TRANSLATING LITERATURE INTO CAUSAL GRAPHS

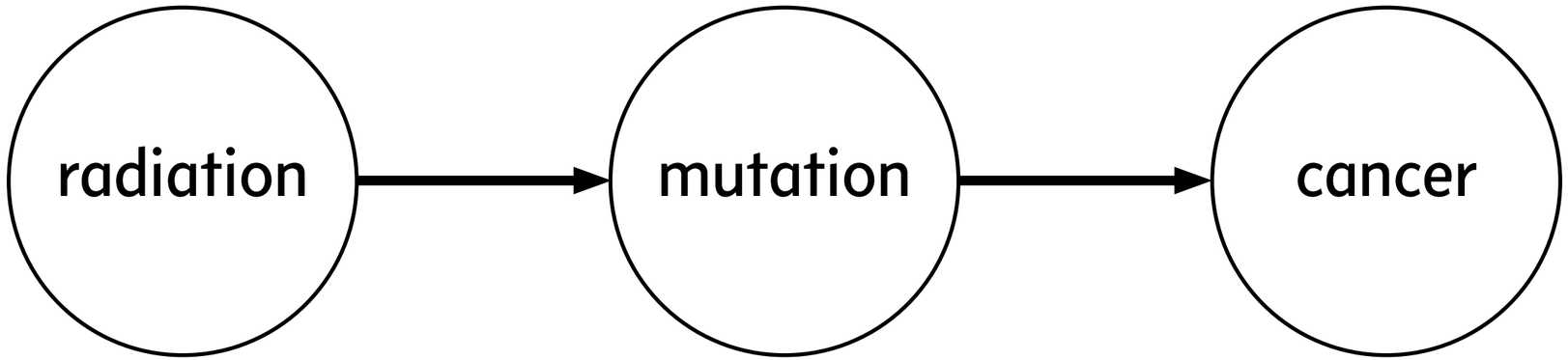
TOWARD AUTOMATED EXPERIMENT SELECTION

NICHOLAS J. MATIASZ

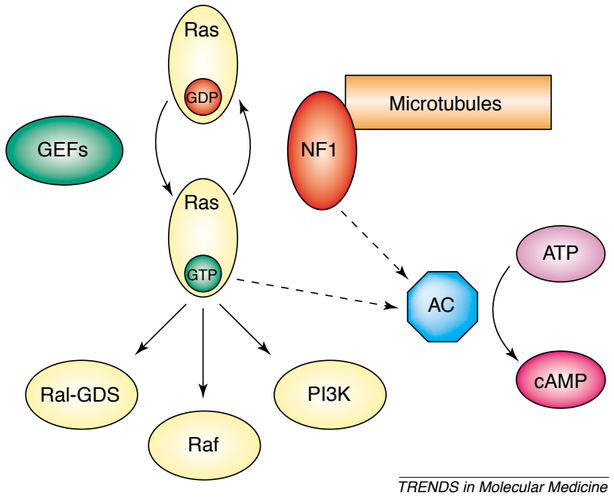
JUSTIN WOOD, WEI WANG, ALCINO J. SILVA, WILLIAM HSU

UCLA

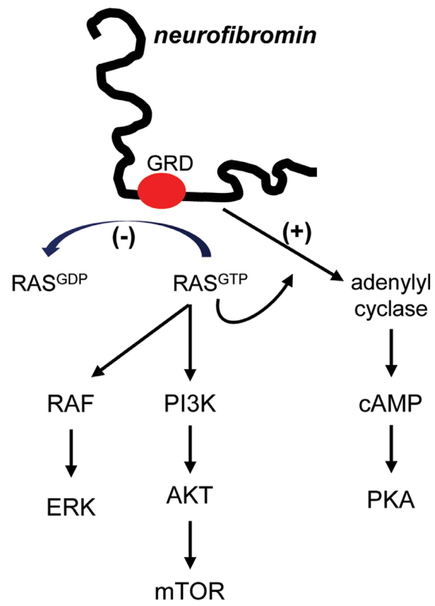
Causal graph



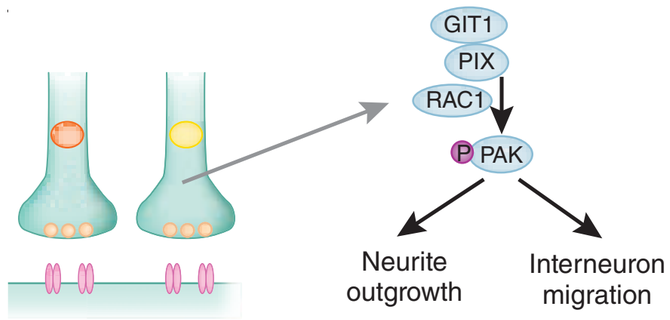
Biological pathway diagrams resemble causal graphs



[1]



[2]



[3]

Biological pathway diagrams can't be stitched together

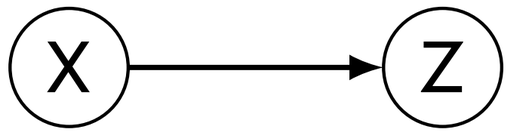


diagram 1

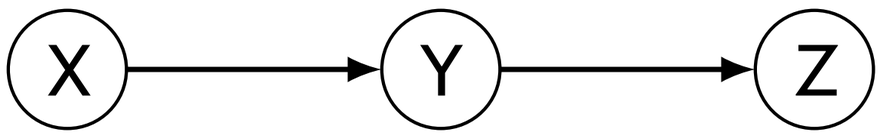
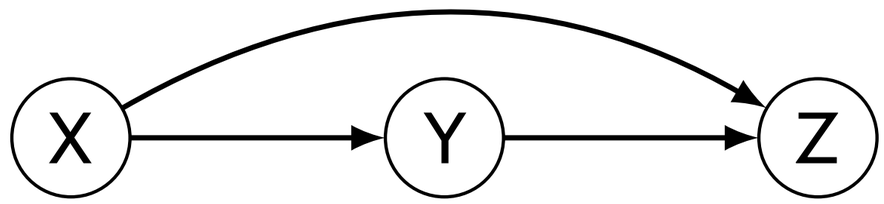
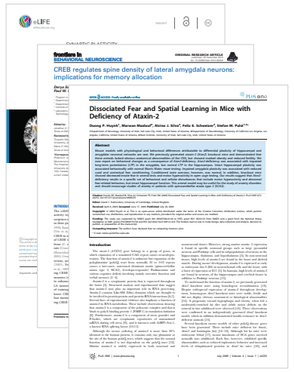


