

EVOLUTION OF CELLULAR NETWORKS

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OUTLINE

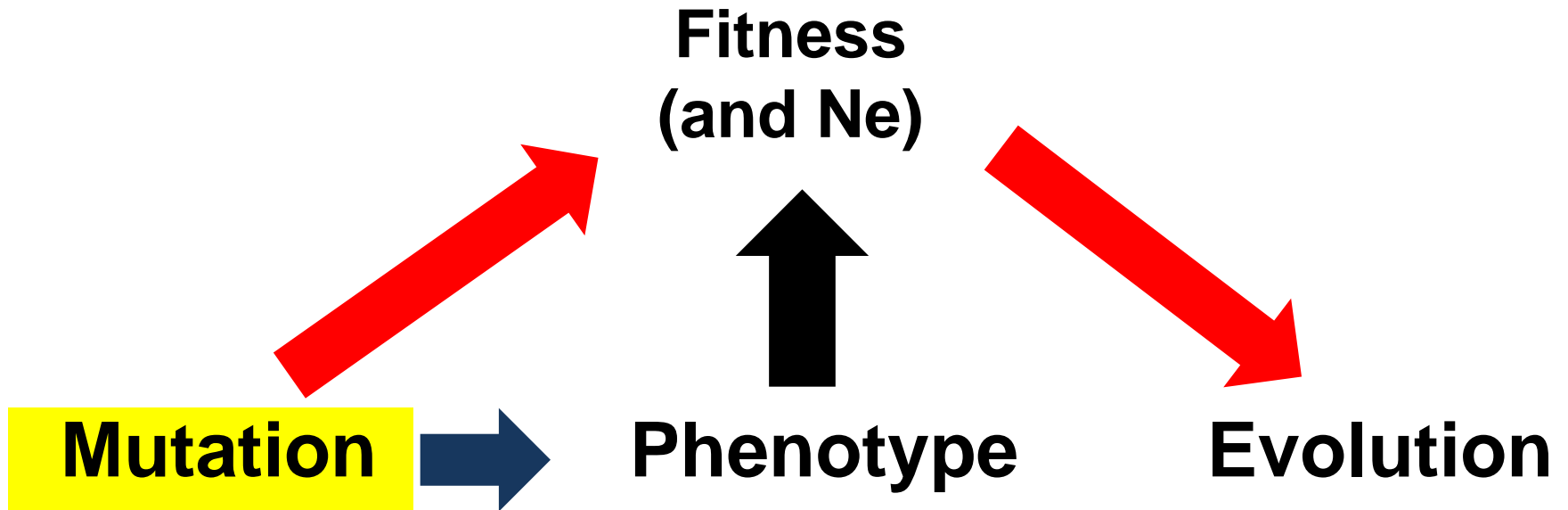
- 1) What (I think) is ECB?
- 2) Genetic redundancy and robustness explained at the molecular level
- 3) How can evolution save you (and not me) from a deleterious mutation?
- 4) Non functional evolution in protein interaction networks

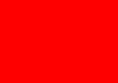

A dark blue rectangular box with a gradient from dark blue on the left to orange on the right. The text "BACK TIME" is written in a bold, sans-serif font. "BACK" is in orange and "TIME" is in white. A small white icon of a film strip is positioned between the two words.

BACK TIME

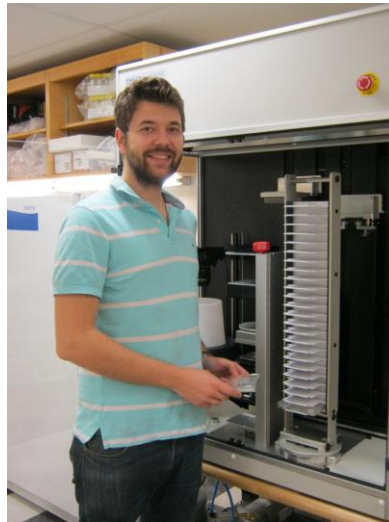
A logo featuring the text "Fast Forward Time.co.uk". "Fast" and "Time" are in a bold, black, sans-serif font. "Forward" is in a larger, bold, black, sans-serif font. A red arrow points to the right, passing through a circular graphic element that resembles a film reel or a globe. The ".co.uk" is in a smaller font size to the right of "Time".

Fast Forward Time.co.uk



 POP GEN
 CELL BIO

Why are some gene deletions worst than others?

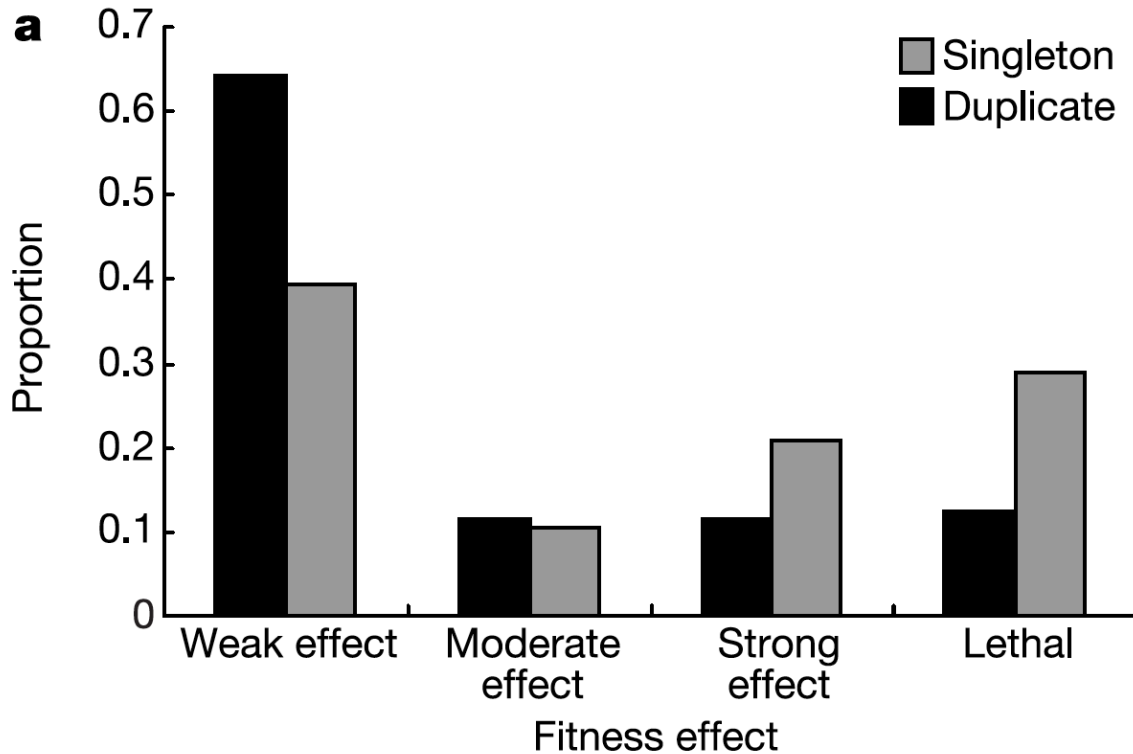


Guillaume Diss

Functional Characterization of the *S. cerevisiae* Genome by Gene Deletion and Parallel Analysis

