

Accurate binding energy calculation

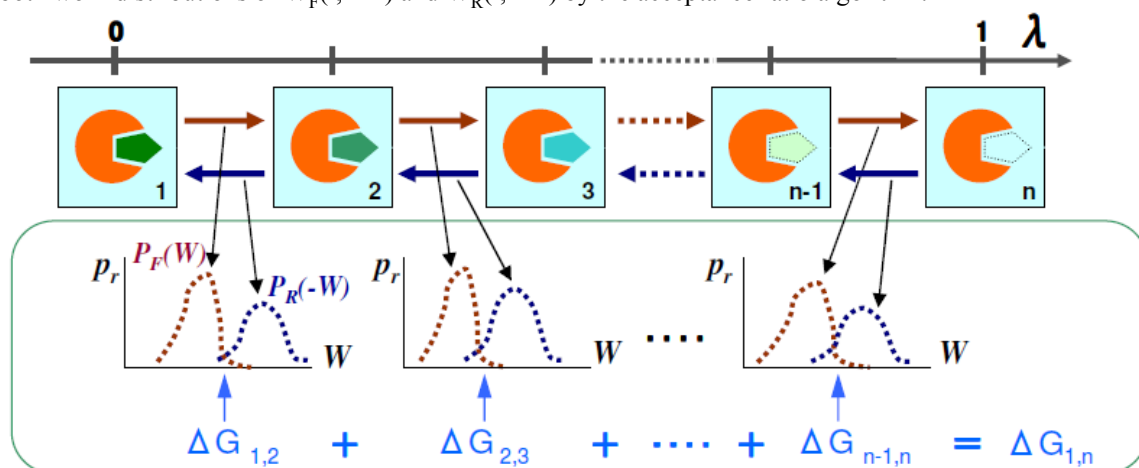
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Abstract

To accurately compute the free energy difference between two thermal equilibrium states is of interest in computational science and of importance in terms of drug discovery. It can help us obtain a quantitative understanding of molecular complexes from atomic-scale, and also provide valuable information for use in structural refinement for drug design. To discuss chemical reaction, we have to determine the free energy change within so-called chemical accuracy of about 1 kcal/mol, which is very challenging.

Method

A trajectory at each λ_i is obtained via the molecular dynamics simulation. The work on the forward path is obtained to compute the potential energy difference as $W_F(i, i+1) = U(\lambda_{i+1}, x_i) - U(\lambda_i, x_i)$. Using a trajectory at λ_{i+1} , the work on the reverse path is also obtained as $W_R(i, i+1) = U(\lambda_{i+1}, x_{i+1}) - U(\lambda_i, x_{i+1})$, while the free energy $\Delta G_{i,i+1}$ can be estimated using both work distributions of $W_F(i, i+1)$ and $W_R(i, i+1)$ by the acceptance ratio algorithm.

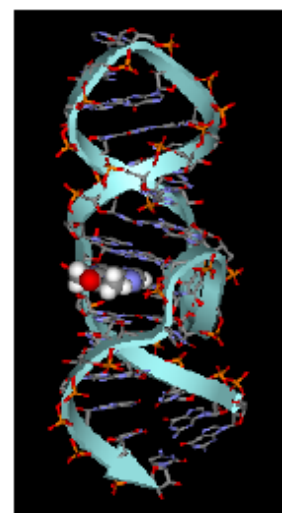
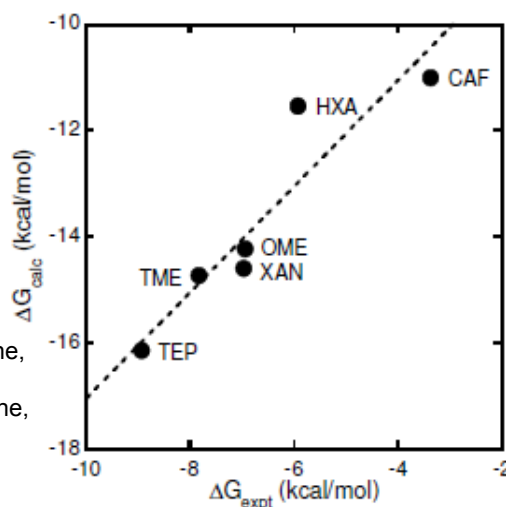


Example

Binding energies for RNA aptamer and ligands

Computed binding free energies ΔG_{calc} vs. measured binding free energies ΔG_{expt} for six ligands.

TEP: theophylline,
TME: 3-methylxanthine,
XAN: xanthine,
OME: 1-methylxanthine,
HXA: hypoxanthine,
CAF: caffeine.



Tanida, Ito, Fujitani, Chemical Physics 337, 135 (2007)