CONNECTING BRAINS WITH MACHINES

The Neural of 2D Cursor Motion

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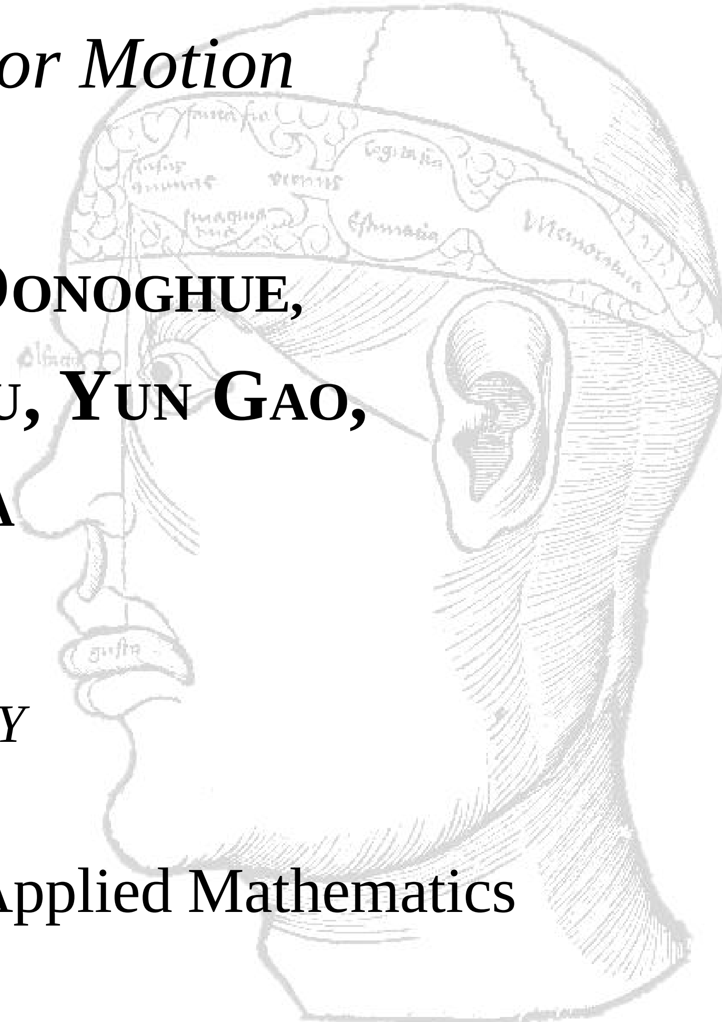
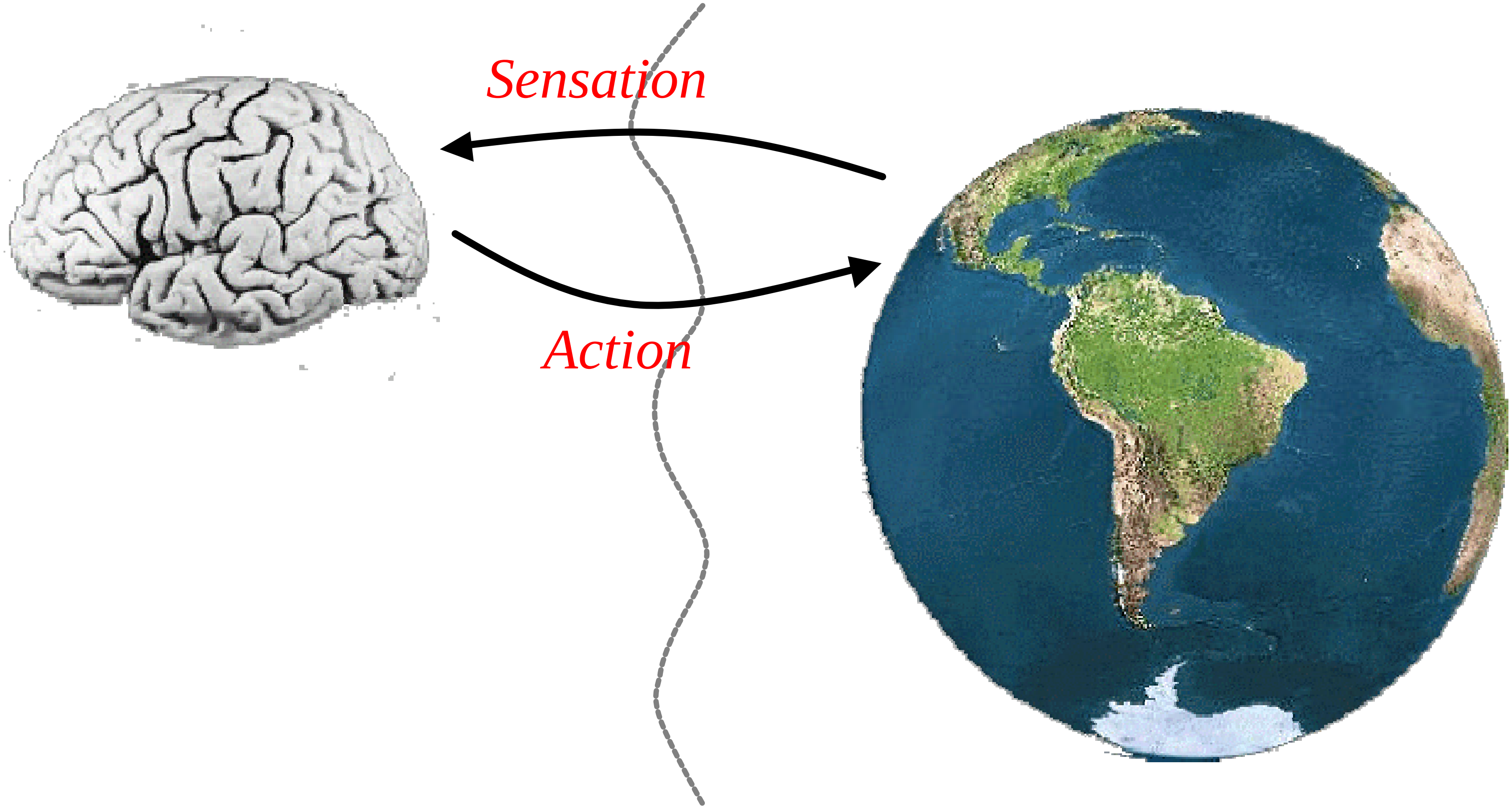
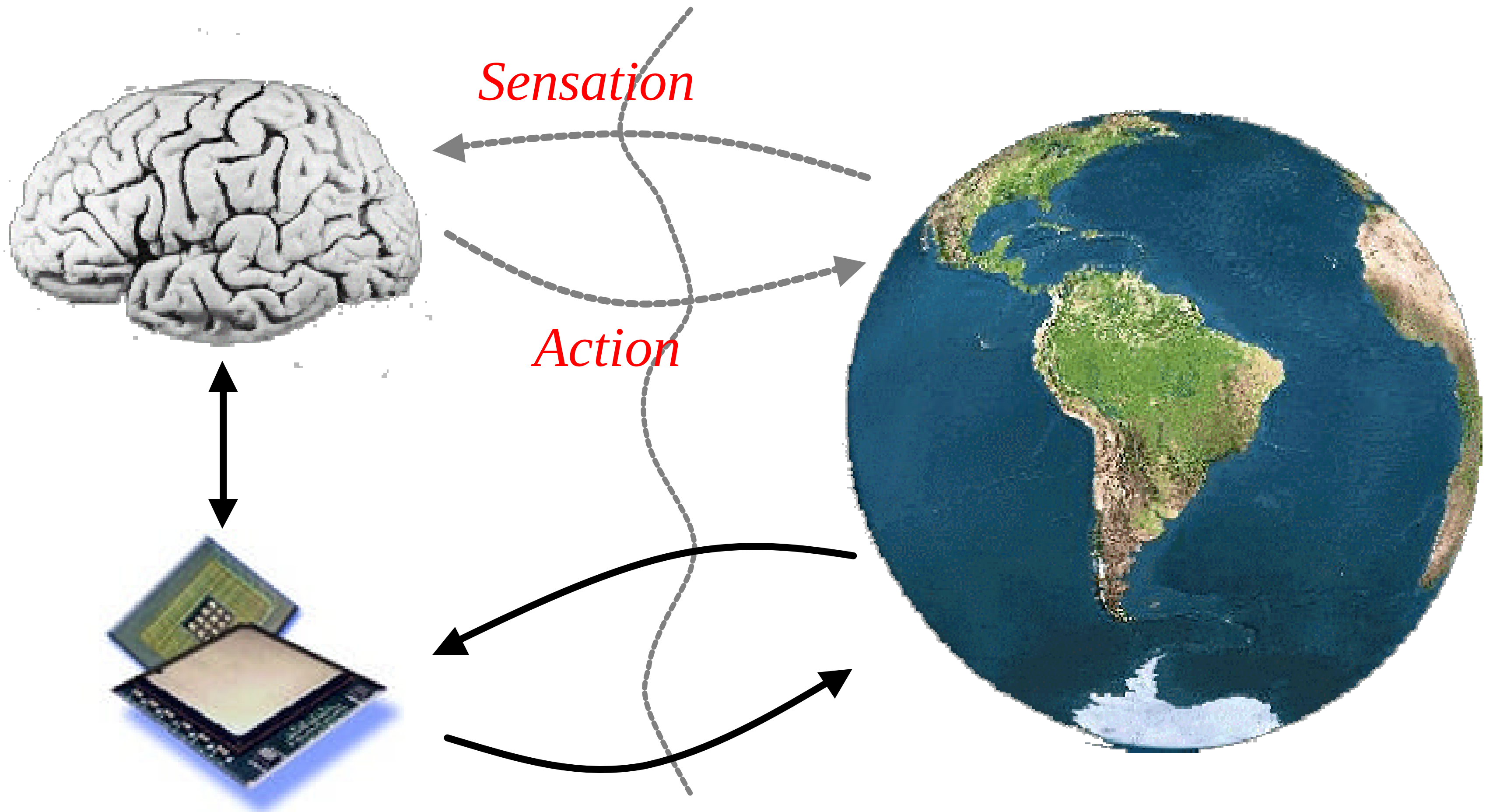
Computer Science Neuroscience Applied Mathematics



NEURAL PROSTHESIS



NEURAL PROSTHESIS



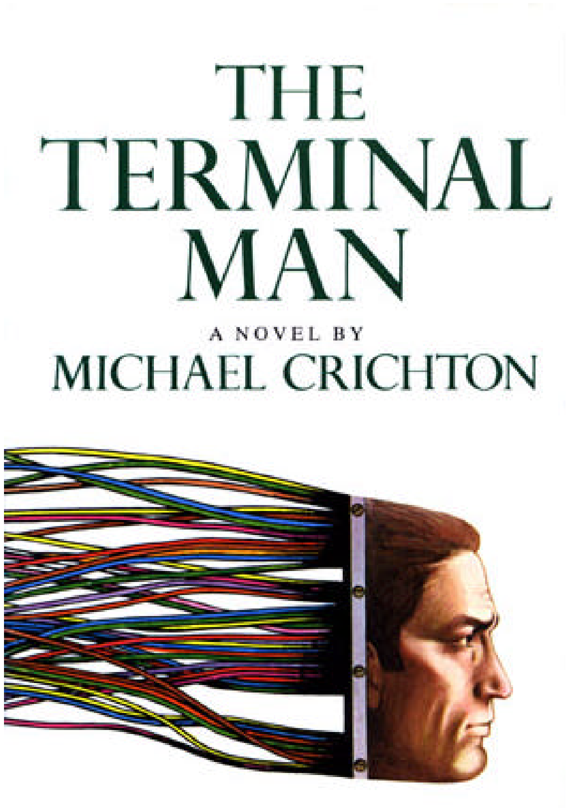
THE LINK SEPARATED

* Stroke (e.g. in brain stem).
* Spinal cord injuries
  - Approximately 200,000 cases in the USA
  - 11,000 new cases/year
  - Fifty-six percent in 16 to 30 year age group
  - 0.7% Recover
* Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's disease)
  - 20,000 cases with 5,000 new cases/year
* Multiple Sclerosis
* Blindness
* Hearing impairment

