BIOC404: Biochemical Methods – Introduction to Biomolecular Simulation

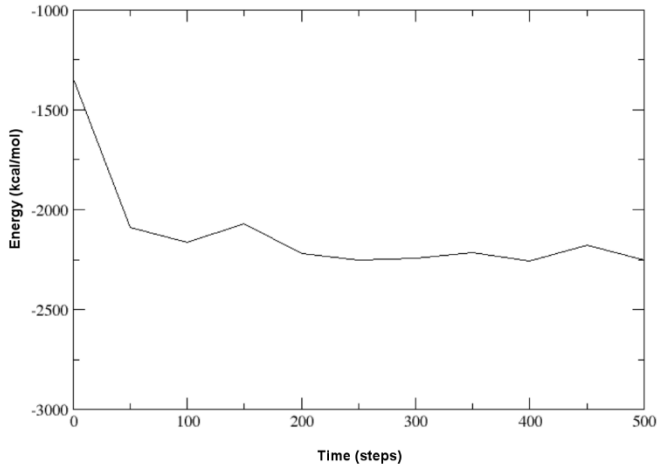
Assignment: Examine each of the example simulations and evaluate them based on your knowledge from the lectures. Recall definitions, techniques, and protocols discussed during class and apply them to these scenarios. Conjecture about the successes and failures within the examples provided and propose possible alternatives. Student evaluation is based on a grading rubric (see below) but is rooted in demonstrating understanding of the lecture material and how it is applied to these specific questions, with a greater focus on attempting to synthesize information rather than, necessarily, being correct.

Case: Now that you have a background in molecular simulation, a collaborator gives you a few different trajectories of a small 10-mer of poly-AT DNA. In these tests, the collaborator varied the solvation model (vac=*in vacuo*; gb= General Born implicit solvation) and the electrostatic cutoff distances between 12 angstroms (a generally accepted distance) and infinite (cut/nocut). After passing the trajectories through your computational pipelines, you now must examine these simulation outputs and report important features back to your collaborator including: (Assume every question ends with “Explain.”)

1. Was minimization necessary and/or sufficient? Are there meaningful differences in the structure before and after minimization? If so, what are they? (3)
2. How are the trends in total, kinetic, and potential energies for the *in vacuo* simulations? Is there something weird here? (3)
3. What happened during the *in vacuo* simulations and why? Which simulation, with or without cutoff, is a better representation of reality? [*HINT: VMD could be very useful here*] (6)
4. Are the *in vacuo* and/or the GB simulations converged? If you were looking to make a ‘production’ run, when would you start collection? (4)
5. Are the tends in energy for the General Born simulations expected? How do they differ from the *in vacuo* simulations? (2)
6. Why would the simulations with no interaction cutoff be expected to take longer (wallclock) than the simulations with a cutoff? (2)
7. Are there noticeable differences in the General Born simulations? (2)
8. How are the differences in walltime in the solvated (explicit and implicit with interaction cutoff)? Is this finding expected? [*HINT: look in output*] (2)
9. What are your recommendations to your collaborator; with the goal of trying to optimize simulation accuracy and efficiency? (6)

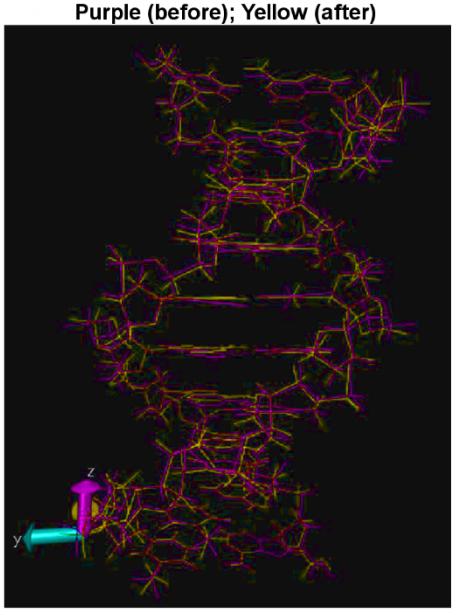
DNA minimization

A



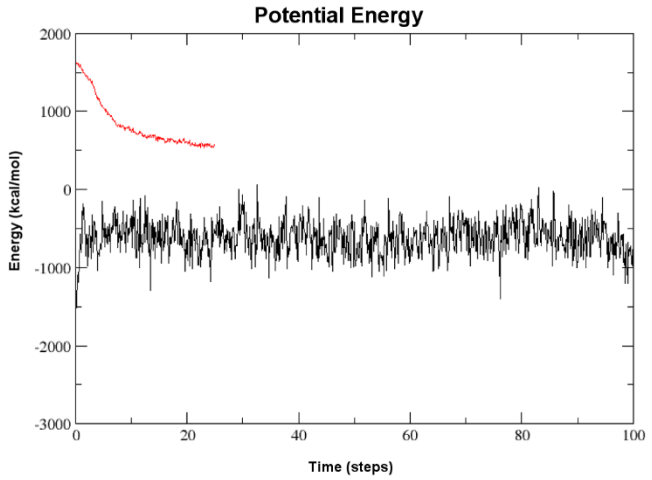
B

Poly-AT DNA Structures Minimization
Purple (before); Yellow (after)

