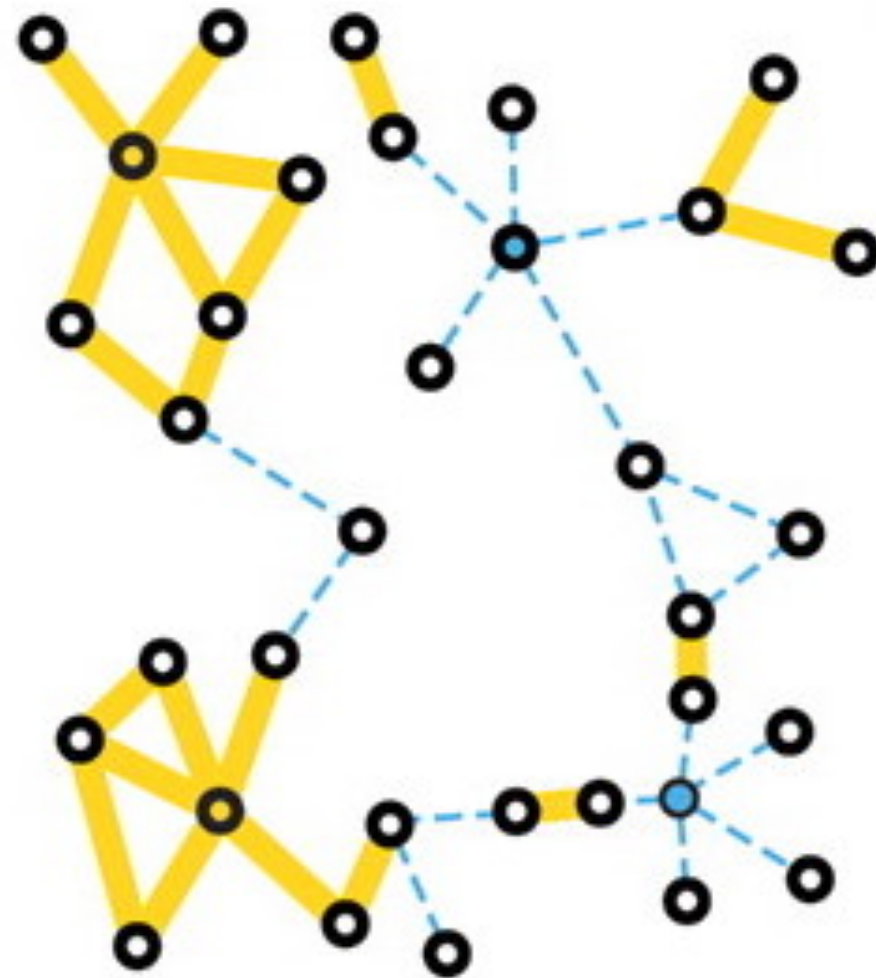


# Relating Three-Dimensional Structures to Protein Networks Provides Evolutionary Insights

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Presented by: Haji Mohammad Saleem

# Traditional studies of protein networks operate on high level of abstraction

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- Multiple studies have explored global aspects PPI network topology, specifically in terms of:
  - ✦ protein function
  - ✦ expression dynamics,
  - ✦ protein essentiality, etc.
- Such studies **do not** consider the role of chemical and structural aspects of protein interactions in their analysis.

