Bayesian optimal experimental design for inferring causal structure

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Session on "Bayesian experimental design for causal inference"

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Outline

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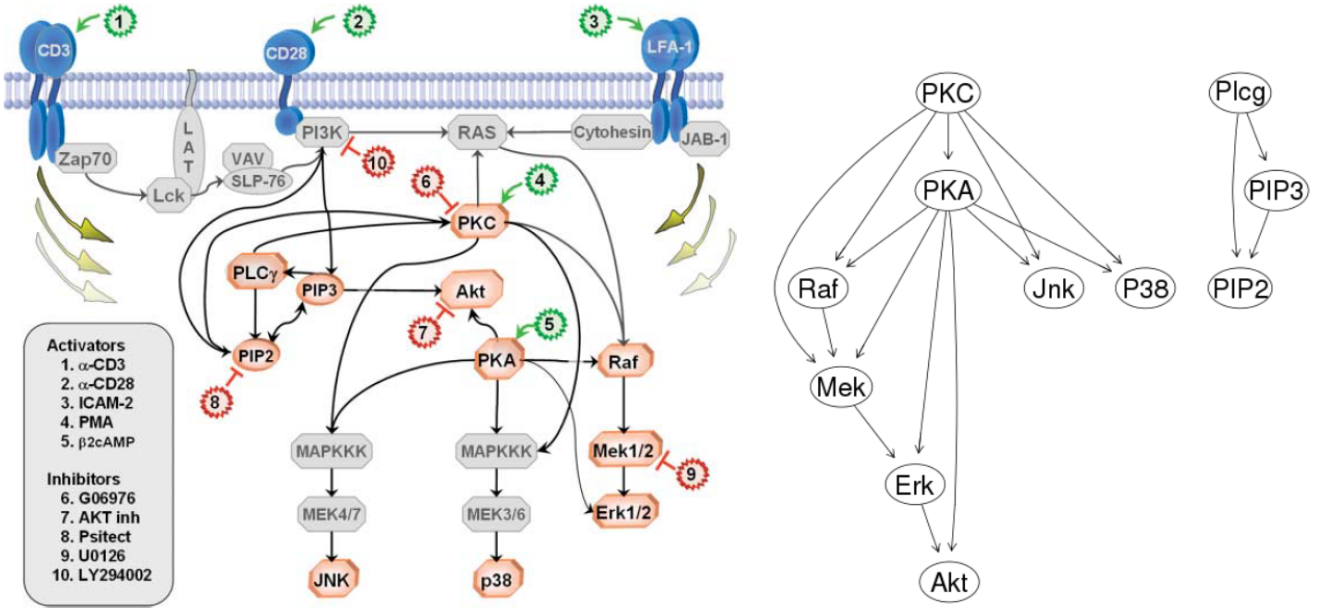
Motivation

- Inferring causal structure is key to understanding many systems.
- Many methods exist for inferring causality from observational data.
- However, observational data only determines the structure of a causal network up to the Markov equivalence class.
- Without strong assumptions, interventional data are needed to fully resolve networks.



Motivation

- Different intervention experiments yield different amounts of information.
- Since experiments are often expensive and time-consuming, it is advantageous to select interventions that provide the most information.
- Optimal experimental design, a.k.a. active learning, attempts to optimize this experiment selection process.

Motivation

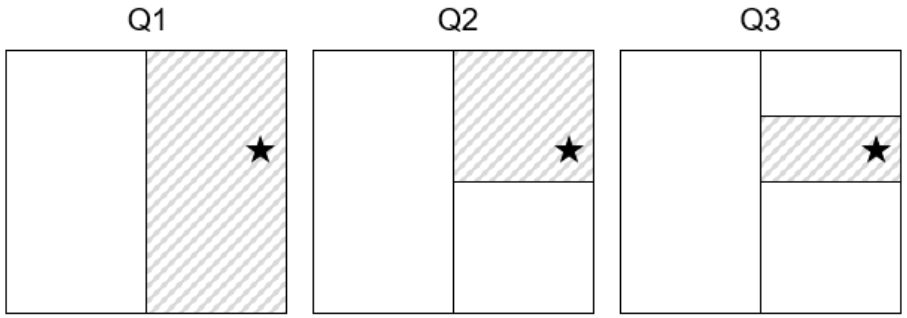
- From the Bayesian perspective, a brute-force approach would be as follows: for each candidate experiment,
  1. generate hypothetical datasets from the posterior predictive,
  2. perform posterior inference on each dataset, and
  3. compute a function of the posterior summarizing the information gain.
- Averaging over many hypothetical datasets would yield an estimate of the posterior expected amount of information gain for each candidate experiment.
- However, this brute-force approach would involve an inordinate amount of computation.

This talk

- We develop a novel Bayesian experiment selection criterion that is principled and computationally tractable.
- Roughly, we consider the asymptotic information gain that each experiment would yield in the limit of infinitely many replicates, as a proxy for the expected gain from finitely many replicates.
- It turns out that the reduction in entropy can be easily computed using samples from the current posterior, without generating or performing inference on any hypothetical datasets.
- This leads to a vast reduction in the computational burden required to select experiments.

Outline

Intuition: Twenty questions game



- Two players: Questioner and Answerer.
- Answerer thinks of an object. Questioner has a prior over objects that the Answerer might select.
- A question such as, "Is the object living?" partitions the objects into two parts: living and non-living.
- Given the answer, the questioner can eliminate objects in one part, and update their beliefs.
- Questioner chooses questions to focus the posterior as fast as possible.

