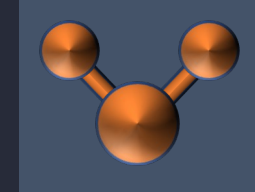


Advancing Chemical Potential Calculations of Polymers Introducing the Effect of Conformational Change



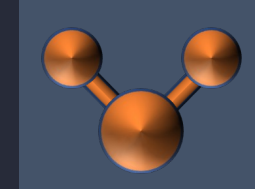
Stefan Hervø-Hansen, Nobuyuki Matubayasi

Graduate School of Engineering Science, Osaka University



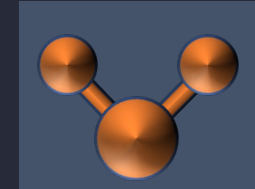
Background

Soft matter systems, like polymers and globular proteins, can be structurally altered by thermal, mechanical, or chemical stress. For instance, proteins typically form compact, folded structures under native conditions but unfold under stress. To describe the thermodynamics of these transformations, obtaining knowledge about the excess chemical potential is essential. We previously developed a methodology to calculate changes in the excess chemical potential due to alterations in liquid composition for various molecular states. However, this method is a linear approximation and does not account for structural transitions induced by changes in solvent composition, which appears as higher-order terms and can be important when the solvent composition is changed much.



Objective

Here we introduce our latest computation scheme for the calculation of the change in free energy of flexible polymers being transferred between solvent compositions formulated through error minimization. The methodology has been applied to describe the solvation of polyethylene glycol (PEG) in aqueous mixtures of urea and NaCl.



Formulation of New BAR-Like Method for Assessing Free Energy Changes Across Solvent Conditions

Usual BAR

\mathbf{X} : system configuration

$U_A(\mathbf{X}), U_B(\mathbf{X})$: potential energies at states A, B

$$\Delta U(\mathbf{X}) = U_B(\mathbf{X}) - U_A(\mathbf{X})$$

$P_A(\mathbf{X}), P_B(\mathbf{X})$: distribution functions of \mathbf{X}

ΔG : free energy change from A to B
identity connecting P_A and P_B

$$P_B(\mathbf{X}) = P_A(\mathbf{X}) e^{\beta(\Delta G - \Delta U(\mathbf{X}))}$$

Fermi function

$$\mathcal{F}(x) = \frac{1}{1 + \exp(\beta x)}$$

Error minimization for ΔG

$$\sum_{\mathbf{X} \in A} \mathcal{F}(\Delta U(\mathbf{X}) - D) = \sum_{\mathbf{X} \in B} \mathcal{F}(-\Delta U(\mathbf{X}) + D)$$

"Solute-Only" BAR

NEW

ψ : solute configuration

$v_A^{\text{solv}}(\psi), v_B^{\text{solv}}(\psi)$: solvation free energies in solvent conditions A, B

$$\Delta v^{\text{solv}}(\psi) = v_B^{\text{solv}}(\psi) - v_A^{\text{solv}}(\psi)$$

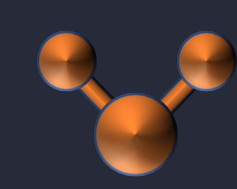
$P_A(\psi), P_B(\psi)$: distribution functions of ψ