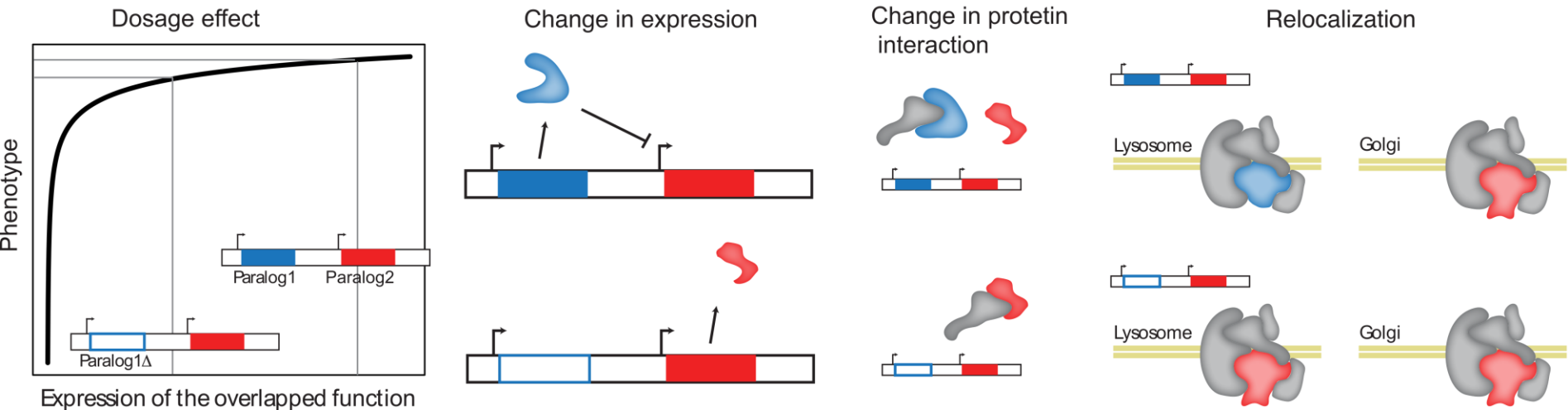
The functions of many open reading frames (ORFs) identified in genome-sequencing projects are unknown. New, whole-genome approaches are required to systematically determine their function. A total of 6925 *Saccharomyces cerevisiae* strains were constructed, by a high-throughput strategy, each with a precise deletion of one of 2026 ORFs (more than one-third of the ORFs in the genome). Of the deleted ORFs, 17 percent were essential for viability in rich medium. The phenotypes of more than 500 deletion strains were assayed in parallel. Of the deletion strains, 40 percent showed quantitative growth defects in either rich or minimal medium.

Cells resist mutations because they have partially redundant parts

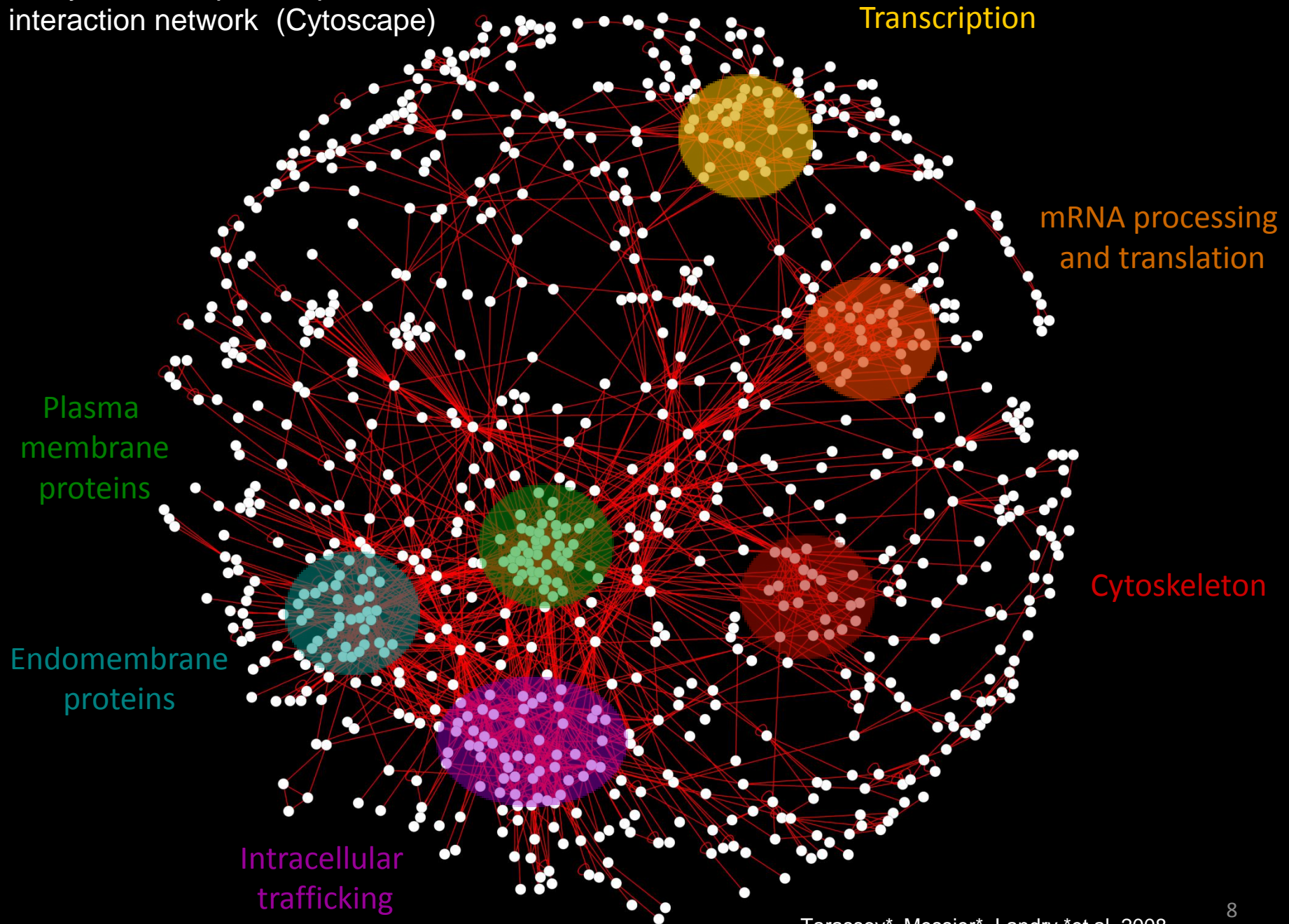


Typical eukaryotic genomes contain from 30 to 65% of duplicated genes

Molecular mechanisms by which paralogous genes can compensate each other's loss

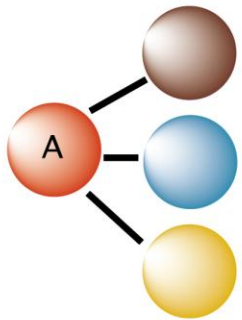


The yeast PCA protein-protein interaction network (Cytoscape)

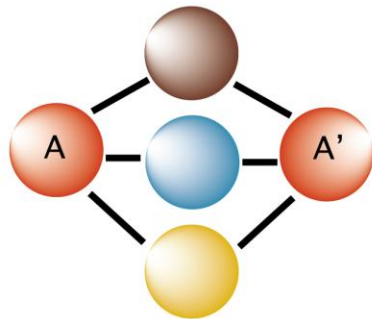


Protein networks grow by gene duplication and divergence

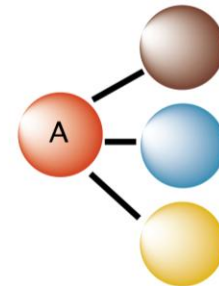
Initial network



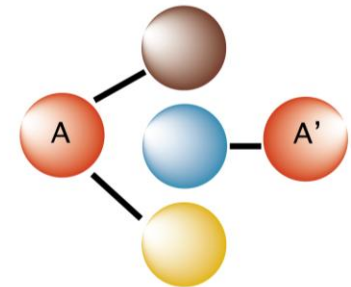
Gene duplication



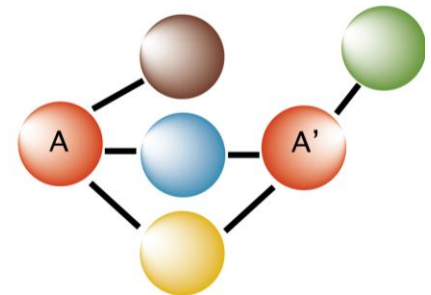
Gene loss



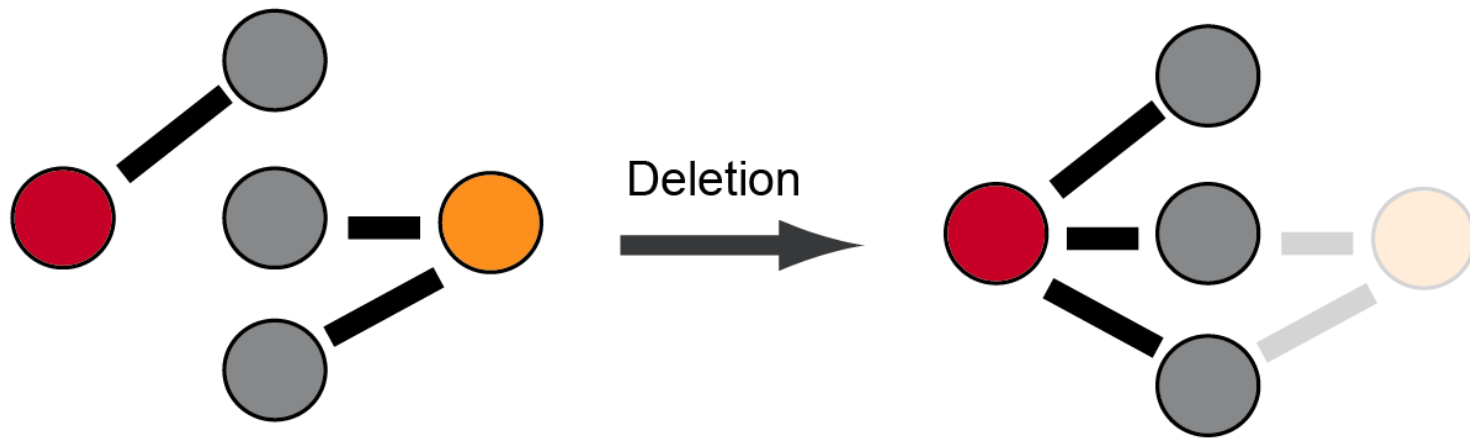
Subfunctionalization
(embellishment)