# Disregarding structural information precludes interaction categorization

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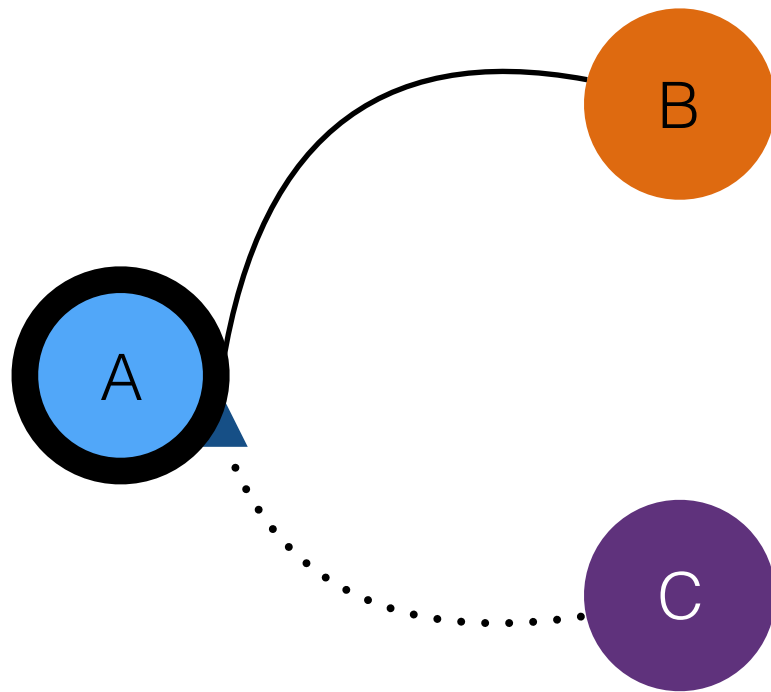
Can't differentiate between the type of interaction:

- Direct
- Loose / transient
- Interaction through a third protein

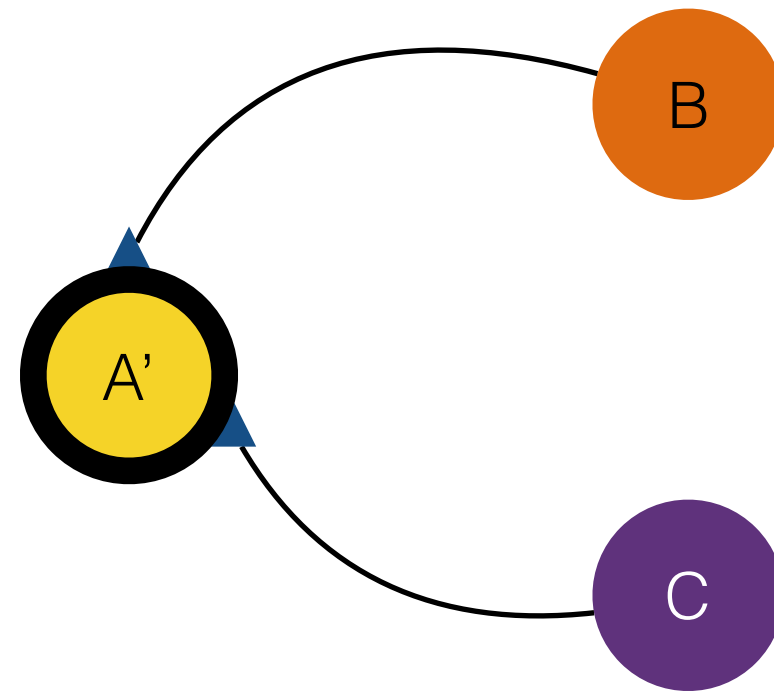
*Solution:* **combine structural modelling with network analysis.**

# Mutually exclusive vs simultaneous interactions

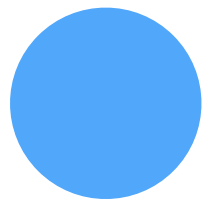
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Mutually Exclusive



