Transforming Mutations into Models: Inferring Causal Networks from Experimental Data

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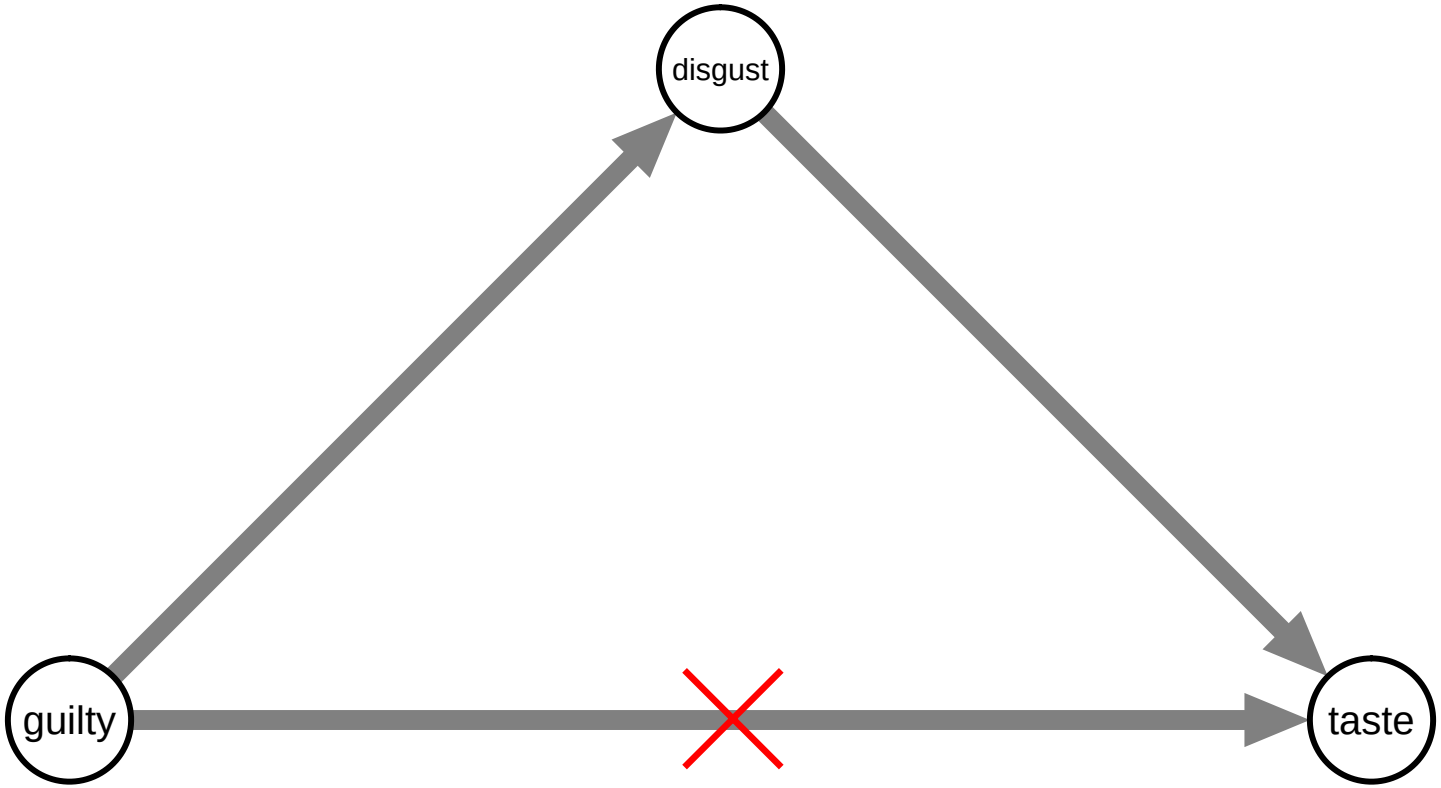
In search for the holy grail

In psychology, we often want to know what the parents of variables are.

"a causal relation is a relation between two variables where, when changing one variable, we expect to observe a change in the other variable"

In search for the holy grail

If there are multiple generations of parents and children in a network, we want to determine a node's true parent(s)