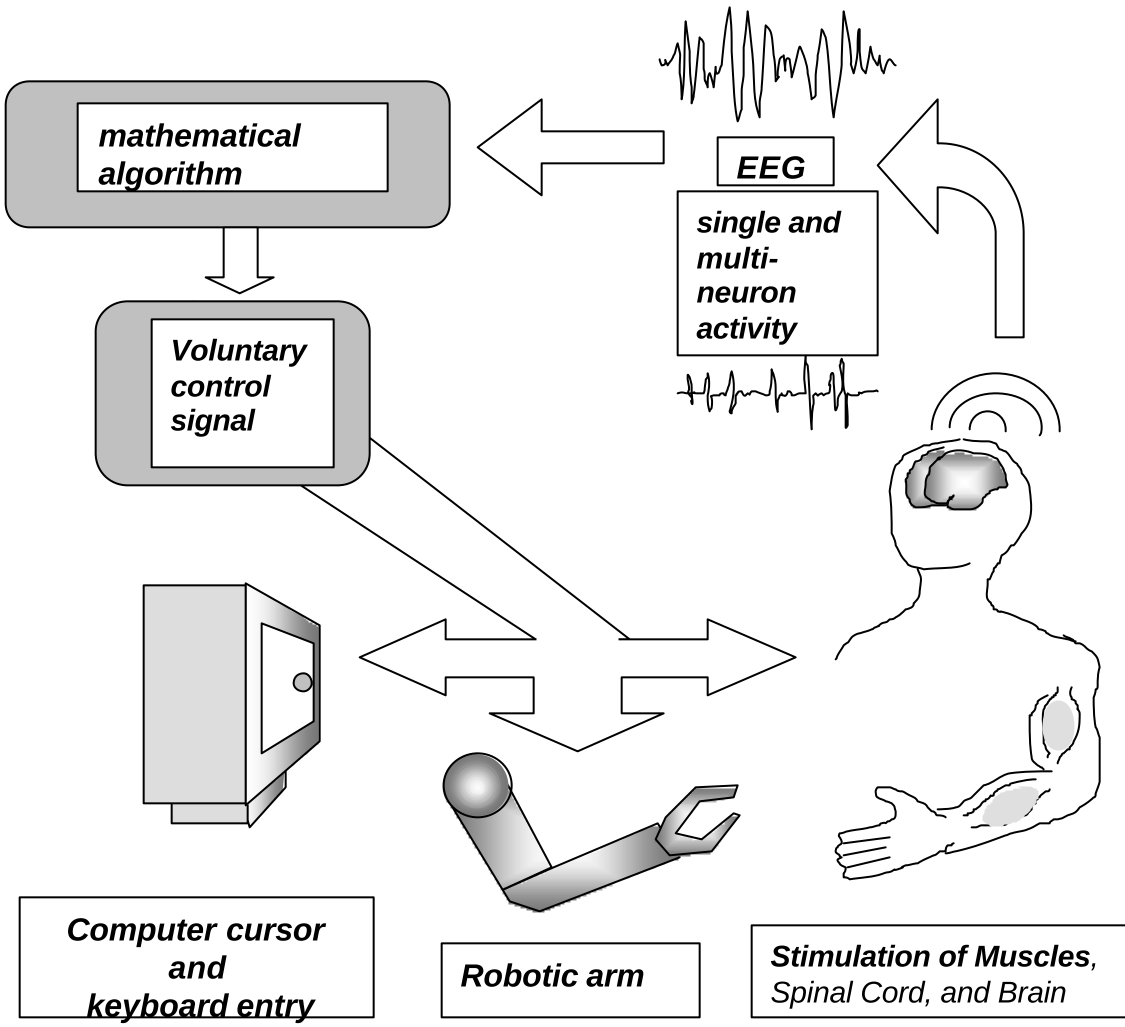
Neural Prostheses

"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



A Neural Motor Prosthesis

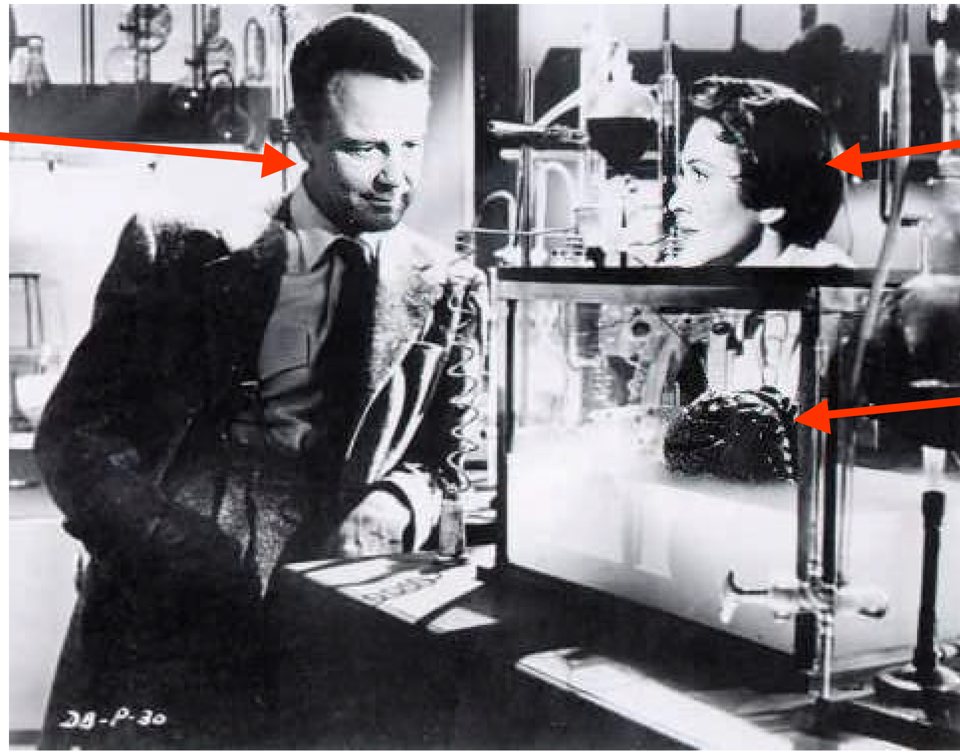


Focus on central rather than peripheral nervous system.

Source: Mijail Serruya

BRAIN-MACHINE INTERFACES

"Mad" scientist



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. What can we measure? From where? How?

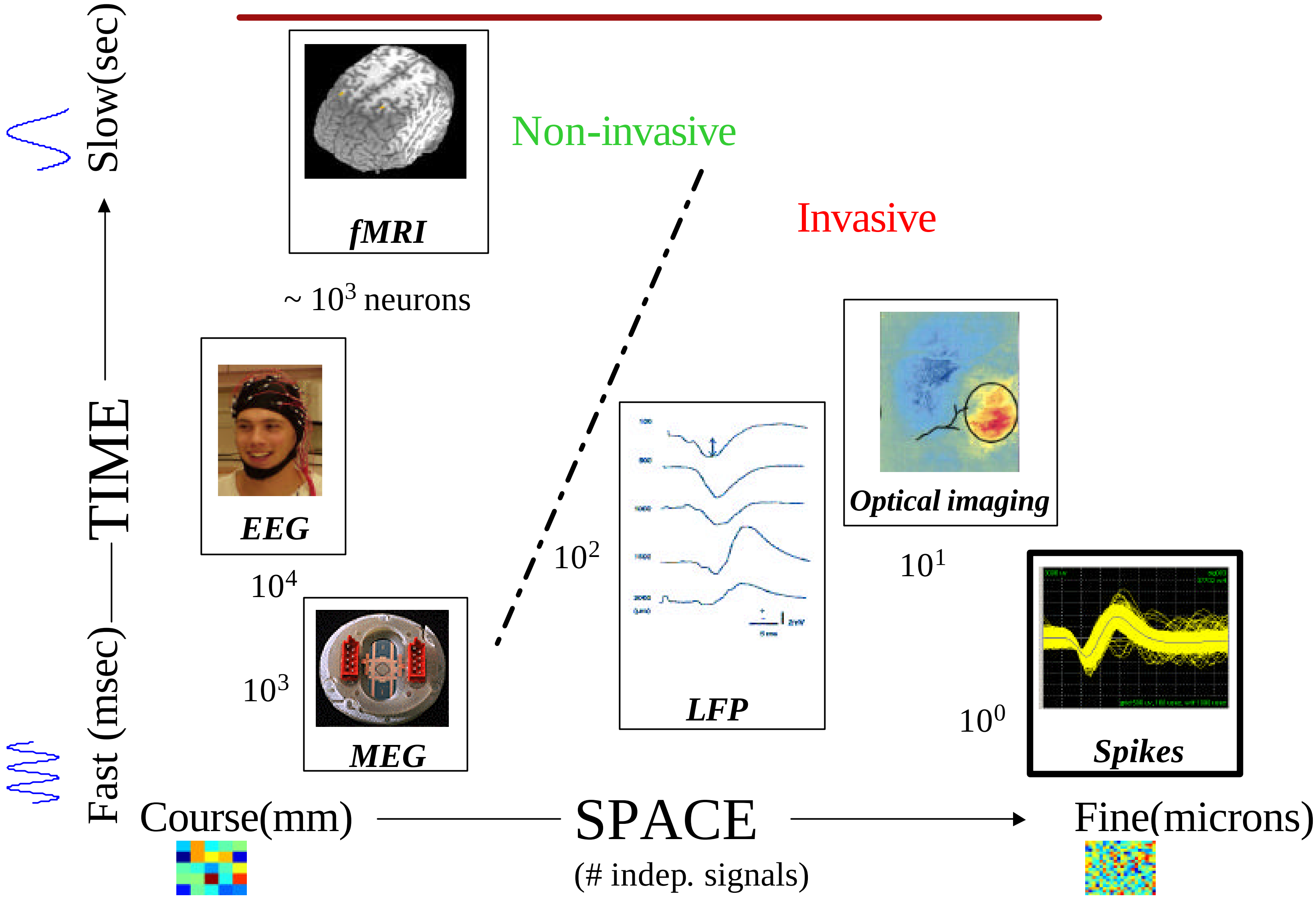
2. **Encoding**: How is information represented in the brain?

