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UCSF

FOUNDATIONS OF COGNITION

APRIL 18, 2017

what is this animal thinking?

an overarching hypothesis

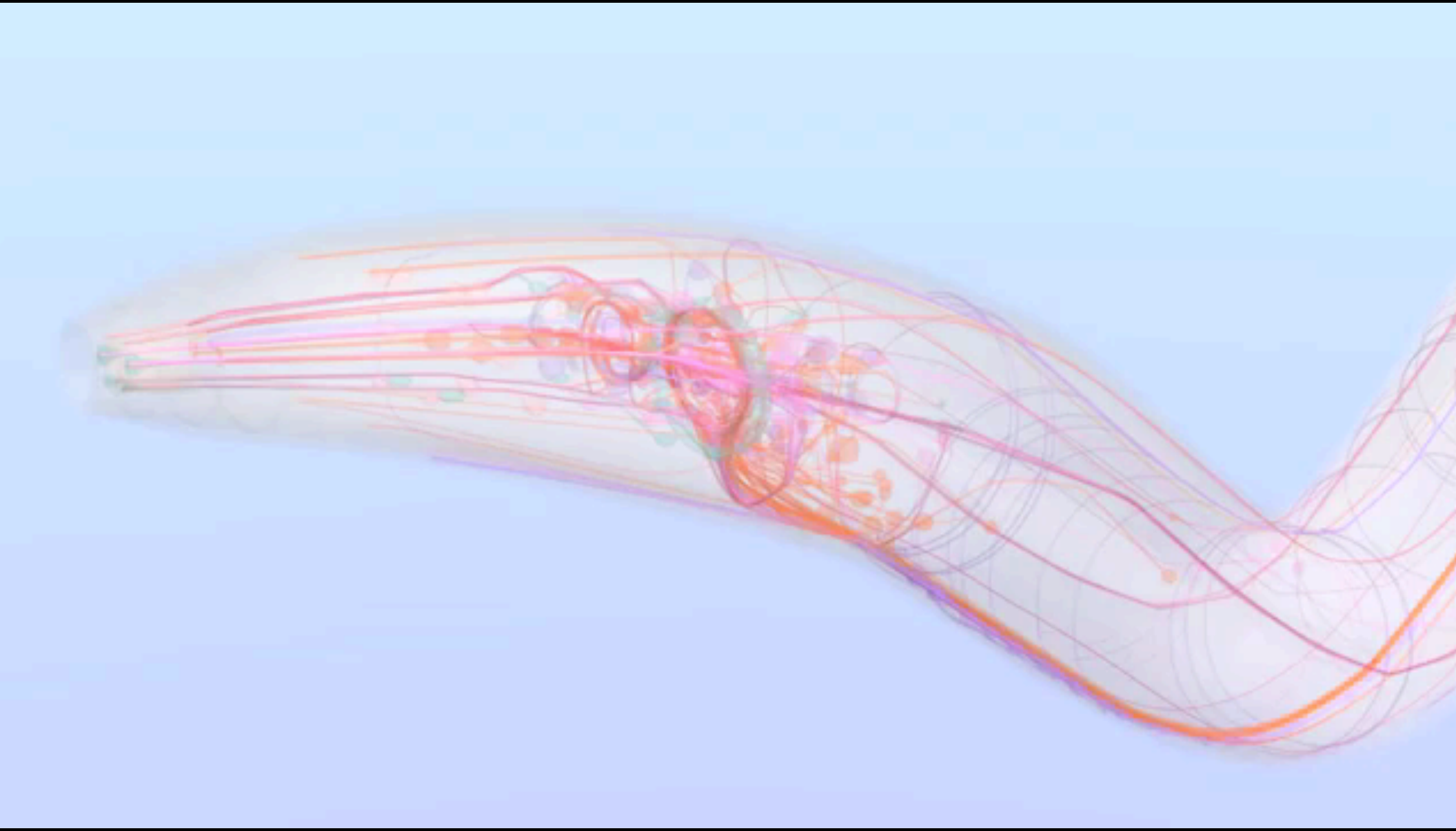
higher cognition originated in the production of **variable but controlled** behavioral sequences in simpler animals.

hot neuroscience organisms

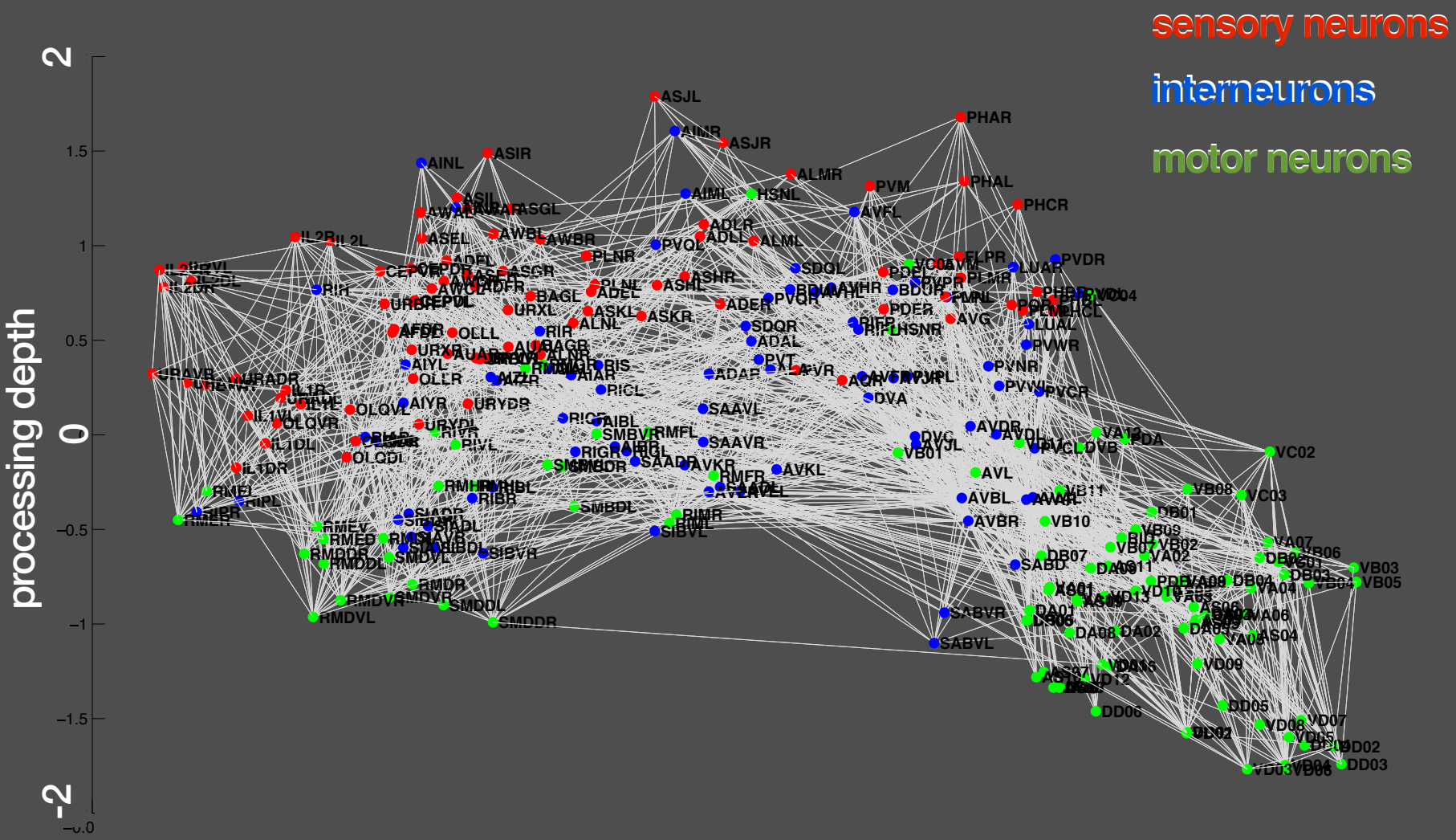
	# neurons
sponge	0
nematode worm	302
zebrafish larva	~100,000
fruit fly	~100,000
mouse	~50 million
macaque	~5 billion
human	~85 billion

