Quantum-Classical Hybrid Machine Learning for Gene Regulatory Pathways

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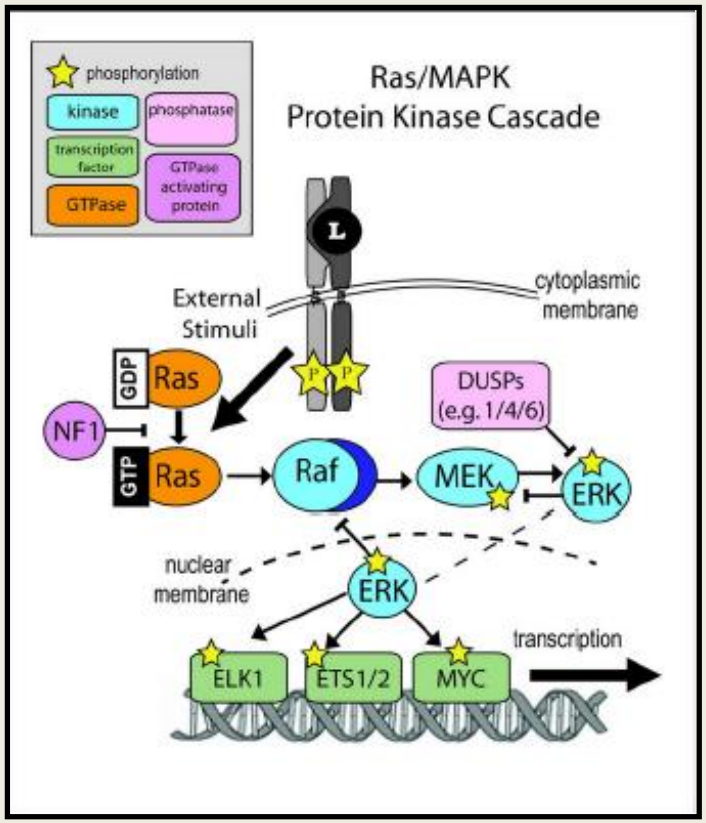
Qubits North America, 09/26/2018, Knoxville, TN

Outline of the Talk

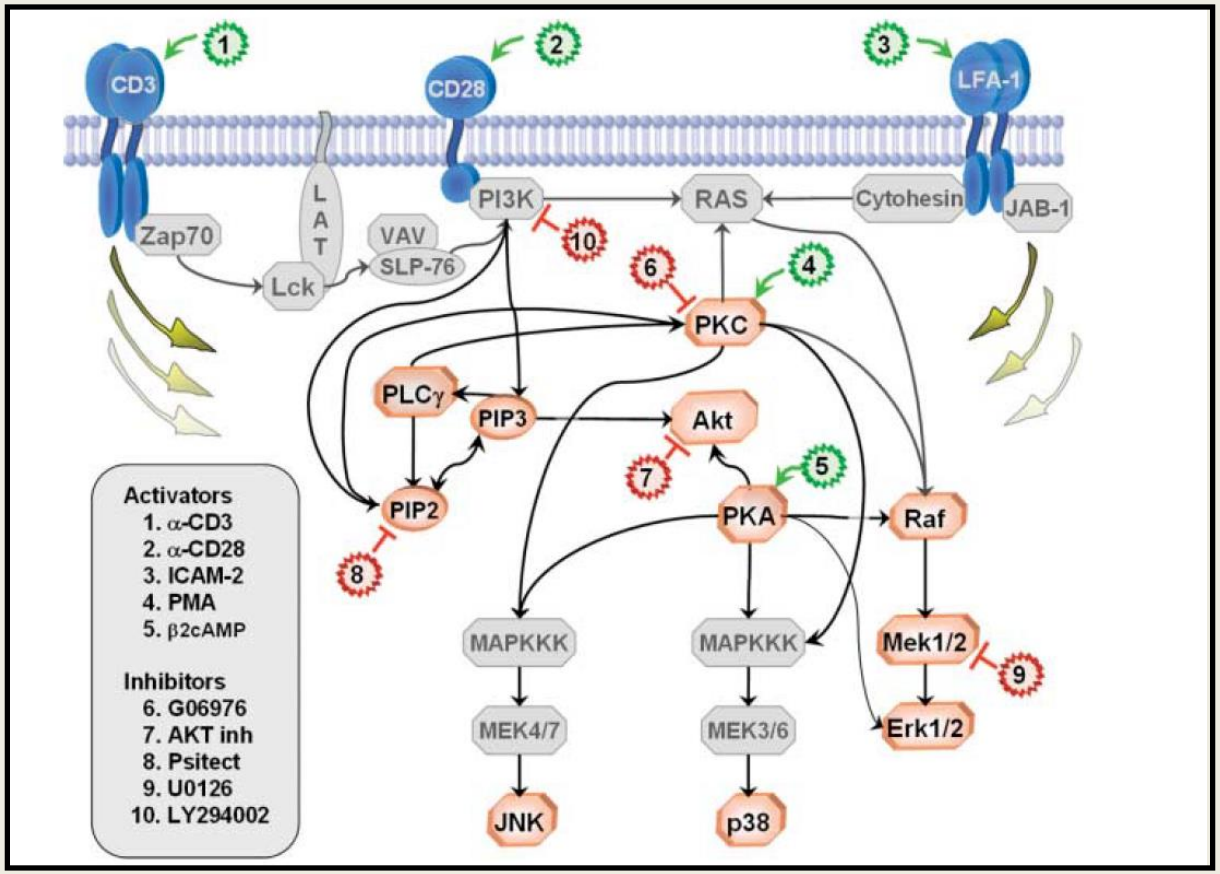
- A Brief introduction to the problem
- Review of Bayesian Networks
- Embedding challenges
- Probabilistic Logic Programming (ML)
- Solution Architecture and Results

MAPK/Raf Pathway



MAPK/Ras pathway. Source: Discovery Medicine

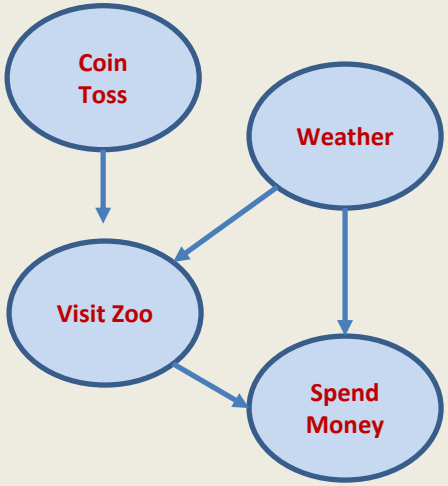
A Bayesian Network based Causal Relationship Elucidation



Sachs, K.; Perez, O.; Pe'er, D.; Laughenburger, A. D.; Nolan, P. G. Causal Protein-Signaling Networks Derived from Multiparameter Single-Cell Data. *Science* 2005, *308*.

