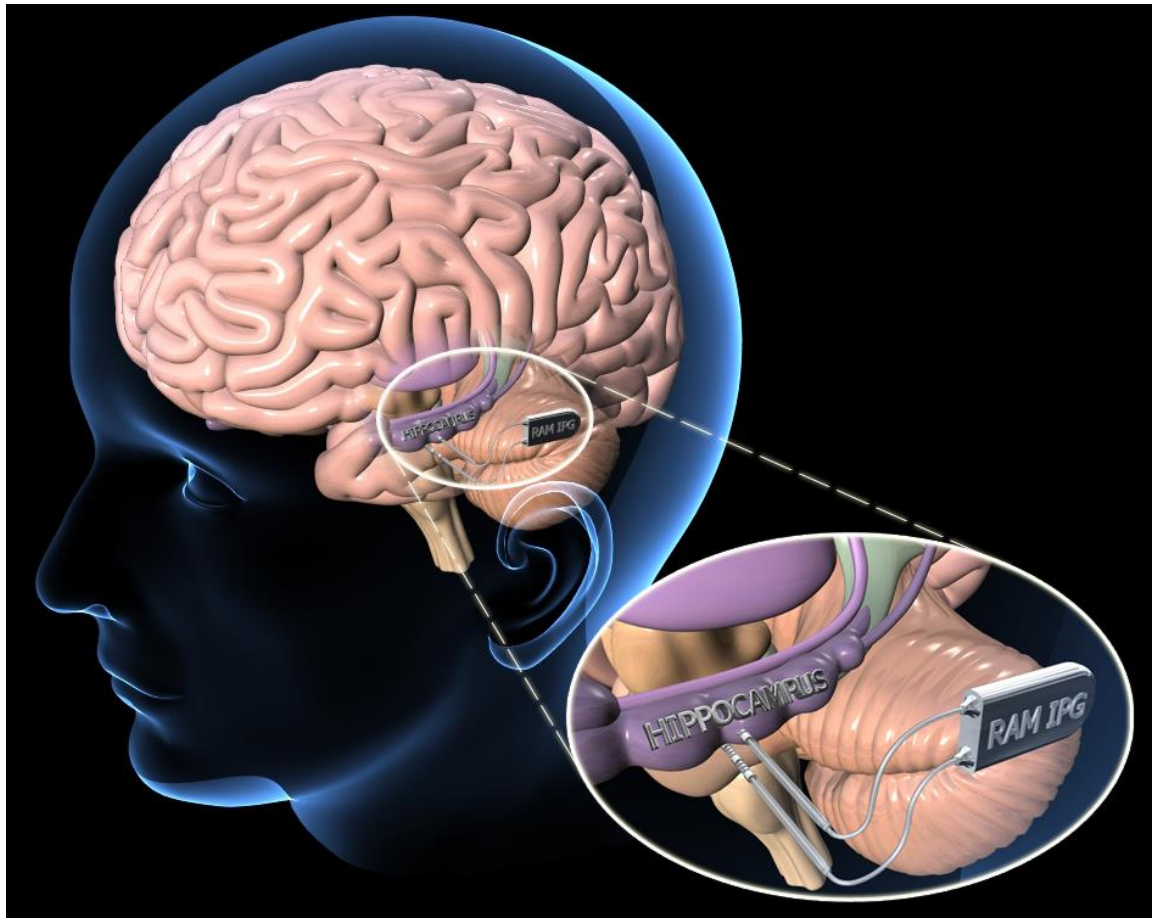
Epilepsy monitoring technology

- Wall-plugged instruments
- Deep intracranial probes
- Hospital environment
- Limited closed-loop

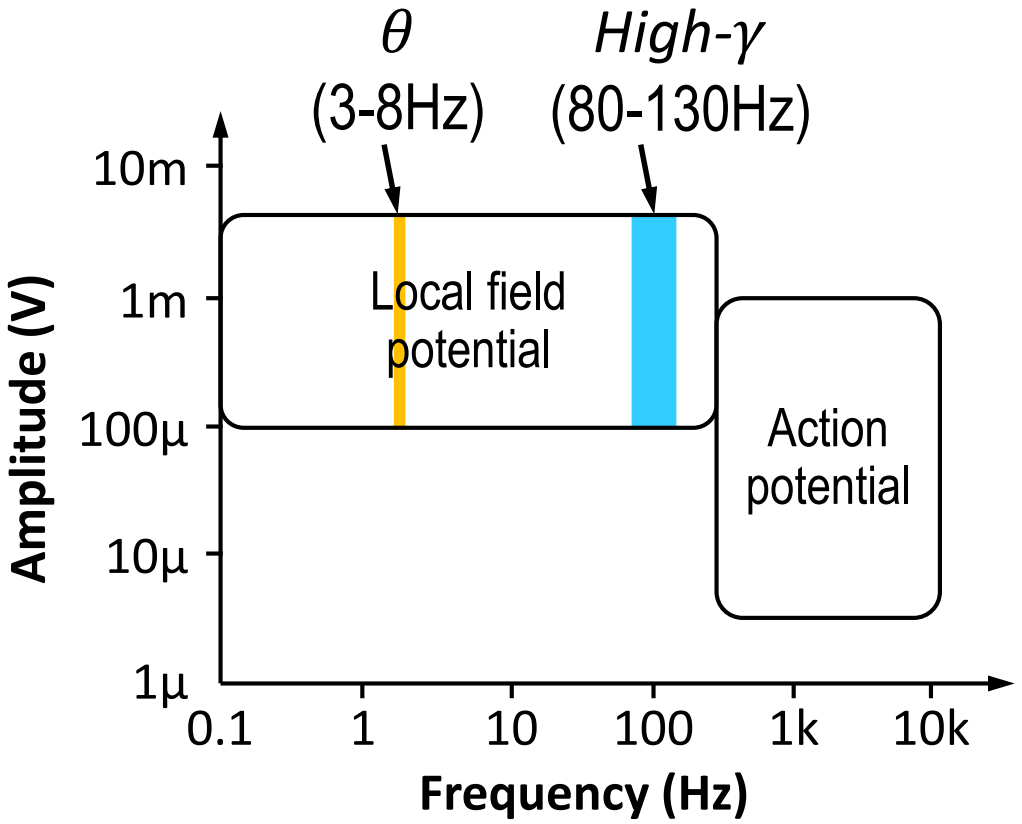
Human Memory Circuits

Our focus: hippocampus and entorhinal cortex





What to Measure?



- Local field potential (LFP)
  - Population activity
  - Analyze frequency bands
- Action potential (AP)
  - Individual neurons
  - Firing (time, rate)
  - **~50x** higher f_{sample}

Also analyze various temporal correlations

Non-Topographic Organization of Memory Cells

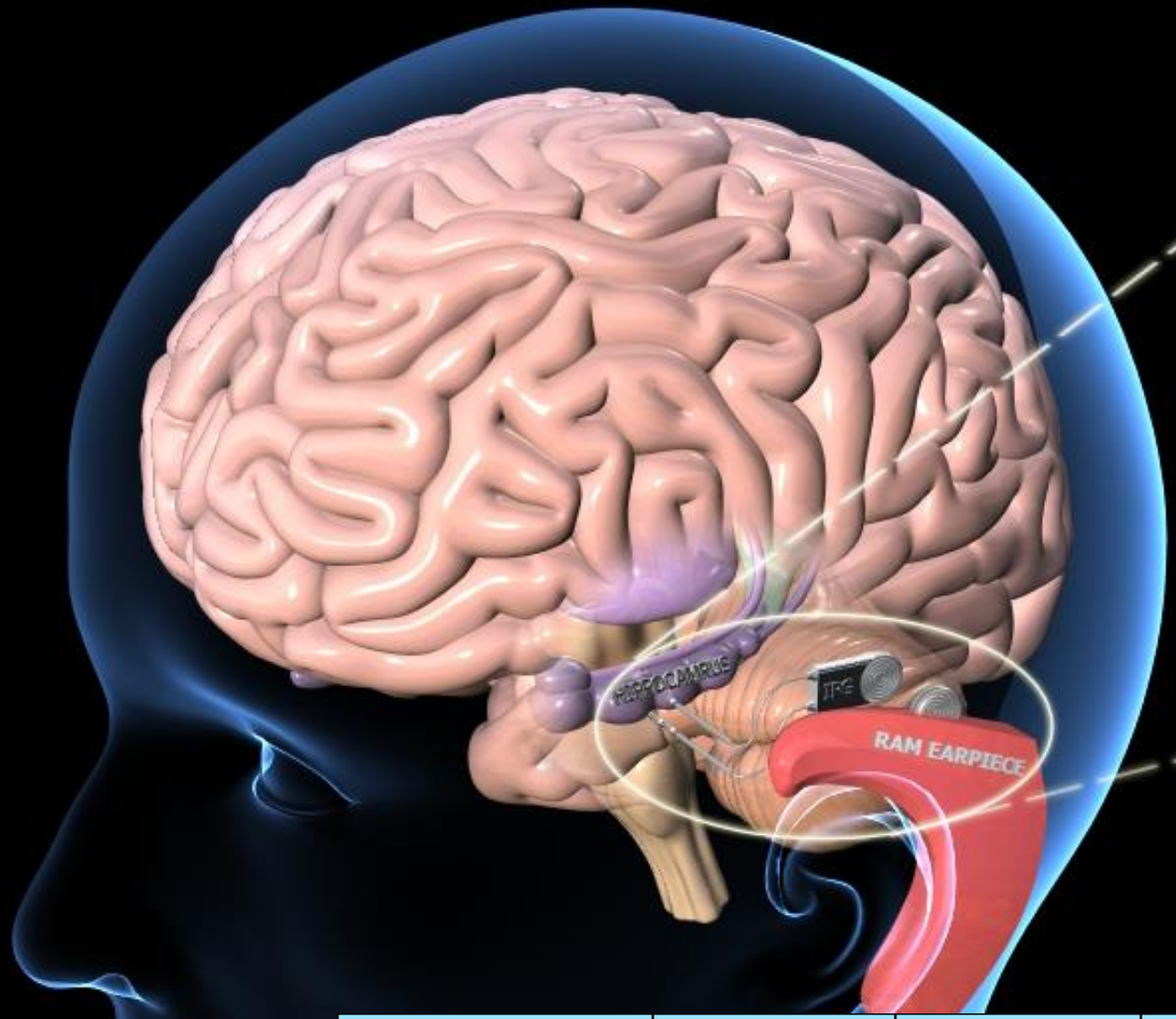
- Adjacent cells encode different concepts
- Response to multiple instances of a concept
- Single units encode **specific memories**

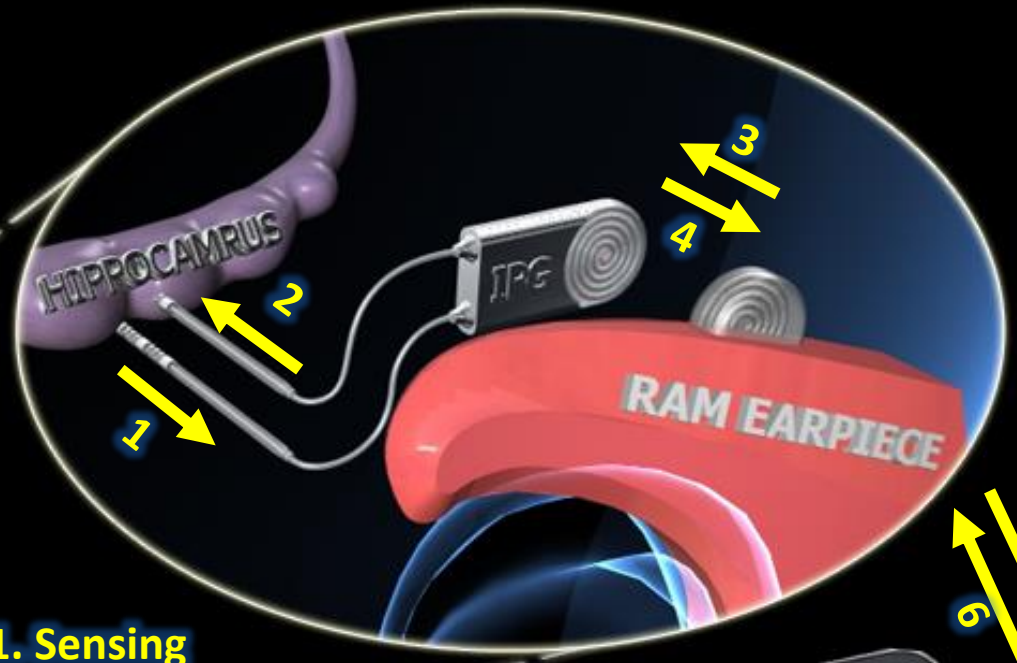
Courtesy: Dr. Itzhak Fried (UCLA)

Why is Engineering Human Memory Hard?

