Brain-computer interfaces for basic science

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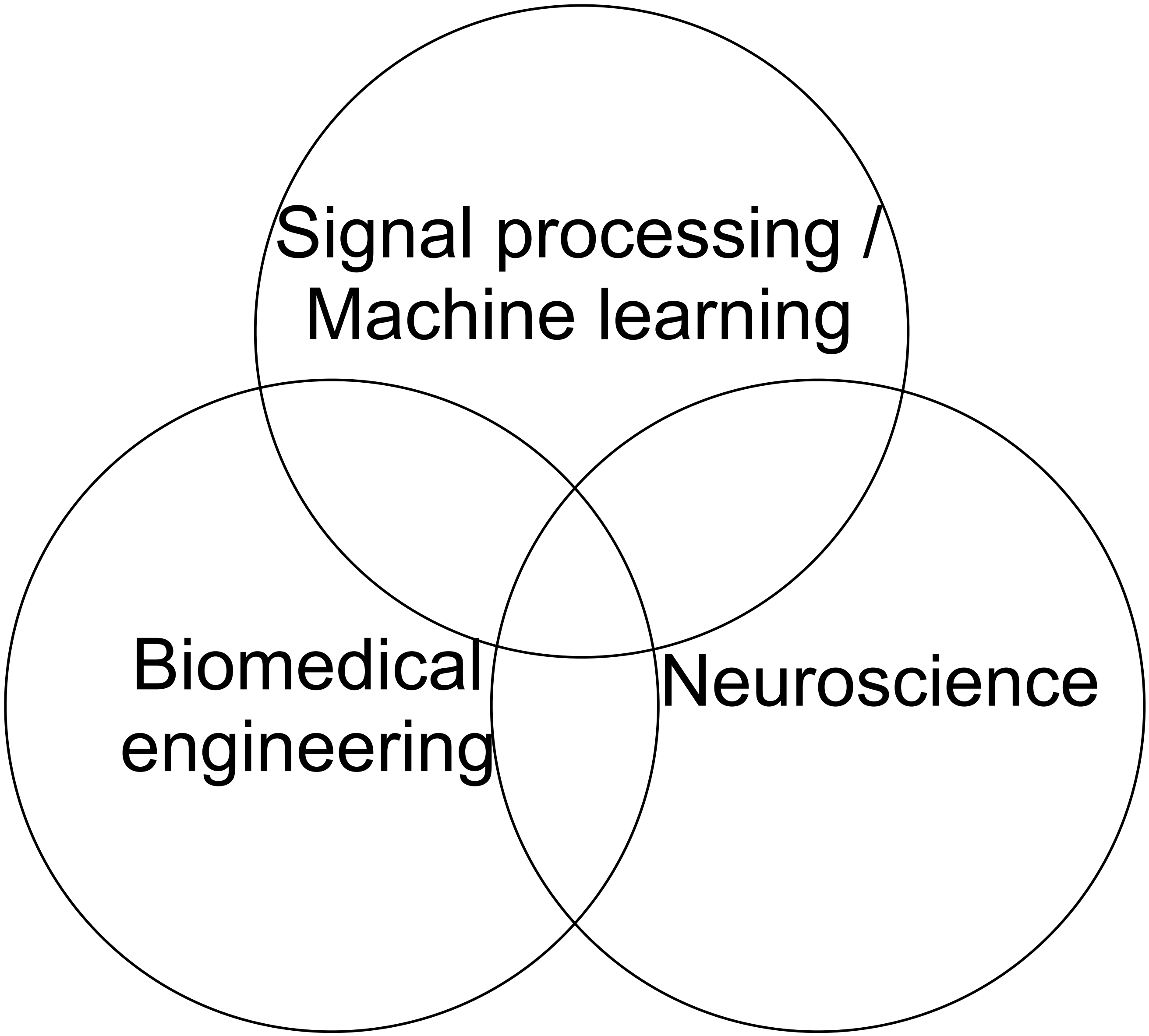
My group’s work



About me

- Undergraduate in Electrical Engineering and Computer Sciences at UC Berkeley

  (didn’t take a single biology class there)

- Graduate school in Electrical Engineering at Stanford

  (research group included neuroscientists and engineers; did neural recordings and worked with animals)

- Post-doc at Stanford and UCL

  (experimental / computational collaboration)

- Started at Carnegie Mellon in 2010

Brain-computer interface

J. Collinger and R. Gaunt
University of Pittsburgh

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Central message:

Brain-computer interface is powerful tool for basic science

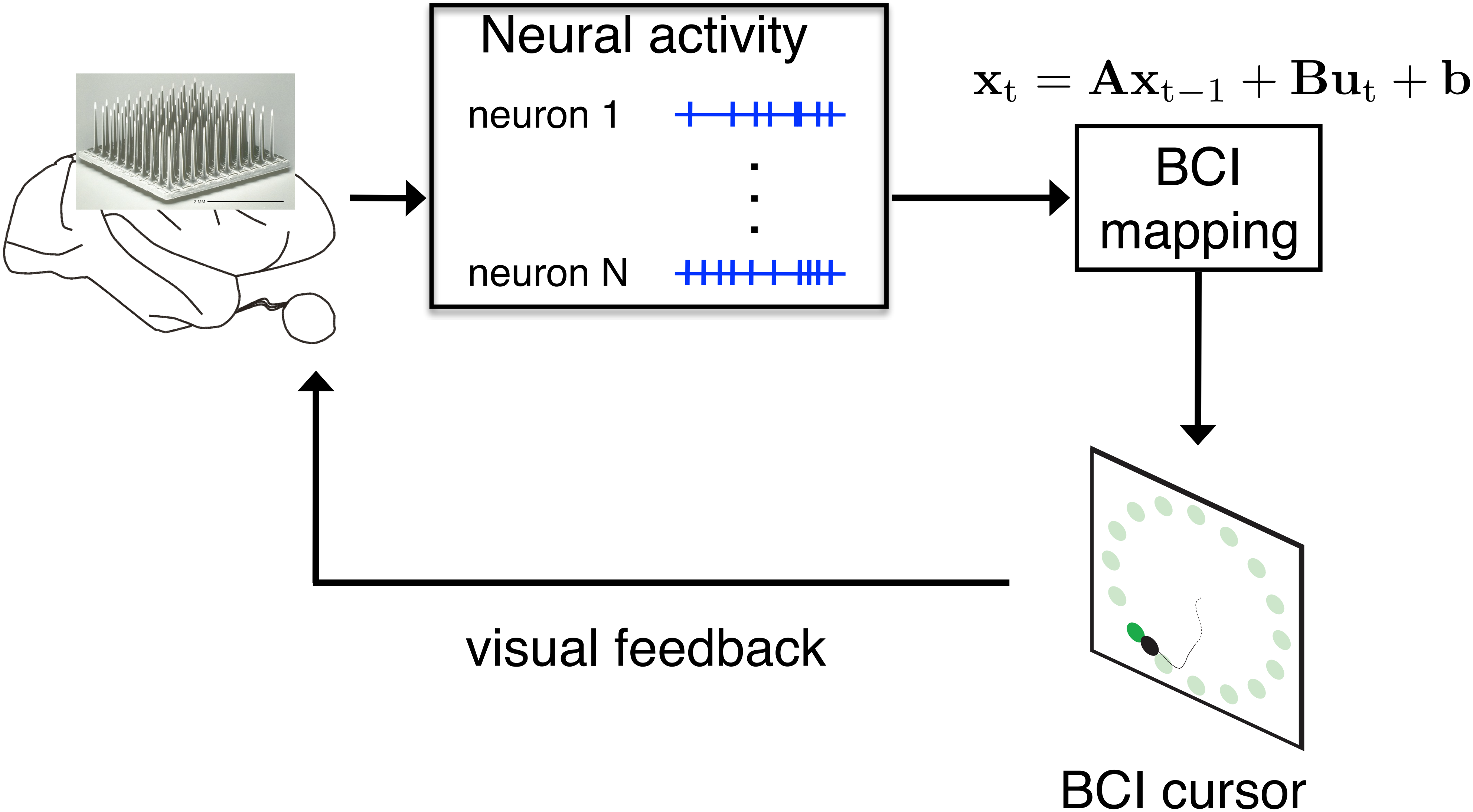
=> Simplify brain's output interface without simplifying away complexity of brain processing we wish to understand

Brain's output interface is complex

	Arm reaching	
Effector	arm	
# Non-output neurons	millions	
# Output neurons	1000's (some recorded)	
Neuron-to-movement mapping	unknown	
Effector dynamics	difficult to measure, nonlinear	
Sensory feedback	tied to arm	

Golub, Chase, Batista, Yu, *Curr Opin Neurobiol*, 2016.

Brain-computer interface (BCI)



BCI represents simplified output interface

	Arm reaching	BCI
Effector	arm	cursor or robotic limb
# Non-output neurons	millions	millions
# Output neurons	1000's (some recorded)	10's-100's (all recorded)
Neuron-to-movement mapping	unknown	known
Effector dynamics	difficult to measure, nonlinear	known, can be linear
Sensory feedback	tied to arm	flexibly manipulable

Golub, Chase, Batista, Yu, *Curr Opin Neurobiol*, 2016.

Proficient control of BCI cursor

Credit: S. Chase

Key advantages of BCI

1) Monitoring all neurons that directly drive movement
2) Distinguishing between output and non-output neurons
3) Defining a simple mapping
4) Changing the mapping
5) Flexibly manipulating sensory feedback

Golub, Chase, Batista, Yu, *Curr Opin Neurobiol*, 2016.

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Learning requires the brain to alter the neural activity it produces

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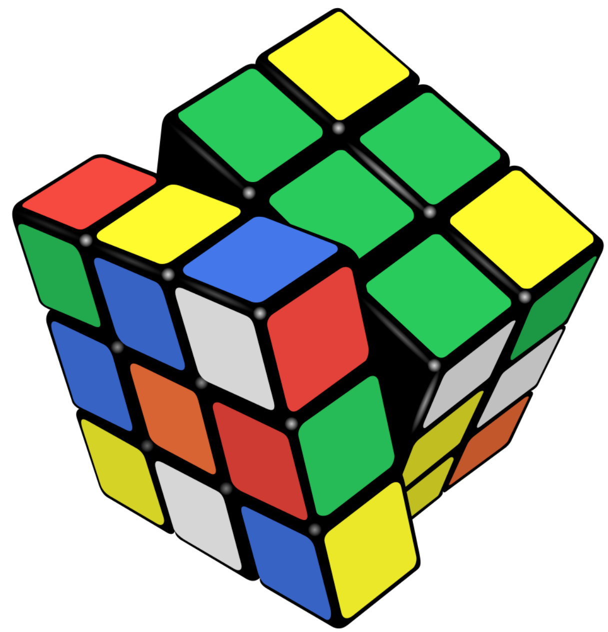

Outline

- Why are some tasks easier to learn than others?

- How does population activity change during learning?