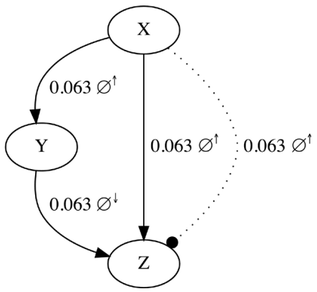
diagram 2

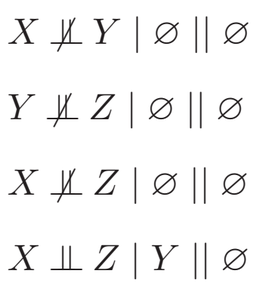


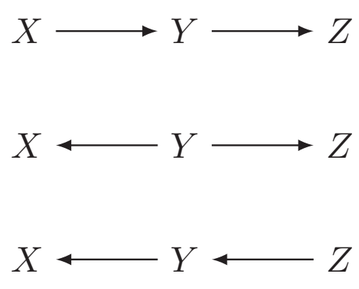
stitched diagram

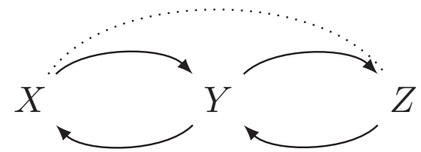
A pipeline for stitching empirical results











studies in literature

research map

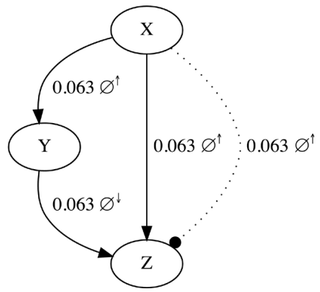
causal constraints

causal graphs

degrees of freedom

A pipeline for stitching empirical results

studies in literature



research map

$X \not\perp\!\!\!\perp Y \mid \varnothing \,||\, \varnothing$

$Y \not\perp\!\!\!\perp Z \mid \varnothing \,||\, \varnothing$

$X \not\perp\!\!\!\perp Z \mid \varnothing \,||\, \varnothing$

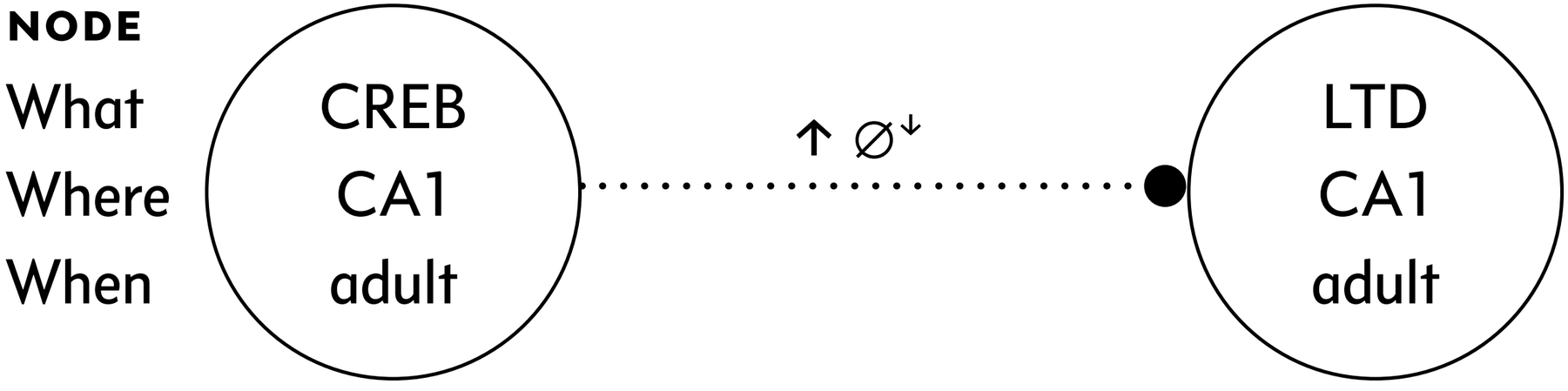
$X \perp\!\!\!\perp Z \mid Y \,||\, \varnothing$

causal constraints

causal graphs

degrees of freedom

The research map representation



STUDY DESIGN

Intervention

- Positive ↑
- Negative ↓

Observation

- Positive ∅↑
- Negative ∅↓

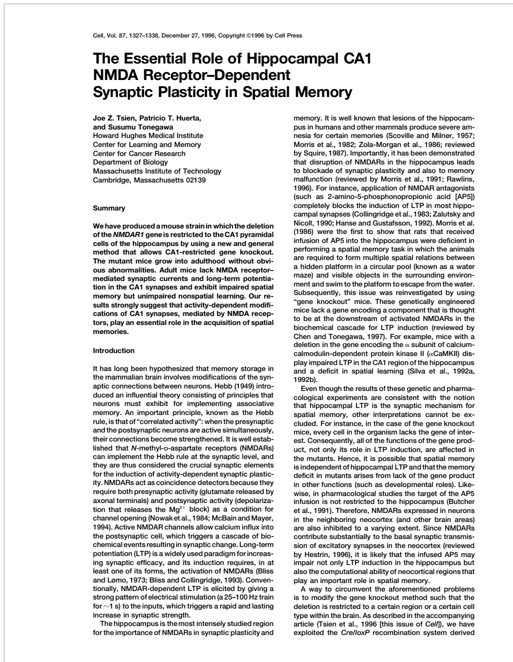
RELATION

- Excitatory →
- Inhibitory ⊣
- None ····●

RESULT

- Increase +
- No change 0
- Decrease –

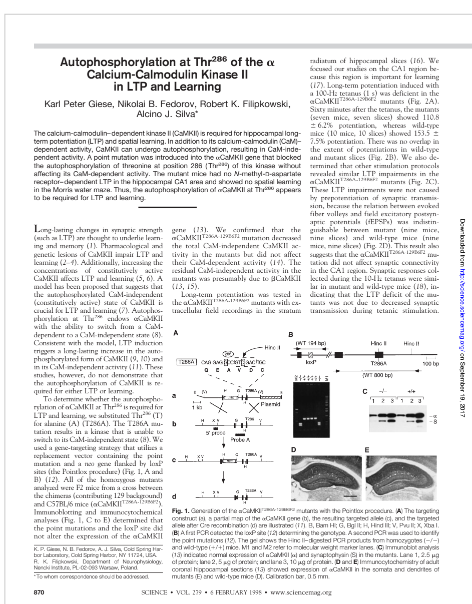
[4]


Cell, Vol. 87, 1327–1338, December 27, 1996, Copyright ©1996 by Cell Press

The Essential Role of Hippocampal CA1 NMDA Receptor–Dependent Synaptic Plasticity in Spatial Memory