- **Access to deep brain areas**
  - Rare clinical situations
- **Need both population and single-unit activity**
  - Very power hungry
- **Need more channels**
  - And higher density…
  - Study specific memories

BF probe (UCLA)

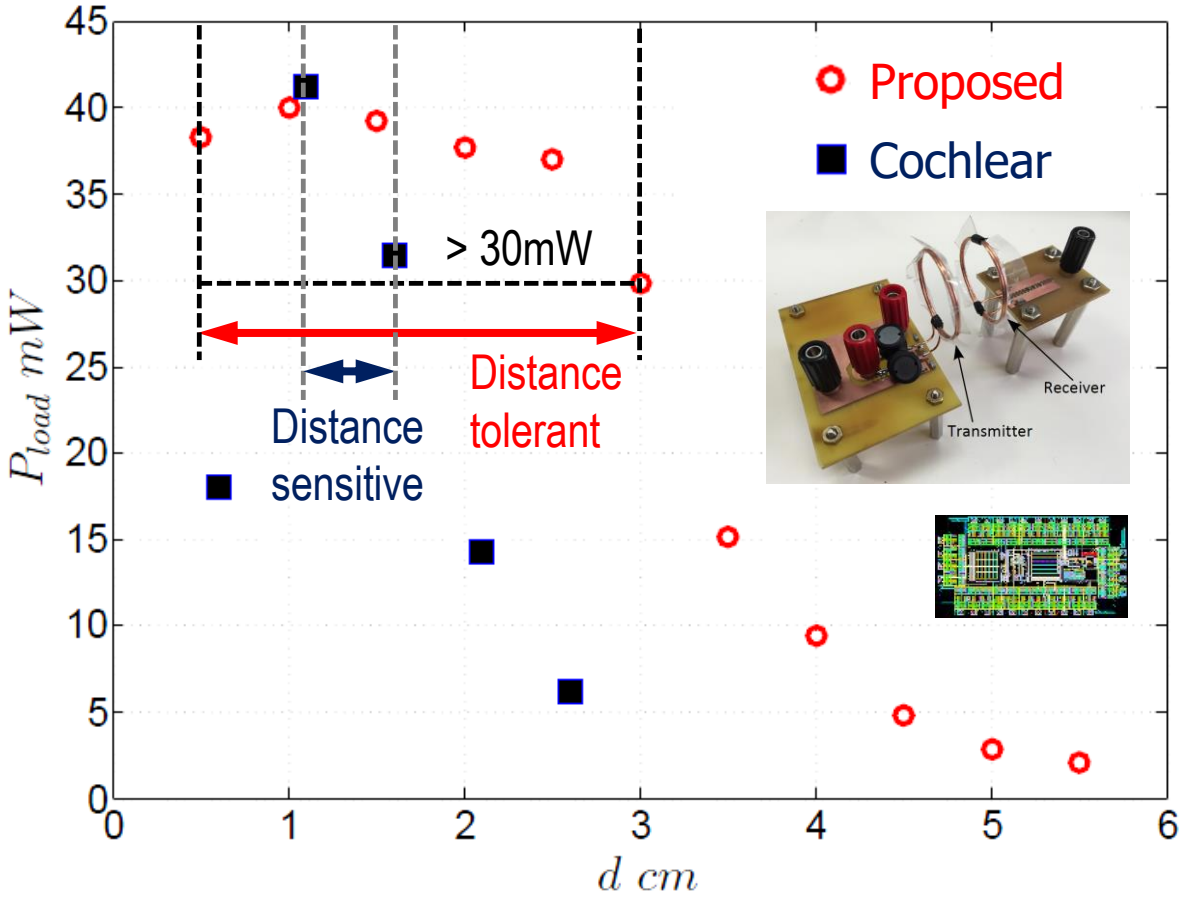


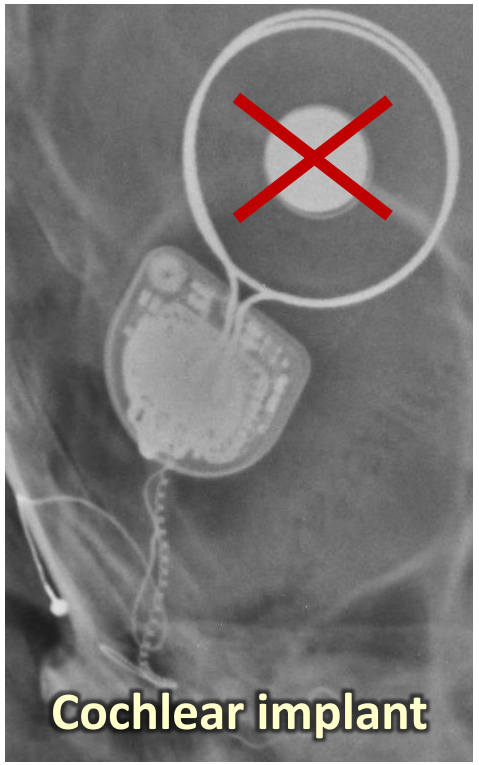


1. Sensing
2. Stimulation
3. Power & Config
4. Data
5. Status and Display
6. Update

Device	Channels	Spacing	AP + LFP	Battery	Volume
Activa PC+S	2 x 4	1.5 mm	N	Y (6.3 Ah)	39 cm^3
RNS-300	2 x 4	3.5 mm	N	Y (0.7 Ah)	13 cm^3
Proposed	2 x 32	0.3 mm	Y	N (RF)	<1 cm^3

Revolutionizing Wireless Power

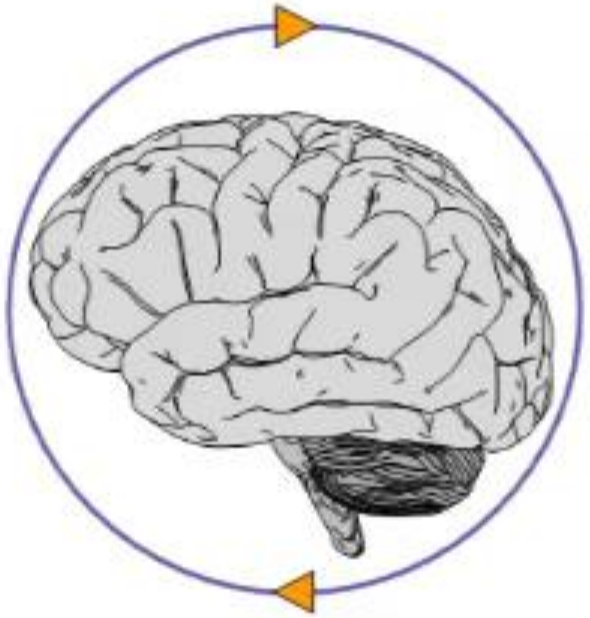




Benefit: no magnet

- Cochlear: stable power only at a narrow distance (→ alignment magnet)
- Proposed: stable power delivery up to 3cm (→ no implant magnet)

DARPA BTO – RAM Program



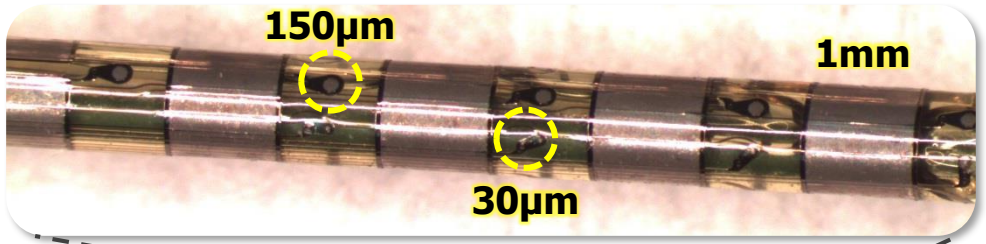
UCLA

Lawrence Livermore National Laboratory

Revolutionizing Wireless Power

Our High-Precision Implantable Lead

- 40 contacts (10x more)
- Multi-scale, high-density
- Same diameter (1.27mm)



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1mm

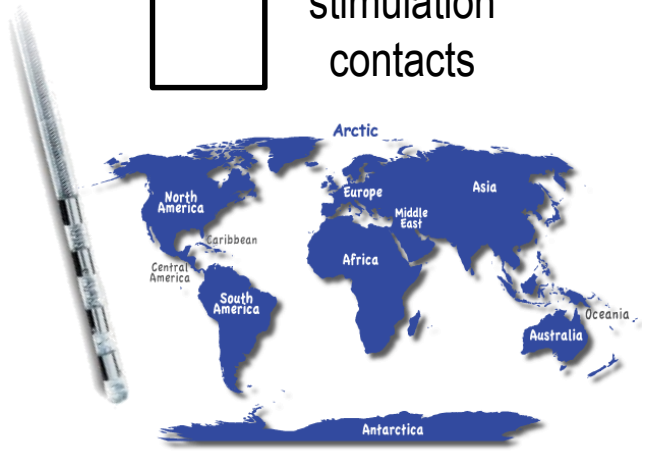
Large defocused stimulation contacts

150µm

Medium-sized focal stimulation contacts

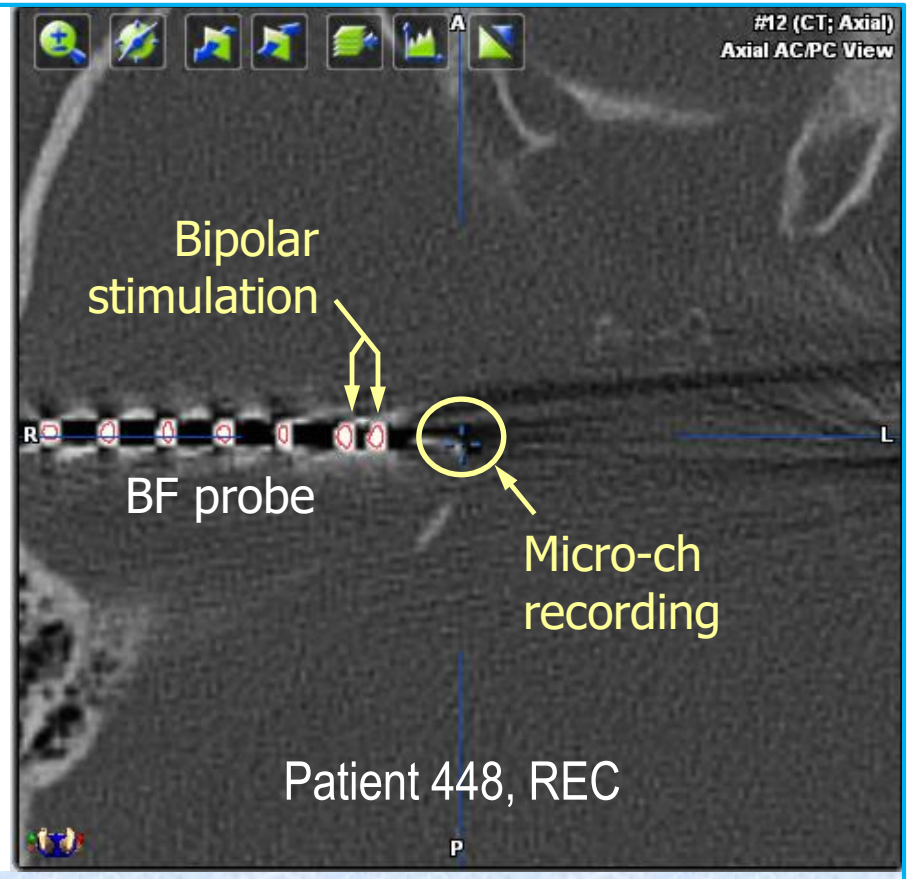
30µm

Small contacts for cell-level recording



Dynamic Range in Closed-Loop Systems?

