Understanding & interfacing with the brain: challenges and opportunities

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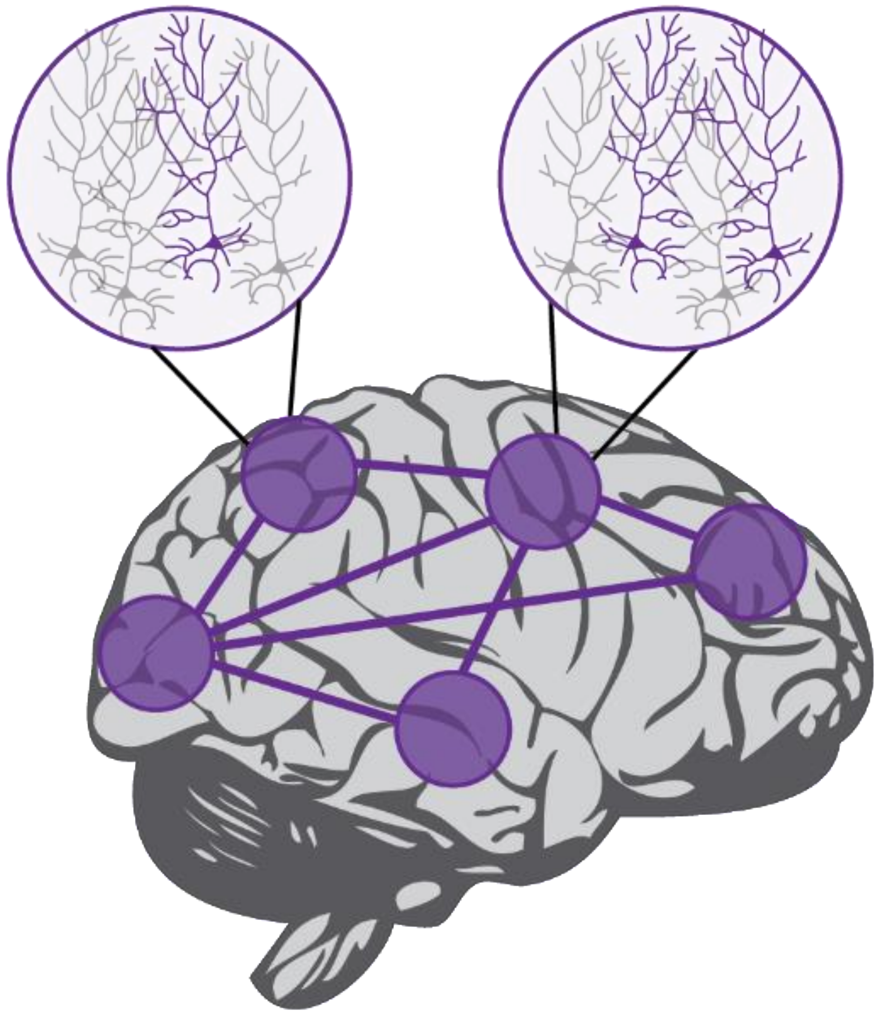
A3D3 seminar

October 25, 2021

Need to understand and treat brain **networks**

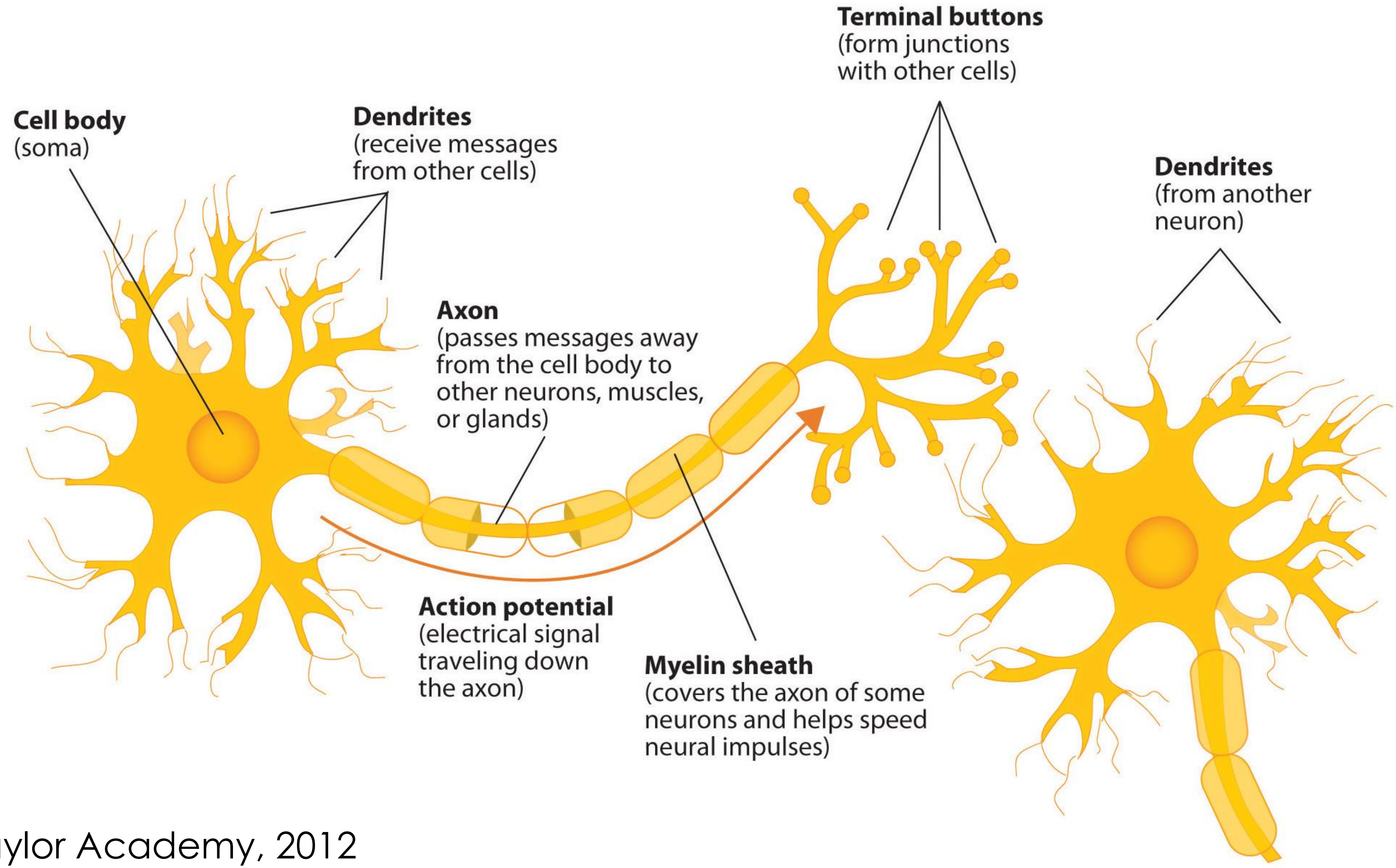


- Brains are big networks
  - Billions of neurons, trillions of connections
  - Distributed computation
  - Multi-scale computation

