Neural Motor Prostheses:

Directly Coupling Brains and Machines to Restore Lost Function

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Brown University

Computer Science Neuroscience Applied Math Engineering

Motivation

Fun fact:

The "Six Million Dollar Man" would cost $22,471,910.11 2002 dollars.

Neural Motor Prosthesis

cerebral palsy

cerebellar disorders

locked-in syndrome

other stroke

spinal cord injury

spinal muscular atrophies

ALS

muscular dystrophy

limb loss

multiple sclerosis

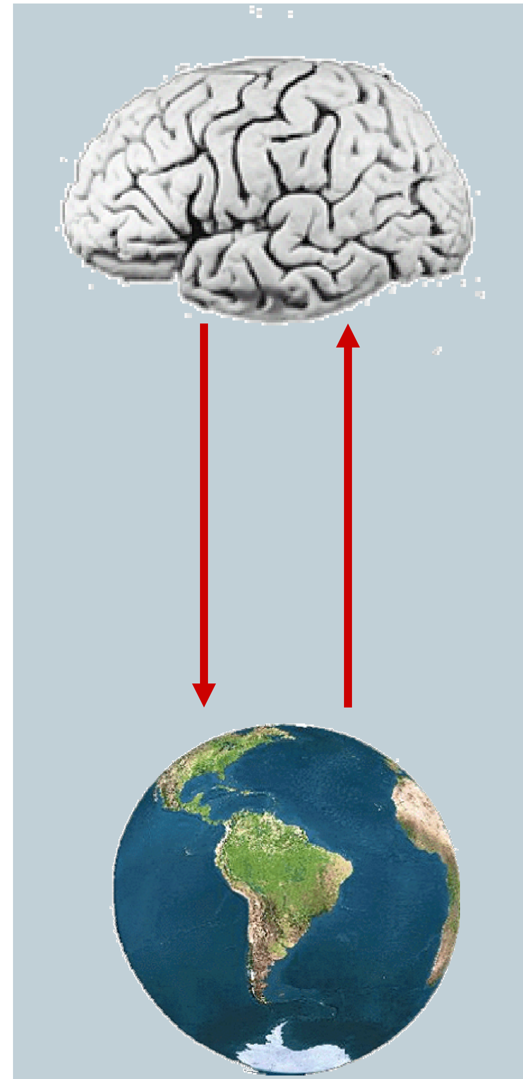
veterans

* Many neurological disorders disrupt the ability to *move* or *communicate*, but leave *cognition* intact.

* Spinal cord injury:
    - ~ 200,000 cases in the USA
    - 11,000 new cases/year
    - mostly young

* Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's disease)
    - 20,000 cases
    - 5,000 new cases/year

* Current assistive technology is limited



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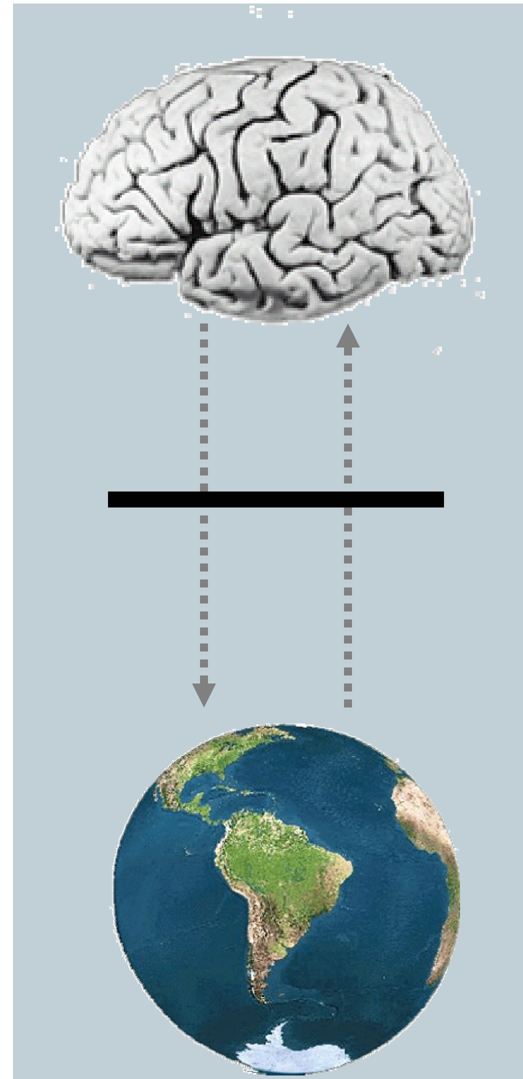

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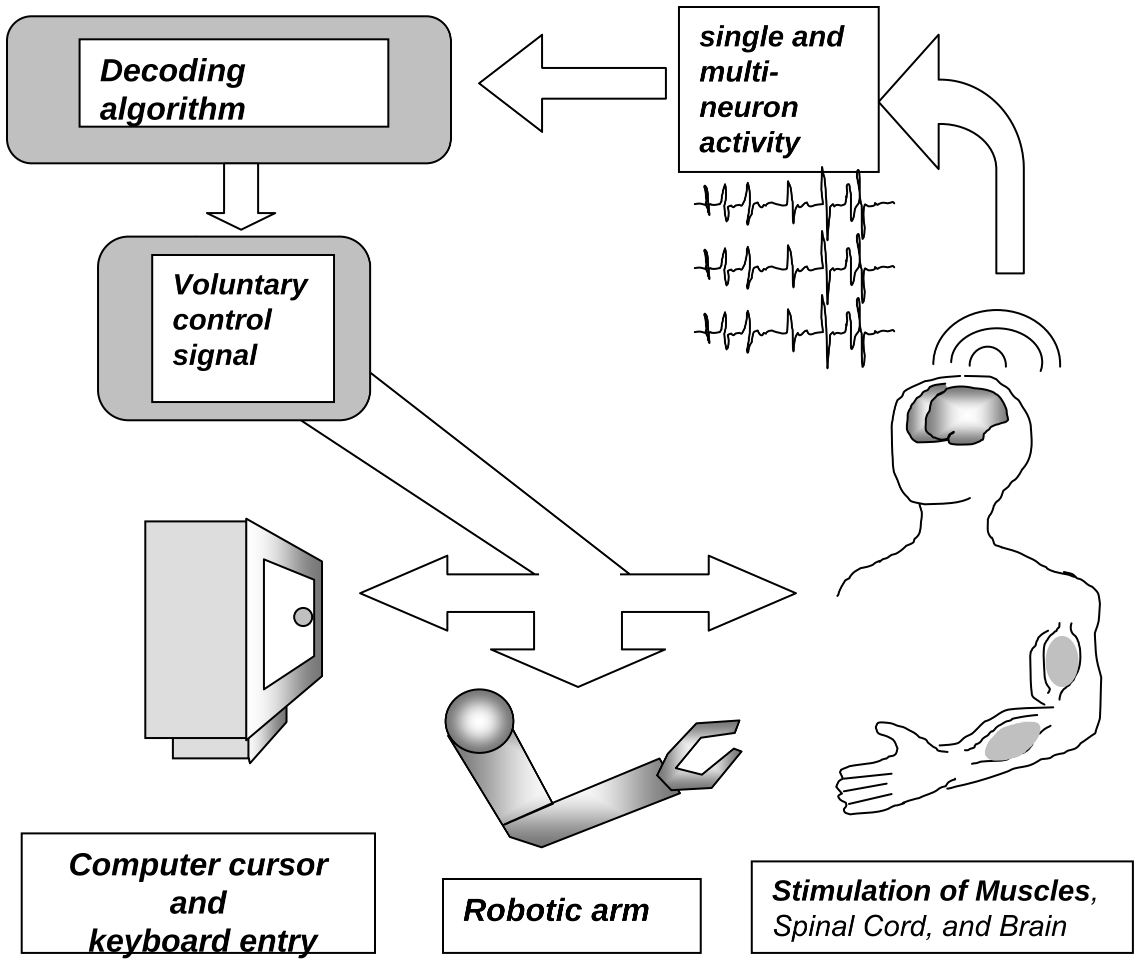
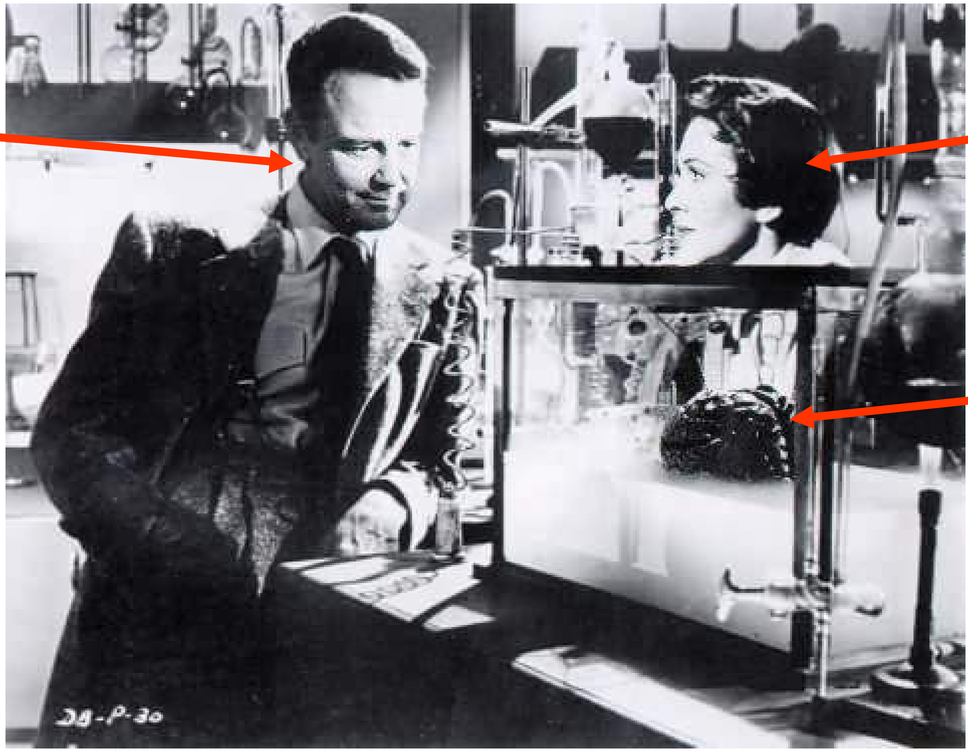


Source: Mijail Serruya

From Science Fiction to Practice

“Mad” scientist



Fun fact:
Nancy Davis
(Reagan)

Brain

*“If I could find … a **code** which **translates** the relation between the reading of the encephalograph and the mental image …the brain could **communicate** with me.”*

“Donovan’s Brain”, Curt Siodmak, 1942

Key Questions

1. **Measurement**: What can we measure? From where? How?

2. **Encoding**: How is information represented in the brain?

