Brain-Computer Interfaces to Replace or Repair the Injured Central Nervous System

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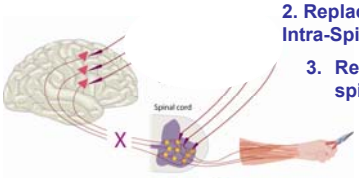
Three approaches to restore movement

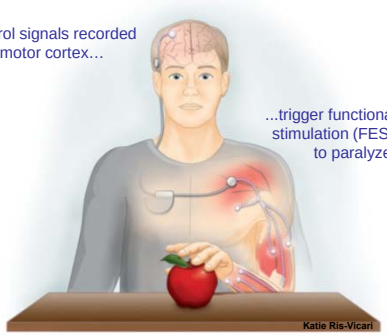
1. Replace: Brain control of muscle stimulation
2. Replace & Repair: Intra-Spinal Stimulation
3. Repair: Brian-triggered spinal stimulation



Brain control of muscle stimulation

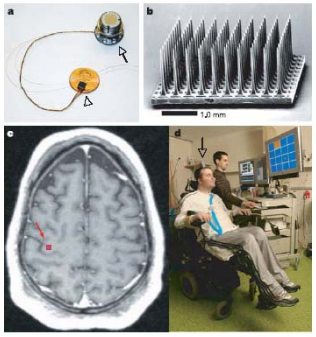
Control signals recorded from motor cortex…

...trigger functional electrical stimulation (FES) delivered to paralyzed muscles



News & Views on Moritz *et al*; S. Scott, *Nature Neuroscience* 2008

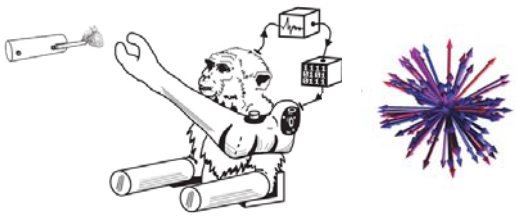
Recording from human motor cortex



100-electrode array

Hochberg et al, *Nature* 2006

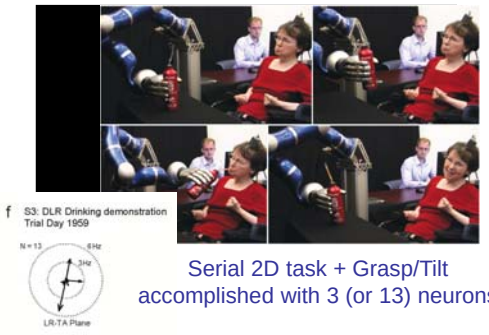
Monkeys use brain activity to control a robotic arm for self-feeding



Activity decoded from groups of neurons to control end-point of a robot arm in 3-dimensions

Velliste et al, *Nature* 2008

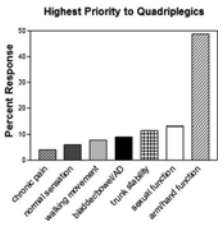
Control robotic arm 5 years after implant



Serial 2D task + Grasp/Tilt accomplished with 3 (or 13) neurons

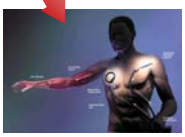
Hochberg et al., *Nature* 2012

Connecting cortical neurons to control muscle stimulation



Extract control signals from brain

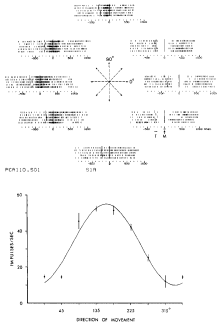
Reanimate limbs using muscle stimulation (FES)



FreeHand, Peckham et al

Anderson, *J Neurotrauma* 2004

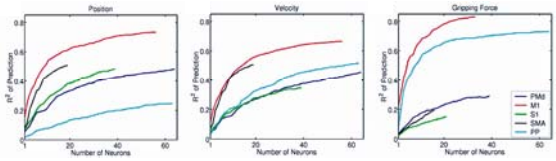
Directional tuning of motor cortex neurons - decoding



- Cosine tuning often observed for direction
- About 1/3 of M1 neurons are directionally tuned
- Can 'decode' movement intention by considering a population of tuned neurons (e.g., population vector, linear model, Kalman filter, etc)

Georgopoulos *et al, J Neurosci* 1982

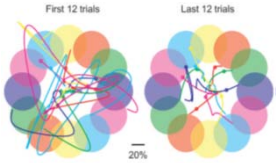
Neuron ensembles largely redundant



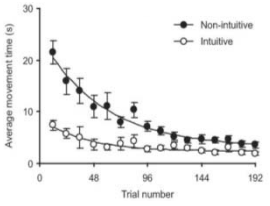
- Performance is never perfect despite large neural populations
- Many neurons contribute redundant information
- Could performance be improved using a small group of neurons trained with explicit feedback?

