A new Tabu-Search based algorithm for solvation of proteins

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Supporting Information

Further Theoretical Details

Dimer method:

The initial dimer is obtained by distorting the starting structure in dihedral space (equation (1)). Φ_{dih0i} and Φ_{dih1i} denote the i-th dihedral angle of the starting point and endpoint, respectively. τ is a unified random vector at the beginning, and is set to the dimer distance later on (equation (2)).

$$\Phi_{dih1i} = \Phi_{dih0i} + \hat{\tau}_i \cdot 5° \tag{1}$$

$$\vec{\tau} = \frac{(\vec{x}_0 - \vec{x}_1)}{2} \ , \ \hat{\tau} = \frac{\vec{\tau}}{|\tau|} \tag{2}$$

The rotational force F_R acting on the dimer is given by equation (3). The rotational step involves the determination of a step size in an optimization algorithm. The adaption to Tabu-Search employs either a Steepest Descent or Conjugate Gradient step. The curvature is given in equation (4), where Δ is the distance of the two end points of the dimer.

$$F_R = -2(g_1 - g_0) + 2[(g_1 - g_0)\cdot\hat{\tau}]\hat{\tau} \tag{3}$$

$$C_\tau = \frac{(g_1 - g_0)\cdot\hat{\tau}}{\Delta} \tag{4}$$

By definition, the dimer lies in the plane spanned by the two vectors τ and Θ. The gradients at the endpoints, the rotational force, and the curvature as well as its derivatives are used to calculate an estimated rotational angle φ_1 and a minimal angle φ_{min}. The rotations about φ_1 and φ_{min} are done alternately until a predefined maximum number of rotations is reached or the rotational angle is smaller than a given threshold (for an illustration see Figure 1).

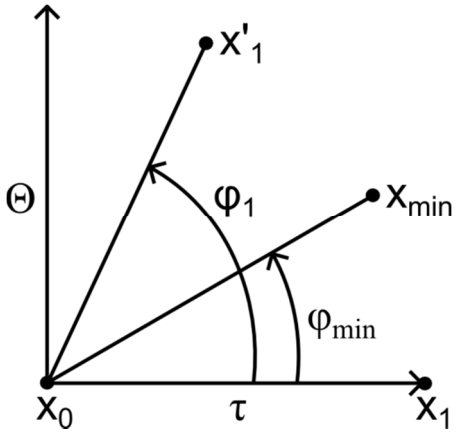


Figure 1 Illustration of the two-step rotation during the first part of the Dimer method (see text).

When the rotational step is converged, the dimer is translated along the translational force. The new dihedral angles of the next starting point are obtained from equation (5).

$$\phi_{dih0} = \phi_{dih1} + \Delta_{trans} \cdot F_T \tag{5}$$

The translational force F_T is given by equation (6) and the translational step by equation (7).

$$\begin{aligned} C_\tau \le 0 &: F_T = -g_0 + 2(g_0 \cdot \hat{\tau})\hat{\tau} \\ C_\tau > 0 &: F_T = -(g_0 \cdot \hat{\tau})\hat{\tau} \end{aligned} \tag{6}$$

$$\Delta_{trans} = \frac{-g_0 \cdot 2}{|F_T|} \tag{7}$$

The rotational and translational steps are iterated until the energy of the dimer end point is lower than the energy of the dimer starting point.

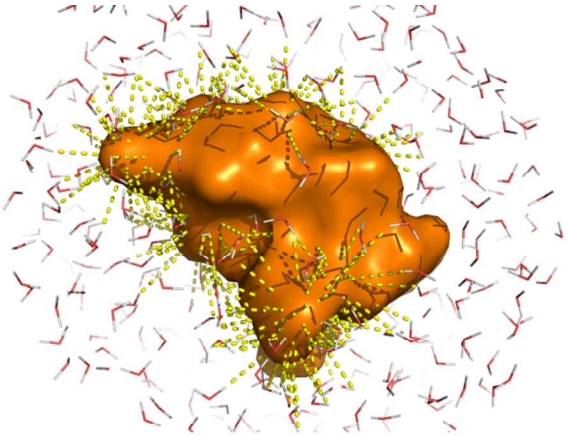
VegaZZ:

The solvation was done with VegaZZ using the Edit→Add→Cluster tool with an increasing solvation radius. This feature is explained in the manual of VegaZZ (chapter 6.10 “Add a solvent cluster”) accessible from: http://nova.colombo58.unimi.it/manual/pages/gl_index.htm .