Simultaneous



Protein



Interaction interface

# Materials and Methods

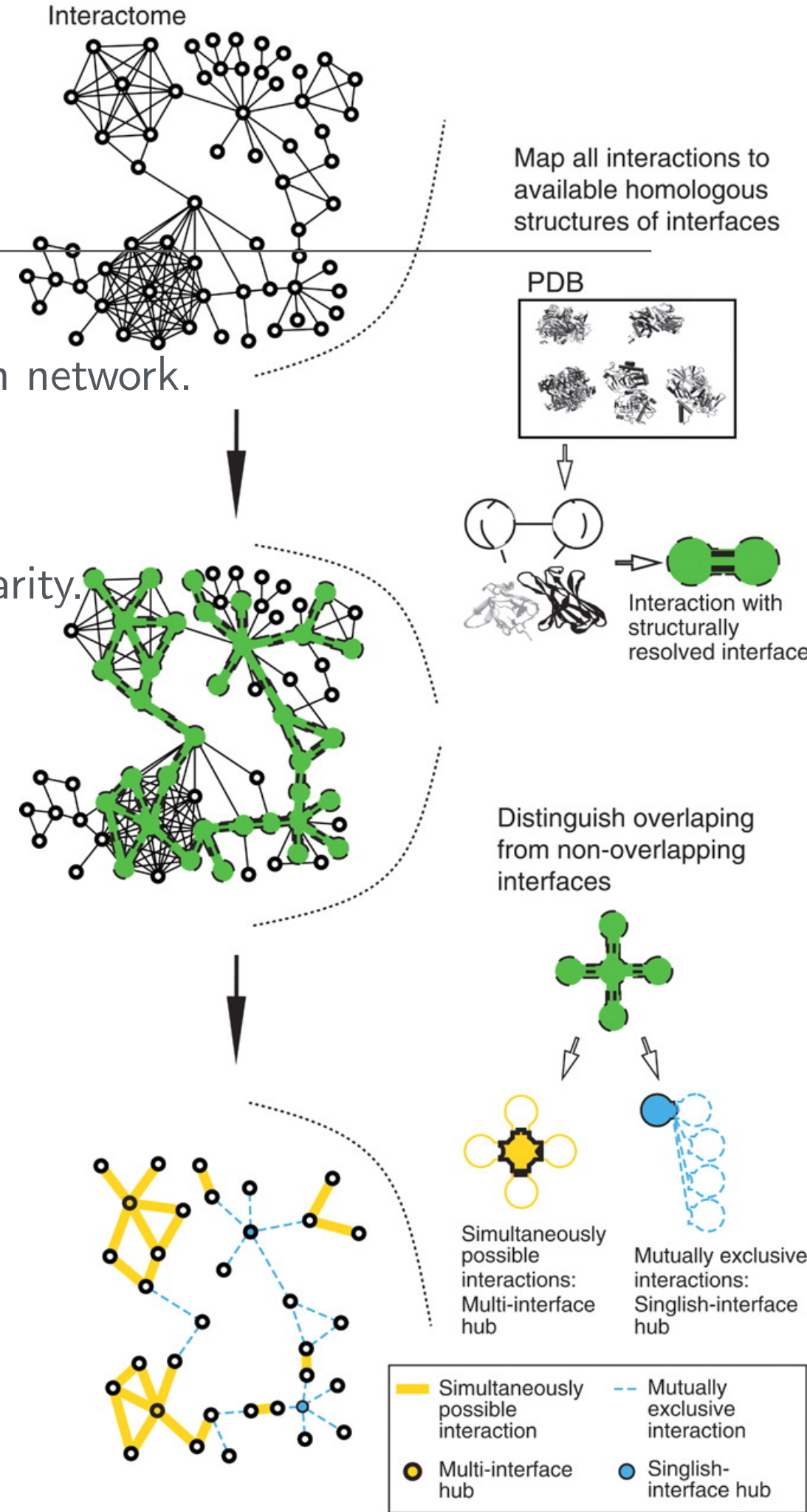
- Compile a multi-source consensus yeast interaction network.
- Filter low-confidence interactions.
- Annotate sequence edges based on sequence similarity.
- Distinguish the interface for each interaction.

