



# Degree Conservation in Protein Interaction Networks

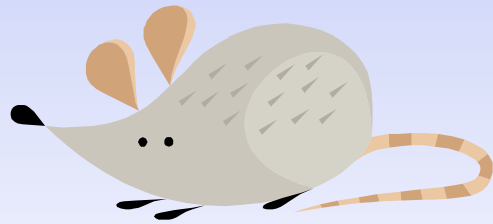
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# Motivation

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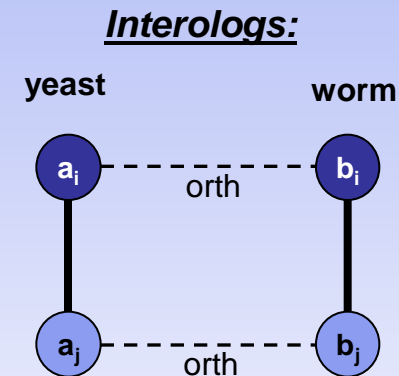
# Motivation

- Network Modules not well conserved

(Wang & Zhang, 2007), (Babu,2004)

- Interologs observed less often than expected

- But we predict the conservation of functionally important interactions / motifs





# Outline

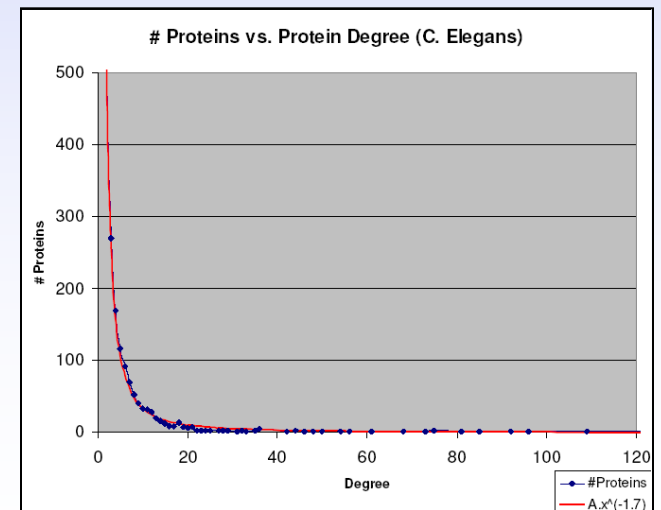
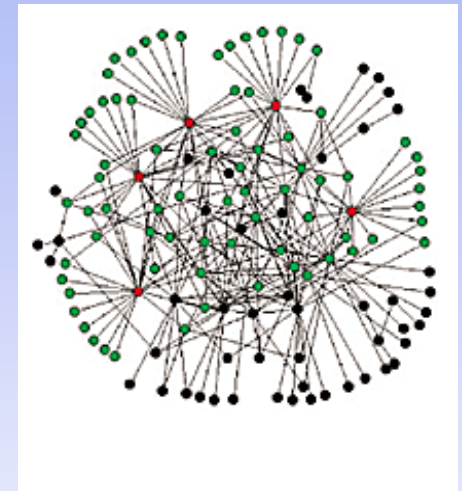
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- Degree Conservation of Hubs
- Hub Interactions Conserved
- Once a Hub, Always a Hub

# Focus on Hubs

Protein interaction networks  
are Scale-free

Hubs  $\leftrightarrow$  increased functional  
importance



# Hubs: Degree Conservation

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Hypothesis:

*(Functionally important) hubs will be hubs in multiple species.*

We call this “degree conservation.”

# Experimental Data

- All protein-protein interaction data from:

*S. cerevisiae, C. elegans, D. melanogaster, H. sapiens*

## Sources:

- IntAct
- MINT
- BioGRID

Data are *noisy*

□ removed inconsistent data (Chiang '07)

Data are *incomplete*

...

Use a (percentile) rank to compare degrees across species.

