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Correction: No simple dependence between protein evolution rate and the number of protein-protein interactions: only the most prolific interactors tend to evolve slowly

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After the publication of this work [1], we became aware of the fact that the *Saccharomyces cerevisiae* physical interaction table from the MIPS database that was used to count the number of protein-protein interactions per *S. cerevisiae* protein contains numerous redundant entries (http://mips.gsf.de/proj/yeast/tables/interaction/physical_interact.html). These redundancies were not removed initially, and as a result the numbers of protein-protein interactions reported for *S. cerevisiae* proteins and compared to the proteins' evolutionary rates were artifactually high. These redundancies have now been removed and the data has been re-analyzed. Here we briefly present the results of the re-analysis with the corrected data sets along with revisions of the relevant tables and figures.

Removal of redundant entries resulted in a substantial decrease in the number of protein-protein interactions per *S. cerevisiae* protein (Figure 1). However, consideration of this revised data with respect to evolutionary rates does not result in any qualitative change in the results or conclusions of our previous report. A total of 2,807 pairs of orthologous proteins, one from *S. cerevisiae* and one from *S. pombe*, were identified, and for 1,061 of these, there was data on protein-protein interactions of the *S. cerevisiae* member in the corrected MIPS data. There appears to be no simple dependence between protein evolution rate and the number of protein-protein interactions; in fact, the slight negative correlation between the number of interactions and the evolutionary rates is no longer statistically significant with the corrected data (Figure 1 and Table 1). There is no significant correlation between the taxonomic distribution of *S. cerevisia*e orthologs and the number of protein-protein interactions ($r^2 = 0.0004$, p = 0.5). The apparent trend whereby the most prolific *S. cerevisiae* interactors have, on average, lower evolutionary rates than proteins that are involved in fewer protein-protein interactions also remains (Figure 2 and Table 2).

We regret any inconvenience that this inaccuracy in the data used for the original analysis might have caused. We wish to thank Dr. Hunter B. Fraser for bringing this matter to our attention.

References

Jordan IK, Wolf YI, Koonin EV: No simple dependence between protein evolution rate and the number of protein-protein interactions: only the most prolific interactors tend to evolve slowly. *BMC Evol Biol* 2003 **3**:1

Table 1 - Correlation between the number of protein-protein interactions and the evolutionary rate.

Data set	Linear correlation coefficient (r)/ P-value	Rank correlation coefficient (R)/P-value
S. cerevisiae – S. pombe (all orthologs, N=1061)	-0.051/0.095	0.022/0.47
S. cerevisiae – S. pombe (only orthologs with >40% identity, N=478)	0.011/0.812	0.096/0.036
H. pylori J99 – *H. pylori* 26695 (N=672)	-0.039/0.310	0.020/0.610
H. pylori – *C. jejuni* (N=458)	-0.013/0.787	0.015/0.747

Table 2 - Statistical significance of the differences in evolutionary rates between groups of proteins with different numbers of interactions.

Bin (# interactions) comparisons[a]	P[b]
S. cerevisiae – S. pombe	
16 – 29 vs. 1 – 15	1.0×10^{-2}
11 – 29 vs. 1 – 10	5.9×10^{-3}
6 – 29 vs. 1 – 5	5.2×10^{-1}
H. pylori 26695 – H. pylori J99	
21 – 55 vs. 1 – 20	1.5×10^{-1}
15 – 55 vs. 1 – 14	1.8×10^{-1}
11 – 55 vs. 1 – 10	3.2×10^{-1}
H. pylori 26695 – C. jejuni	
21 – 47 vs. 1 – 20	9.8×10^{-1}
11 – 47 vs. 1 – 10	5.1×10^{-1}

[a] Orthologous pairs of proteins were placed into bins based on the number of protein-protein interactions.
[b] *P*-value for the Student's ttest comparing the mean evolutionary rates between orthologs for bins with distinct ranges in the number of protein-protein interactions.
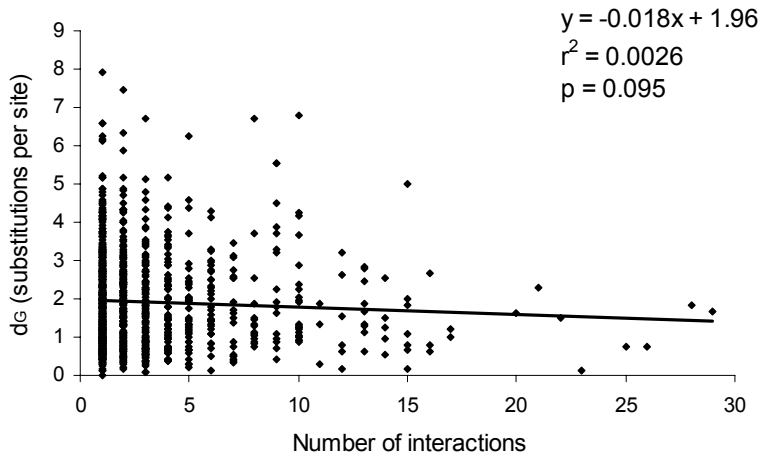
Figure Legends

Figure 1 - The relationship between the number of protein-protein interactions for _S. cerevisiae_ proteins and the evolutionary rates between _S. cerevisiae_ and _S. pombe_ orthologs.

Shown for each plot is the equation that describes the linear trend line, the r^2 value that describes the fraction of the variability in the evolutionary rates that is accounted for by the variability in the number of protein-protein interactions and the p value, which is the probability that the correlation between the number of protein-protein interactions and evolutionary rates could be due to chance. (a) All 1,061 observations. (b) 478 observations that correspond to orthologous protein pairs with $\geq$40% amino acid sequence identity.
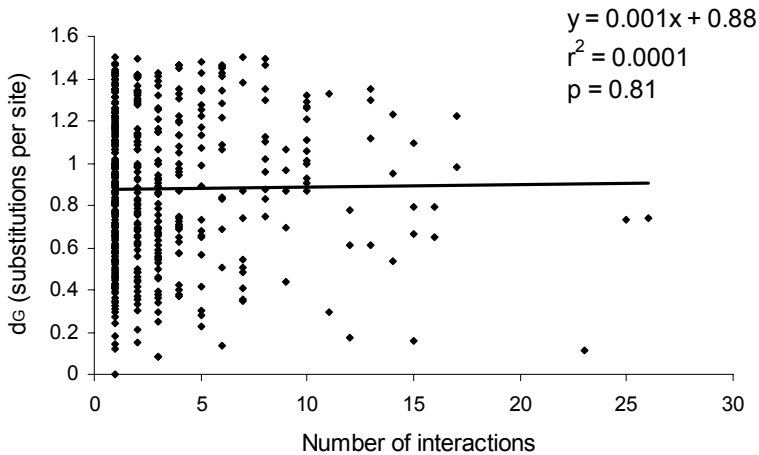
Figure 2 – Mean evolutionary rates between _S. cerevisiae_ and _S. pombe_ orthologs for bins of proteins with different numbers of interactions.

The range of the number protein-protein interactions per _S. cerevisiae_ protein for each bin (x-axis) and the mean evolutionary rate (substitutions per site) for each bin (y-axis).

(a)

$y = -0.018x + 1.96$
$r^2 = 0.0026$
$p = 0.095$

(b)

$y = 0.001x + 0.88$
$r^2 = 0.0001$
$p = 0.81$

S. cerevisiae - S. pombe

Mean dG (subs per site) vs. # interactions (range)