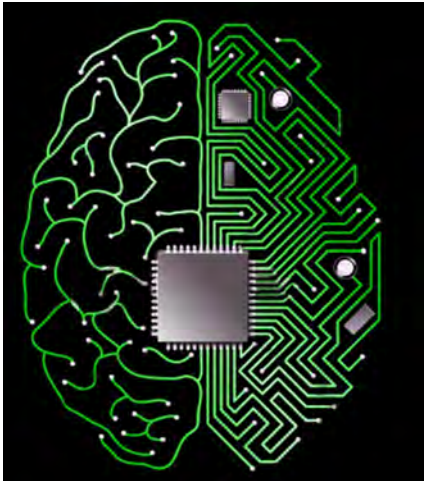
**Osher Mini Medical School**
"UCSF Scientists Outline What's to Come"
November 22, 2019

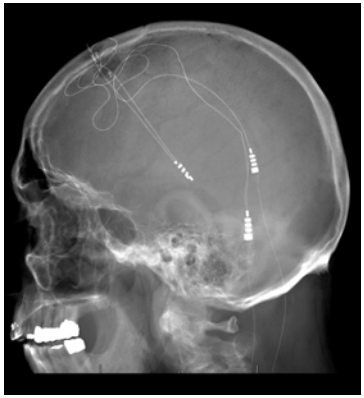
UCSF Department of Neurology
Weill Institute for Neurosciences



# Development of Implantable Interfaces to Restore Motor Function

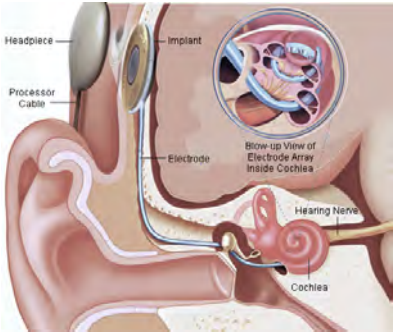
**Karunesh Ganguly, MD PhD**

# Introduction



- Concept of bio-interactive neural interfaces dates to early 20th century
- Successful translation of
  - Cochlear implants
  - Deep brain-stimulation (DBS)
  - Responsive stimulation (RNS)
- Neural Interface for paralysis and rehabilitation
  - 'Brain-Machine Interfaces'/'Brain-Computer Interfaces'

# Cochlear Implants




- Auditory nerve stimulation research starting in the 1950s
- ~22,000 adults and ~15,000 children live in the US with cochlear implants

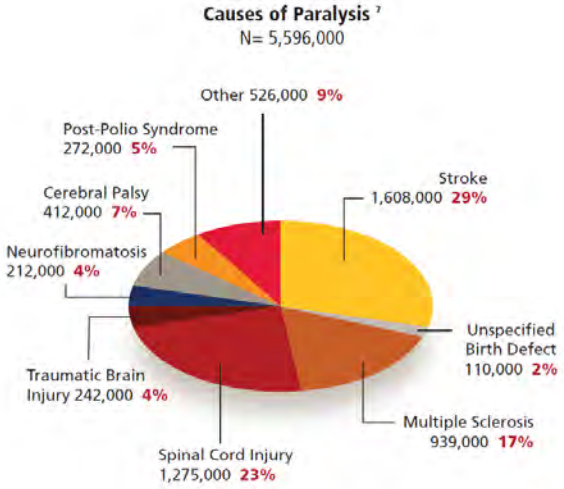
Image credit: UCSF Benioff Children's Hospital

