Implicit Solvent Parametrisation by Force Matching

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Introduction

Molecular dynamics simulations of biomolecules are routinely performed in a water box with periodic boundary conditions. While the explicit representation of water molecules provides a high level of detail in regard to solute-solvent interactions, treating their degrees of freedom becomes gradually prohibitive with increasing system size. For systems whose detailed water interactions are not relevant to the properties under study, implicit solvation is a suitable method to represent the solvent-solute interactions [1, 4].

SASA Model

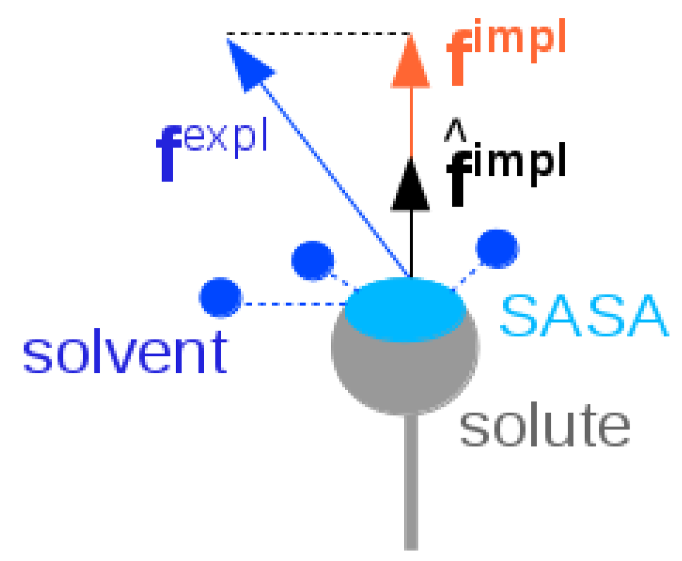
The interaction potential V^{impl} between the solvent and all solute atoms i can be assumed to be proportional to its solvent accessible surface area (SASA) [3], scaled by an atom-specific energy term σ_i^{SASA}:

$$V^{impl}(\mathbf{r}^N) = \sum_{i=1}^{N} \sigma_i^{SASA} A_i(\mathbf{r}^N) . \qquad (1)$$

The implicit solvent forces per atom are obtained from the derivative of the above equation with respect to r_i:

$$\mathbf{f}_i^{impl} = -\sigma_i^{SASA} \frac{\partial A_i(\mathbf{r}^N)}{\partial \mathbf{r}_i} . \qquad (2)$$

Force Matching



$$\left|\mathbf{f}_i^{impl}\right| = \hat{\mathbf{f}}_i^{impl} \cdot < \mathbf{f}_i^{expl} > \qquad (3)$$

$$\sigma_i^{SASA} = -\frac{\frac{\partial A_i}{\partial \mathbf{r}_i}}{\left|\frac{\partial A_i}{\partial \mathbf{r}_i}\right|^2} \cdot < \mathbf{f}_i^{expl} > \qquad (4)$$

Fig. 1 : Force matching: Explicit solvent forces (blue arrow) exerted on the solute are projected on the normal of its SASA (black arrow), yielding the implicit solvent force (orange arrow).

Eq. for Fig. 1 : Using the concept of force projection shown left, the expression for σ_i^{SASA} combines the observed forces in explicit solvent with the derivative of the atomic SASA.

σ_i^{SASA} Parameters

Using the solvation forces of 188 topologically diverse proteins in explicit and implicit solvent, a robust set of σ_i^{SASA} parameters was derived by force matching [2, 5]. Hydrophilic N and O atoms adopt negative σ_i^{SASA} parameters, those of hydrophobic C atoms are positive.

