# *Learning and control of sensorimotor Functions in Motor Cortical Fields*

**Eilon Vaadia**

MotorCortex lab
**http://motorcortex.huji.ac.il**

**The Edmond and Lily Center for Brain Sciences**
**The Jack H. Skirball Chair & Research Fund in Brain Research**
**The interdisciplinary center for neural computation**
**Dept. of Physiology, Faculty of Medicine**
**The Hebrew University of Jerusalem**
**Israel**

# Acknowledgments


*The MotorCortex lab*

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# The Edmond and Lily Center for Brain Sciences

**( to be the largest in Israel)**

- State of the art Labs and facilities

  From Genes and Molecules to Cognition
- New Faculty positions and Post doctoral training funds
- New PhD Program and courses

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# Outlines

- Chapter 1: Sensorimotor Control:  The Notion of Internal Models
  1. The sensorimotor loop
  2. The notion of Internal models
  3. The notion of Active Perception

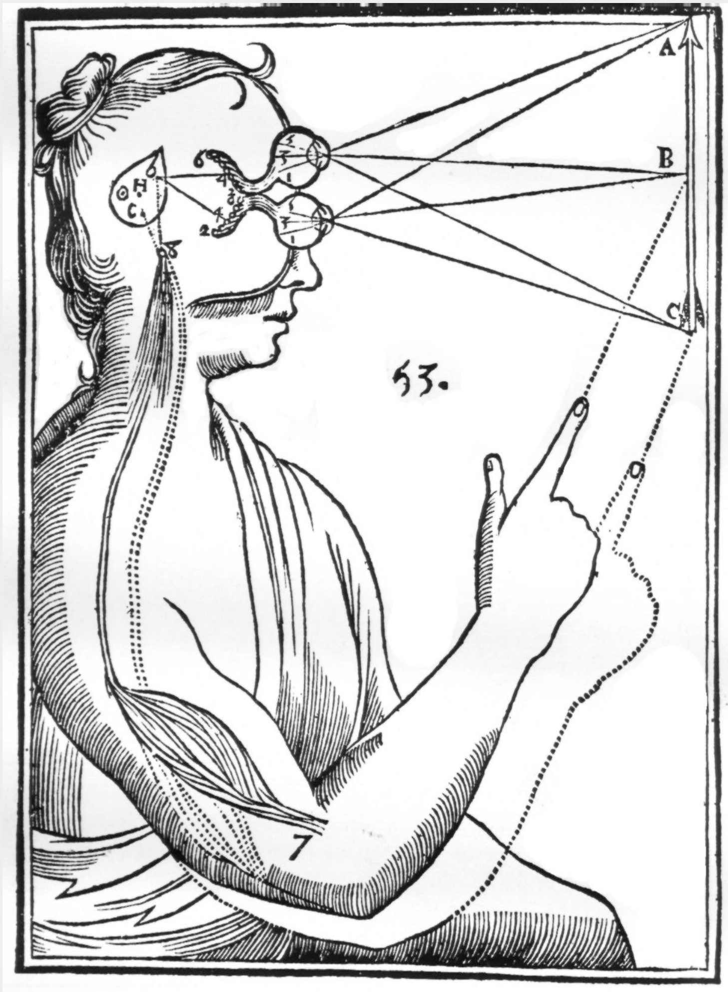
- Chapter 2: Understanding Neuronal Basis of Sensorimotor Control
  1. Population Codes in Motor Cortex
  2. Learning Related Activity in Motor cortical Fields

- Chapter 3: Brain Machine Interface (BMI)
  1. BMI - Requirements
  2. BMI – Algorithms
  3. BMI – The Karma Algorithm

- Chapter 4: BMI Experiments
  1. Reaching movements
  2. Learning and Performance in BMI settings

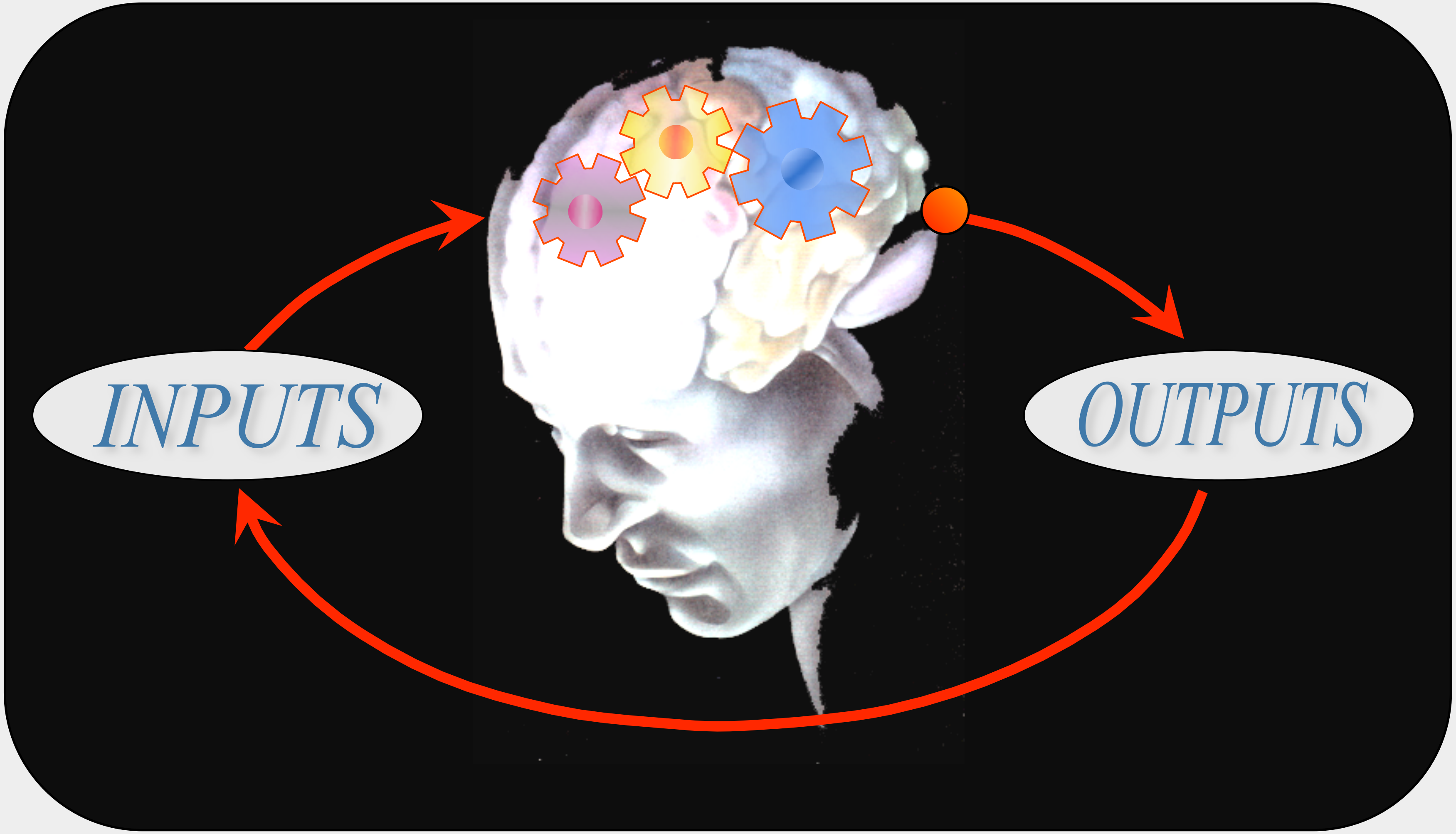
René Descartes
(1596-1650)

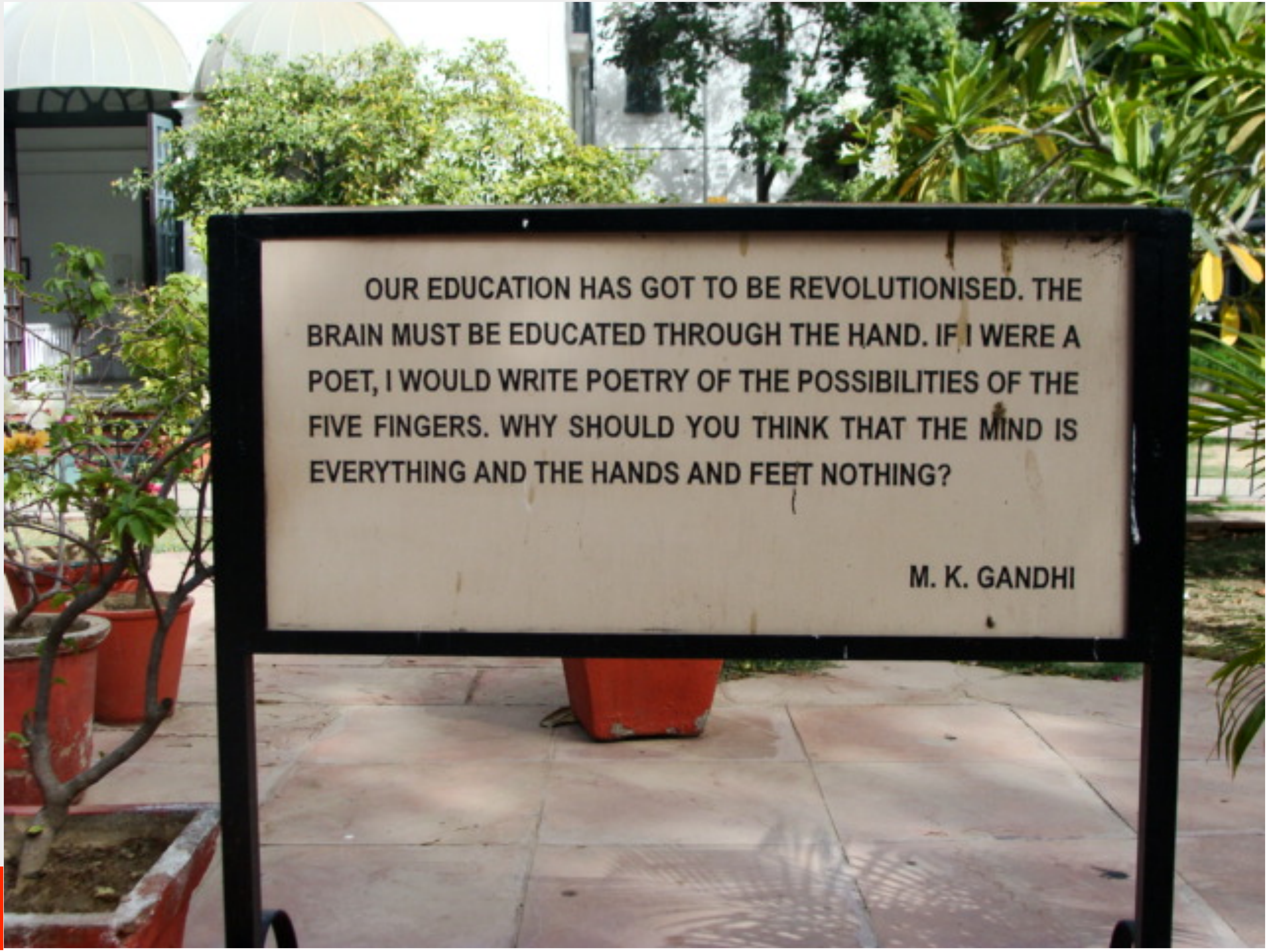
# René Descartes **1569 - 1650**



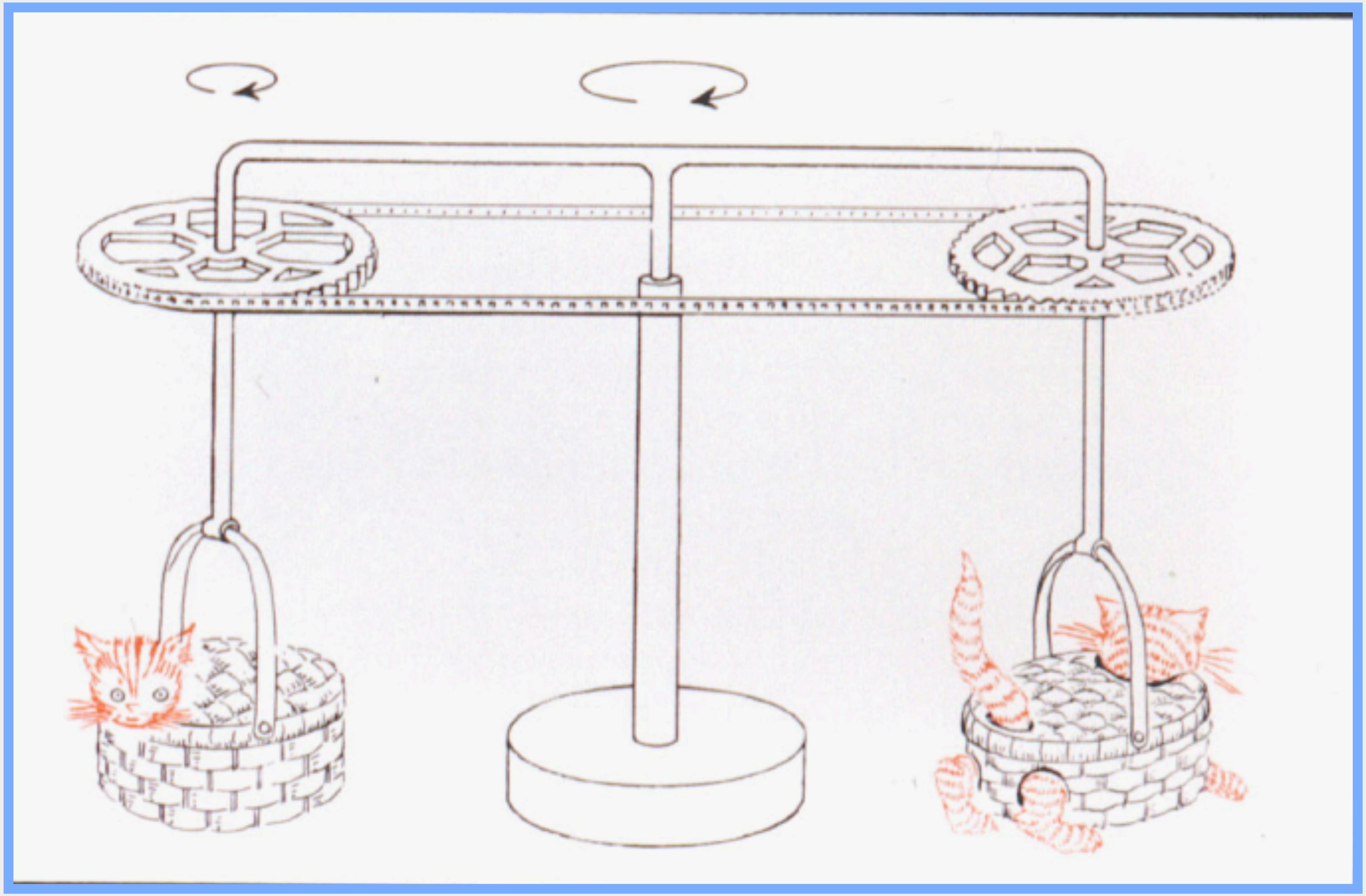

*…Animal spirits is united to the pineal gland, by the aid of which* ***the mind is enabled to feel all the movements which are set going in the body, and also external objects,*** *and which the mind by a simple act of volition can put in motion in various ways (De homine, 1662)*

# The Sensory-motor Loop



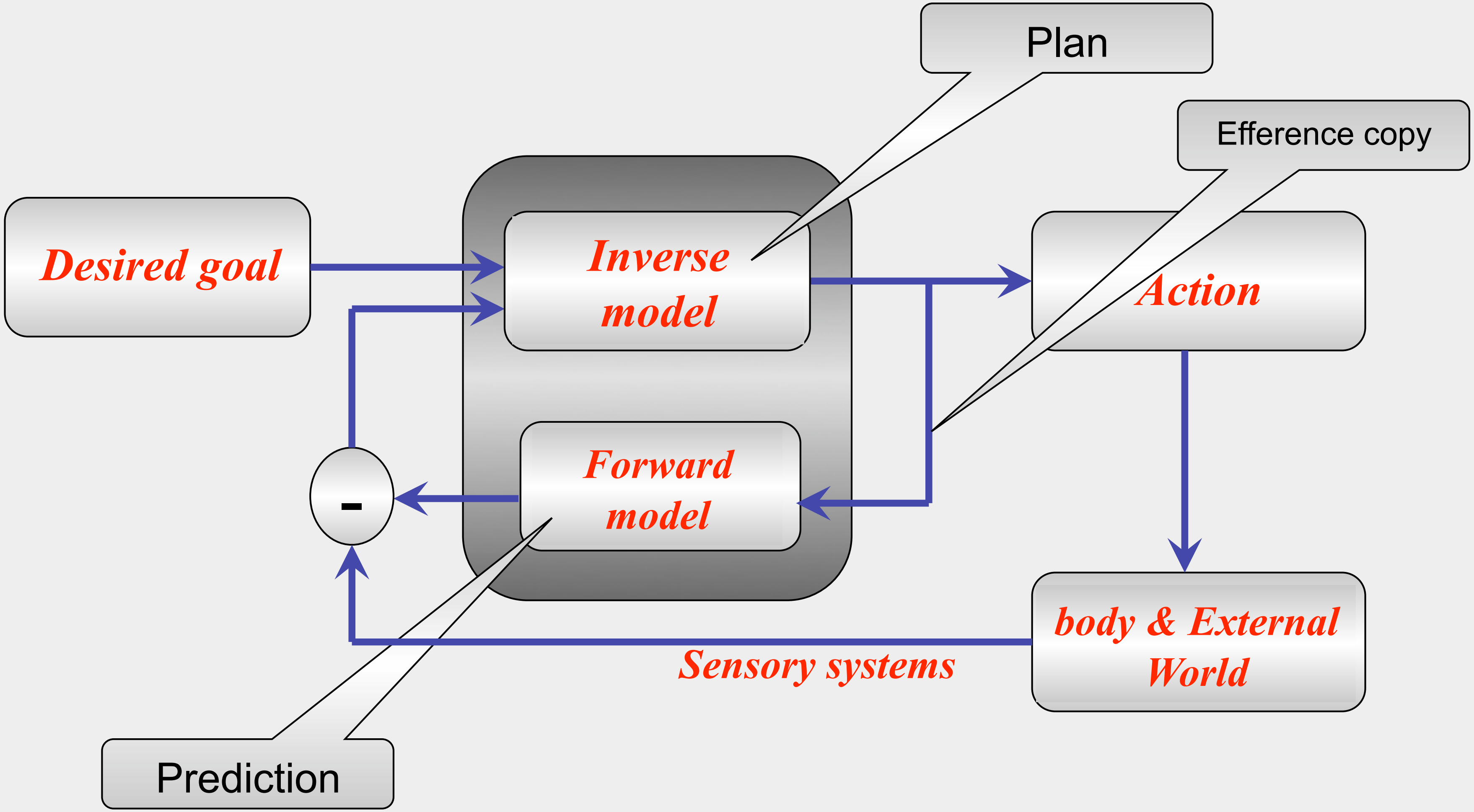

OUR EDUCATION HAS GOT TO BE REVOLUTIONISED. THE BRAIN MUST BE EDUCATED THROUGH THE HAND. IF I WERE A POET, I WOULD WRITE POETRY OF THE POSSIBILITIES OF THE FIVE FINGERS. WHY SHOULD YOU THINK THAT THE MIND IS EVERYTHING AND THE HANDS AND FEET NOTHING?
M. K. GANDHI

# *Action is essential for learning  and perception*



*Hein and Held 1969*

# Modeling the Action-Perception Loop: "Internal Models"




*Lalazar and Vaadia, Current Opin. Bilo. 2009*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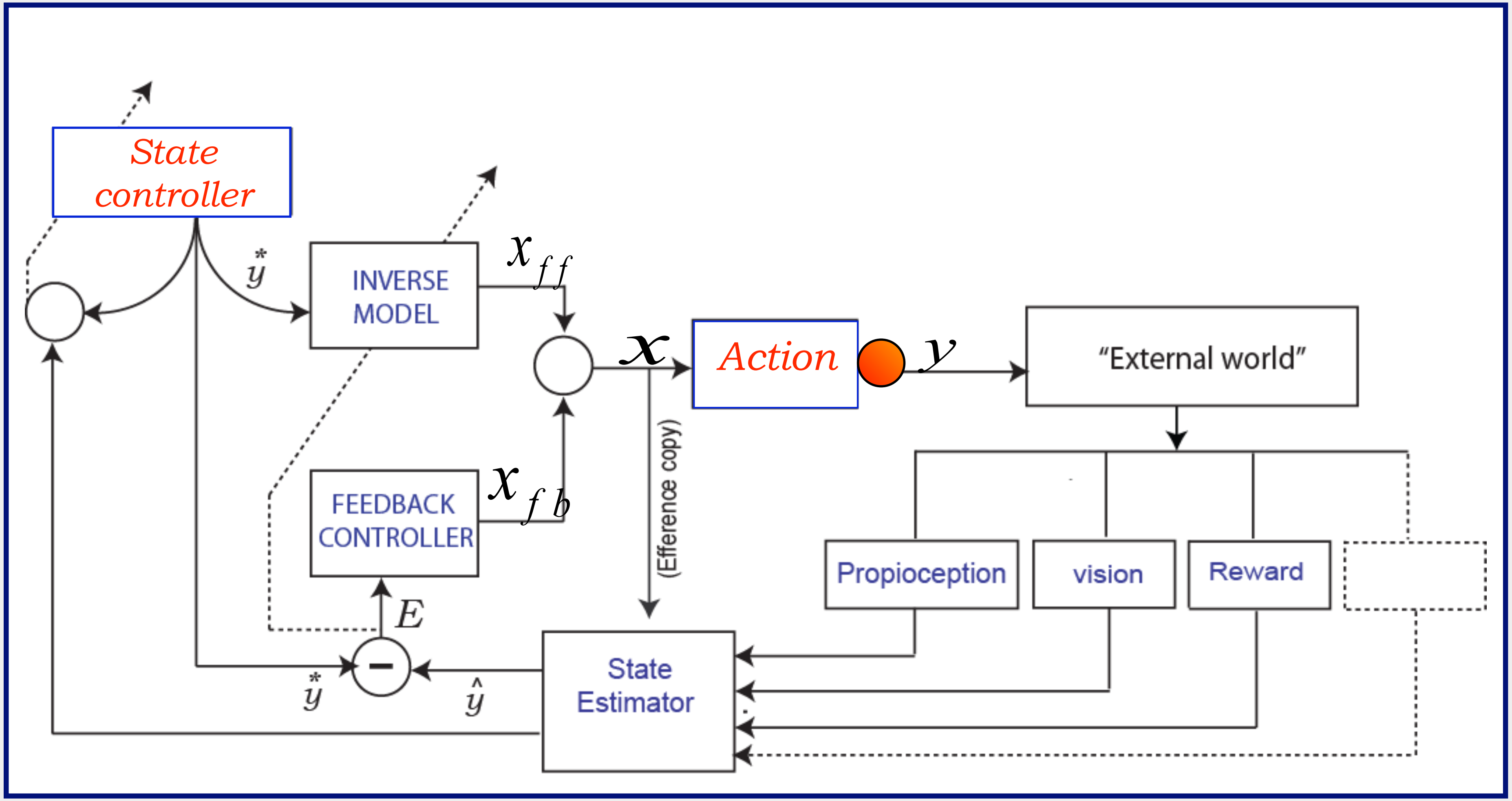
# The Significance of Previous Knowledge

# Action-perception loop




$y^*$ - Desired State

$y$ - Actual state

$\hat{y}$ - Estimated state

$x$ - Neural 'Commands'

$x_t$ Neuronal activity

$y_t$ Behavioral state (Action, movement)

# Kalman Filter

$$\hat{y}_t = \underbrace{A\hat{y}_{t-1}}_{\substack{\text{Predictor of } y_t \\ \text{(Based previous state} \\ \text{alone)}}} + \underbrace{K_t}_{\text{Kalman Gain}}\underbrace{(X_t - HA\hat{y}_{t-1})}_{\substack{\text{Error of predicted current} \\ \text{observation}}}$$

$\hat{y}_t$ Current state

$\hat{y}_{t-1}$ Previous state

$X_t$ Set of current observations

$A$ Weights matrix to predict the current state, based only on previous state (s)

$K_t$ Kalman Gain

$H$ Weights matrix to estimate the expected observation, based on the current state

