

Supporting online material for: Protein-protein interactions more conserved within than across species

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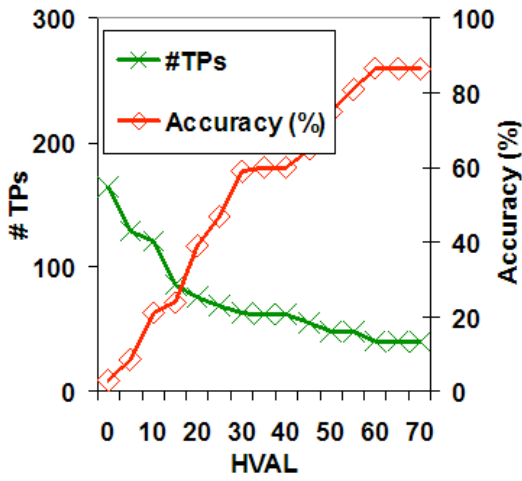
Material

Table App_1: Large-scale protein-protein interaction data sets from IntAct [1] ^Δ

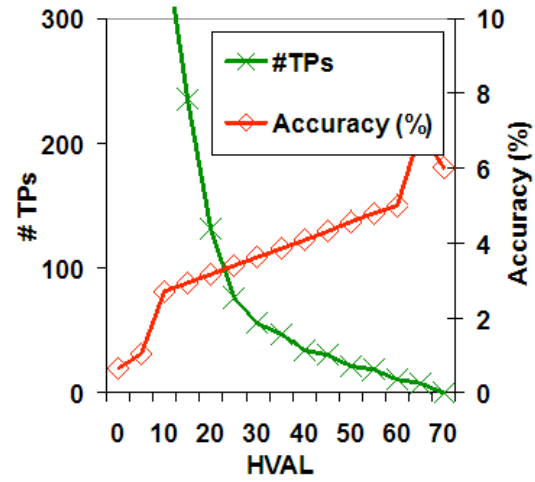
Dataset	Organism	Method	Number of pair interactions
Ito (2001) [2]	<i>Saccharomyces cerevisiae</i>	Y2H	4524
Uetz (2000) [3]	<i>Saccharomyces cerevisiae</i>	Y2H	1495
Ho (2002) [4]	<i>Saccharomyces cerevisiae</i>	MS	29098
Gavin (2002) [5]	<i>Saccharomyces cerevisiae</i>	TAP	19254
Giot (2003) [6]	<i>Drosophila melanogaster</i>	Y2H	20667
Stanyon (2004) [7]	<i>Drosophila melanogaster</i>	Y2H	1615
Formstecher (2005) [8]	<i>Drosophila melanogaster</i>	Y2H	1674
Li (2004) [9]	<i>Caenorhabditis elegans</i>	Y2H	4037
Bouwmeester (2004) [10]	<i>Homo sapiens</i>	TAP + others	1670

^Δ Numbers as taken unfiltered directly from IntAct [1].