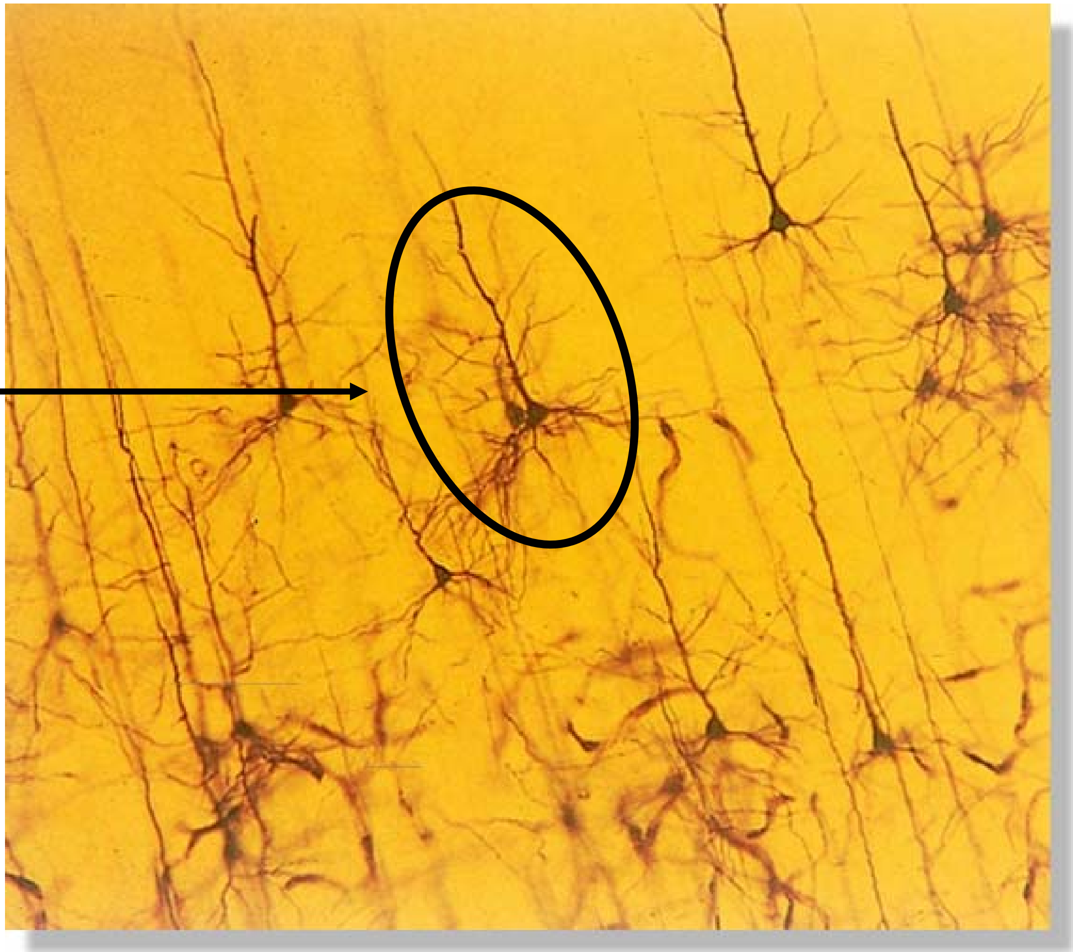
3. **Decoding**: What algorithms can we use to infer the internal "state" of the brain?

4. **Interface**: How can we build practical interfaces and train people to use them?

