Bidirectional interactions between the brain and implantable computers

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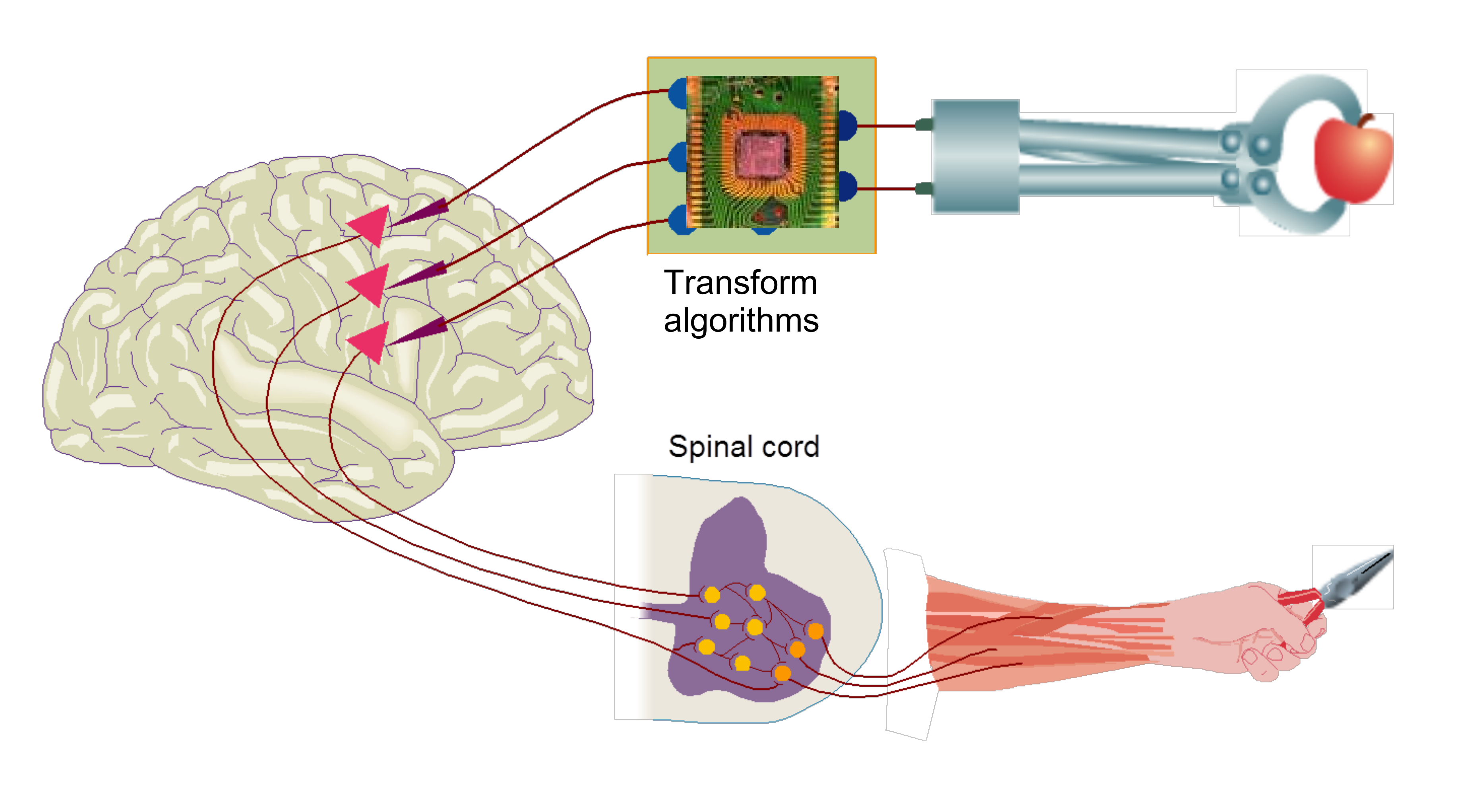
Brain-computer interface to transform cortical activity to control signals for prosthetic arm

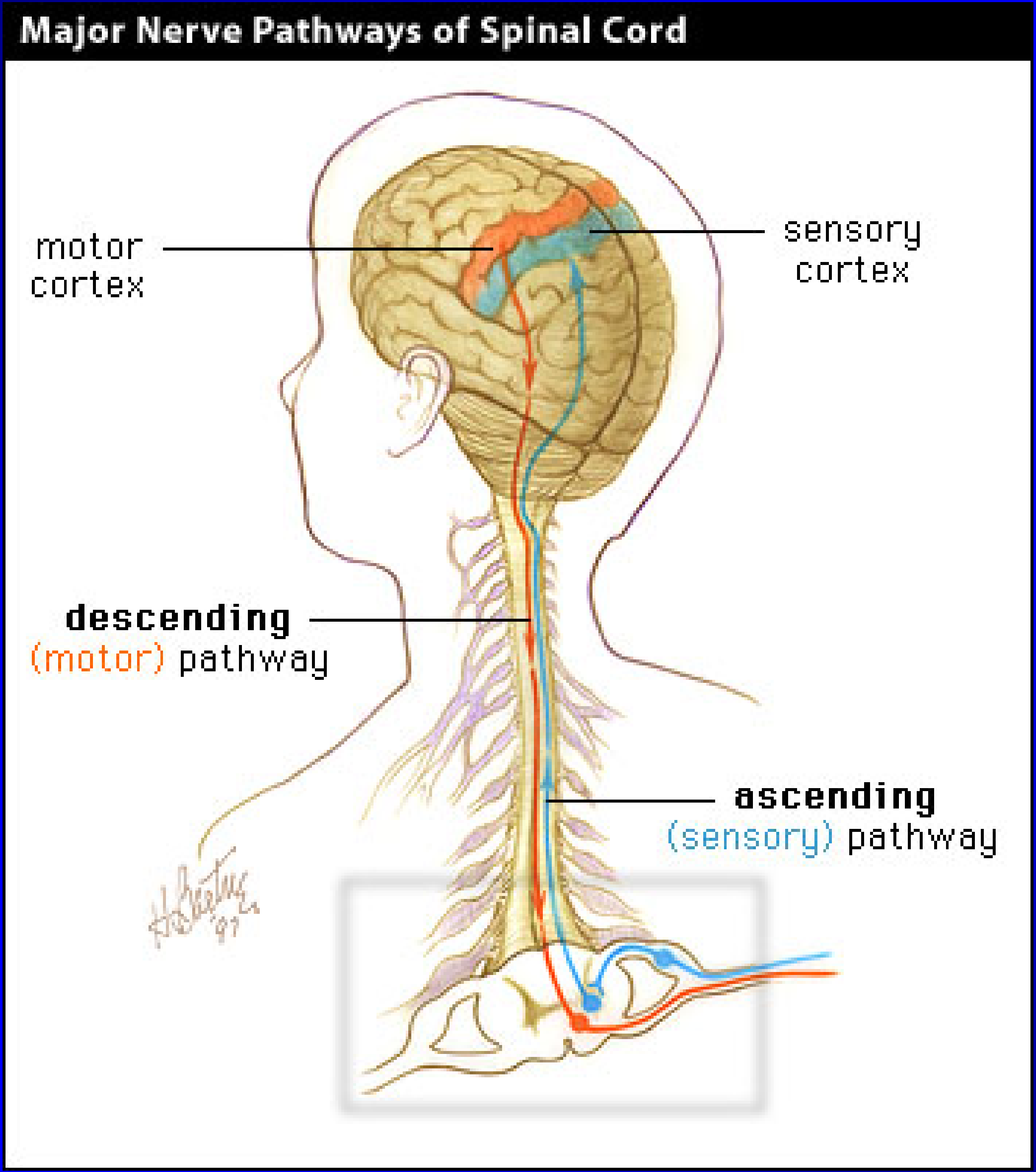


Adaptive control of cortical neurons is required to generate appropriate control signals

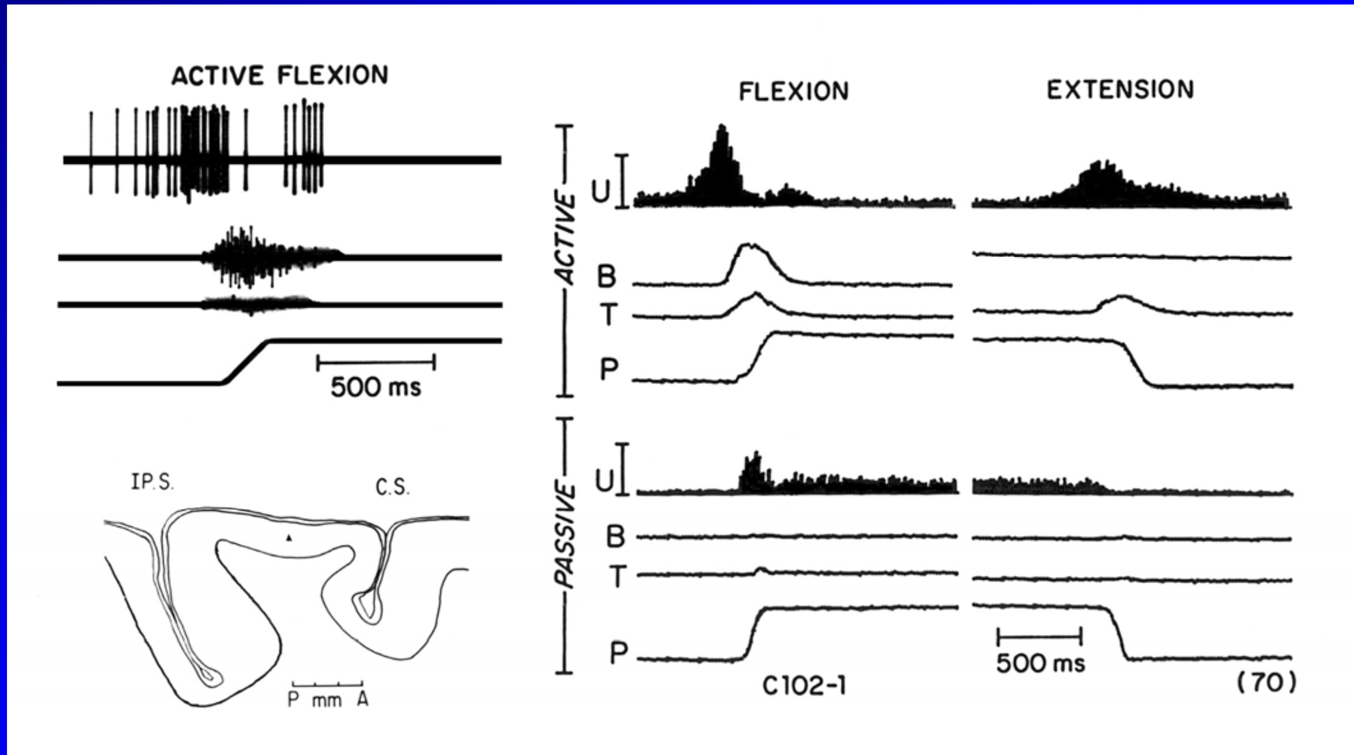
Fetz, *Nature Neuroscience* 2: 583, 1999

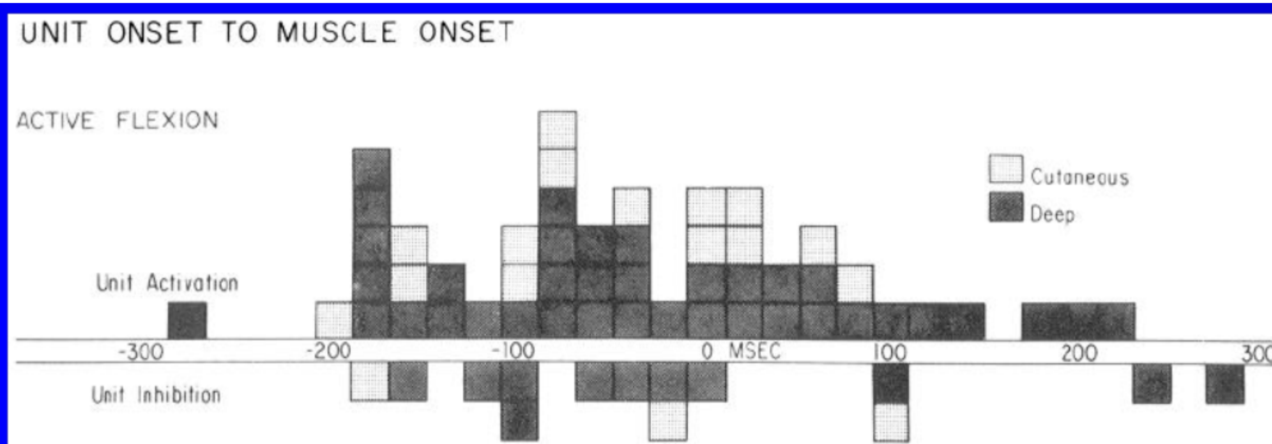
Volitional control of neural activity & recurrent brain-computer interfaces

1. Volitional modulation of cortical neurons
2. Volitional control of neural activity
   through biofeedback
3. Volitional control of brain-computer and
   brain-machine interfaces
4. Implanted recurrent brain-computer interface


Major Nerve Pathways of Spinal Cord
motor cortex
sensory cortex
descending
(motor) pathway
ascending
(sensory) pathway

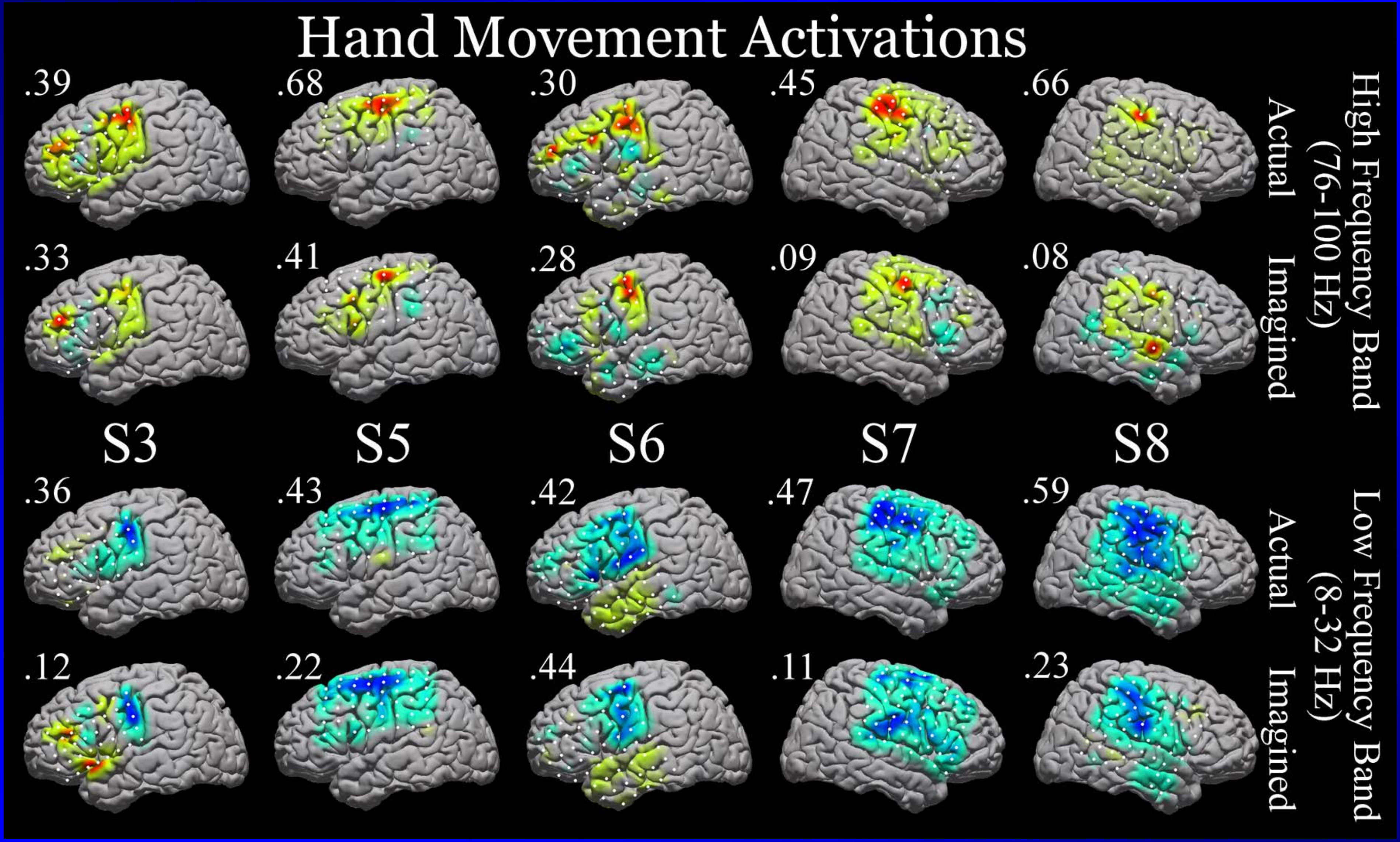
Central input to many sensory cortex cells





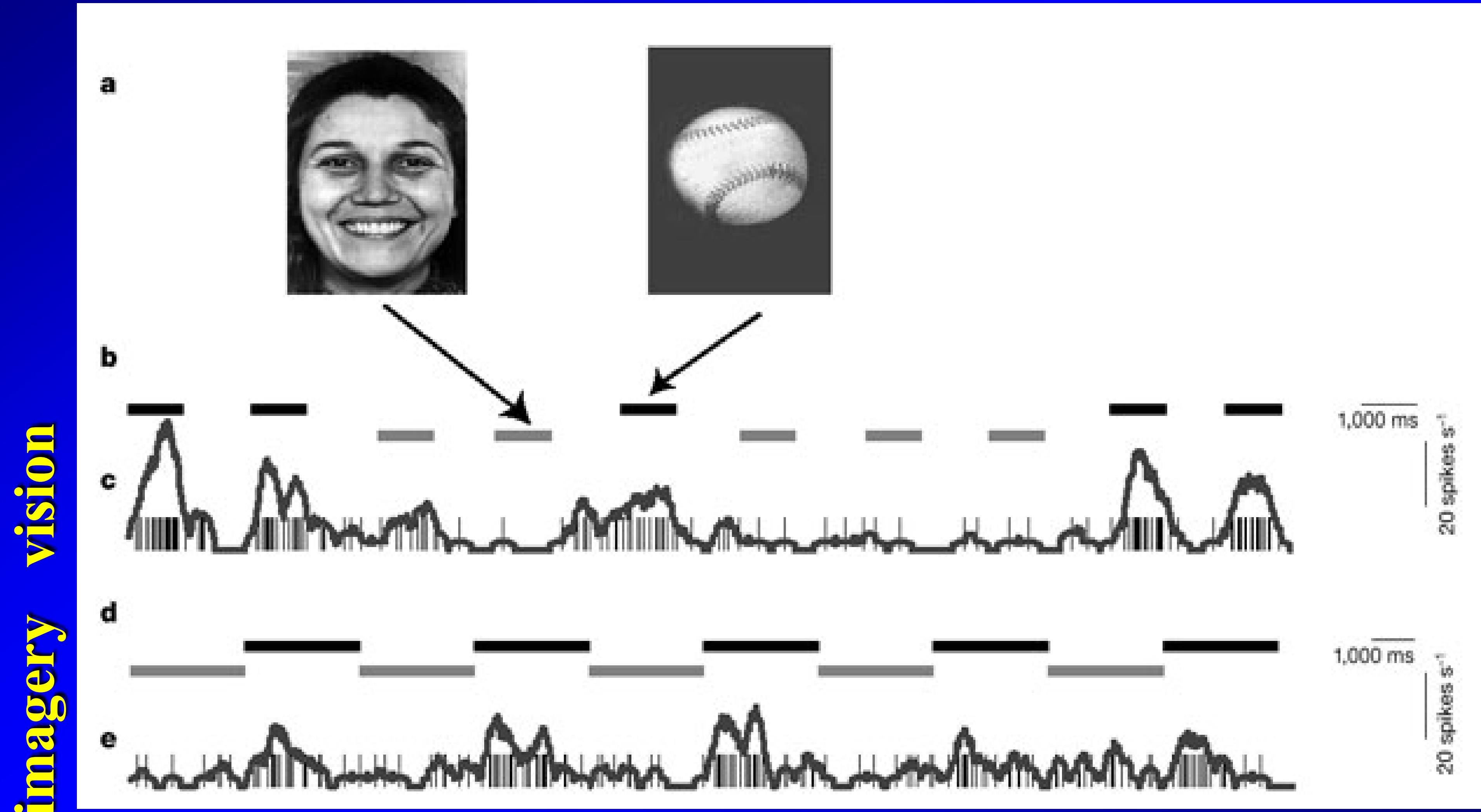
Soso & Fetz, *J. Neurophysiol*. 41, 1090 – 1110, 1980

Cortical ECoG power with real and imagined movement



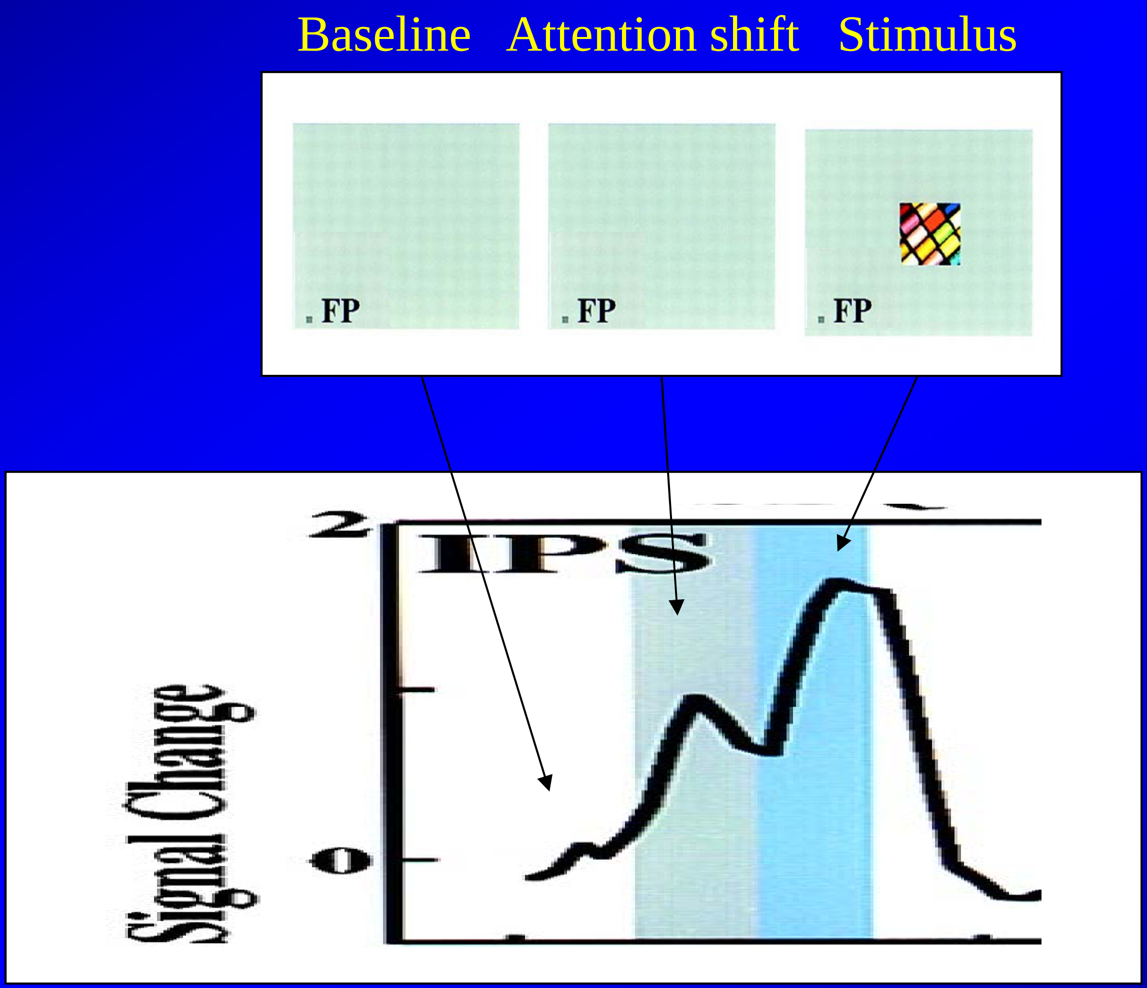
Miller, Ojemann, Rao et al, *PNAS 107: 4430–4435 , 2010*