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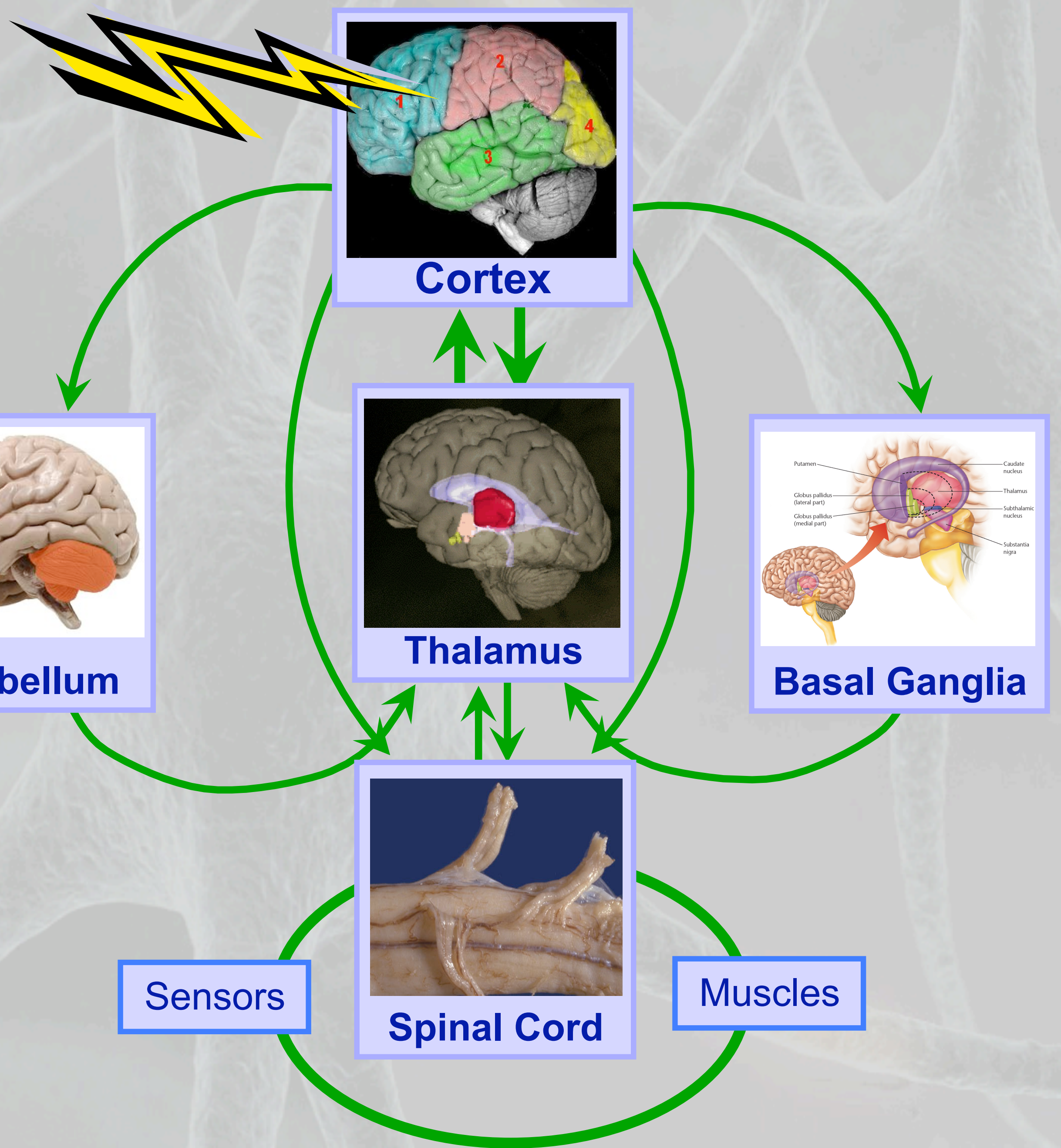
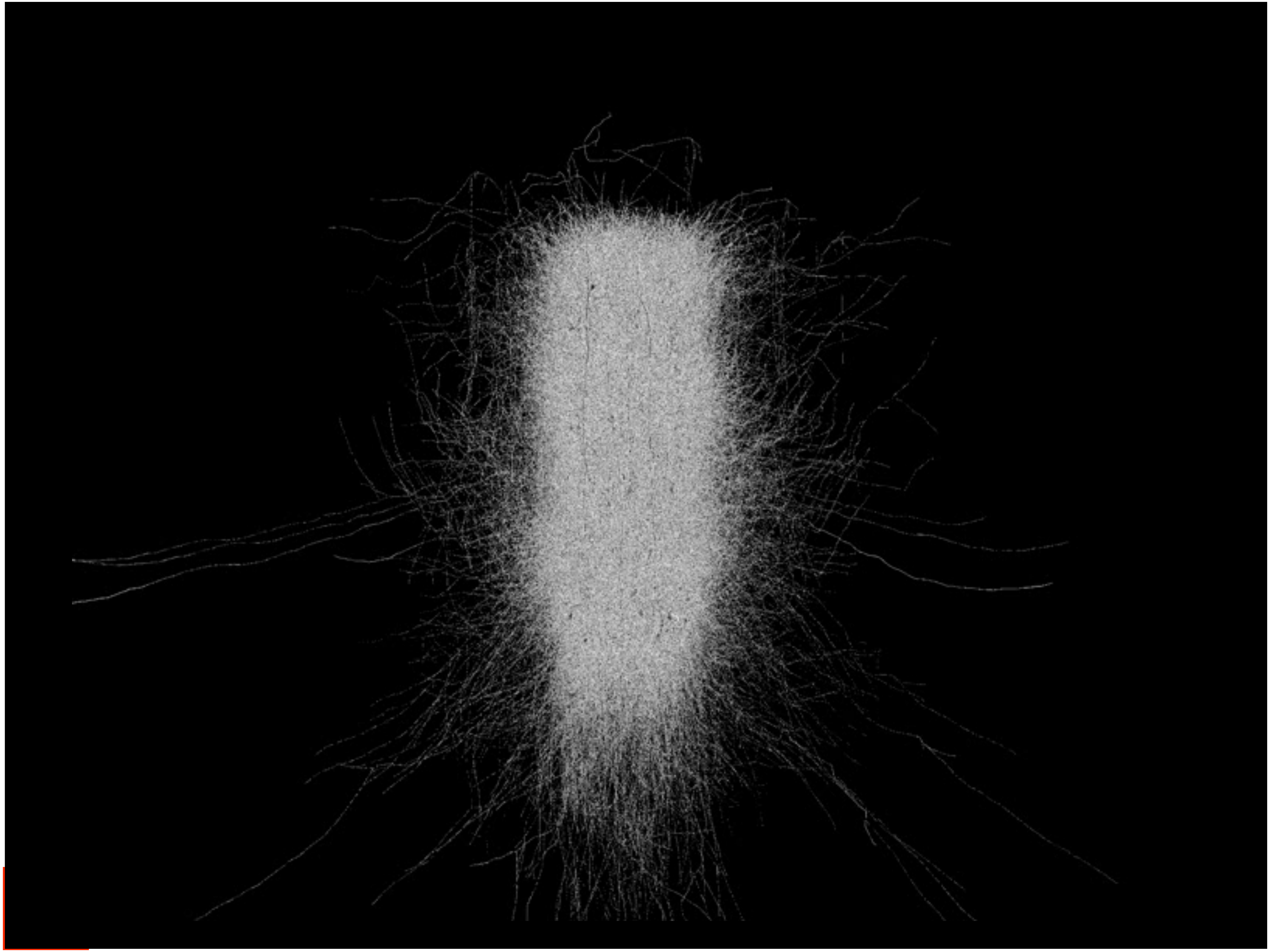
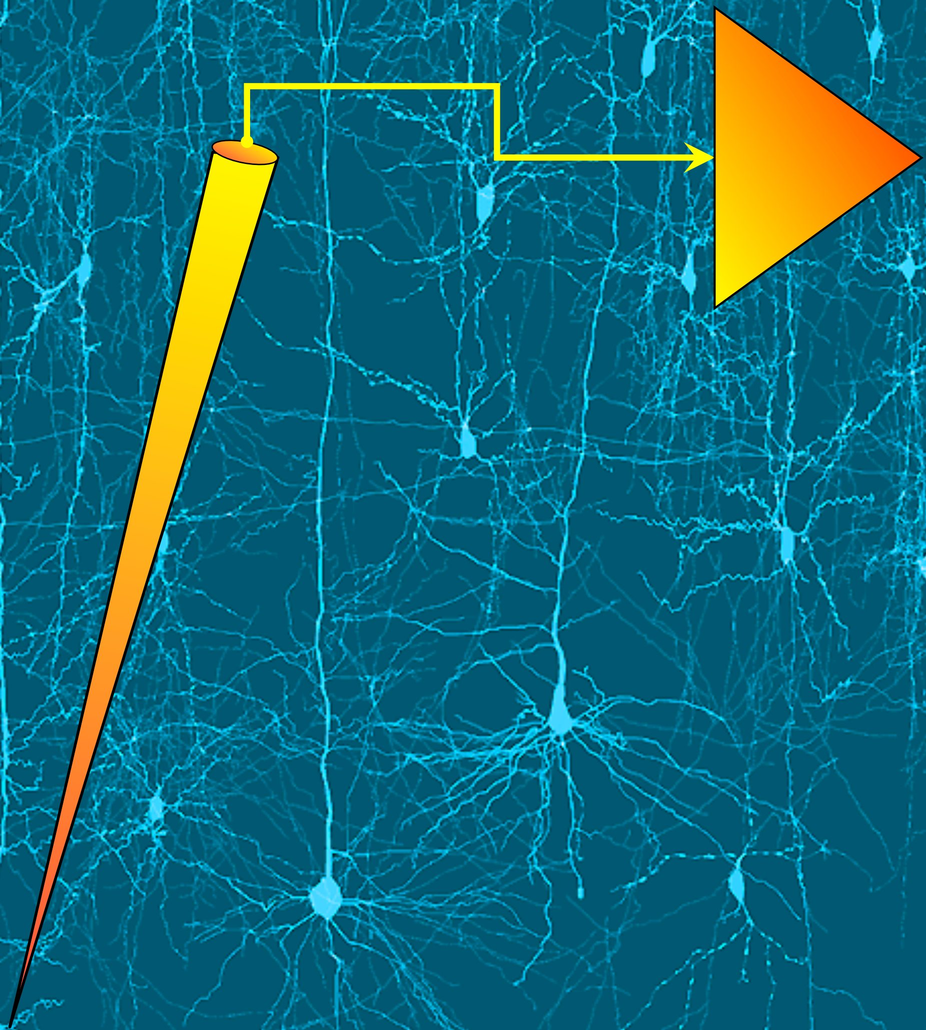
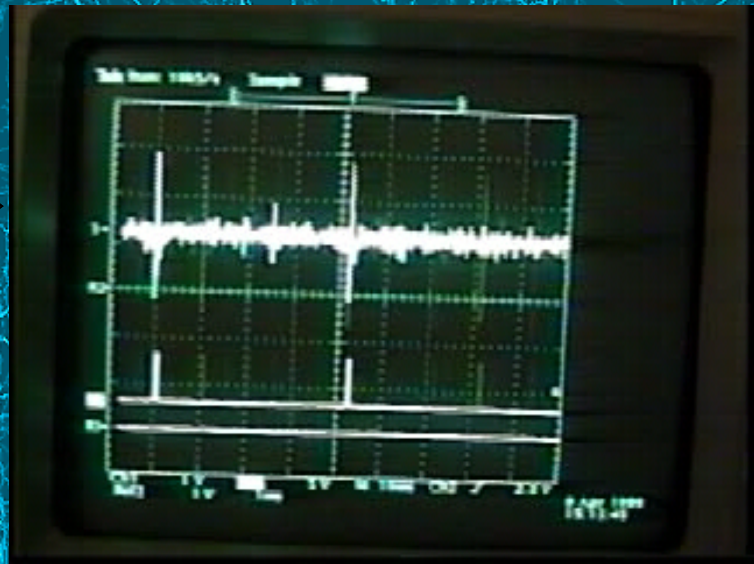
# *Billions of nerve cells in many brain regions orchestrate behavior*





# Single Units Recordings

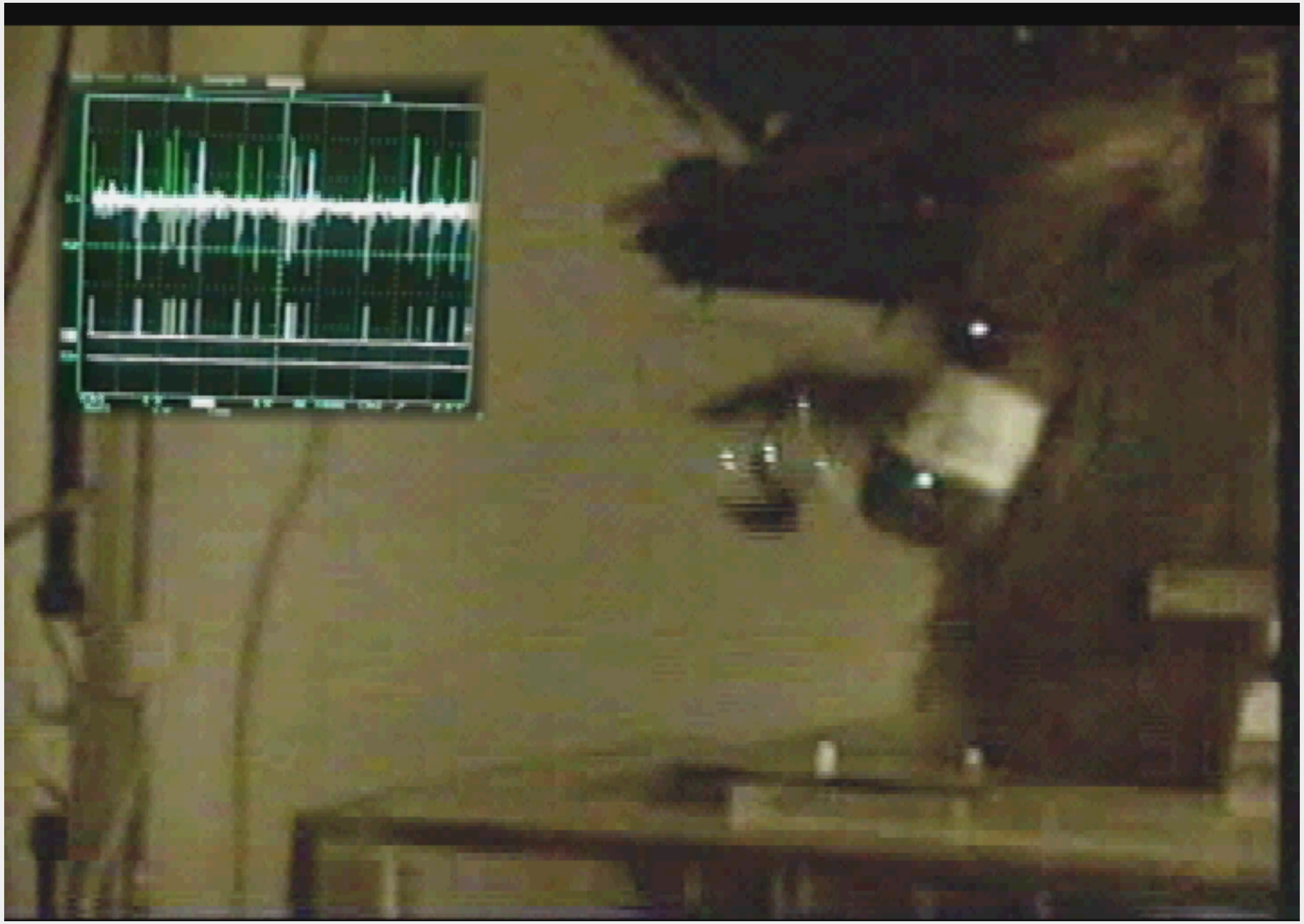




Recording by: A.B. Schwartz

(Background: H. Markram

# *The Voice of a single neuron in motor cortex*



*By: Dr. Andrew Schwartz*

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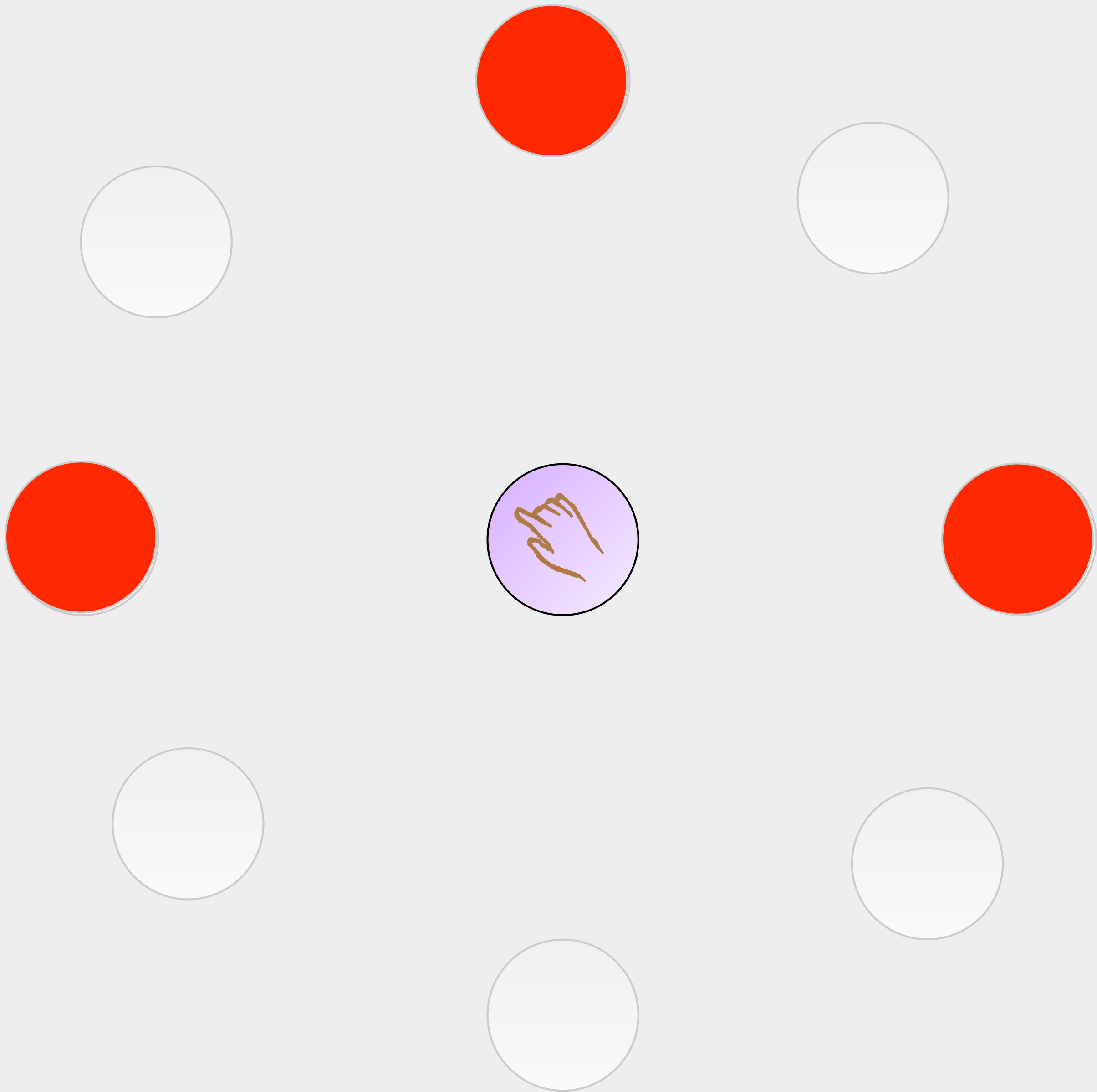
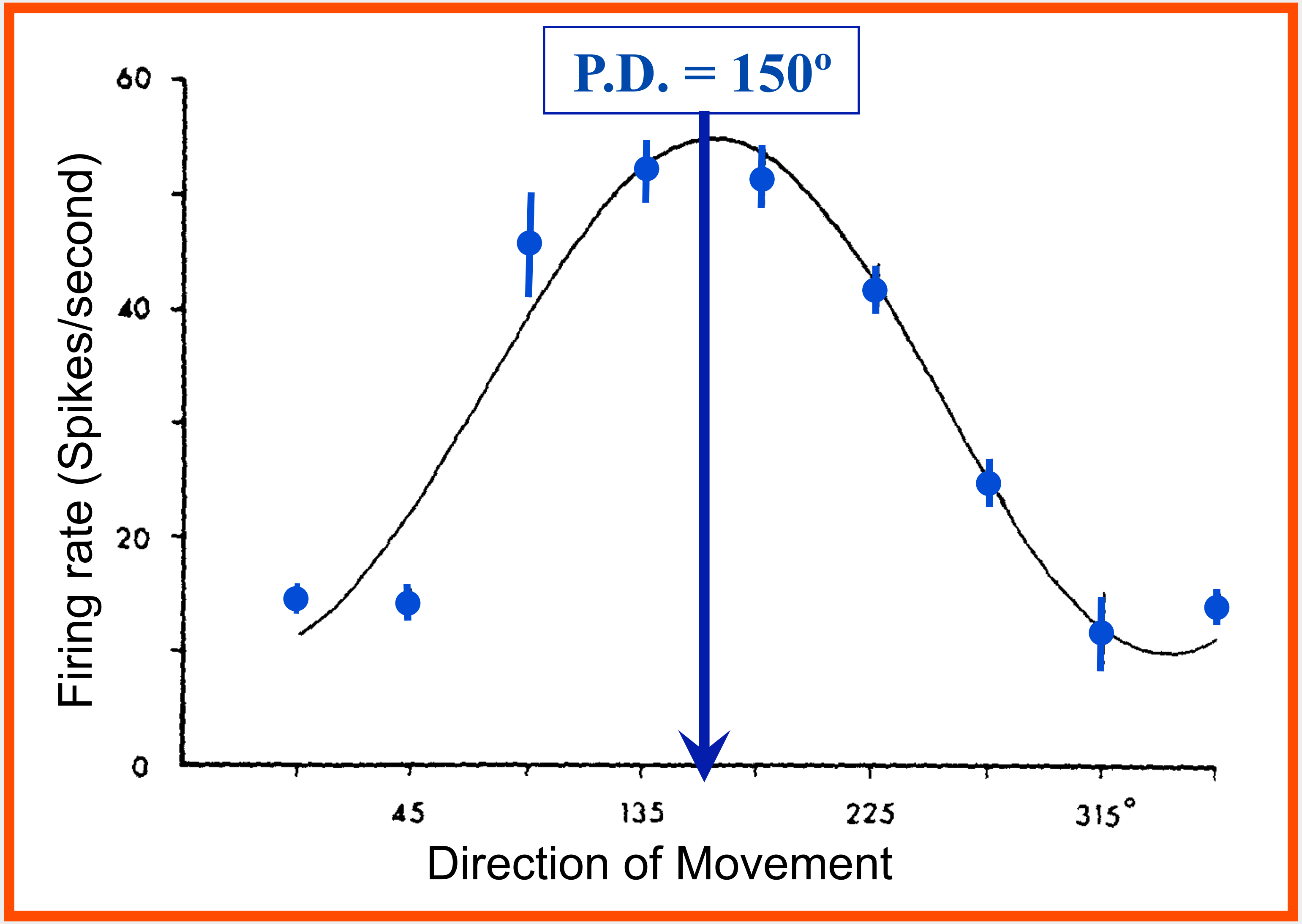
# The "Center Out" Task



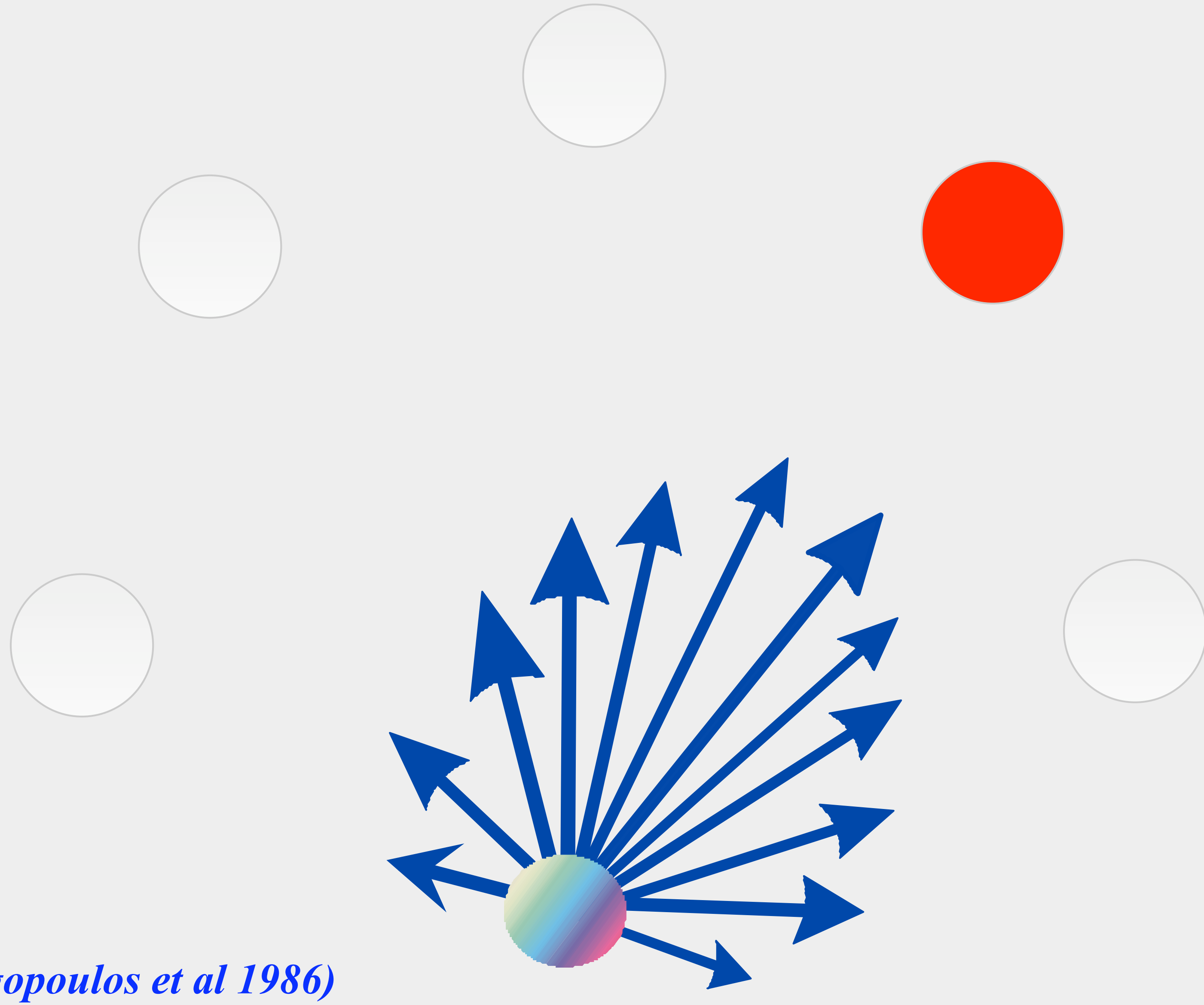
# *Directional Tuning of Single cells in motor cortex*




