Supporting information for: Spatial decomposition of solvation free energy based on the 3D integral equation theory of molecular liquid: Application to miniproteins

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Root mean square deviation of peptide backbones

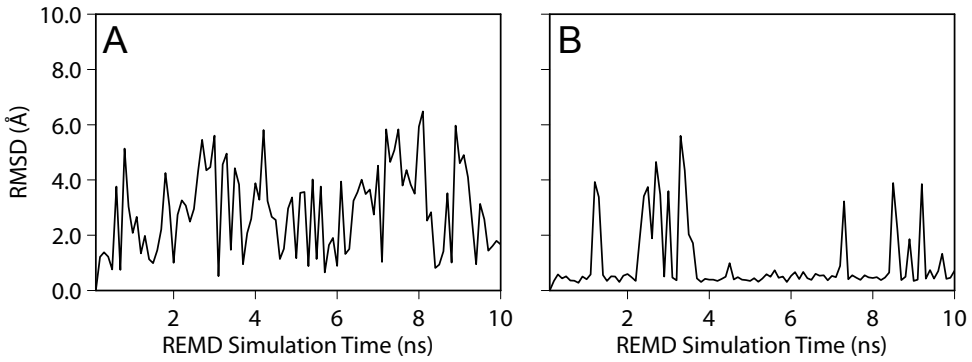

Figure S1: Root mean square deviation of the peptide backbone (backbone alpha and carbonyl carbon and nitrogen atoms) as a function of simulation time at 25 °C for Chignolin (left panel) and CLN025 (right panel).

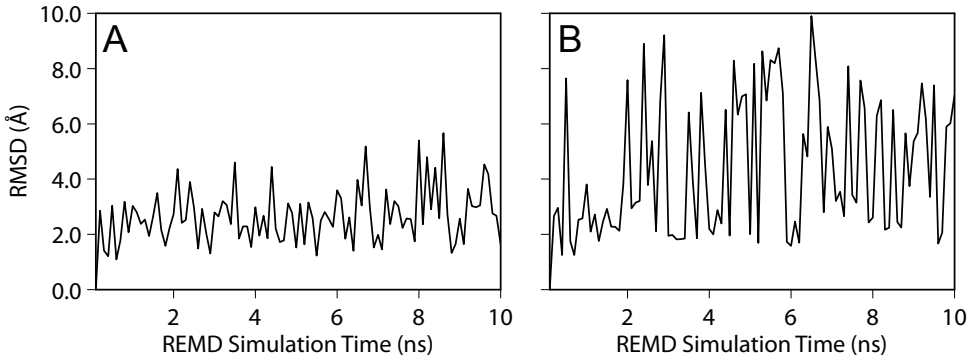

Figure S2: Root mean square deviation of the peptide backbone (backbone alpha and carbonyl carbon and nitrogen atoms) as a function of simulation time at 25 °C for Trp-cage (left panel) and FSD-1 (right panel).

Hydrogen bond analysis in the sampled conformations of Trp-cage

In order to figure out how many percentage of the sampled conformations are the conformations that have the hydrogen-bonds involving the R16 residue, the REMD trajectory at 25 °C was processed by the ptraj module in Amber 10[1] to search the atomic sites as a counterpart of hydrogen

bond with the NE, NH1, and NH2 atoms of R16 residue. The labeling for the atomic sites is presented in Figure S3. The hydrogen-bond pairs observed in the trajectory are summarized in Table S1.

Table S1

R16@NE	–	D9@OD1
	–	D9@OD2
	–	G11@O
	–	S14@OG
R16@NH1	–	D9@O
	–	D9@OD1
	–	D9@OD2
	–	G10@O
	–	S14@OG
R16@NH2	–	D9@O
	–	D9@OD1
	–	D9@OD2
	–	G10@O
	–	S14@OG