Cells are activated by visual imagery
in amygdala, entorhinal cortex, hippocampus



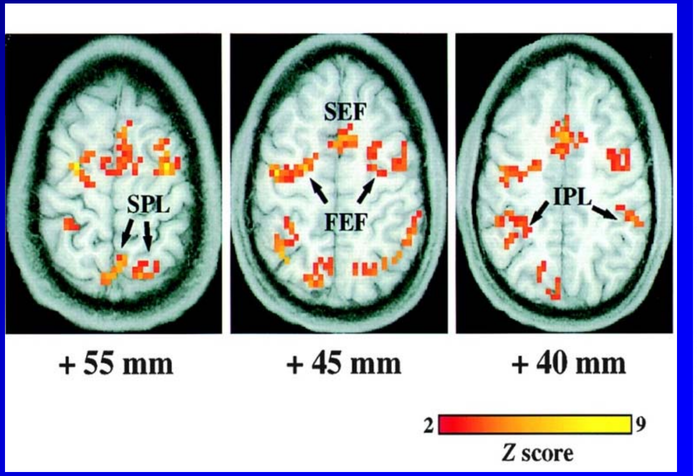
Kreiman, Koch & Fried, *Nature* 408: 357, 2000

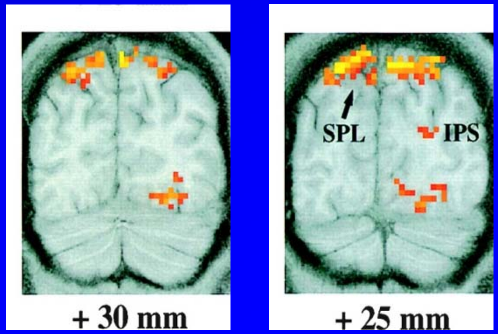
Cortical cells are activated by volitional shifts of attention

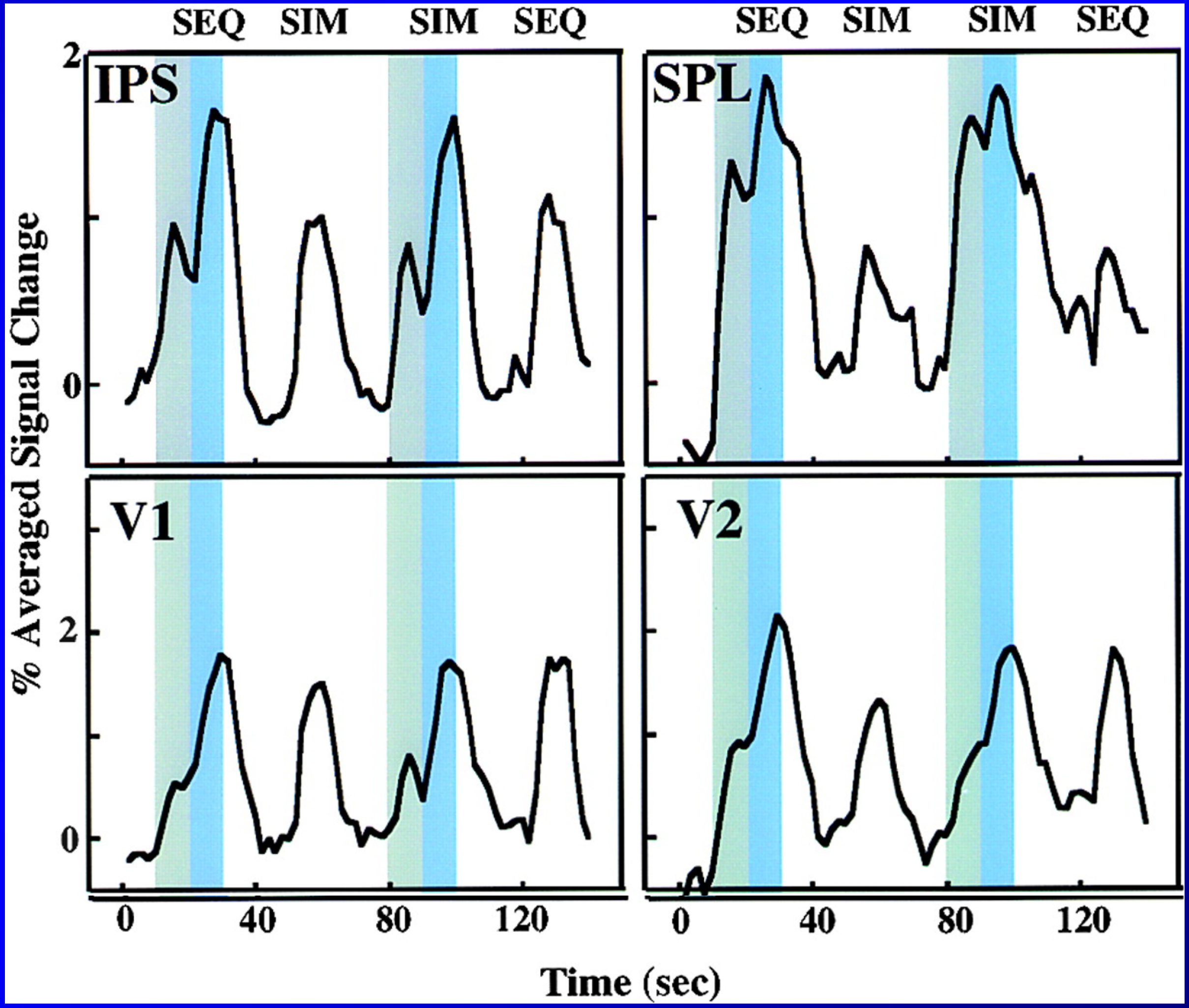


Kastner, Desimone, Ungerleiter et al, *Neuron* 22: 751, 1999

Many cortical areas activated by shifts of attention





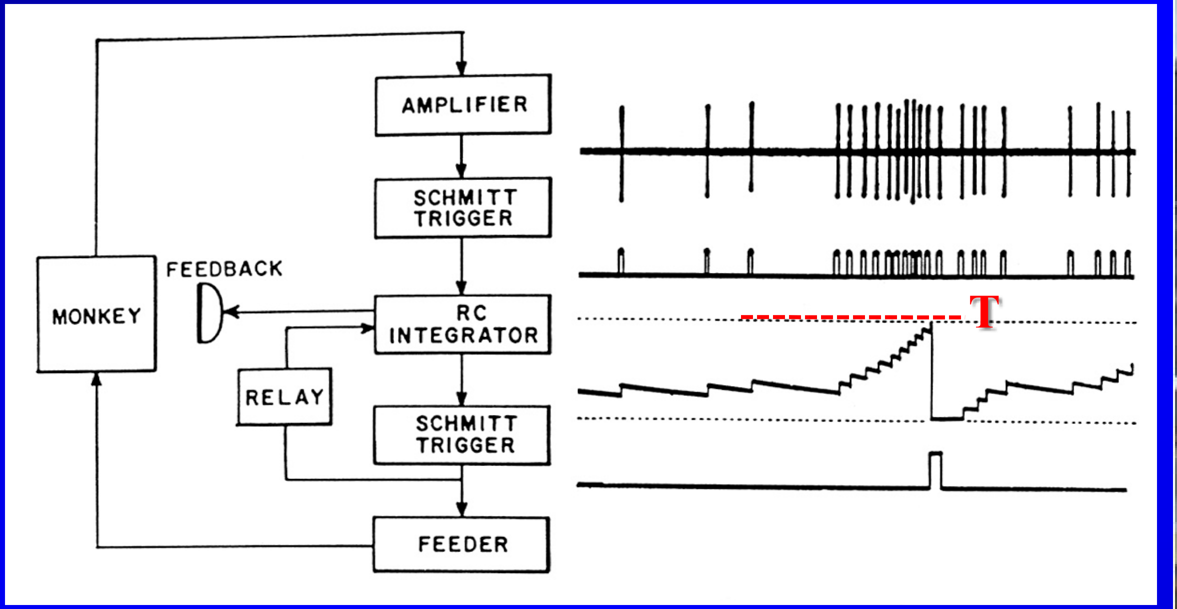


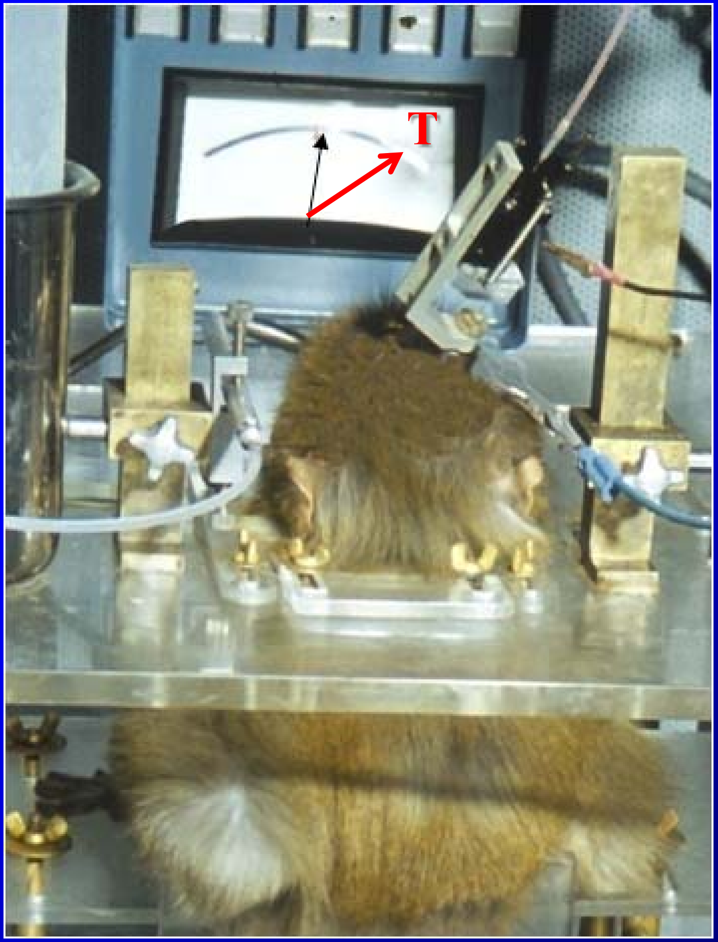
Kastner et al, *Neuron* 22: 751, 1999

Volitional activation of neural activity

1. Volitional movements [real & imagined]
2. Preparatory activity
3. Activation of internal representations
4. Shifts of attention [“top down” signals]
5. Cognitive processing [“thinking”]
6. Directly evoked with biofeedback

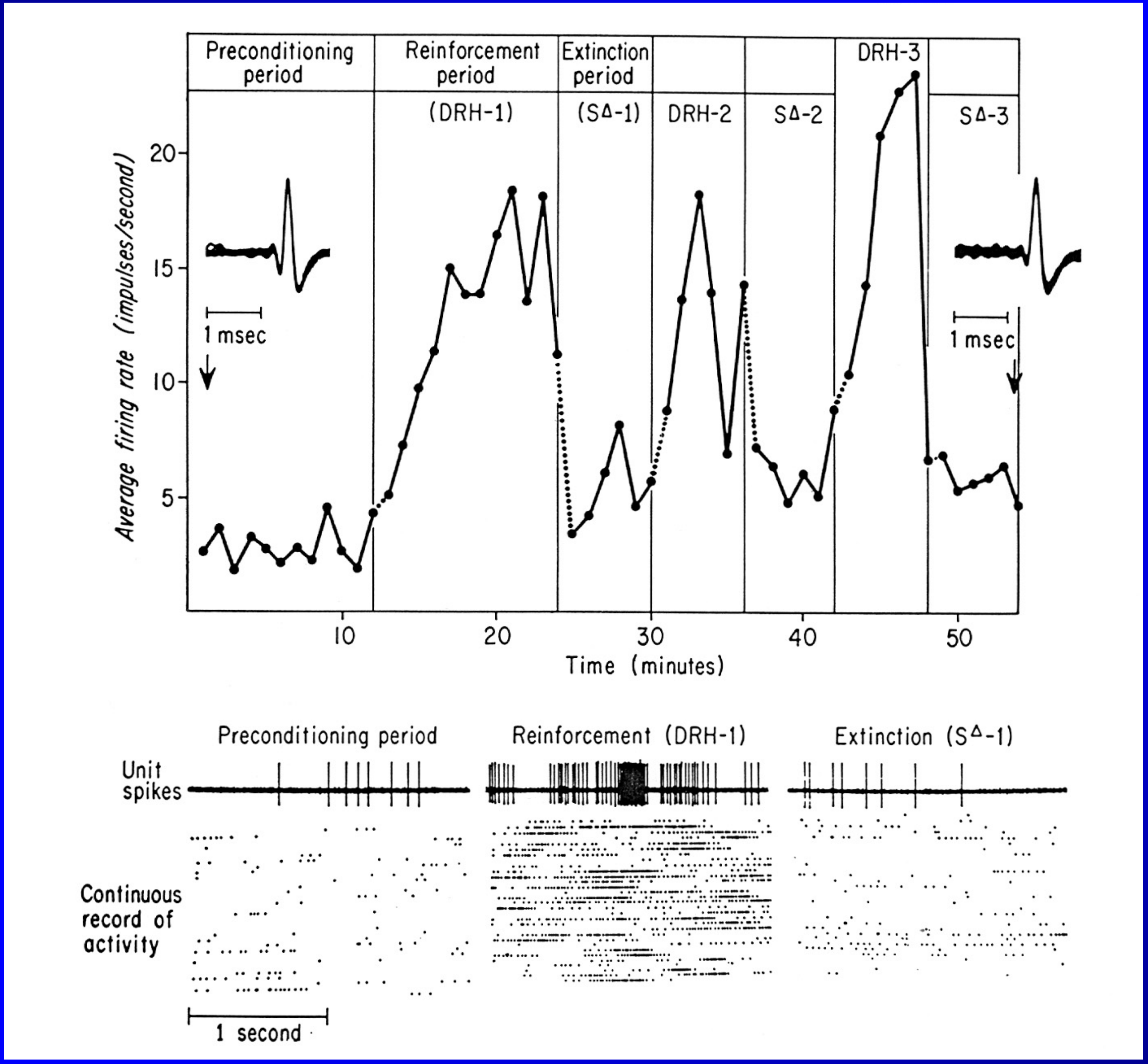
Cortical cell activity controls biofeedback meter arm





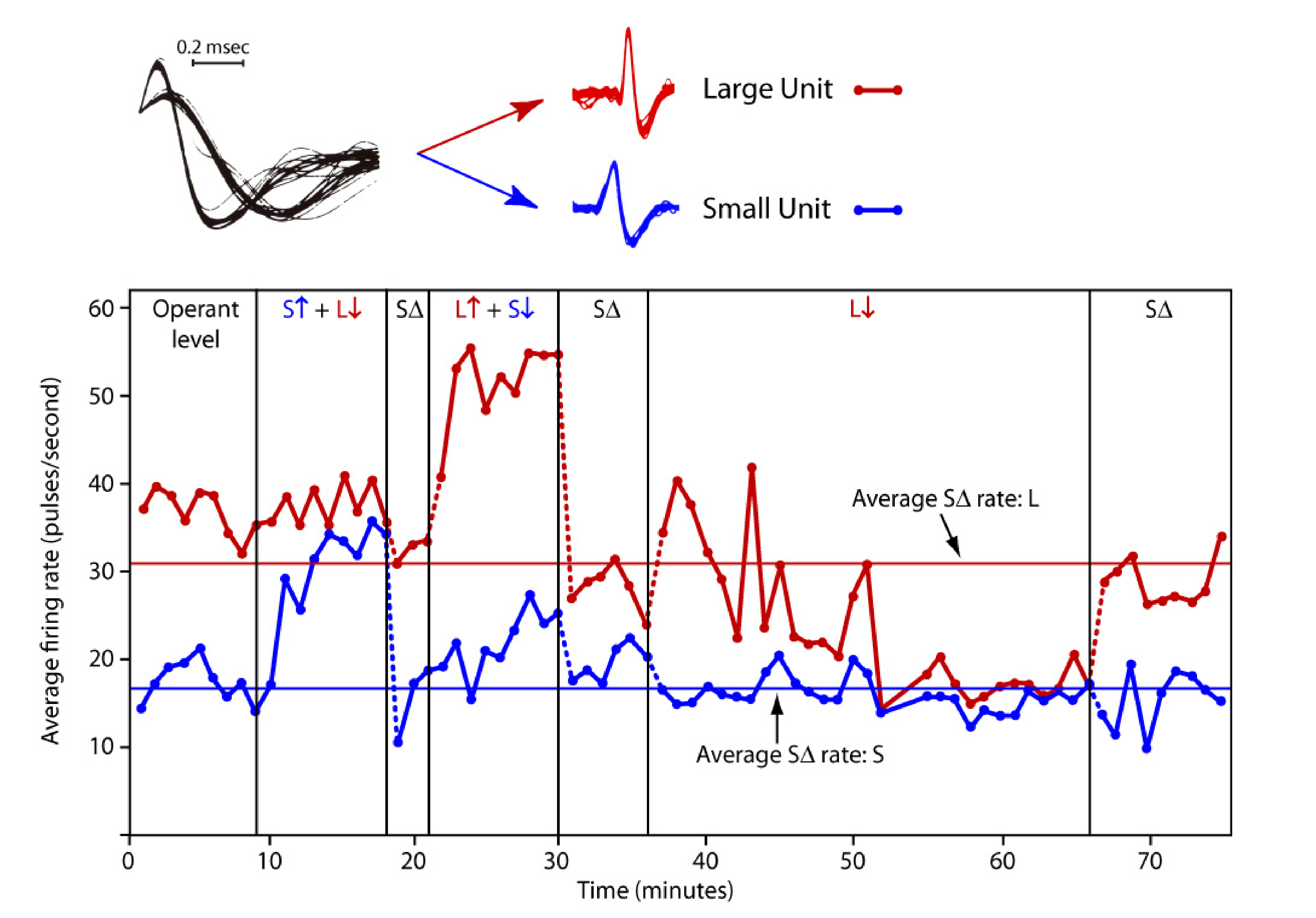
Fetz, *Science 163*: 955-958, 1969

Monkey increases activity of new cell



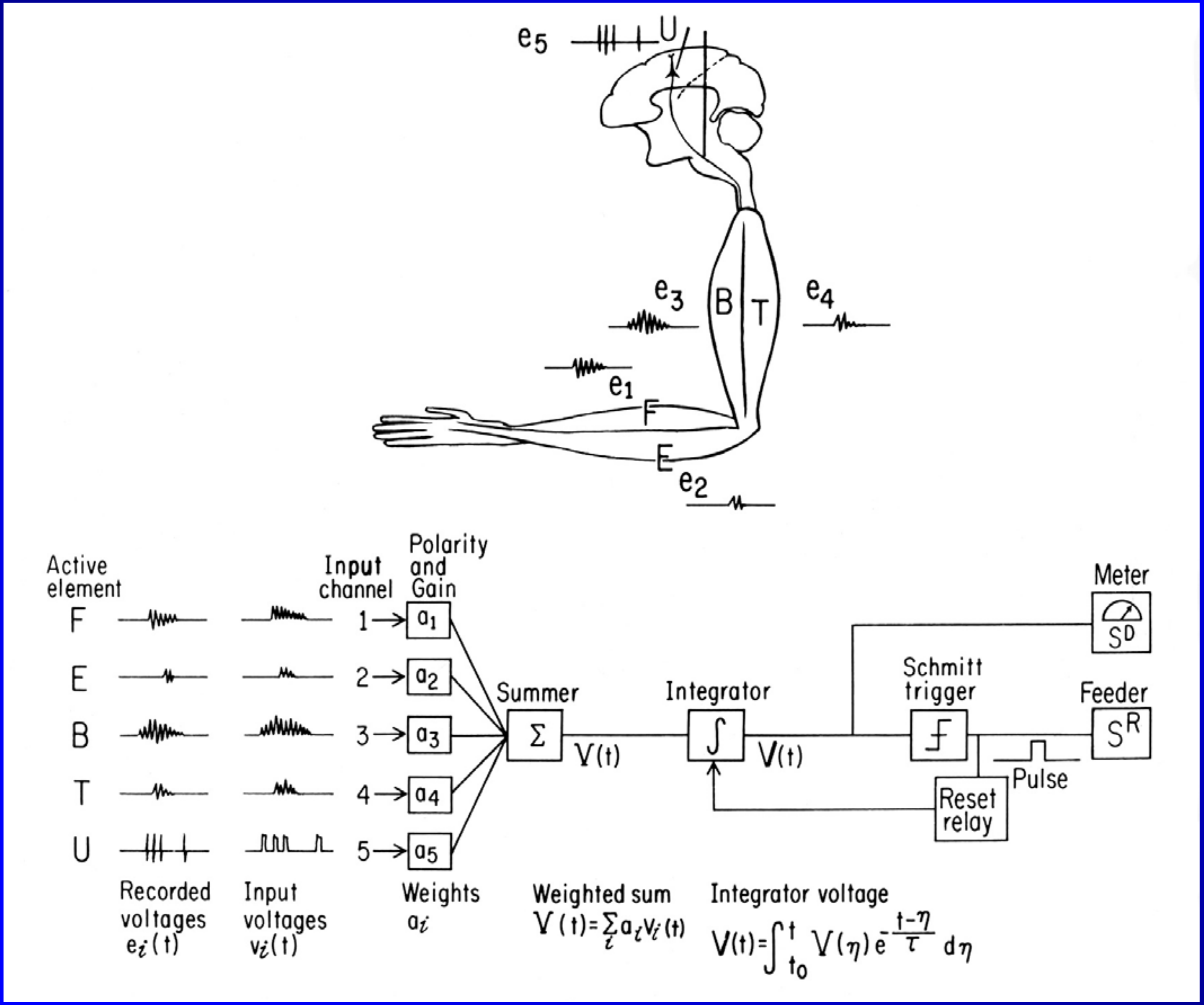
Fetz & Baker, *J. Neurophysiol 36*:179-204, 1973