Computational Elements of the Brain

Single cells of the nervous system

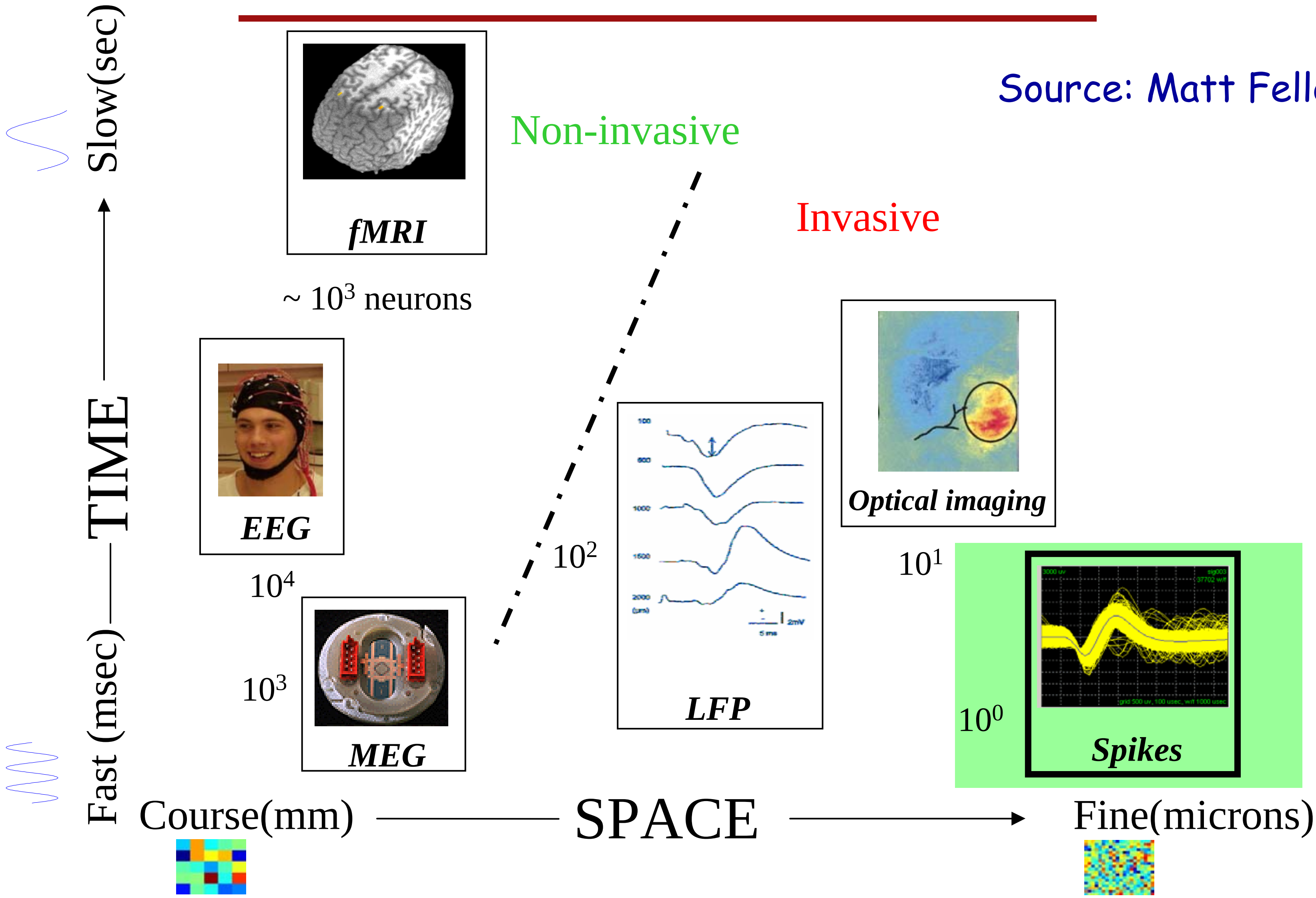
NEURON



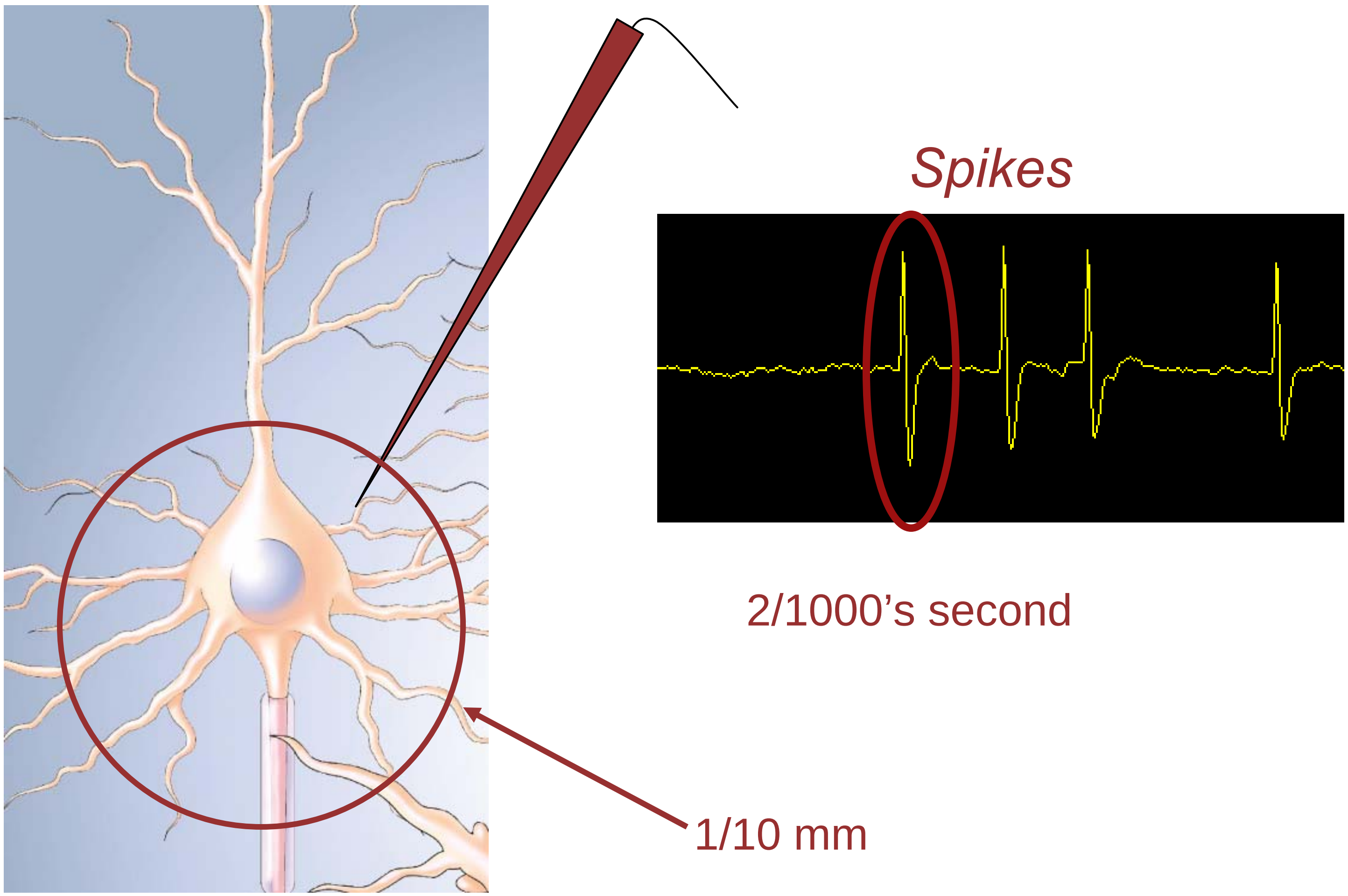
100,000,000,000 in your brain

Sensing the Brain

Source: Matt Fellows

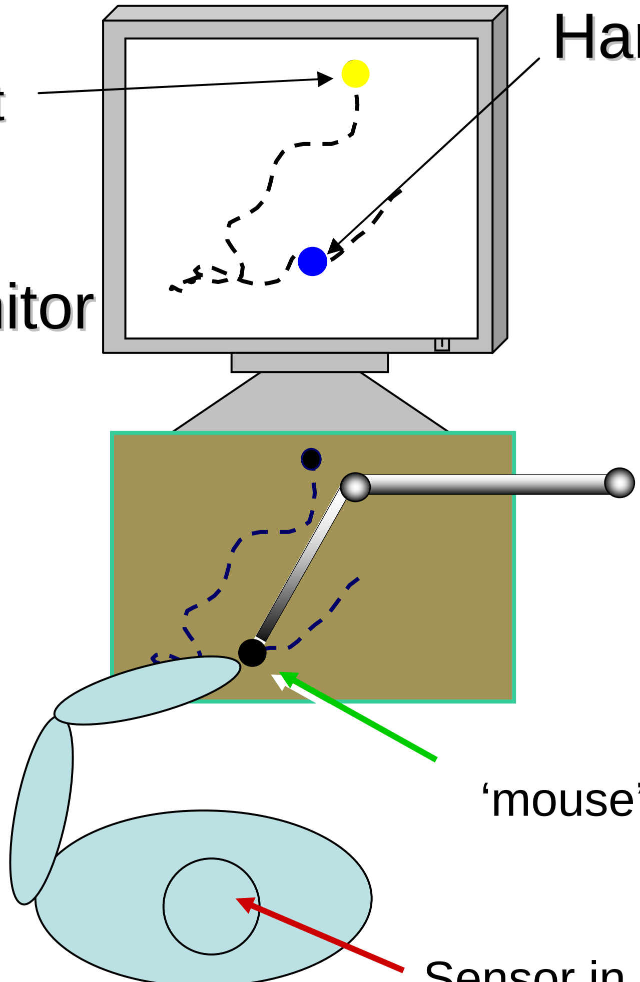


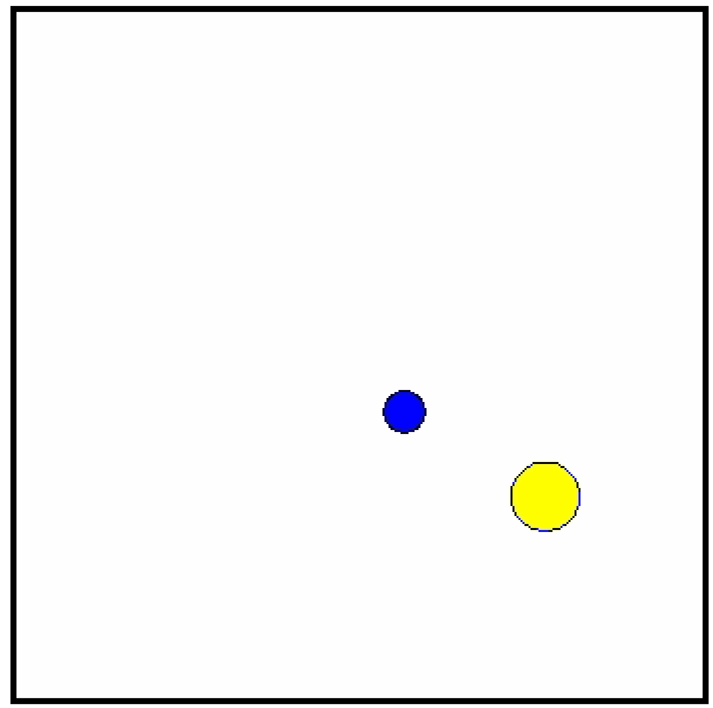
Computational Elements of the Brain



Source: David Sheinberg

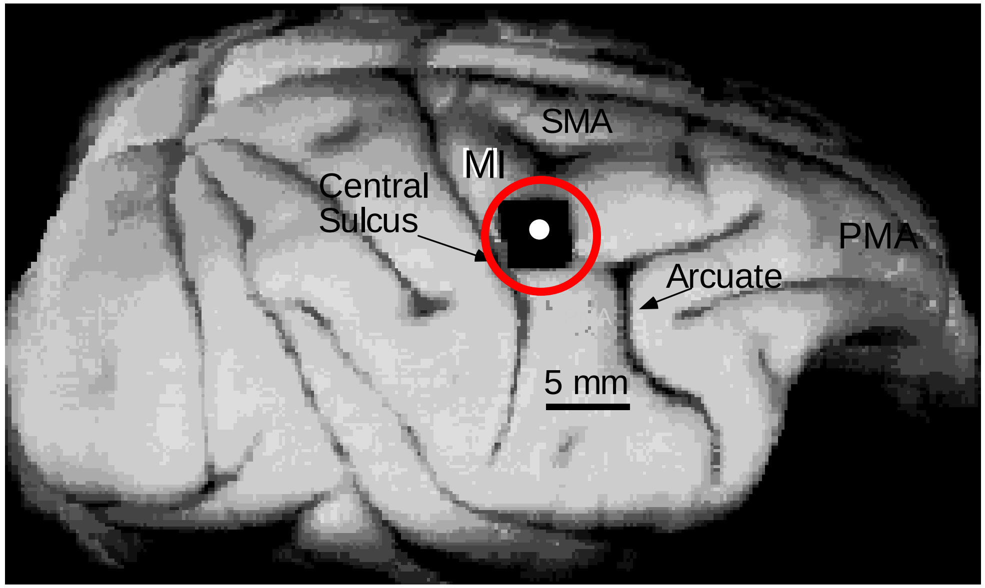
Behavior and Neural Firing





Motions are 2D, fast, continuous, and "natural".

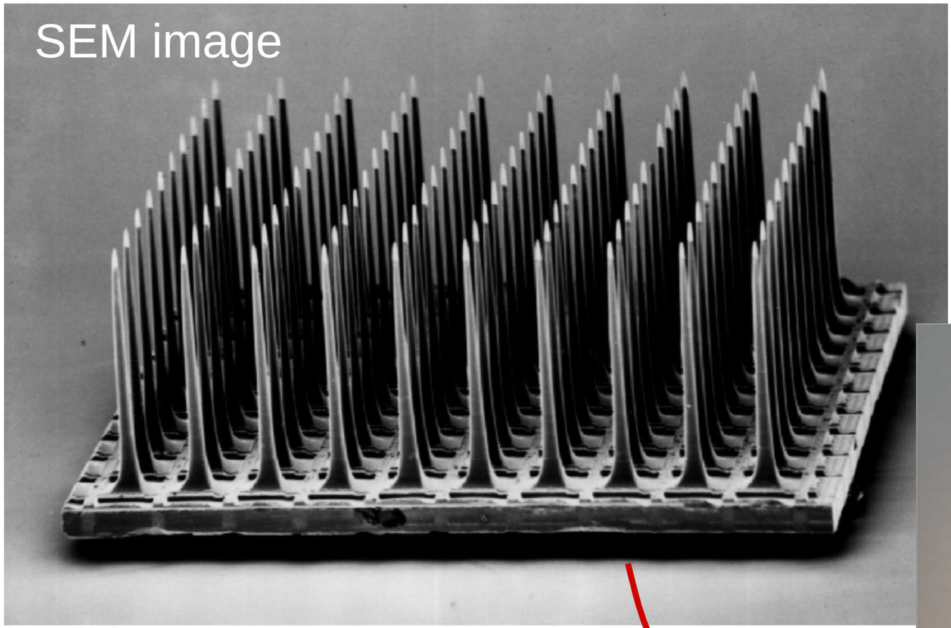
Implant Area

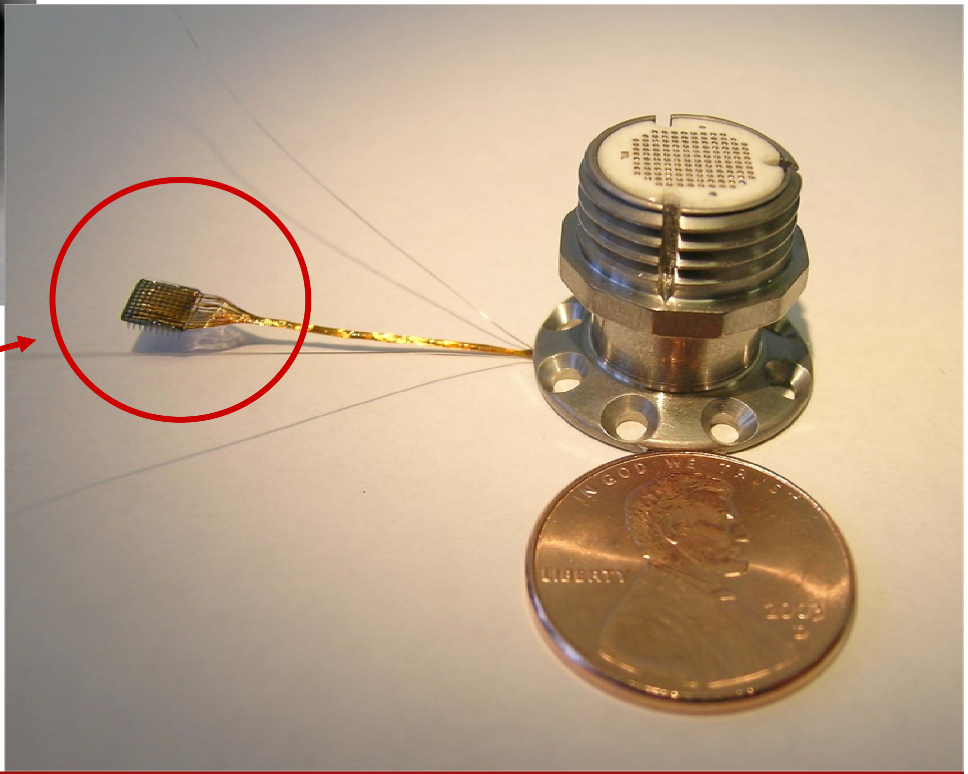


MI arm area of motor cortex.

* know that activity of cells related to hand motion
* accessible (in monkeys and humans)
* ***hypothesis***: natural for controlling continuous motion of a prosthesis

