Modeling uncertain interventions

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Joint work with
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Outline

- Reducing causality to decision theory
- Learning DAGs with “fat hands”
- Beyond DAGs

2 types of causality

- Phil Dawid distinguishes 2 types of causality
- Effects of Causes
  - e.g., if I take an aspirin now, will that cause my headache to go away?
- Causes of Effects
  - e.g., my headache has gone; would it be gone if I had not taken the aspirin?

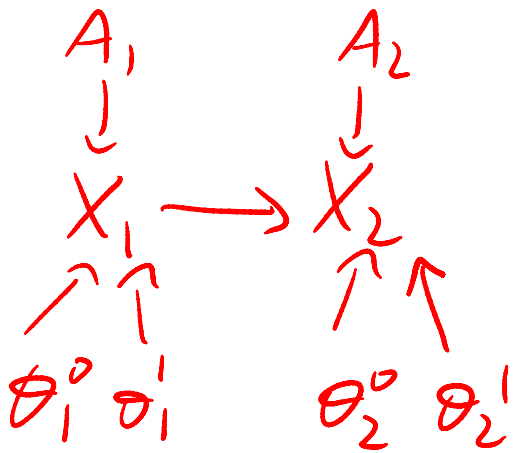
- "Causal inference without counterfactuals", JASA 2000
- "Influence diagrams for causal modeliling and inference", Intl. Stat. Review, 2002
- "Counterfactuals, hypotheticals and potential responses: a philosophical examination of statistical causality", Tech Report, 2006

Causality -> decision theory

- Most applications of causal reasoning are concerned with Effects of Causes. This can be modeled using standard decision theory.
- Reasoning about Causes of Effects requires counterfactuals, which are fundamentally unidentifiable, hence dangerous.
- We shall focus of Effects of Causes (Pearl 2000, ch 1-6).

Intervention DAGs

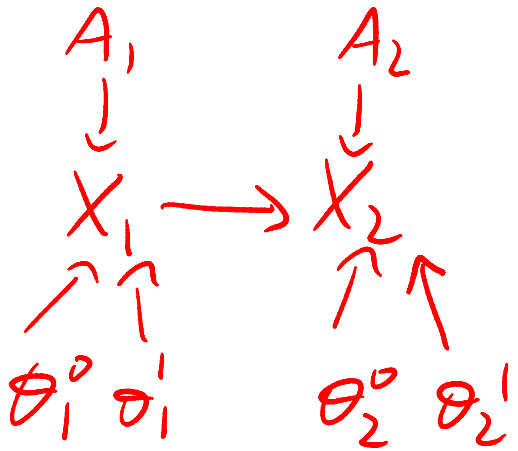
- Each intervention/ action A_j node determines if X_j is sampled from its normal or 'mutated' mechanism
- Perfect intervention means cutting incoming arcs: $p(X_2|X_1,A_2=1,\theta_2)=\delta(X_2 - \theta_2^1)$



Observing vs doing

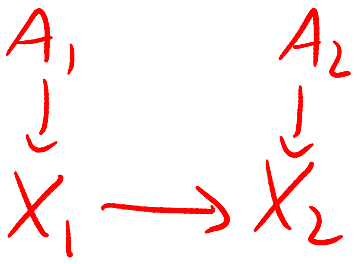
- I-DAGs make the do-operator and edge-cutting unnecessary

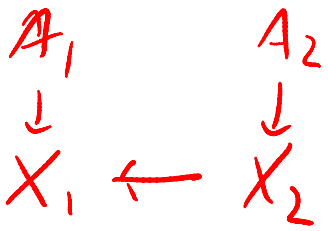
$$p(X_1|X_2 = x_2) = p(X_1|X_2 = x_2, A_1 = 0, A_2 = 0)$$
$$p(X_1|\mathsf{do}(X_2 = x_2)) = p(X_1|X_2 = x_2, A_1 = 0, A_2 = 1)$$



Distinguishing causally different DAGS

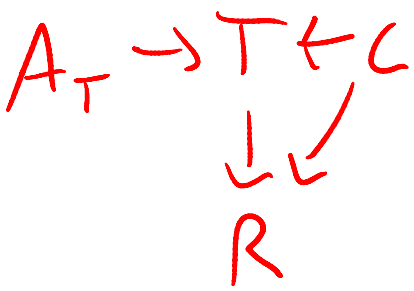
- I-DAGs can resolve Markov equivalence





Back-door criterion

- D-separation in I-DAG can be used to derive all of Pearl's results (in ch1-6) and more



$$C \perp A_t$$
$$R \perp A_t | C, T$$

$$p(r|A_t = t) = \sum_c p(r|A_t = t, c)p(c|A_t = t)$$
$$= \sum_c p(r|A_t = 0, T = t, c)p(c|A_t = 0)$$

Dawid, Intl Stat Review 2002

Structure learning

- Posterior over graphs given interventional and observational data:

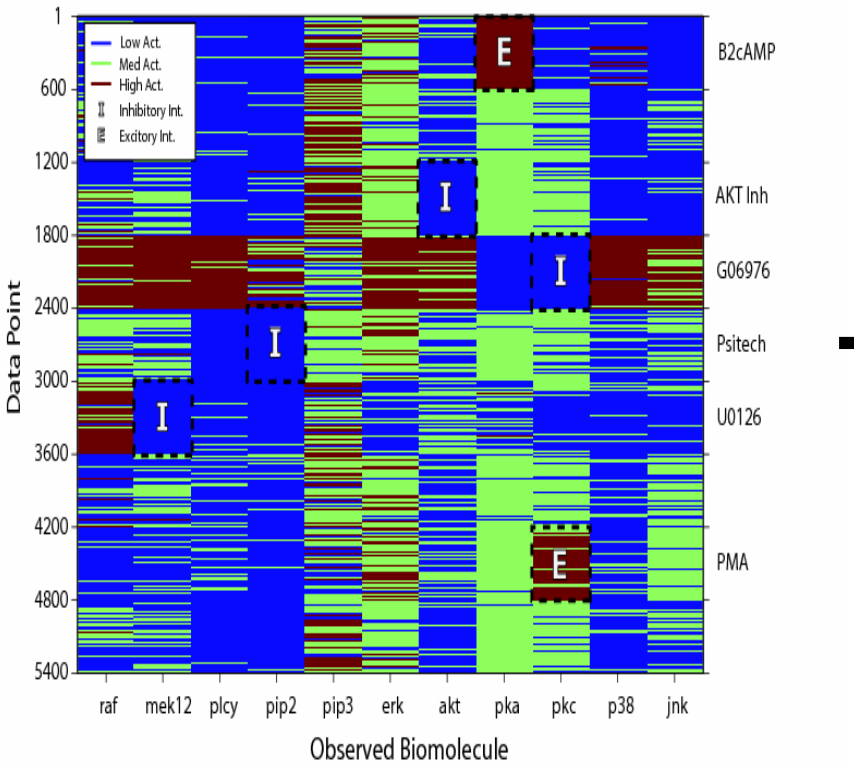
$$p(G|X,A) \quad \propto \quad p(G)p(X|G,A)$$

