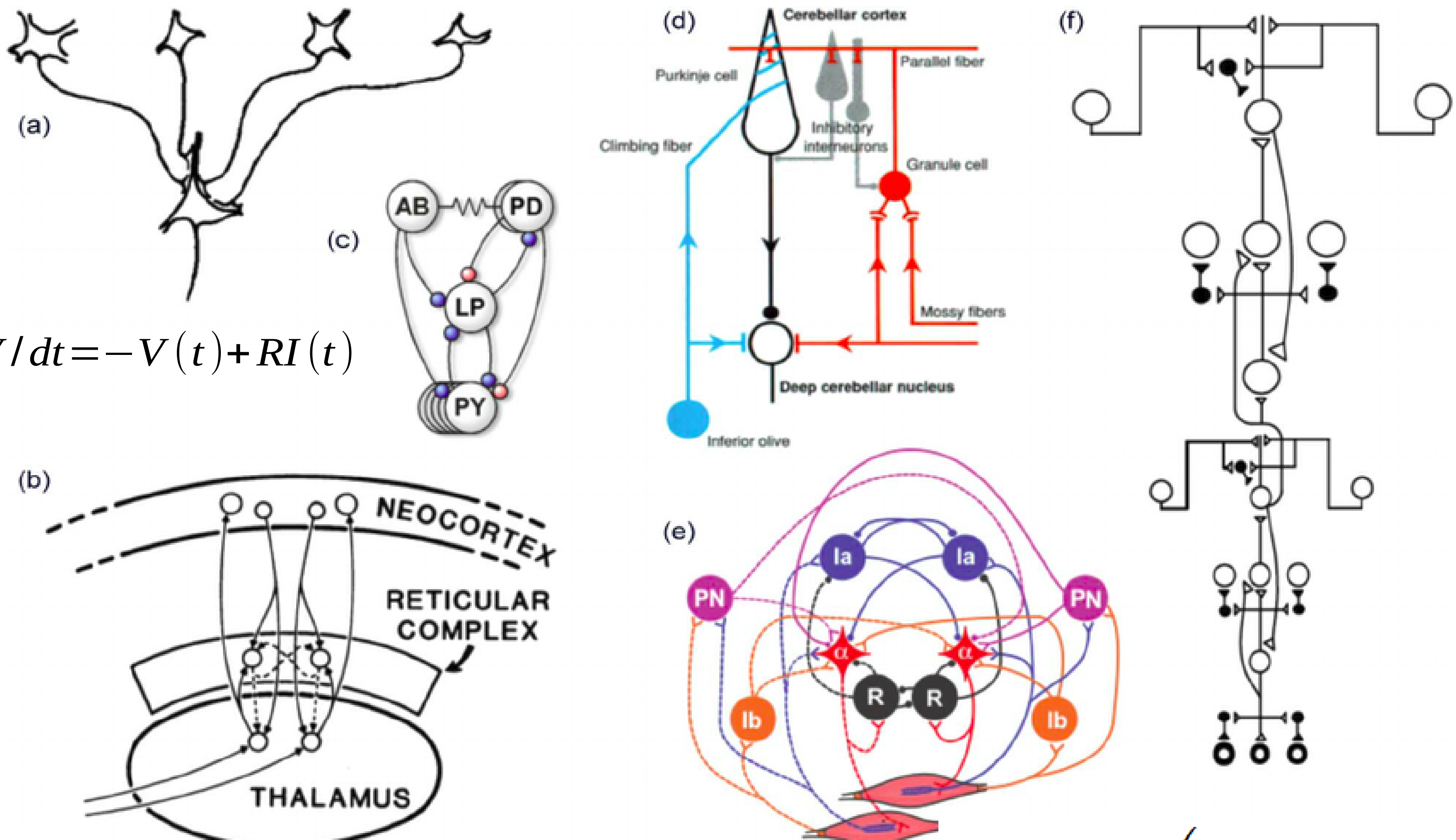
Synthesizing Experimental Data with Circuit Models

Grace Lindsay, PhD
Columbia University

Overview

- Defining Circuit Models
- The 3 A's (a framework for circuit modeling)
- Example
- Tips for making & taking

What are circuit models?



$$\tau_m dV/dt = -V(t) + RI(t)$$

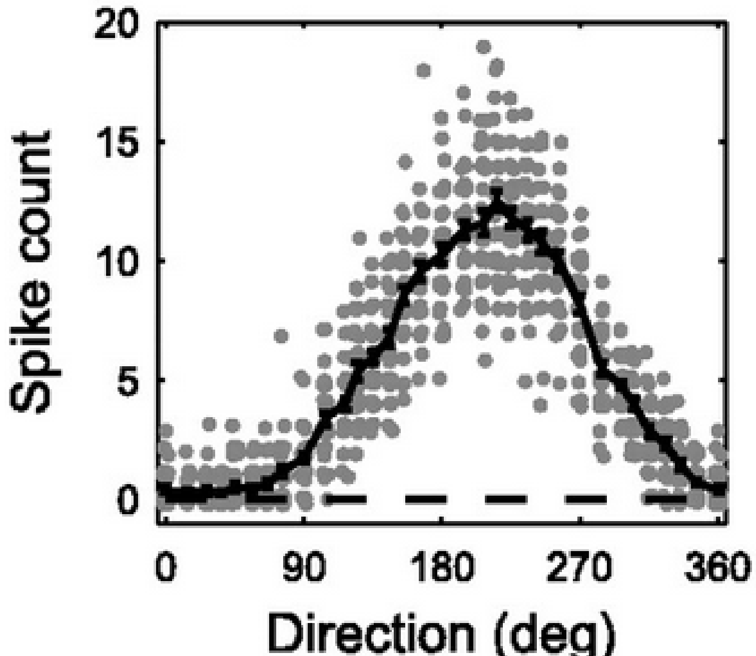
$$r_i^t = k\ \phi\left(\sum_j w_{ij} x_j^t + \epsilon_A^t - \Theta_i\right)$$

Jadi et al., 2014

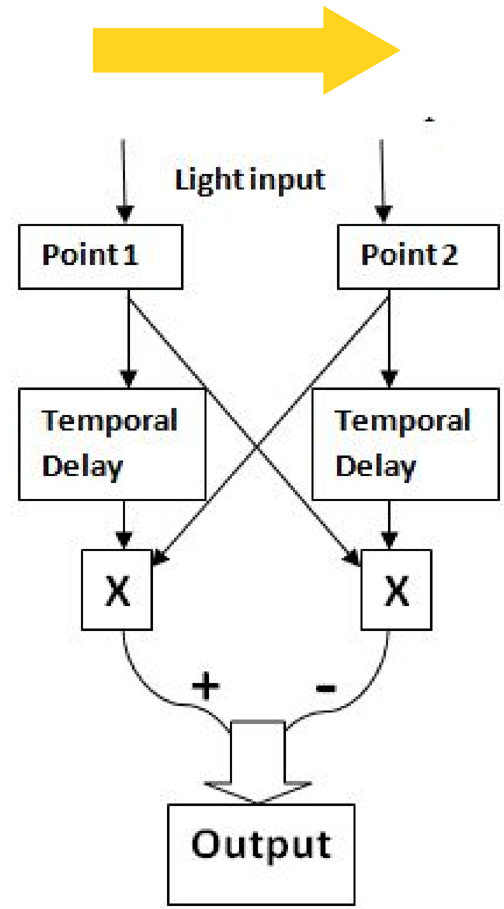
Well-known Examples

- Hodgkin-Huxley for single cell physiology
- Hopfield Network for memory/recall
- Balanced network for E-I interaction

