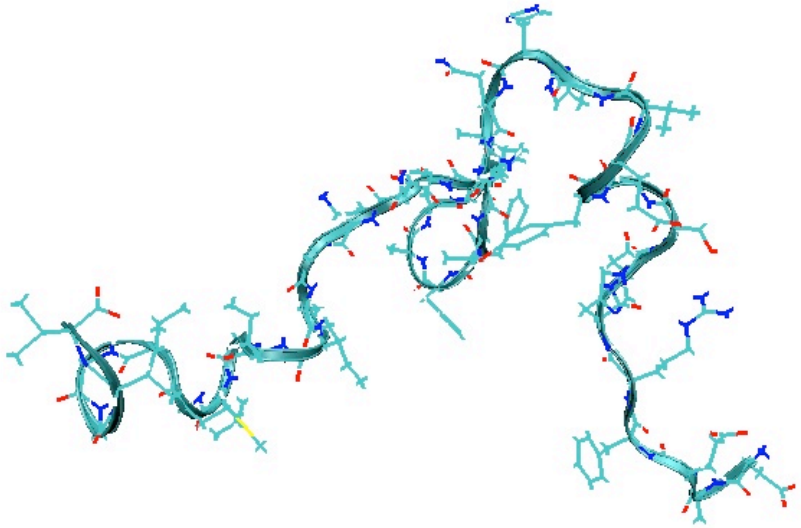
Replica Exchange Molecular Dynamics (REMD) for Amber's Particle-Mesh Ewalds MD (PMEMD) code



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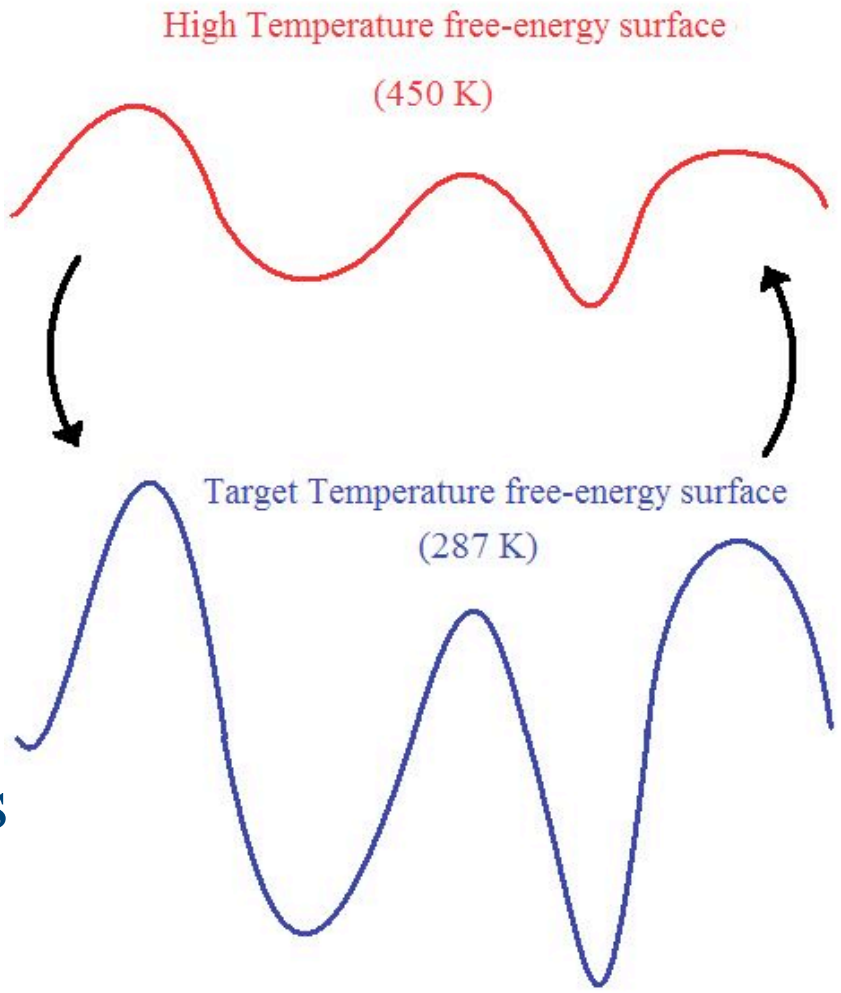
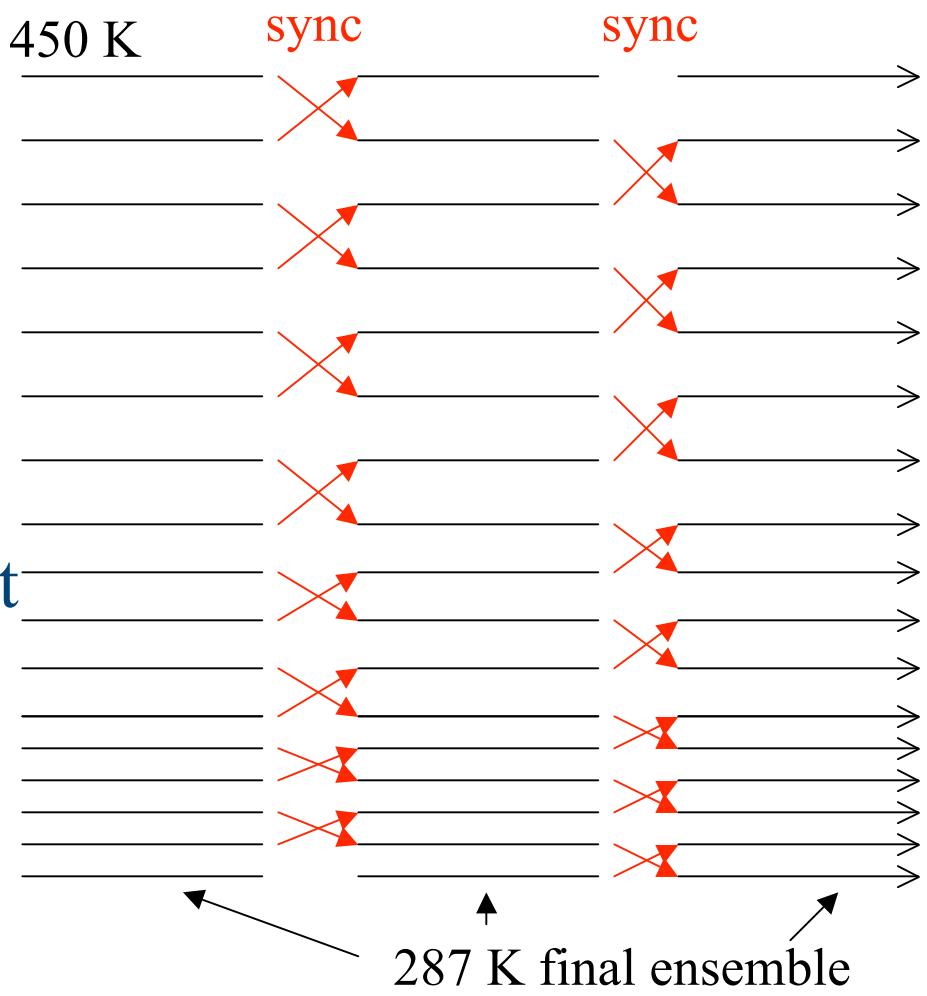
Goal: Converging Aβ monomer Molecular Dynamics simulations