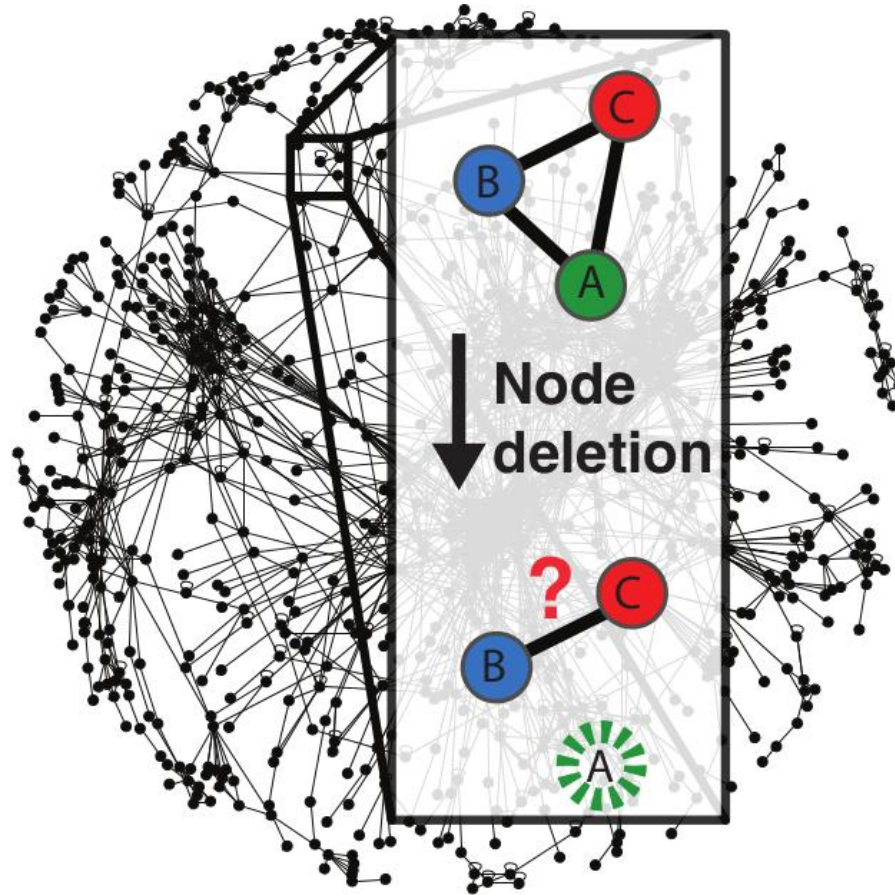


Neofunctionalization
(innovation)

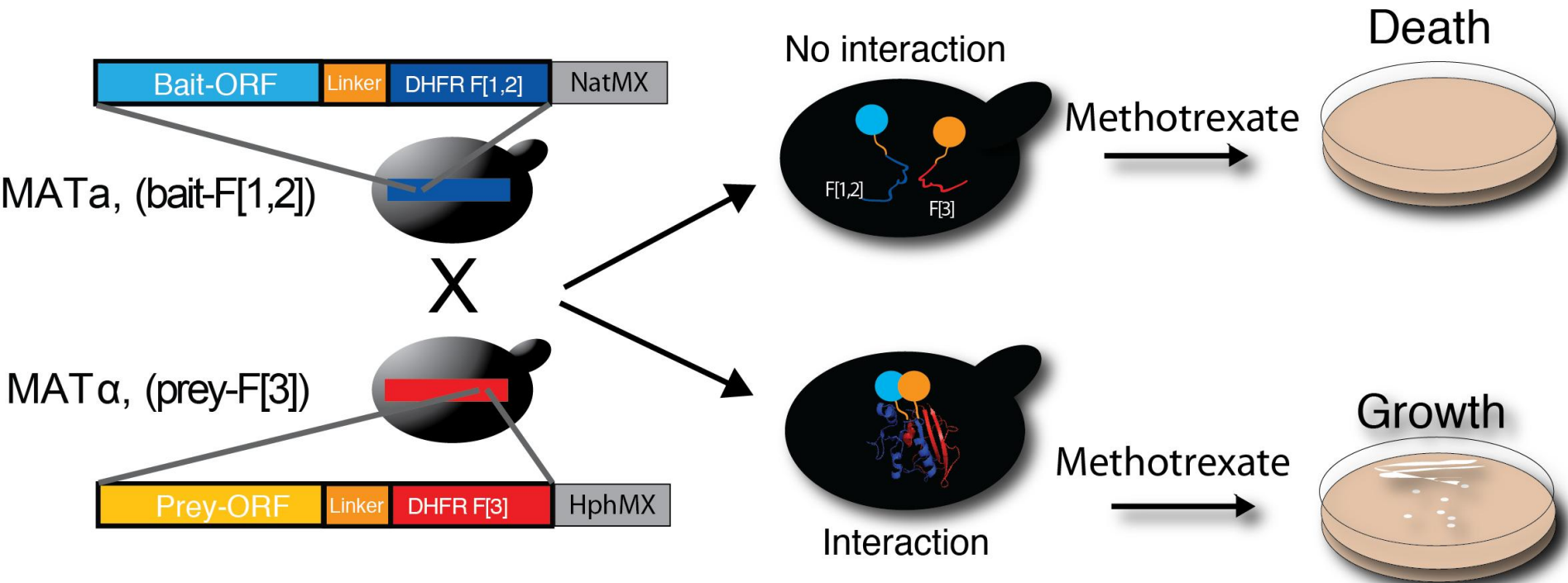


Compensation at the level of protein-protein interactions (PPIs)



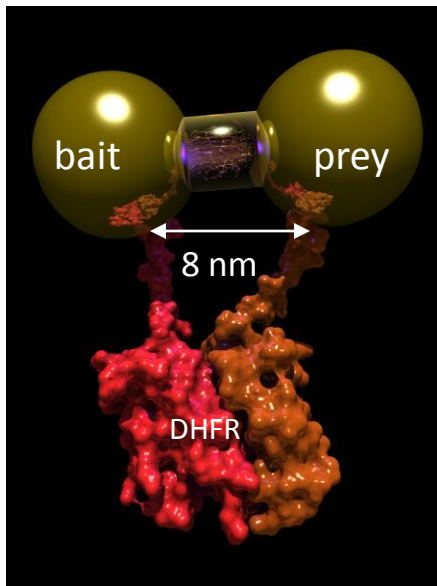


Measuring PPIs in living cells using Protein-fragment Complementation Assay (PCA)