Mechanistic vs. Descriptive



$$y = ae^{\frac{-(x-\mu)^2}{2\sigma^2}}$$



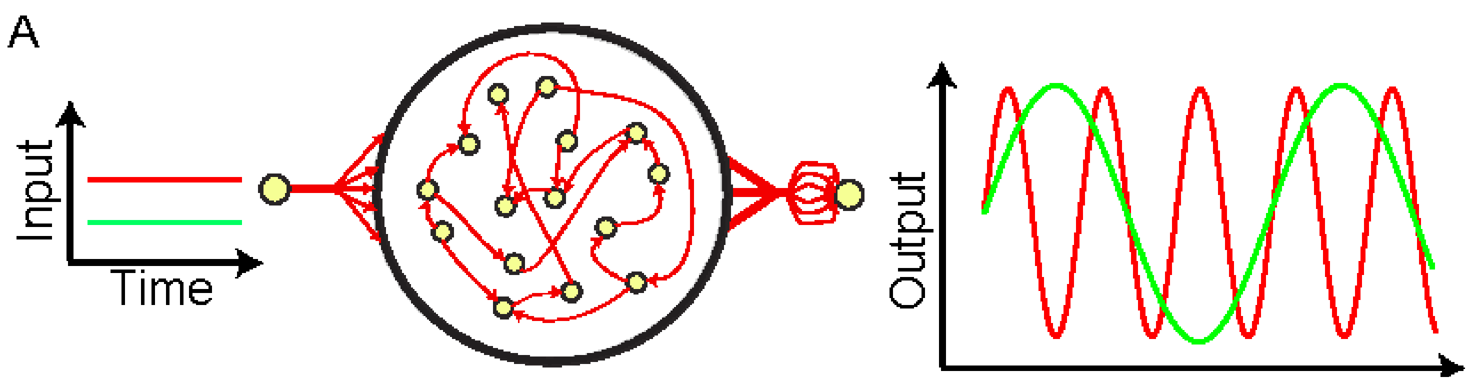
Circuit models are mechanistic, meaning components of the model correspond to known physical entities

Mechanistic vs. Normative

Performance-optimized hierarchical models predict neural responses in higher visual cortex

Daniel L. K. Yamins, Ha Hong, Charles F. Cadieu, Ethan A. Solomon, Darren Seibert and James J. DiCarlo

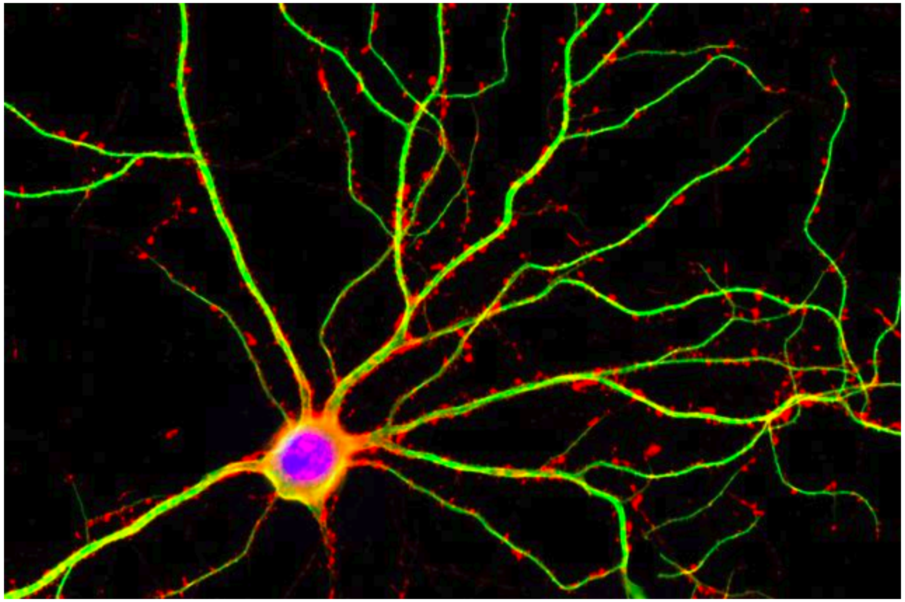
PNAS 2014 June, 111 (23) 8619-8624. https://doi.org/10.1073/pnas.1403112111

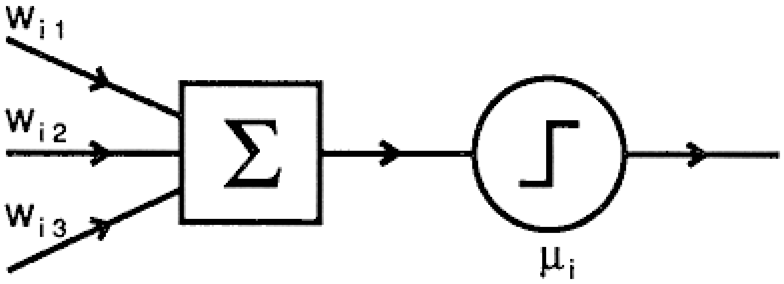


Sussillo & Barak, 2013

Circuit models are mechanistic, but can formalize constraints for normative models

Incompleteness





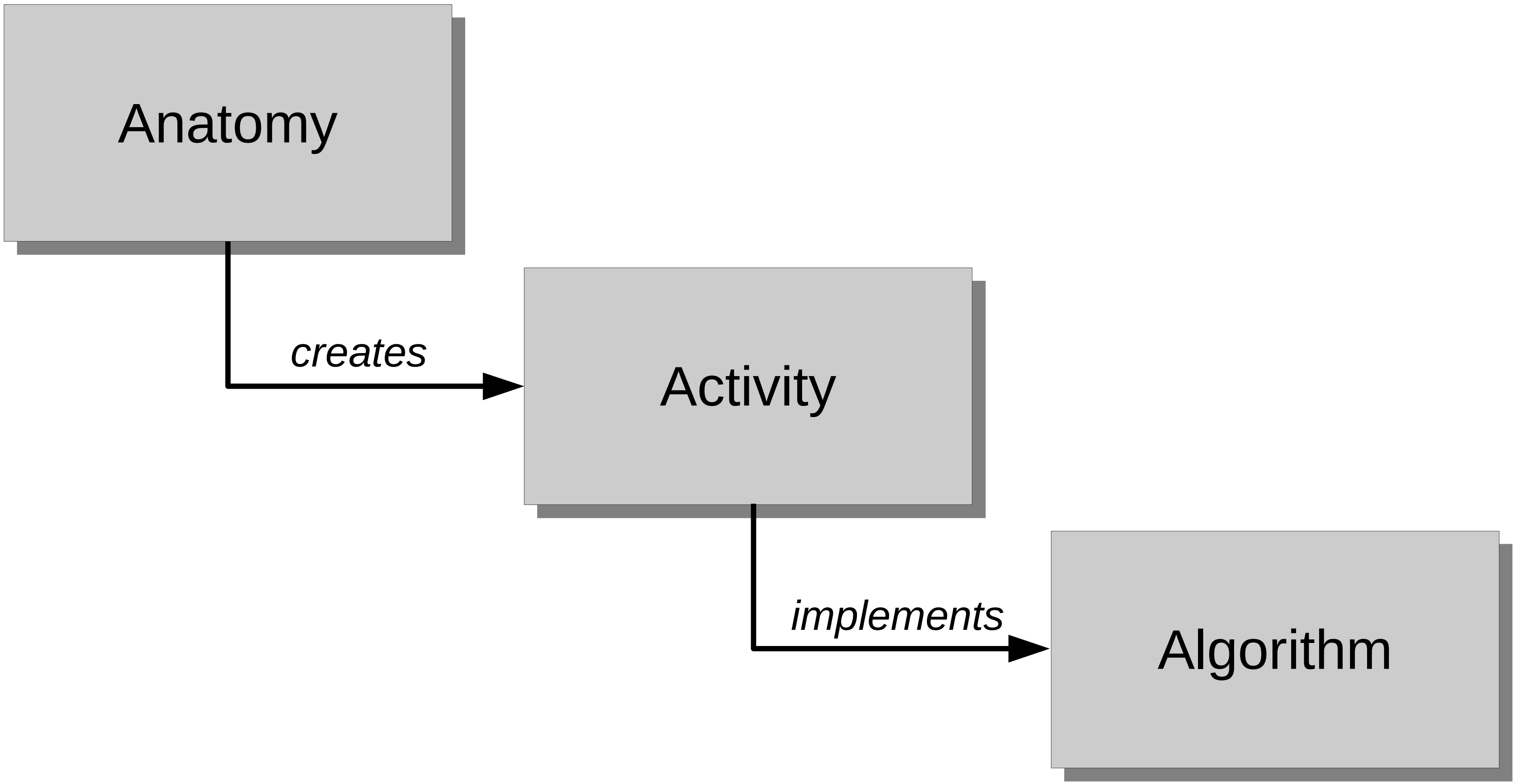
By both necessity and design, all circuit models are wrong. But some are useful.