*(Georgopoulos et al 1982)*

# Hypothesis:

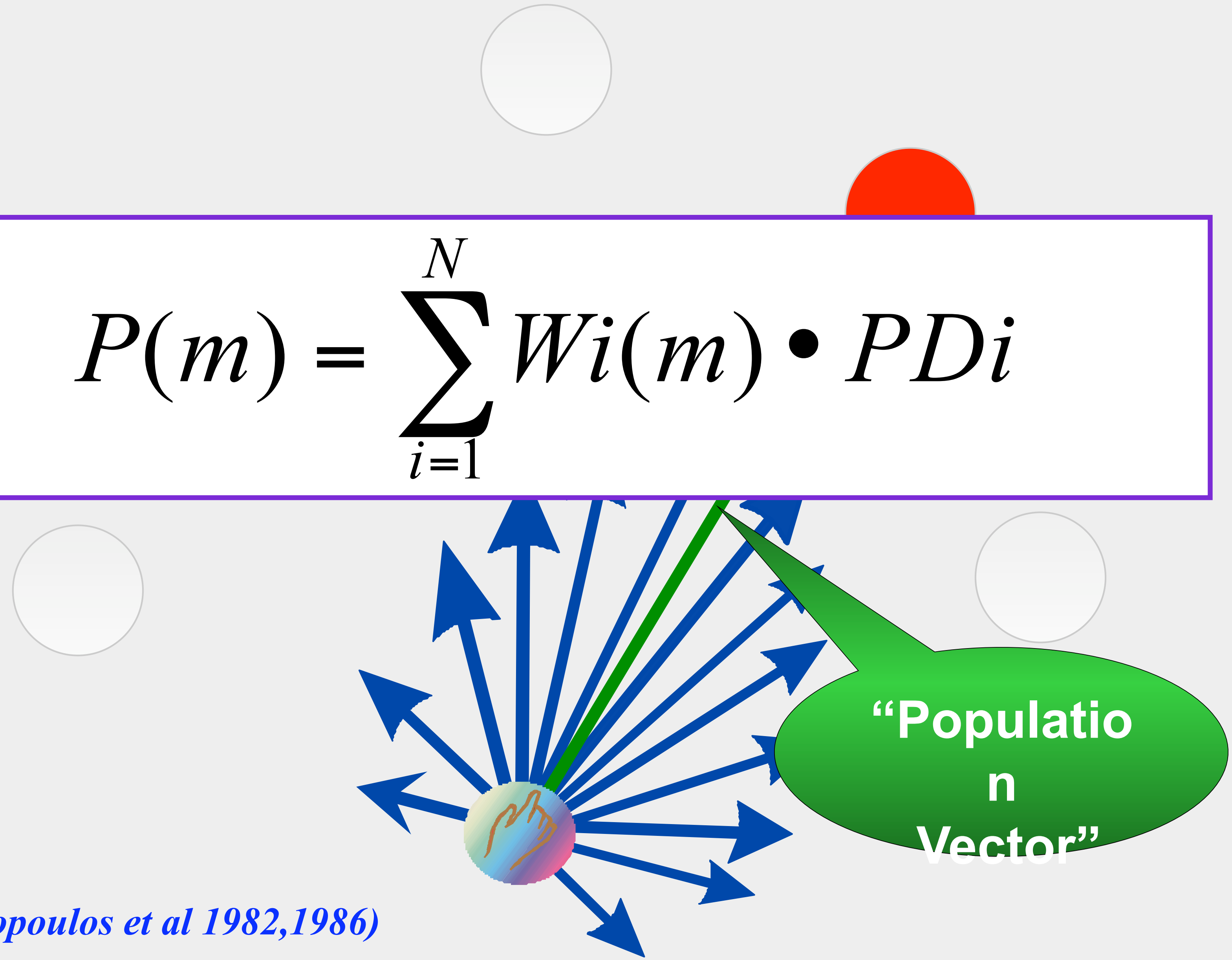
## *1.Each neurons has a “preferred direction”*



*(Georgopoulos et al 1986)*

# 2. A Population of neurons encodes accurately movement direction

$$P(m) = \sum_{i=1}^{N} Wi(m) \bullet PDi$$




*(Georgopoulos et al 1982,1986)*

## Simultaneous Recordings allow on-line inference of movements from Neuronal Activity: Example : OLE* / Linear Regression

Movement $y$ at time $t$ where $\mathbf{X}$ is the matrix of units activity and $\mathbf{w}$ is a set of impulse response functions (weights).

$$\hat{y}(t) = \mathbf{b} + \sum_{\tau,i} w_i(\tau)\mathbf{X}_i(t-\tau) + \varepsilon(t)$$

$X$ = observed neural activity

$y$ = movement (unobserved during inference)

$\mathrm{w}_{i,\tau}$ = weights for each neuron and each time bin

$\varepsilon$ = error (to minimize)

* Salina and Abbott: Vector reconstruction from firing rate 1994



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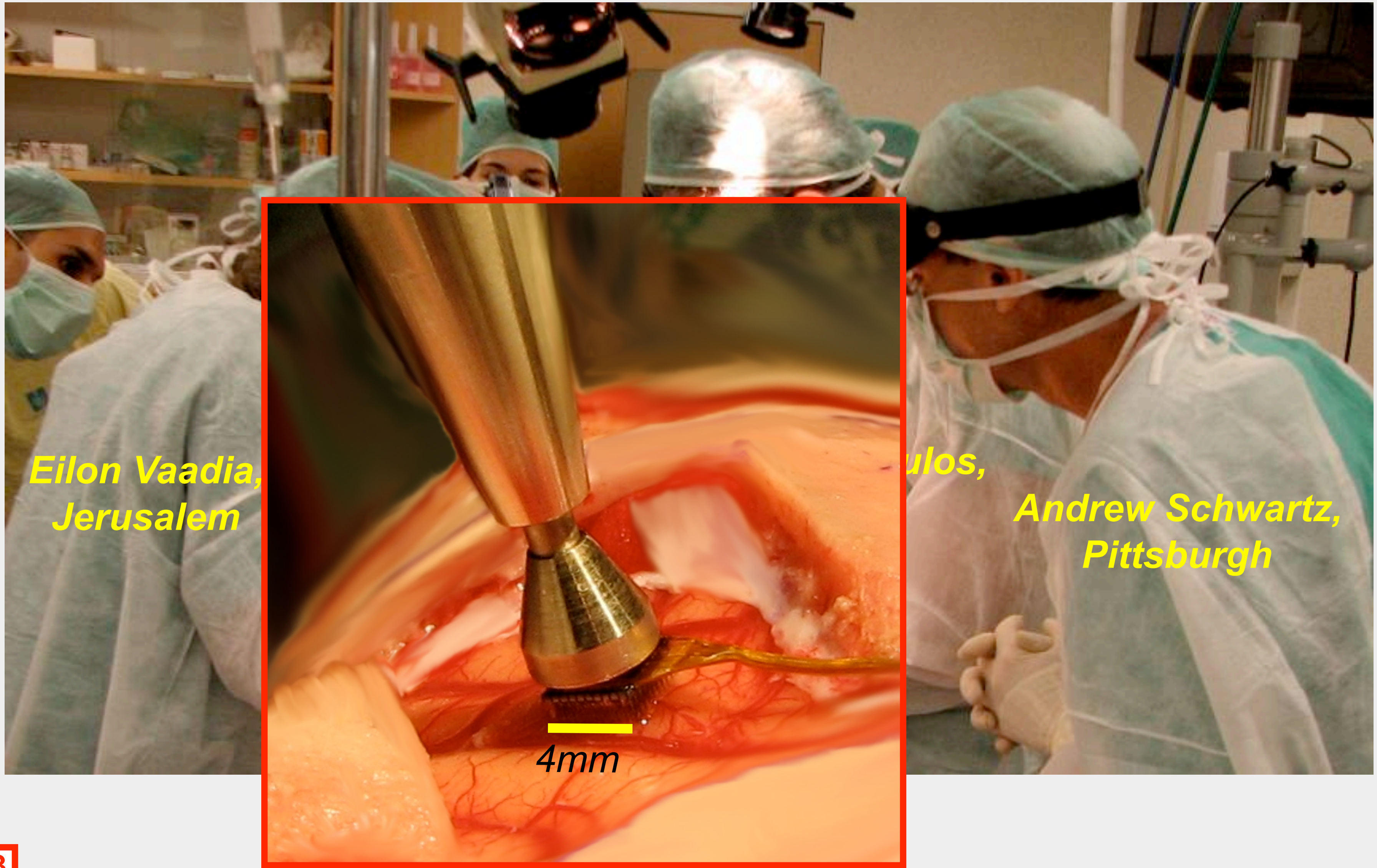
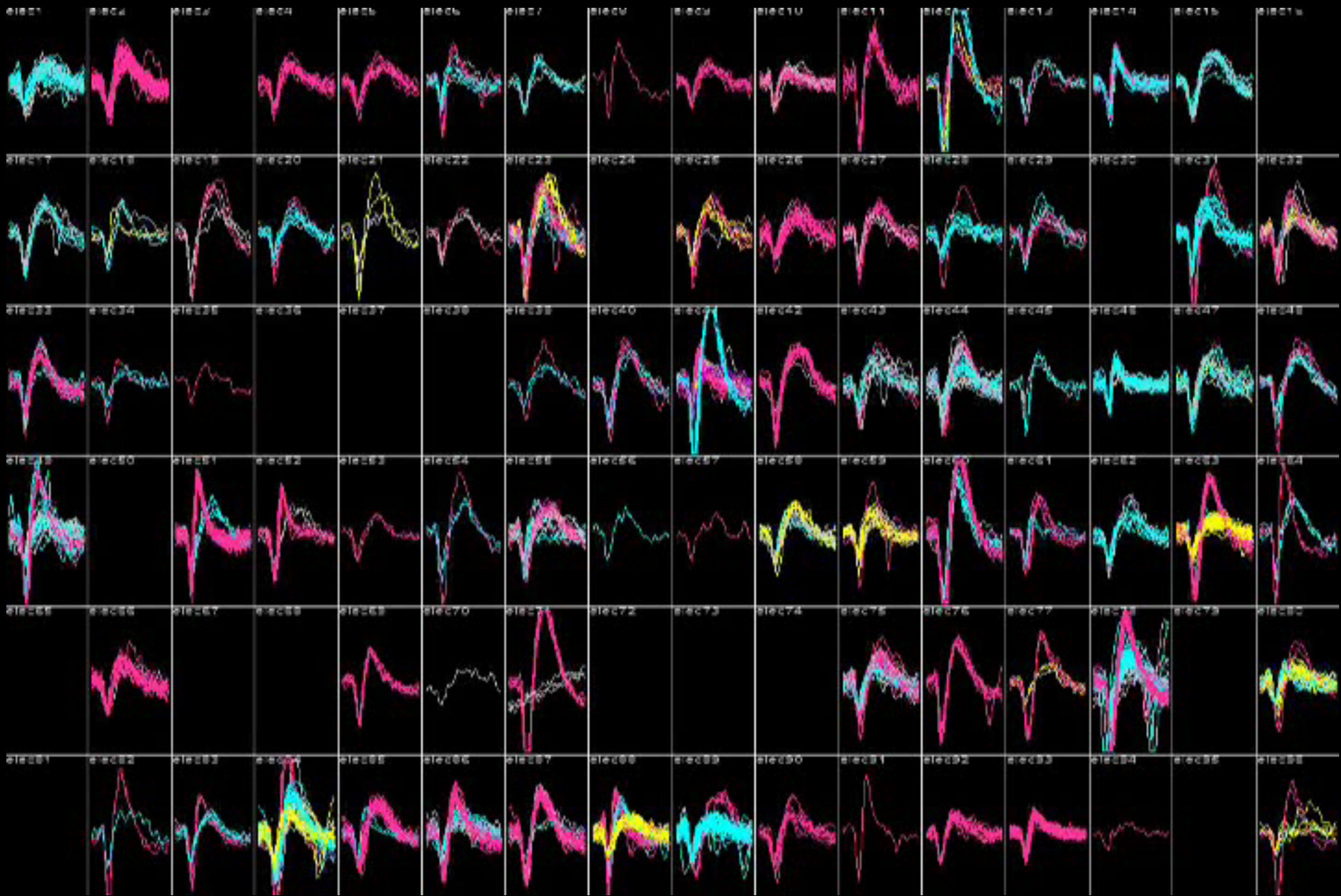
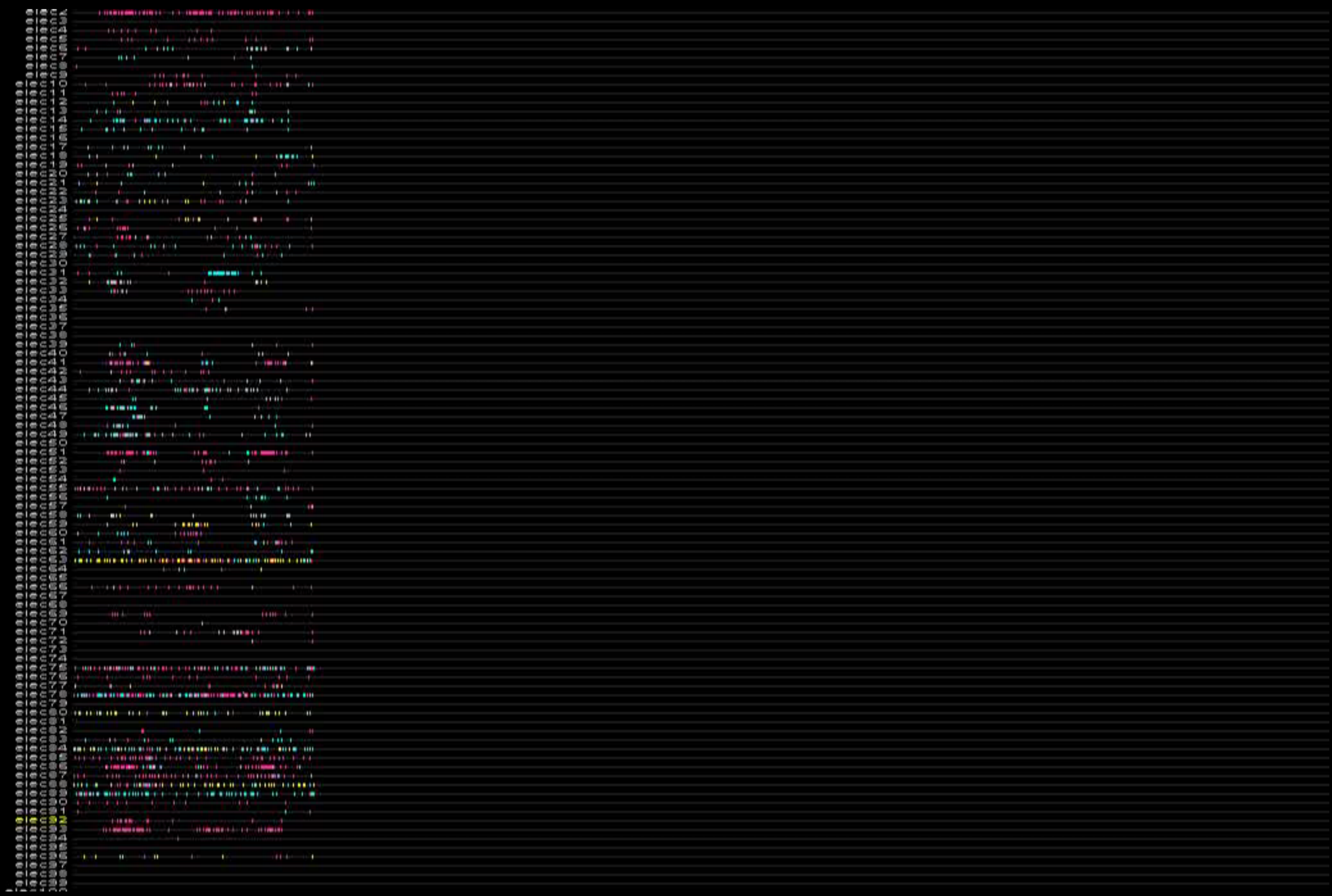
# *Multi channel recordings of brain signals*



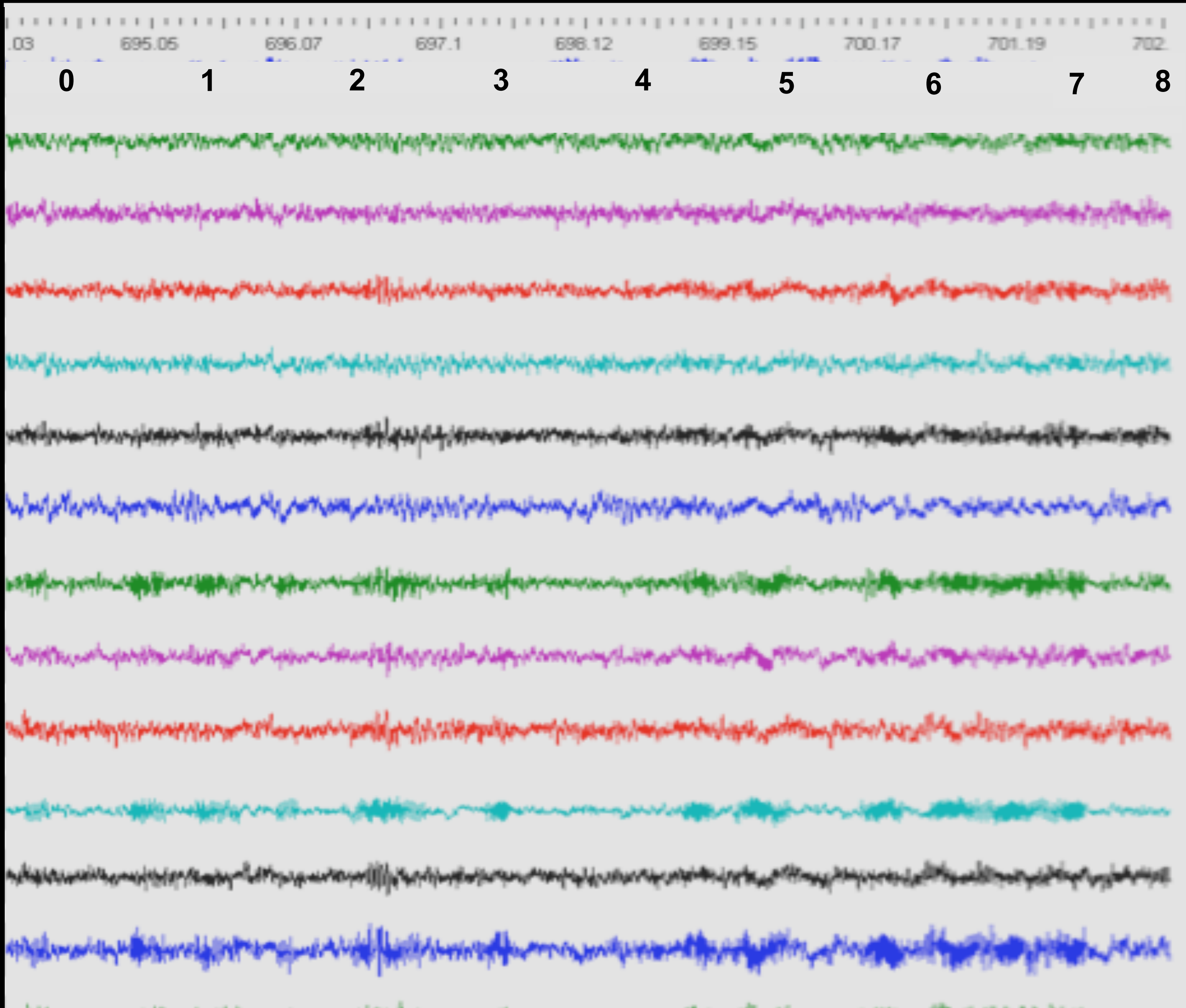
# *Simultaneous Recordings and Spikes Sorting*



## *Simultaneous Recordings of ~200 Spikes Channels*



# Local Field Potentials - LFP



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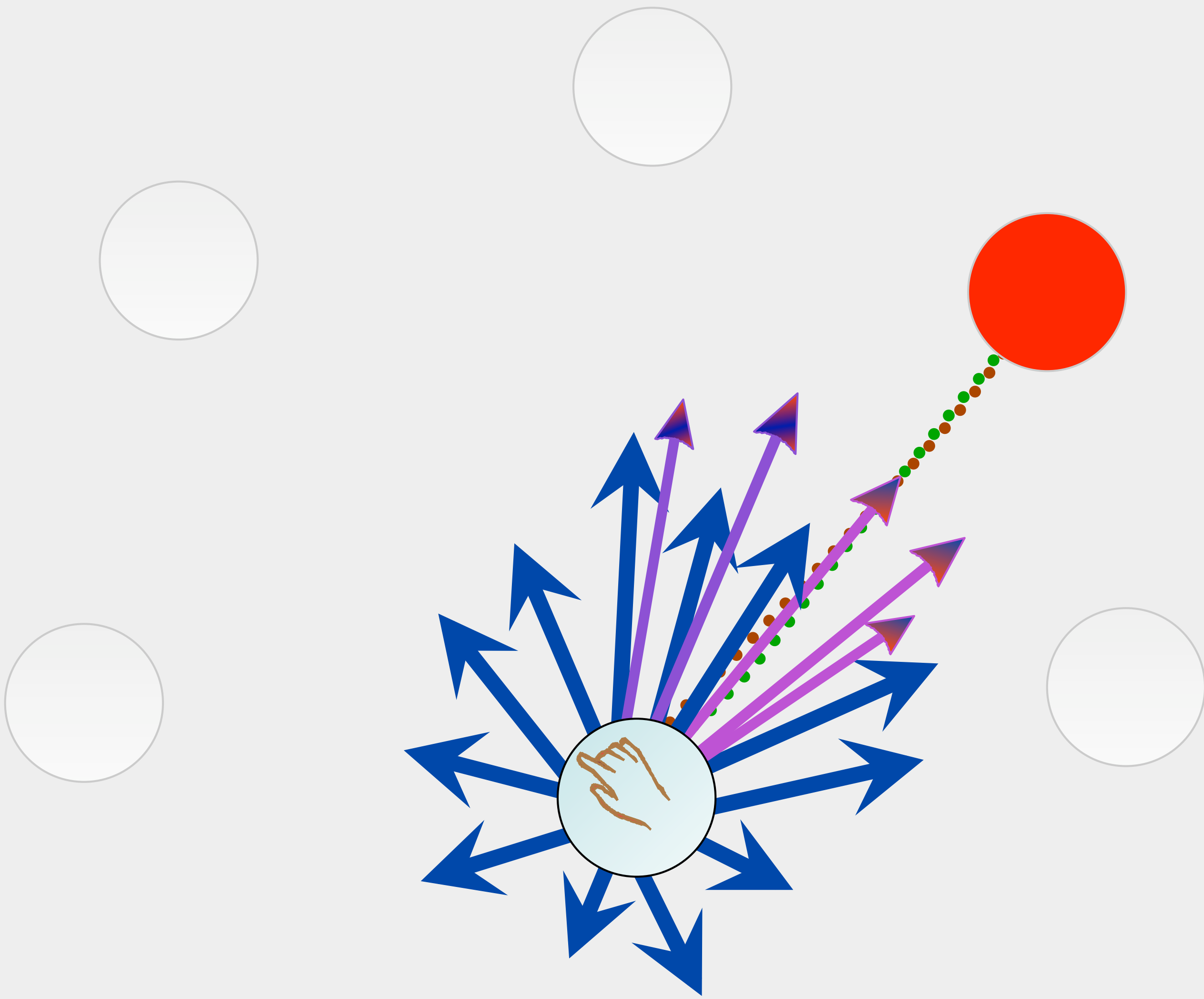
# *Sensorimotor Learning*

- Are tuning properties modulated by learning?
- Can the cells learn new tricks?