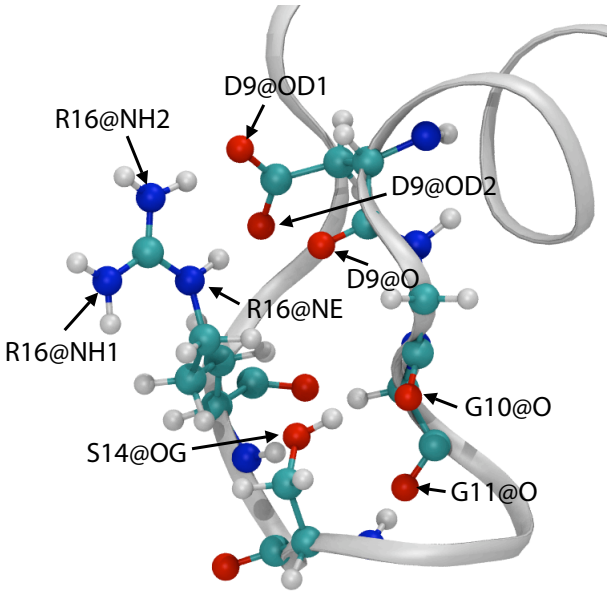

Figure S3: Labeling for the atomic sites of R16 residue and its counterparts of hydrogen-bond observed in the trajectory of Trp-cage protein.

The following figures represents the distances between the NE, NH1, or NH2 atoms of R16

residue and their counterpart of hydrogen bond observed in the trajectory, as a function of the REMD simulation time, and the histogram for the minimal distance of those pairs at each snapshot. For example, Figure S4 A shows the distances between the NE atom of R16 residue and the D9 (OD1 and OD2 atoms), G11 (O atom), and S14 (OG atom) residues. Figure S4 B represents the histogram for the minimal distance of the pairs at each snapshot. The solid line in Figure S4 B indicates the cumulative curve of the histogram. We considered the distance up to the minimal distance of 3.0 Å as a criterion for a possible hydrogen bond.

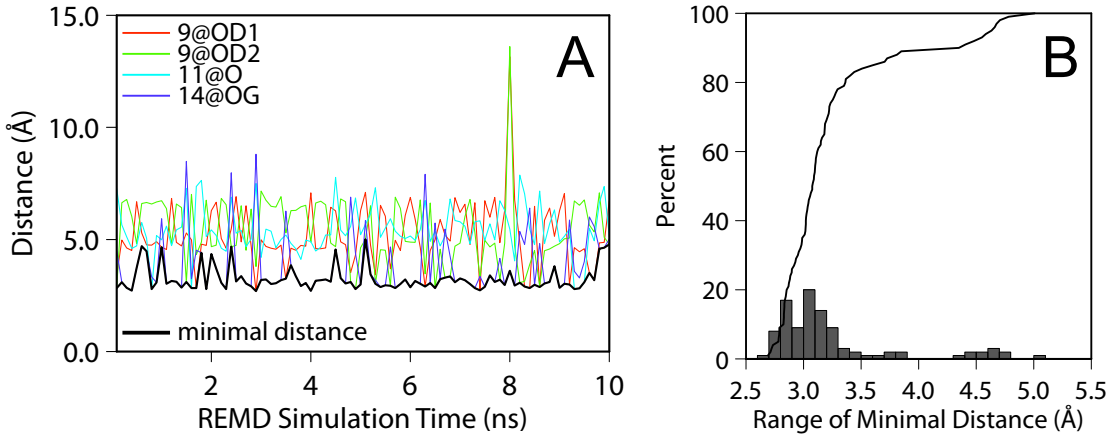

Figure S4: Part (A) shows the distance between the NE atom of R16 residue and its counterparts of hydrogen bond. Part (B) shows the histogram for the minimal distance of the pairs at each snapshot. The solid line in part (B) indicates the cumulative curve of the histogram. In 35% of the sampled conformations, the NE atom is possibly forming hydrogen bonds.