General setup

- More generally, suppose:
  - θ is a parameter of interest,
  - ν is a nuisance parameter,
  - $\pi(\theta, \nu)$ is the prior,
  - $f(\theta)$ is the answer to a research question f (for example, is a certain hypothesis true), and
  - $X_{1:N} = (X_1, \ldots, X_N)$ are data from N replicates of an experiment performed to obtain information about $f(\theta)$.

- By analogy with Twenty Questions, θ is the object to be inferred, f is the question, and $X_{1:N}$ is a noisy "answer".

Conditions

- Suppose:

$$(\theta, \nu) \sim \pi$$
$$X_1, \ldots, X_N | \theta, \nu \sim P_{\theta,\nu} \text{ i.i.d.}$$

and $f(\theta)$ is a function of θ with the following three properties:

1. $\theta \perp\!\!\!\perp X_{1:N} \mid f(\theta)$,
2. $f(\theta)$ is identifiable, in the sense that there is a function g such that $g(P_{\theta,\nu}) = f(\theta)$ almost surely, and
3. $f(\theta)$ can only take one of finitely many values.

- Condition 1 is that if we know the true answer to question f, then the experiment provides no additional information about θ.
- Condition 2 is that the answer $f(\theta)$ is uniquely determined by the distribution of X_n.

General criterion

- We seek experiments that minimize the posterior entropy $H(\theta \mid X_{1:N})$.

- **Theorem**: *Under the conditions above,*

$$H(\theta \mid X_{1:N}) \xrightarrow[N \to \infty]{} H(\theta) - H(f(\theta)).$$

- The information gain, in terms of reduction of entropy, is

$$H(\theta) - H(\theta \mid X_{1:N}).$$

- Thus, when N is large, the information gain is approximately $H(f(\theta))$, the entropy of the answer $f(\theta)$ *under the prior*.

- Thus, to approximate the information to be gained by a particular question f, we need only work with the prior — not the posterior $\theta|X_{1:N}$ for a yet unobserved dataset $X_{1:N}$.

Sequentially selecting experiments

- Now, suppose that instead of $\pi(\theta, \nu)$ being the prior, $\pi(\theta, \nu)$ is the current posterior given all the data from any previous experiments.

- For each candidate experiment e, let $X_1^e, \ldots, X_N^e | \theta, \nu \sim P_{\theta,\nu}^e$ i.i.d. be hypothetical random data from N replicates of experiment e.

- Suppose $f_e(\theta)$ satisfies our assumed conditions above.

- Our proposed method of choosing the next experiment e is:
  1. Generate samples $\theta_1, \ldots, \theta_T$ from the current posterior π.
  2. Compute $\hat{p}_e(y) = \frac{1}{T} \sum_{t=1}^{T} \mathbb{1}\big(f_e(\theta_t) = y\big)$ for each candidate experiment e.
  3. Select the experiment e with the largest value of the entropy

$$\widehat{H}(f_e(\theta)) := -\sum_y \hat{p}_e(y) \log \hat{p}_e(y).$$

Features of the proposed approach

- All it requires is posterior samples given the current data — no need to simulate or do inference on hypothetical future data.
- While the justification is asymptotic, our criterion accounts for finite sample uncertainty in a natural way.
  - The posterior π quantifies uncertainty in θ based on finitely many previous experiments and finitely many replicates of each experiment.
- A further advantage is that $f_e(\theta)$ often takes a small number of values, and thus, $H(f_e(\theta))$ is often much easier to approximate than $H(\theta \mid X^e_{1:N})$ or even $H(\theta)$.

Outline

Selecting experiments for causal networks

- Causal network models specify the joint distribution of the data when variables are manipulated (or unmanipulated).

- It is common to specify causal networks via:
  1. a directed acyclic graph G and
  2. the conditional probability distribution (CPD) of each node given the values of its parent nodes.

- In general, an intervention partitions the set of graphs into equivalence classes such that
  - the graphs in each class are indistinguishable with respect to this intervention (corresponding to our Condition 1), and
  - graphs in different classes are distinguishable (corresponding to Condition 2).

- Thus, in our notation, θ is the graph G, and the "question" f corresponds to this partition.

Selecting experiments for causal networks

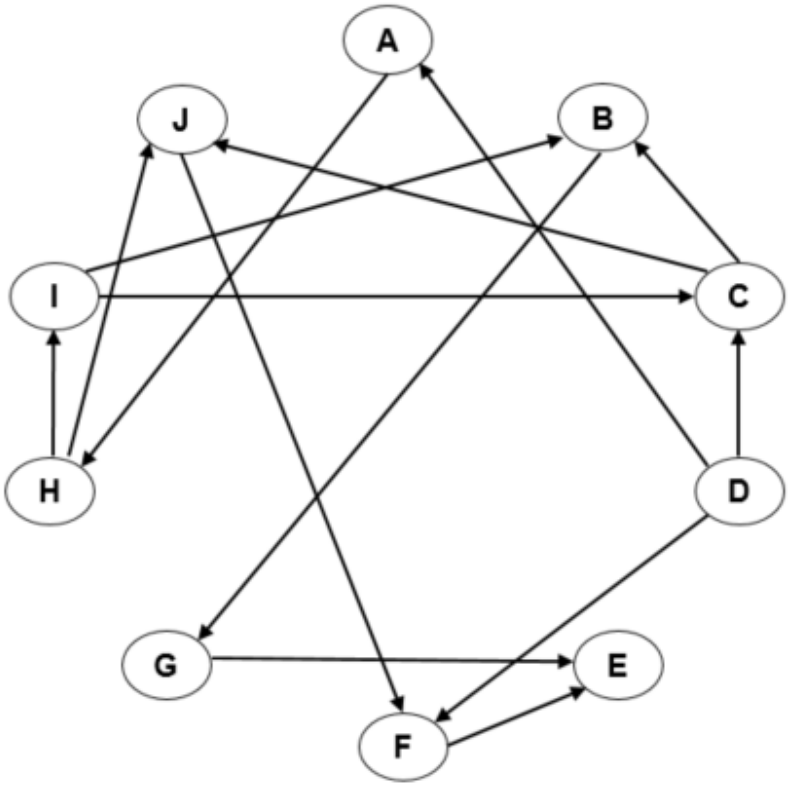
- The Markov equivalence class (MEC) is a natural choice of function f to use in our criterion.
- However, it may be possible to obtain good performance using other partition schemes as well.
- To this end, we considered the following array of partition schemes:
  1. MEC: $f_e(G) =$ Markov equivalence class when intervening on node e,
  2. Child Set (CS): $f_e(G) =$ set of children of node e,
  3. Descendant Set (DS): $f_e(G) =$ set of descendants of node e,
  4. Parent Set (PS): $f_e(G) =$ set of parents of node e.