# Deep-Brain Stimulation

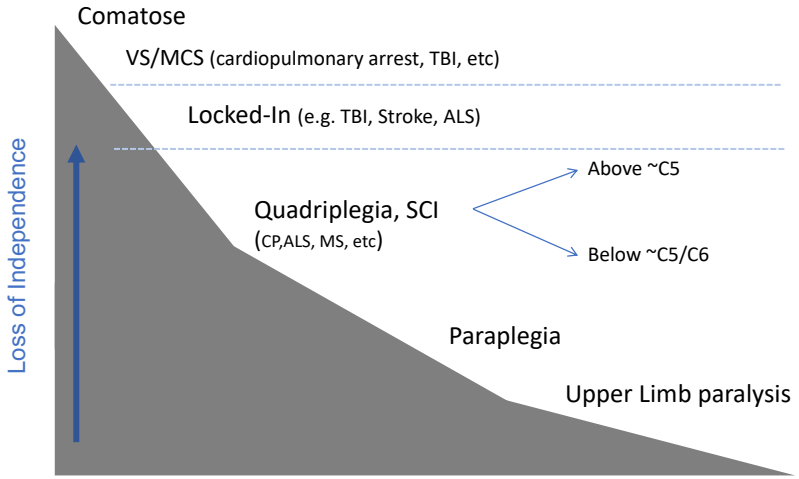

Source: NIH, *Neurology*

# Neural Interfaces for Communication and Movement

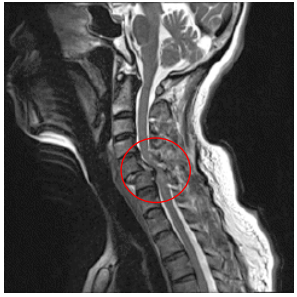
# Motor Disability in the US

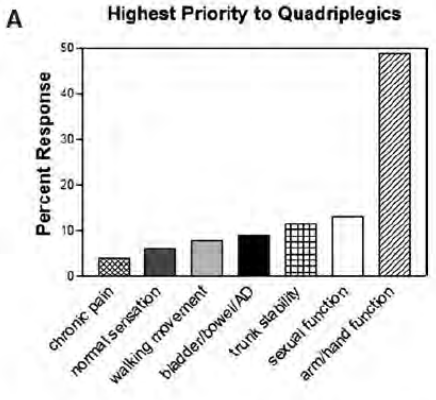


# Rehabilitation Needs Vary



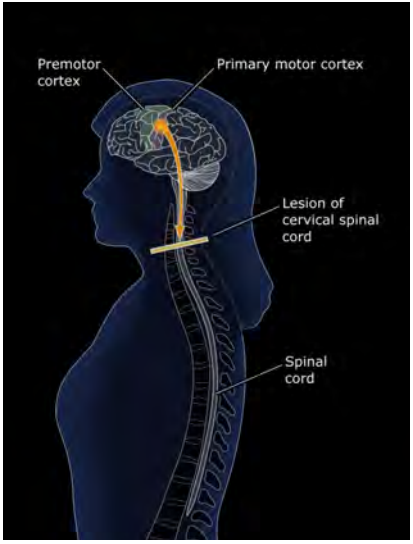
# Patient Rehabilitation Goals



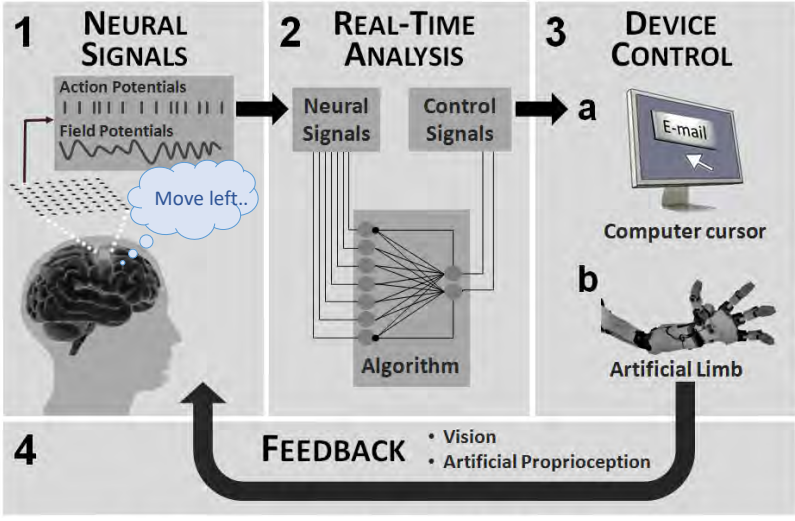



Anderson, *J Neurotrauma* (2004)