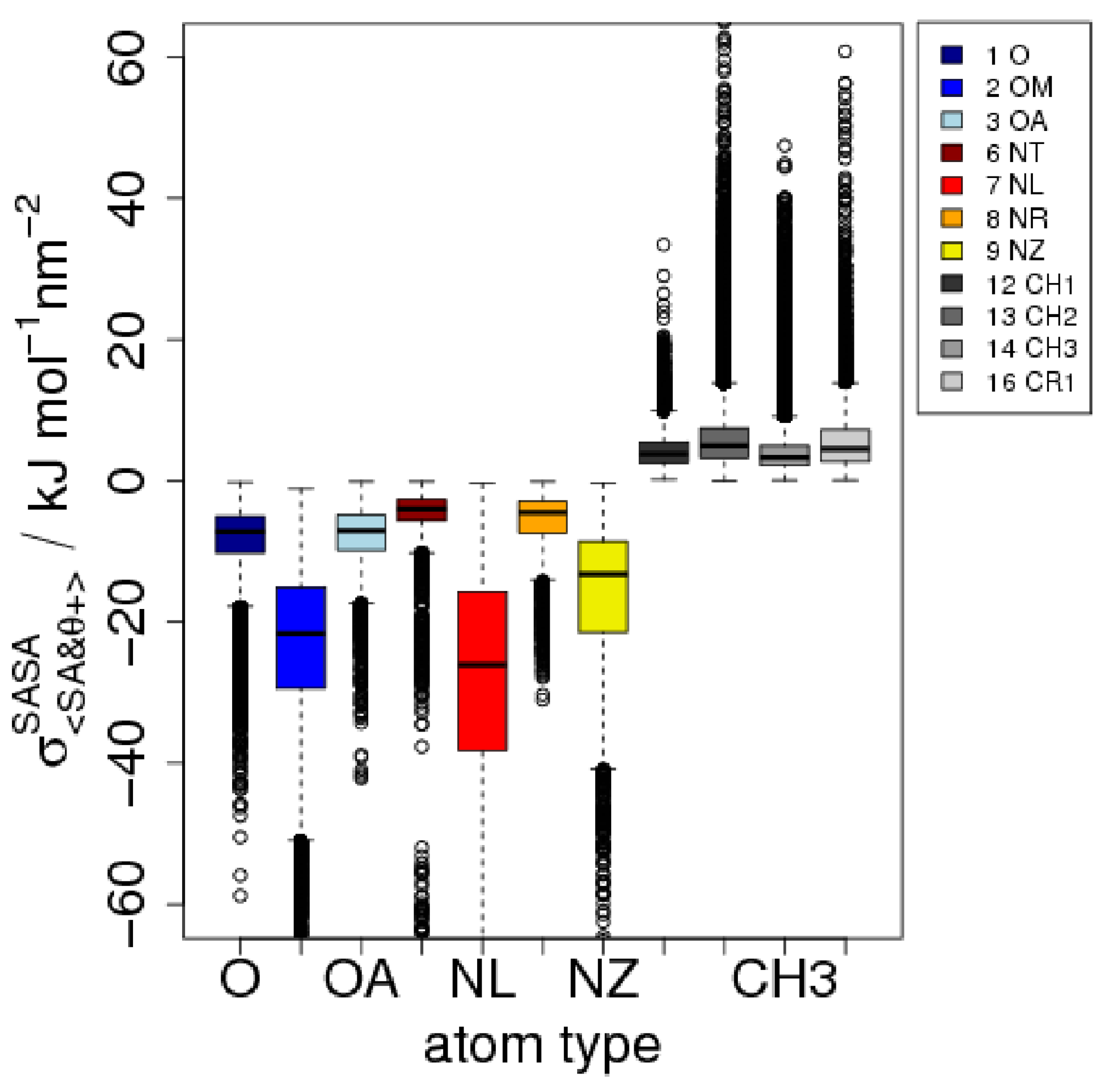


Fig. 2 : σ_i^{SASA} parameters derived by force matching.