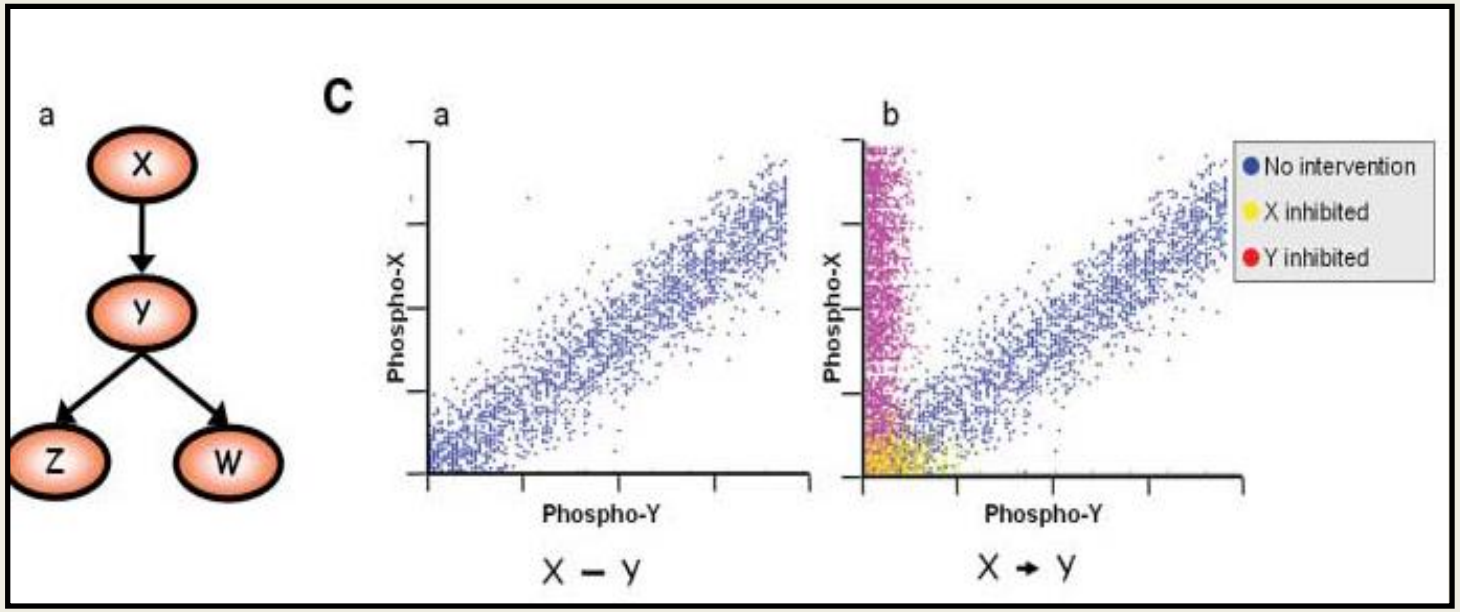
Bayesian Networks

- BN is a pair (B_s, B_p).
- B_s is directed acyclic graph representing the model
- B_p is the set of conditional probabilities
- X_i state of node – gene is activated or not
- Probability of X_i conditioned on the joint state of its parents $\pi_i(B_S)$
- Parents: Arcs in the structure to X_i