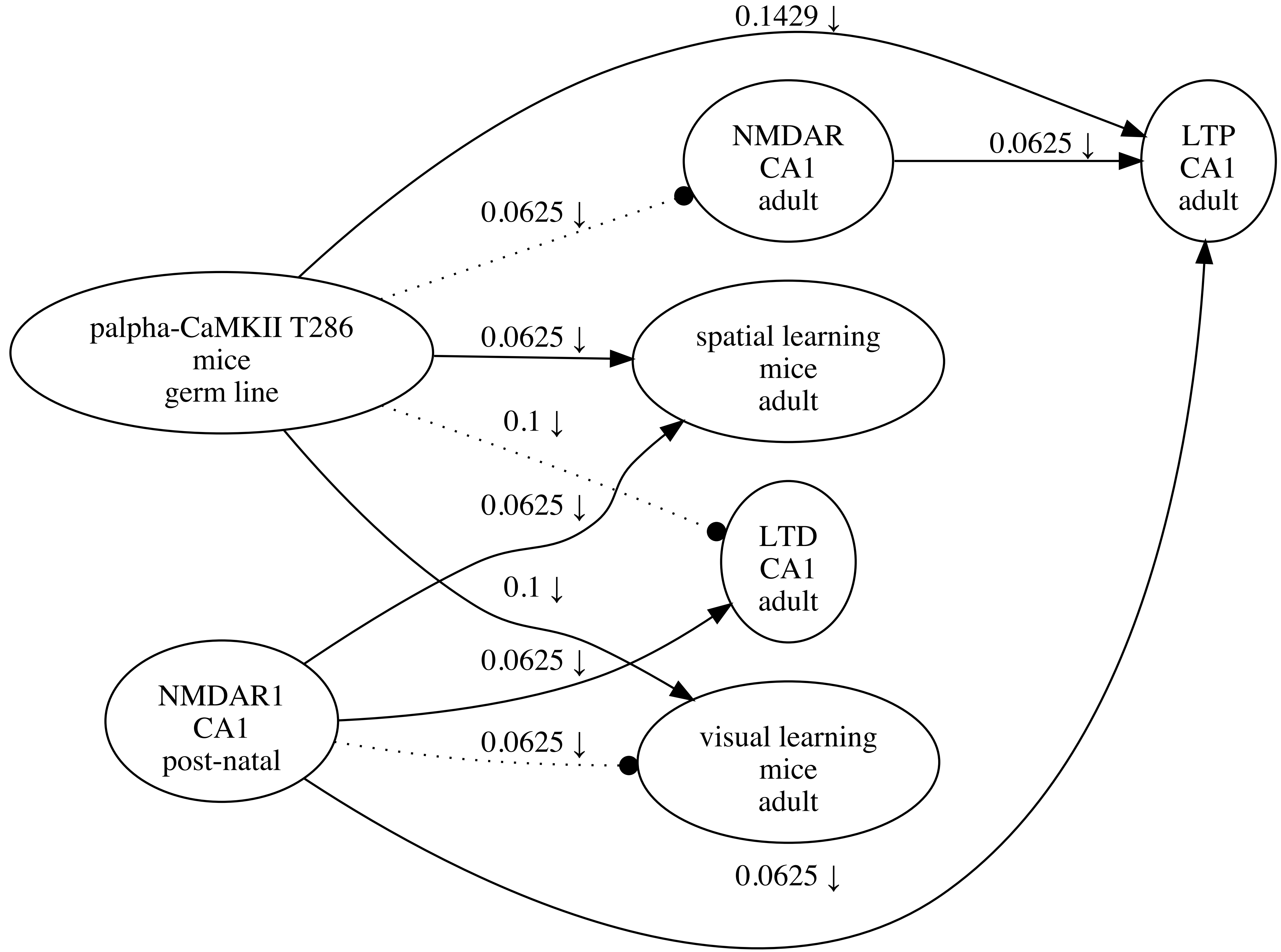
Joe Z. Tsien, Patricio T. Huerta, and Susumu Tonegawa

[5]


Autophosphorylation at Thr286 of the α Calcium-Calmodulin Kinase II in LTP and Learning

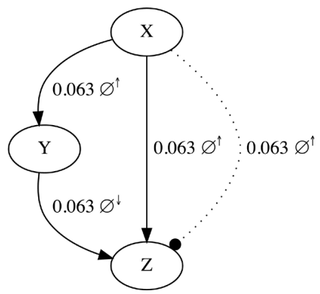
Karl Peter Giese, Nikolai B. Fedorov, Robert K. Filipkowski, Alcino J. Silva*

studies in literature



research map

A pipeline for stitching empirical results



$$X \not\perp\!\!\!\perp Y \mid \varnothing \mid\mid \varnothing$$

$$Y \not\perp\!\!\!\perp Z \mid \varnothing \mid\mid \varnothing$$

$$X \not\perp\!\!\!\perp Z \mid \varnothing \mid\mid \varnothing$$

$$X \perp\!\!\!\perp Z \mid Y \mid\mid \varnothing$$

studies in literature

research map

causal constraints

causal graphs

degrees of freedom

Constraint on causal structure

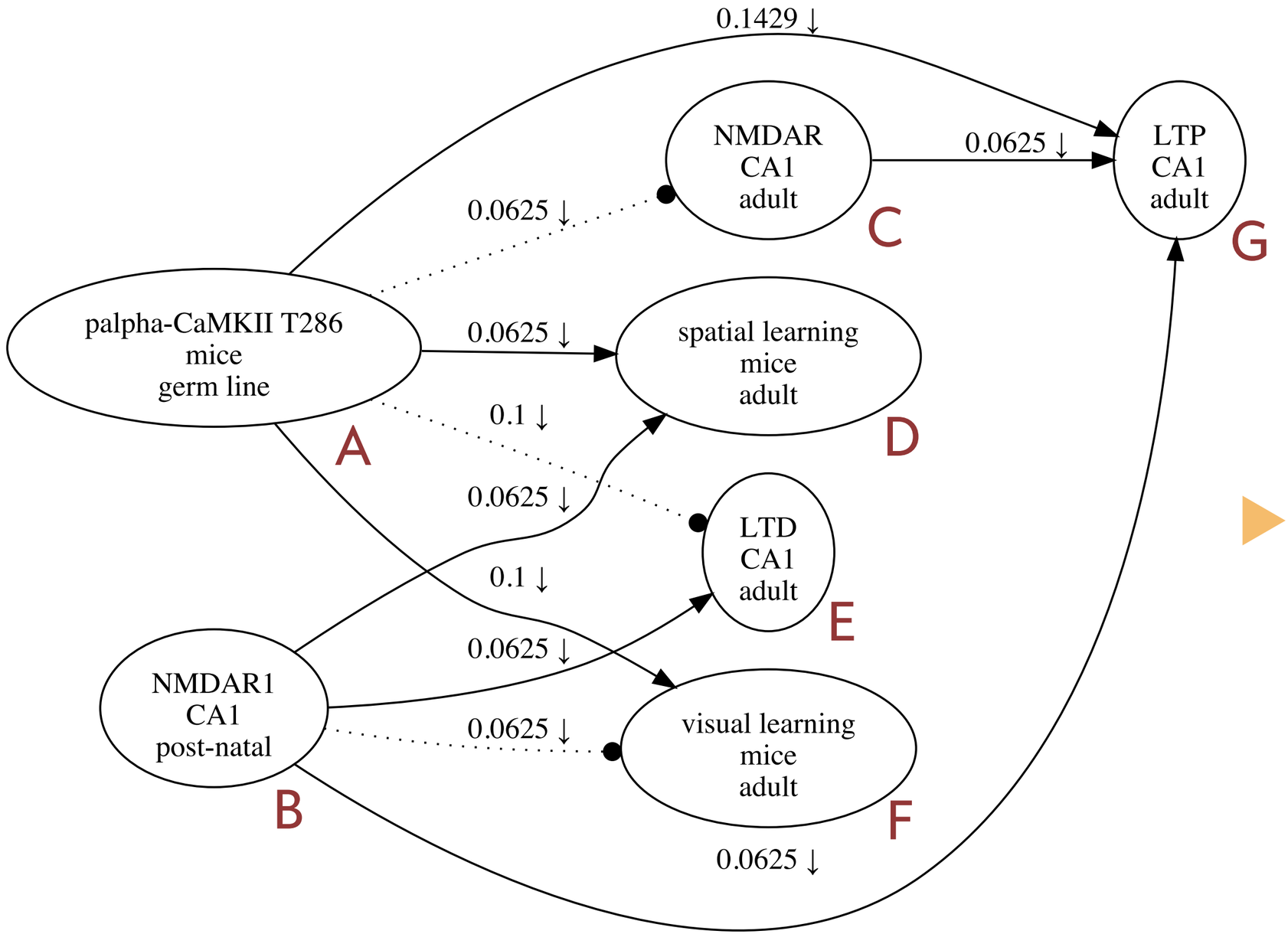
$X \perp\!\!\!\perp Y \mid \mathbf{C} \,||\, \mathbf{J}$