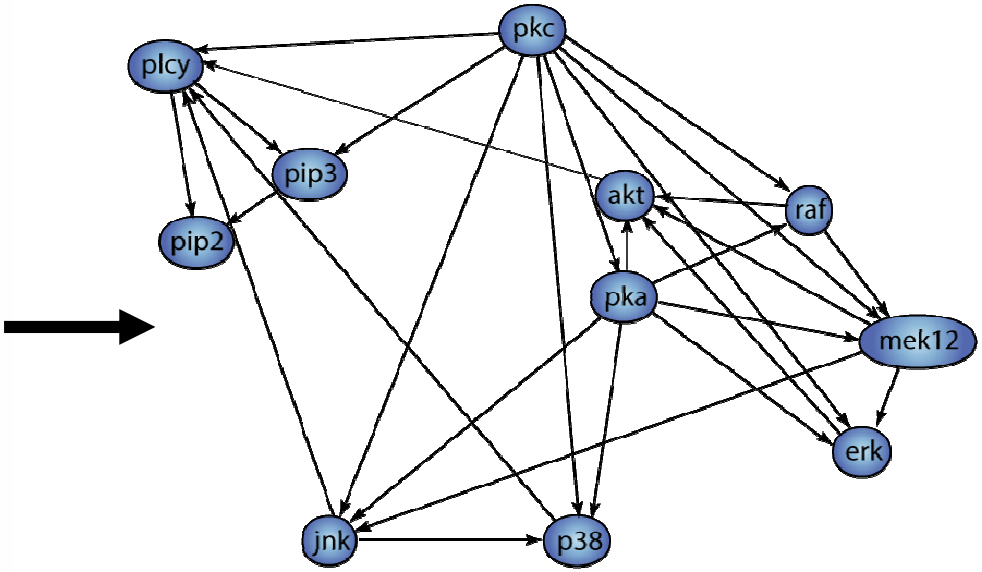
$$= \quad p(G)\prod_{j=1}^{d}\int \prod_{i:A_{ij}=0} p(X_{ij}|X_{i,G_j},\theta_j)d\theta_j$$

- We just modify the marginal likelihood (or BIC) criterion to exclude training cases where node was set by intervention

Cooper & Yoo, UAI'99

Learning T-cell signaling pathway





"Causal Protein-Signaling Networks derived from multiparameter Single-Cell Data", Sachs, Perez, Pe'er, Lauffenberger, Nolan, Science 2005

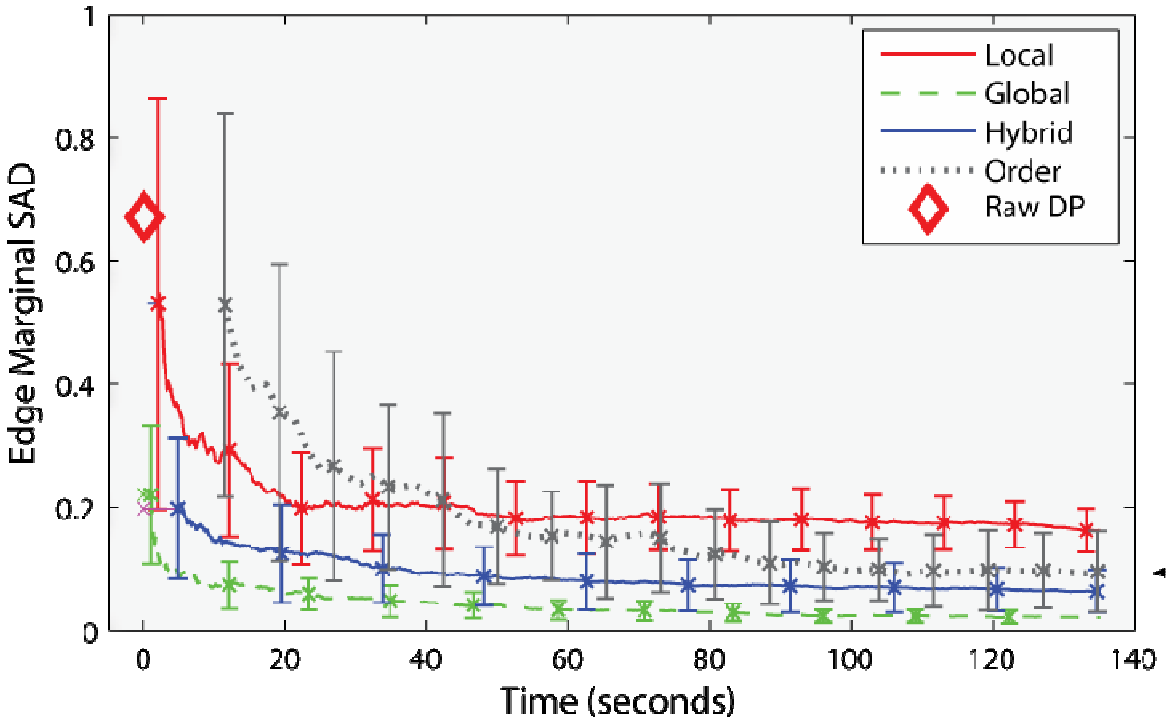
Aside on algorithms

- Sachs et al. used simulated annealing
- Ellis & Wong used equi-energy sampling
- Eaton & Murphy used dynamic programming (Koivisto) to compute the exact posterior mode and exact edge marginals $p(G_{ij}=1|X,A)$.
- Can use DP as proposal for MH.

-Byron Ellis and Wing Wong, “Learning causal Bayesian networks from experimental data”, JASA 2008
- Daniel Eaton and Kevin Murphy, “Exact Bayesian structure learning from uncertain interventions”, AI/Stats 2006
-“Advances in exact Bayesian structure discovery in Bayesian networks”, M. Koivisto, UAI 2006

Error vs compute time (5 nodes)

$$\sum_{ij} |p(G_{ij} = 1|D) - \hat{p}_t(G_{ij} = 1|D)|$$



- Eaton & Murphy," Bayesian structure learning using dynamic programming and MCMC", UAI 2007