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

4. How can we build practical interfaces?

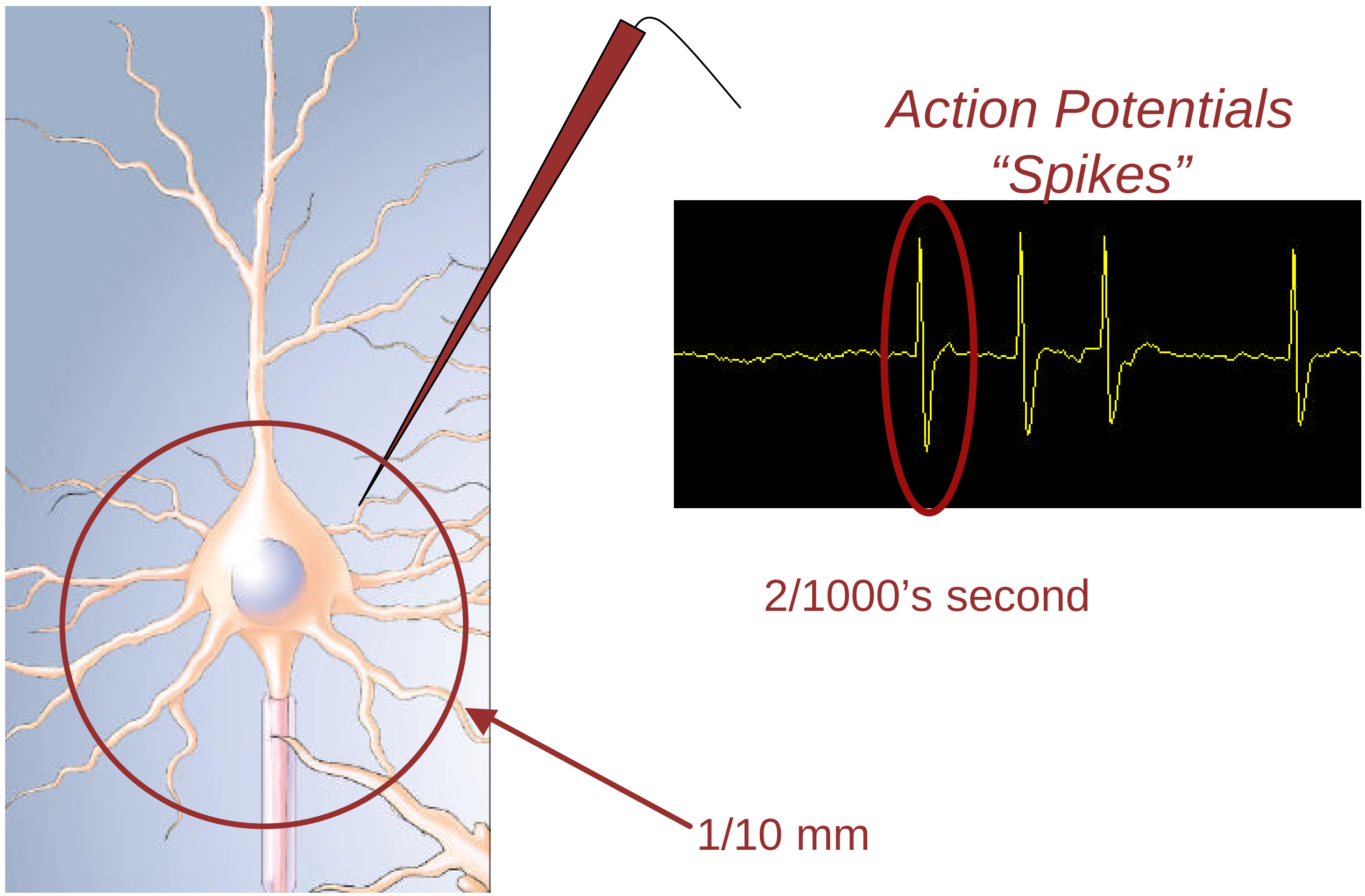
    * learning/training
    * adaptation (human versus computer)
    * user interface design

SENSING THE BRAIN



Source: Matt Fellows

SINGLE UNIT ACTIVITY



100,000,000,000 neurons in brain versus 50,000,000 transistors on a Pentium IV

NEURAL "CODING"

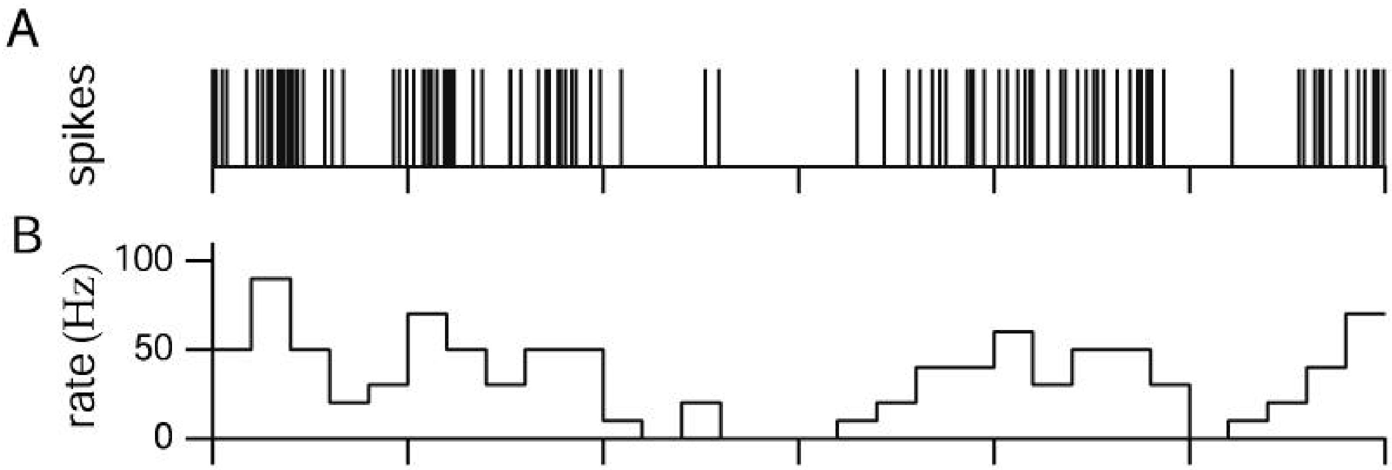
* How do cells represent information?

    * How is the representation "coded" in action potentials?

* If we understand the encoding then we can tackle the "decoding" problem.

    * *Inference* – from neural activity to encoded "state".

RATE CODING

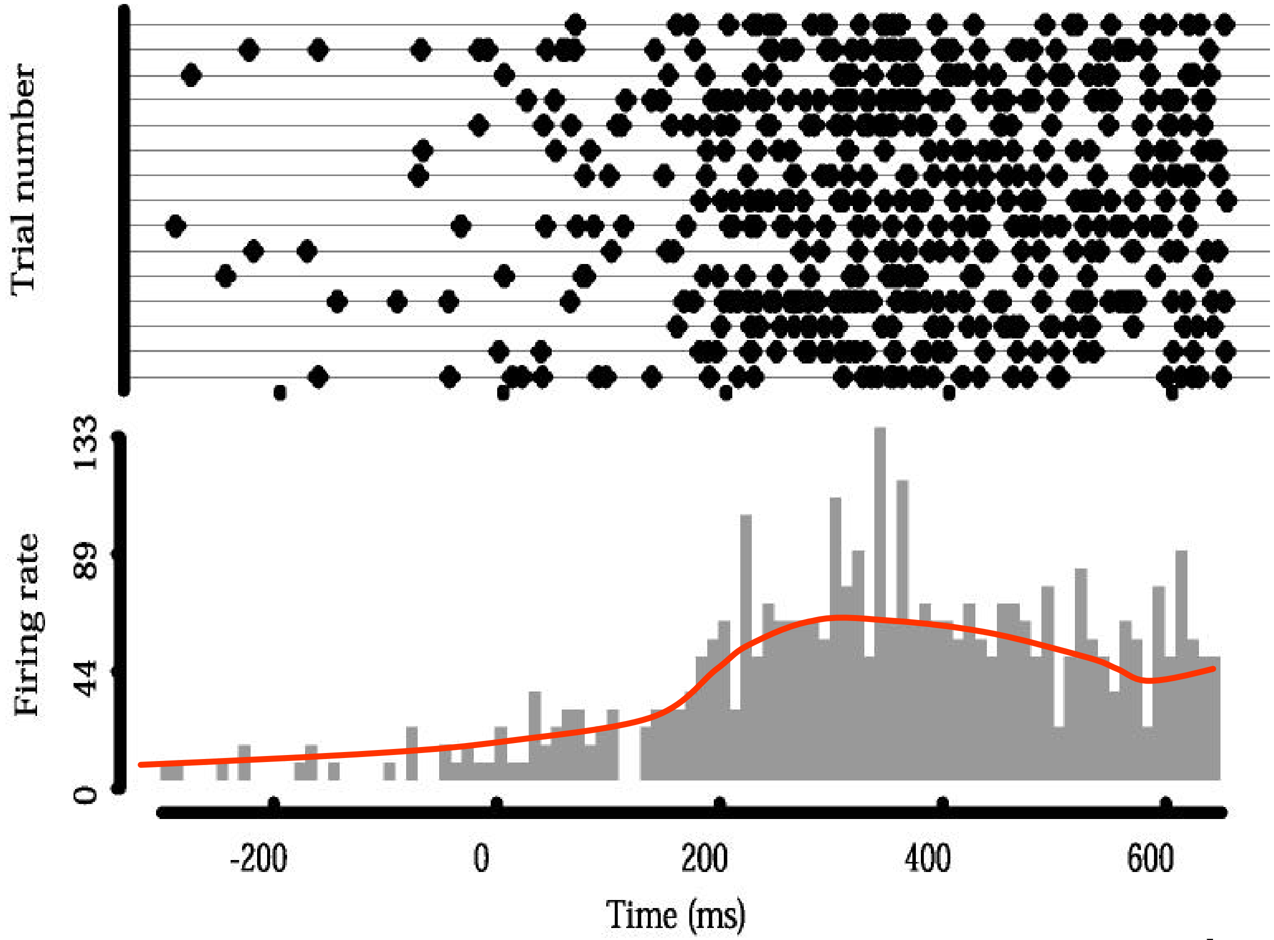


source: Zemel & McNaughton, NIPS2000 tutorial

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

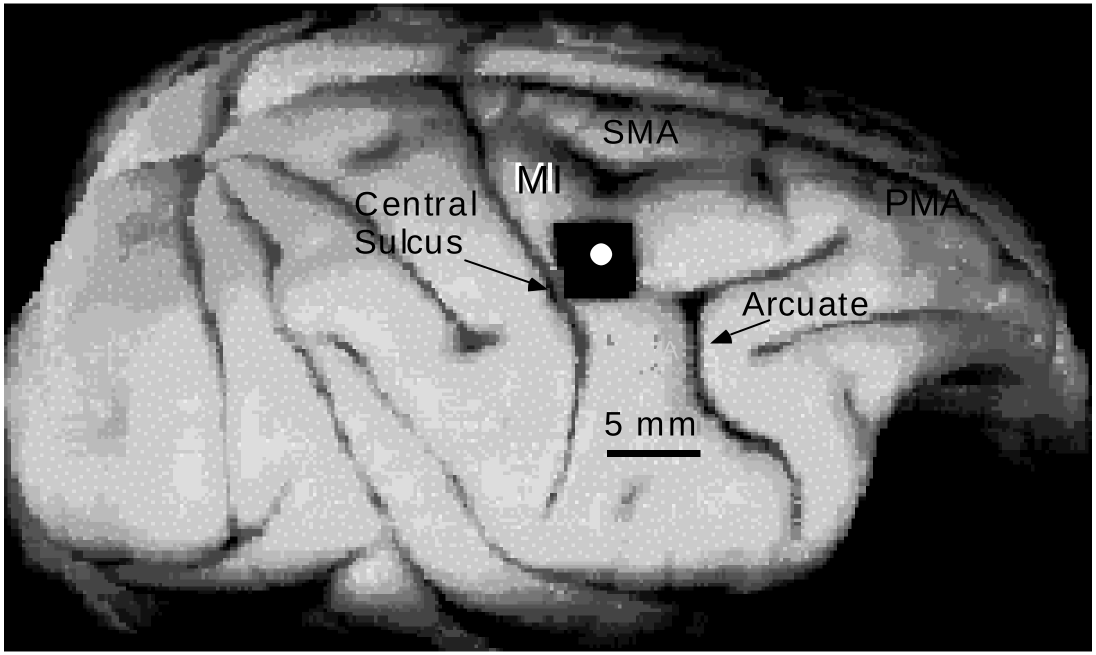
Rate is related to the probability the cell will spike in a given time interval