- All behaviors involve distributed brain activity

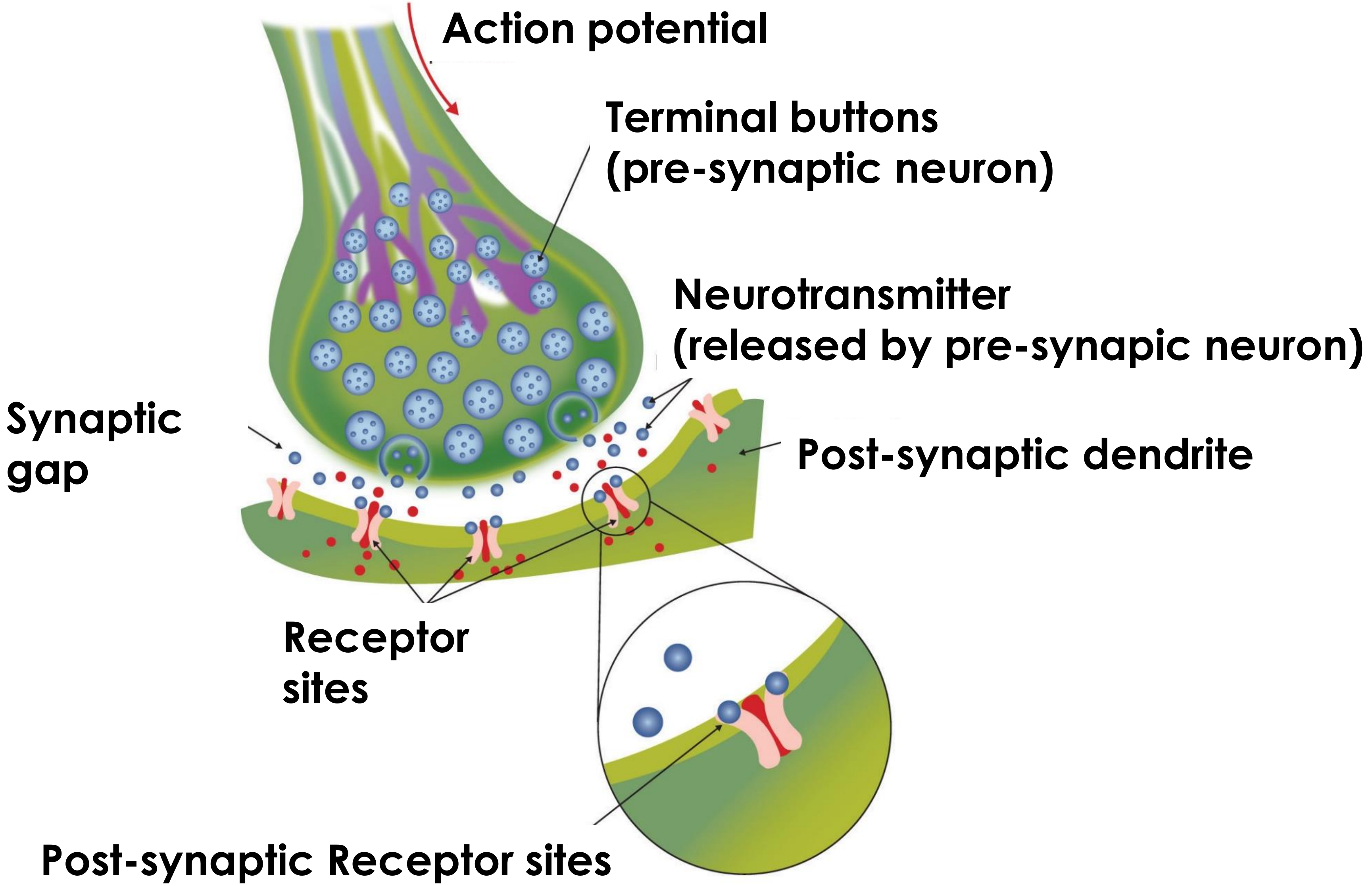
- Neurological disorders = disrupted network function
  - Parkinson's
  - Alzheimer's
  - Stroke
  - …

Neurons communicate via electro-chemical signaling



Saylor Academy, 2012

Neurons communicate via electro-chemical signaling



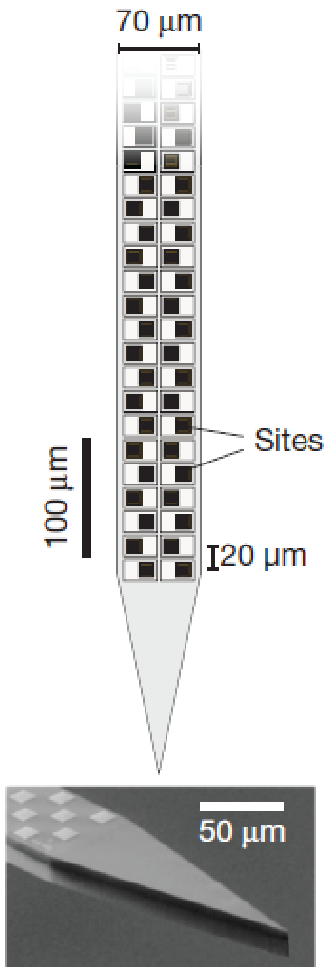
Saylor Academy,
2012

Many ways to measure neural activity

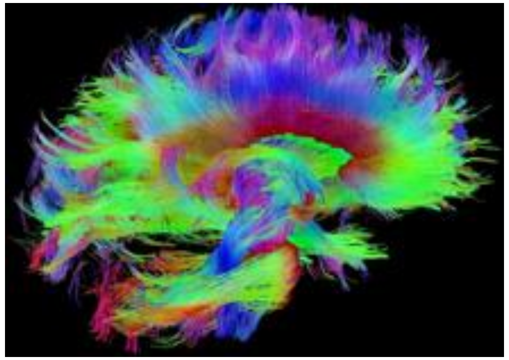
- Electrical
  - Detect currents/voltages inside or outside of neurons
- Chemical
  - Detect changes in ion flow inside of neurons
  - Detect neurotransmitter release
- Metabolic indicators (e.g. bloodflow)
  - Detect changes in energy consumption by neurons

- Many different scales of measurement across modalities

Technology to define, monitor & manipulate networks



Neuropixels
Jun et al., *Nature* 2017



Diffusion image,
Human connectome project

Optogenetics

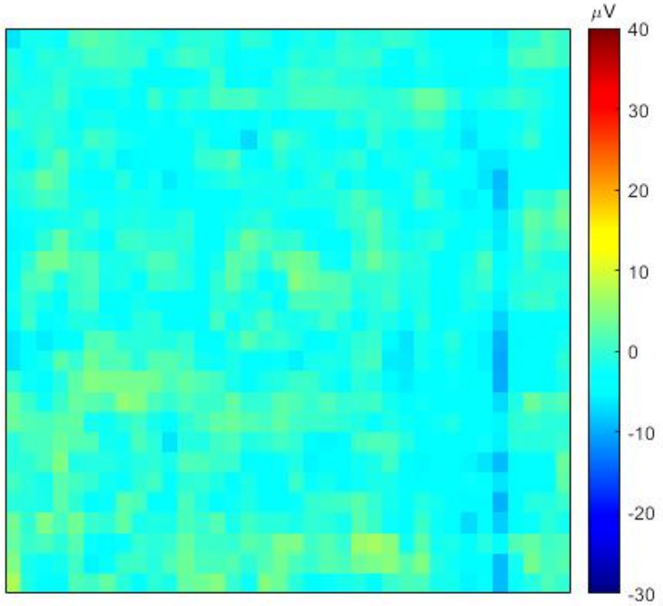
- BRAIN Initiative–**B**rain **R**esearch **A**dvancing **I**nnovative **N**eurotechnology
  - Electrodes
  - MRI
  - Light
  - Ultrasound
  - Combinations
    - Optoelectrical
    - Optoacoustics
- Translation from animals to humans

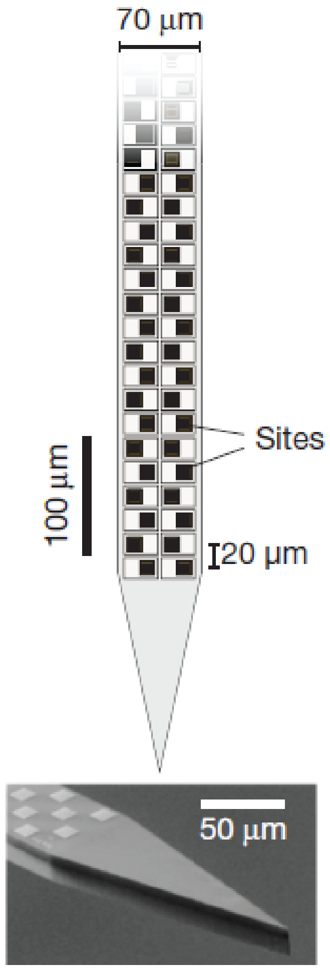
Modern neurotechnologies: rapid data scaling

- Electrical
  - Active, integrated electronics
    - → Denser sampling
  - Thin-film devices
    - → Increased biocompatibility (record longer)