Friction Model

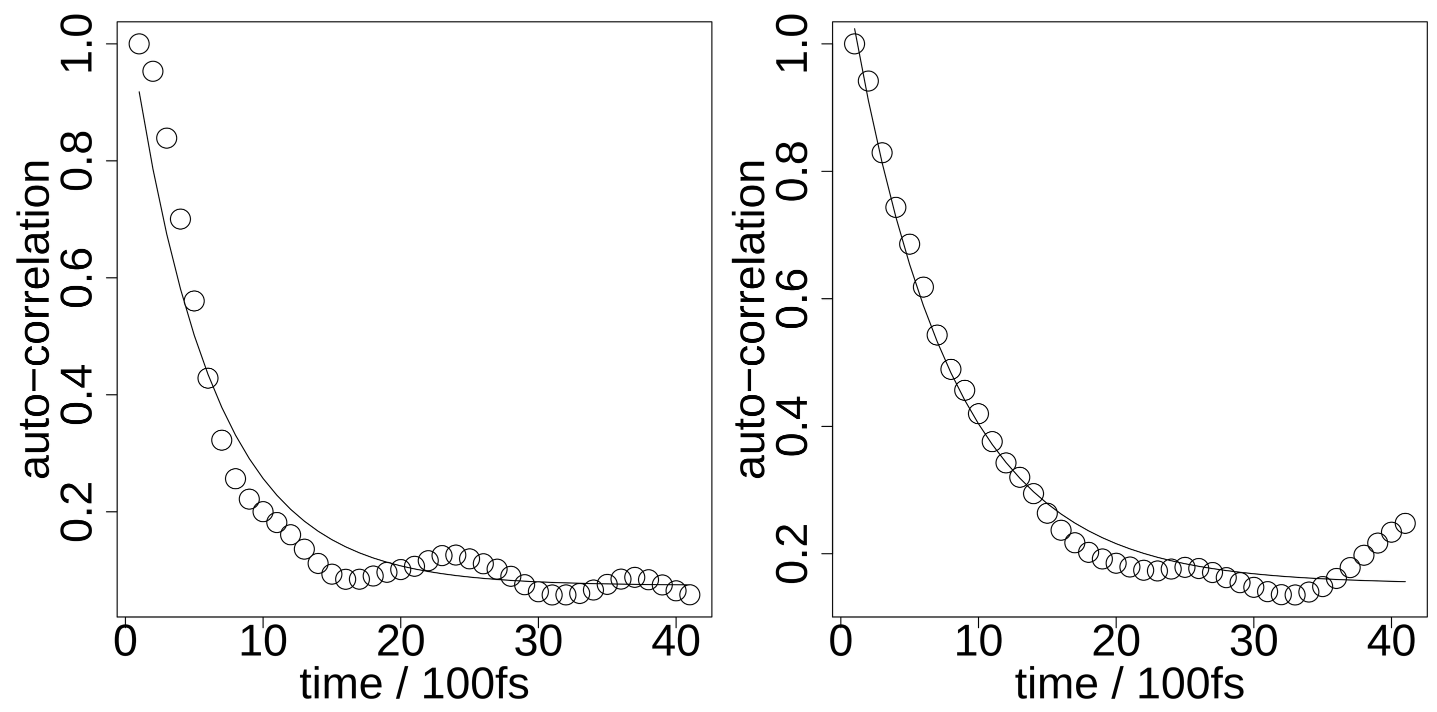
Forces occurring in molecular dynamics fluctuate over time, yielding charcteristic force distributions. While the σ_i^{SASA} term models the mean force between solute and solvent, the variance of the force distributions are coupled to the friction parameter γ_i:

$$\left\langle (\mathbf{f}_i^{stoch})^2 \right\rangle \tau^{solv} = 6\, m_i\, \gamma_i\, k_B\, T . \qquad (5)$$

Here, $\left\langle (\mathbf{f}_i^{stoch})^2 \right\rangle$ is the mean correlation of the friction force and τ^{solv} is the autocorrelation time of the solvent friction. Using the fractional solvent accessibility ω_i as scaling factor, we can derive the atom-specific friction parameter γ_i^0:

$$\gamma_i^0 = \frac{\tau^{solv}}{6\, k_B\, T} \cdot \frac{\left\langle (\mathbf{f}_i^{stoch}(t) - < \mathbf{f}_i^{stoch} >)^2 \right\rangle}{m_i} \cdot \frac{1}{\omega_i(t)} . \qquad (6)$$

Autocorrelation



(a) d1luqa_ Gly1 CA

(b) d1luqa_ Asn34 ND2

Fig. 3 : Exemplary exponential fits (solid line) of the auto-correlation function (circles) of the solvation forces on atoms C, N, O and S. The unit lag of the auto-correlation functions corresponds to 100 fs of simulated time.