source: BioNumbers **and** ***Wikipedia***

a 500 million year old brain

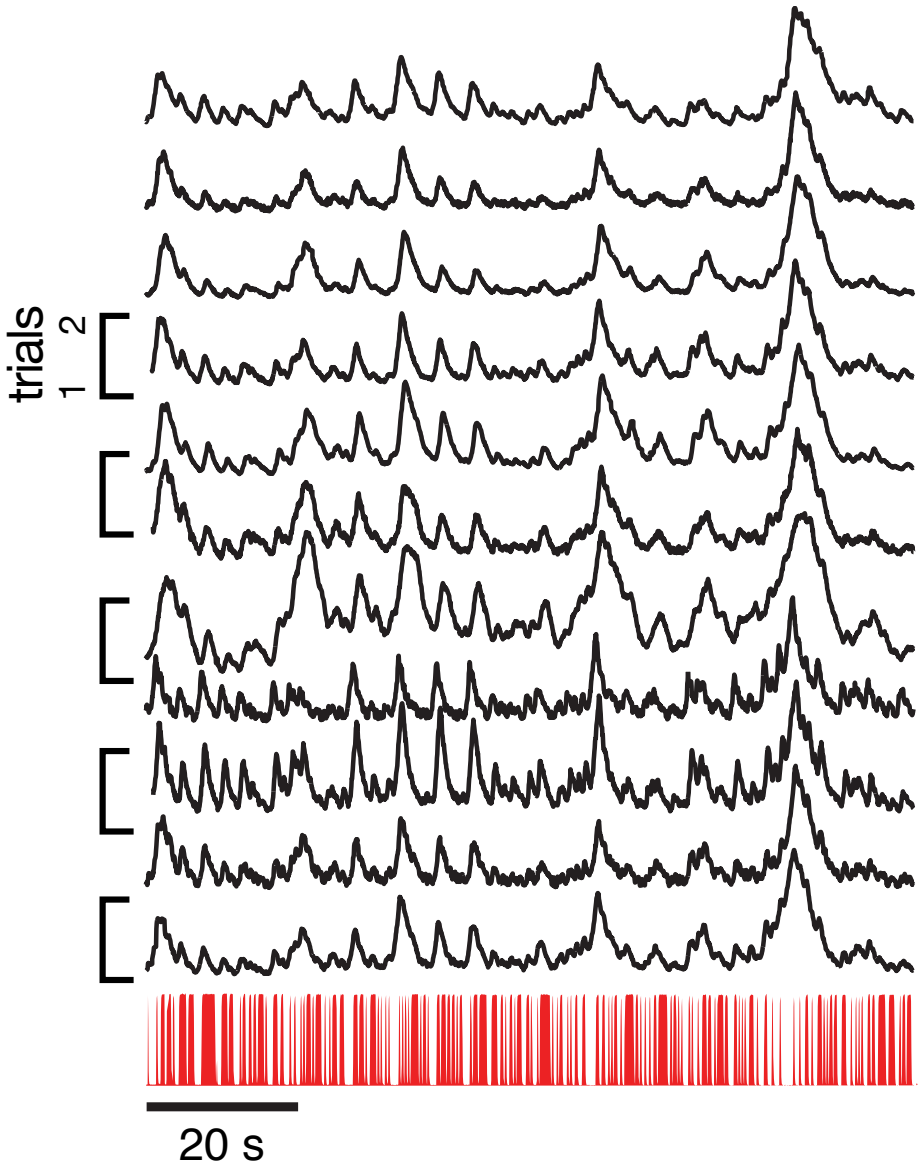


the worm connectome



Chen 2011

C. elegans neurons are highly reliable information processors



output trials

input

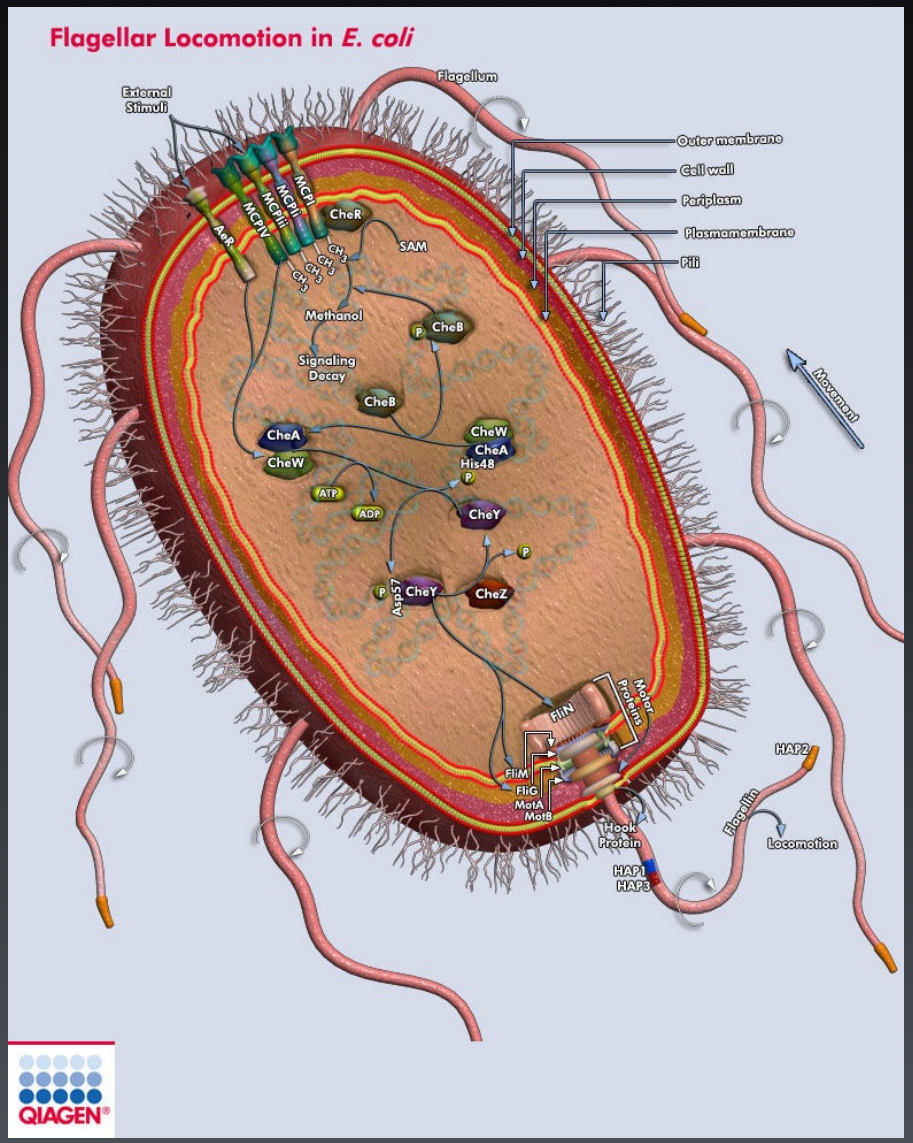
Kato et al, Neuron 2014

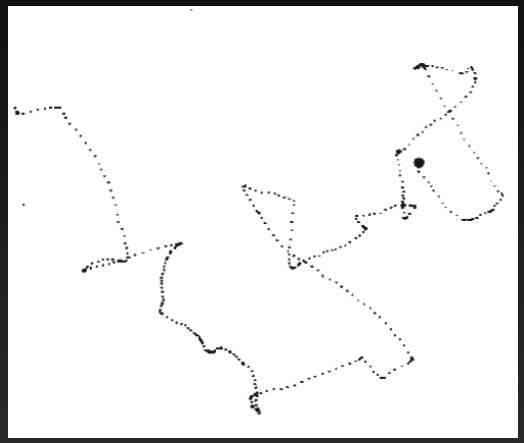
what would a “complete” story of how a nervous system generates behavior look like?

a complete story of neurons-to-behavior should:

explain single trials	organism behavior is competent on a single trial basis
explain behavior as as a time series	behavior is a continuous, on-line output of a nervous system
be self-contained	cannot rely on a homunculus or components outside of the model