Carmena *et al., PLoS Biol* 2003

Human subjects learn non-intuitive muscle control

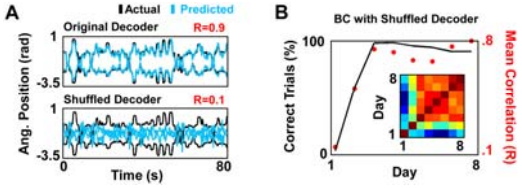


Randomly assigned transform from muscles to movement directions is learned within one practice session.



Radhakrishnan *et al, J Neurophysiol.* 2008

Monkeys learn random decoder equally well



Monkeys learn cursor control with shuffled decoder

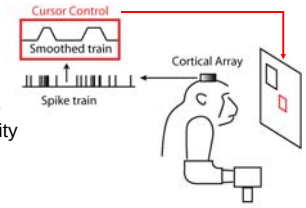
Performance is nearly perfect after 3 days of practice

Ganguly & Carmena, *PLoS Biol*, 2009

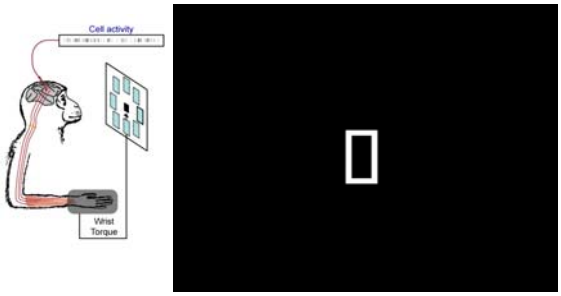
Train single neurons to control muscle stimulation

Methods

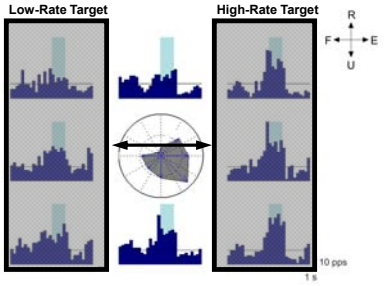
1. Neurons recorded during wrist movements
2. Neural activity then displayed as cursor movements
3. Monkeys conditioned to modulated neuron activity



1. Cell activity during wrist movement

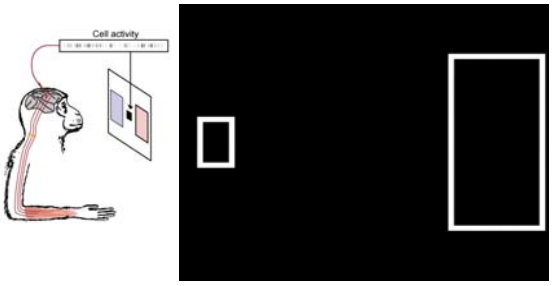


2. Direction tuning sets visual feedback

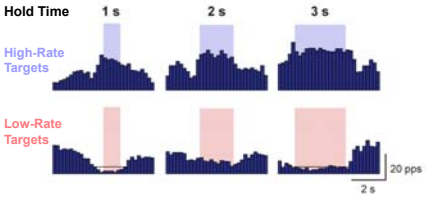


Visual feedback of cell rate with targets oriented in preferred direction

3. Monkey controls cursor with neuron



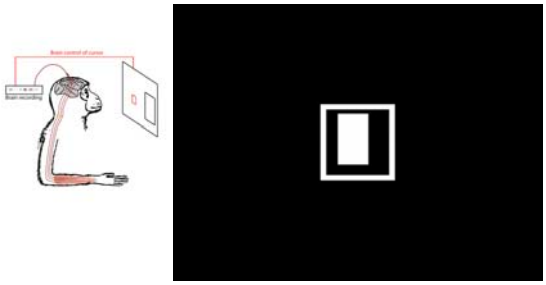
Monkeys can maintain cell activity for prolonged periods