In search for the holy grail

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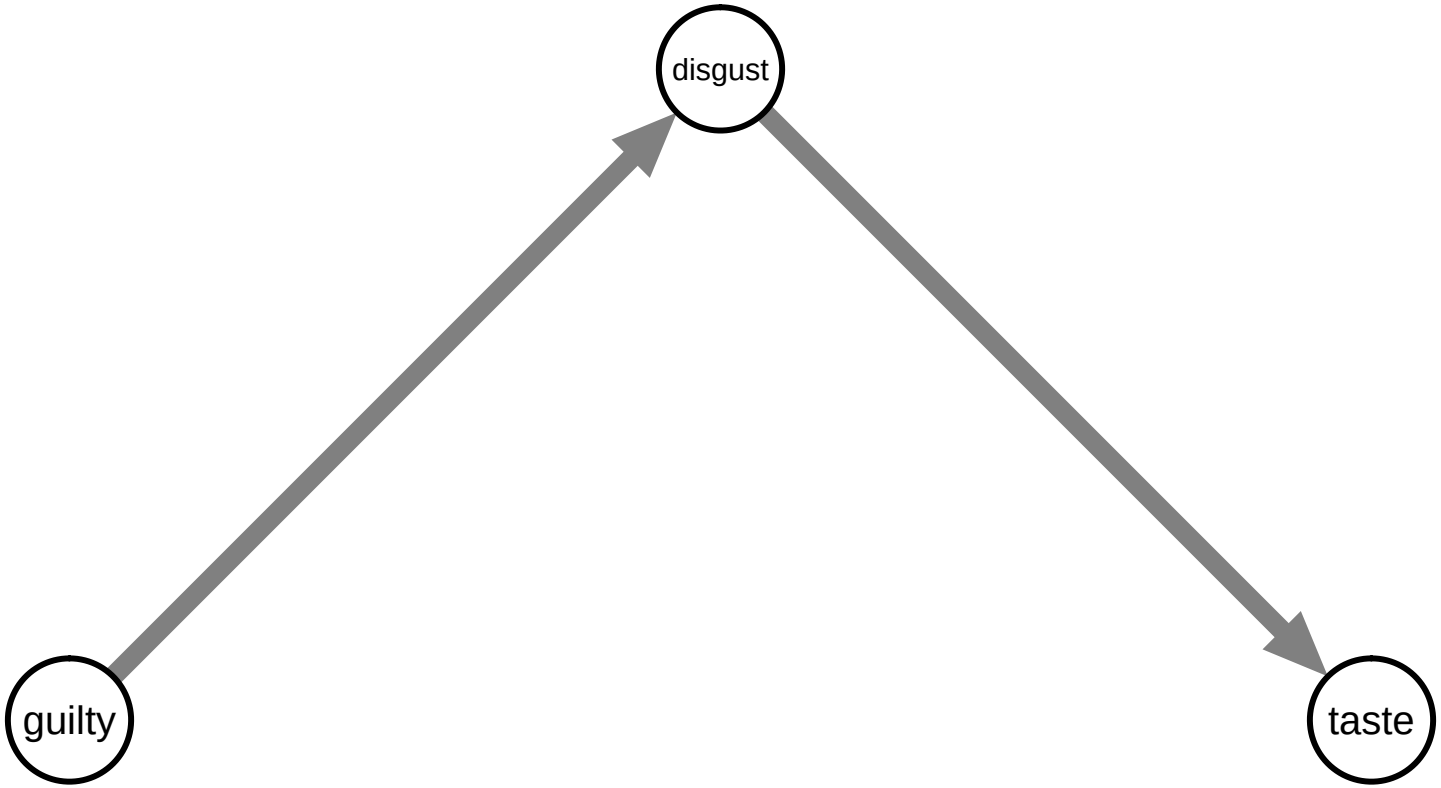
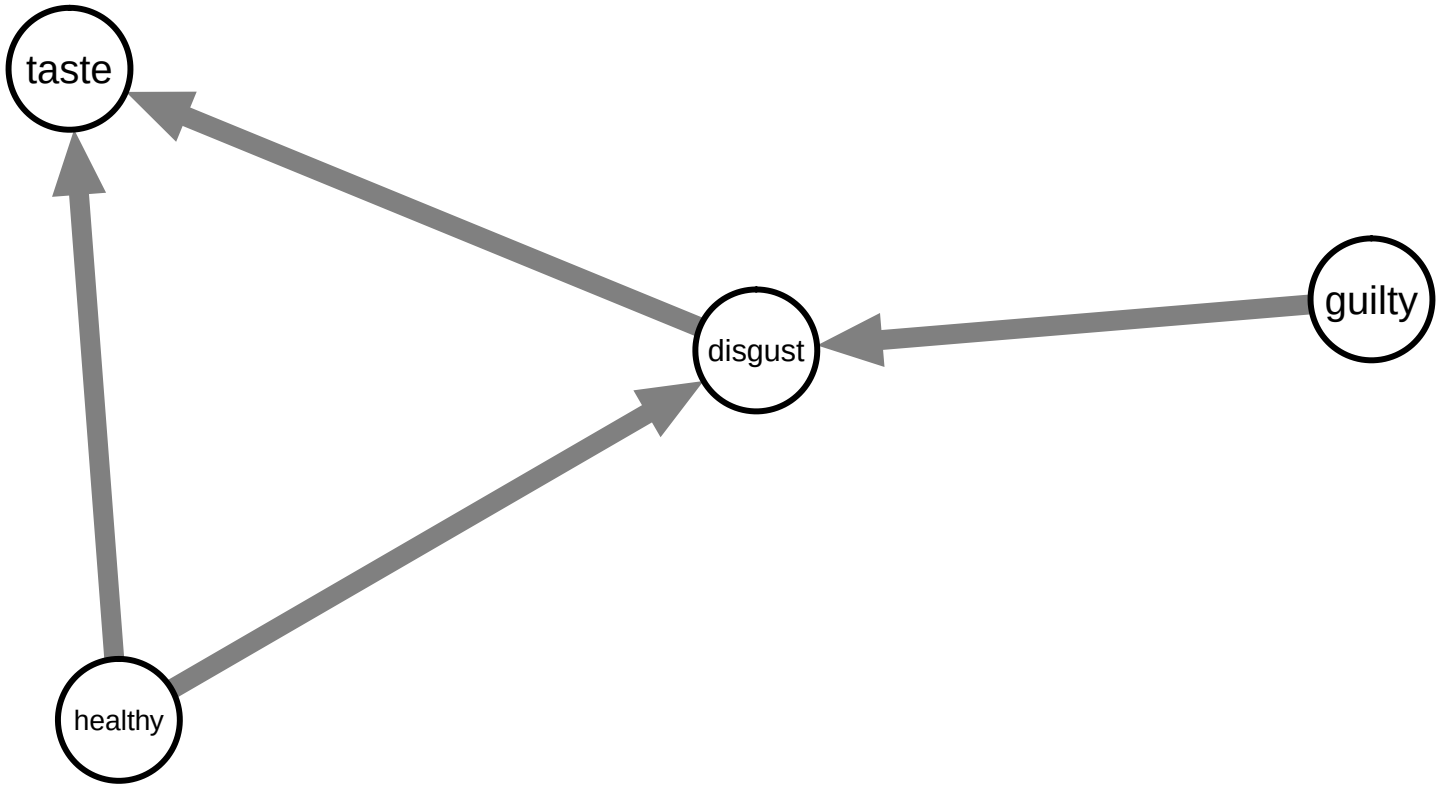


