Program : A constant pressure replica exchange molecular dynamics technique in the NVT ensemble.

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A. Compiling

- download gromacs-4.5.5 from www.gromacs.org
- tar -xvf gromacs-4.5.5.tar
- cd gromacs-4.5.5
- copy repl_ex.c md.c to gromacs-4.5.5/src/kernel/ (to overwrite the 2 existing source files in /src/kernel/)
- perform : configure –enable-mpi –enable-double –prefix=/your-path-to-install-binary/ either –enable-all-static or –enable-shared NOTE : you have to have fftw3 installed and use : export LDFLAGS="-L/path-to-fftw3/lib", export CPPFLAGS="-I/path-to-fftw3/include". NOTE : if you compile with –enable-double, fftw3 has to be compiled with double precision. Otherwise, fftw3 should be in single-precision and gromacs-4.5.5 as well.
- perform : make -j12 (number of cores for parallel compilation) install-mdrun
- in the ideal case, the binary should now be in /your-path-to-install-binary/bin/, called mdrun_d
- Use gcc version > 4.9
- The new exchange term can be found in line 682 in repl_ex.c :

$$\xi \leq \exp(-(\beta_m - \beta_n)(U_m - U_n) + (\beta_m P_m - \beta_n P_n)\Delta V) \\ (1 - \exp(-(\beta_m - \beta_n)(U_m - U_n) + (\beta_m P_m + \beta_n P_n)\Delta V)) \, . \tag{1}$$

- Other pointers had to be invoked in md.c to measure the pressures and volumes in NVT.
- The exchange of volumes has been switched off.

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B. System preparation

1. Start using temp0.mdp (attached) at 298 K with Nosé Hoover thermostat and vary the box coordinates written at the bottom-line of the .gro file :
   - start with a set of box-coordinates.
   - use grompp -f temp0.mdp -c .gro -p .top -o .tpr
   - run the system for 10-30 ps.
   - check the pressure using g_energy (! The output-frequency of ener-data must be approx. every 2-5 steps)
   - re-adjust the box-coordinates and goto point 2 using grompp - NOTE : Equilibrate with a switched off barostat, since the production and the algorithm run in the NVT ensemble.
2. ! Store each of the single coordinate files after you have equilibrated it. Use following order, e.g. start_#replica-index.gro
3. ! Note that you maybe will never reach a precise average of 1.0 atm. Rather you will reach an average in the range from -4.0 to +10 atm. It is always better to reach a positive average pressure, but a slightly negative pressure might get compensated by the dynamics of the peptide (conformation transitions). You should consider that the variance of the pressure can be $\pm 50 - 100\ atm$. Always change the last digits of the box-coordinates first and only one of the box-vectors.
4. ! Use each of the coordinate files for the subsequent run at elevated temperatures for the new equilibration, e.g. start_0.gro for the next trial of start_1.gro - start_1.gro for the 3rd trial, etc.
5. Use a script to write the individual run-input files in .tpr format in the order of the equilibrated structures, e.g. grompp -f temp0.mdp -c start_0.gro -p topol.top -o topol_0.tpr corresponding to 298 K, etc.
6. Run the program using : mpirun -np (total number of cores) /your-path-to-install-binary/bin/mdrun_d -v -s topol_.tpr -multi number_of_replicas -replex 1000 (exchange attempt frequency) -deffnm traj_ (all files have replica

index and traj_ in their file-name) -np (number of cores per replica, very important for speedup)

7. Use about 1 single core for approx. 1000 particles.

8. Have a lot of fun !

C. Files

1. unpack CONST_P_NVT_SOURCE.tar.gz using tar -xvf

2. start.top, start_0.gro topology and .gro structure files for Dialanine, equilibrated for 298 K

3. temp.txt : file with temperatures, used in write_tpr.f90

4. Two source files md.c and repl_ex.c which have to be moved into /src/kernel/ of your gromacs-4.5.5 source code

5. write_tpr.f90 : a short fortran90 program to read temp.txt, to write run-input files for the individual temperatures and to print tpr-files using temp.txt, start_$i.gro and start.top. Compile with pgf90 (pgi), ifort (intel) or gfortran (gnu).

D. Notes

1. Please cite : E. K. Peter, I. V. Pivkin, J-E. Shea, A constant pressure replica exchange molecular dynamics technique in the NVT ensemble. (manuscript in preparation) (2015).

2. Although I have continuously tested this software, it goes without saying that I cannot be held responsible for any damage caused by errors in the software or data files.