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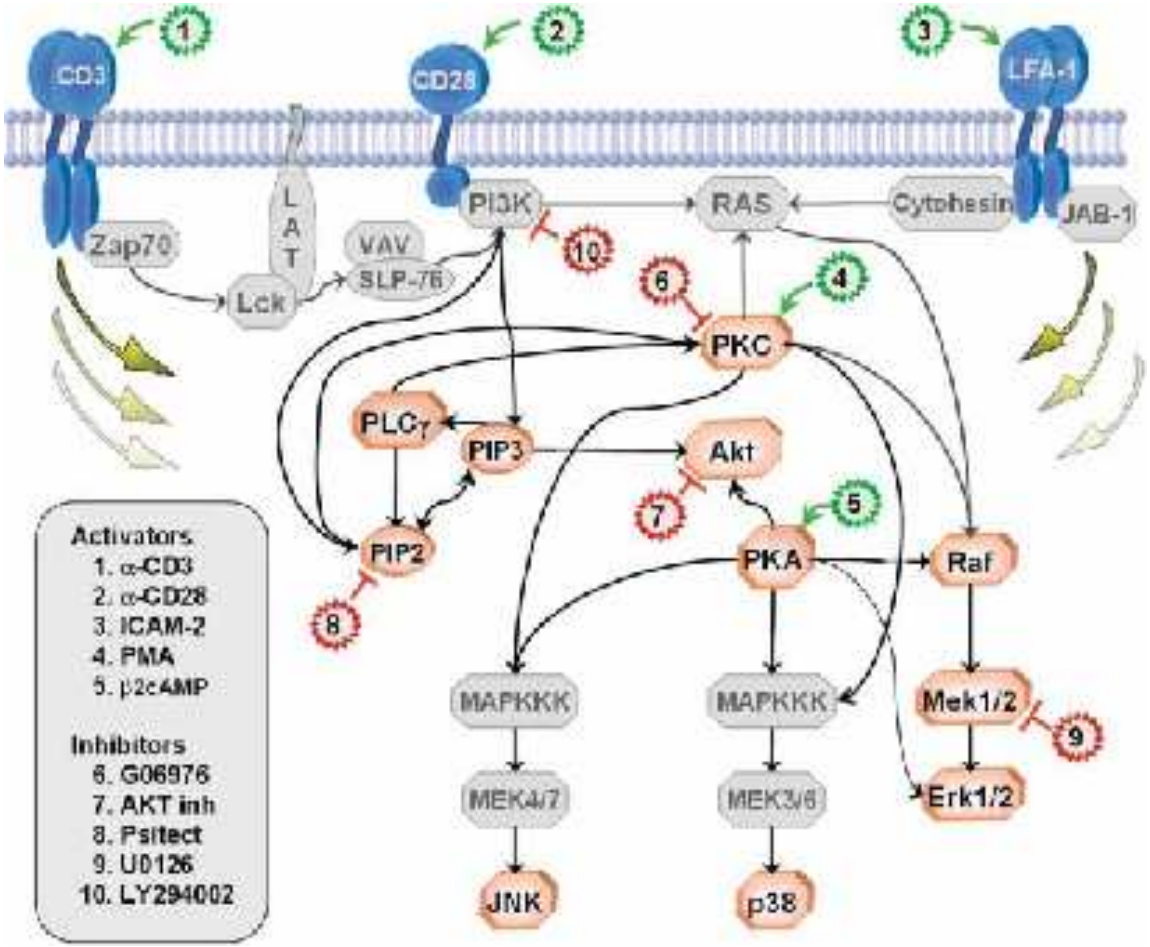
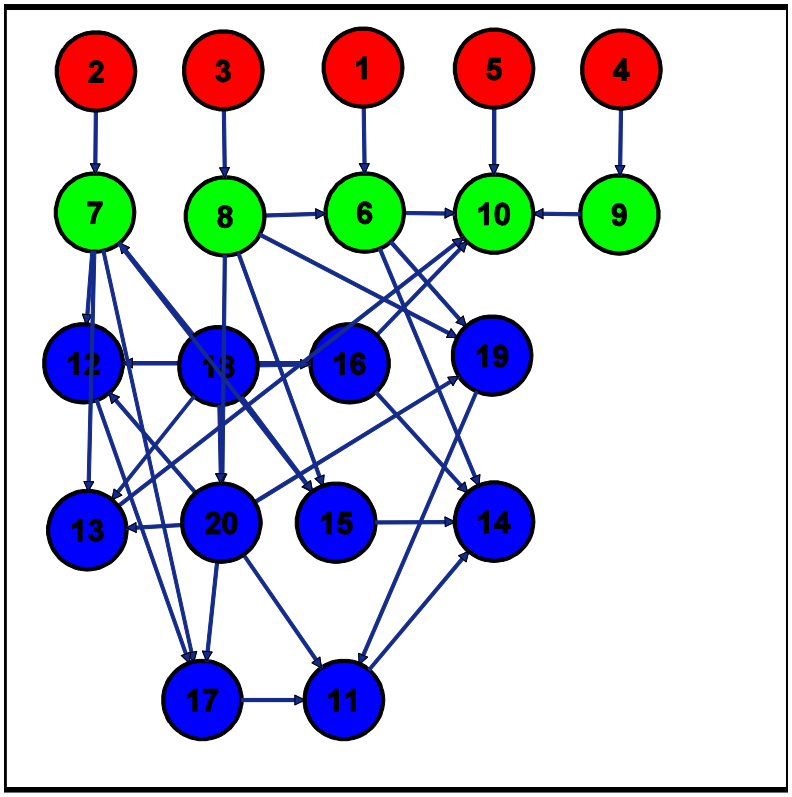
T-cell interventions



Sachs et al, Science ‘05

Intervening on hidden variables

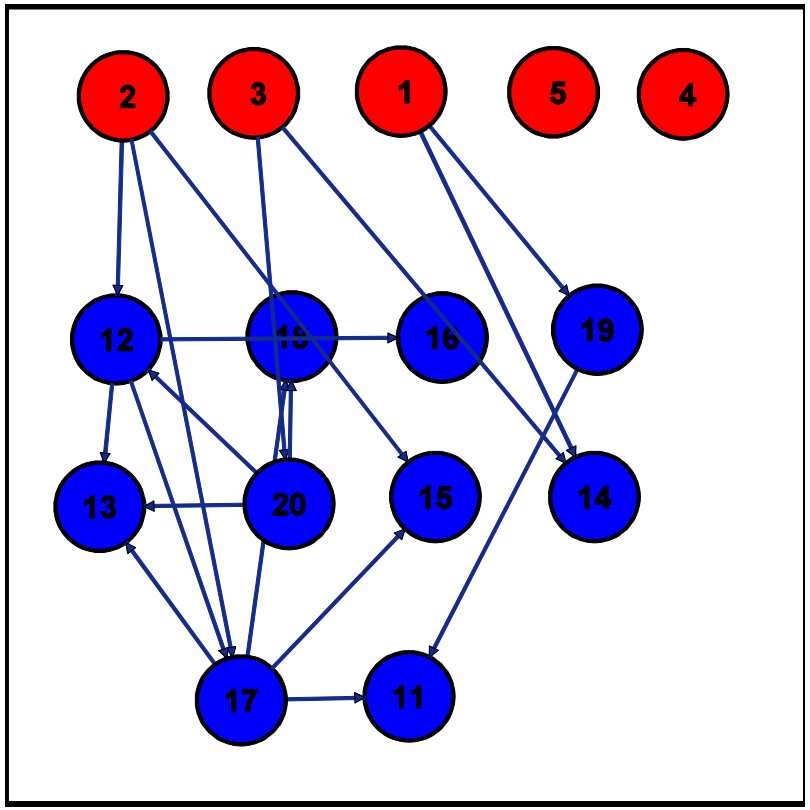


Intervention Nodes

Hidden Nodes

Observed Nodes

Actions appear as “fat hands”