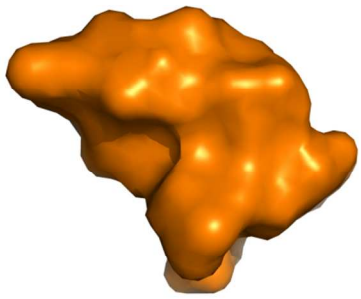
We used the cluster files provided by the VegaZZ program, selected “Sphere” for solvation, and placed a solvent sphere around the geometric center of the solute. This was done for each solvation step taking the best result of the previous step as input structure.

Tabu criteria:

The Tabu criteria were applied in internal dihedral coordinates. Structures were compared due to their dihedral angles and were assigned as Tabu if the dihedral angles were the same within 5°. Furthermore, total energy values were taken as Tabu criteria.

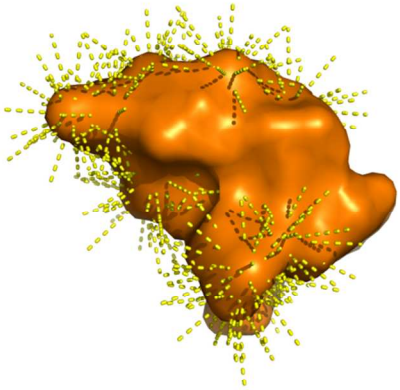


a) TOT: complete system

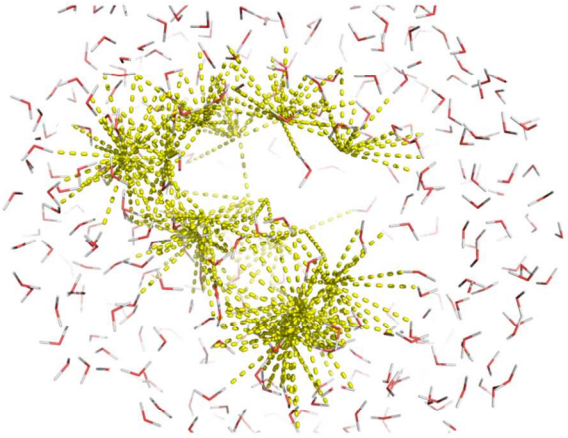


b) ENZ: only enzyme

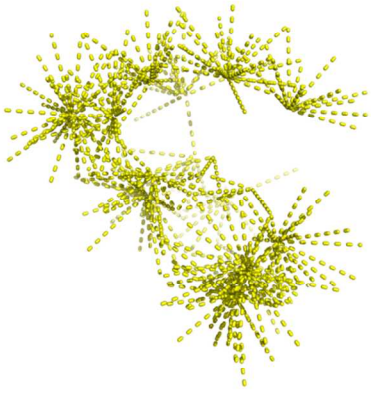
c) WAT: only water



d) TOT-WAT: enzyme + stabilization from water



e) TOT-ENZ: water + stabilization from enzyme



f) TOT-ENZ-WAT: stabilization energy

Figure 2 Illustration of the subsystems and difference systems used for the calculation of the energies shown in Table 3 of main document.