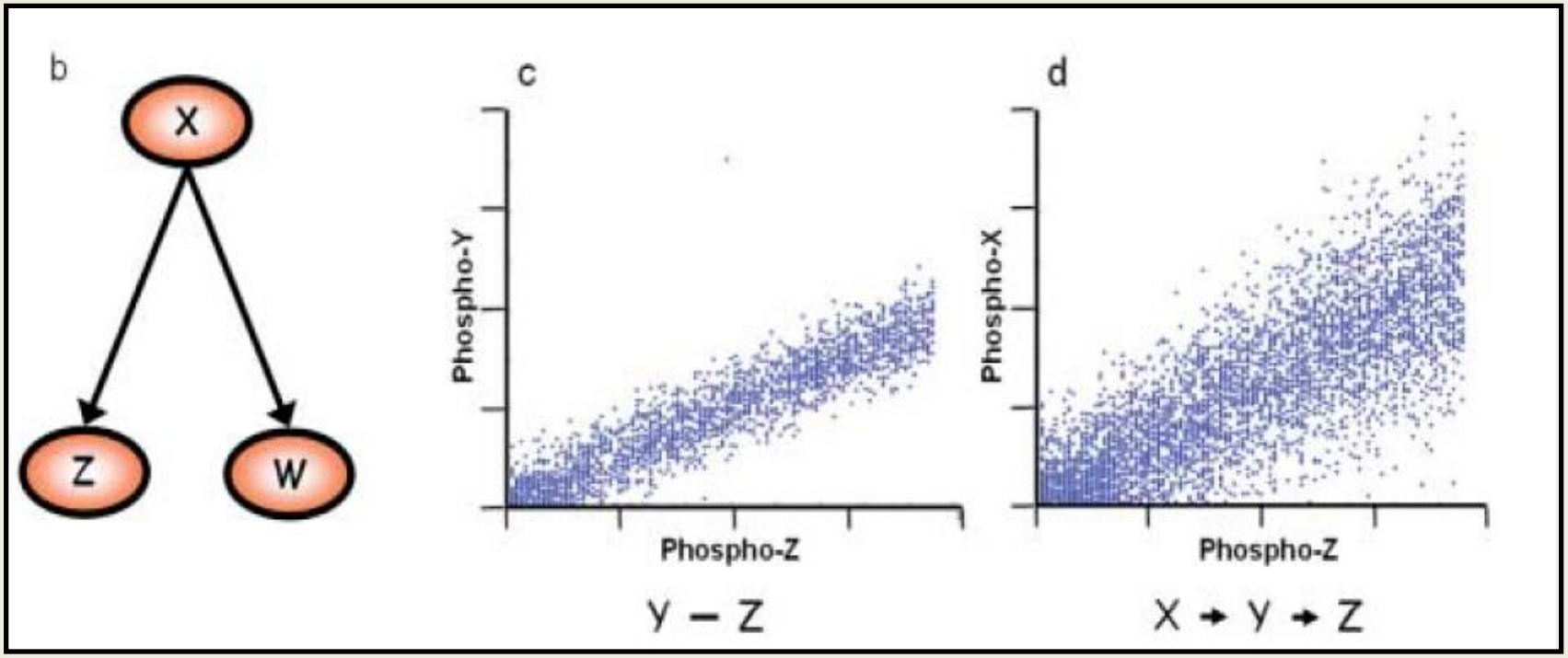
Bayesian Networks

Proteomics data from flow cytometry
Concentrations of proteins as probabilities



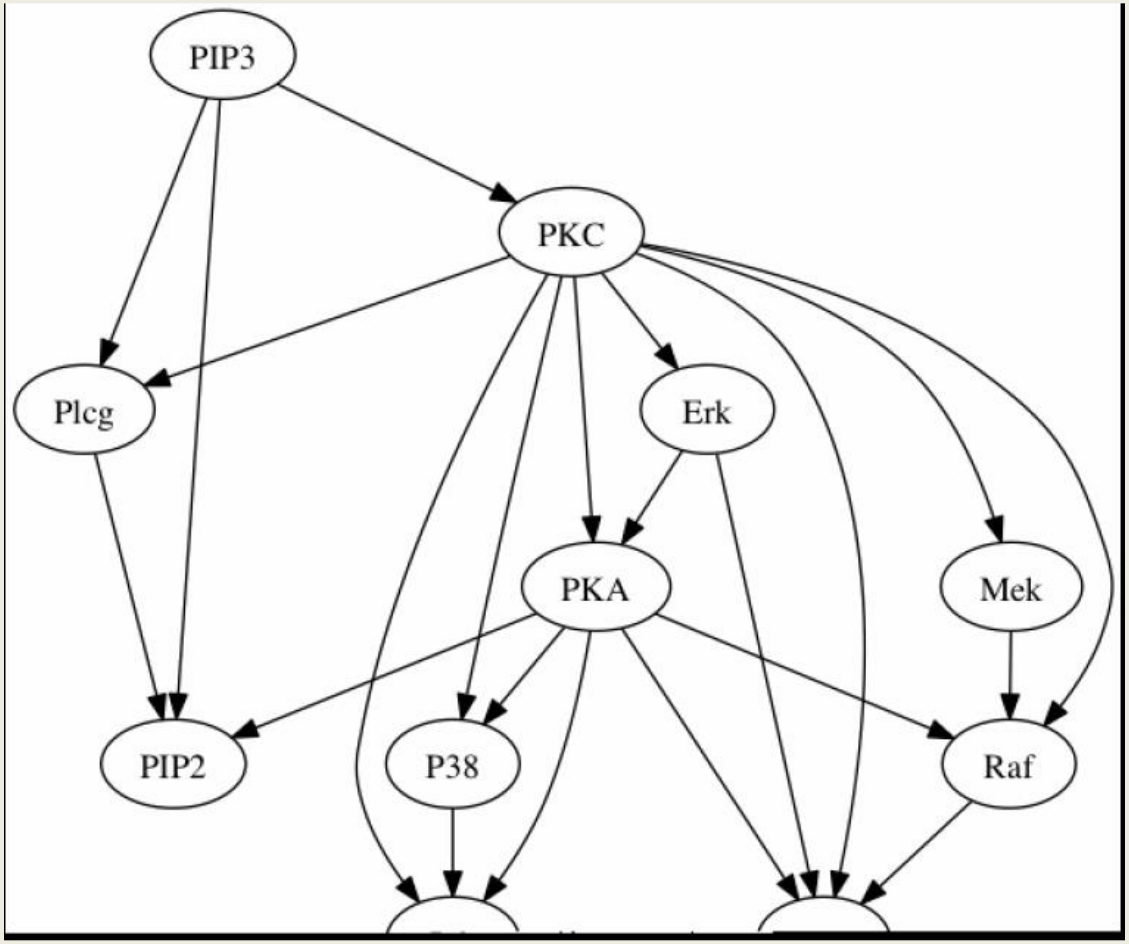
Bayesian networks for hypothetical proteins X, Y, Z, and W. In this model, X influences Y, which, in turn, influences both Z and W.

Acyclic directed graphs



- Biological pathways may contain cycles
- BN May miss some dependencies

PRISM Generated BN



Nand Kishore, Radhakrishnan Balu, and Shashi P. Karna, “Modeling Genetic Regulatory Networks Using First-Order Probabilistic Logic”, **ARL-TR-6354**, 2013.

(Quantum) Probabilistic Logic

- Non-commutative Probability
- Quantum Probability Space
- Attach Probability Amplitudes to H-interpretations
- Projections of H
- ρ - State

Denotational Semantics

⇕

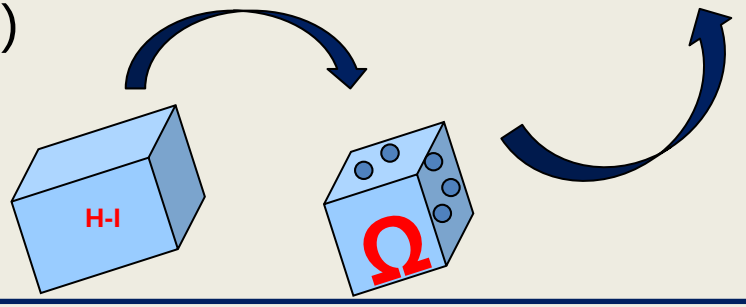
Distribution Semantics (PRISM)