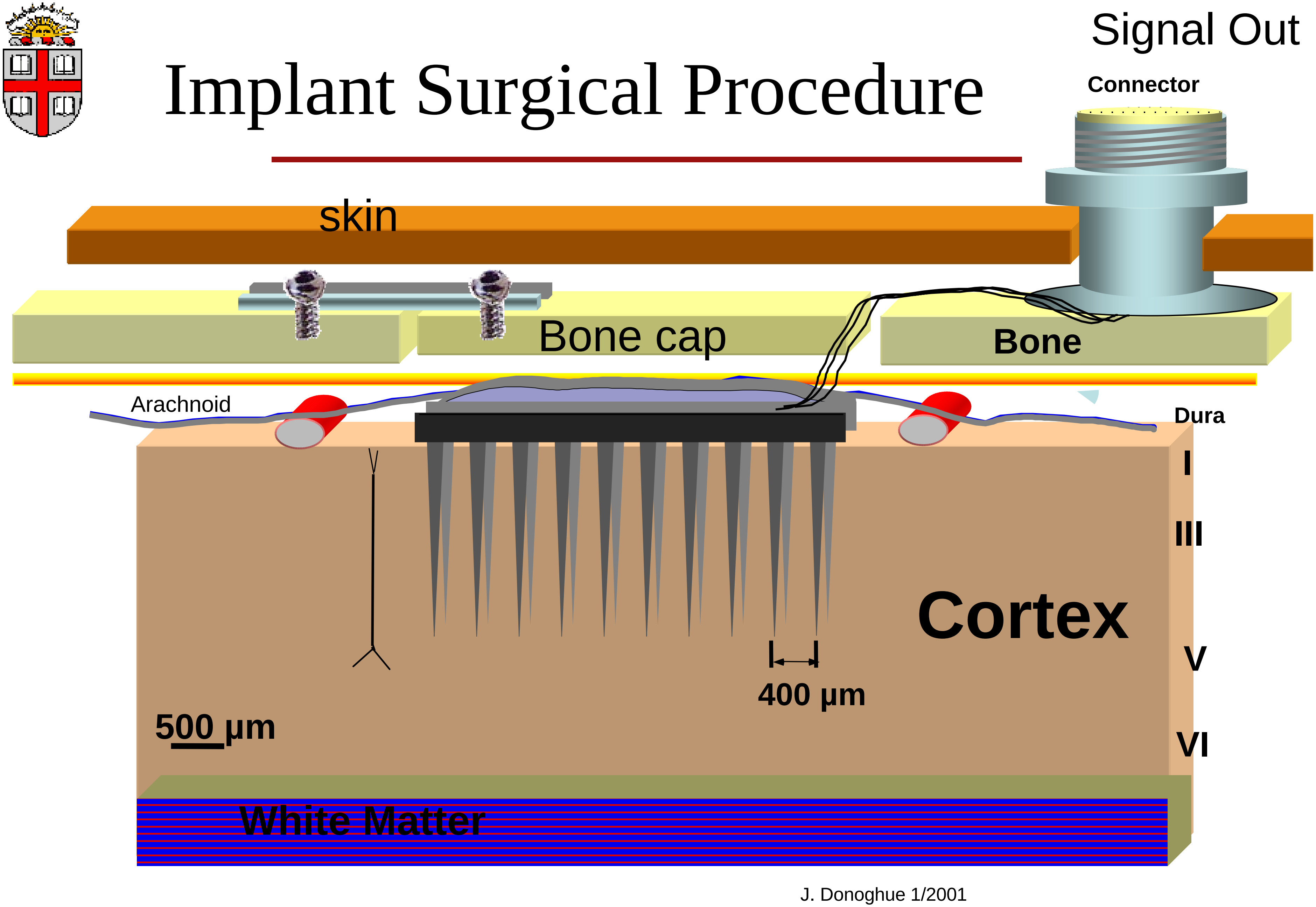
Cyberkinetics-Bionic Array

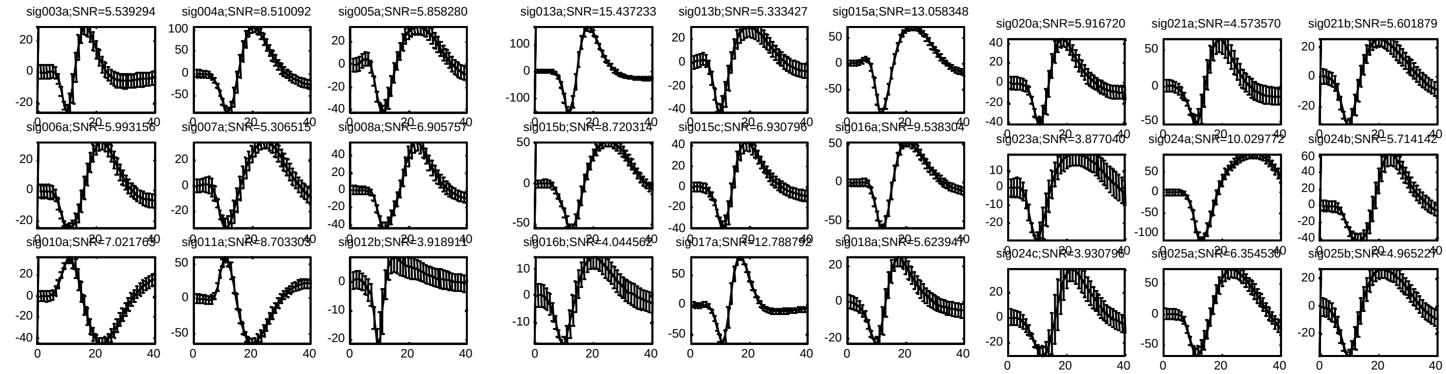


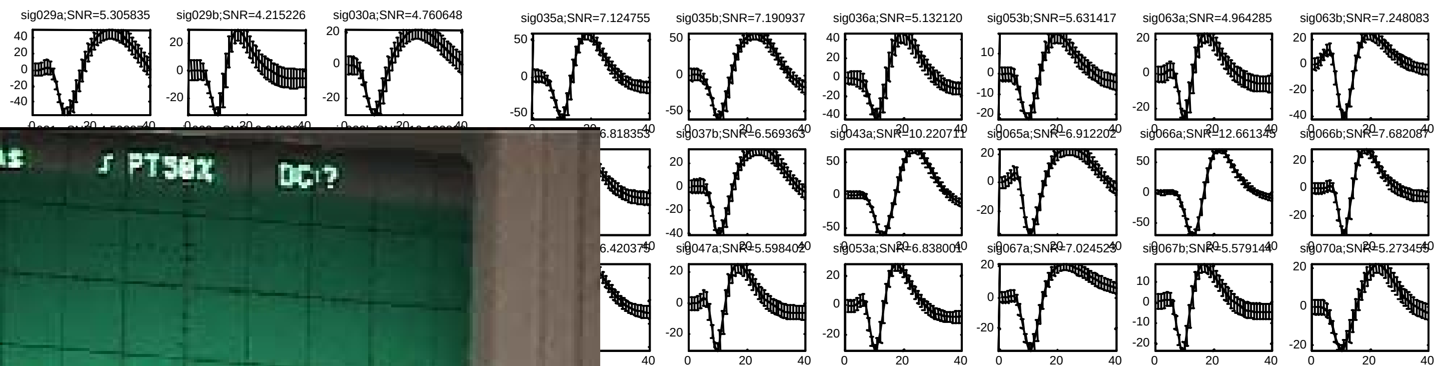


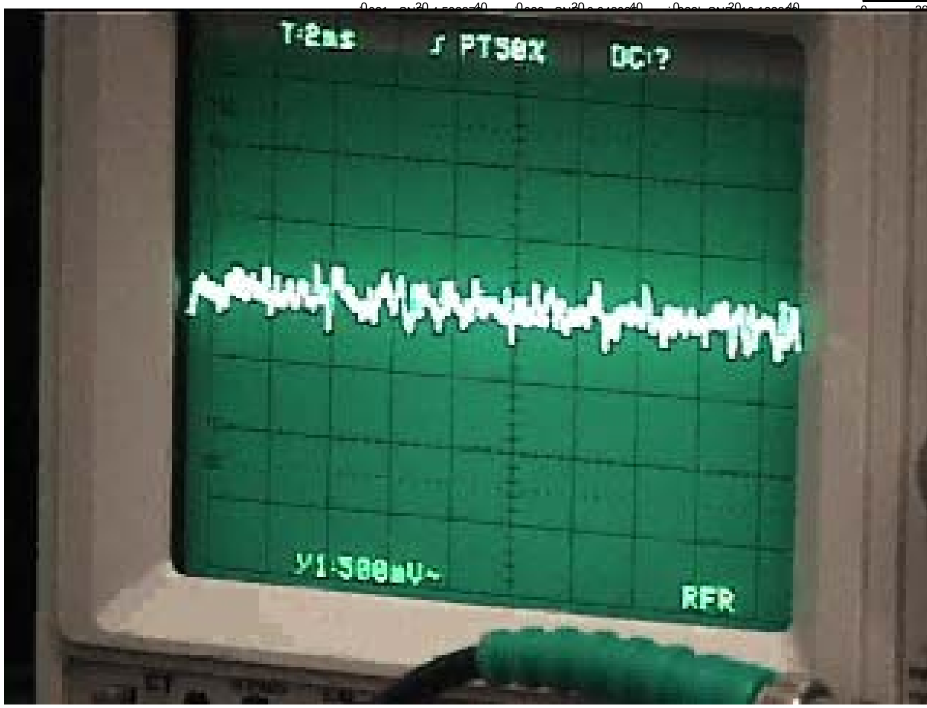
100 “ideal” microelectrodes
10x10 grid,
4x4 mm platform
1 or 1.5 mm long, Si shafts,
Pt coated tips
Glass separation
Parylene insulation coating

