GROMACS SCC Problem Set:

This problem set contains three different tasks with GROMACS, ranging from standard simulations to force-field comparisons to enhanced sampling simulations relevant to the study of SARS-CoV-2 proteins.

Task 1 Default Scaling Performance (CHARMM Force-Field) [30-points possible]:

Evaluate scaling performance for standard GROMACS simulations using five different trial systems (see below). For this trial, we aim to replicate the first step of any major MD study: to test and see how well the simulation systems of interest will scale using GROMACS. For this task the aim is to obtain computational performance profiles for each system using at least 10 different variations on the number of mpi ranks for running gromacs and compare scaling with and without the use of gpus. The aim is identifying the best use of an allocation.

For task 1 the following five systems should be simulated for 750ps each:

(1) 5nm x 5nm x 5nm box of water (system name: water)
(2) SARS-CoV-2 Nucleocapsid Protein N-terminus monomer (system name: protein_mono)
(3) SARS-CoV-2 Nucleocapsid Protein N-terminus complex (system name: protein_complex)
(4) Pure Membrane (system name: Memb)
(5) Membrane + SARS-CoV-2 pore-protein ORF3a (system name: ORF3a)

These systems will be provided for you with prepared gromacs input files: input_[system_name].gro, em.mdp, pr.mdp, production.mdp. You will need to modify the production.mdp file to reflect 750ps of simulation time.

Evaluation File Instructions:

For each system generate a plot that shows number of ns/day (estimated from the gromacs logs) on the y-axis and number of mpi-ranks on the x-axis. Be sure to include standard-deviations for each ns/day reported (as error-bars). This will require running the benchmarks *5 times for each data point* in the scaling plot.

Name these files: “system_name_scaling_profile_noGPU.png” and “system_name_scaling_profile_wGPU.png” also provide the raw, plain-text formatted, data to these plots as “system_name_scaling_profile_wGPU.dat” and “system_name_scaling_profile_noGPU.dat.”

Also generate a file, in plain text, named “turning-points.txt” where each system is noted in column 1 and in column 2 is the number of ranks before the scaling curve saturates (i.e. the point where the scaling curve shifts from being near linear to ‘flat’ in the profile).

As a final note, record the mdrun flags (your command-line flags that were associated with mdrun) that resulted in your optimal performance into a file named “optimal_run_commands.txt”

Scoring*: Task 1 is worth a maximum of 30 points.*

*1.25 point per scaling file (the plain-text and png figure files) will be awarded (5 systems * 4 scaling files per system * 1.25 = a maximum of 25 points). This means that each “png” and the “dat” are effectively worth 1.25 points each.*

For each both with and without GPU tests, each team may earn up-to 2.5 additional points by having the "best performance" for that category (2.5 points for runs with GPU and 2.5 points for non-GPU runs). The "best performance" will be taken taken to be the team's final scaling performance data-point (in ns/day) noted before the "turning point", divided by the number of ranks used.

The team with the "best performance" with GPUs will earn 2.5 additional points, the second-best performance will receive 2 points, third place will receive 1.5 points, fourth will receive 1 point, & fifth will receive 0.5 points

The team with the "best performance" without GPUs will earn 2.5 additional points, the second-best performance will receive 2 points, third place will receive 1.5 points, fourth will receive 1 point, & fifth will receive 0.5 points

Penalties. For this task a few point penalties may be given. Note that no team will receive negative points, if the deduction would result in negative points, the team will simply be given zero so that no penalty from this section extends to the other tasks.

2 Points will be deducted from a team's total if the "turning-points.txt" file is missing.

2 Points will be deducted if the "optimal_run_commands.txt" file is missing.

Additionally, if error-bars are missing in the performance files (the dat and png files), no points for those files will be awarded. If the error-bars are found to be so small that they are not visible in the png file but are present in the raw (dat) file that corresponds to the png, the png file will not be penalized.

Task 2 Force-Field Dependent Performance Metrics [50 Points] :

Occasionally, it is necessary to compare the dynamics of a protein system under different force-fields. In this task, it will be necessary to compare the results of 10ns long simulations of the SARS-CoV-2 Nucleocapsid protein's c-terminal domain complex under 4 different force-fields.

1) Amber03 (VDW cutoff: 0.9nm)
2) Amber99SB-ILDN (VDW cutoff: 0.9 nm)
3) OPLS-AA/L (VDW cutoff: 1nm)
4) GROMOS (VDW cutoff: 0.85nm)

The coordinate files for these simulations are provided as 7C22_OPLS.gro, 7C22_GROMOS.gro, 7C22_Amber03.gro, & 7C22_Amber99SB-ILDN.gro and topologies are named as 7C22_OPLS.top, 7C22_GROMOS.top, 7C22_Amber03.top, & 7C22_Amber99SB-ILDN.top. From these starting files: generate a cubic box of (SPC/E) water that has the protein centered and has at least 1.3nm of distance between the protein and the periodic box before running. There is no need to neutralize the system, these are already included in the gro coordinate files and topology files.

From these starting coordinate files and using the em.mdp, pr.mdp, and md.mdp files provided in task 1, modify the vdw cutoffs to be consistent with the table noted above and perform a scaling test (as in Task 1, at least 3 independent runs per test, at least 4 different ranks, there is **no restriction** on the use of GPUs) and report your best average ns/day for each force-field. After identifying your optimal scaling, generate **five** 10ns long trajectories with each force-field and the report the time-to-solution.

To obtain an estimate for the time-to-solution for each system, place all of your mdrun commands into a shell-script and execute the command and use "time" and report the 'real-time' in a file named: "simulation_time-to-solution_systemX.txt" where systemX should be replaced with the force-field being used.