Outline

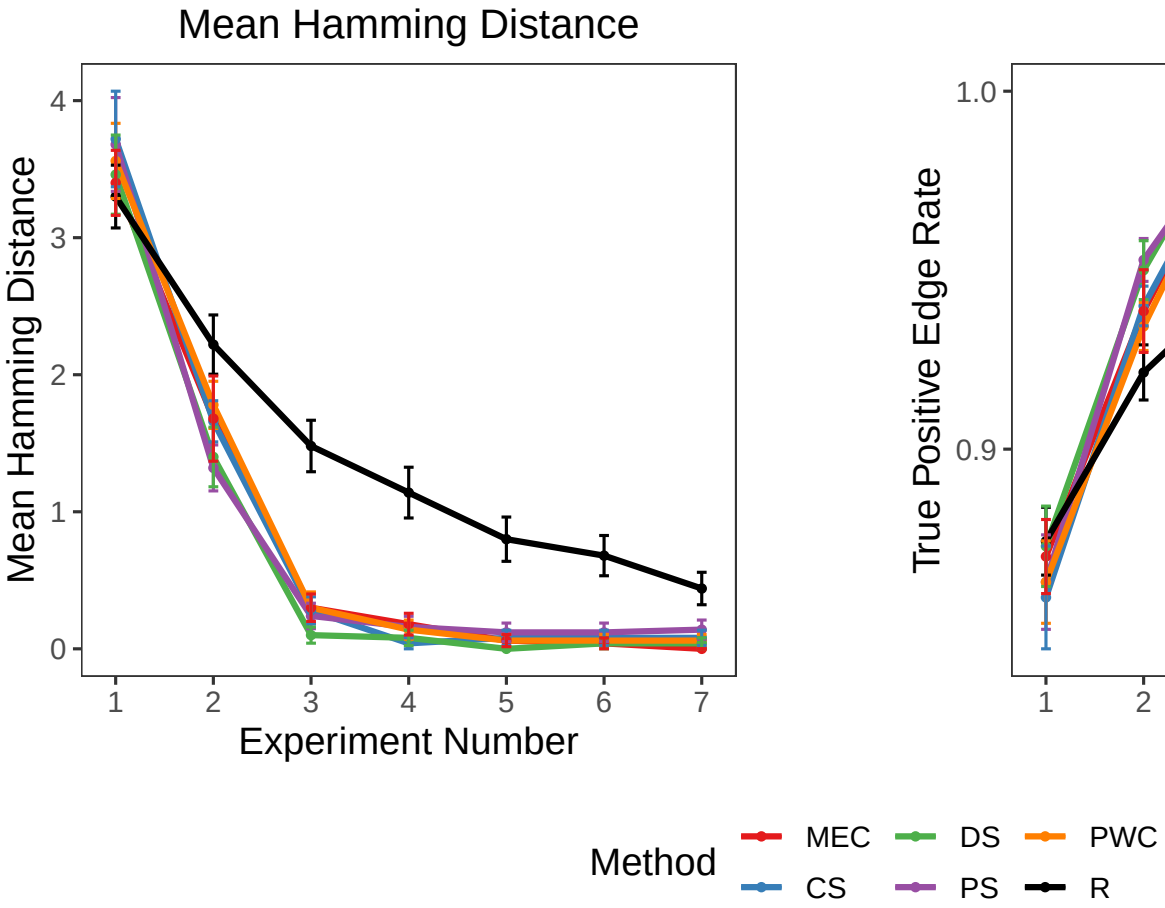
Simulations: Comparing partition schemes