# Motor Dysfunction

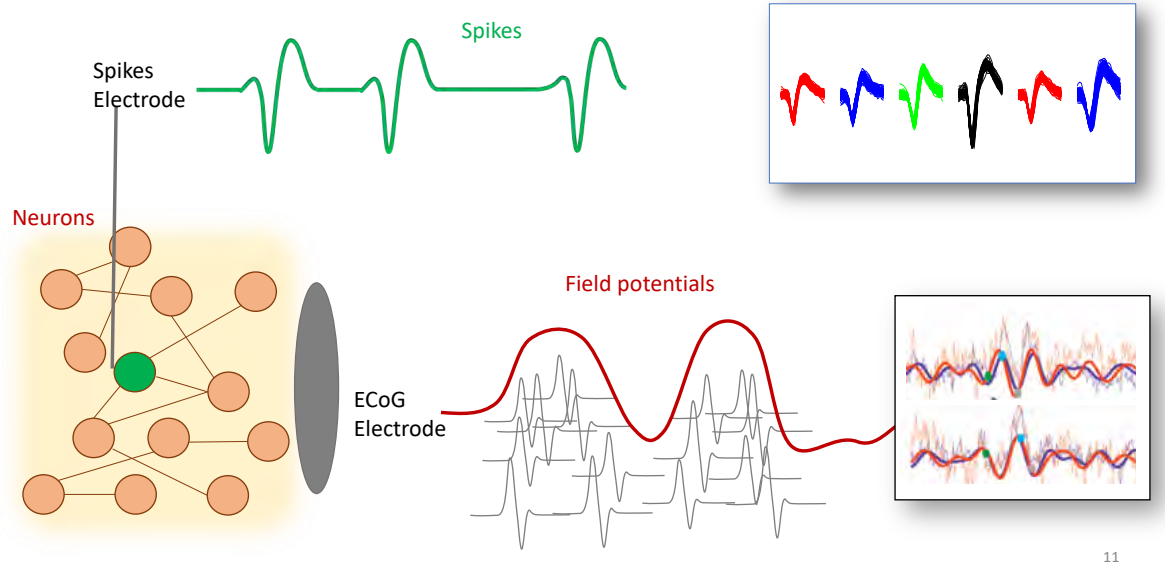


# Brain-Computer Interface (BCI)

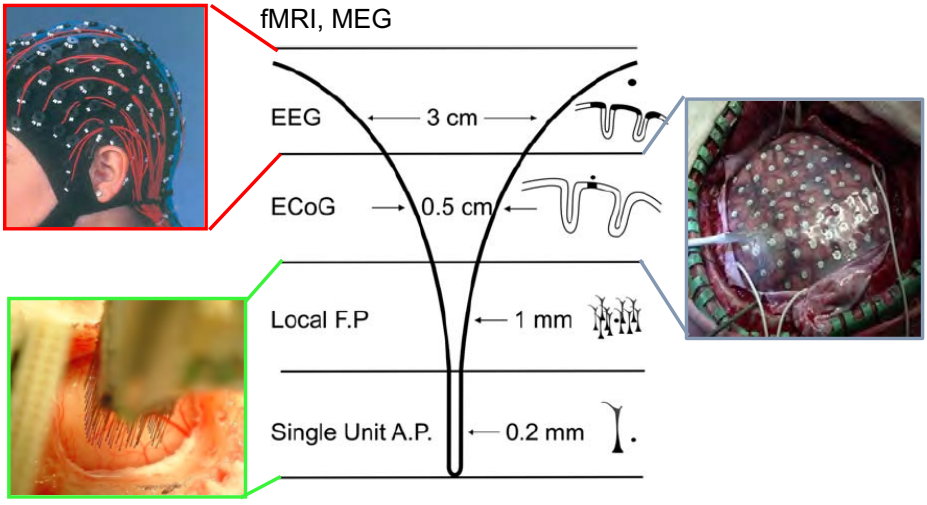



Also known as “Neural Interface” and “Brain-Machine Interface/BMI”

# Extracellular Recording of Activity

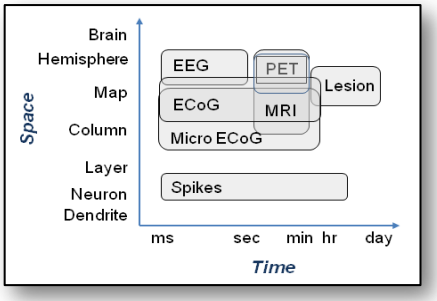


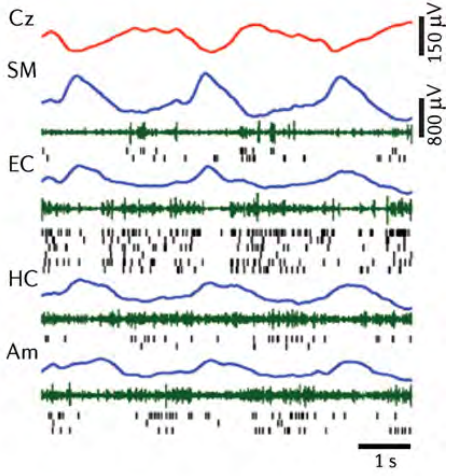
# Recording neural activity from the brain




Schwartz et al. *Neuron*, 2006

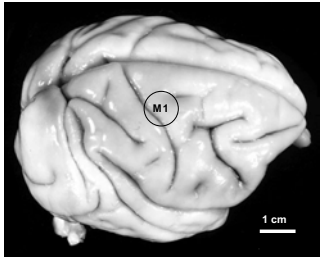
# Recording neural activity from the brain

