Protein Structure Prediction and Design in a Biologically Realistic Implicit Membrane

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To compute the $\Delta\Delta G$ of mutation results (Test 2, presented in Figure 3, Supplementary Figure 8B, and Supplementary Figure 13), the score function used an *fa_water_to_bilayer* weight value of 1.5 instead of the reported value of 0.5. In addition, the $\Delta\Delta G$ results were erroneously computed allowing all residues within 8 Å of the host site to change identities (that is, to be designed). The figures were annotated with R^2 values, but the numbers shown are in fact the correlation coefficients, R . The script has been corrected to restrict these residues to repacking only. The updated data and correlation coefficients (*fa_water_to_bilayer* weight of 1.5) are presented in the updated Figure 3 below and in updated Supporting Material, in which Supplemental Tables 4 and 8 and Supplemental Figures 4–6, 8B, and 13 have been corrected and replaced. Supplemental Table 10 also has been replaced to correct a typographical error.

FIGURE 3 Comparison between computationally predicted and experimentally measured $\Delta\Delta G^{\text{mut}}$ for mutations in PagP. For all correlation plots (B–D), proline is not shown because of steric clashes resulting in a large $\Delta\Delta G^{\text{mut}}$ -value. The dotted gray line is the line of best fit, and the solid gray line is $y = x$. In addition, amino acids are colored according to the following categories: charged (orange), nonpolar (red), aromatic (blue), polar (purple), and special case (green). (A) The structure of the PagP scaffold (PDB: 3GP6) with the mutation site V111 highlighted in dark gray is shown. The implicit solvent phases in (A) are colored in a similar manner as in Fig. 1. The $\Delta\Delta G^{\text{mut}}$ predictions for mutations in PagP by M07, M12, and M19 are shown in (B)–(D), respectively. To see this figure in color, go online.

The corrected analysis preserves the original observation that, relative to the M07 and M12 models, the M19 energy function improves the correlation of predicted PagP $\Delta\Delta G$ values with the experimental values ($R = 0.830, 0.822, 0.403$, and 0.919 for the M07, M12, R15M, and M19 models, respectively). The improvement is more pronounced than previously reported since noise arising from inadvertent design is now removed. The conclusion also holds for the contribution of polar side chains to the correlation coefficient ($R = 0.778, 0.755, 0.484$, and 0.920 for the M07, M12, R15M, and M19 models, respectively). The amino acids G, T, V, Y, and L remain the residues with the largest deviation from the experimental values.

The other three benchmark tests were carried out at the originally reported weight of 0.5. As the $\Delta\Delta G$ test is independent from the fitting and benchmarking of the energy function, this correction does not affect any other results or the conclusions of the paper.

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