The MD trajectories should contain at least 5,000 snapshots/frames (i.e. the trr format trajectories files that are created and written to disk by GROMACS should have the "nstxout" variable within the mdp files used to generate the tpr run files set such that 10ns/(timestep in picoseconds) > 4999). Upon completing the MD simulation, compute the radius of gyration (Rg), solvent accessible surface area (SASA), number of hydrogen-bonds (HB), and potential energy for each trajectory (PE). The Rg, SASA, HB, can be computed from the output trajectory by running the gmx gyrate (Rg), gmx sasa (SASA), and gmx hbond along with the tpr file used to run the MD trajectory with mdrun. The PE can be obtained by either parsing the trajectory's log files or by using the gmx energy utility with the md_replica_[trajectory_number].edr file as the input.

Evaluation File Instructions: Run each simulation in a separate directory name after each force-field. For the production phase of the simulations be sure to name the final output files md_replica_[trajectory_number].trr (for the trajectory), md_replica_[trajectory_number].log, & md_replica_[trajectory_number].edr (for the raw binary energy file).

Also redirect and save the standard-out from gromacs to a file name "RunLog" If the job must be restarted, be sure to save the older RunLog file as RunLog.part0, RunLog.part1, RunLog.part2, and so on.

Generate a figure containing time-series plots of the radius of gyration, sasa, potential energy, and number of hydrogen-bonds per MD frame name this "Trajectory_comparison.png". For this plot should be arranged into four sub-plots, one per time-series type, and should have the timeseries of each trajectory plotted together (i.e. run 0's PE timeseries should be in the same sub-plot as run 1's PE timeseries, and so on) be should be in the same plot.

Finally, report the scaling performance and optimal identified computational performance (in ns/day) for each force-field. Place this information in files named: FFComparison_scaling.txt FFComparison_Optimal_Performance.txt. For the scaling performance file, have column one be the number of ranks used, and column 2 be the performance for Amber03, column 3 be Amber99SB-ILDN, column 4 be OPLS, and column 5, be GROMOS. For the optimal performance report the force-field in column 1, optimal ns/day performance reported in column 2, and time-to-solution in column 3.

Scoring: *Task 2 is worth up-to a total of 50 points.*

4 points will be awarded for a complete FFComparision_scaling.txt file.

4 points will be awarded for a complete FFComparison_Optimal_Performance.txt file.

An additional 2 points will be award to the team with the overall best performance (averaged over all force-fields in the FFComparison_Optimal_Performance.txt file).

Up to 20 points will be awarded for the MD trajectories (1 per completed 4ns trajectory).

4 points will be awarded to the team with the fastest time-to-solution per force-field, 3 points to the second fastest, and 2 points for the third fastest, and 1 point for the fourth fastest. (A total of 16 points are possible, if a team has the fastest time-to-solution over all of the force-field tests)

1 point will be awarded for each of the Trajectory comparison plots generated (for a total of 4 points if the trajectory comparisons plots are generated for each force-field).

Task 3: Perform Temperature Replica-Exchange Simulations of NSP3 X-Domain [20-points]

Using the input files provided in NSP3-X-domain.tar.gz perform a temperature replica-exchange simulation with temperatures ranging from 283K to 400K for 1ns with the exchange flag set to -replex 1, -replex 2, -replex 10, -replex 100, -replex 1000. The temperature windows are provided in the file TempRamp for these simulations. You will need to modify the remd.mdp and relax.mdp files so that each tpr file has a different temperature corresponding to those in the TempRamp plain-text file.

Evaluation File Instructions. Performing a temperature replica exchange simulation requires two sets of trajectories, one set of temperature relaxations (one trajectory per temperature window, no exchanges) and the exchanging/communicating simulations. For evaluation there should be six sets of directories: Relax and Production_Replex_1, Production_replex_2, Production_Replex_10, Production_Replex_100, Production_Replex_1000, and within each should be a set of subdirectories named replica_[replica index number]. All output files should have a prefix of either "remd_replex_[replex number here]", as in the case of the production simulation, or simply "relax" in the case of the relaxation simulation. The ns/day for the lowest temperature replicate production simulations should be reported in a file named "best_performance_TREMD_vs_replexFrequency.txt", where the first column is the replex flag input value, and second column is the ns/day performance.

Scoring. *Task 3 is worth a total of 20 points.*

5 points will be awarded for the completion of the relaxation simulations.

5 points will be completion of all of the different REMD simulations (the Production_Replex_1, Production_Replex_2, Production_Replex_10, Production_Replex_100, Production_1000).

*5 Points will be awarded to the team with the best average TREMD performance over all replex schedules, 4 points for the second-best average over all replex schedule TREMD performance, 3 points for the third-best average over all replex schedule TREMD performance, 2 for the fourth-best average over all replex schedule TREMD performance, and 1 point-best average over all replex schedule TREMD performance for the fifth. The decisions will be made based on the noted in the "*best_performance_TREMD_vs_replexFrequency.txt" file

*5 Points will be awarded to the team with the best performance for the TREMD simulations with a replex of 100, 4 points for the team with the second-best performance for the TREMD simulations using a replex of 100, 3 points for the third best performance for the TREMD simulations using a replex of 100, 2 points for the fourth best performance for the TREMD simulations using a replex of 100, and 1 points for the fifth best performance for the TREMD simulations using a replex of 100. The decisions will be made based on the noted in the "*best_performance_TREMD_vs_replexFrequency.txt" file

Results Submission

The results should be submitted to the designated Azure cloud storage container, “gromacs”.

To prepare for the submission step, create the following directory structure on your local cluster filesystem:

a. Create a top-level directory for placing this application’s results.
b. Create a directory for each task and name the directories task1, task2, task3
c. Place the results files for each task in the corresponding directory
d. Recursively copy the task directories to the “gromacs” storage container location.