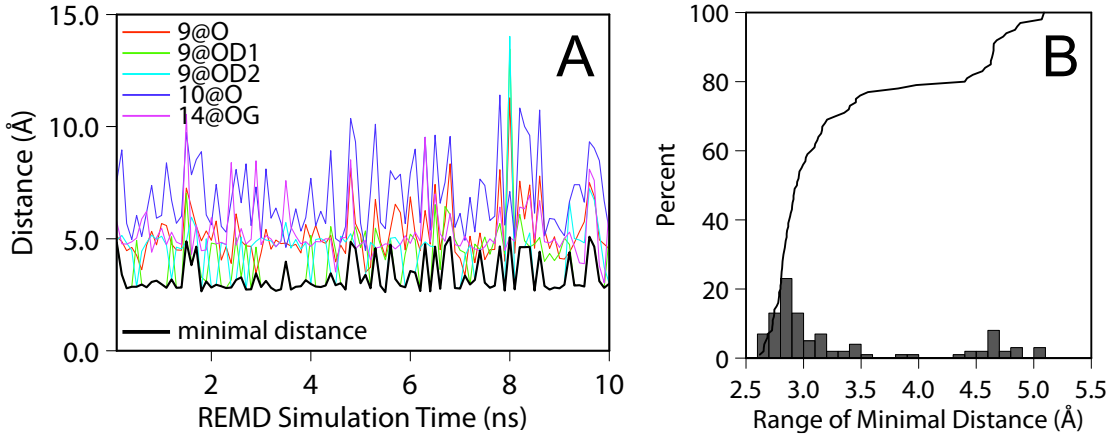

Figure S5: Same as Figure S4 but for the NH1 atom of R16 residue. In 56% of the sampled conformations, the NH1 atom is possibly forming hydrogen bonds.

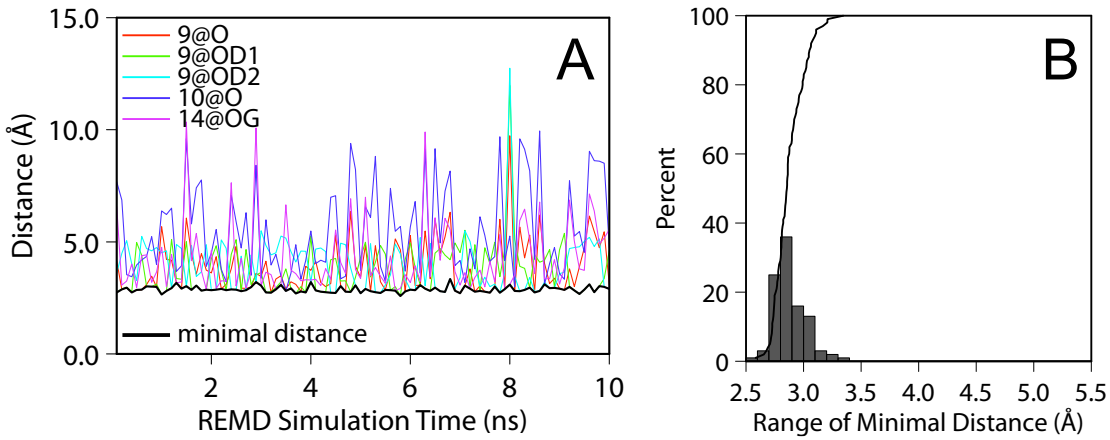

Figure S6: Same as Figure S4 but for the NH2 atom of R16 residue. In 81% of the sampled conformations, the NH2 atom is possibly forming hydrogen bonds.

Hydrogen bond analysis in the sampled conformations of FSD-1

Analysis similar to in the case of Trp-cage described above was carried out for the OE1 and OE2 atoms of E17 residue in FSD-1 protein. The labeling for the atomic sites is presented in Figure S7. Hydrogen bond pairs observed in the trajectory are summarized in Table S2. The distances between the hydrogen bond pairs and the histogram for the minimal distance are presented in Figure S8 and Figure S9.

Table S2

E17@OE1	–	R10@NH1
	–	R10@NH2
	–	R13@N
	–	R13@NE
	–	R13@NH1
	–	R13@NH2
E17@OE2	–	R10@NH1
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	–	R13@NE
	–	R13@NH1
	–	R13@NH2

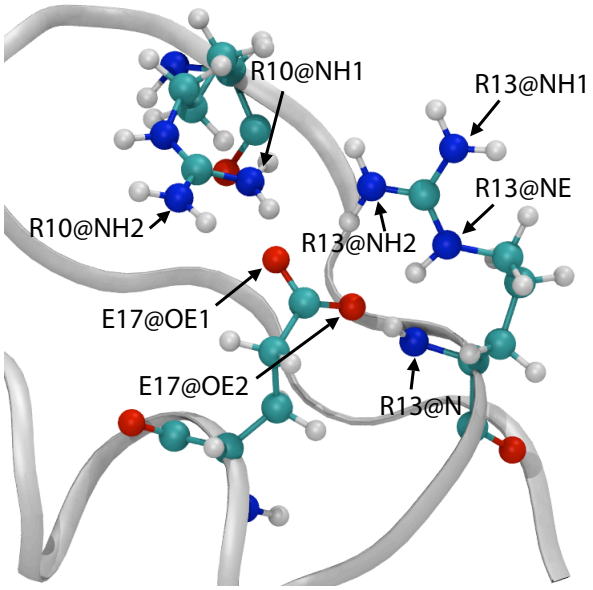

Figure S7: Labeling for the atomic sites of E17 residue and its counterparts of hydrogen-bond observed in the trajectory of FSD-1 protein.

