Supplementary information

Tables:

Table S1. Details of the yeast PPI dataset used in our work.

| DataSet | Number of Nodes | Number of Interactions | Platform |
|---------------------------|-----------------|------------------------|--------------------|
| LC-Kim ¹ | 3268 | 12058 | Literature-curated |
| IDBOS-Gavin ² | 1274 | 7879 | AP/MS |
| IDBOS-Krogan ³ | 1719 | 3640 | AP/MS |
| Y2H-Union ⁴ | 2019 | 2923 | Y2H |

1. Data is from [1]; 2. This data is from [2], we used the default cutoff 5.95; 3. This data is from [2], we used the default cutoff 12.92; 4. Data is from [3].

| dataset | motif size | number of age- homogenous | deltaD after removing interactions within age- | original deltaD | p-value |
|--------------|------------|------------------------------|---|--------------------|-------------------|
| | | motifs | nomogeneous motifs | | |
| LC-Kim | 3 | 2212 | 0.11909275 | 0.54 | ~10-3 |
| | 4 | 44562 | -0.461184082 | 0.54 | ×10 ° |
| IDBOS-Gavin | 3 | 4644 | -0.29278693 | 0.49 | <10-3 |
| | 4 | 39456 | -0.314663703 | 0.48 | |
| IDBOS-Krogan | 3 | 1272 | 0.127818538 | 0.00 | <10 ⁻³ |
| | 4 | 3879 | 0.203066283 | 0.88 | |
| Y2H-Union | 3 | 40 | 0.5975674 | 0.7 | -10-3 |
| | 4 | 195 | 0.588700861 | 0.7 | <10° |

Table S2. The significance of the interactions within the age-homogeneous motifs.

Table S3. The number of motifs containing paralogs in age pattern #3 and 4#. The percentage is simply computed by the second column/third column to show a direct result.

| Motif | Number of Motifs Containing Paralogs | Number of Motifs Containing Paralog PairS in Age Patterns 3# and 4# | Percentag e | Dataset |
|-------|---|---|----------------|--------------|
| В | 69 | 24 | 34.78% | LC |
| Е | 509 | 46 | 9.03% | LC |
| G | 72 | 8 | 11.11% | LC |
| Н | 16 | 3 | 18.75% | LC |
| В | 50 | 7 | 14% | IDBOS-Gavin |
| Е | 289 | 14 | 4.84% | IDBOS-Gavin |
| G | 52 | 4 | 7.69% | IDBOS-Gavin |
| Н | 6 | 0 | 0 | IDBOS-Gavin |
| В | 93 | 9 | 9.67% | IDBOS-Krogan |
| Е | 328 | 2 | 0.60% | IDBOS-Krogan |

| G | 152 | 3 | 1.97% | IDBOS-Krogan |
|---|-----|---|-------|--------------|
| Н | 87 | 2 | 2.29% | IDBOS-Krogan |

| Table S4. Param | neters for all t | he canonical | models. |
|-----------------|------------------|--------------|---------|
|-----------------|------------------|--------------|---------|

| Model | Node Size | Parameters | Initial network |
|-------------------------------------|-----------|---|-------------------------|
| PA Model ¹ | 3000 | connections of new node m ₀ =4 | 4 isolated nodes |
| Symmetric DD Model ² | 3000 | Divergence prob p=0.6, mutation prob q=0.1 | 4 fully connected nodes |
| Asymmetric DD Model ³ | 3000 | Divergence prob p=0.587 | 4 fully connected nodes |
| CG Model ⁴ | 3000 | Newman algorithm to divide the communities | 4 fully connected nodes |

1. Preferential Attachment Model 2. Symmetric Duplication-Divergence Model 3. Asymmetric Duplication-Divergence Model 4. Crystal Growth Model





Figure S1. The degree distribution P(k), clustering coefficient C(k) and the average degree of nearest neighbors k<nn> of the four yeast PPI networks.



Figure S2. The number of proteins within/without network motifs across the four yeast PPI datasets. The p-value shows that proteins within network motifs among three datasets are significantly enriched in SGD_complexes where as no such tendency observed in Y2H-Union data. Same result holds for CYC_2008 copmlexes.



Figure S3. An illustration for our Network Motif model

- 1. Kim WK, Marcotte EM (2008) Age-dependent evolution of the yeast protein interaction network suggests a limited role of gene duplication and divergence. PLoS Comput Biol 4: e1000232.
- 2. Yu X, Ivanic J, Wallqvist A, Reifman J (2009) A novel scoring approach for protein co-purification data reveals high interaction specificity. PLoS Comput Biol 5: e1000515.
- 3. Yu H, Braun P, Yildirim MA, Lemmens I, Venkatesan K, et al. (2008) High-quality binary protein interaction map of the yeast interactome network. Science 322: 104-110.