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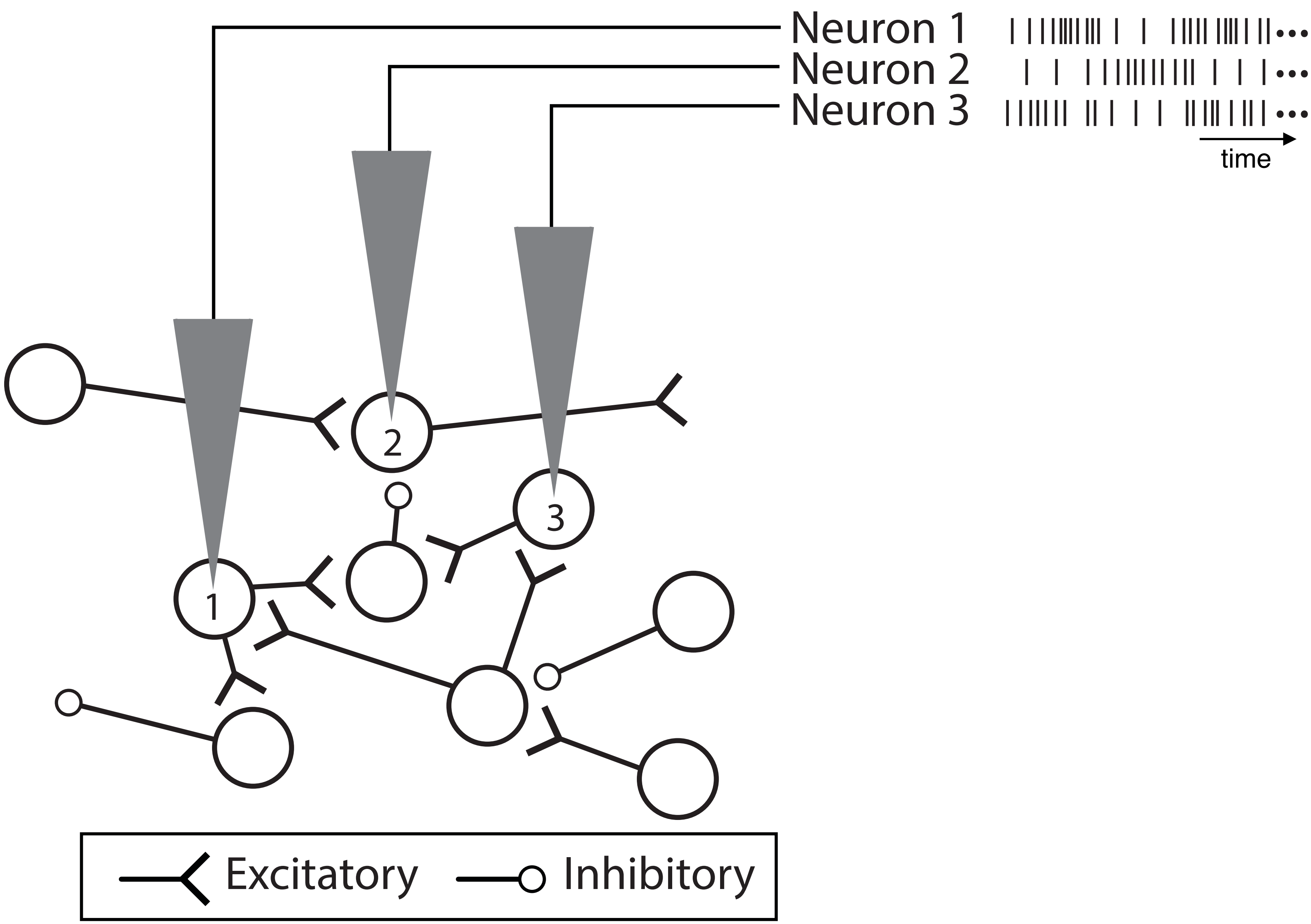
Why are some tasks easier to learn than others?

- Perhaps certain types of neural activity patterns are easier to produce than others

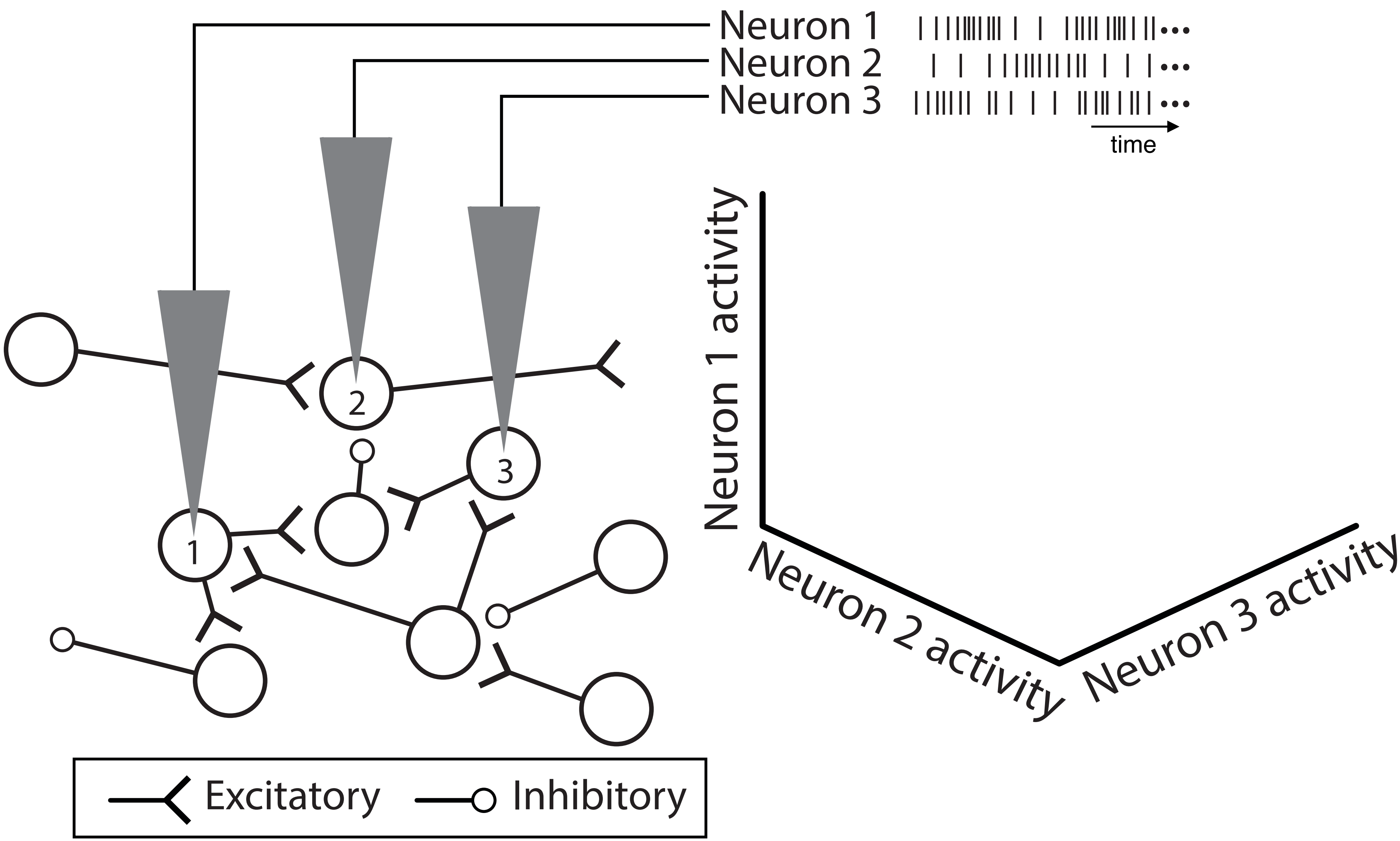
- Can subjects learn to produce arbitrary population activity patterns?

- If not, what defines the constraints on learning?