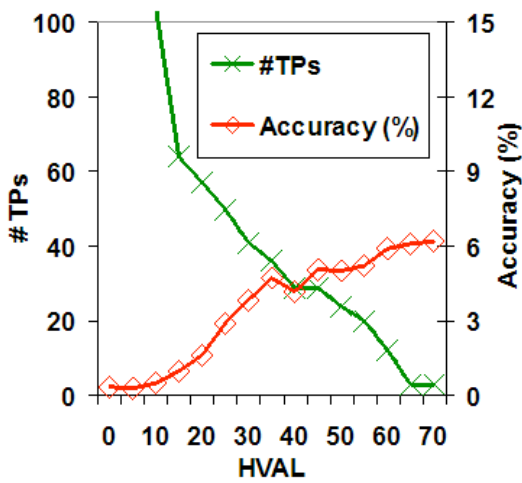
yeast vs yeast



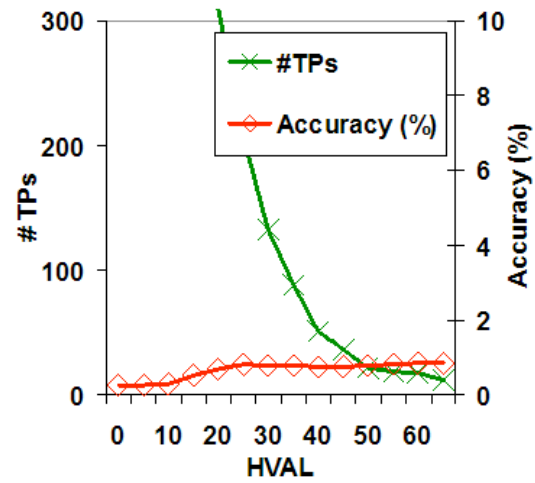
non-yeast vs yeast



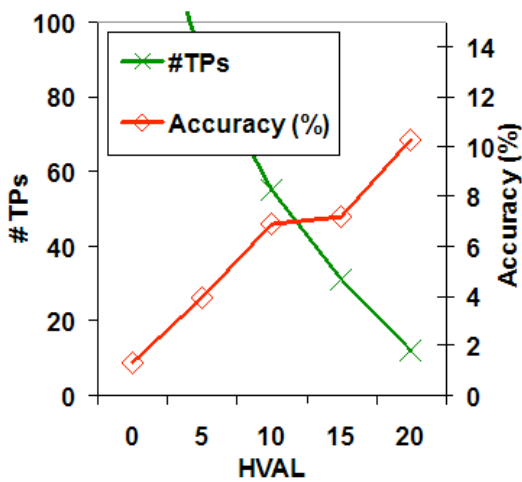
fly vs fly



non-fly vs fly



worm vs worm



non-worm vs worm

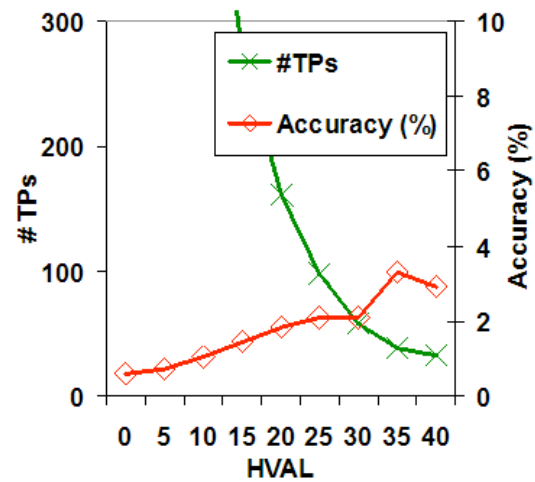
