

# Protein Hypernetworks

Johannes Köster, Eli Zamir, Sven Rahmann

TU Dortmund, Informatik LS 11  
Max-Planck-Institute of Molekular Physiology Dortmund

June 12, 2011

9th Int. Conference on Pathways, Networks, and Systems Medicine

# Protein Network Modelling

Differential equations  
(Law of Mass Action),  
Bayesian Networks, ...

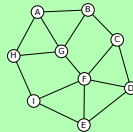
$$\frac{d[C]}{dt} = k[A][B]$$

# Protein Network Modelling

Differential equations  
(Law of Mass Action),  
Bayesian Networks, ...

$$\frac{d[C]}{dt} = k[A][B]$$

Interaction maps (undirected graphs)

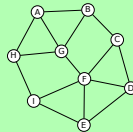


# Protein Network Modelling

Differential equations  
(Law of Mass Action),  
Bayesian Networks, ...

$$\frac{d[C]}{dt} = k[A][B]$$

Interaction maps (undirected graphs)



accuracy ↑  
large scale feasibility ↓

# Protein Network Modelling

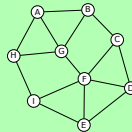
Differential equations  
(Law of Mass Action),  
Bayesian Networks, ...

$$\frac{d[C]}{dt} = k[A][B]$$

Protein Hypernetworks

?

Interaction maps (undirected graphs)



accuracy

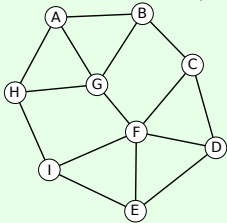
large scale feasibility

# Structure

- 1 Protein Hypernetworks
- 2 Prediction of Protein Complexes
- 3 Prediction of Functional Importance

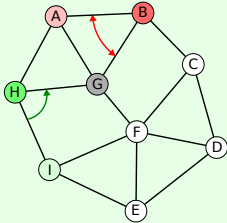
# Idea

Protein Network (P,I)



# Idea

Protein Network (P,I)

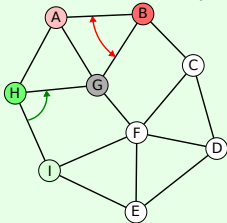




# Idea

## Protein Hypernetwork (P,I,C)

### Protein Network (P,I)



### Boolean Logic Constraints C

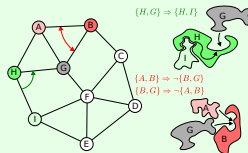
$$\{G, H\} \Rightarrow \{I, H\}$$

$$\{A, B\} \Rightarrow \neg\{G, B\}$$

$$\{G, B\} \Rightarrow \neg\{A, B\}$$

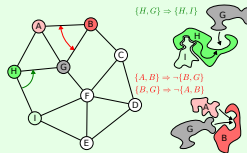
# Mining Protein Hypernetworks

Protein Hypernetwork  $(P, I, C)$



# Mining Protein Hypernetworks

Protein Hypernetwork  $(P, I, C)$

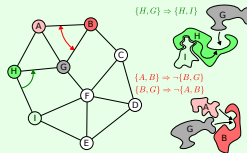


For each protein or interaction  $q$ :

$$q \wedge \bigwedge_{c \in C} c$$

# Mining Protein Hypernetworks

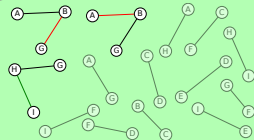
Protein Hypernetwork  $(P, I, C)$



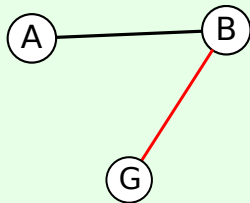
For each protein or interaction  $q$ :