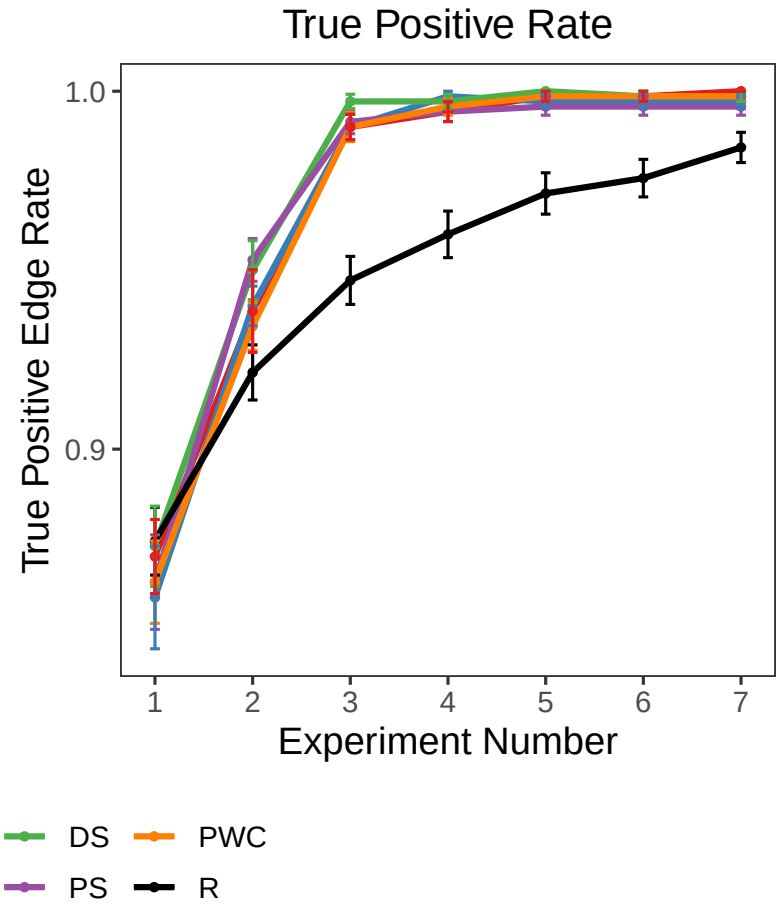
- First, we compare various partition schemes that could be used in our method.

- We simulate binary data using the following 10-node network as ground truth:



Simulations: Comparing partition schemes

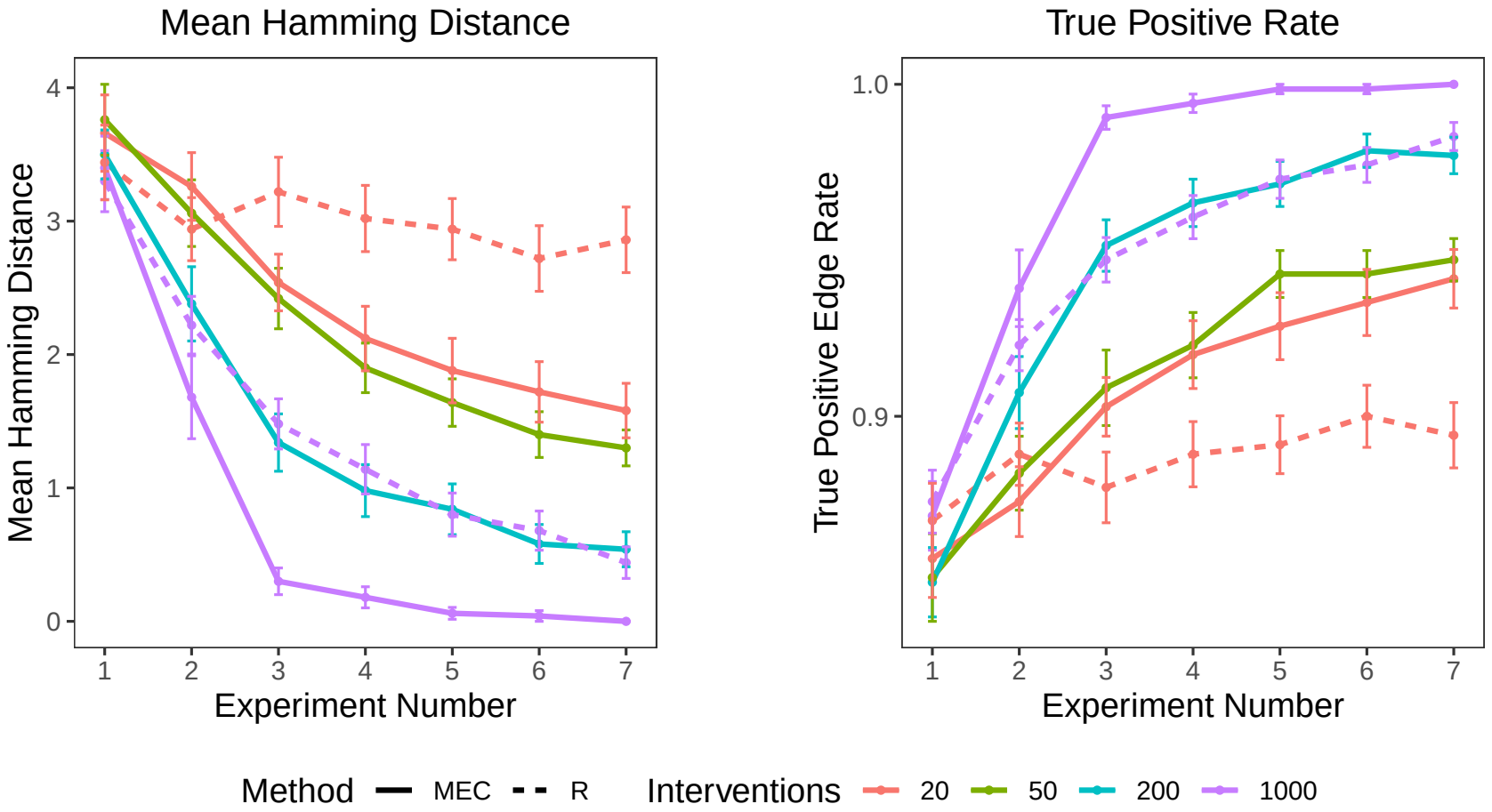




- Settings: $n_{sim} = 50$ simuation runs, $n_{exp} = 7$ interventional experiments per run, $n_{obs} = 1000$ observational data points, $n_{intv} = 1000$ data points for each interventional experiment.
- "R" = randomly selecting a node to intervene on.