RATE CODING



Source: Rob Kass

PRIMARY MOTOR CORTEX

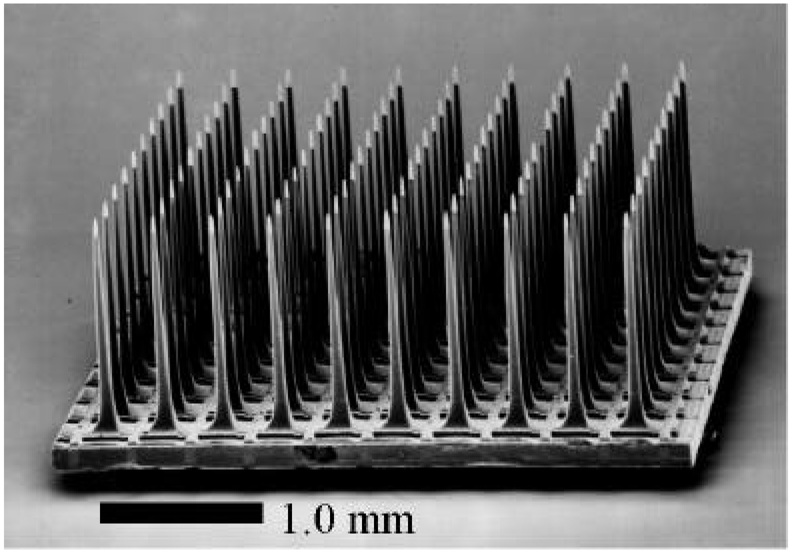


MI arm area of motor cortex.

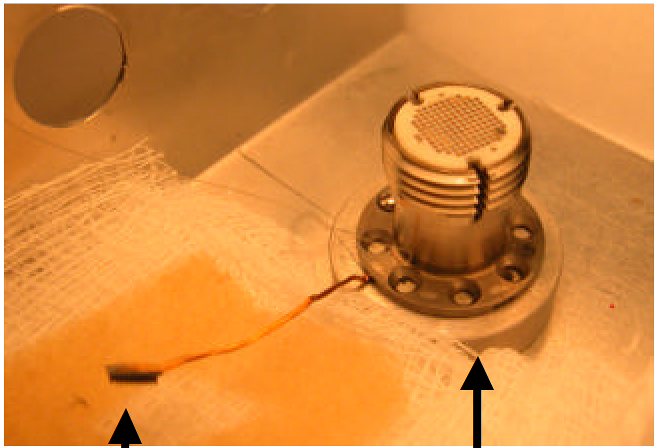
* firing rates of cells correlated with hand motion (velocity, position, acceleration?)
* *hypothesis*: natural for controlling motion of a prosthesis.

NEURAL IMPLANT

Bionic Technologies:

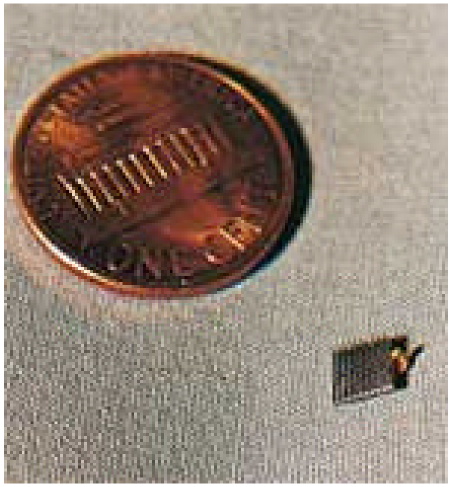


Utah Array



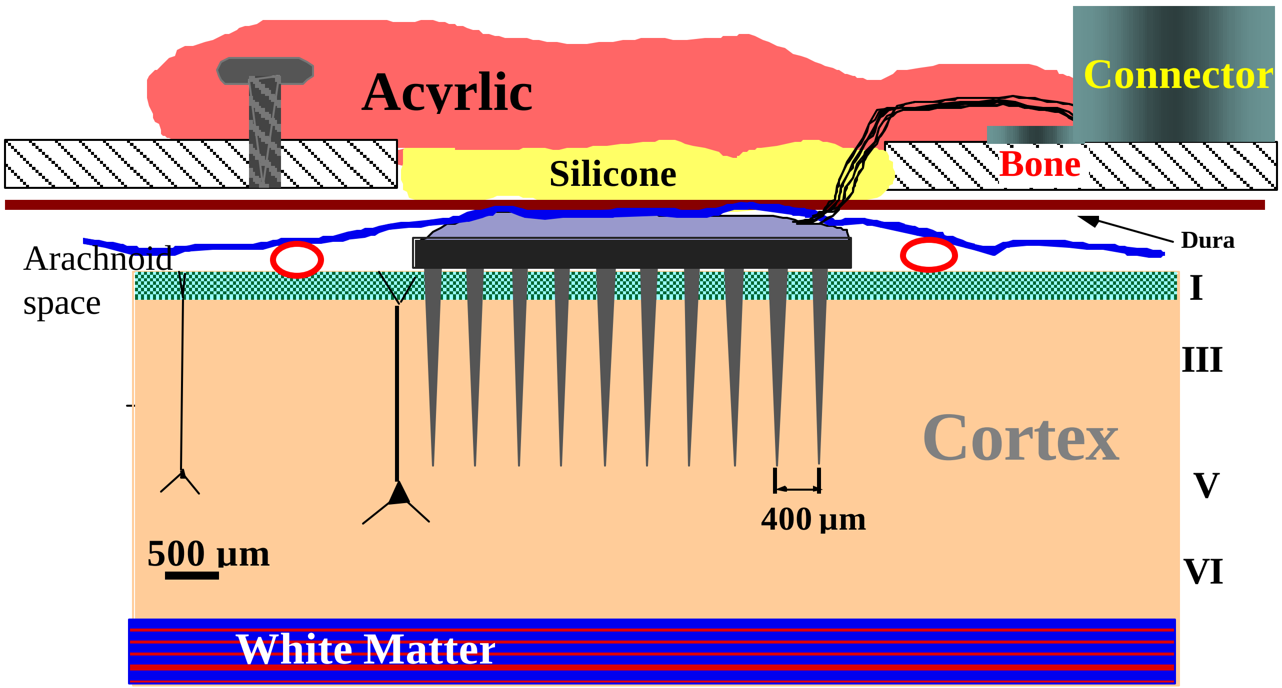
Electrode array

Neural connector



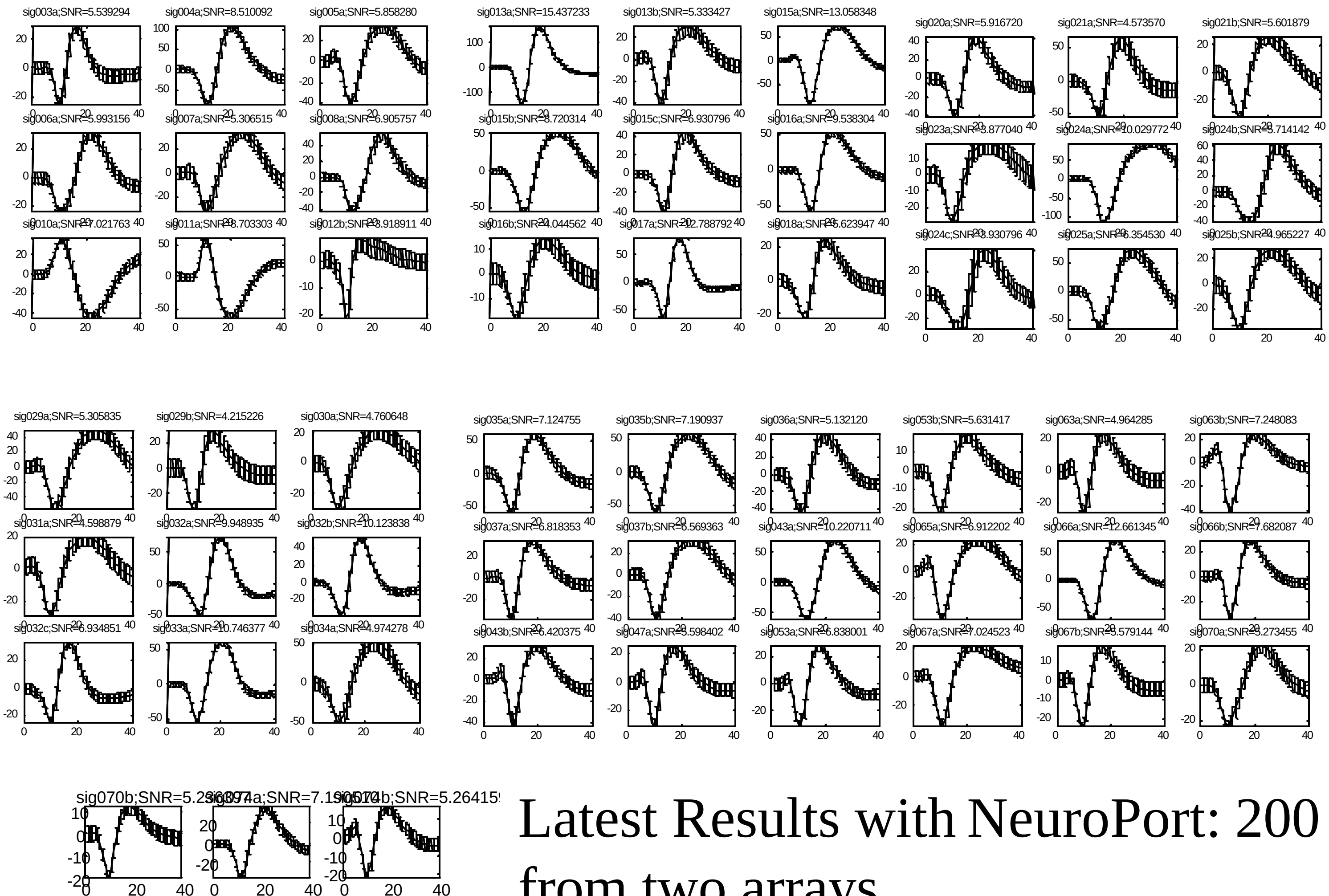
100 electrodes,
400µm separation
4x4 mm

NEURAL IMPLANT



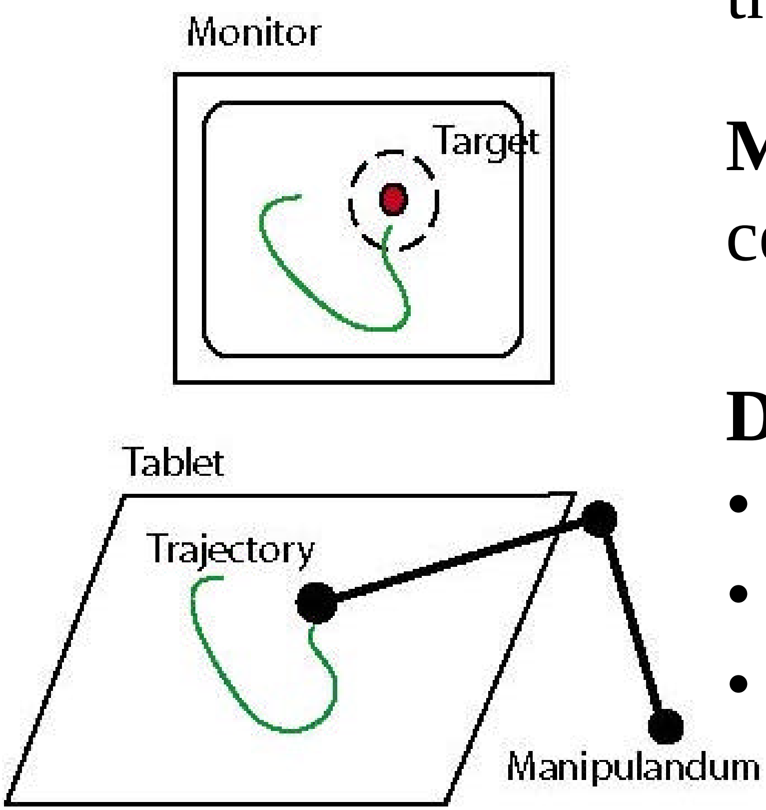
Chronically implanted.
Stable recording for 2-3 years (not necessarily same cells every day).
Spikes as well as local field potentials.
Take what you get.