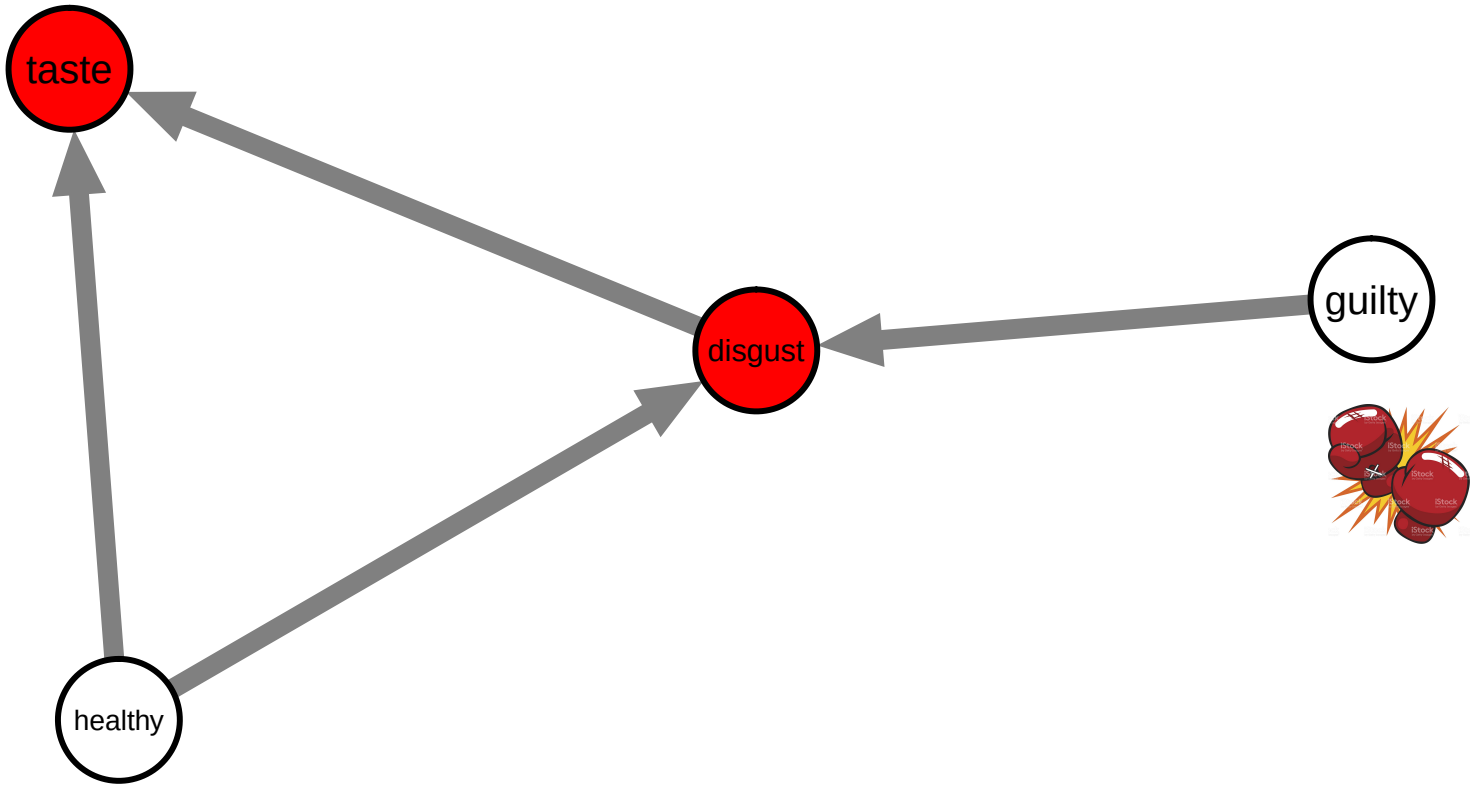
From observational to experimental data

Observational data



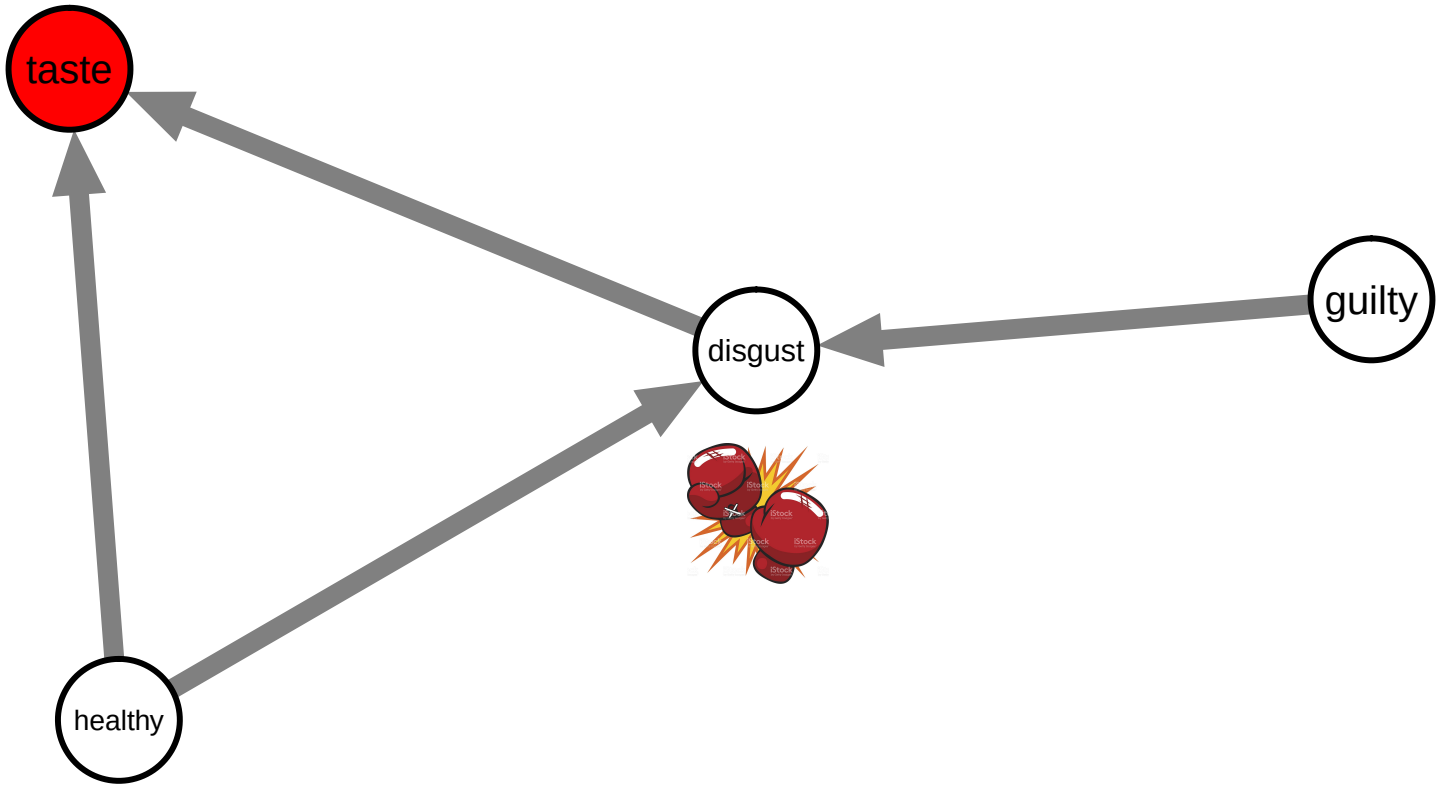
From observational to experimental data

