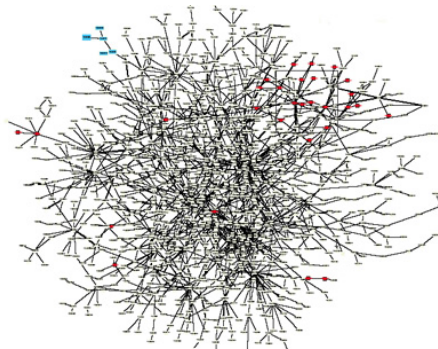


# Comparative Annotation of Protein Interaction Networks (PINs)

24.3.10

Objective: To give a presentation of about 60 minutes at the end of the week covering the key aspects of the comparative annotation of protein interaction networks.



The experimental techniques that allowed detection of protein complexes were established in the late 90s and quickly produced large amount of protein interaction (PIN) data. PIN data is extremely interesting as they make statements about which protein groups work together in for instance multimers. However, the data is noisy and dependent on the experimental conditions and techniques used. Additionally, a true observation between two proteins is not easily translated into a functional statement. This has made the PINs the object of much study and modelling. PINs are also fascinating for modellers as they represent the ideal graph – labelled nodes and standard edges – to apply stochastic modeling to. There are stochastic models for graphs that described the probability of each graph and models have been developed describing the evolution of such graphs over time. Because of experimental noise and the difficulty of interpreting an interaction as functional, it is important to compare PINs from related species to see how conserved interactions are. Proper evolutionary models and phylogenetic methods additionally allow the inference of ancestral PINs.

## The Big Questions Are:

- What are the experimental noise on an interaction ?
- How fast does interactions evolve from specie to specie ?
- What evidence for positive and negative selection is there ?
- How are interactions translated into functional statements ?
- Which probability model describes a PIN the best and is there any biological interpretation ?
- Which evolutionary model is most appropriate for PIN evolution ?
- Can one annotate a PIN in the same way a genome is annotated ?
- Are there cases where the simple graph is not appropriate to represent a PIN ?

## Possible Contents of Presentation

1. The History of PINs
2. Detailed examples of present knowledge of PINS
3. A few examples of important use of PINs in biological discovery
4. Null model (equilibrium distributions) for PINS
5. Evolutionary models for PINs
6. Technical problems in statistical analysis of PINs
7. Annotation of PINs
8. Combining PINs with other data types

## Recommended literature

Aloy, R.B. Russel: Structural systems biology: Modelling protein interactions, Nat. Rev. Mol. Cel. Biol. 7, 188–196 (2006).  
Beltrao and Serrano (2007) Specificity and Evolvability in Eukaryotic Protein Interaction Networks PLOS compu biol. 3.2.25-  
Dittrich et al. (2008) Identifying Functional Modules in Protein-Protein Interaction Networks: An Integrated Exact Approach, Bioinf 24:i223-i231,  
Erdos, A. Rényi: On random graphs, Publicationes Mathematicae 6, 290 –297(1959).  
Erdos, A. Rényi: On the evolution of random graphs, Publications of the Mathematical Institute of the Hungarian Academy of Sciences 5, 17–61 (1960).  
Hakes (2009) Protein-protein interaction networks and biology—what’s the connection? Natu Biotech 26.1.69-  
Jensen et al. (2009) STRING 8 – a global view on proteins and their functional interactions in 630 organisms, Nucl. Acids.Res. 37, D412–D416 (2009).  
Pinney et al(2007) "Reconstruction of ancestral protein interaction networks for the bZIP transcription factors" Proc. Natl. Acad. Sci. USA 104 (51): 20449  
Schwikowski et al. (2000) A network of protein–protein interactions in yeast Natu Biotech 18.12.1257  
Sharan et al. (2005) Conserved patterns of protein interaction in multiple species PNAS 102.6. 1974–1979  
SINGH et al. (2008) GLOBAL ALIGNMENT OF MULTIPLE PROTEIN Pacific Symposium on Biocomputing 13:303-314(2008)  
Stumpf, C. Wiuf, R. May: Subnets of scale-free networks are not scale-free: Sampling properties of networks, Proc. Natl. Acad. Sci. 102, 4221–4224 (2005).  
Stumpf et al.(2007)Evolution at the system level: the natural history of protein interaction networks, Trends Ecol. Evol. 22, 366–373  
Wagner (2001) The Yeast Protein Interaction Network Evolves Rapidly and Contains Few Redundant Duplicate Genes Mol Biol Evol 18(7):1283–1292  
Wiuf et al. (2006) A likelihood approach to analysis of network data, Proc. Natl. Acad. Sci. 103 (2006), 7566–7570.

“Big Questions”, “Contents” and “Recommended Literature” are only suggestions from which the student is welcome to depart from or completely ignore.