



Title: ...

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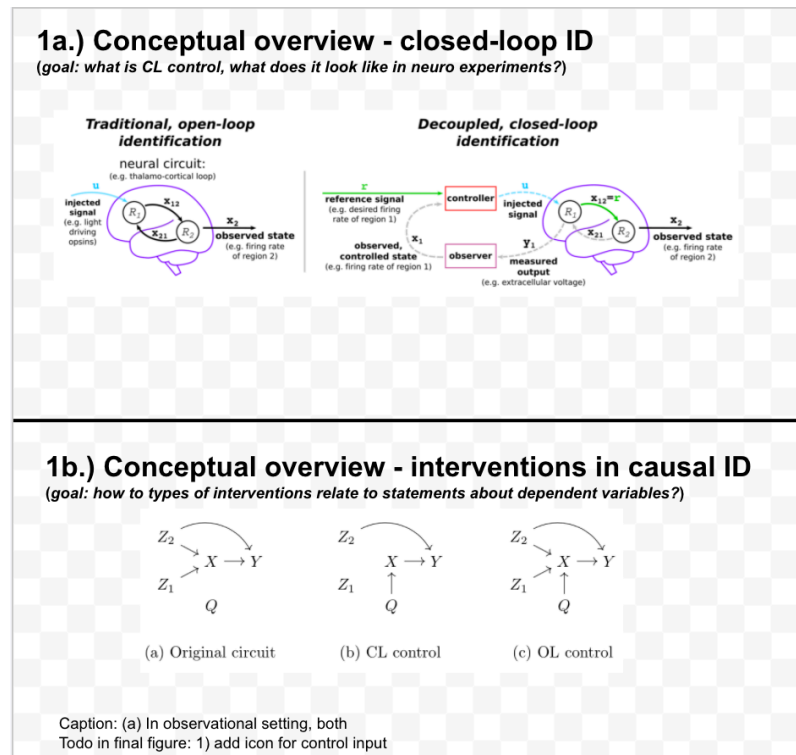
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Abstract

The necessity of intervention in inferring cause has long been understood in neuroscience. Recent work has highlighted the limitations of passive observation and single-site lesion studies in accurately recovering causal circuit structure. The advent of optogenetics has facilitated increasingly precise forms of intervention including closed-loop control which may help eliminate confounding influences. However, it is not yet clear how best to apply closed-loop control to leverage this increased inferential power. In this paper, we use tools from causal inference, control theory, and neuroscience to show when and how closed-loop interventions can more effectively reveal causal relationships. We also examine the performance of standard network inference procedures in simulated spiking networks under passive, open-loop and closed-loop conditions. We demonstrate a unique capacity of feedback control to distinguish competing circuit hypotheses by disrupting connections which would otherwise result in equivalent patterns of correlation. Our results build toward a practical framework to improve design of neuroscience experiments to answer causal questions about neural circuits.

Introduction

Estimating causal interactions in the brain



https://github.com/awillats/clinc/blob/main/figures/core_figure_sketches/figure1_sketch.png

@ import "section_content/background_causal_network_id.md"

Interventions in neuroscience & causal inference

@ import "section_content/background_intervention_neuro.md"

@ import "section_content/background_intervention_causal_inf.md"

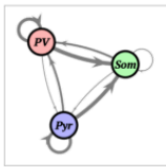
Representations & reachability

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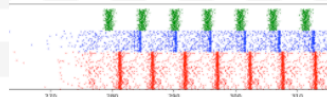
2a.) Methods overview

(goal: introduce language of graphs, adj matrices, dynamical systems, interventions)

A. Circuit view



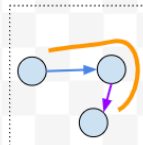
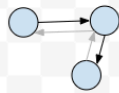
Data



Point 1.)
"All of these are related"

B. Dynamical systems view

$$\begin{bmatrix} \dot{x}_A \\ \dot{x}_B \\ \dot{x}_C \end{bmatrix} = \begin{bmatrix} w_{AA} & w_{AB} & w_{AC} \\ w_{BA} & w_{BB} & w_{BC} \\ w_{CA} & w_{CB} & w_{CC} \end{bmatrix} \begin{bmatrix} x_A \\ x_B \\ x_C \end{bmatrix}$$