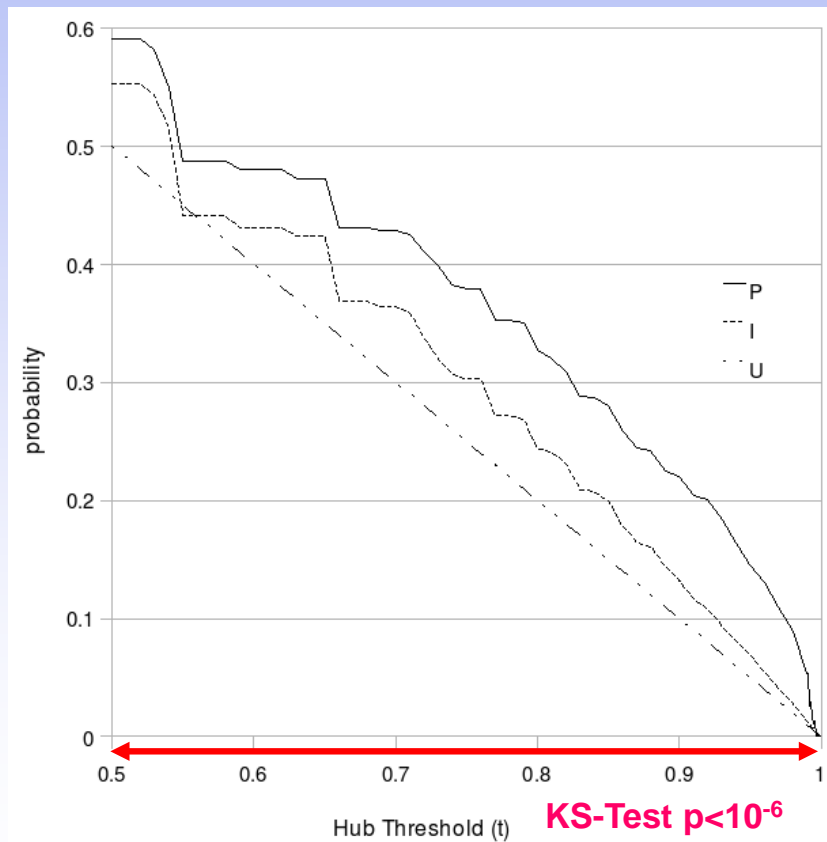
DEFINE:  $\text{hub}_t(\mathbf{p}): \text{rank}(\mathbf{p}) > t$

# Having an Orthologous Hub Increases Hub Likelihood

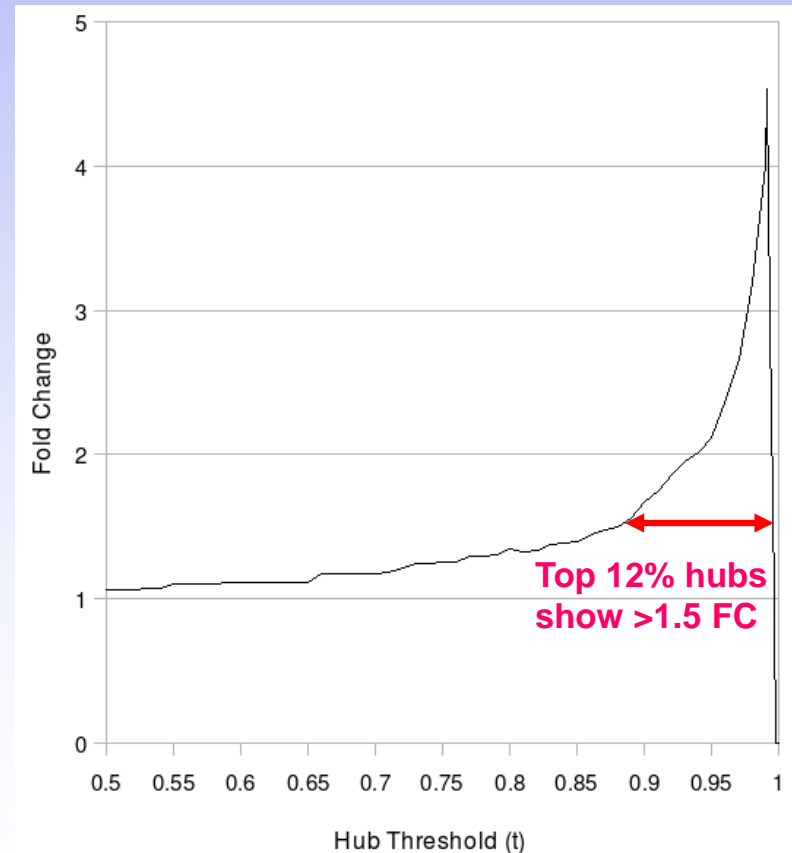
$$P(t) = \Pr\{ \text{hub}_t(\mathbf{p}) \mid \mathbf{p} \text{ has orthologous } \textit{hub} \text{ (at } t)\}$$

$$I(t) = \Pr\{ \text{hub}_t(\mathbf{p}) \mid \mathbf{p} \text{ has an ortholog} \}$$