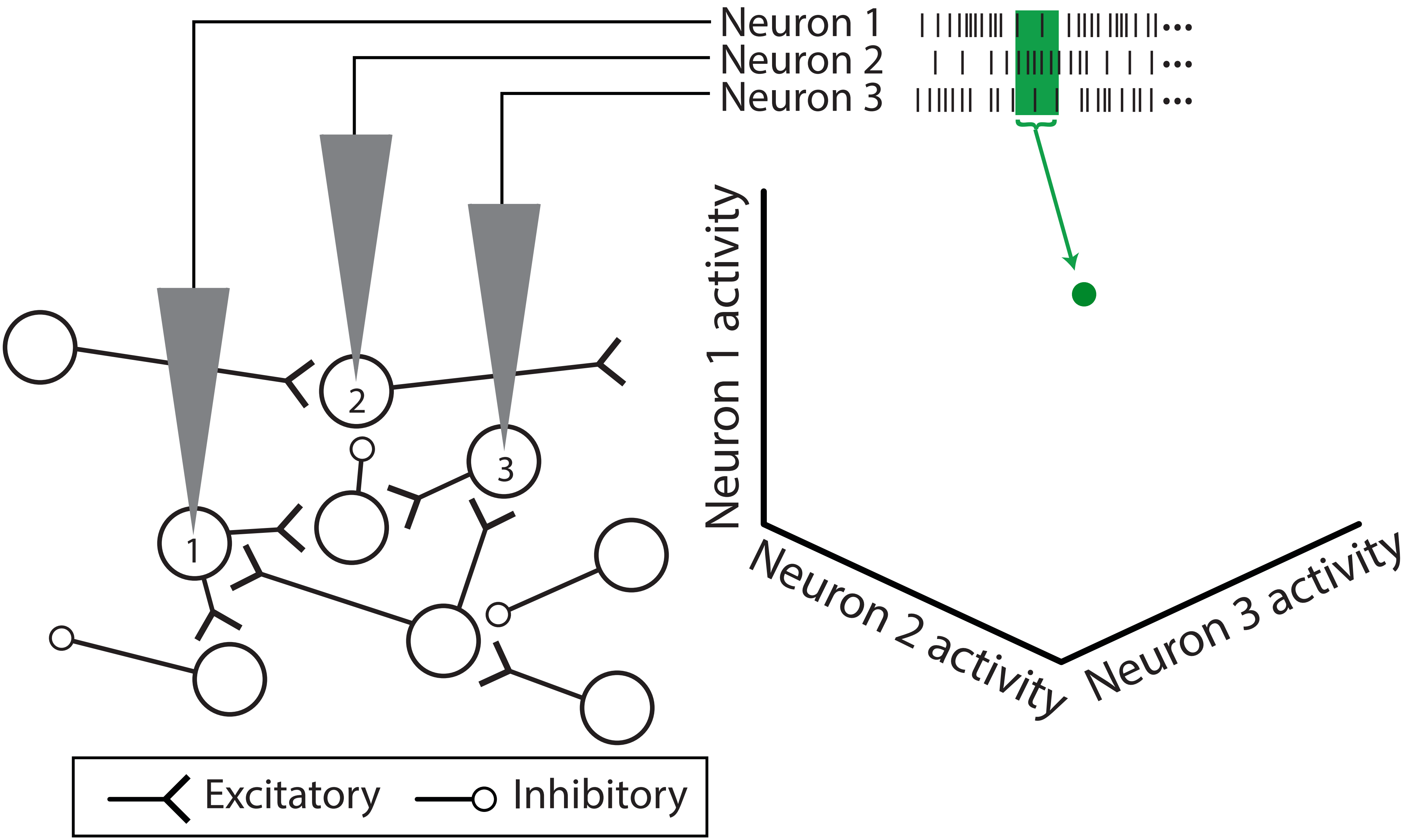
Record activity of tens of neurons



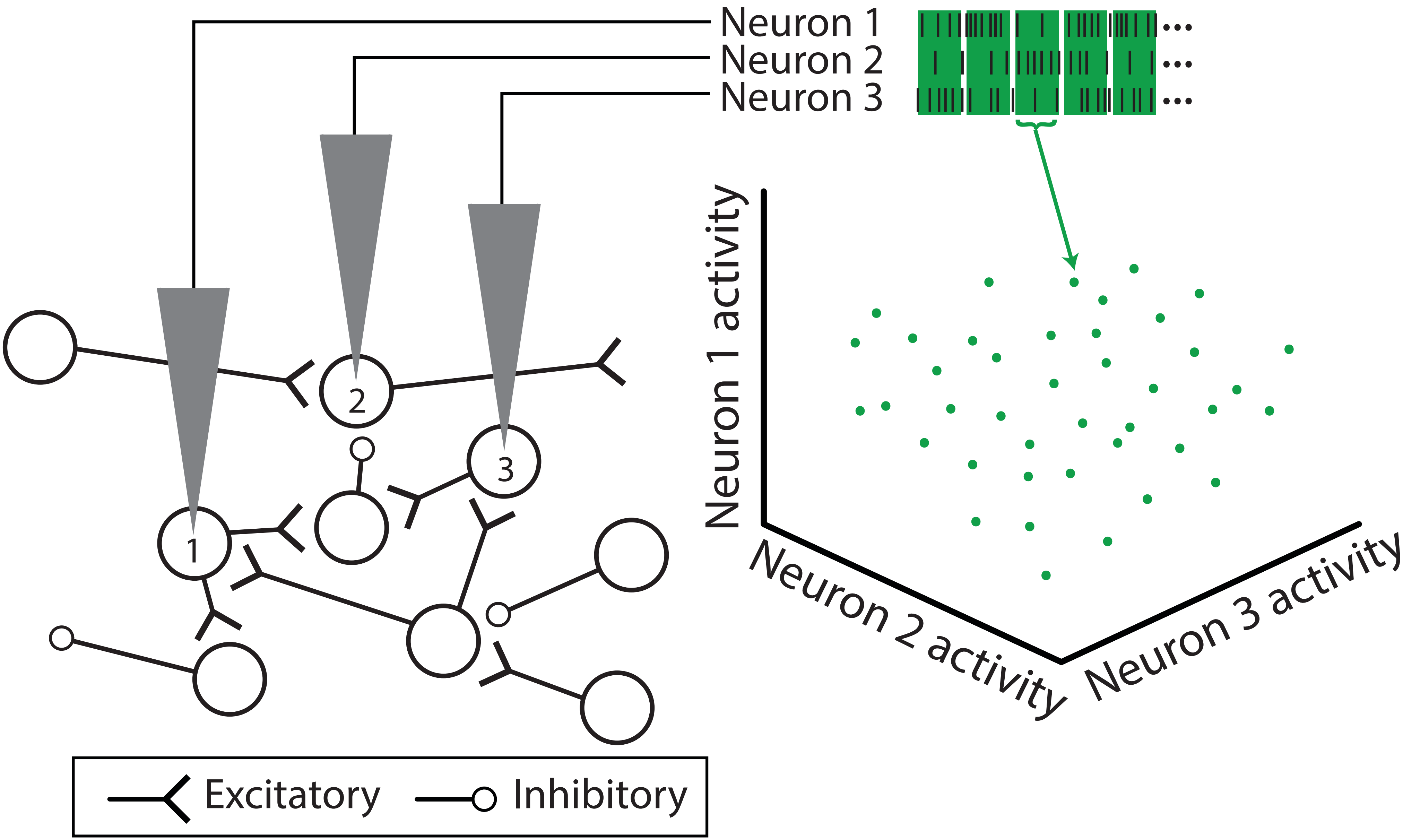
Define population activity space



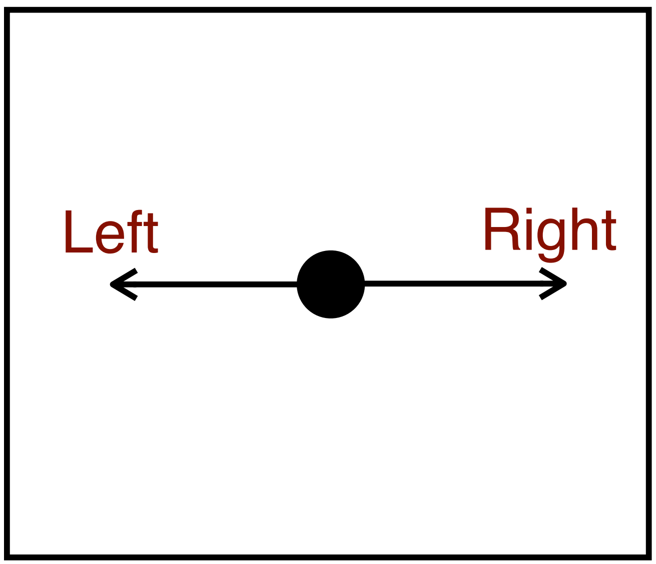
Represent recorded activity in this space



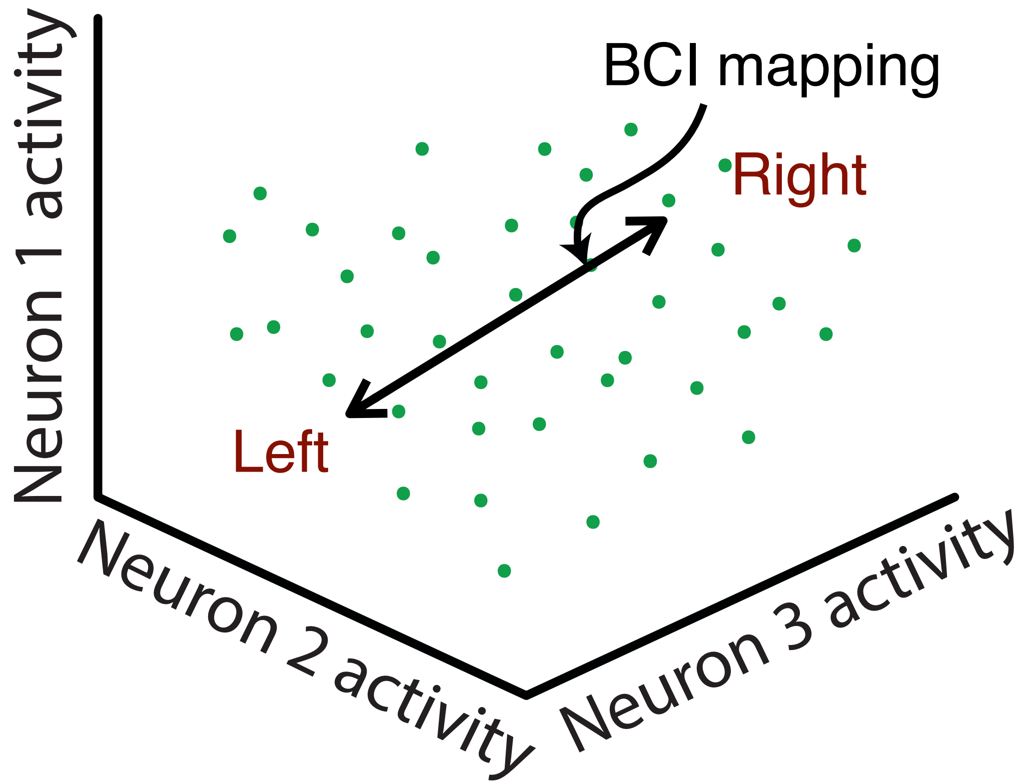
Represent recorded activity in this space



Define BCI mapping

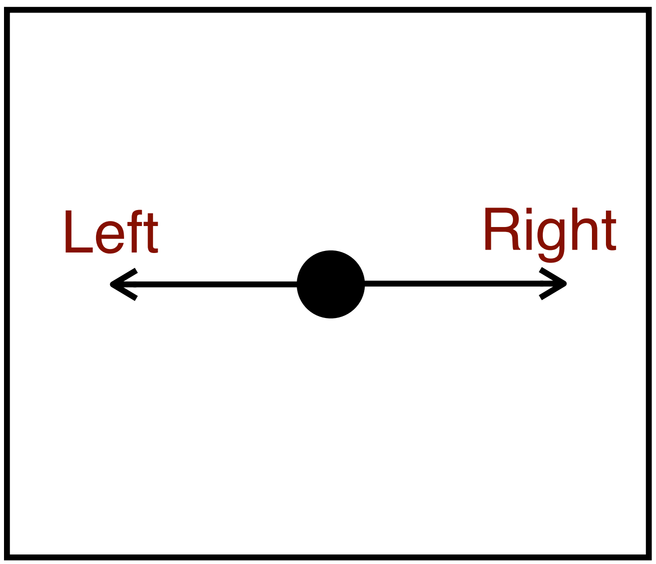


Subject's workspace

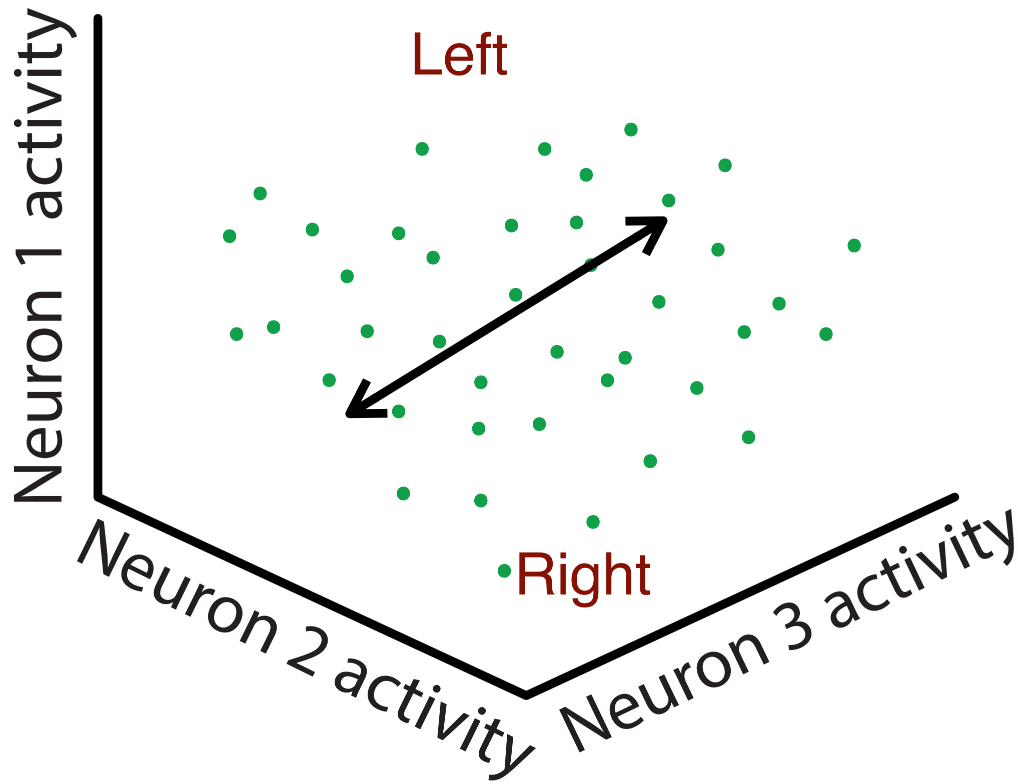


Key manipulation: Switch BCI mapping

Can subject learn to use the new mapping?