$$P_B(\psi) = P_A(\psi) e^{\beta(\Delta G - \Delta v^{\text{solv}}(\psi))}$$

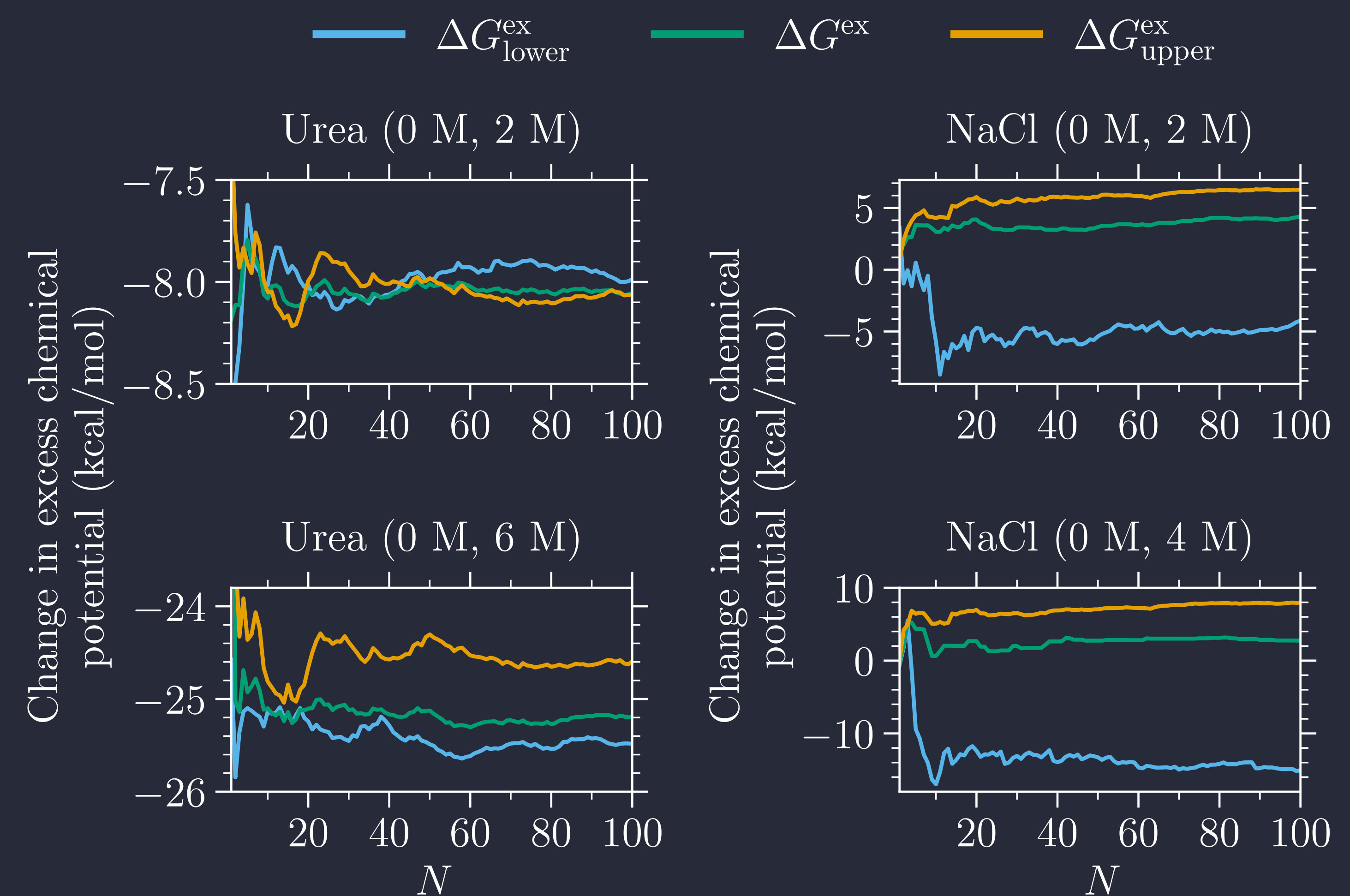
N_A, N_B : number of samples in A, B

$$D = \Delta G + \beta^{-1} \ln \frac{N_B}{N_A}$$

$$\sum_{\psi \in A} \mathcal{F}(\Delta v^{\text{solv}}(\psi) - D) = \sum_{\psi \in B} \mathcal{F}(-\Delta v^{\text{solv}}(\psi) + D)$$



Convergence of the "Solute-only BAR" Method and Establishing an Upper and Lower Limit of ΔG

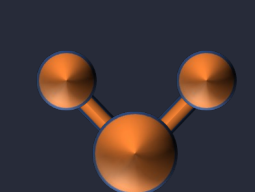


$$\Delta G = \int P_A(\psi) \Delta v^{\text{solv}}(\psi) d\psi + \beta^{-1} \int P_A(\psi) \ln \frac{P_B(\psi)}{P_A(\psi)} d\psi$$