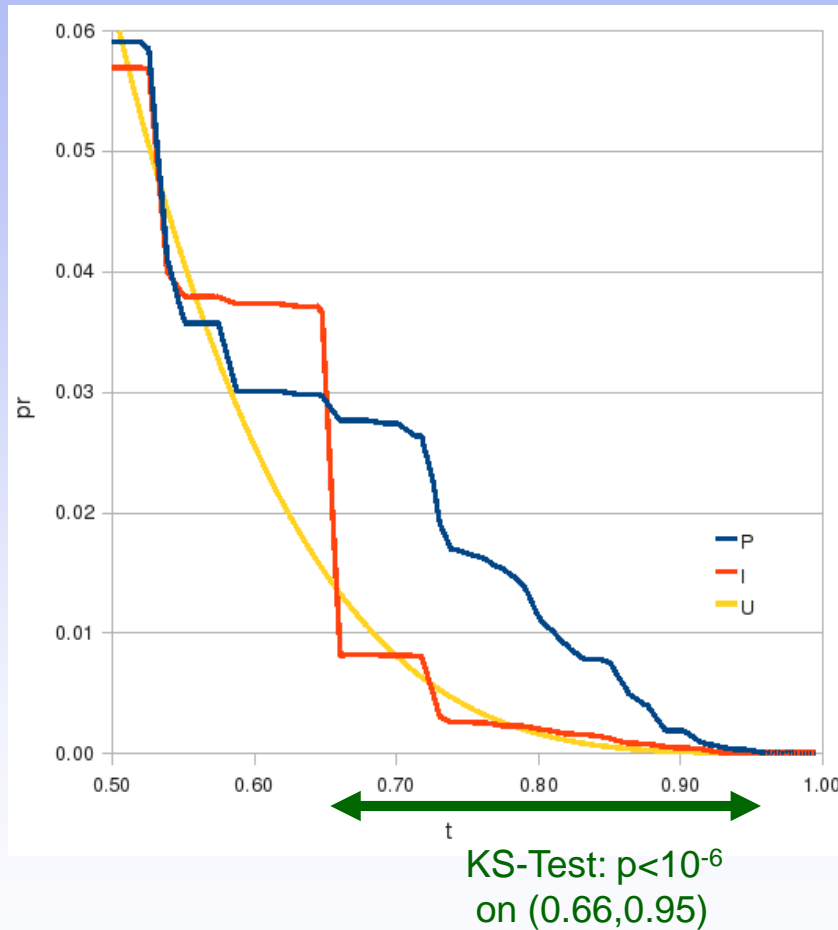
$$\text{Fold-Change}(t) = P(t) / I(t)$$



KS-Test  $p < 10^{-6}$   
 $t \in (0.5, 0.99)$




# Four-Species Degree Conservation



$H_0$  : Degree is NOT conserved  
by orthology

$P(t)$ : Observed Posterior  
 $I(t)$ : Informed Expectation |  $H_0$   
 $U(t)$ : Uninformed Expectation |  $H_0$

$[ P > I ]$  for top ~33% proteins



# Which Hubs are Degree-Conserved?

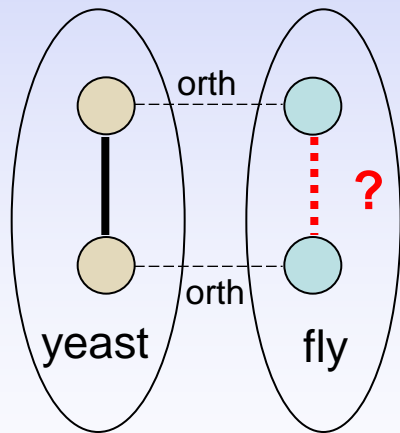
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- Yeast vs. Other
  - Metabolism
  - Ribosomal
  - Structural
  - Cell Cycle
  - DNA repair
  - Splicing
- Human vs. Fly
  - Differentiation
  - Development
  - Signal Transduction
    - *p53, Wnt, ErbB, Notch, TGF- $\beta$*
  - Post-translational Protein Modification
  - Regulation of Kinase activity