Experimental data



From observational to experimental data

Experimental data



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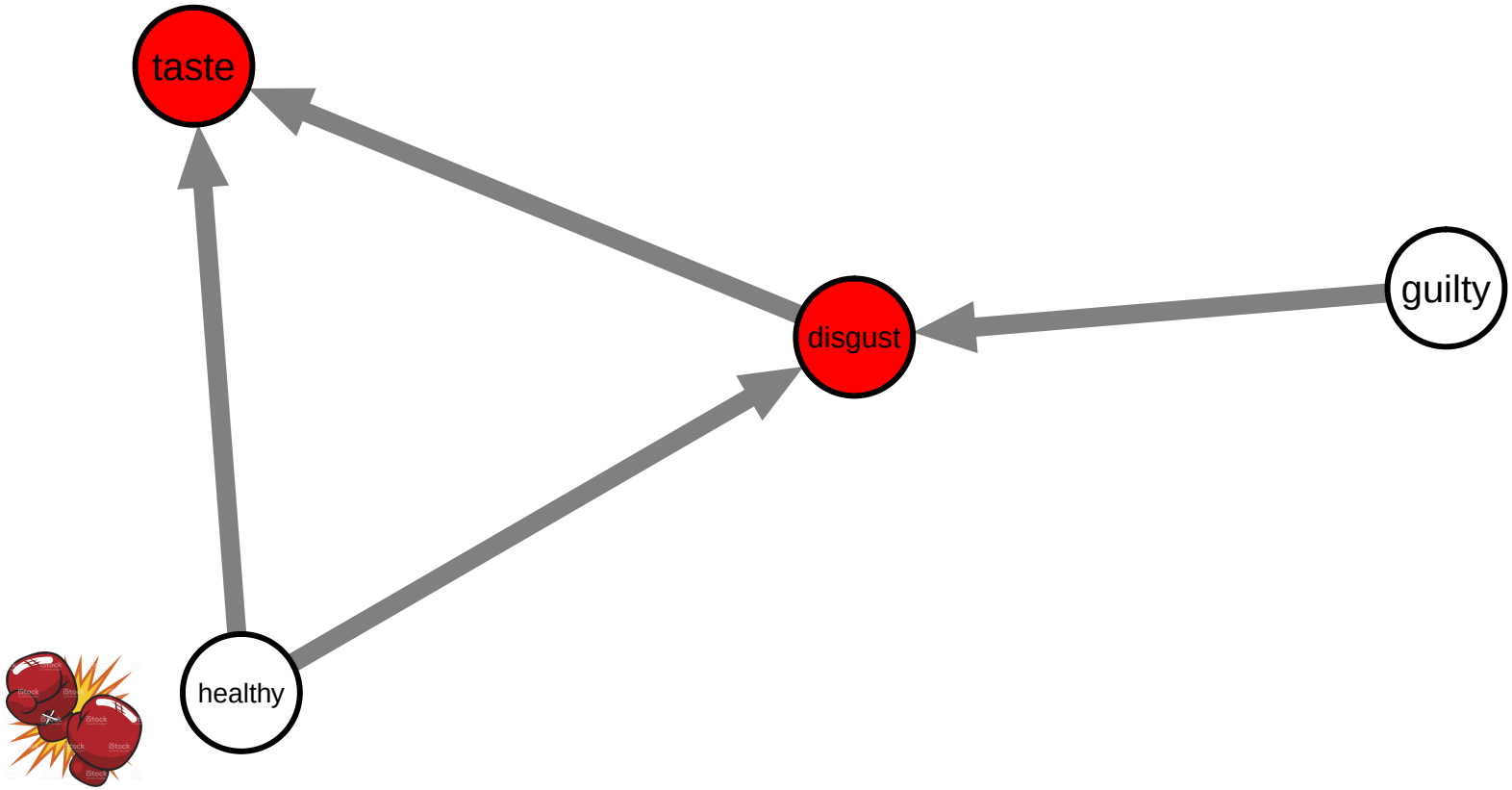