Simulations: Effect of sample size

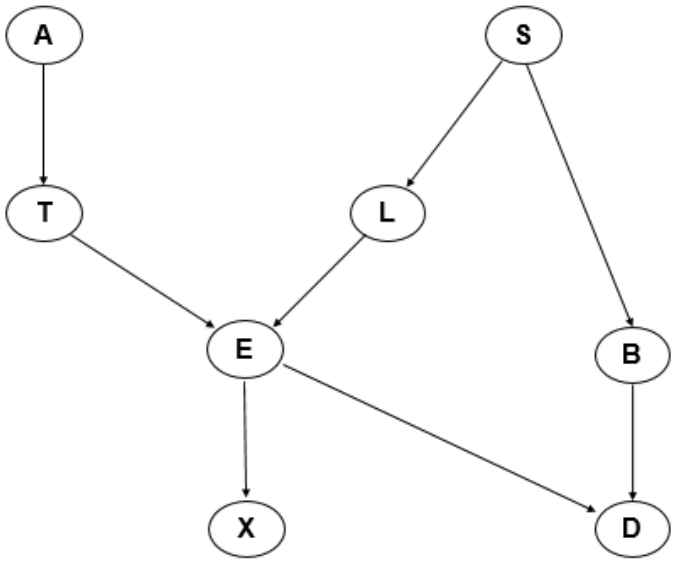
- We see the same pattern for smaller numbers of data points as well.
- Settings: Same as previous, but with $n_{intv} \in \{20, 50, 200, 1000\}$.

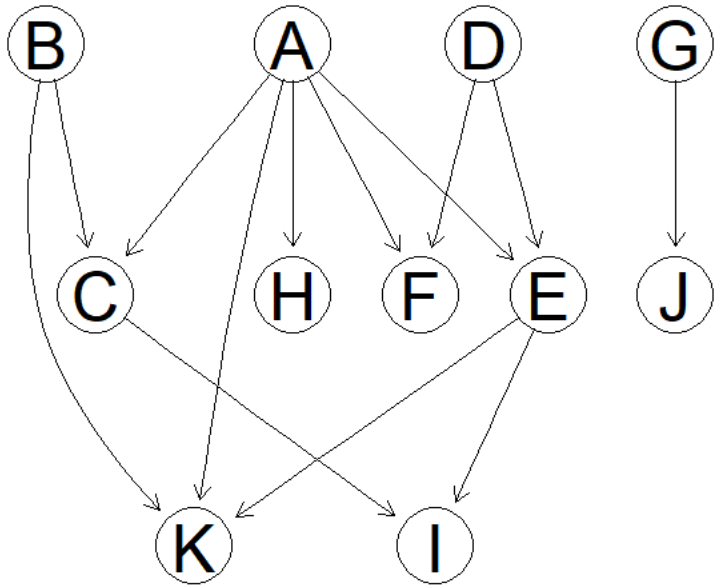


Simulations: Comparing with other methods

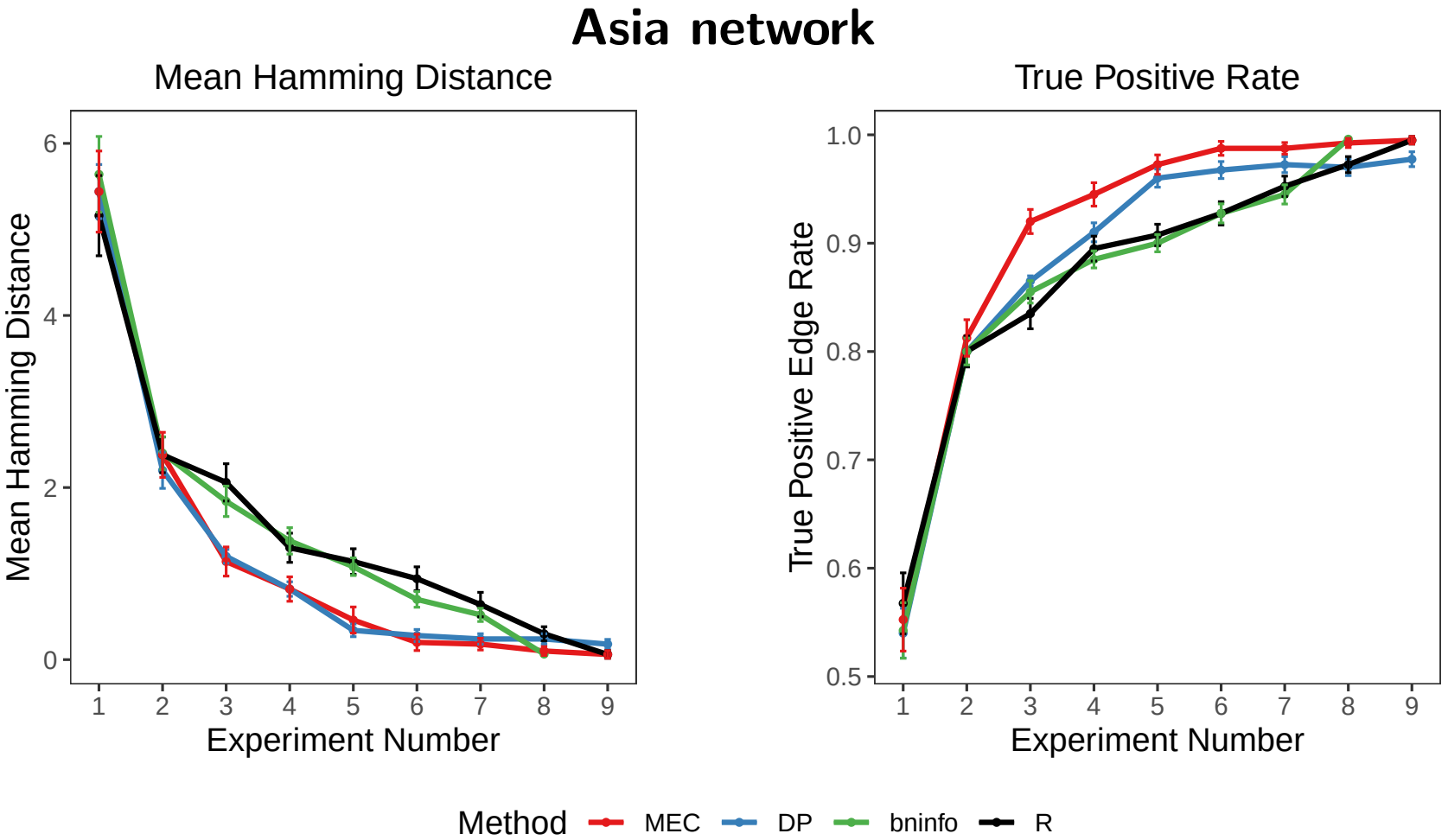
- We compared our algorithm to several other methods:
  - "bninfo" method of Ness et al. (2018)
  - dynamic programming (DP) method of Li and Leong (2009)
  - greedy equivalence search (GES) method of Chickering (2002)
  - greedy interventional equivalence search (GIES) method of Hauser and Bühlmann (2012)

