The cost of brain state transitions

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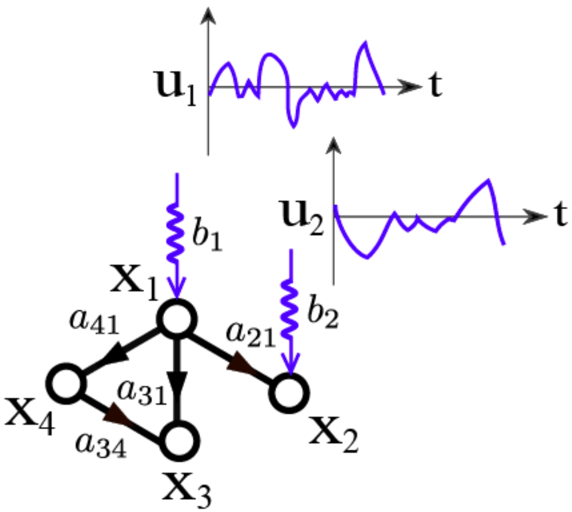
Overview

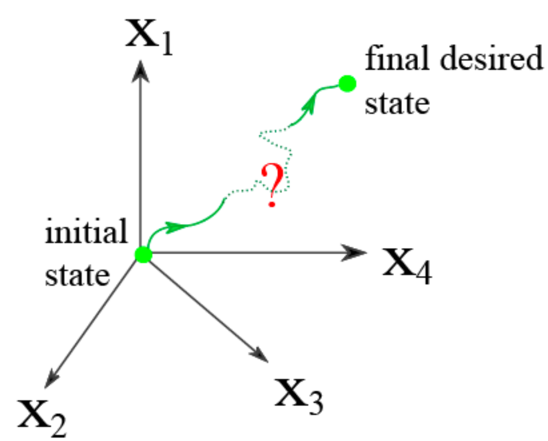
I. Network control theory and its application to neural systems

II. Examining cognitive and neurobiological correlates of control energy

III. Extension: multiplex network control

The network control model





Network control theory is a mathematical framework that determines which perturbations can drive the whole system to a desired state. It is typically applied to the study of the power grid, mechanical systems, air traffic control systems, & robotics.

Figure from Liu et al. (2011) *Nature*

A network control model for the brain

The model stipulates how activity flows along structural connections.

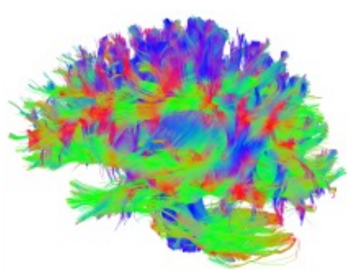
Number of regions being controlled

$$x(t+1) = Ax(t) + B_{\mathcal{K}} u_{\mathcal{K}}(t)$$

State of brain regions over time

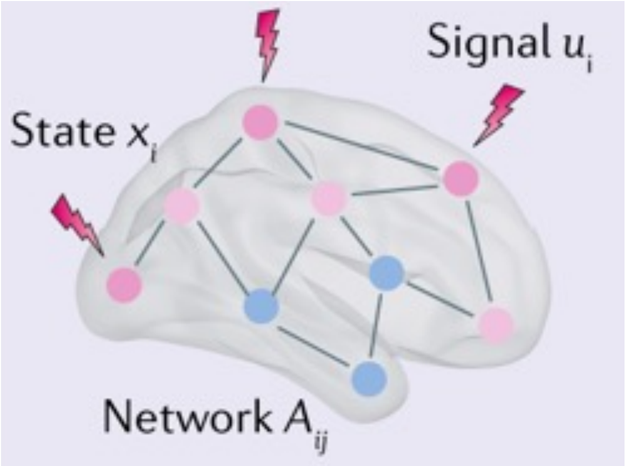
Weighted adjacency matrix

Control energy



Kim *et al.* (2018) Nature Physics; Kim *et al.* 2020 In Press arXiv:1902.03309

What are the inputs and outputs of NCT?



Network control theory

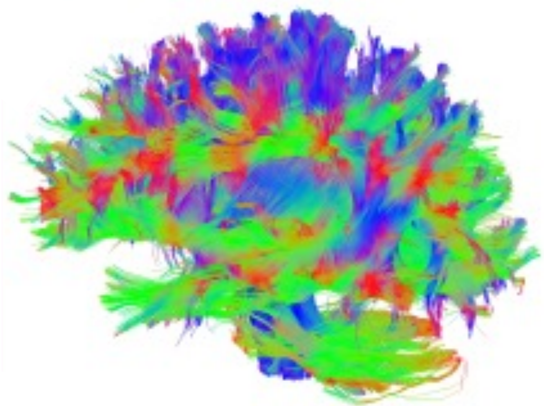
Inputs:
- Mapping of network
- Model of dynamics

Outputs:
- Design of perturbation

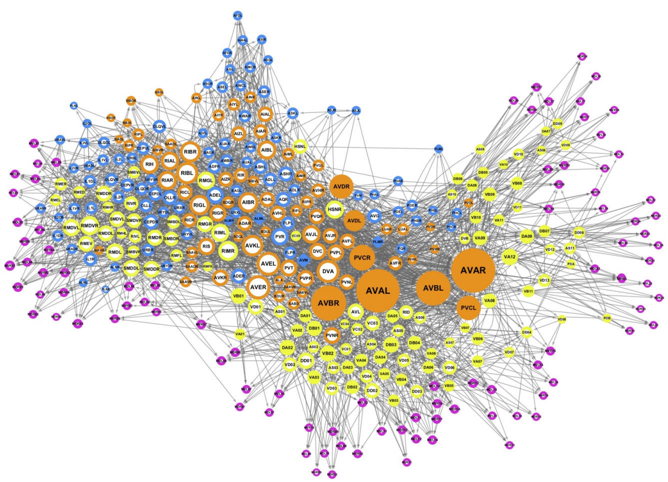
Tang *et al.* Reviews of Modern Physics 2018

Complex Systems

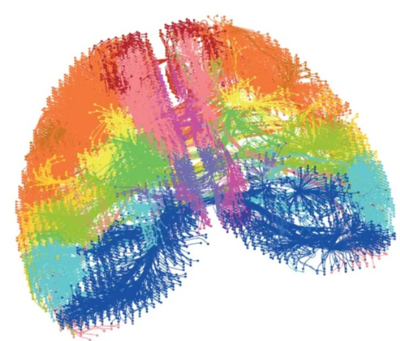
Input: A map of the network



Diffusion tractography

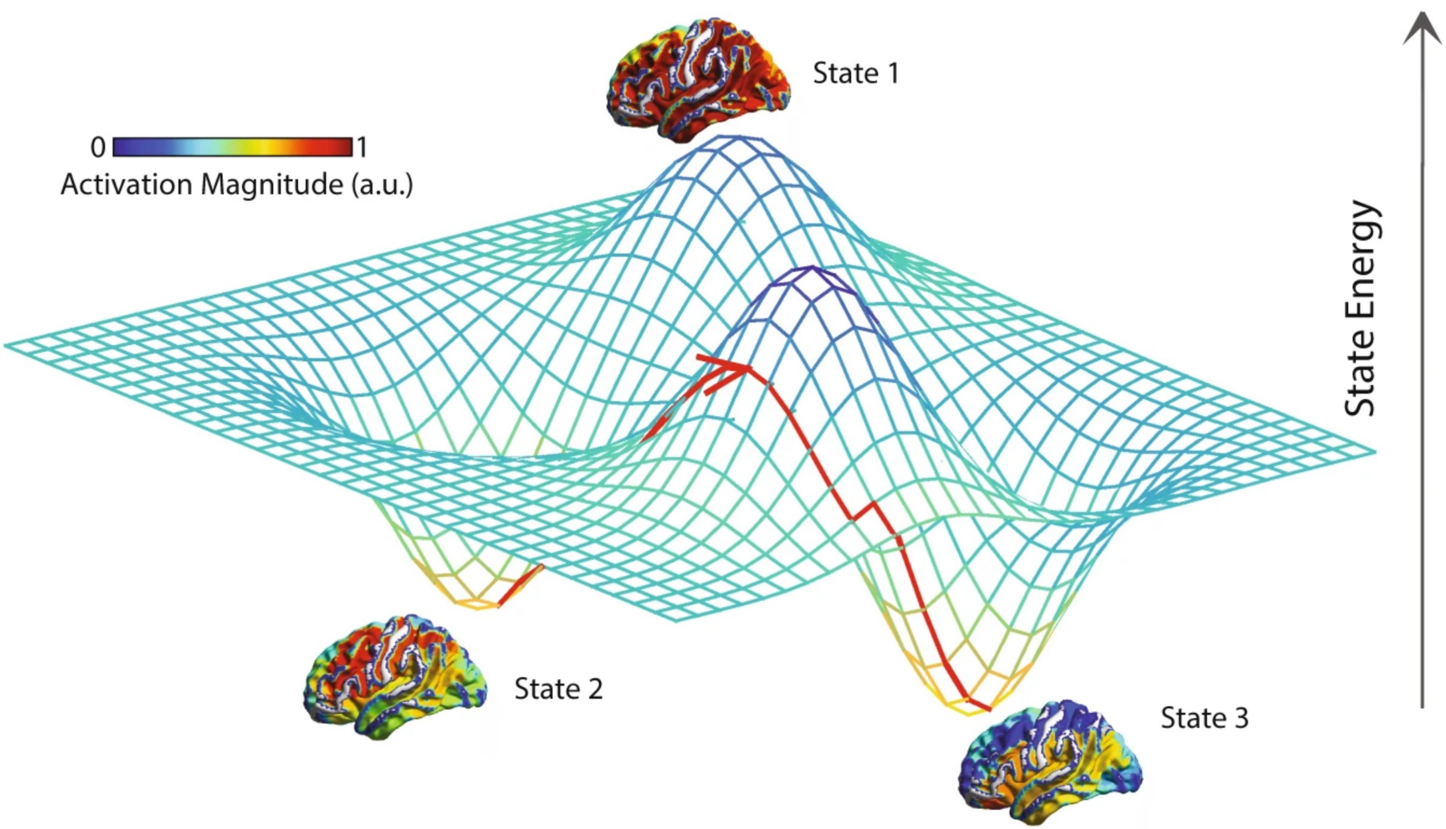


Electron microscopy



Tract tracing

Input: A model of the dynamics



Gu et al. (2018) *Sci Rep*

Input: A model of the dynamics

complexity

- Linear, time-invariant models

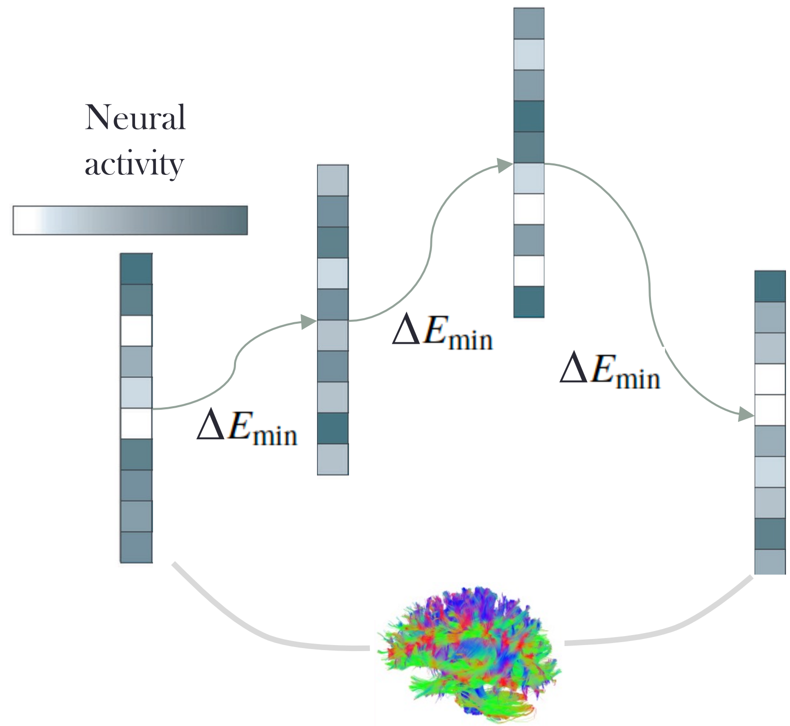
$$\frac{d}{dt}\mathbf{x}(t) = \mathbf{A}\mathbf{x}(t) + \mathbf{B}\mathbf{u}(t)$$
$$\mathbf{y}(t) = \mathbf{C}\mathbf{x}(t).$$