Device with 1k electrodes/ 1cm^2

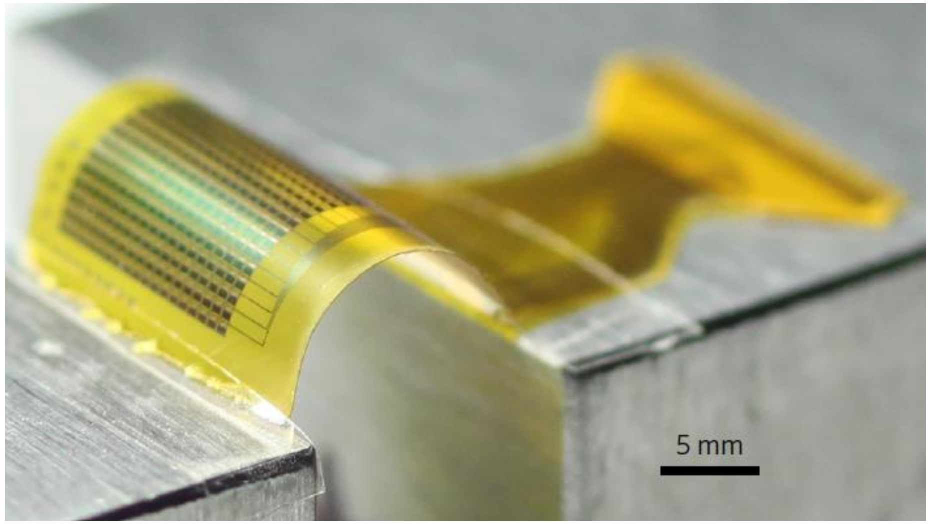
Chiang, Won, Orsborn, Yu et al., *Sci Trans Med* 2020





Neuropixels
- ~400 ch
- 1k sites
- 20um pitch

Jun et al., *Nature* 2017



Active Arrays
- Flexible, stretchable

Fang et al., *Nature BioEng* 2017

Modern neurotechnologies: rapid scaling

- Electrical
  - Active, integrated electronics
    - → Denser sampling
  - Thin-film devices
    - → Increased biocompatibility (record longer)
- Optical
  - Sensing (Ca+, voltage indicators)
  - Actuation (light-sensitive ion channels)
  - Higher resolution & specificity
  - Larger volumes

Mesocope imaging
- Hemispheric coverage (mouse brain,surface)
- ROI high-res imaging

Sofroniew et al., eLife 2016

Modern neurotechnologies: rapid scaling

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- Comprehensive behavioral monitoring
  - Video tracking
  - Text
  - Voice

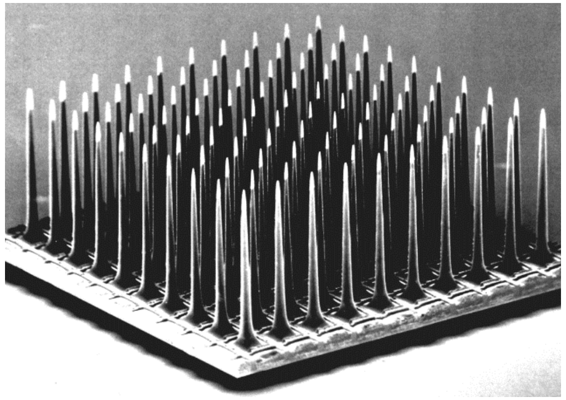
Real-time motion tracking in 3D
(Bala et al., *Nature Communications* 2020)

Neuro data is getting bigger

Functional Magnetic Resonance Imaging

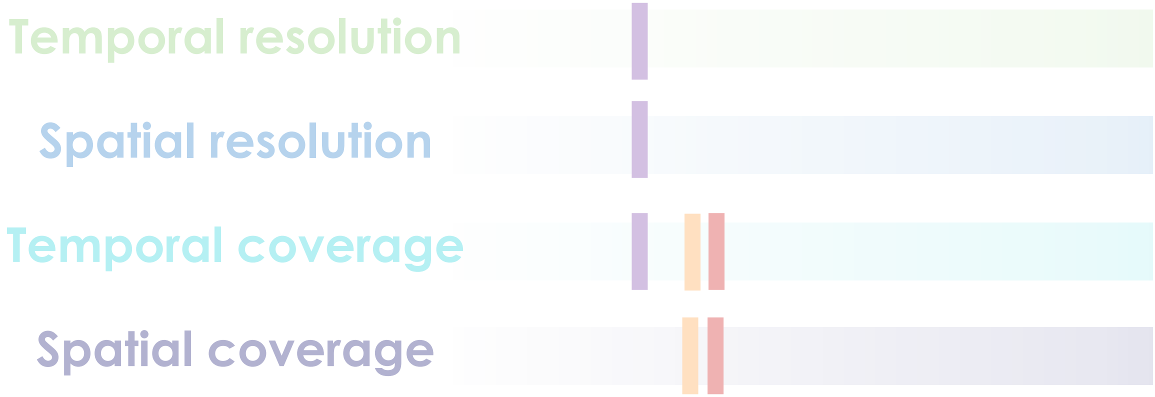
- 1 Hz sampling
- ~8mm^3 voxels
- 1 hr
- 5 x 10^3 voxels
- Whole human brain

Electrodes



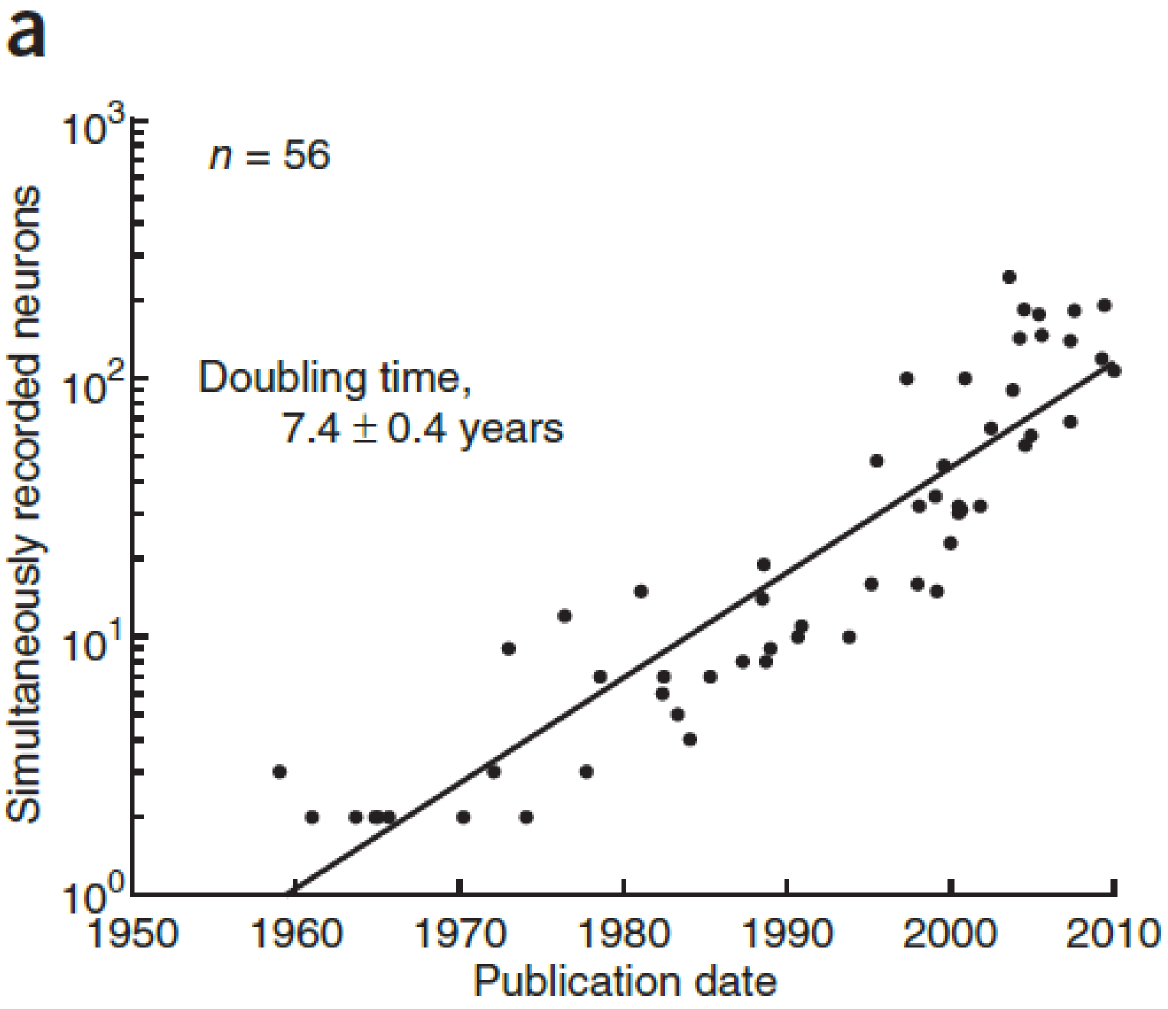
- 30 kHz sampling
- ~500 um^3 sampling volume
- 1 hr
- 100 electrodes
- 1,000 mm^3