- We considered the 8-node "Asia" binary network and an 11-node Gaussian network:



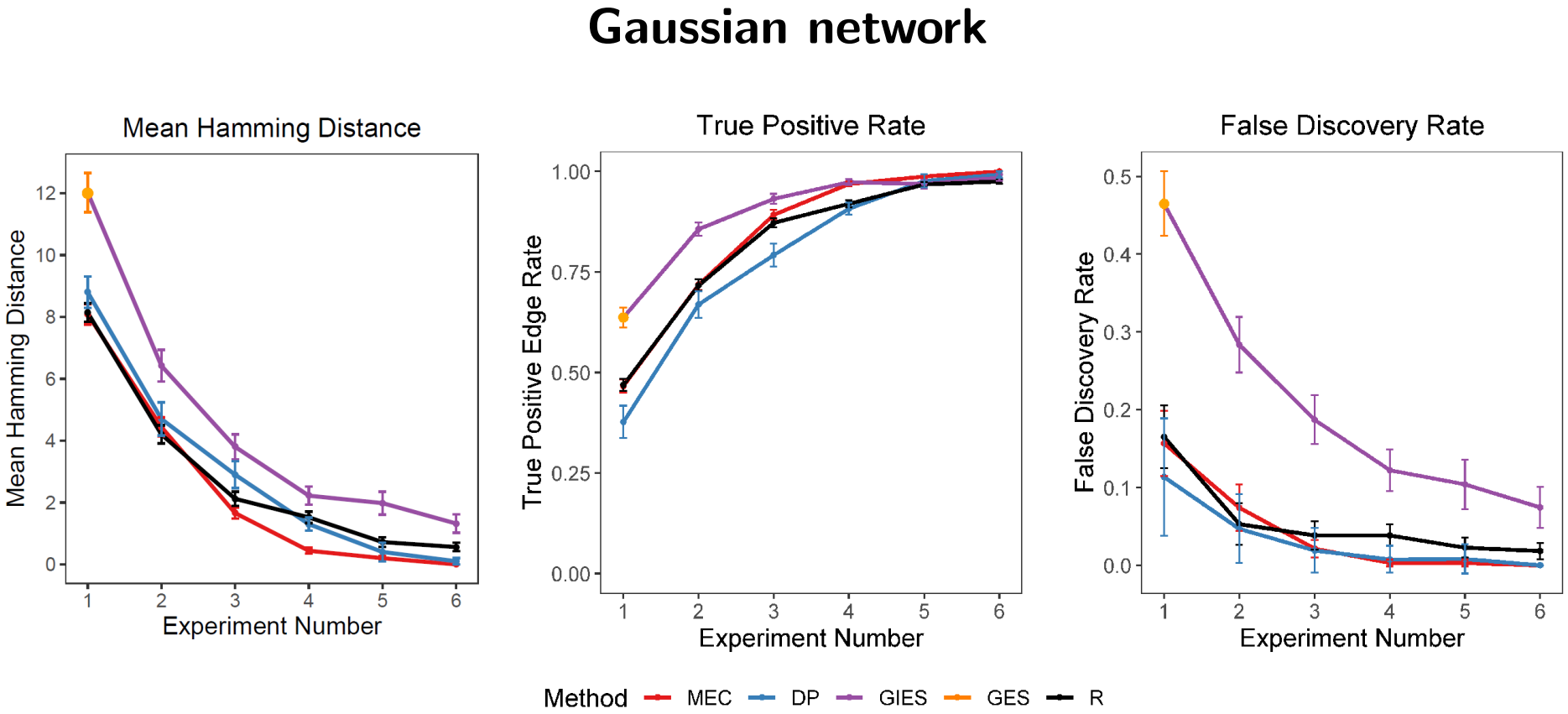


Simulations: Comparing with other methods



- Settings: $n_{sim} = 50$ simuation runs, $n_{exp} = 9$ interventional experiments per run, $n_{obs} = 300$ observational data points, $n_{intv} = 300$ data points for each interventional experiment.