- Linear, time-varying models

$$\frac{d}{dt}\mathbf{x}(t) = \mathbf{A}(t)\mathbf{x}(t) + \mathbf{B}(t)\mathbf{u}(t)$$
$$\mathbf{y}(t) = \mathbf{C}(t)\mathbf{x}(t).$$

- Nonlinear models

$$\frac{d}{dt}\mathbf{x}(t) = f(\mathbf{x}(t), \mathbf{u}(t), t)$$
$$\mathbf{y}(t) = h(\mathbf{x}(t), t).$$



Srivastava et al. (2021) *Network Neuroscience*; Motter (2015) *Chaos*

Input: A model of the dynamics

nature biomedical engineering

Article https://doi.org/10.1038/s41551-023-01117-y

Macroscopic resting-state brain dynamics are best described by linear models

Received: 23 December 2020

Accepted: 26 September 2023

Erfan Nozari[1,2,3], Maxwell A. Bertolero[4], Jennifer Stiso[4,5], Lorenzo Caciagli[4], Eli J. Cornblath[4,5], Xiaosong He[4], Arun S. Mahadevan[4], George J. Pappas[6] & Dani S. Bassett[4,6,7,8,9,10]

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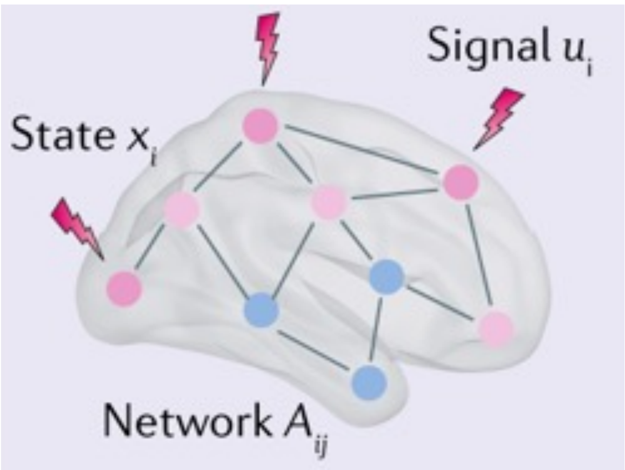


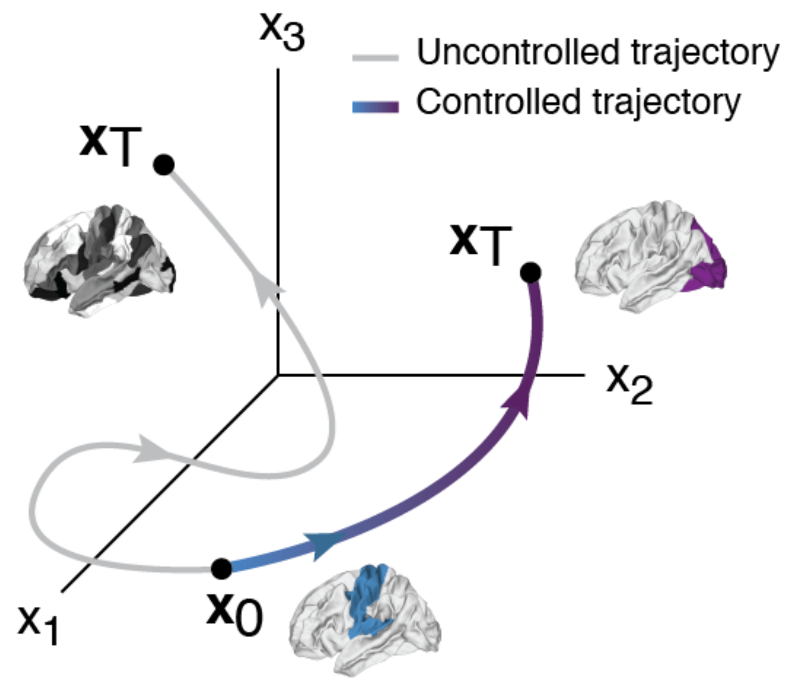
Network control theory

Inputs:
- Mapping of network ✓
- Model of dynamics ✓

Outputs:
- Design of perturbation ?

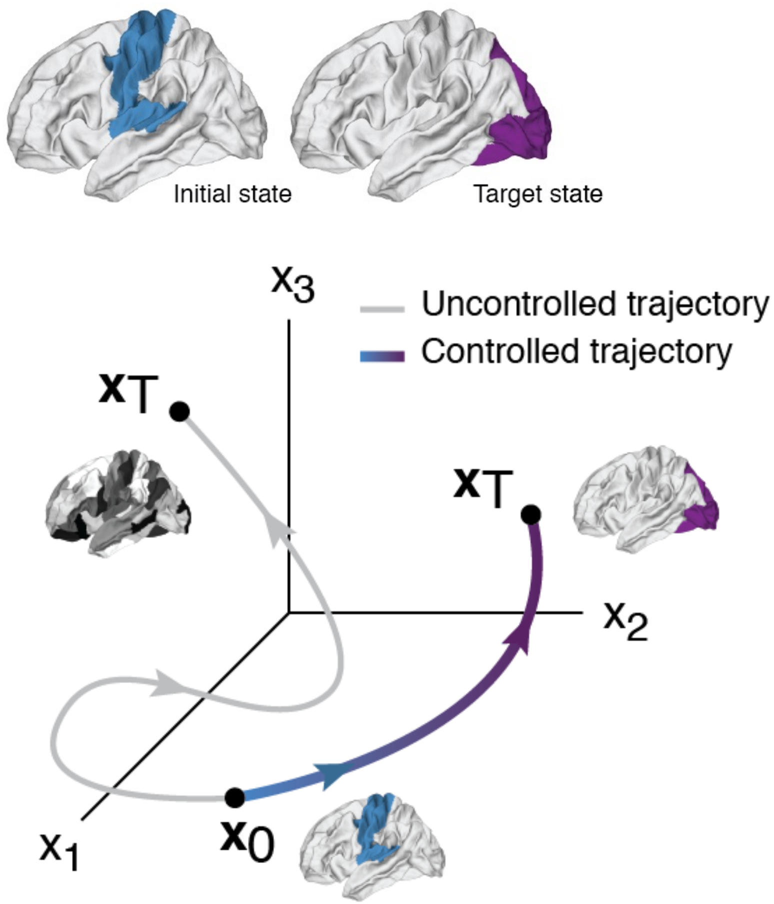
Outputs of NCT

- **Controlled response:** the system's response to some controlling input u(t) from some initial state x_0.
- **Controllability:** A system is controllable if there is a control input that brings our system from any initial state to any final state in finite time.
- **Achieving desired state transitions through minimum energy control:** Designing the control input u(t) to minimize the control energy E (and possibly other factors) to drive the desired response.



Betzel et al. (2016) *Sci Reports*

Quantifying ease and difficulty of state transitions



Given the model of network dynamics, we can define a cost function that penalizes control energy required and distance of x(t) from the target state

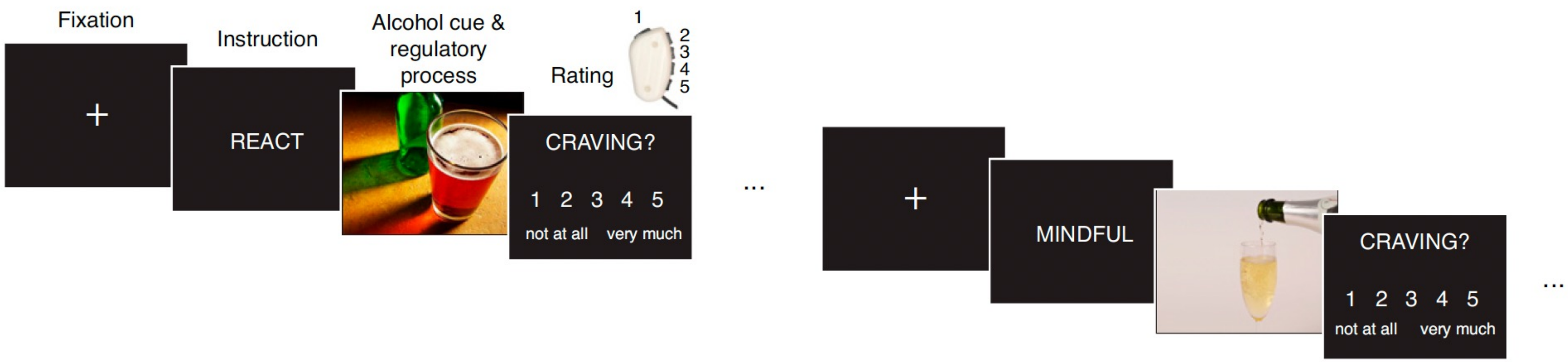
$$\min_{\mathbf{u}} \int_0^T \underbrace{(\mathbf{x}_T - \mathbf{x})^T (\mathbf{x}_T - \mathbf{x})}_{\text{distance}} + \underbrace{\rho \mathbf{u}_{\mathcal{K}}^T \mathbf{u}_{\mathcal{K}}}_{\text{energy}}$$

II. Examining cognitive and neurobiological correlates of control energy

Complex Systems

Relating control energy and cognitive effort

Does a brain state associated with higher cognitive effort require more control input to reach and to maintain?