a one neuron animal





Chemotaxis in E. coli Analysed by 3D Tracking
Berg & Brown, Nature 1972

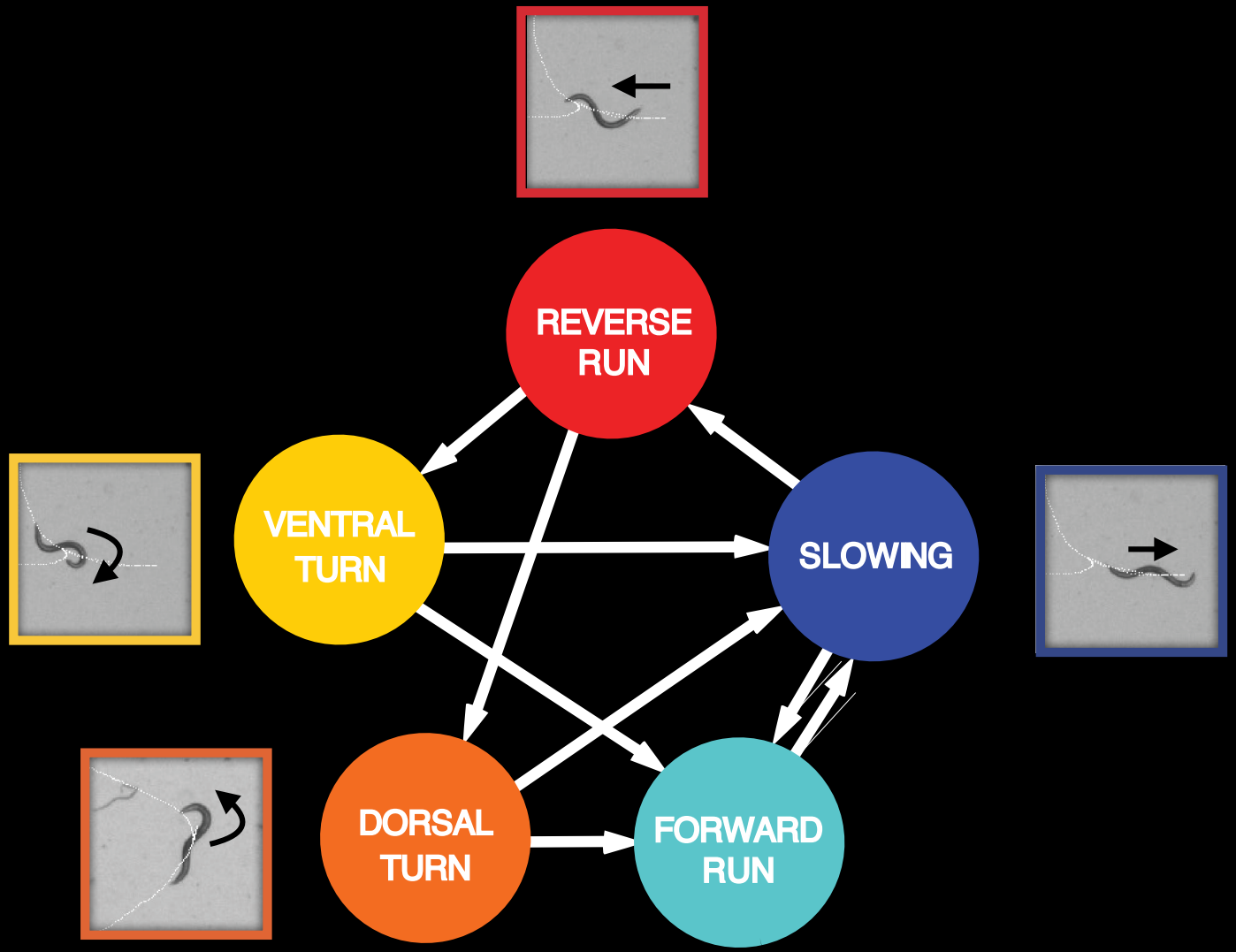
$$G' = k_m(1-I)A - k_p IG + k_r$$

$$A' = -k_m A(1-I) - \frac{k_b A}{A + K_{mm}} + k_p GI$$

$$p(CW \to CCW) = f_1(G)$$
$$p(CCW \to CW) = f_2(G)$$

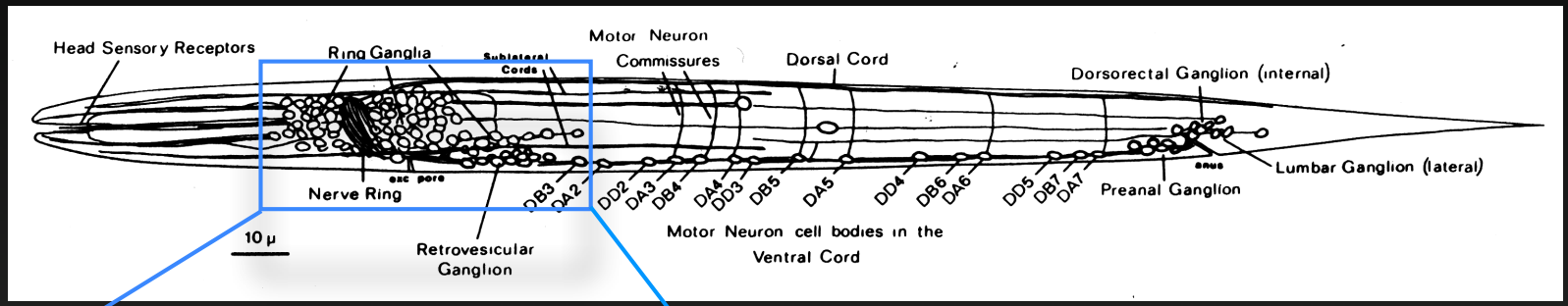
worm ethology

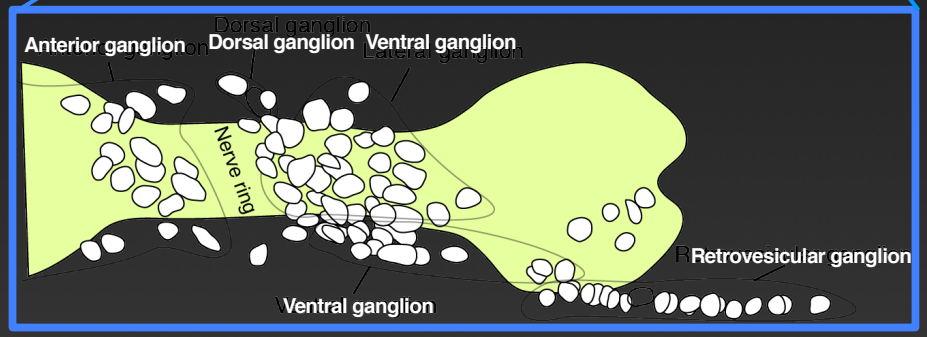