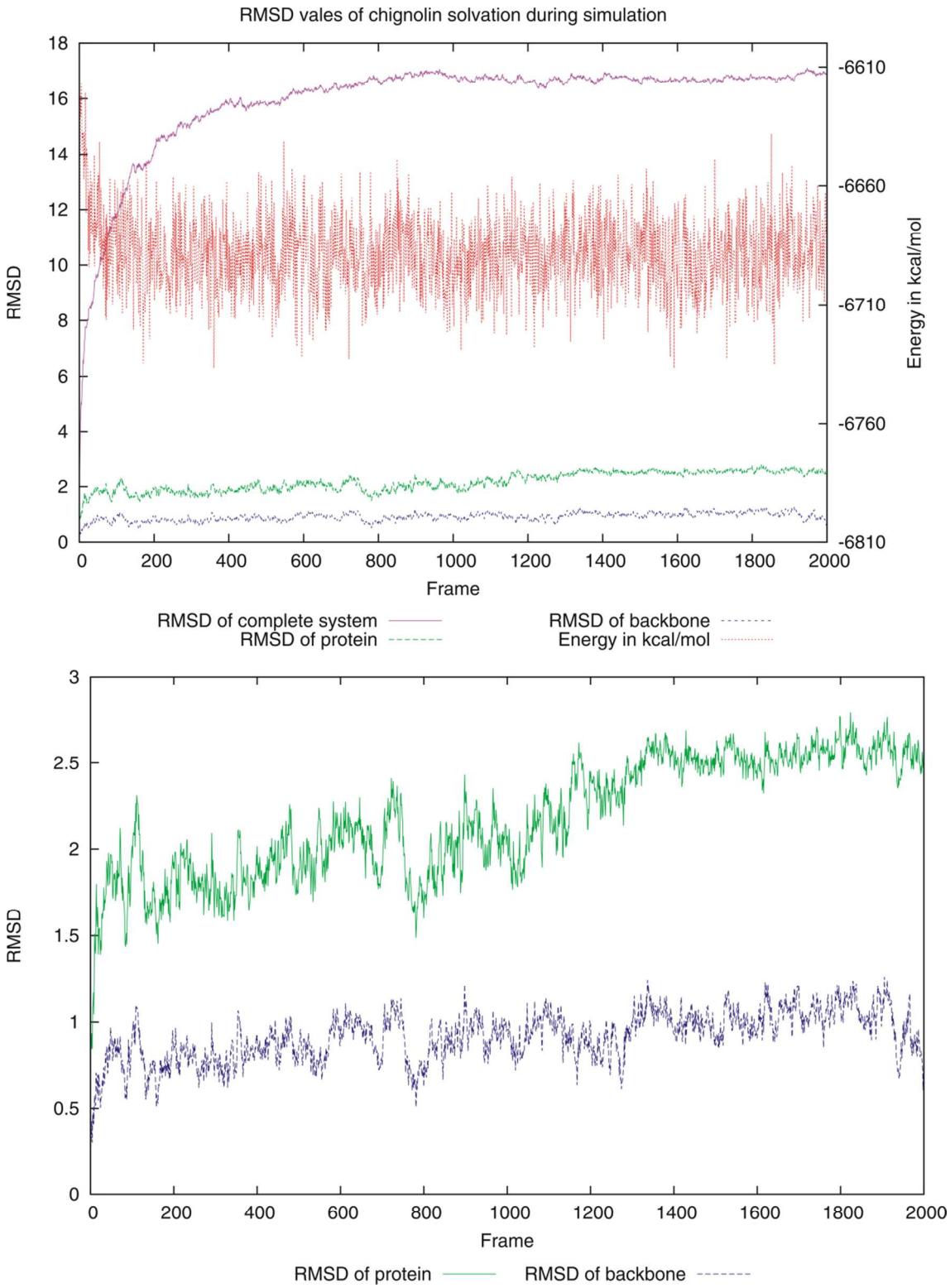


Figure 3 RMSD values (relative to the NMR structure) of the MD free approach; Red: absolute energy in kcal/mol, Blue: RMSD value of backbone, Green: RMSD value of the protein, Violet: RMSD value of the complete system.