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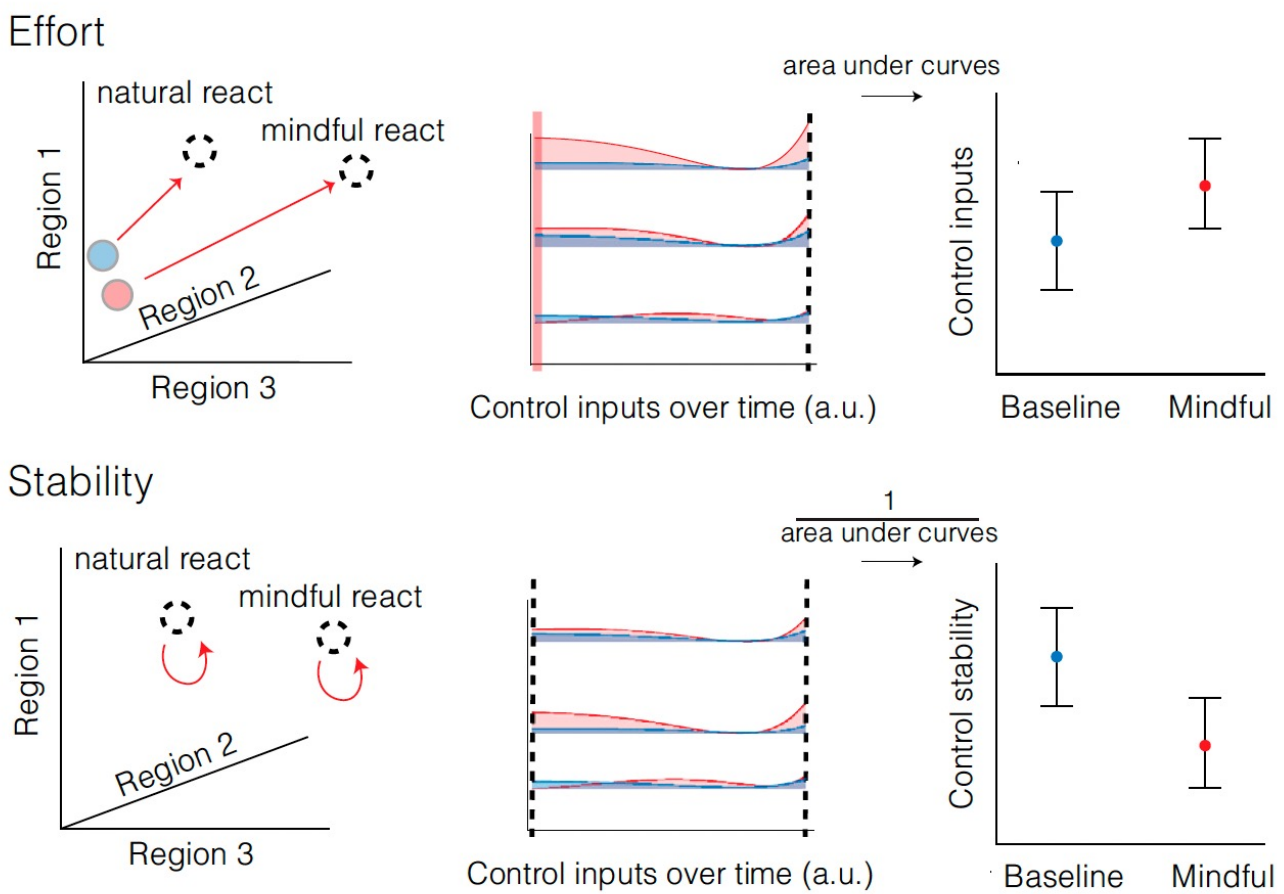

Zhou et al. (2023) *PNAS*

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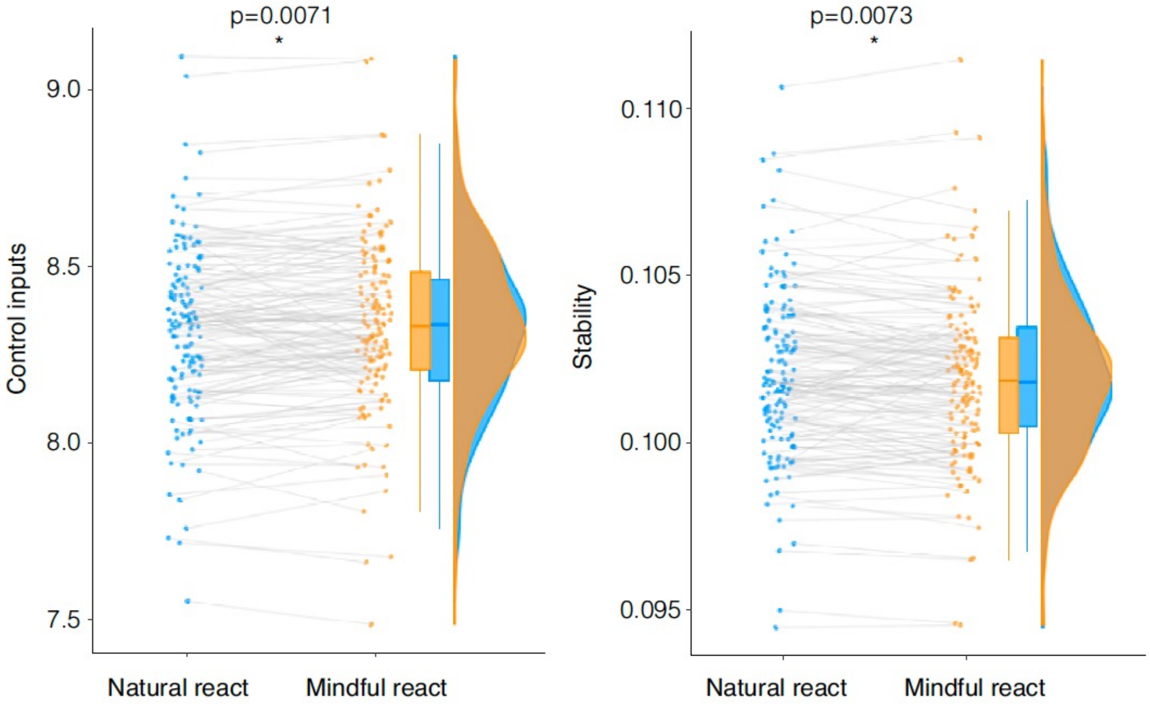

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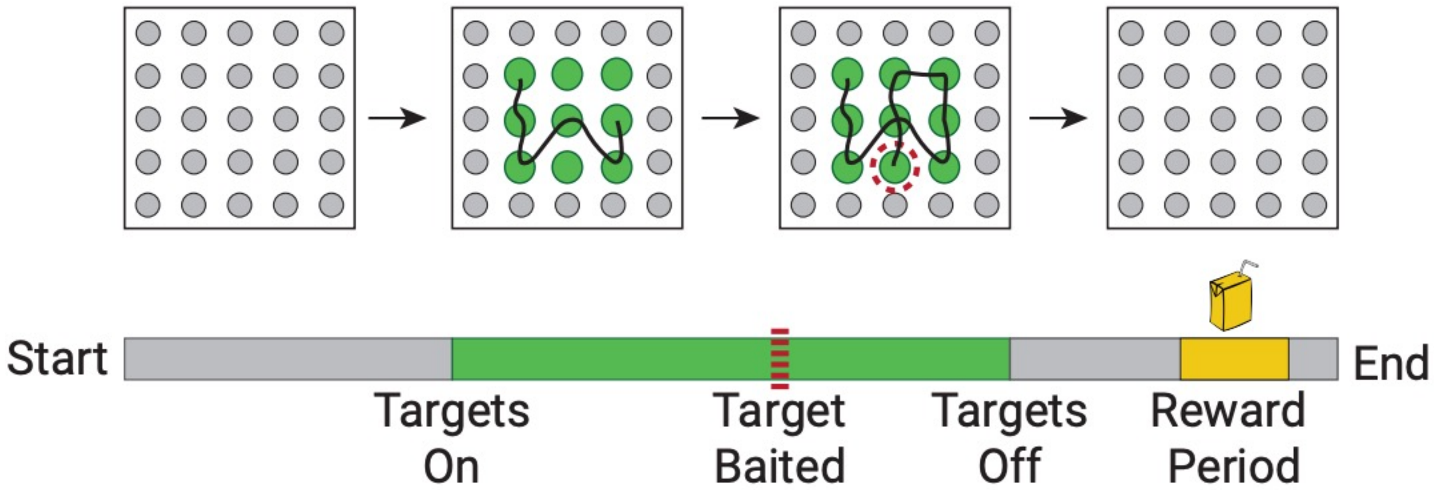
Complex Systems

Relating control energy and cognitive effort

Do task-associated brain state transitions become less costly over the course of habit learning?



Szymula*, Brynildsen*, Fotiadis* et al. (in revision)

Complex Systems

Relating control energy and cognitive effort

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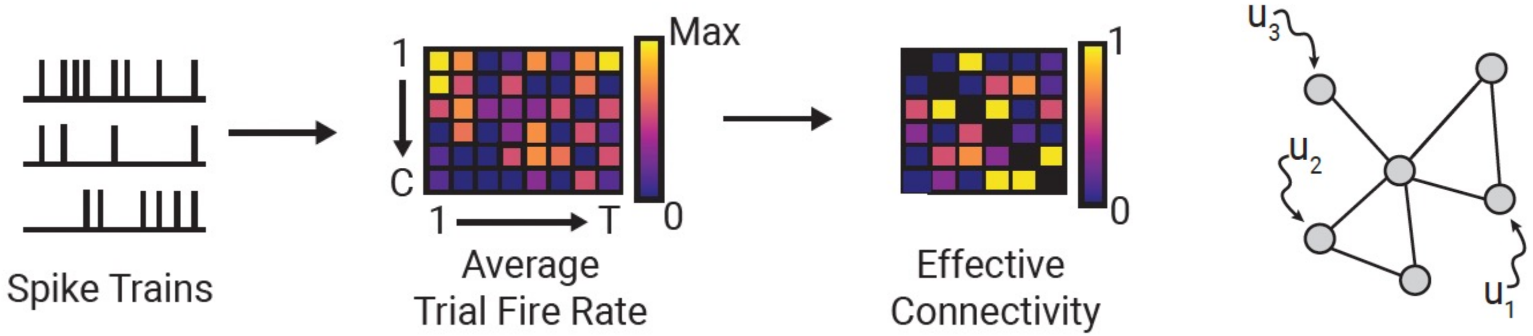