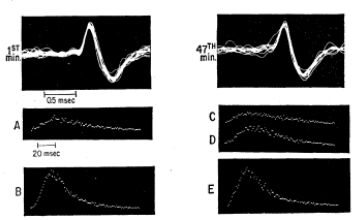


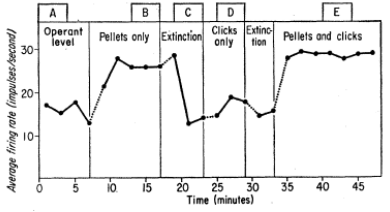



# Principles Underlying BCI Control

# Volitional control of brain activity



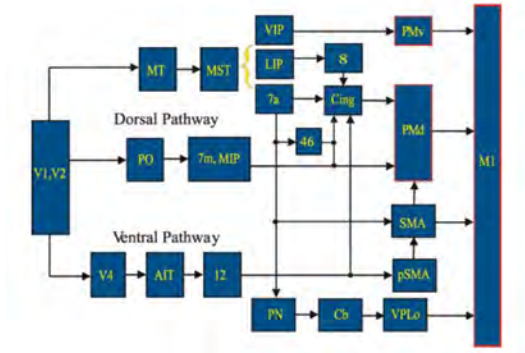



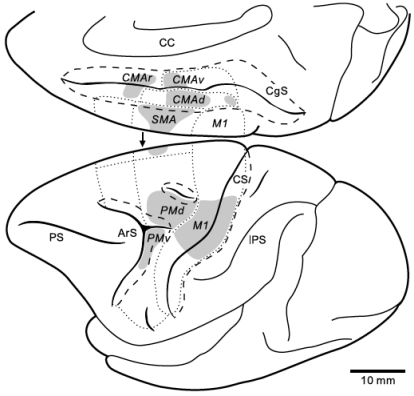

Fetz, E, Science, 1969

# Volitional control of movements

A



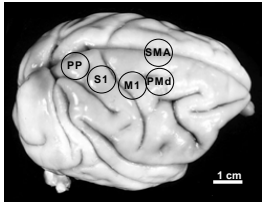

B

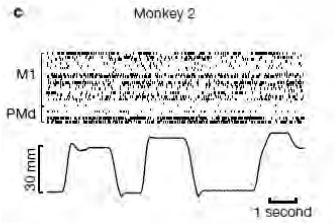


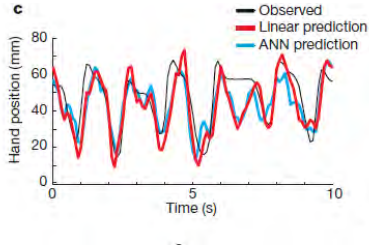

BCIs grounded by > 40 years of research into movement control!

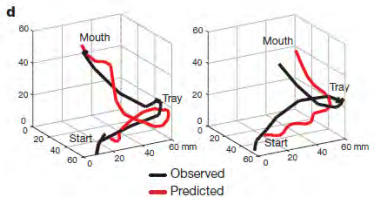
Georgopoulos AP, J. Neurosci (1982); Dum & Strick (2002); Schwartz, J. Physiology (2006)

# Distributed neural population activity



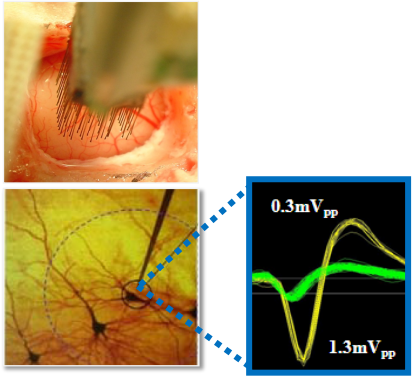



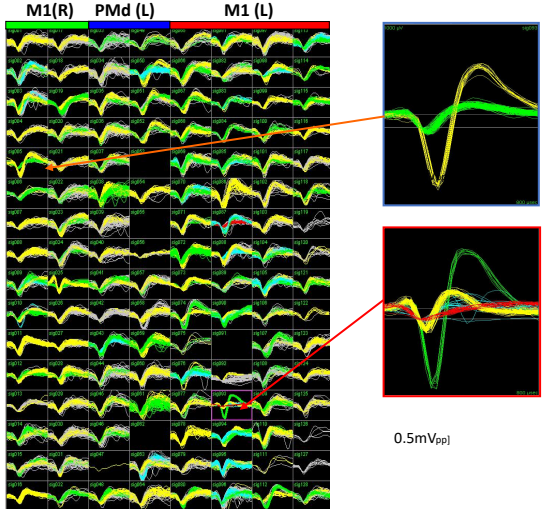



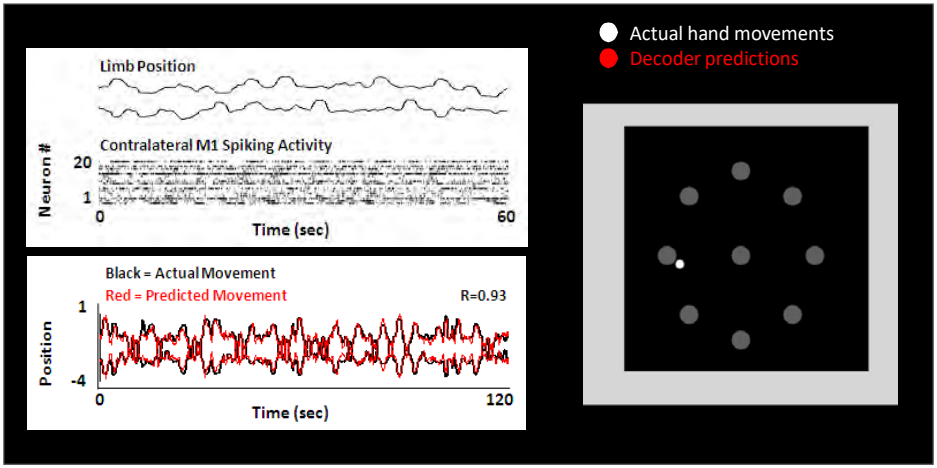

From Wessberg et al., 2000;
but see also Chapin et al., 1999, Serruya et al., 2002; Taylor et al., 2002; Carmena et al., 2003; Velliste et al., 2008; Pohlmeyer et al., 2009

