Comparison of SASA calculated with LCPO vs Molsurf

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Test System

- Trpzip2 (PDB 1LE1)
- FF10, mbondi radii
- MD: GB HCT, Langevin Thermostat (gamma = 5 ps^{-1}), 999.0 Å cutoff, 1 fs timestep, SHAKE on hydrogens, no SASA term.
- Two runs, 1 ns at 300K and 400K
- All analysis (LCPO, Molsurf, RMSD) performed with Cpptraj. Molsurf probe radius 1.4 Å

Results

300 K

The SASA calculated with LCPO and molsurf methods for Trpzip2 at 300 K, as well as the correlation between the two methods is shown in Figure 1, left. During the simulation Trpzip2 stays quite close to the native conformation, as indicated by the low average backbone RMSD (0.52 +/- 0.12 Å). In general, the average SASAs from both methods agree reasonably well with each other. There is a general decrease in SASA from about 400 ps to 700 ps corresponding to the interaction of LYS12 with GLU5 which serves to obstruct one face of the hairpin. During this decrease in SASA the behavior of the LCPO method diverges slightly from molsurf; while the average SASA calculated by molsurf stays around 1060 $Å^2$, the average LCPO SASA decreases first to around 1050 $Å^2$, then around 1020 $Å^2$ before the two methods begin to agree again.

The correlation between LCPO and molsurf at 300 K is shown in Figure 1, right. The overall correlation between the two methods is decent (0.86), although in general LCPO underestimates the SASA at small values and overestimates at large values vs molsurf.

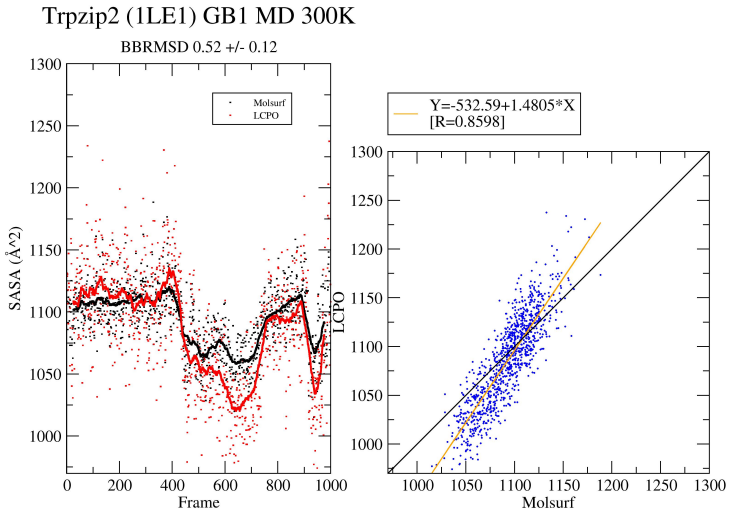

Figure 1: Left: SASA calculated using LCPO and molsurf methods for Trpzip2 at 300K. Lines are running average of data, window size 50 ps. Right: Correlation of LCPO to molsurf data.

400 K

The SASA calculated with LCPO and molsurf methods for Trpzip2 at 400 K, as well as the correlation between the two methods is shown in Figure 2, left. During the simulation Trpzip2 unfolds just before 600 ps. While the average SASAs calculated from both methods initially agree, the results diverge after unfolding, with the SASA calculated by the LCPO method around 200 Å^2 larger than that from the molsurf method.

The correlation between LCPO and molsurf at 400 K is shown in Figure 2, right. The overall correlation between the two methods is quite good (0.99), although again LCPO underestimates the SASA at small values and overestimates at large values vs molsurf.

The fact that LCPO overestimates the SASA in the unfolded state compared molsurf (arguably a more accurate method) by a significant amount has implications for using LCPO SASA for estimating non-polar solvation free energy. For a quick BOE calculation let's use the data here; say that in the unfolded state the LCPO SASA is about 1600 Å^2, and the molsurf SASA is about 1400 Å^2, while in the folded state the average SASA for both methods is about 1100 Å^2. That would mean the change in SASA upon folding is -500 Å^2 for LCPO and -300 Å^2 for molsurf. Using the default value of surface tension used in Amber that corresponds to -2.5 kcal/mol for LCPO and -1.5 kcal/mol for molsurf. The end result is that all other factors being equal, using the LCPO SASA

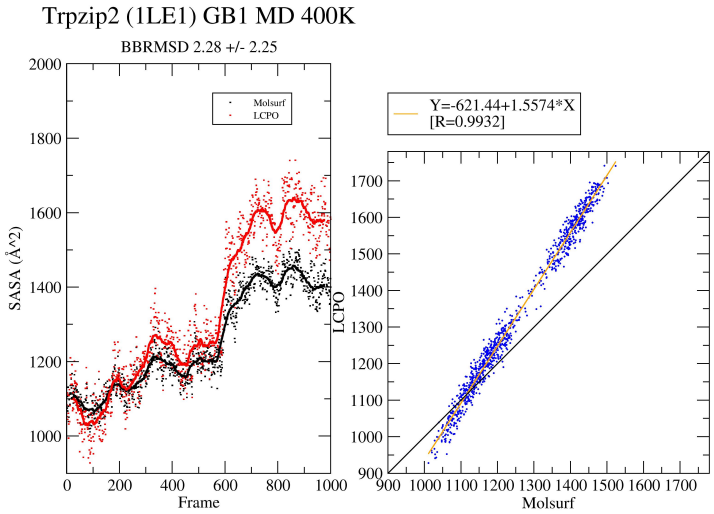

Figure 2: Left: SASA calculated using LCPO and molsurf methods for Trpzip2 at 400K. Lines are running average of data, window size 50 ps. Right: Correlation of LCPO to molsurf data.

term to estimate the nonpolar solvation free energy results in folding being 1 kcal/mol more favorable than it otherwise would be, which could certainly throw off population estimates.

Future Directions

- More systems / secondary structure types; look at more "realistic" cases (FtuFabI)?