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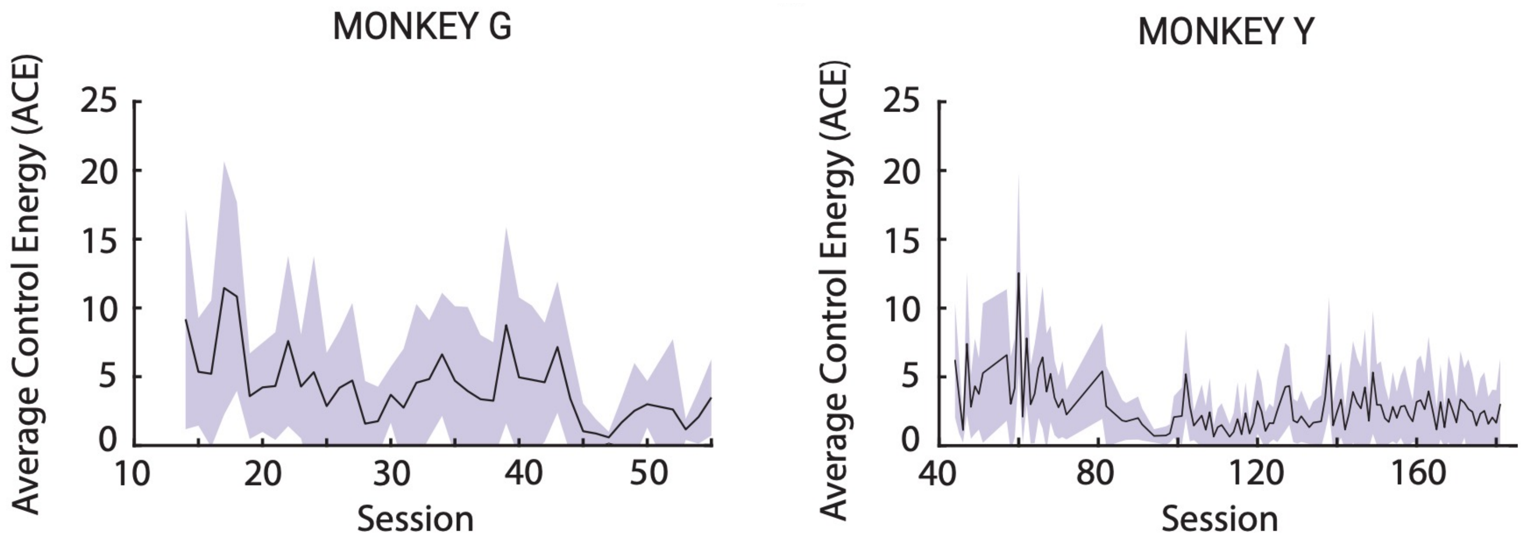

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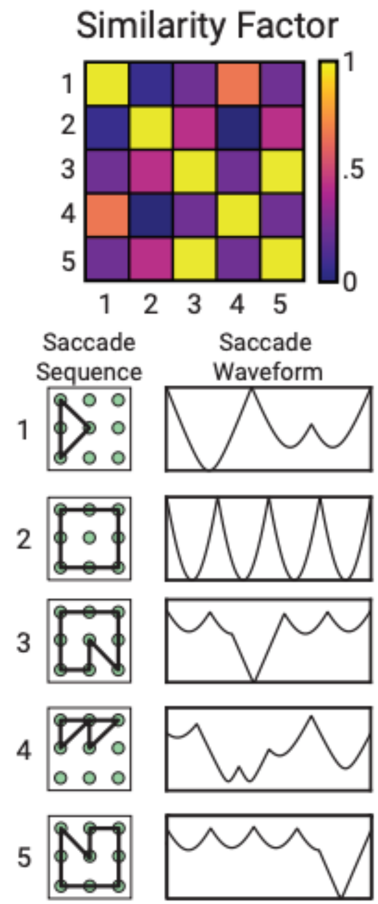
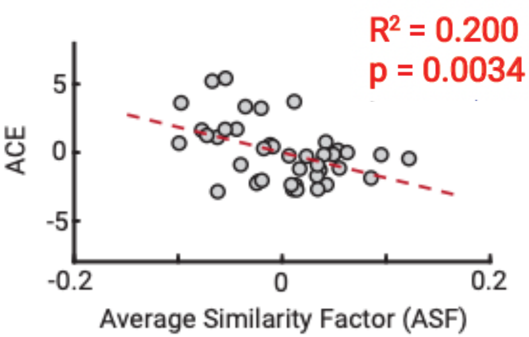
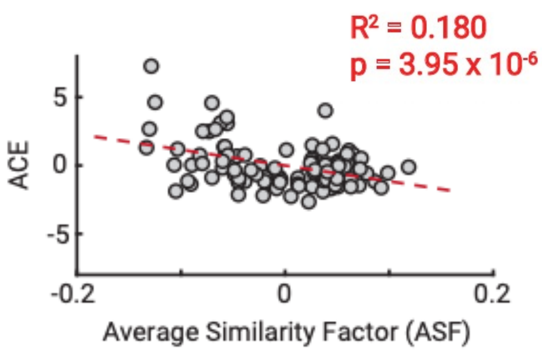
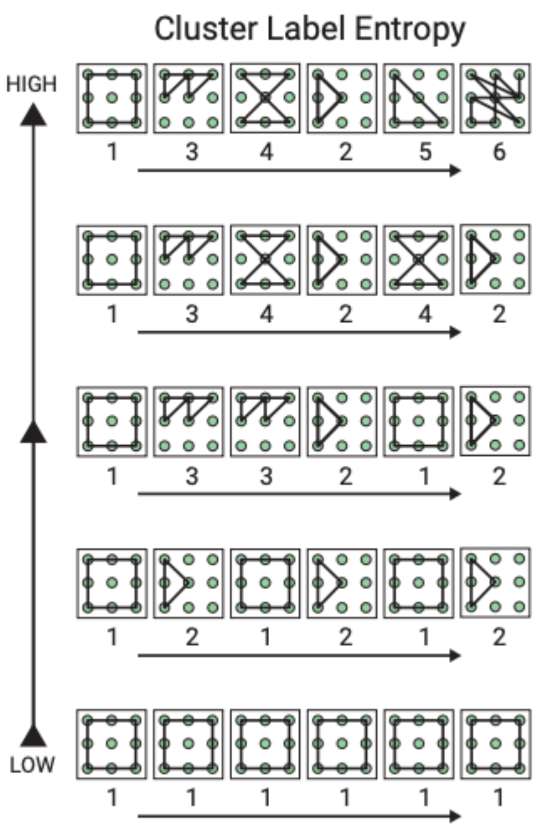


Is the monkey performing increasingly similar patterns the longer she engages in the task?

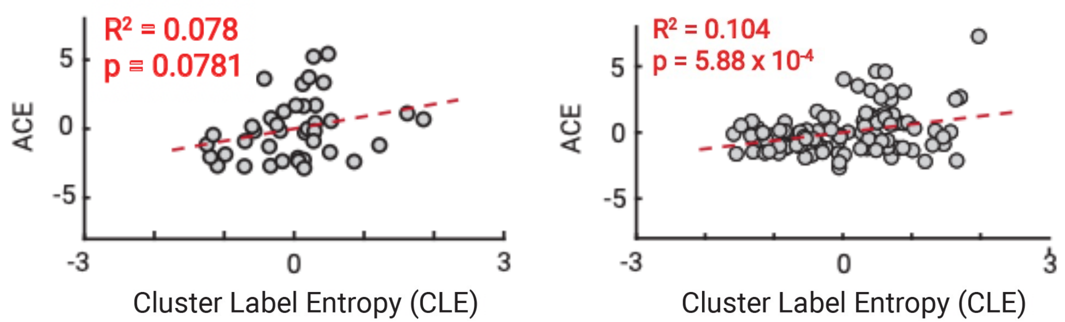




Relating control energy and cognitive effort



Is the monkey choosing to explore many different saccade patterns across trials or does she continuously exploit a select few?

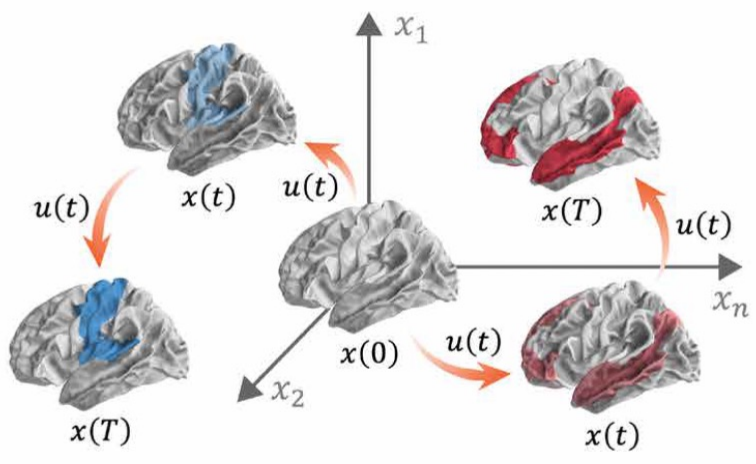


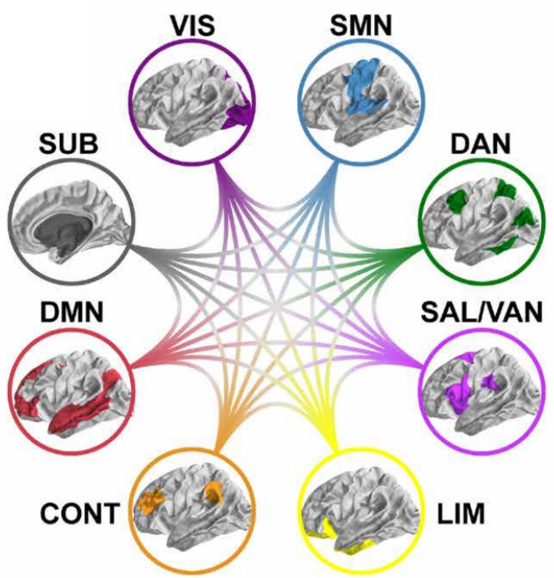
Szymula*, Brynildsen*, Fotiadis* et al. (in revision)

Complex Systems

The biological basis of control energy

Does control energy reflect glucose utilization in the brain?

