# Information-Theoretic Reconstruction of Interaction Graphs in Complex Networks

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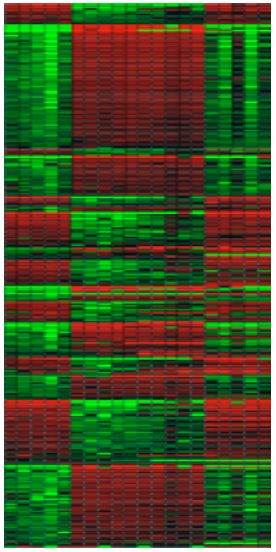
(CCS-3)

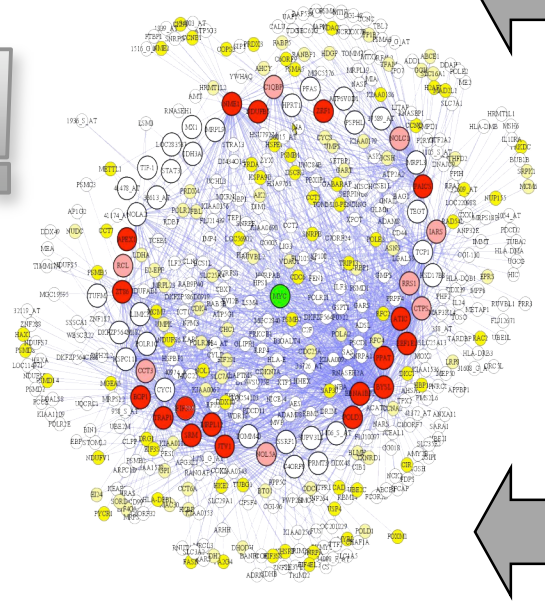
# Interaction models in gene regulation

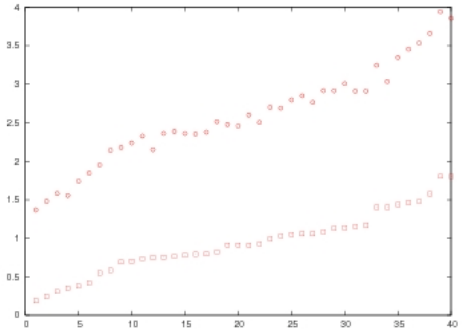
Measurement of ~1e4 chemical concentrations in cultures simultaneously



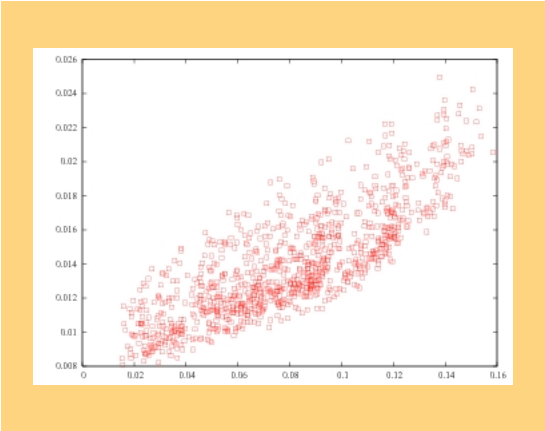
(B-cell lymphomas, Basso et al, 2004)

Holy Grail !





Time series



Steady states

Reducibility?

# Interaction models

$$\frac{dx_i}{dt} = f_1\left(\left\{CL_1(x_i)\right\}\right) + \cdots + f_{N_1}\left(\left\{CL_{N_1}(x_i)\right\}\right) - rx_i$$

$$\bar{x}_i = \frac{1}{r}\left[f_1\left(\left\{CL_1(x_i)\right\}\right) + \cdots + f_{N_1}\left(\left\{CL_{N_1}(x_i)\right\}\right)\right]$$

$$P\left(x_i \mid Ne(x_i)\right) \propto \exp\left\{-\frac{1}{2\sigma^2}\left[x_i - \bar{x}_i\right]^2\right\}$$

$$P\left(x_i \mid Ne(x_i)\right) \propto \exp\left\{-\lambda\left[x_i, \left\{CL_1(x_i)\right\}\right] - \cdots - \lambda\left[x_i, \left\{CL_{N_1}(x_i)\right\}\right]\right\}$$

$$P(x_1, \ldots, x_N) \propto \exp\left\{-\sum \lambda_i - \sum \lambda_{ij} - \sum \lambda_{ijk} - \cdots\right\}$$