## Structural Interaction Network (**SIN**)

873 Nodes / proteins

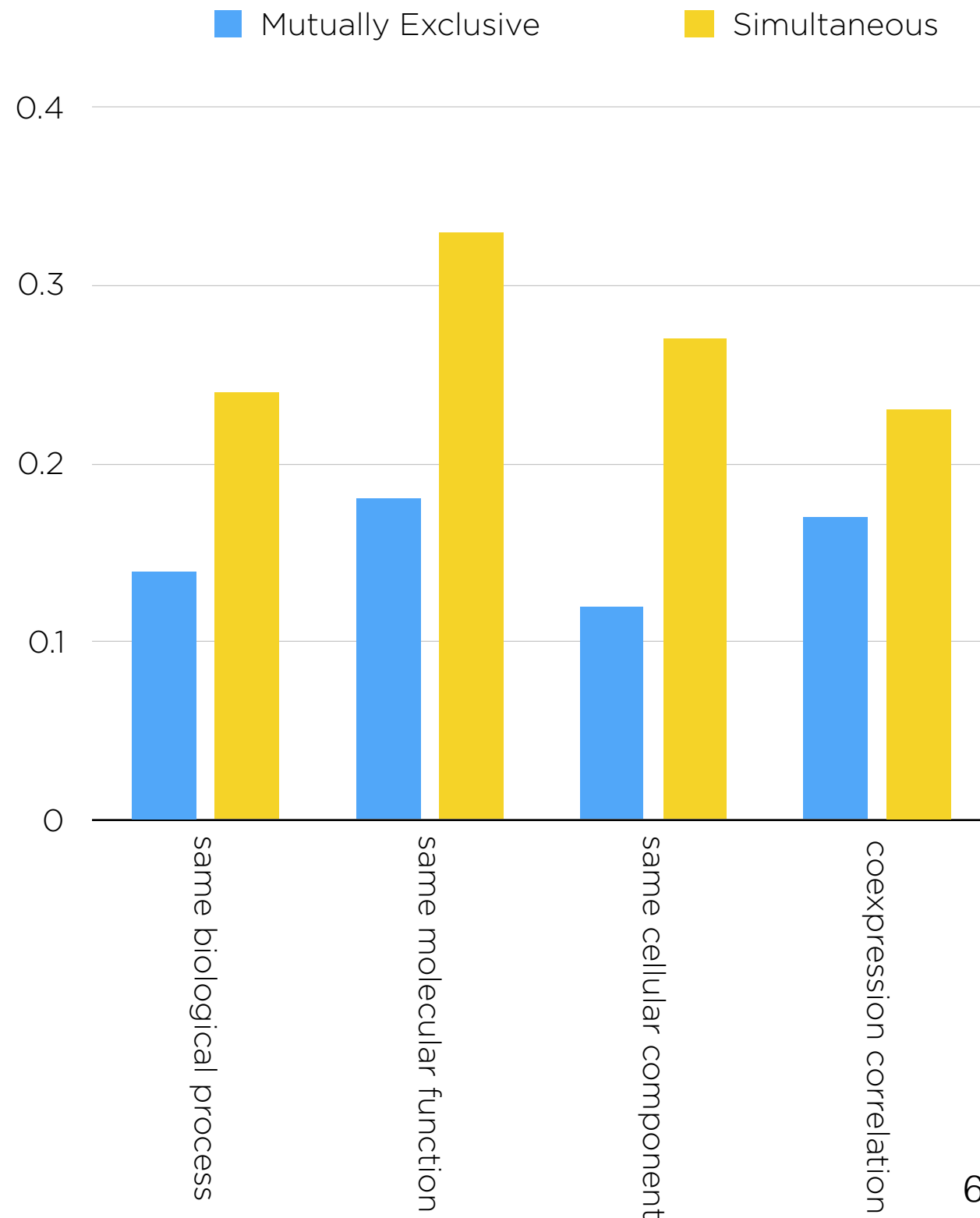
1269 Edges / interactions

438 mutually exclusive



# Mutually exclusive and simultaneous interaction proteins are significantly different

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In terms of gene-ontology, simultaneous interactions are more likely to:

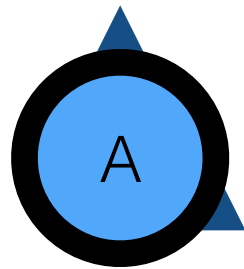
- share the same function
- be expressed at the same time
- be enriched with permanent associations

# Protein hubs behave significantly different based on the number of interfaces

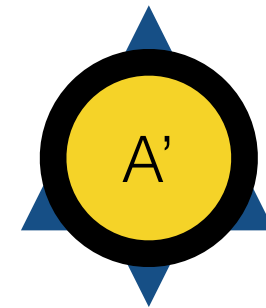
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Empirically define hubs to nodes with  $\geq 5$  partners.