γ_i^0 Parameters

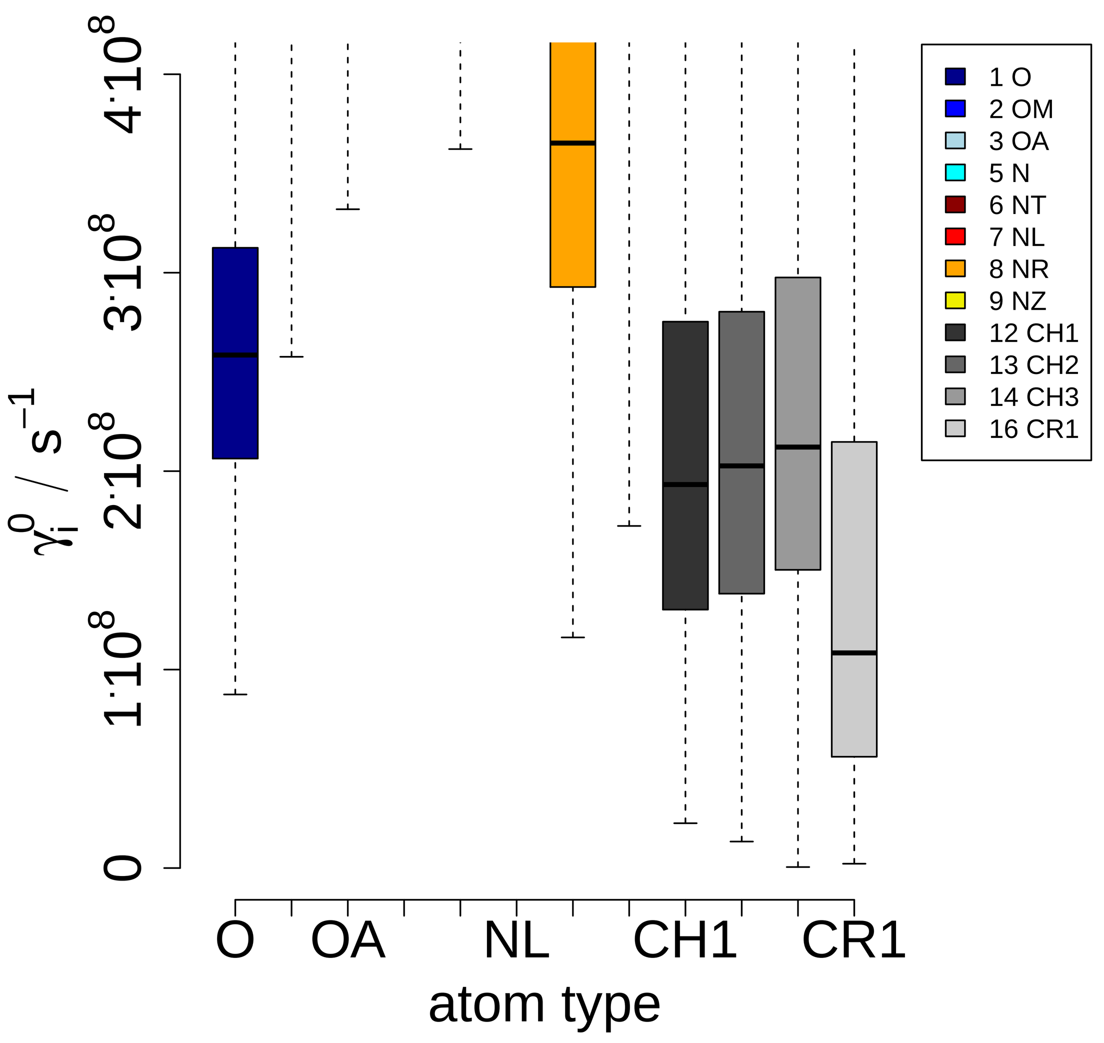


Fig. 4 : Boxplot of distributions of γ_i^0 parameters.

References

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