RECORDED ACTION POTENTIALS



Latest Results with NeuroPort: 200 neurons from two arrays.

“PINBALL” TASK

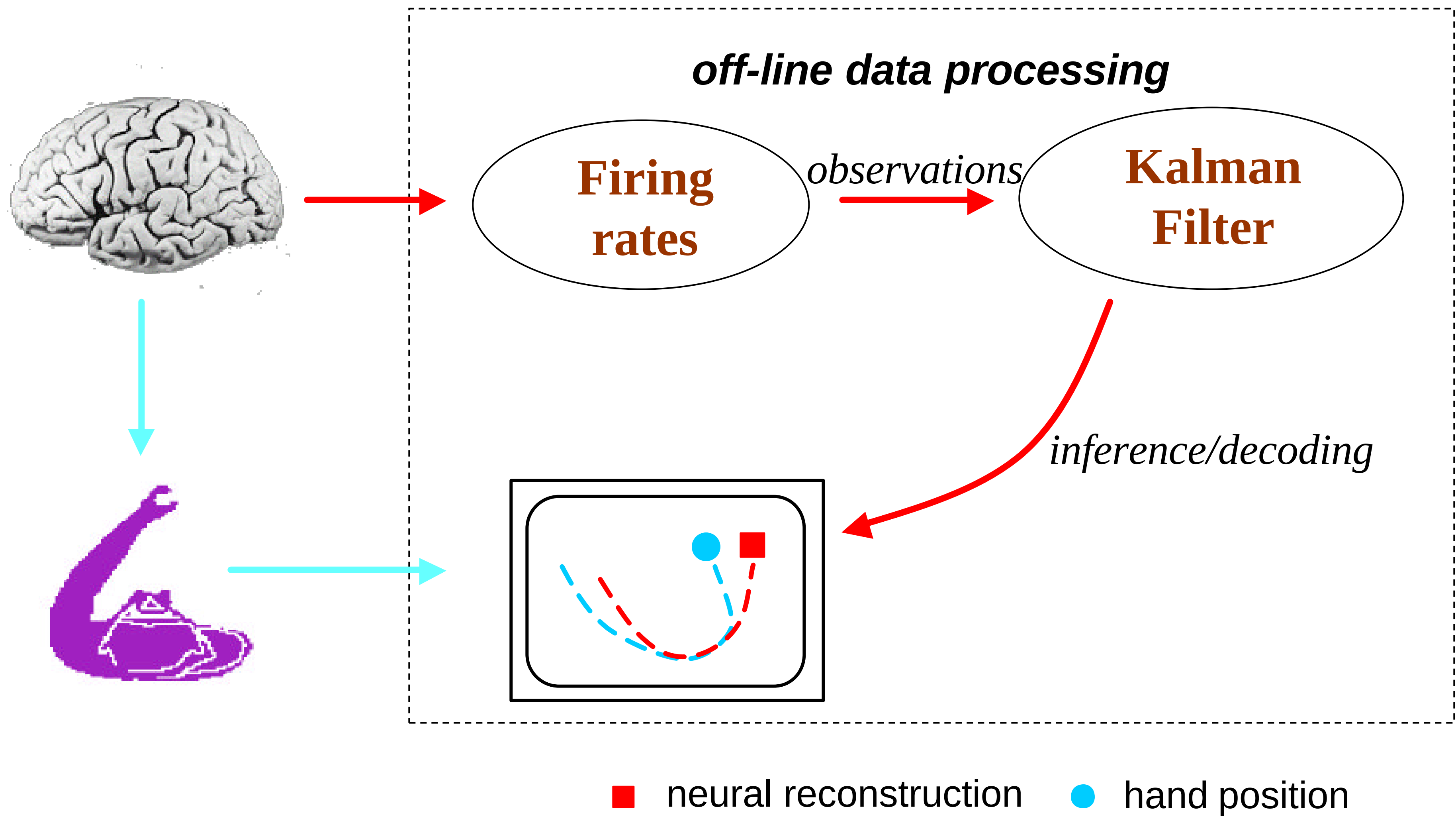


Task: Hit random targets on the screen.

Motions: fast, unconstrained (not center-out)

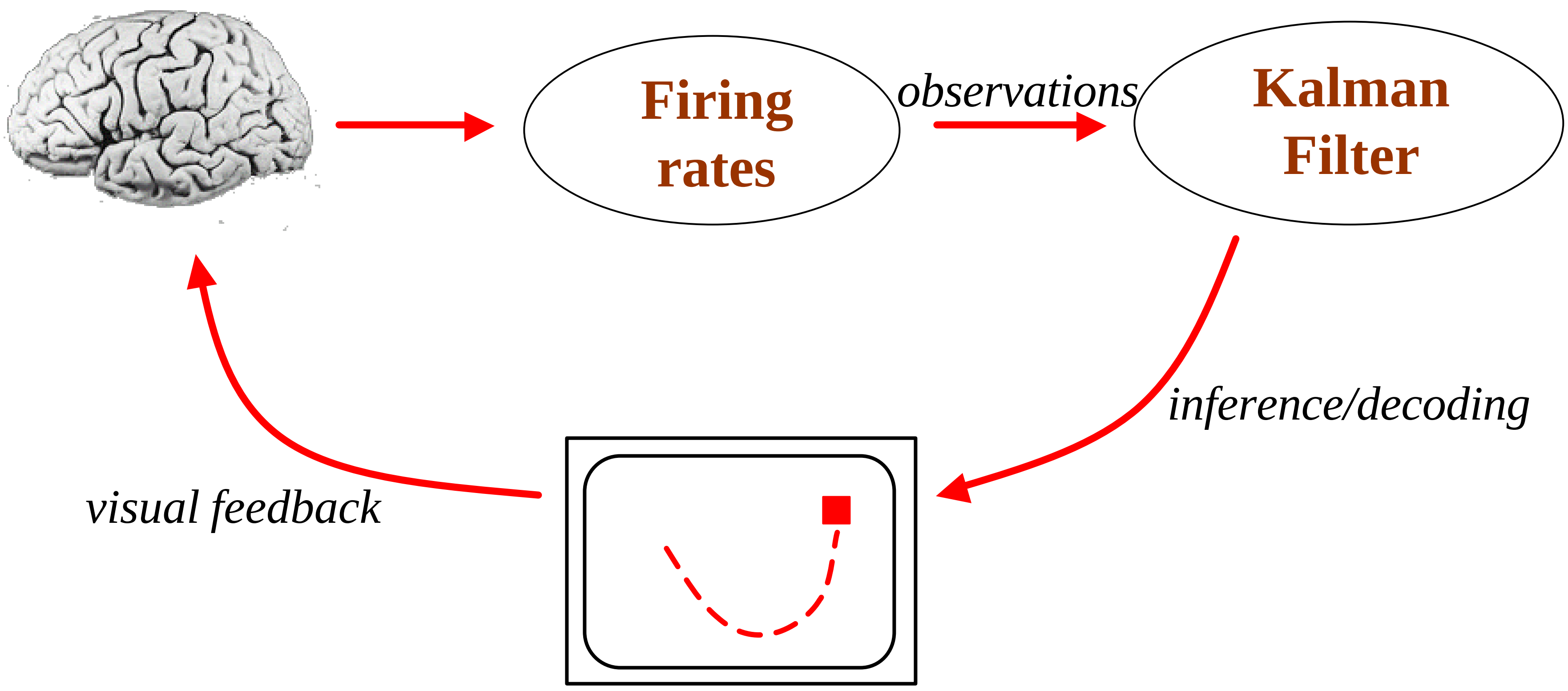
Data (4.5 minutes)**:**
- Position (Velocity, Acceleration)
- 1.5 minutes needed for training
- Firing rate (42 cells, non-overlapping 70ms bins)

EXPERIMENAL PARADIGM



CLOSED-LOOP CONTROL

on-line direct neural control



■ neural reconstruction

Generative Model

Encoding:

linear, non-linear?

$$\vec{z}_k = f_1(\vec{x}_k) + \vec{q}_k$$

noise (e.g. Normal or Poisson)

$$\vec{x}_k = f_2(\vec{x}_{k-1}) + \vec{w}_k$$

neural firing rate of N=42 cells in M=70ms

behavior (e.g. hand position, velocity, acceleration)

ENCODING (HAND DIRECTION)

Cosine tuning (Georgopoulos et al ’82). Single cell:

$$z_k = h_0 + h_x \sin(q_k) + h_y \cos(q_k)$$

q_k = hand direction at time k

Not sufficient for continuous control.

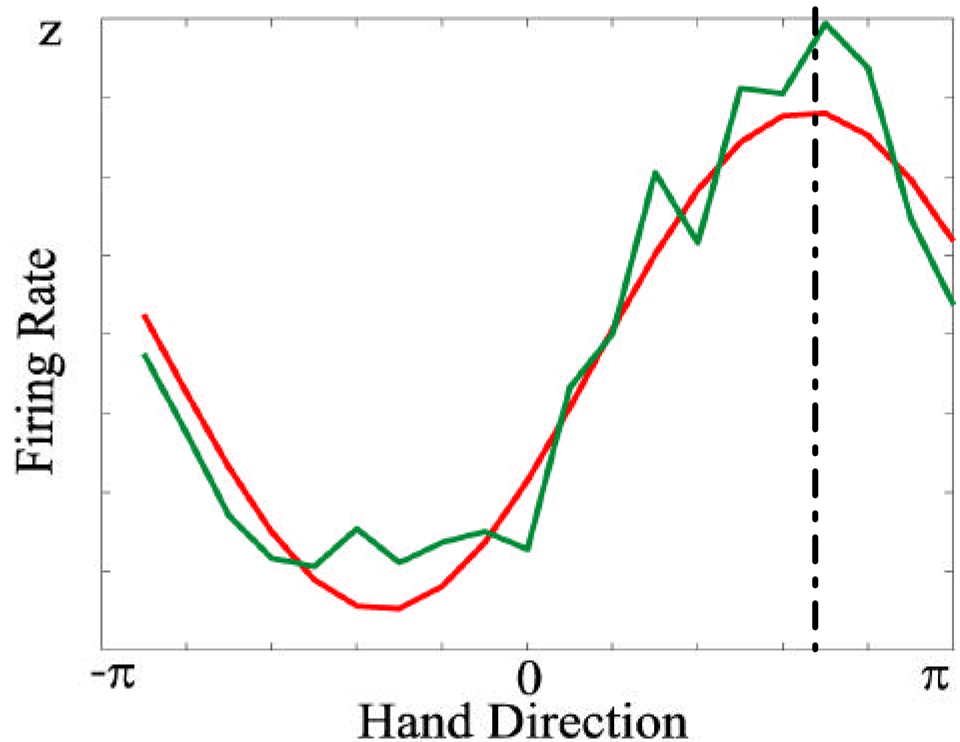
Speed?