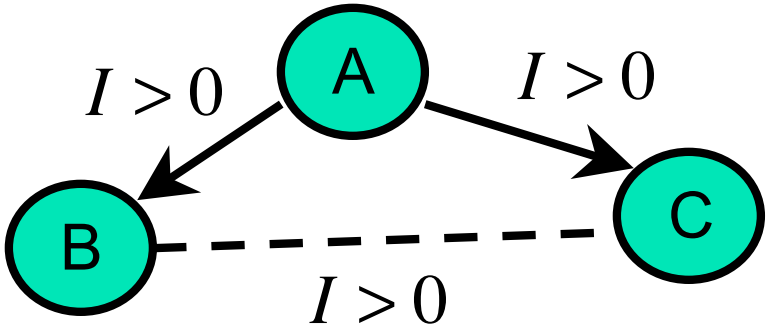
MaxEnt determination of interactions:

$$S[X] \equiv -\sum_{x=1}^{K} p_x \log p_x = -\langle \log p_x \rangle$$

$$Q_{i_1 \ldots i_M} = \arg\max\left\{S[Q] - \sum_{\text{others}} \lambda_{\text{others}} \cdot P_{\text{marginal}}\right\}$$

$$\Delta_{i_1 \ldots i_M} \equiv S[Q] - S[P] > 0 \quad \Rightarrow \quad \text{interaction}$$

# Example




$$P_{ABC} = \frac{P_{AB} P_{AC}}{P_A} = \frac{1}{Z} f_{AB} f_{BC}$$

MaxEnt approximation without BC: No interaction!

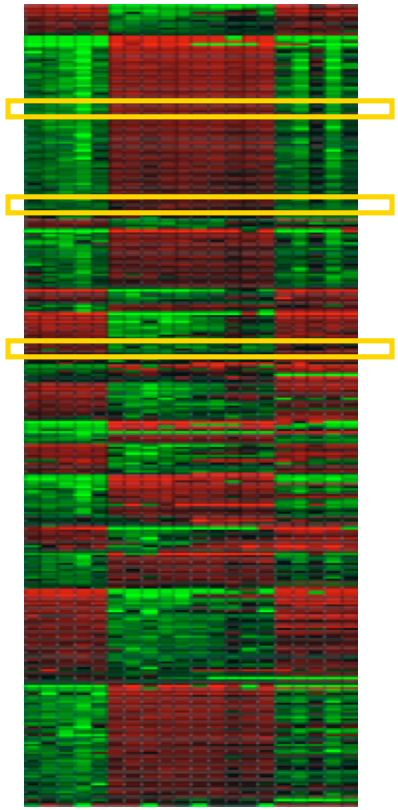
$$Q_{ABC} = \frac{1}{Z} \exp(-\varphi_{AB} - \varphi_{AC}) \quad \Rightarrow \quad \Delta = 0$$

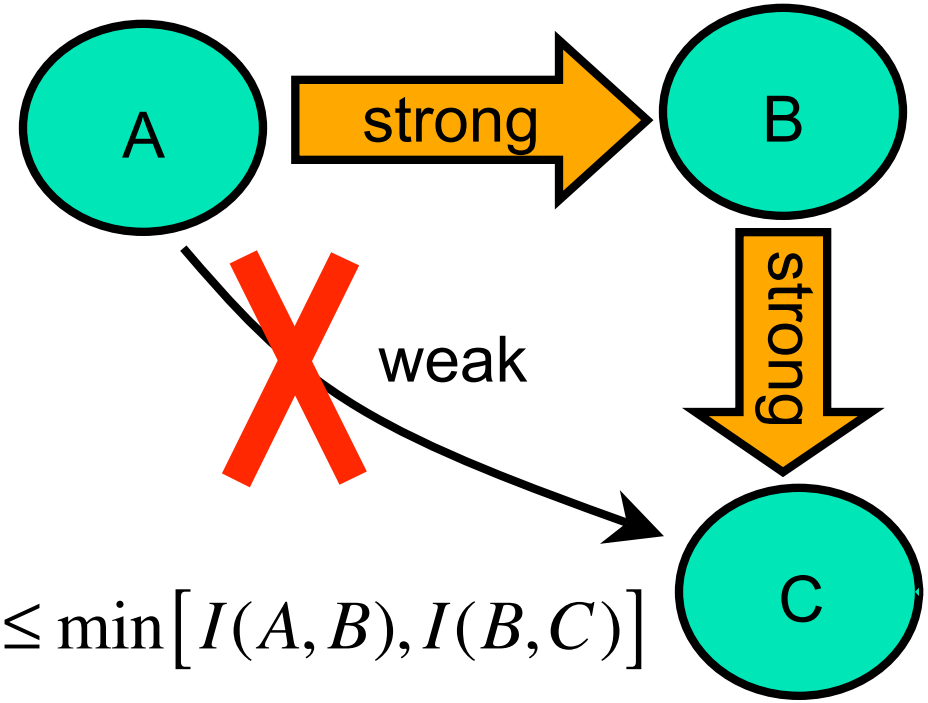
MaxEnt approximation without AB: Interaction!