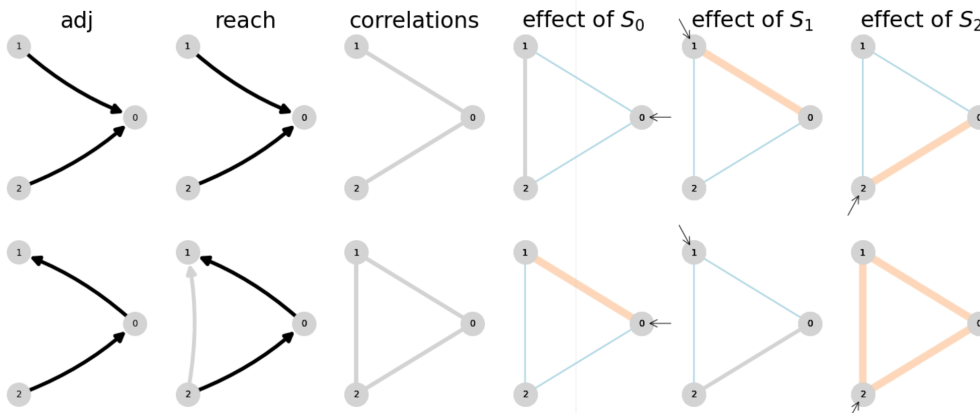


Point 2a.) From the adjacency matrix view we can derive reachability measures (which will be useful later)

C. Adjacency matrix view

https://github.com/awillats/clinc/blob/main/figures/core_figure_sketches/figure2_sketch.png

Interventions



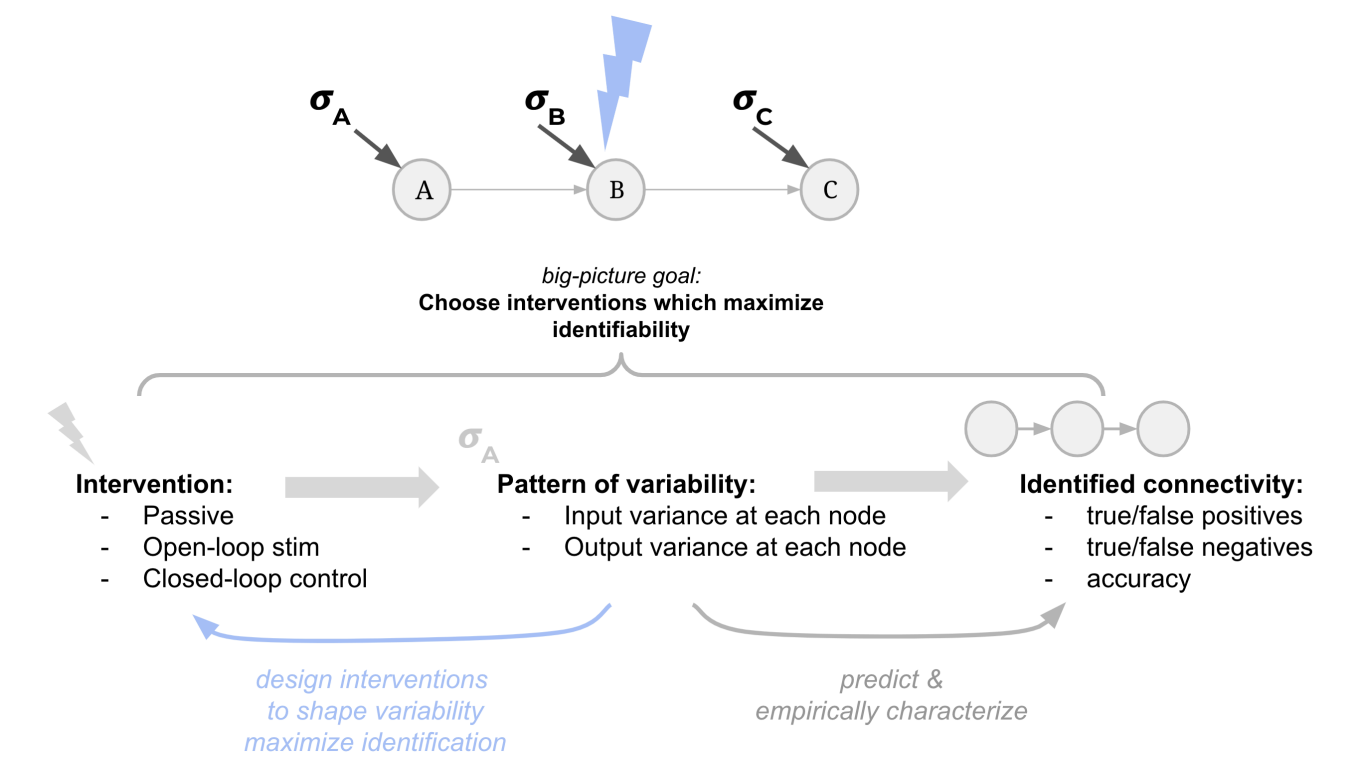
https://github.com/awillats/clinc/blob/main/figures/misc_figure_sketches/two_circuit_case_study_mockup.png