# Recording from neural populations



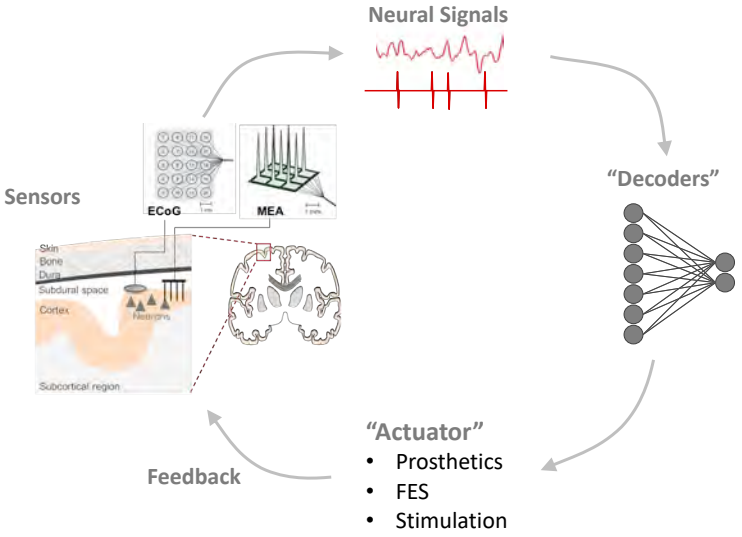



# Real-time decoding of hand position

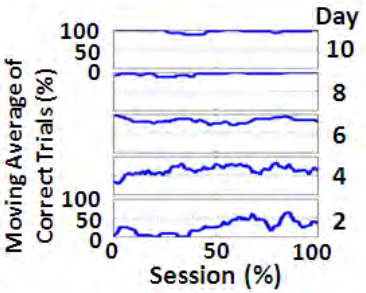


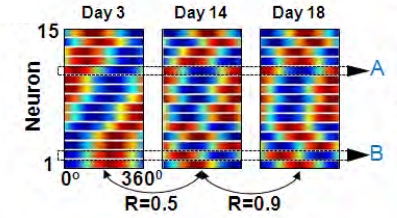

Ganguly et al., 2009

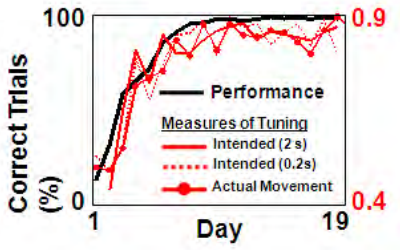
# “Closed-Loop” Brain-Computer Interfaces



# Neural plasticity key for stable BCI control




Ganguly et al., PLoS Biology, 2009; Ganguly et al., Nat Neuro 2011; Gulati et al, Neuro Neuro 2014, 2017 Nat Neuro; Kim et al., Cell 2019

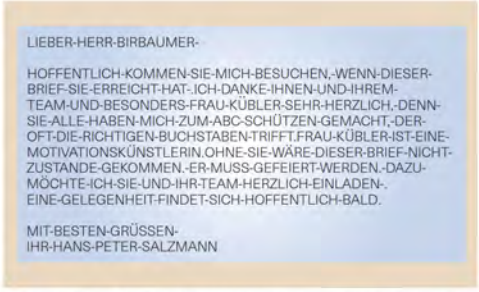
# Examples of BCI Control in Human Subjects

# Development of BCI Control

- Real-time recording of ensembles
  Chapin et al., 1999; Wessberg et al., 2000
- Multiple demonstrations of ‘closed-loop’ control over an external device
  Serruya et al., 2002; Taylor et al., 2002; Carmena et al., 2003; Velliste et al., 2008; Pohlmeyer et al., 2009
- Human subjects can learn direct neural control of a computer cursor
  Kennedy et al., 2000; Leuthardt et al., 2004; Hochberg et al., 2006
- Clear demonstration that a subject’s intentions can be translated

# EEG-interface for communication

- Two patients with advanced ALS (ventilated, PEG tube for > 4 years) could learn to communicate
- Patients were 'locked-in' (no voluntary muscle movements)
- EEG signals could be used to type a message (but very slow!)



LIEBER-HERR-BIRBAUMER-

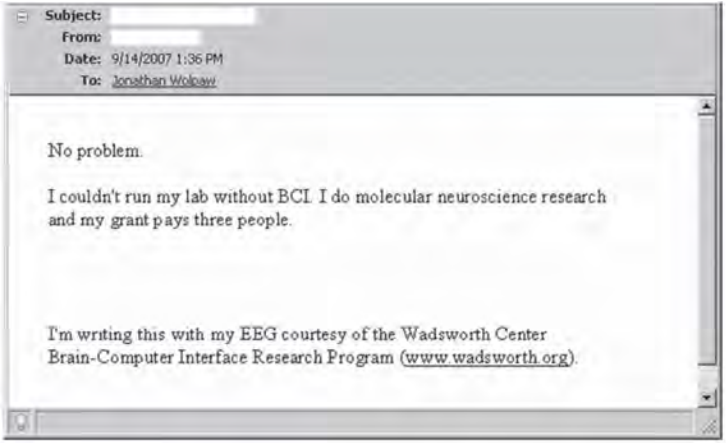
HOFFENTLICH-KOMMEN-SIE-MICH-BESUCHEN,-WENN-DIESER-BRIEF-SIE-ERREICHT-HAT-.ICH-DANKE-IHNEN-UND-IHREM-TEAM-UND-BESONDERS-FRAU-KÜBLER-SEHR-HERZLICH,-DENN-SIE-ALLE-HABEN-MICH-ZUM-ABC-SCHÜTZEN-GEMACHT,-DER-OFT-DIE-RICHTIGEN-BUCHSTABEN-TRIFFT.FRAU-KÜBLER-IST-EINE-MOTIVATIONSKÜNSTLERIN.OHNE-SIE-WÄRE-DIESER-BRIEF-NICHT-ZUSTANDE-GEKOMMEN.-ER-MUSS-GEFEIERT-WERDEN.-DAZU-MÖCHTE-ICH-SIE-UND-IHR-TEAM-HERZLICH-EINLADEN-. EINE-GELEGENHEIT-FINDET-SICH-HOFFENTLICH-BALD.