describing high-level behavior



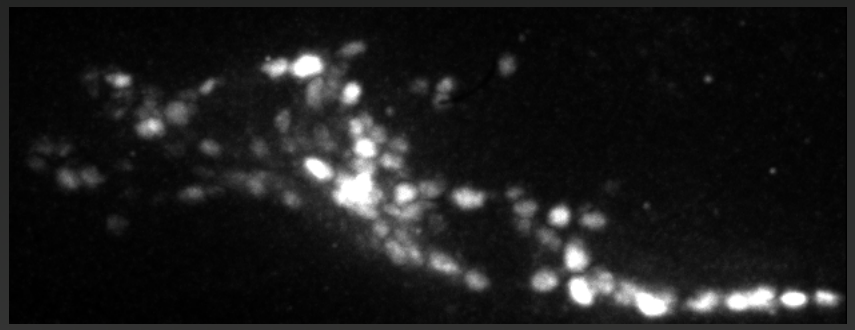
state transition diagram

C. elegans has a stereotypic neuroanatomy



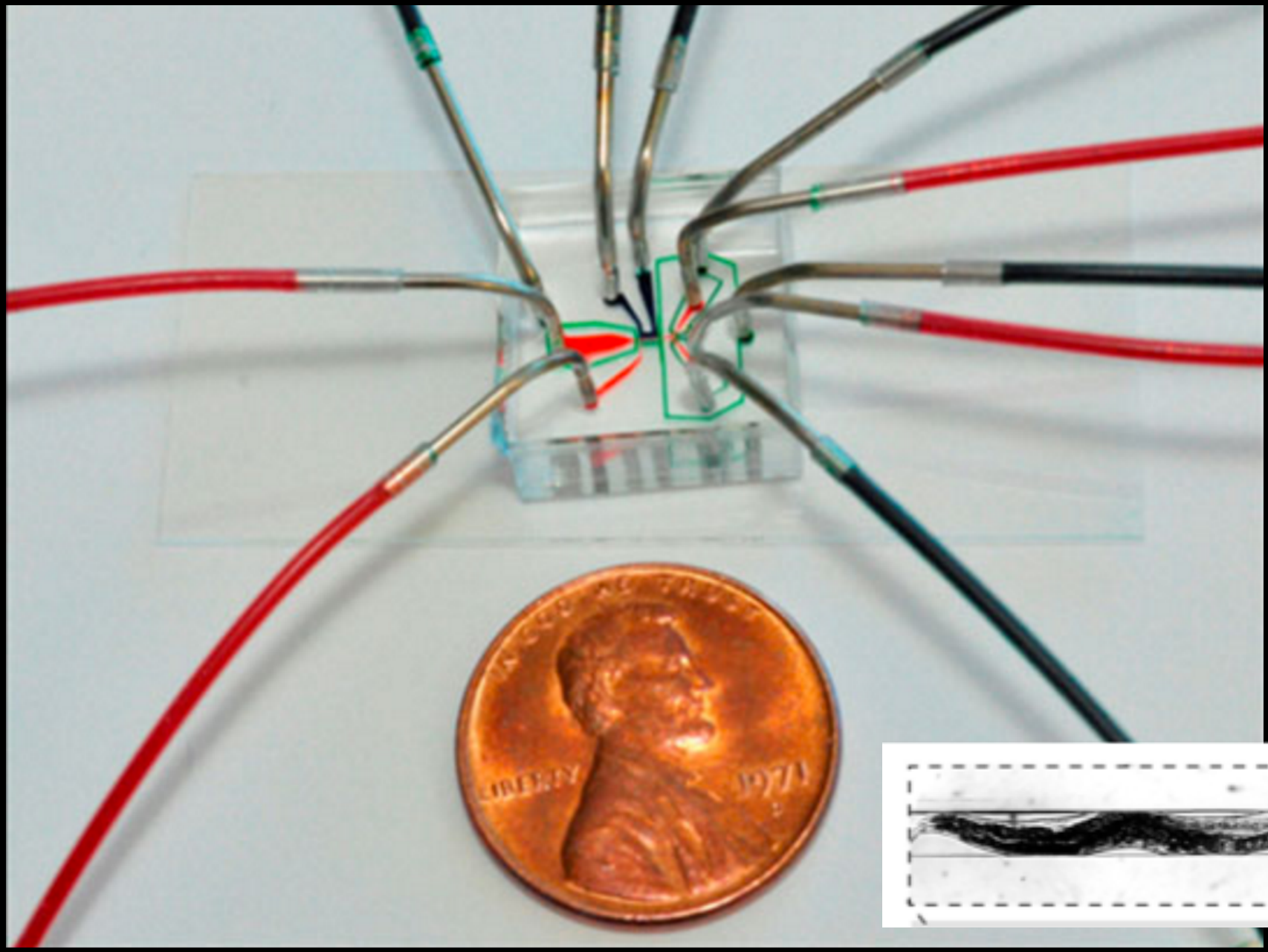


10 μm

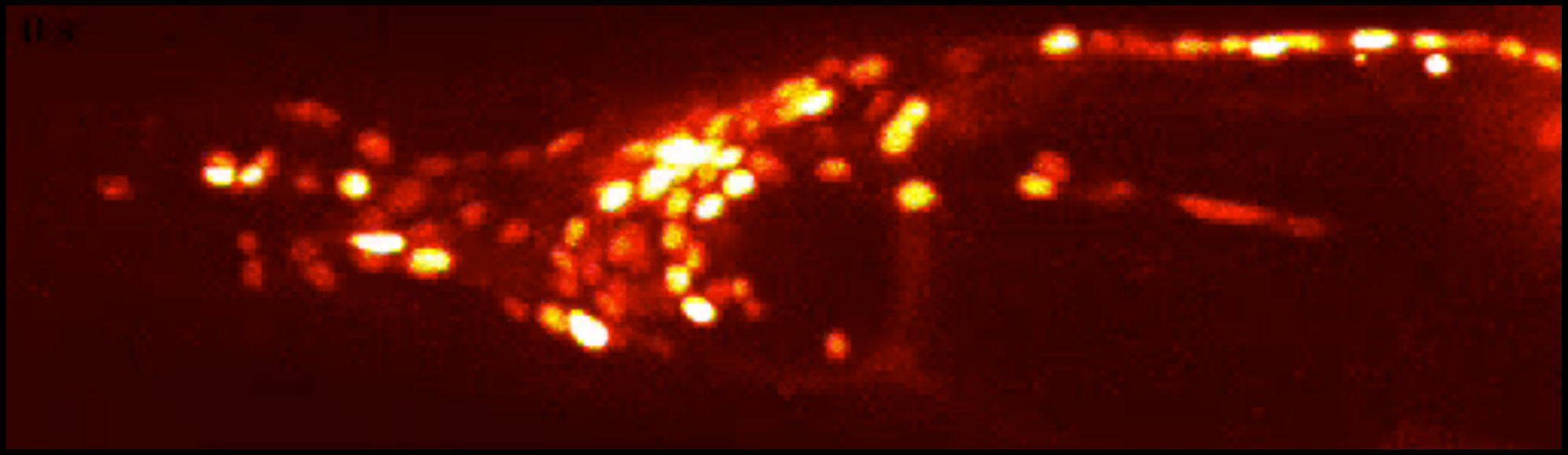


adapted from
White, 1986

microfluidics for animal and fluid handling

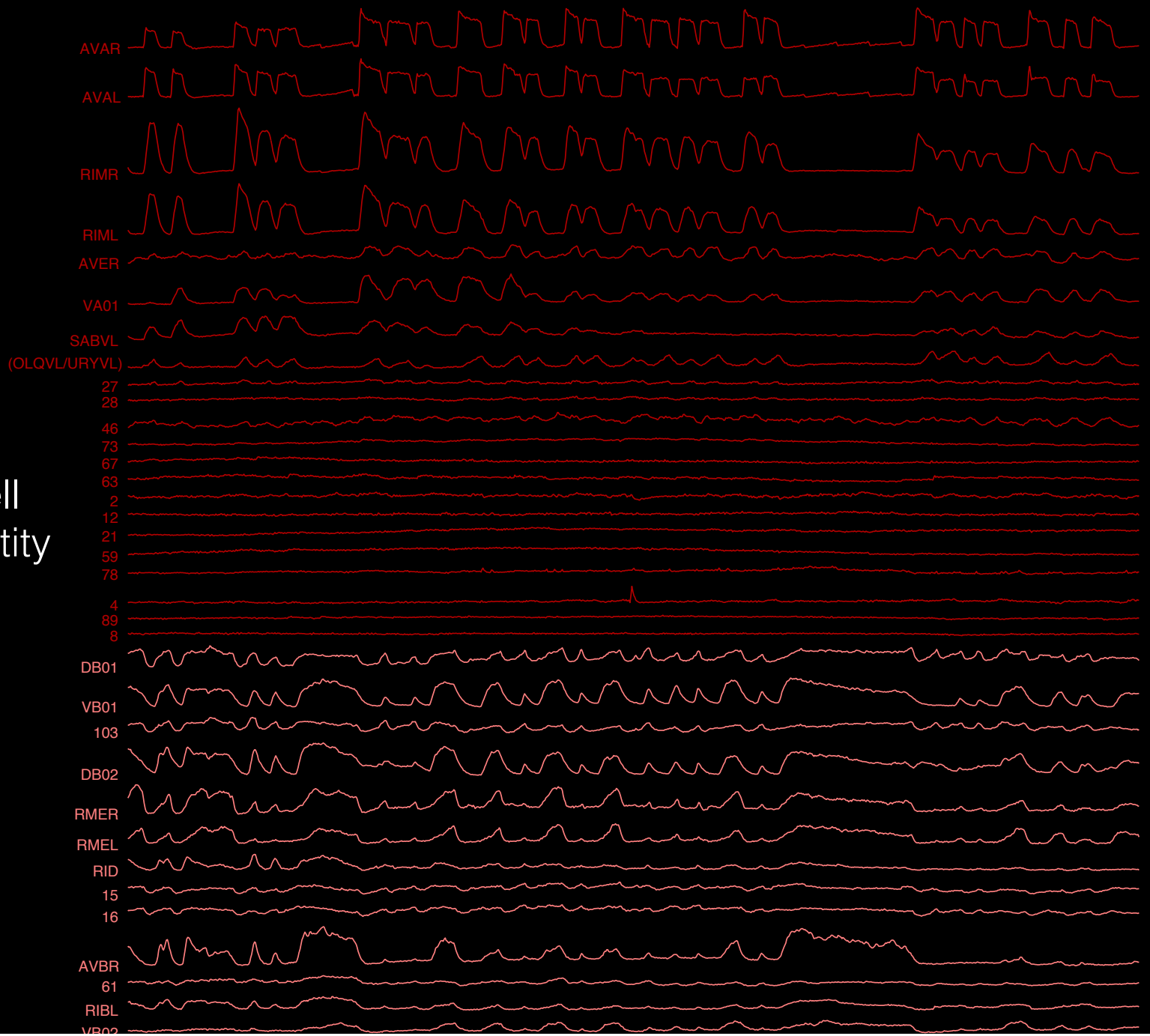


monitoring the brain at cellular resolution