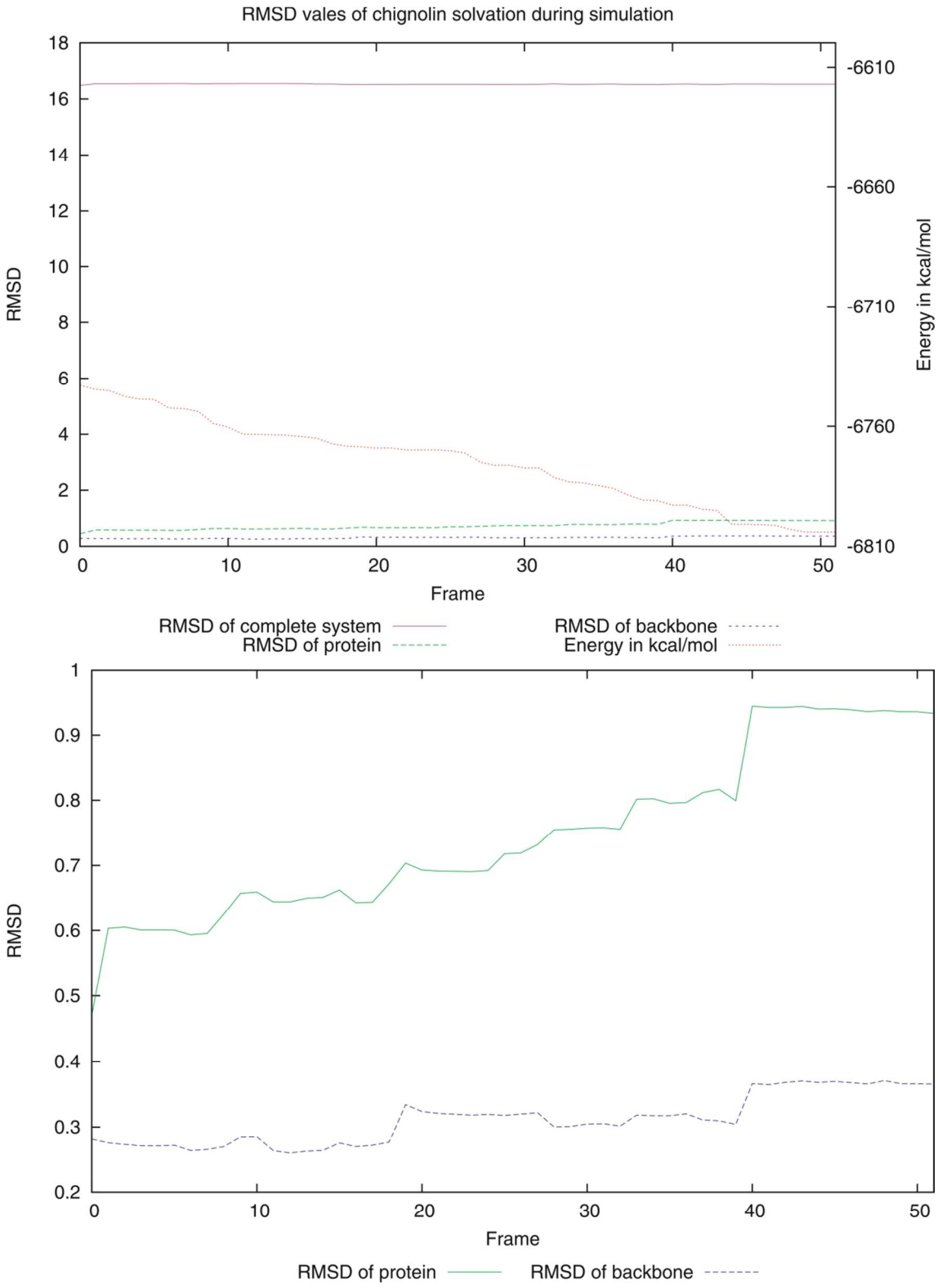


Figure 4 RMSD values (relative to the NMR structure) for the Tabu-Search fixed approach. The figure shows the final global optimization run. For more information see Figure 3.