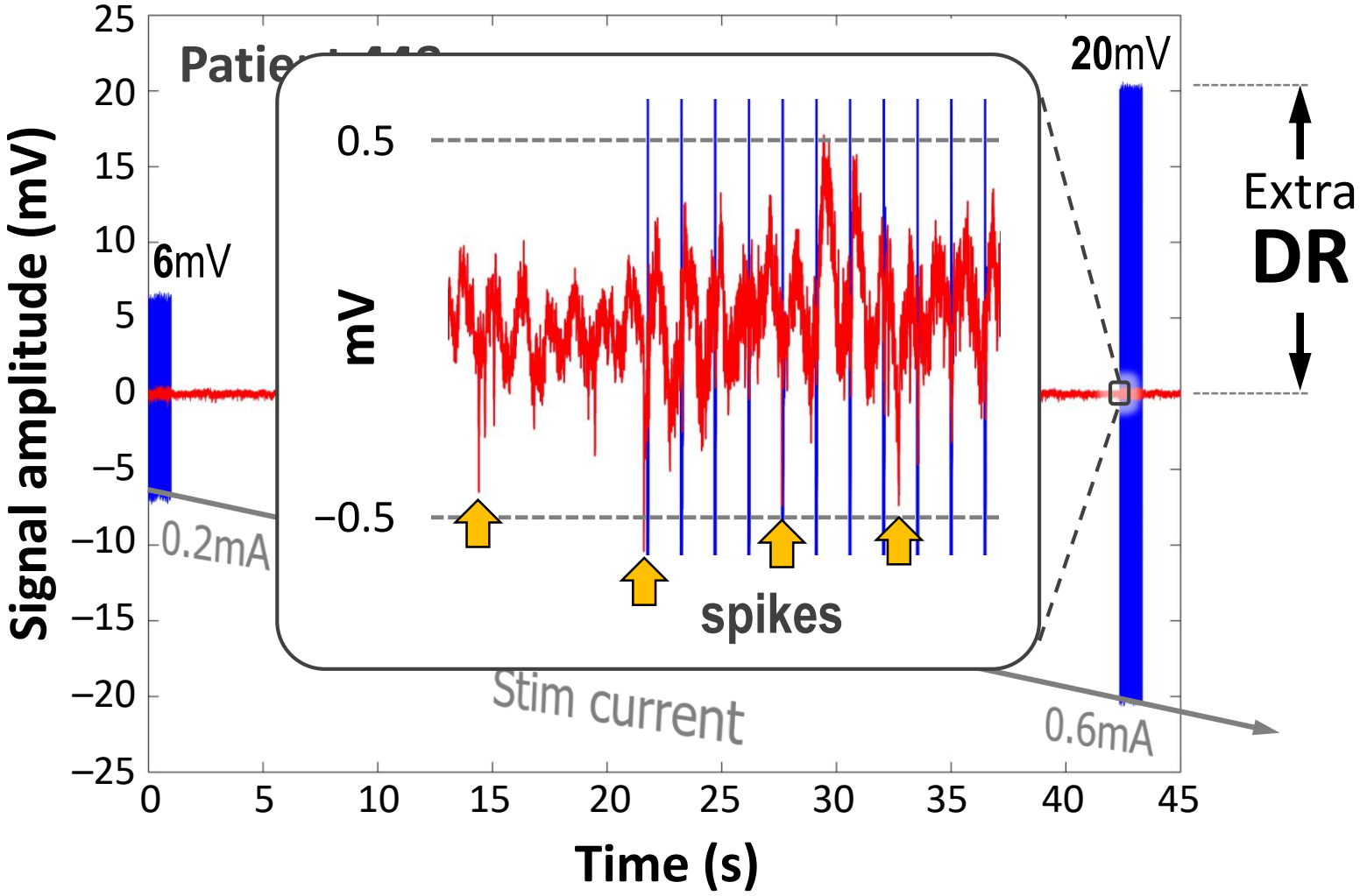
- **Stimulation:** 0.2-0.6mA
  - 2 distal macro channels
  - 300µs per phase
  - 50Hz pulses for 1s
- Micro-channel recording (**7.3mm** away from the stimulation site)
- **Recording:** 30kHz sampling



This setup uses **wall-plugged electronics** to achieve sufficient input **dynamic range**

~5b of Headroom at Microwatt Power?

Headroom: 20mV / 0.5mV = **40 (32dB) → +5bits**

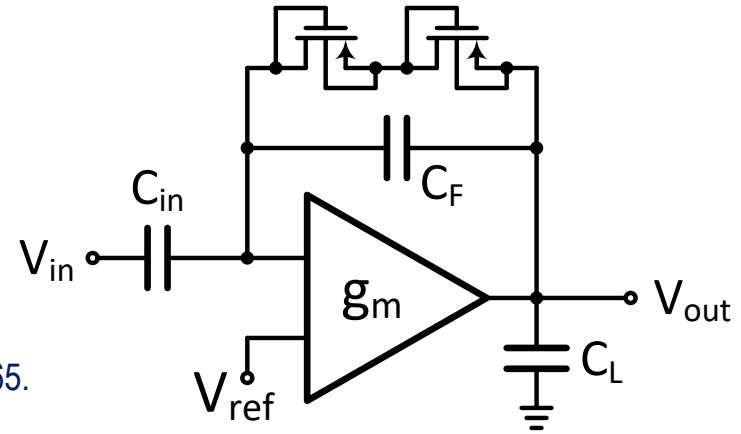


Key Requirements for Implantable Amplifiers

1 High DR 2 High Z_{in} 3 Low HP corner 4 Low power

Single-unit front-end

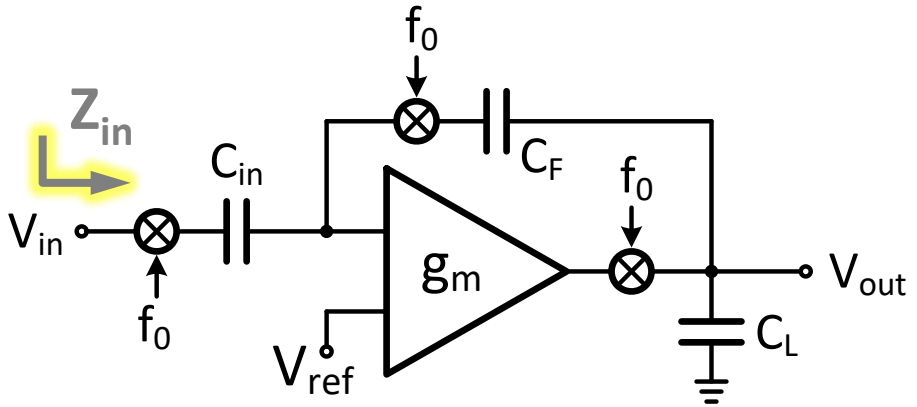
- Pseudo-R nonlinearity distorts V_{out}
- R<5GΩ & large caps for low HPC
- Sensitive to process and temp

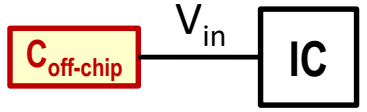


[1] R. Harrison, et al., IEEE J. Solid-State Circuits, June 2003, pp 958–965.
[2] F. Zhang, et al., IEEE Trans. BioCAS, Jan. 2012, pp 344–355.

Chopper-based LFP front-end

- Electrode offset = large DC current due to reduced Z_{in}
- SoA designs: Z_{in} < 30MΩ (need >1GΩ to avoid $C_{off\text{-}chip}$)



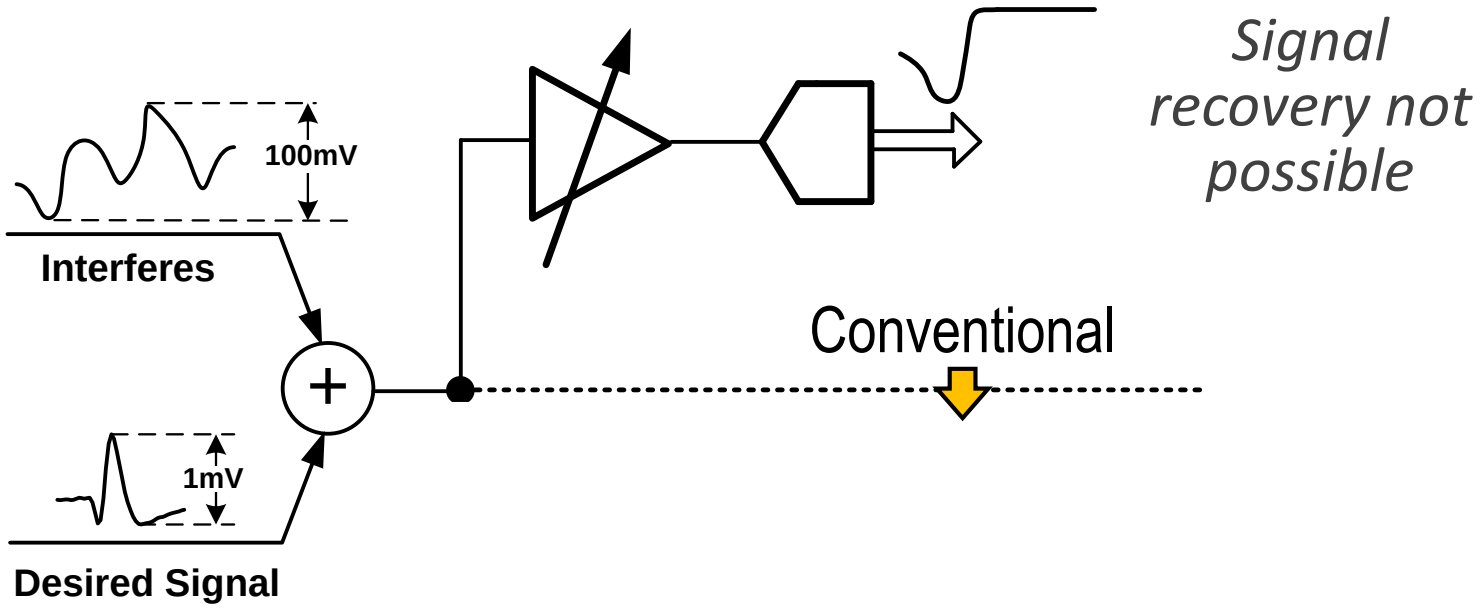


[3] T. Denison, et al., IEEE J. Solid-State Circuits, Dec. 2007, pp 2934–2945.
[4] Q. Fan, et al., IEEE J. Solid-State Circuits, July 2011, pp 1534–1543.

Addressing the Dynamic Range Issue

(conventional receive chains are inadequate)

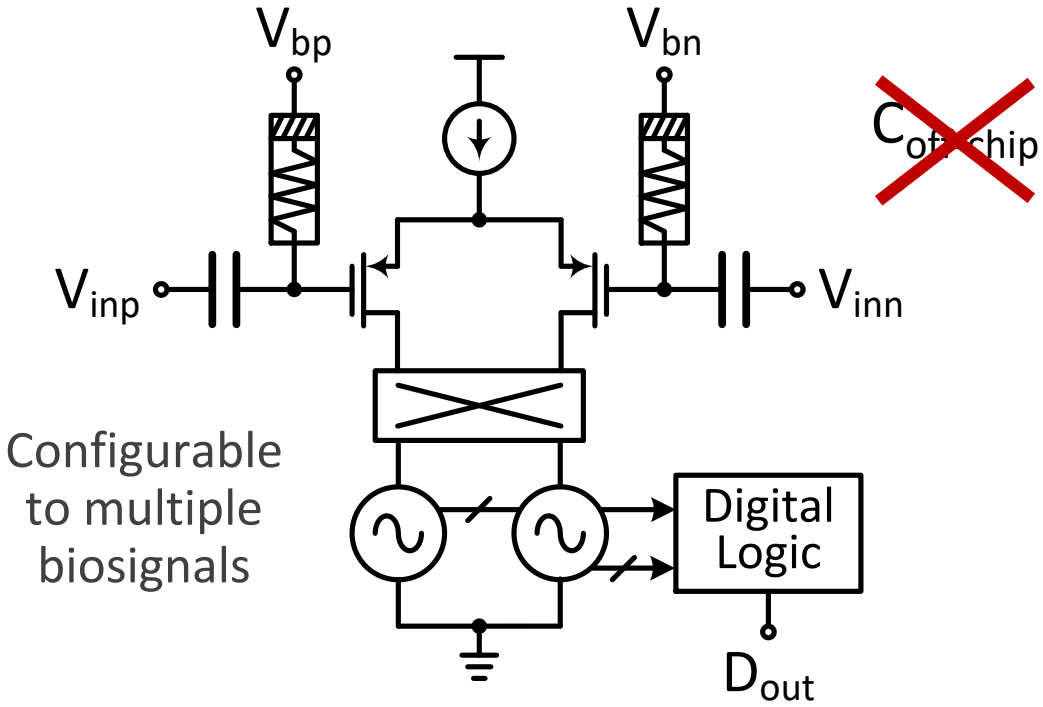
Voltage-to-voltage/current gain: output saturates



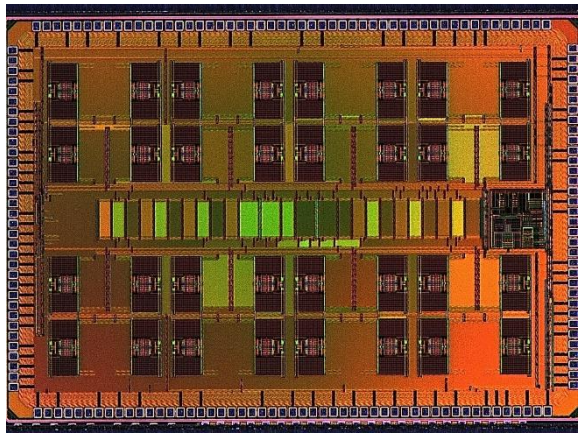
Voltage-to-phase gain: output does not saturate