X and Y are **independent**, conditioned on set **C**, intervening on set **J**

$X \not\perp\!\!\!\perp Y \mid \mathbf{C} \,||\, \mathbf{J}$

X and Y are **dependent**, conditioned on set **C**, intervening on set **J**

C and **J** can be the empty set ($\varnothing$)



research map

$$
\begin{array}{lllll}
A & \not\perp\!\!\!\perp & G & \mid \varnothing \mid\mid & A \\
A & \perp\!\!\!\perp & C & \mid \varnothing \mid\mid & A \\
A & \not\perp\!\!\!\perp & D & \mid \varnothing \mid\mid & A \\
A & \perp\!\!\!\perp & E & \mid \varnothing \mid\mid & A \\
A & \not\perp\!\!\!\perp & F & \mid \varnothing \mid\mid & A \\
B & \not\perp\!\!\!\perp & D & \mid \varnothing \mid\mid & B \\
B & \not\perp\!\!\!\perp & E & \mid \varnothing \mid\mid & B \\
B & \perp\!\!\!\perp & F & \mid \varnothing \mid\mid & B \\
B & \not\perp\!\!\!\perp & G & \mid \varnothing \mid\mid & B \\
C & \not\perp\!\!\!\perp & G & \mid \varnothing \mid\mid & C
\end{array}
$$

causal
constraints

A pipeline for stitching empirical results

studies in literature

research map

$$X \not\perp\!\!\!\perp Y \mid \varnothing \,||\, \varnothing$$

$$Y \not\perp\!\!\!\perp Z \mid \varnothing \,||\, \varnothing$$

$$X \not\perp\!\!\!\perp Z \mid \varnothing \,||\, \varnothing$$

$$X \perp\!\!\!\perp Z \mid Y \,||\, \varnothing$$

causal constraints

$$X \longrightarrow Y \longrightarrow Z$$

$$X \longleftarrow Y \longrightarrow Z$$

$$X \longleftarrow Y \longleftarrow Z$$

causal graphs

degrees of freedom

Constraint-based Causal Discovery: Conflict Resolution with Answer Set Programming [6]

Antti Hyttinen and **Frederick Eberhardt**
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Pasadena, CA, USA

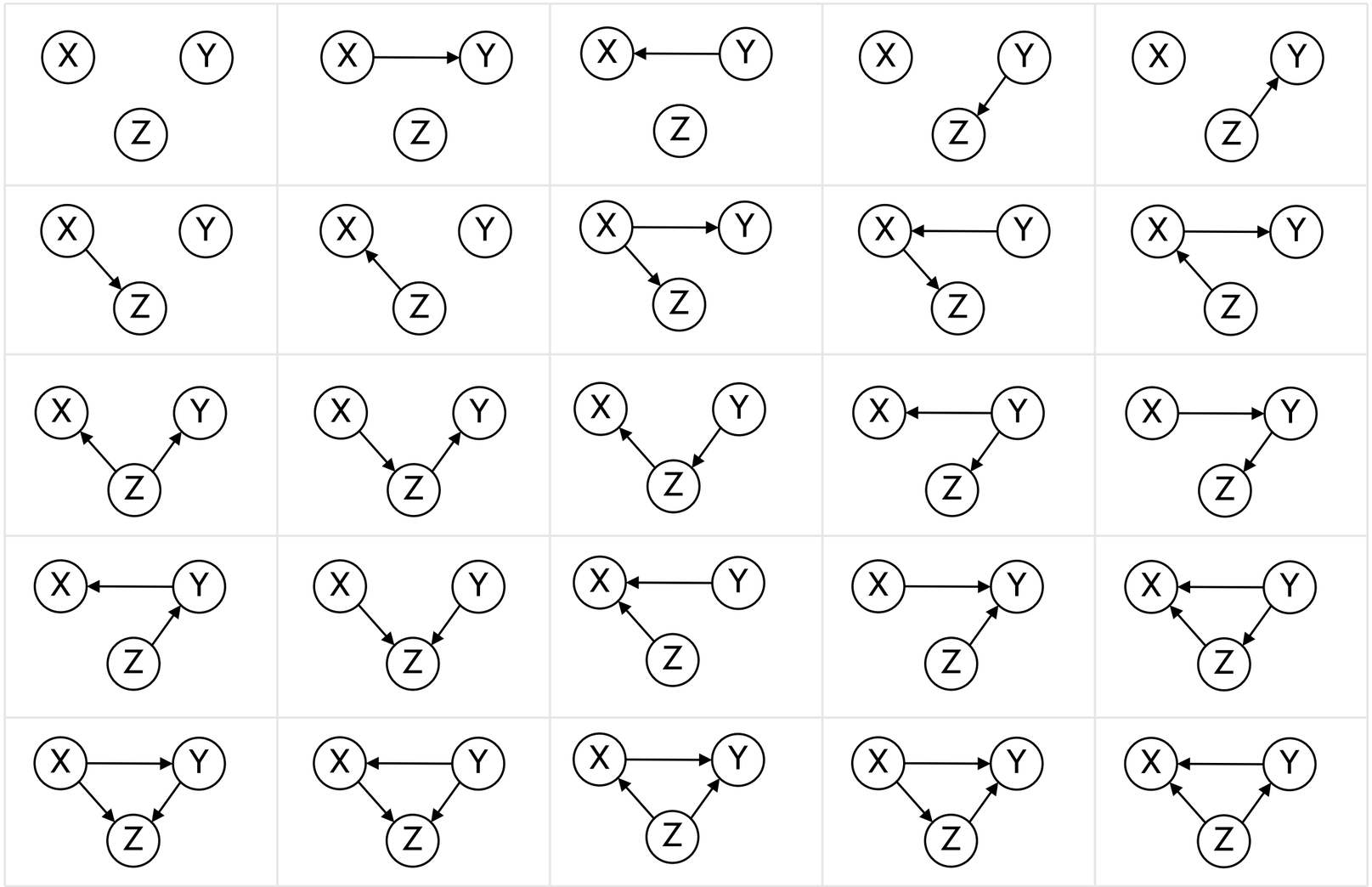
Matti Järvisalo
HIIT & Department of Computer Science
University of Helsinki, Finland