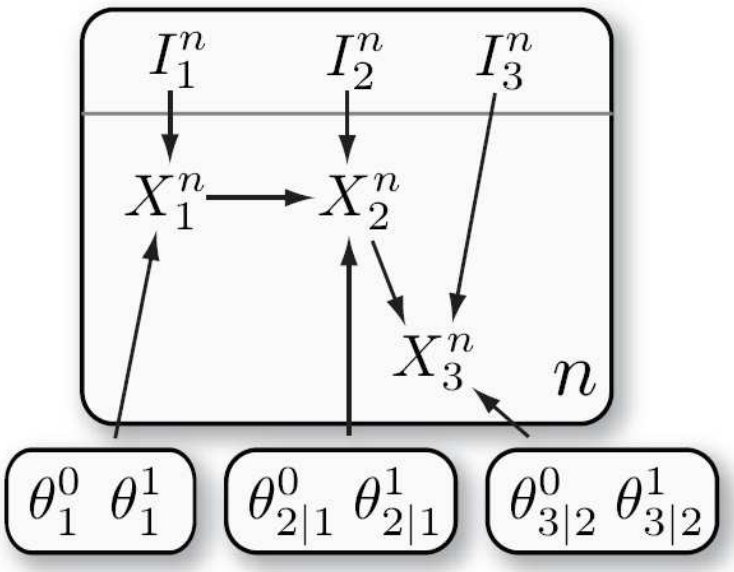


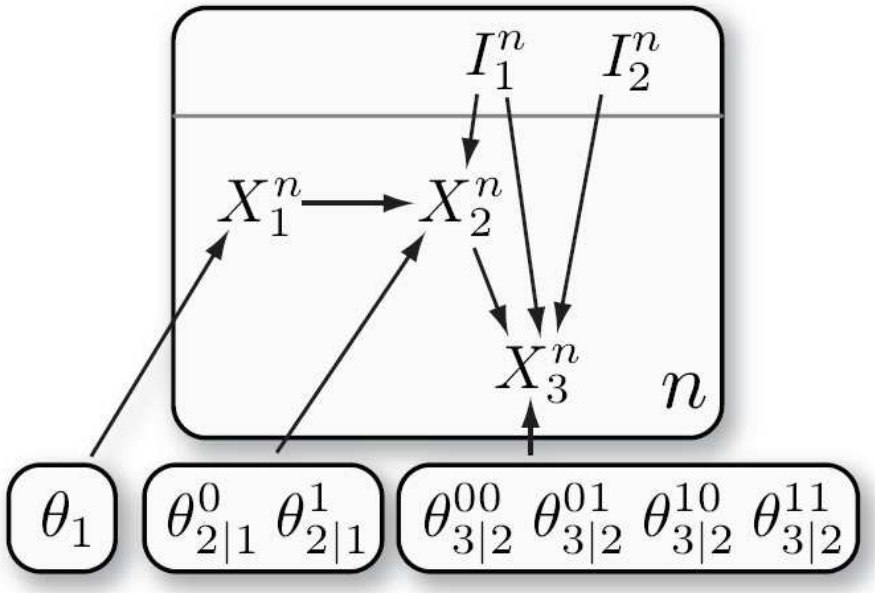
Intervention Nodes

Observed Nodes

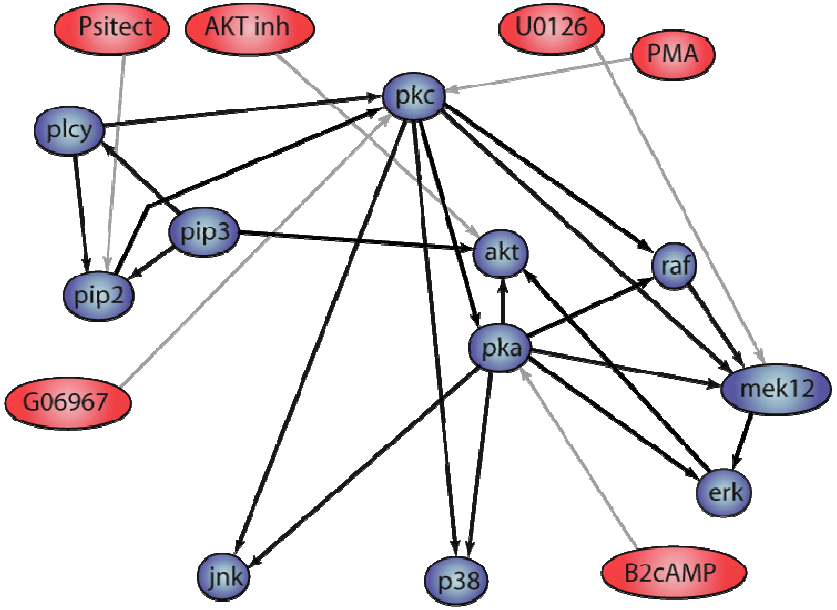
MAP DAG computed exactly by DP from large training set