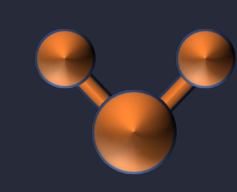
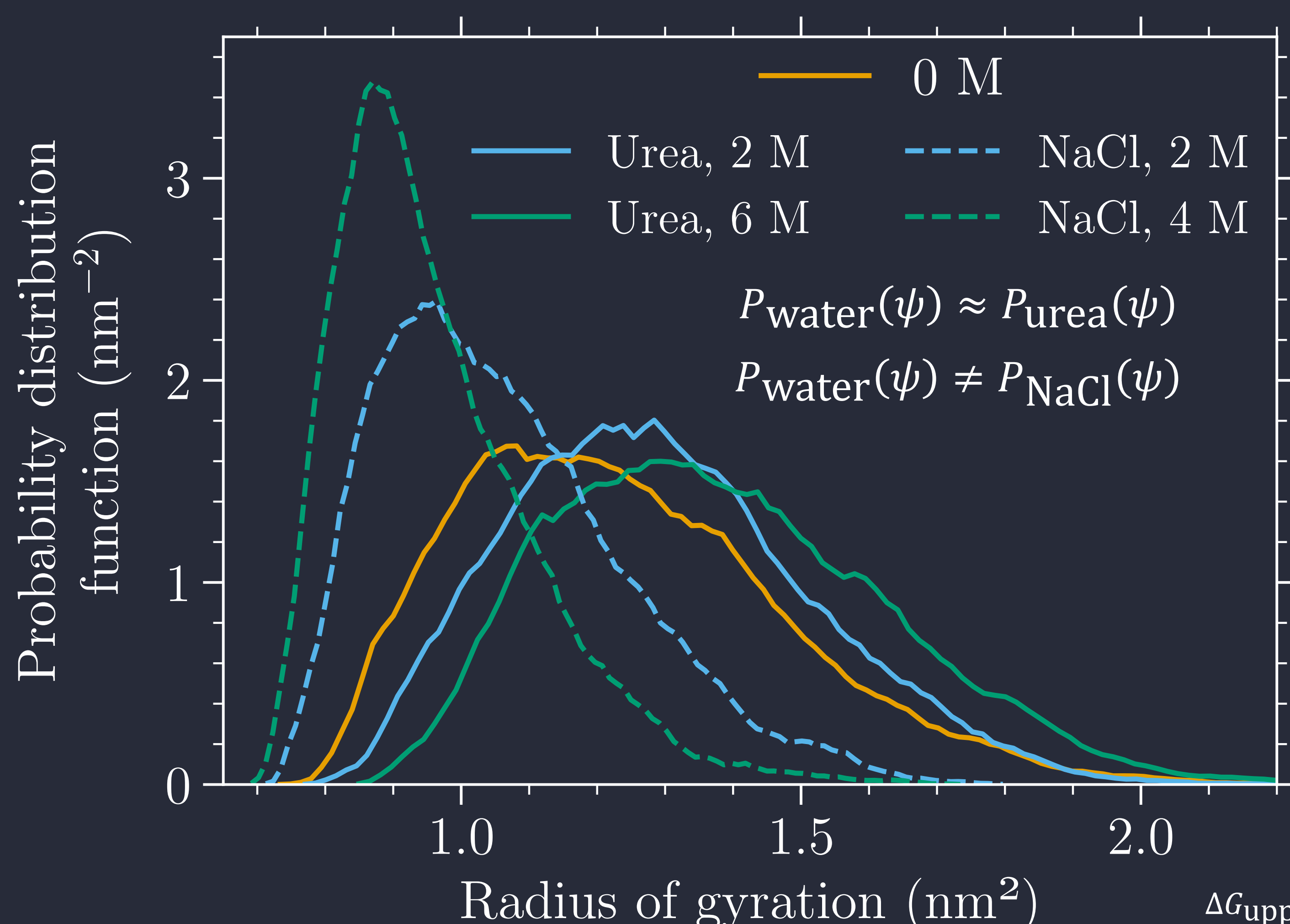
$$= \int P_B(\psi) \Delta v^{\text{solv}}(\psi) d\psi + \beta^{-1} \int P_B(\psi) \ln \frac{P_B(\psi)}{P_A(\psi)} d\psi$$