From observational to experimental data

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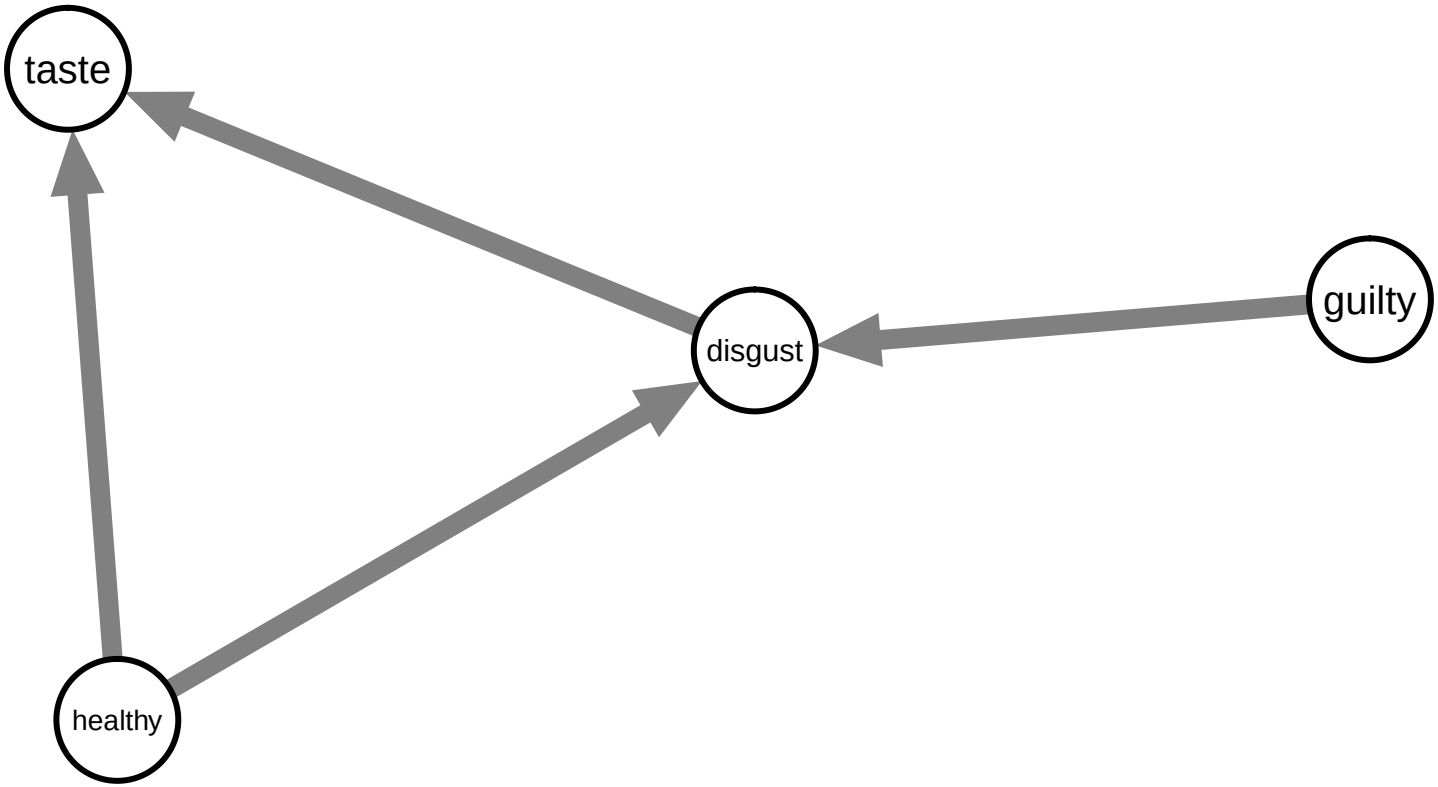
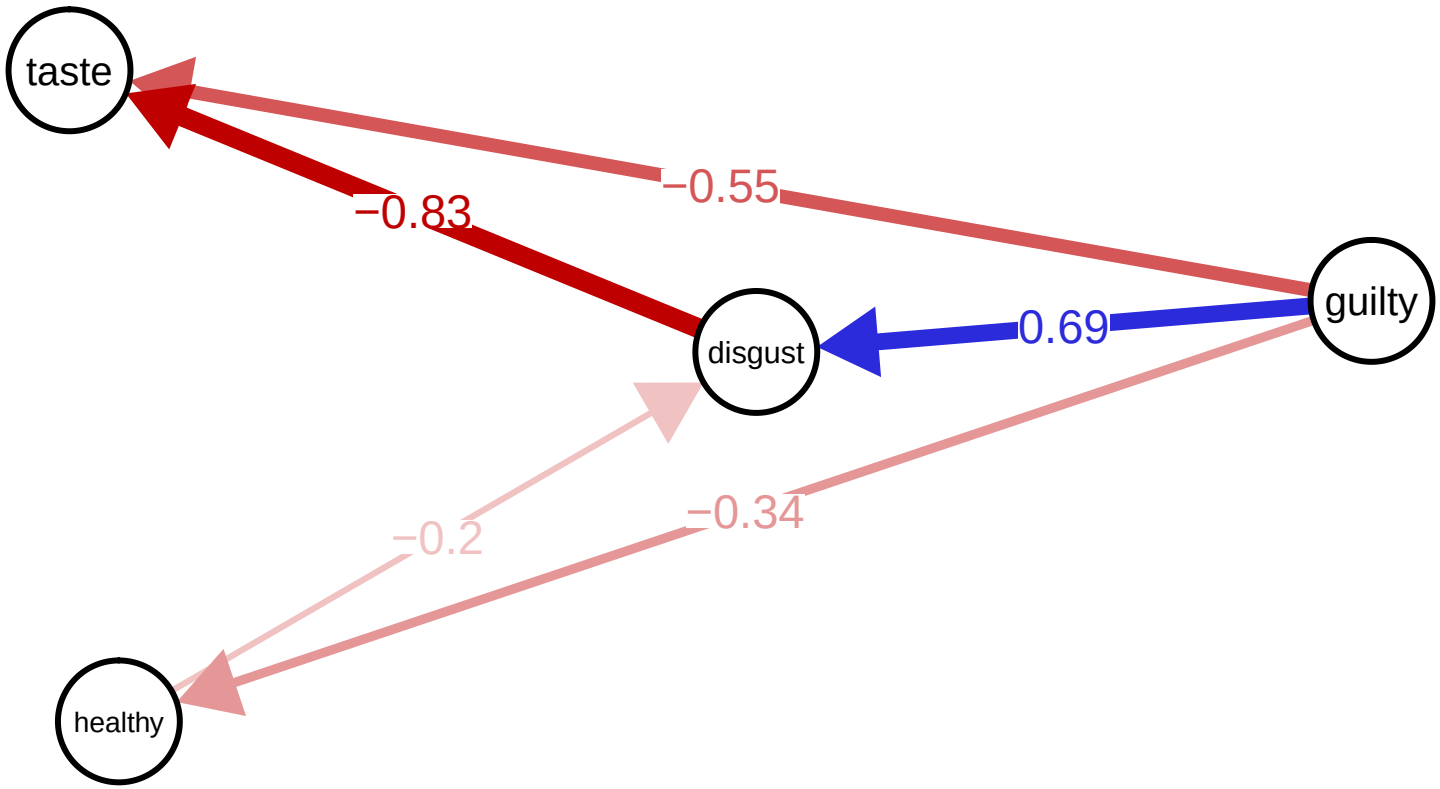