Learning is:

1. A tool to investigate how internal models operate and updated
2. A tool in developing Brain Machine interface

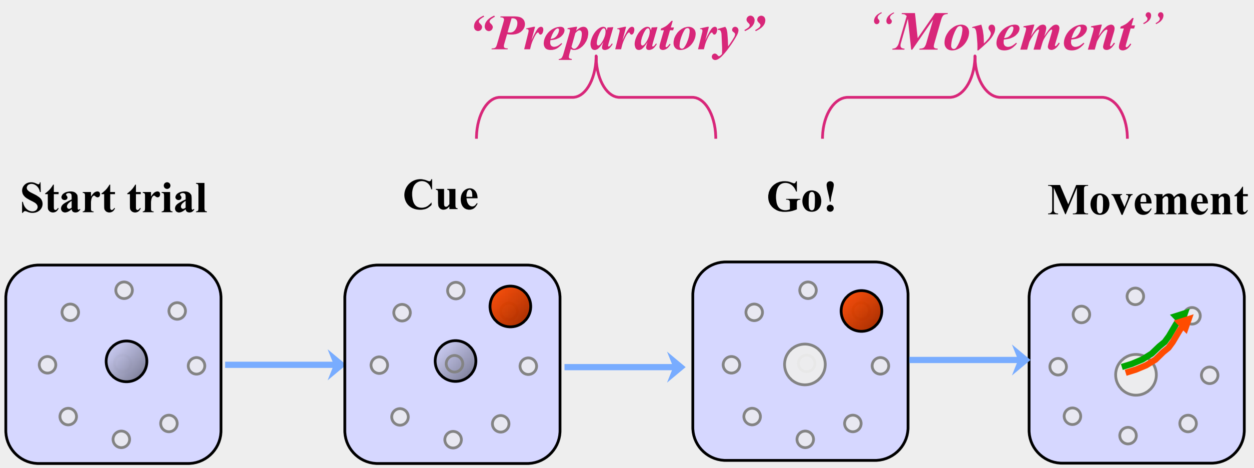
# The hypothesis: The population code is shaped by learning



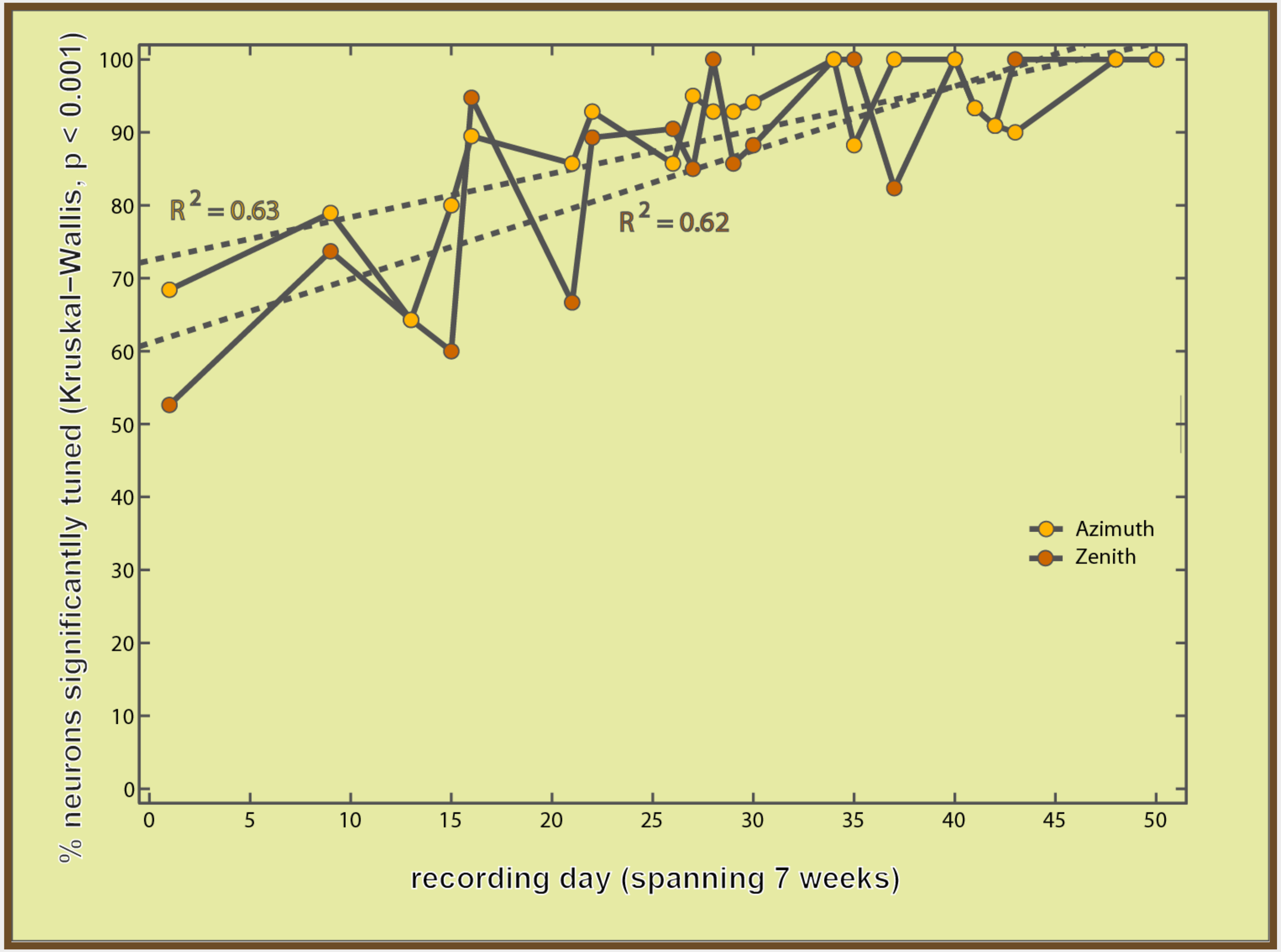
# *Three learning tasks*

1. Learning reaching movements
2. Learning Visuomotor rotation
3. learning arbitrary associations

# *In All Experiments: Delayed Reaching Tasks*

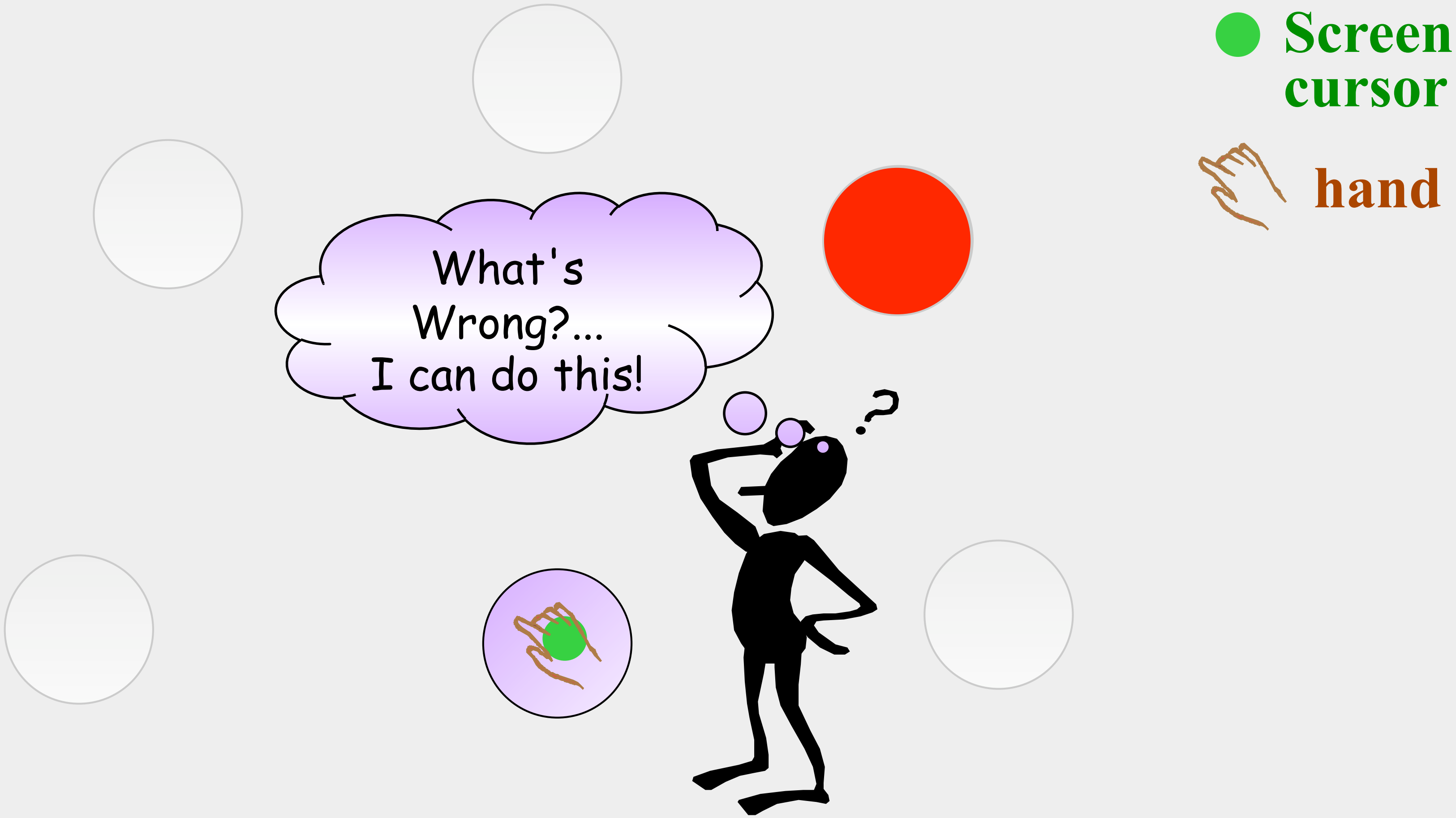


# *1. Learning Reaching: More tuned cells as learning*



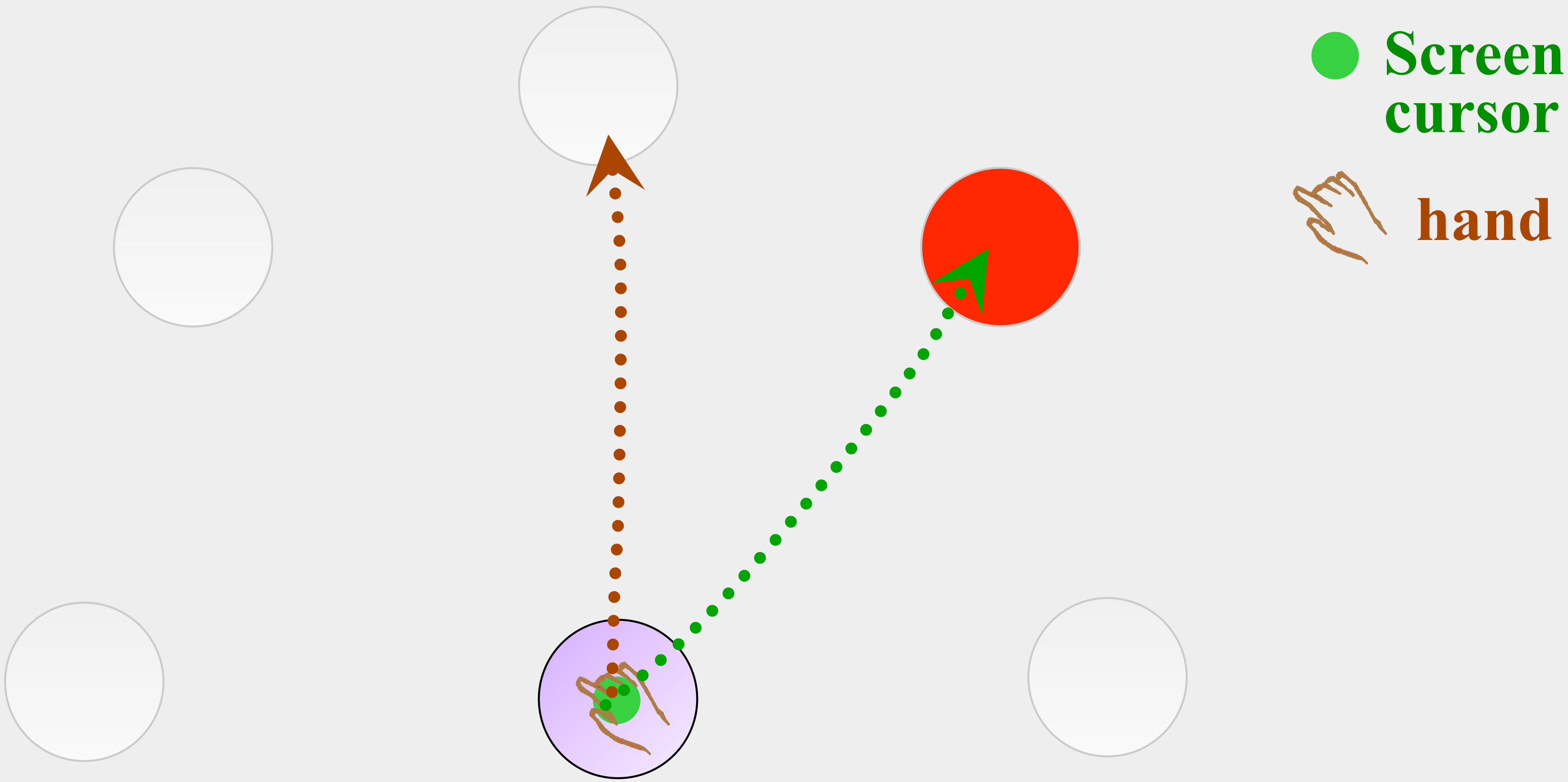

***Lalazar, Shpigelman et.al, Cosine 2008***

# 2. Learning Visuomotor Rotation



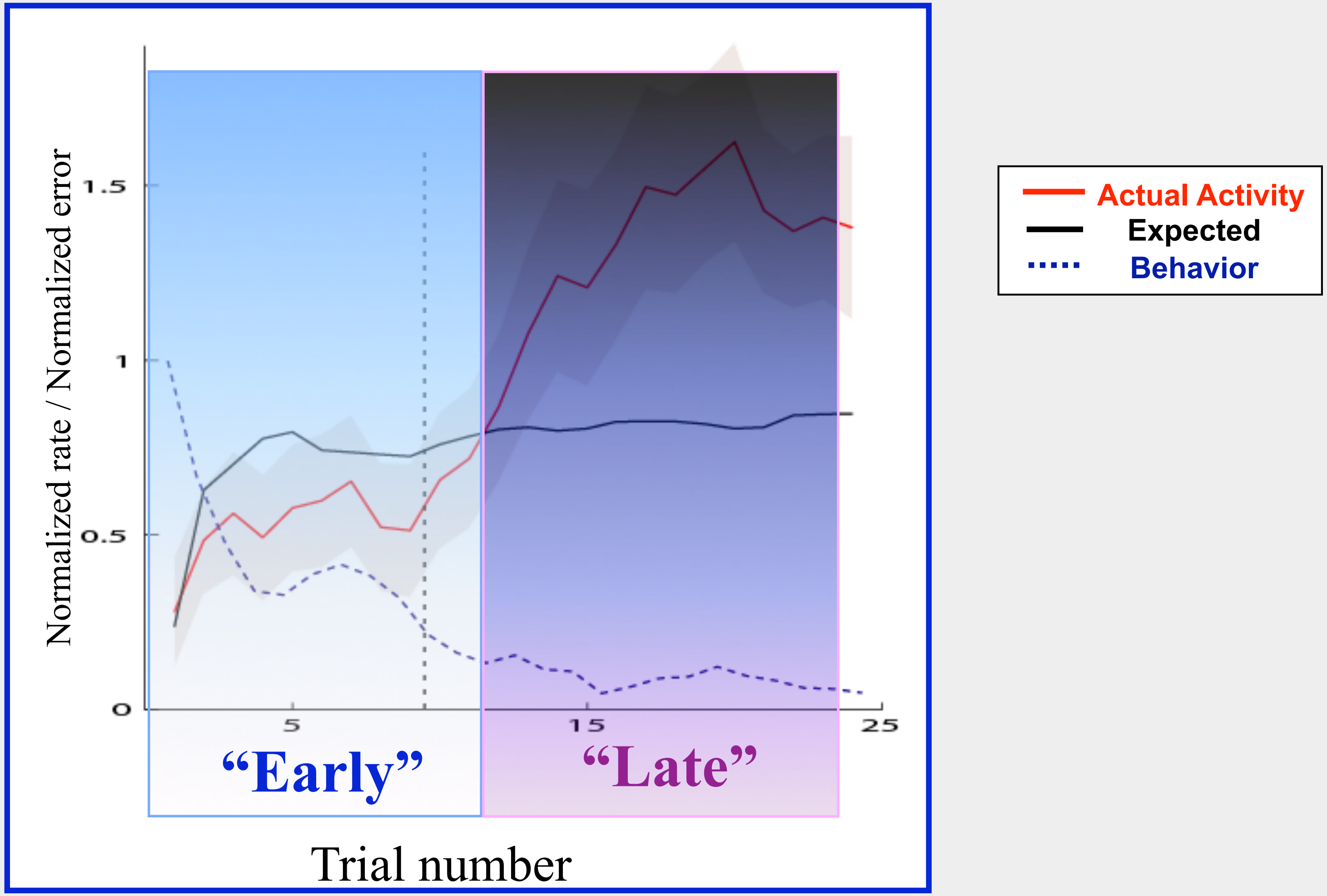

*Study by R. Paz, C. Natan, T. Boraud*

# After learning Visuomotor rotation of 45°




*Two learned directions per recording session !*

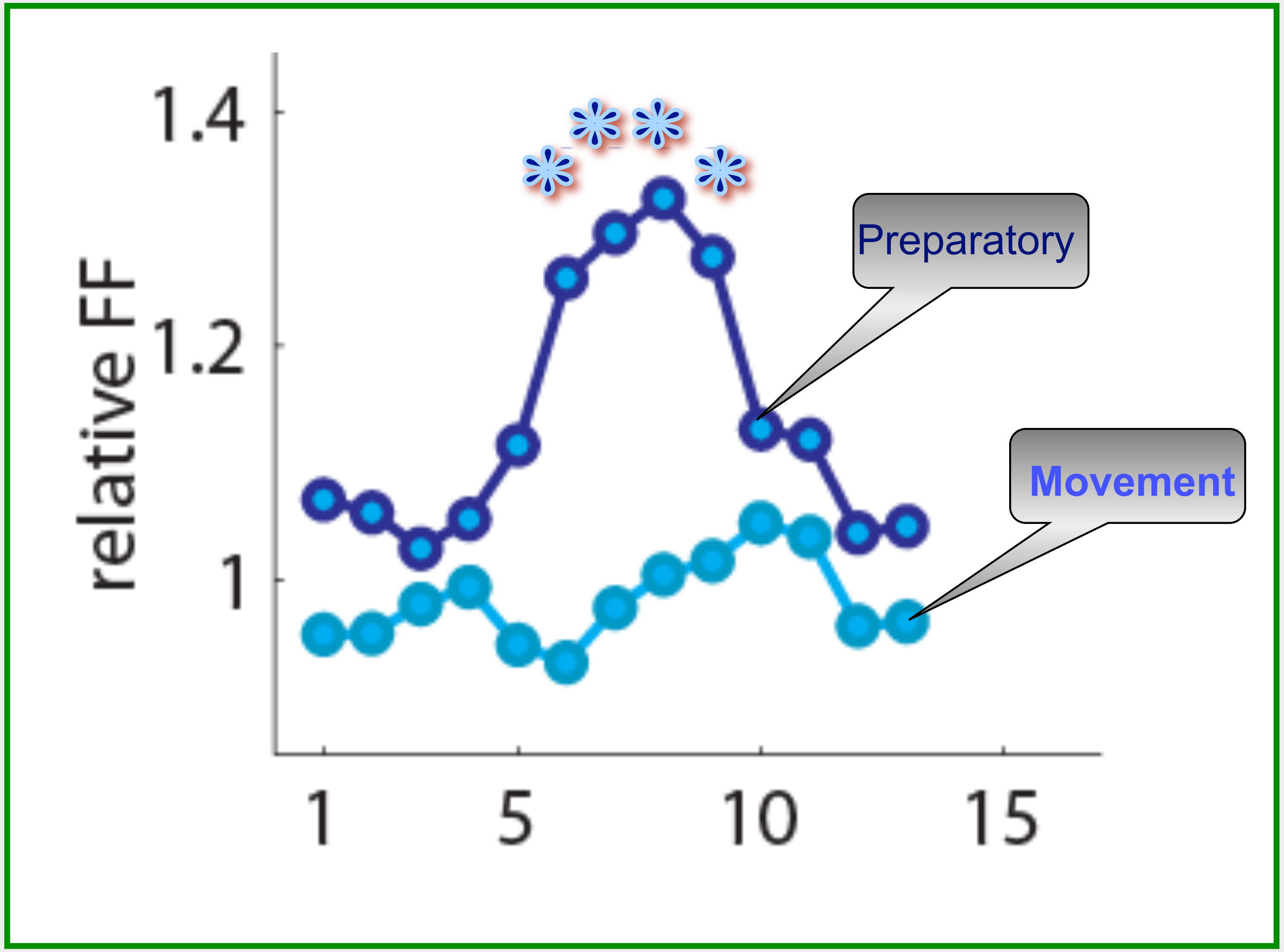
## *Increased firing rate in selected population during learning*
## *Single units Activity changes only in the preparatory period*





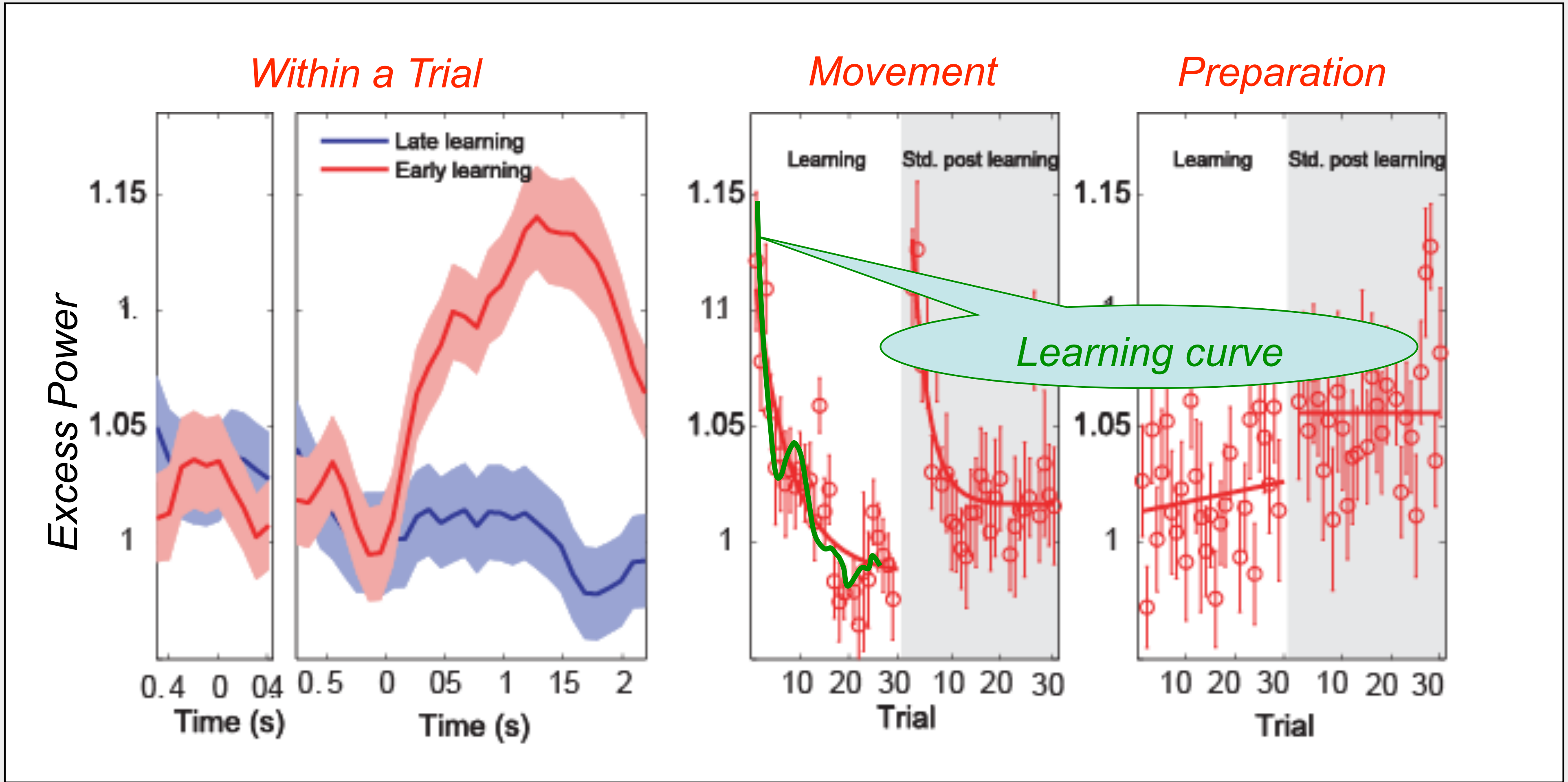
*Paz et al. Nature Neurosc. 2003*

## *Single units Trial-to-Trial Variability : Modulation only in the preparatory period!*




*Yael Madelblat, Paz Vaadia Submitted 2009*

# Modulation of Local Field Potentials
# Gamma Excess – Only During movement execution!





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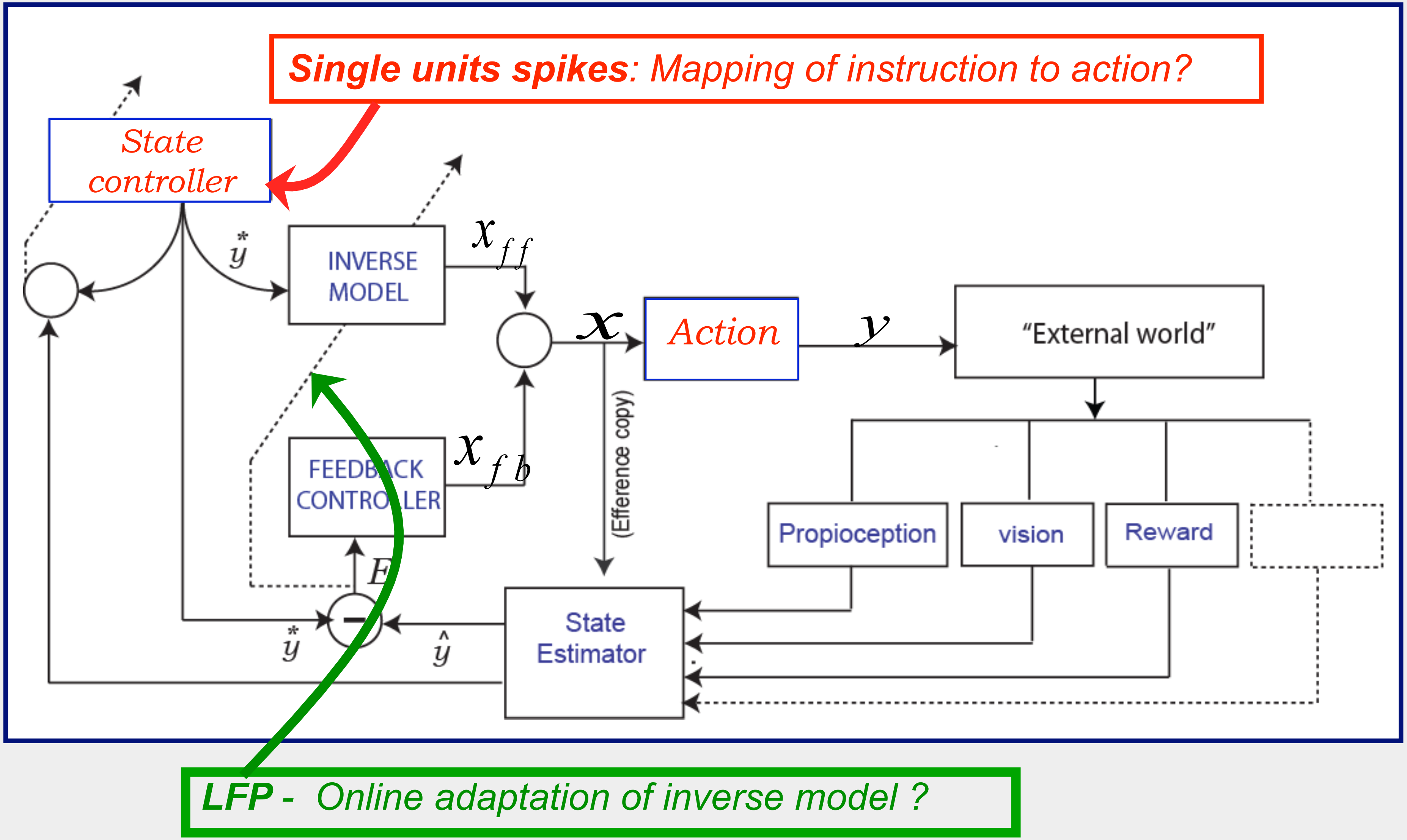
# LFP and Spikes reflect different aspects of Learning?