MIT-BESTEN-GRÜSSEN-
IHR-HANS-PETER-SALZMANN

Figure 2 The first full message written by subject A.

Birbaumer et al., Nature (1999)

# Case Report: A 51yo molecular biologist with ALS…



Subject:
From:
Date: 9/14/2007 1:36 PM
To: Jonathan Wolpaw

No problem.

I couldn't run my lab without BCI. I do molecular neuroscience research and my grant pays three people.

I'm writing this with my EEG courtesy of the Wadsworth Center Brain-Computer Interface Research Program (www.wadsworth.org).

Sellars et al., Amyotroph Lateral Scler. (2010)

# BCI Control of a Computer Cursor

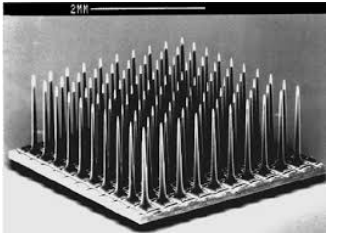

FROM Collinger et al., Lancet (2013)
See also Hochberg et al., 2006, 2012; Wodlinger et al., 2014

# BCI Control in a tetraplegic subject

FROM Pandarinath et al., eLife(2017).

# Translational Challenges

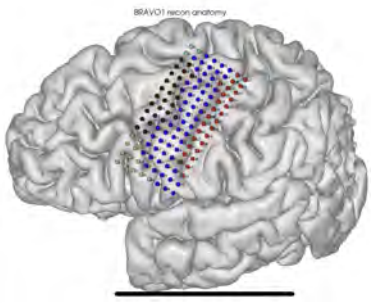
- Signals are not stable → Utah Array
- Daily training required because of signal stability
- Complex setups that require lot of support
- Currently not wireless (this will be solved soon)



# Ongoing UCSF studies

- ECoG BCI Trial
- Neural Interfaces for Stroke

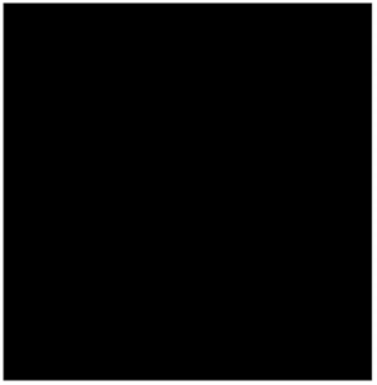
# ECoG based chronic implant



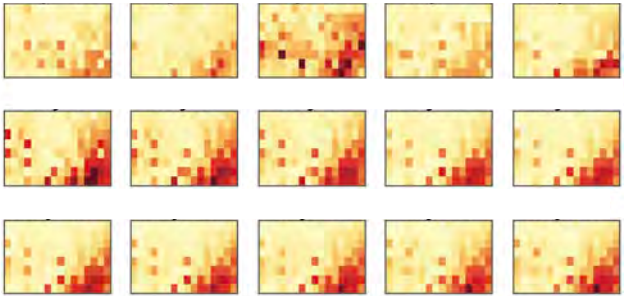

- FDA cleared testing of a chronic ECoG based device
- Addresses a downside of current trials
  - Signal instability
  - Daily training
- Two primary goals are control of a typing interface and a complex robotic arm
- Leverage stability of ECoG signals to engage learning and plasticity

** Experimental Device → FDA Investigational Device Exemption (IDE)

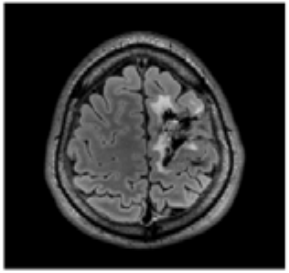
# ‘Plug-and-Play’ BCI Control



‘Neural maps’ Across Days

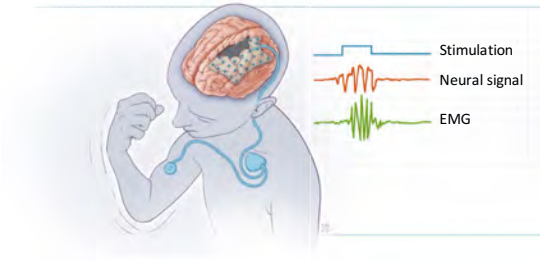


# Impaired hand function after stroke



- ~700,000 strokes/year
- >$15K for rehabilitation per patient
  - Limits of rehab (ICARES Trial, 2018)
- ~50% with hand impairments, limits independence