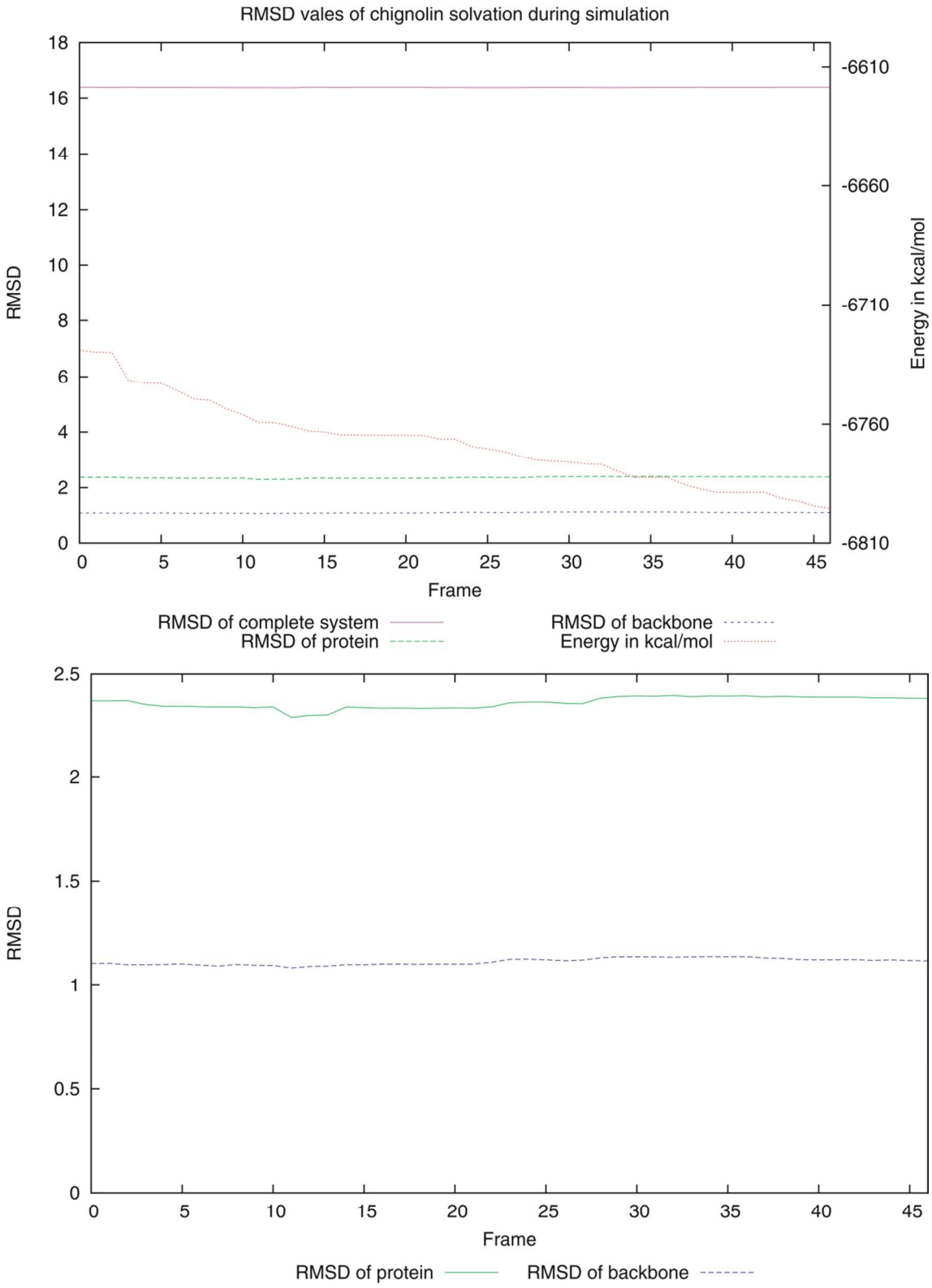


Figure 5 RMSD values (relative to the NMR structure) for the Tabu-Search free procedure. For more details see Figure 3.