Simulations: Comparing with other methods



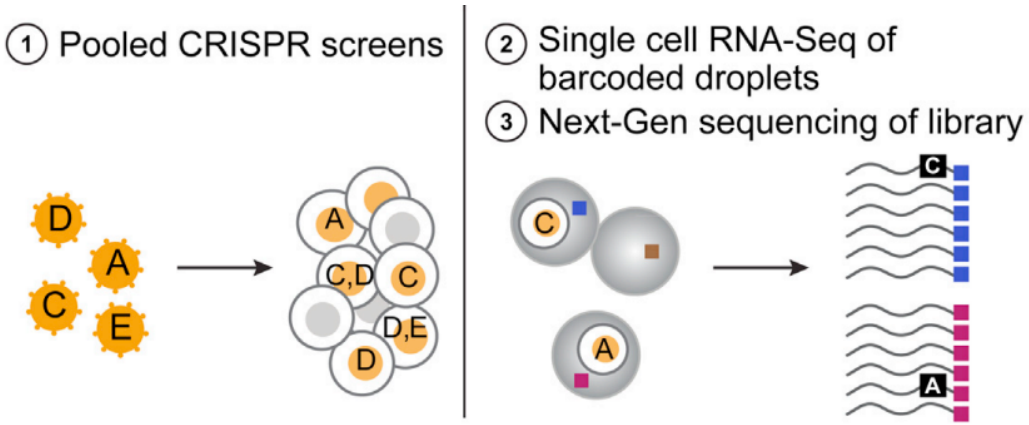
- Settings: $n_{sim} = 50$ simuation runs, $n_{exp} = 6$ interventional experiments per run, $n_{obs} = 50$ observational data points, $n_{intv} = 50$ data points for each interventional experiment.

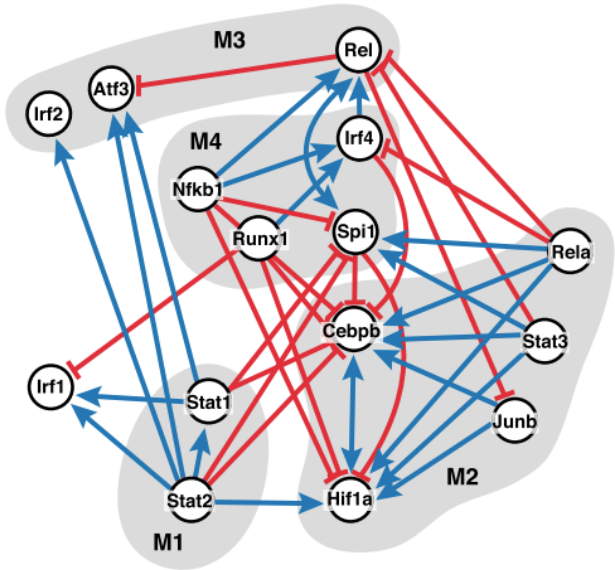
Outline

Application: Perturb-seq gene expression dataset

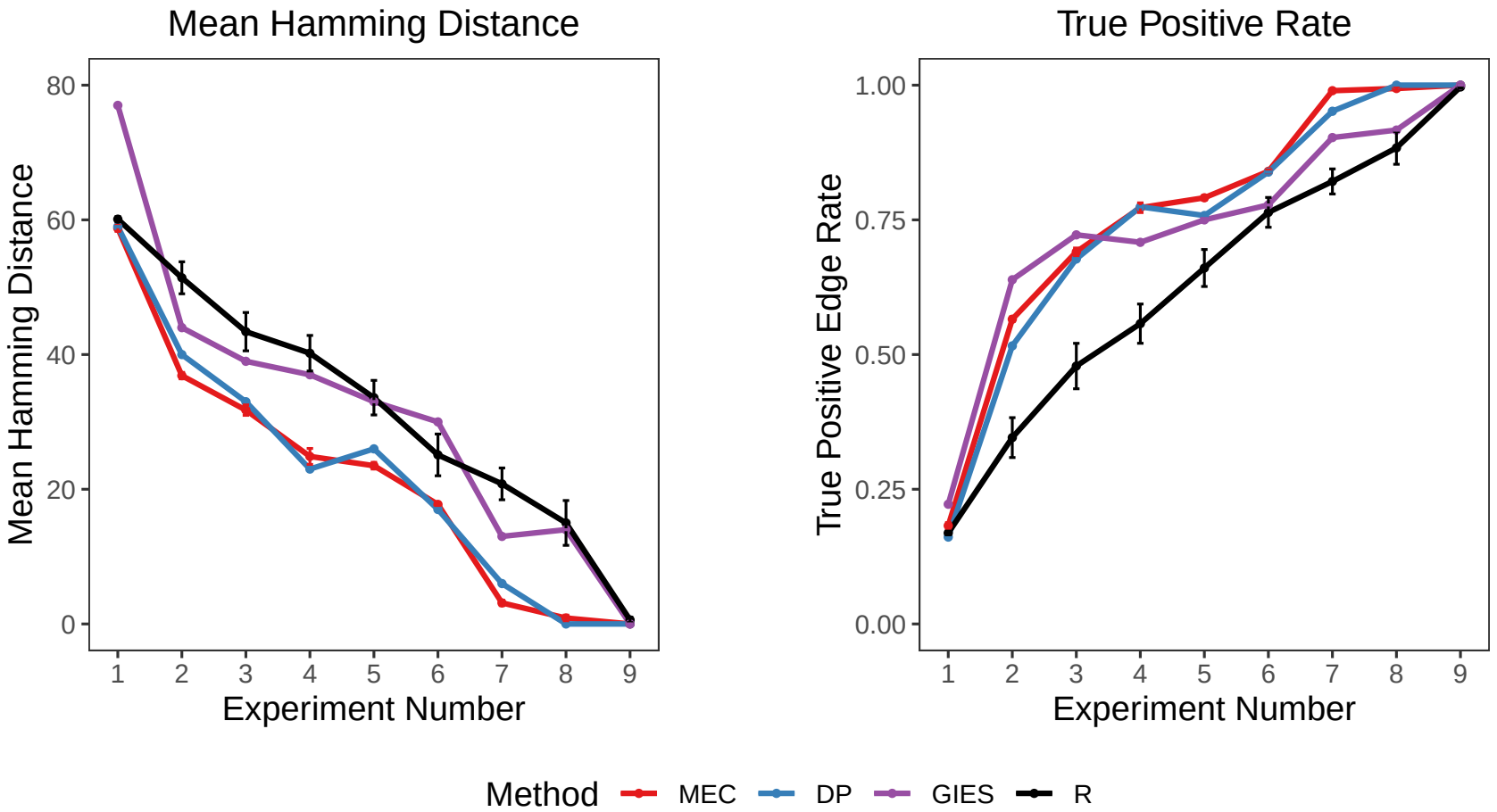
- We apply our method to the Perturb-seq data (Dixit et al., 2016), and compare with the interventional greedy sparsest permutation (IGSP) structure learning algorithm of Wang et al. (2017).