Neuro data is getting bigger



Next-gen technologies

- 30 kHz samplinc
- ~500 um^3 samp volume
- 1000+ hr
- 10^6 electrodes
- 10^4 mm^3

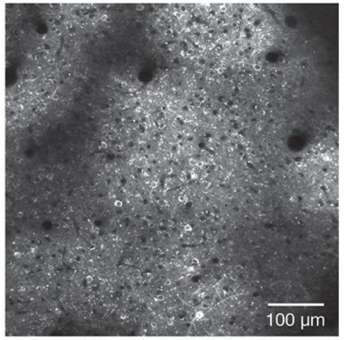


Stevenson & Kording, *Nature Neuroscience* 2011

Data is becoming multi-modal

- No recording method is a panacea

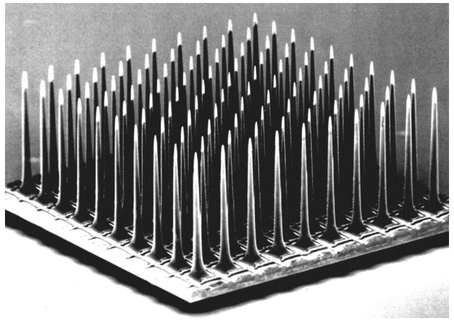
Imaging



- Dense spatial sampling
- Low temporal resolution

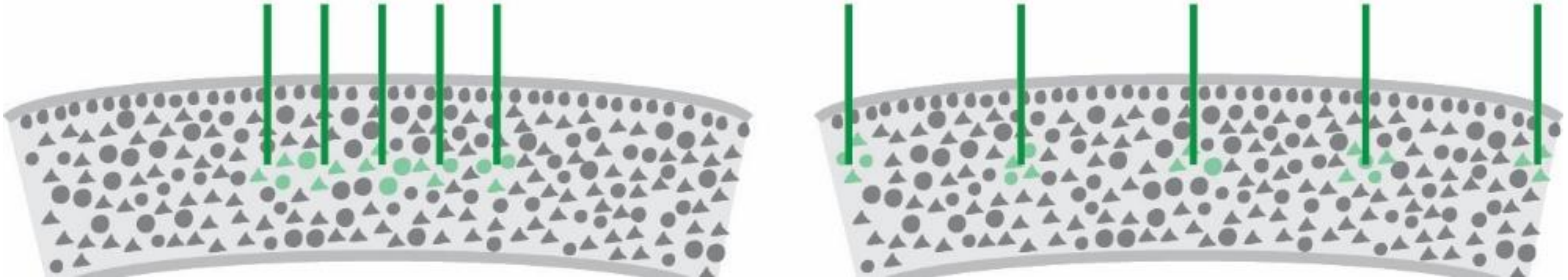
Sofroniew et al., eLife 2016

Electrodes

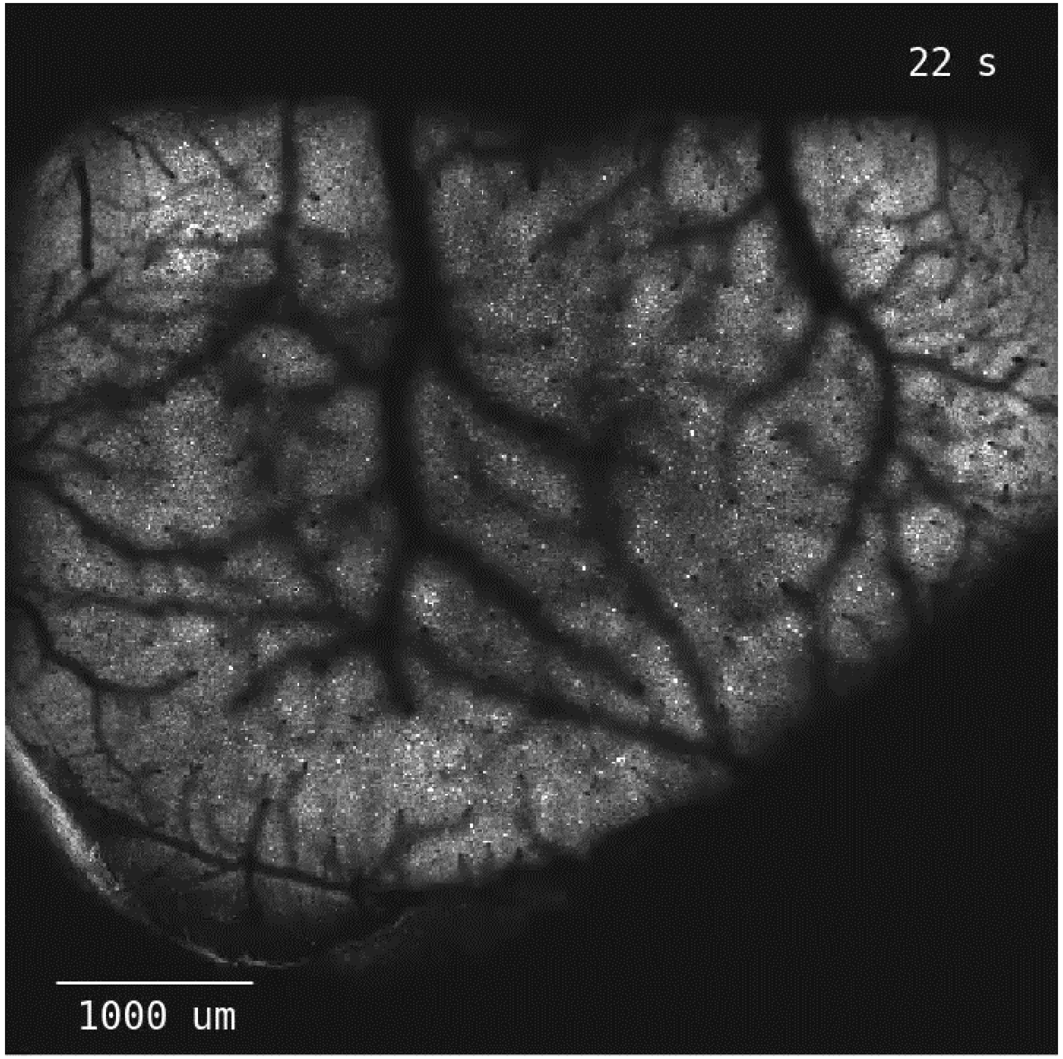


- Low spatial sampling
- High temporal resolution

- Trade offs in resolution and coverage



Towards multi-modal, multi-scale sampling



Low-resolution, large field of view imaging

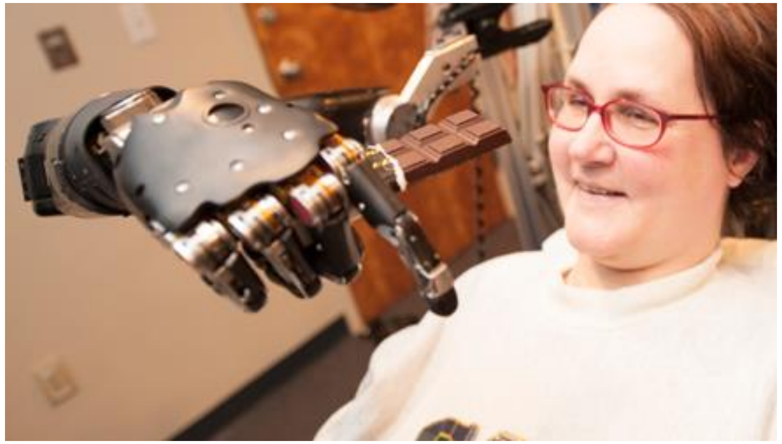
Use to guide ROI selection for high-res imaging