Oscillator-based Analog Front End

(suitable for kHz-rate biosignals)



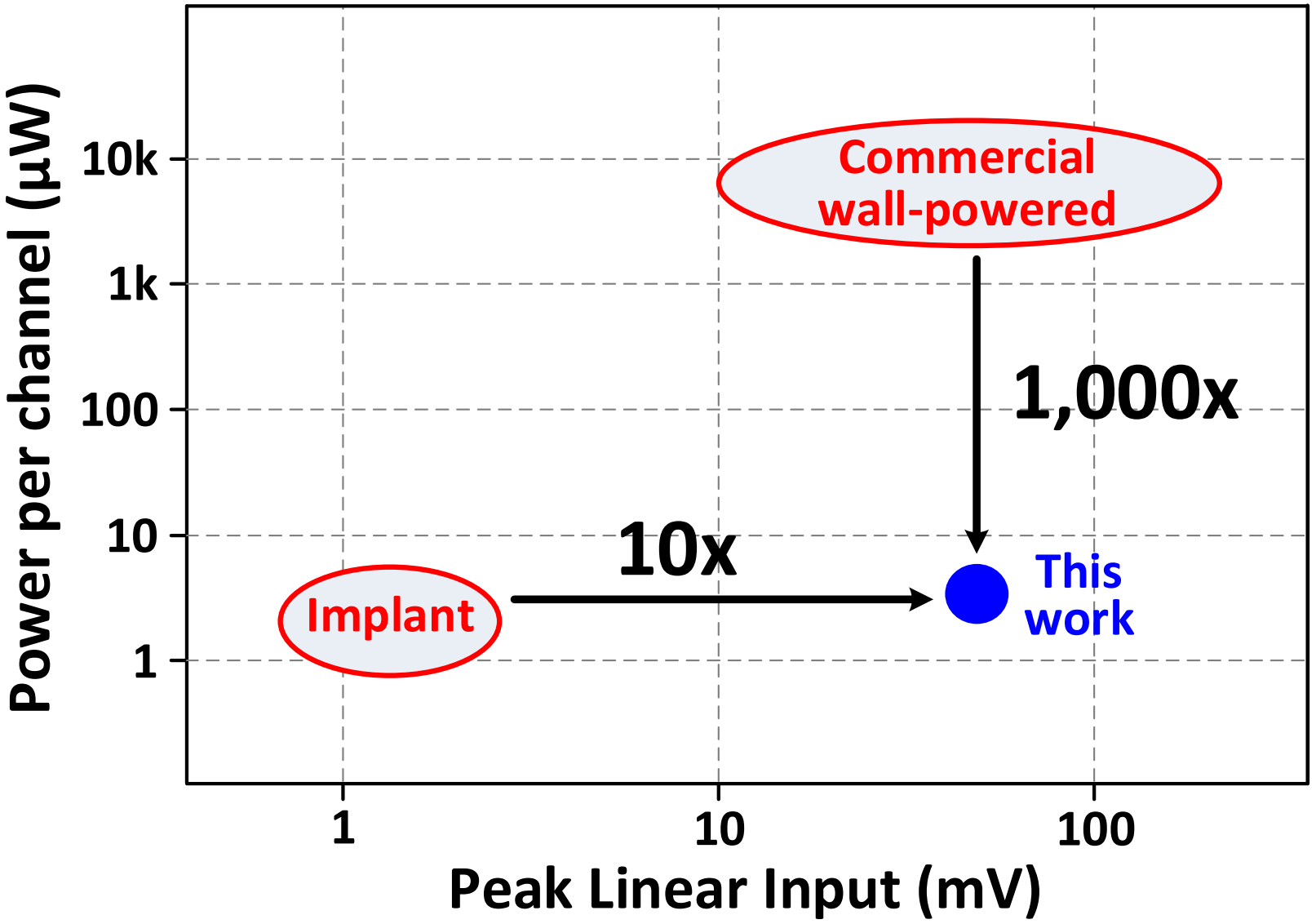
EEG	ECG	EMG
< 1μW	< 1μW	~ 5μW



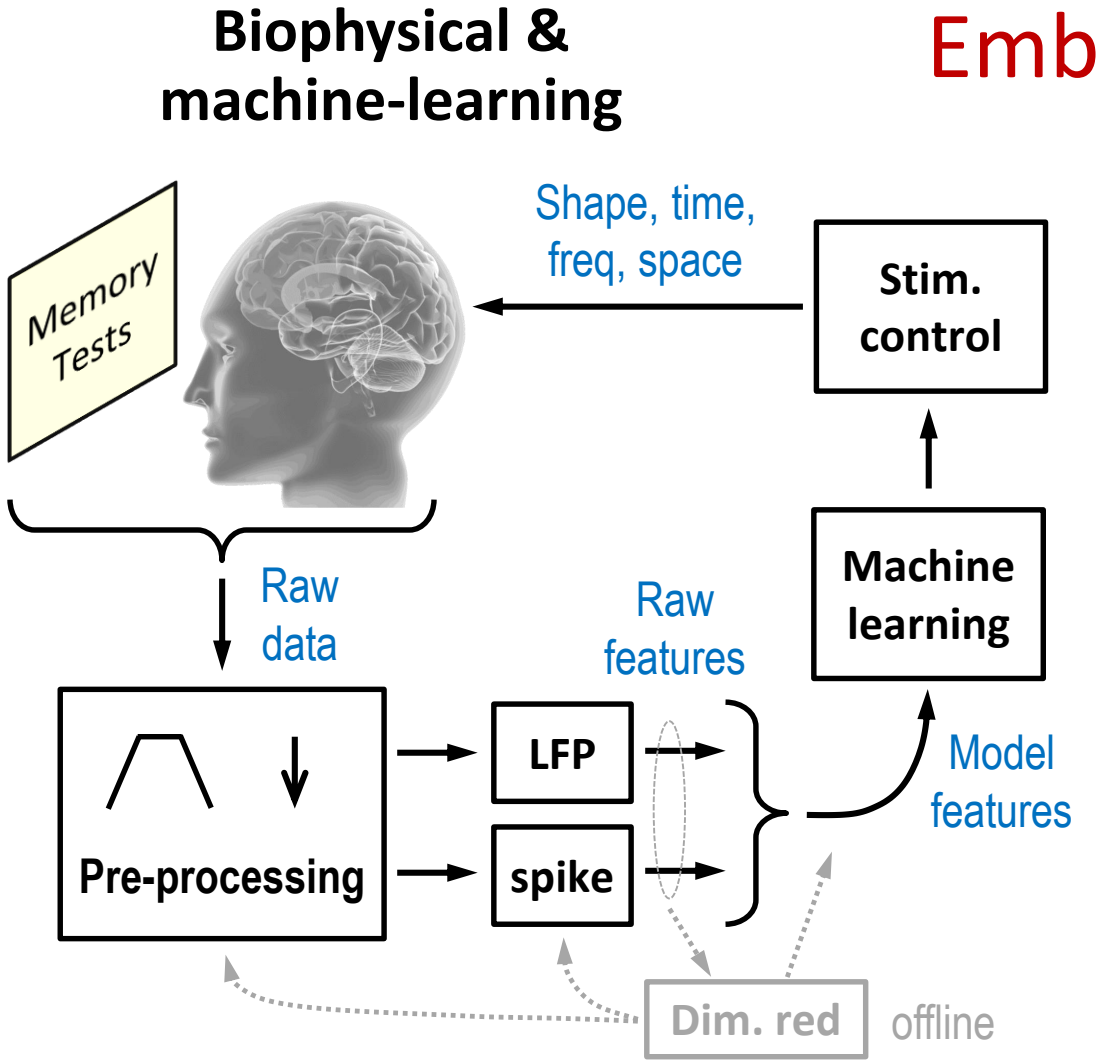
Reference	DR	THD	V_{pk}	Z_{in}	$V_{n,rms}$	V_{DD}	Power
Denison, JSSC'07	74dB	−60dB	2.5mV	8MΩ	1μV	1.8V	2μW
Muller, ISSCC'14	52dB	−48dB	0.5mV	28MΩ	1.3μV	0.5V	2.3μW
This Work	**91dB**	**−87dB**	**100mV**	**>1GΩ**	2μV	1.2V	**3μW**

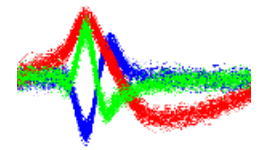
W. Jiang, V. Hokhikyan, H. Chandrakumar, V. Karkare, D. Marković, ISSCC 2016, pp. 484-485.

Full-Duplex Recording and Stimulation

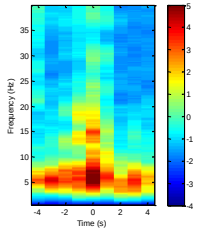


Embedded Computational Memory Model

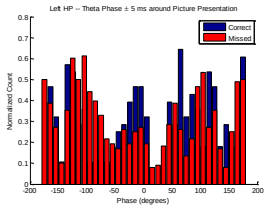




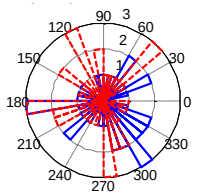
Spike Activity



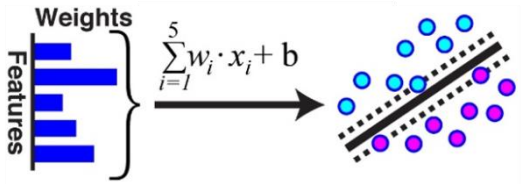
LFP Spectum



LFP Phase



Spike-Phase Coherence



- **Patient specific:** offline learning & online adaptation
- **Closed-loop:** non-linear adaptive stim-artifact removal

Demo of UCLA NMU

DARPA SUBNETS Program

Demonstration of
Concurrent Sensing and Stimulation

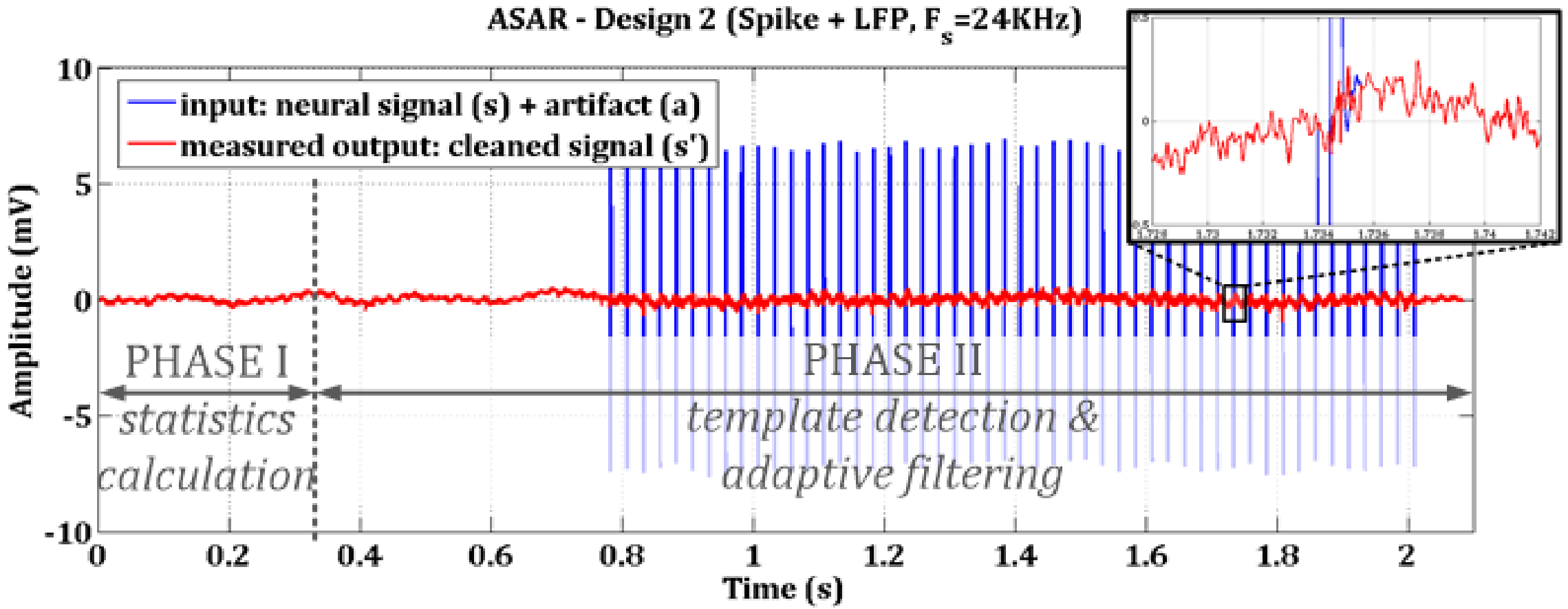
TA2 Team: Wenlong Jiang, Vahagn Hokhikyan, Dejan Rozgić, Dejan Marković (TA2 PI)