Independent control of neighboring neurons



Fetz & Baker, *J. Neurophysiol 36*:179-204, 1973

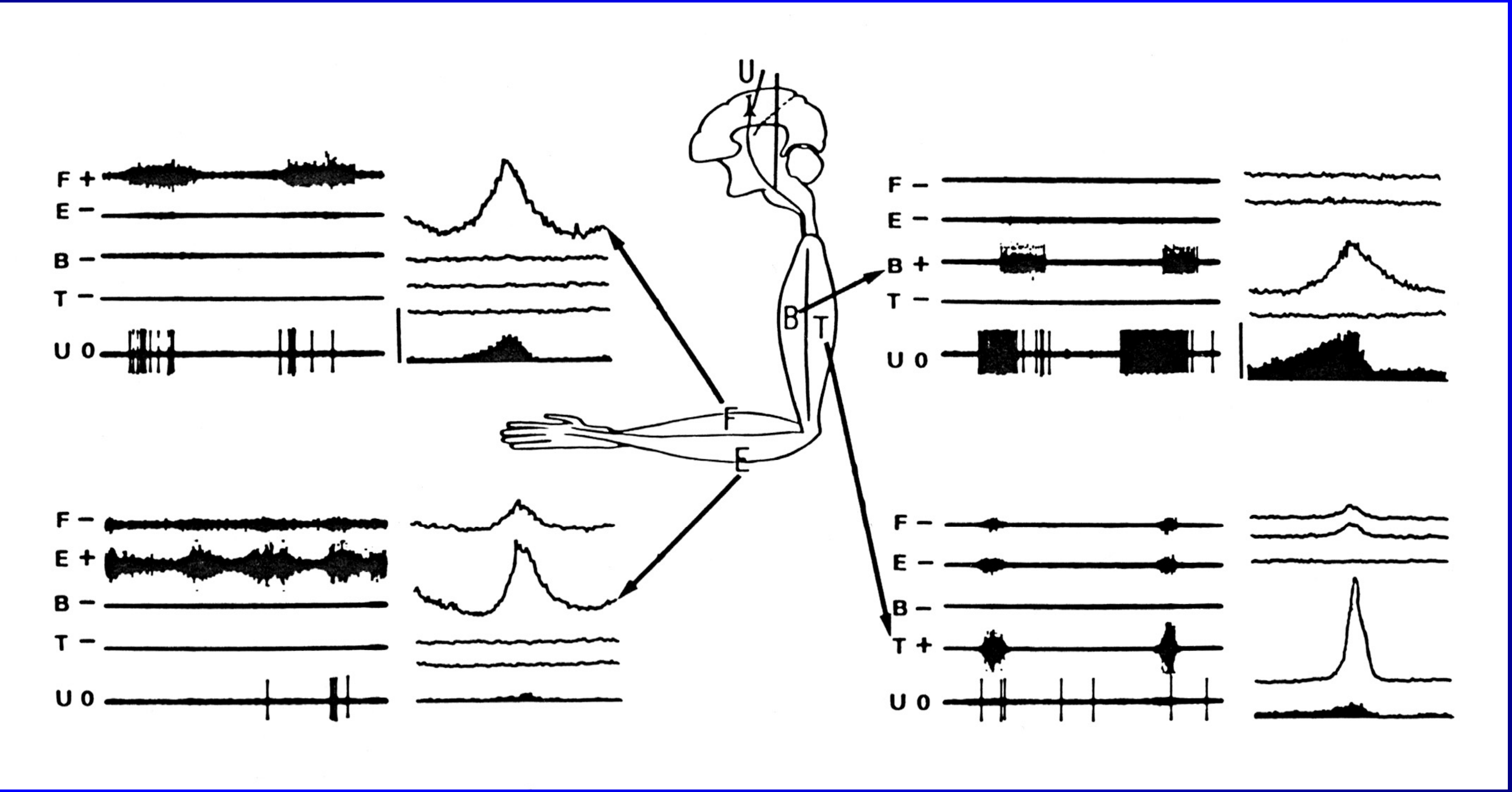
Conditioning cell and muscle activity



Fetz & Finocchio, *Science* 174:431-435, 1971

Isolated isometric EMG bursts

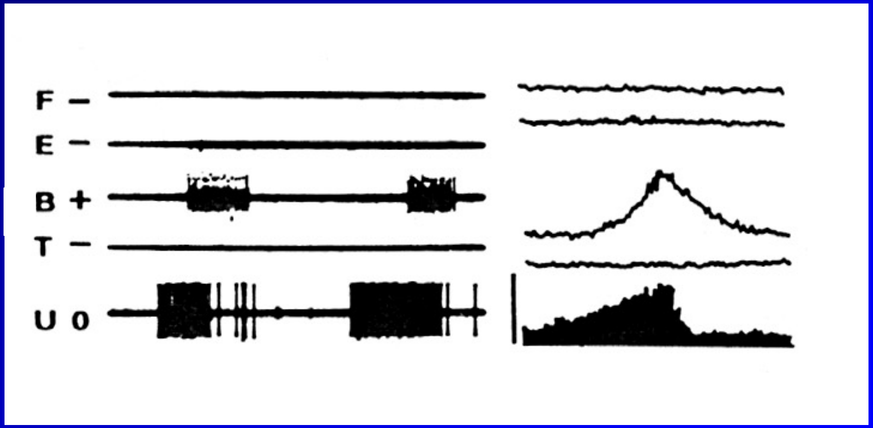
Cell fires with biceps and wrist flexor



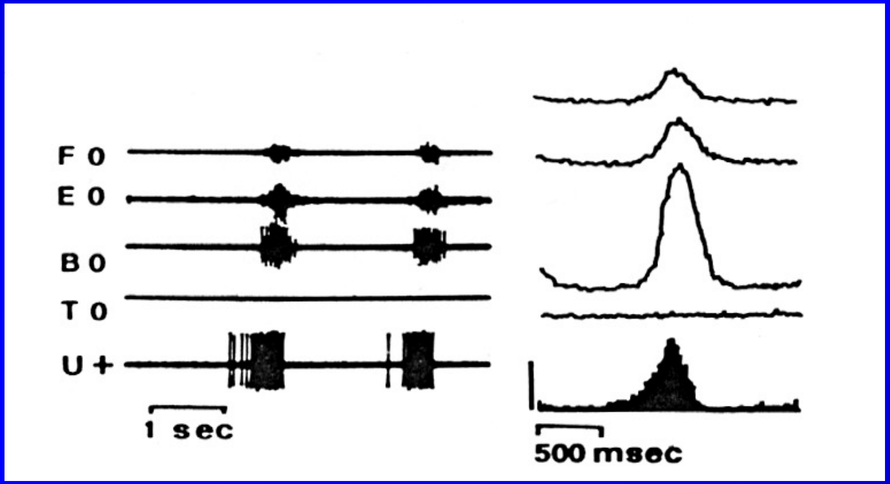
Fetz & Finocchio, *Science* 174:431-435, 1971

Motor cortex cells could be dissociated from muscles

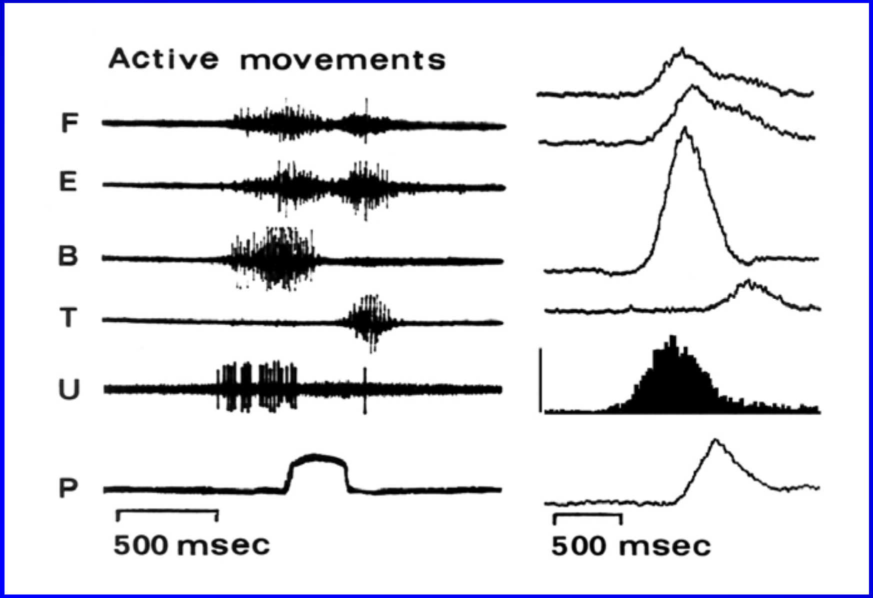
Isometric biceps bursts



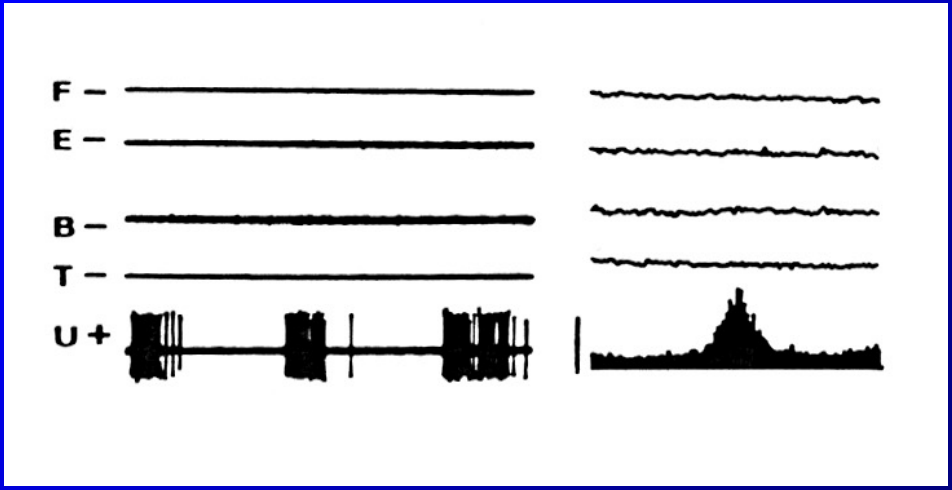
Isometric unit bursts



Active elbow flexion

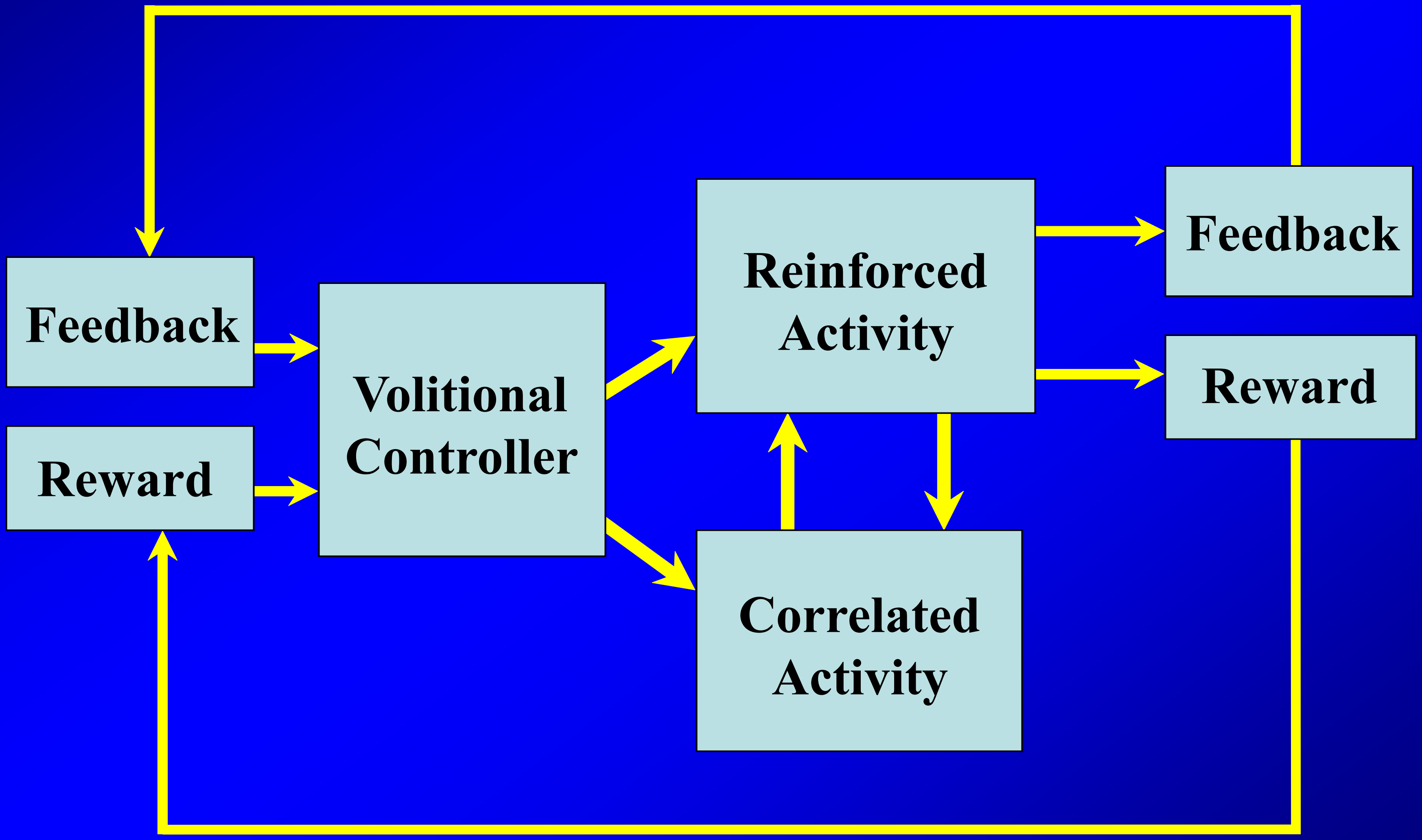


Unit increase and muscles decrease



Fetz & Finocchio, *Exp. Brain Res.* 23:217-240, 1975

Basic biofeedback paradigm



Biofeedback conditioning of CNS activity
[cf. "Biofeedback and Self-Control" Annuals 1970-77]

1. Single neurons

Motor units *[human]* Harrison 1962; Basmajian 1967

Motor cortex *[monkey]* Fetz 1969, 1973; Schmidt 1977

Midbrain *[rat]* Olds 1961, 1965

2. Spontaneous EEG & LFP

Cortical Alpha *[human]* Kamiya 1968; Sterman 1969

Hippocampal Theta *[dog]* Black 1970, 1972

Amygdala spindling *[chimpanzee]* Delgado 1970

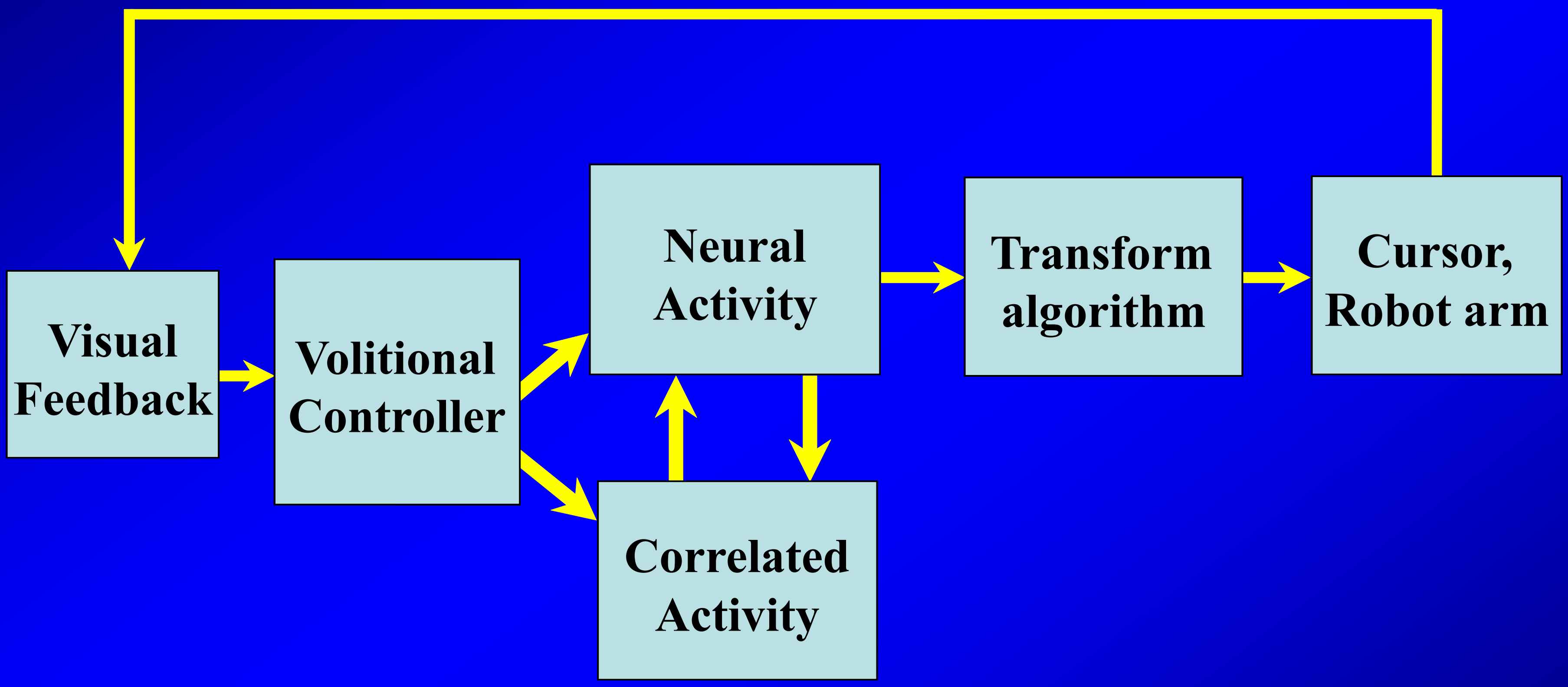
3. Evoked potentials

Visual cortex *[cat]* Fox & Rudell 1968, 1970

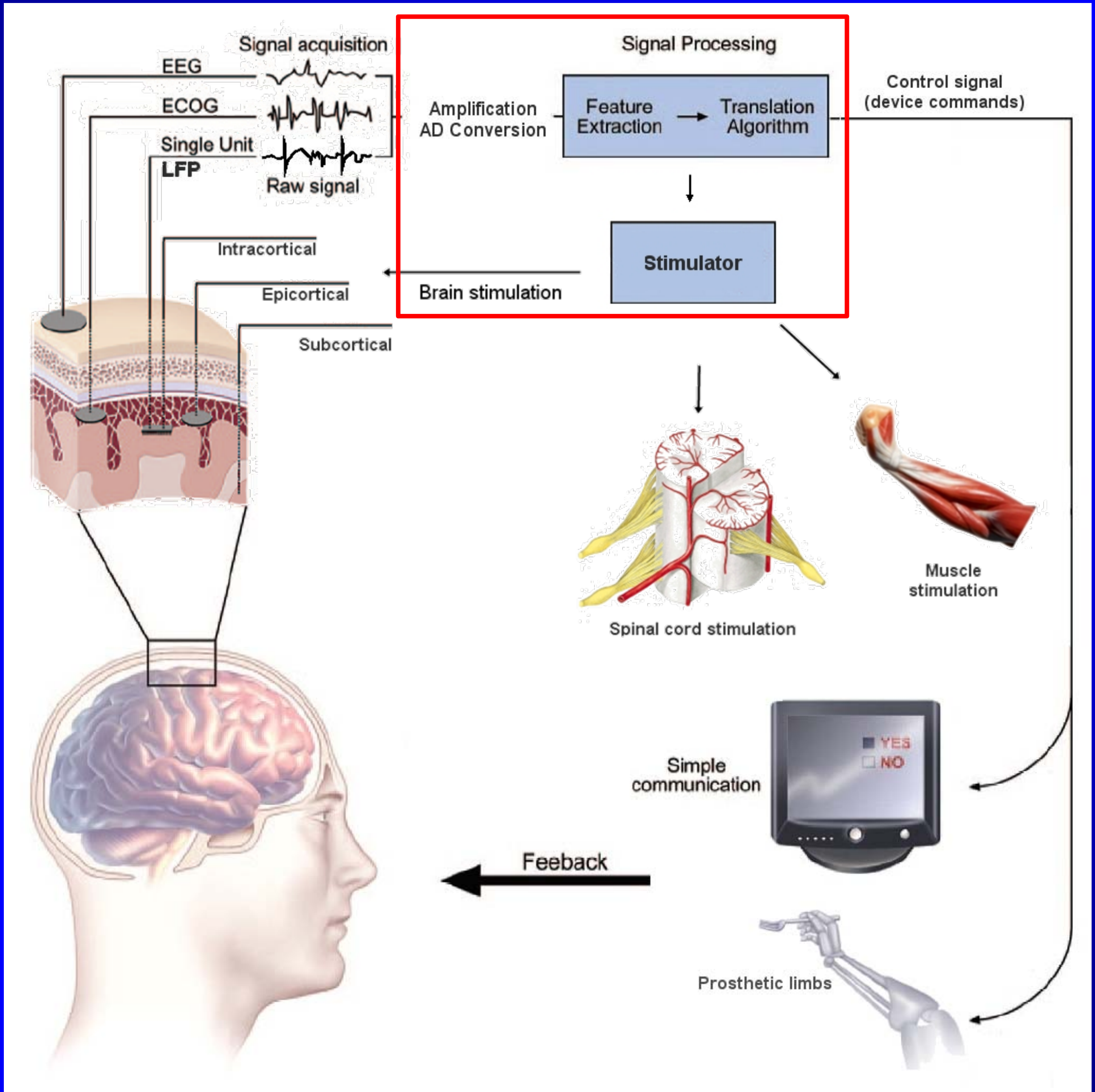
Auditory cortex *[human]* Rosenfeld 1970

Spinal stretch reflex *[monkey, rat]* Wolpaw et al 1983

Basic BCI/BMI paradigm



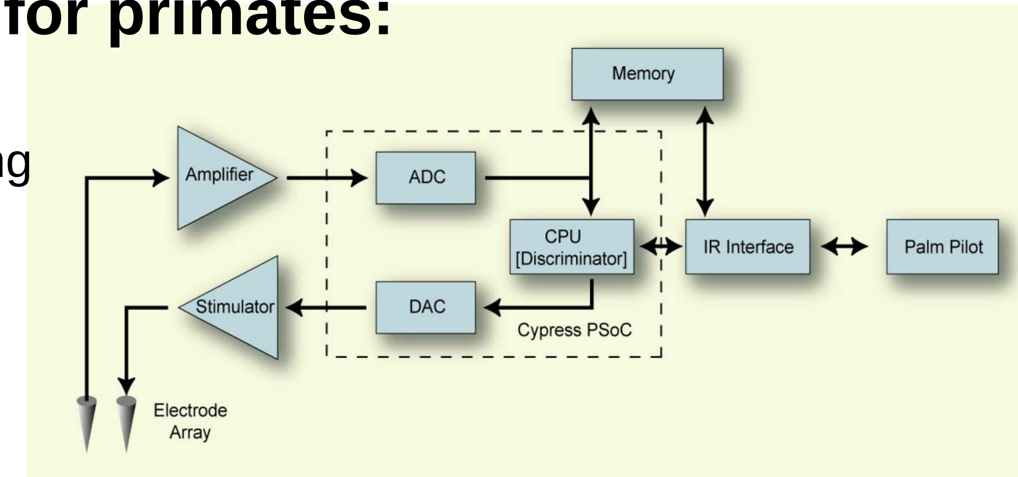
Interfacing brain and computers

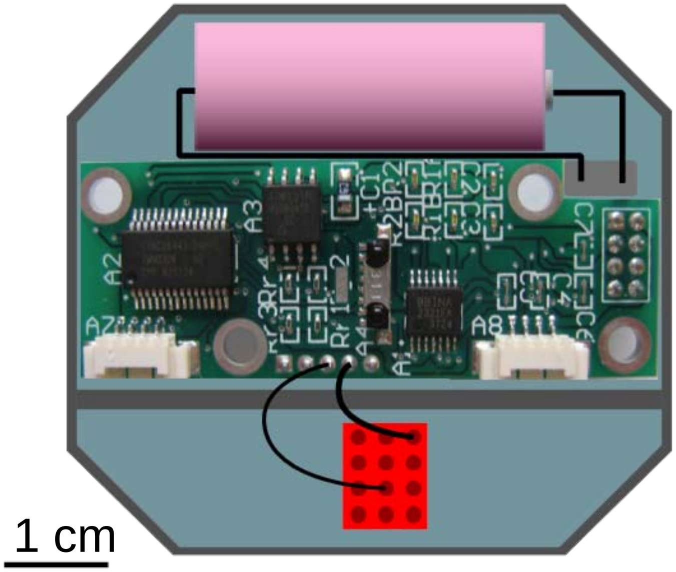


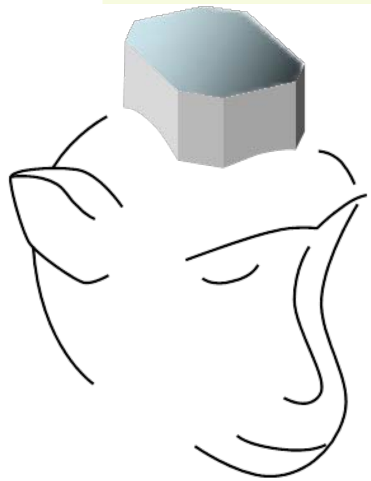
Modified from
Leuthardt, et al
Neurosurgery 59, 2007

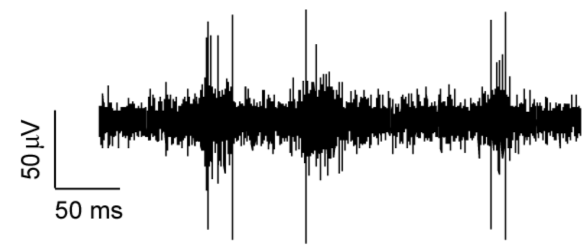
The Neurochip implant for primates:

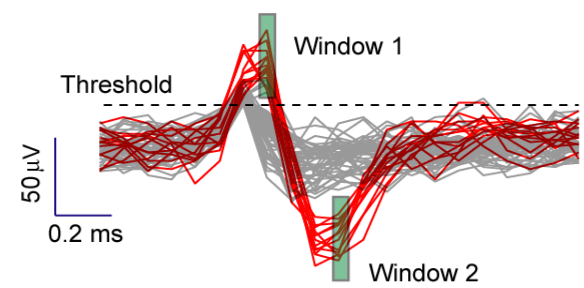
- Autonomous implant
- Neural and muscle recording
- Spike discrimination
- On-board processing
- Non-volatile memory
- Constant-current stimulator
- Infra-red link to PC
- Battery-powered





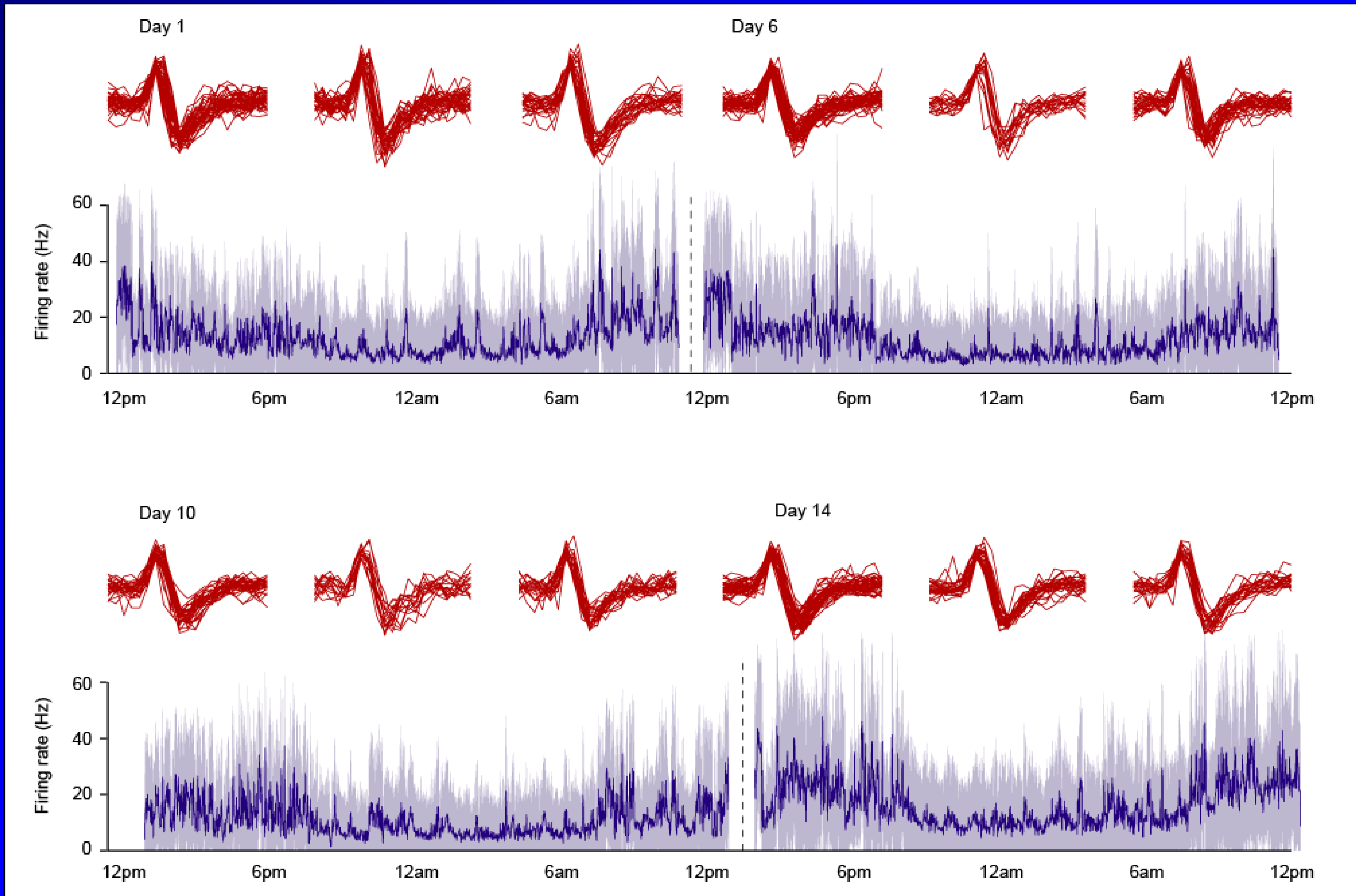






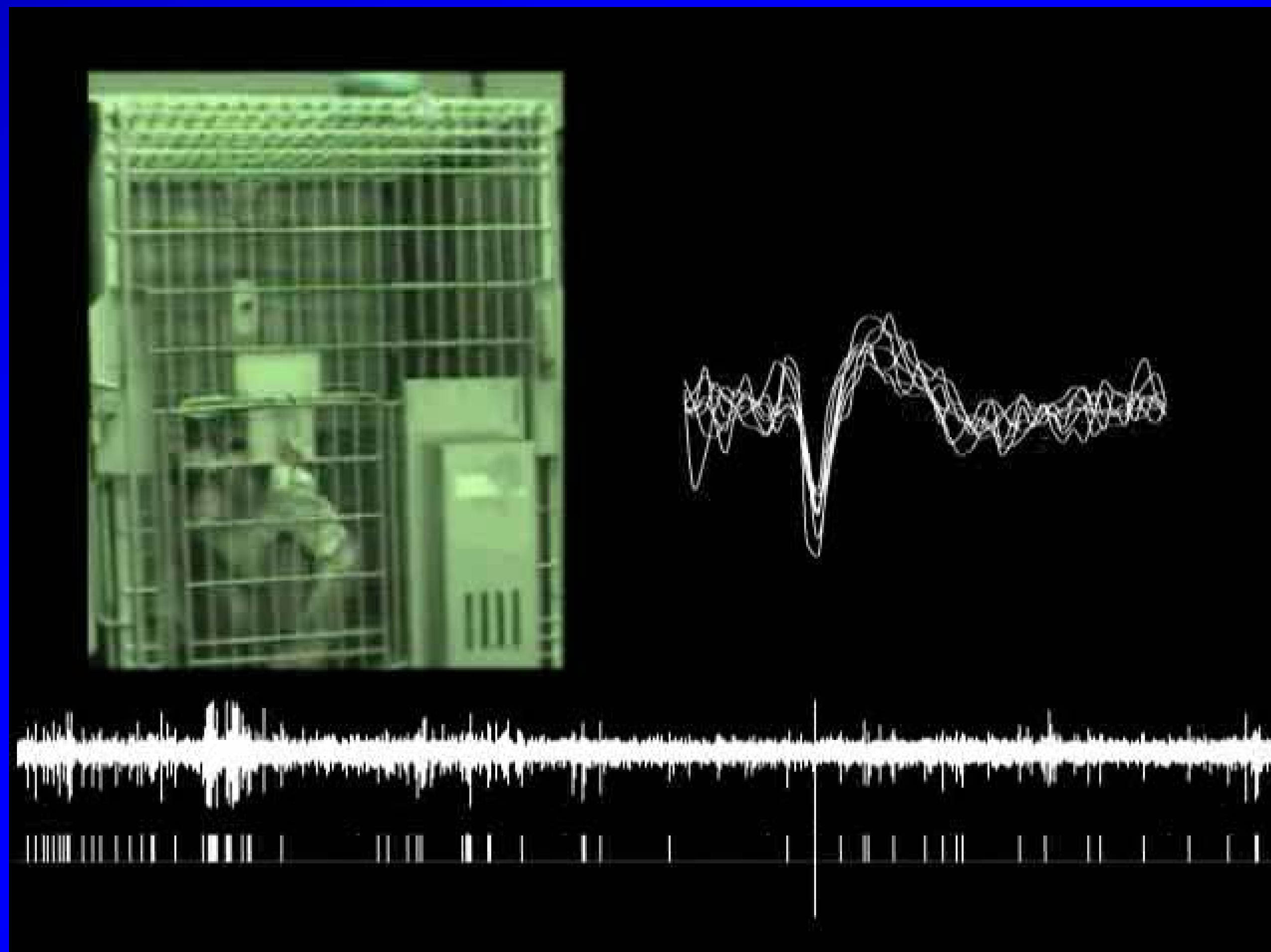
Mavoori, Jackson et al. J. Neurosci Meth. 148: 71,. 2005

Continuous recording of a single M1 neuron for 2 weeks.



Jackson et al, *J. Neurophysiol*, 97, 360-374, 2007

Stable unit recordings during free movement



Neural activity

Unit pulses

Recurrent BCIs: Two types of applications

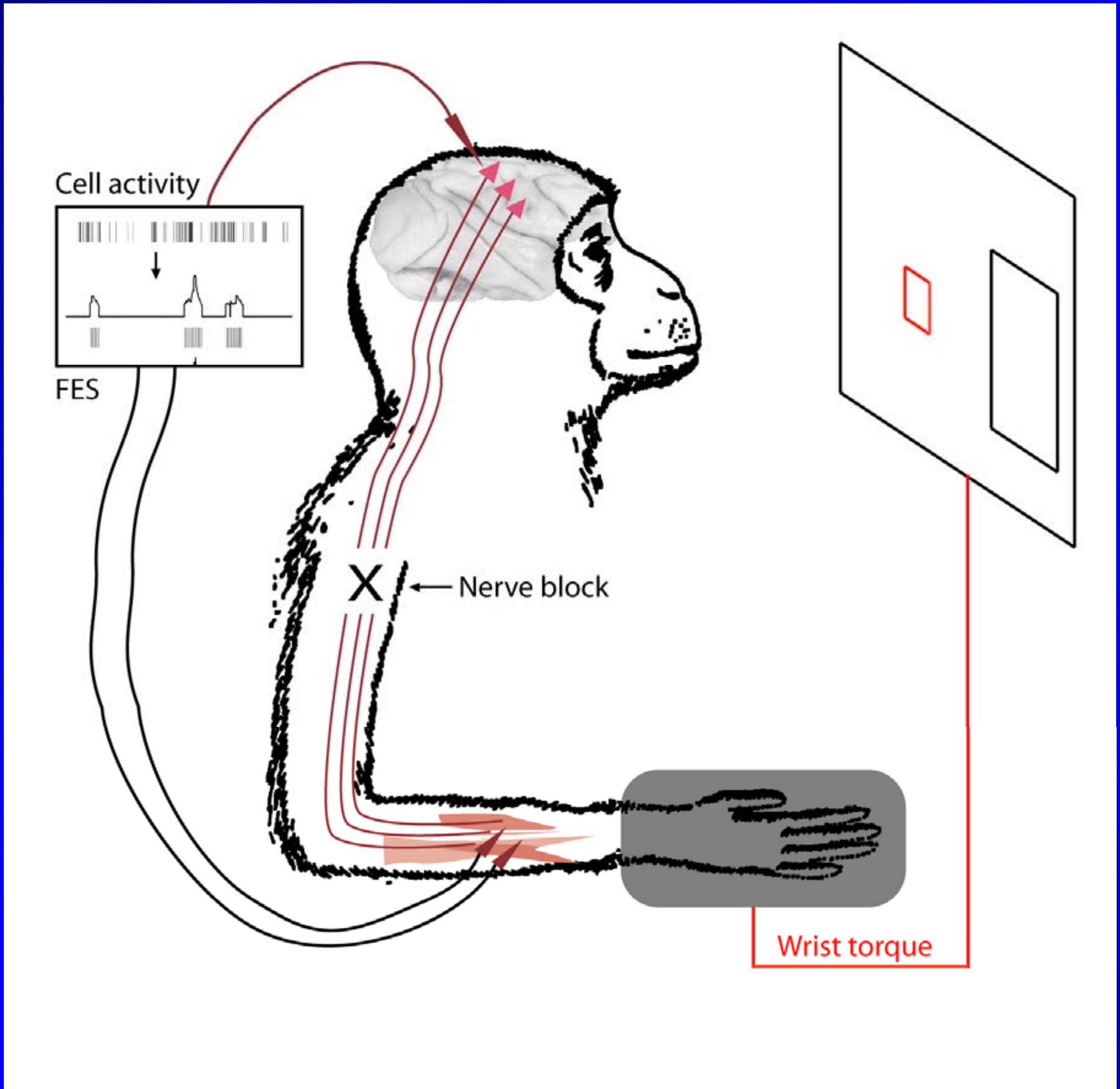
1. Create artificial recurrent connections

   Brain adapts to consistent sensorimotor conditions and could learn to incorporate the R-BCI

2. Create synaptic (Hebbian) plasticity

   Spike-triggered stimulation strengthens synaptic connections

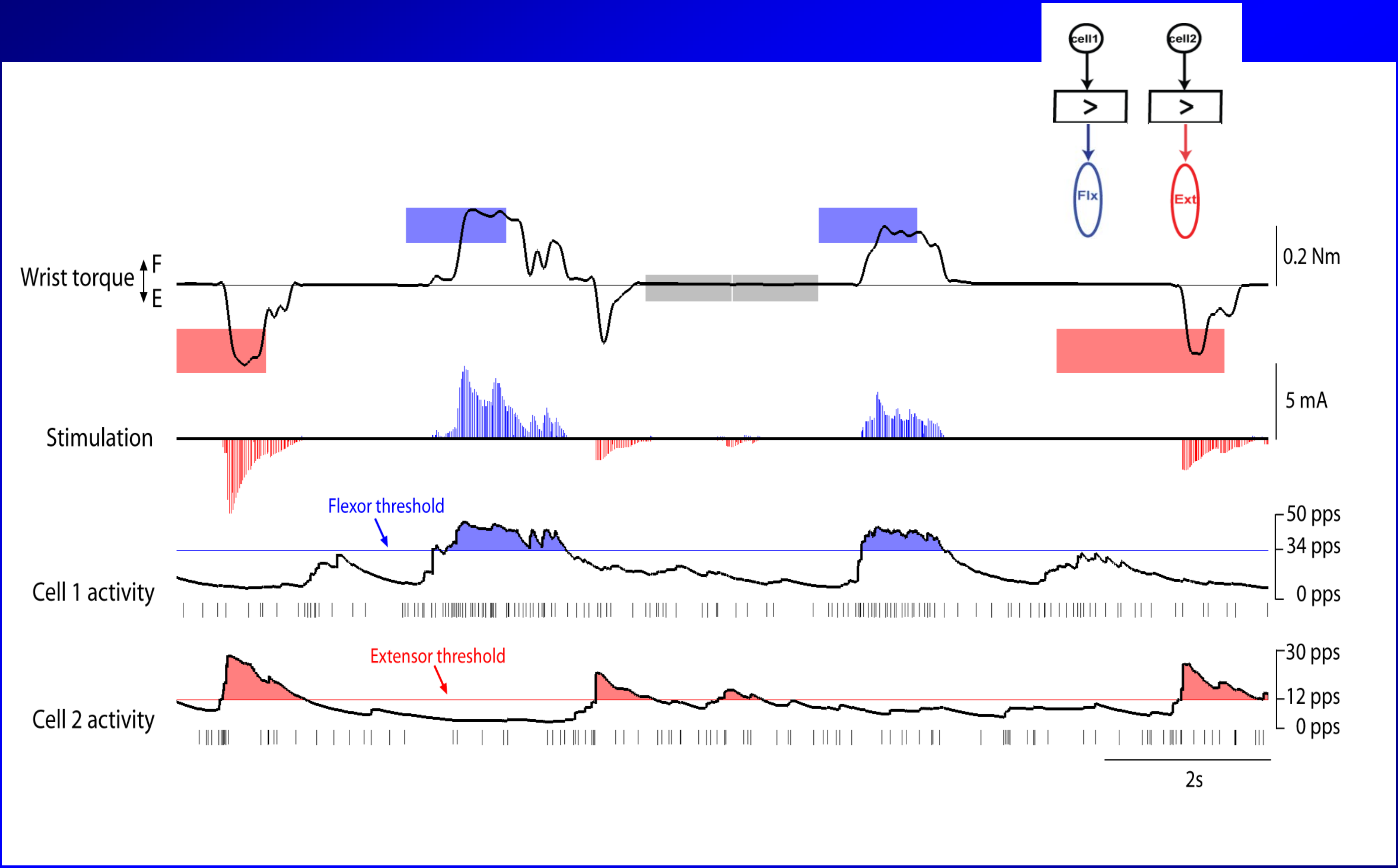
Artificial connections via Recurrent BCI: cortical spikes control FES of muscle



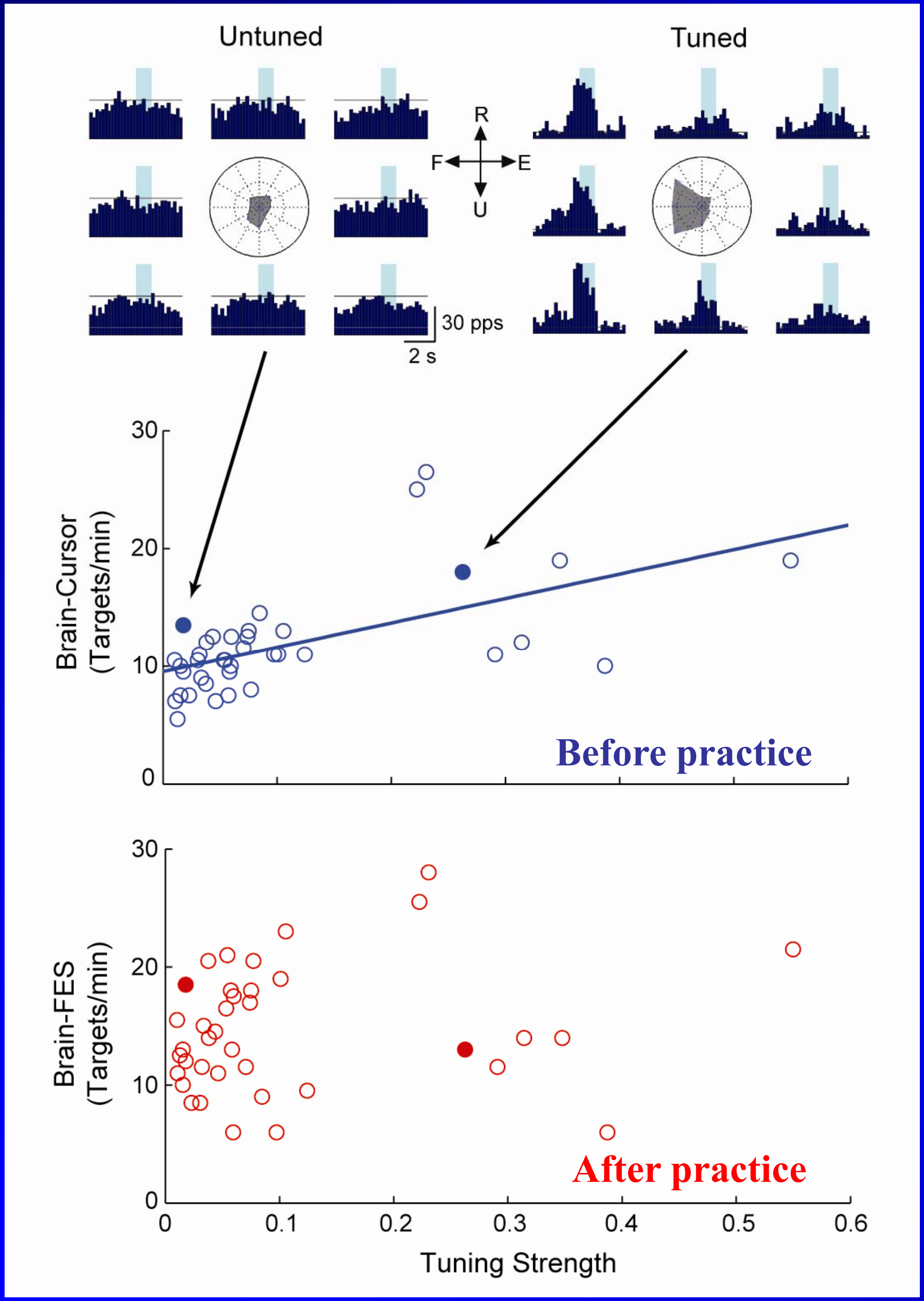
Activity of cortical cell triggers electrical stimulation of paralyzed muscles, allowing monkey to reach the force target

Moritz, Perlmutter Fetz, *Nature* 456: 639-42, 2008

Two cortical units drive two muscles (flexor and extensor)



Moritz et al, *Nature* 456: 639-42, 2008



Cell tuning does not predict control of FES

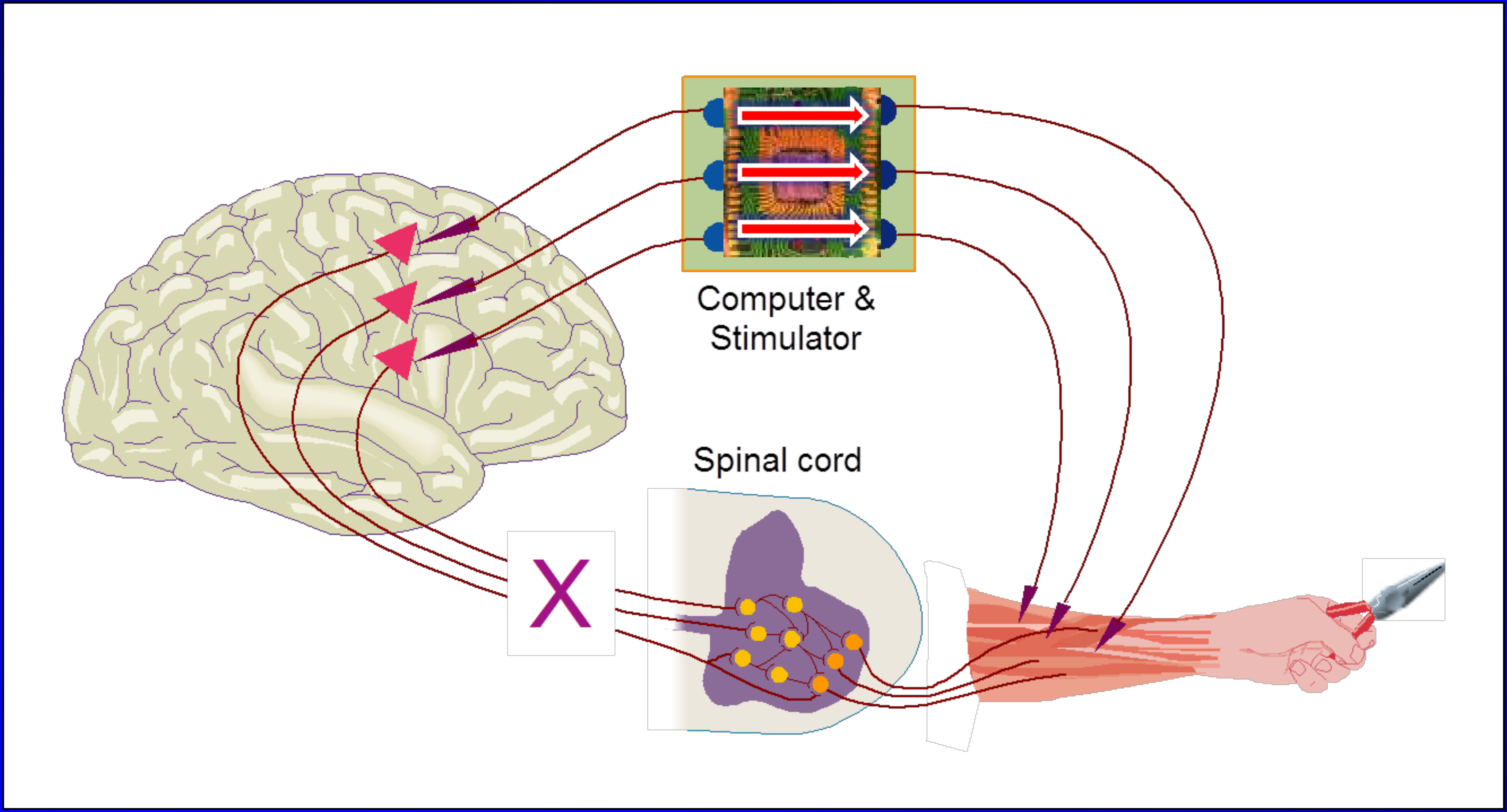
Tuned neurons initially control cursor faster