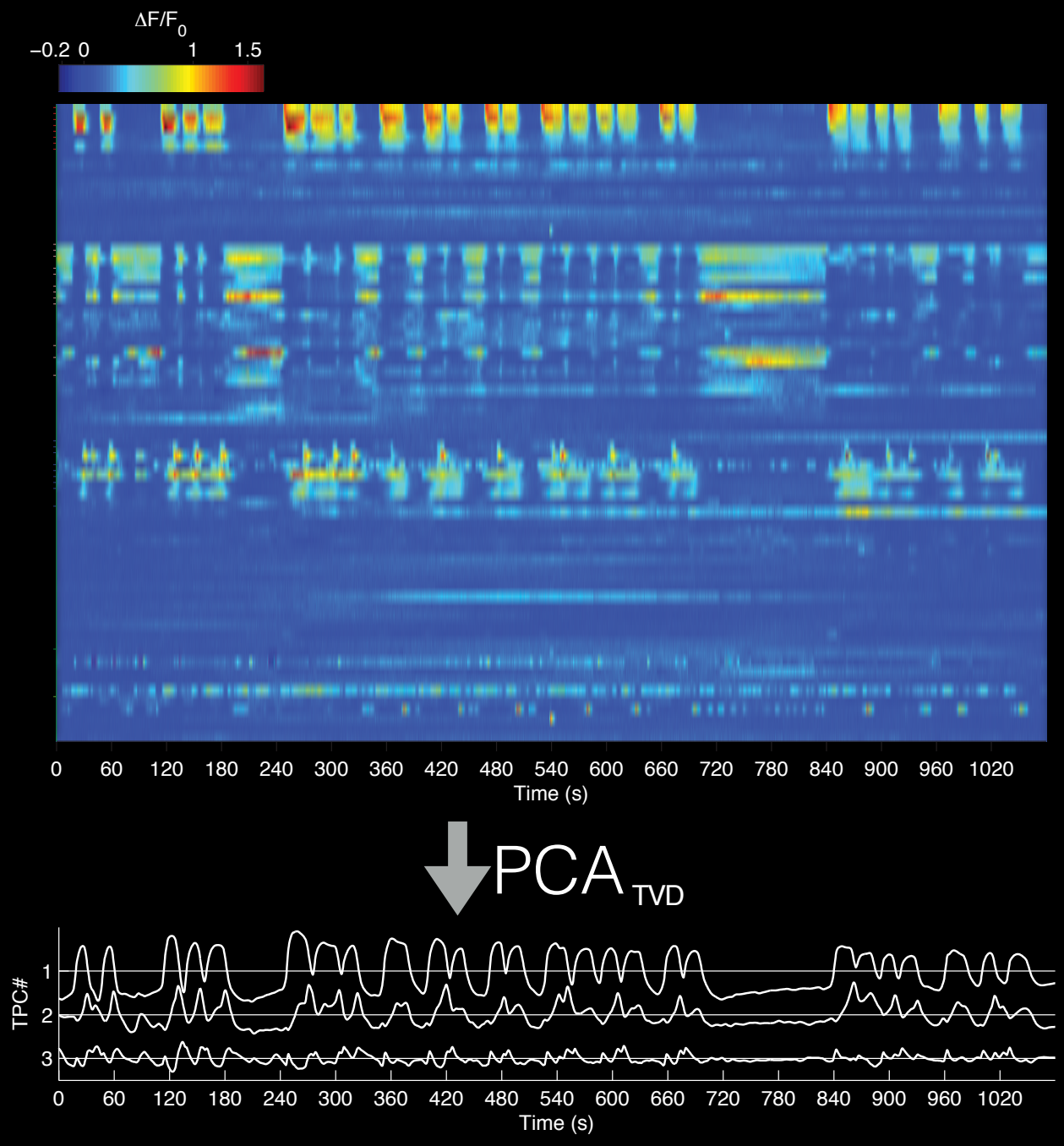


monitoring the brain at cellular resolution

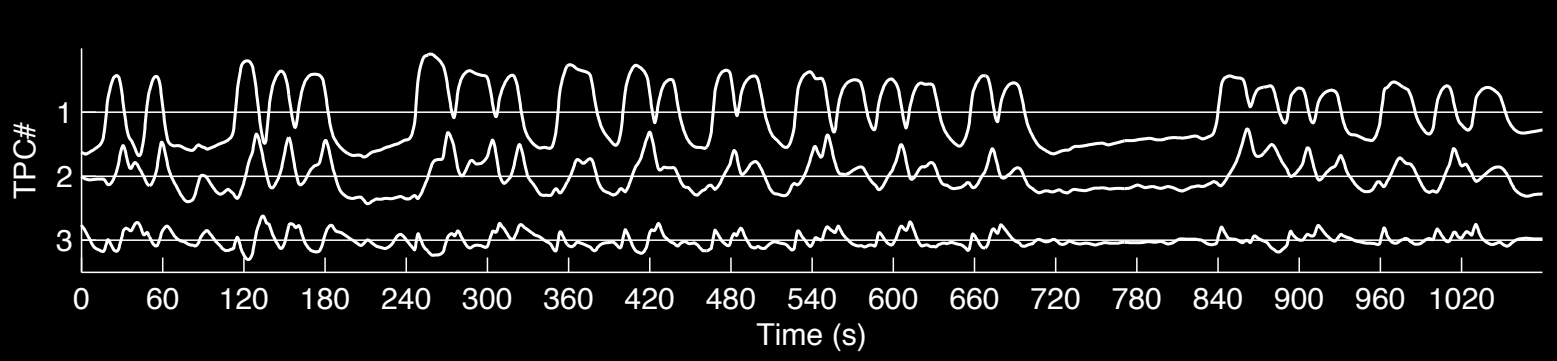
Cell Identity

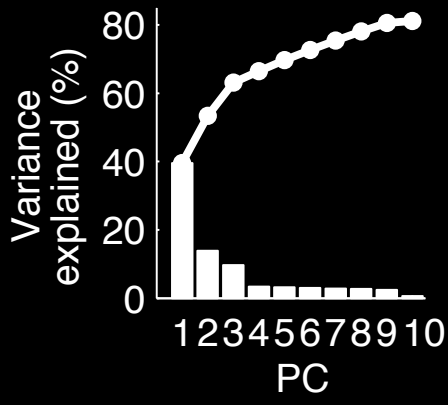


neural dynamics exhibit a widely shared, cyclical signal

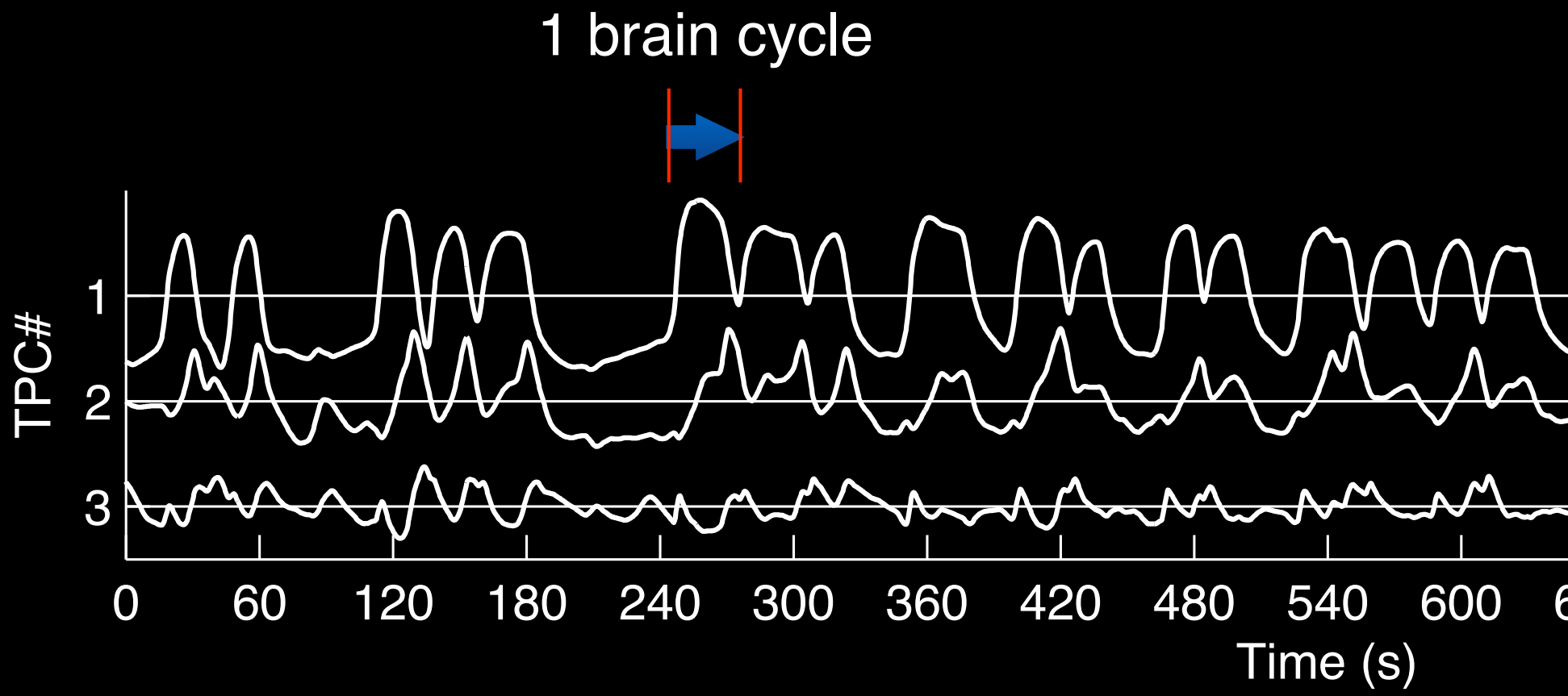


neural dynamics exhibit a widely shared, cyclical **low-dimensional** signal

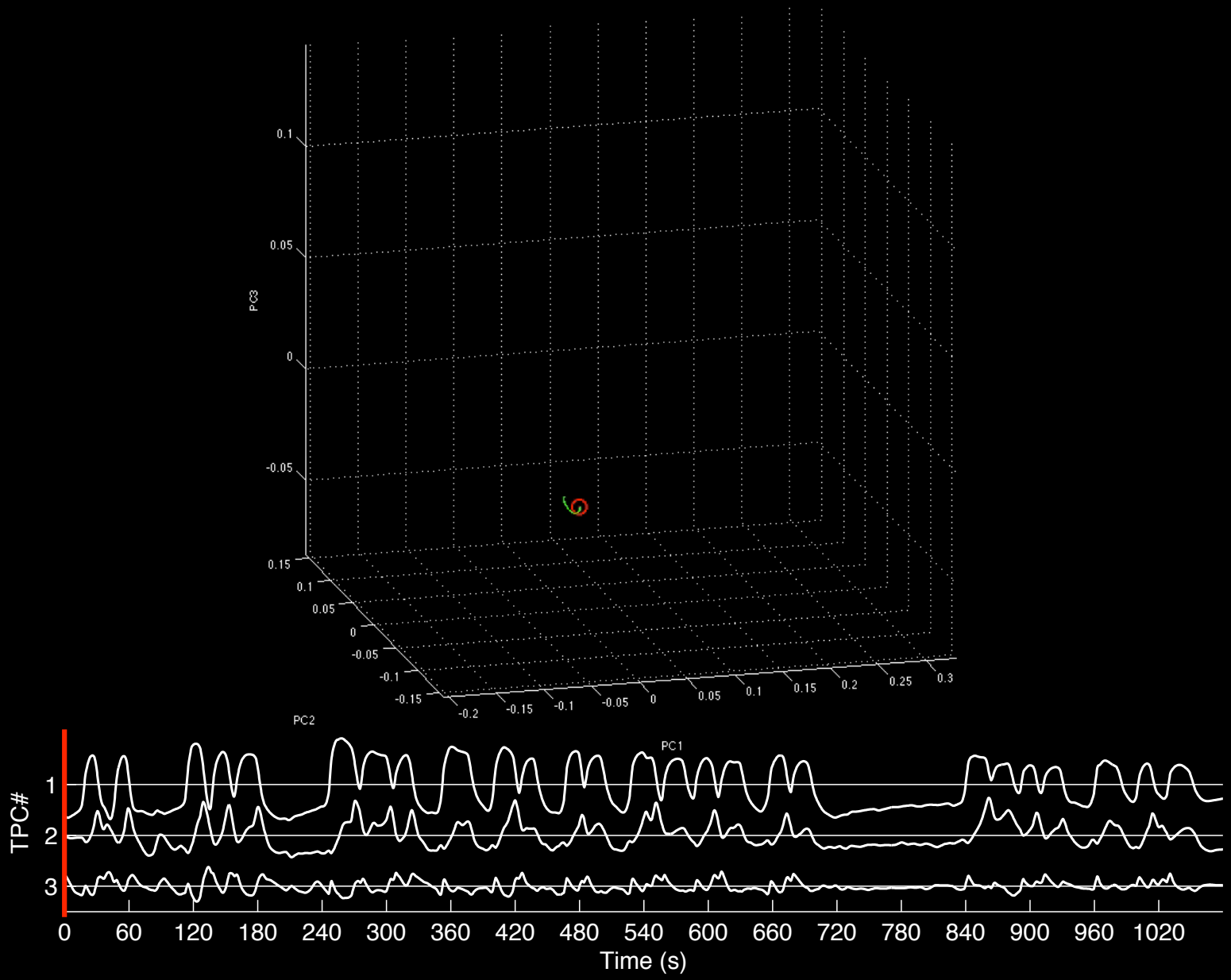