Implant Surgical Procedure



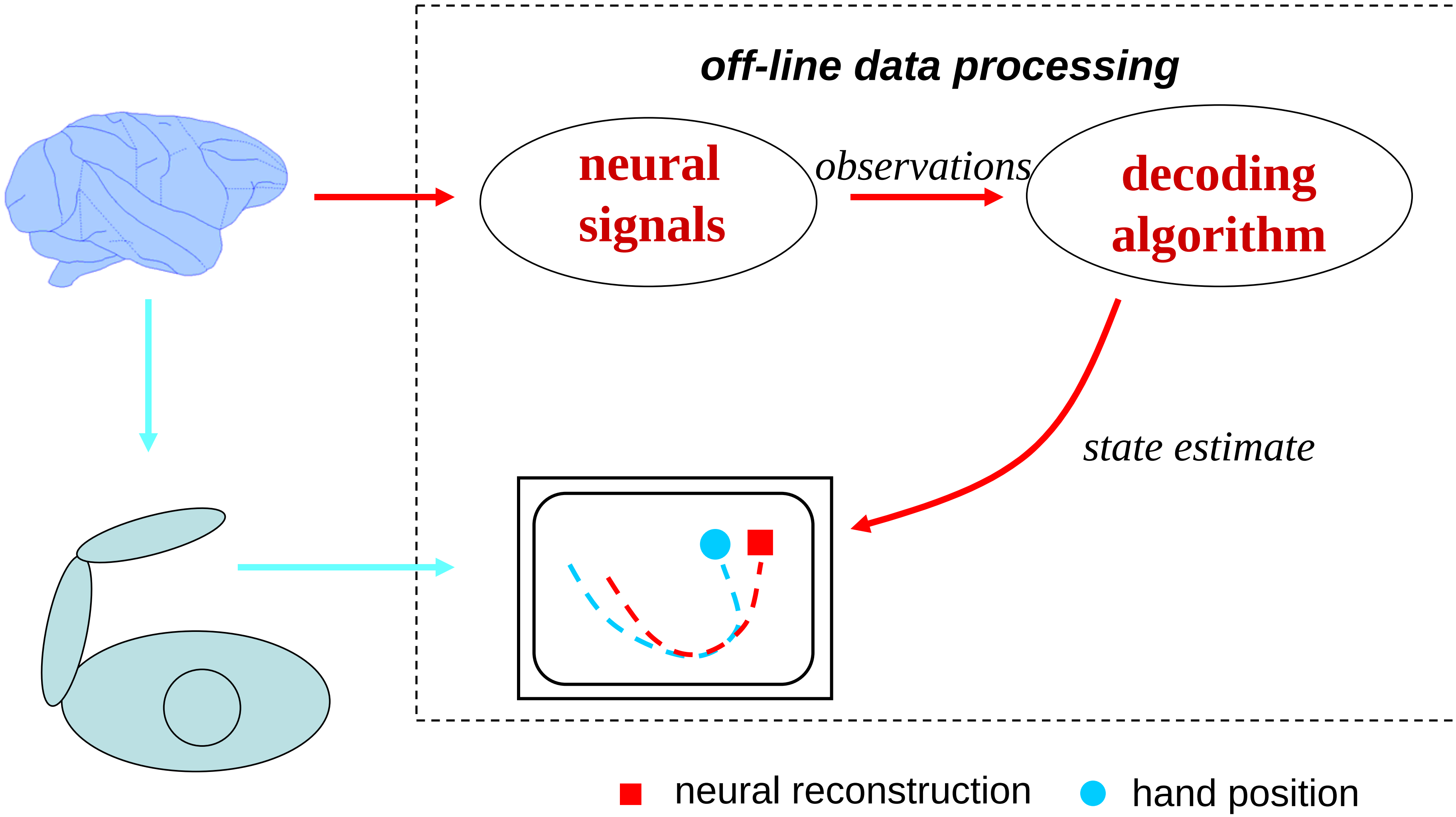






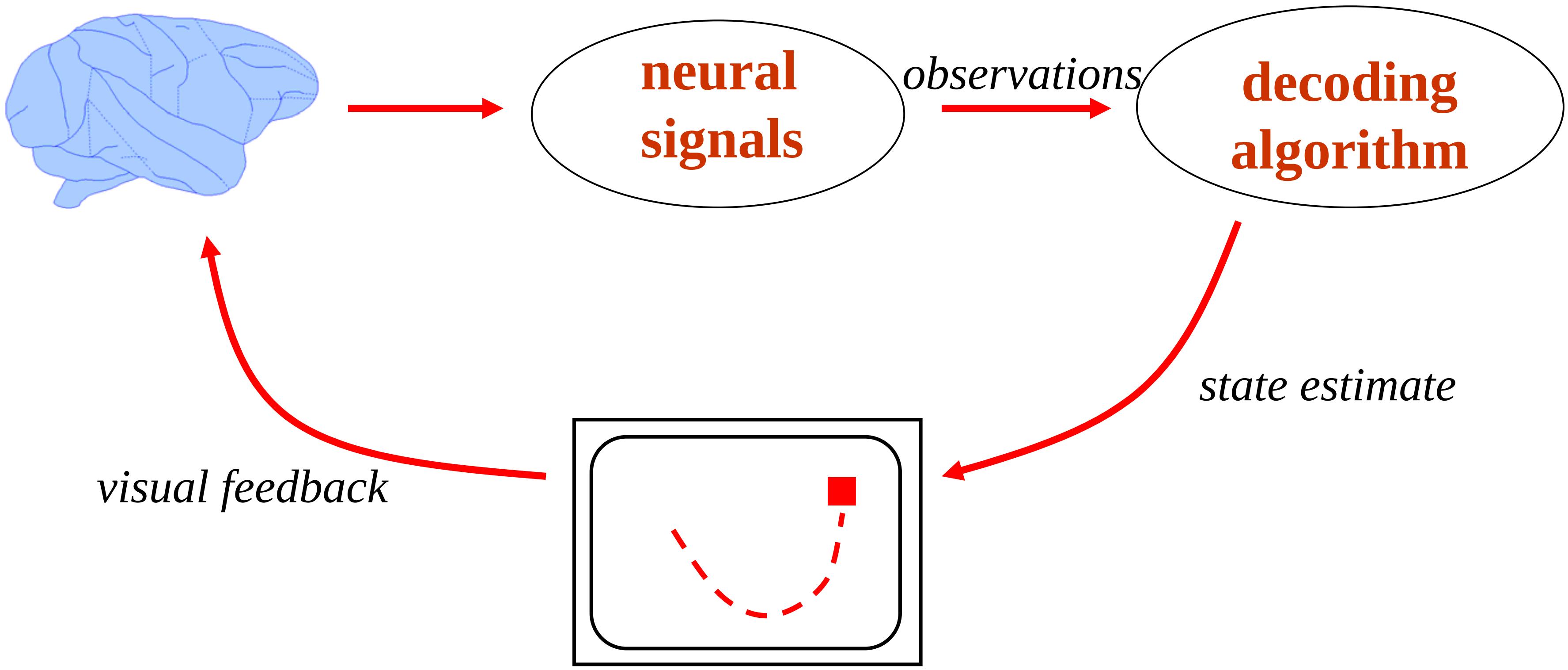
Recorded waveforms

Off-line Reconstruction



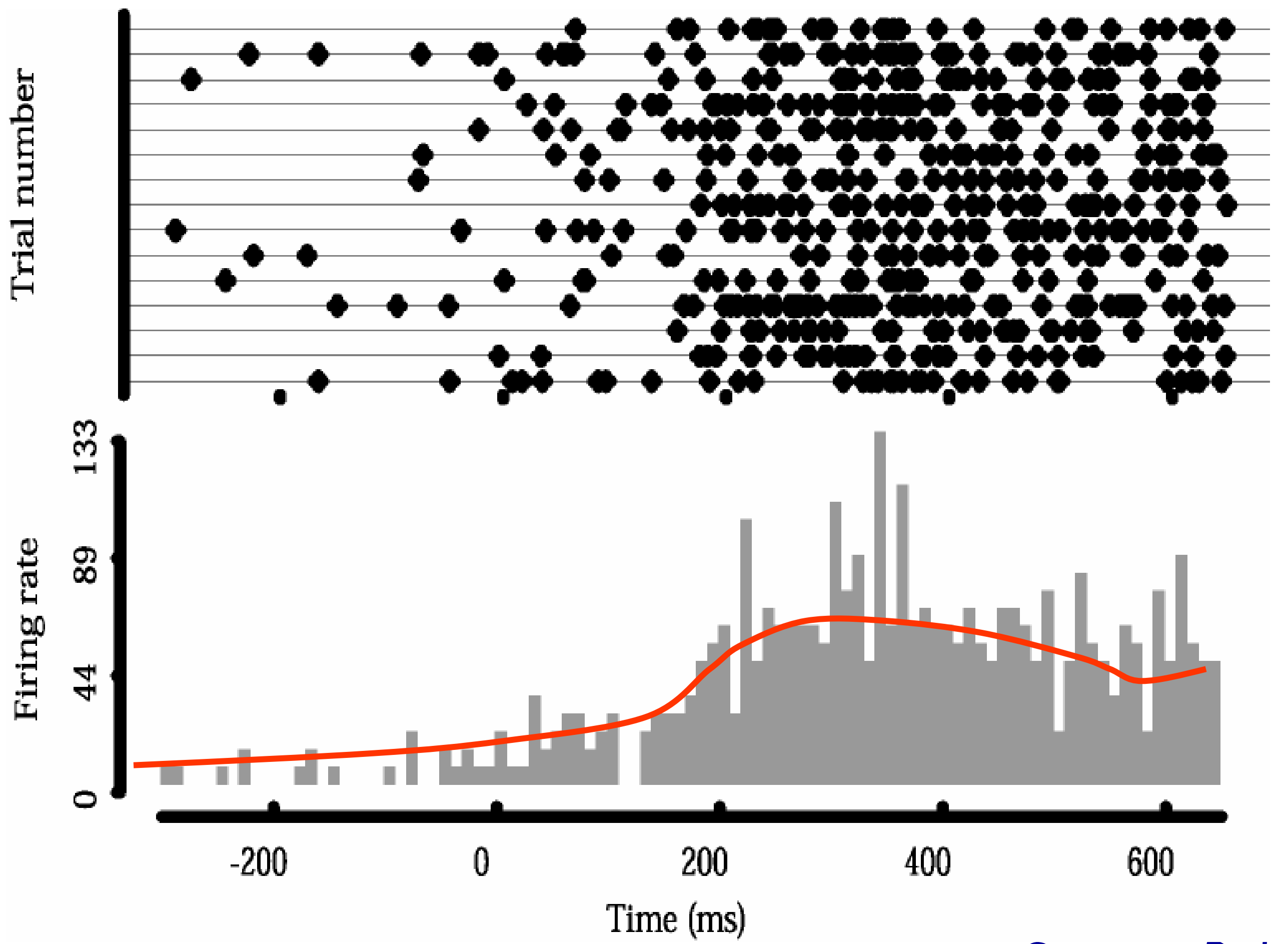
Closed-loop Neural Control

on-line direct neural control



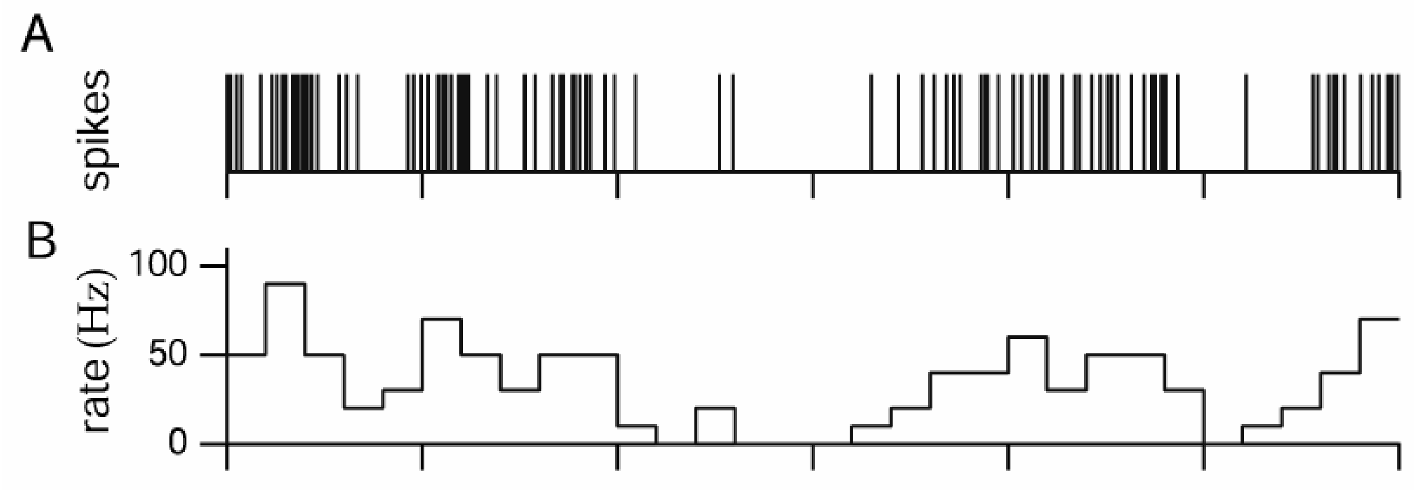
- Cursor under neural control

Cracking the Neural Code



Source: Rob Kass

Cracking the Neural Code



Source: Zemel & McNaughton, NIPS2000 tutorial

rate = (# of spikes in time bin) / (length of time bin)

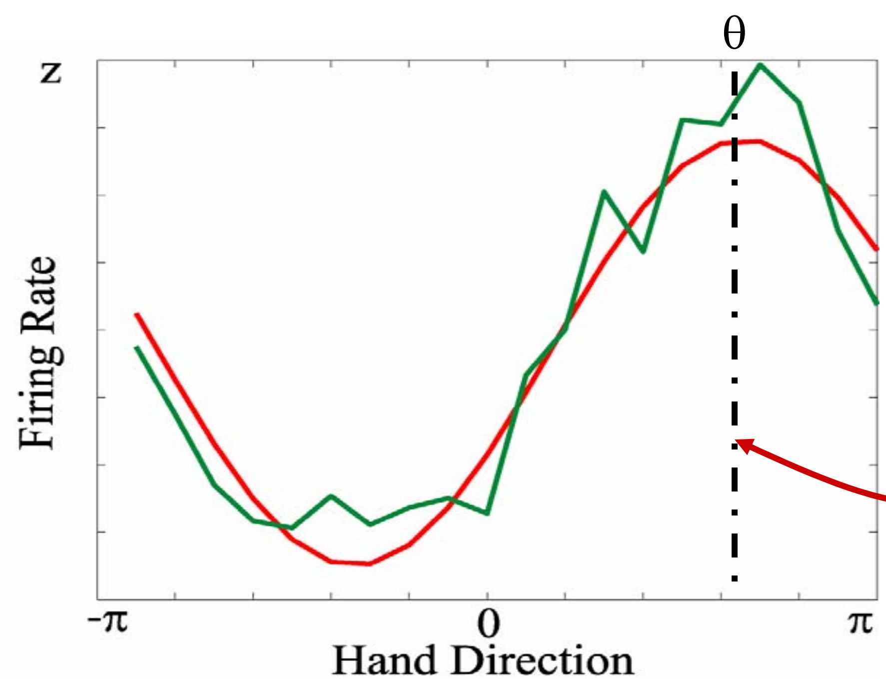
Related to the probability a cell will spike (fire) in a given time interval

Encoding

Georgopoulos et al ('82): (***cosine tuning*** of single cells)

$$z_k = h_0 + h\cos(\theta_k - \theta)$$
$$= h_0 + h_x \cos(\theta_k) + h_y \sin(\theta_k)$$

z_k = firing rate, θ_k = hand direction



Preferred direction θ

Encoding

Georgopoulos et al ('82): (***cosine tuning*** of single cells)

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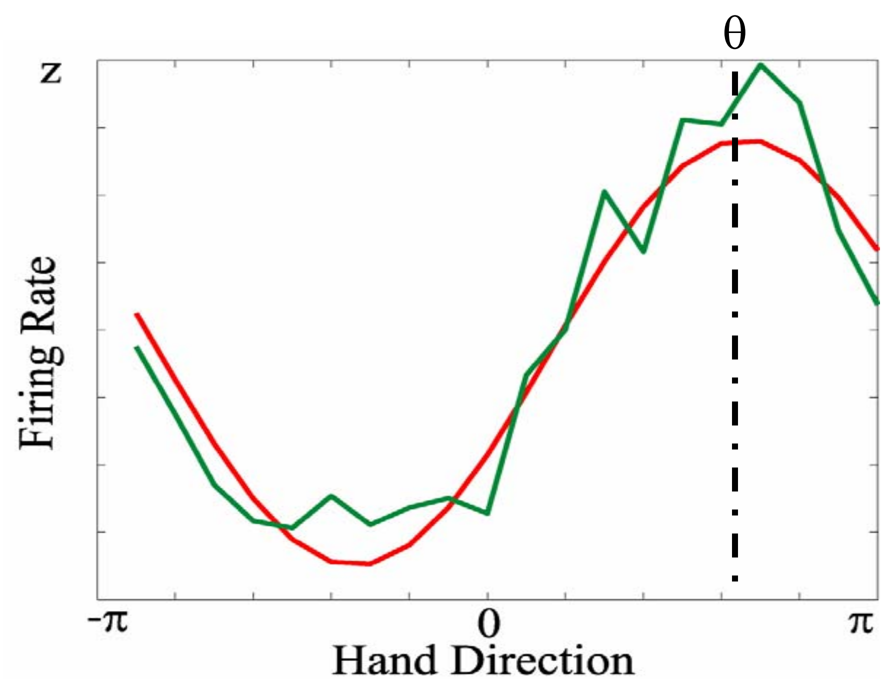