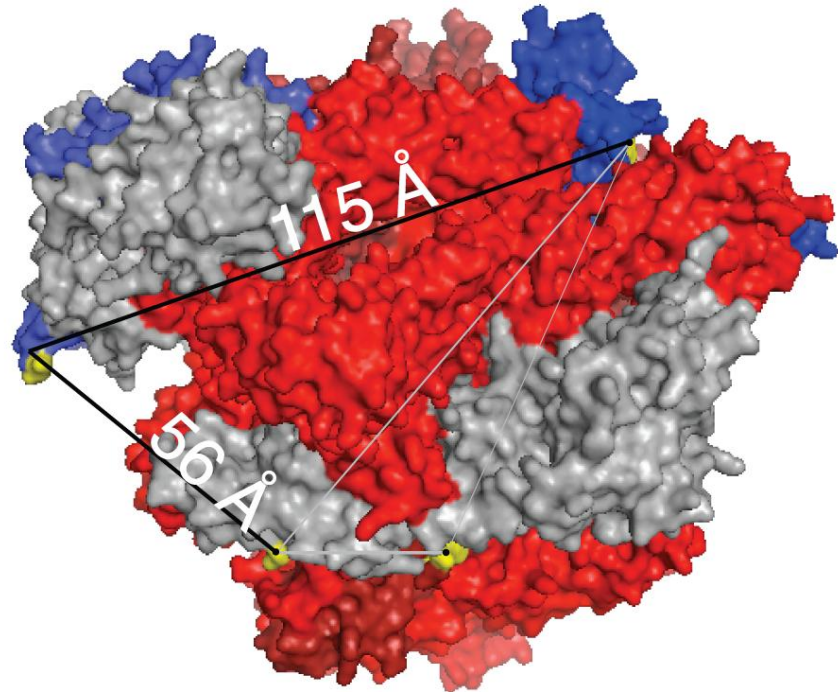


Quantitative interaction score based on growth
Entire yeast proteome ready for PCA