⇕

Entanglement Semantics

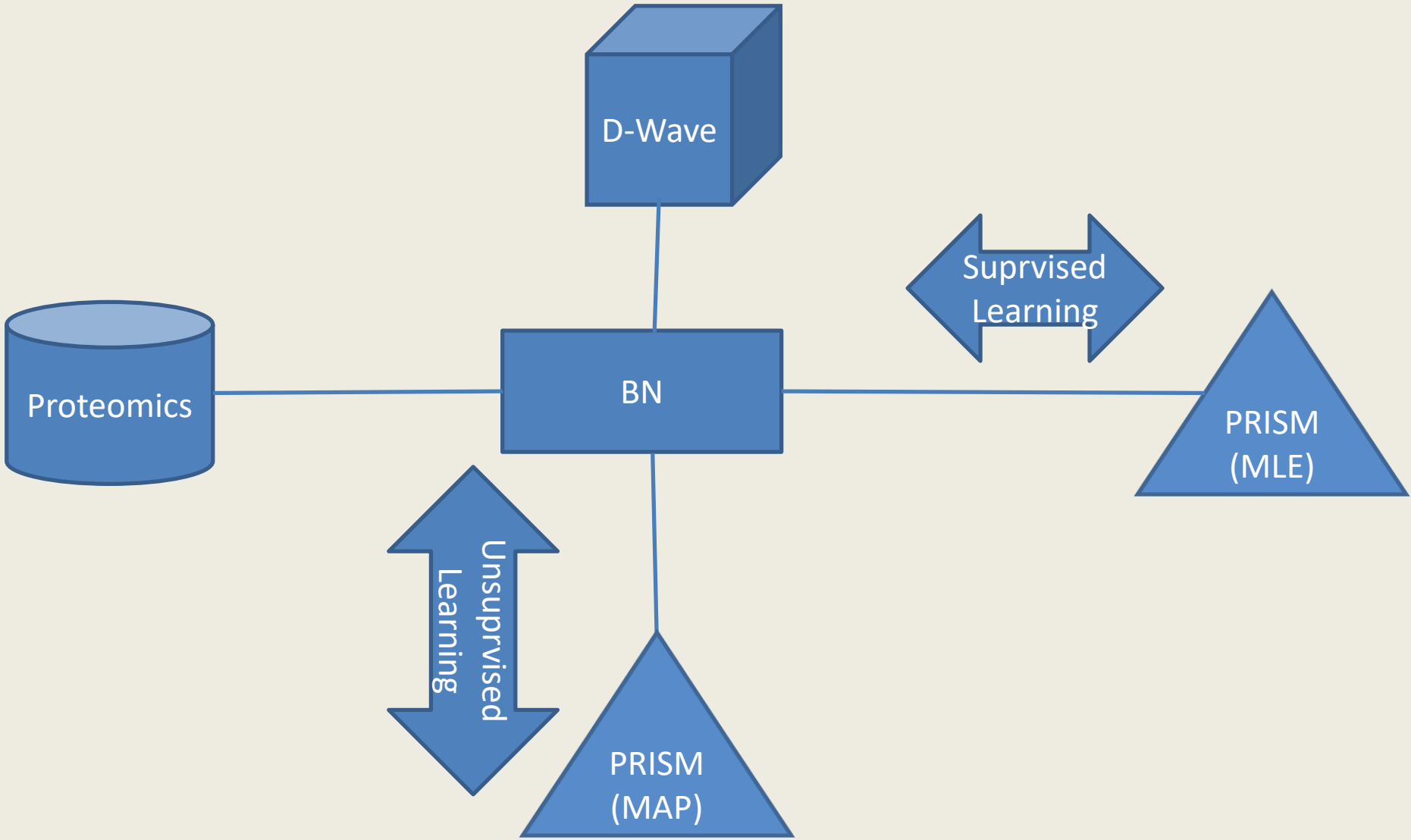
$$QP = \left(\mathrm{H}^{\infty}, P(H), P\right)$$

$$\frac{1}{\sqrt{2}}\left(|01\rangle + |10|\right)$$



Radhakrishnan Balu: Quantum probabilistic logic programming, Proc. SPIE-DSS, quantum information and computation, Baltimore MD (2015)

Hybrid Architecture



Quantum Annealing

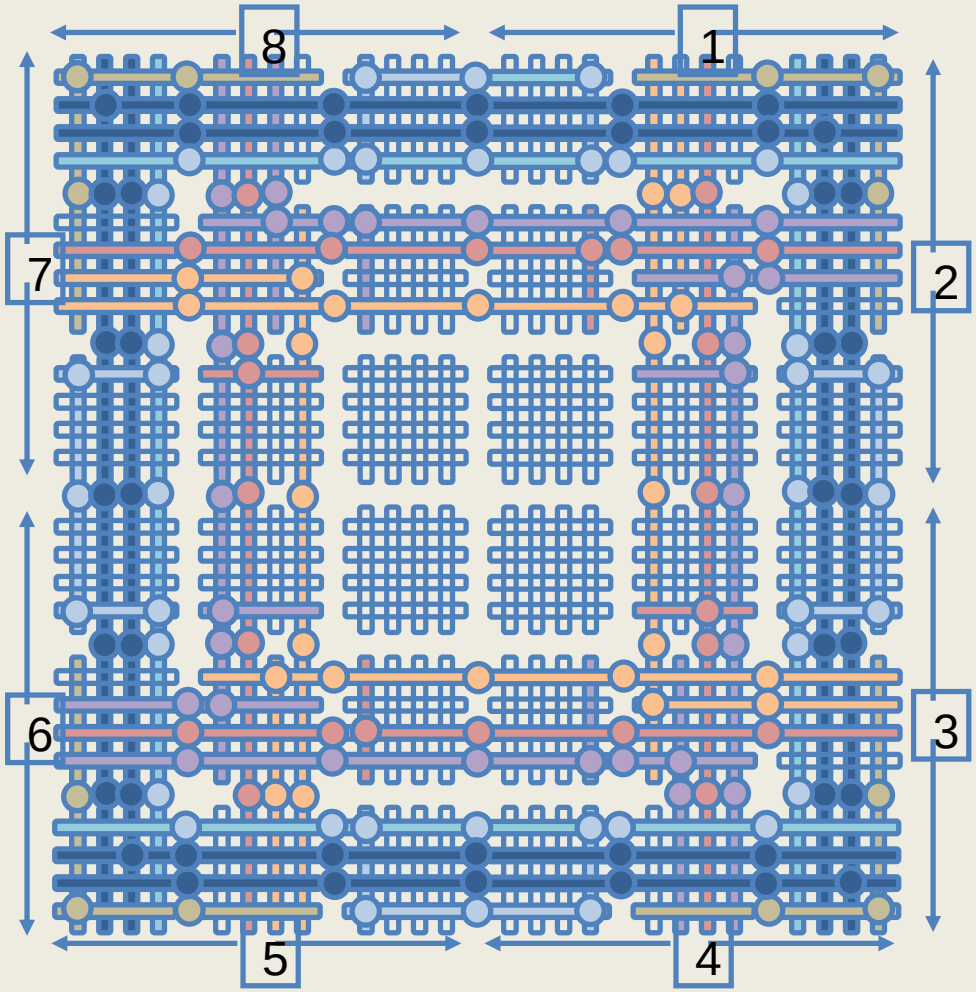
- 2000 qubit processor
- Restricted class of optimization problems
- Quadratic Unconstrained Binary Optimization (QUBO)