$$Q_{ABC} = \frac{1}{Z} \exp(-\varphi_{BC} - \varphi_{AC}) \quad \Rightarrow \quad \Delta > 0$$

Empirically: interactions >2nd order are (almost) negligible in genetic and many other networks.

# Fast Approximation: 2nd order tree-like



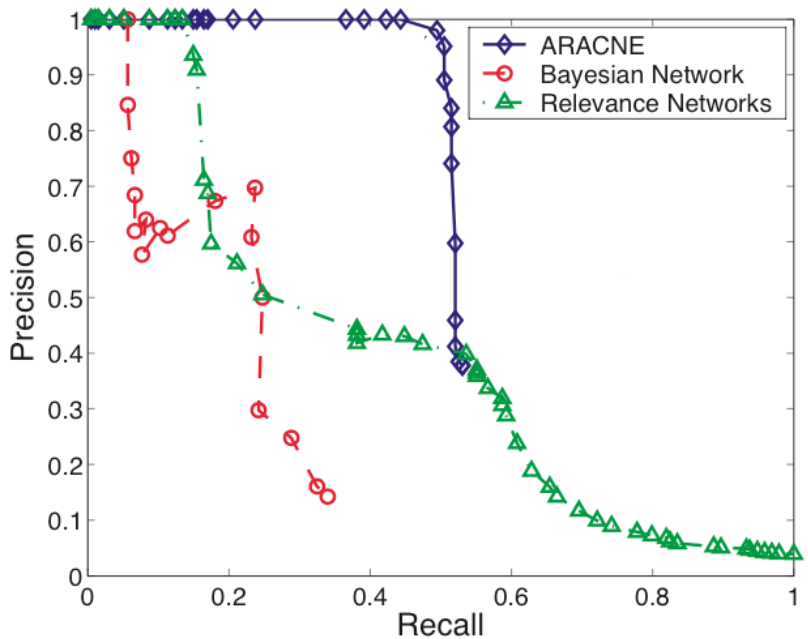




$$I(A,C) \le \min\left[I(A,B), I(B,C)\right]$$

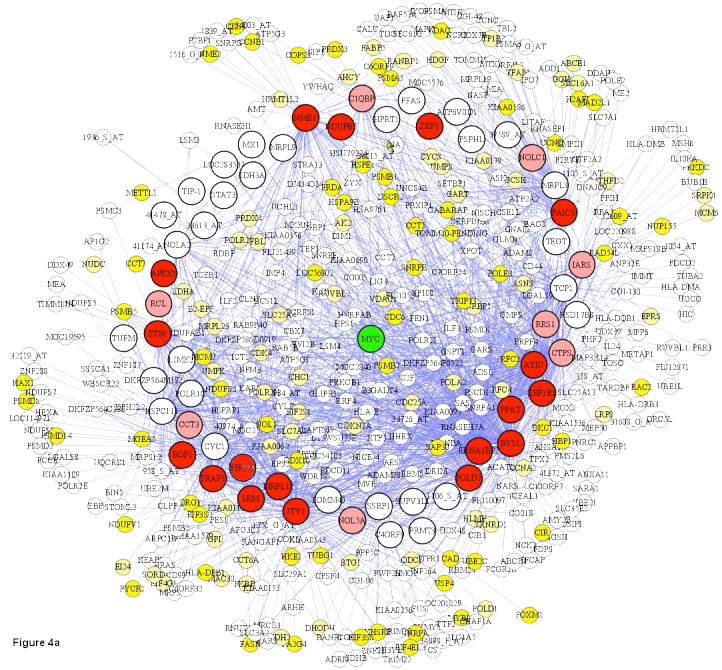
Tree-like: strongest contribution to *I(A,B)* from the shortest link; some relation to BP.

# Performance

## Synthetic




## B-cells




Total interactions: 56
Pre-known: 22
Ch-IP validated: 11/12