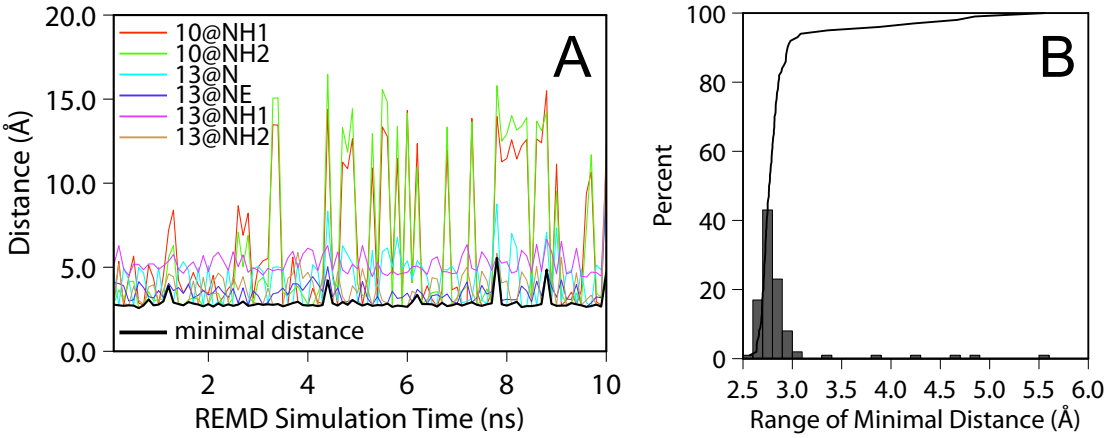

Figure S8: Same as Figure S4 but for the OE1 atom of E17 residue in FSD-1 protein. In 92% of the sampled conformations, the OE1 atom is possibly forming hydrogen bonds.

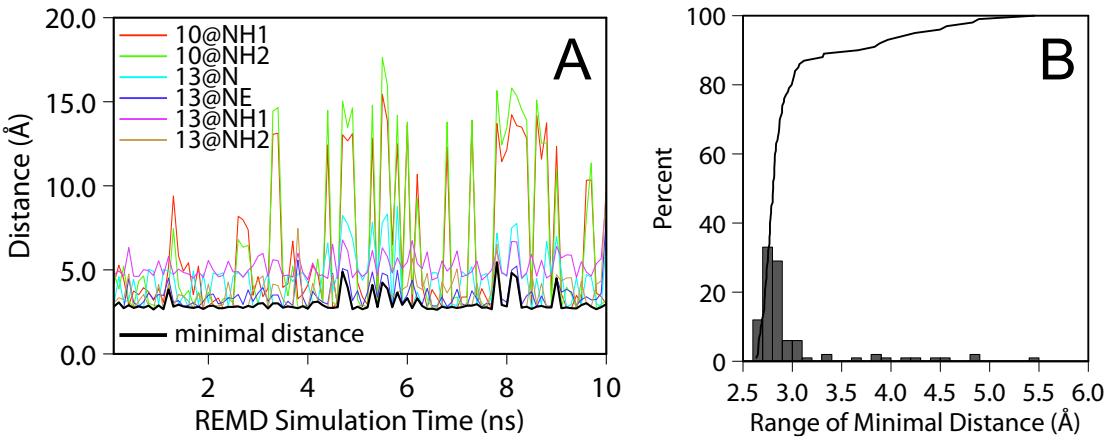

Figure S9: Same as Figure S4 but for the OE2 atom of E17 residue in FSD-1 protein. In 80% of the sampled conformations, the OE2 atom is possibly forming hydrogen bonds.

Hydrogen bond analysis in the sampled conformations of Trp-cage with the explicit water solvent

A similar analysis was carried out for the Trp-cage protein conformations sampled with the explicit water solvent model. The labeling for the atomic sites is the same as presented in Figure S3. Hydrogen bond pairs observed in the trajectory are summarized in Table S3. The distances between the hydrogen bond pairs and the histogram for the minimal distance are presented in Figure S10, Figure S11, and Figure S12.