Thin vs fat hands

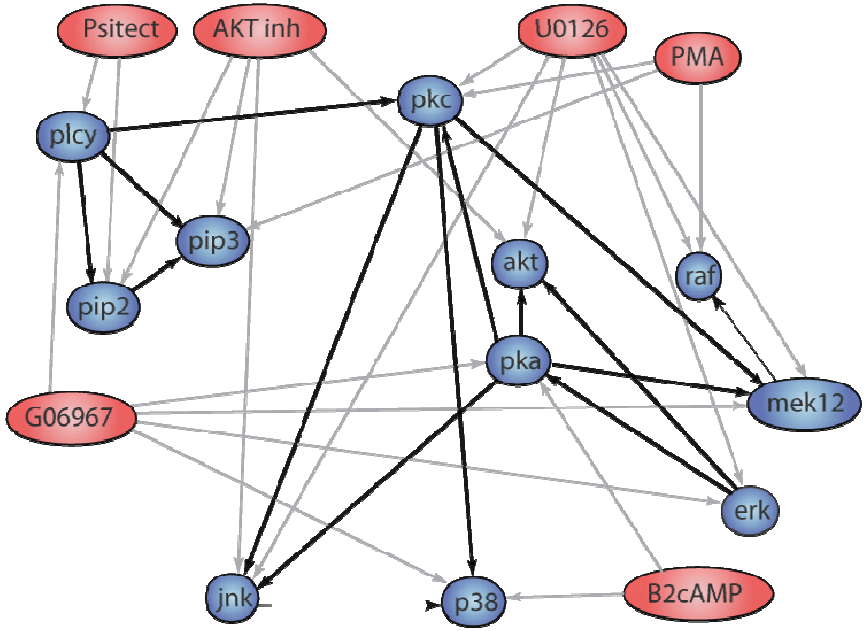




Thin vs fat in T-cell example



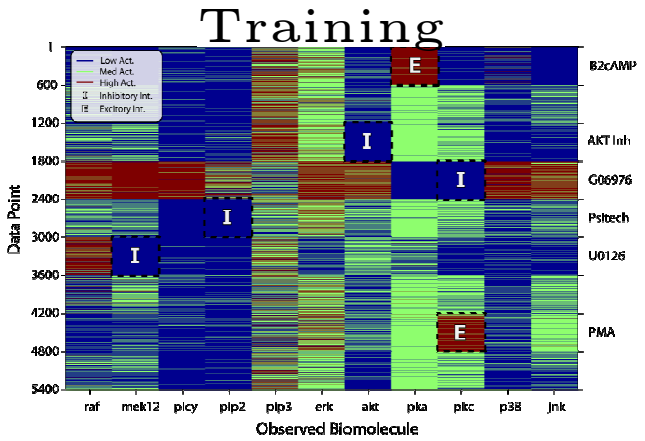
"Ground truth" DAG

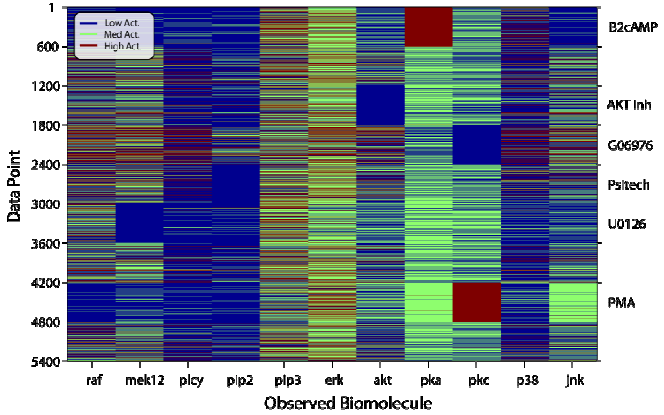


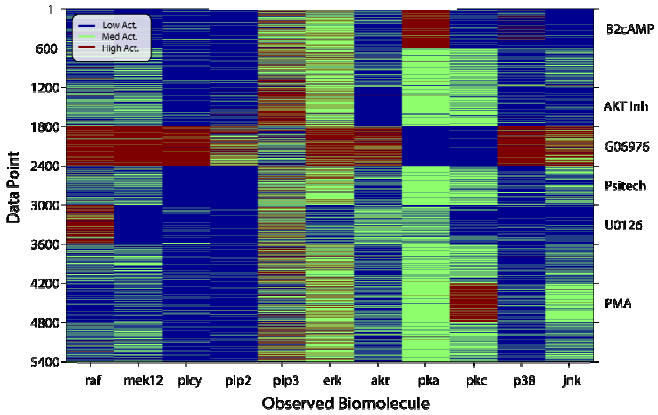
Learned fat-hand DAG

DAG learned with perfect intervention assumption is quite similar…

Samples from learned models

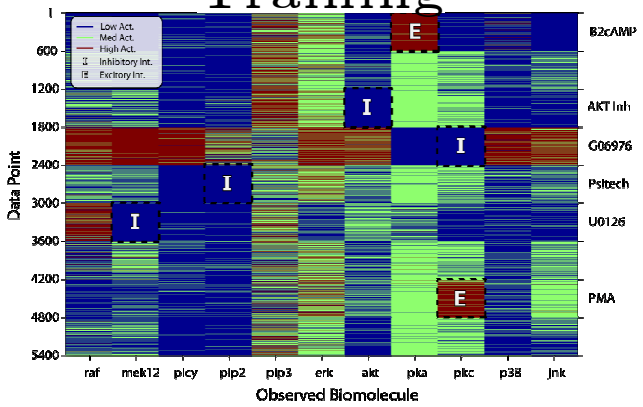




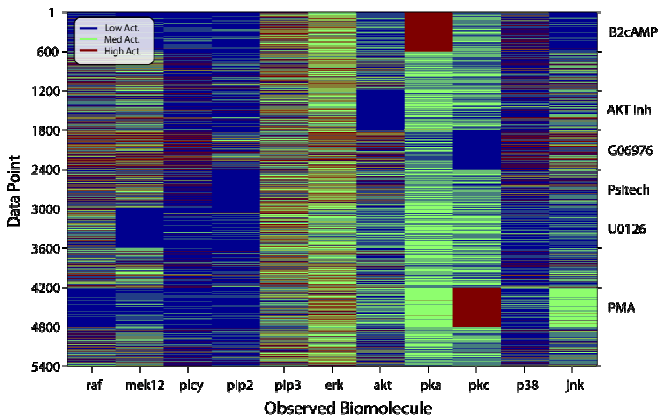


Samples from learned models

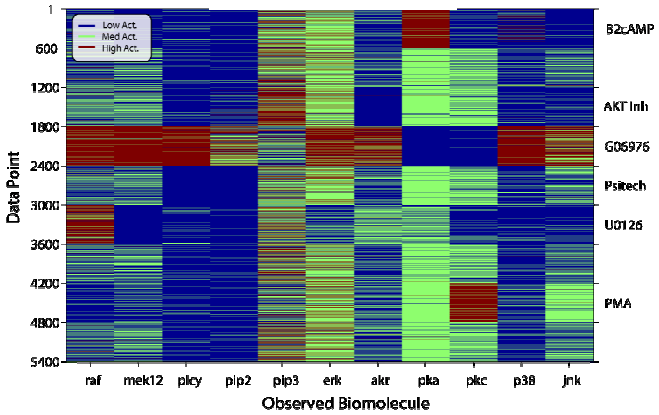
Training



Perfect interventions



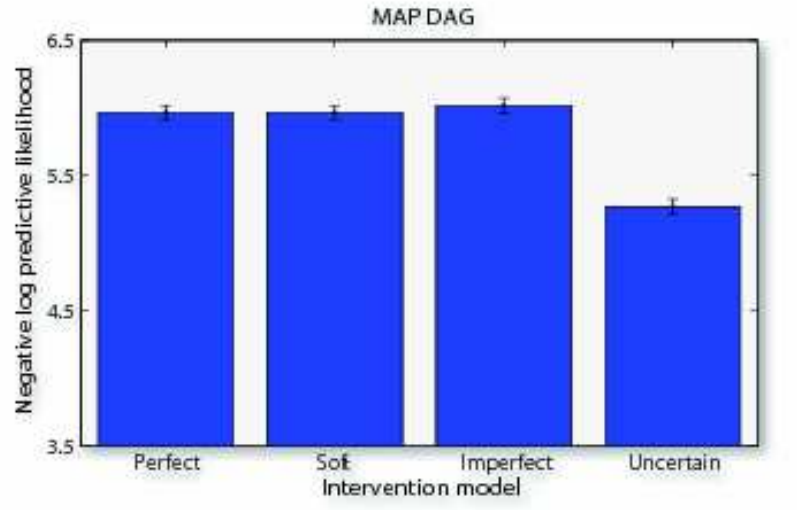
Learned interventions

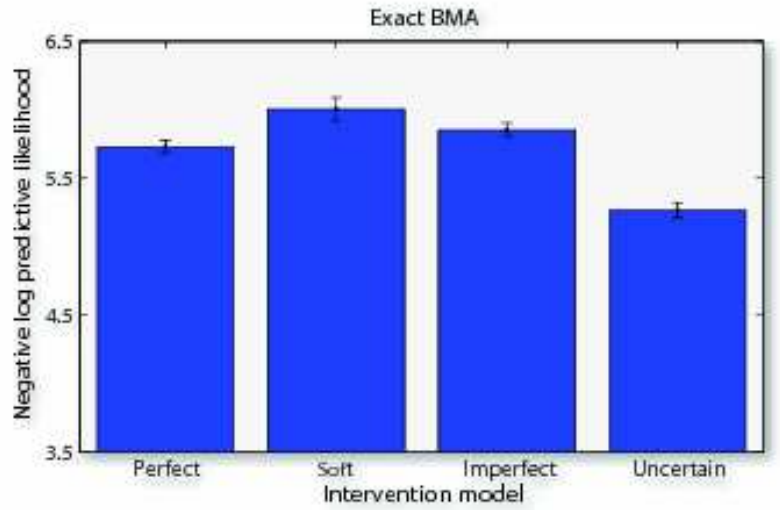


Posterior predictive checking, without reference to “ground truth” DAG

Cross validation

- Negative log-likelihood on 10-fold CV



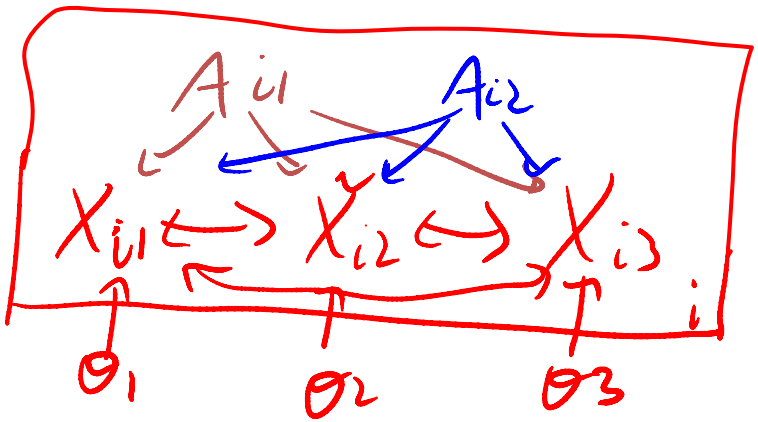


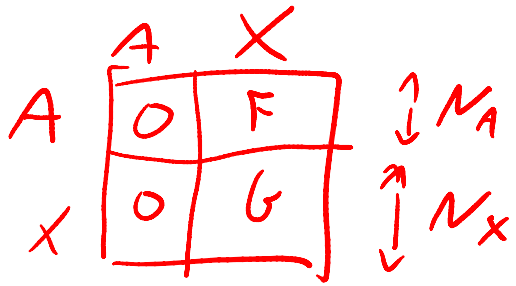
- Learning effects of intervention is better than assuming they are perfect.

