THE JOURNAL OF PHYSICAL CHEMISTRY B

Addition/Correction

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Correction to "Symmetry Numbers for Rigid, Flexible, and Fluxional Molecules: Theory and Applications"

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J. Phys. Chem. B **2010**, *114* (49), 16304−16317. DOI: 10.1021/jp110434s

Equation 12 of the original paper is in error, so the example represented in the original Figure 3 did not correctly illustrate the intended point. The following figure and text should be substituted.

A rigid protein (figure, hatched) binds any of three rigid compounds (filled), A, B, or C. Compound A has one group that fits the binding site, compound B has two such groups and a symmetry number of 2, and compound C is identical to B but has an additional feature that breaks its symmetry. We will isolate the role of symmetry as a determinant of affinity by assuming that the binding groups of all three compounds interact identically with the protein. Solvent is neglected, because including it would add complexity without changing the conclusions. The configuration integrals of the free compounds and protein at standard concentration C° [1] are

$$Z_A = 2Z_B = Z_C = Z_P = \frac{8\pi^2}{C^\circ}$$

where the factor of 2 results from the symmetry of compound B. For simplicity, we will approximate the binding potential as a square energy well of depth E and volume ωv, where ω is an angular volume in the three Euler angles defining the relative orientation of the protein and bound compound and v is a Cartesian volume based on the relative translational freedom of the two molecules in their bound state. The configuration integrals of the three protein-compound complexes become[1]

$$Z_{AP} = Z_{BP} = \frac{1}{2}Z_{CP} = \frac{8\pi^2}{C^\circ}\omega v e^{-\beta E}$$

The equivalence of Z_{AP} and Z_{BP} follows from the indistinguishability of the two binding groups of B, which can adopt either of two indistinguishable orientations in the binding site, whereas Z_{CP} is double because C has two distinguishable binding groups with identical affinities. (If the groups had similar but different affinities, this would be accounted for via a Boltzmann sum.) The standard binding free energies are given by $\Delta G^\circ_{XP} = -RT \ln[Z_{XP}/(Z_X Z_P)]$, where X = A, B, or C:

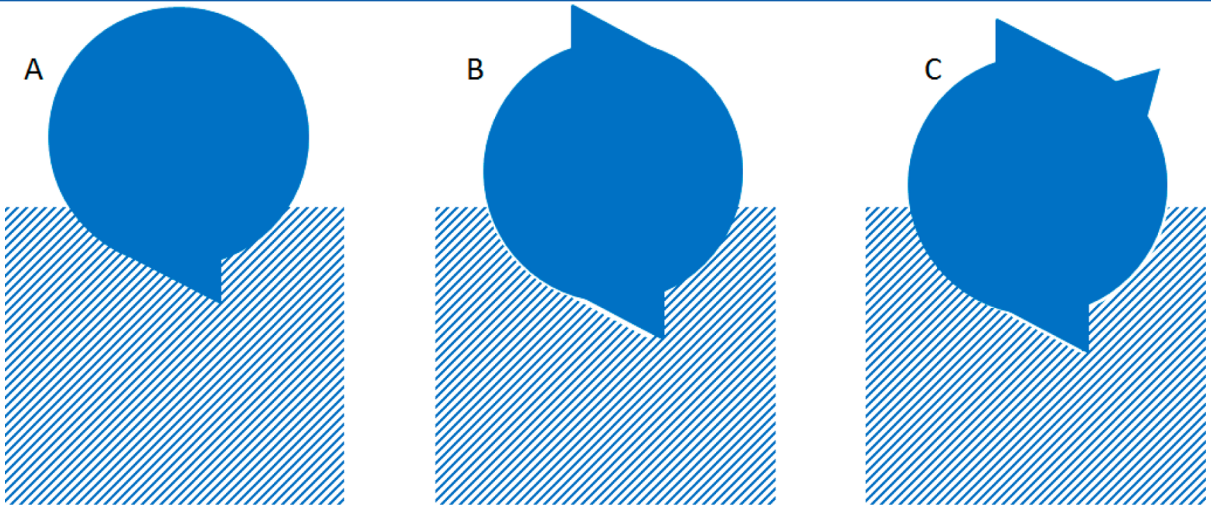
$$\Delta G^\circ_{AP} = -RT \ln\left[\frac{C^\circ}{8\pi^2}\omega v e^{-\beta E}\right]$$

$$\Delta G^\circ_{BP} = \Delta G^\circ_{CP} = \Delta G^\circ_{AP} - RT \ln 2$$

Thus, the compounds with two binding groups (B and C) have the same affinity for the protein, although one is symmetric and the other is asymmetric, and their binding free energies are more negative (favorable) than compound A, with its single binding group, by $-RT \ln 2$. The greater symmetry of ligand B leads neither to increased nor decreased affinity relative to the less symmetric, but otherwise matched, ligand C, because the presence of symmetry has an equal effect on the configuration integrals of the bound and free states. If one neglected indistinguishability in the case of compound B, then $Z_B = Z_C$ and $Z_{BP} = Z_{CP}$, so again, there would be no difference in affinity between ligands B and C.

REFERENCES

(1) *Biophys. J.* **1997**, *72*, 1047.



Published: March 5, 2013