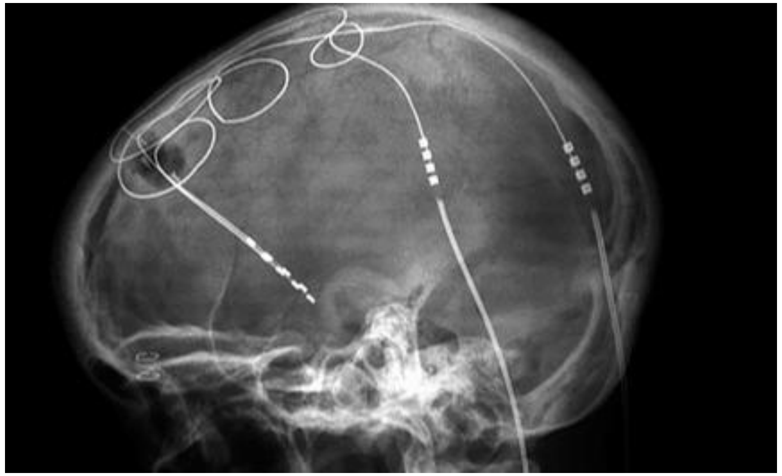
Sofroniew et al., eLife 2016

More data, more problems: processing, manipulation, interpretation

- Efficient data processing
  - Computationally efficiency
  - Person-hour efficiency (i.e. automation)

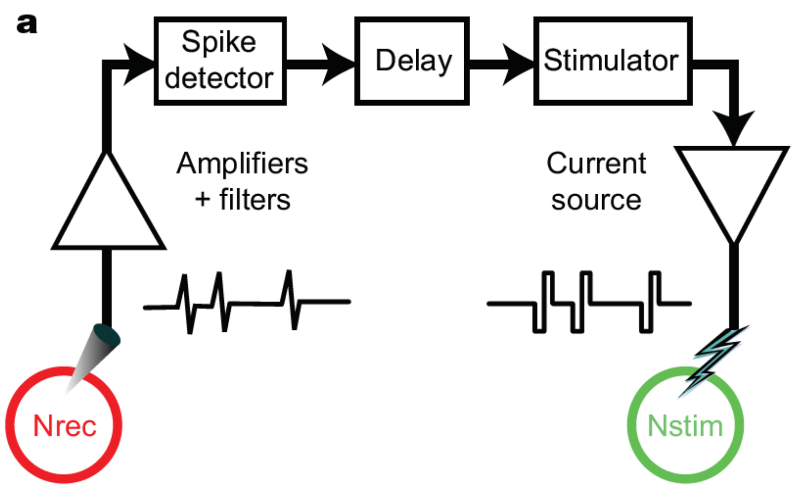
- Real-time processing, manipulation → treatments
  - Motor brain-machine interfaces
  - Closed-loop stimulation





Real-time ("Closed-loop") manipulations for studying brain-behavior relationships

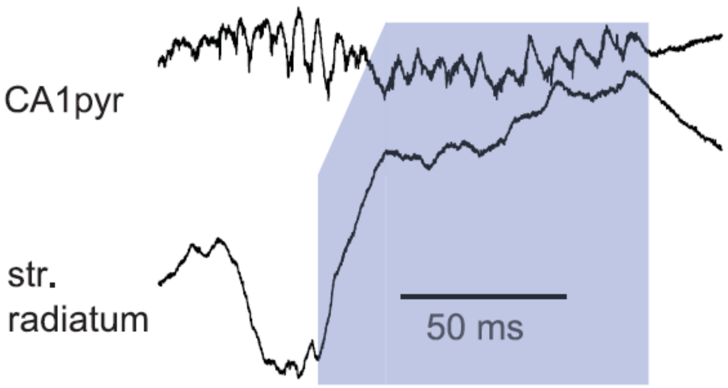
Stimulate based on activity → induce plasticity, study impact on behavior



timing-dependent:
<50ms +; >50ms -

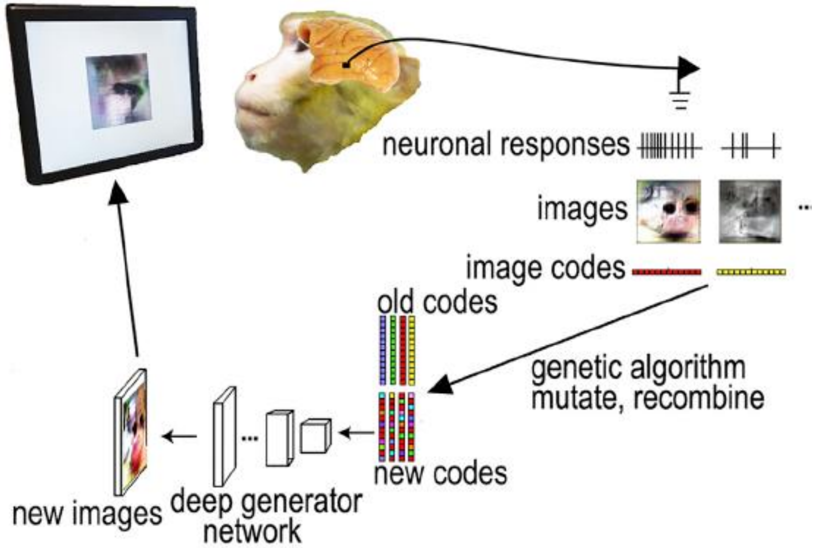
Jackson et al., *Nature* 2006

Stimulate to alter detected brain states → study impact on behavior



Fernández-Ruiz et al., *Science* 2019

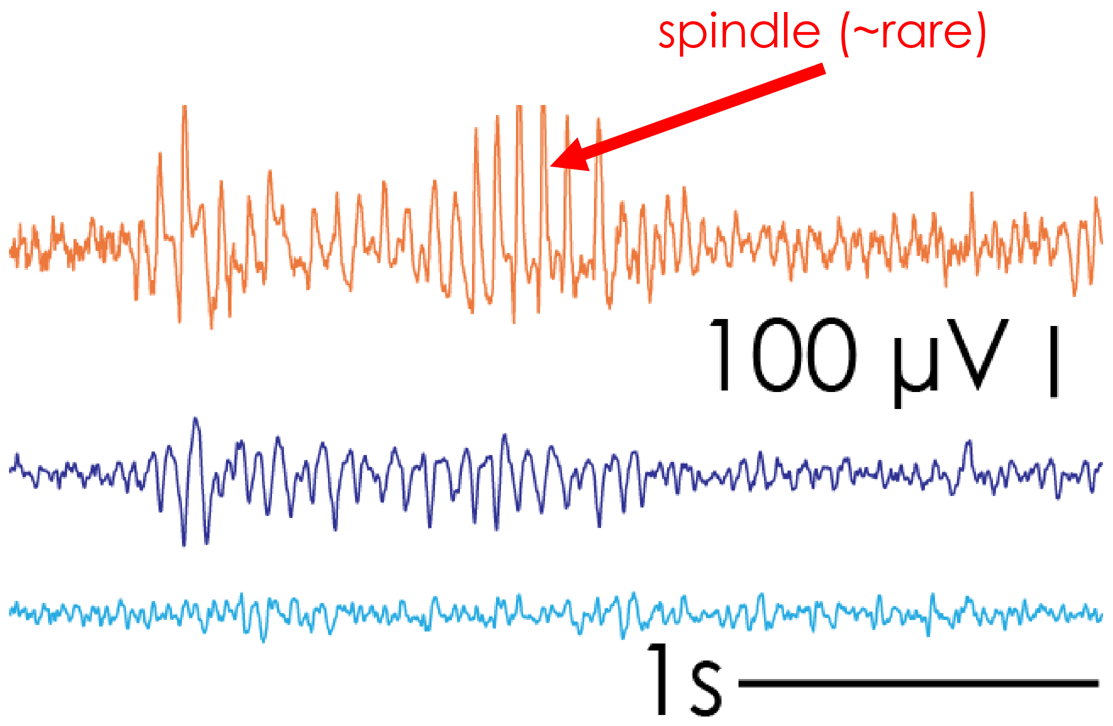
Change stimuli based on brain activity→ map responses quickly



Ponce et al., *Cell* 2019

Example application: closed-loop stimulation to alter sleep-spindle events

Local field potential measurements
(electrical activity of groups of neurons)