z_k = firing rate, θ_k = hand direction

Note that this is a *generative* model of neural firing:

$$z = f(\theta) + \text{noise}$$

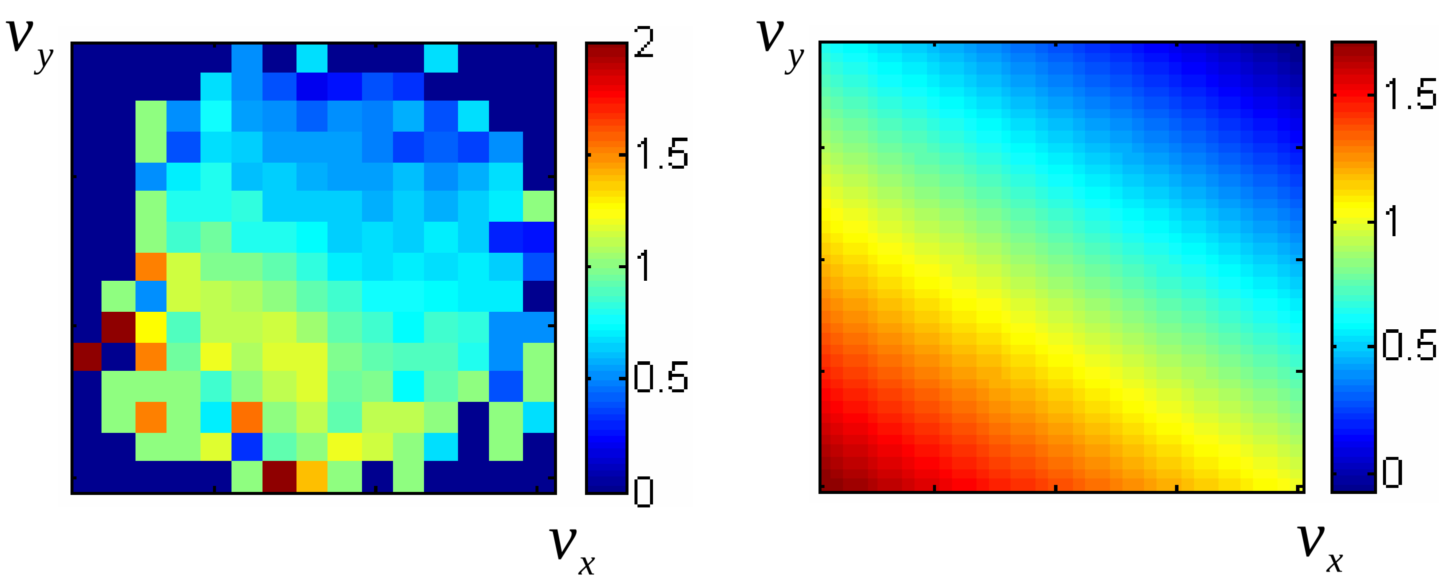
What should $f(.)$ be?

Encoding

Moran & Schwartz ('99):

$$z_k = h_0 + speed\,(h_x \cos(\theta_k) + h_y \sin(\theta_k))$$

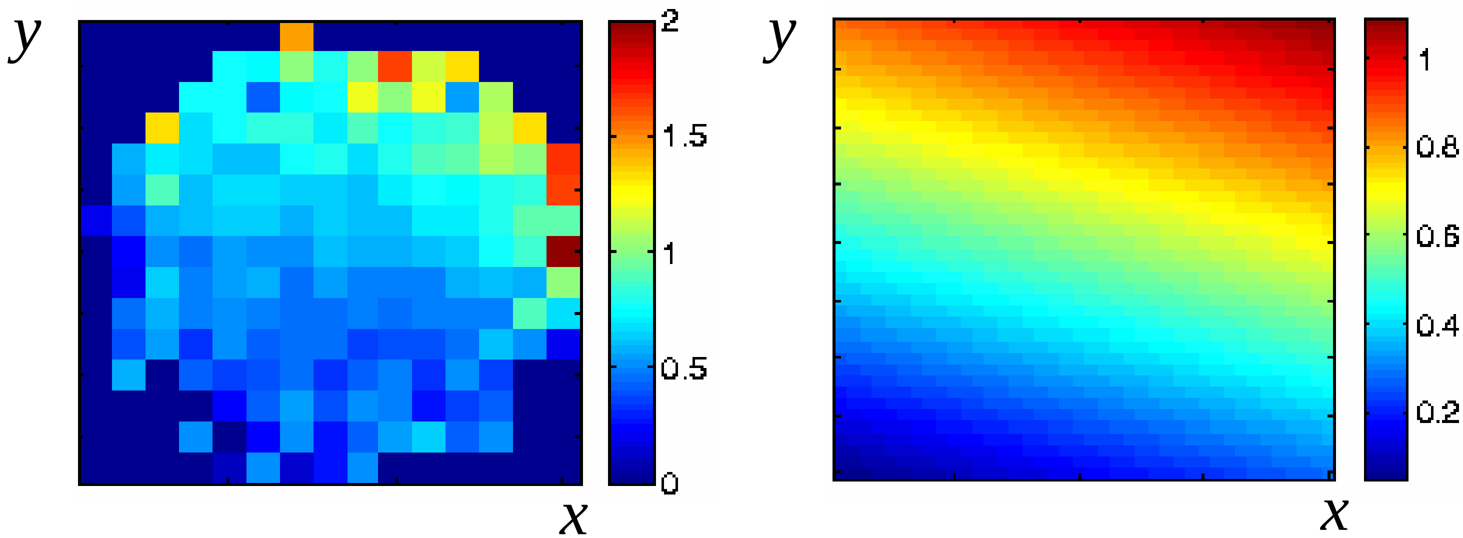
$$= h_0 + h_x v_{x_k} + h_y v_{y_k} \qquad \text{(\textit{Linear} in velocity)}$$



Encoding

Kettner et al ('88):

$$z_k = b_0 + b_x x_k + b_y y_k$$ (*Linear* in position)



Flament et al ('88): Firing rate is also related to hand acceleration

Encoding Summary

* Firing rate is approximately linearly related to position, velocity, acceleration (see Paninski et al. '04).
  - Decoding models should exploit this.

* Firing rates of cells are not statistically independent (need to model the correlations) (Hatsopoulos et al '98).

* Encoding models above don't model uncertainty in hand motion or neural firing rates.

Previous Decoding Algorithms

* **Population Vectors**

  Georgopoulos et al. (1986), Moran & Schwartz (1999), Taylor et al. (2002)

* **Linear Regression Methods**

  Wessberg et al.(2000), Serruya et al. (2002), Carmena et al. (2003)

* **Artificial Neural Networks**

  Wessberg et al.(2000)

* **Bayesian Inference (e.g. particle filter)**

  Gao et al. (2002), Brockwell et al. (2004), Wu et al. (EMBS'04)

Decoding Methods

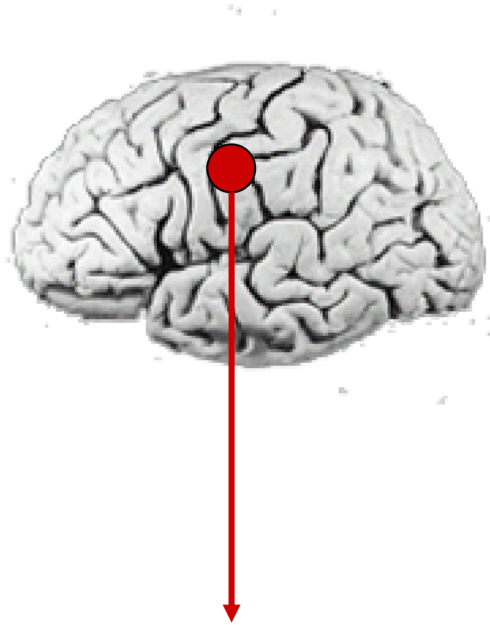
Direct decoding methods:

$$\vec{x}_k = f(\vec{z}_k, \vec{z}_{k-1}, \ldots)$$

In contrast to generative encoding models:

$$\vec{z}_k = f(\vec{x}_k)$$

Need a sound way to exploit generative models for decoding.

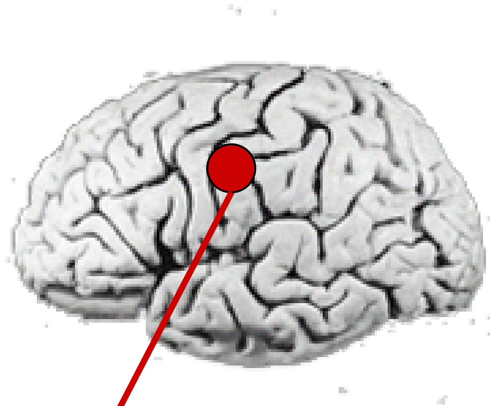


Bayesian Inference.

$$p(\text{kinematics}_t \mid \text{history of firing rates}_{t\text{-}j})$$

$$= k \; \underbrace{p(\text{firing rates}_{t\text{-}j} \mid \text{kinematics}_t)}_{\text{likelihood}} \; \underbrace{p(\text{kinematics}_t)}_{\text{prior}}$$

Hand kinematics



Approach:

probabilistic formulation, model uncertainty

$$p(\vec{x}_t \mid \vec{Z}_{t-j}) = p(\vec{x}_t \mid \vec{z}_{t-j}, \ldots, \vec{z}_1)$$

lag

$$\begin{pmatrix} x_t \\ y_t \\ v_{x_t} \\ v_{y_t} \\ a_{x_t} \\ a_{y_t} \end{pmatrix}$$

system state vector (zero mean) at time *t*

$$\begin{pmatrix} z_{t-j}^{(1)} \\ z_{t-j}^{(2)} \\ \vdots \\ z_{t-j}^{(n)} \end{pmatrix}$$

firing rate vector (zero mean, sqrt)

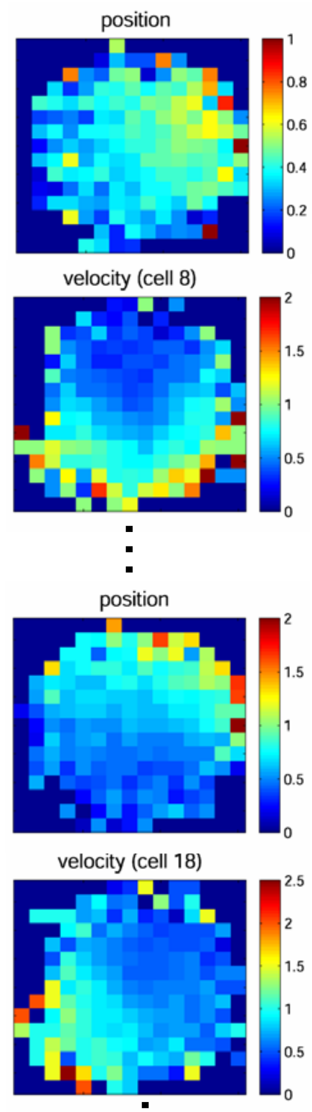
Learn rich probabilistic models of the encoding

Bayesian approach.

$$p(\vec{x}_t \mid \vec{Z}_{t-j})$$

$$= \kappa \underbrace{p(\vec{z}_{t-j} \mid \vec{x}_t)}_{\text{likelihood}} \underbrace{p(\vec{x}_t \mid \vec{Z}_{t-j-1})}_{\text{prior}}$$

$$p(\vec{x}_t \mid \vec{Z}_{t-j-1}) = \int \underbrace{p(\vec{x}_t \mid \vec{x}_{t-1})}_{\text{temporal prior}} \underbrace{p(\vec{x}_{t-1} \mid \vec{Z}_{t-j-1})}_{\text{posterior at } t\text{-}1} d\vec{x}_{t-1}$$



"cell 8"