Table S3

R16@NE	–	D9@OD1
	–	D9@OD2
R16@NH1	–	D9@OD1
	–	D9@OD2
R16@NH2	–	D9@OD1
	–	D9@OD2

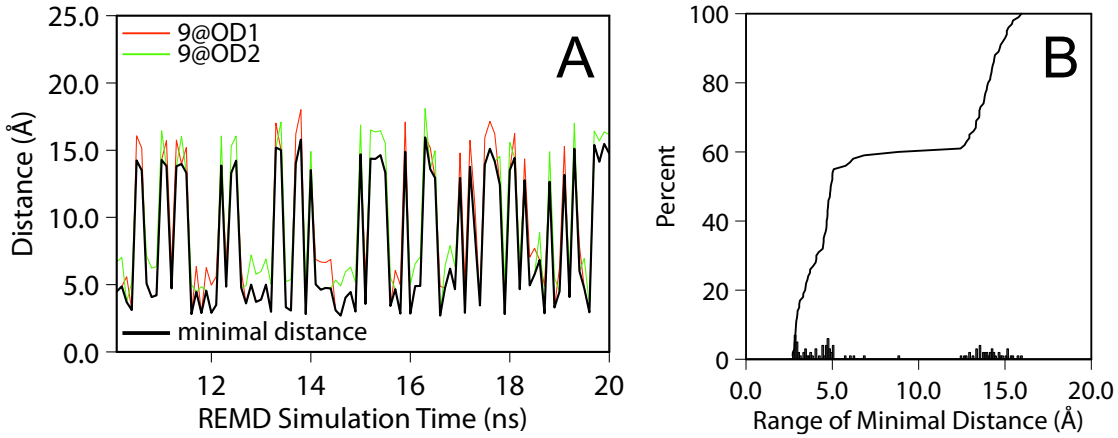

Figure S10: Same as Figure S4 but for the NE atom of R16 residue for the Trp-cage protein conformations sampled with the explicit water solvent model. In 14% of the sampled conformations, the NE atom is possibly forming hydrogen bonds.

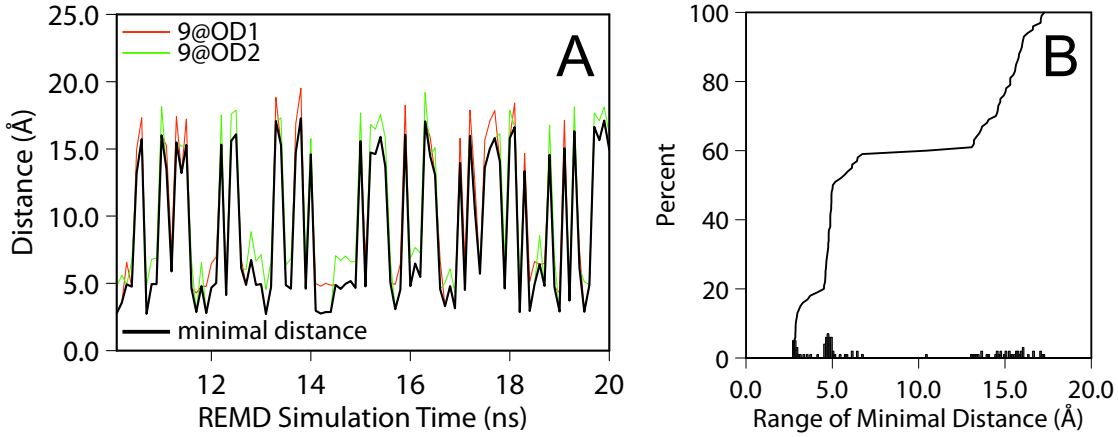

Figure S11: Same as Figure S4 but for the NH1 atom of R16 residue for the Trp-cage protein conformations sampled with the explicit water solvent model. In 13% of the sampled conformations, the NH1 atom is possibly forming hydrogen bonds.