Turning experimental data into a network

A high conditional correlation occurs when the effect shown in the observational data is also shown in the experimental data.

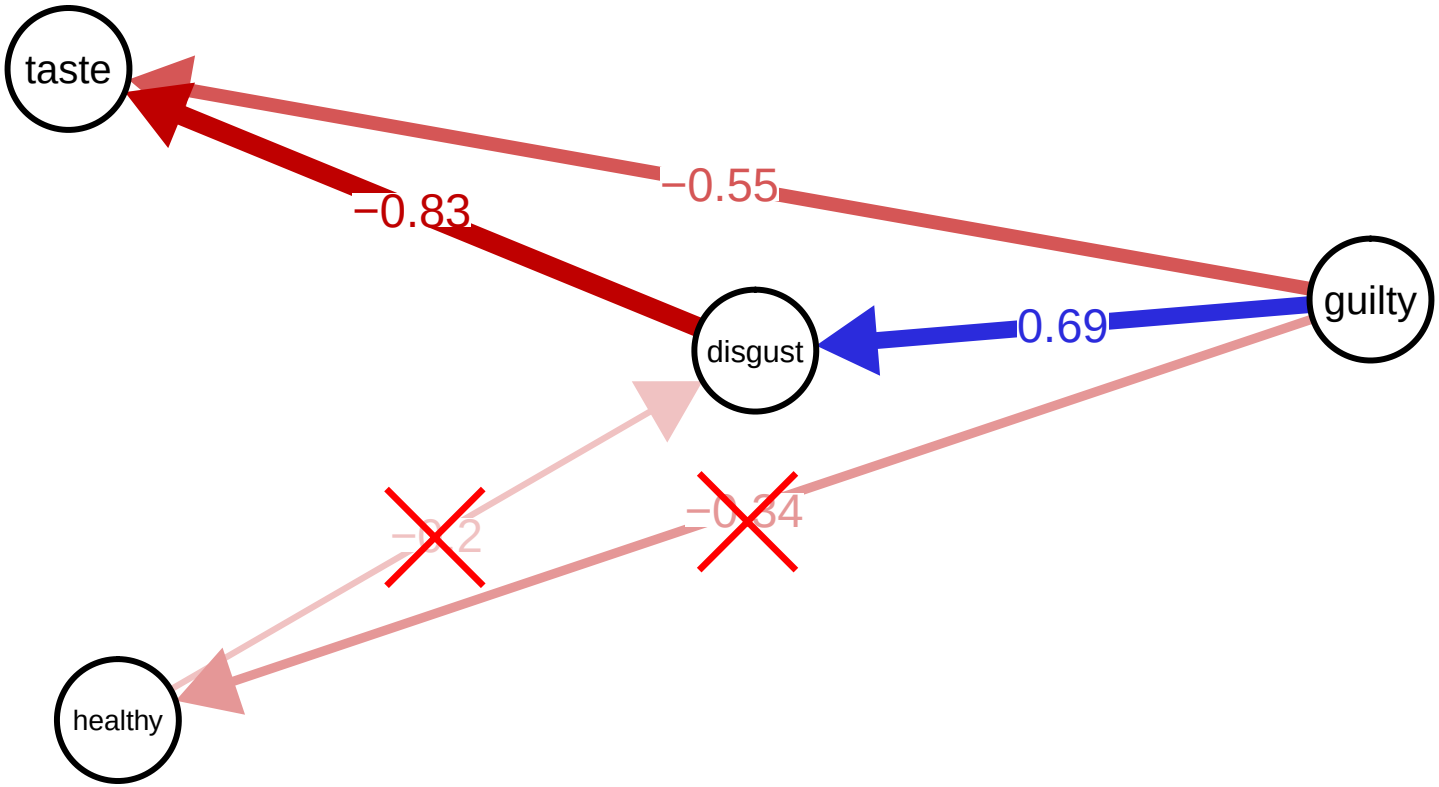


How do we determine if the relation between “guilty“ and “taste“ is a direct or indirect relation?

Current Methods for causal networks

Transitive Reduction

Transitive reduction prunes relations whose conditional correlation do not exceed some threshold:



$|0.20|$ & $|0.34| <$ threshold

Current Methods for causal networks

Transitive Reduction

- Transitive reduction algorithms start out with a graph that contains edges between variables whose conditional correlation exceed some threshold
- Edges are stepwise removed when alternative paths between those variables satisfy certain conditions
- DR-FFL[1] and TRANSWESD[2] are two methods that use transitive reduction
- DR-FFL and TRANSWESD vary in their usage of the conditional correlation when pruning relations from a network

[1] Pinna et al. (2010) From knockouts to networks: Establishing direct cause-effect relationships through graph analysis

[2] Klamt et al. (2010) TRANSWESD: inferring cellular networks with transitive reduction

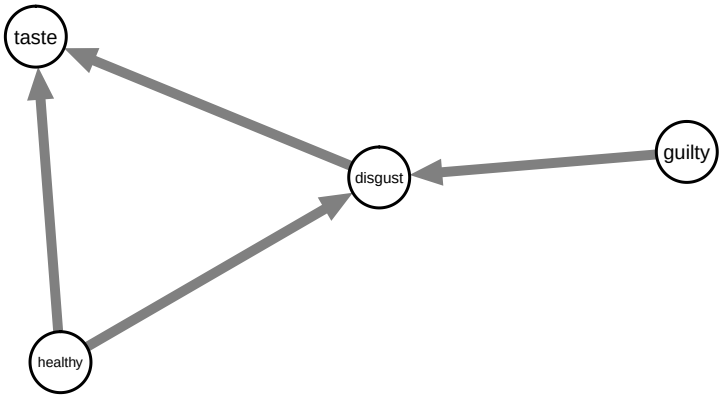
Current Methods for causal networks

IC-algorithm

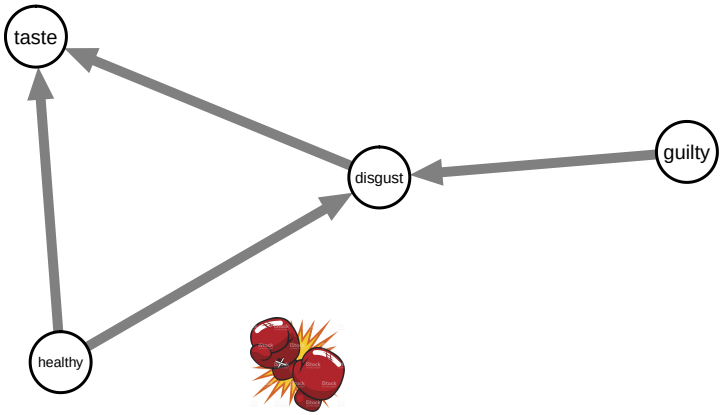
- Based on work by Pearl[3]
- Uses only observational data
- Sometimes finds unlogical relations