Position?

Acceleration?

Noise model?

“Preferred” direction

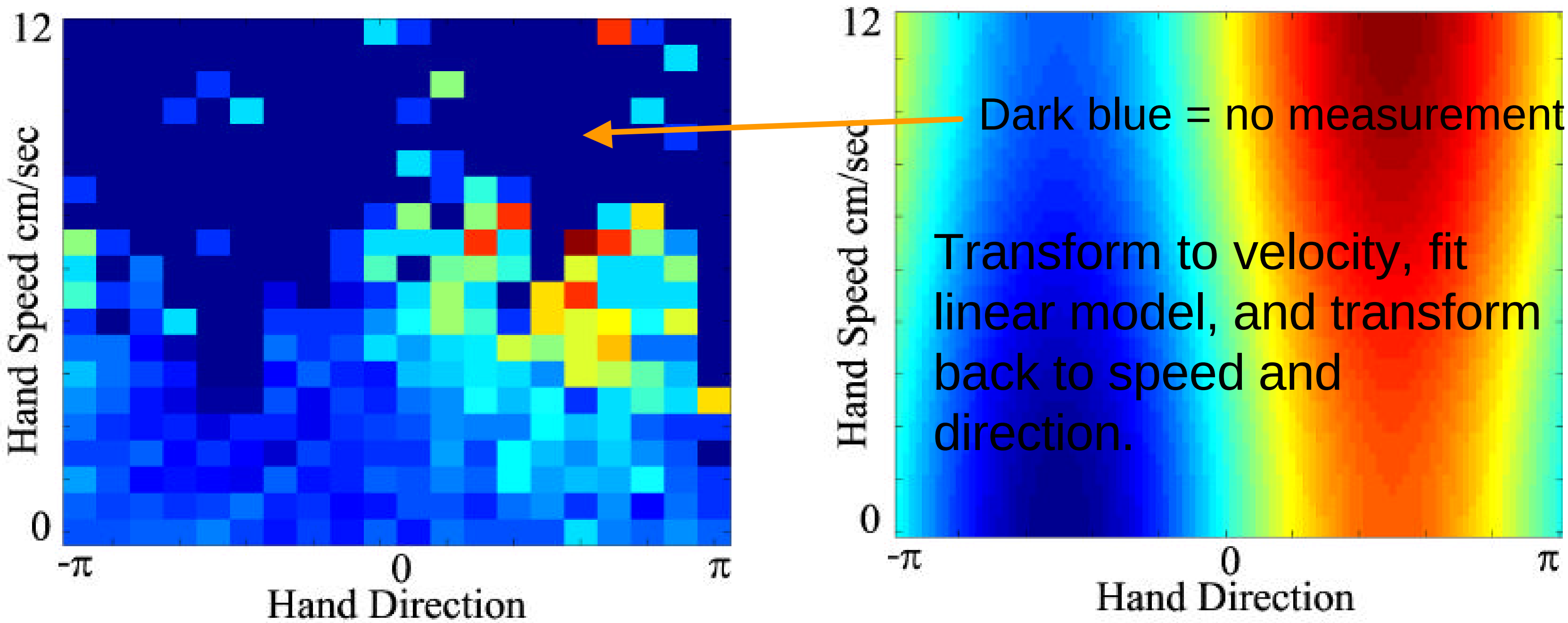


ENCODING (HAND VELOCITY)

Moran & Schwartz ('99):

$$
\begin{aligned}
z_k &= s_k(h_0 + h_x \sin(q_k) + h_y \cos(q_k)) \\
&= h_1 + h_x v_{x,k} + h_y v_{y,k}
\end{aligned}
$$

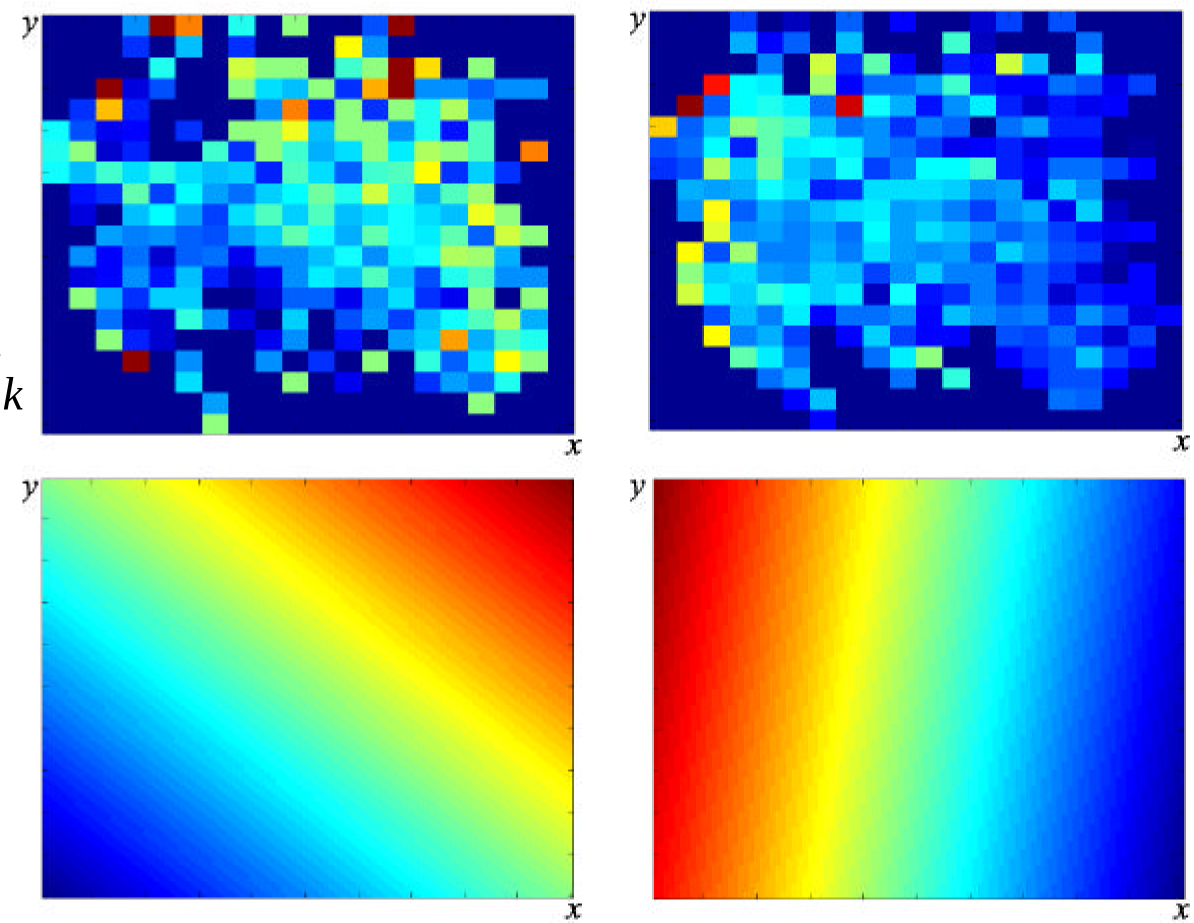
(*Linear* in velocity).



ENCODING (POSITION)

Linear encoding of position

$$z_k = b_0 + b_x x_k + b_y y_k$$



We do the same for acceleration.

ENCODING SUMMARY

* Linear models of position and velocity seem reasonable.

* Linear models relating firing to acceleration, jerk, snap, … also improve the encoding but with diminishing returns.

* Firing rates of cells are not conditionally independent (need to model the correlations) [Hatsopoulos et al ’98].

GENERATIVE MODEL

Observation Equation:

firing rate vector (zero mean, sqrt)

$$\begin{pmatrix} z^1_{k-j} \\ z^2_{k-j} \\ \vdots \\ z^{42}_{k-j} \end{pmatrix}$$

$$\vec{z}_{k-j} = H_k \vec{x}_k + \vec{q}_k$$

$$\begin{pmatrix} x_k \\ y_k \\ v_{x_k} \\ v_{y_k} \\ a_{x_k} \\ a_{y_k} \end{pmatrix}$$

system state vector (zero mean)

42 X 42 matrix

$$\vec{q}_k \sim N(0, Q)$$

$$k = 0,1,2,\cdots$$

42 X 6 matrix

System Equation:

6 X 6 matrix

$$\vec{x}_{k+1} = A_k \vec{x}_k + \vec{w}_k$$

$$\vec{w}_k \sim N(0, W)$$

$$k = 0,1,2,\cdots$$

6 X 6 matrix

TRAINING

$$H = \underset{H}{\operatorname{argmin}} \sum_k \| \vec{z}_k - H\vec{x}_k \|^2$$

$$A = \underset{A}{\operatorname{argmin}} \sum_k \| \vec{x}_{k+1} - A\vec{x}_k \|^2$$

$$\begin{aligned} Q &= \mathbf{cov}(\{\vec{z}_k - H\vec{x}_k\}_k) \\ &= (\mathbf{z} - H\mathbf{x})(\mathbf{z} - H\mathbf{x})^{\mathrm{T}} \end{aligned}$$

$$\begin{aligned} W &= \mathbf{cov}(\{\vec{x}_{k+1} - A\vec{x}_k\}_k) \\ &= (\mathbf{x}_{k+1} - A\mathbf{x}_k)(\mathbf{x}_{k+1} - A\mathbf{x}_k)^{\mathrm{T}} \end{aligned}$$

Centralize the training data, such that

$$\mathrm{E}(\{\vec{z}_k\}) = 0, \quad \mathrm{E}(\{\vec{x}_k\}) = 0$$

DECODING: BAYESIAN INFERENCE

Infer (decode) behavior from firing.

p(behavior at k | firing up to k) =

$$p(\vec{x}_k \mid \vec{Z}_k) = k\, p(\vec{z}_k \mid \vec{x}_k)\, p(\vec{x}_k \mid \vec{Z}_{k-1})$$

likelihood

prior

observation model

$$\vec{z}_k \sim ?\ (H\ \vec{x}_k,\ Q)$$

$$p(\vec{x}_k \mid \vec{Z}_{k-1}) = \int p(\vec{x}_k \mid \vec{x}_{k-1})\, p(\vec{x}_{k-1} \mid \vec{Z}_{k-1})\, d\vec{x}_{k-1}$$