Abstract

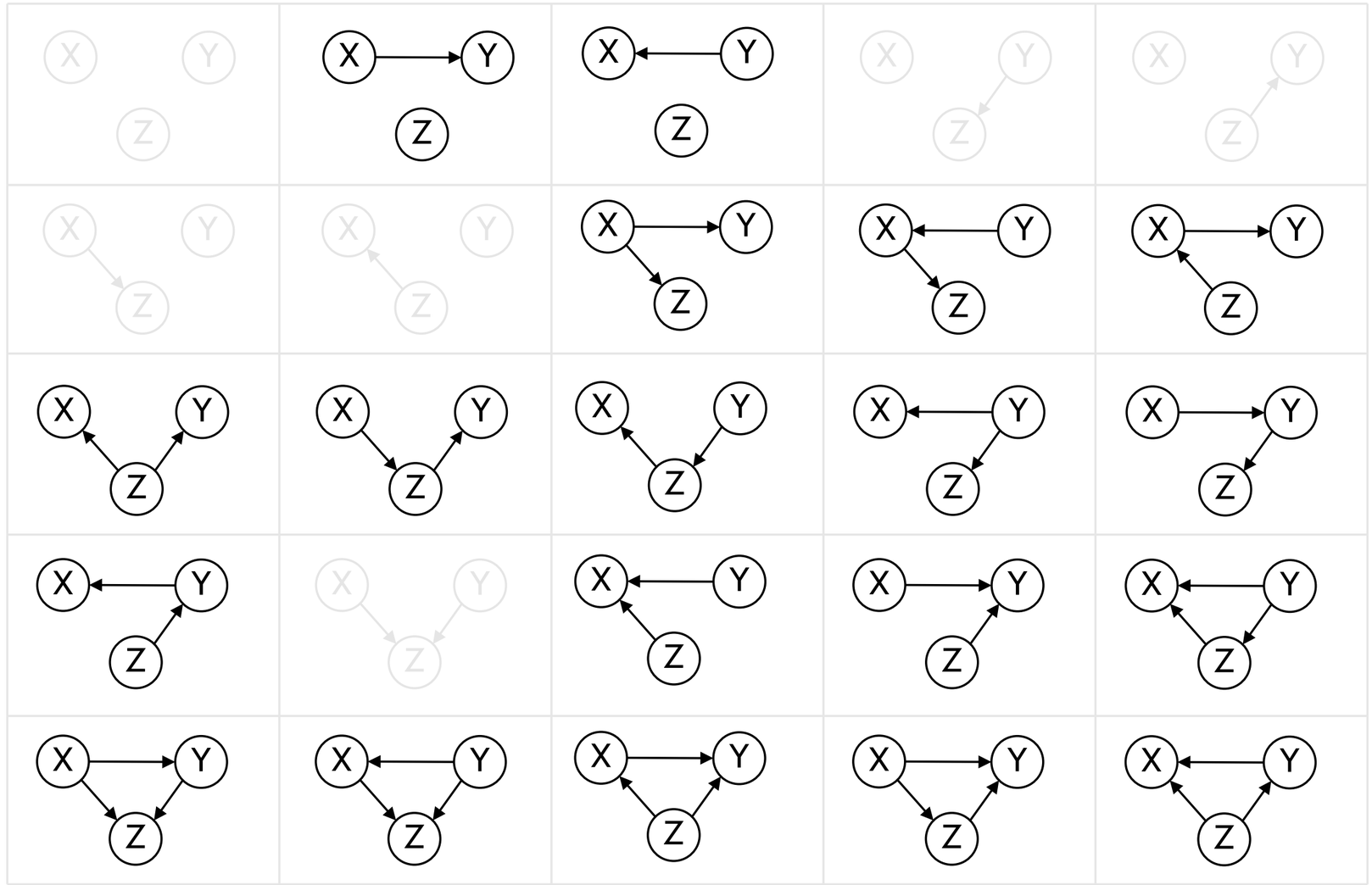
Recent approaches to causal discovery based on Boolean satisfiability solvers have opened new opportunities to consider search spaces for causal models with both feedback cycles and unmeasured confounders. However, the available methods have so far not been able to provide a principled account of how to handle conflicting constraints that arise from statistical variability. Here we present a new approach that preserves the versatility of Boolean constraint solving *and* attains a high accuracy despite the presence of statisti-

faithfulness (Spirtes et al., 1993). Unlike many other approaches, these constraint-based causal discovery methods can allow for the presence of latent confounders, feedback cycles and the utilisation of several (partially overlapping) observational or experimental data sets.

Even without experimentation (or additional assumptions, such as time order), and despite the generality of the model space, constraint-based methods can infer some causal orientations on the basis of *v-structures* (unshielded colliders). A v-structure in a graph is a triple of variables, such as $\langle x, z, y \rangle$ in Figure 1, where z is a common child of x and y, but x and y are non-adjacent in the graph. V-structures can be identified because of the specific (in)dependence rela-