O'Gorman, B. A., Perdomo-Ortiz, A., Babbush, R., Aspuru-Guzik, A. & Smelyanskiy, V. *Bayesian network structure learning using quantum annealing*. *European Physics Journal Special Topics* **224**, 163–188 (2015)

Current Implementation

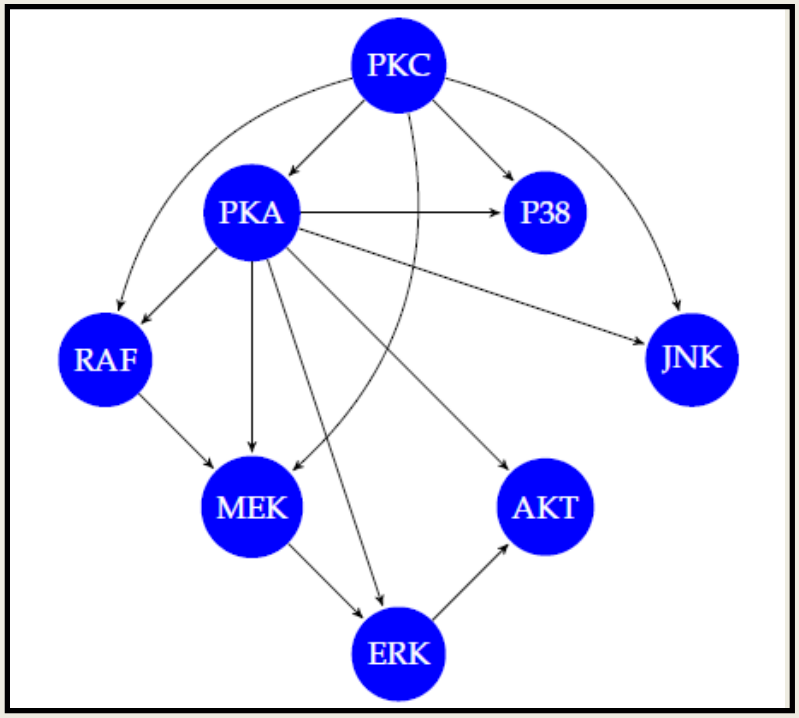
- Number of nodes of BN = 8
- Number of parents allowed = 3
- Number of logical qubits = 230
- Number of Physical qubits ~ 2000

Embedding Challenge



- Denny's help with manual embedding
- Routine based embedding also worked

MAPK/Raf Pathway



Bayesian Network encoding the causal relationship in MAPK/Raf signal transduction pathway in human T-cells. Only eight of the units are considered here.

Bayesian Theorem

$$p(B_S|D) = \frac{p(D|B_S)p(B_S)}{p(D)}$$

$$p(D|B_S) = \Pi_{i=1}^{n} \Pi_{j=1}^{q_i} \frac{\Gamma(\alpha_{ij})}{\Gamma(N_{ij}+\alpha_{ij})} \Pi_{k=1}^{r_i} \frac{\Gamma(N_{ijk}+\alpha_{ijk})}{\alpha_{ijk}}$$

D – Data

B_S – BN

α – Dirichlet priors (assumed uniform here)

$$s_i(\Pi_i(B_S)) = -log\left(\Pi_{j=1}^{q_i} \frac{\Gamma(\alpha_{ij})}{\Gamma(N_{ij}+\alpha_{ij})}\right) \Pi_{k=1}^{r_i} \frac{\Gamma(N_{ijk}+\alpha_{ijk})}{\alpha_{ijk}}$$