Eaton & Murphy, AI/Stats 2006

Aside on algorithms

- The DAG is block-structured, since no X->A or A->A edges.
- Can exploit this in the DP algorithm so computation is $O(2 \cdot 2^d)$ not $O(2^{2d})$





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I-DAGs represent p(x|a)

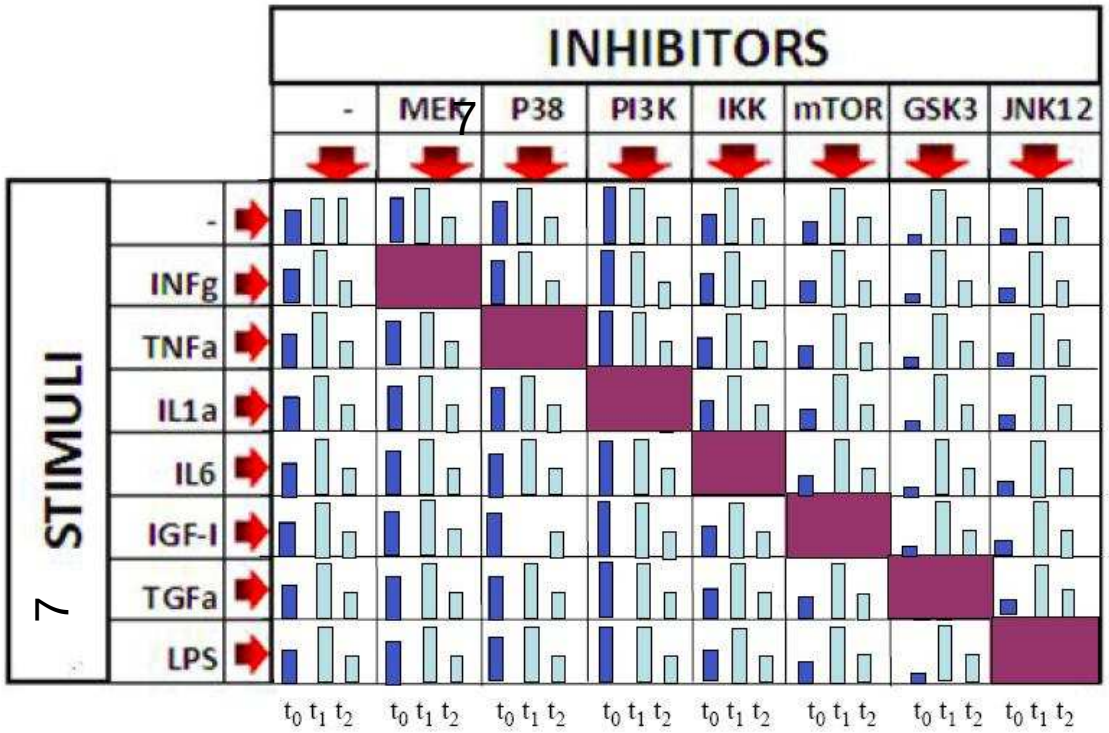
- DAGs are a way of representing joint distributions p(x) in factored form.
- I-DAGs are a way of representing conditional distributions p(x|a) in factored form, assuming actions have local effects.
- This lets us fit fewer than $O(2^d)$ separate distributions, so we can pool data, and allows us to generalize to new conditioning cases.

Predicting fx of novel interventions

- Main focus of current literature: predict effects of interventions given observational data, i.e., predict $p(x|do(x_j)) = p(x|a_j=1,a_{-j}=0)$ given samples from $p(x|a=0)$
- Other possible questions: predict $p(x|a_j=1,a_k=1,a_{-jk}=0)$ given samples from $p(x|a_j=1,a_j=0,a_{-jk}=0)$ and $p(x|a_j=0,a_k=1,a_{-jk}=0)$

DREAM 3 signaling response challenge

Predict value of 17 phosphoproteins and 20 cytokines at 3 time points in 2 cell types under novel combinations of stimulus/ inhibitor



Dialogue on Reverse Engineering and Assessment Methods

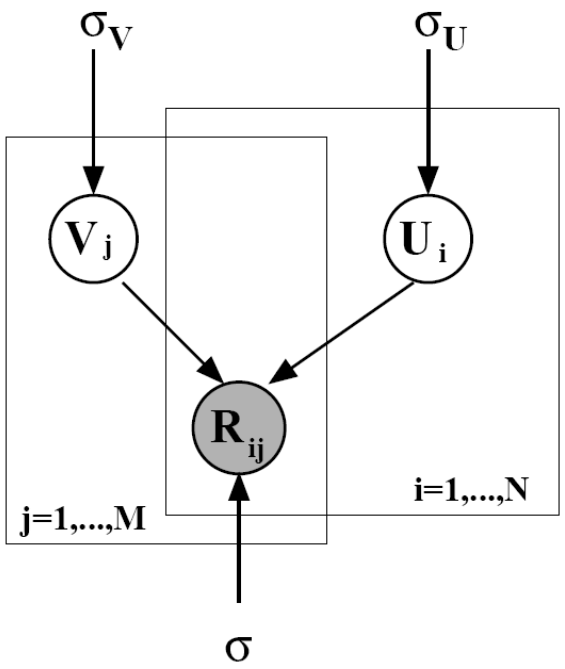
How to Fill in a Matrix?

- Need to borrow statistical strength from your (unordered) row and column neighbours
- Almost like predicting what rating someone will give a movie…

$$\begin{pmatrix} 3 & 2 & 4 & \mathbf{?} \\ 8 & 5 & 7 & \mathbf{?} \\ 9 & \mathbf{?} & 6 & 9 \end{pmatrix}$$

Probabilistic Matrix Factorization

- Singular Value Decomposition with missing entries, plus some L2 regularization



$$\begin{pmatrix} 3 & 2 & 4 & ? \\ 8 & 5 & 7 & ? \\ 9 & ? & 6 & 9 \end{pmatrix}$$

$$x_{ij} = \mathbf{u}_i^T \mathbf{v}_j + \epsilon_{ij}$$

Salakhutdinov & Mnih, NIPS 2007

Linear regression

If u_i, v_j are scalar, we can use linear regression

$$\begin{pmatrix}
1 & 0 & 0 & 1 & 0 & 0 & 0 \\
1 & 0 & 0 & 0 & 1 & 0 & 0 \\
1 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 1 & 0 & 1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 1 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 1 & 1 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 1 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 1
\end{pmatrix}
\begin{pmatrix} u_1 \\ u_2 \\ u_3 \\ v_1 \\ v_2 \\ v_3 \\ v_4 \end{pmatrix}
=
\begin{pmatrix}
u_1 + v_1 \\ u_1 + v_2 \\ u_1 + v_3 \\ u_2 + v_1 \\ u_2 + v_2 \\ u_3 + v_3 \\ u_3 + v_1 \\ u_3 + v_3 \\ u_3 + v_4
\end{pmatrix}
=
\begin{pmatrix} 3 \\ 2 \\ 4 \\ 8 \\ 5 \\ 7 \\ 9 \\ 6 \\ 9 \end{pmatrix}$$

$$\begin{pmatrix}
3 & 2 & 4 & ? \\
8 & 5 & 7 & ? \\
9 & ? & 6 & 9
\end{pmatrix}$$