Electrical Engineering Department

UCLA

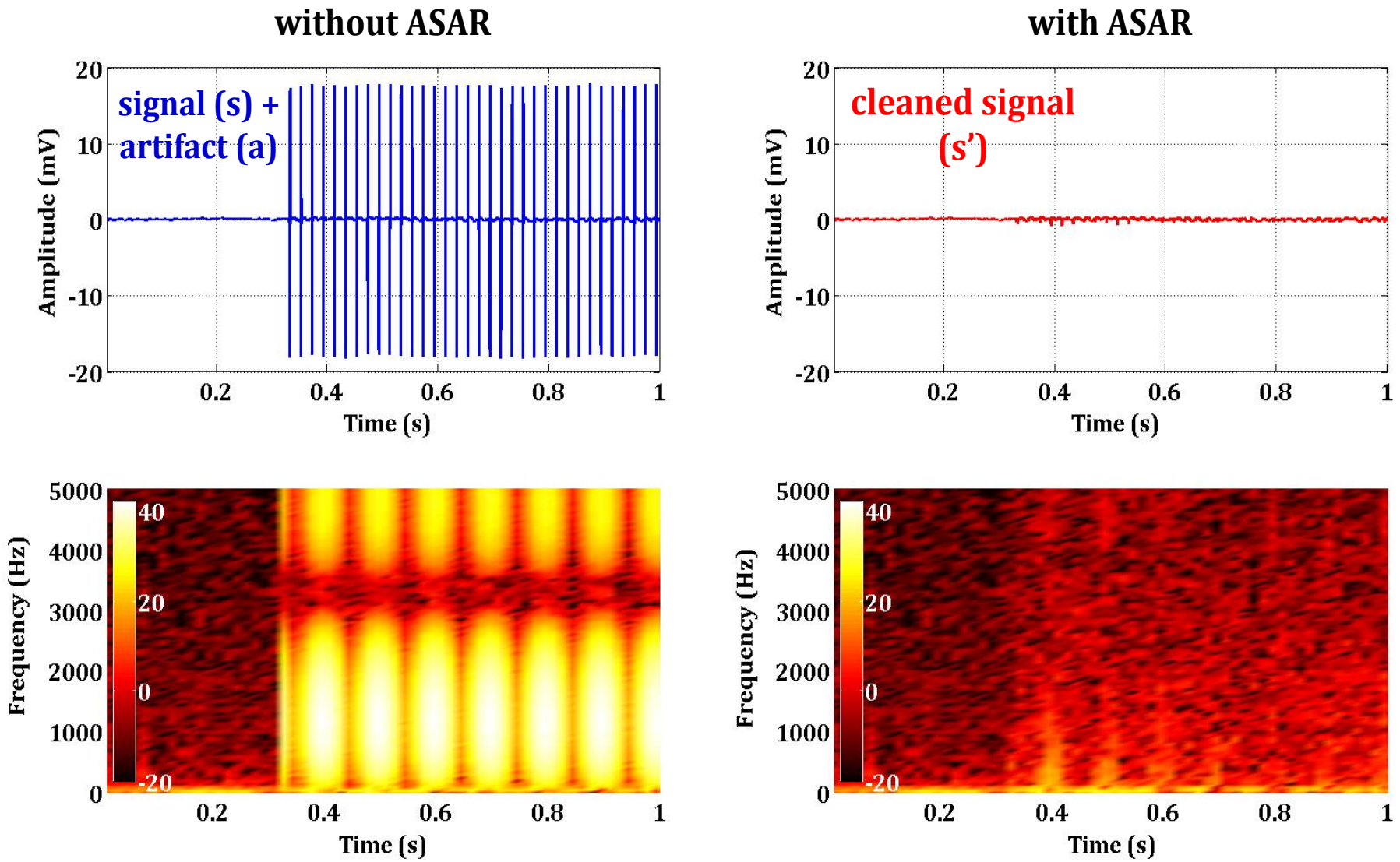
Waveform Shape Agnostic Adaptive Stimulation Artifact Rejection

Measurements on adjacent channel(s)

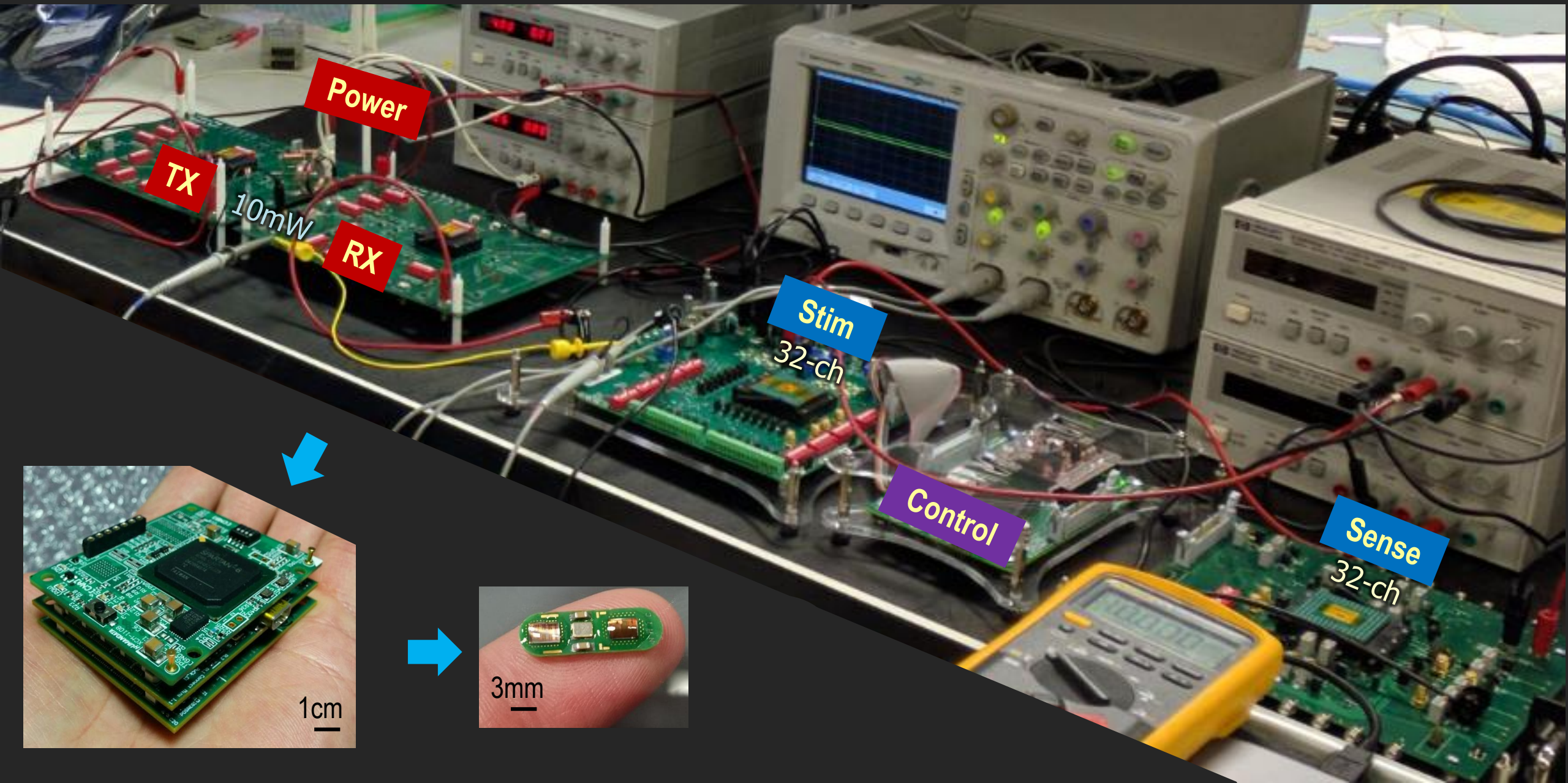


S. Basir-Kazeruni, S. Vlaski, H. Salami, A.H. Sayed, and D. Marković, IEEE EMBS Conf. on Neural Eng., pp. 186-189, May 2017.