neural dynamics exhibit a widely shared, cyclical **low-dimensional** signal



neural dynamics live on a low-dimensional **manifold**

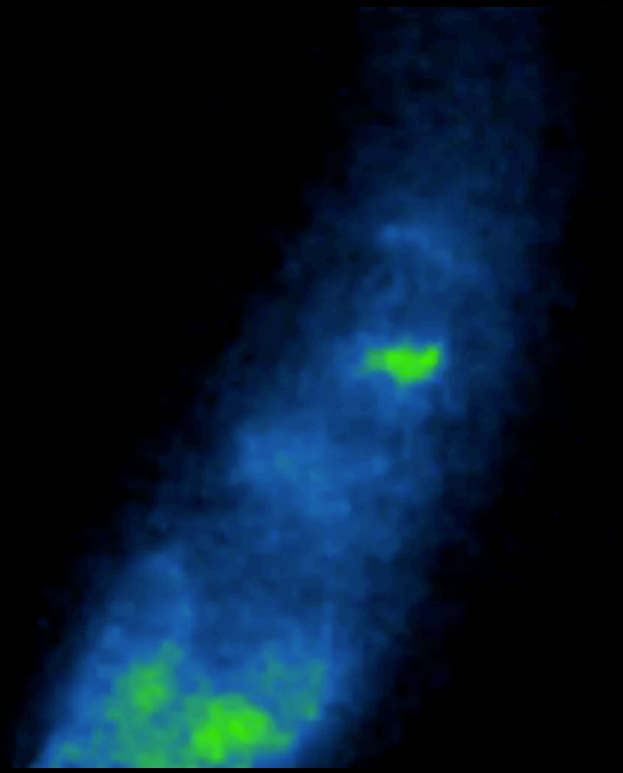


experimental techniques

I. Whole-brain imaging

II. Free-moving single neuron imaging

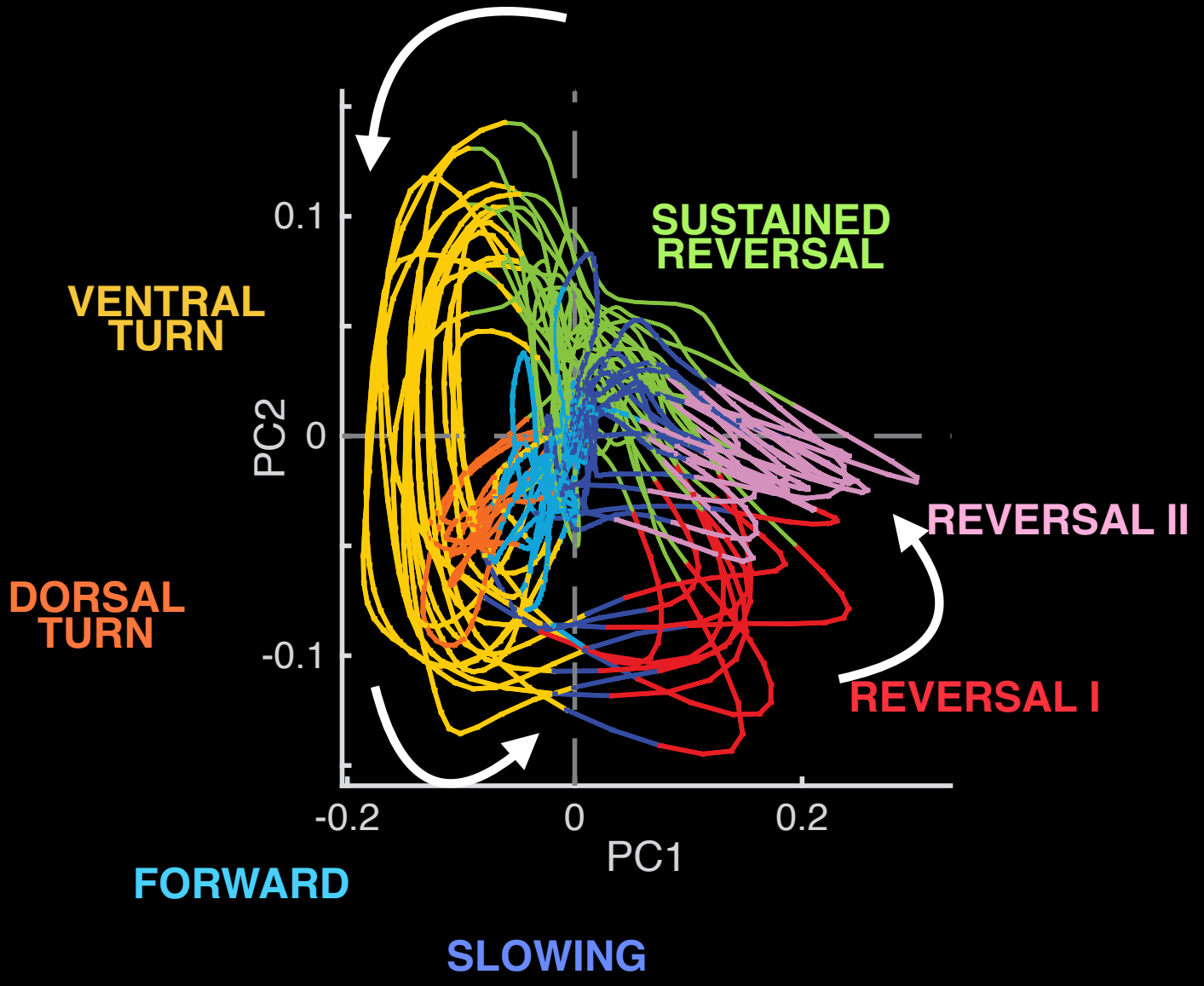
Faumont et al, 2011



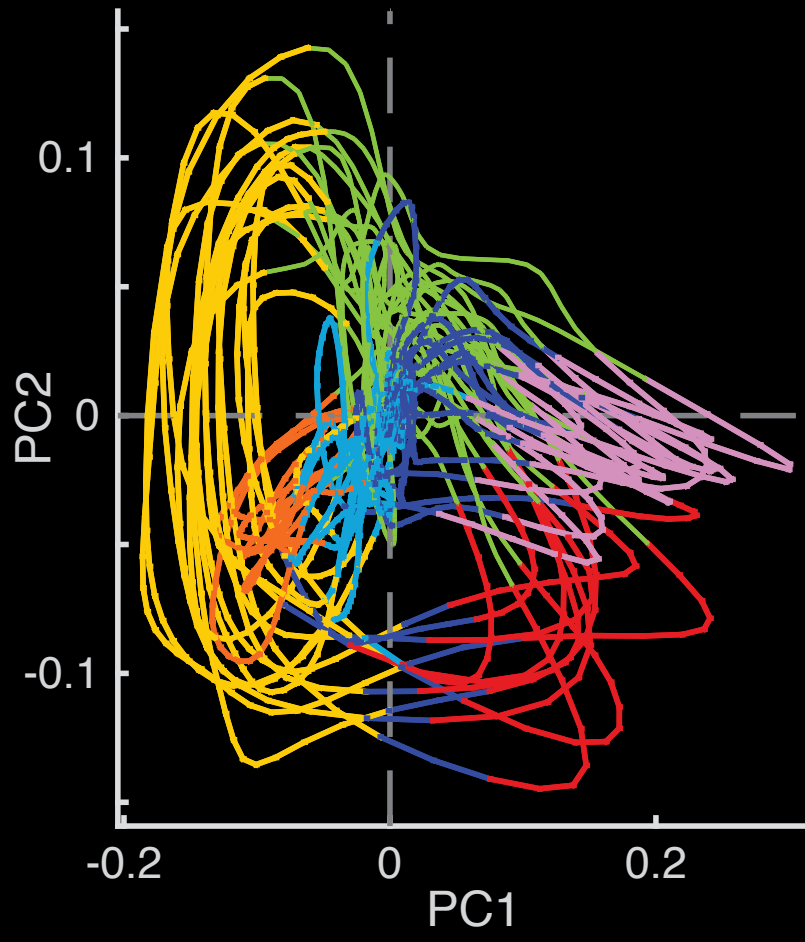
30 Hz epifluorescence