An 8 nm map of the interactome



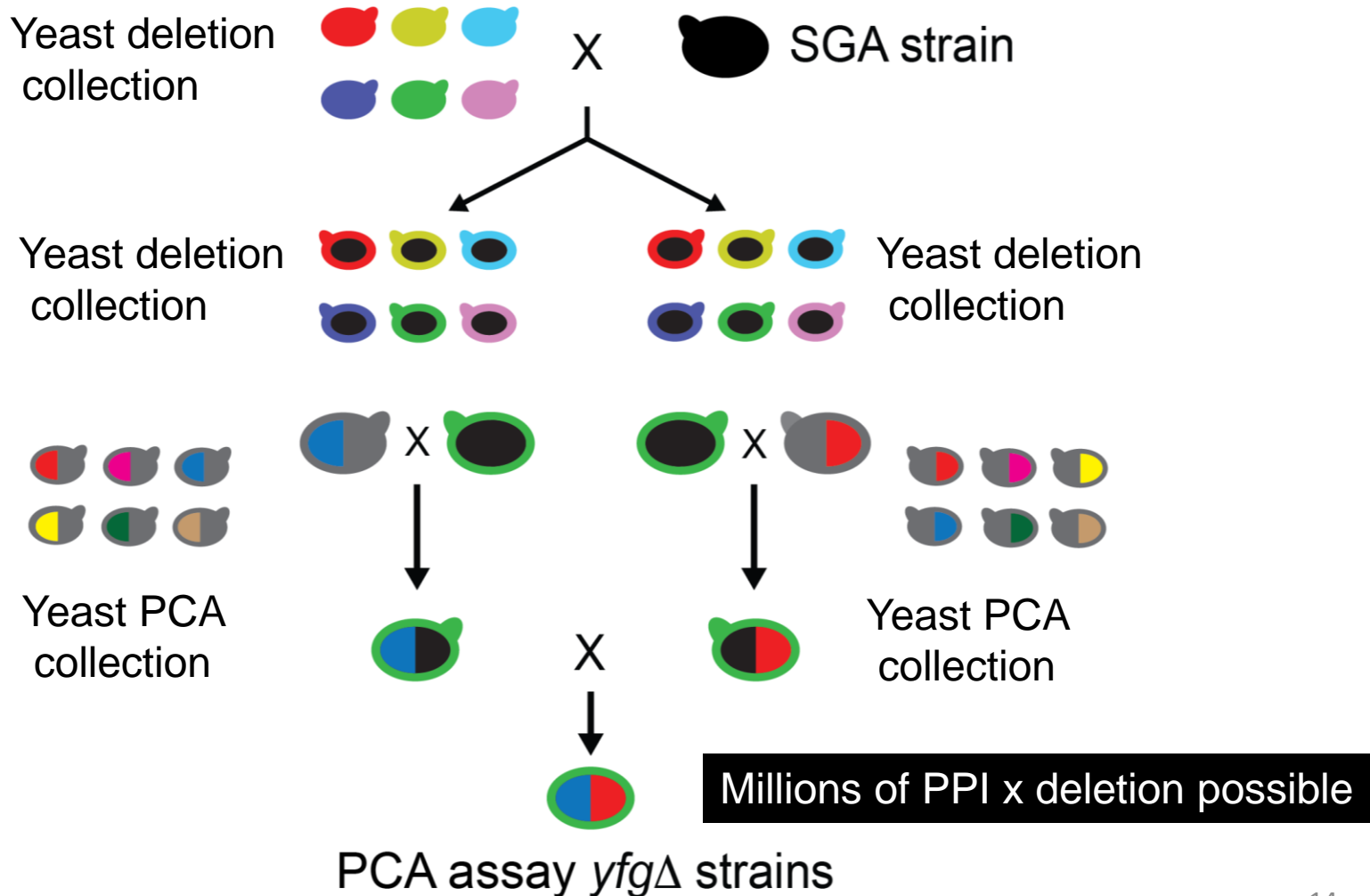
Space constraints
on interactions



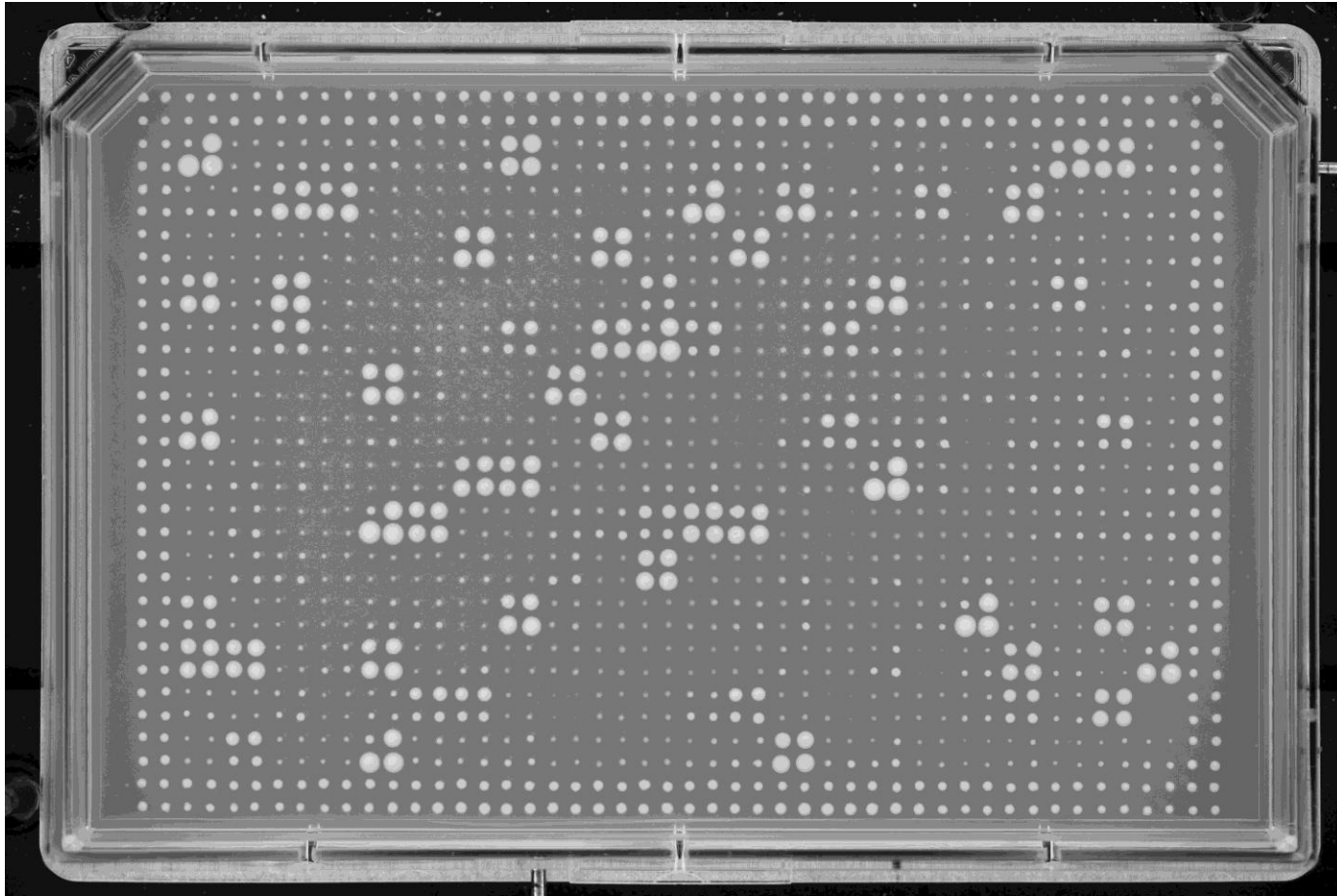
RNApol II small scale

	Distance within 82 Å	Distance above 82 Å	} 6X
Detected	17	4	
Not detected	10	14	

Combination of deletion and PCA with yeast genetics



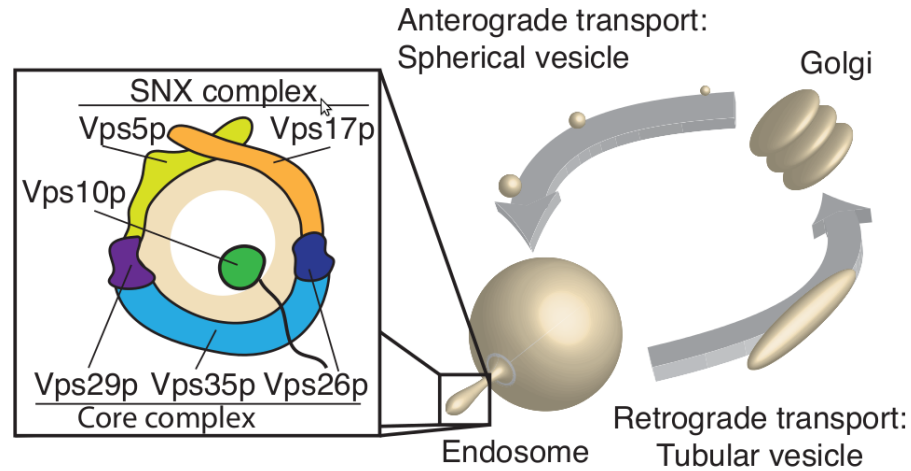
In vivo colony arrays



Systematic perturbation of two protein complexes

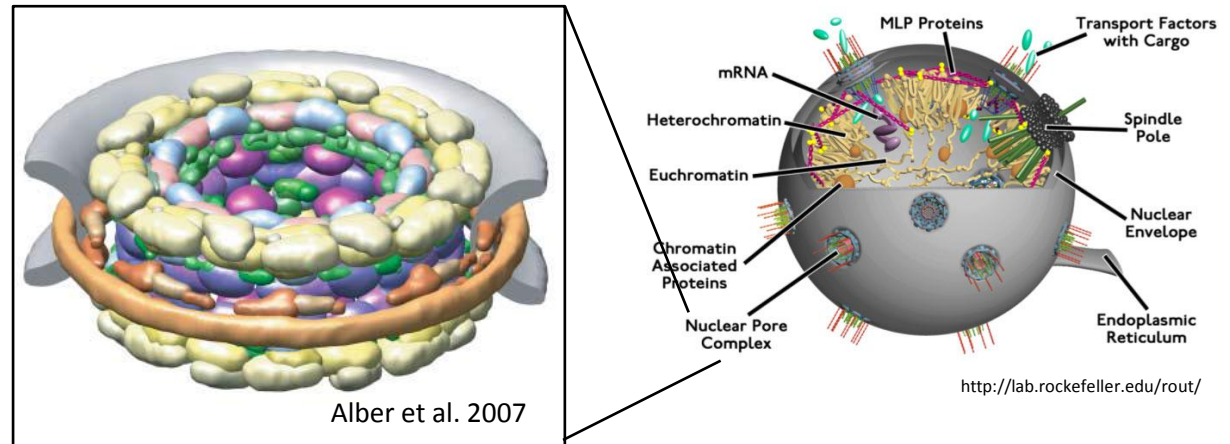
Retromer Complex (6)

No paralogs
Dispensable

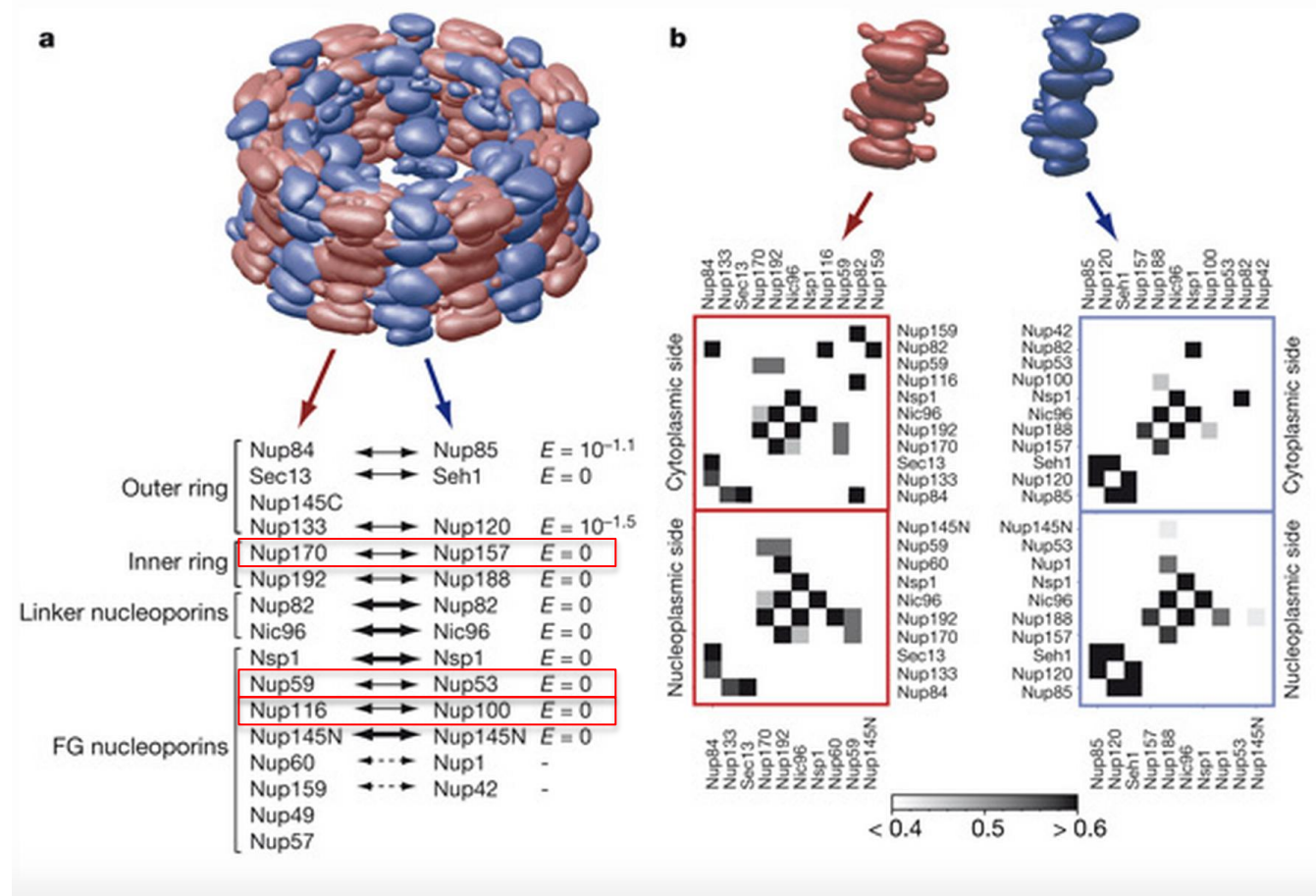
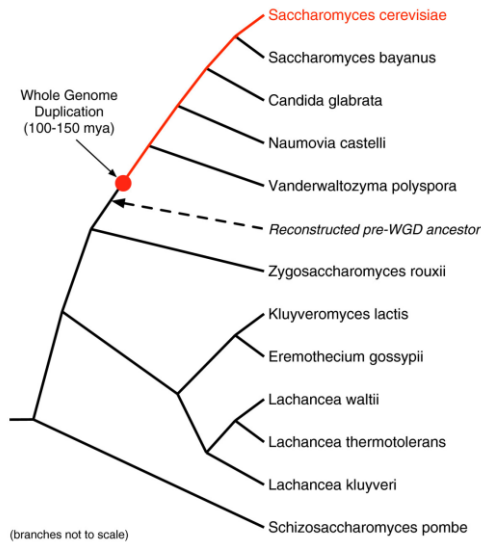


Nuclear Pore Complex (40)