But: the brain learns to use all neurons equally well to control FES with practice

Therefore: biofeedback triples population of useful neurons

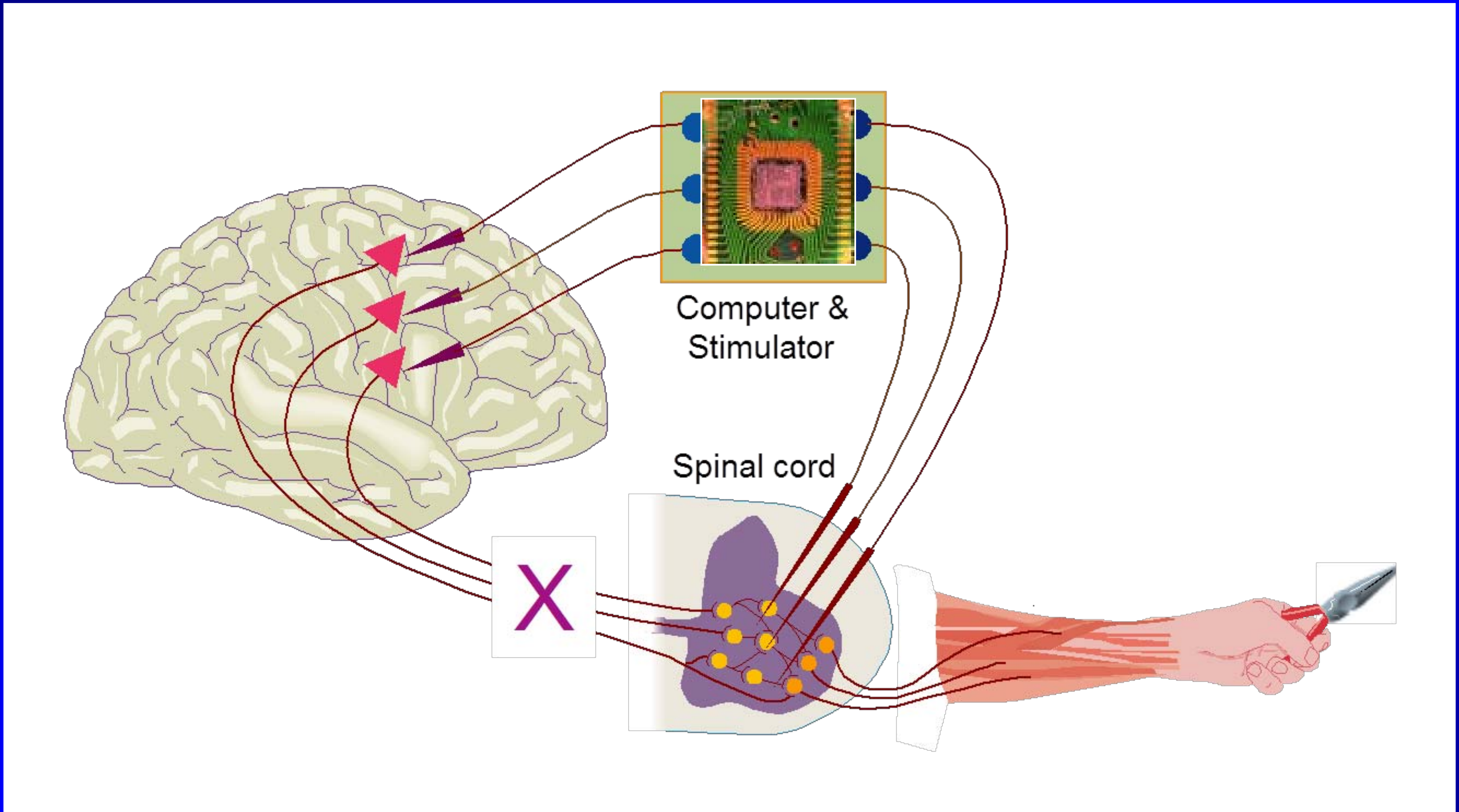
Moritz et al, *Nature* 456: 639-42, 2008

Recurrent BCI allows cortical cell activity to control muscle stimulation



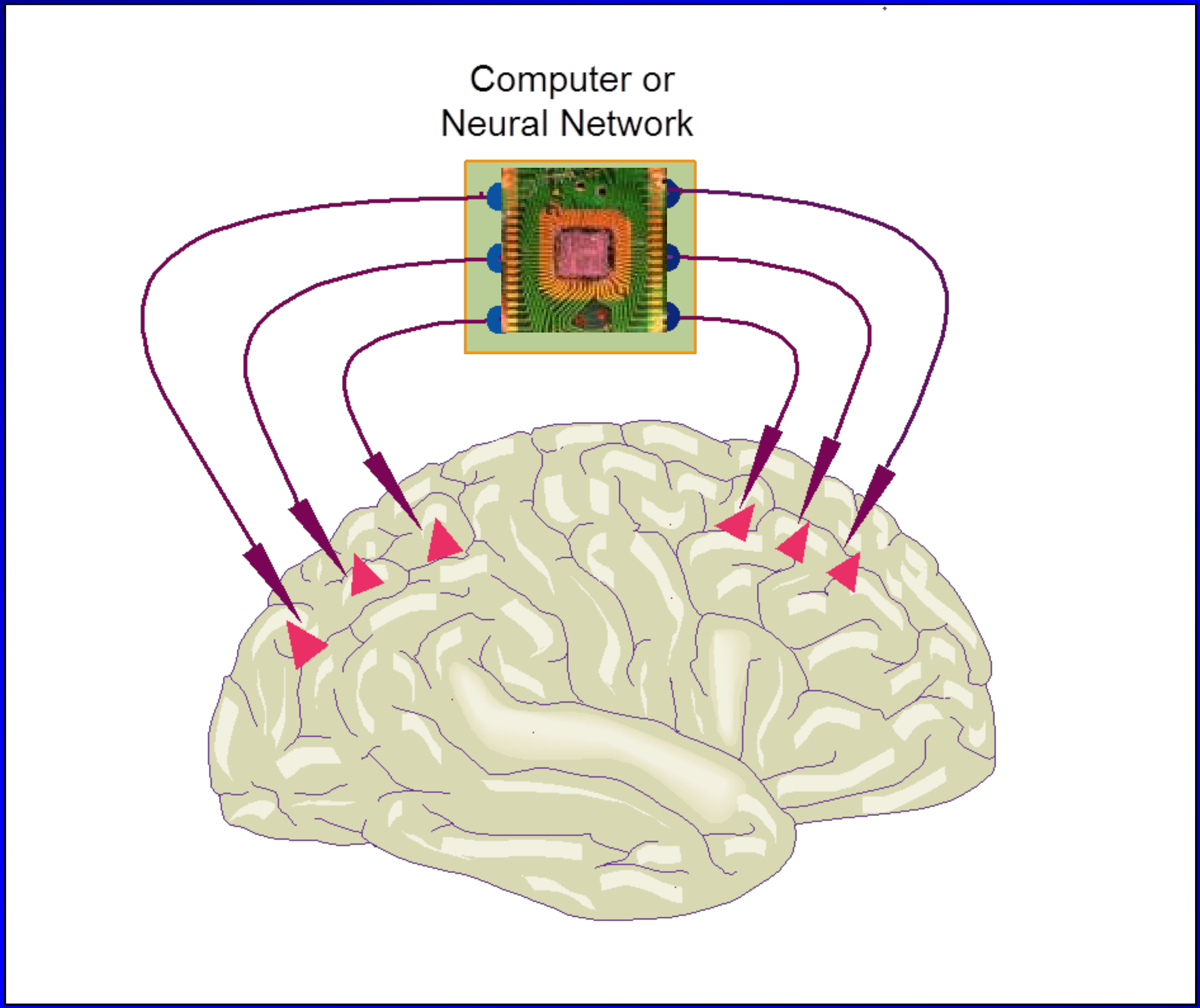
1. Utilizing muscles is more natural than prosthetic arm
2. Chronically implanted circuit will allow relearning

Cortical activity could stimulate spinal cord



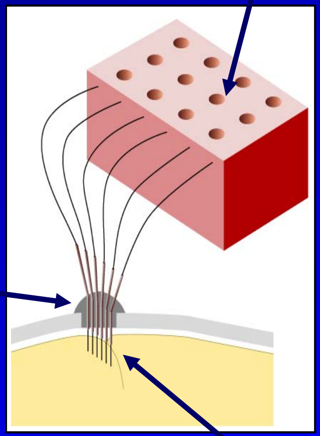
1. Stimulating spinal circuits recruits motor units in natural order
2. Spinal sites typically evoke co-ordinated movements
3. Effect of implant will be integrated with any remaining spinal function

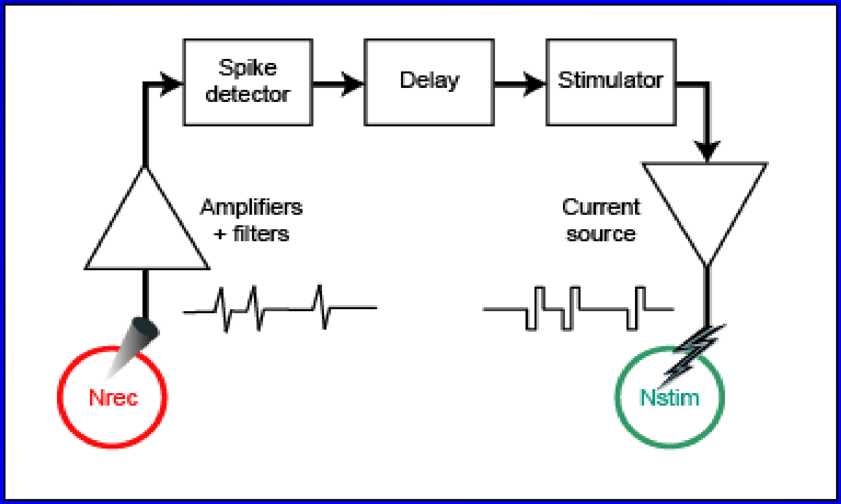
Cortical activity could stimulate other brain sites

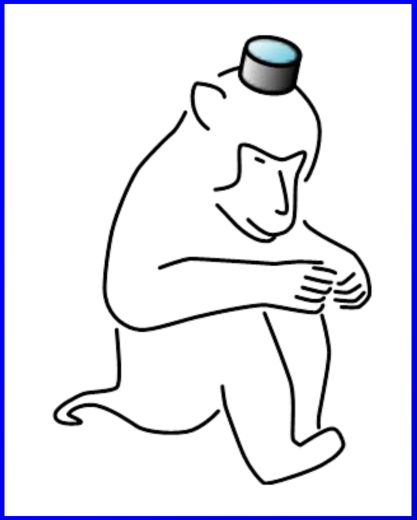


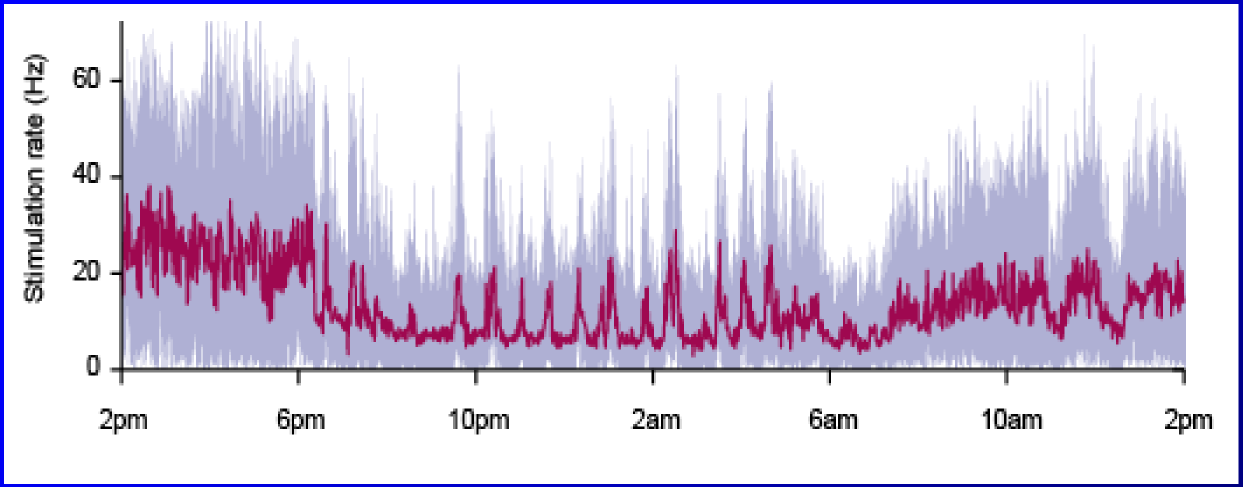
1. Test adaptation to artificial connections
2. Effect of implant may be integrated with ongoing brain function
3. Spike-triggered stimulation strengthens connections between sites

Plasticity example 1
Recurrent BCI connects neighboring motor cortex sites



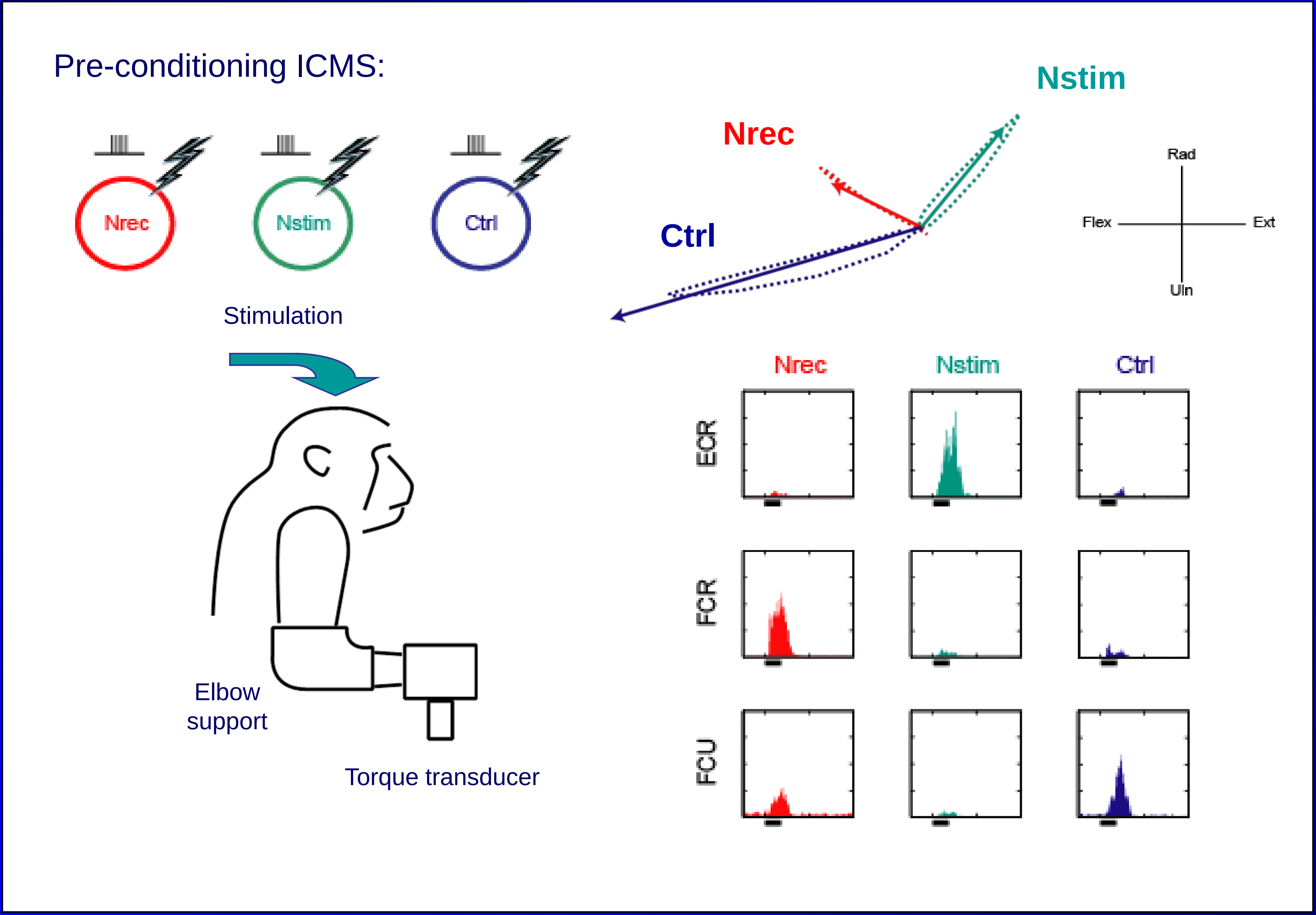






Jackson , Mavoori, Fetz, *Nature* 444: 56-60, 2006

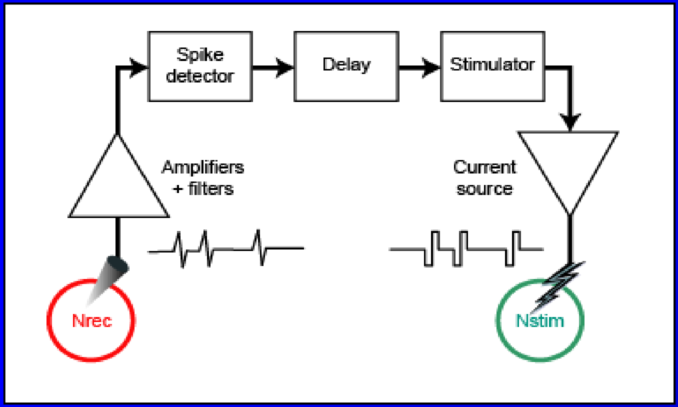
1. Intracortical microstimulation (ICMS) mapping of motor output

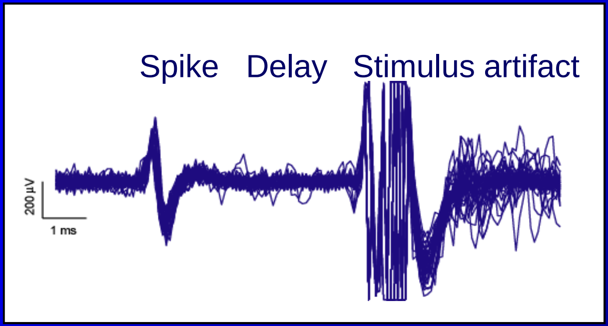


2. A recurrent connection is implemented between cortical sites Nrec and Nstim

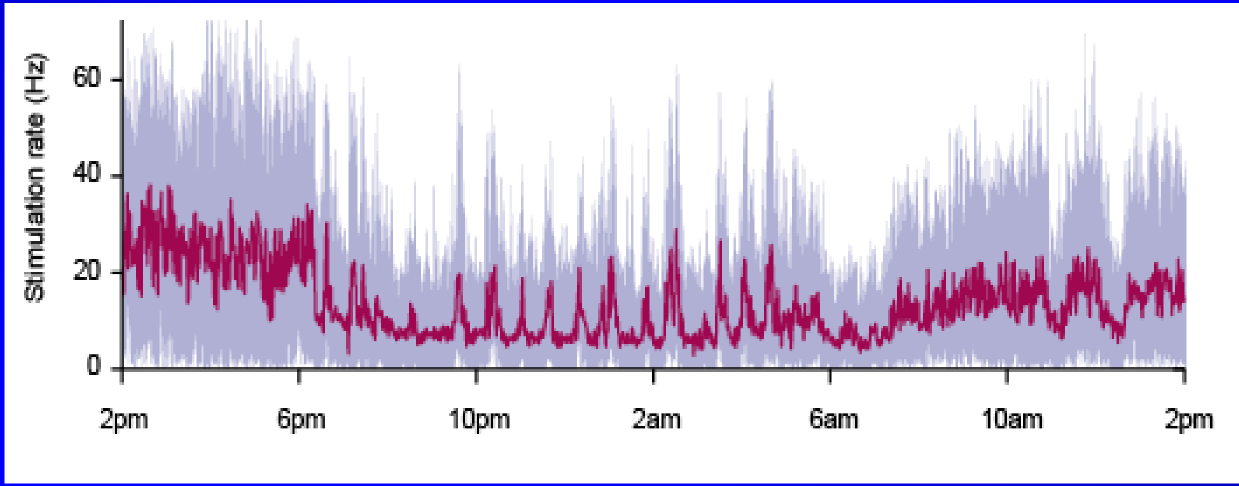
Spikes recorded at the Nrec electrode trigger stimuli delivered to the Nstim electrode after a pre-defined delay. (5ms)

This artificial connection operates continuously during free behavior and sleep



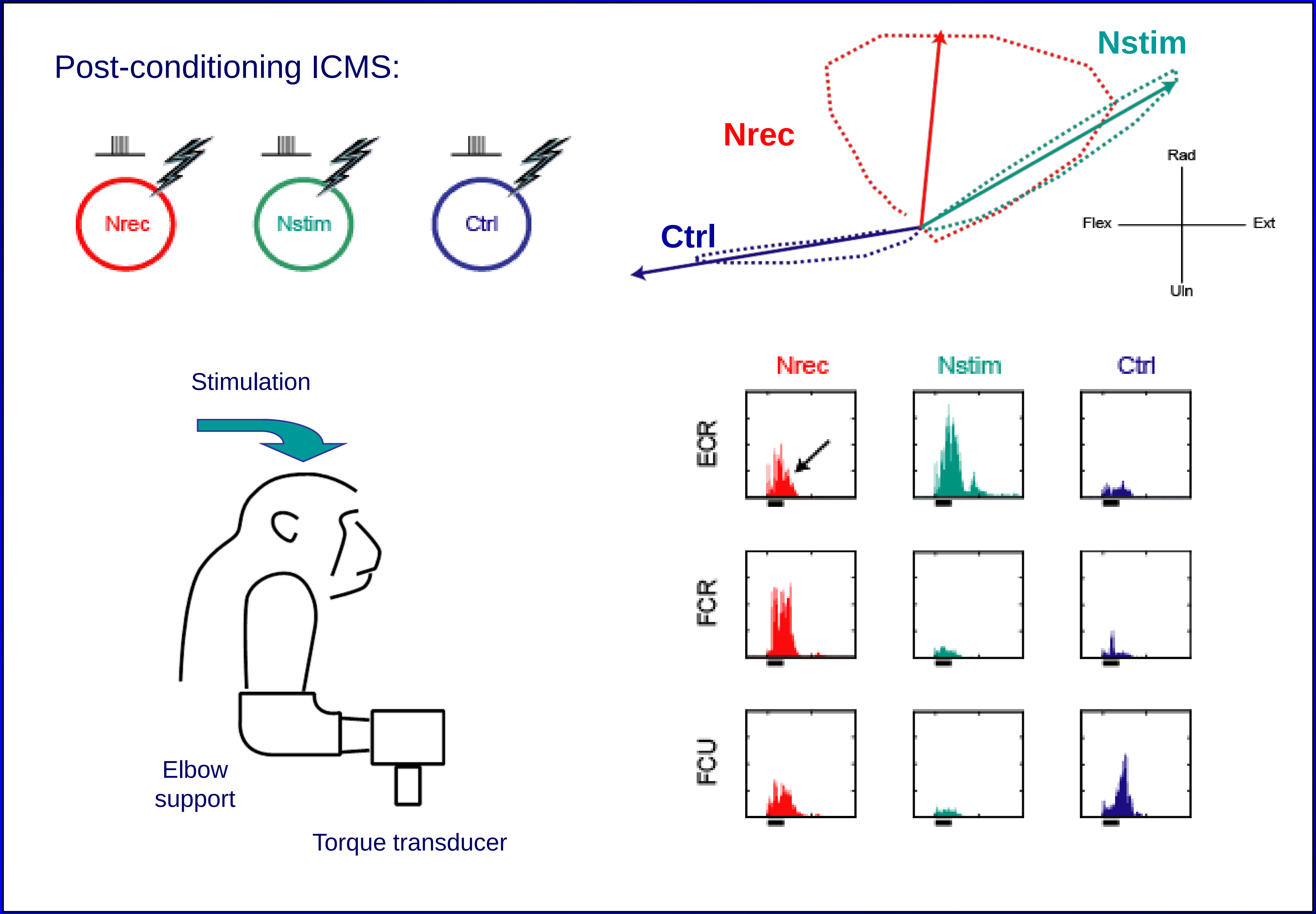


Recording from Nrec electrode showing spike and stimulus artifact.