Benefits of Circuit Models

- Explicit representation of a hypothesis
- Highlights what is unknown
- Can perform impossible “experiments”
- Introduces tools of mathematical analysis

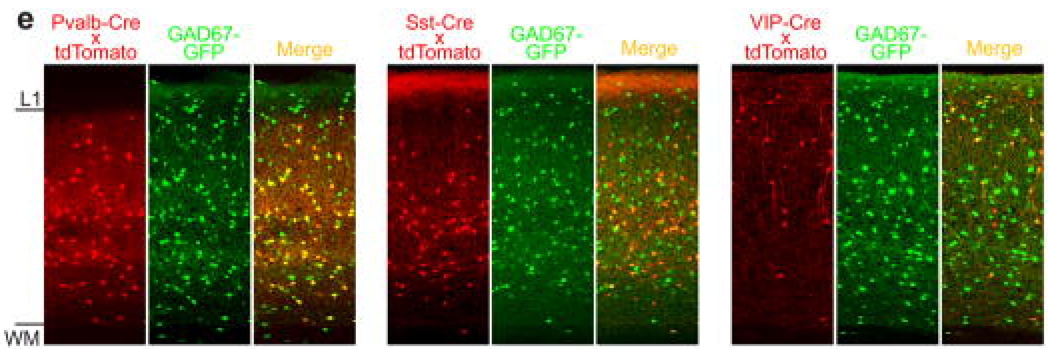
The 3 A's of Circuit Modeling

The 3 A's of Circuit Modeling

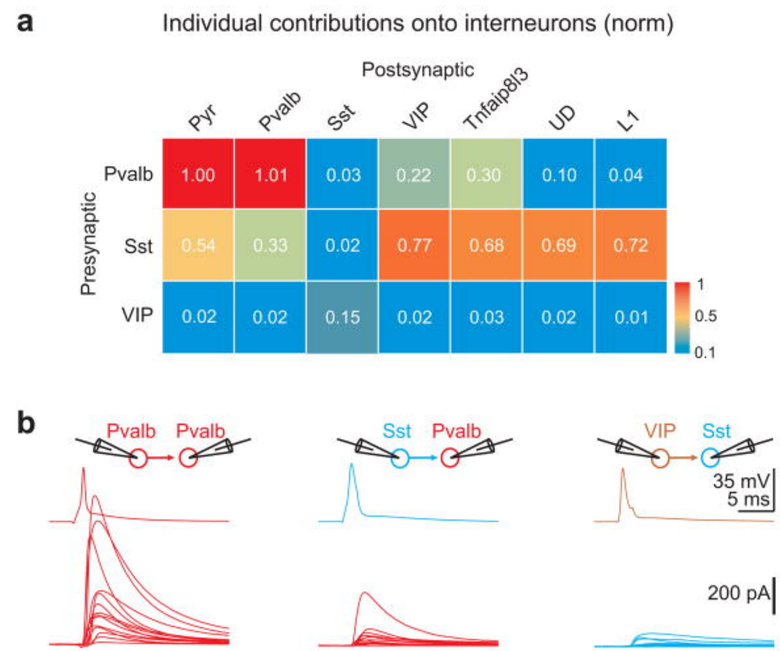


Data for: Anatomy

Types of studies – tracer studies, paired recordings & stimulation, molecular profiling, dendritic spine imaging



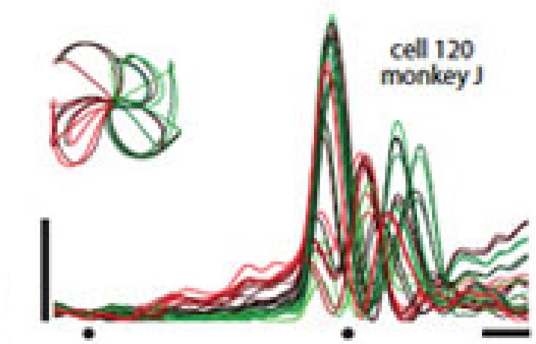
Inhibition of Inhibition in Visual Cortex: The Logic of Connections Between Molecularly Distinct Interneurons, Pfeffer et al., 2013

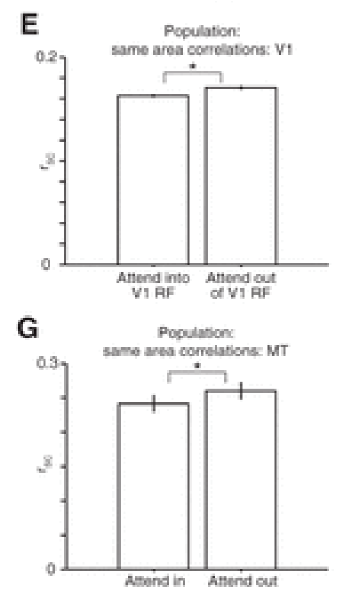


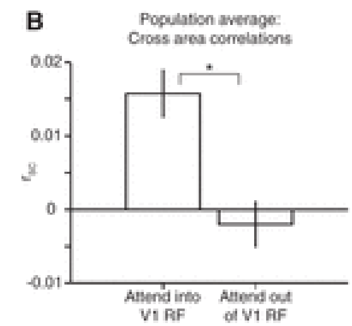
Example findings – inter-area connectivity, distance-dependent connections, cell-type specific connectivity, dendritic vs somatic targeting