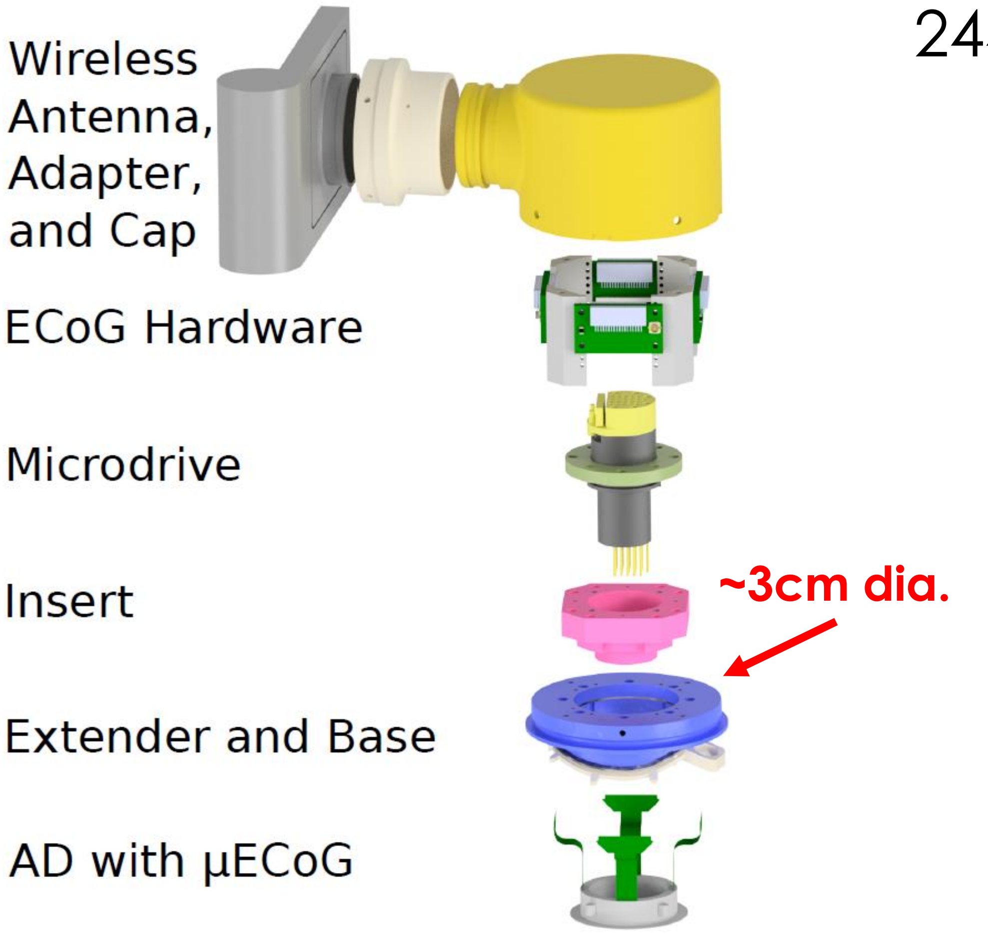
- “Spindles” are oscillation events that occur during sleep/rest
- Thought to contribute to learning

- **Currently:** *detect* a spindle starting and stimulate to disrupt

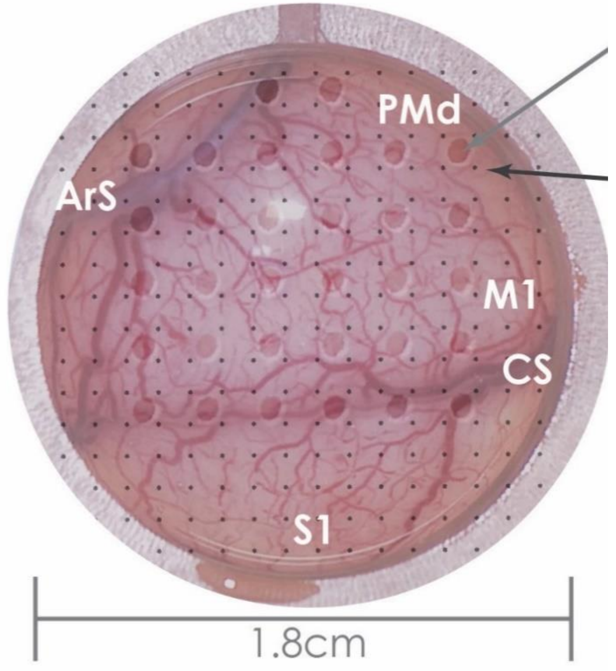
- **Goal:** predict spindle will occur, stimulate to prevent

Example application: closed-loop stimulation to alter sleep-spindle events

Example implant system for a monkey



244 measurement sensors

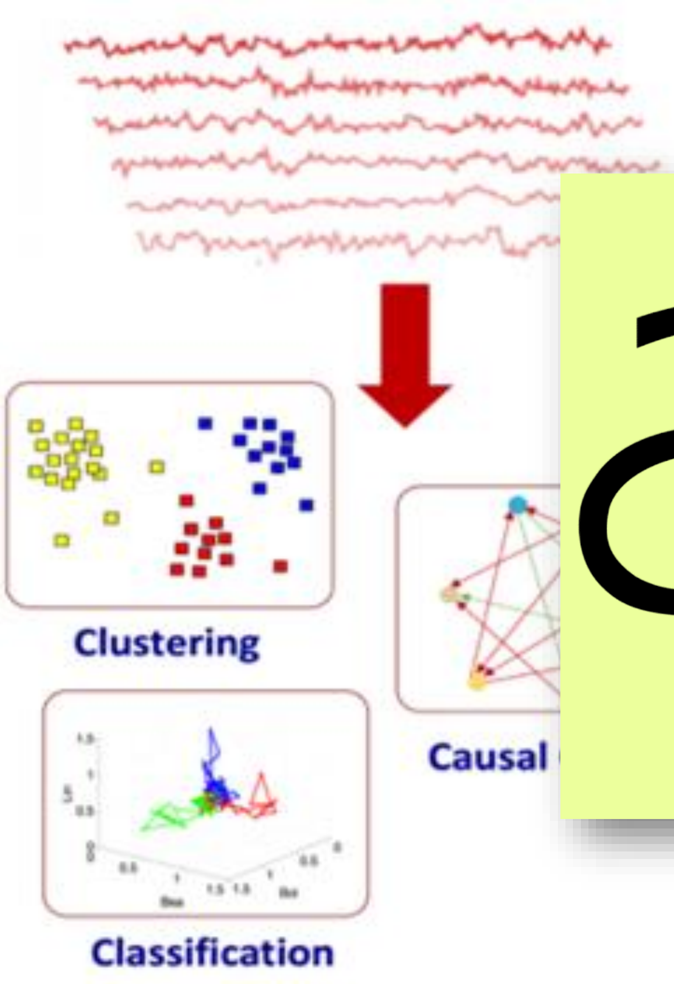


- **Goal:** packaged in hardware to be wearable on an animal
  - Local processing (preferred)

  OR

  - Wireless transmission to processing unit

Data-**Interpretation** for Neural Systems

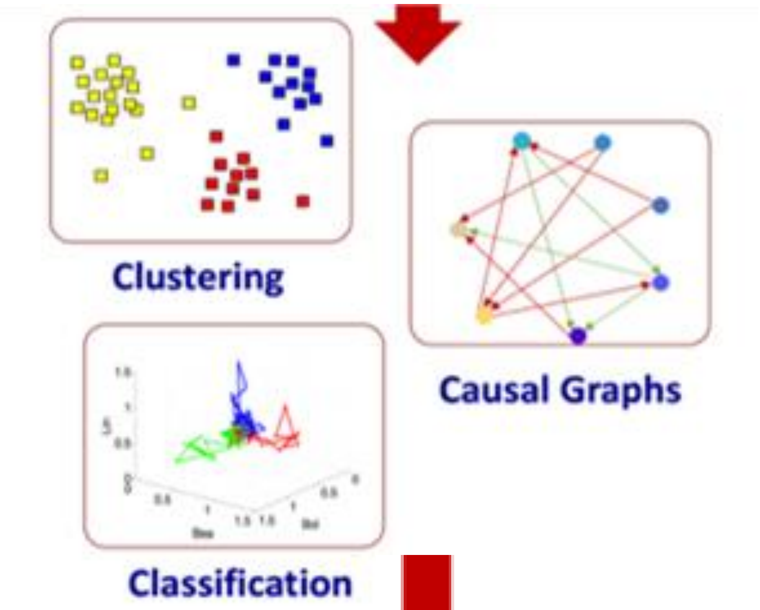


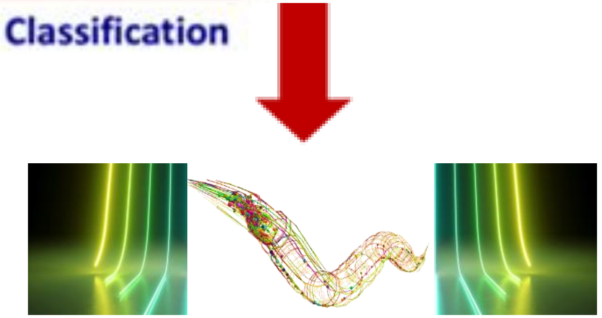
- With multi-neural recordings we would like to perform
  - (Data Organization)
  - **ion** (Data Labeling)
  - **Information** (Network Architecture)