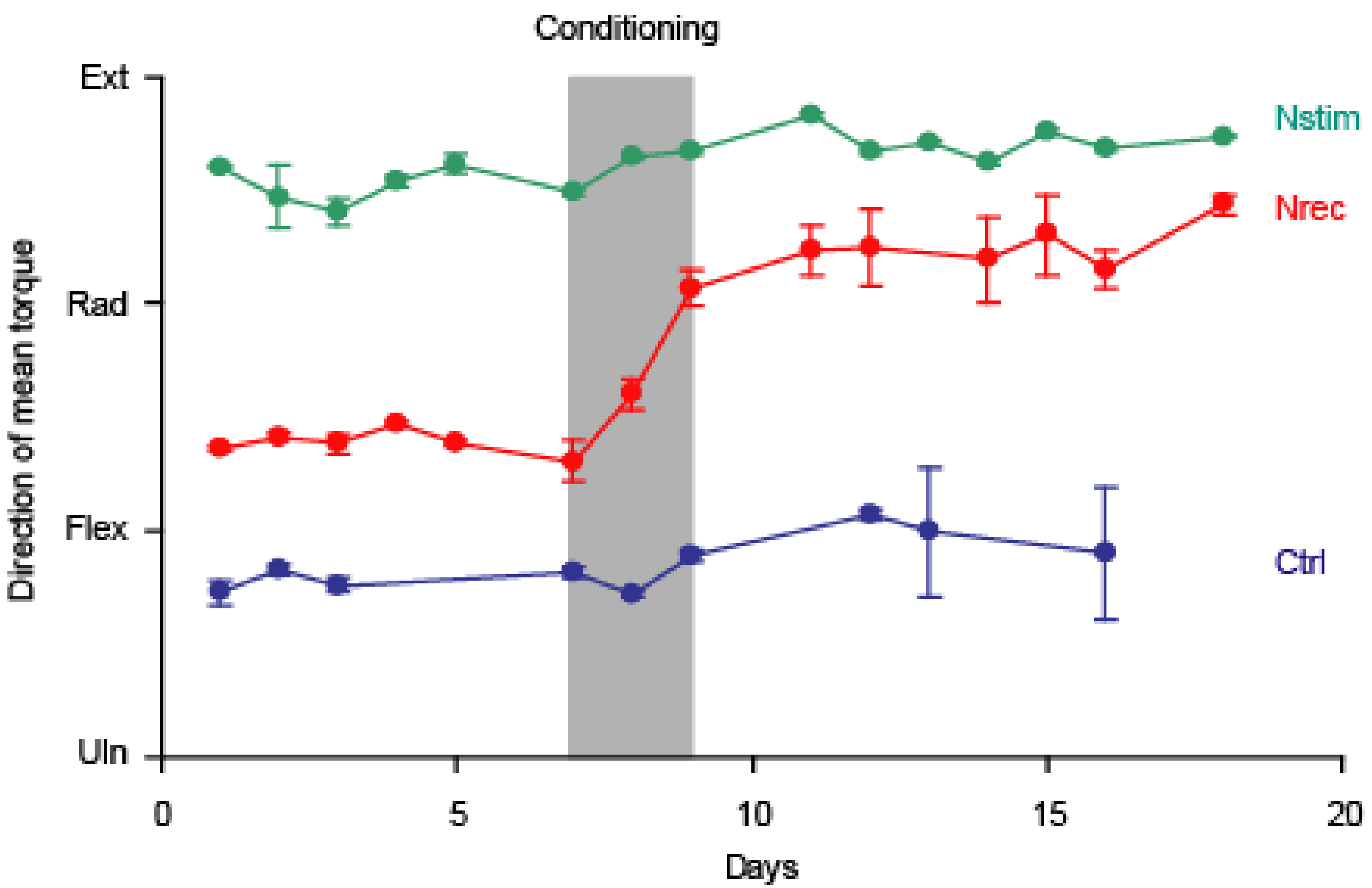


Average stimulation rate (red) during day and night

3. Post-conditioning ICMS testing shows changed output from Nrec



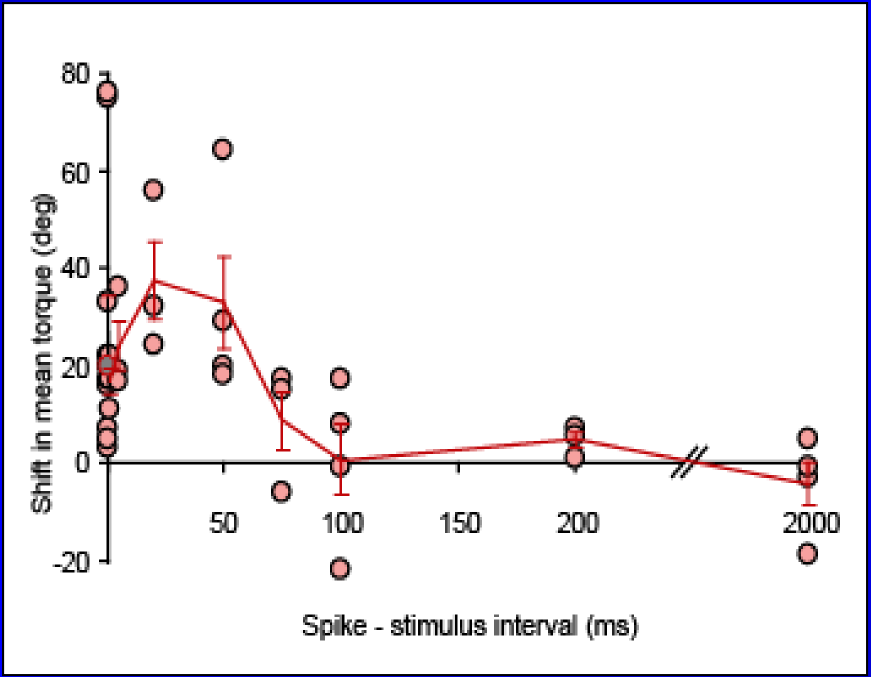
Modified cortical output persists for over 1 week post-conditioning

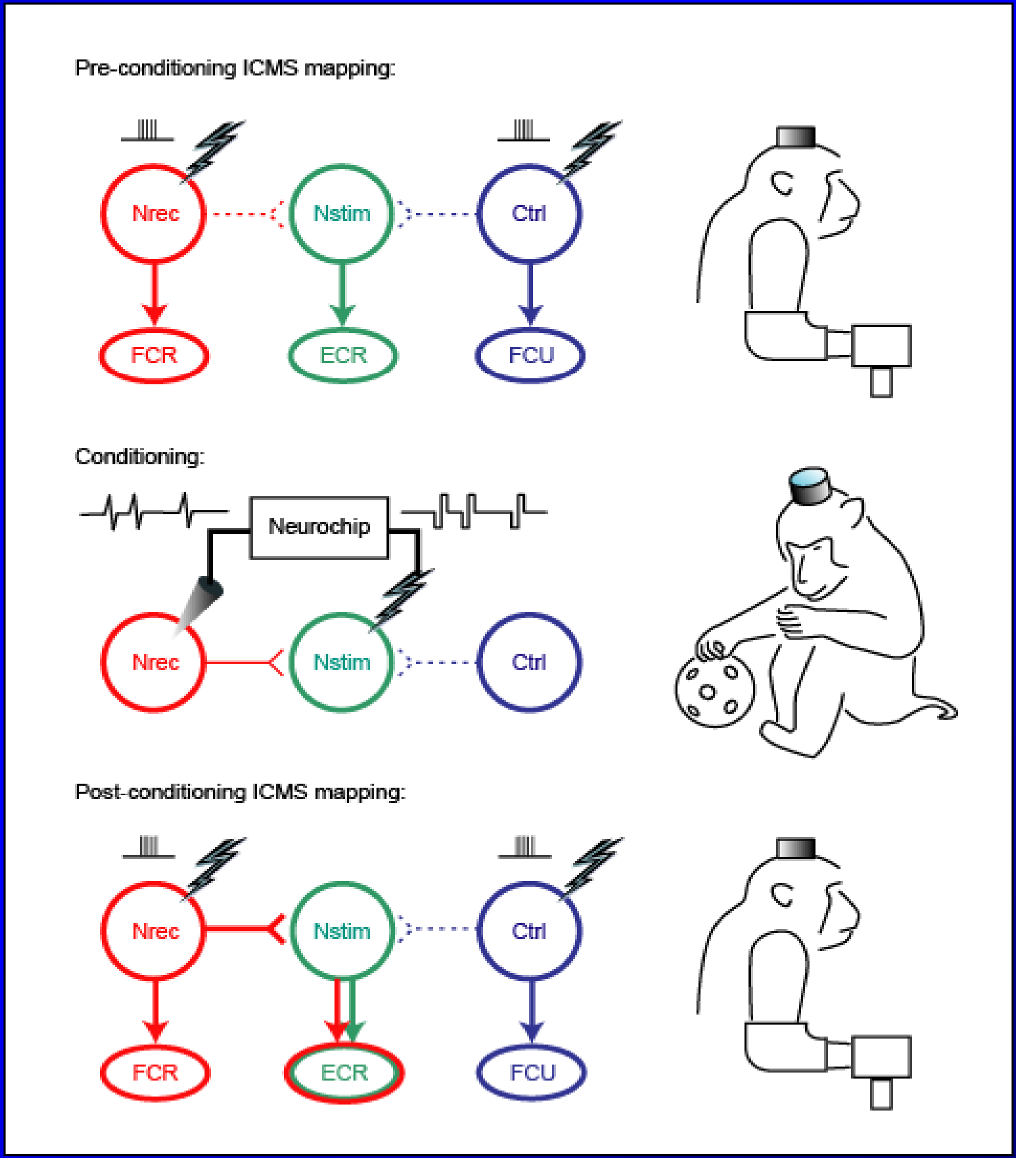


Changed output probably produced by Hebbian plasticity

Motor remapping caused by Neurochip conditioning may be explained by a timing-dependent Hebbian strengthening of pathways between synchronized Nrec and Nstim [or downstream sites]

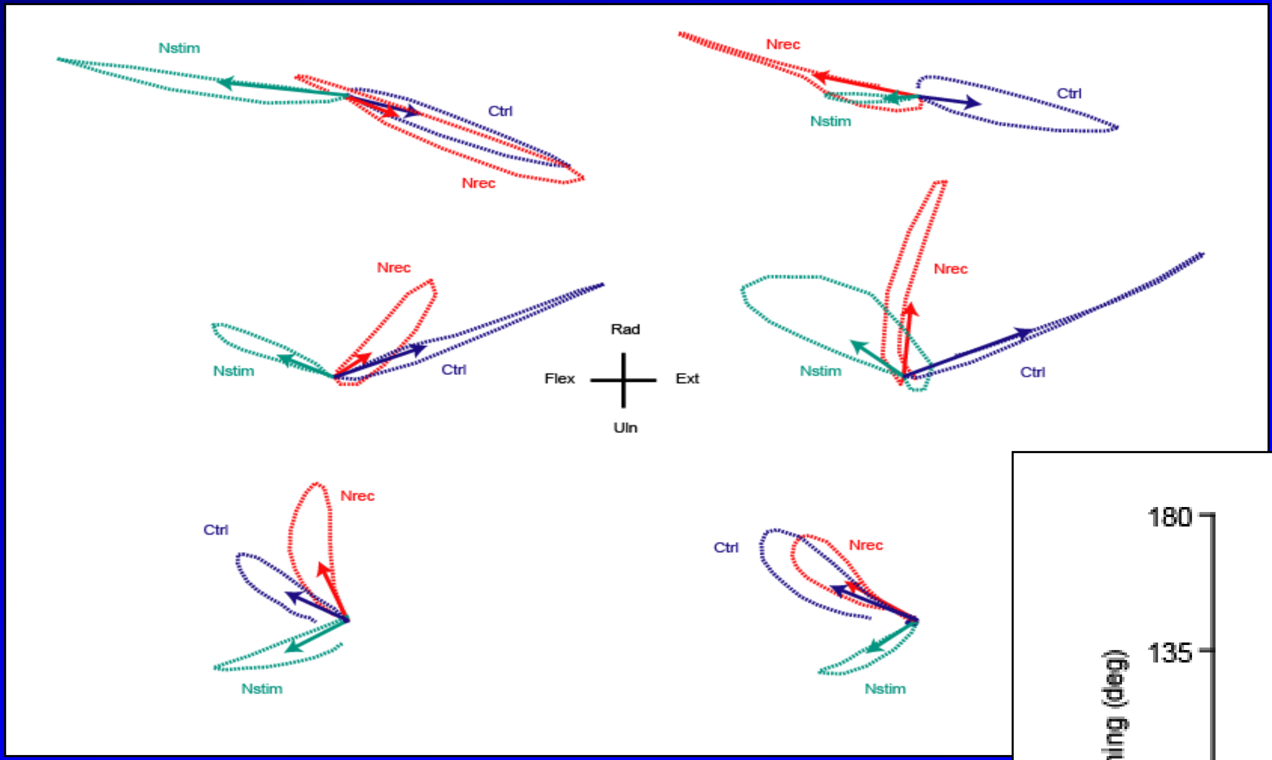
Conditioning requires a coincidence of spikes and stimulation within approx. 50 ms.

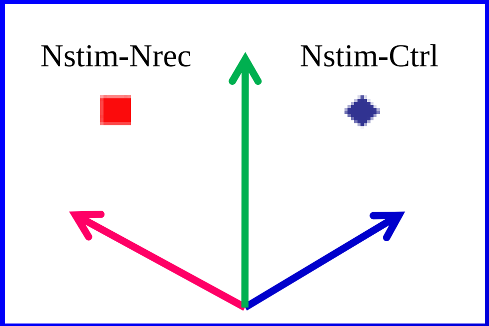


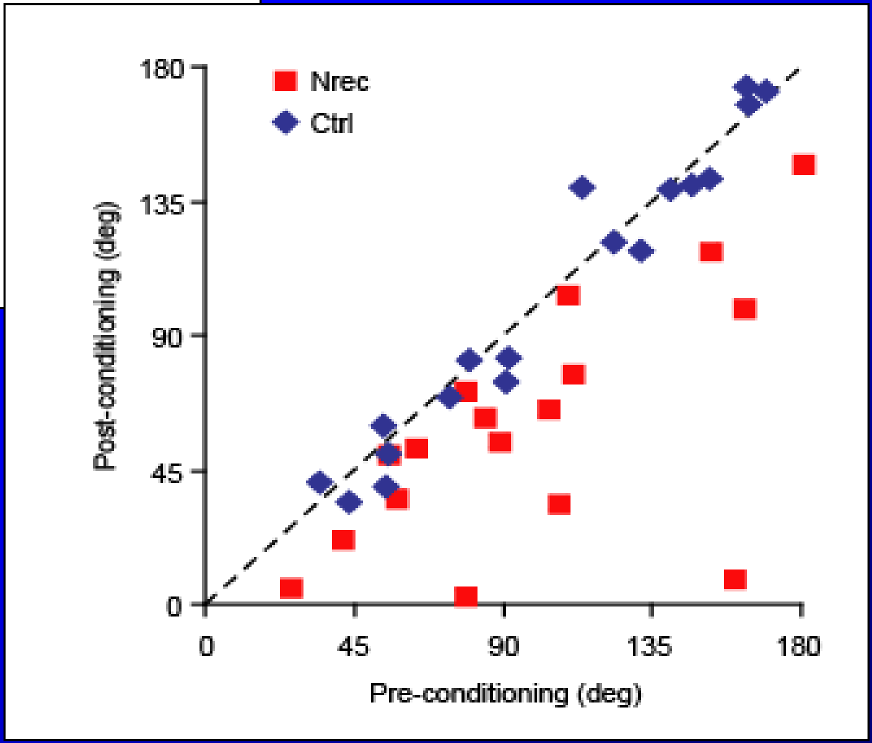


Jackson et al, *Nature* 444: 56-60, 2006

Summary of cortical conditioning experiments:

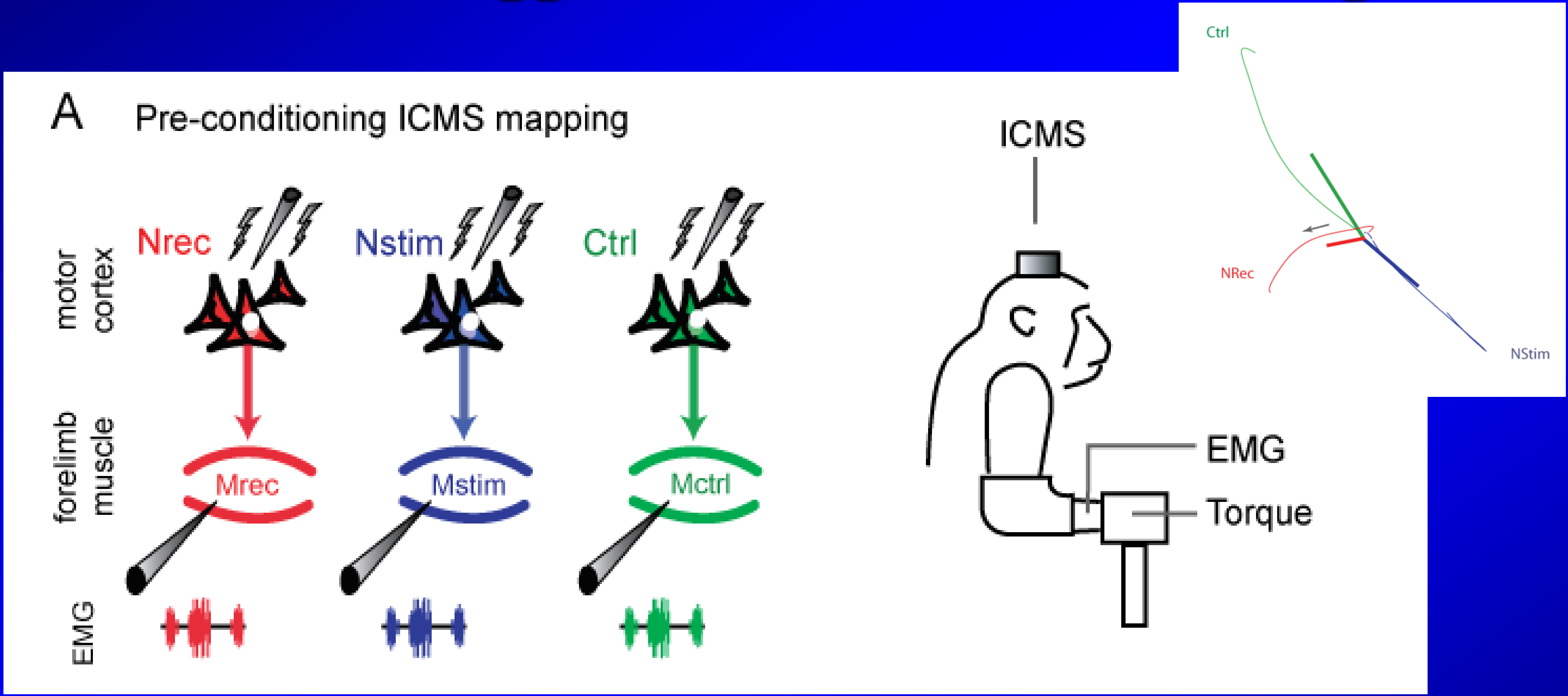






Angular separation from Nstim effect before and after conditioning, plotted for Nrec and Ctrl sites.

Plasticity example 2
EMG-triggered cortical conditioning



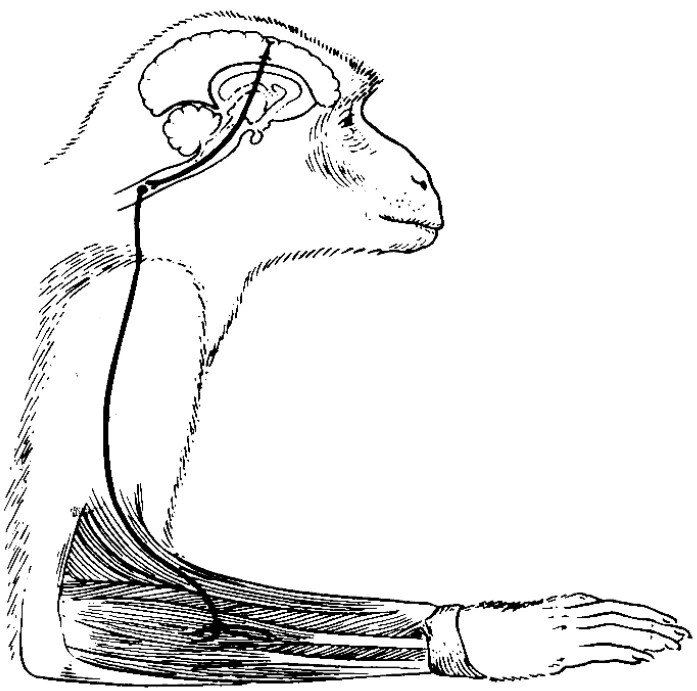
Cortical sites are closely associated with corresponding muscles.

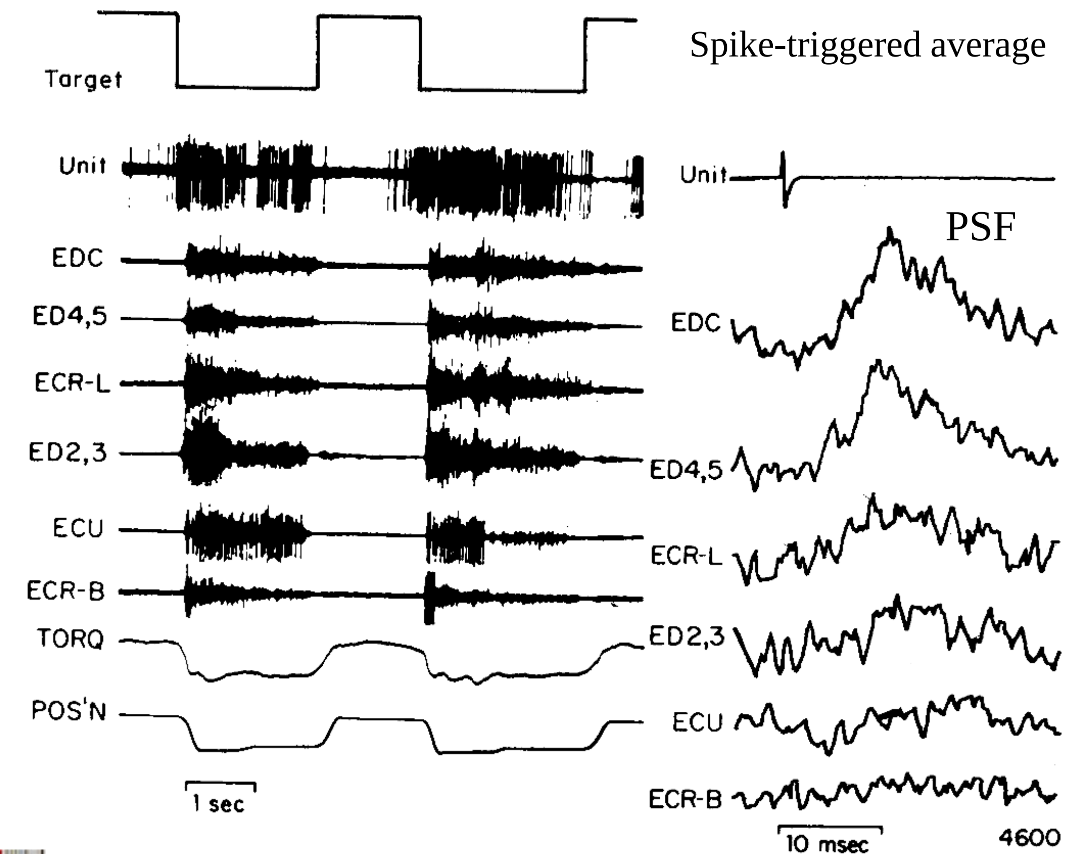
Can muscle activity serve as surrogate for cortical activity?