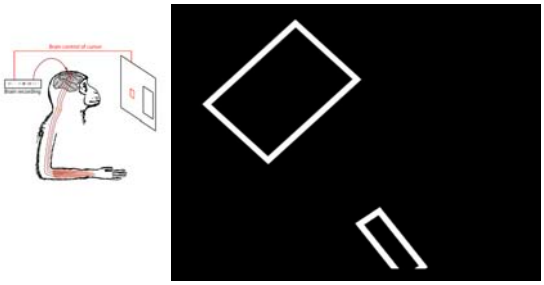
Neurons can be trained to produce or suppress activity for sustained periods of time

Moritz & Fetz, *J Neural Engineering* 2011

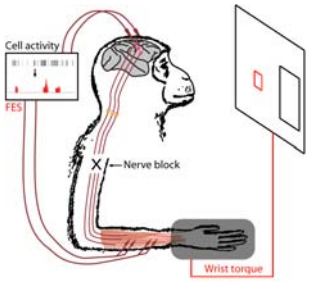
Monkey controls 2D cursor directly using only 2 neurons



Monkey directly controls 3D cursor using only 3 neurons



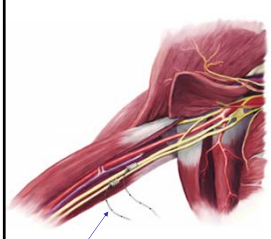
Brain-controlled muscle stimulation

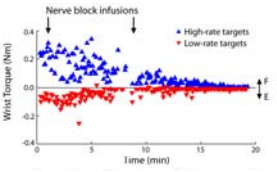


- Cell activity directly converted to muscle stimulation (FES)
- Wrist muscles temporarily paralyzed by nerve block

Moritz et al, *Nature* 2008

Model of reversible paralysis

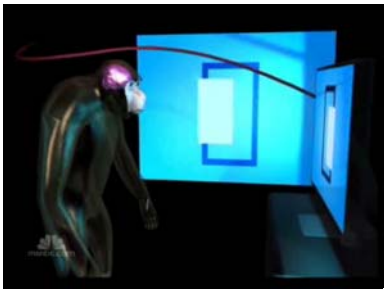




Catheters deliver anesthetic to nerves

Moritz et al, *Nature* 2008

Cortical control of muscle stimulation

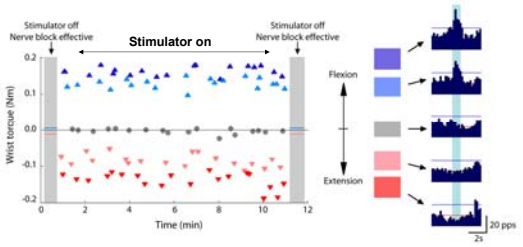


Cortical neurons move cursors on computer screen

Cortical neurons trigger FES of paralyzed muscles via standard or miniature computer

Moritz et al, *Nature* 2008

Brain-control of muscle stimulation

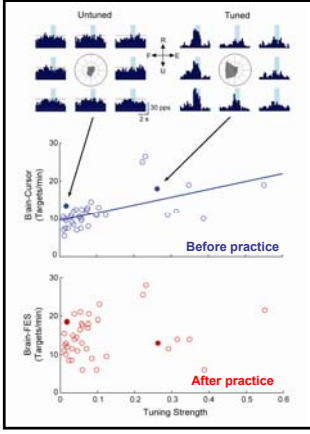


Monkeys match 5 levels of wrist torque using cortically-controlled FES

Only 5-10% of torque can be produced without stimulator

Moritz et al, *Nature* 2008

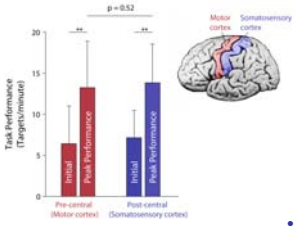
Cell tuning does not predict control of FES



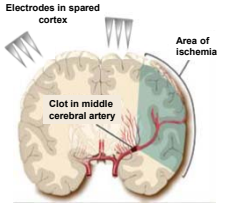
- Tuned neurons initially control cursor faster
- The brain learns to use all neurons equally well to control FES with practice
- Feedback triples population of useful neurons

Moritz et al, *Nature* 2008

Can other cortical areas be used to control FES?