Establish exact lower and upper bounds

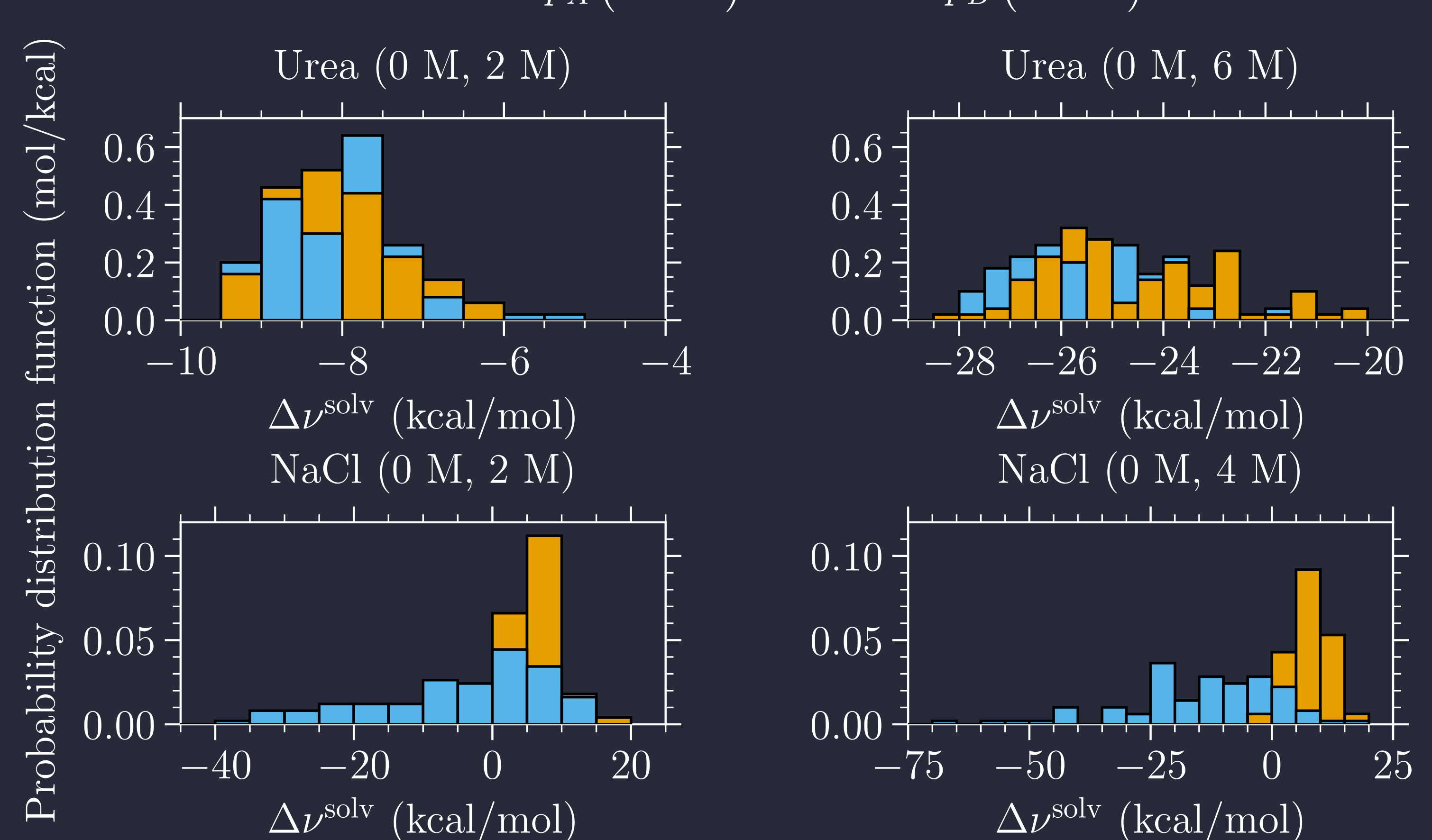
$$\int P_B(\psi) \Delta v^{\text{solv}}(\psi) d\psi \leq \Delta G \leq \int P_A(\psi) \Delta v^{\text{solv}}(\psi) d\psi$$



PEG Conformational Ensemble is Invariant with Urea, but Structure is Collapsed with the Addition of NaCl



Relative Entropy is the Statistical Thermodynamic Origin of the Inequality of the Lower and Upper Limits



$$\Delta G_{\text{upper}} + \beta^{-1} \int p_A(\Delta v^{\text{solv}}) \ln \frac{p_B(\Delta v^{\text{solv}})}{p_A(\Delta v^{\text{solv}})} d(\Delta v^{\text{solv}}) = \Delta G = \Delta G_{\text{lower}} + \beta^{-1} \int p_B(\Delta v^{\text{solv}}) \ln \frac{p_B(\Delta v^{\text{solv}})}{p_A(\Delta v^{\text{solv}})} d(\Delta v^{\text{solv}})$$