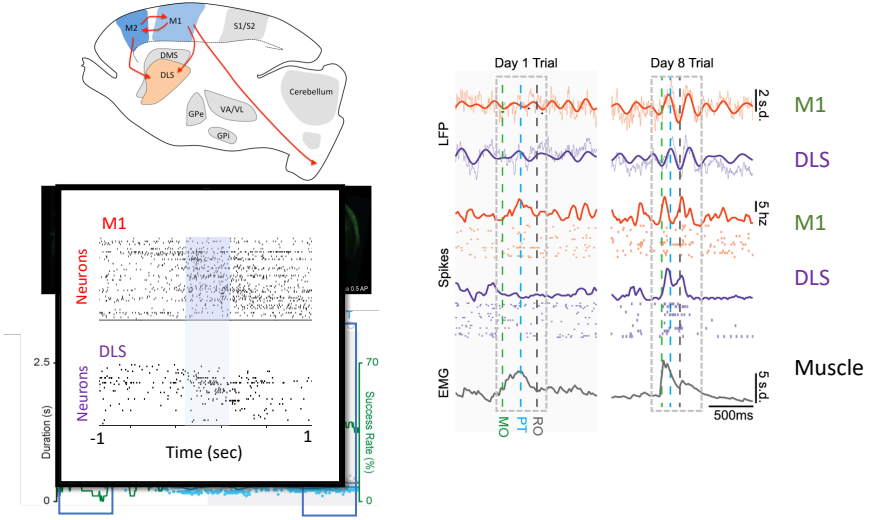
# Towards the Development of a Closed-Loop Neural Interface for Stroke



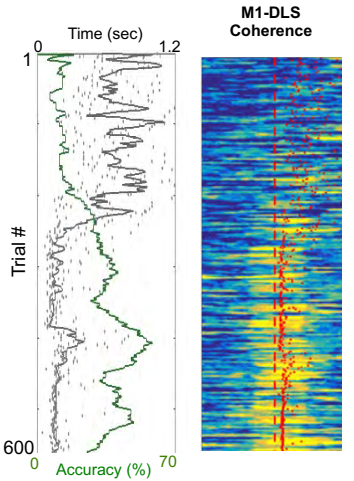

**What is required for closed-loop modulation?**

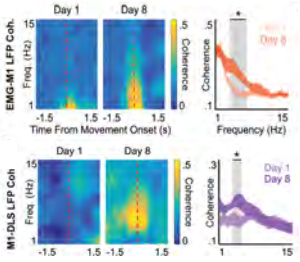
- Electrophysiological targets?
- Predictor of good/poor recovery?
- Can targeted stimulation help chronic deficits?

# Synchronous Network Activity During Skilled Movements



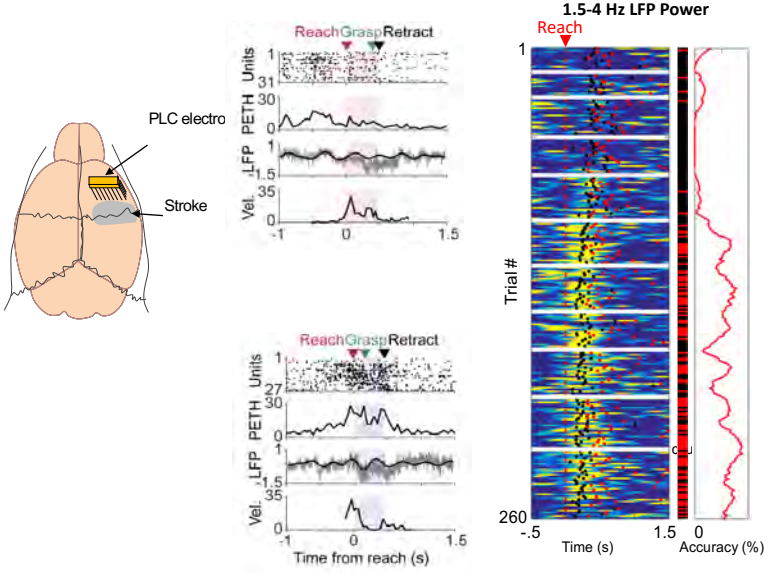
# Changes in Speed/Consistency with Learning