DAVID (*fdr*<5%)

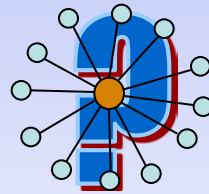
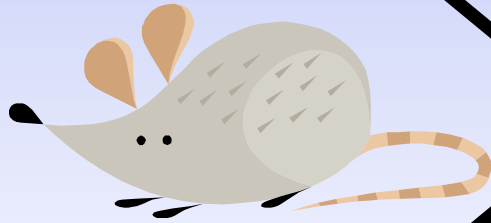
# Conservation of Individual Hub Interactions

- High **Degree** conserved
- Are hubs' interactions conserved?



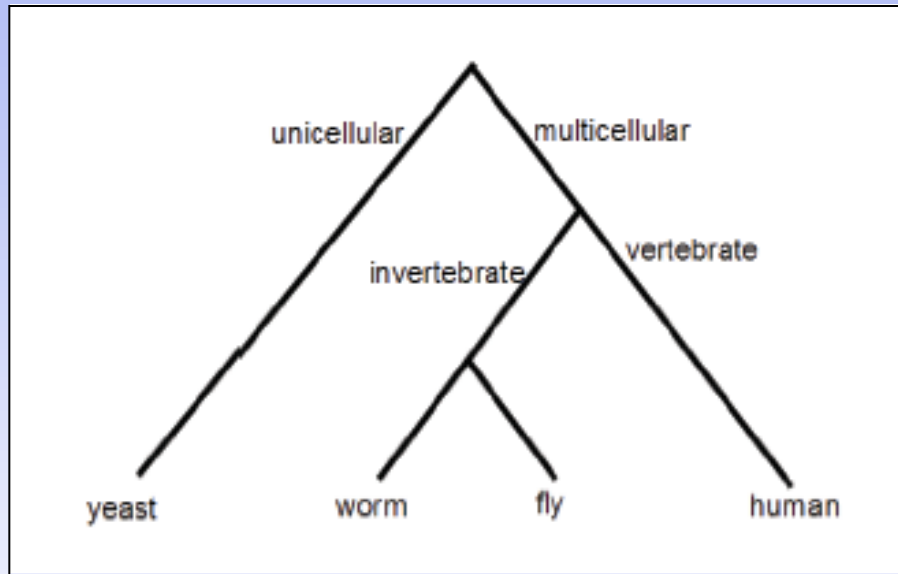
# Evolution of Hubs

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# Once a Hub, Always a Hub

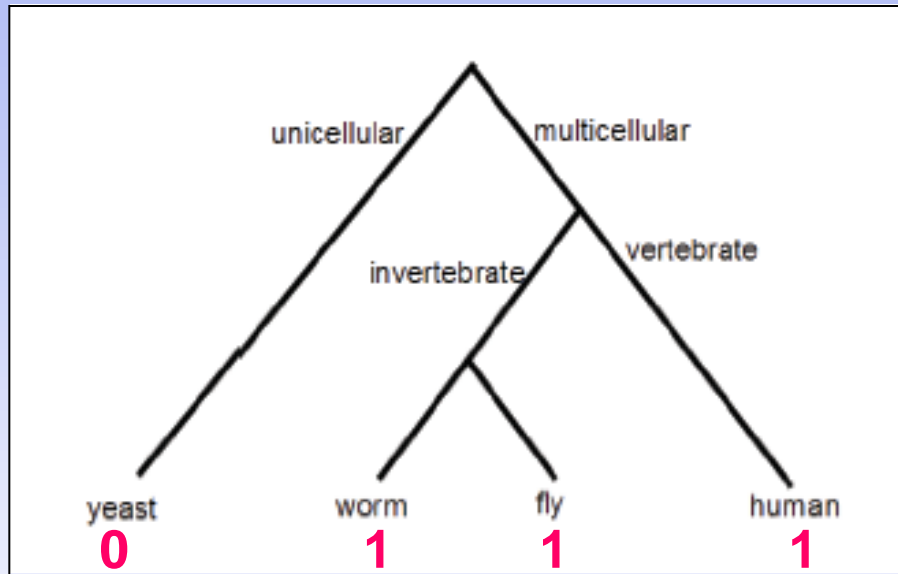
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Ex: y w f h