Kalman Filter

$$\vec{x}_k \sim \mathcal{N}(A\vec{x}_{k-1}, W) \qquad \mathcal{N}(\hat{x}_{k-1}, P_{k-1})$$

system model

KALMAN FILTER ALGORITHM

Time Update

Prior estimate

$$\hat{x}_k^- = A\hat{x}_{k-1}$$

Error covariance

$$P_k^- = AP_{k-1}A^T + W$$

Measurement Update

Posterior estimate

$$\hat{x}_k = \hat{x}_k^- + K_k(\vec{z}_k - H\hat{x}_k^-)$$

Error covariance

$$P_k = (I - K_k H)P_k^-$$

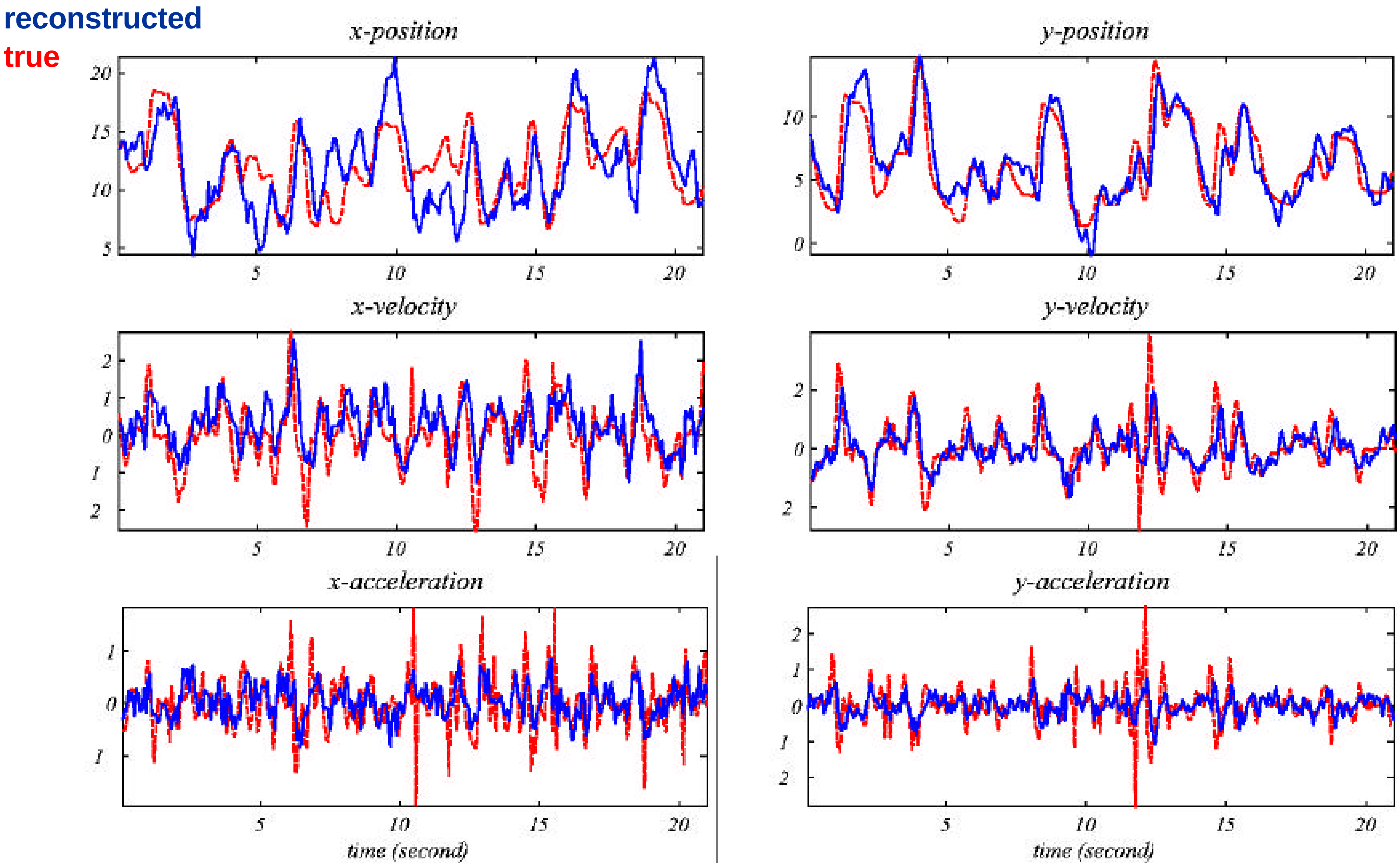
Kalman gain

$$K_k = P_k^- H^T (HP_k^- H^T + Q)^{-1}$$

Initial estimate of $\hat{x}_{k-1}$ and P_{k-1}

Welch and Bishop 2002

RECONSTRUCTION (TEST DATA)



OPTIMAL "LAG"

Measurement Equation

$$\vec{z}_k = H\ \vec{x}_k + \vec{q}_k$$

Firing precedes motion:

* Uniform: lag j time steps (1 time step = 70ms)

$$\vec{z}_{k-j} = H\ \vec{x}_k + \vec{q}_k \qquad j = 0,1,2,3,4$$

* Non-uniform: lag $(j_1, j_2, \cdots, j_{42})$ time steps

RECONSTRUCTION AND LAG

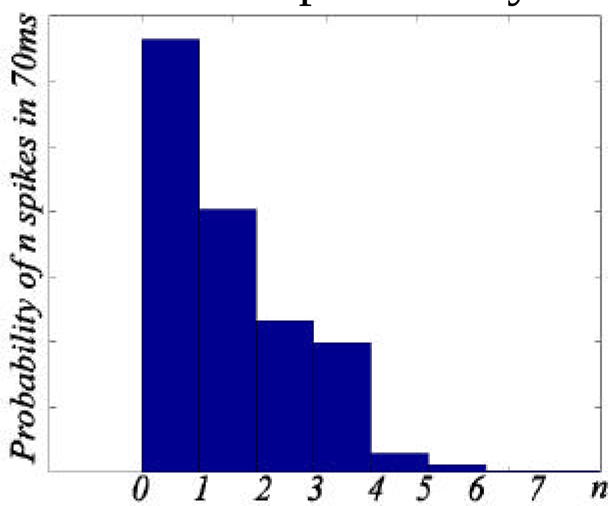
Methods	CC (x, y)	MSE (cm^2)
Kalman (0ms lag)	(0.77, 0.91)	6.96
Kalman (70ms lag)	(0.79, 0.93)	6.67
Kalman (140ms lag)	**(0.81, 0.93)**	**6.09**
Kalman (210ms lag)	(0.81, 0.89)	6.98
Kalman (280ms lag)	(0.76, 0.82)	8.91
Kalman (non-uniform)	(0.82, 0.93)	5.24

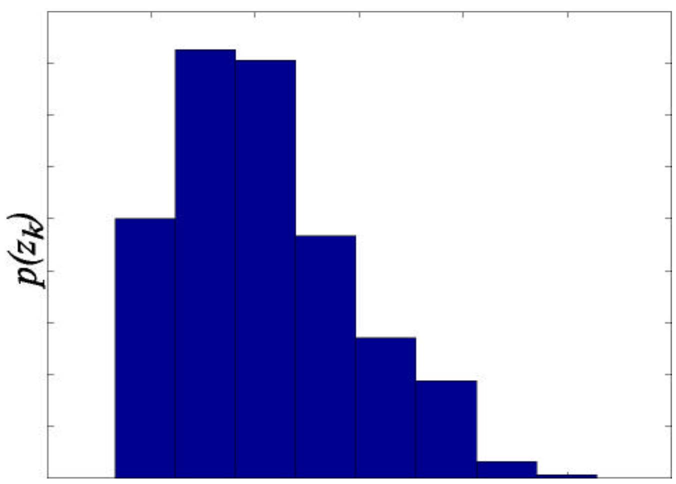
TRANSFORMED RATE

Fitting the linear models with LS assumes Gaussian noise.

$$\tilde{z}_k = \sqrt{z_k + 1} - mean(\sqrt{z_k + 1})$$

Poisson probability





$$\vec{\tilde{z}}_{k-j} = H\ \vec{x}_k + \vec{q}_k$$

Kalman (140ms lag) (0.82, 0.93) 5.87

MIXTURE MODEL

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

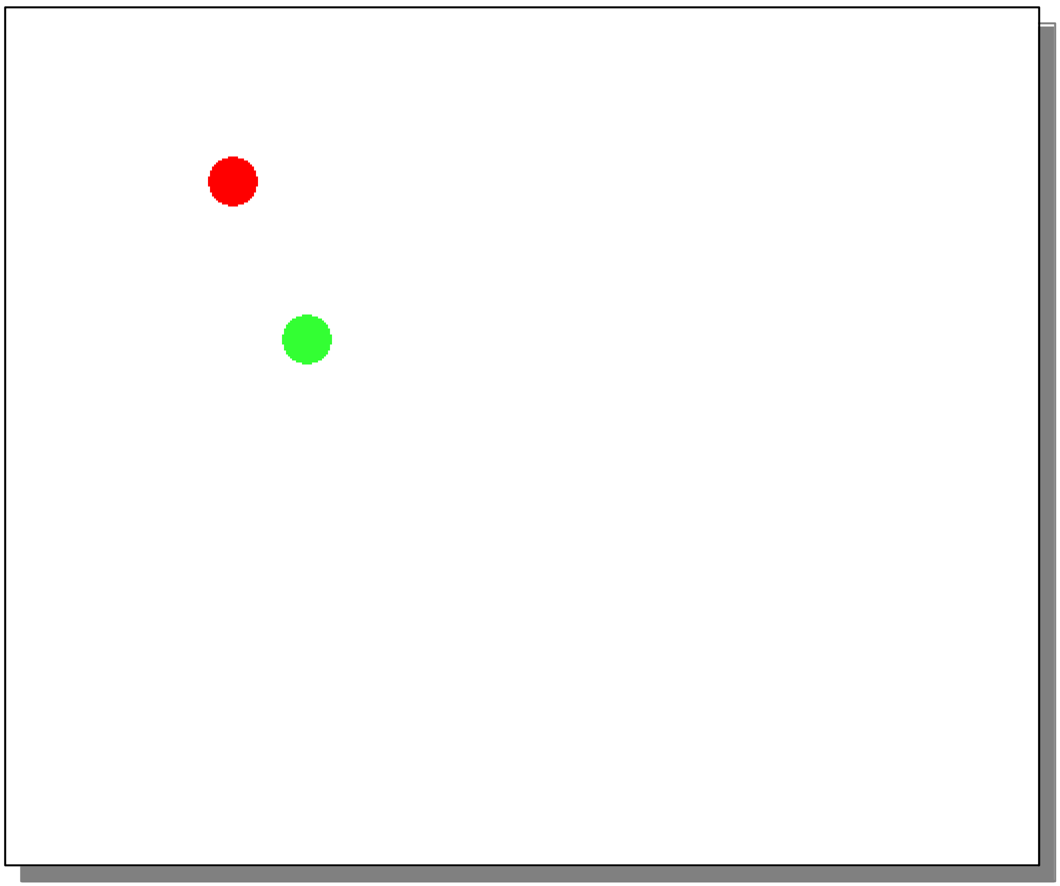
$$p(\vec{z}_{k-j} \mid \vec{x}_k, S_t = i) = G(H_i\, \vec{x}_k, Q_i)$$

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

MSE = 5.5 cm^2

REAL-TIME DEMO

Closed Loop Neural Control



Target

Neural control

Linear filters
built on-line.