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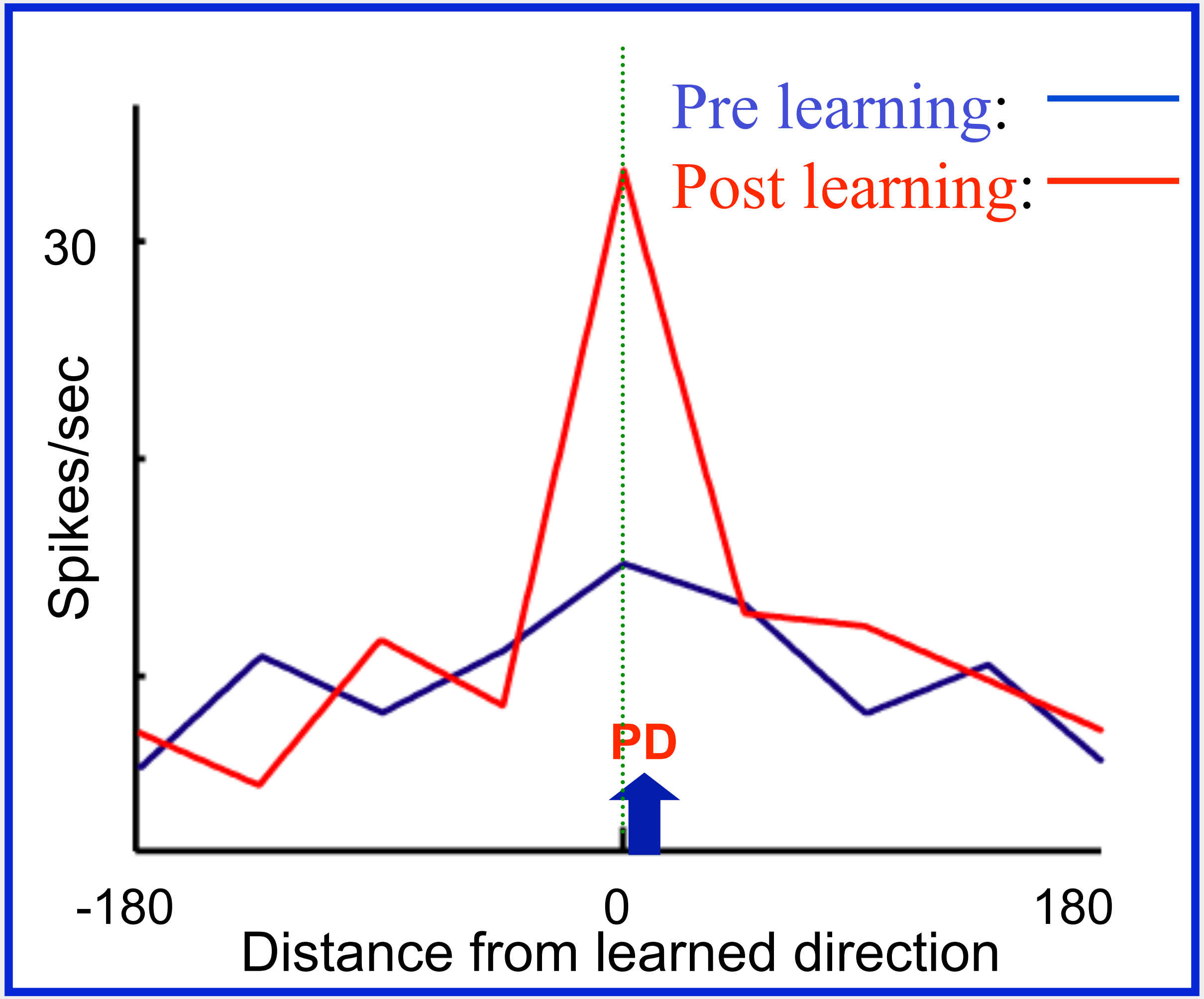
# *After Learning: memory traces?*

Cells change:

- Only near PD
- Only near the learned direction
- Only in preparatory epoch




*Paz et al, Nature Neuroscience, 2003*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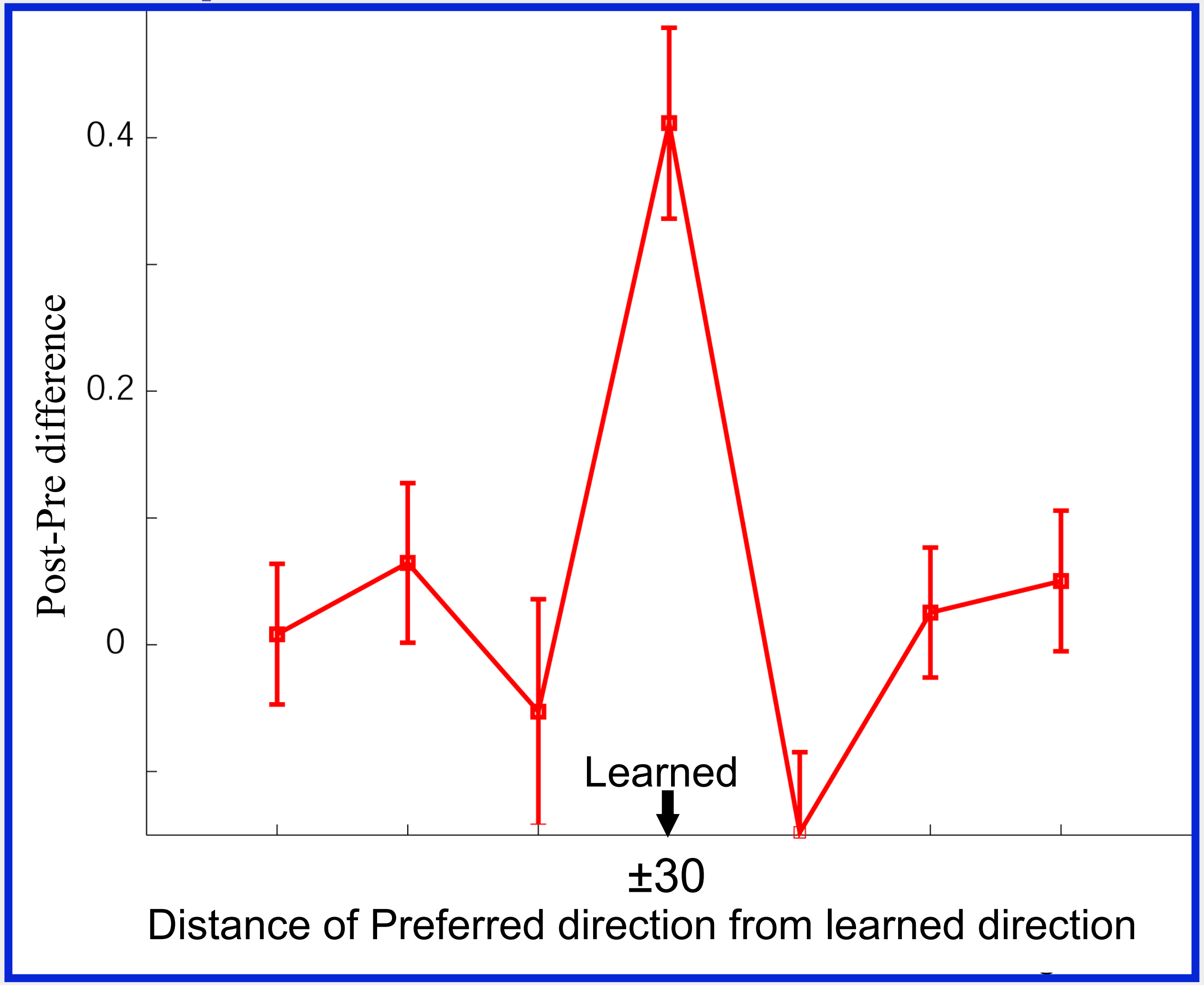
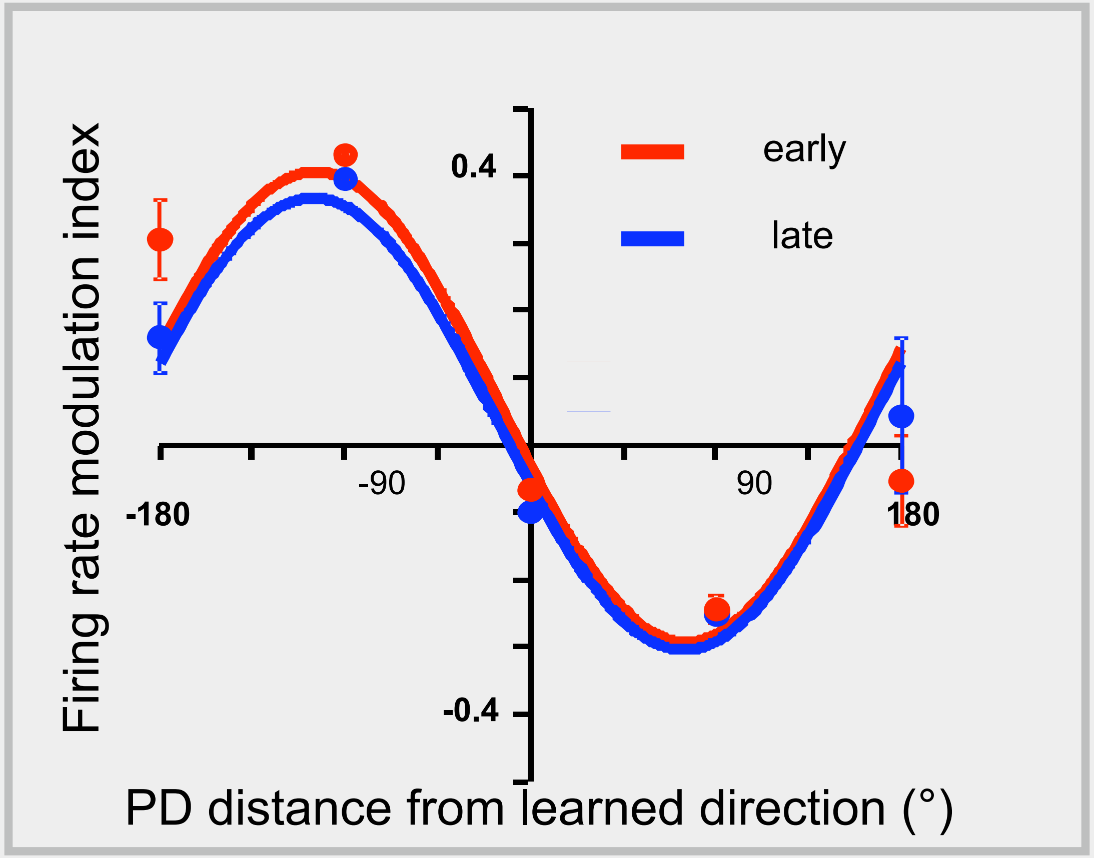
# *After Learning:*
## *Better Representation of Learned movements*




- ***Only Cells with PD near a learned direction change***

# *Force Field Adaptation:*
# *Modulation of the whole population Depending on cells' PDs!*




Mean Modulation Index

Unlike visuomotor rotation:
Cells with PD near learned change less than others!

*Fritzie Arce with: Ithai Novick and Yael Mandelblat-Serf 2009*



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## *Intermediate Conclusions*

*These Studies Indicate that:*

1. Learning improves neural encoding
2. We know how to teach the neurons new tricks!

*These notions, are important for*

*Brain Machine interface*

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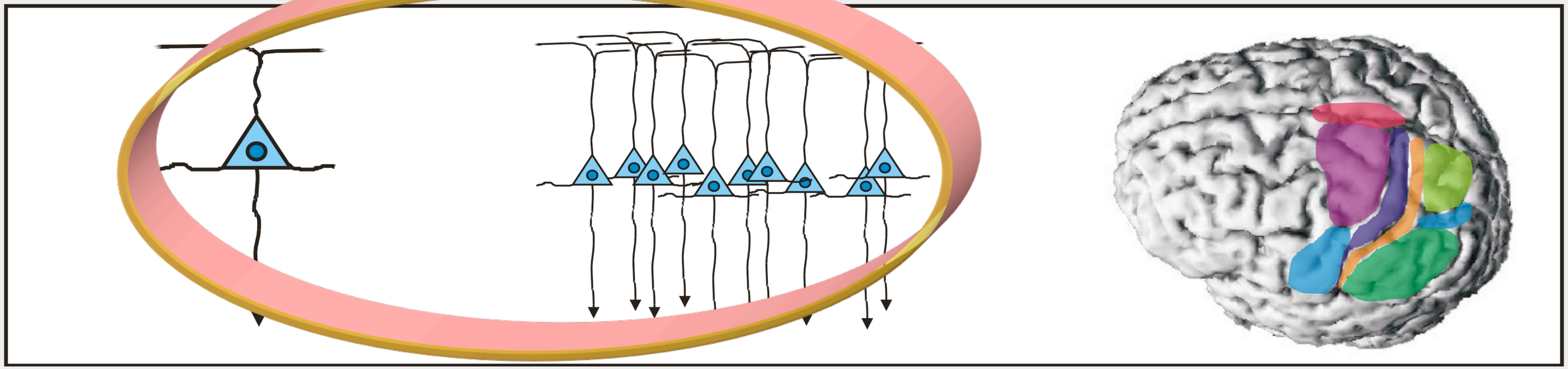
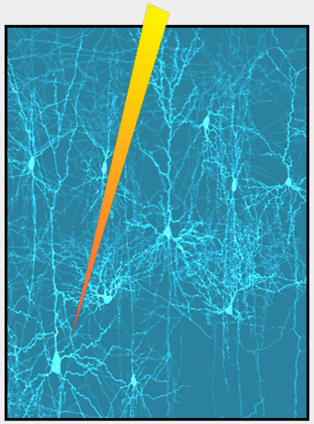
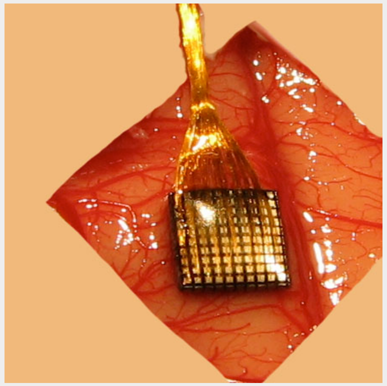
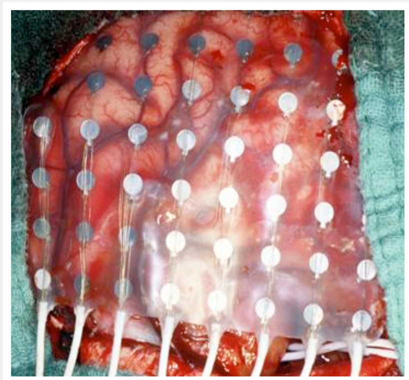
# *Neuronal signals*

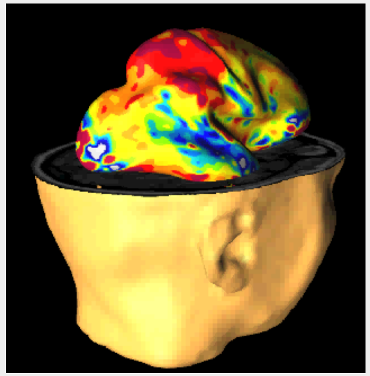
Single Neurons | Local Circuits | Brain Areas











**Action Potentials**

**Extra / Intra Cellular**

**Local Field Potential**

**EcOG**

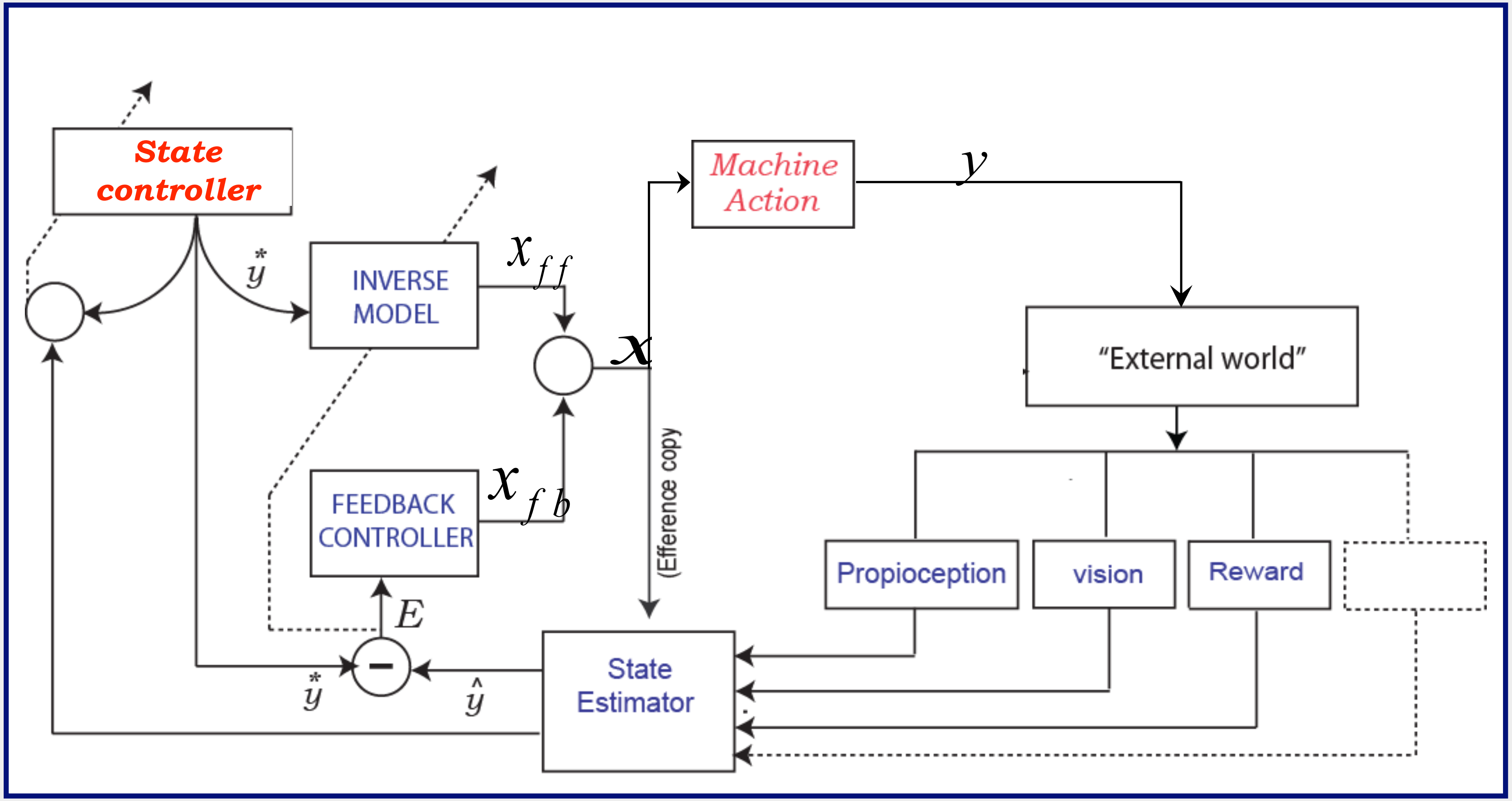
**EEG**

**F-MRI**

*Lower Spatial Resolution* →

← *More invasive*

# BMI action-perception loop




$\overset{*}{y}$ - Desired State

$y$ - Actual state

$\hat{y}$ - Estimated state

$x$ - Neural 'Commands'

$x_t$ Neuronal activity

$y_t$ Behavioral state (Action, movement)



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# *Model Requirments: Choosing a BMI algorithm*

1. Real time Performance
2. “Action-Perception” autoregressive loop
3. Adaptivity – Day to Day and online
4. On line adaptivity:  Learning and performance in parallel

Neural activity

Movement

**Goal:** find mapping $f : \mathbf{x}_t \rightarrow \mathbf{y}_t$

Linear Regression: $\mathbf{y}_t = \mathbf{A} \cdot \mathbf{x}_t$ (***Population Vector***)

**Add history**

**Add nonlinearity (using Kernels)**

1st order movement model:

$$\mathbf{y}_t = \mathbf{A}_t \cdot \mathbf{x}_t + \mathbf{B}_t \cdot \mathbf{y}_{t-1}$$

(Gaussian noise ⇨ ***Kalman Filter***)

Nonlinear input-output:

$$\mathbf{y}_t = \mathbf{W}_\psi \cdot \psi(\mathbf{x}_t)$$

(*Support Vector Regression; SVR*)

Nth order neural & movement:

$$\mathbf{y}_t = \sum_m \mathbf{A}_m \cdot \mathbf{x}_{t-m} + \sum_n \mathbf{B}_n \cdot \mathbf{y}_{t-n}$$

(*Auto Regressive Moving Average; ARMA*)

Nonlinear input-output & movement:

$$\mathbf{y}_t = \mathbf{W}_\psi \cdot \psi(\mathbf{x}_t) + \mathbf{W}_\chi \cdot \chi(\mathbf{y}_{t-1})$$

Add history

Add nonlinearity (using Kernels)

Kernel Auto Regressive Moving Average (***KARMA***):

$$\mathbf{y}_t = \underbrace{\mathbf{W}_\psi}_{\text{Weights matrix}} \cdot \underbrace{\psi}_{\text{Nonlinear Transform}} \Big( \underbrace{\mathbf{x}_{t:t-M}}_{\text{Neural activity history}} \Big) + \mathbf{W}_\chi \cdot \chi \Big( \underbrace{\mathbf{y}_{t-1:t-N}}_{\text{Movement history}} \Big)$$

Martinez-Ramon M., et al. *Support vector machines for nonlinear kernel ARMA system identification*.
IEEE Transaction of Neural Networks, 2006

Add history

Add nonlinearity (using Kernels)

## Kernel Auto Regressive Moving Average (***KARMA***):

$$\boxed{\mathbf{y}_t = \mathbf{W}_\psi \cdot \psi\left(\mathbf{x}_{t:t-M}\right) + \mathbf{W}_\chi \cdot \chi\left(\mathbf{y}_{t-1:t-N}\right)}$$

Nonlinear input-output

History neural activity

Nonlinear movement model

Movement history

(1) $$\mathbf{y}_t = \mathbf{W}_\phi \cdot \phi\left(\mathbf{v}_t\right)$$

(2) $$\mathbf{W}_\phi = \sum_\mu \boldsymbol{\alpha}_\mu \phi\left(\mathbf{v}_\mu\right)^T$$

(3) $$\mathbf{y}_t = \sum_\mu \boldsymbol{\alpha}_\mu \cdot \phi\left(\mathbf{v}_\mu\right)^T \cdot \phi\left(\mathbf{v}_t\right)$$

(4) $$\boxed{\mathbf{y}_t = \sum_\mu \boldsymbol{\alpha}_\mu \cdot K\left(\mathbf{v}_\mu, \mathbf{v}_t\right)}$$

$$\mathbf{v}_t \equiv \begin{bmatrix} \mathbf{x}_t \\ \vdots \\ \mathbf{x}_{t-M} \\ \mathbf{y}_{t-1} \\ \vdots \\ \mathbf{y}_{t-N} \end{bmatrix}$$

Martinez-Ramon M., et al. *Support vector machines for nonlinear kernel ARMA system identification*. IEEE Transaction of Neural Networks, 2006

# *Modeling choices*

- Gaussian kernels:

$$\boxed{K\left(\mathbf{v}_{\mu}, \mathbf{v}_{t}\right) = \exp^{a\cdot\left\|\mathbf{x}_{\mu}-\mathbf{x}_{t}\right\|^{2}} \otimes \exp^{b\cdot\left\|\mathbf{y}_{\mu}-\mathbf{y}_{t}\right\|^{2}}}$$

$$\otimes \equiv + \text{ or } \times$$

- *Neural vector*: Spike counts (50msec bins), from well isolated single-units (20-40), medium and multi-units (100-150), 7 bins history window (350msec)

- *Movement vector*: 3D cursor position *(x,y,z)*, 3 bins history window (150msec)

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# *Learning*

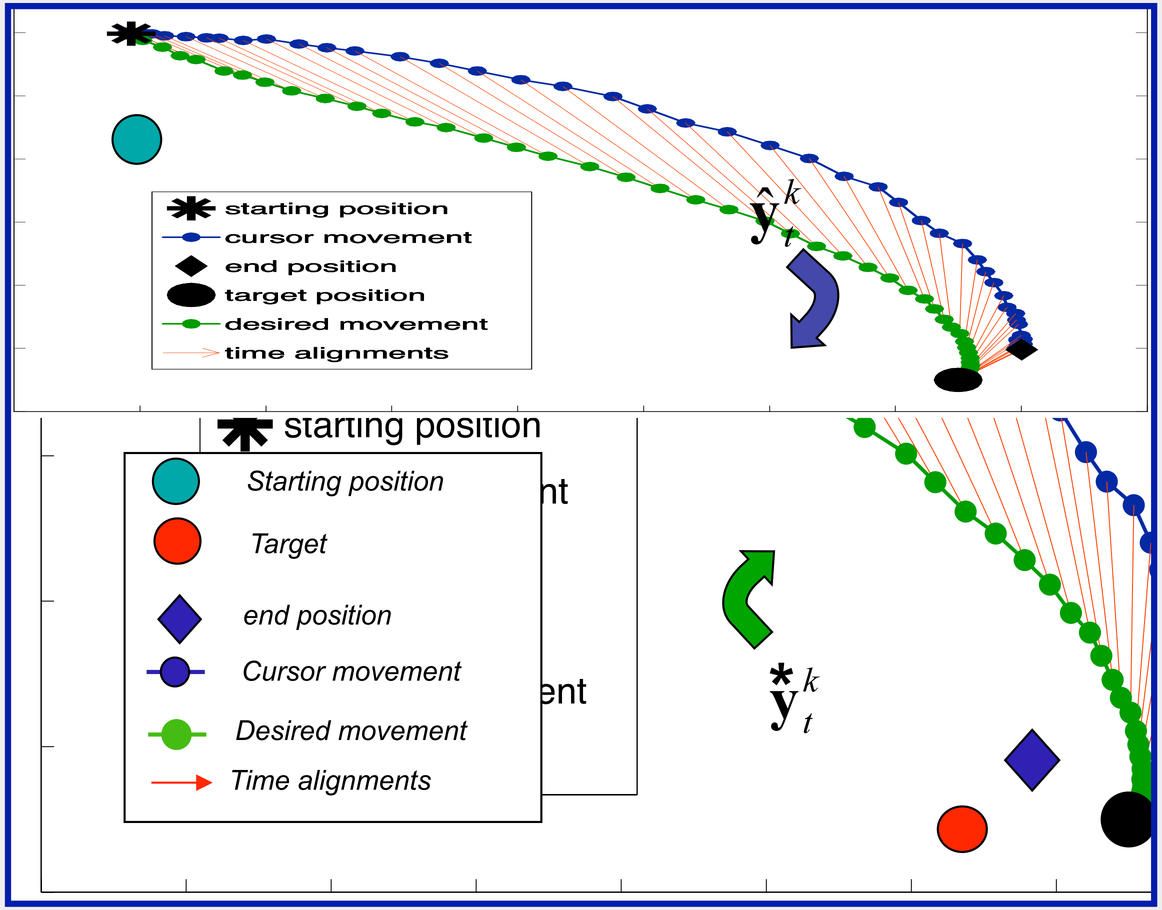
Minimize the error function:

$$\boxed{E\left(\mathbf{W}_{\phi}\right)=\sum_{\mu}\left|\mathbf{y}_{\mu}-\mathbf{W}_{\phi}\cdot\phi\left(\mathbf{v}_{\mu}\right)\right|_{\varepsilon}+c\cdot\left\|\mathbf{W}_{\phi}\right\|^{2}}$$