$$log(p(D|B_S)) = -s(B_S) = \sum_{i=1}^{n} s_i(\Pi_i(B_S))$$

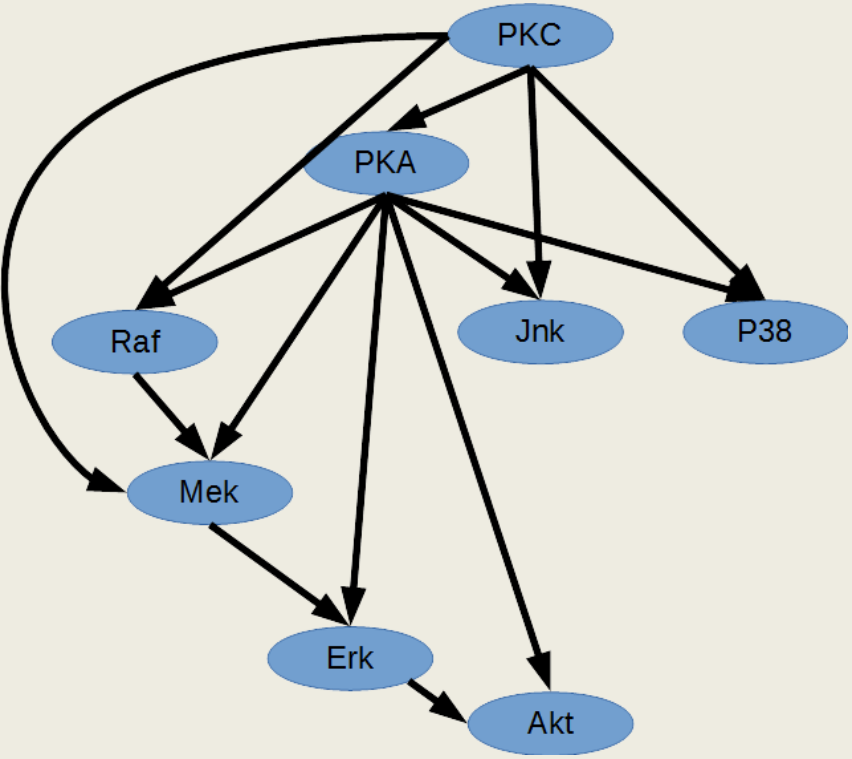
QUBO

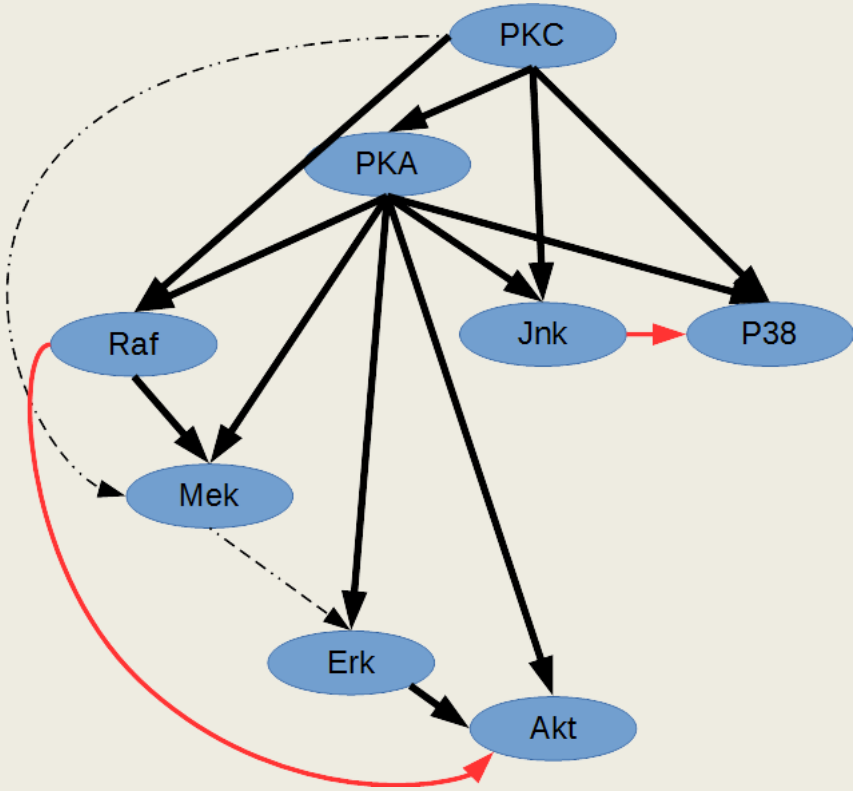
- BN with at most three parents constraint
- No cycles constraint

- $H_{total} = H_{score} + H_{max} + H_{cycle}$
- QUBO conversion

O'Gorman, B. A., Perdomo-Ortiz, A., Babbush, R., Aspuru-Guzik, A. and Smelyanskiy, V.: Bayesian network structure learning using quantum annealing, European Physics Journal Special Topics 224, 163-188 (2015).

Expt. vs PRISM Score





Legend :
Black arcs : Correct edges (True Positives)
Dotted arcs : Missed edges (False Negatives)
Red arcs : Wrong edges (False Positives)
Green arcs : Reversed edges (False Positive + False Negative)