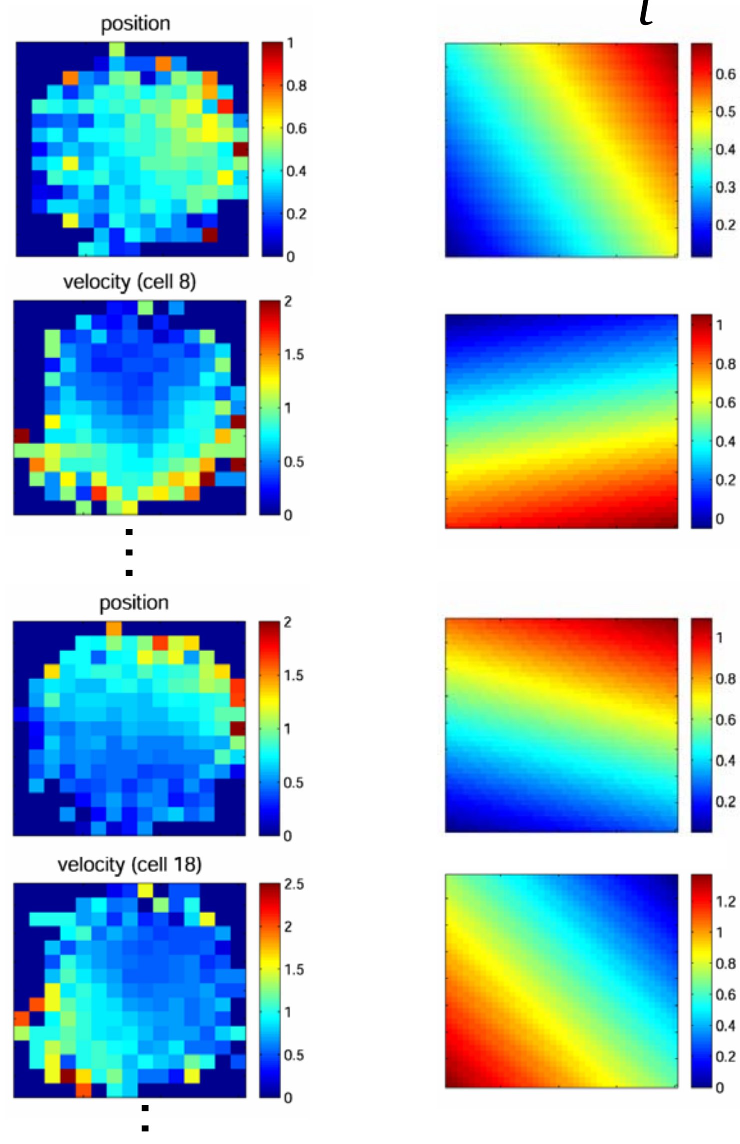
"cell 18"

empirical "marginal" **rate** functions for

* position,
* velocity,
* etc.

Approximation: Linear Gaussian (generative) model

$H\ \vec{x}_t$



observation model

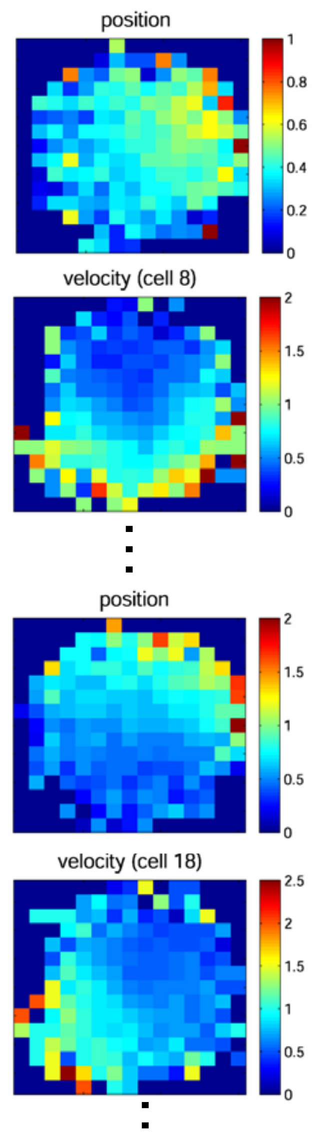
$$\vec{z}_{t-j} \sim \mathcal{N}(H\ \vec{x}_t,\ Q_t)$$

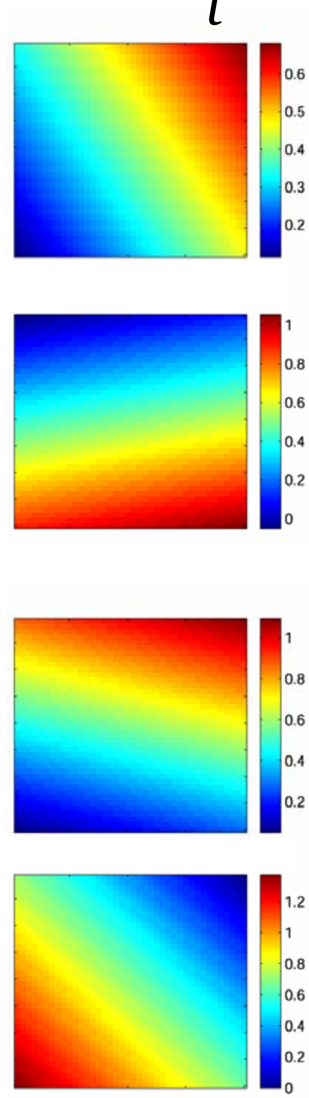
Full covariance Q matrix models correlations between cells.

H models how firing rates relate to full kinematic model (position, velocity, and acceleration).

$$H \; \vec{x}_t$$

Approximation: Linear Gaussian (generative) model





likelihood

$$p(\vec{z}_t \mid \vec{x}_t) =$$

$$\frac{1}{D}\exp\left(\tfrac{-1}{2}(\vec{z}_t - H\vec{x}_t)^{\mathrm{T}} Q_t^{-1}(\vec{z}_t - H\vec{x}_t)\right)$$

Kalman Filter

Likelihood

$$p(\vec{z}_{t-j} \,|\, \vec{x}_t) \longrightarrow$$

observation model:

$$\vec{z}_t \sim \mathcal{N}(H_t\, \vec{x}_t,\, Q_t)$$

Temporal prior

$$p(\vec{x}_t | \vec{x}_{t-1}) \longrightarrow$$

system model:

$$\vec{x}_t \sim \mathcal{N}(A_t \vec{x}_{t-1}, W_t)$$

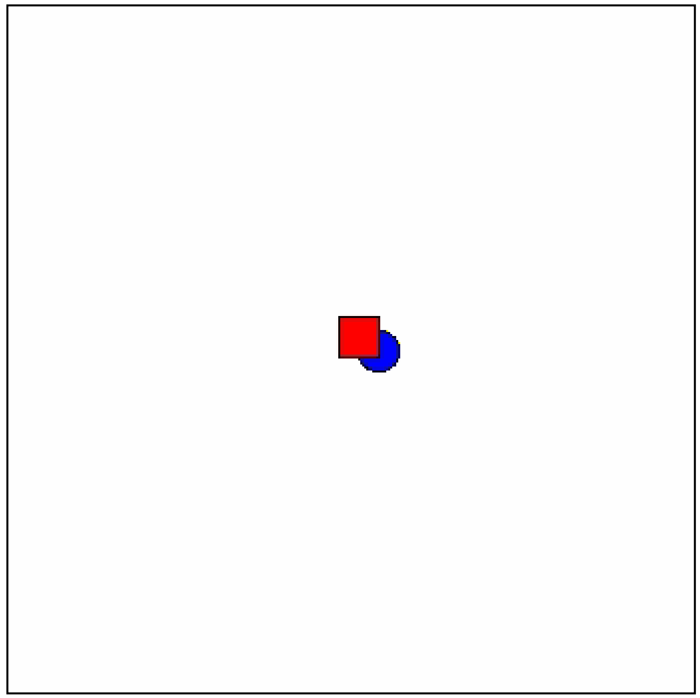
Posterior is also Gaussian

$$p(\vec{x}_t \,|\, \vec{Z}_t) = \kappa\, p(\vec{z}_t \,|\, \vec{x}_t) \int p(\vec{x}_t | \vec{x}_{t-1})\, p(\vec{x}_{t-1} \,|\, \vec{Z}_{t-1})\, d\vec{x}_{t-1}$$

Kalman filter.

Real-time, recursive, decoding.

Off-line Reconstruction



69 cells with
1.5 minutes of
training data

Actual hand position

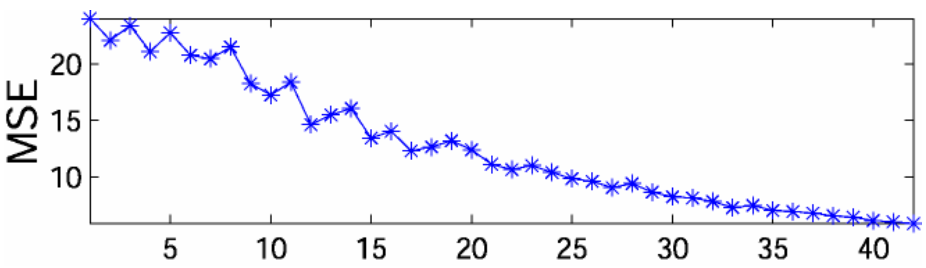
Estimated/decoded position (reconstruction)

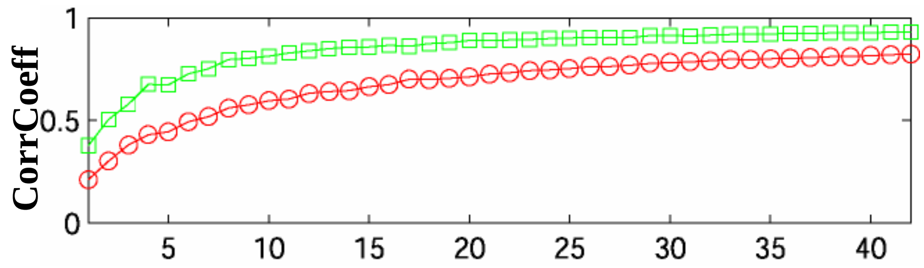
Accuracy

Continuous 2D hand motion (off-line reconstruction):

Method	MSE (cm^2)
Population vector	75.0
Linear regression method	6.48
Kalman filter	4.75

As number of cells increases:





Mixture Model Likelihood

$$p(\vec{z}_{k-j} \mid \vec{x}_k) = \sum_{i=1}^{N} p(S_t = i)\, p(\vec{z}_{k-j} \mid \vec{x}_k, S_t = i)$$

$$p(\vec{z}_{k-j} \mid \vec{x}_k, S_t = i) = G(H_i\, \vec{x}_k, Q_i)$$

- Model non-Gaussian probability.
- Training using EM algorithm.
- Decoding using Switching Kalman filter.
- Real-time decoding.

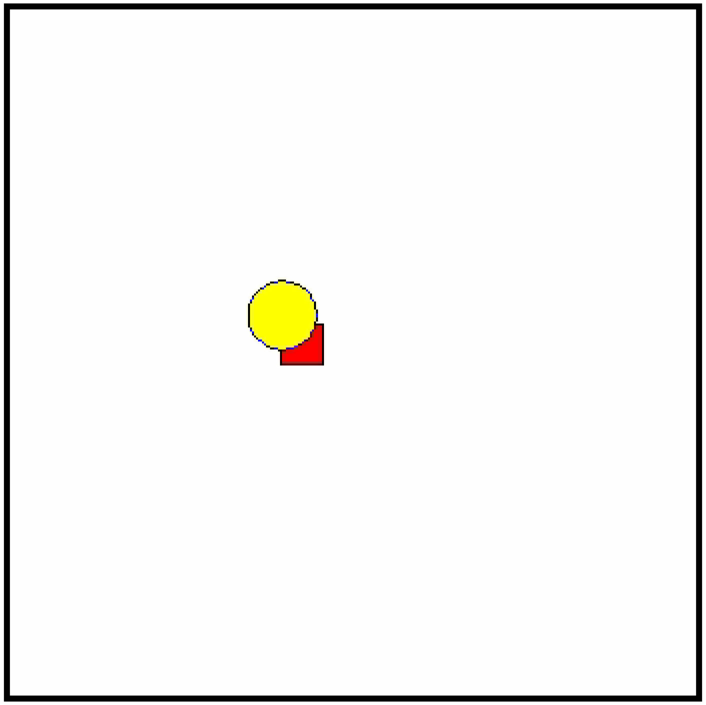
MSE: Kalman = 5.87 cm^2

Switching Kalman = 5.39 cm^2

On-line Neural Control

Neural control of a computer cursor in real time.