Data for: Activity

- Type of studies – Electrophysiology, calcium imaging, fMRI





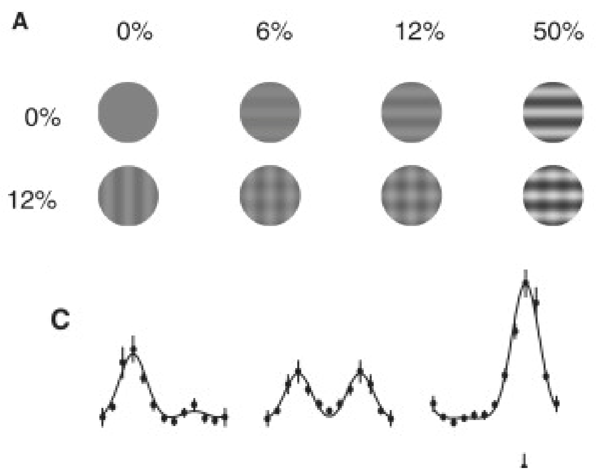


Ruff & Cohen, 2016

- Example findings – tuning curves/preferences, population codes, response trajectories, activity changes with learning/attention

Data for: Algorithms

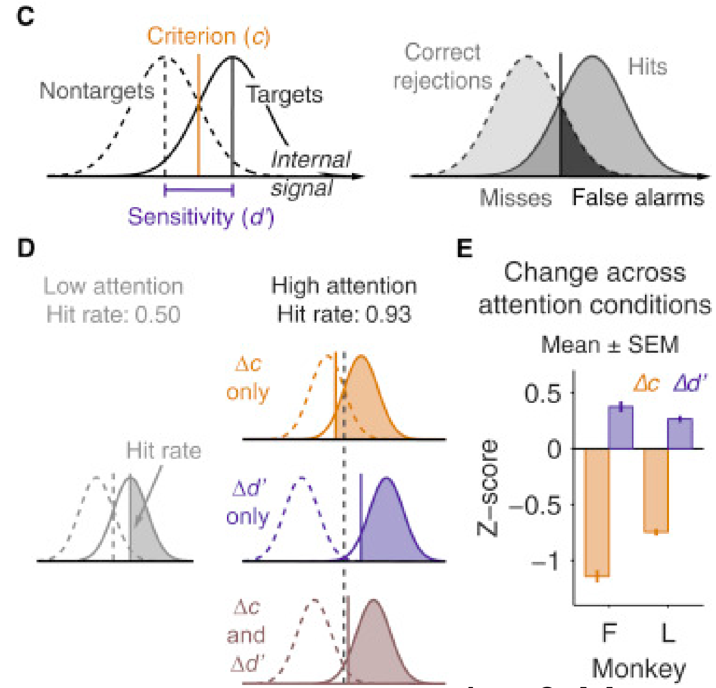
- Types of studies – behavior/performance quantification, normative or descriptive theory



$$f(c) = r_{max}\frac{c^n}{c_{50}^n + c^n}, \quad R_\varphi(\theta, c) = G_\varphi(\theta) f(c).$$

$$\mathbf{R}_{1+2}(c_1, c_2) = w_1(c_1, c_2)\mathbf{R}_1(c_1) + w_2(c_1, c_2)\mathbf{R}_2(c_2),$$

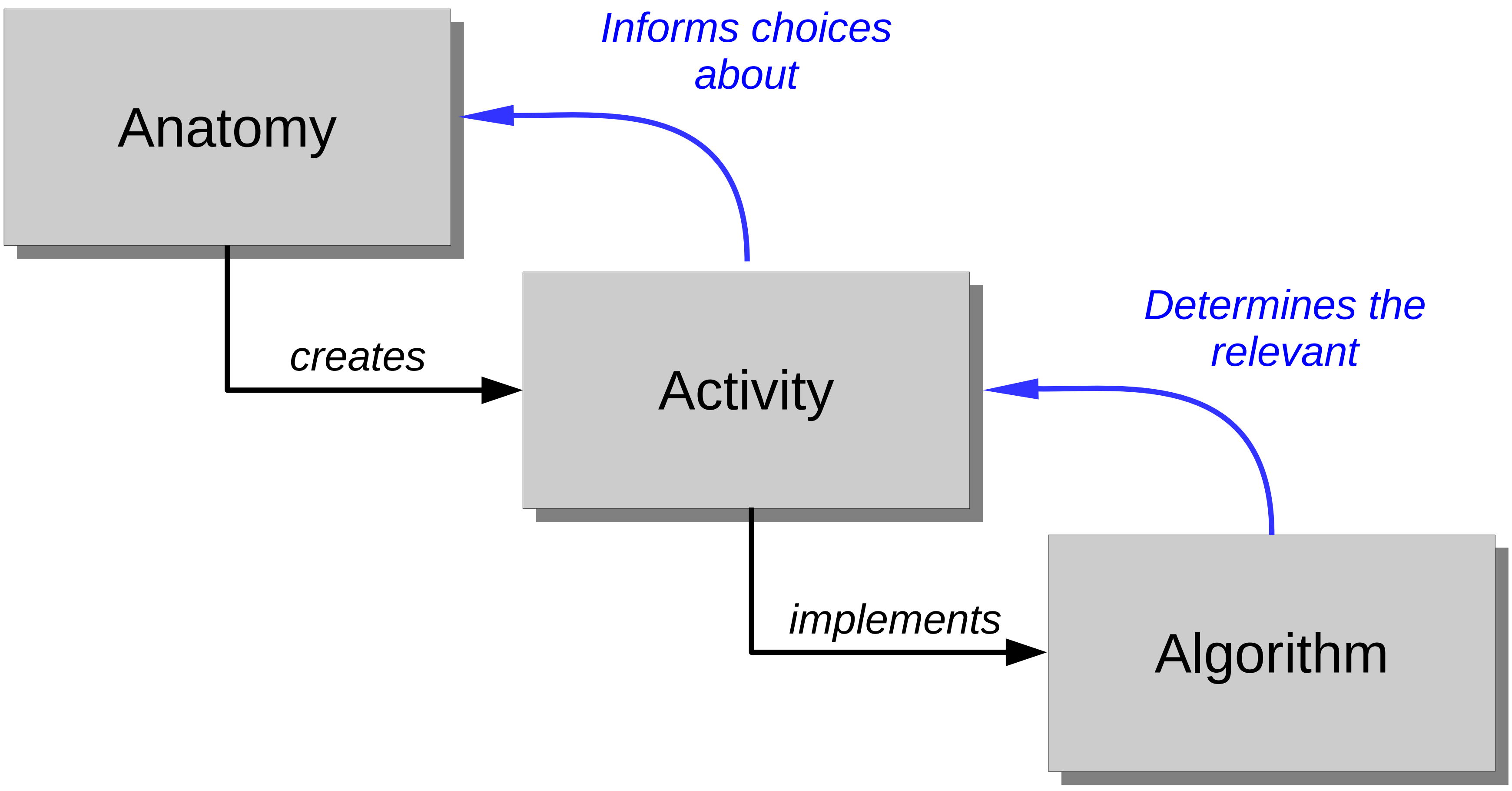
Busse et al., 2009



Lu & Maunsell, 2015

- Example findings – signal detection theory, reaction times, canonical computations, information theory, Bayesian computations