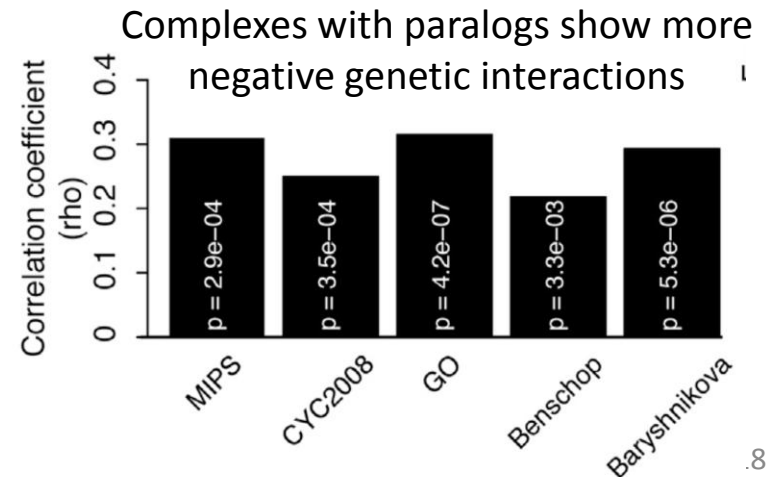
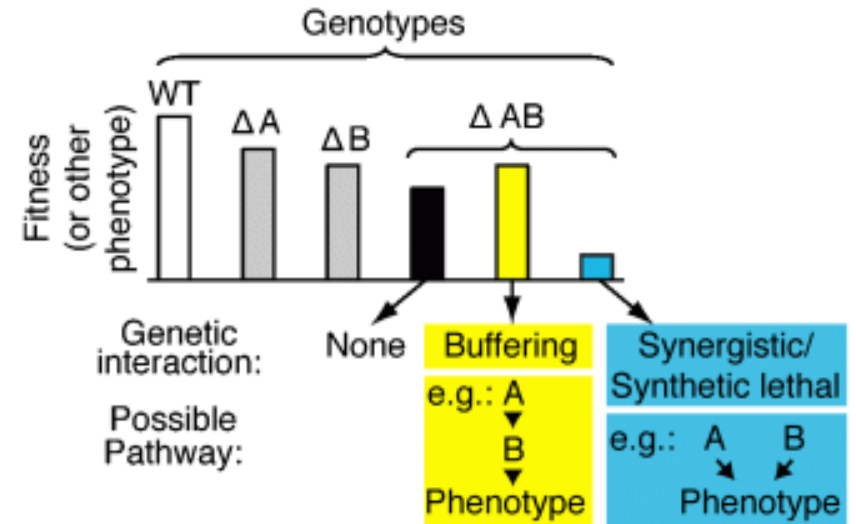
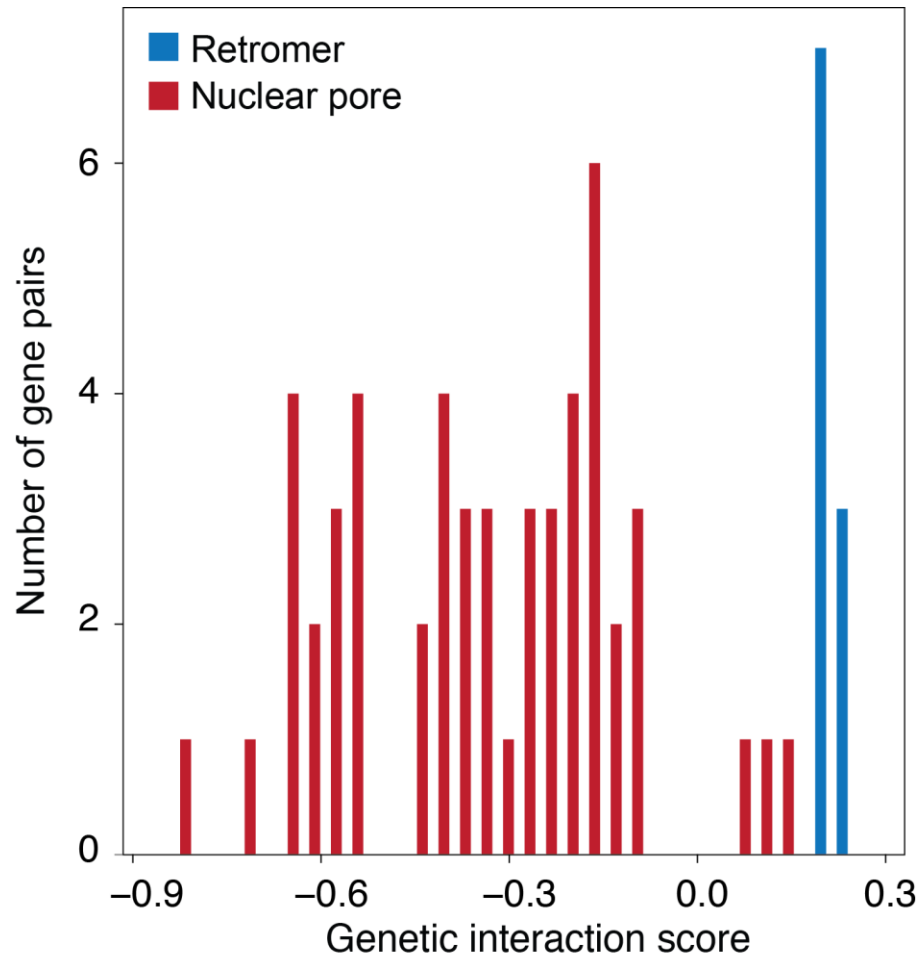
Evolved by gene duplication
Essential



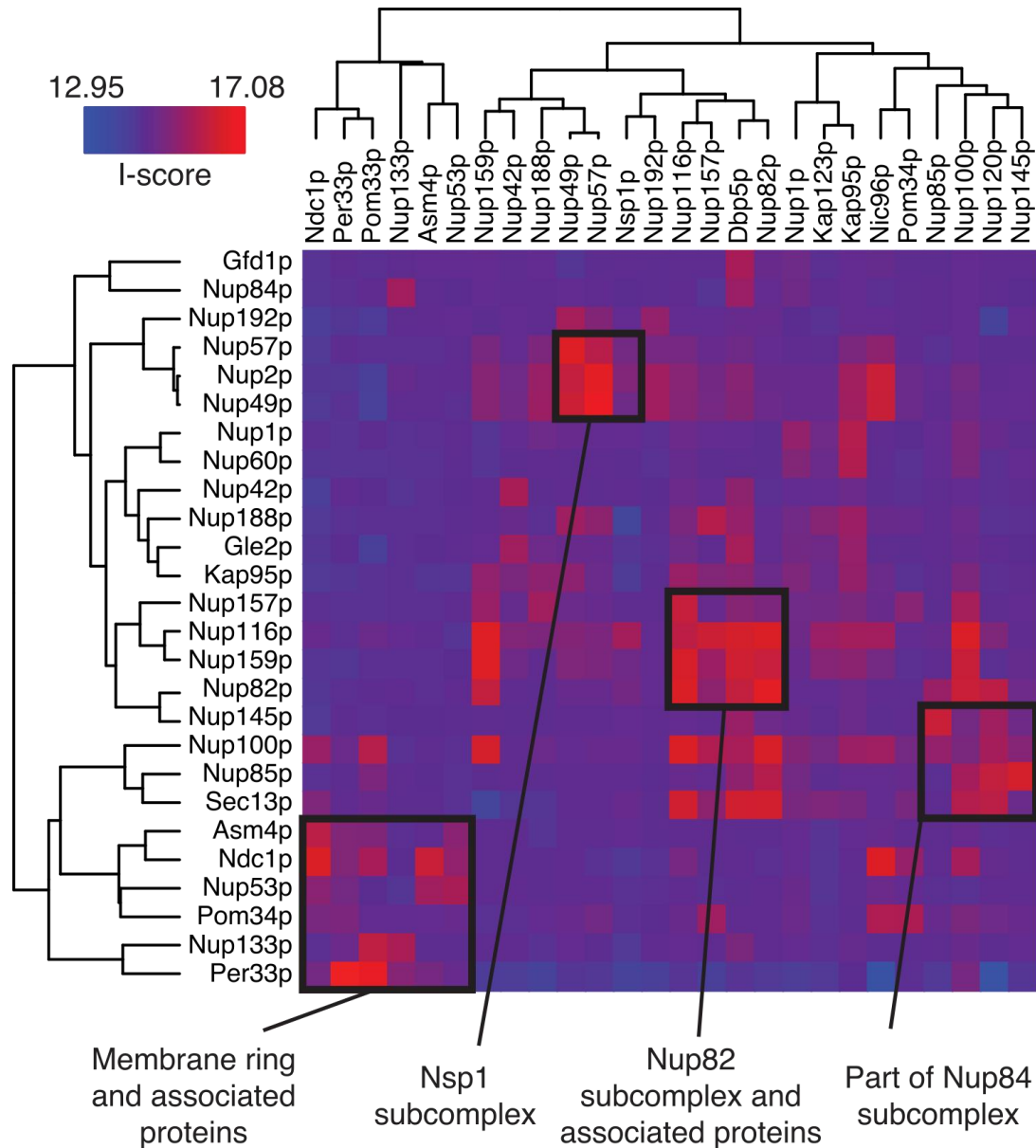
Evolution of the nuclear pore complex by gene duplication