g1 .8 .91 .87 .93

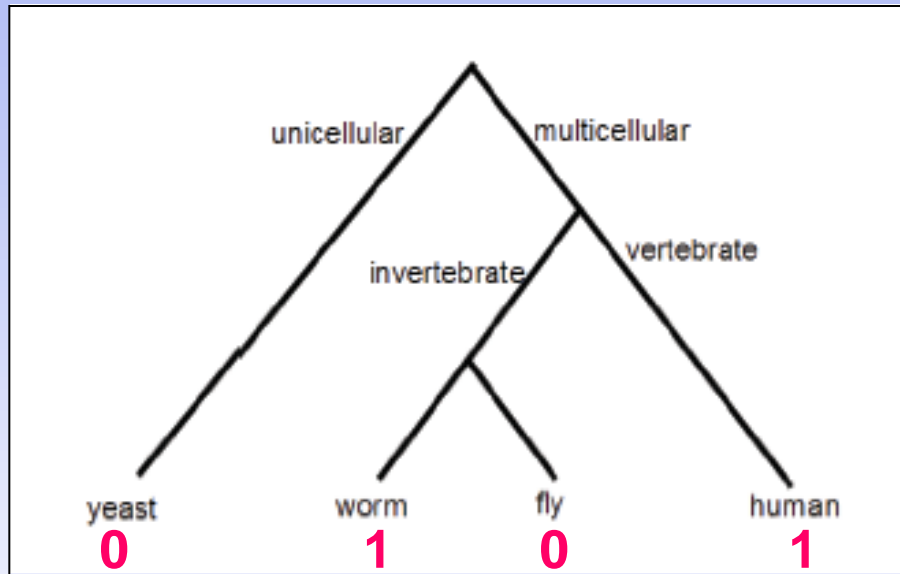
# Once a Hub, Always a Hub



Ex: y w f h | Hub(.85)