**Prediction error**

**Regularization**

# *Learning* the model in BMI mode




**y** - Trajectory
**x** - neural data
*k* - trials index
*t* - time (within trial *k*)
*T – Time from "Go" to "Reach"*

$$\mathbf{y}_t^{\text{intended}} = \left(1 - \frac{t}{T}\right) \cdot \mathbf{y}_t + \left(\frac{t}{T}\right) \cdot \text{target}$$

**Desired movement** is created as a time varying combination of the **estimated trajectory** and ***target location***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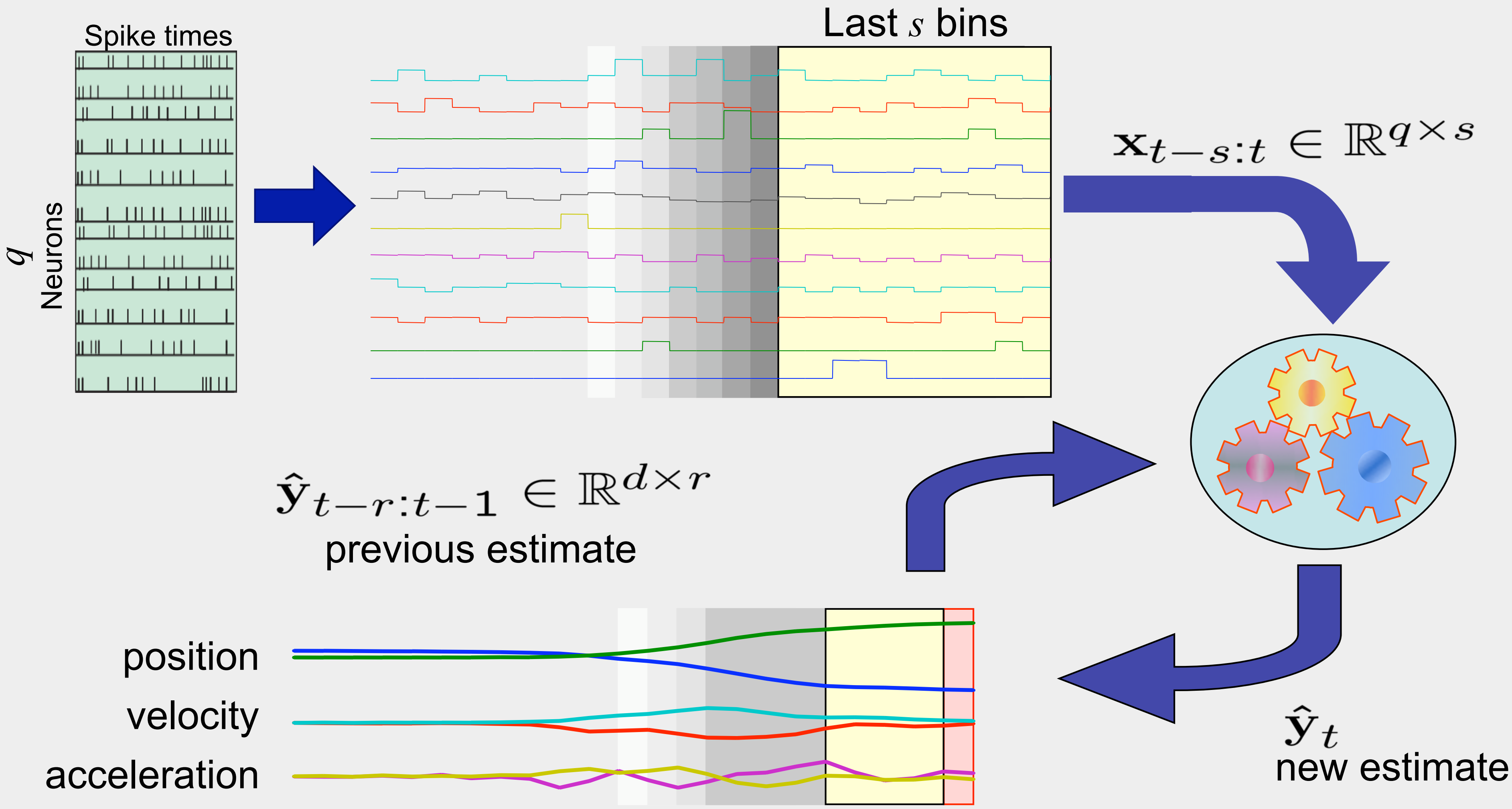
# KARMA: General scheme




*Shpigelman et al 2006, Shpigelman, Lalazar et al 2008*

# *Making KARMA Adaptive*

1. Learning: The learning algorithm produces a sequence of models for predicting trajectories (**Y***k*) from neural data (**X***k*)

$$\{\mathbf{f}^{1}, \ldots, \mathbf{f}^{k}, \ldots, \mathbf{f}^{N}\}$$

2. Performance: At trial *k*, the model produces a trajectory

$$\mathbf{y}_t^{*k} = \mathbf{f}^{k}(\mathbf{x}_{0:t}^{k}, \mathbf{y}_{0:t-1}^{k})$$

3. The previous trajectory is used as feedback for the learning algorithm

4. Part of the old examples are randomly removed to learn new models


Experiments
Hagai Lalazar
Lavi Shpigelman
Maayan Shachar

# Outlines

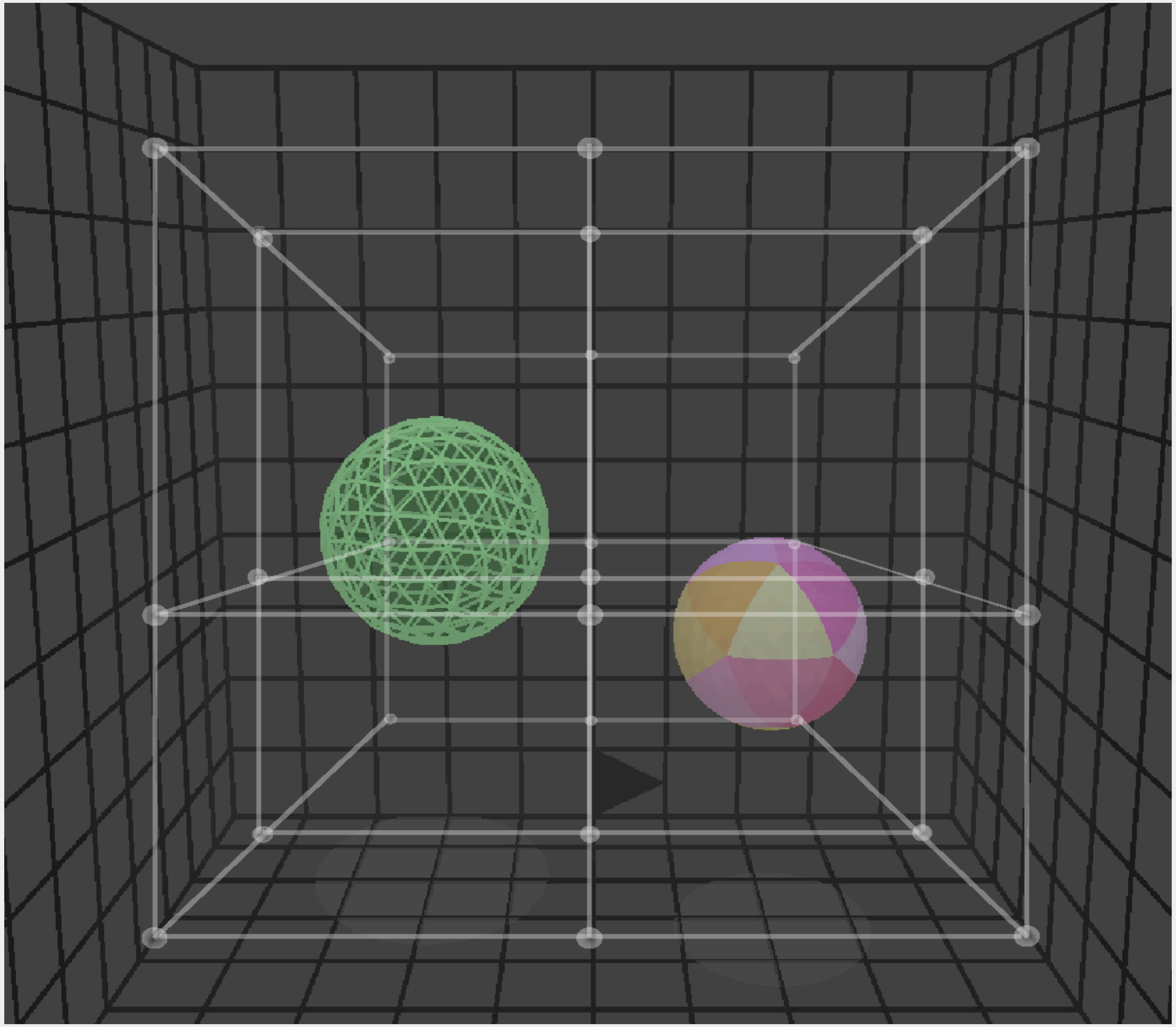
- Chapter 1: The Notion of Internal Models
  1. The sensorimotor loop
  2. The notion of Internal models
  3. The notion of Active Perception

- Chapter 2: Understanding Neuronal Basis of Sensorimotor Control
  1. Population Codes in Motor Cortex
  2. Learning Related Activity in Motor cortical Fields

- Chapter 3: Brain Machine Interface (BMI)
  1. BMI - Requirements
  2. BMI – Algorithms
  3. BMI – The Karma Algorithm

- Chapter 4: BMI Experiments
  1. Reaching movements
  2. Learning and Performance in BMI settings

# *3D instructed-delay with continuous target-to-target reaching*





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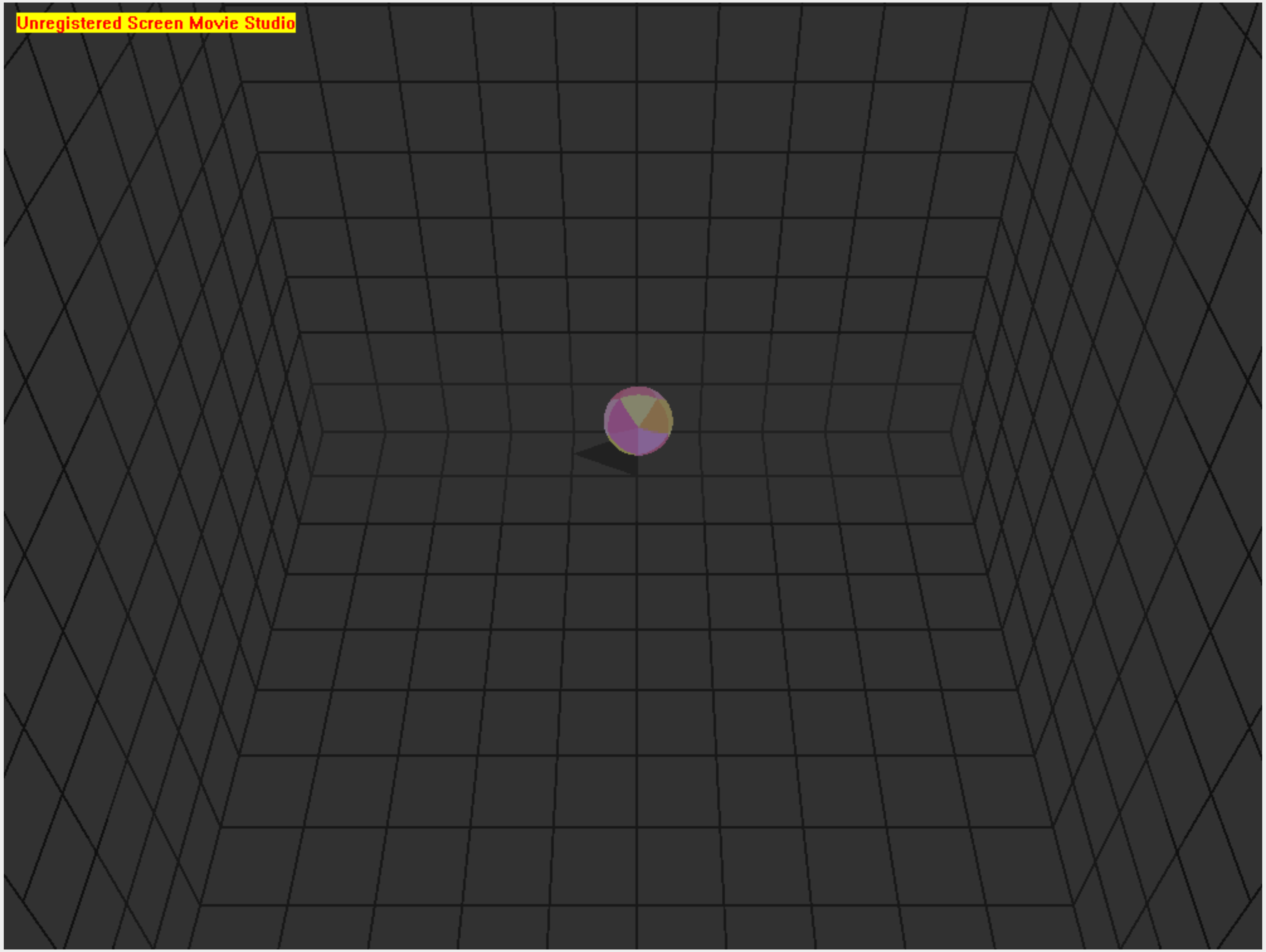
Unregistered Screen Movie Studio

# Arm Control



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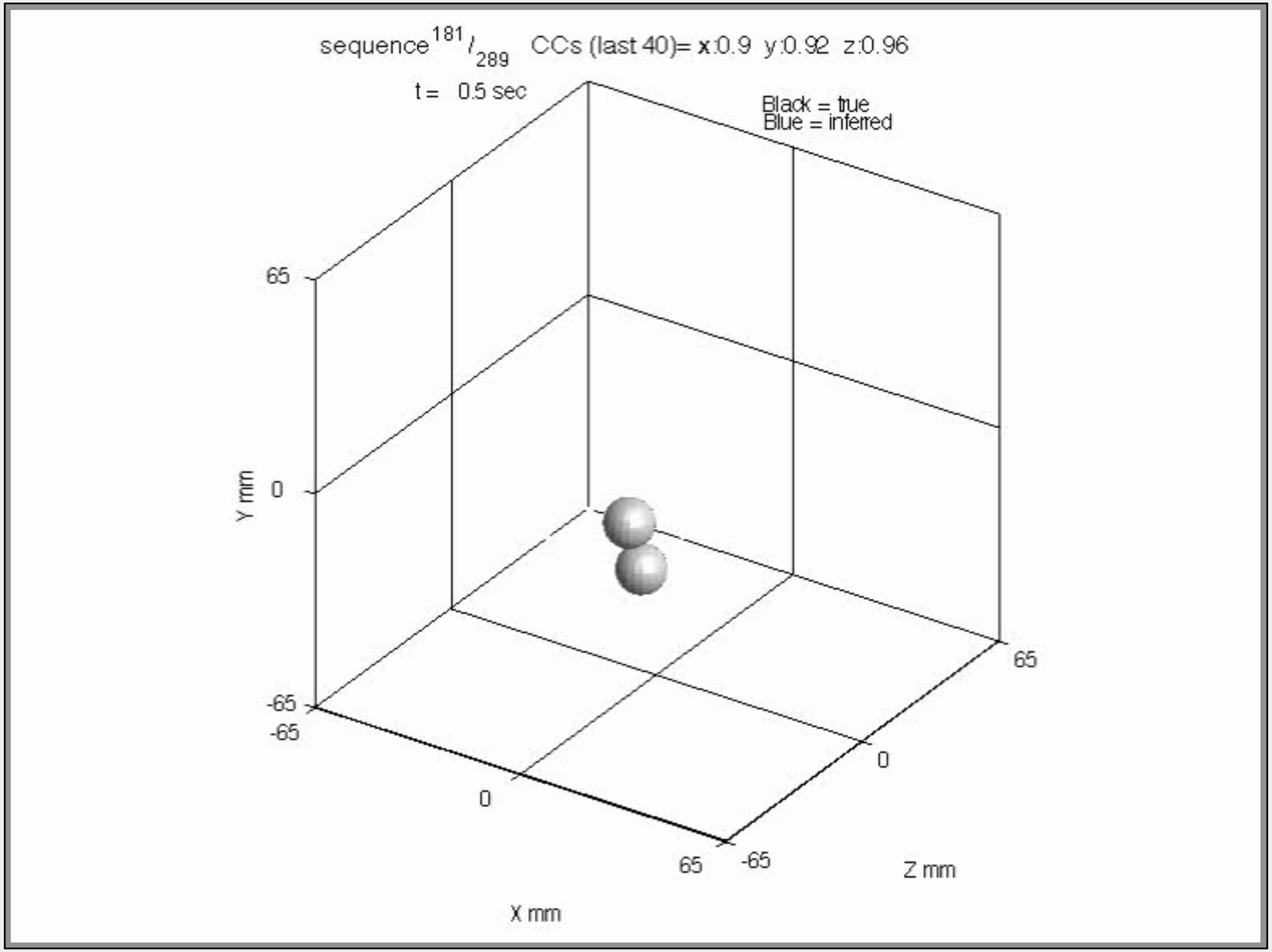
# *Real Time tracking of hand movements by KARMA*





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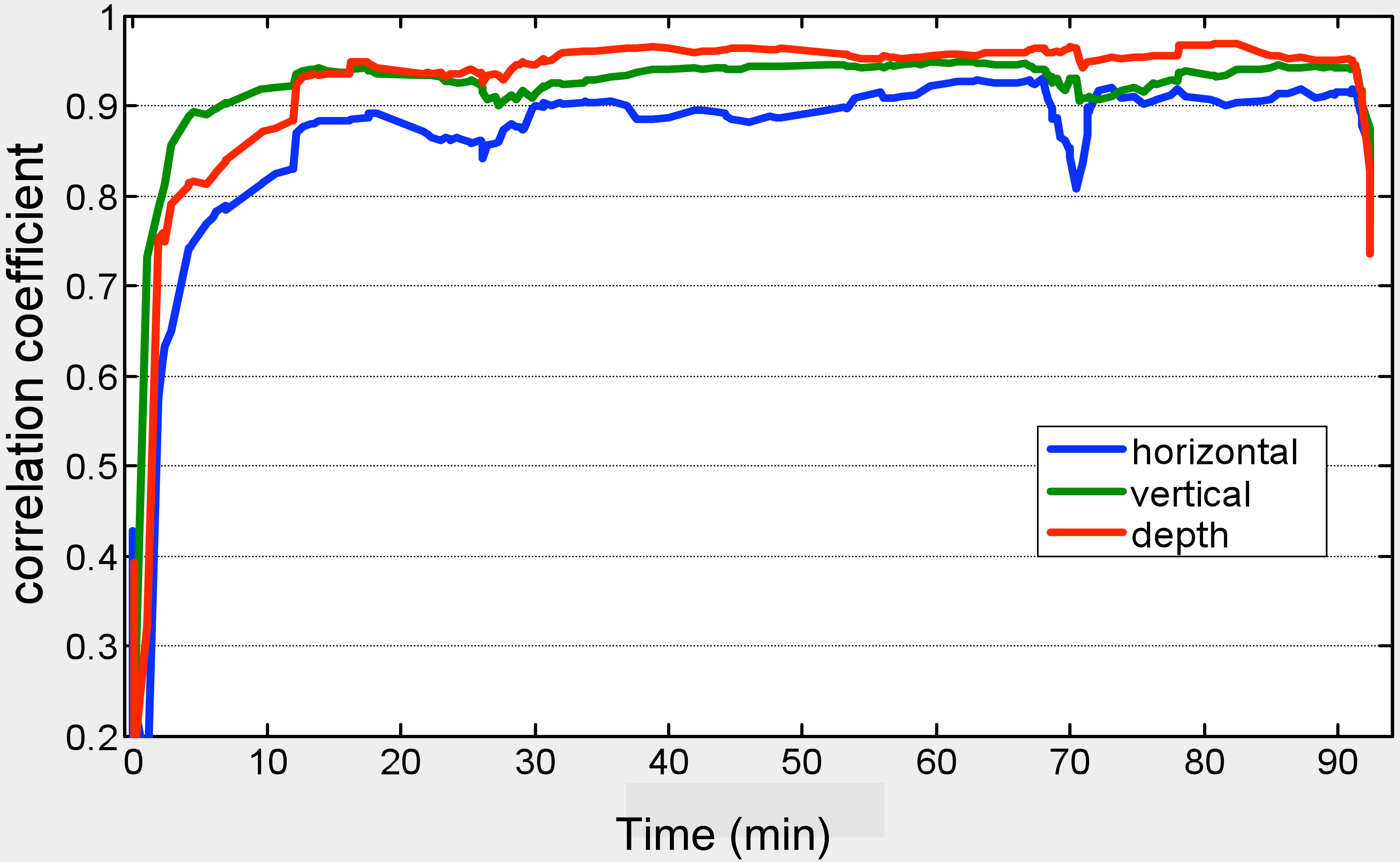
# *Tracking performance*





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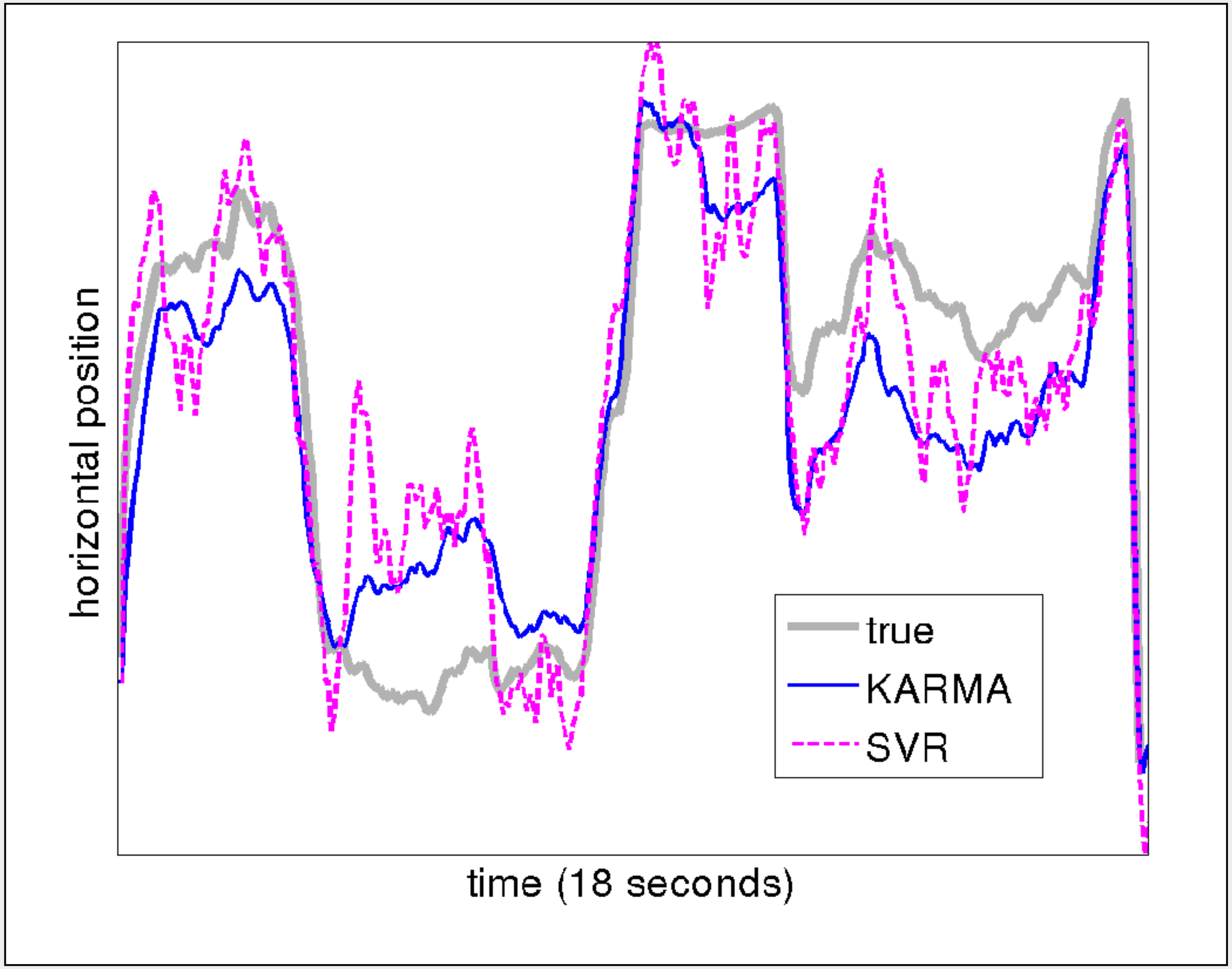
# Comparing KARMA to SVR