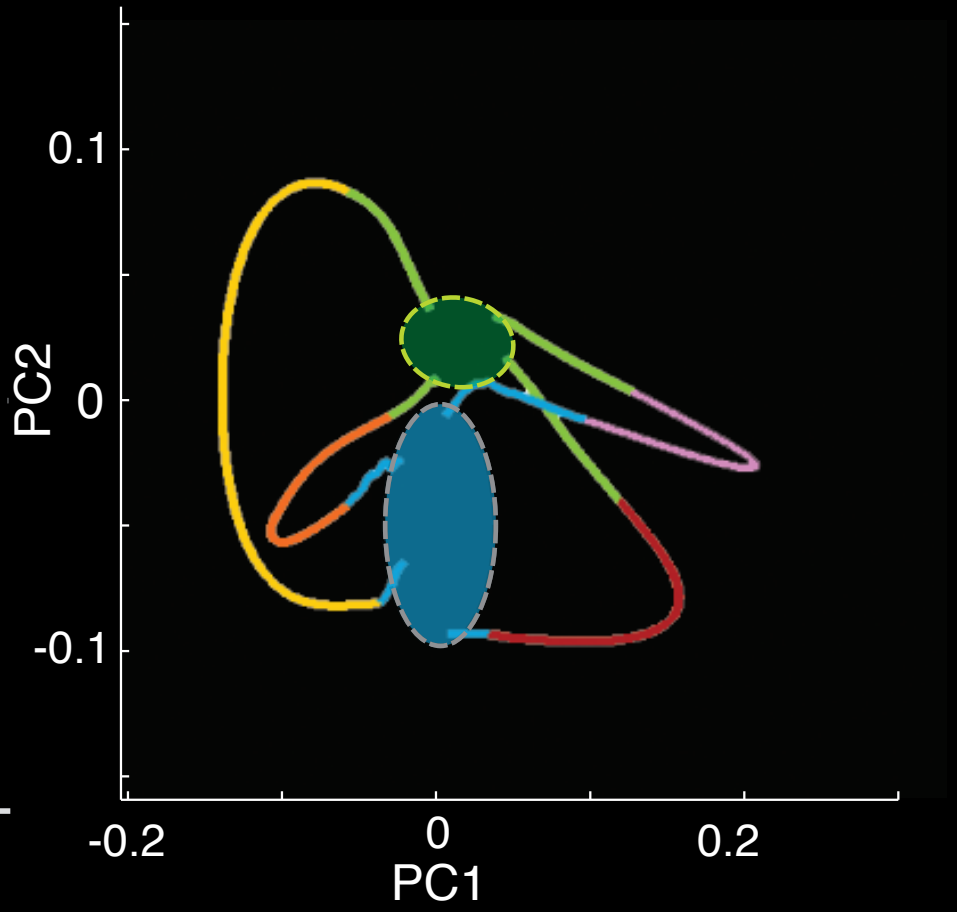
10 Hz infrared

dictionaries from free-moving studies allow decoding of behavioral command state

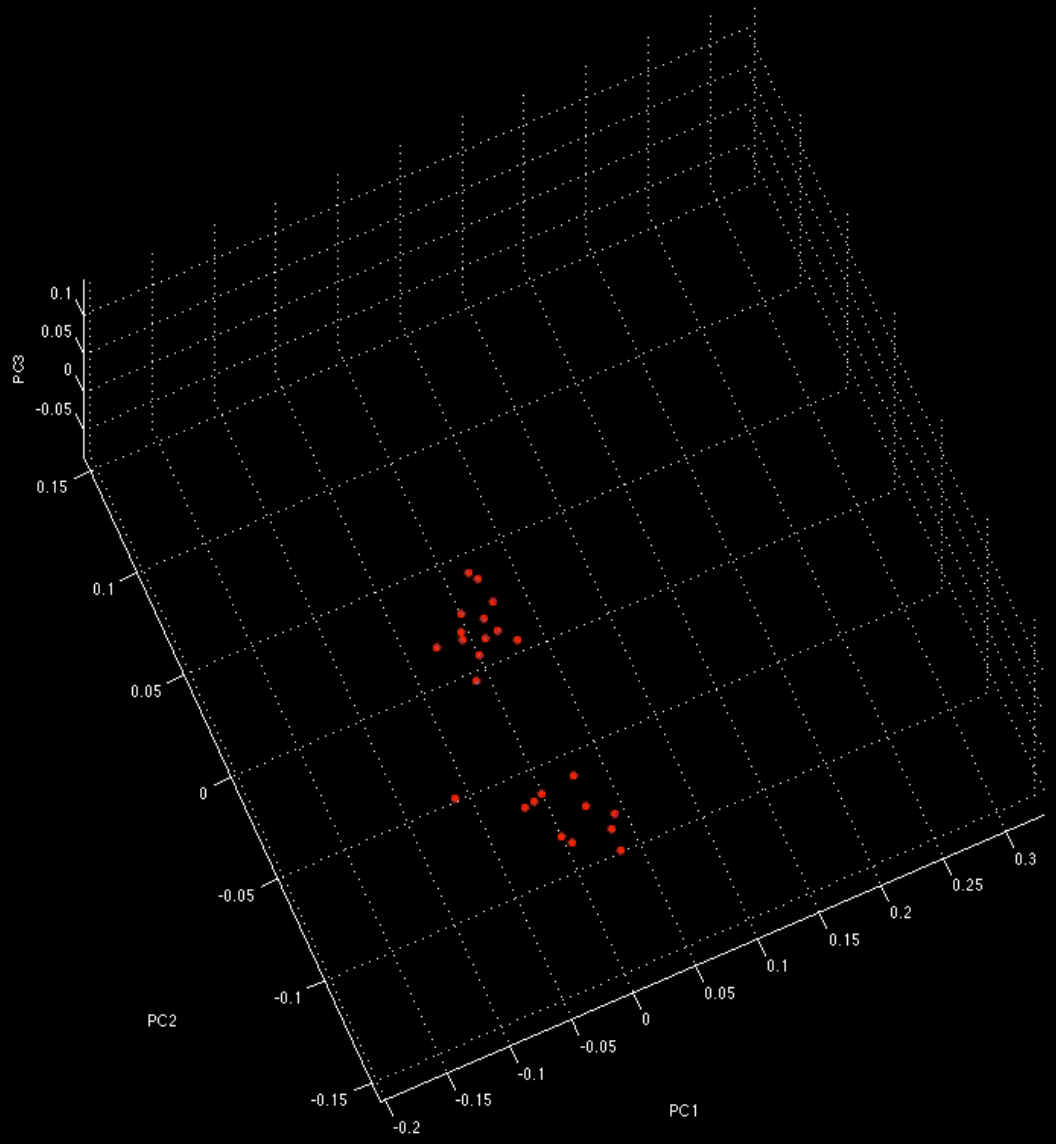


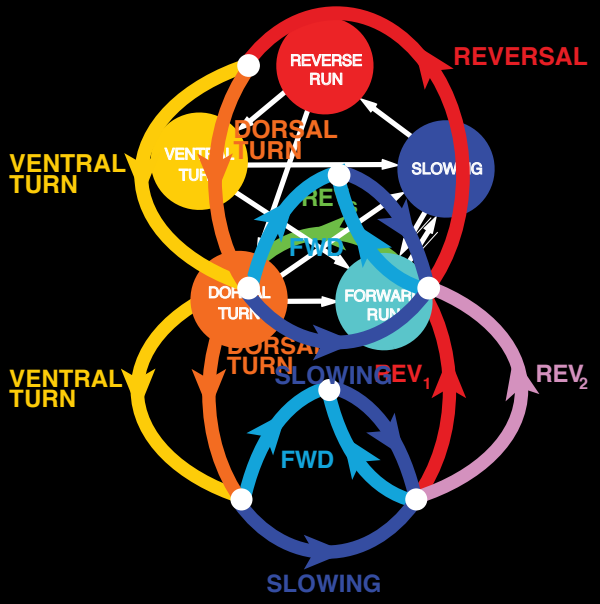
trajectory clustering allows bundle averaging





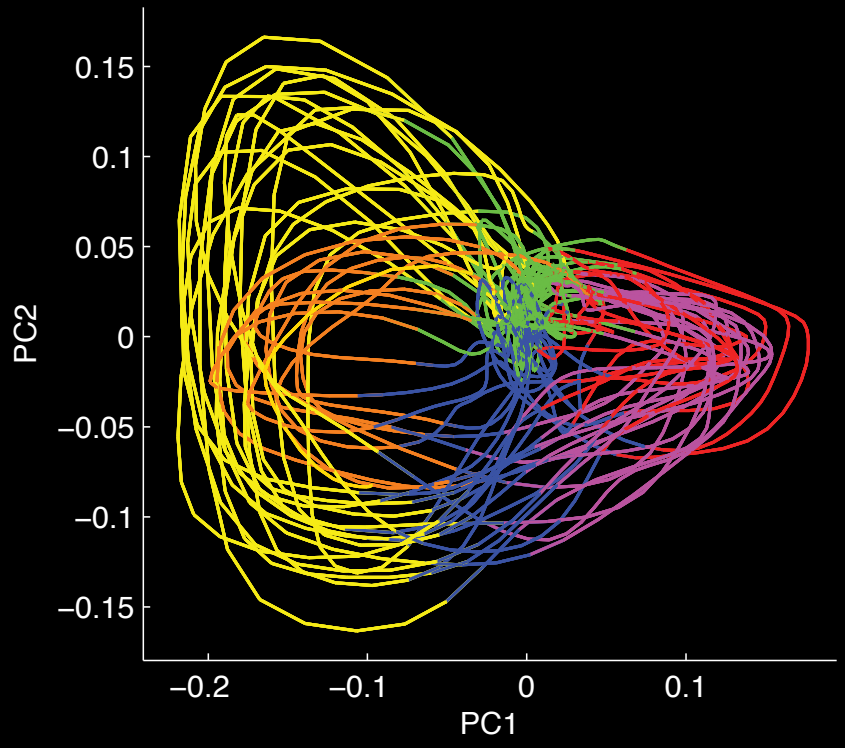
the behavioral graph is embedded in the abstract space of neural dynamics!