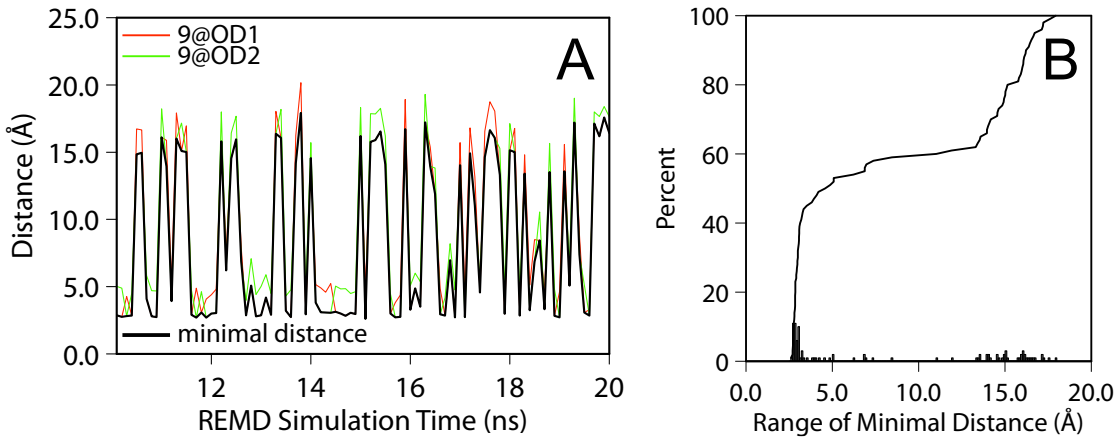

Figure S12: Same as Figure S4 but for the NH2 atom of R16 residue for the Trp-cage protein conformations sampled with the explicit water solvent model. In 29% of the sampled conformations, the NH2 atom is possibly forming hydrogen bonds.

Transfer solvation free energy of miniprotein from water to octanol by using the OPLS-UA force field

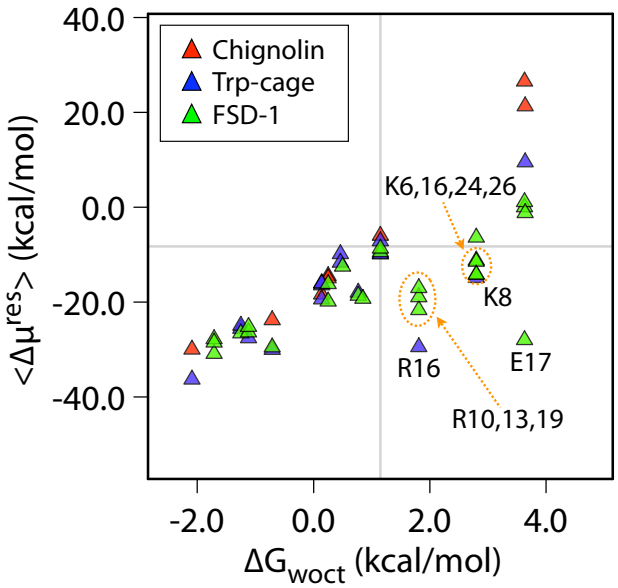

Figure S13: Same as Figure 6 in the manuscript but the octanol solvent was modeled by the OPLS-UA force field.

The correlation coefficients were calculated to be 0.98, 0.75, and 0.76 for Chignolin, Trp-cage,

and FSD-1, respectively. As can be seen from Figure S13, the charged residues (the upper triangles with indices) were estimated to prefer the transfer from water to octanol, which may be related to the assignment of the partial charges of octanol hydroxyl group. In the GROMOS96 45A3 force field, the partial charges are assigned as 0.150, -0.548, and 0.398 for the CH_2 next to the hydroxyl group, the hydroxyl oxygen, and the hydroxyl hydrogen groups. In the OPLS-UA force field, these are assigned as 0.265, -0.700, and 0.435, respectively.

References

(1) Case, D. A.; Darden, T. A.; Cheatham, T. E., III; Simmerling, C. L.; Wang, J.; Duke, R. E.; Luo, R.; Crowley, M.; Walker, R. C.; Zhang, W.; Merz, K. M.; Wang, B.; Hayik, S.; Roitberg, A.; Seabra, G.; Kolossváry, I.; Wong, K. F.; Paesani, F.; Vanicek, J.; Wu, X.; Brozell, S. R.; Steinbrecher, T.; Gohlke, H.; Yang, L.; Tan, C.; Mongan, J.; Hornak, V.; Cui, G.; Mathews, D. H.; Seetin, M. G.; Sagui, C.; Babin, V.; Kollman, P. A. *AMBER 10*; University of California, San Francisco, 2008.