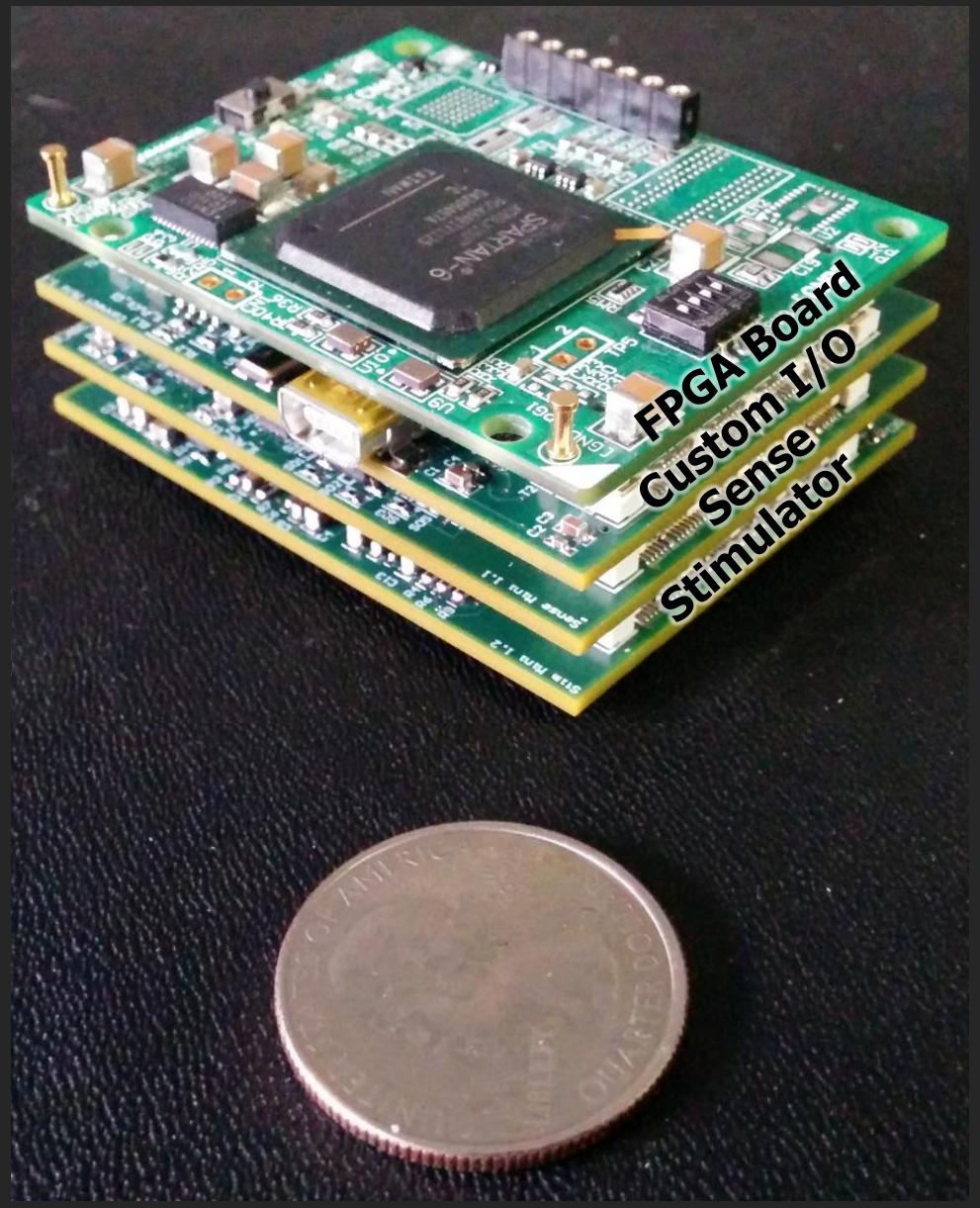
True Concurrent Stimulation + Sensing



System Approach to Integration & Miniaturization



Companion External (Trial) Device

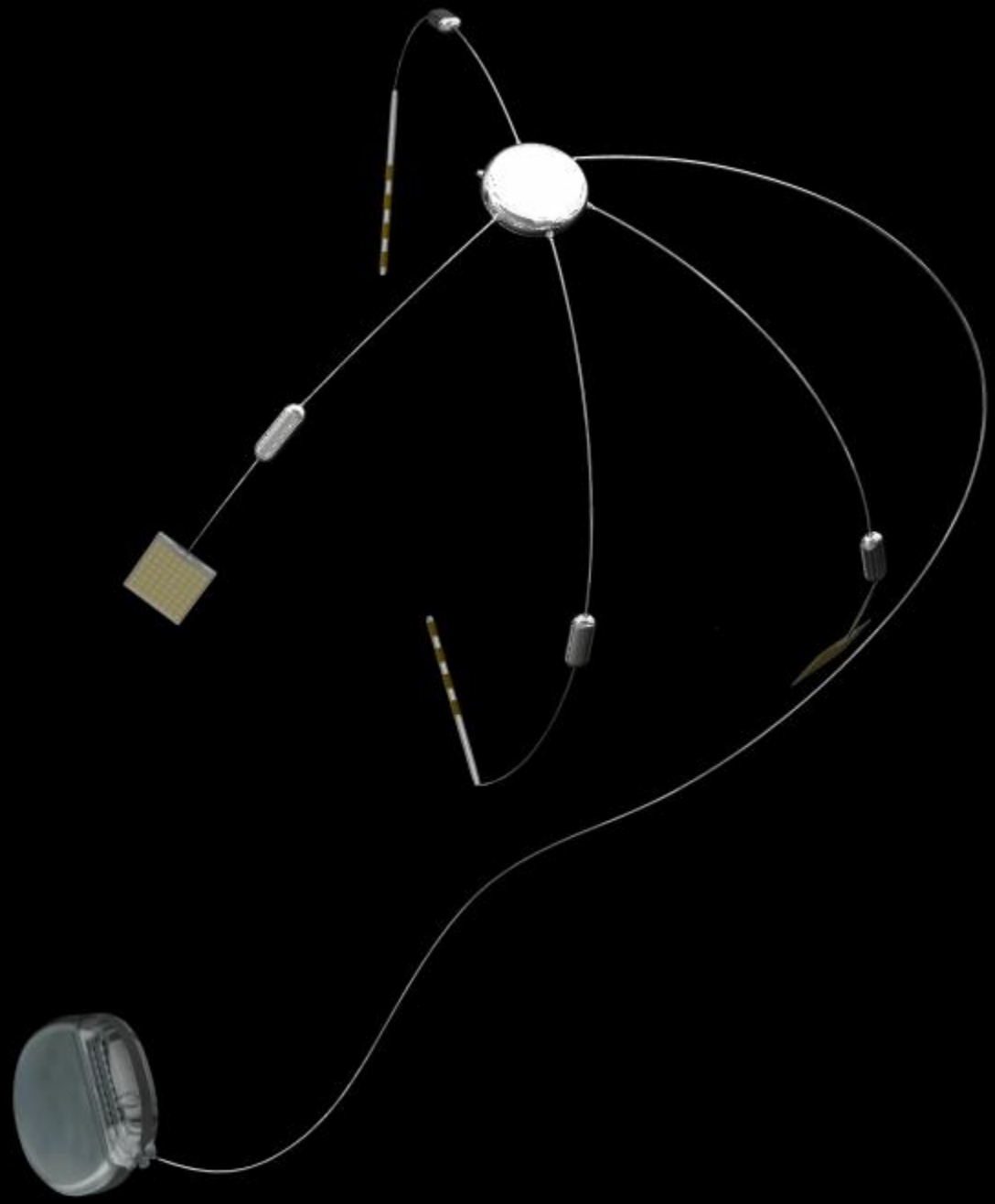


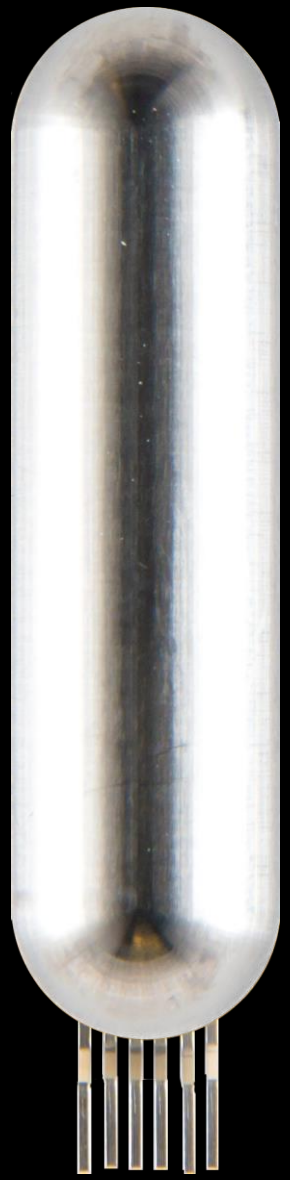
LEGO-style assembly

IRB-approved for human recordings at UCLA

Modular Implant Device

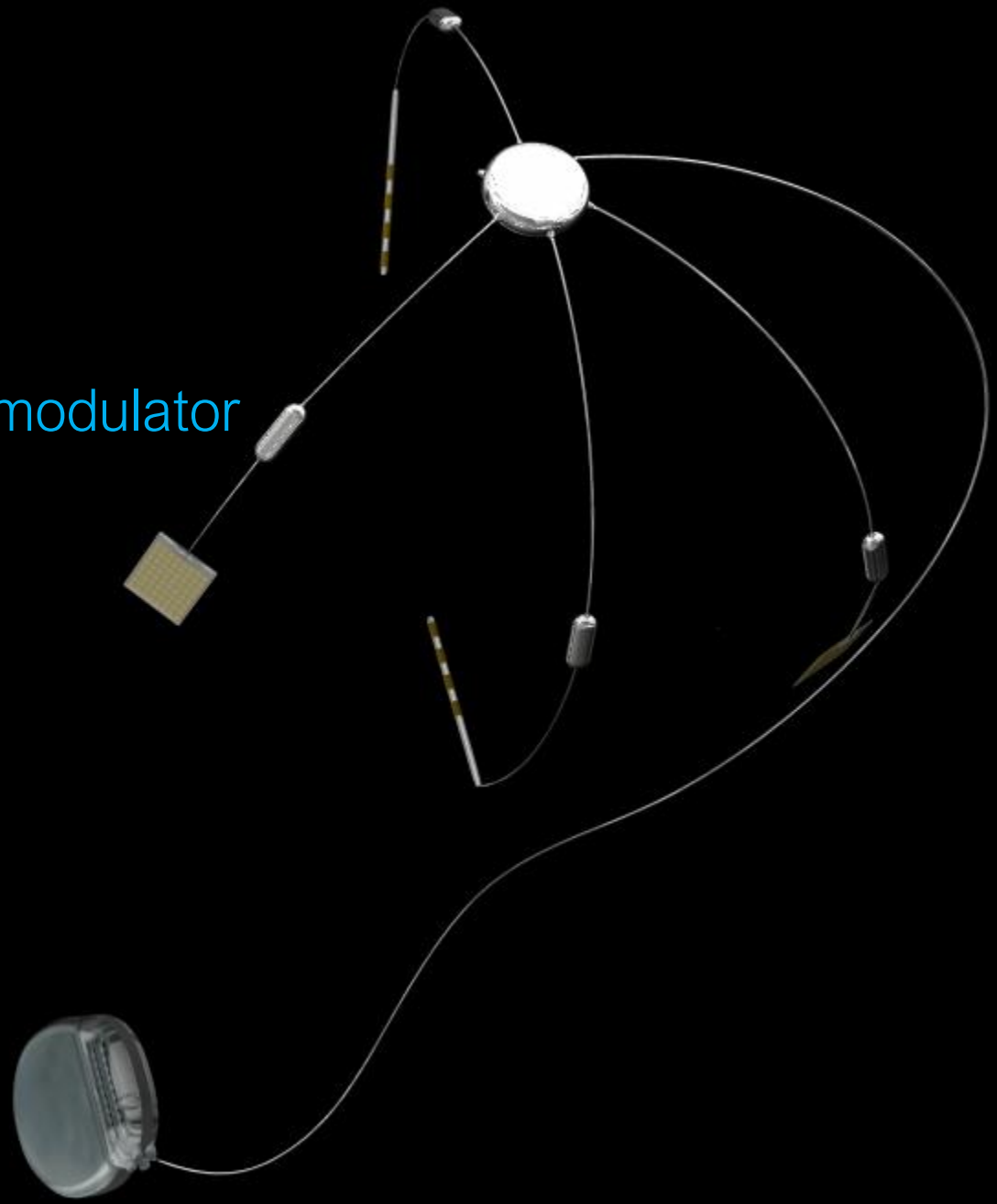
- Closed-loop stimulation
- Up to 256 channels
- Wireless charging
- Wireless data