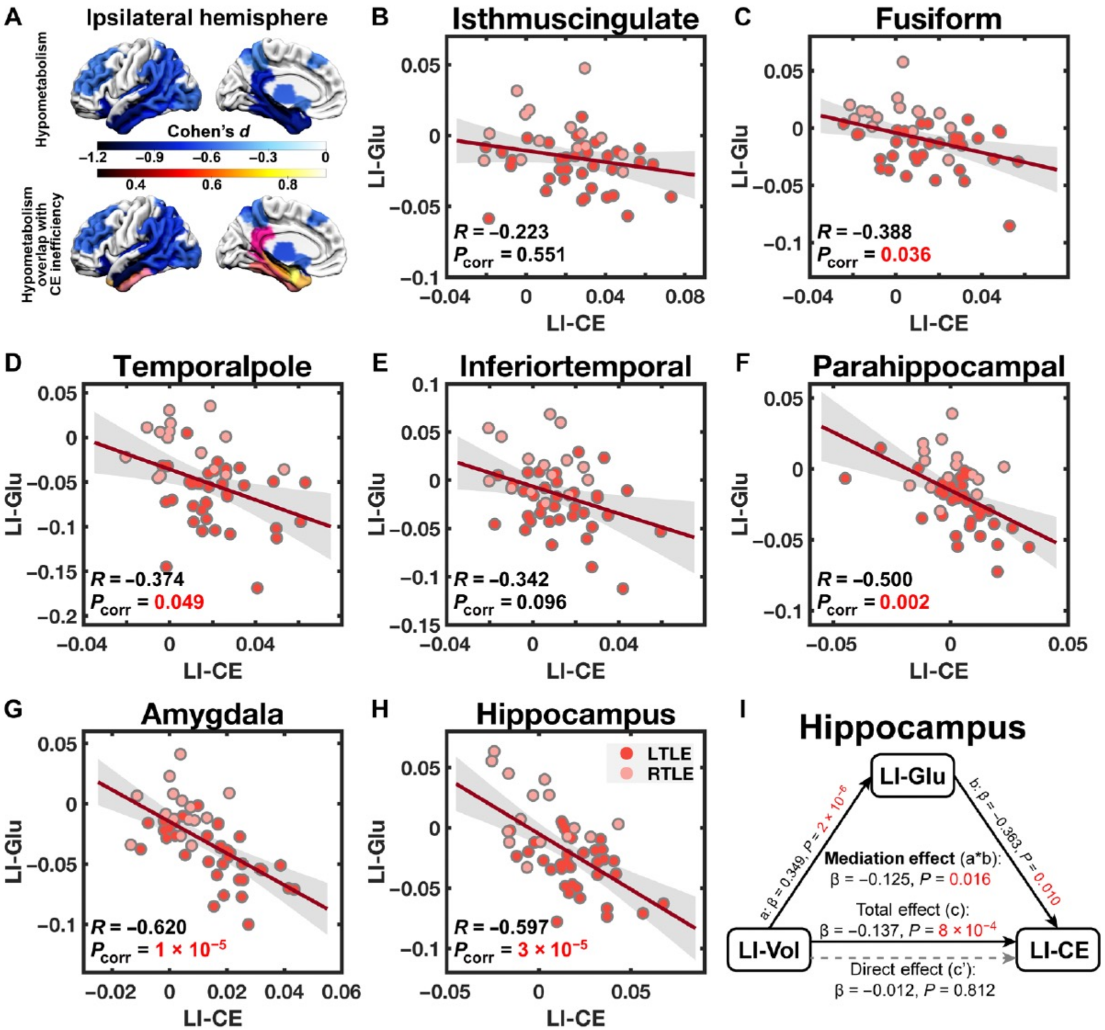




He et al. (2022) *Sci Adv*

Complex Systems

The biological basis of control energy



Summary

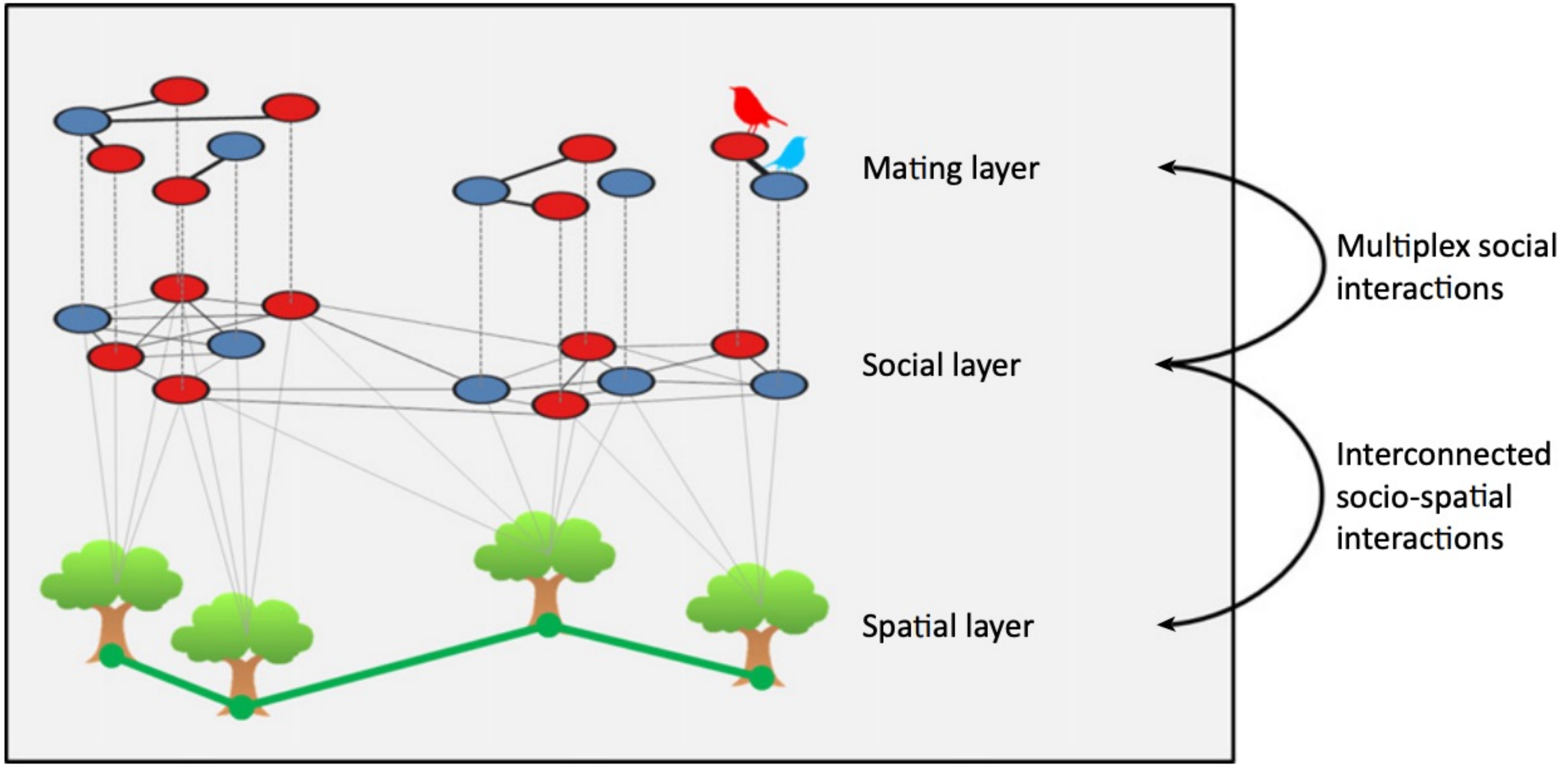
- Engaging mindful attention requires more control input into cognitive-control associated regions than reacting naturally to cues (Zhou et al., *PNAS* 2023)
- Control energy for state transitions decreases over the course of repeated task trials (Szymula, Brynildsen, Fotiadis et al.)
  - Changes in behavior associated with habit learning are correlated with control energy
- Regional glucose hypometabolism in TLE is associated with greater control energy requirements (He et al., *Sci Adv* 2022)

Complex Systems

III. A multilayer network control framework for modeling interactions between neural activity and gene expression

Control of multilayer networks

Multilayer networks model multiple types of interactions between components of a system.



Silk et al. (2018) *Trends Ecol Evol*

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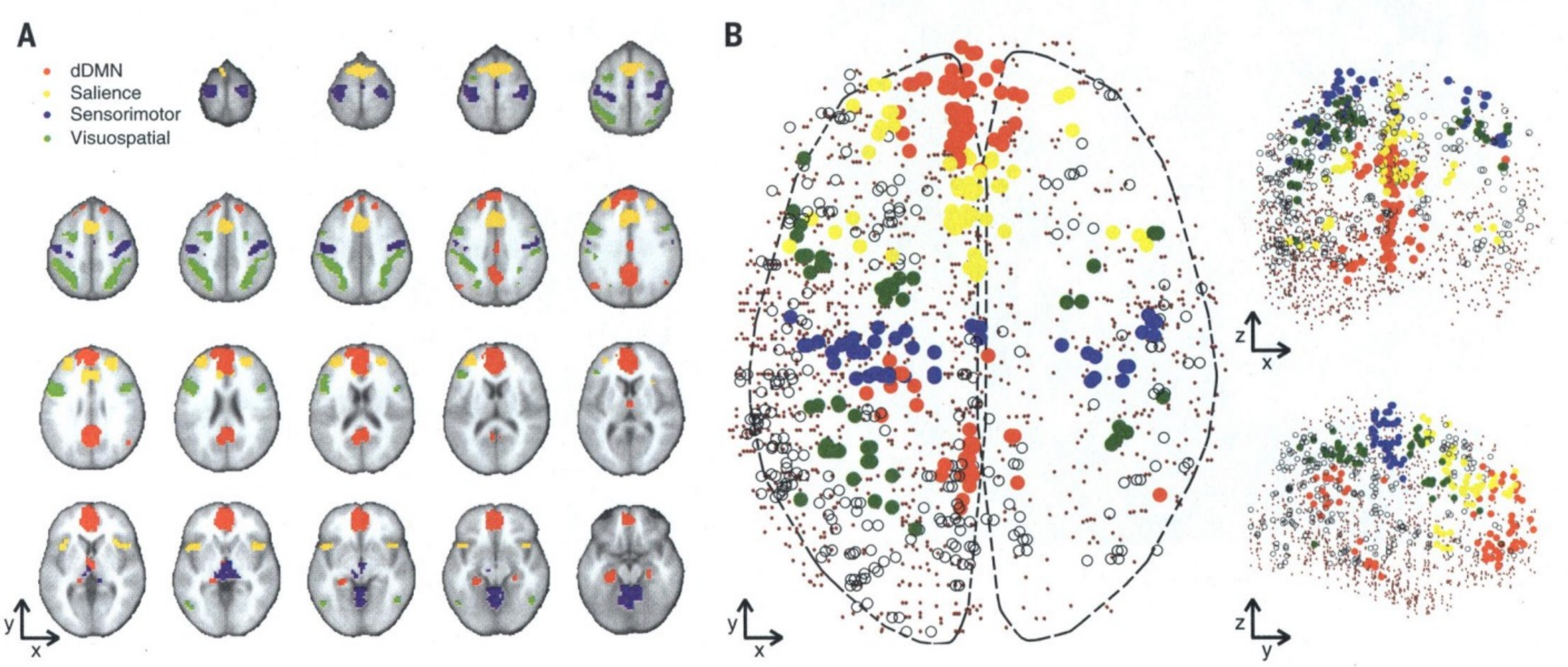

Richiardi et al. (2015) *Science*

Applying NCT to multilayer networks

Given access to only one layer, how can we drive a multilayered system to a desired state?