- To facilitate comparison with IGSP, we follow Wang et al. (2017) in using 992 observational samples and 13,435 interventional samples under 8 gene interventions for 14 transcription factors of interest.





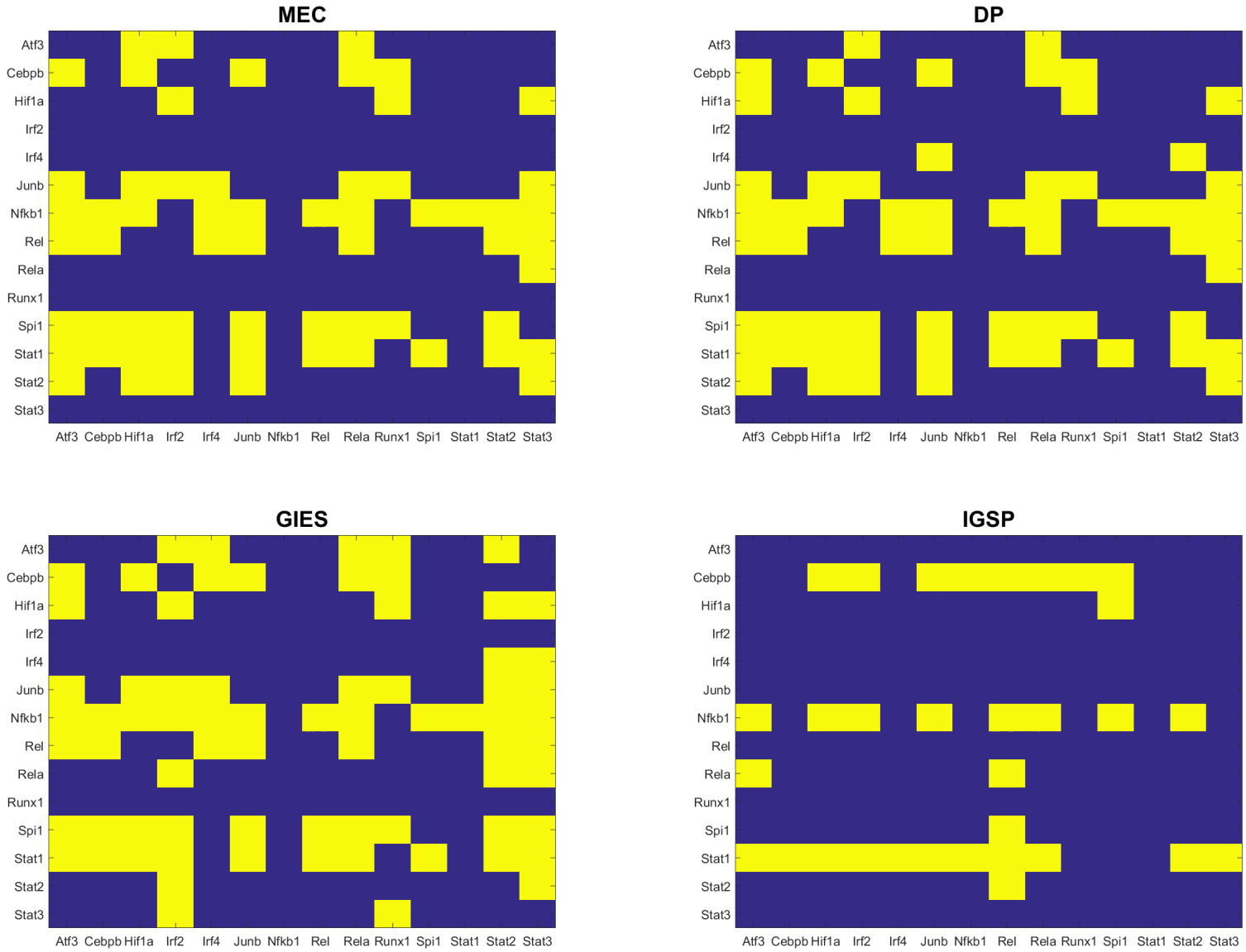
Application: Perturb-seq gene expression dataset



- Since ground truth is unknown, we self-benchmark each method by treating the final estimated network for each method as its ground truth.

Application: Perturb-seq gene expression dataset

Adjacency matrices of final estimated networks



Conclusion

- Our general criterion provides a computationally fast way to select experiments that optimize an approximation to the information gain.
- Empirically it works well for a range of natural partition schemes.
- Challenges and future work:
  - Existing posterior inference algorithms for causal networks are too slow to handle larger numbers of nodes.
  - Relaxing the acyclicity assumption is important for some real-world networks.
  - It would be interesting to try the method on other settings, beyond causal networks.

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