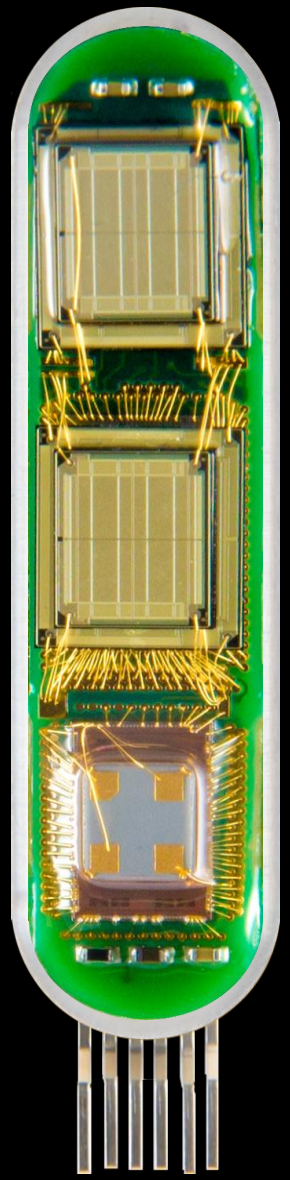




23 mm
5 mm

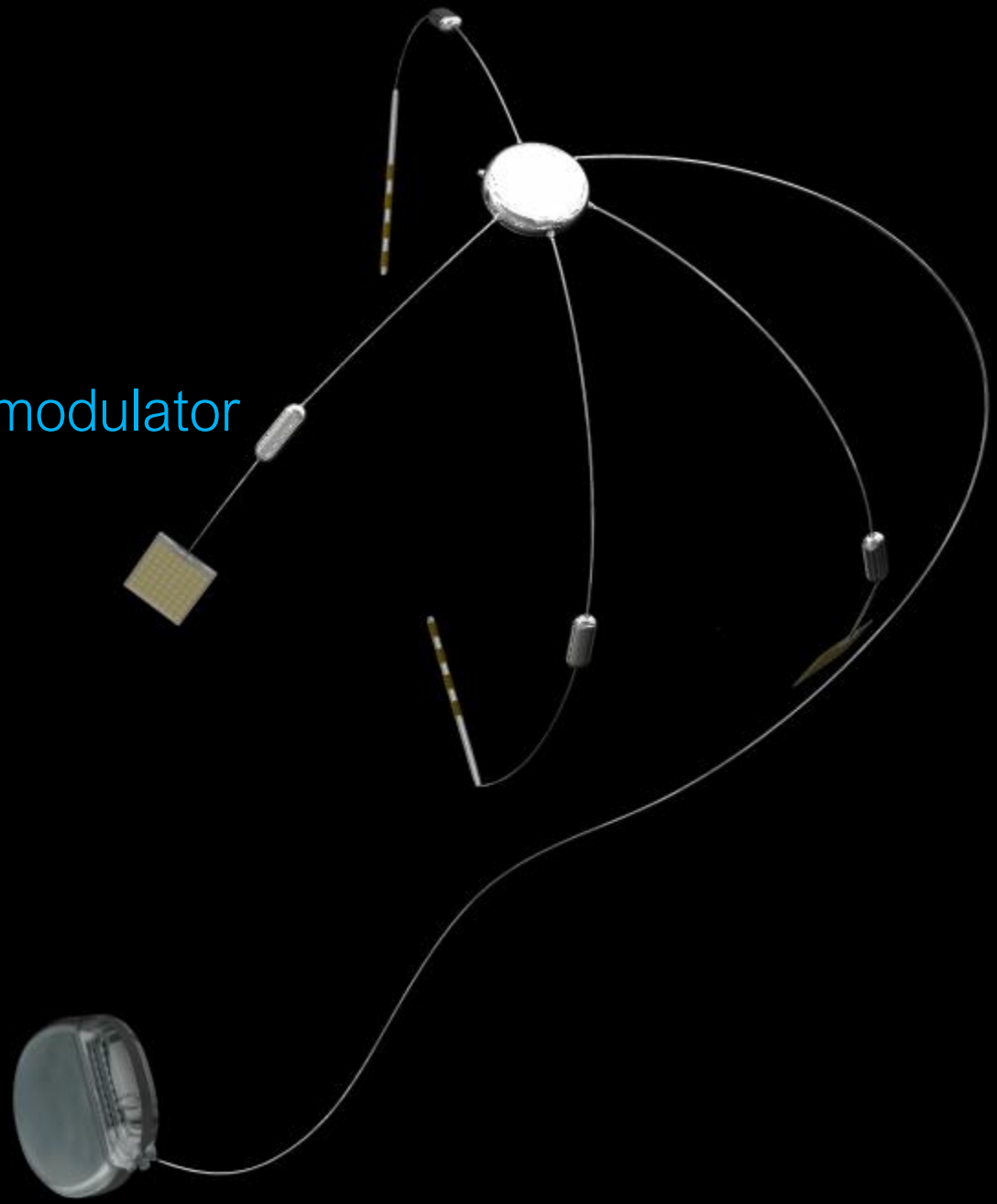
Neuromodulator

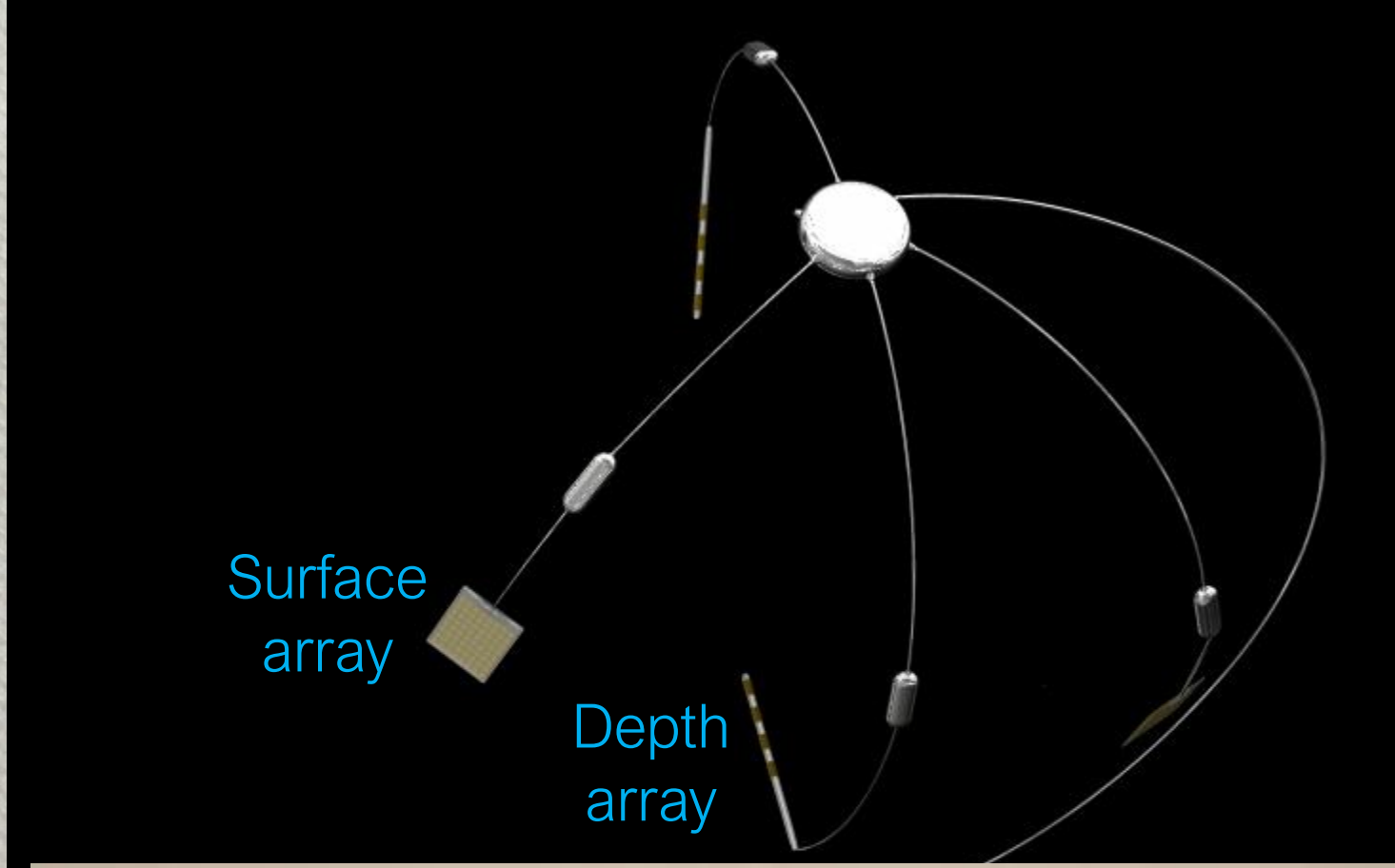




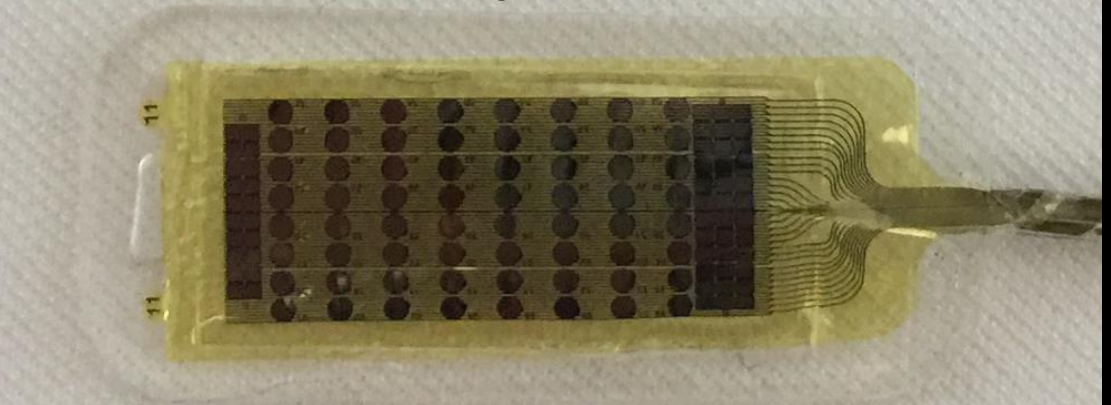
64-channel
sensing and
stimulation

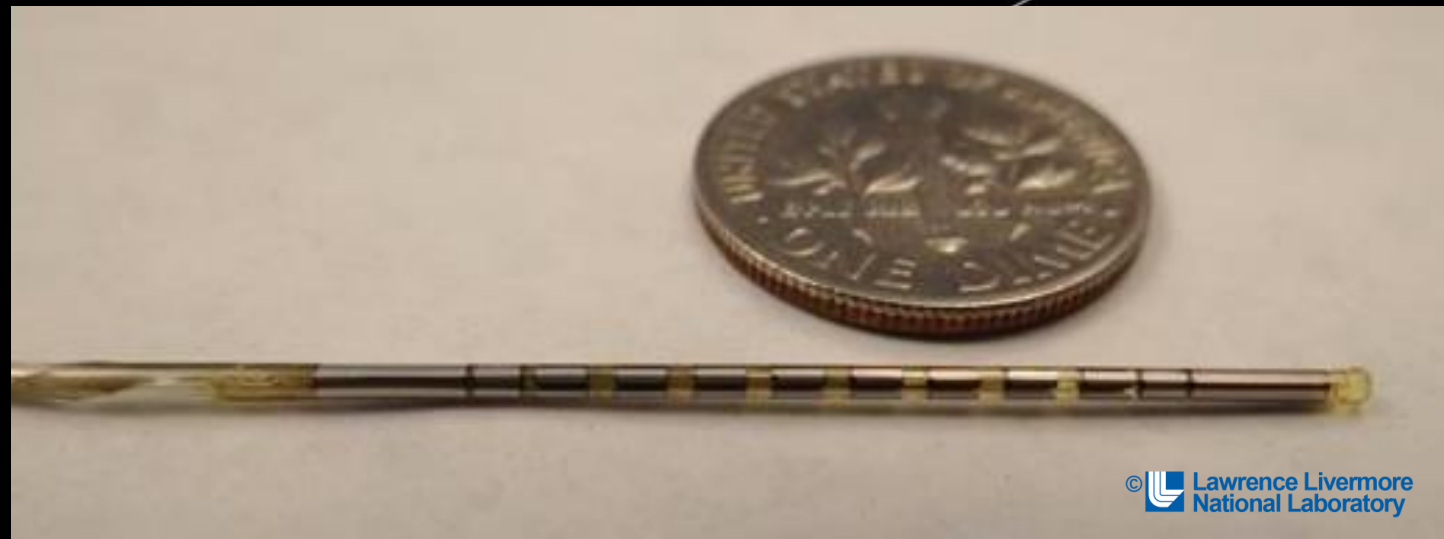
Neuromodulator

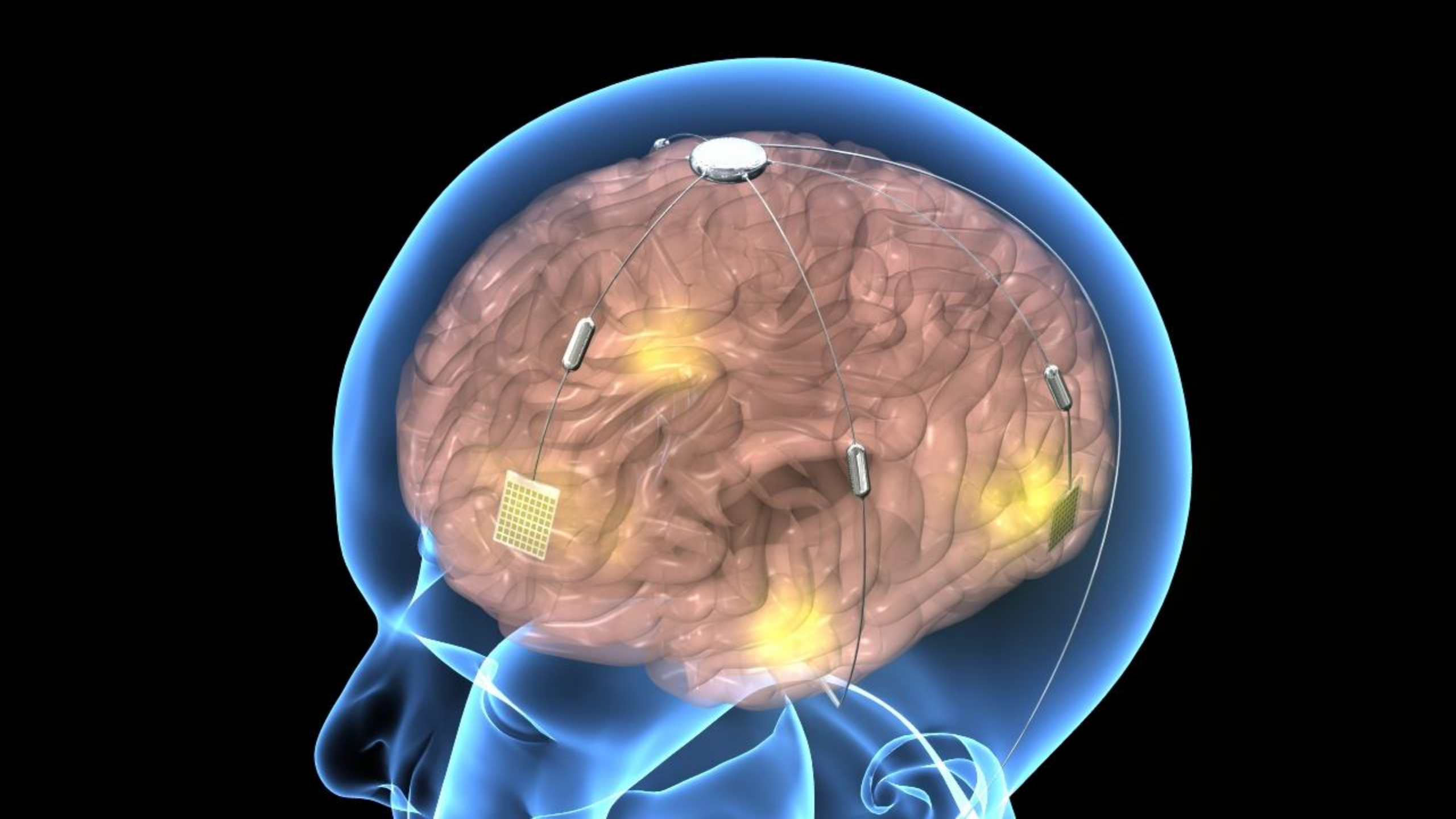




64 contacts







Demonstration of Autonomous Energy

780µW/cm²

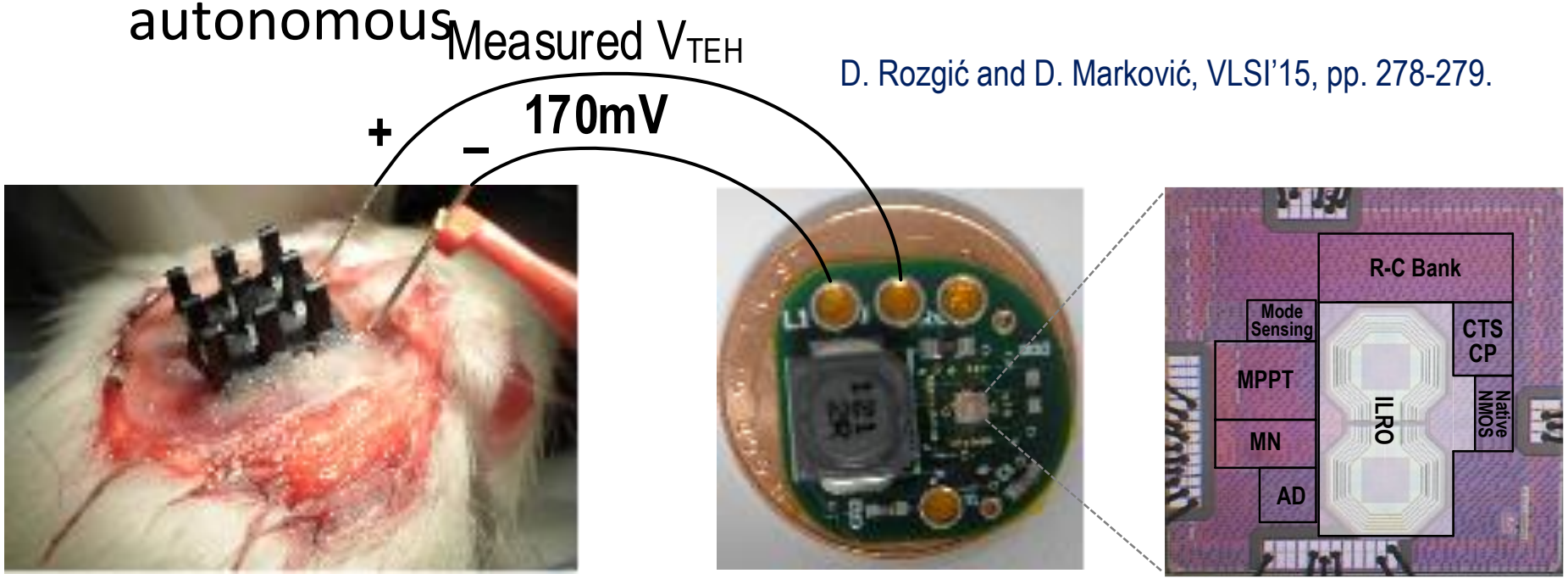
in-vivo (3.5K) fully autonomous

Early feasibility study

- **Smallest** footprint (by **>6x**)
- Best power density (by **>7x**)

Next: anatomical integration

D. Rozgić and D. Marković, VLSI'15, pp. 278-279.



ΔT=3.5K effective

Regulated P_{out} **= 645µW**

1.4mm x 1.4mm

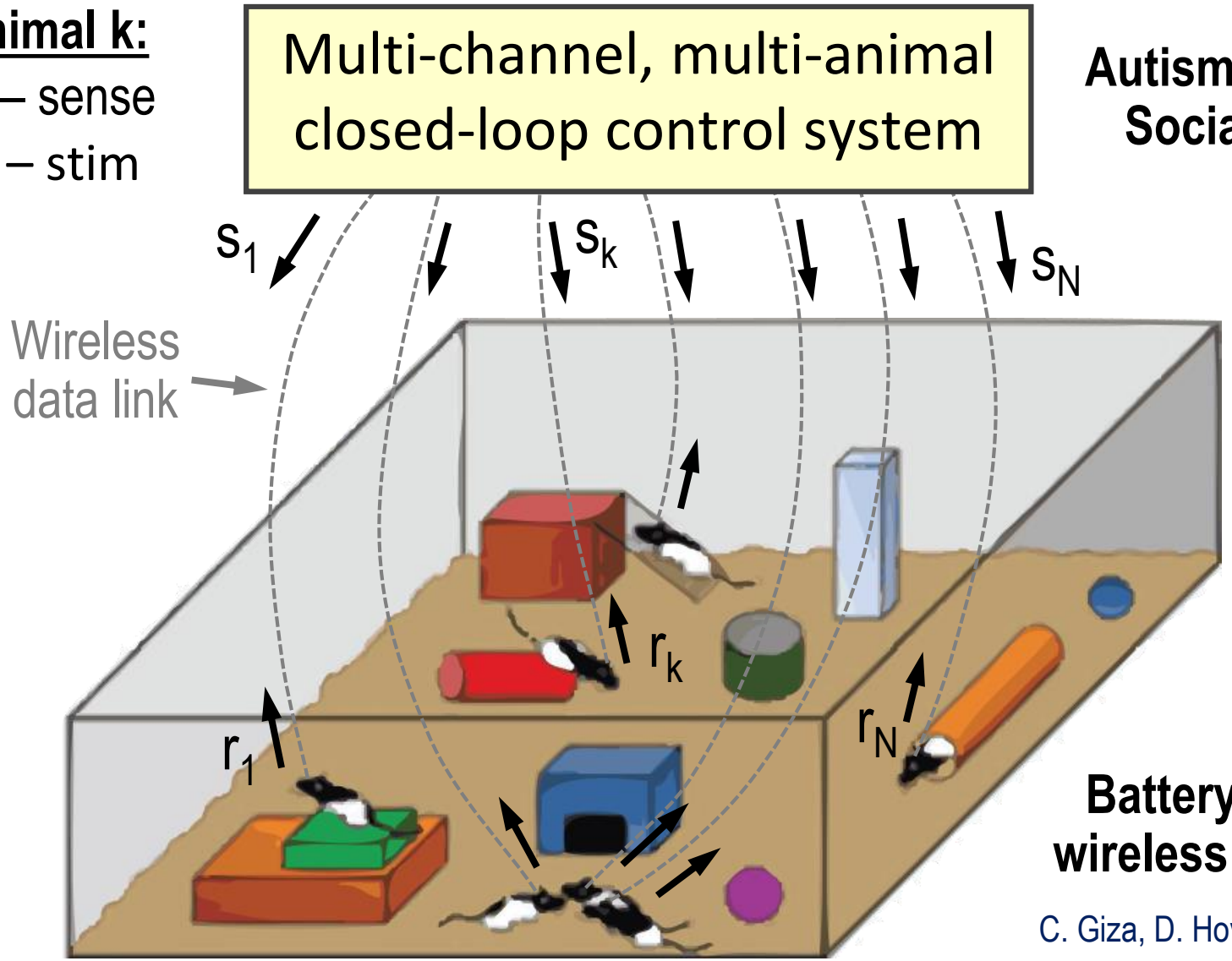
Acknowledgment: Rick Staba and Joyel Almajano (UCLA Neurology)