Hub categorization:

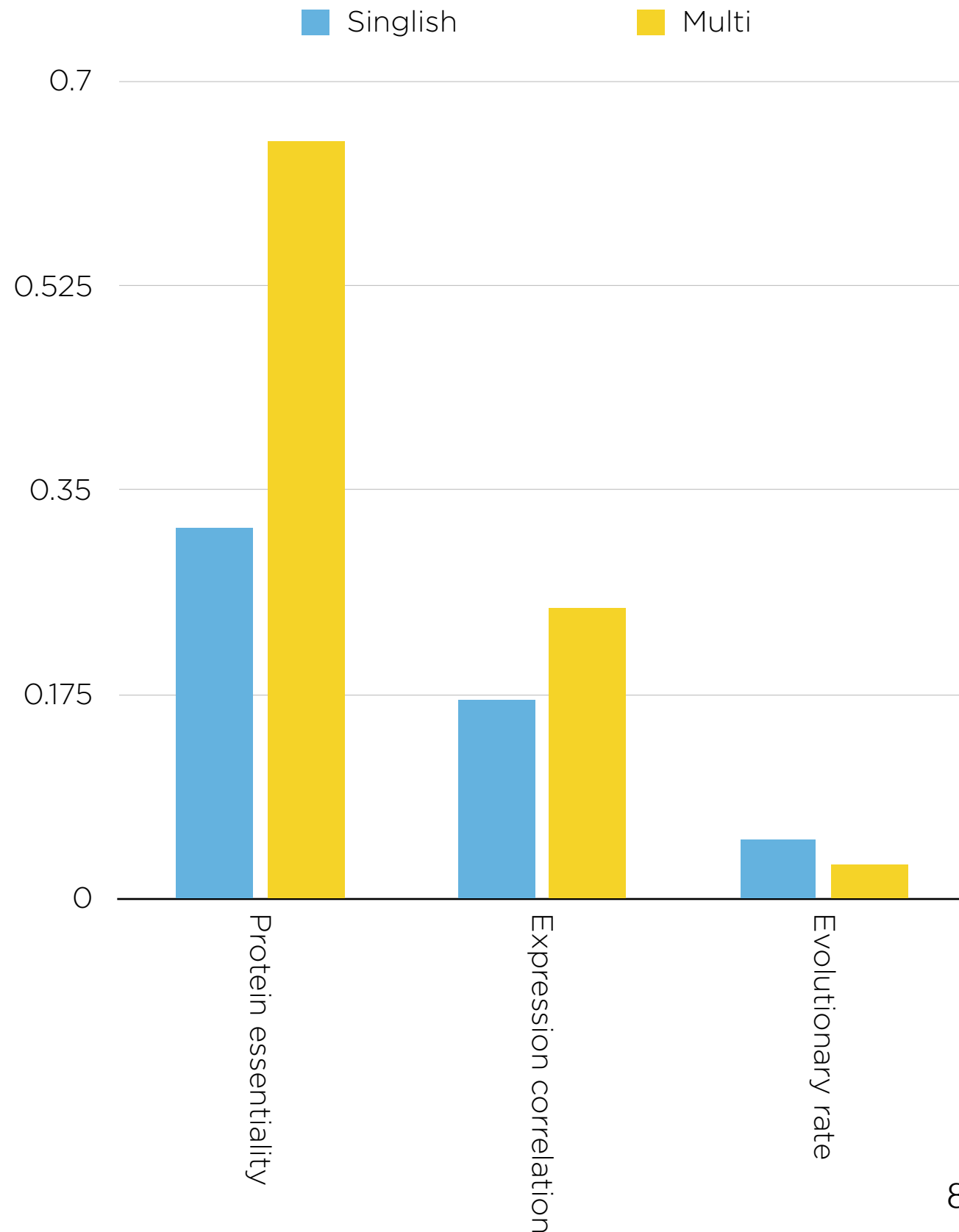


singlish-interface



multi-interface

# Protein hubs behave significantly different based on the number of interfaces



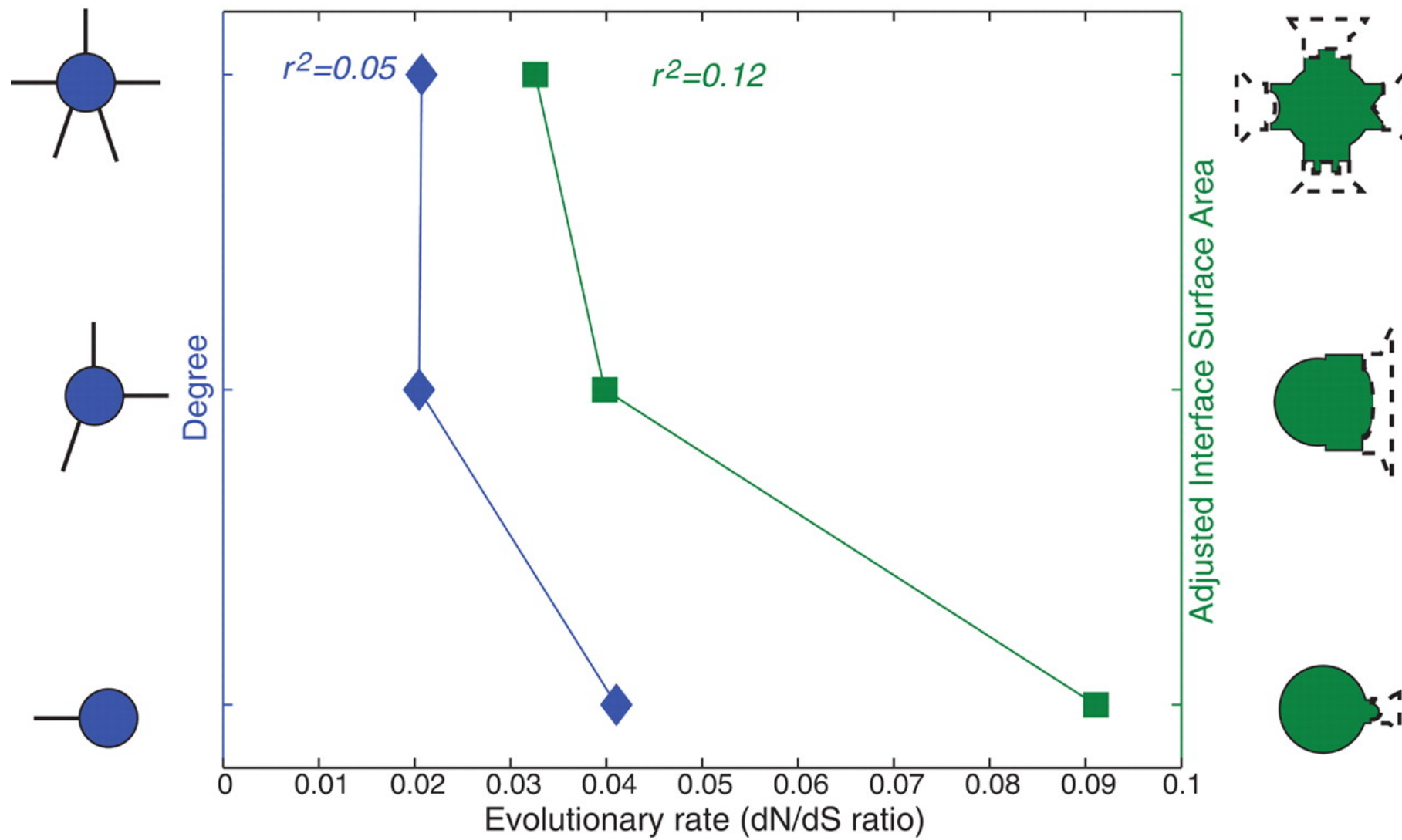
## Multi-interface hubs:

- are twice likely to be essential.
- are more likely to be expressed with their partners (*party-hubs*).
- have a significantly slower evolution rate.