TRUE POSITIVE : 12
FALSE POSITIVES : 2
FALSE NEGATIVES : 2

U.S. ARMY RDECOM®

R vs PRISM

ARL

Legend :
Black arcs : Correct edges (True Positives)
Dotted arcs : Missed edges (False Negatives)
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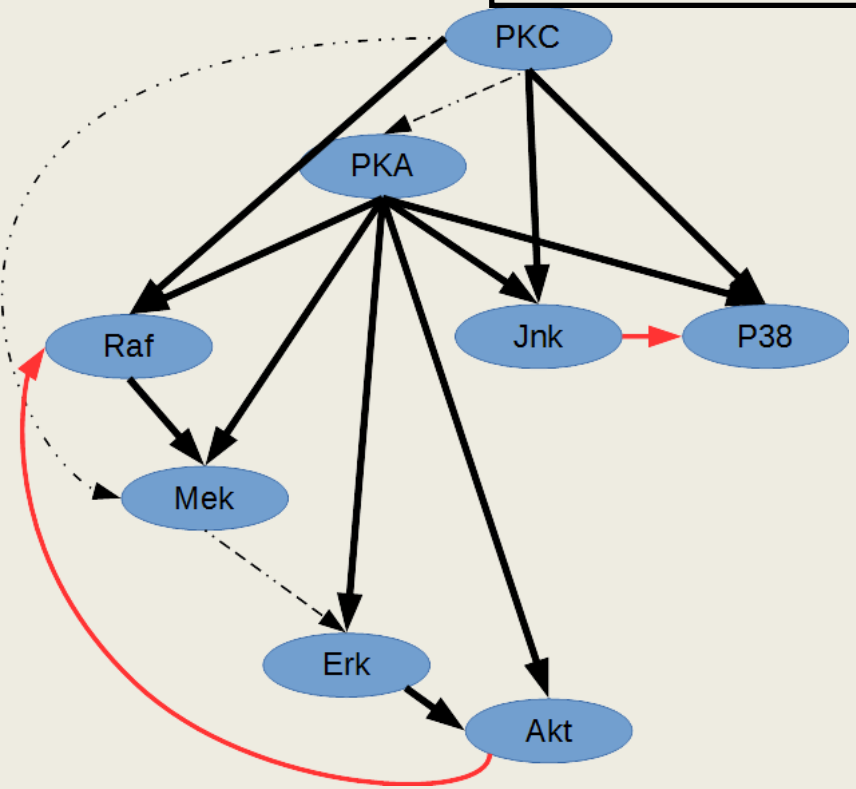
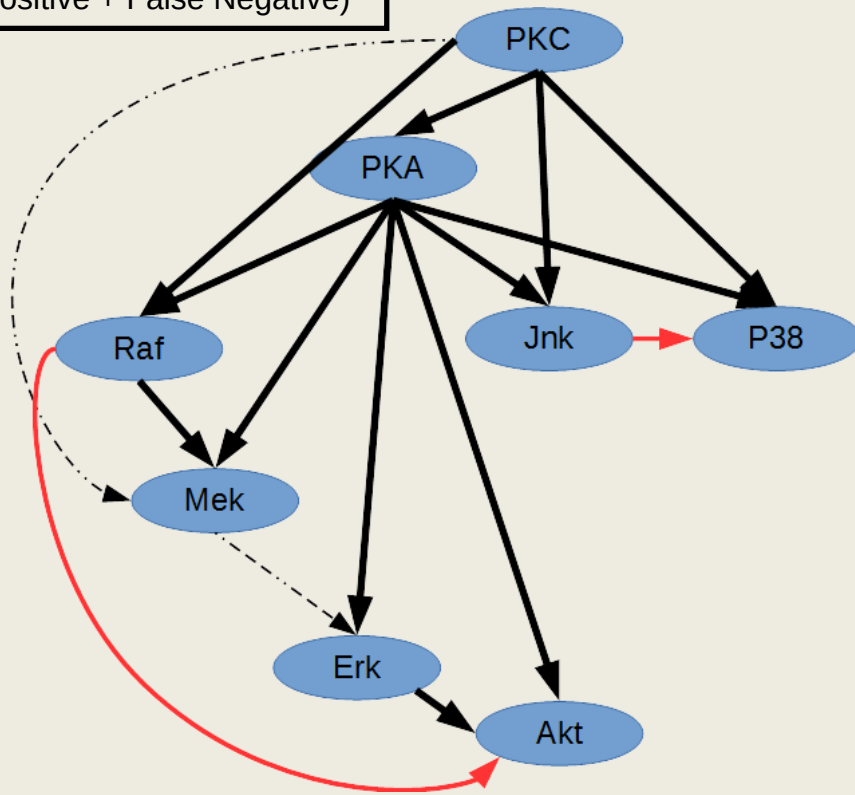
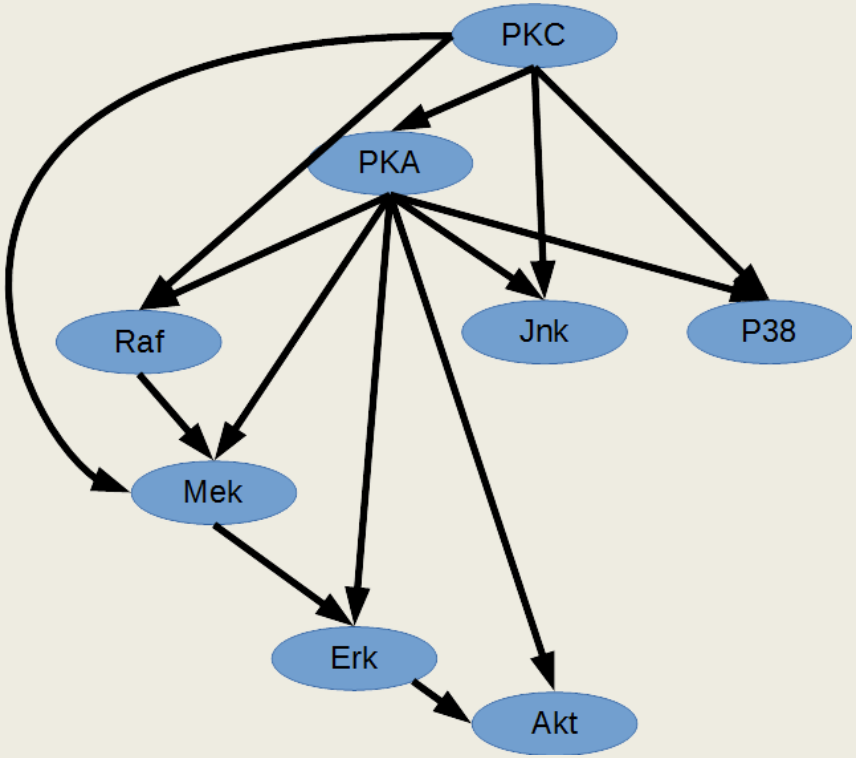


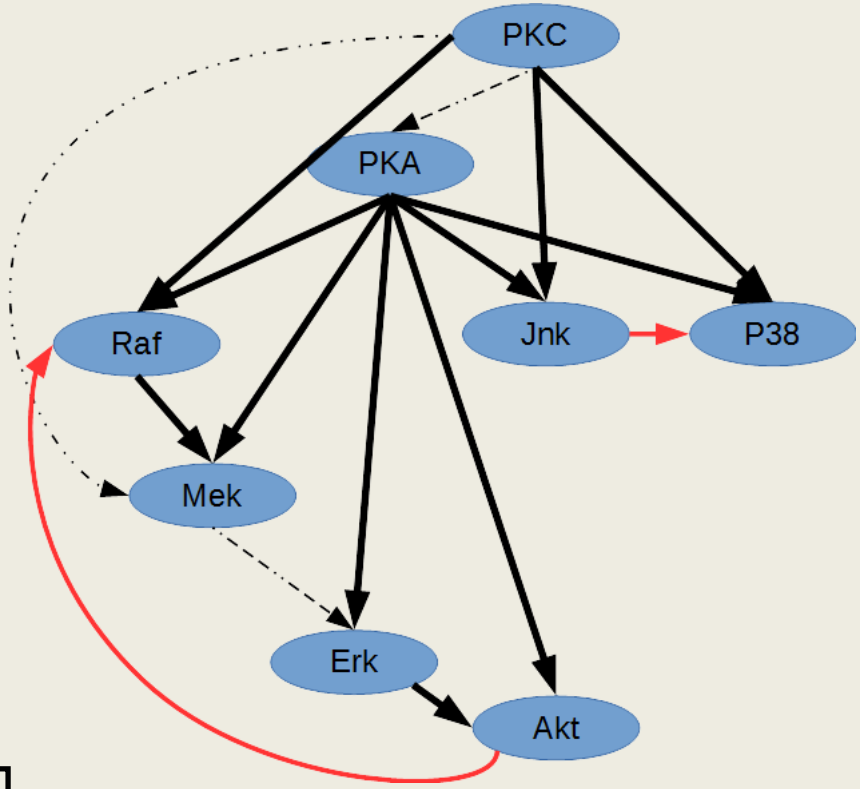
TRUE POSITIVE : 11
FALSE POSITIVES : 2
FALSE NEGATIVES : 3