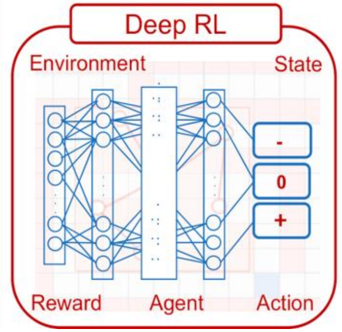
a3d3
Accelerated AI Algoritms for Data-Driven Discovery

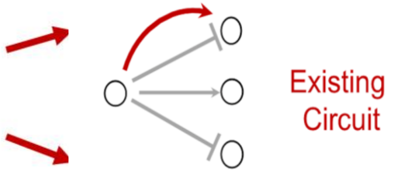
System-Understanding and **Applications** from Data

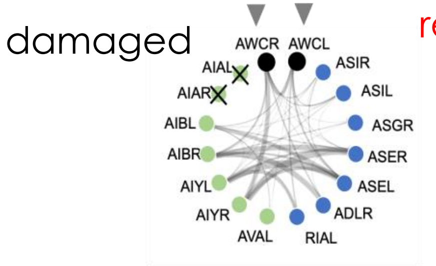
- From Data to
  - **Modeling** Neural Dynamics
  - **Control**
    - Neuromodulation Control
    - Structure Control

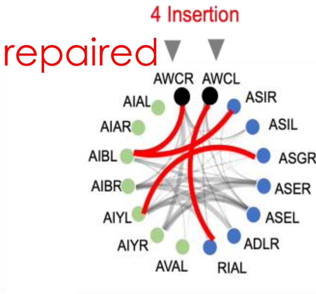






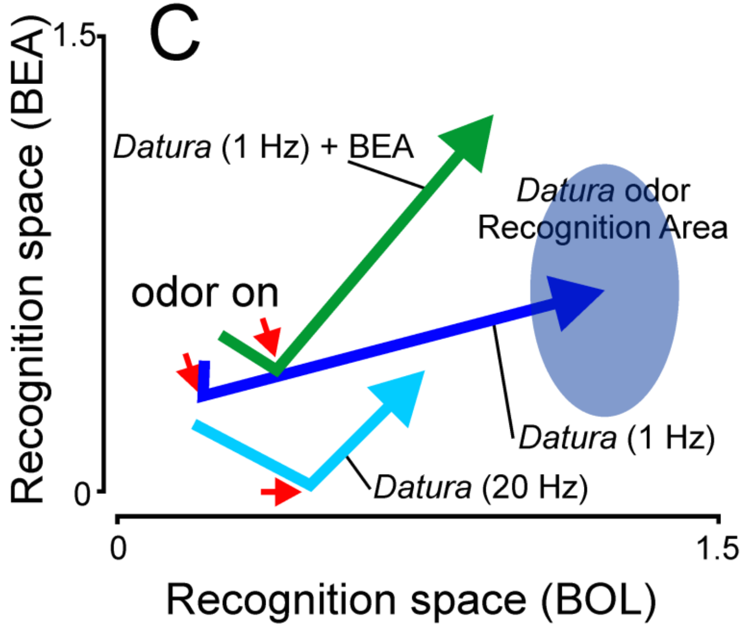






Clustering Multi-dimensional Timeseries

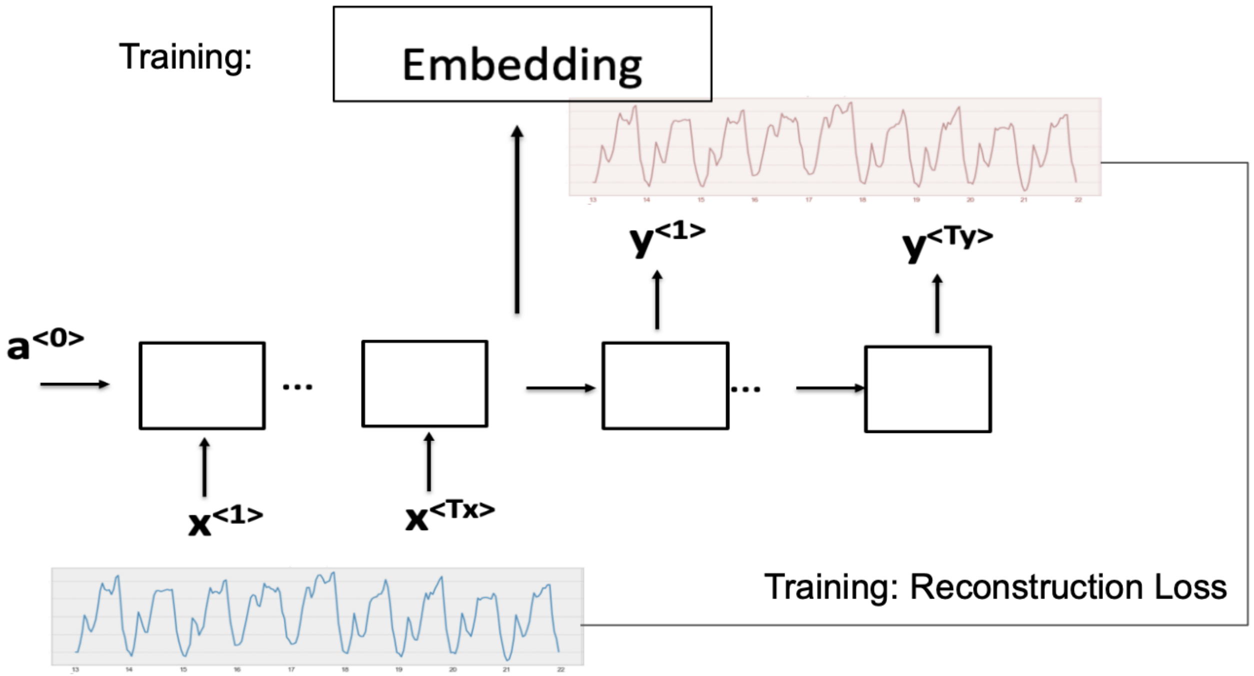
- **Classical** Machine Learning Methods
  - Low Dimensional Embeddings
  - Exclusive Threshold Reduction
  - Optimal Exclusive Threshold Reduction
  - **More neurons -> better**



Riffell et al. Science, 2014, Shlizerman et al., Front. Comp. Neuro 2014, Blaszka & Shlizerman, Front. Comp. Neuro 2017

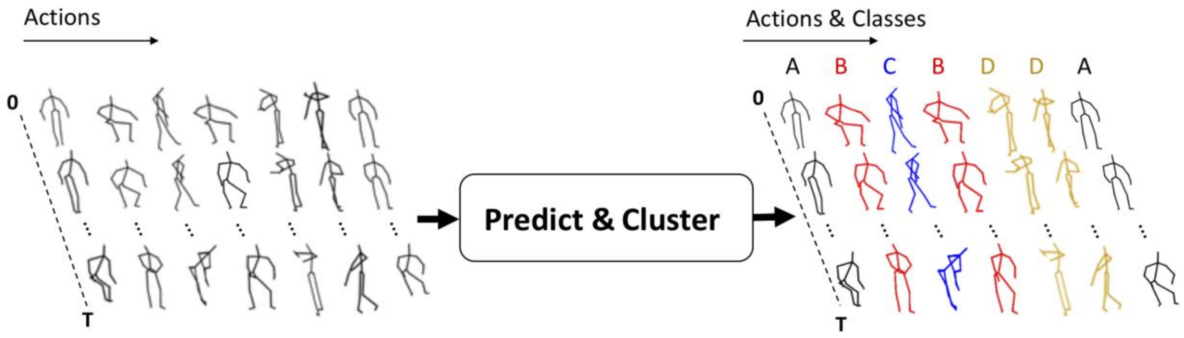
Clustering Multi-dimensional Timeseries

- **Deep** Learning Methods
  - Encoder-Decoder
  - Task:
    Prediction/Reconstruction
  - Latent Representation