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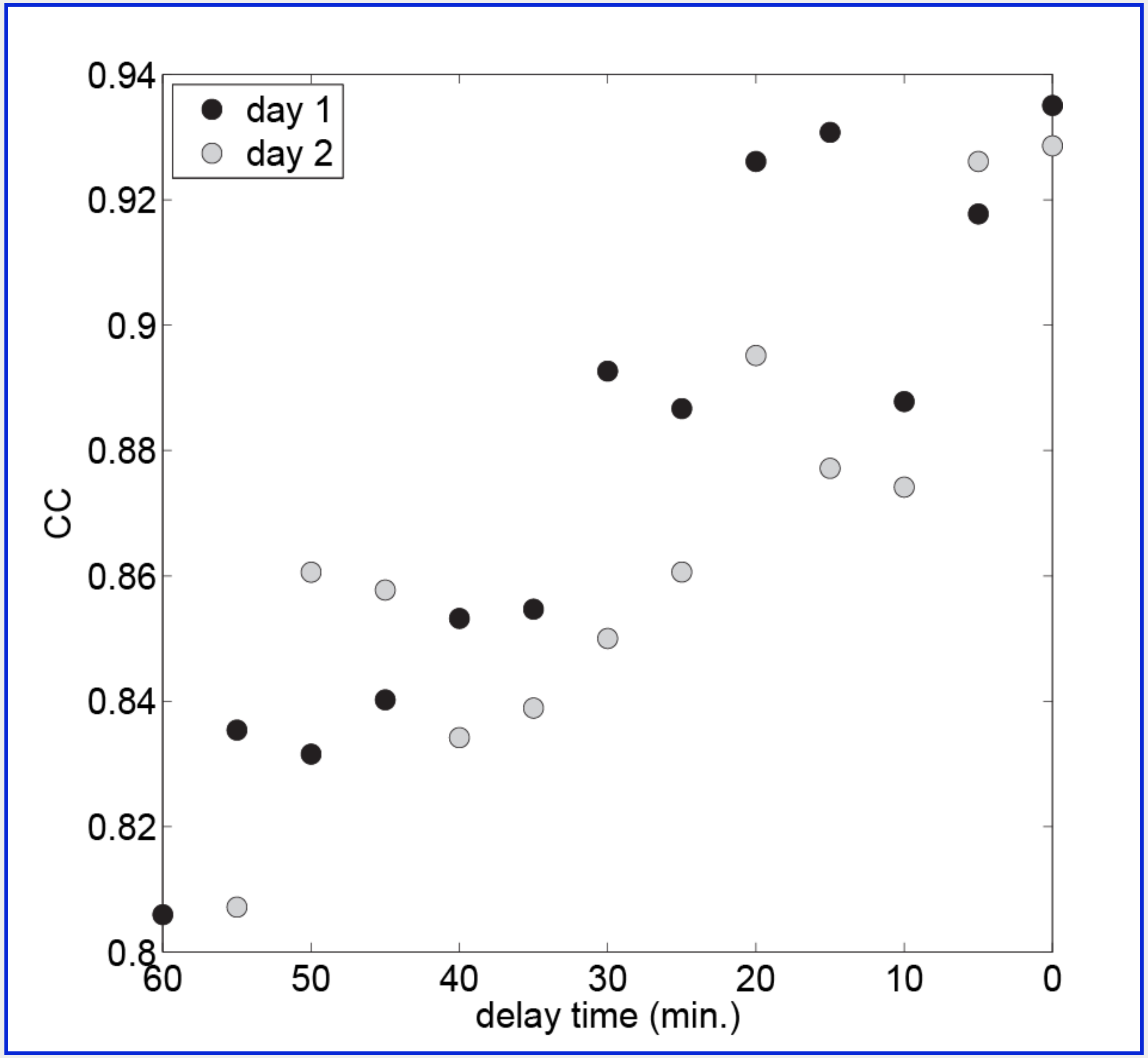
# *Adaptivity model is helpful in tracking*





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# Adaptive Models are Useful for These Brains


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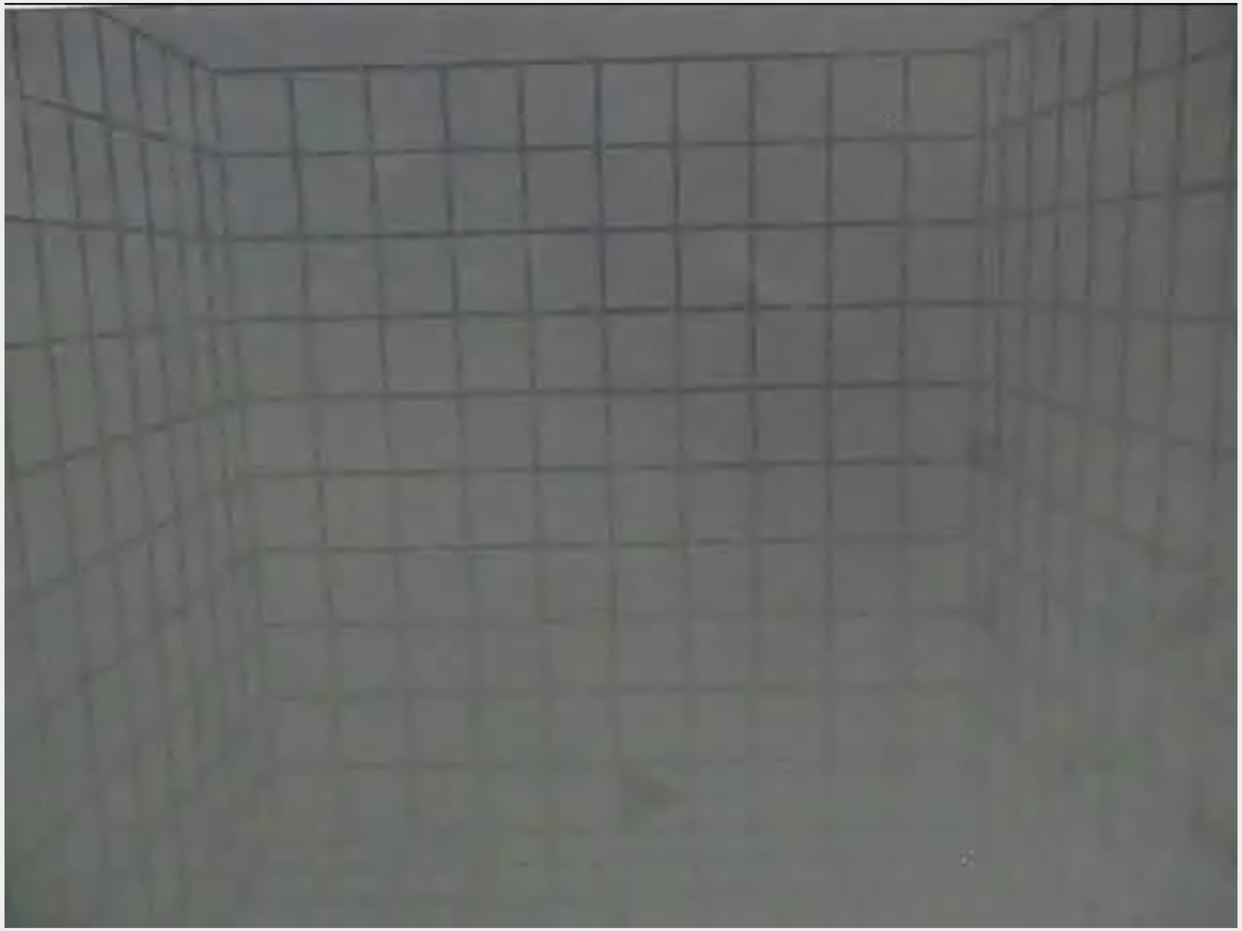
# *Brain Control – Reaching Targets in 3-D*





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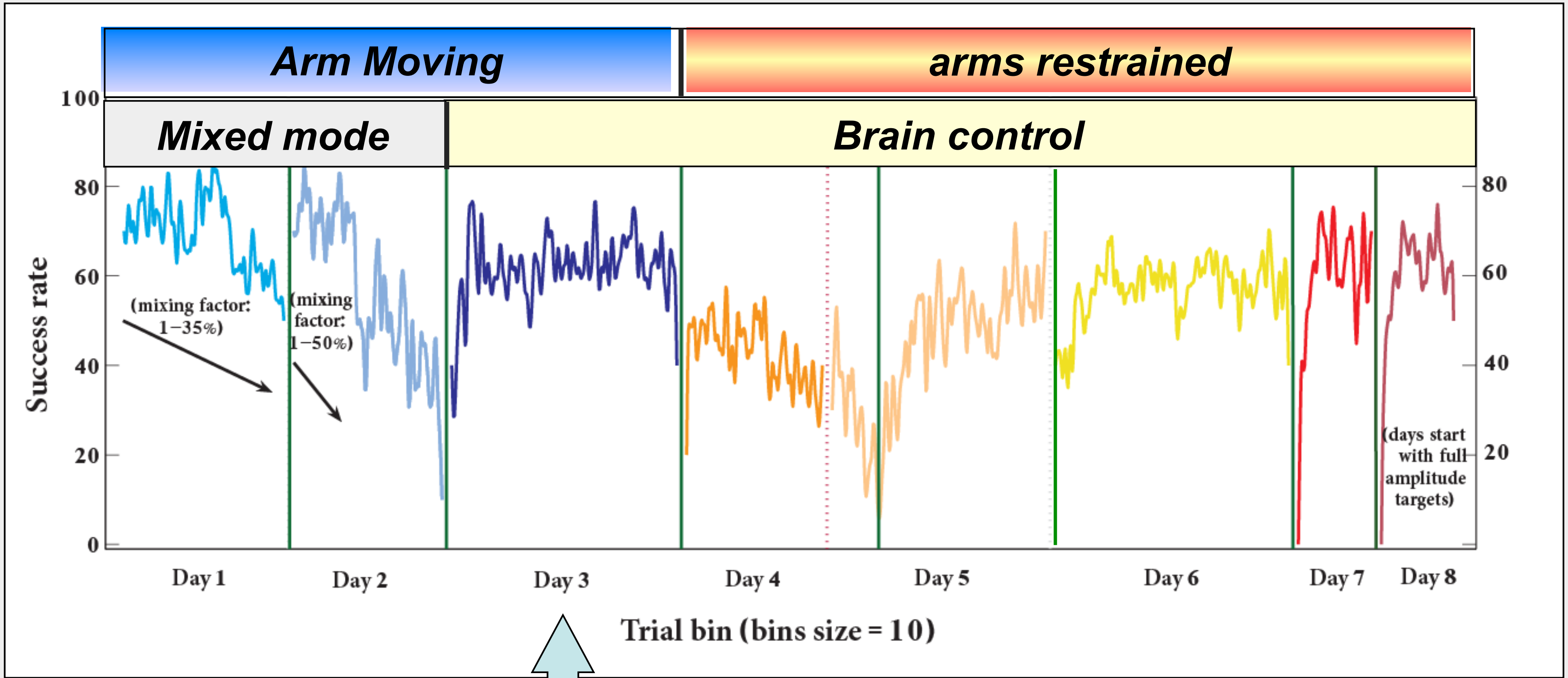
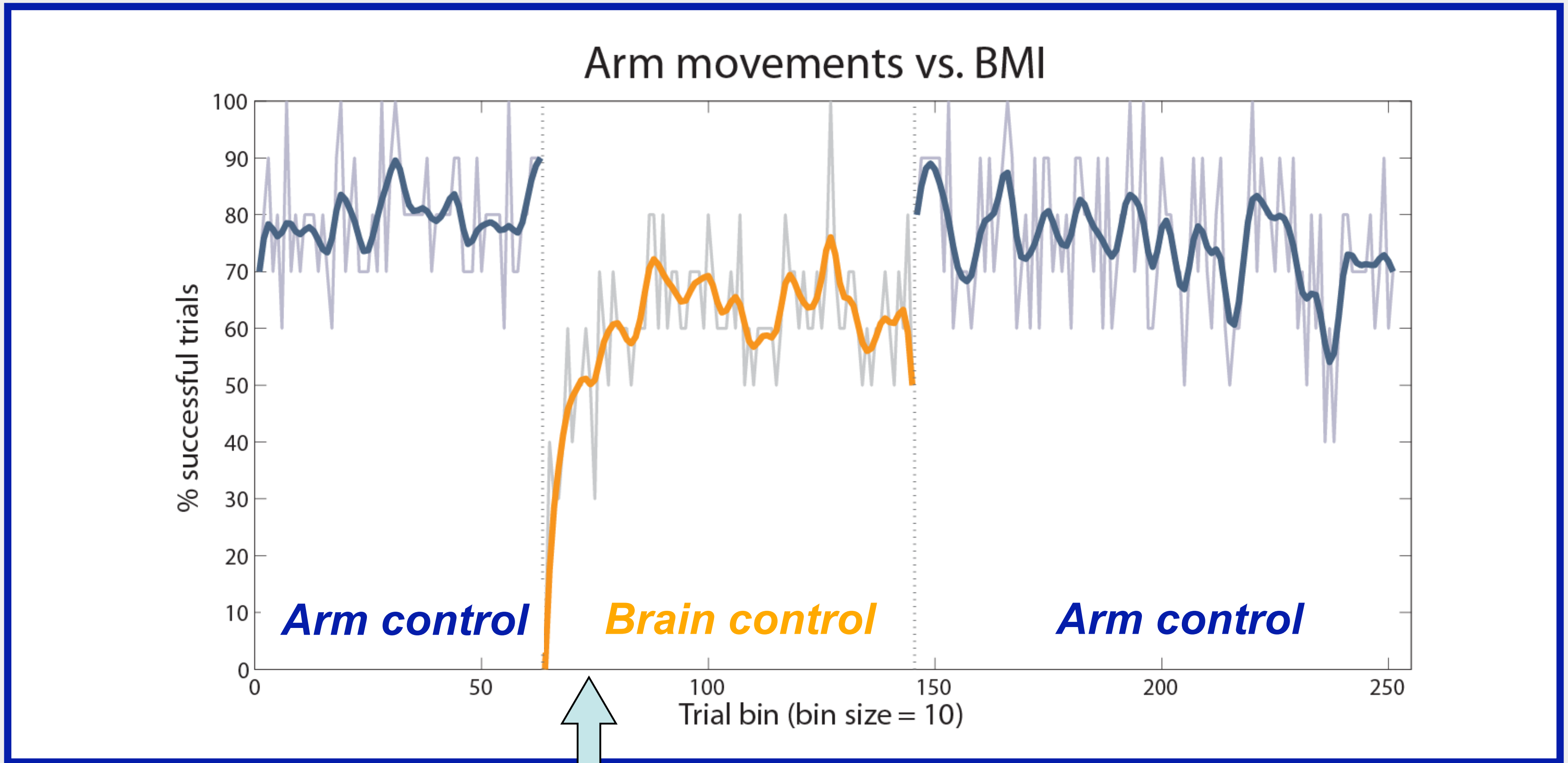
# First days of BMI adaptation




FIRST DAY OF FULL BRAIN CONTROL

# Switching from Arm control to Brain Control is fast!




plateau in ~30 trials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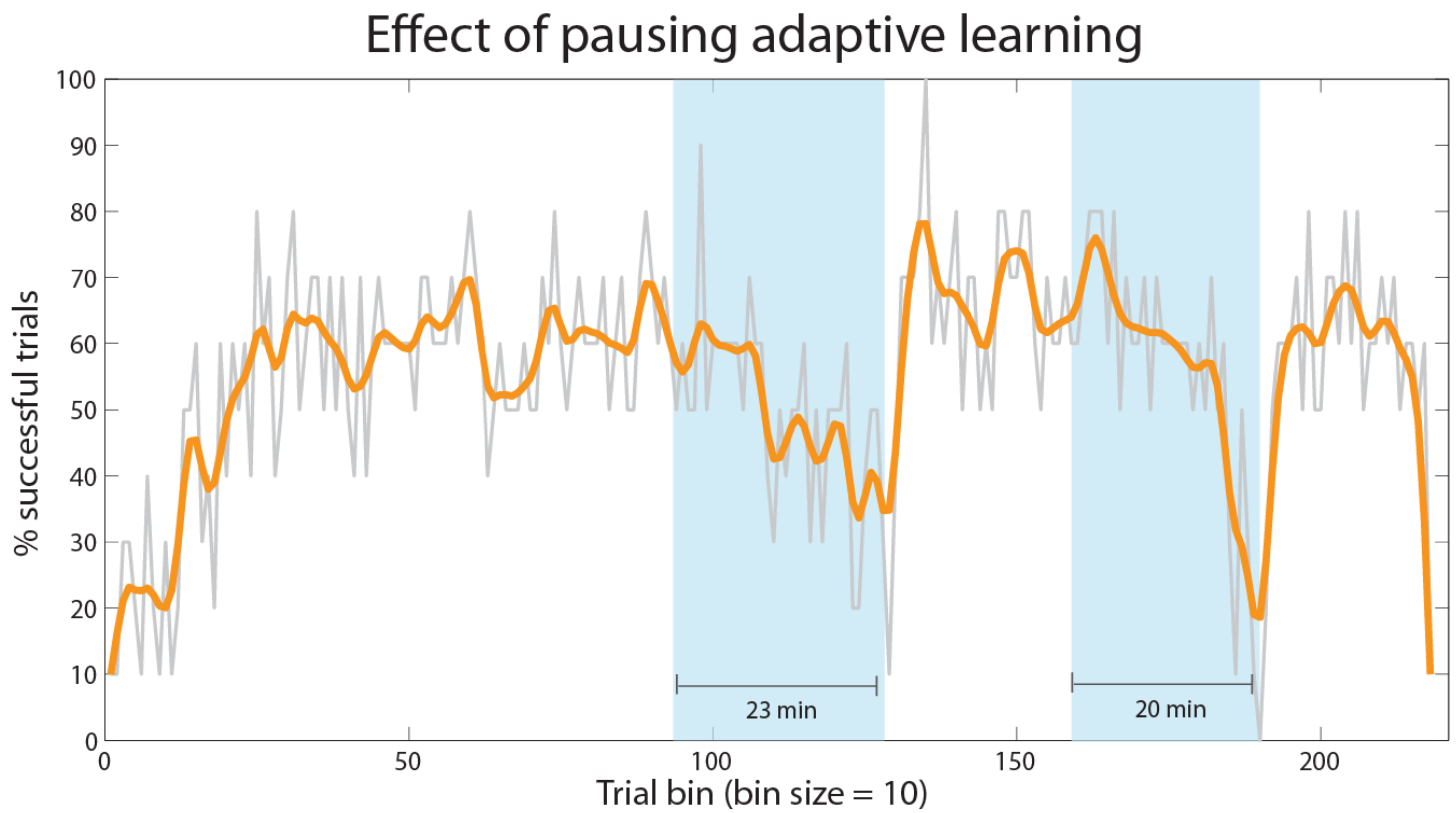
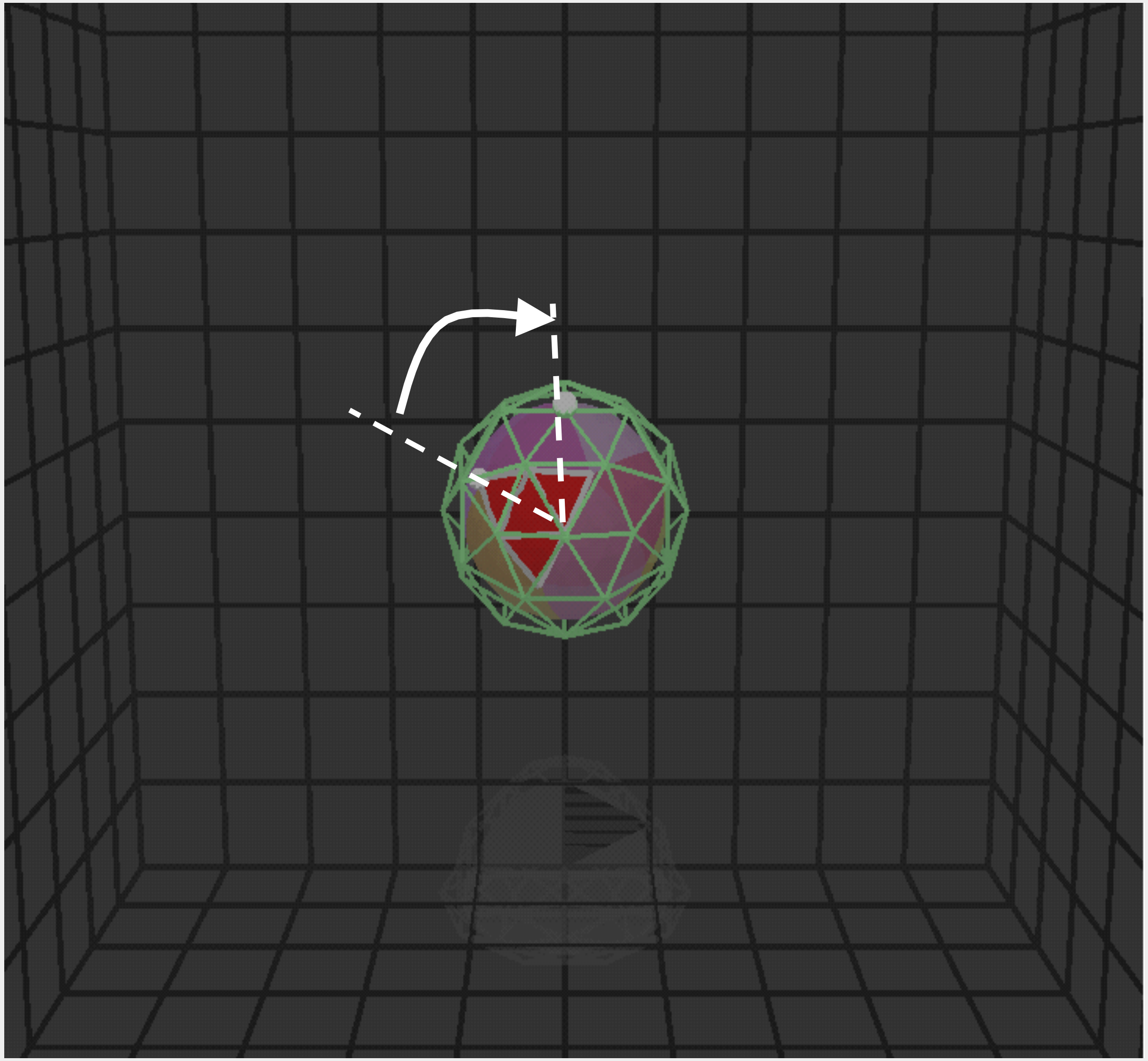
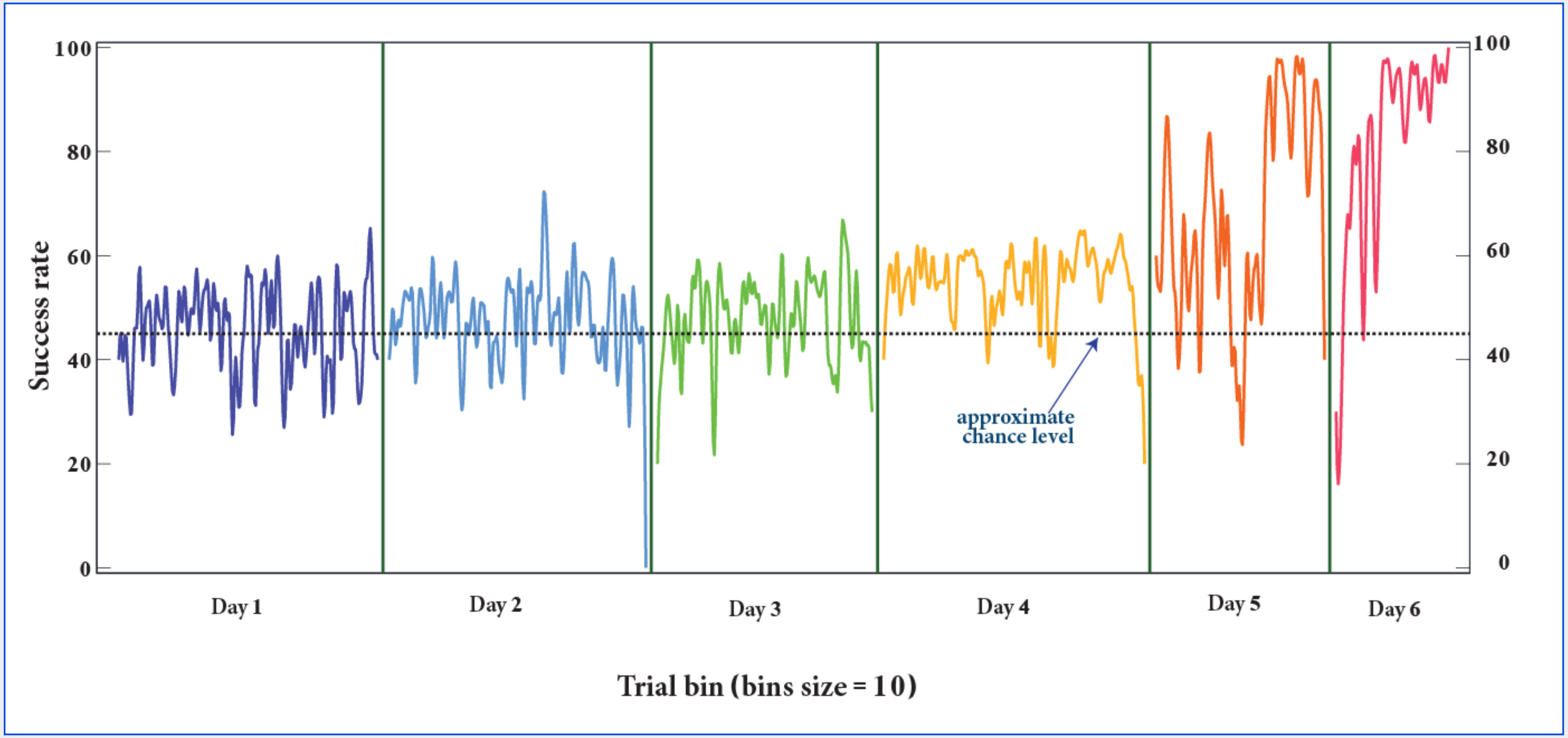
# *Adaptive model performs better in Brain control*