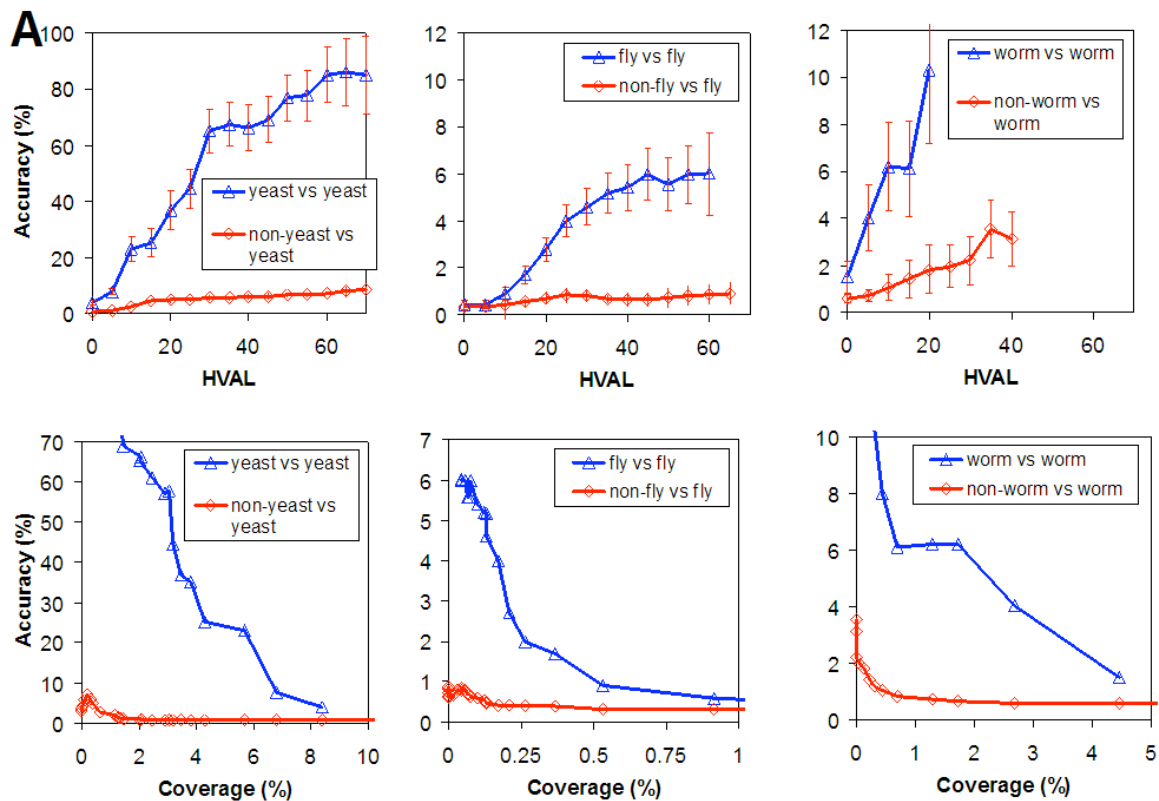
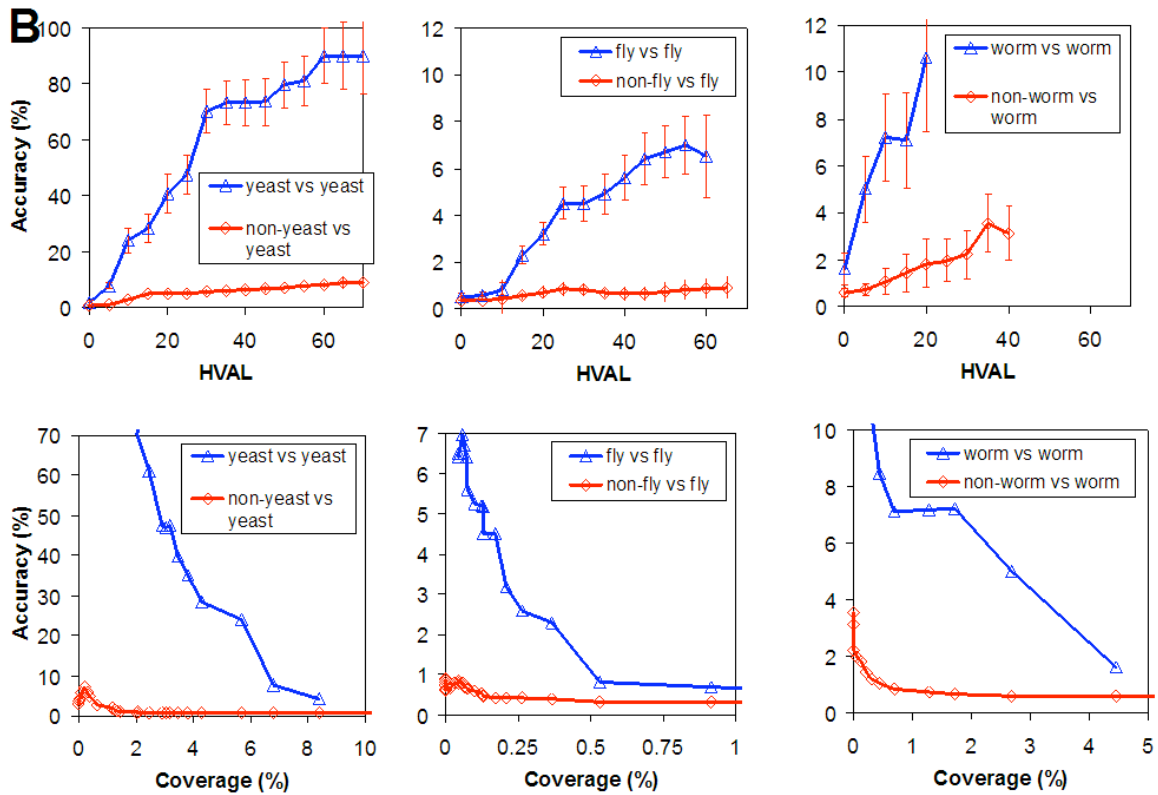


Fig App_1: Each curve above shows the accuracy (red) as shown in Figure 3 (manuscript) and the number of true positives counted at a certain HSSP-value cutoff (green).