$$q \wedge \bigwedge_{c \in C} c$$

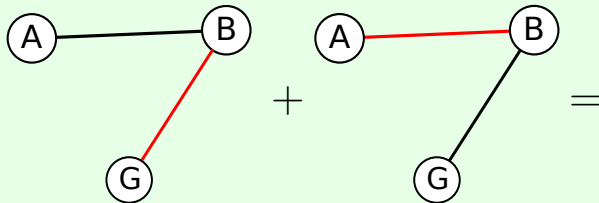
Minimal Network States  $(Nec, Imp)$



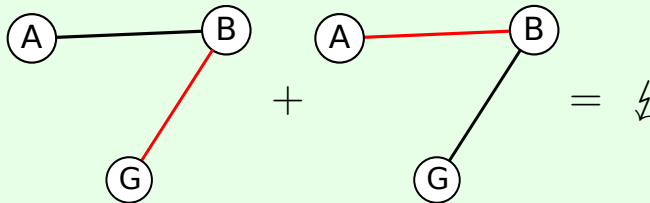
## Minimal Network States



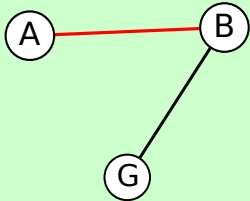
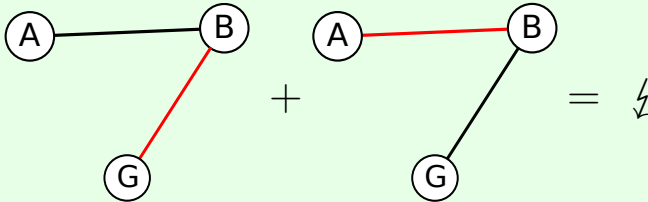
## Minimal Network States



## Minimal Network States

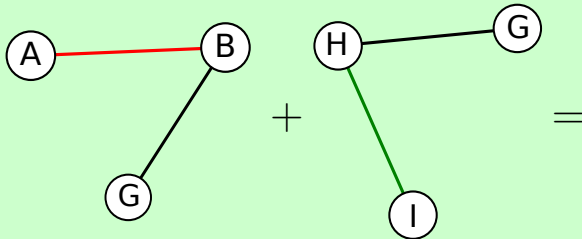
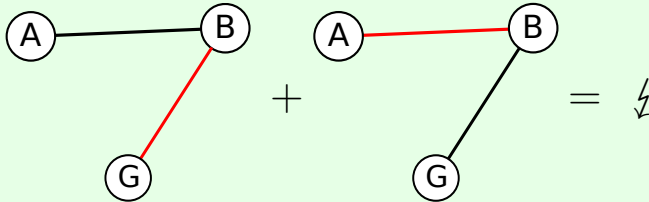


## Minimal Network States

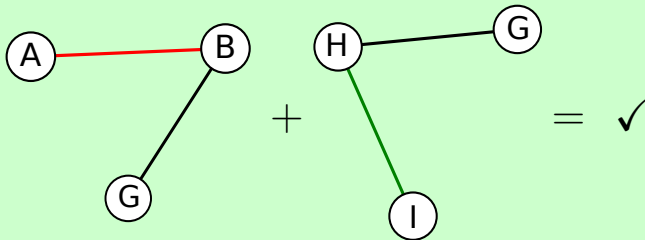
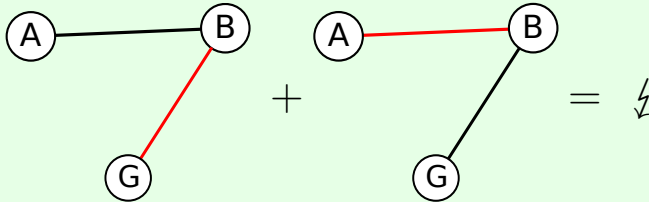




## Minimal Network States



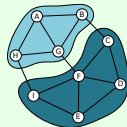
## Minimal Network States



# Prediction of Protein Complexes

Network based complex prediction

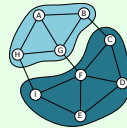
- e.g. dense regions



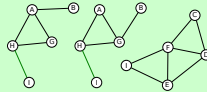
## Prediction of Protein Complexes

Network based complex prediction

- e.g. dense regions



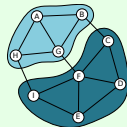
Maximal combinations of minimal network states