Figure DEMO: Applying CLINC to distinguish a pair of circuits

Theory / Prediction

Computing reachability (theory)

Predicting correlation structure (theory)



https://github.com/awillats/clinc/blob/main/figures/misc_figure_sketches/intervention_identifiability_concept.png

Simulation

Network simulations (simulation)

@adam

Implementing interventions (simulation)

@adam

Extracting circuit estimates (empirical)

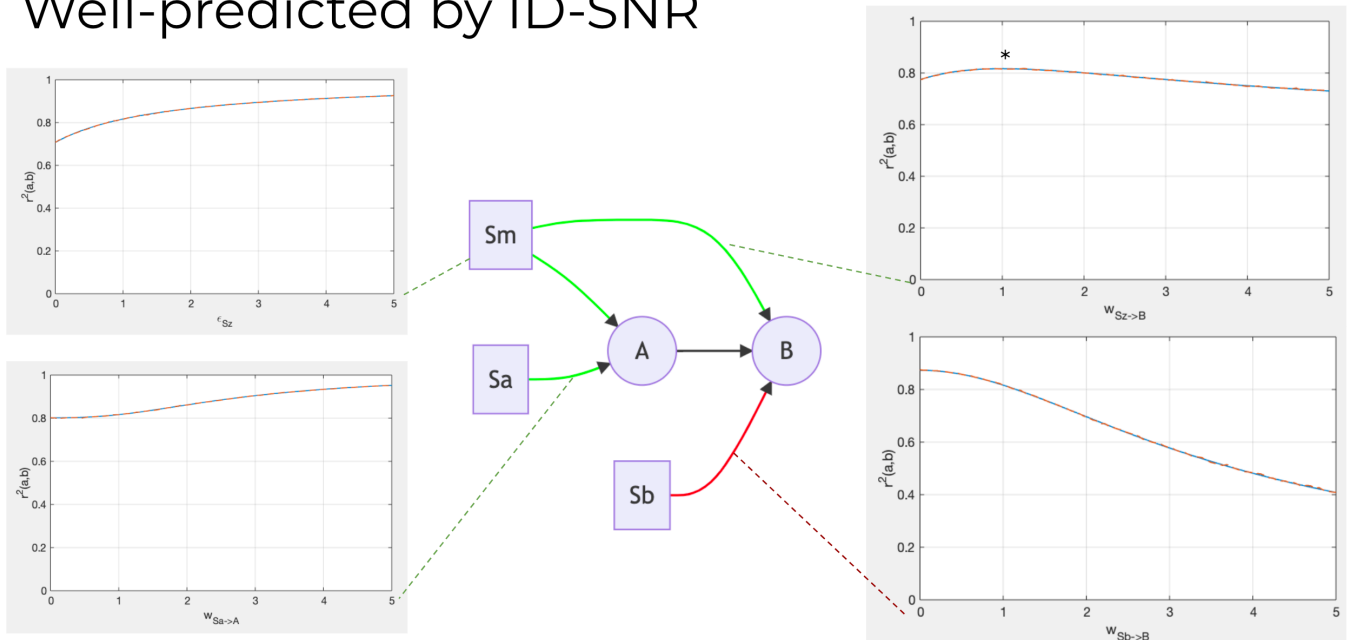
Information-theoretic measures of hypothesis ambiguity