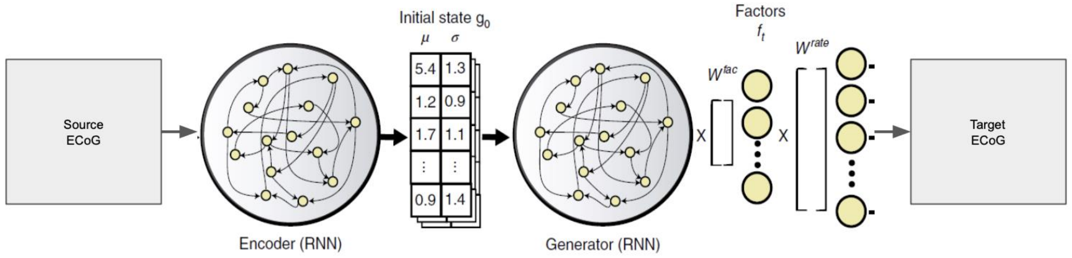
Clustering Multi-dimensional Timeseries

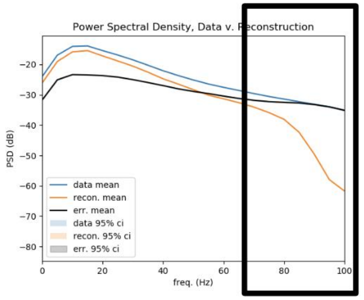
Behavioral Data: Unsupervised Human Action Recognition *(Predict and Cluster)*



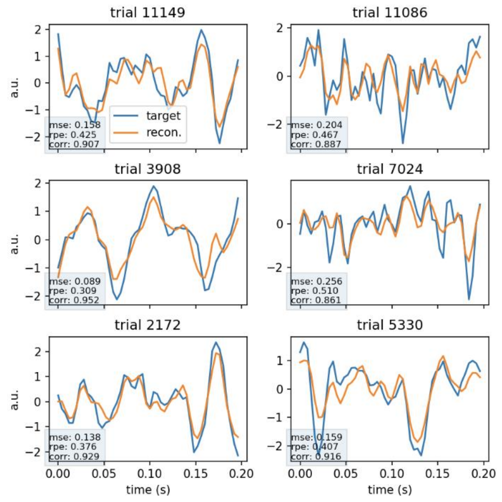
Su et al. CVPR, 2020, Su & Shlizerman, Front. AI 2020

Neural Data: Spike train data or Electrocorticogram (ECoG)





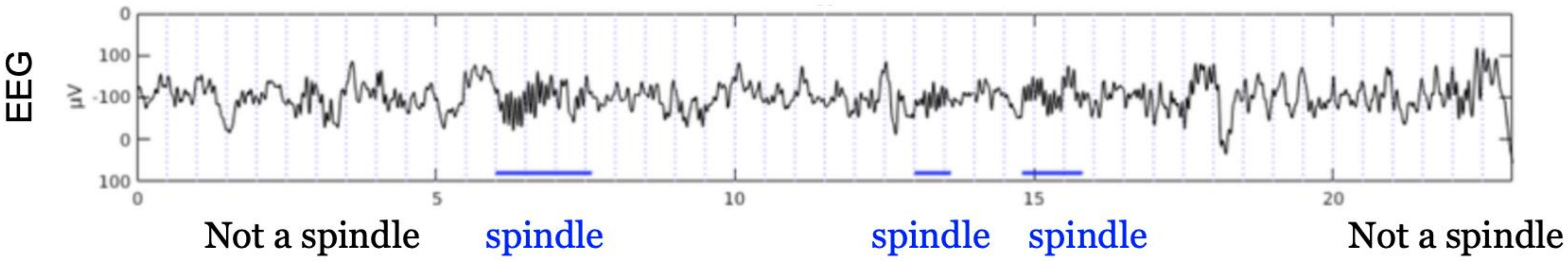
In progress to improve



Work in progress w. Amy Orsborn

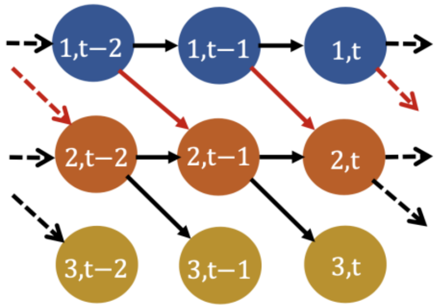
Applications of Prediction & Reconstruction

- Denoising
- Channel Reconstruction
- Tracking
- Anomaly Detection

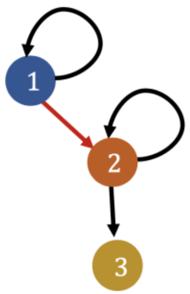


From Recordings to Structure

- Causal Graph Models
- Directed Markov Property
- Neuro-PC



Unrolled causal graph
between time instances of neurons



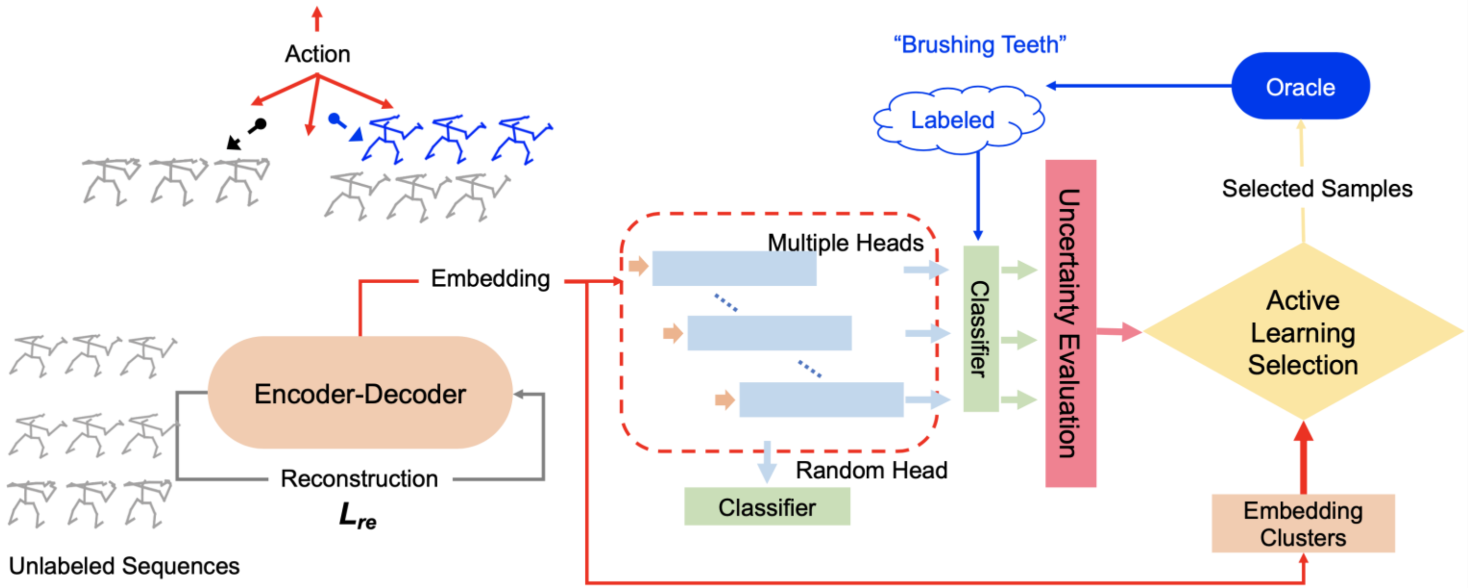
Causal Functional Connectome
(CFC-DPGM)

Biswas & Shlizerman, Arxiv 2021

Classification of Multi-dimensional Timeseries

- From Unsupervised to Semi-Supervised

Behavioral Data: Active Learning (Semi-Supervised)



Li & Shlizerman, Arxiv 2020