TRUE POSITIVE : 12
FALSE POSITIVES : 2
FALSE NEGATIVES : 2

Expt. vs R SCORE





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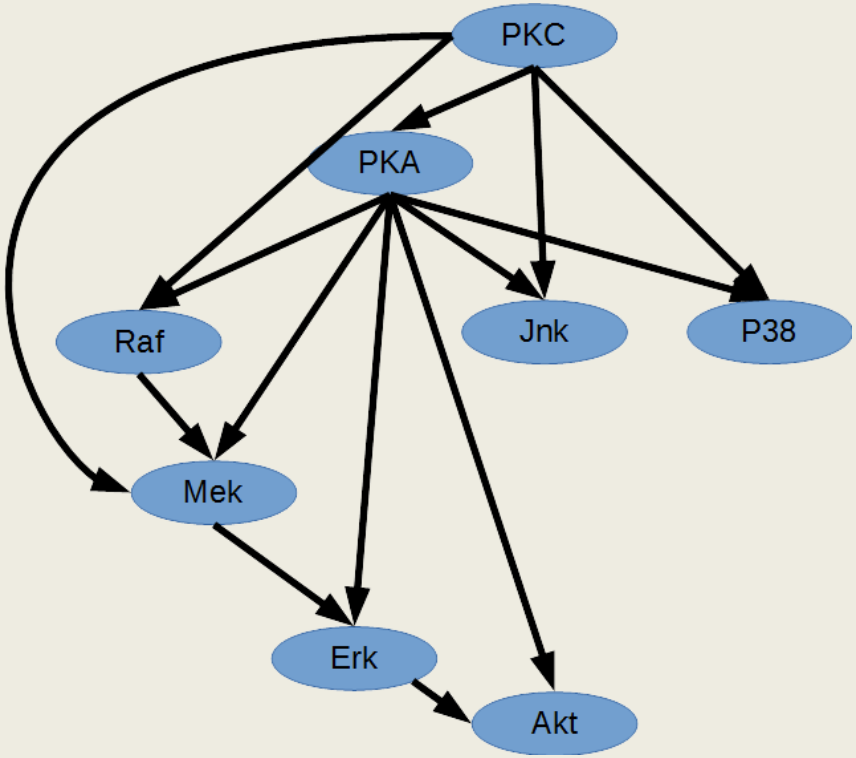
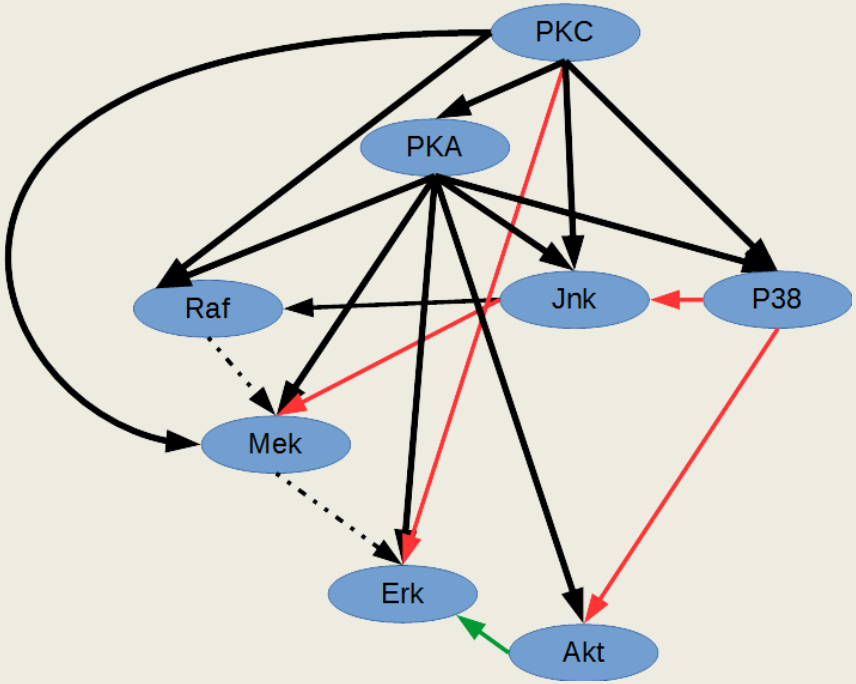
Green arcs : Reversed edges (False Positive + False Negative)

TRUE POSITIVE : 11
FALSE POSITIVES : 2
FALSE NEGATIVES : 3

Expt. VS D-Wave II





True Positives : 11
False Positives : 4
False Negatives : 3

LEGEND:
BLACK EDGES : CORRECT
DOTTED : MISSING
RED : EXTRA EDGES
GREEN : REVERSED

MAPK/Raf Pathway

	Raf BN	Raf BN with Error Correction
No of instances with cycles	0	1
No of false positives	6-13	6-14
Average true positives	8.3	8.6
Median of true positives	9	9

Results from 30 annealing schedules for the MAPK/Raf BN with 14 arcs.

Summary and Future Plans

- Real world application embedded
- Limited error correction applied
- Essential features of BN captured
- Scalability beyond 8-nodes BN
- ML applied to QUBOs (U. Calgary)
- Benchmarking against classical solutions
- Dynamic BN and Bayesian Neural Networks

Acknowledgements

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Thank you for your attention