Linear regression for dream 3

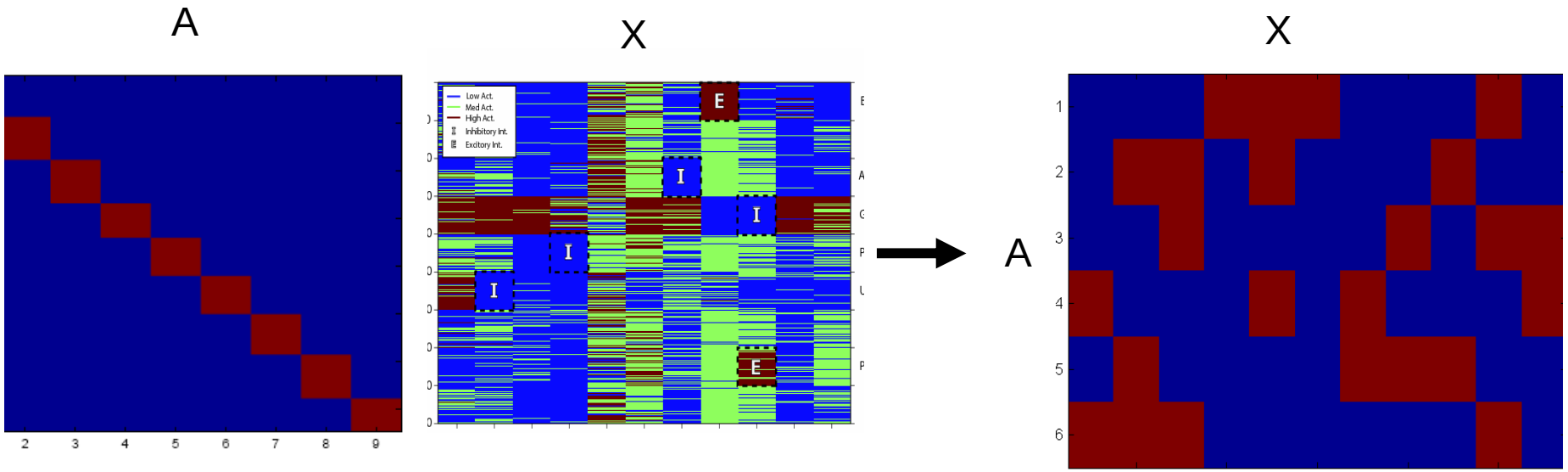
Stimulus								Inhibitor								
None	INFg	TNFa	IL1a	IL6	IGF1	TGFa	LPS	None	MEK	P38	P13K	IKK	mTOR	GSK3	JNK12	Response
1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	5578
1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	4544
1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	5108
1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2796
1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	4409
1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	4269
								.								.
								.								.
								.								.
0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	5485
0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	4720
0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	5317

Results

Team	Normalized Squared Error	P Value
UBC PMF	1483.961	2.116e-024
UBC Index-Based	1828.389	5.771e-024
Team 102	3101.950	2.080e-022
Team 106	3309.644	3.682e-022
Team 302	11329.398	7.365e-014

- We won!
- However, the contest was already over ☹
- Also, none of the other methods used DAGs…
- How do these simple methods compare to DAG-based approaches on the T-cell data?

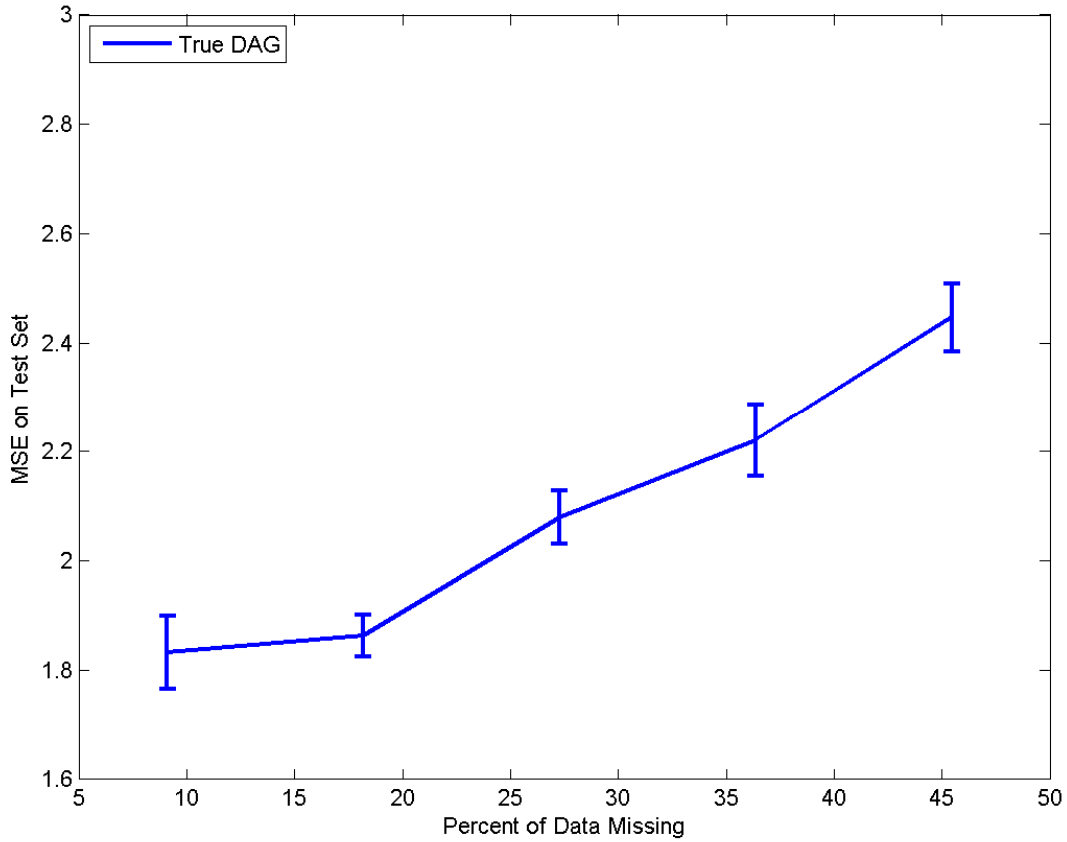
Modified T-cell data



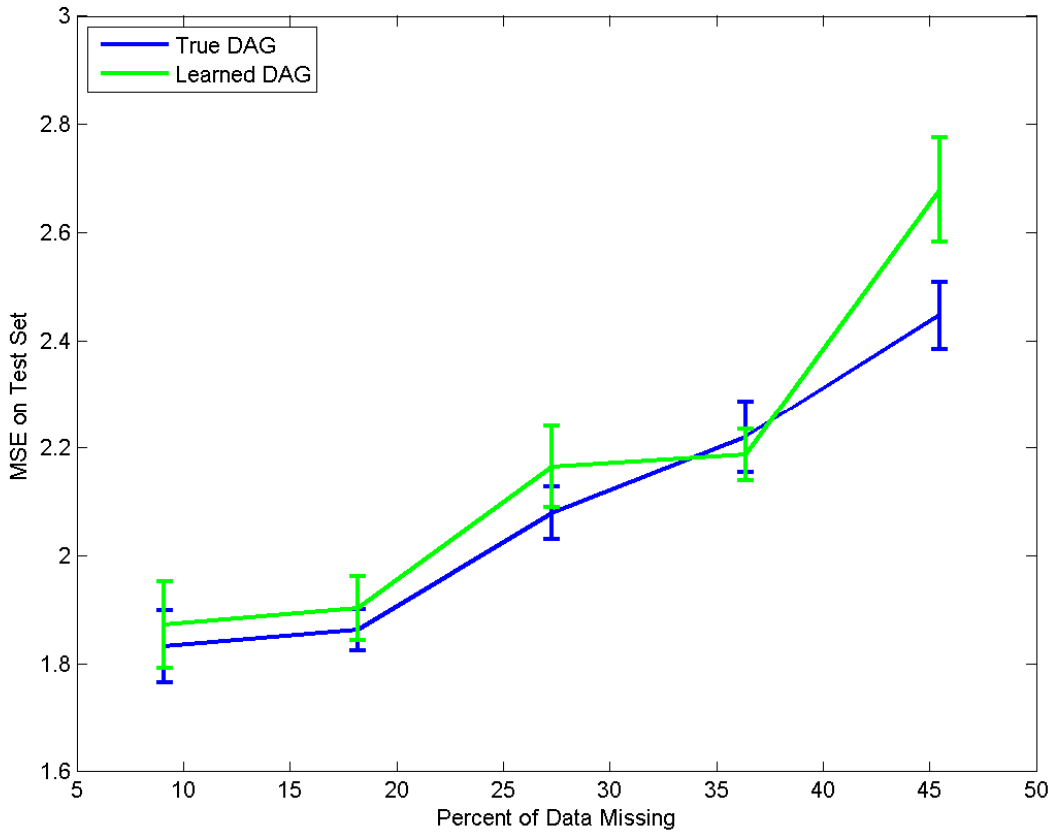
We have observations of $X_{i,1:d}$ for i=1:1000, given A_a=1, A_{-a}=0, for a=1:6. From this, compute average response of each variable to each action.