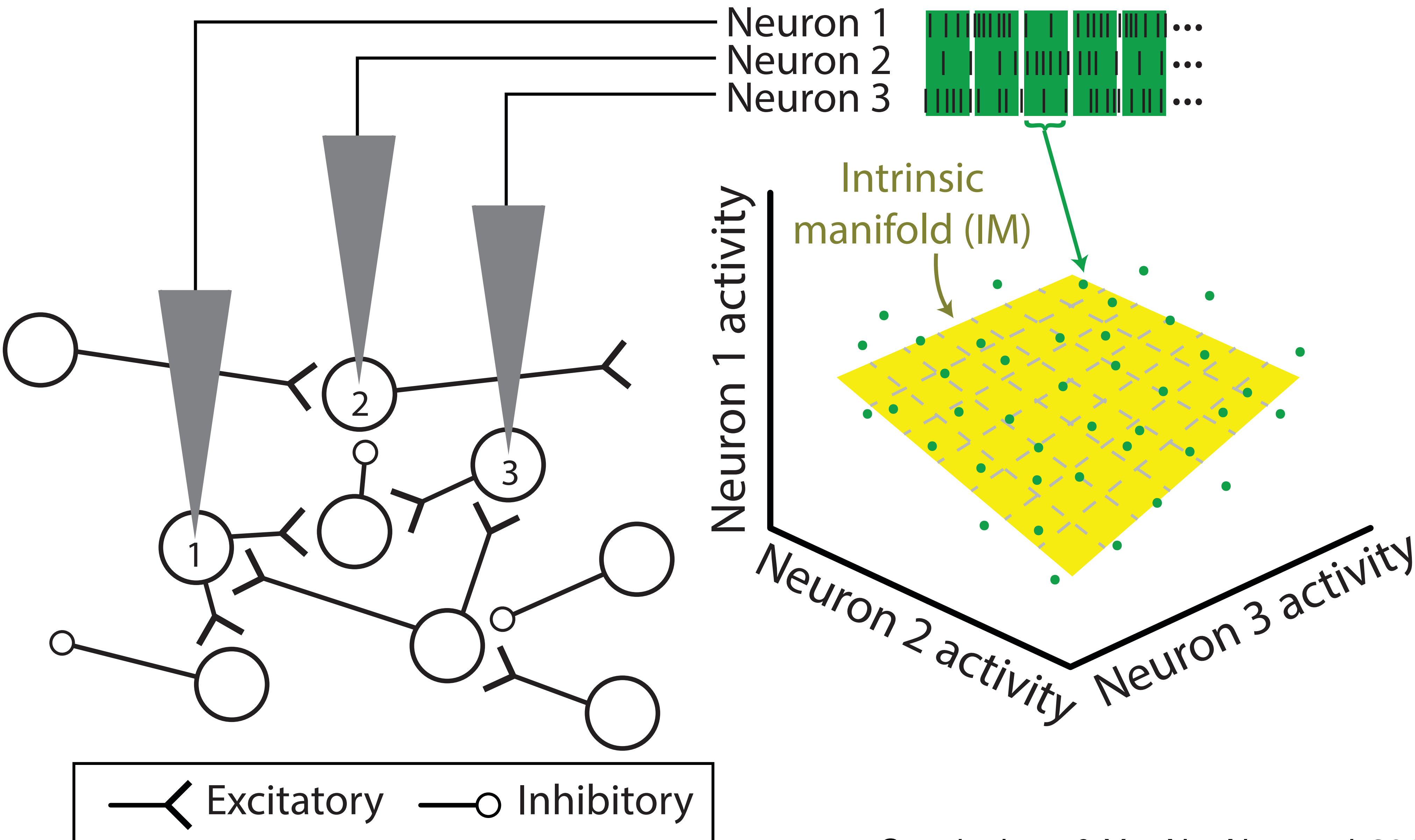


Subject's workspace



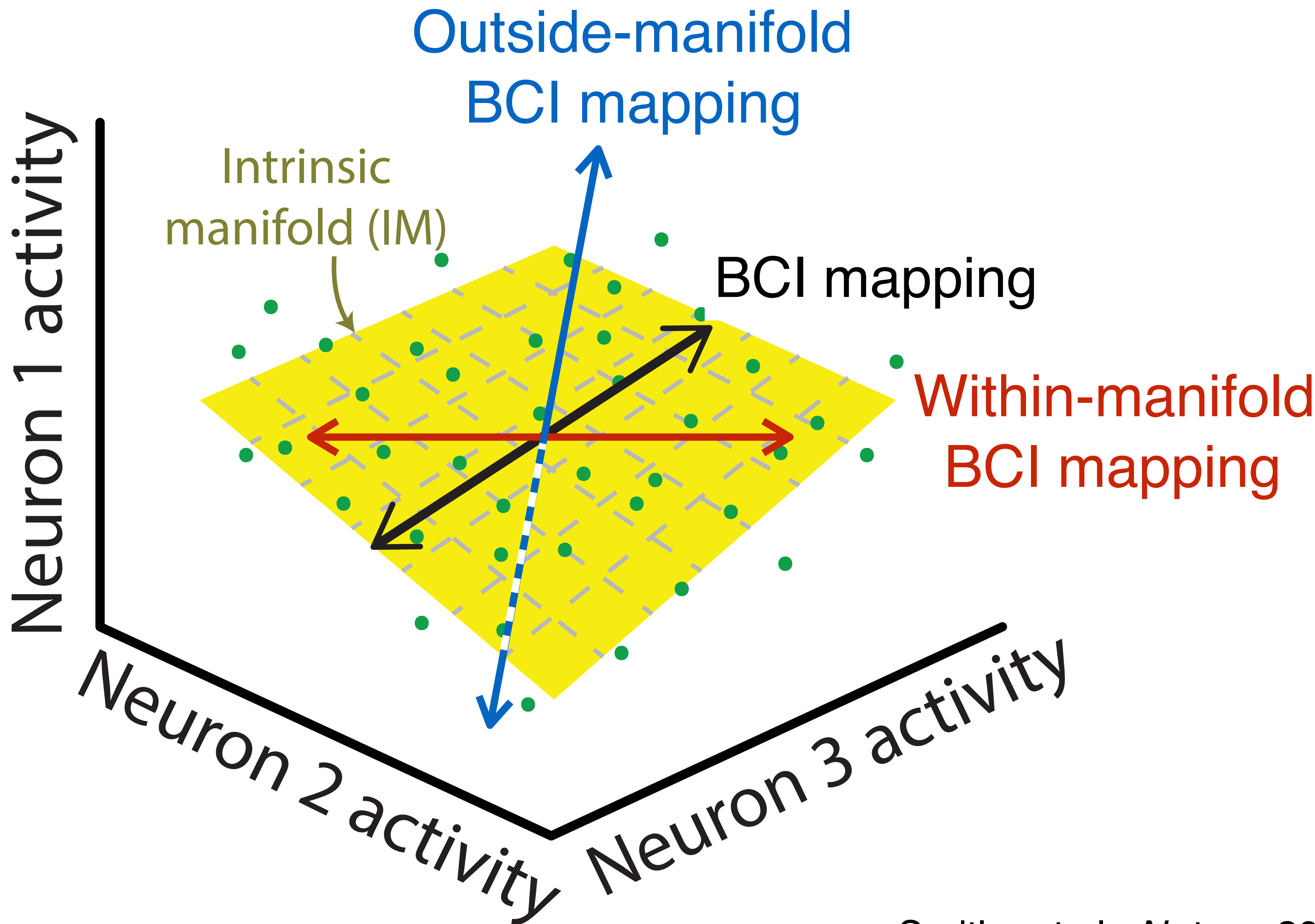
Sadtler et al., *Nature*, 2014.

Intrinsic manifold represents network constraints



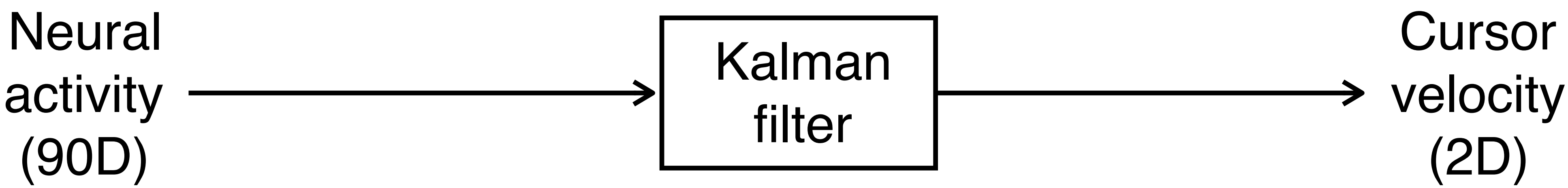
Cunningham & Yu, *Nat Neurosci*, 2014.
Yu et al., *J Neurophysiol*, 2009.

<u>Central hypothesis</u>: Easier to learn within than outside of intrinsic manifold

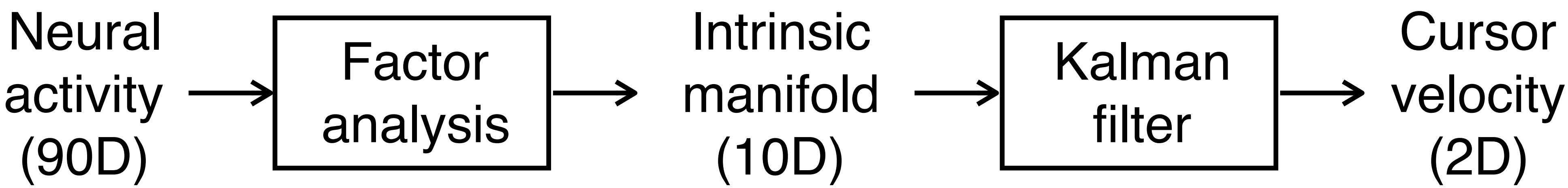


Sadtler et al., *Nature*, 2014.