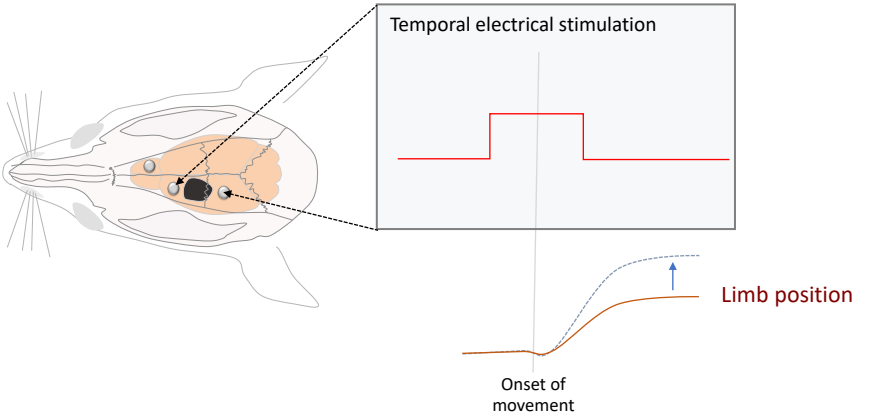




*Lemke et al., Nature Neuroscience, 2019*

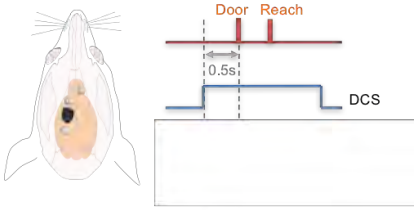
# Reemergence of synchronous activity

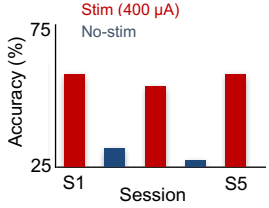


# Responsive Stimulation

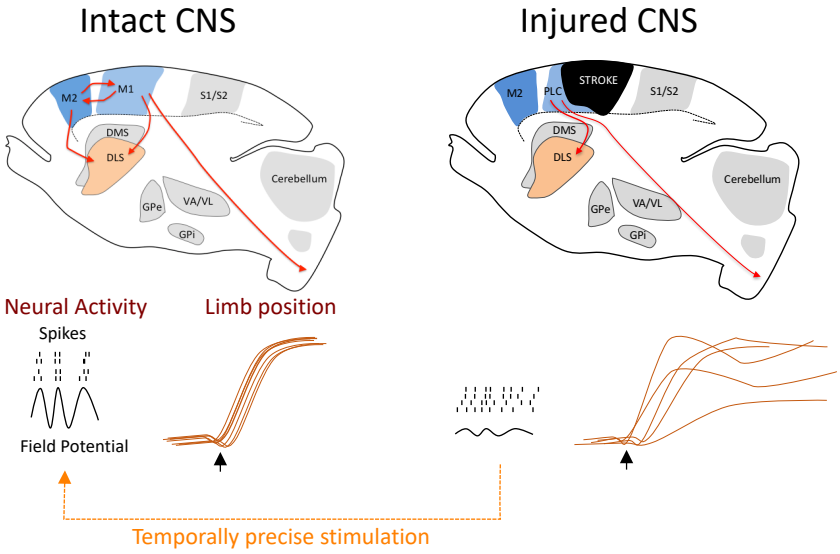


# Responsive Stimulation

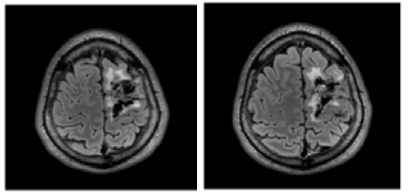


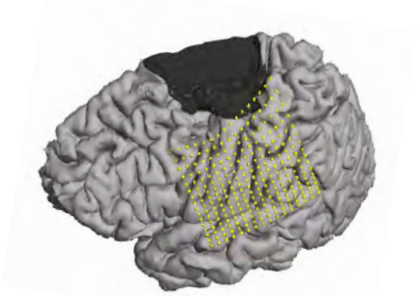



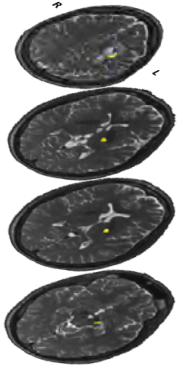
# Summary


Intact CNS
Injured CNS
M2
M1
S1/S2
DMS
DLS
Cerebellum
GPe
VA/VL
GPi
PLC
STROKE
Neural Activity
Limb position
Spikes
Field Potential
Temporally precise stimulation

# ECoG in Stroke



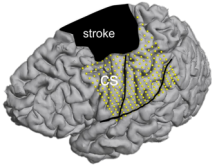


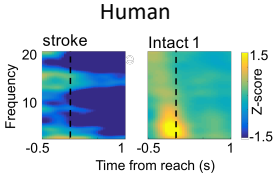


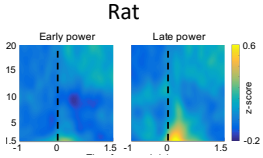
Fugl-Meyer of 35

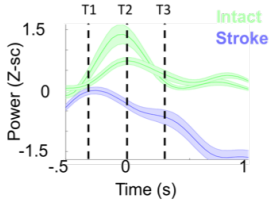
Ramanathan*, Guo*, Gulati* et al. *Nature Medicine (2018)*

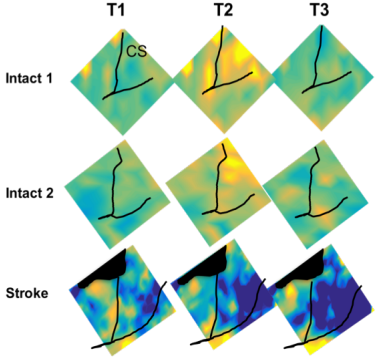
# Reduced task-related slow-oscillations



# Thanks for your attention!

**Research Funding**