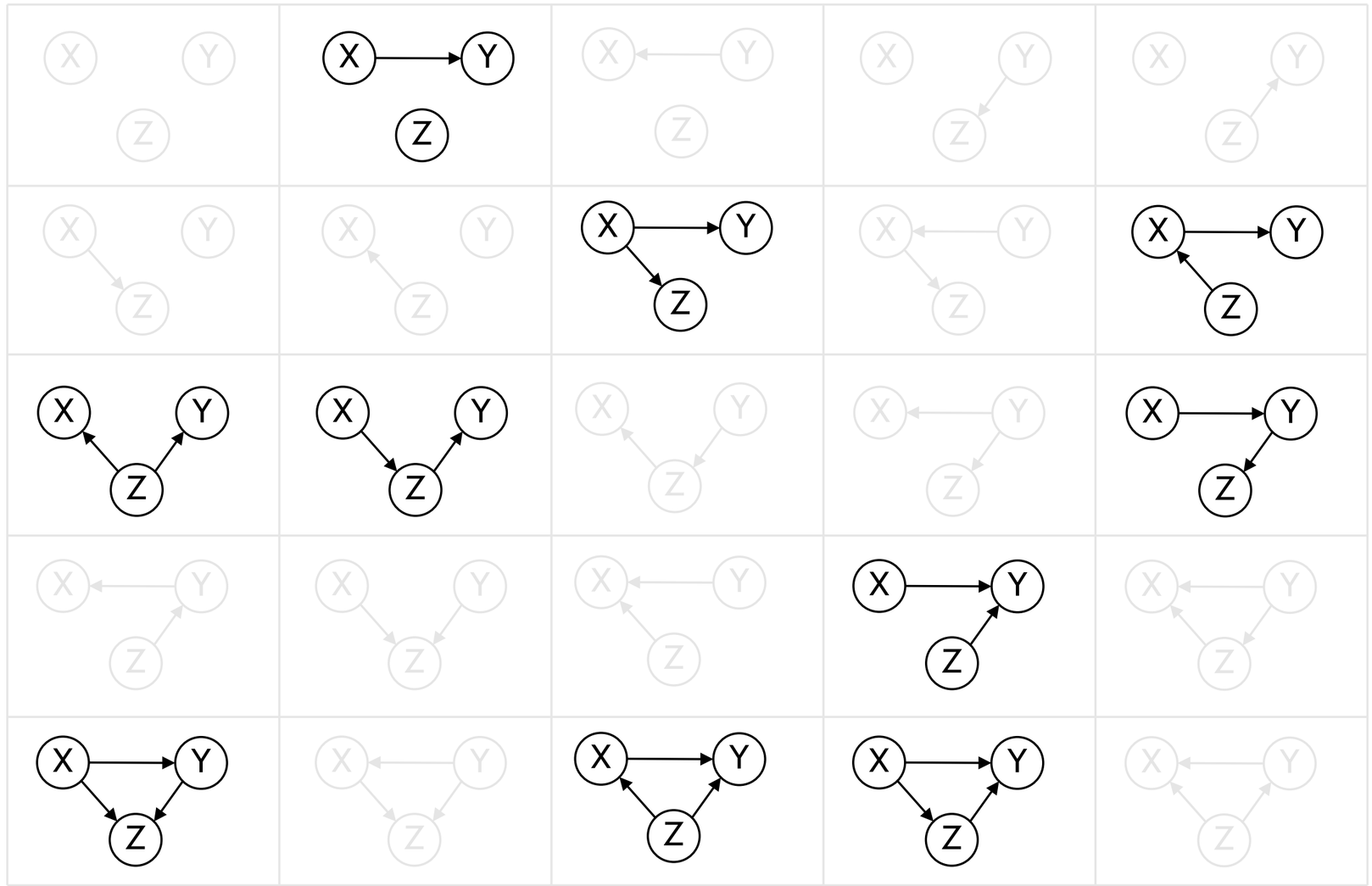

X
Y
Z

$$X \not\perp\!\!\!\perp Y \mid \varnothing \mid\mid \varnothing$$



$$X \not\perp\!\!\!\perp Y \mid \varnothing \;||\; \varnothing$$

$$X \perp\!\!\!\perp Y \mid \varnothing \;||\; Y$$



$X \not\perp\!\!\!\perp Y \mid \varnothing \mid\mid \varnothing$

$X \perp\!\!\!\perp Y \mid \varnothing \mid\mid Y$

…

…

…

…

…

…

$X \not\perp\!\!\!\perp Y \mid \varnothing \mid\mid \varnothing$

$X \perp\!\!\!\perp Y \mid \varnothing \mid\mid Y$

…

…

…

…

With conflicting constraints, we minimize the summed weight of unsatisfied constraints.

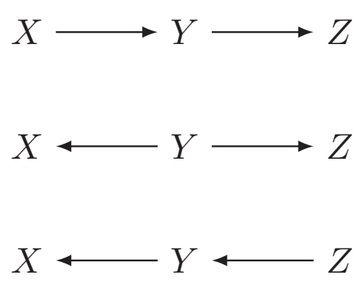
$$G^* \in \operatorname*{argmin}_{G \in \mathcal{G}} \sum_{k \in \mathbf{K}: G \not\models k} w(k) \quad [6]$$