BCI mapping



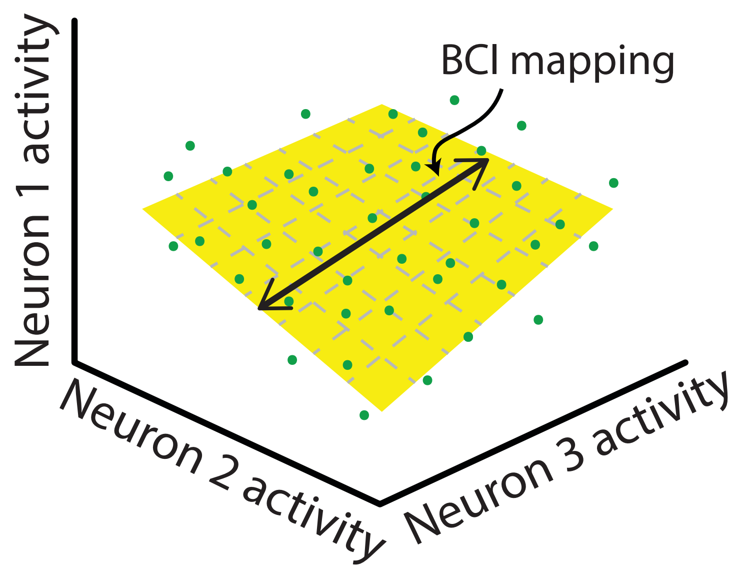
BCI mapping



Sadtler et al., *Nature*, 2014.

BCI mapping

Neural activity (90D) → Factor analysis → Intrinsic manifold (10D) → Kalman filter → Cursor velocity (2D)



(3D-2D-1D)

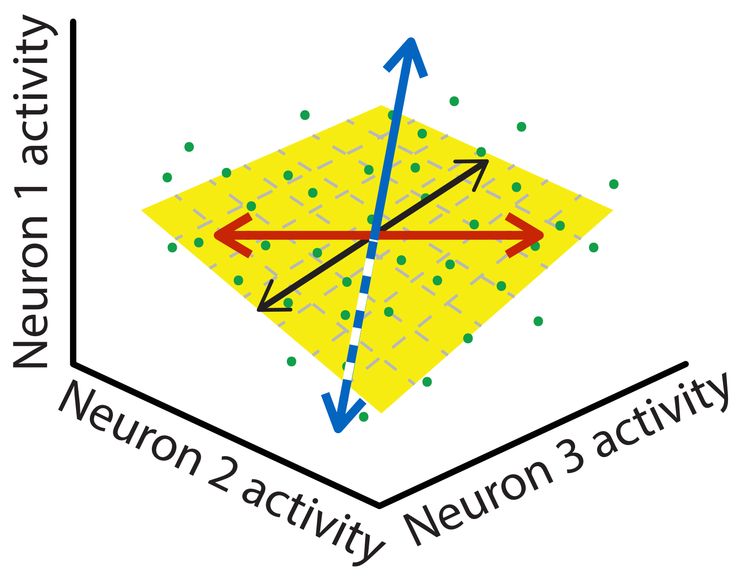
Sadtler et al., *Nature*, 2014.

How BCI mappings were perturbed

Neural activity (90D) → **Factor analysis** → Intrinsic manifold (10D) → **Kalman filter** → Cursor velocity (2D)

outside-manifold perturbation

within-manifold perturbation

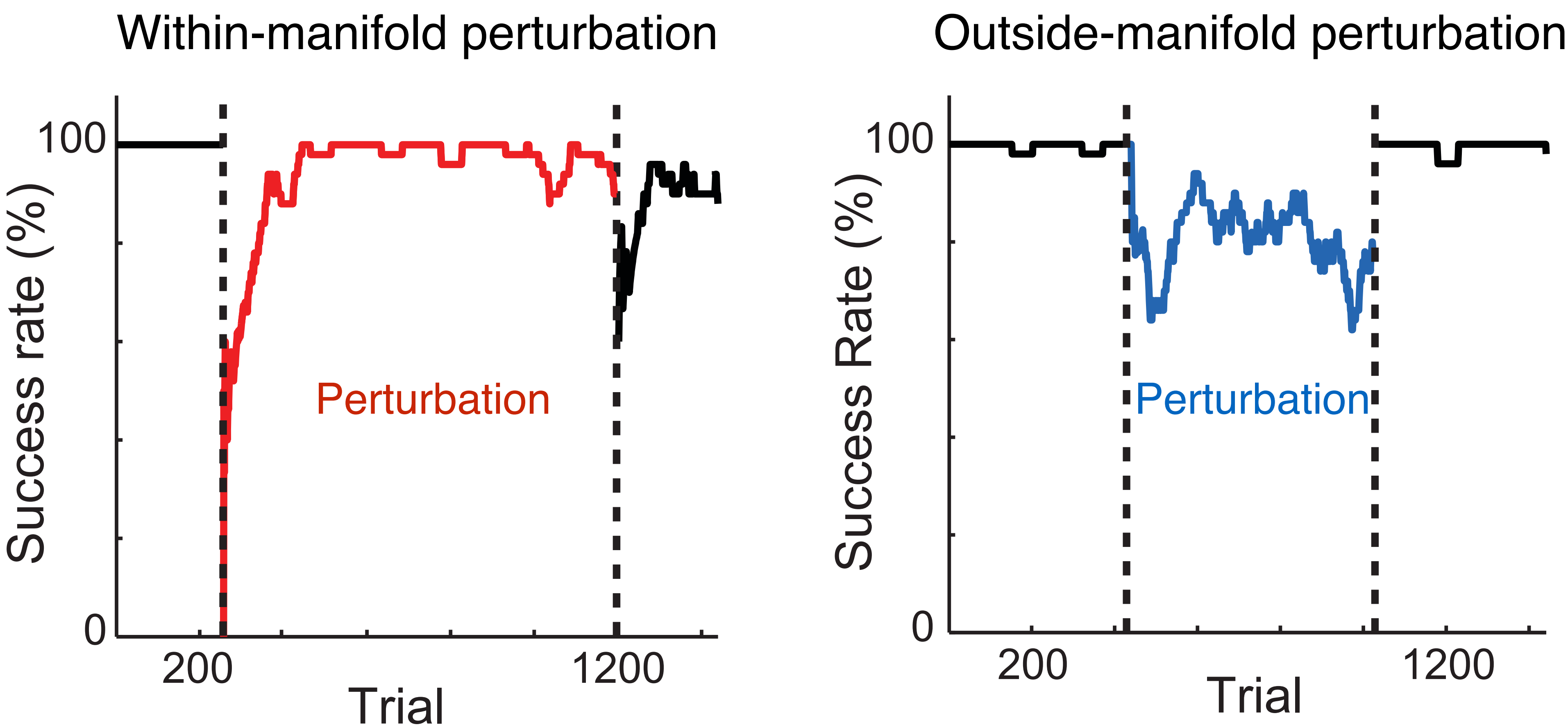


Sadtler et al., *Nature*, 2014.

Experimental methods

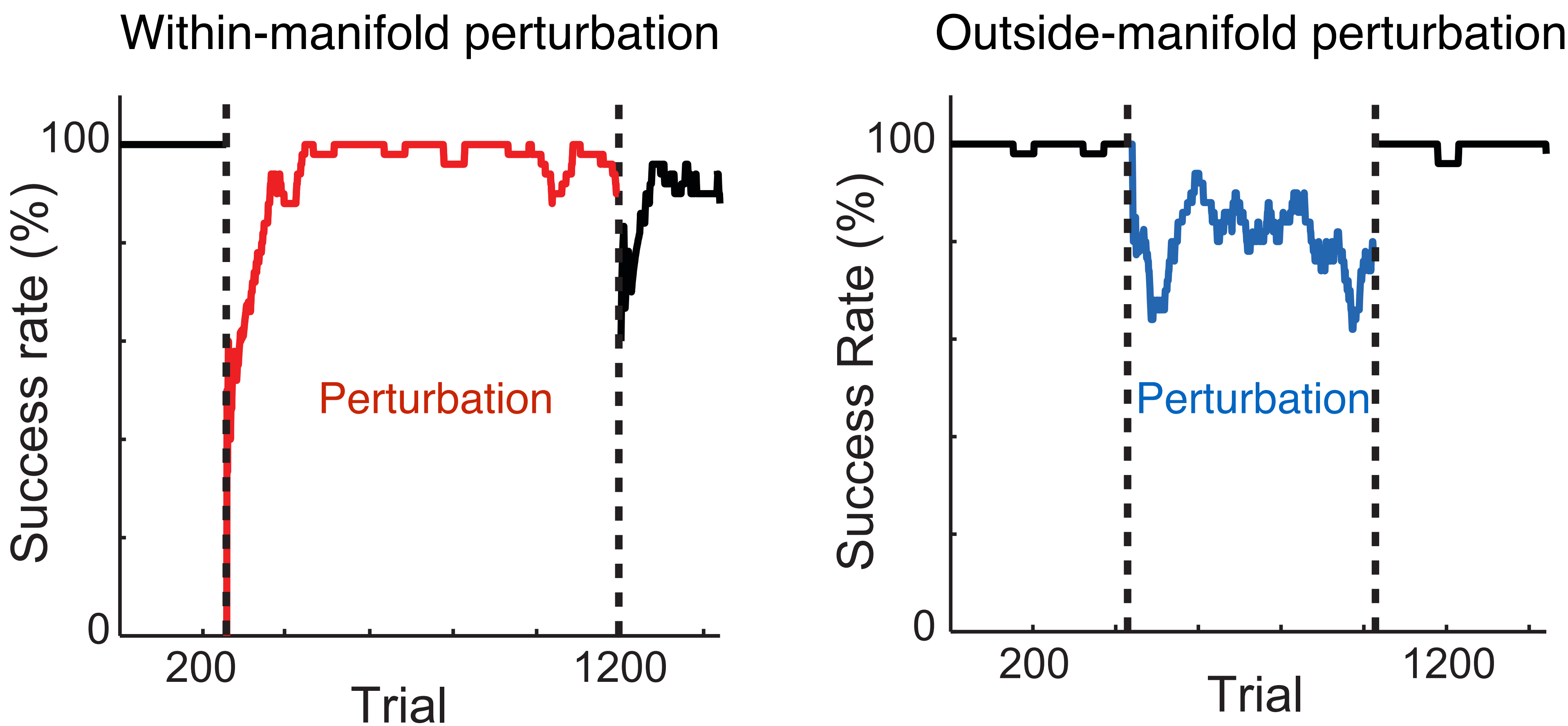
- Utah array recordings in motor cortex (M1) of macaque monkeys
- Used threshold crossings (no spike sorting)
- Spike counts taken in non-overlapping 45ms bins
- 8-target center-out task

Representative sessions



Sadtler et al., *Nature*, 2014.