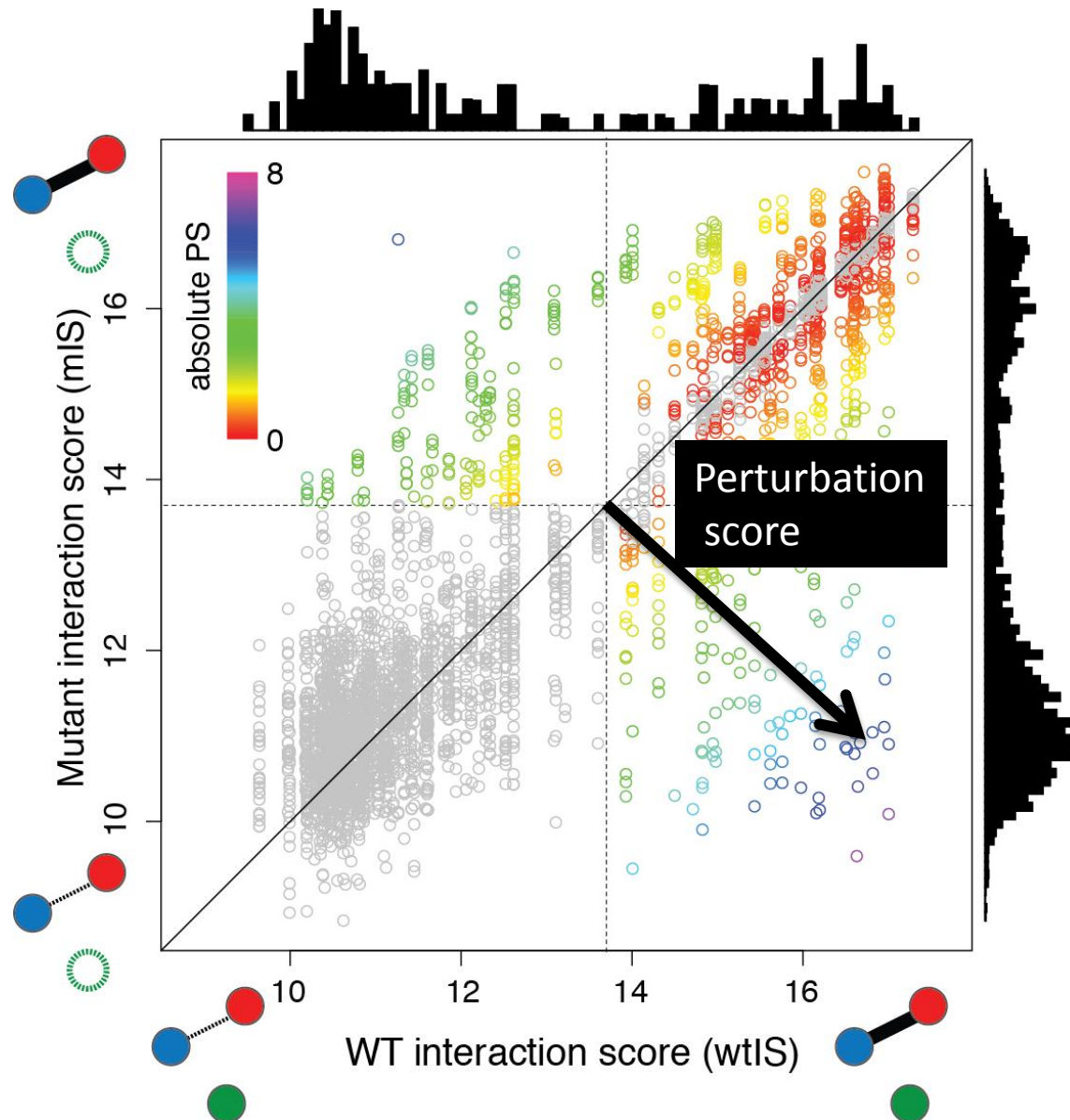
Genetic interactions in these two complexes