Mijail Serruya

RELATED WORK

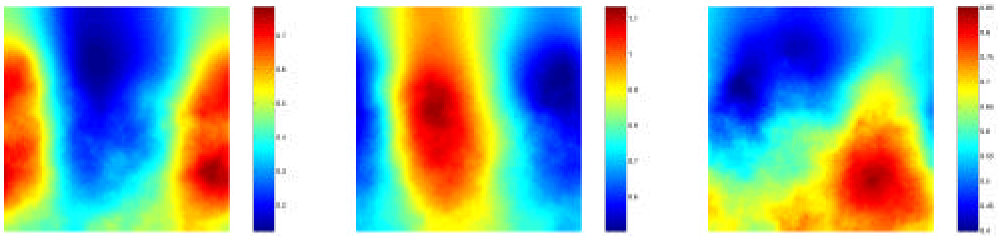
* Georgopoulos *et al*. (1986) * Taylor *et al*. (2002)	Population Vector (velocity)
* Zhang *et al* (1998)	“two step Bayes”
* Brown *et al*. (1998)	Recursive Bayesian (hippocampal place cells)
* Wessberg *et al*.(2000)	Linear filter, ANN
* Gao *et al*. (2002)	Particle filter
* Principe *et al* (2002)	non-standard Kalman model
* Serruya *et al*.(2002)	Linear filter (position) (closed loop)

BAYESIAN APROACH

* sound probabilistic framework.
  - explicit assumptions about the model and noise.
* requires a small amount of “training” data.
* provides on-line estimation of hand position with short delay (< 200ms).
* more accurate than previous linear filtering and population vector methods.
* extendable to non-linear and non-Gaussian models.

CURRENT/FUTURE WORK

* 3D motion and joint angles.
* Incorporating local field potentials.
* Non-linear and non-parametric tuning functions



* Recognizing patterns of motion (gestures).
* Plasticity.
* Robot control (service robots, semi-autonomous).
* Recording from multiple brain areas.

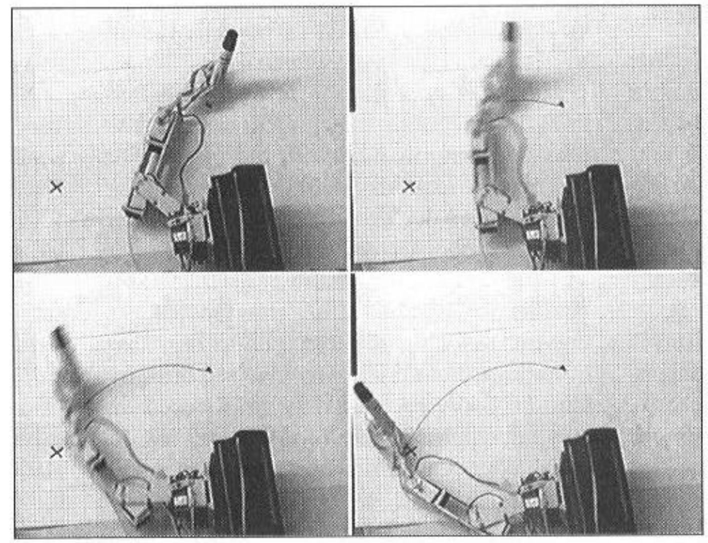
HUMANS?

* Implanted Electrodes
  + Good biocompatibility.
  + No motor impairment.
  + Can be explanted.
  + Can be re-implanted.
  + Effective control signals in animal models.
  + Commercialization and regulatory approval is underway.

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

(Unanswered) QUESTIONS AT THE INTERFACE

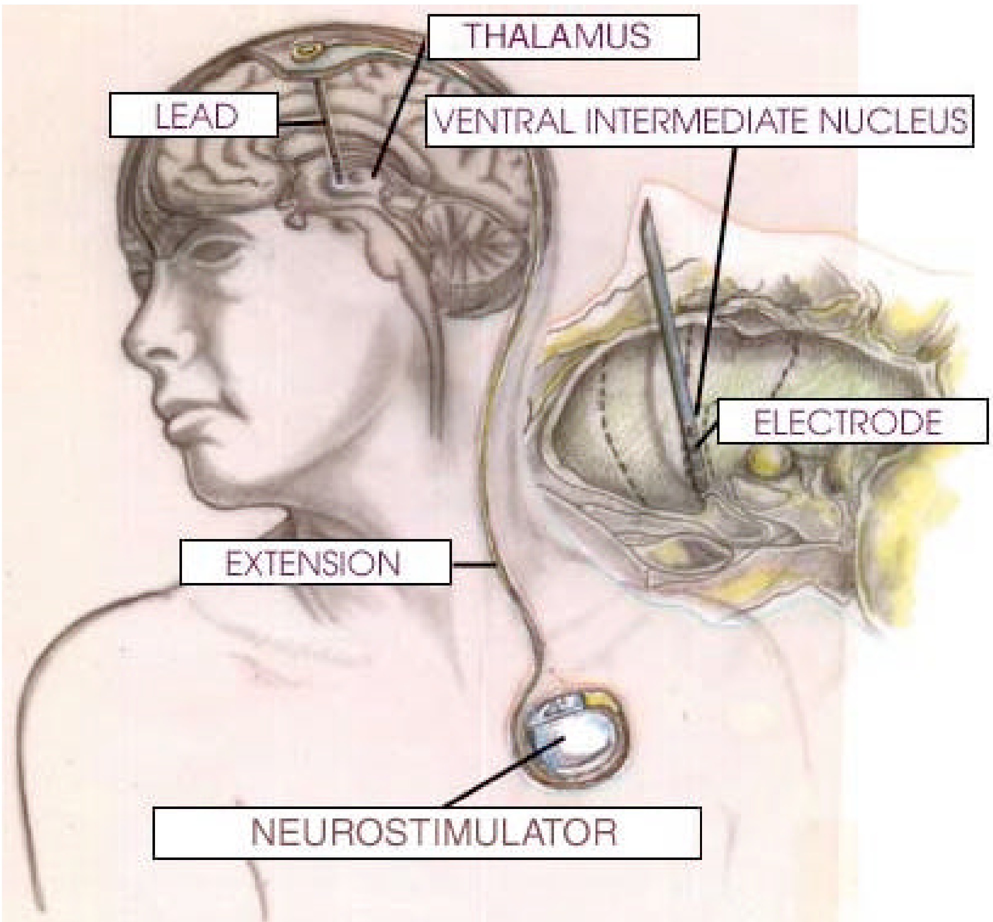
* training paralyzed subjects
* controlling "unnatural" devices
  • cursors
  • robotic arms, hands.
  • mobile robots



* controlling multiple devices
  - switching contexts
  - adaptation

* Where should the computation take place (brain or computer)?
* What level of autonomous control/perception is needed?

DEEP BRAIN STIMULATION



Neurostimulator Control Magnet Model 7452

Parkinson's

Epilepsy

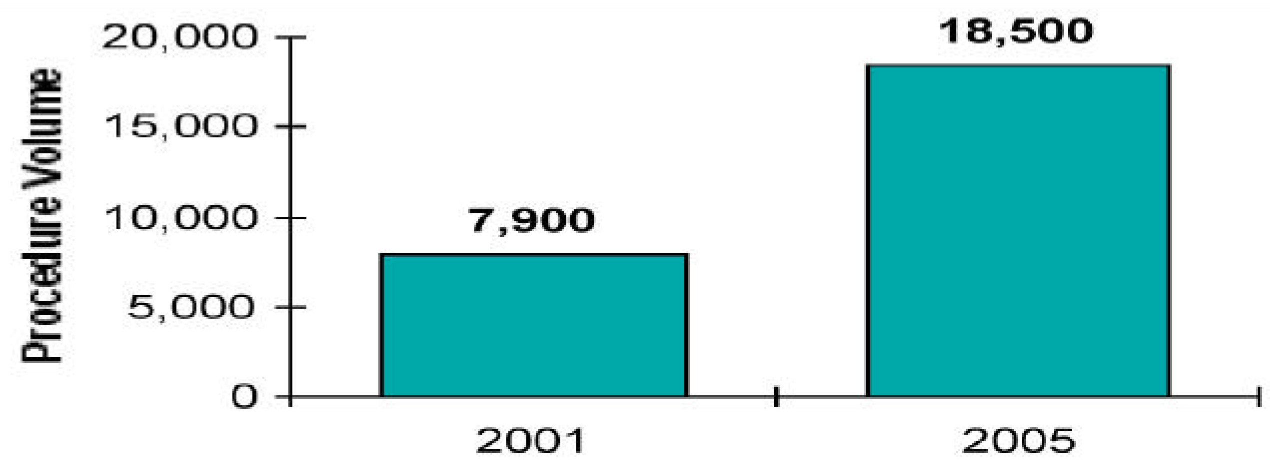
Obsessive-Compulsive Disorder.

…

Medtronic Inc.

HUMAN BRAIN IMPLANTS

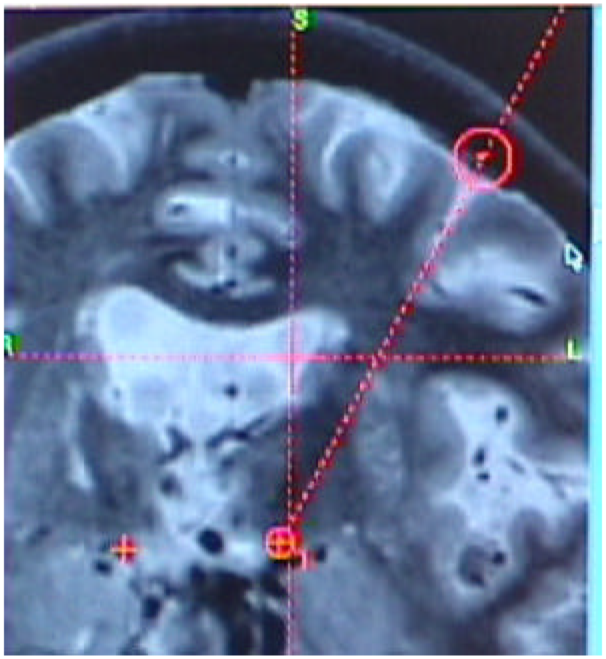
Worldwide DBS Implants[1]



- Analysts estimate a 24% growth rate in the DBS market over the next four years.[2]
- Medtronic's Activa® DBS implant was originally approved in 2000 for essential tremor, and most recently in January 2002 for Parkinson's Disease.
- Sales of Activa® for DBS have more than doubled between Q1Y01 and Q1Y02.[3]

Source: Cyberkinetics

HUMANS?



MRI of electrode track for this DBS implant procedure.

* Patients undergoing DBS procedure for Parkinson’s.
* Exact copy of our lab environment in the operating room.
* Stop in cortex and record for approx 45 minutes.
* Expect approximately 10 cells.
* Learn the encoding then test closed loop cursor control.

CONCLUSIONS

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

In animal models we have demonstrated continuous 2D cursor control and limited robotic control.

The work opens opportunities to study

- 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.

THANKS

M. Fellows, *Neuroscience*

D. Sheinberg, *Neuroscience*

N. Hatsopoulos, *Neuroscience*

W. Patterson, *Engineering*

A. Nurmikko, *Engineering*

G. Friehs, *Brown Medical School*

S. Geman, *Division of Applied Mathematics*

D. Mumford, *Division of Applied Mathematics*

L. Paninski, *NYU, Center for Neural Science*

S. Shoham, *Princeton*

Support:

National Science Foundation, ITR Program.

The Keck Foundation

The National Institutes of Health