The 3 A's of Circuit Modeling



Circuit models are ideally well-constrained by these elements

Example

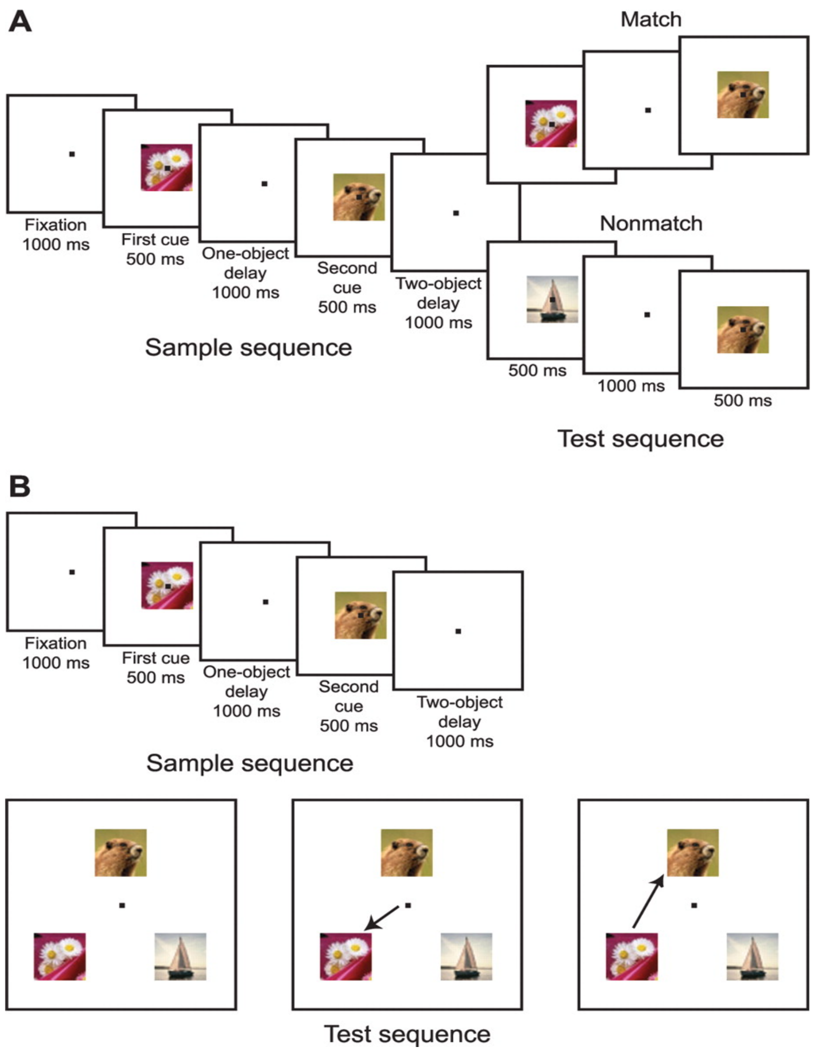
The Journal of Neuroscience, November 8, 2017 • 37(45):11021–11036 • **11021**

Systems/Circuits

Hebbian Learning in a Random Network Captures Selectivity Properties of the Prefrontal Cortex

Grace W. Lindsay,[1,2] Mattia Rigotti,[1,4] Melissa R. Warden,[5,6] Earl K. Miller,[6] and Stefano Fusi[1,2,3]
[1]Center for Theoretical Neuroscience, College of Physicians and Surgeons, [2]Mortimer B. Zuckerman Mind Brain Behavior Institute, College of Physicians and Surgeons, and [3]Kavli Institute for Brain Sciences, Columbia University, New York, New York 10027, [4]IBM Thomas J. Watson Research Center, Yorktown Heights, New York 10598, [5]Department of Neurobiology and Behavior, College of Agriculture and Life Sciences, Cornell University, Ithaca, New York 14853, and [6]The Picower Institute for Learning and Memory & Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Data

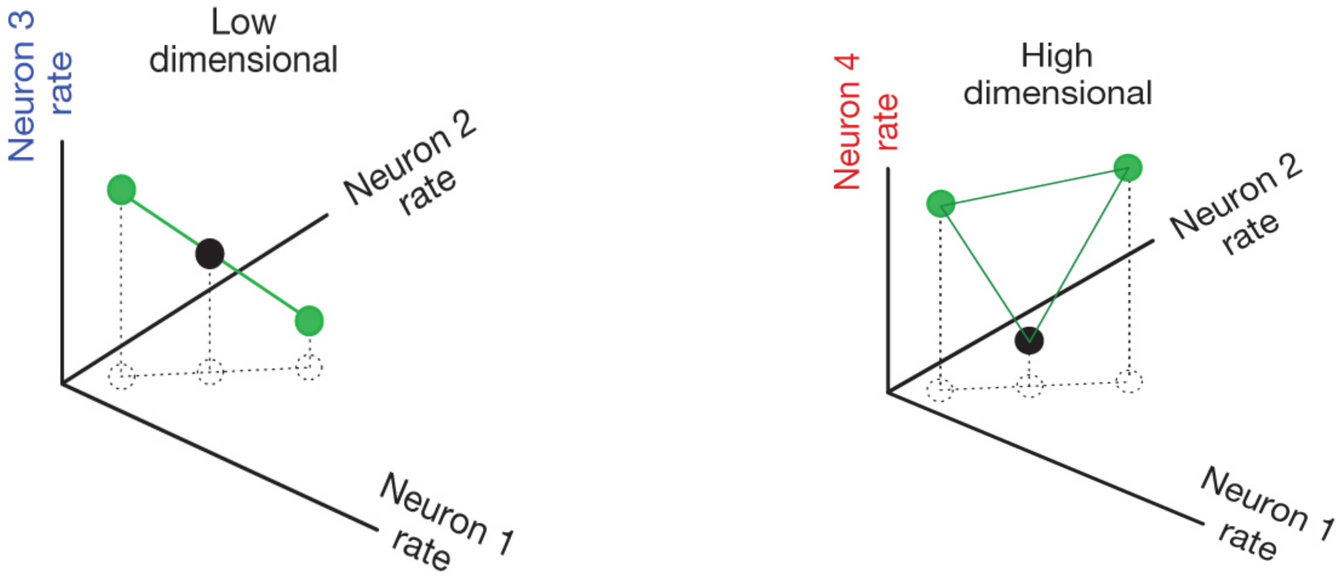


- Task Type (defined blockwise): Recognition or Recall
- Two cue identities (chosen without replacement from 4 options)
- 90 PFC cells