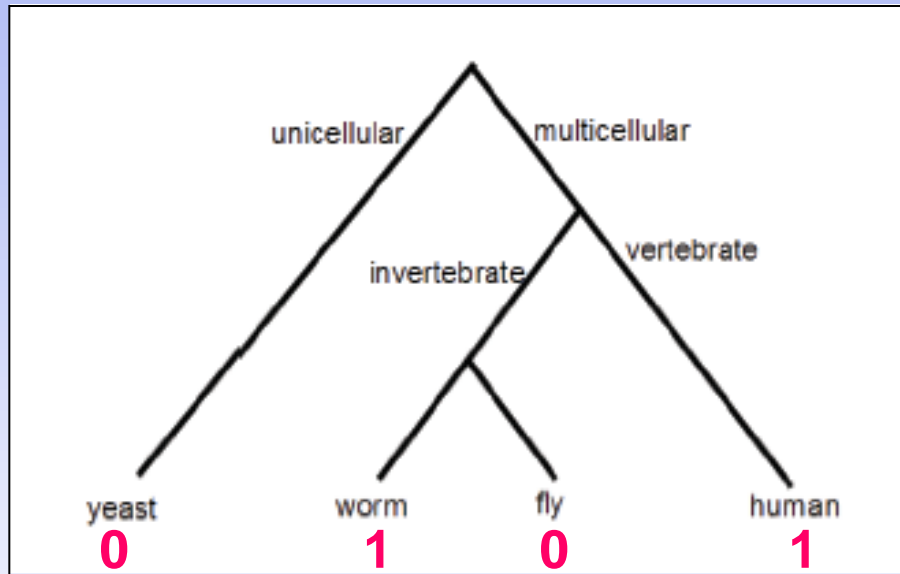
g1 .8 .91 .87 .93 | 0111

# Once a Hub, Always a Hub



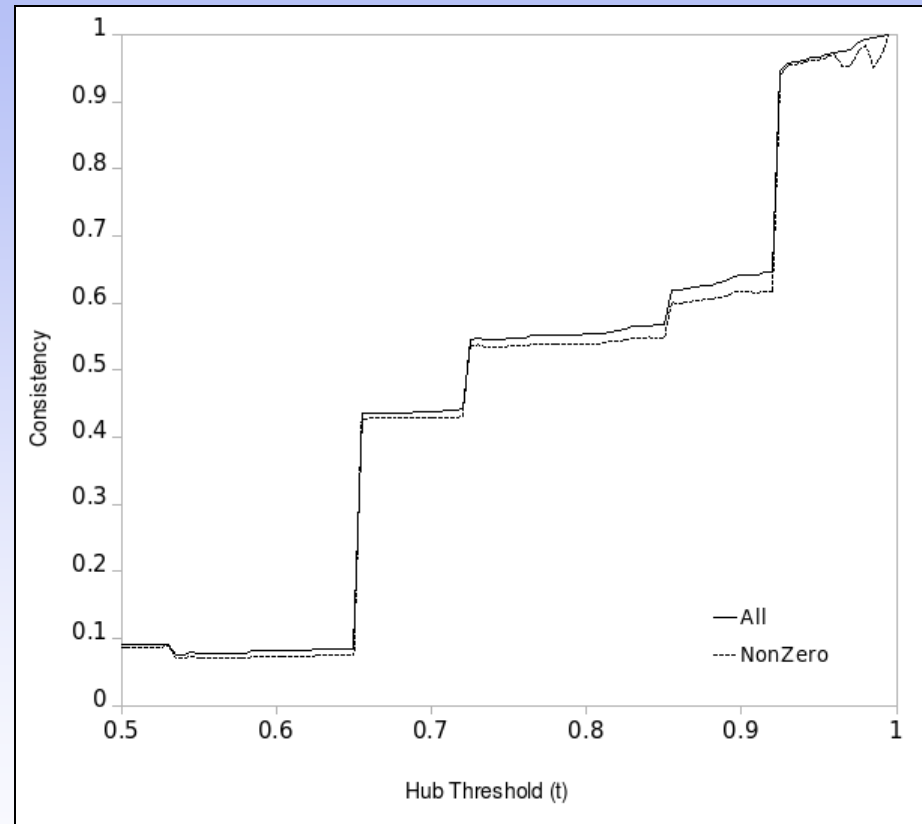
Ex:	y	w	f	h	Hub(.85)	Hub(.9)
g1	.8	.91	.87	.93	0111	0101

# Once a Hub, Always a Hub



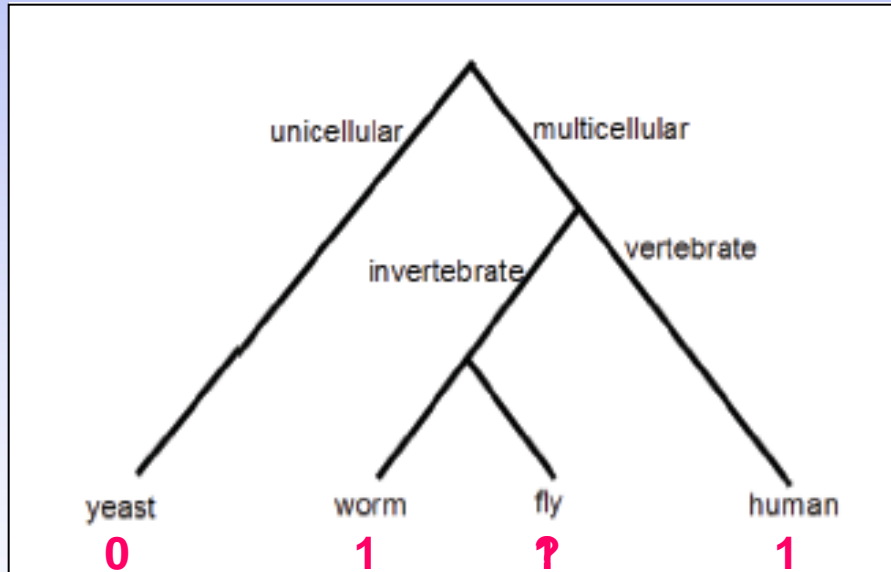
Ex: y w f h | **Hub(.85)** | **Hub(.9)**

g1 .8 .91 .87 .93 | **0111** | **0101**



# Once a Hub, Always a Hub

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# Hub Conservation Conclusions

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- Functional modules around network hubs are likely to persist across species.
- Even when individual interactions are not conserved, functional importance of high degree proteins persists once evolved.
- These results may help us identify putative important hub proteins *without complete PPI data*.

# Acknowledgements

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- Daniel Taylor
- Donna Slonim
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