T. Lucas, 2009, *unpublished Ph.D. thesis*

Plasticity example 3: corticospinal connections

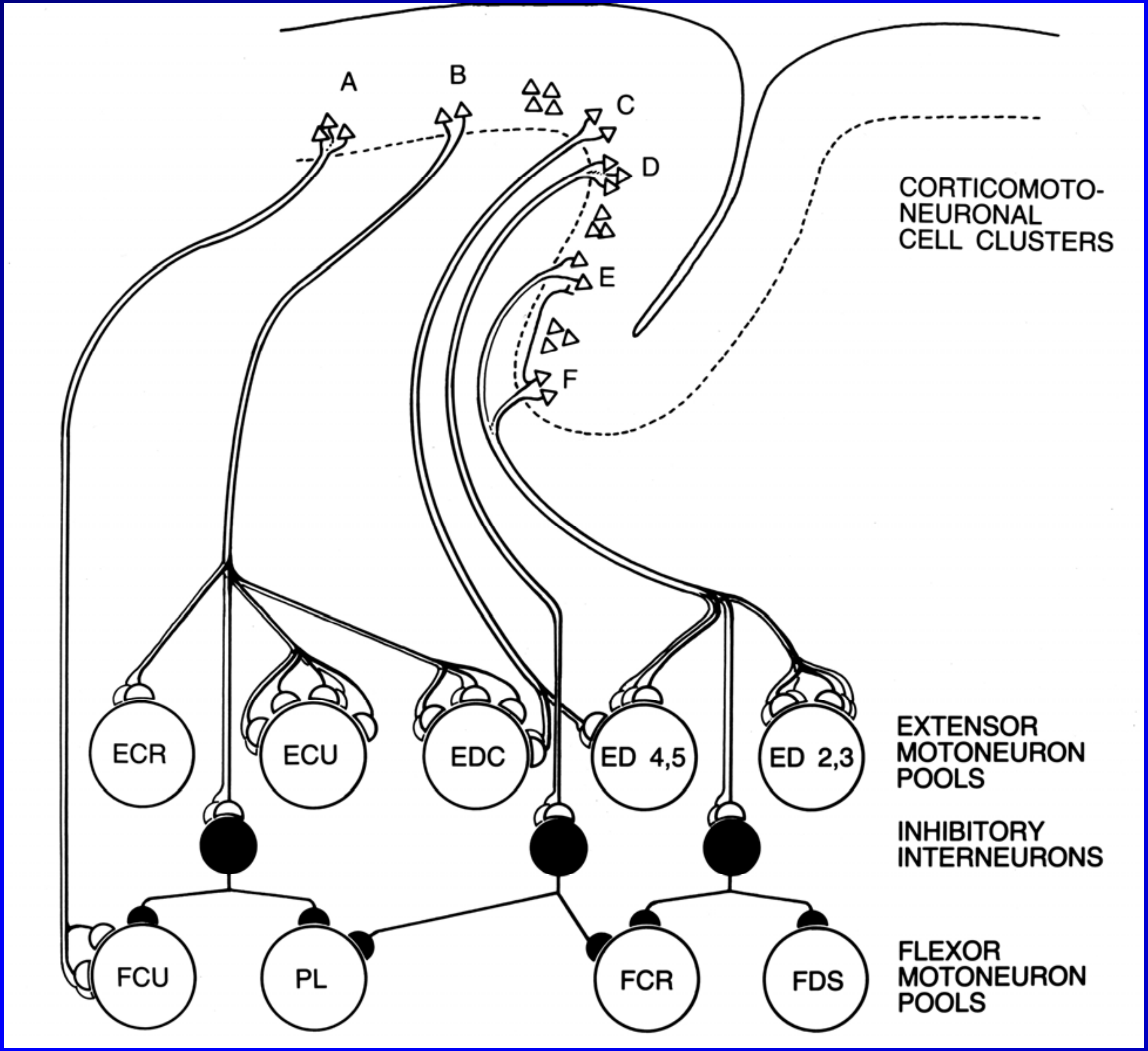
Corticomotoneuronal cells have correlational effects in STAs of EMG

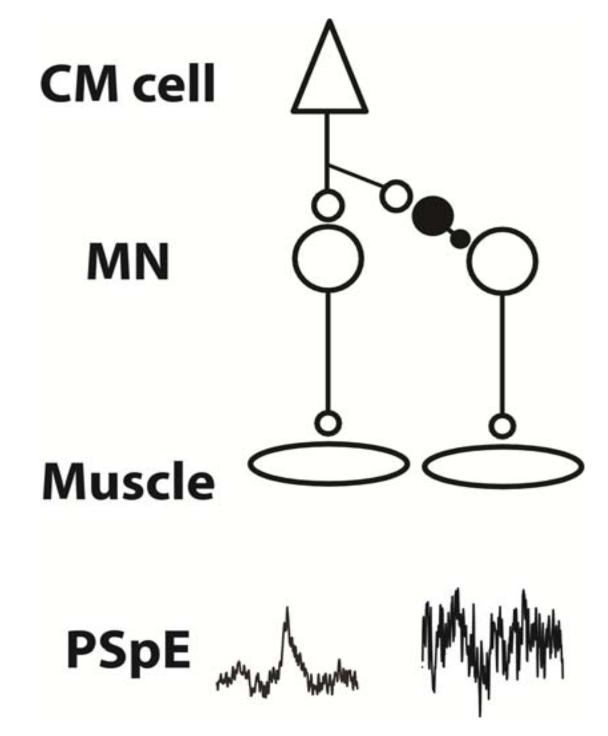




Cheney & Fetz, *J Neurophys* 44:773-791, 1980

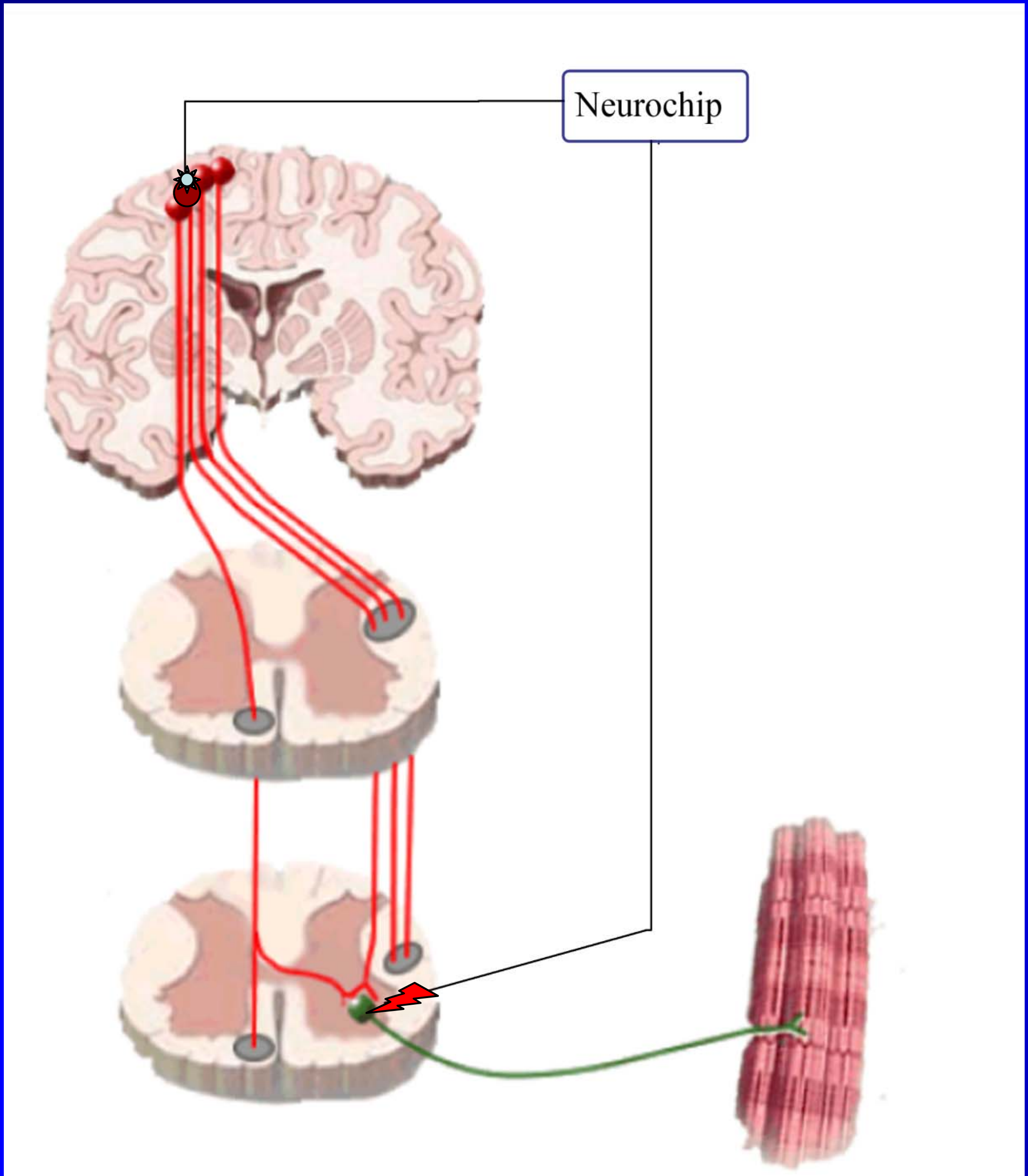
Muscle fields of CM cells



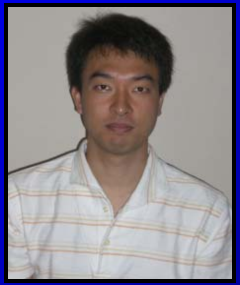


Cheney & Fetz, *J Neurophys* 44:773-791, 1980

Hebbian conditioning of CM pathway with Neurochip

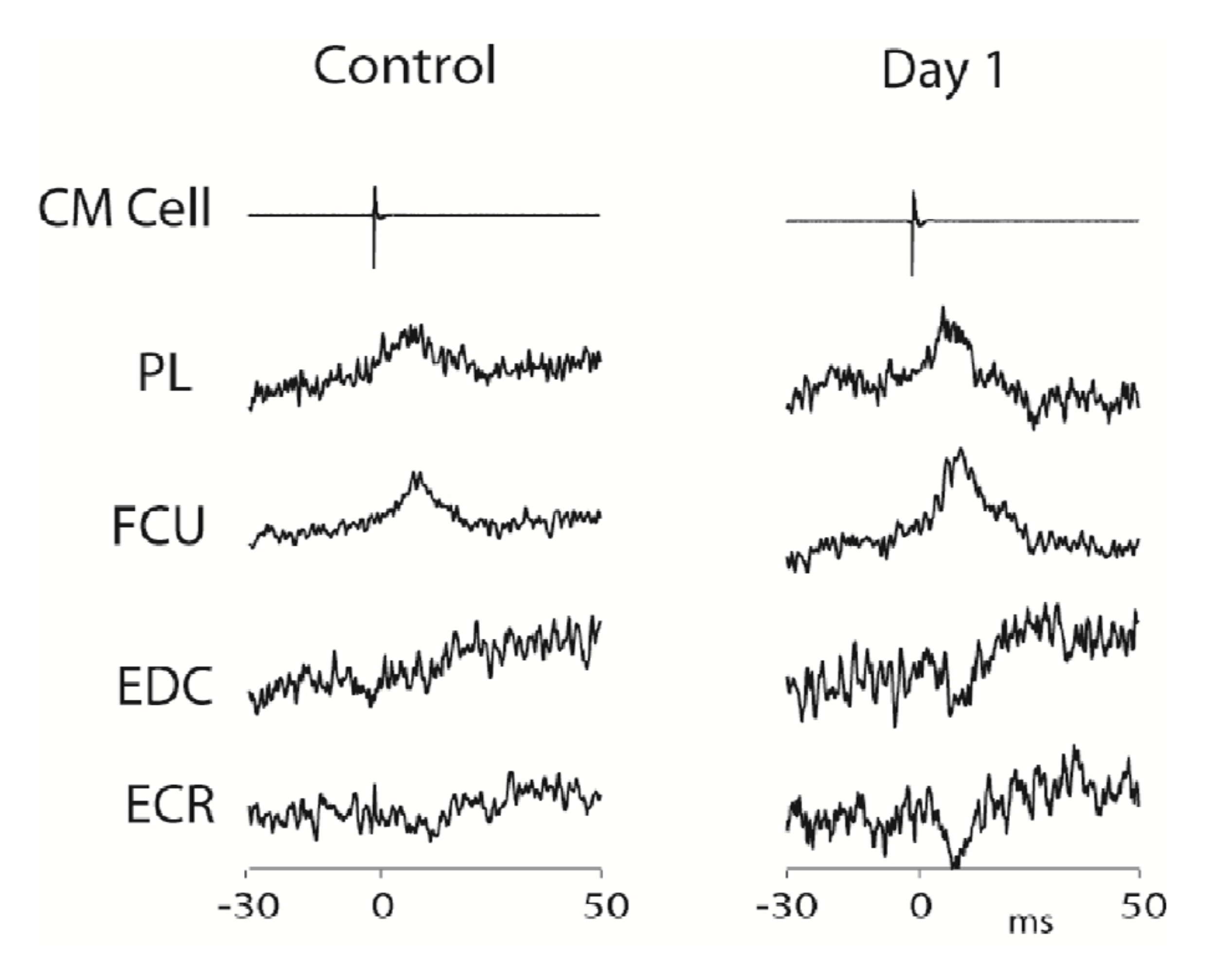


Neurochip delivers spike-triggered intraspinal stimuli near terminals of CM cell during ~20 hours of free behavior



Nishimura, et al, *unpublished*

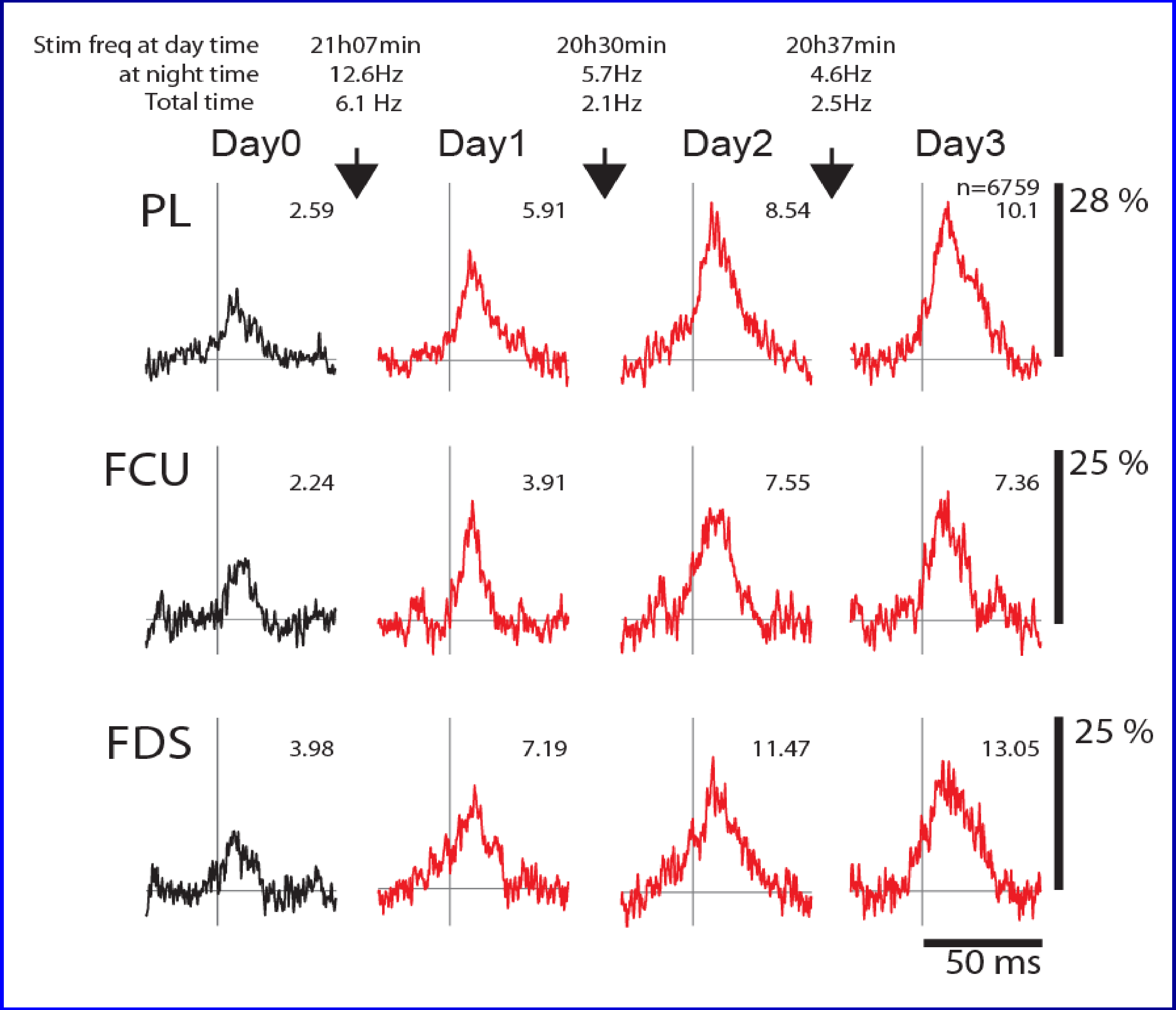
Neurochip conditioning enhances size of post-spike effects



Conditioning
time: 22 hrs.
Spike-stim delay
25 ms
Mean stim. freq.
16.8/sec day
8.3 /sec night

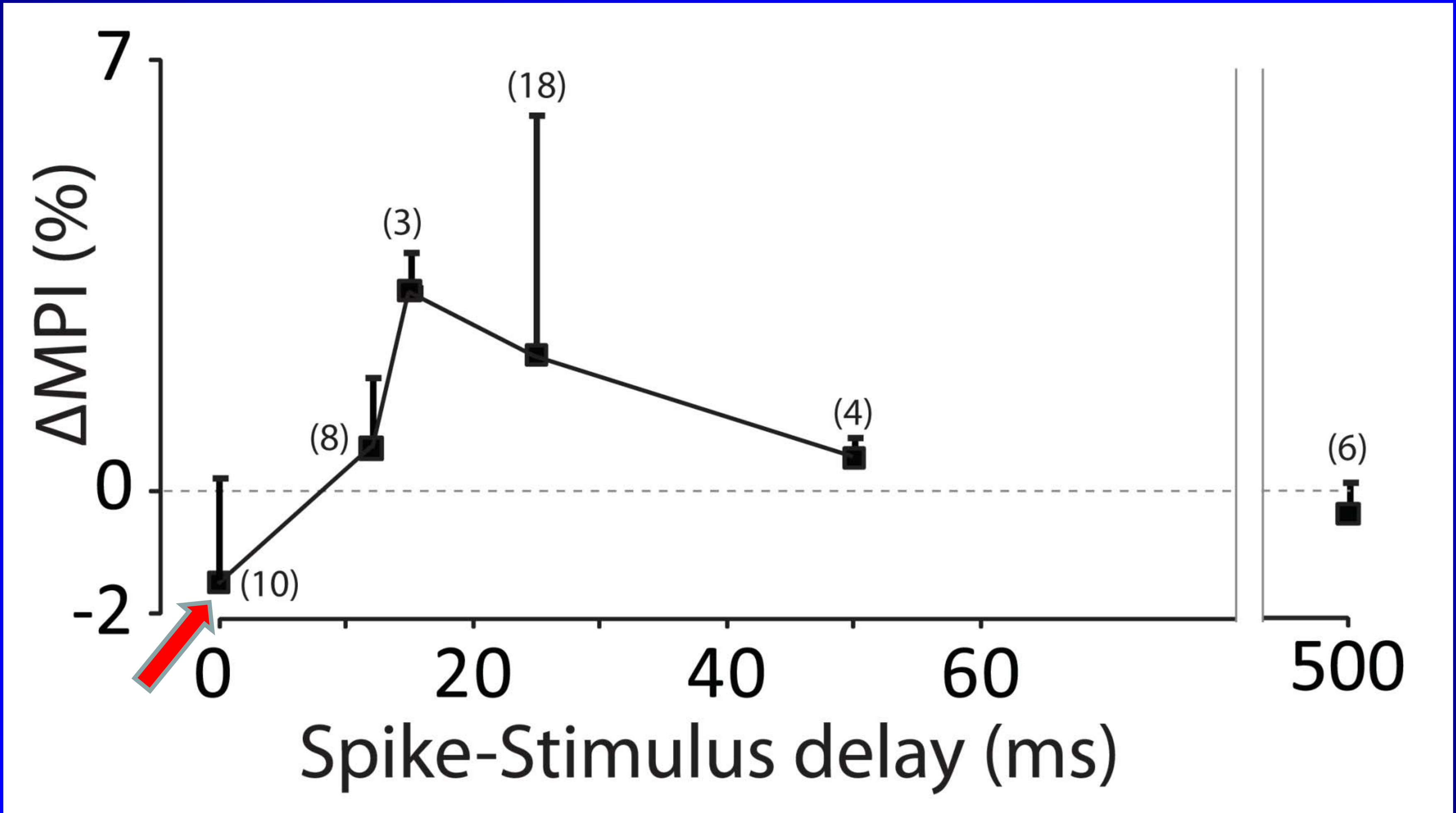
Nishimura et al *unpublished (SfN 2010)*

Neurochip conditioning of CM cell output



Nishimura et al *unpublished (SfN 2010)*

Change in mean percent increase of PSF as function of spike-stimulus delay

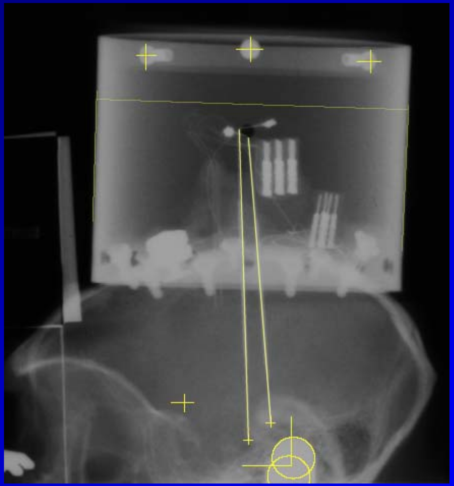


Nishimura et al *unpublished (SfN 2010)*

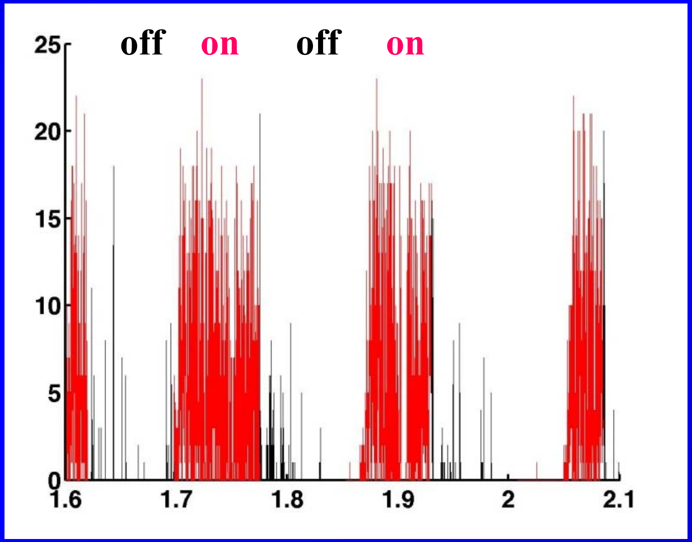
Applications for Recurrent BCI

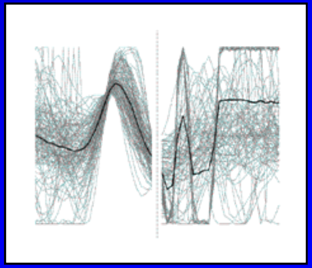
Sources	Transforms	Targets
Cortical neurons	Direct conversion	Muscles
Multiunit activity	Computed function	Spinal cord
Field potentials	Neural network	Cortex
EMG	Modifiable	Reward center
ECoG		
Various sites		