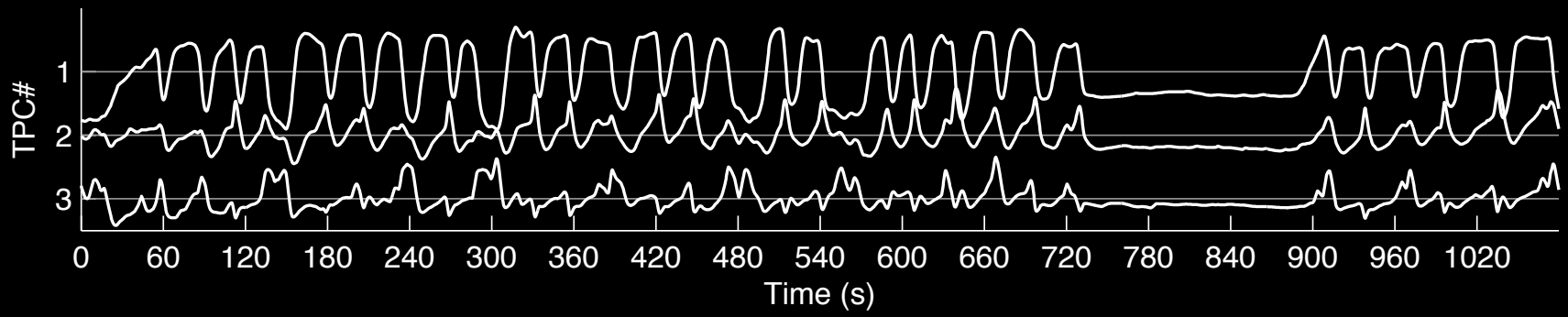


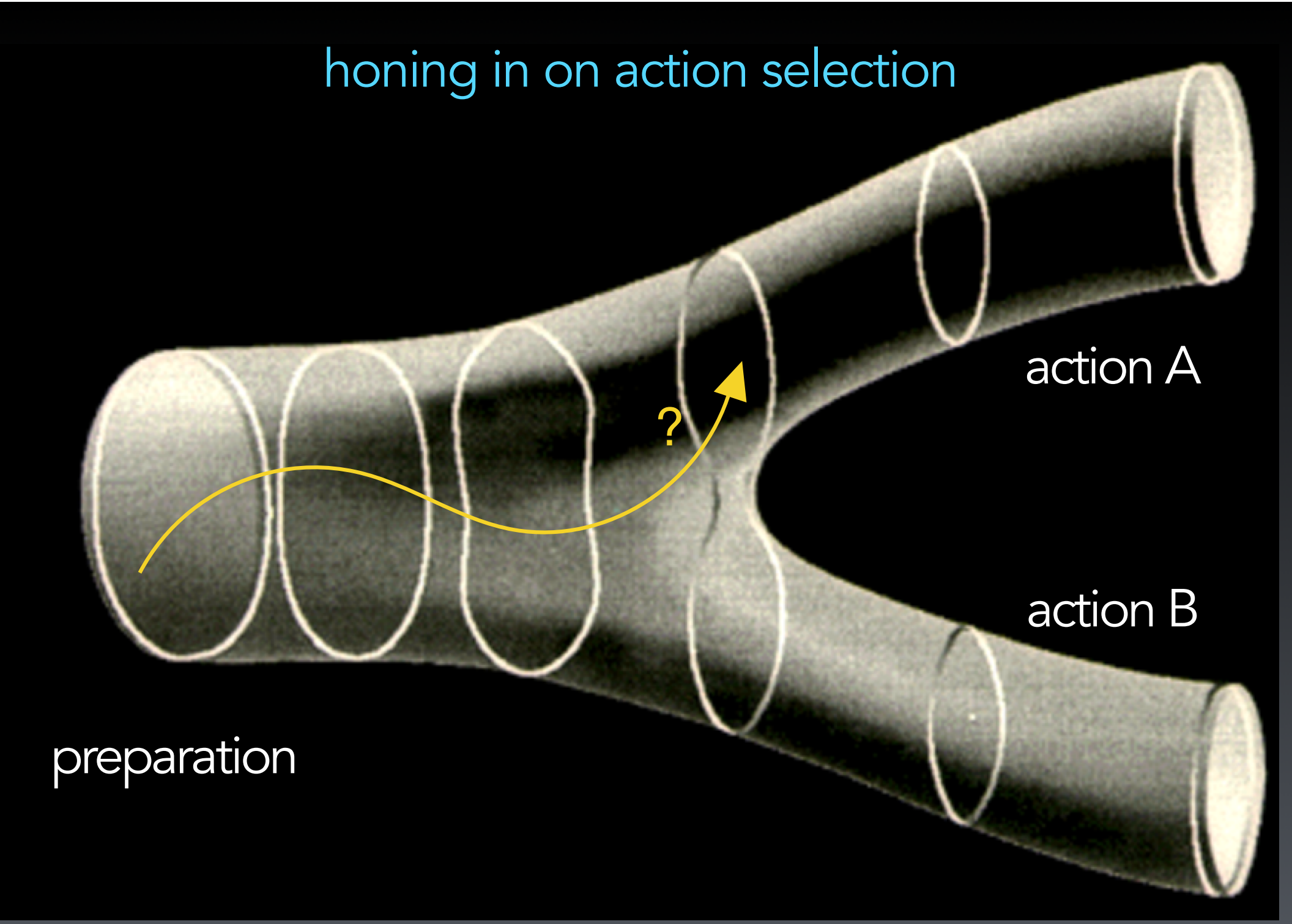
the command sequence pattern is preserved despite decoupling from motor output

AVA:: HisCl



Pokala, PNAS 2014




honing in on action selection
action A
?
action B
preparation

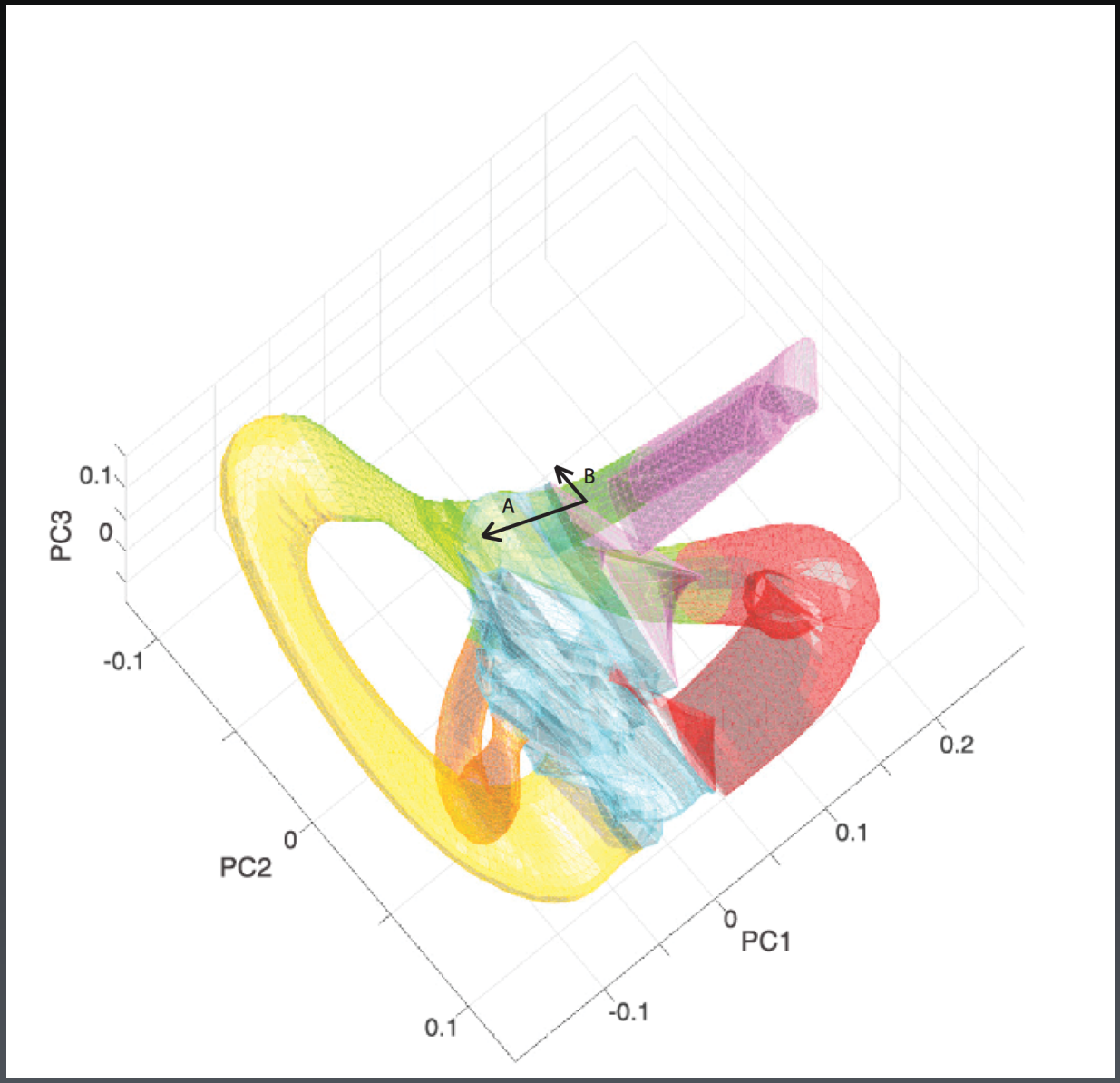
honing in on action selection: closed-loop perturbation

optogenetic patterning:

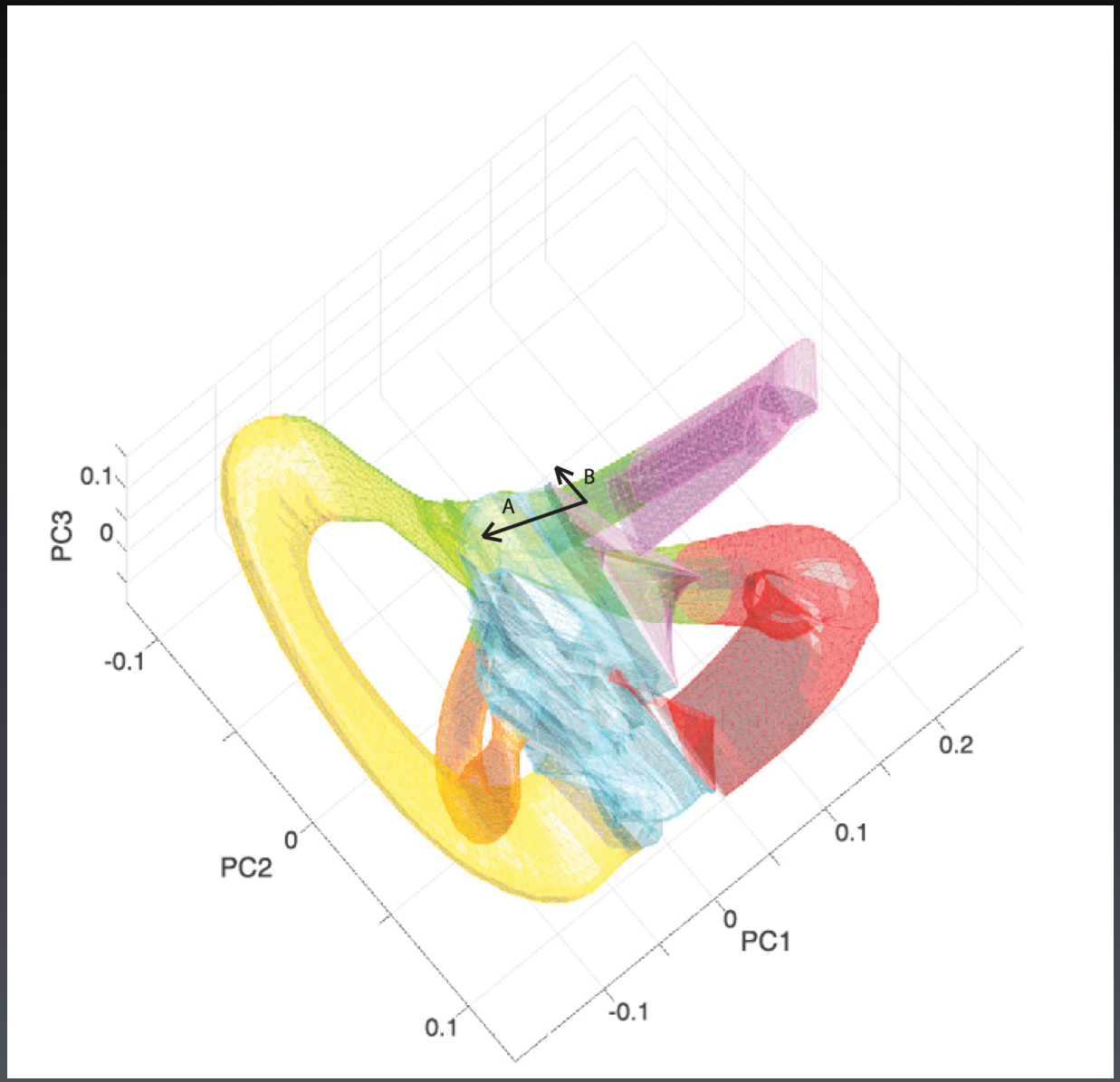
spatial light modulation

+

intersectional genetics



honing in on action selection: closed-loop perturbation



thank
you!