# Learning novel visuomotor task using a BMI



# Target Rotation Task





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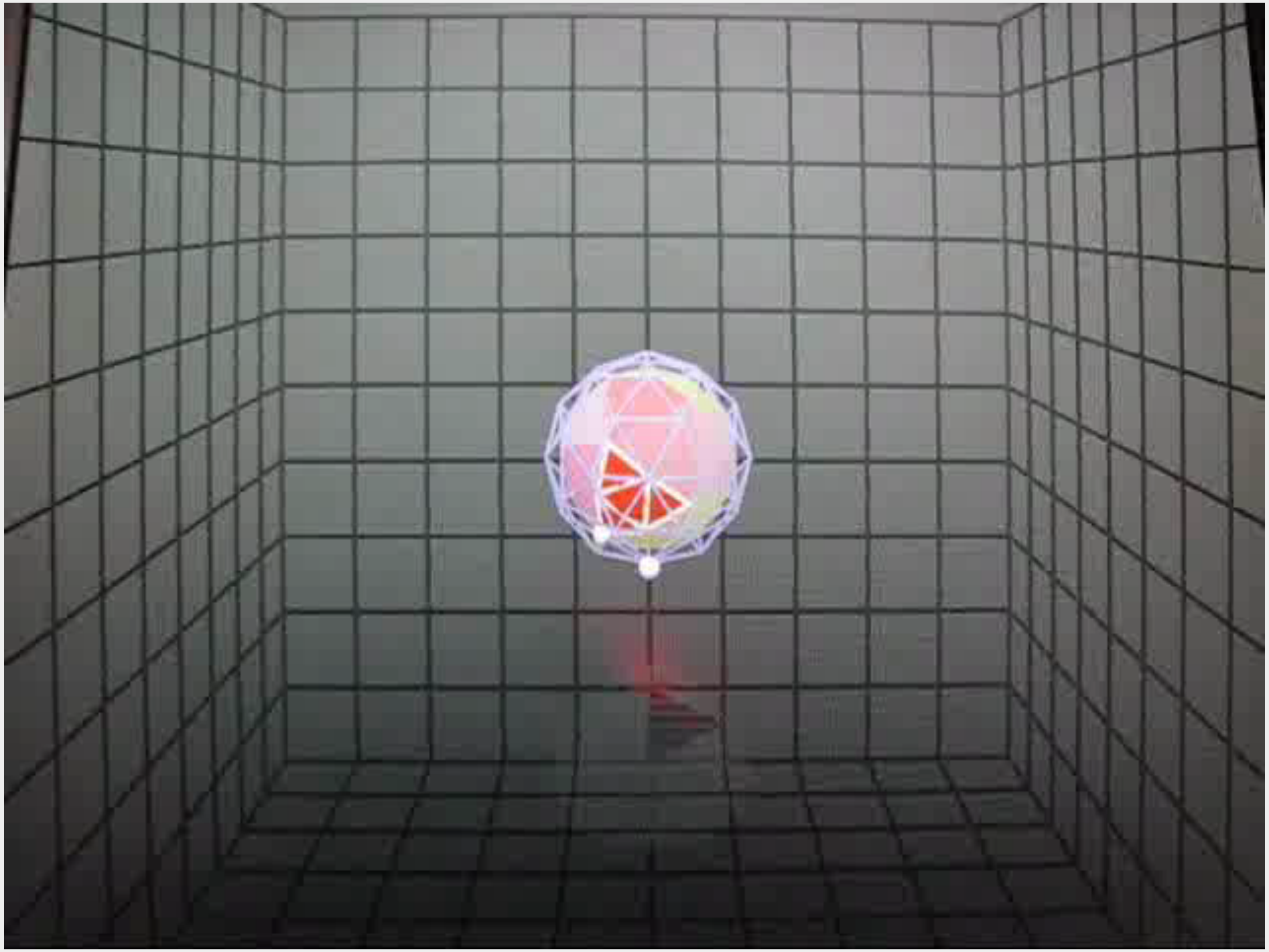
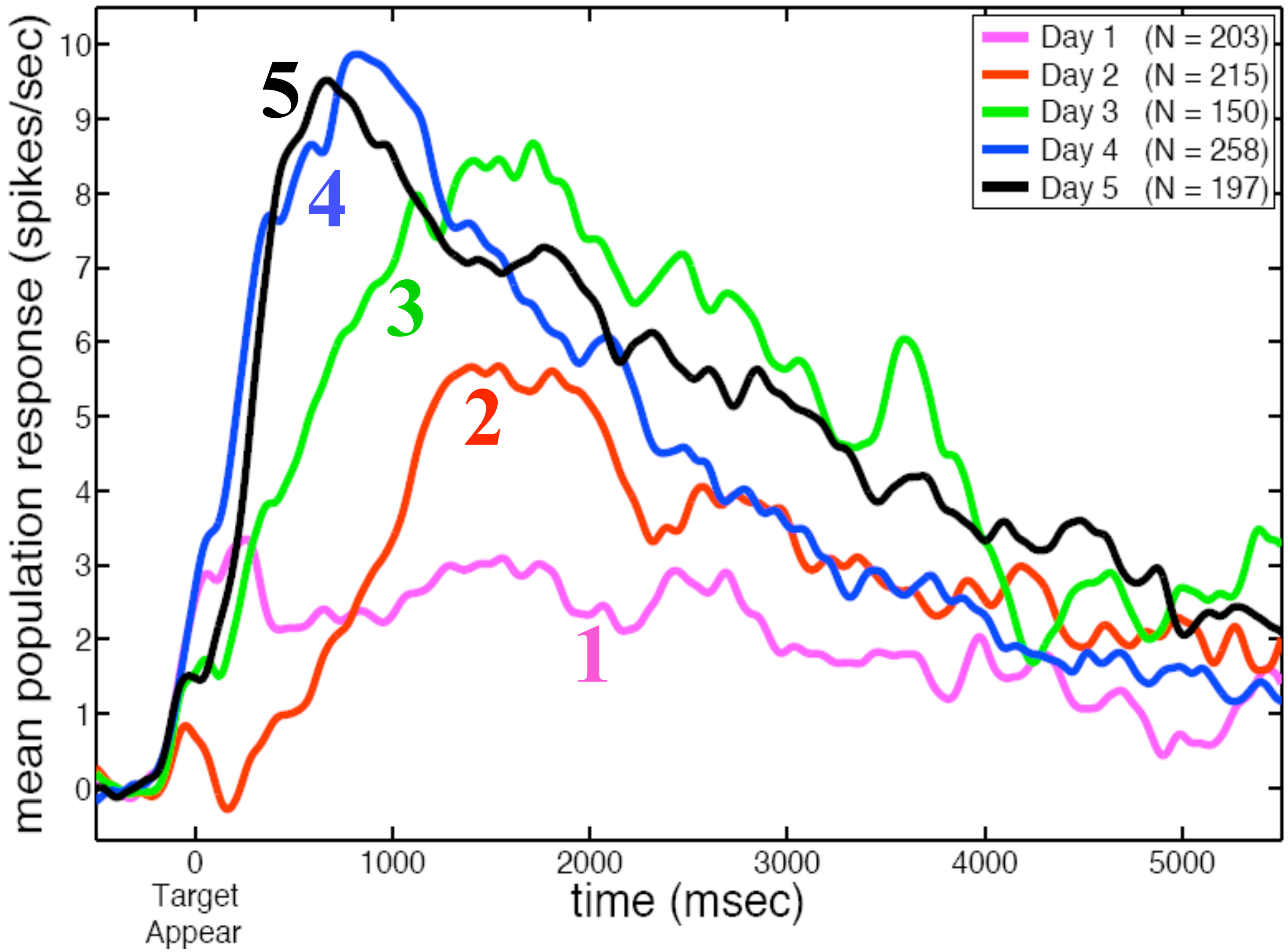
# Learning anew in BMI - Target Rotation Task



# Gradual emergence of Population responses



# *Reach and Rotate*

# Summary and conclusions

- The model is learned practically instantly (20 trials – few minutes).
- Handful of cortical units can produce good results
- New task can be learned in BMI without training on natural movements.
- The model's learning is completely automatic and does not involve any explicit training of the subject
- The model is adaptive and reliable

Promising model for clinical applications!

## *More investment in funds and manpower will put us on the yellow brick road*



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# Acknowledgments

Thank you

תודה רבה

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- Ben Engelhard
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- Haim Sompolinsky
- Yoram Singer



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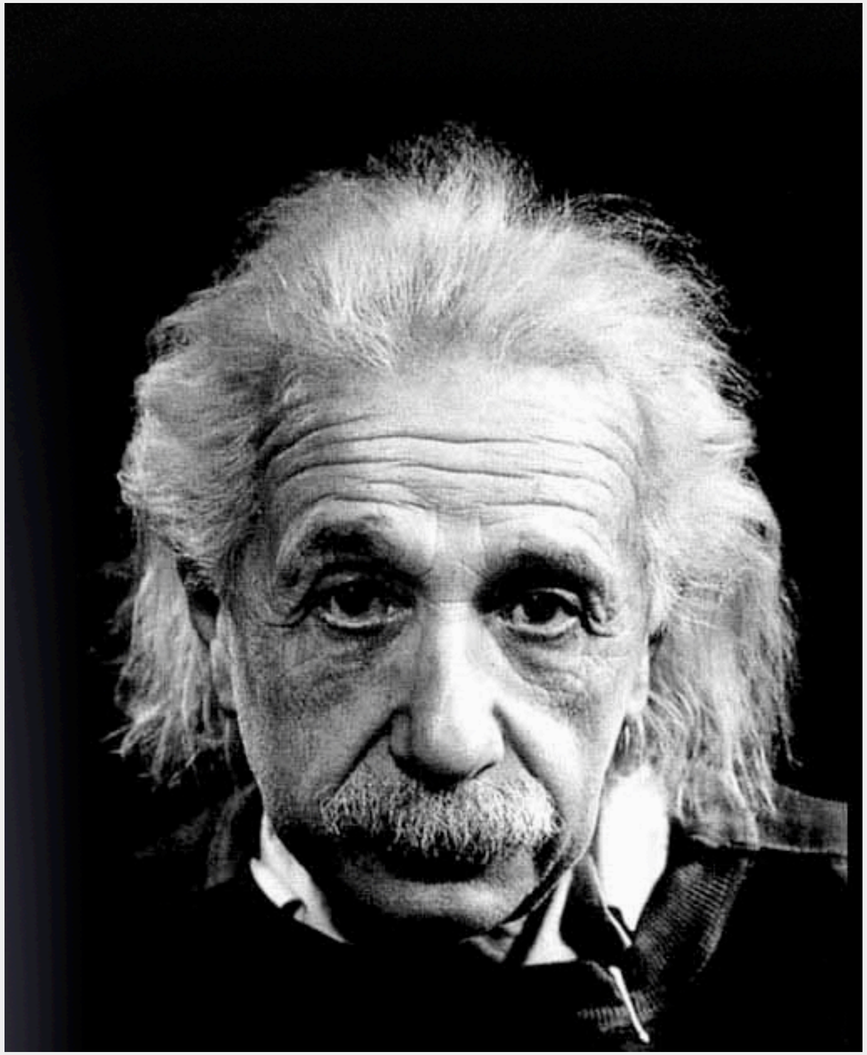
[redacted]

$$\min_{\mathbf{W}} \quad \frac{1}{2}\|\mathbf{W}\|^2 + c\sum_i \left|\hat{\mathbf{y}}_t^i - \mathbf{y}_t^i\right|_\varepsilon$$

*Learning problem:*
*Minimize total size of Weights (W)  and the error (to epsilon)*

# *Can we understand the brain enigma ?*



*The most beautiful and most profound experience*
*is the sensation of the* ***mystical.***

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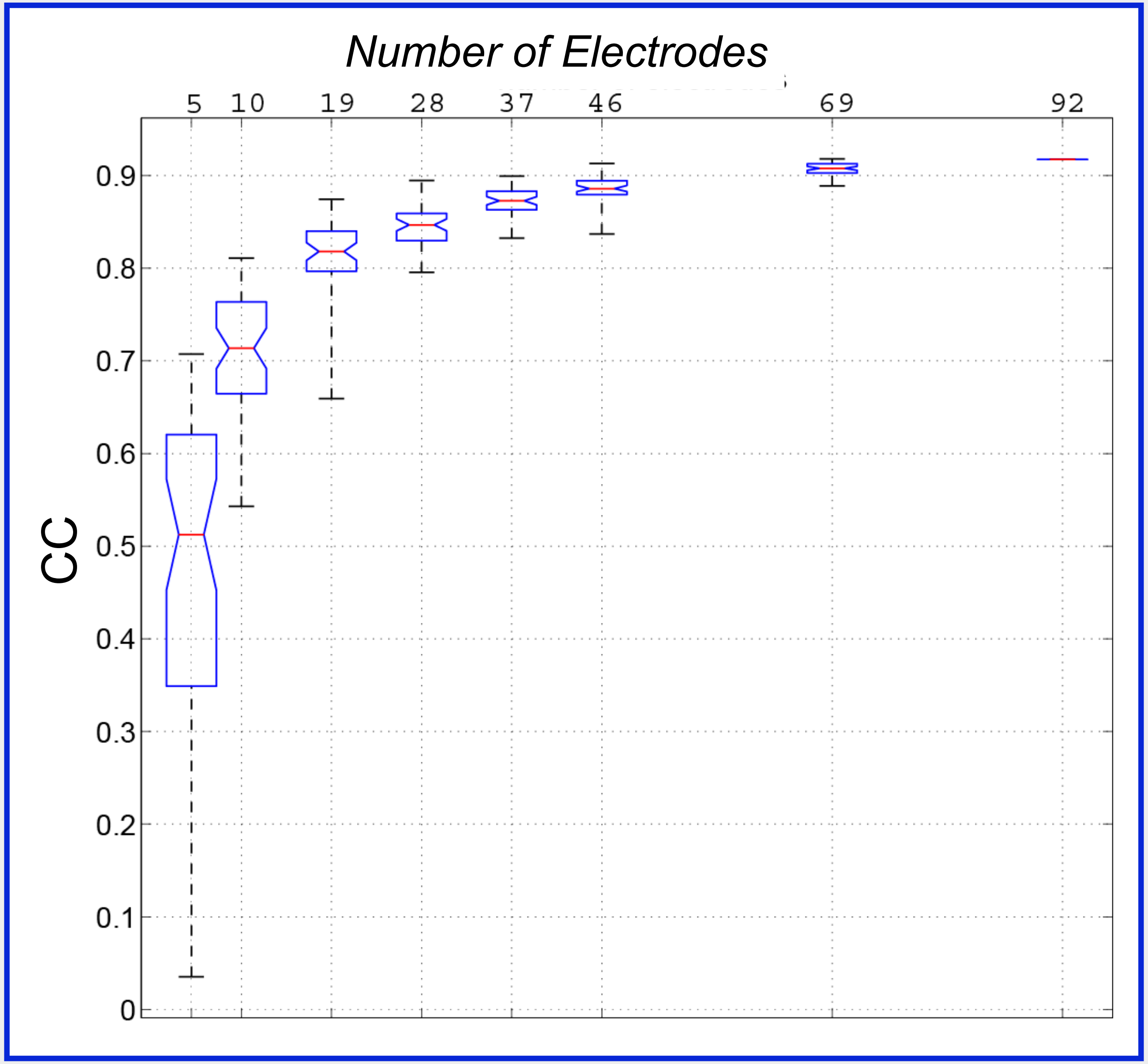
# Neurons dropping





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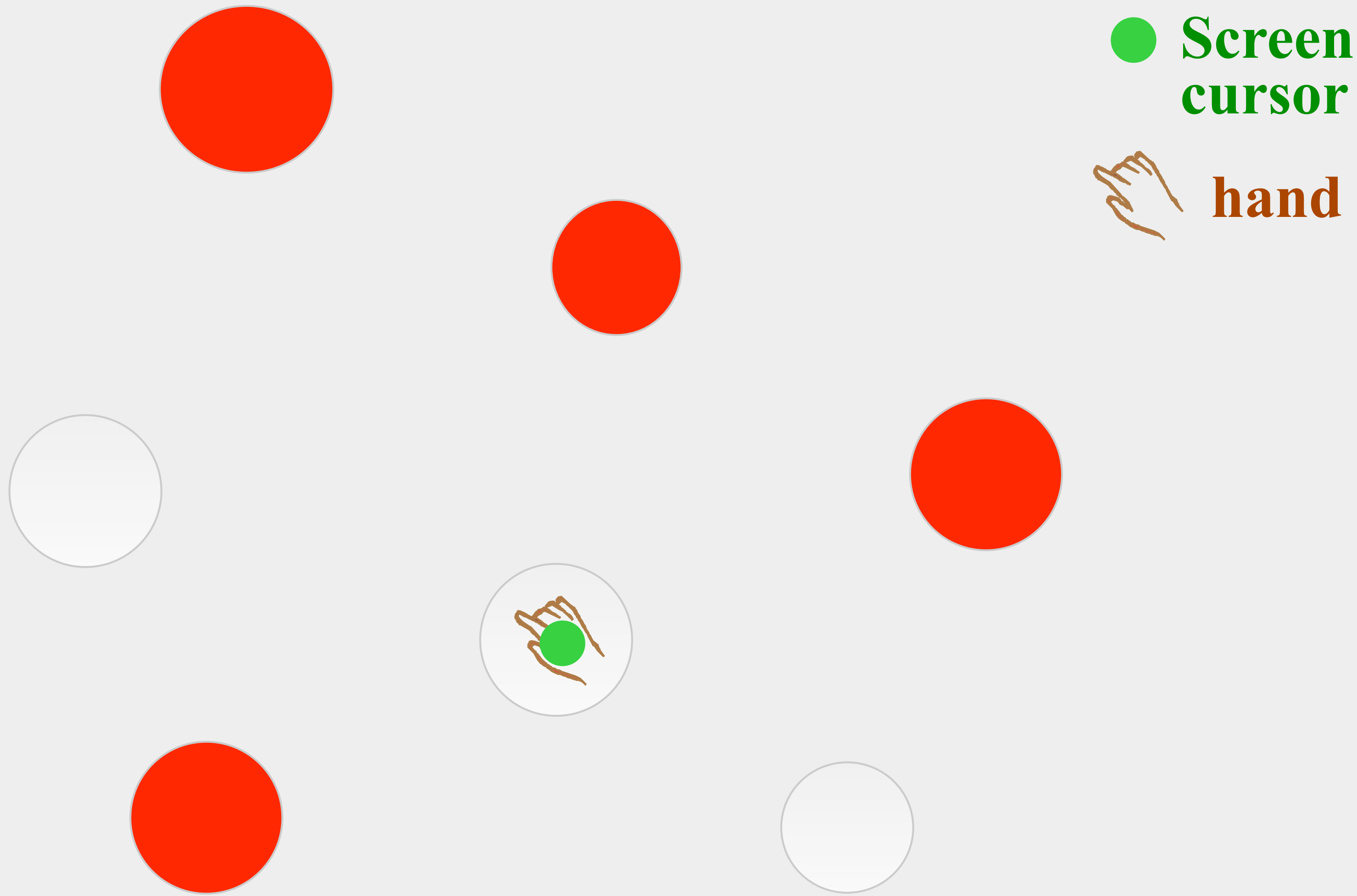
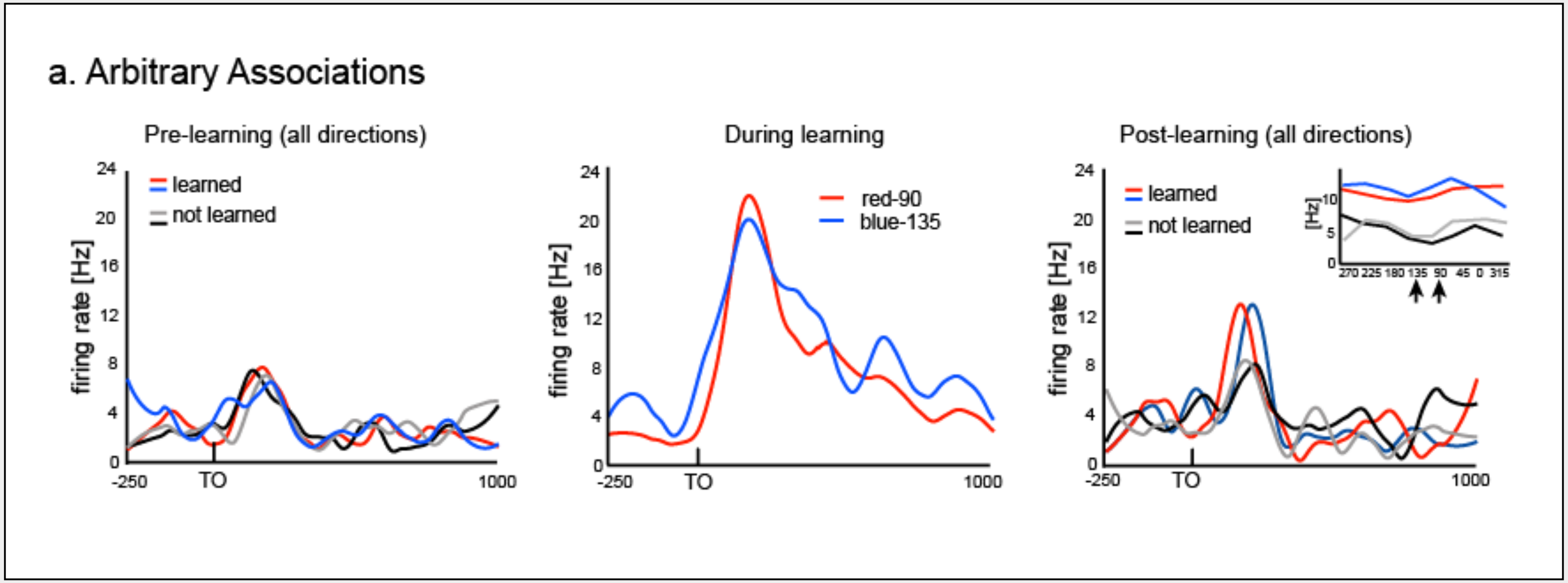
# *Reaching task*



# Arbitrary Association – Example of one cell



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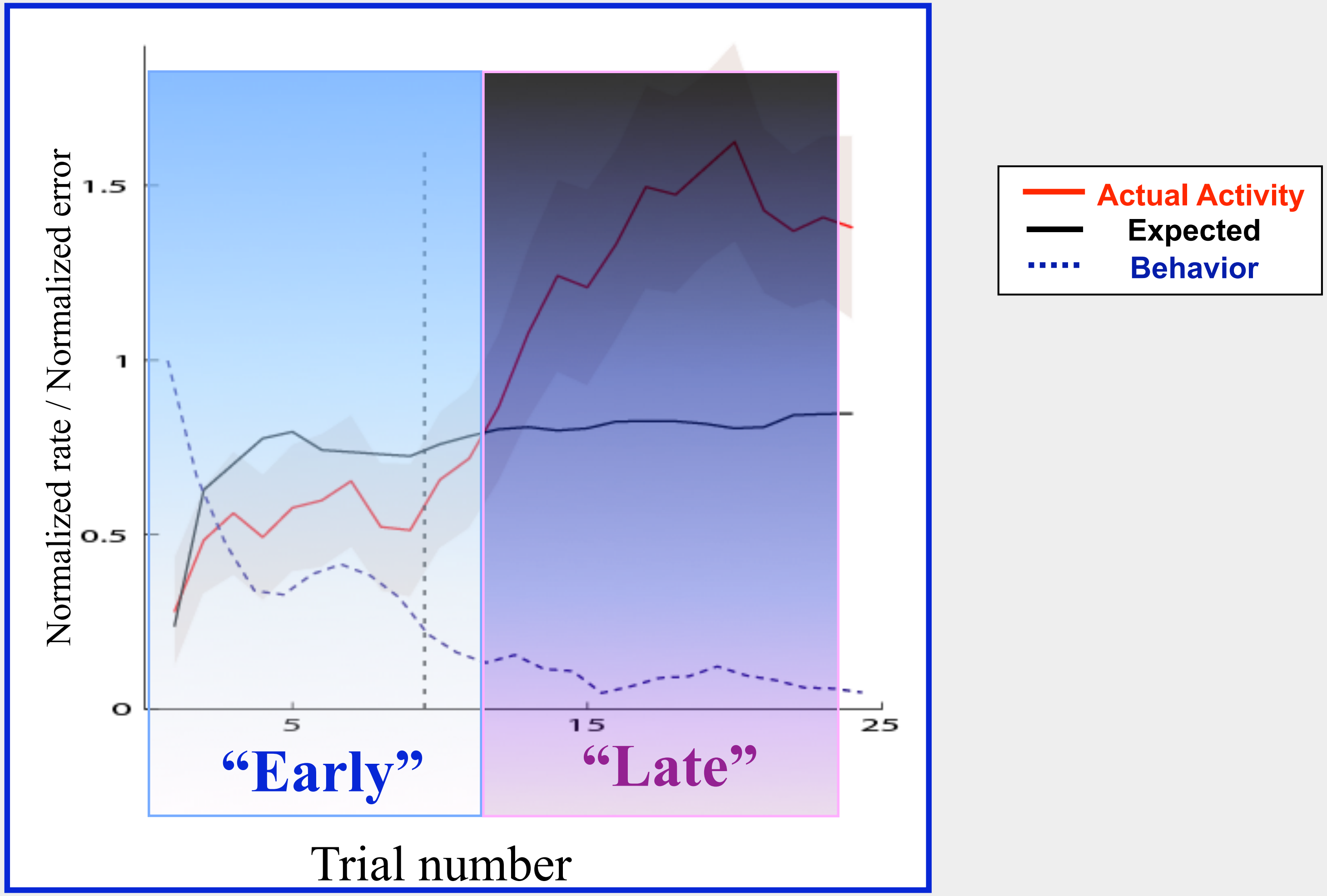
## *Increased firing rate in selected population during learning (from Visuomotor Rotation)*




*Paz et al. Nature Neurosc. 2003*

# Conclusions – Why BMI, Why KARMA?

1. Good Neural prosthetic  Desired features:
   - High quality predictions (accurate, fast, natural-like)
   - Fast learning
   - No daily active training – The models learns from scratch in 1-2 minutes
   - Adaptivity
   - Real-time performance
2. Science 1: Using the internal model notion “like the brain” May Reveal significance of neural and behavioral features by analyzing algorithm’s characteristics
3. Science II: Experimental tool for studying encoding and learning in the motor system with causal relations between neural activity and “behavior”

## *How far BMI can take us?*

**Basic assumption:**

**IF There is nothing but Physical processes in the brain.**

**Then: In principle BMI can lead far into the realm of Science fiction.**

- Technological Issues
- Ethical Issues
- Economical Issues

# Predicting behavior from Neuronal activity

| | *No-state* | *State based* |
|---|---|---|
| *Linear* | (standard) Linear Regression<br>$y(t) = \mathbf{b} + \sum_{u,i} w_i(u)\mathbf{X}_i(t-u) + \varepsilon(t)$<br>⬇<br>$\hat{\mathbf{y}}_t = \mathbf{W}\mathbf{x}_t$ | Population Vector<br>$\hat{\mathbf{y}}_t = \hat{\mathbf{y}}_{t-1} + \mathbf{W}\mathbf{x}_t$<br>(standard) Kalman Filter<br>$\hat{\mathbf{y}}_t = \mathbf{A}\hat{\mathbf{y}}_{t-1} + \mathbf{K}_t(\mathbf{x}_t - \mathbf{H}\mathbf{A}\hat{\mathbf{y}}_{t-1})$ |
| *Non-linear* | Support Vector Regression<br>$\hat{y}_t = W\phi(X_t)$ | **KARMA**<br>$\hat{y}_t = W\phi(X_t, Y_t)$ |

$y$ is state (movement) at time $t$
$\mathbf{X}$ is the matrix of neural activity
$\mathbf{W}$ is matrix of weights.

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