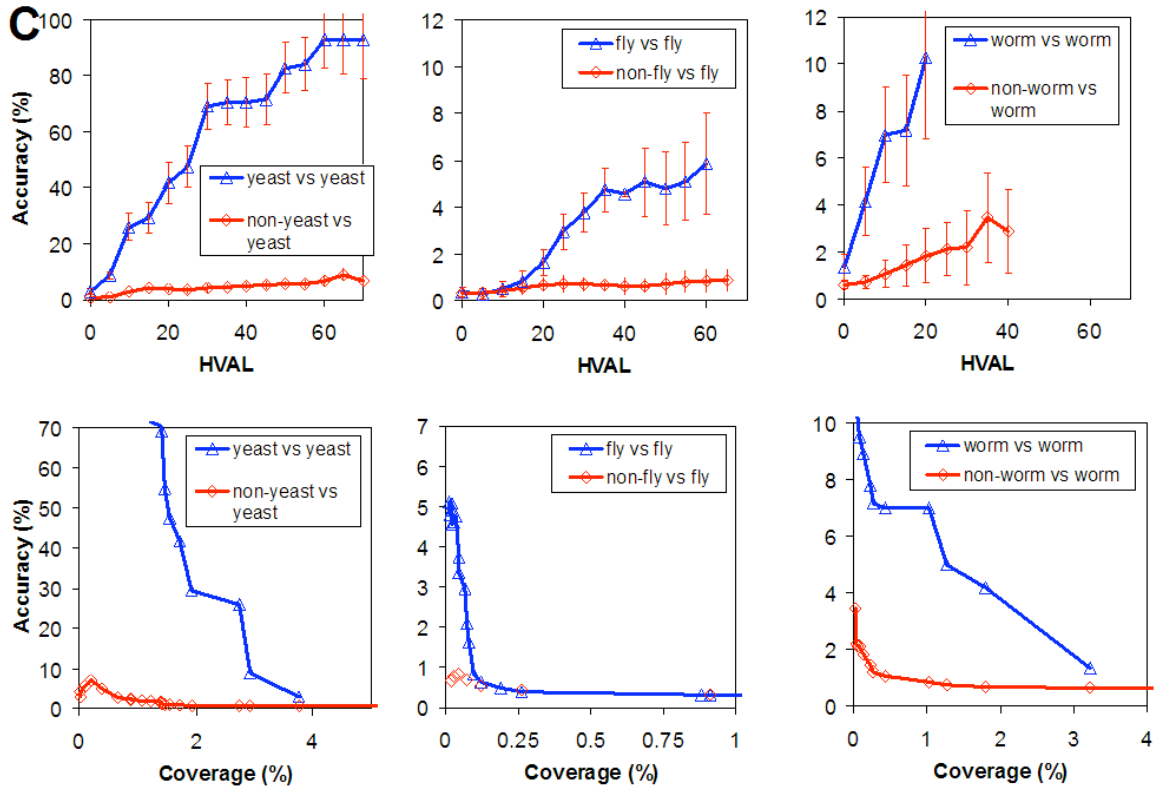
Fig App_2: Results of varying the parameters of our experimental setup to measure the performance of homology inference of protein-protein interactions. Four experiments (A-D) were performed with differences to the experimental setup of Fig 3 (Methods section in manuscript) described below:



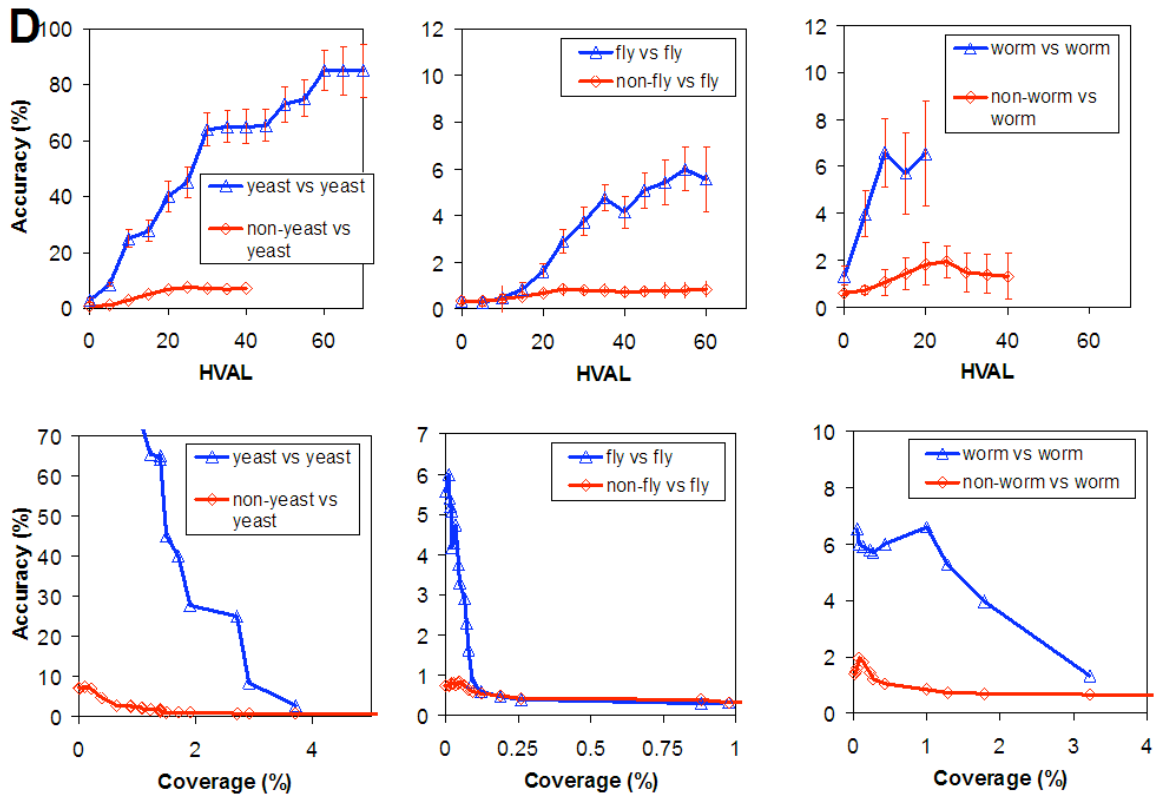
A: Different sampling of intra- vs. inter-species: we allowed transfers of the type A-B to A'-B or A-B to A-B' (Methods). The performance became significantly better for intra-species PPI-transfers, thus further widening the gap between intra and inter-species transfers.



B: Inclusion of transfers within the same data set: we included homology transfers within the same experimental dataset (Methods). The effect was very similar to those observed for different sampling (#1), i.e. widening the gap between intra- and inter-species inferences.



C: Using TAP-like data (Table App_1, Supplementary Online Material) as a constraint for the negatives. To illustrate this assume that TAP pulled down a complex of six proteins. While we cannot infer that all 15 possible interactions are physical, all could be. Therefore, we ignored a false positive prediction (did not count it) if we could find the interaction in those 15 TAP protein-protein pairs. The accuracy slightly increased for both yeast vs yeast (intra-species) comparisons as well as for non-yeast vs yeast (inter-species) comparisons. Note that yeast is the only organism with available TAP-like data.



D: We used a redundant dataset (instead of a non-redundant, bias-reduced set) from organism o (Fig. 7) to hunt for interologs in organism p (Fig. 7). The main message indicated by the results for this latter experiment (#4) stays the same as in our original procedure (Methods): Intra species comparisons are more accurate than inter-species comparisons. Due to more samples in the dataset for organism o (Fig. 7) and thus higher counts, the errors slightly decreased.

References for 'Supporting online material'

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2. Ito T, Chiba T, Ozawa R, Yoshida M, Hattori M, et al. (2001) A comprehensive two-hybrid analysis to explore the yeast protein interactome. *Proc Natl Acad Sci U S A* 98: 4569-4574.
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4. Ho Y, Gruhler A, Heilbut A, Bader GD, Moore L, et al. (2002) Systematic identification of protein complexes in *Saccharomyces cerevisiae* by mass spectrometry. *Nature* 415: 180-183.
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6. Giot L, Bader JS, Brouwer C, Chaudhuri A, Kuang B, et al. (2003) A protein interaction map of *Drosophila melanogaster*. *Science* 302: 1727-1736.
7. Stanyon CA, Liu G, Mangiola BA, Patel N, Giot L, et al. (2004) A *Drosophila* protein-interaction map centered on cell-cycle regulators. *Genome Biol* 5: R96.
8. Formstecher E, Aresta S, Collura V, Hamburger A, Meil A, et al. (2005) Protein interaction mapping: a *Drosophila* case study. *Genome Res* 15: 376-384.
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10. Bouwmeester T, Bauch A, Ruffner H, Angrand PO, Bergamini G, et al. (2004) A physical and functional map of the human TNF-alpha/NF-kappa B signal transduction pathway. *Nat Cell Biol* 6: 97-105.