Warden and Miller, 2010

Algorithm

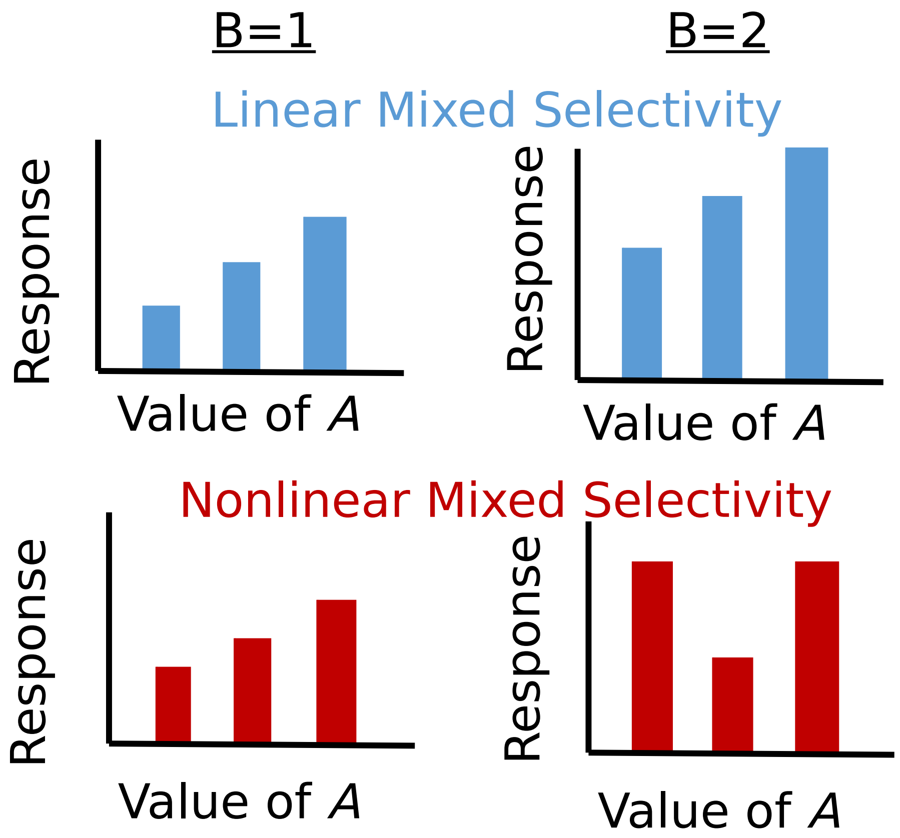
- High dimensional representations allow for more linear readouts, and better/more flexible performance



Rigotti et al., 2013

Activity

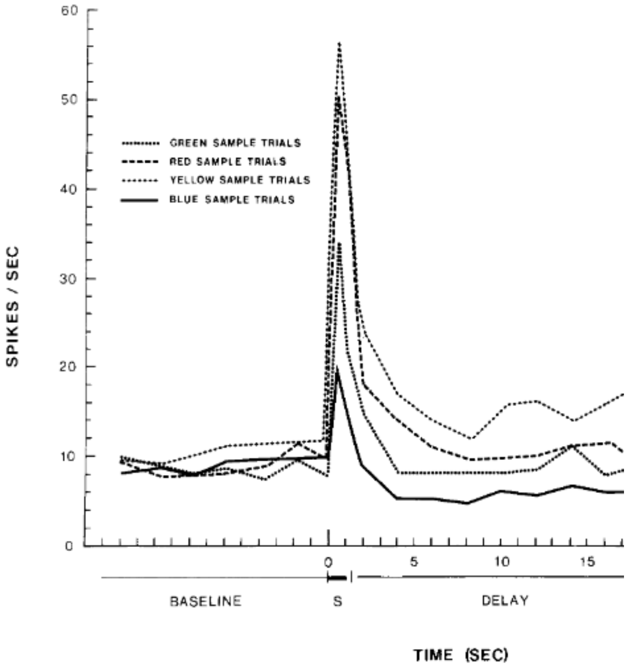
- Cells with nonlinear mixed selectivity increase the dimensionality of the network representation



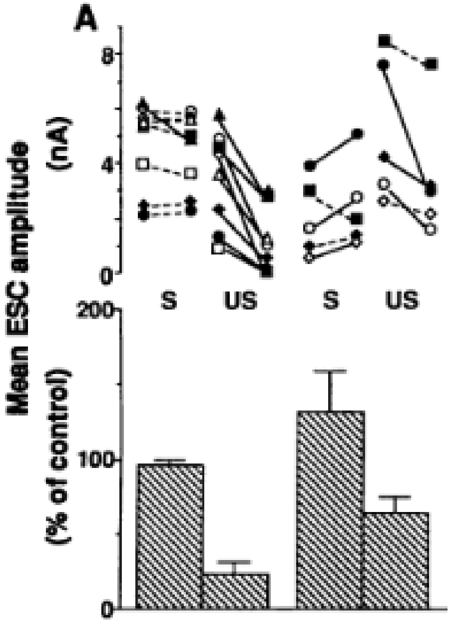
*With constraints on firing rate, noise, and selectivity distributions

Anatomy

- PFC cell selectivity is primarily determined by feedforward inputs from cue-representing cells.
- Hebbian learning has “rich get richer” and “poor get poorer” dynamics