A pipeline for stitching empirical results

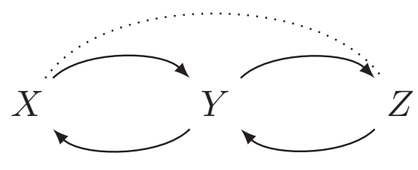
studies in literature

research map

causal constraints



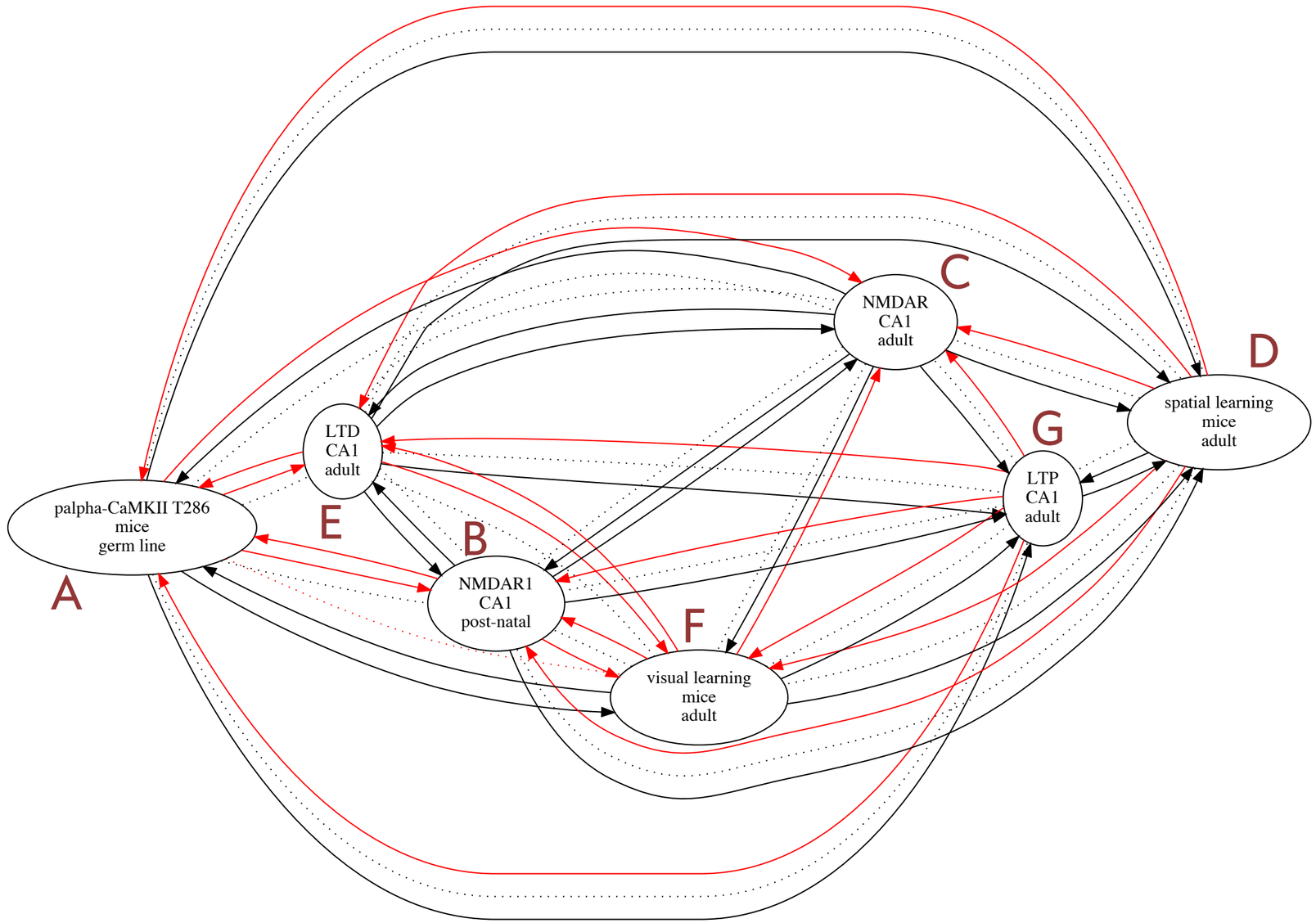
causal graphs



degrees of freedom

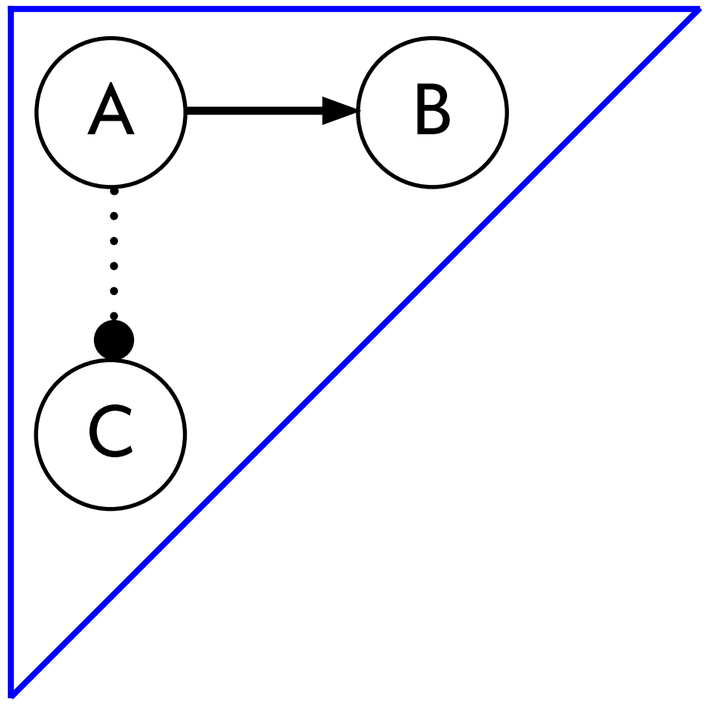
$$A \not\perp G \mid \varnothing \mid\mid A$$
$$A \perp\!\!\!\perp C \mid \varnothing \mid\mid A$$
$$A \not\perp D \mid \varnothing \mid\mid A$$
$$A \perp\!\!\!\perp E \mid \varnothing \mid\mid A$$
$$A \not\perp F \mid \varnothing \mid\mid A$$
$$B \not\perp D \mid \varnothing \mid\mid B$$
$$B \not\perp E \mid \varnothing \mid\mid B$$
$$B \perp\!\!\!\perp F \mid \varnothing \mid\mid B$$
$$B \not\perp G \mid \varnothing \mid\mid B$$
$$C \not\perp G \mid \varnothing \mid\mid C$$

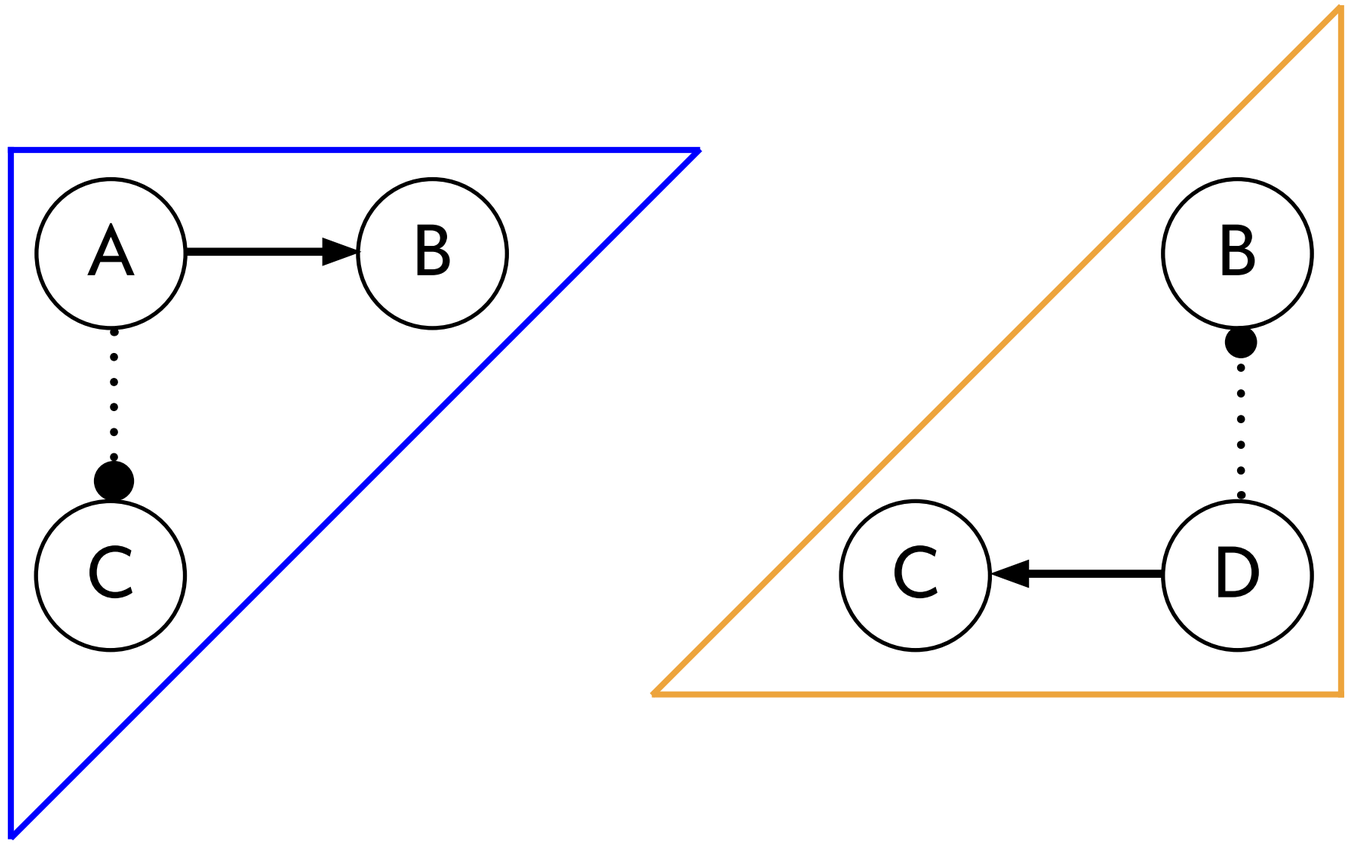
edge(A,B)?