The Brain Basis for Group Dynamics

Animal k:
$\mathbf{r_k}$ – sense
$\mathbf{s_k}$ – stim

Multi-channel, multi-animal closed-loop control system

Autism, ADD, Social NS



Battery-less wireless motes

C. Giza, D. Hovda (UCLA)

Brain Stethoscope: EEG in Your Pocket

Linking Neurology and Computer Music

with Josef Parvizi and Chris Chafe (Stanford)

Seizure or No Seizure?

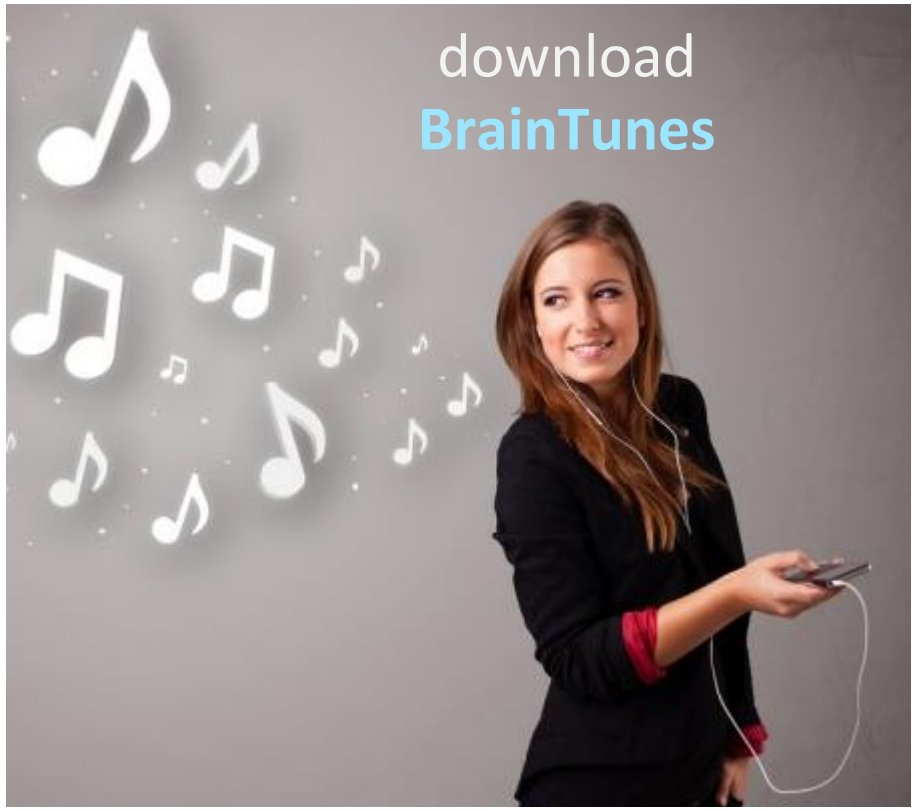



Hear Brains of Other People?

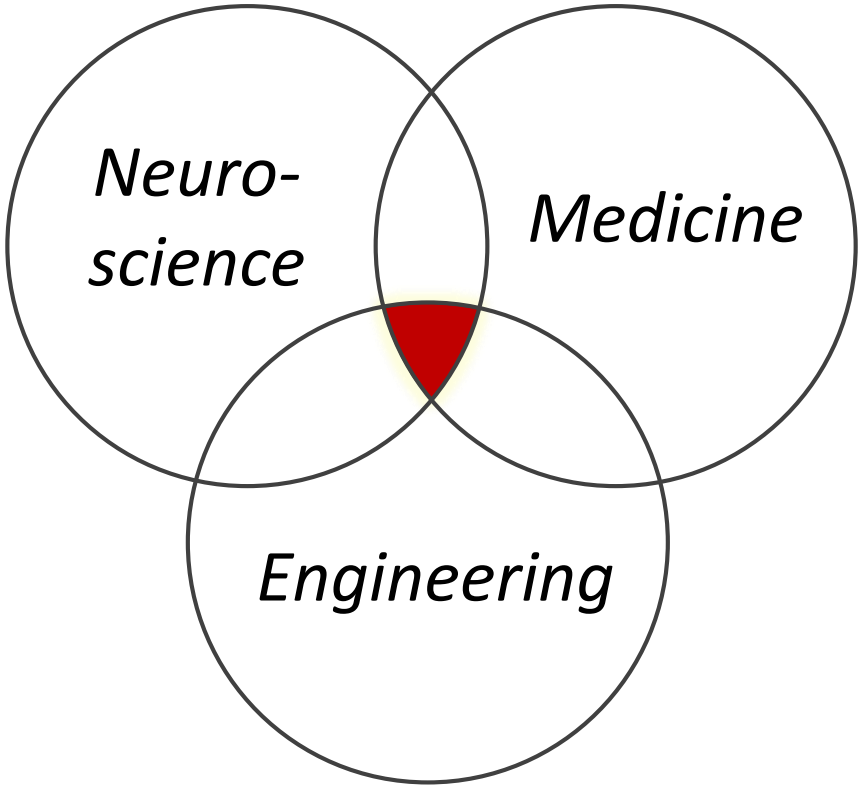
Technology:

dense EEG array

+ vocal synthesis



Revolutionizing Brain Therapies



- **Network neurotechnology**
- **Electrical engineering:** Signal processing, control, circuits, power, data, …

- **Facilitate new clinical science**
  - Translation to therapy

CENT
Center for **NeuroTechnology**