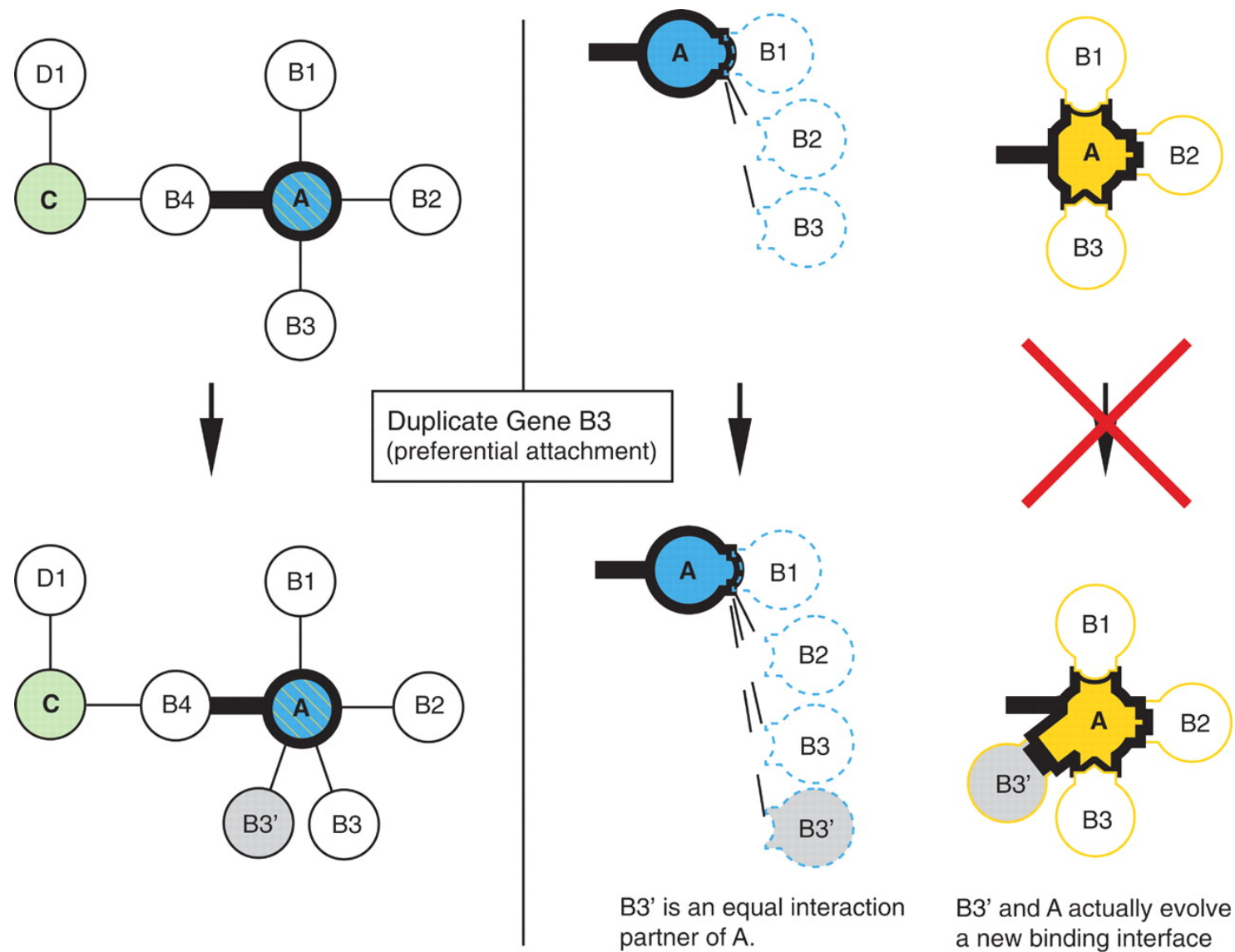


# Evolutionary rate is better explained by interface area

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# Multi-hubs do not follow traditional evolutionary patterns



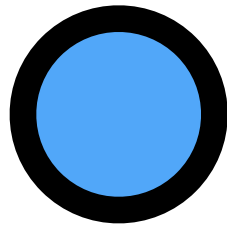
# Multi-hubs do not follow traditional evolutionary patterns

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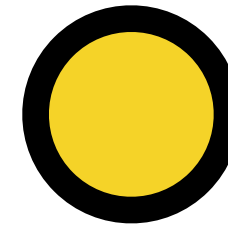
- The dominance of hubs is like due to preferential attachment.
- If a hub evolves by gene-duplication, its interaction partners are expected to be enriched in paralogs.
- Two proteins are significantly more likely to be paralogs if they share a common partner and also share an interaction interface.
- However this trend is only found in singlish-hubs.

## In conclusion

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- Mutually exclusive interactions
- Associated with singlish-interface hubs
- Not likely to be essential
- Not conserved
- Have a transient character
- Follow canonical preferential gene duplication network growth model



- Simultaneously possible interactions
- Associated multi-interface hubs
- More likely to be essential
- More conserved
- Most likely members of large and stable complexes
- Do not follow canonical models of network evolution, growing through gene duplication