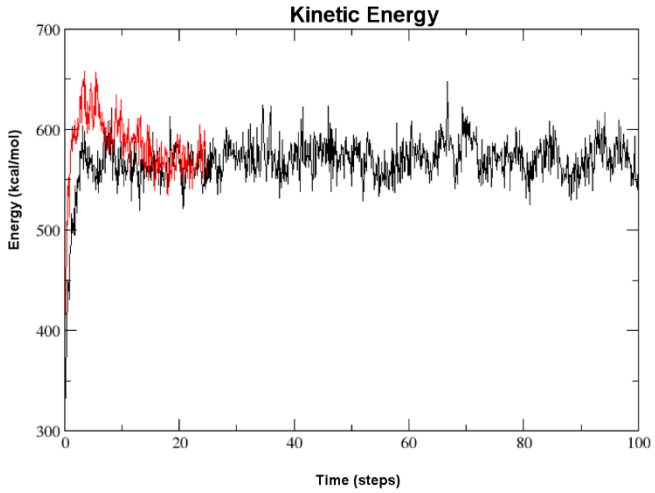


Simulation *in vacuo*

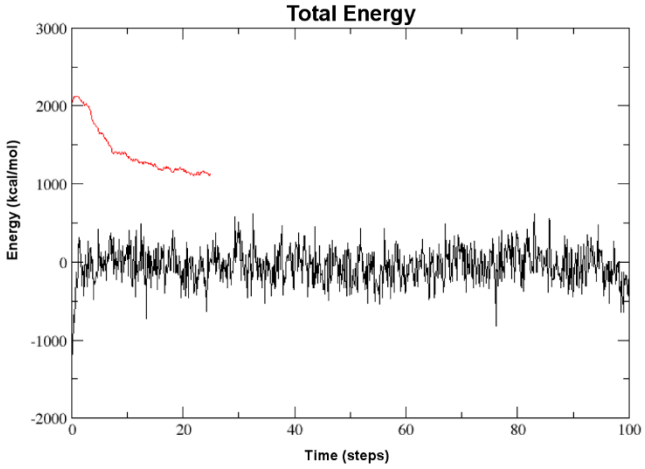
A



B

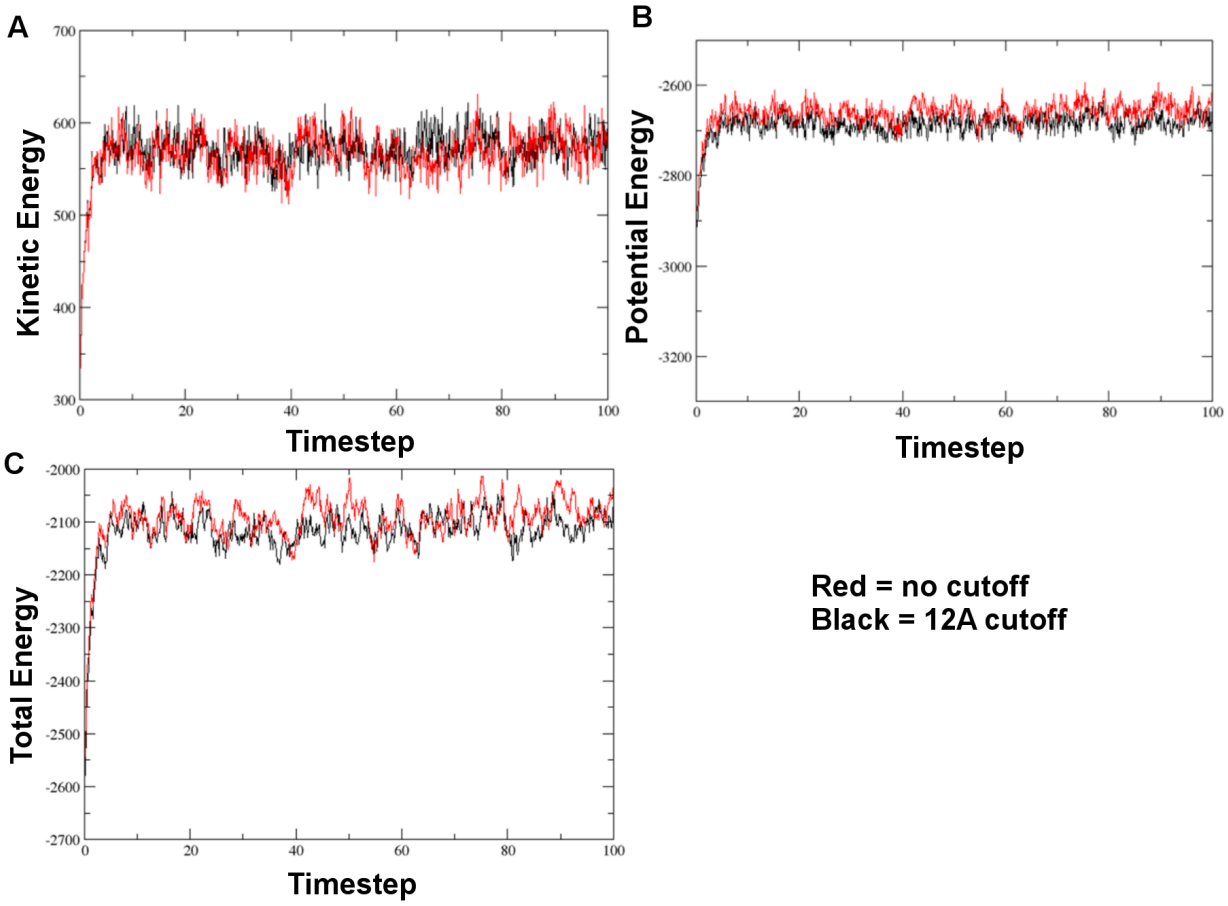


C



Red = nocut
Black = 12A cut

General Born Solvent Simulation



Red = no cutoff
Black = 12A cutoff

General Rubric:

A weight is listed after each question (#), these values will be multiplied by a score (0.0-3.0) for each where 1.0 is “Answered the question in any meaningful way” and 3.0 is “Answered the question in a thoughtful way, drawing on course materials, and the student demonstrated understanding of the material”. There is an additional 10 points that will be assigned for clarity/effort. Total out of 100.