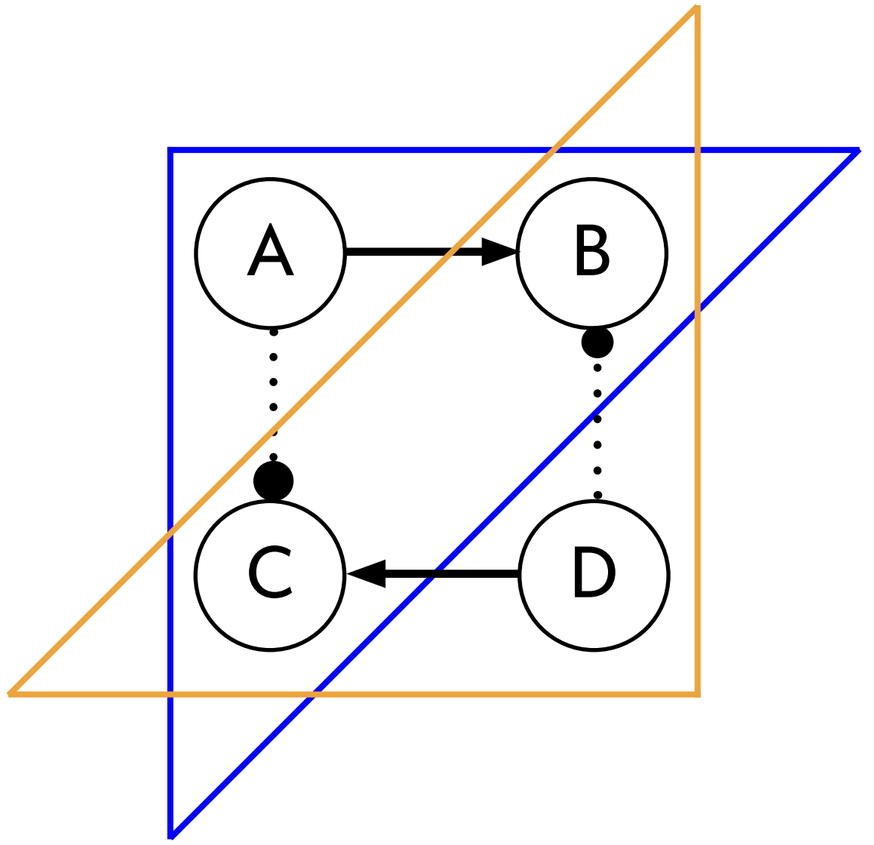


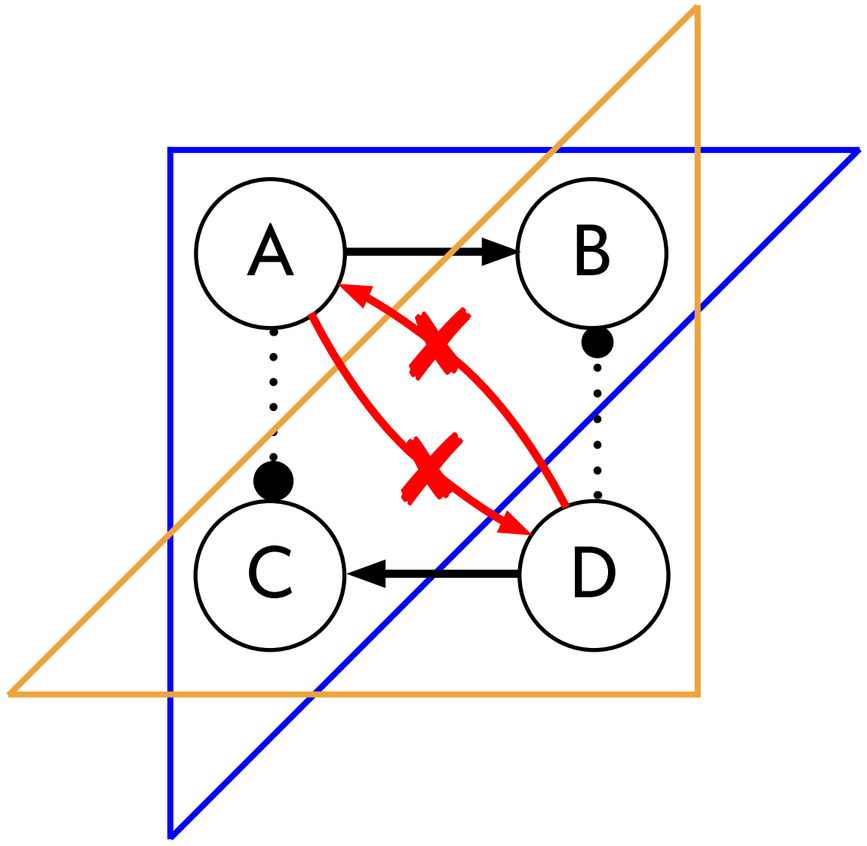
possible

ruled-out

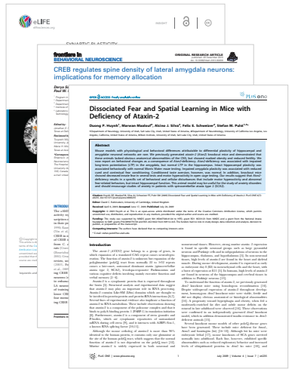

A
B
C

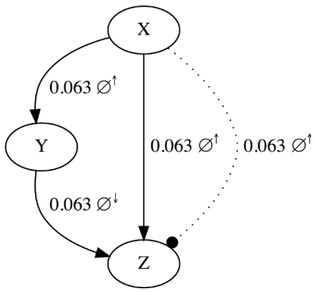

A
B
C
B
C
D

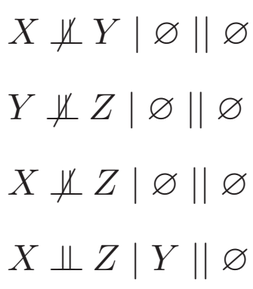

A
B
C
D

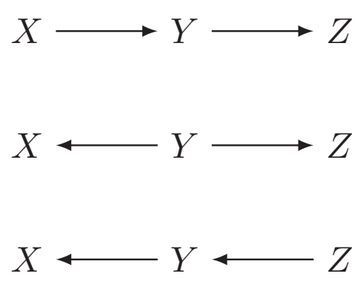

A
B
C
D

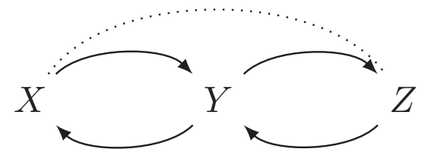
A pipeline for stitching empirical results











studies in literature

research map

causal constraints

causal graphs

degrees of freedom

[1] R. M. Costa & A. J. Silva (2003). Mouse models of neurofibromatosis type I: bridging the GAP. In *TRENDS in Molecular Medicine* 9(1):19–23.

[2] D. H. Gutmann, L. F. Parada, A. J. Silva, & N. Ratner (2012). Neurofibromatosis type 1: Modeling CNS dysfunction. In *Journal of Neuroscience* 32(41):14087–14093.

[3] Y. S. Lee & A. J. Silva (2011). Modeling hyperactivity: of mice and men. In *Nature Medicine* 17(5):541–542.

[4] J. Z. Tsien, P. T. Huerta, & S. Tonegawa (1996). The essential role of hippocampal CA1 NMDA receptor-dependent synaptic plasticity in spatial memory. In *Cell* 87(7):1327–1338.

[5] K. P. Giese, N. B. Fedorov, R. K. Filipkowski, & A. J. Silva (1998). Autophosphorylation at Thr^{286} of the calcium-calmodulin kinase II in LTP and learning. In *Science* 279(5352):870–873.

[6] A. Hyttinen, F. Eberhardt, & M. Järvisalo (2014). Constraint-based causal discovery: Conflict resolution with answer set programming. In *Proceedings of the 30th Conference on Uncertainty in Artificial Intelligence (UAI)*.

TRANSLATING LITERATURE INTO CAUSAL GRAPHS

TOWARD AUTOMATED EXPERIMENT SELECTION

NICHOLAS J. MATIASZ

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