Applying NCT to multilayer networks

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Addressing this question is relevant to considering:

- How the brain transitions between health and disease states in which disease pathology impacts multiple layers

Applying NCT to multilayer networks

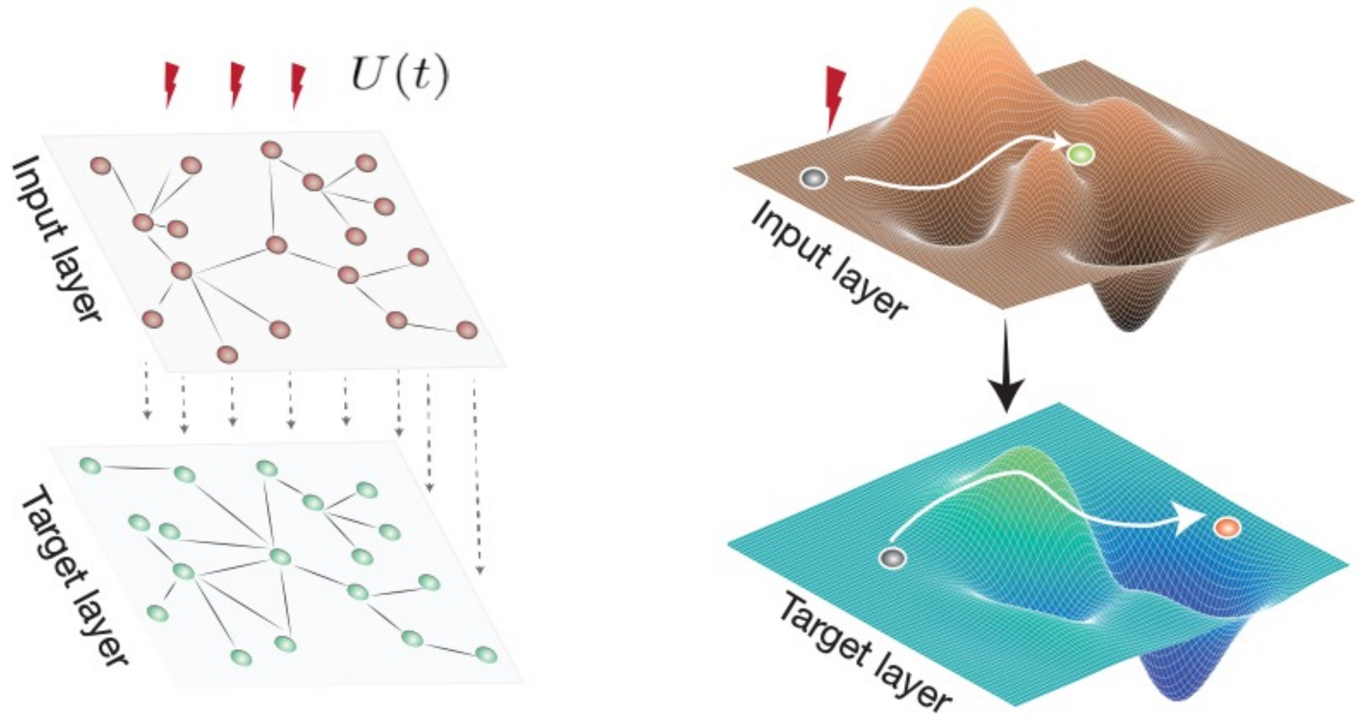
Given access to only one layer, how can we drive a multilayered system to a desired state?

Addressing this question is relevant to considering:

- How the brain transitions between health and disease states in which disease pathology impacts multiple layers
- How to target an intervention to impact multiple layers when only one layer is accessible

Applying NCT to multilayer networks

Given access to only one layer, how can we drive a multilayered system to a desired state?

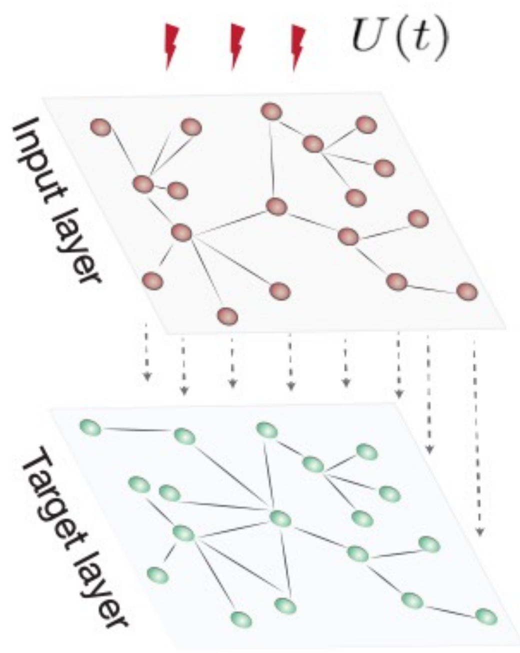


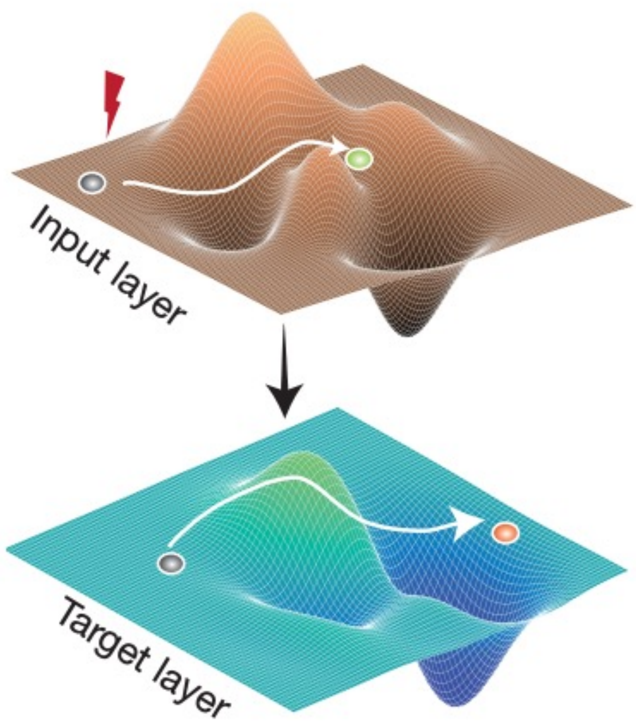
Applying NCT to multilayer networks

Given access to only one layer, how can we drive a multilayered system to a desired state?