$$\mu_{a,j} = \frac{1}{n_a} \sum_{i:A_a=1} x_{i,j}$$

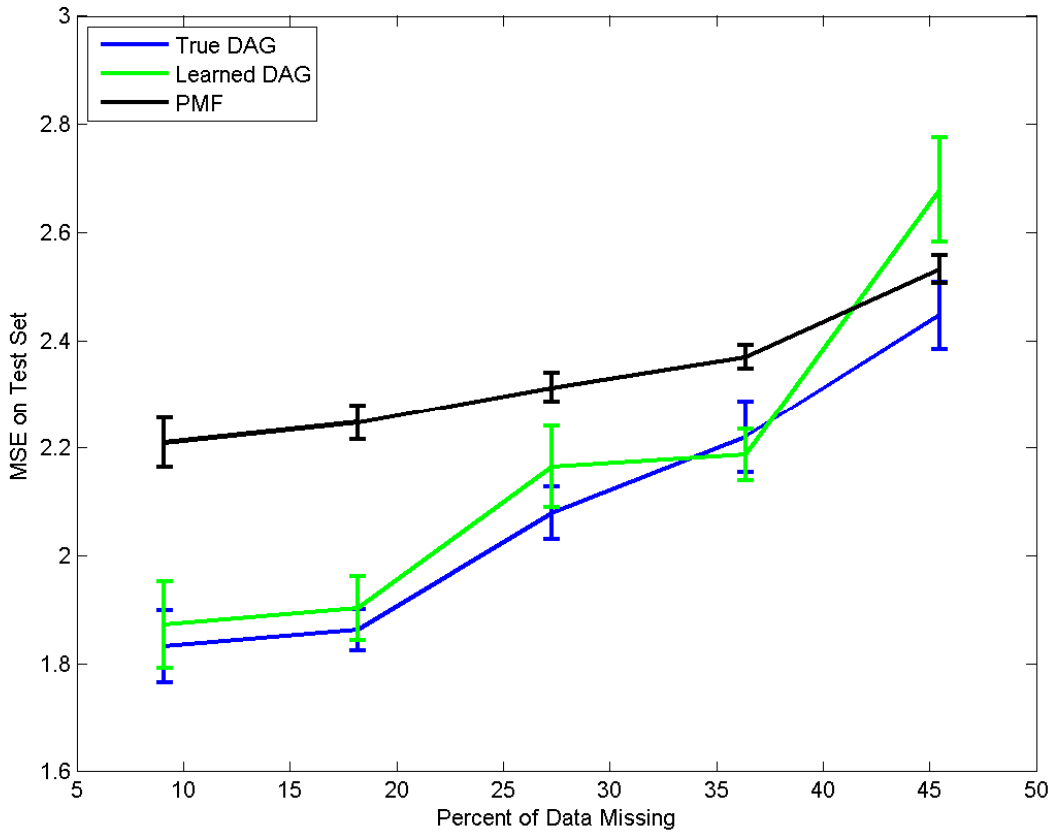
Predictive accuracy on modified T-cell



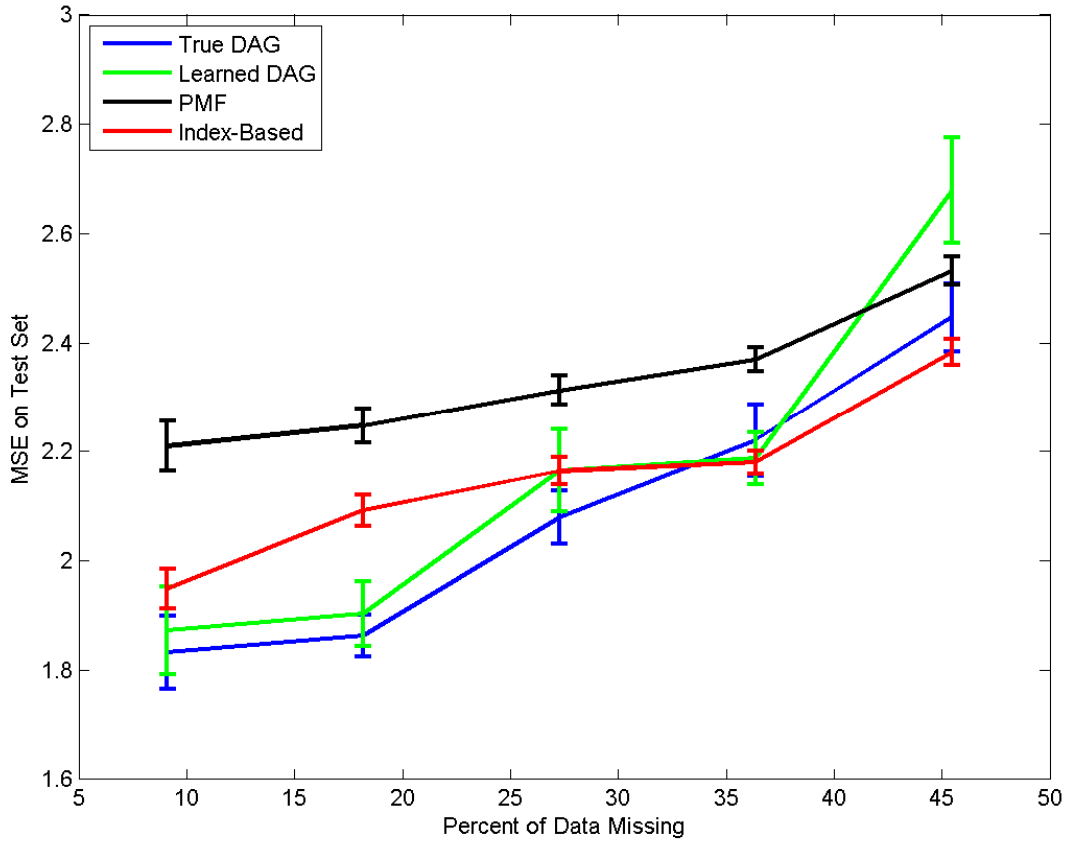
Predictive accuracy on modified T-cell



Predictive accuracy on modified T-cell



Predictive accuracy on modified T-cell



Summary

- Effects of Causes can be modeled using influence diagrams, which can be learned from data using standard techniques.
- Other kinds of conditional density models can also be used, and work surprisingly well.
- We need to assess performance without reference to graph structures, which, for real data, can never be observed.