[3] Pearl. Causality

Difference between IC-algorithm and Transitive Reduction



IC-algorithm

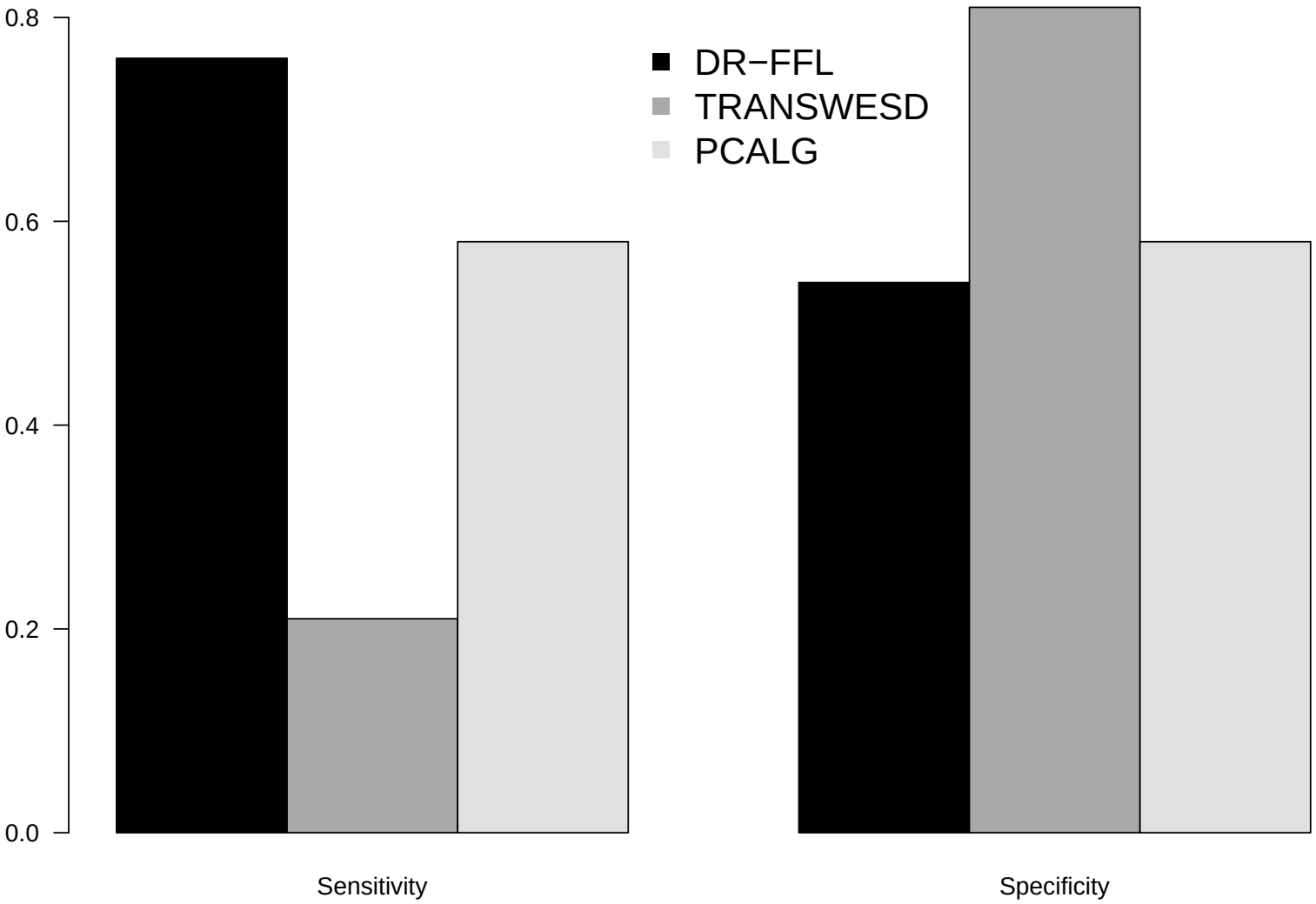


DR-FFL/TRANSWESD

Differences between IC-algorithm and Transitive Reduction

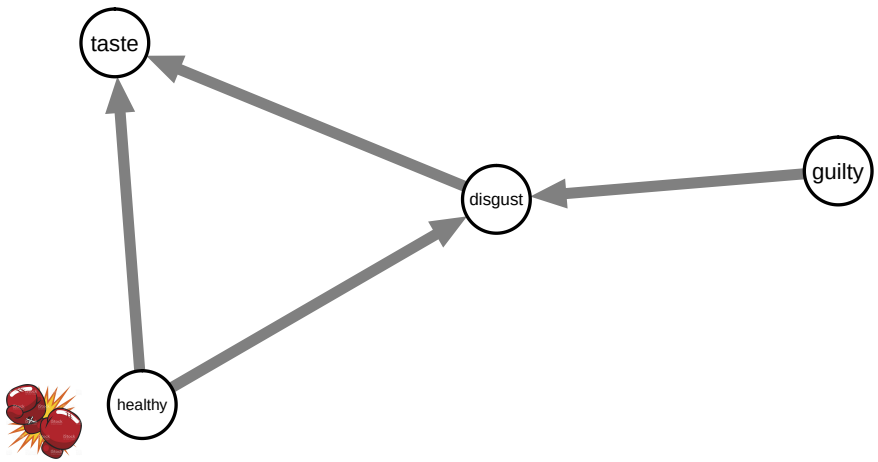
	Pro		Con
DR-FFL	Creates network	single-subject	Causal network is always unweighted
TRANSWESD	Creates network	between-subject	Computation time is long for reasonably sized networks
IC	Computationally fast		Uses solely observational data

Comparing methods



The future

- **Invariant prediction**[4]is a new and promising method to infer causal networks from experimental data.
- Invariant prediction checks for each edge whether it holds across experiments.



[3]Meinshausen, et al. (2016) Methods for causal inference from gene perturbation experiments and validation

The future

We are currently working on a model that combines the advantages of transitive reduction and invariant prediction

Collaborators

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