Neurons in somatosensory cortex can be controlled equally well



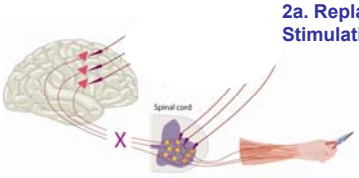
- MCA stroke → arm paresis
- Record from spared cortex for control? (e.g. leg area or cortex contralateral to injury)

Moritz & Fetz, *J Neural Engineering* 2011

Outline: Intra-Spinal Stimulation

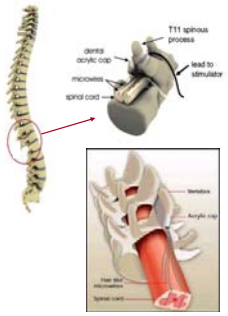
1. Replace: Brain control of muscle stimulation

2a. Replace: Intra-Spinal Stimulation



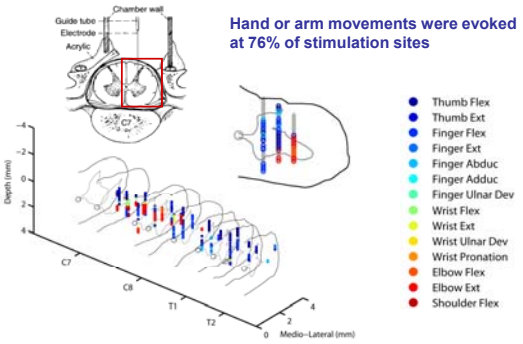
Advantages of spinal stimulation

- More natural recruitment order of motor units
  (Mushahwar & Horsch, *2000*)
- Elicit functional muscle synergies or reflex circuits from single stimulating electrodes, reducing number of electrodes & controllers
  - Evoke complete stepping movements in spinal cats with only 4 electrodes
    (Mushahwar *et al.* 2002)



Mushahwar *et al., J Neural Eng* (2007)

Spinal stimulation evoked movements

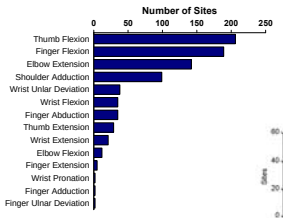


Hand or arm movements were evoked at 76% of stimulation sites

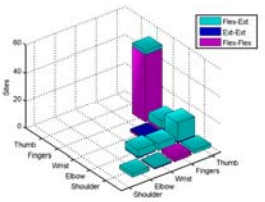
Moritz *et al. J Neurophysiol* 2007

Example: Intra-spinal microstimulation

Synergies evoked by spinal stimulation



Simultaneous flexion of fingers & thumb was the most common synergistic movement evoked



Movements of the digits were most commonly evoked

Moritz *et al. J Neurophysiol* 2007

Replace: Spinal stimulation

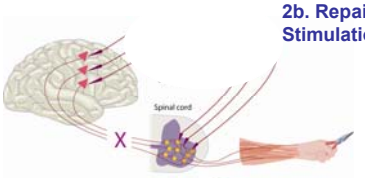
- **Hand and arm movements are readily evoked throughout cervical spinal cord.**
- **Synergist muscles are commonly co-activated by spinal stimulation.**
- **Perhaps brain-controlled spinal stimulation is the ideal neuroprosthesis to restore hand & arm function**

Vivian Mushahwar

Outline: Intra-Spinal Stimulation

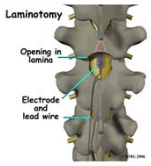
1. Replace: Brain control of muscle stimulation

2b. Repair: Intra-Spinal Stimulation



Epidural stimulation promotes movement

- Case Study: 23-year-old man with paraplegia from a C7–T1 subluxation
- ASIA – B: abnormal sensation present below the lesion, but no motor function of trunk or leg muscles
- Multisite epidural electrode array over L1-S1
- Therapeutic stimulation duration 40-120 min per session
- 7 months of stimulation paired with movement training (standing, stepping, etc.)



Harkema et al, Lancet 2011

Without Epidural Stimulation

Attempts of voluntary movements (leg, ankle, and toe) **without** epidural stimulation

Harkema et al, Lancet 2011

With Epidural Stimulation ON

Voluntary movements (leg, ankle, and toe) **with epidural stimulation** (4 V, 30 Hz)

Harkema et al, Lancet 2011

Intra-spinal stimulation for sustained recovery?