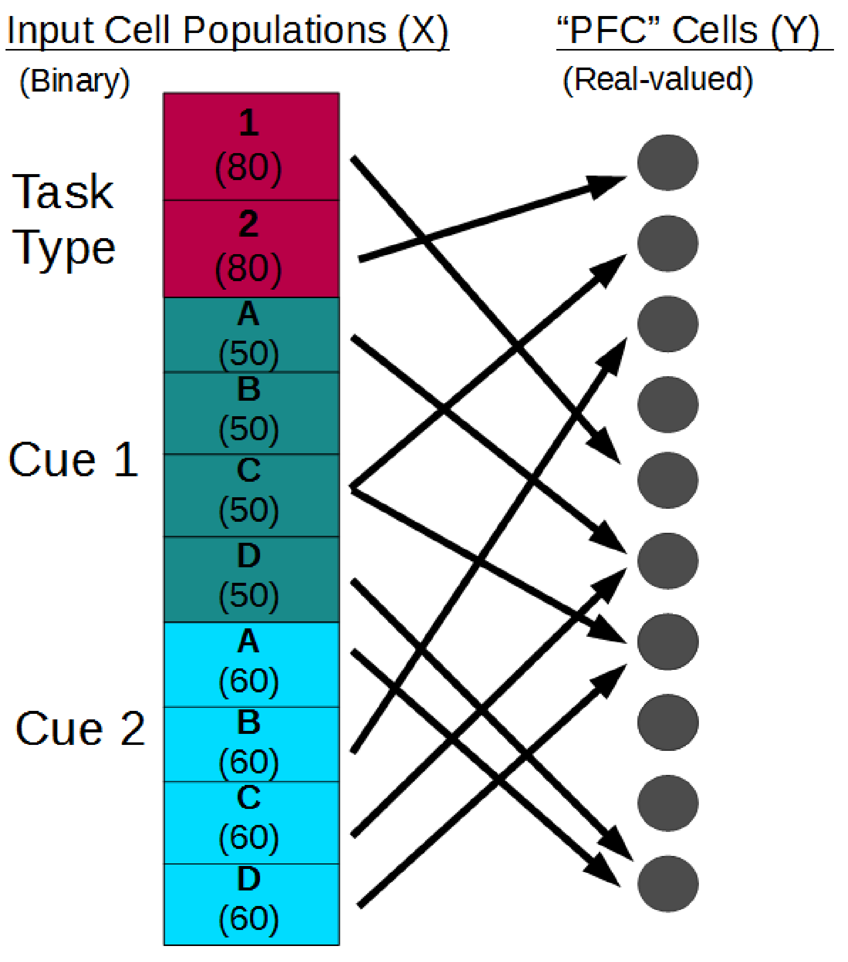


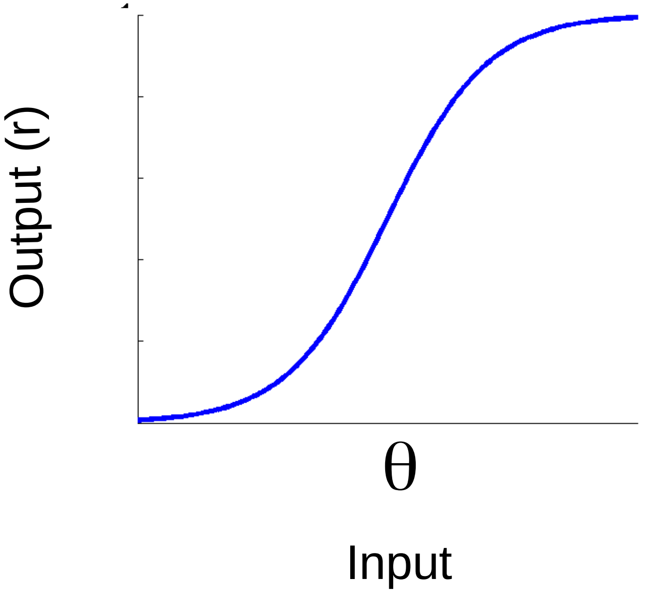
Fuster & Jervey, 1982



Lo & Poo, 1991

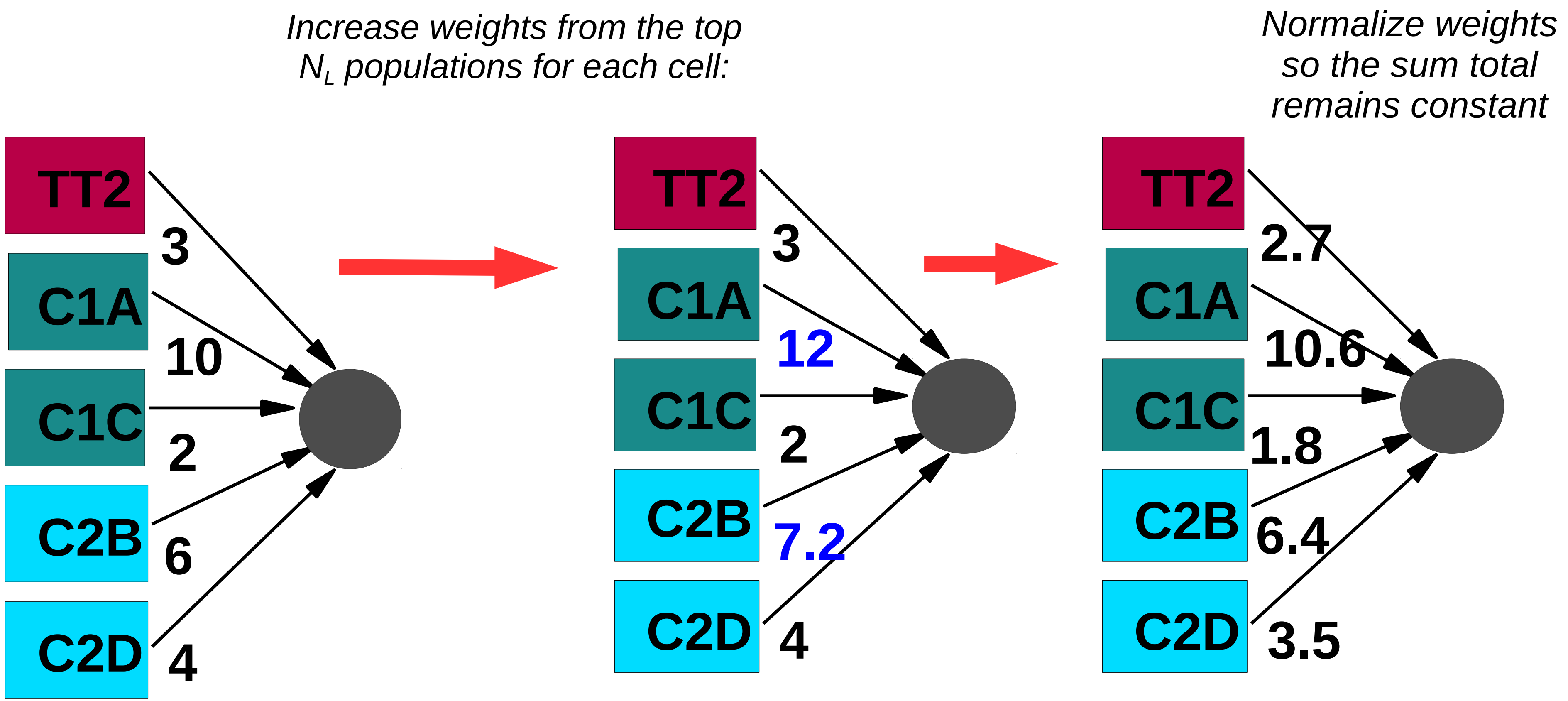
The Circuit Model





- *Weights are drawn from non-negative Gaussian distribution, 25% connection probability.*
- *PFC cell activity is a sigmoidal function of the weighted sum of its input, plus noise.*
- *The threshold is defined as a fraction of the total weight into a cell*