<u>Key result</u>: Greater learning for within-manifold perturbations than outside-manifold perturbations



Sadtler et al., *Nature*, 2014.

Part 1: Summary

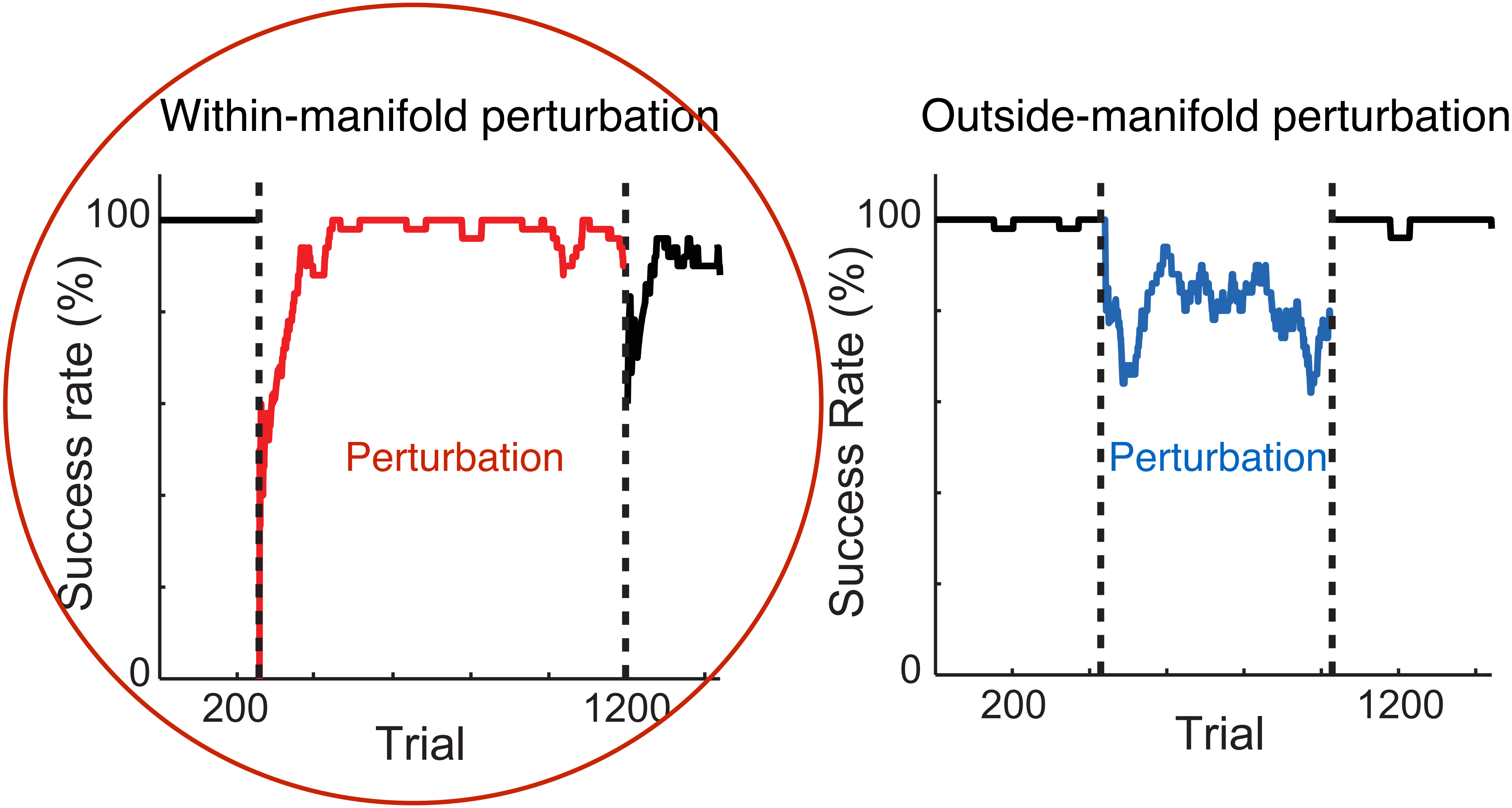
- Learning within intrinsic manifold > learning outside of intrinsic manifold
- Thus, existing structure of a network can shape learning
- Dimensionality reduction can reveal causal constraints on activity patterns attainable by networks of neurons

Outline

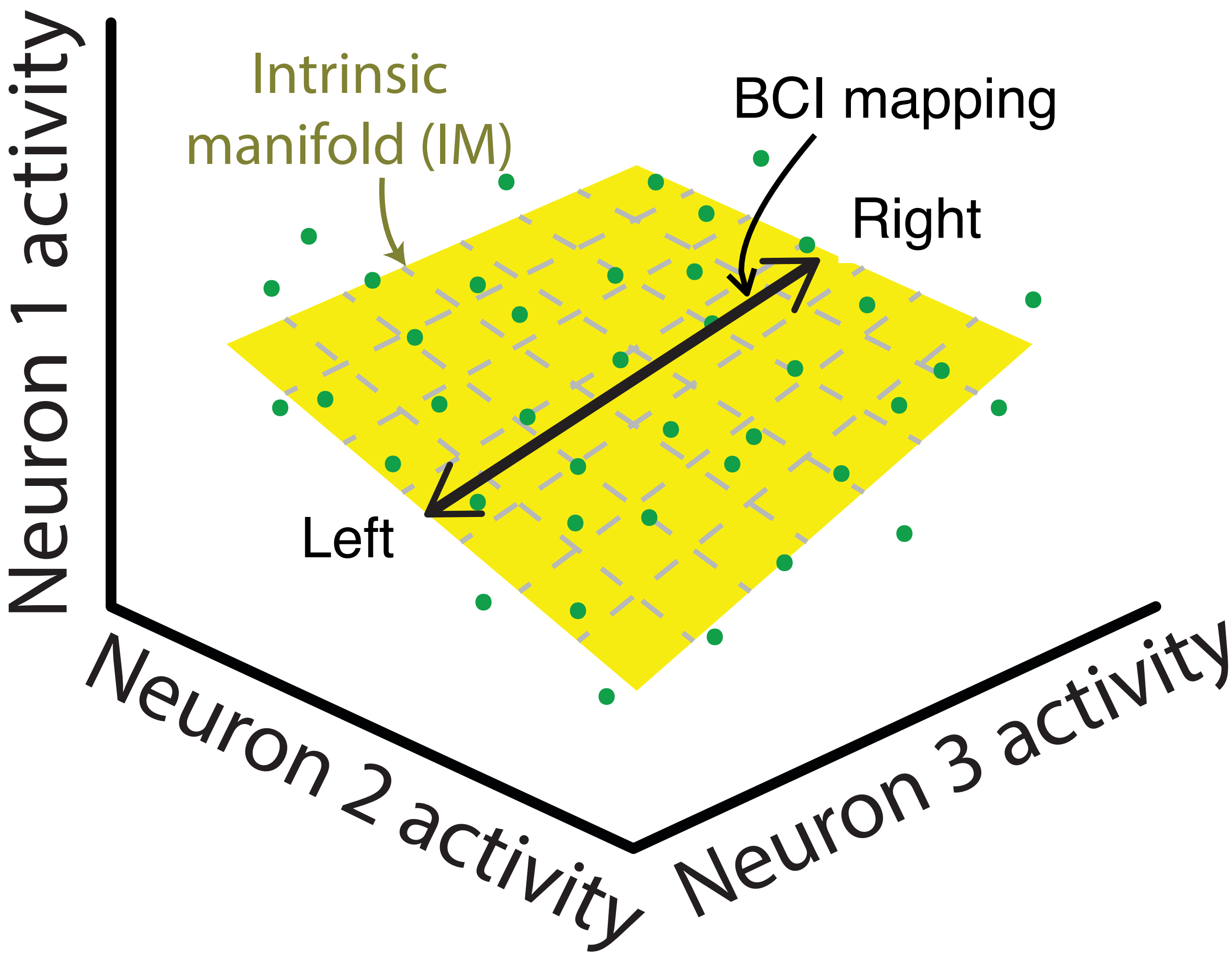
- Why are some tasks easier to learn than others?

- How does population activity change during learning?