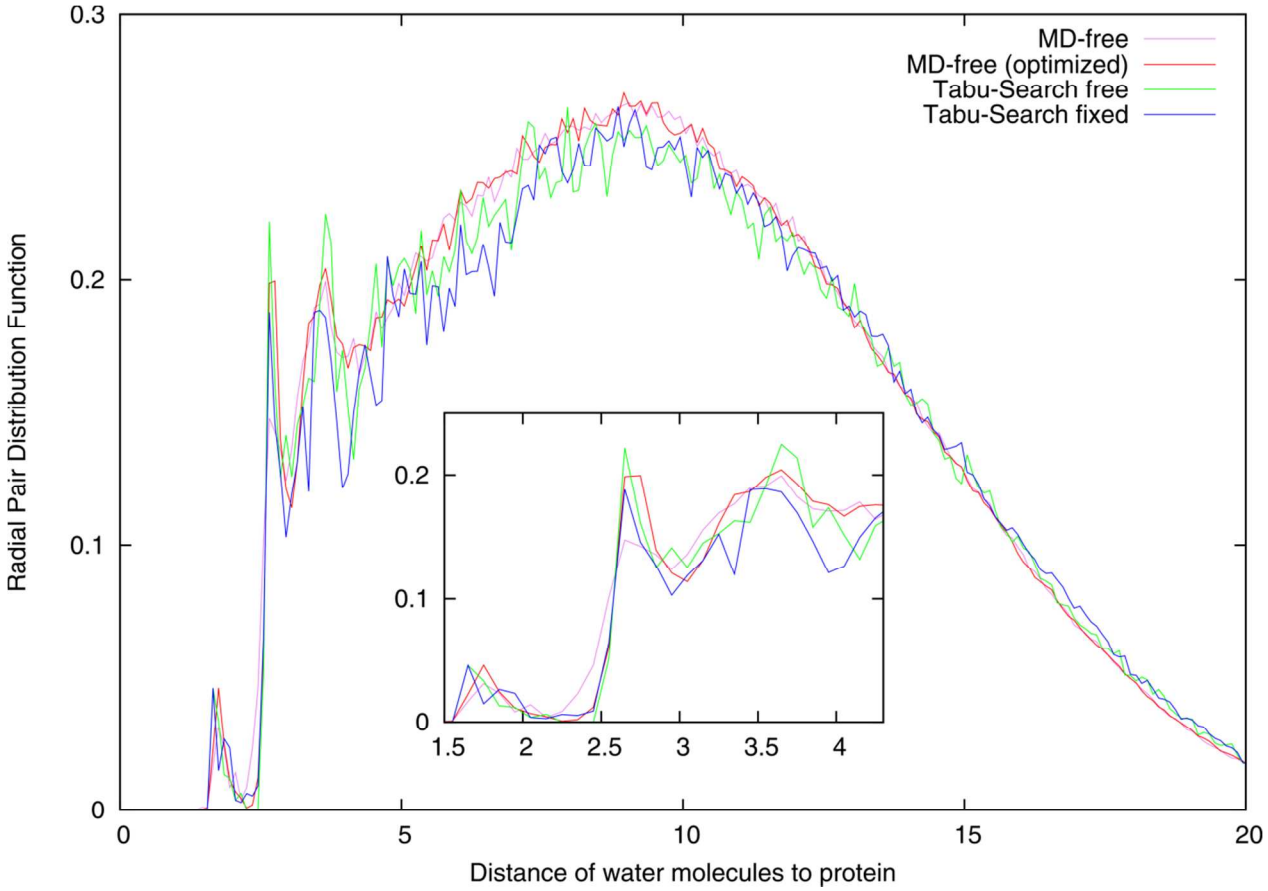


Figure 6 Radial pair distribution function (radial PDF) of water molecules around the chignolin protein. Radial pair distribution function (radial PDF) of water molecules around the chignolin protein. The 20 lowest structures of each simulation were included in the calculation of the radial PDF. The radial PDF was calculated with the corresponding tool implemented in VMD.[1]

References:

(1) Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* 1996, *14*, 33-38.