- Epidural stimulation on cord dorsum activates sensory afferents
- Intra-spinal stimulation in ventral horn activates spinal motor neurons and interneurons
- Intra-spinal stimulation may promote sustained recovery of function after incomplete spinal cord injury

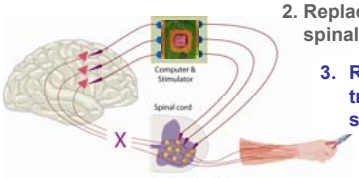
Epidural stimulation

Intra-spinal stimulation

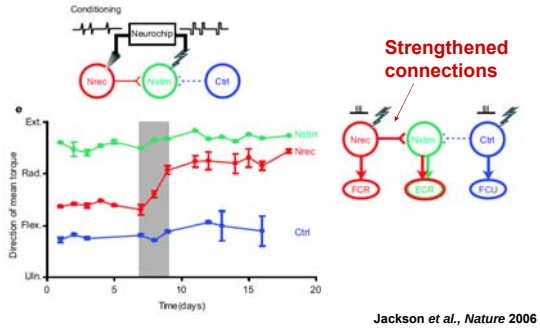
Mushahwar *et al., J Neural Eng* (2007)

Three approaches to restore movement

1. Replace: Brain control of muscle stimulation
2. Replace & Repair: Intra-spinal microstimulation
3. **Repair: Brain-triggered spinal stimulation**

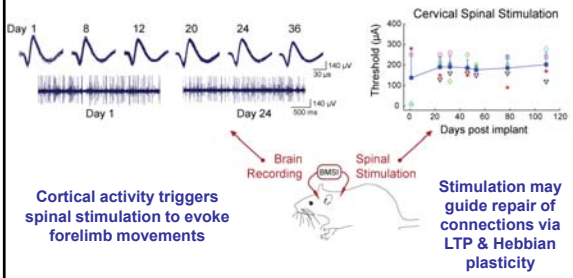


Synchronizing cortical sites leads to stronger connections



Jackson *et al.*, *Nature* 2006

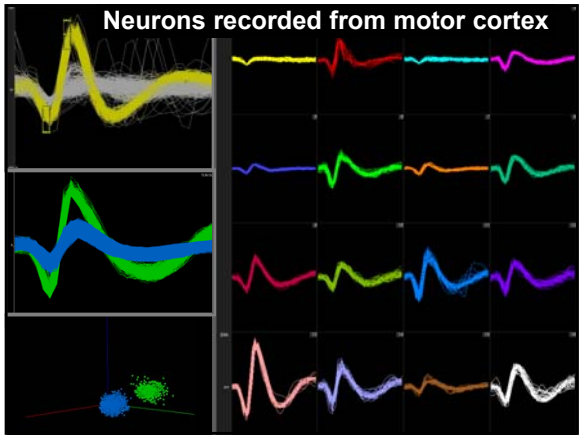
Promoting repair of functional connections after injury



Cortical activity triggers spinal stimulation to evoke forelimb movements

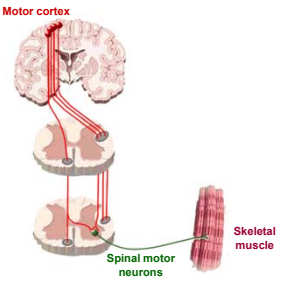
Stimulation may guide repair of connections via LTP & Hebbian plasticity

Neurons recorded from motor cortex



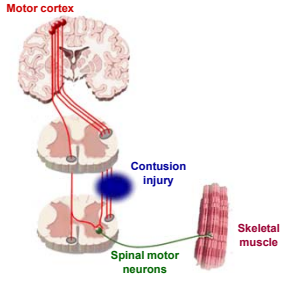
Brain-triggered spinal stimulation

Intact motor system



Brain-triggered spinal stimulation

Incomplete spinal cord injury

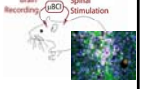


Summary: BCI to restore movement

1. **Replace**: Monkeys can use arbitrary neurons to control muscle stimulation and move a paralyzed arm. Could alternative brain areas be used for control following stroke?

2. **Replace**: Spinal stimulation can evoke forelimb movements & functional muscle synergies. Is BCI-controlled ISMS the ideal combination for limb reanimation?

3. **Repair**: Spinal stimulation enhances recovery after injury. Can synchronous stimulation collaborate with stem cells to promote spinal cord regeneration?



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Spinal Stimulation
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