Operant conditioning of EMG activity via Neurochip
Pulses from biceps EMG trigger n. accumbens stimulation

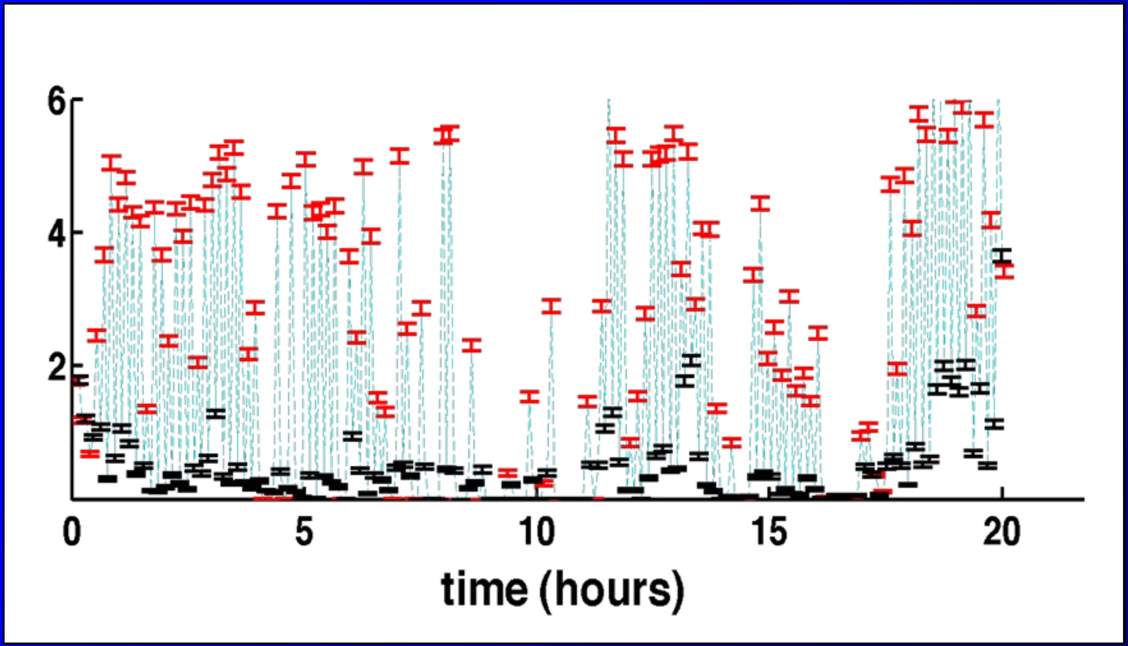


EMG pulse rate during 5-min periods of stim **on** and **off**



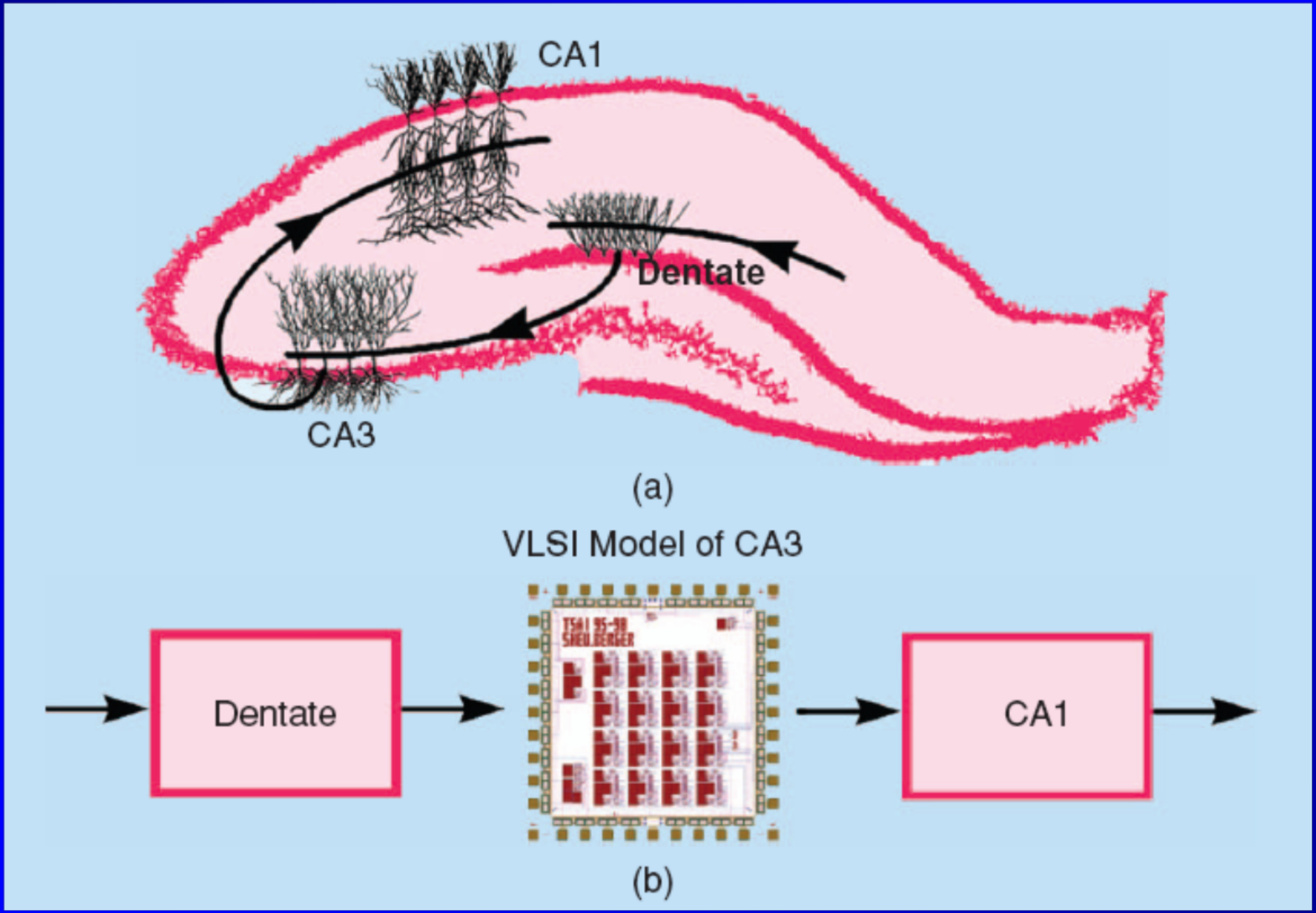


Average EMG pulse rate during 5-min of stim **on** and **off**



Eaton, Zanos, Fetz, *SfN Abstr, 2008*

Proposal for a "cognitive prosthesis"

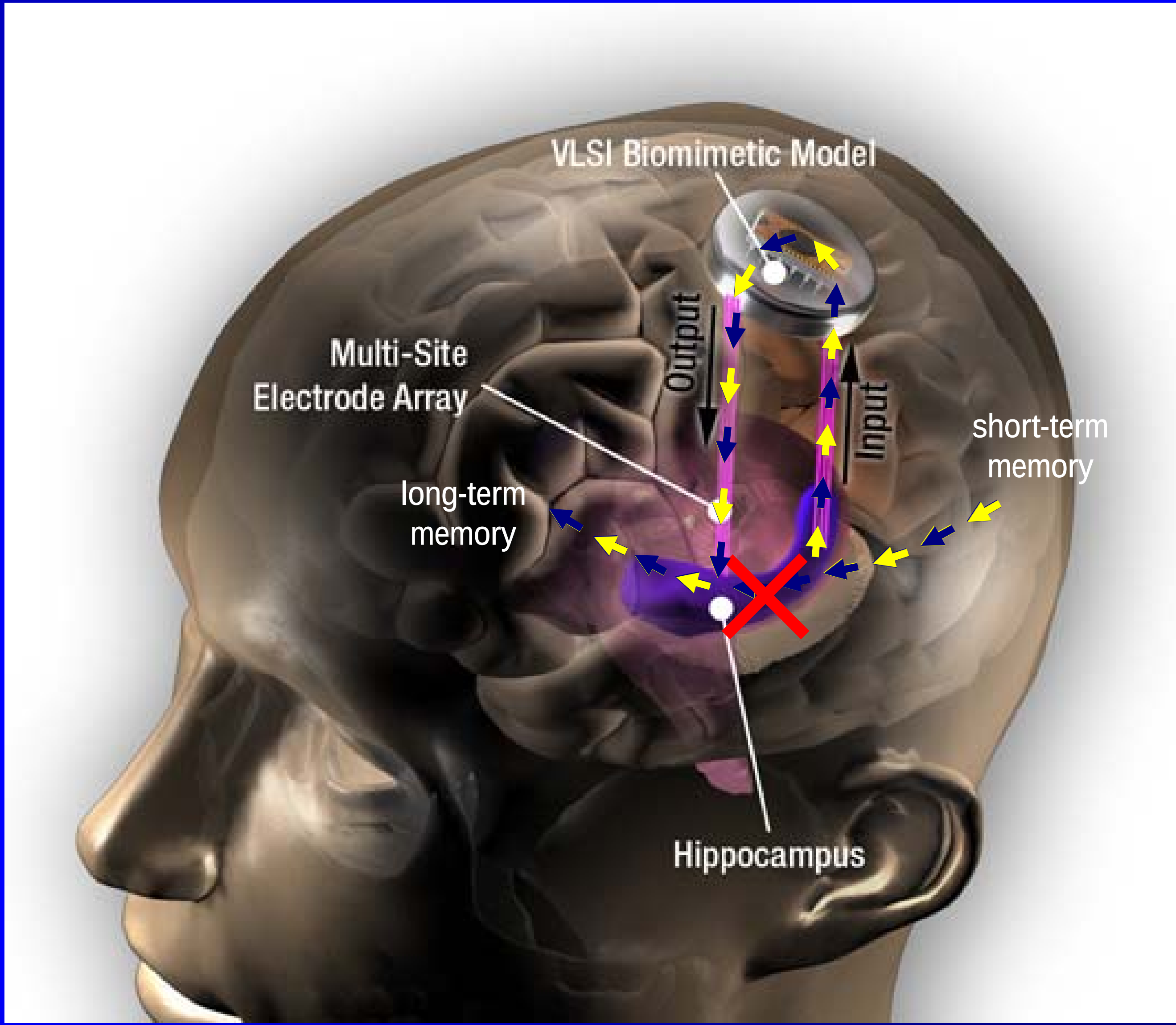


Berger et al, *IEEE Eng Med Biol Mag* 24, 30-44 , 2005

Neural Prosthesis for Lost Cognitive Function

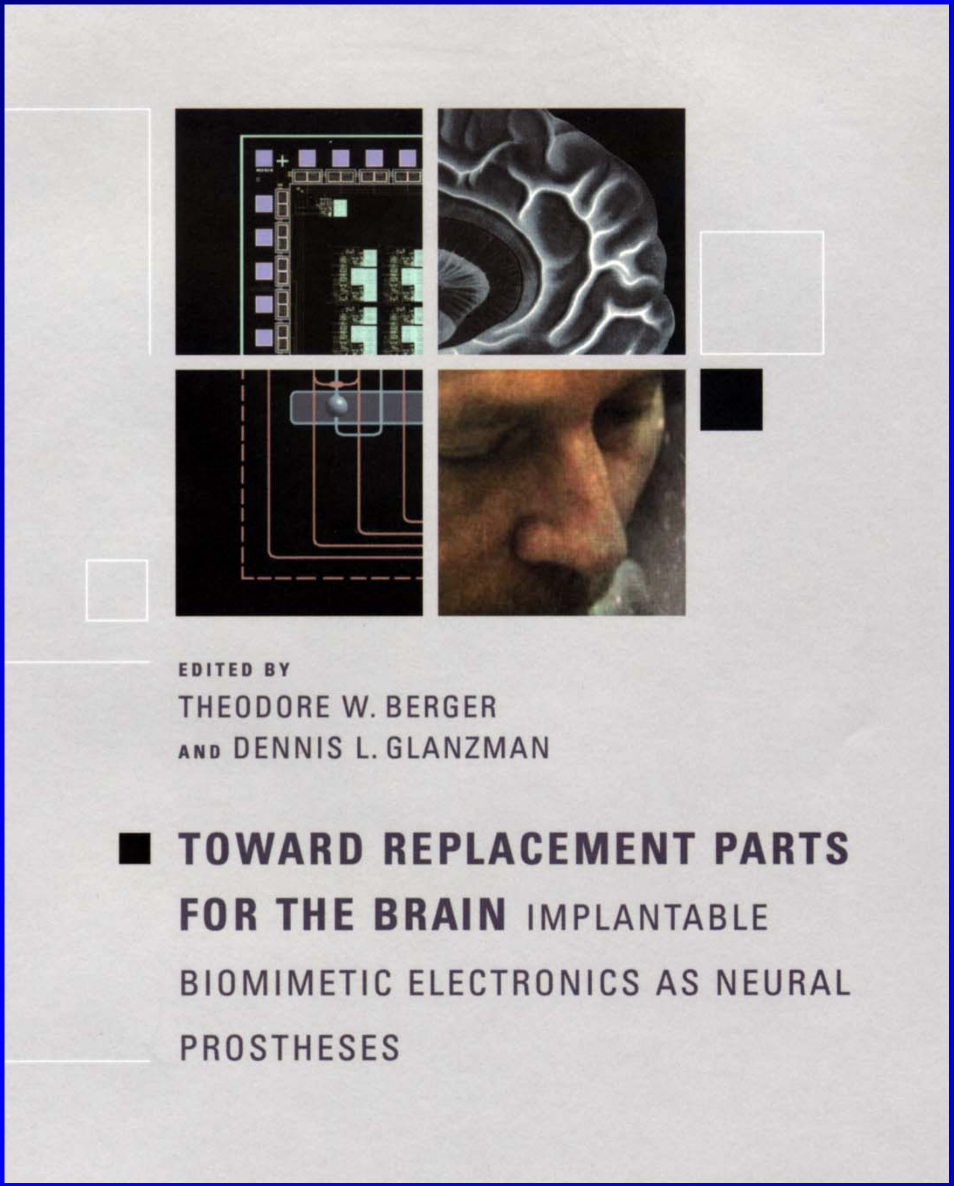
Strategy:

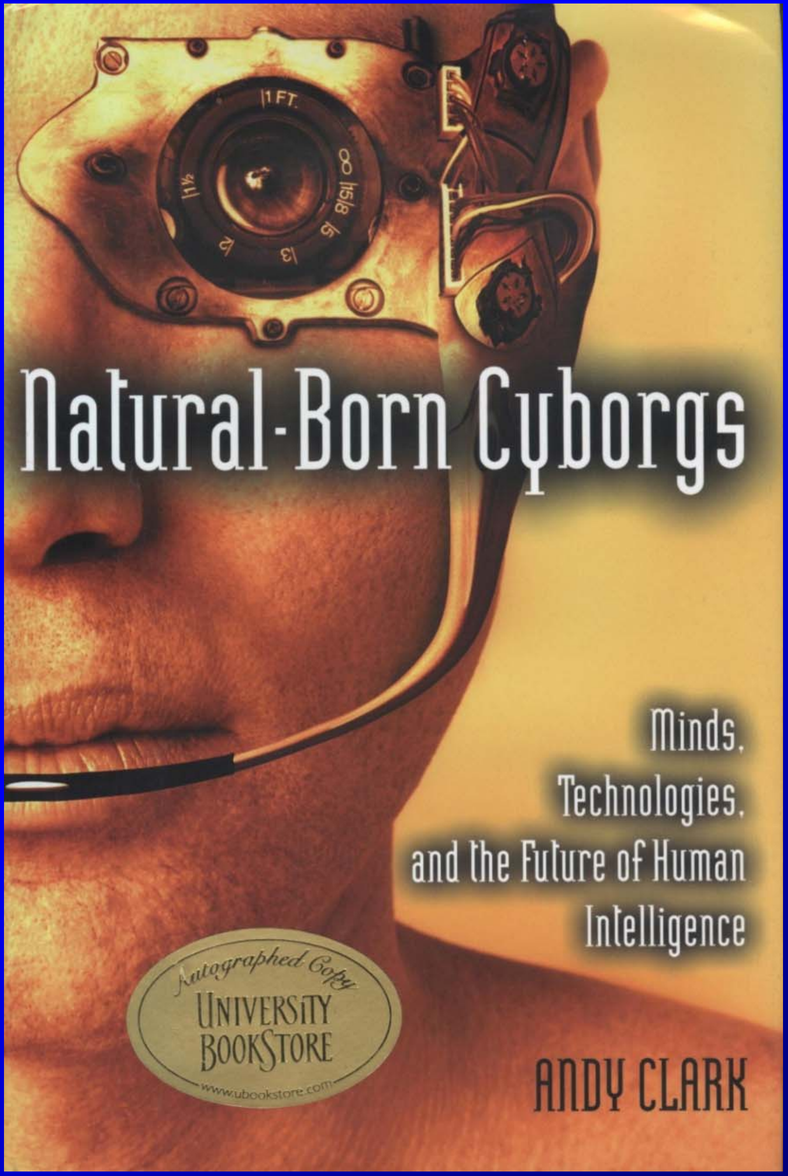
1. Biomimetic model/device that mimics signal processing function of hippocampal neurons/circuits
2. Implement model in VLSI for parallelism, rapid computational speed, and miniaturization
3. Multi-site electrode recording/stimulation arrays to interface biomimetic device with brain
4. Goal: to "by-pass" damaged brain region with biomimetic cognitive function



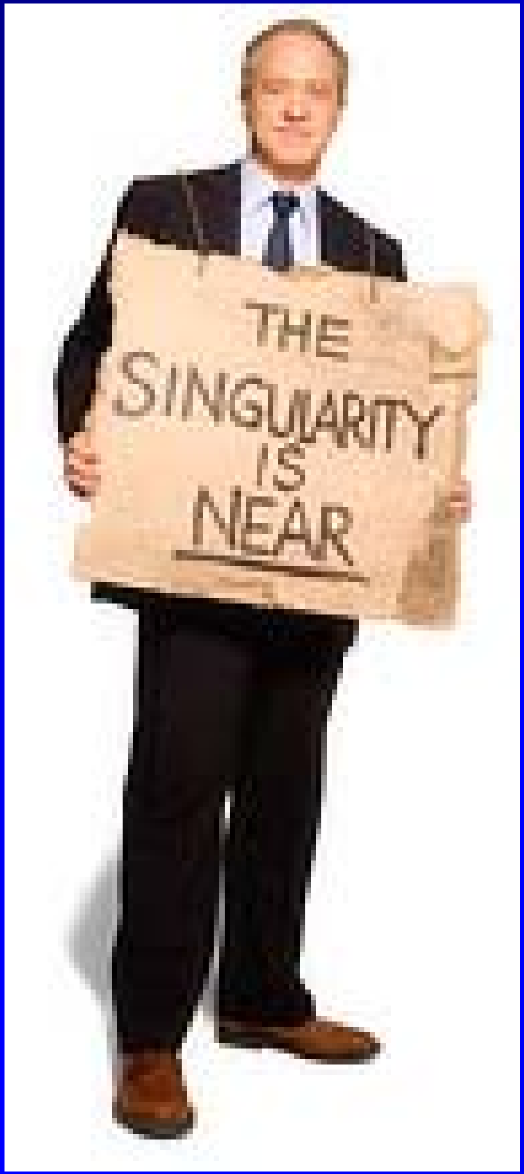
Berger et al, *IEEE Eng Med Biol Mag* 24, 30-44 , 2005

Further reading…

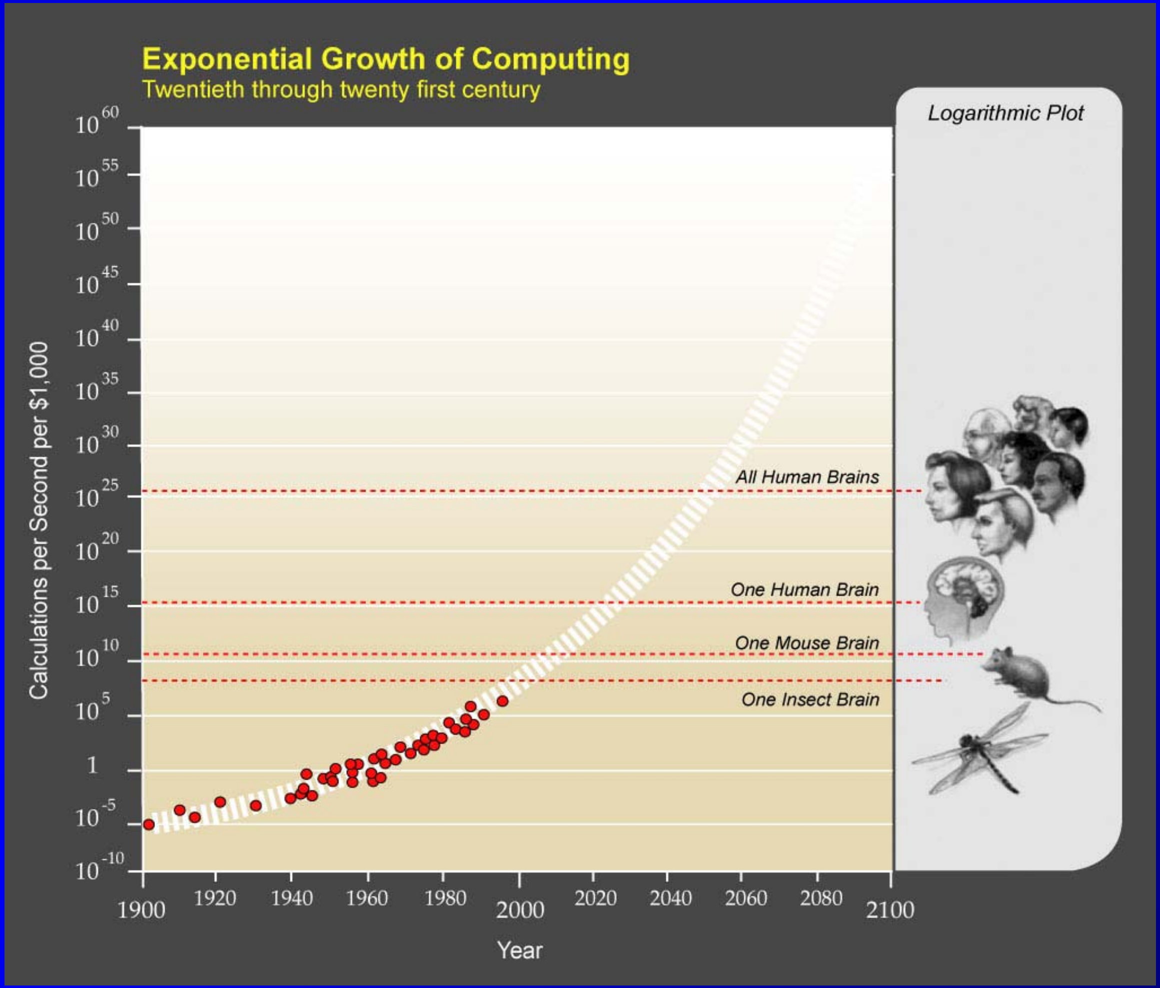




Technologies are advancing exponentially



…Ray Kurzweil



Thanks to:

…and support from NIH; UW RRF; WTC; CDRF; ITHS; LSDF; Keck Foundation

Neurochip 2

1. Three differential input channels.
   Low cutoff: 1 Hz or 500 Hz
   High cutoff: 7.5 KHz or 2.5 KHz.

2. A-D conversion 8 or 12 bit; @ 256-24Ks/sec

3. Removable flash memory: 1 GB.
   Records 35 hrs of 8bit LFP/ECoG/EMG @ 2 Ks/sec on 3 channels
   16 hrs of unit data @ 12 Ks/sec plus 2 channels @ 2Ks/sec

4. Bipolar stimulation switchable to 3 output channels [<20 μs]
   10 μa – several ma [50 volt output for high-range stimulator]

5. Stimulus artifact suppression

6. Rechargeable battery [2 batteries for high stim]