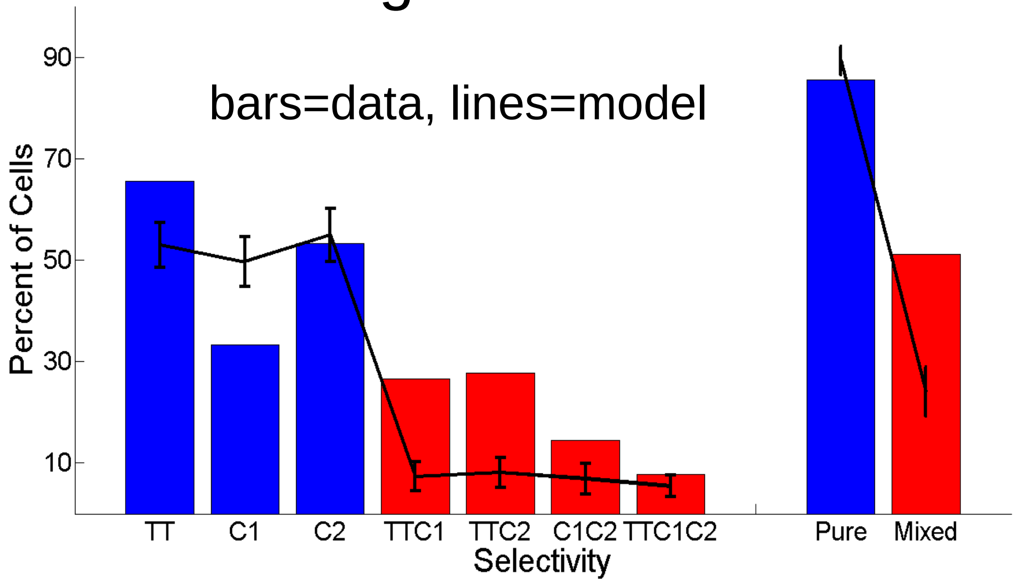
Learning in the Model



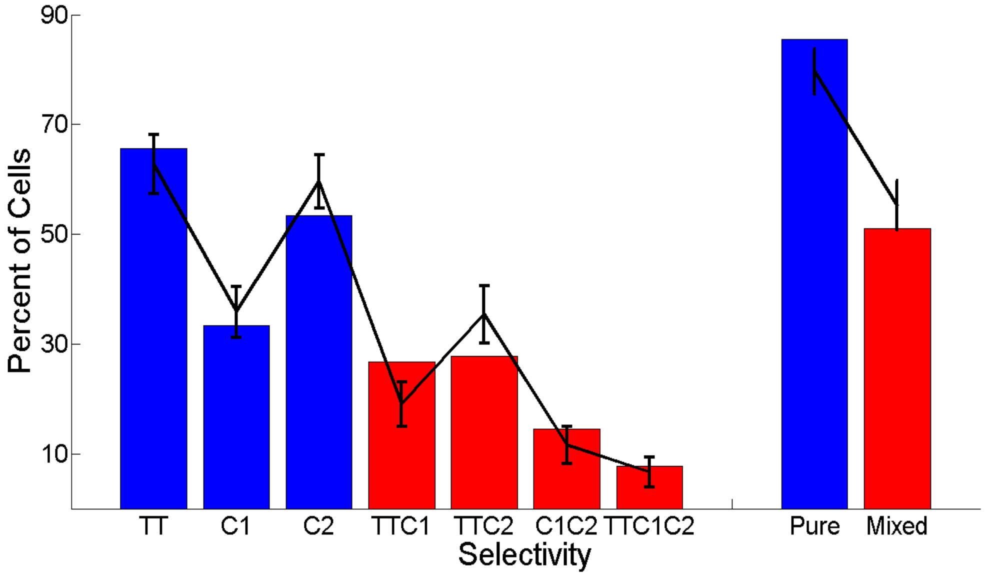
Implements “rich get richer” while keeping overall input to a cell constant

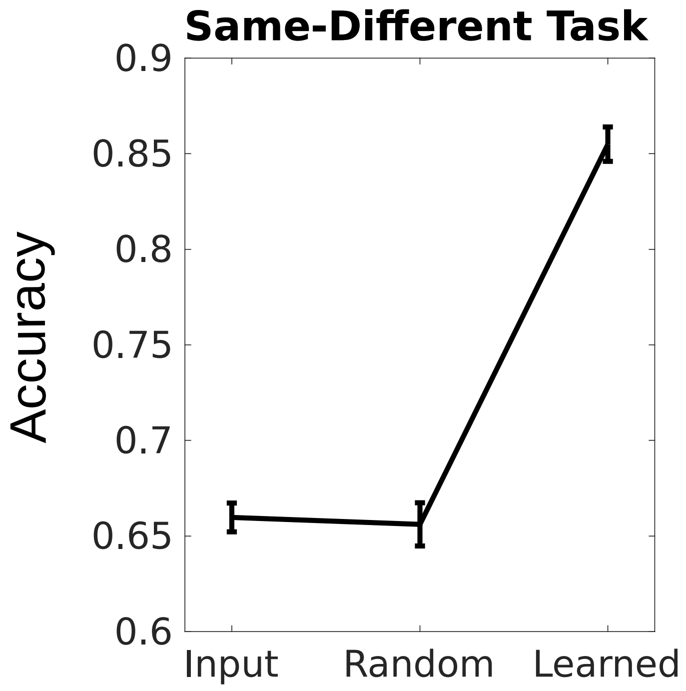
Data vs Model

Before Learning:



After Learning:

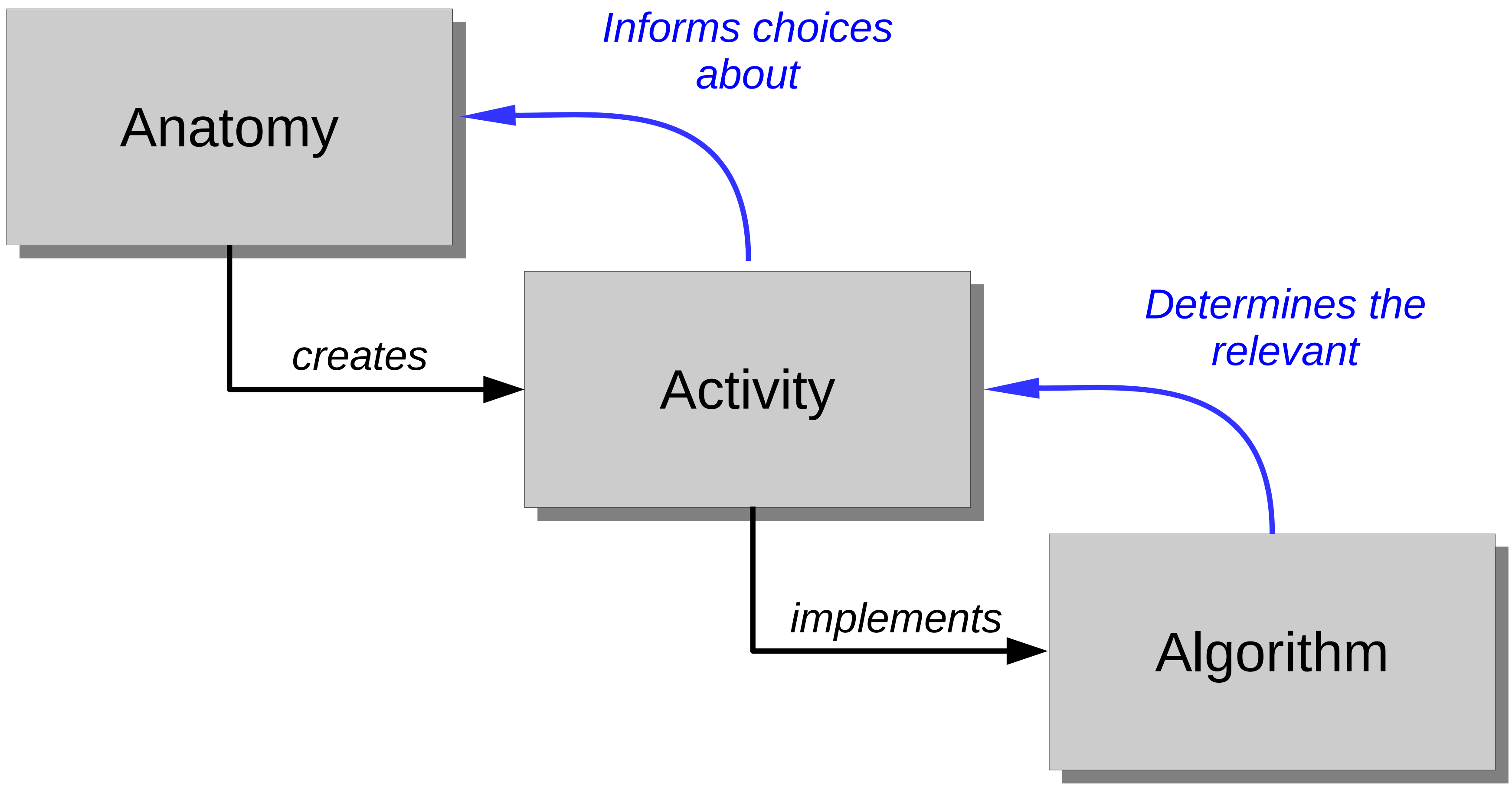




“Post-dictions”

- Mixed selectivity increases with learning
- Pure selectivity decreases with learning
- Noise decreases with learning

The 3 A's of Circuit Modeling



When building circuit models...

- Know your purpose (is this model useful)
- Draw from existing, & think about how yours can be extended
- Know your assumptions
- Motivate each component, and know how components align with reality
- State what could be tested (map back to reality)

When assessing circuit models...

- Know the purpose of the model
- Assess the assumptions wrt that purpose
- An absence of a feature is not (necessarily) a flaw
- The line between assumptions and predictions is thin
- What did you learn from this model?

Thanks!