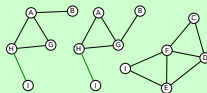
## Prediction of Protein Complexes

Network based complex prediction

- e.g. dense regions

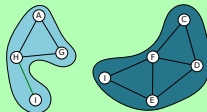


Maximal combinations of minimal network states



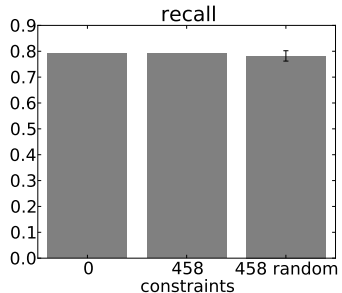
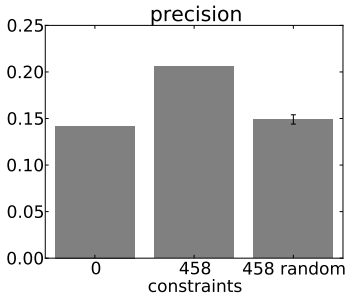
Refined complexes

- no violated constraints



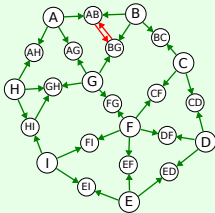
## Results on the Yeast Protein Network

- Network: CYGD (4579 proteins, 12576 interactions)
- Constraints: Competition on binding sites (Jung et al. 2010)
- Complexes: CYGD (55 connected complexes)
- Network based complex prediction: LCMA (Li et al. 2005)

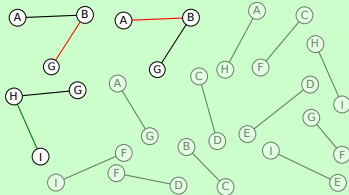


## Prediction of Functional Importance

Minimal network state graph

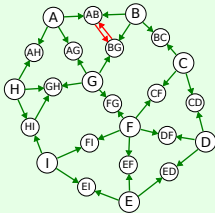


Minimal network states

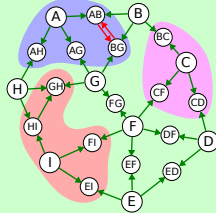


## Prediction of Functional Importance

Minimal network state graph



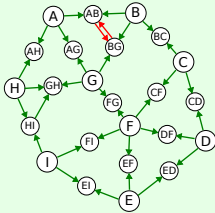
Breadth first search from each node



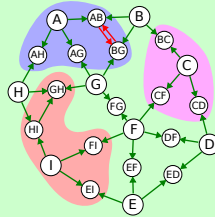


## Prediction of Functional Importance

Minimal network state graph



Breadth first search from each node

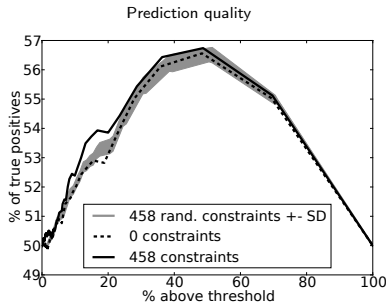


Perturbation Impact Score

$$PIS_{(P,I,C)}(Q_{\downarrow}) := \sum_{q \in reach_{Q_{\downarrow}}^{BFS}} dist_{Q_{\downarrow}}^{BFS}(q)$$

## Results

- Network: CYGD (4579 proteins, 12576 interactions)
- Constraints: Competition on binding sites (Jung et al. 2010)
- Perturbations classified as lethal/sick and viable: SGD

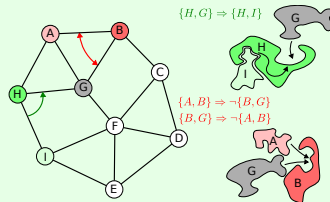


TP: lethal/sick and  $PIS \geq t$ , viable and  $PIS < t$

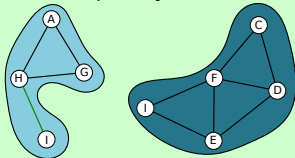
## Conclusion

### Protein Hypernetworks

- extension of graph model
- boolean logic constraints
- minimal network states



### Improvements in complex prediction quality



### Improvements in functional importance prediction quality