Functional connectivity

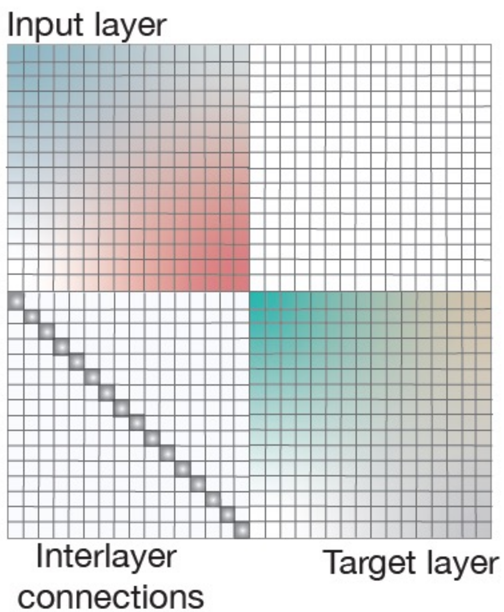
Gene coexpression

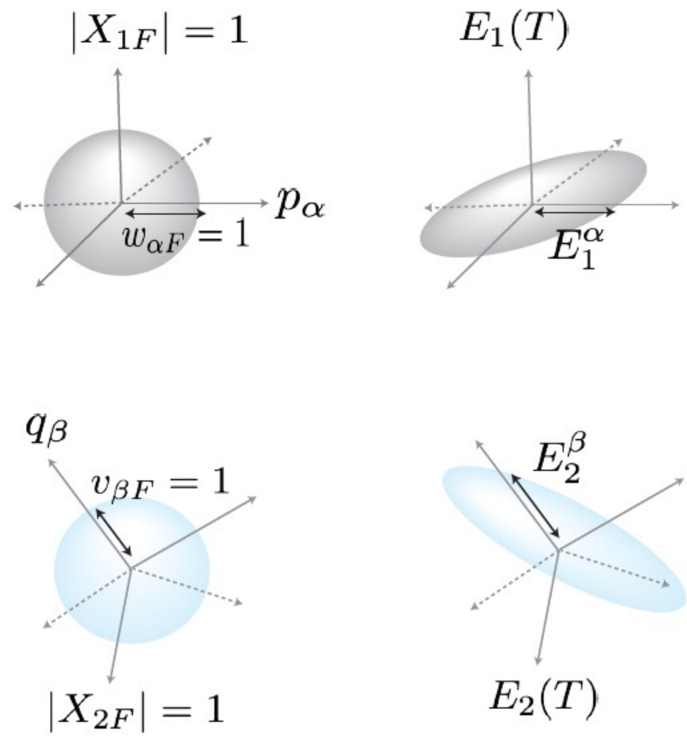




Srivastava et al. (2021) *arXiv*

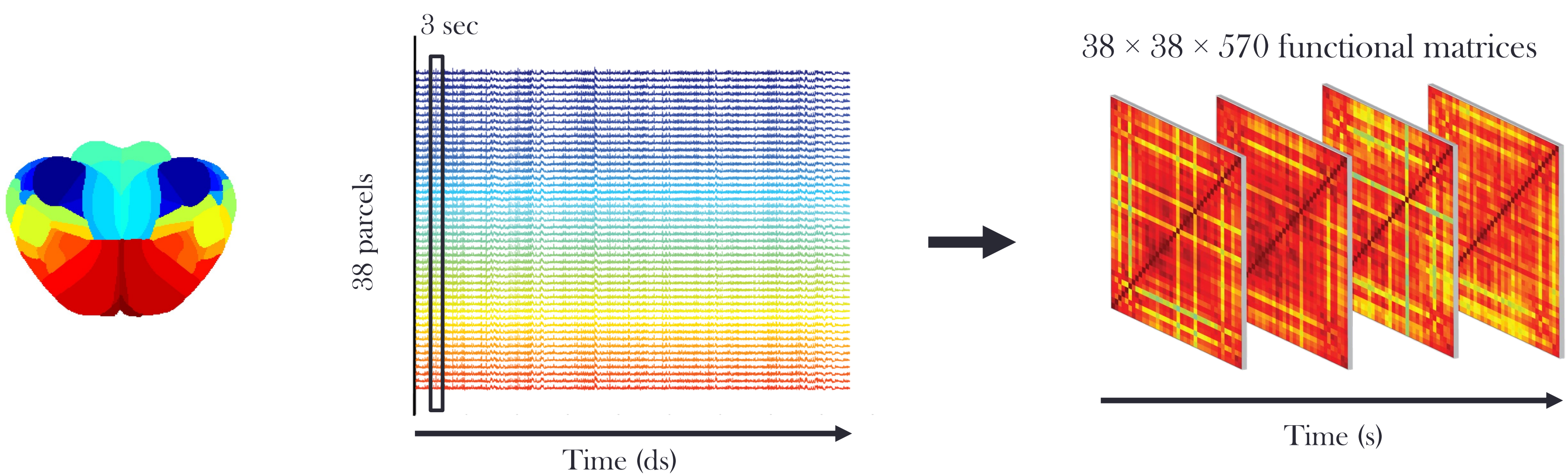
Applying NCT to multilayer networks



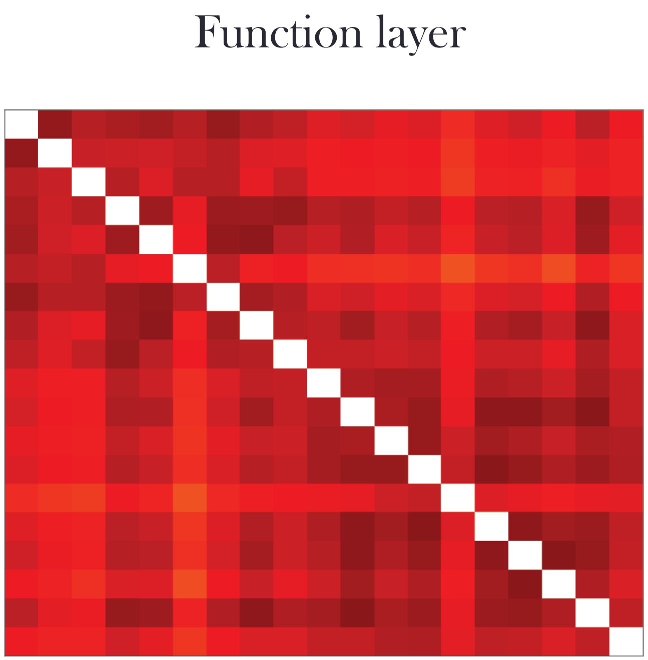


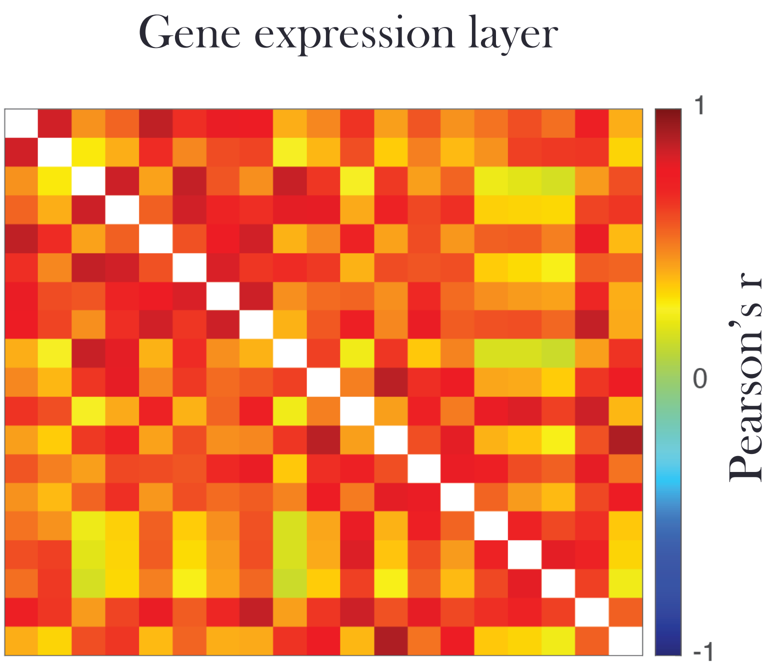
Srivastava et al. (2021) *arXiv*

Overview of functional data



Construction of the duplex network

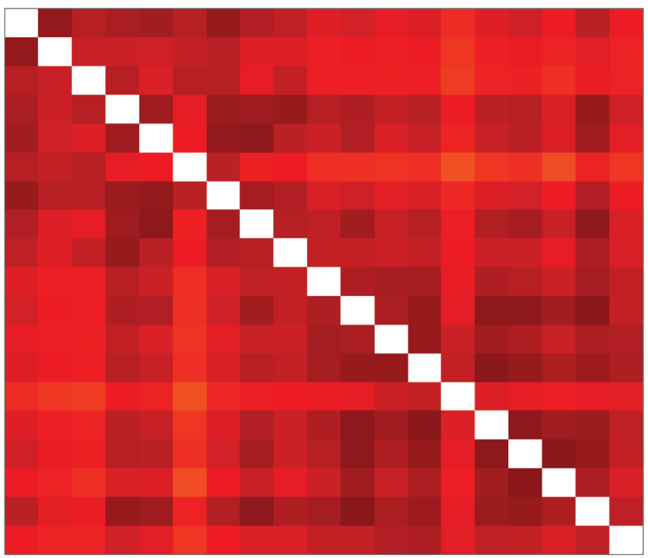




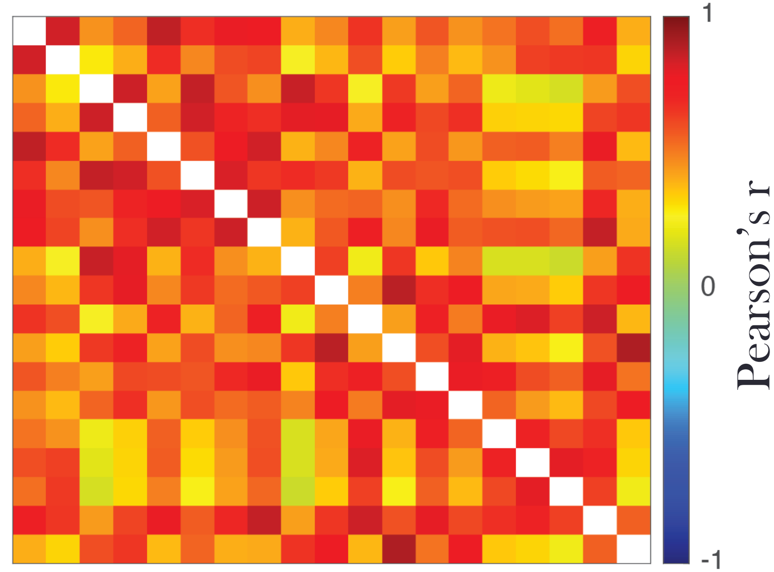
Interregional correlations across ~7,000 genes

Construction of the duplex network

Function layer



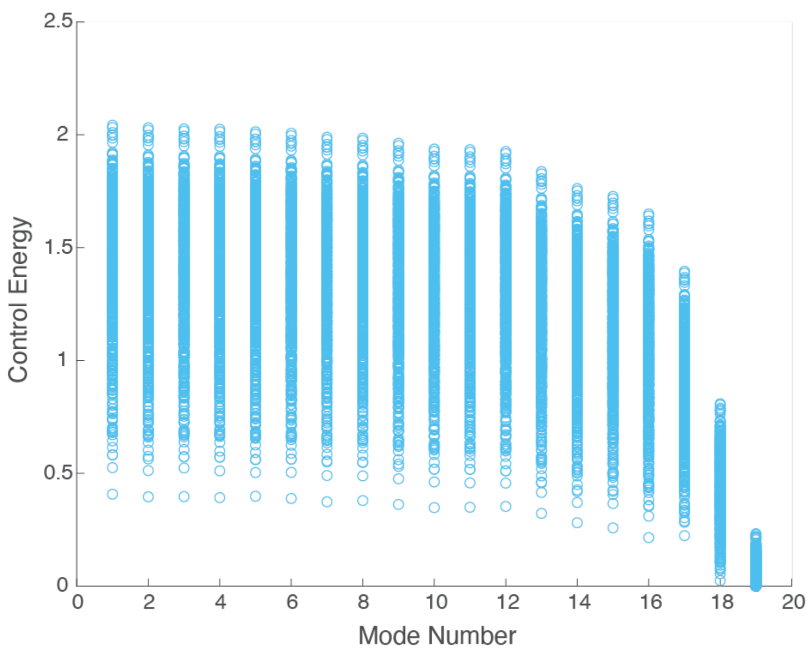
Gene expression layer



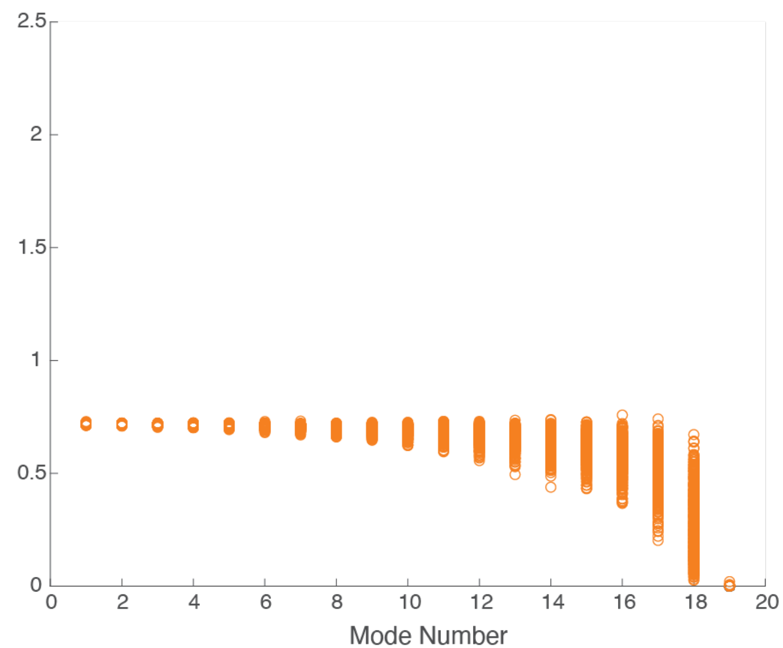
Into which layer is it more energetically favorable to give control input?

Duplex network control in mouse

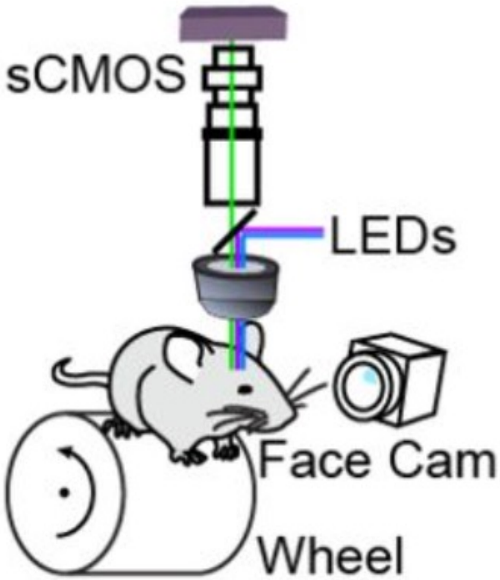
Control spectra
Function to gene:



Gene to function:



Duplex network control in mouse



Pupil size

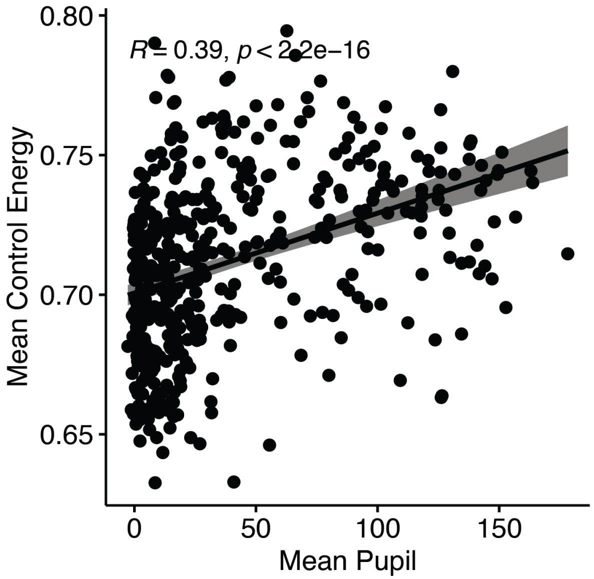
Facial movement

Running speed

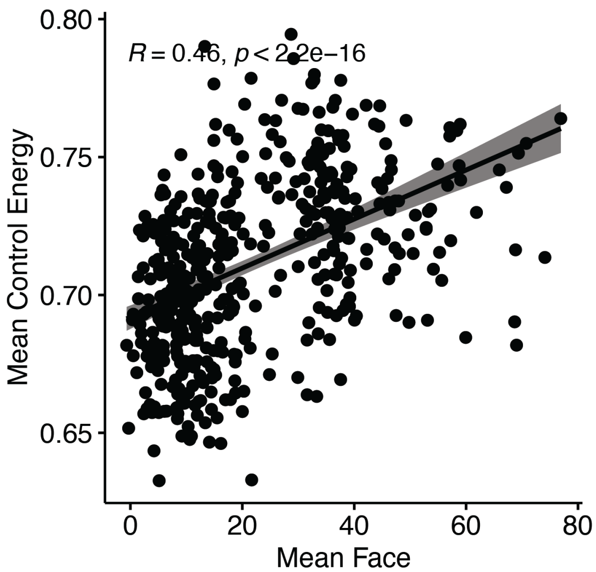
Duplex network control in mouse

Hypothesis: Less control input is required for the functional layer to control the gene expression layer during rest as compared to active states

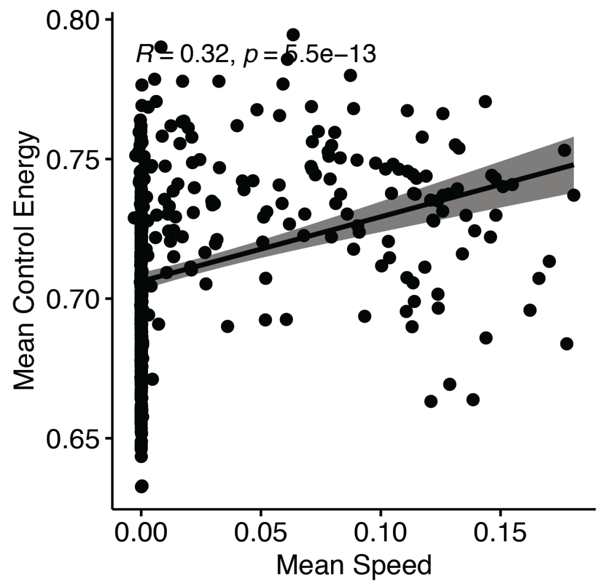
Pupil size



Facial movement



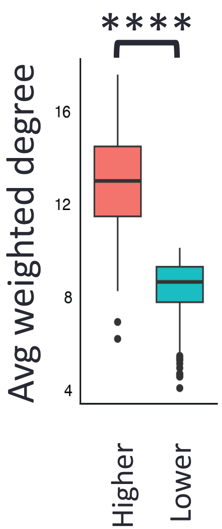
Running speed

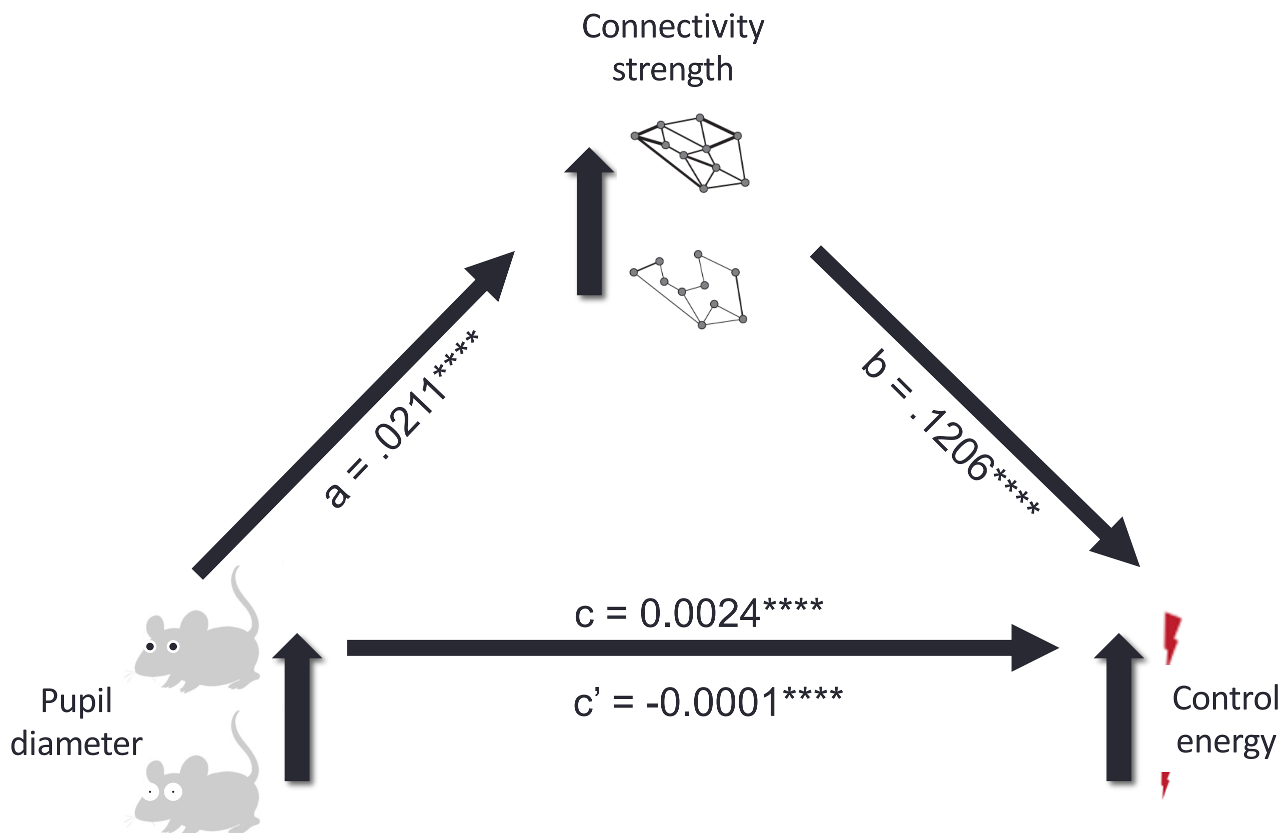


Complex Systems

Linking duplex network control with behavioral states

Relative cost of function to gene control:





Open questions

- How can we examine changes in gene expression across time, and their relation to changes in neural activity?
- Which genes matter?

And more…

Network control theory protocol

Cold Spring Harbor Laboratory

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Confirmatory Results

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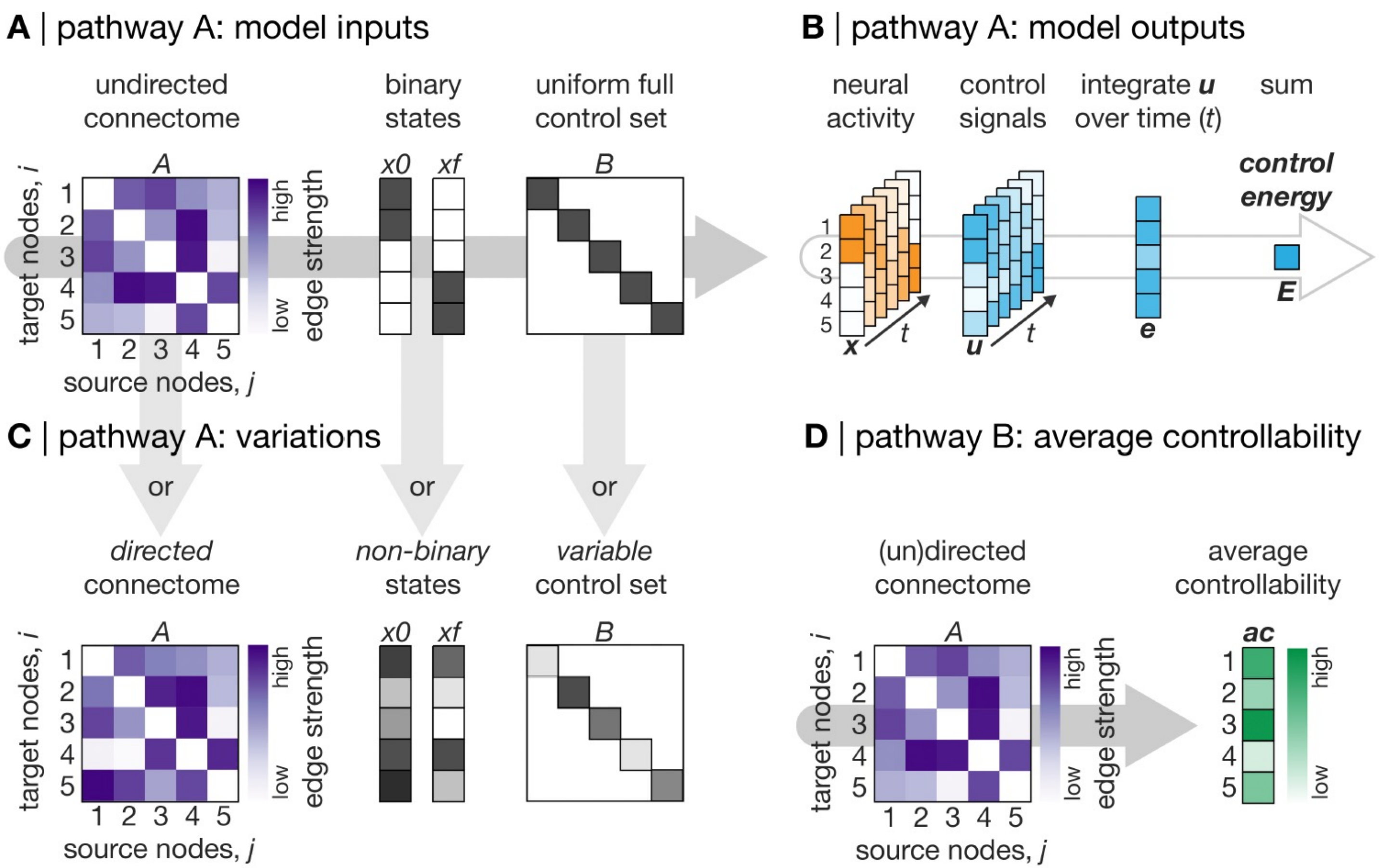
Using network control theory to study the dynamics of the structural connectome

Linden Parkes, Jason Z. Kim, Jennifer Stiso, Julia K. Brynildsen, Matthew Cieslak, Sydney Covitz, Raquel E. Gur, Ruben C. Gur, Fabio Pasqualetti, Russell T. Shinohara, Dale Zhou, Theodore D. Satterthwaite, Dani S. Bassett

doi: https://doi.org/10.1101/2023.08.23.554519

Network control theory protocol



Parkes*, Kim* et al. (2023) *bioRxiv*

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Aligning Science Across Parkinson's