Brain substitutes for hand.



Kalman filter decoder.
Only 18 cells.

Directly exploits the generative encoding model.

Target

Visual feedback

On-line Task Performance

# of cells	Kalman filter			Linear regression		
	time	targets	rate	time	targets	rate
17	60*sec*	38	**38/*min***			
30	105*sec*	55	**31/*min***	58*sec*	24	**25/*min***
36	57*sec*	28	**29/*min***	42*sec*	15	**21/*min***
69	45*sec*	28	**37/*min***	60*sec*	22	**22/*min***

Average results: 50% improvement

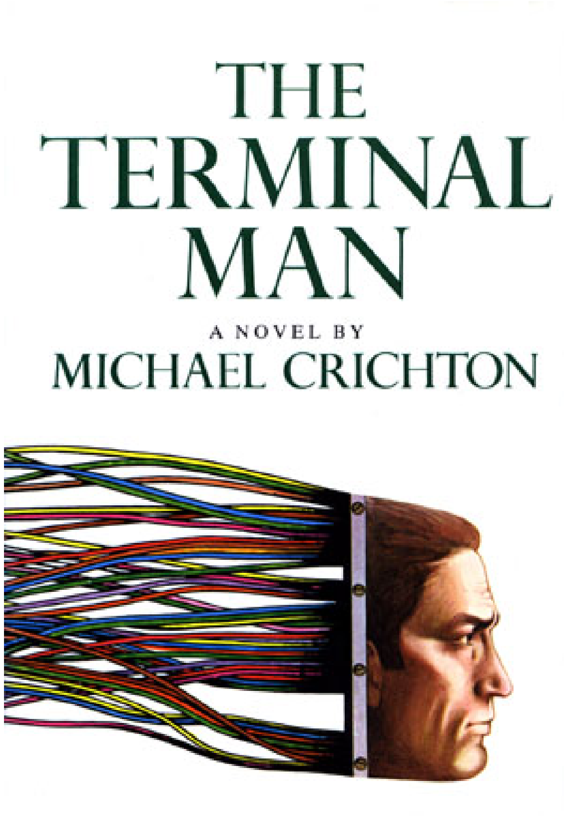
Kalman filter 33.75 targets/min

Linear regression 22.67 targets/min

Human Neural Prostheses

"One might think of the computer in this case as a prosthetic device. Just as a man who has his arm amputated can receive a mechanical equivalent of the lost arm, so a brain-damaged man can receive a mechanical aid to overcome the effects of brain damage. … It makes the computer a high-class wooden leg."

Michael Crichton,
The Terminal Man, 1972

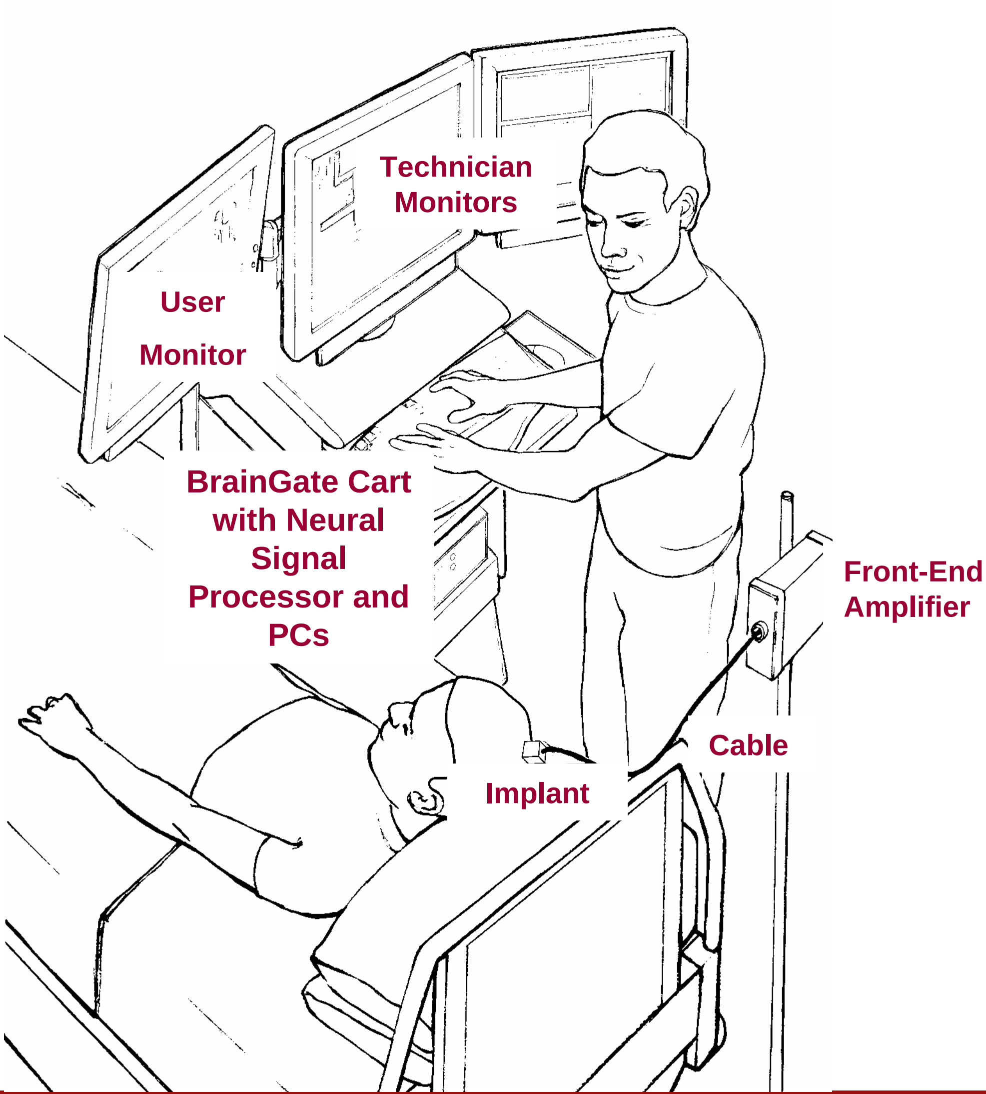


Humans?

- Implanted Electrodes
  - + Good biocompatibility.
  - + No motor impairment.
  - + Can be explanted.
  - + Can be re-implanted.
  - + Effective control signals in animal models.

  - \- Invasive (benefits must outweigh risks of surgery).
  - \- Limited to accessible regions.
  - \- Requires a percutaneous connector.
  - \- Bulky signal processing hardware.

Human Neural Prostheses



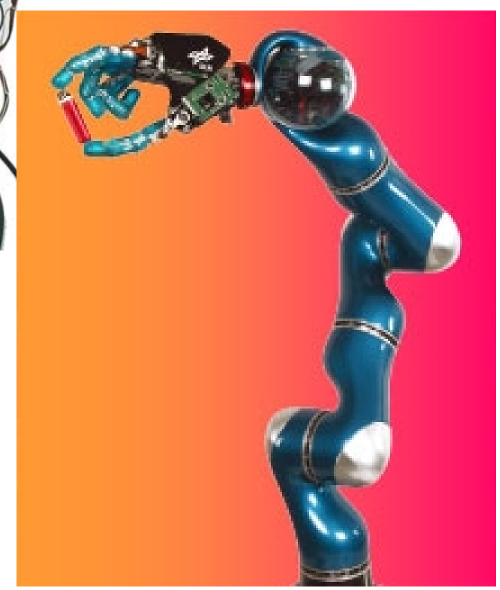
FDA approval granted.

Clinical trials ongoing.

(Unanswered) Questions at the Interface

* training paralyzed subjects
* controlling "unnatural" devices
  • cursors
  • robotic arms, hands.
  • mobile robots
* controlling multiple devices
  • switching contexts
  • adaptation
* Where should the computation take place (brain or computer)?
* What level of autonomous control/perception is needed?

DLR hand and arm.



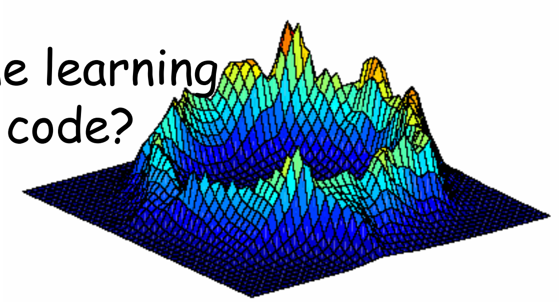
Current Directions

* Adaptive control algorithms
  - Adaptive Kalman filter

* Studying neural adaptation
  - Do the statistical properties of the cells adapt to more closely fit the model assumptions?

* Multi-modal control
  - Will the population of cells maintain multiple distinct representations? Will distinct sub-populations emerge for the different tasks?

* Modeling joint probability $p(\vec{x}_t, \vec{z}_t)$
  - Non-Gaussian, non-linear high-dimensional; machine learning
  - Can we "mine" the joint to understand the neural code?
  - What should $\vec{x}$ be? What should $\vec{z}$ be?



Conclusions

We are on the verge of having *biologically-embedded* hybrid neural-computer systems.

We have demonstrated continuous 2D cursor control and limited robotic control.

The work opens opportunities to study

* basic problems in machine learning and inference
* how the brain represents and processes information
* computational models of biological control
* novel hybrid control systems
* new robotic systems and prostheses

First applications will be for the severely disabled. Promises new model for treating disease and injury of the CNS.

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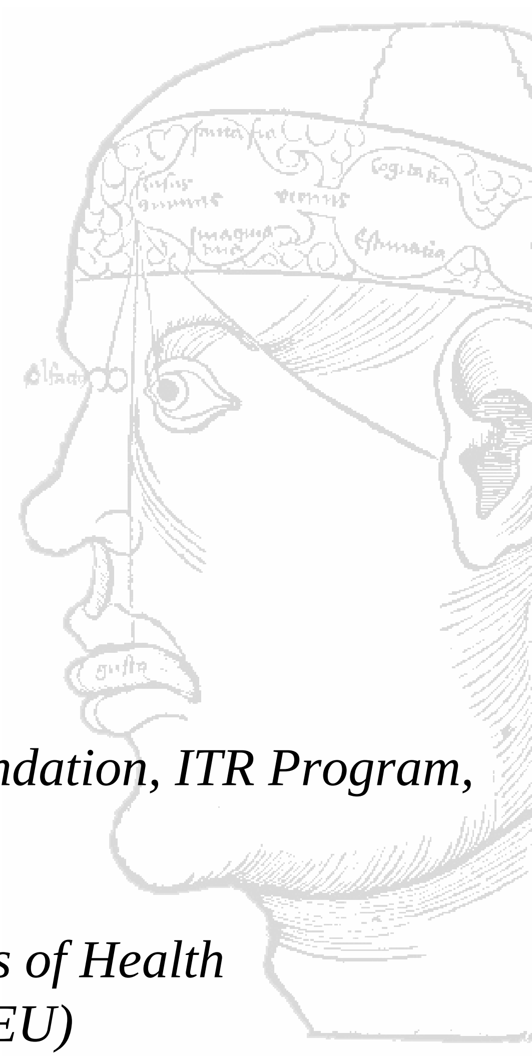
A. Nurmikko, *Brown Engineering*
G. Friehs, *Brown Medical School*
L. Paninski, *NYU, Center for Neural Science*
S. Shoham, *Princeton*
Cyberkinetics Inc.



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