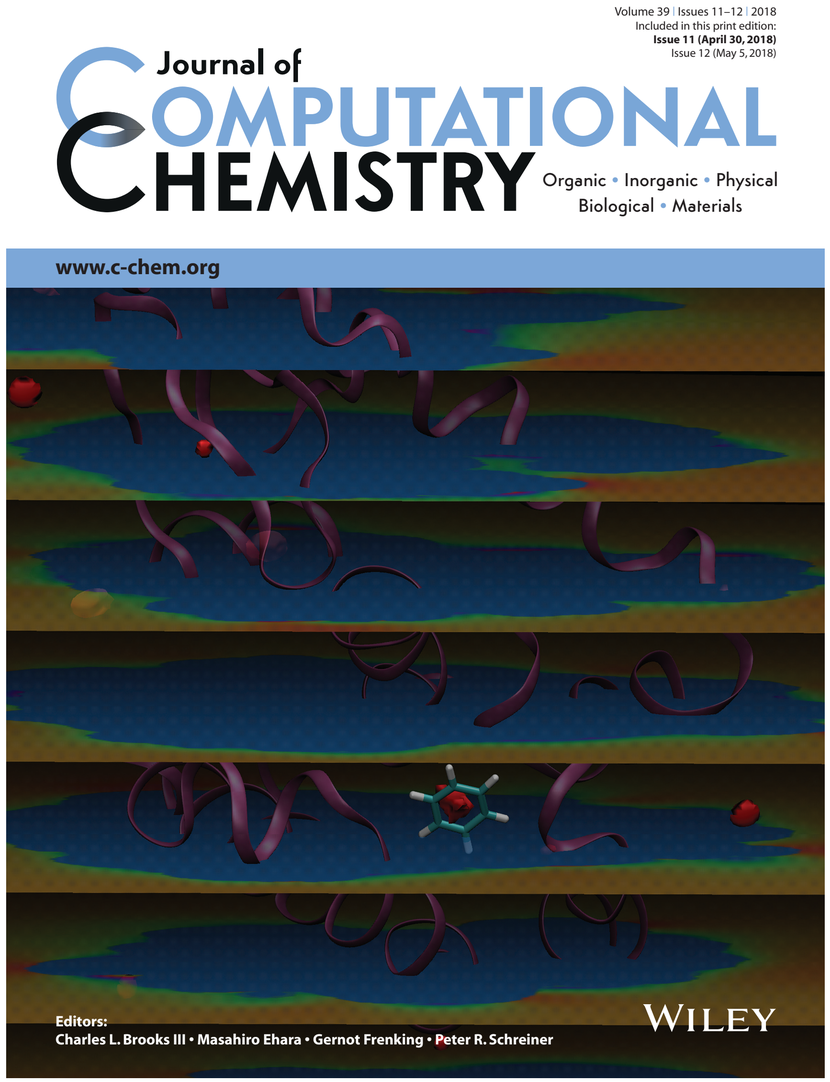
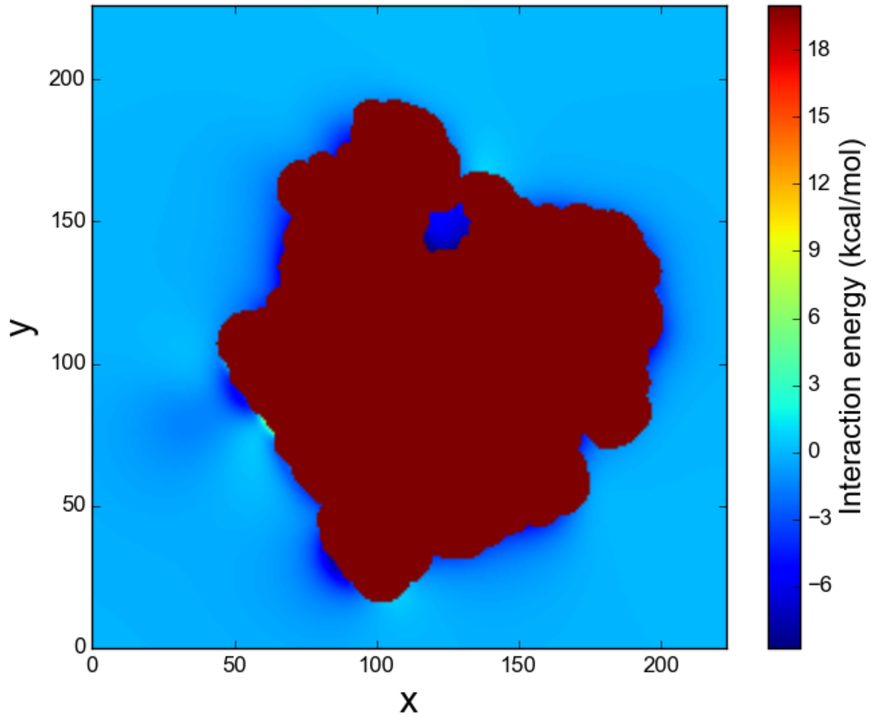
FFT can also be used to estimate binding ΔG





2D cross section of the interaction energy

[Nguyen, Zhou, and Minh, 2018]

How well does docking work? How can it get better?

- How well does it work?
  - Fairly successful at generating binding poses [Damm-Ganamet et al, 2013]. Usually successful (~80%) at ranking them.
  - Poorly correlated with binding free energies [Warren et al, 2006].
  - Unreliable at separating actives from decoys [Cross et al, 2009].
  - Sometimes successful at virtual screening. Hit rates < 20%.
- How can it be better?
  - Free energy includes both enthalpy and entropy. Docking scores usually exclude entropy.
  - Water often mediates protein-ligand interactions. Docking usually does not consider it.
  - Polarizability. Ligands can adapt to the protein environment. Docking usually does not consider this.