A Molecular Dynamics Investigation of Ternary Phase Diagrams

Names: William M. Ames, Benjamin Cunningham
Department of Chemistry and Biochemistry, Juniata College.

Introduction

Determining the efficacy of molecular dynamics simulations holds promise for physical chemistry and for confirming the reliability of specific softwares in computational chemistry. (1) Prior work from Pivirotto and Harijanto at Juniata has shown that molecular-dynamics CHARMM36 force field results work well in providing qualitative results for virtual titrations that can be plotted on a ternary phase diagram and compared realistically with real lab titrations. Similarly, this work focuses on comparing CHARMM-GUI and GROMACS-made, virtual simulations with each other and with a set of real lab titrations in terms of each method's qualitative and quantitative results, giving glimpses into how well computer systems represent mixtures of miscible and immiscible compounds.

Methods

Solutions for the lab titrations

- On an analytical balance
  - Weighed beaker, DI water massed; organic layer massed
  - added stir-bar, covered with punctured parafilm
  - Titrated with 1-propanol titrant into water/alkane mixture or water into alkane/1-propanol mixture
  - Incrementally measured titrant used at approximately 1-5 ml intervals based on turbidity duration remained before reaching equivalence point.

GROMACS files produced through gmx commands

- Generated *CRD, * PSF, and *PDB files for hexane, 1-propanol, and water on the CHARMM-GUI
- In GROMACS, minimized, equilibrated, and ran production runs with *.tpr files.
- Simulations were for 10 ns, 2 fs time step, at 300 K and 1 bar, with Nose-Hoover thermostat and Parrinello-Raham barostat

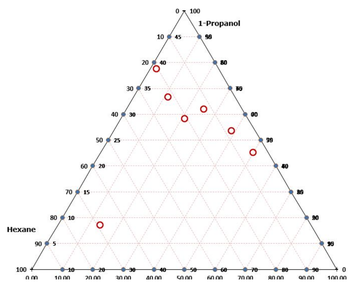

Figure 5: Ternary Phase diagram of lab-produced miscibility of hexane in water with 1-propanol as a solvent

Discussion

CHARMM force field simulations have recognition among biological chemists as a tool for modeling proteins, fats, and other macromolecules in different solvents. This research expands from previous investigations to see if the CHARMM-GUI and/or GROMACS-based simulations are feasible. CHARMM-GUI seems to give micro-molecules results consistent with laboratory results. GROMACS tends to produce qualitative results when plotting the data from its production runs on a ternary phase diagram. This may be because the random-insertion method used to build the files used in the GROMACS simulations spaced the molecules in the virtual box unrealistically. Alternatively, the equilibration step involved in preparing the virtual boxes should have allowed the molecules simulated to coalesce in their proper phases but could also have trapped molecules arbitrarily throughout the box.

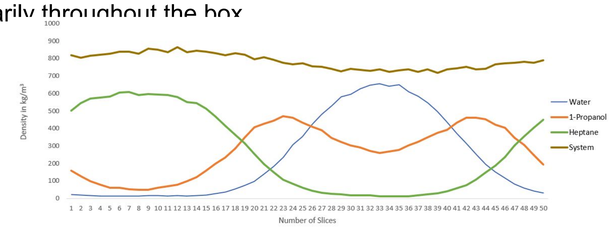

Figure 2: Density of three phases throughout 50 slices--heterogenous simulation

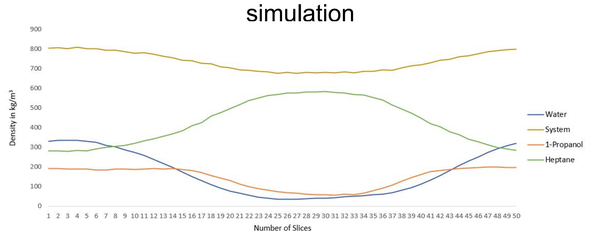

Figure 3: Density of three phases throughout 50 slices--simulation with two developing phases

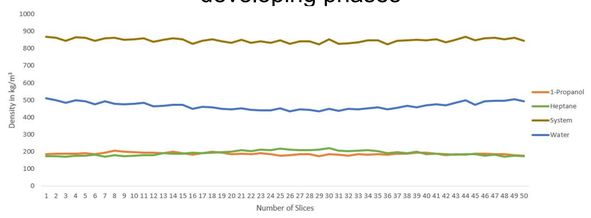

Figure 4: Density of three phases throughout 50 slices--generally homogeneous simulation

References

1) Brooks, B. R., et al. "CHARMM: The Biomolecular Simulation Program." *Journal of Computational Chemistry*, vol. 30, no. 10, July 2009, pp. 1545–614. *DOI.org (Crossref)*, https://doi.org/10.1002/jcc.21287.

Conclusion and Future Work

GROMACS is a powerful tool that allows individuals to simulate various molecular interactions of immense scopes; its utility should not be doubted. Despite this, the accuracy of its simulations for these investigations varies between productions. GROMACS functions well with the accessible, online platform, CHARMM-GUI. CHARMM-GUI, requires less work to learn and operate than native GROMACS commands. Our results indicate that CHARMM force field molecular simulations do not consistently allow researchers to distinguish phases within those boxes based on the densities of the molecules involved; it can only serve as a qualitative basis for judging the miscibility of micro-molecules in solution. Though lab methods are imperfect, they continue to produce the data necessary to plot ternary-phase diagrams desirable for research.

- Mass Percent Data
  - Figure 2: Water-- 44.23 Heptane-- 16.73 1-Propanol-- 39.04
  - Figure 3: Water-- 8.00 Heptane-- 70.30 1-Propanol-- 12.70
  - Figure 4: Water-- 37.14 Heptane-- 16.64 1-Propanol-- 46.21

Future work could cater to the utilization of native, GROMACS commands over the CHARMM-GUI. Additionally, the simulations could run longer (100+ ns) to give the system more time to arrange molecules as accurately as possible. Also, the method of randomly inserting the molecules into the files used for the simulations could take a layered approach instead. An extension of the work here could use larger and smaller molecules in the organic and aqueous layers, and different titrants could be used, too. Lastly, the data could be analyzed differently; instead of considering the data across the whole simulation time, it could be gathered from only the last few nanoseconds of a simulation.

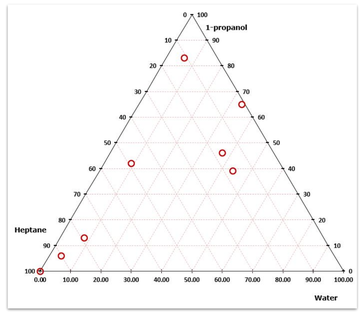

Figure 1: Ternary Phase diagram of GROMACS simulated miscibility of hexane in water with 1-propanol as a solvent