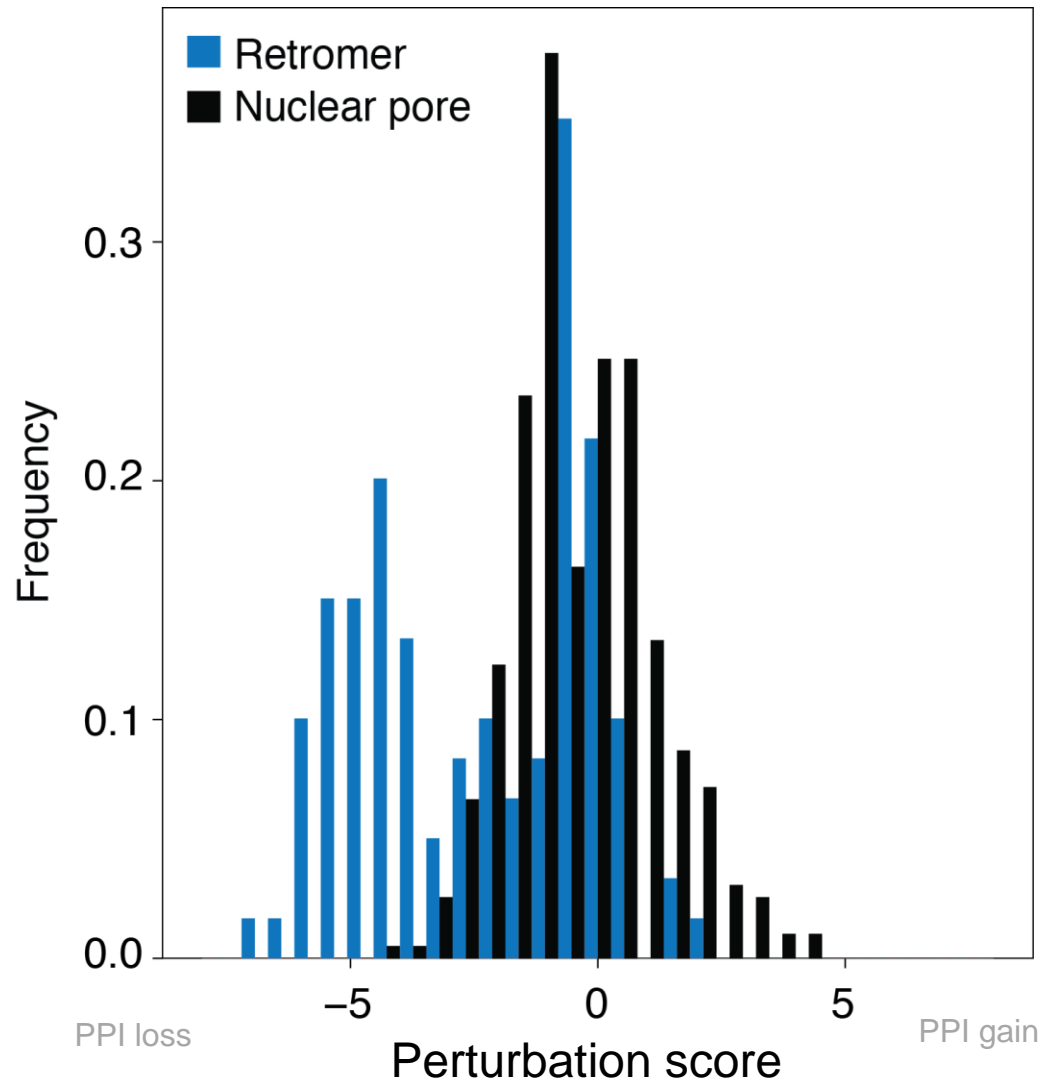
The NPC seen by PCA



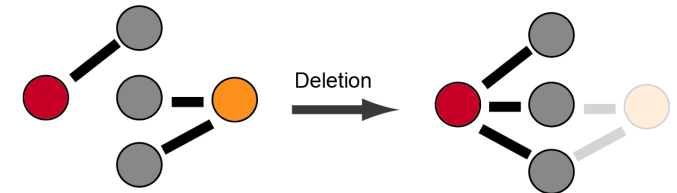
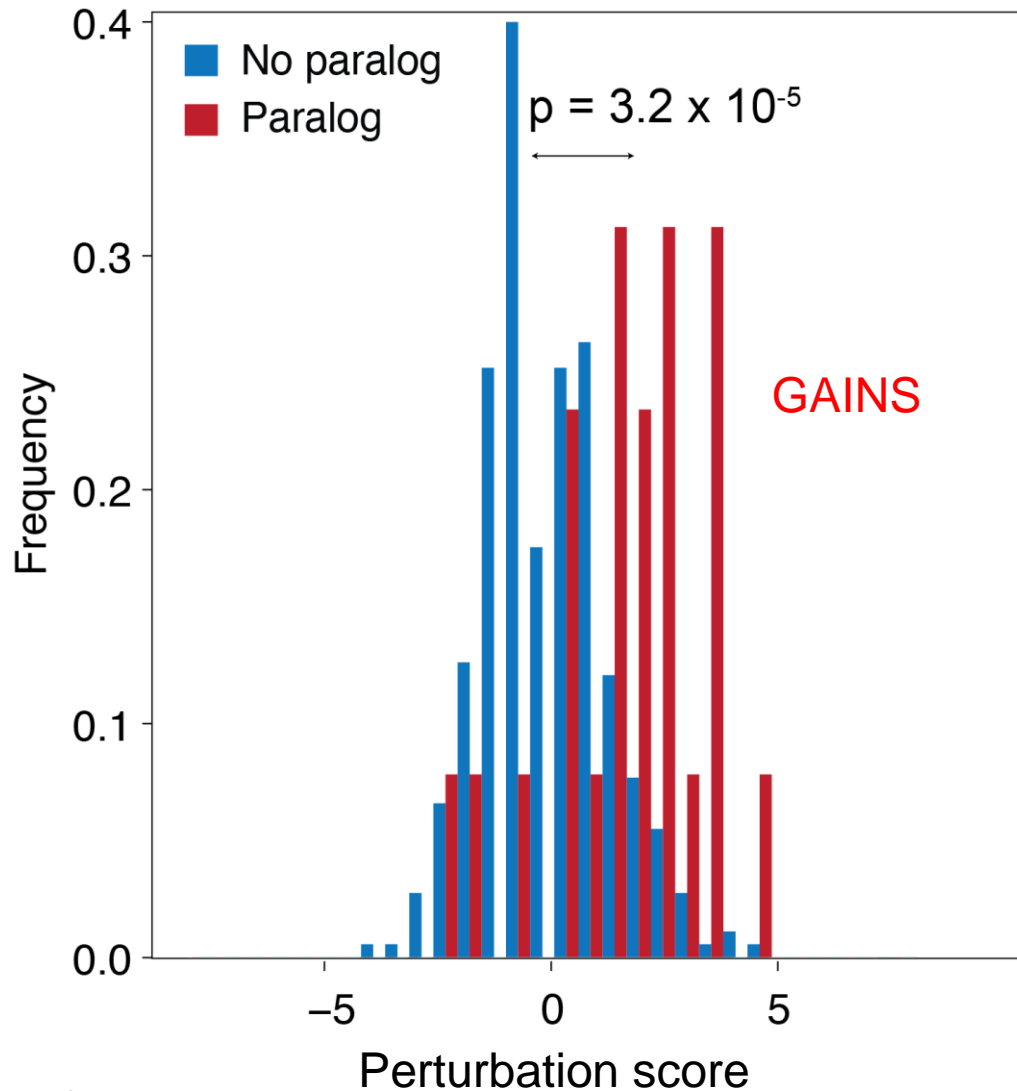
Interactome in WT and deletion strains



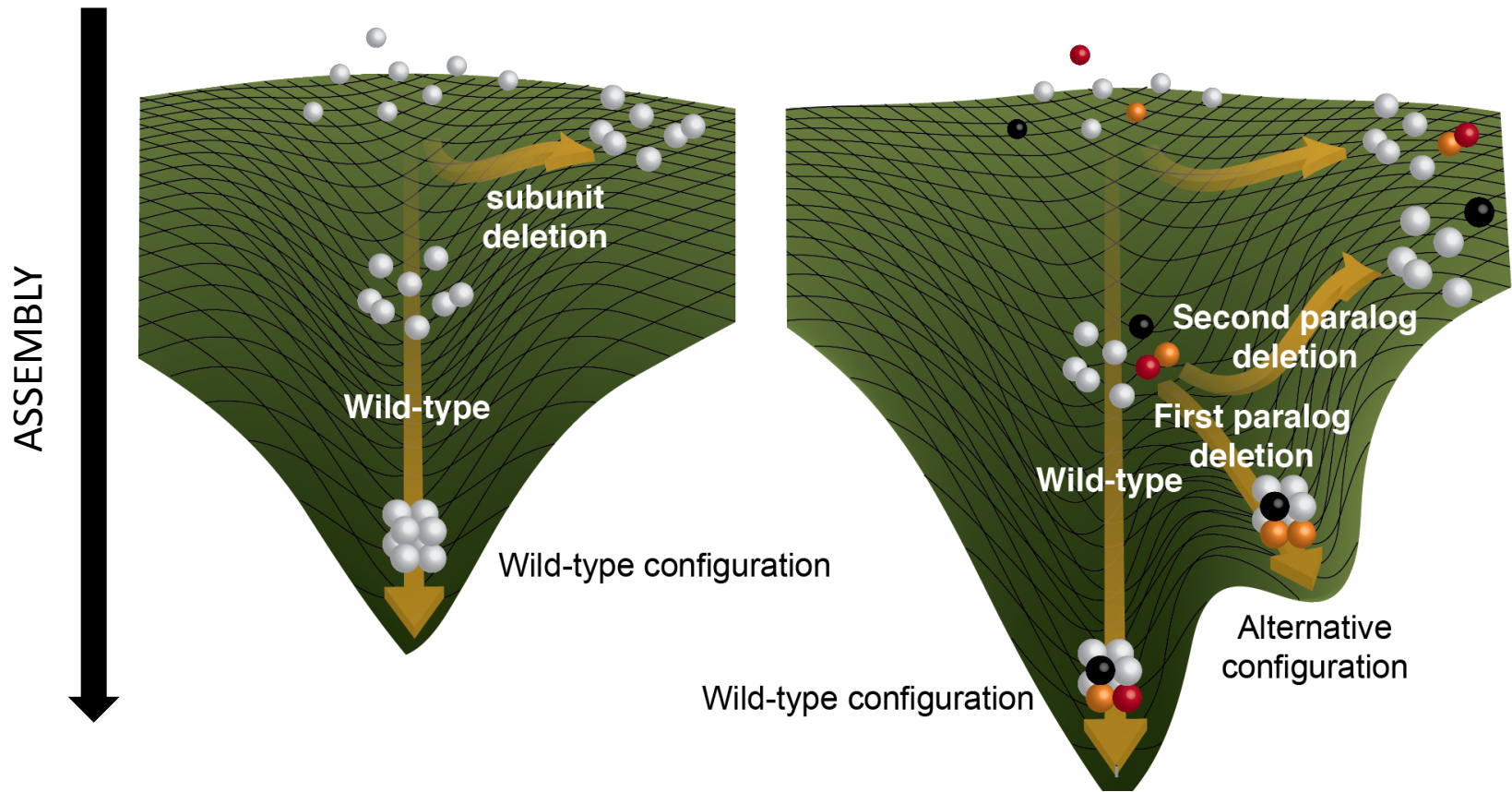
The two complexes have different responses to perturbation



Nuclear pore subunits have enhanced interactions upon the deletion of their paralogs



Paralogous genes allow alternative protein complex configurations



Perspectives

Protein complexes that contain paralogous proteins may be an ensemble of different complexes -> single complex analysis

How would ancestral orthologs position themselves in these complexes?

Acknowledgements