Results

Impact of node, network parameters on estimation performance

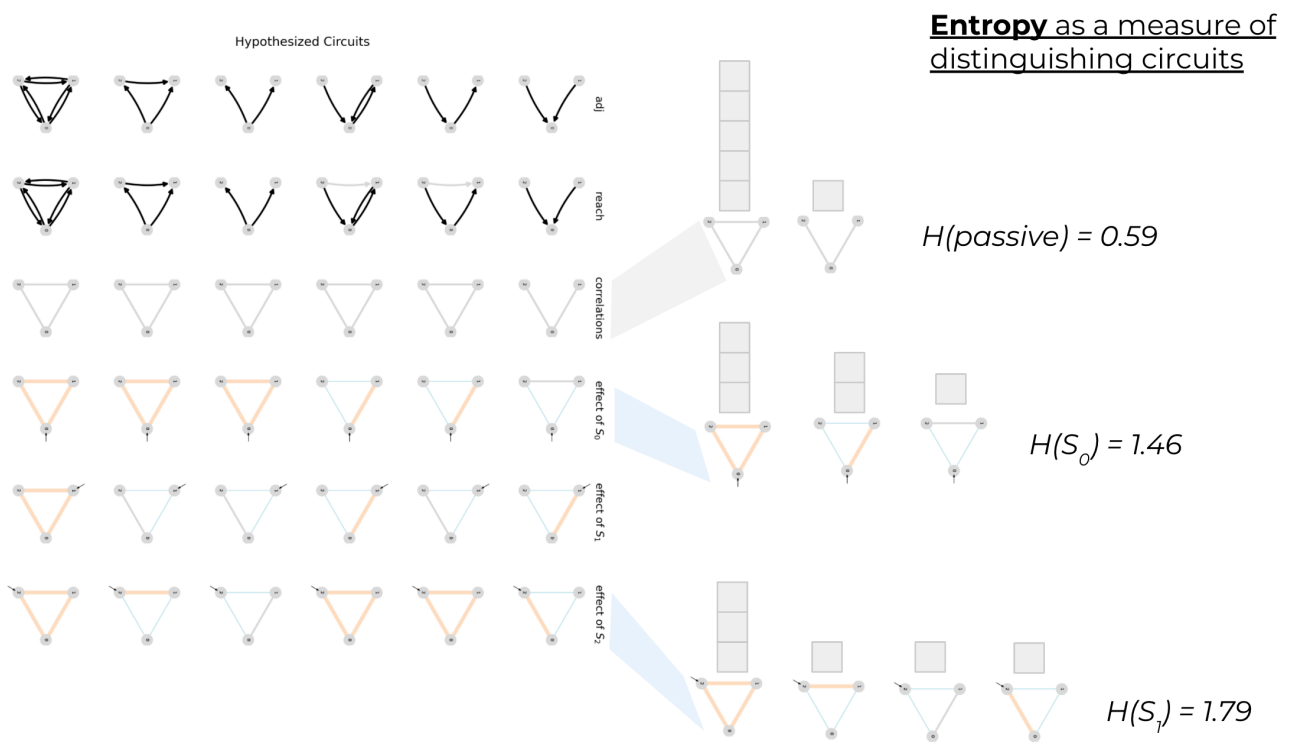
Quantitative impact of parameters

Well-predicted by ID-SNR



https://github.com/awillats/clinc/blob/main/figures/misc_figure_sketches/quant_r2_prediction_common.png

Impact of intervention & circuit structure



https://github.com/awillats/clinc/blob/main/figures/misc_figure_sketches/circuit_intervention_entropy_mockup.png

Discussion

References

Supplement