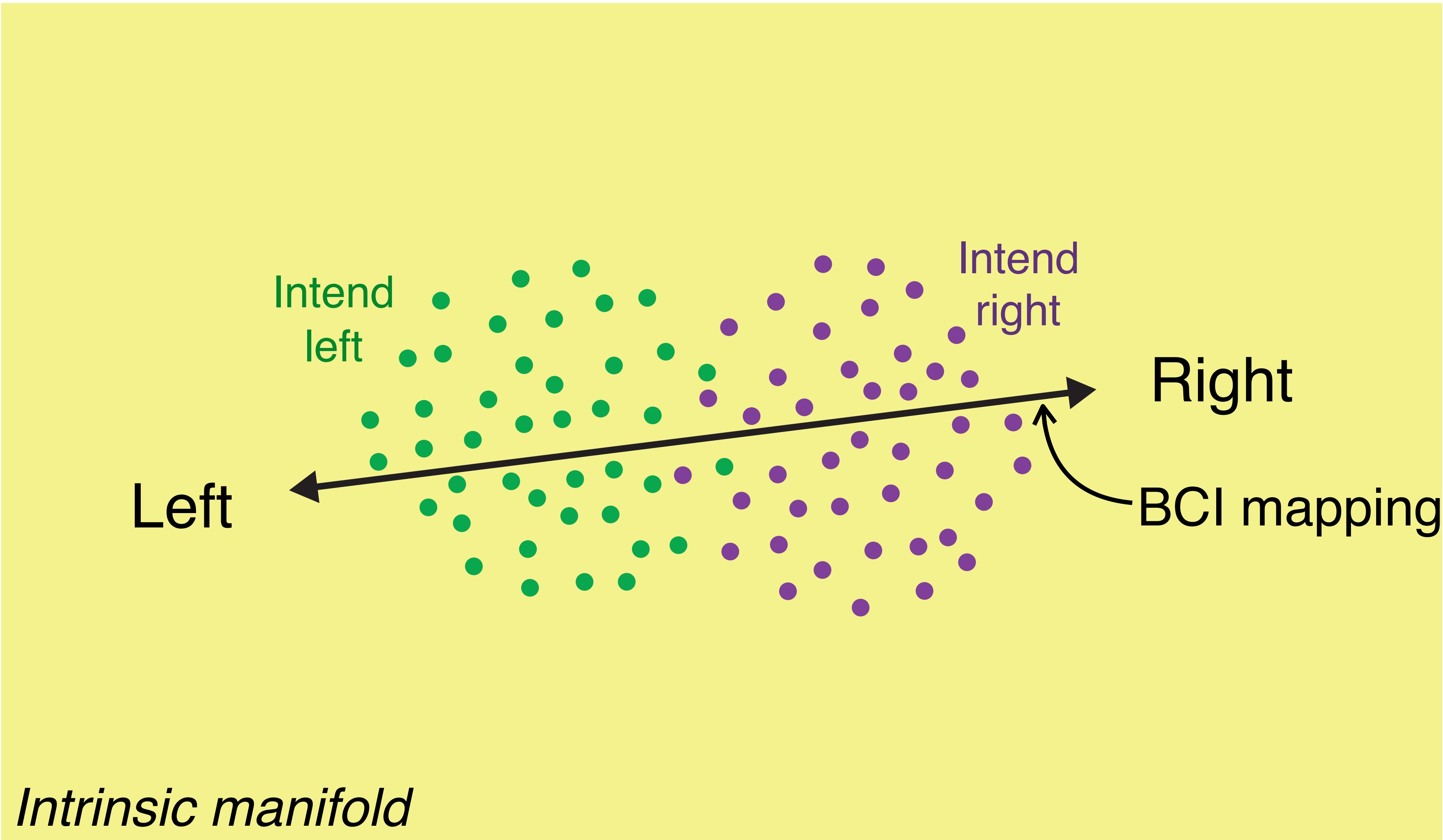
Focus on within-manifold perturbations



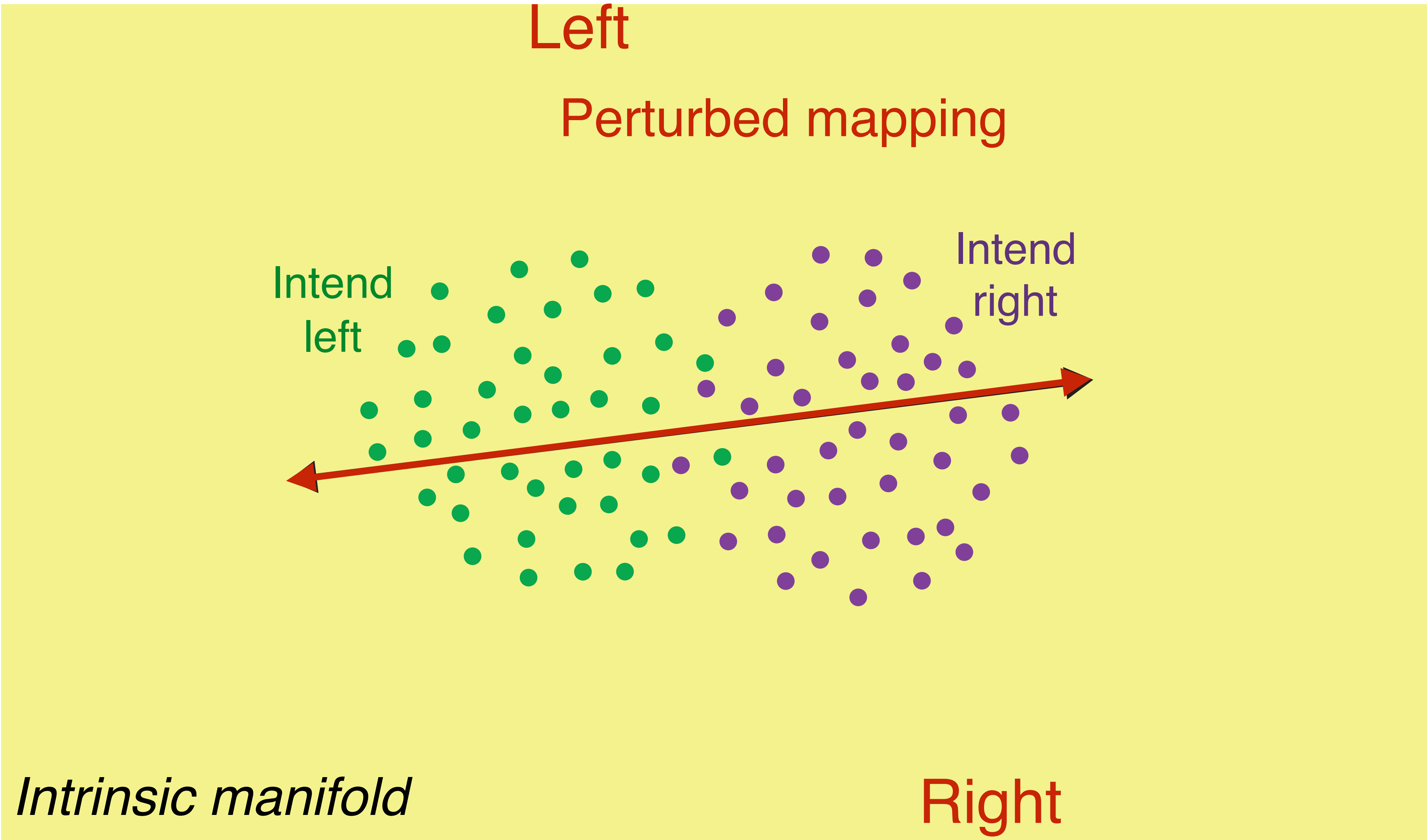
Learning within intrinsic manifold



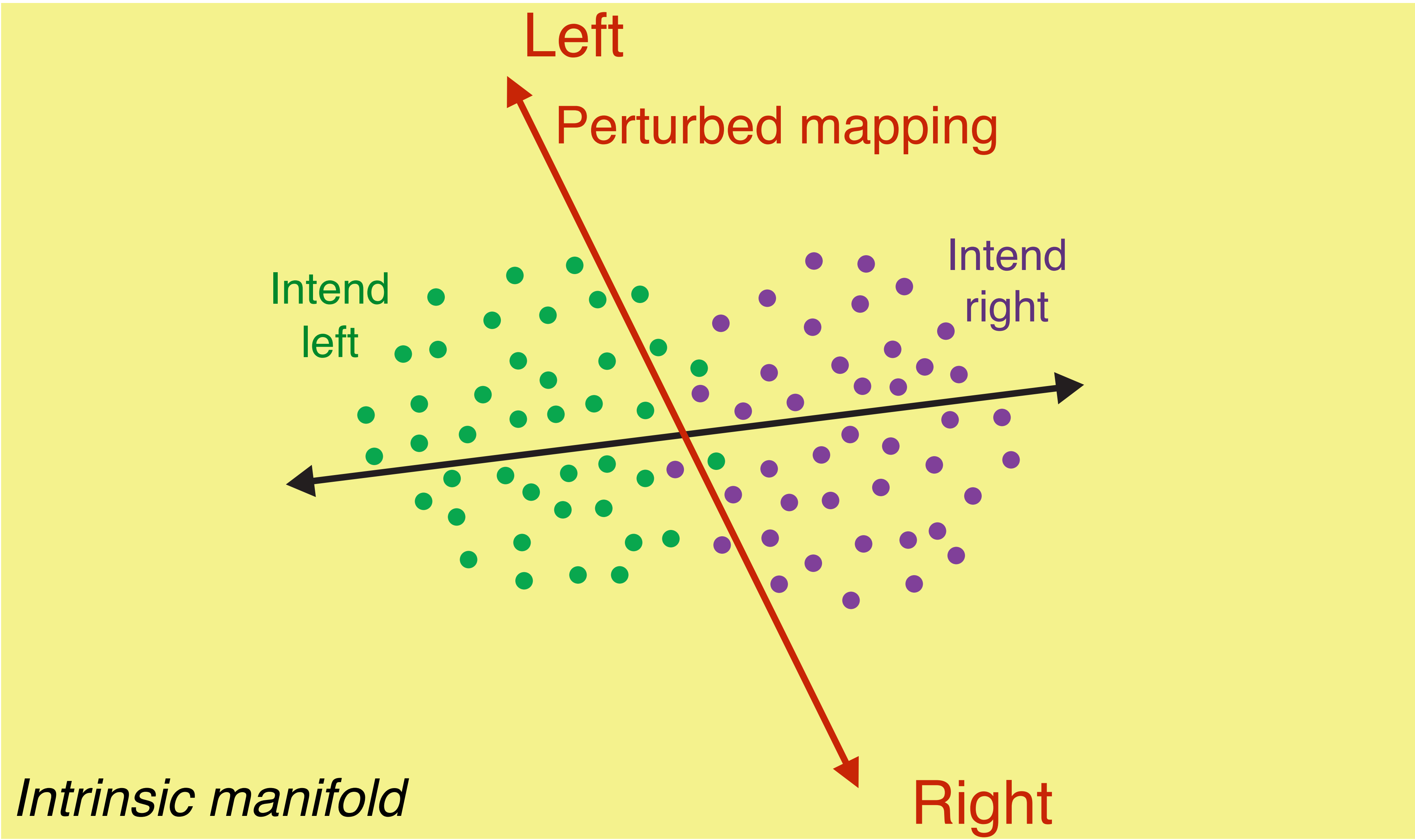
Neural activity <u>before</u> learning



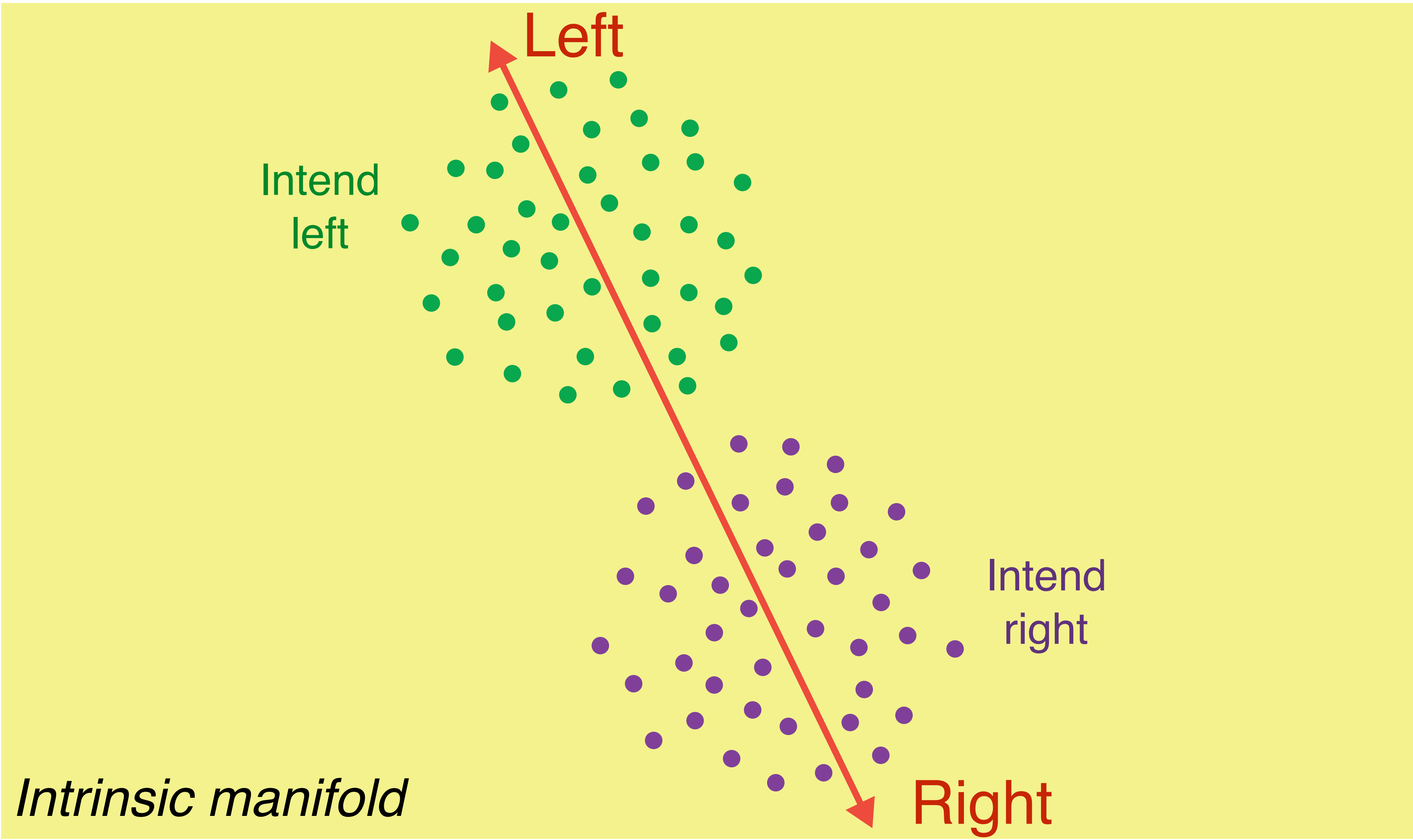
Neural activity <u>before</u> learning



How does animal reorganize its neural activity to regain control of cursor?



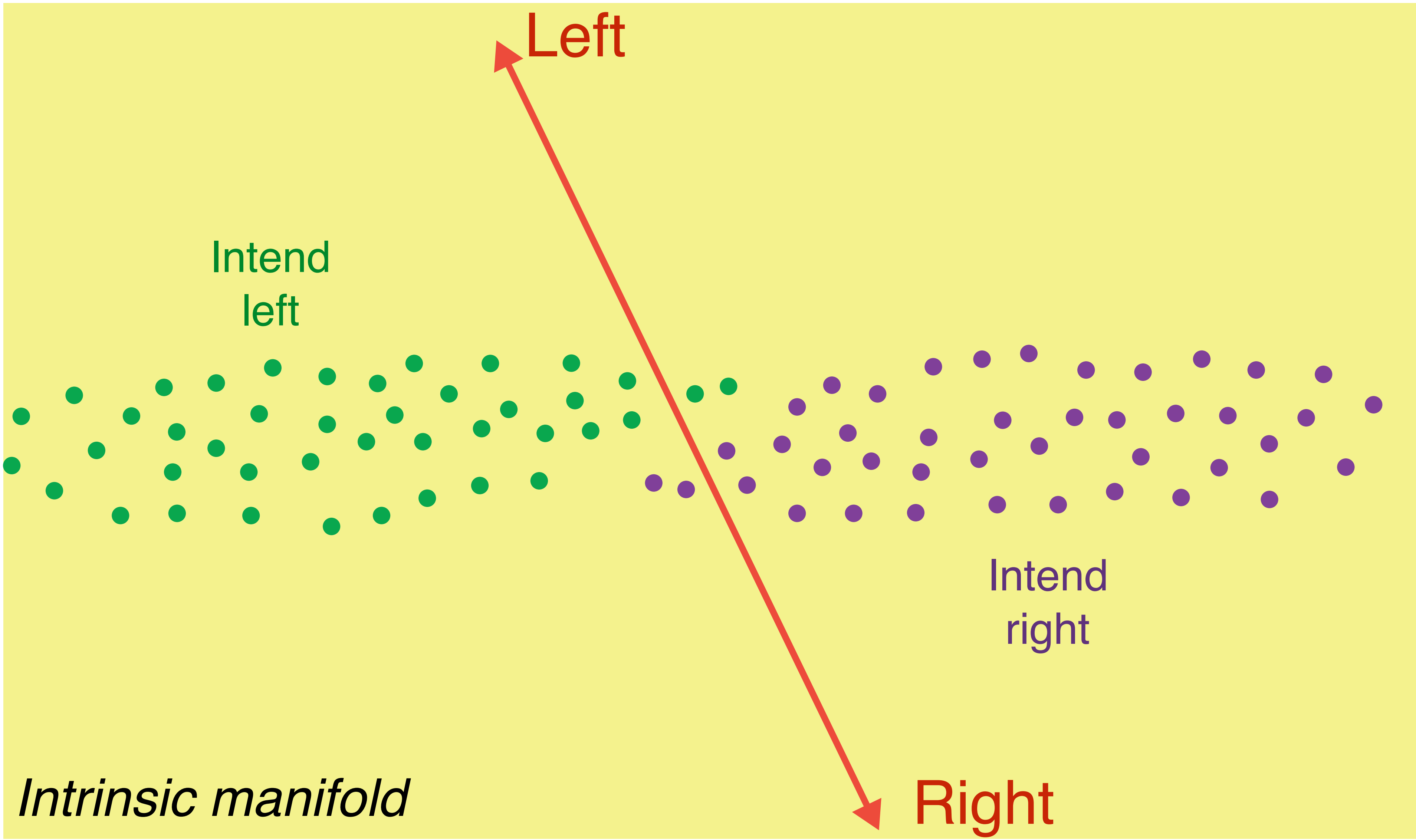
Hypothesis 1: Realignment
"Maximize behavioral performance"



Golub et al., *Nat Neurosci*, 2018.

Hypothesis 2: Rescaling

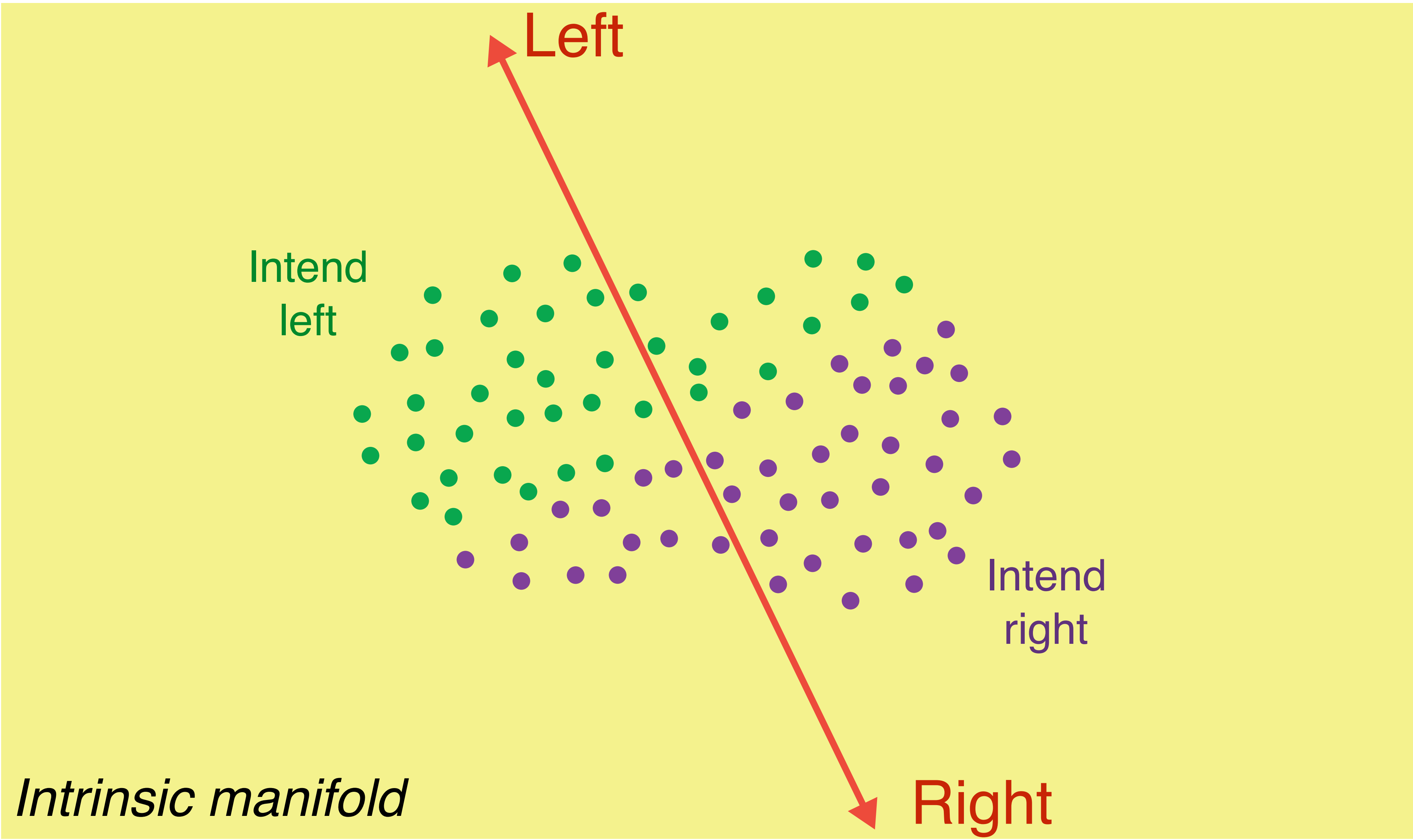
"Restore influence of activity on behavior"



Golub et al., *Nat Neurosci*, 2018.

Hypothesis 3: Reassociation

"Repurpose existing activity patterns"



Golub et al., *Nat Neurosci*, 2018.

Part 2: Summary

- Learning is not only constrained by an intrinsic manifold (Part 1), it is further constrained by a neural repertoire
- Learning is sub-optimal on timescale of hours
- Learning over <u>multiple days</u> can overcome these constraints (Oby et al., *PNAS*, 2019)

BCI enabled this work

- Put task requirements directly on neurons rather than on arm (or eye) movements
- Can <u>causally</u> attribute behavioral (i.e., cursor) learning to specific changes in recorded activity
- Neuron-to-movement mapping known and linear

BCI is a powerful tool for basic science

- BCI simplifies brain's output interface without (hopefully) simplifying complexity of brain processing
- BCIs engage many of same cognitive processes as in arm reaching (learning, internal models, and more)
- BCI can be used to study other sensory, motor, cognitive processes

Group members

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- Darby Losey
- Joao Semedo
- Akashi Umakantha
- Hillary Wehry
- Ryan Williamson

Alumni
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- Patrick Sadtler (PhD)

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  - Erin Grigsby
  - Emily Oby
  - Kristin Quick
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- Brent Dorion (Pitt)
- Adam Kohn (Einstein)
- Christian Machens (Champalimaud)
- Stephen Ryu (Stanford)
- Matthew Smith (Pitt)
- Elizabeth Tyler-Kabara (Pitt)

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