- Use Amber ff99SB force field and TIP4P-ew explicit water model to sample an all-atom representation of Aβ conformational ensemble
- High temperature simulations allow sampling of minima separated by large energy barriers
- Replica Exchange Molecular Dynamics (REMD) runs several independent simulations run at different temperatures in parallel



REMD from 450 K to 287 K

- Run PMEMD simulations independently for all replicas
- Every picosecond of simulation time attempt to exchange two replicas that are close in temperature
- Energy minima accessed at high temperature will exchange down to the low temperature replica over time

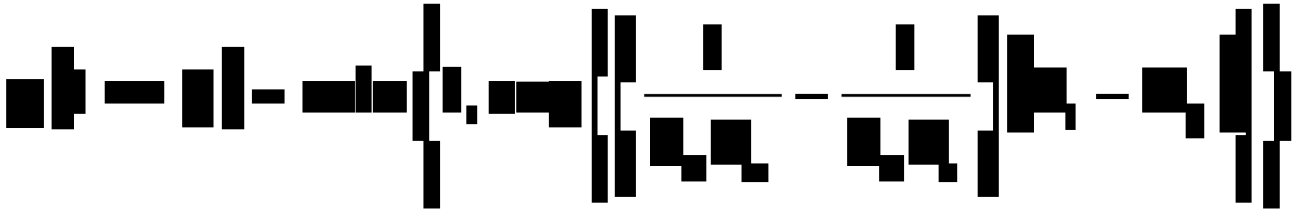


PMEMD is faster than Sander

- PMEMD is a version of Sander MD code that is optimized to perform parallelized particle-mesh Ewalds calculations, which use Fast-Fourier Transforms to calculate the long-range forces on atoms.

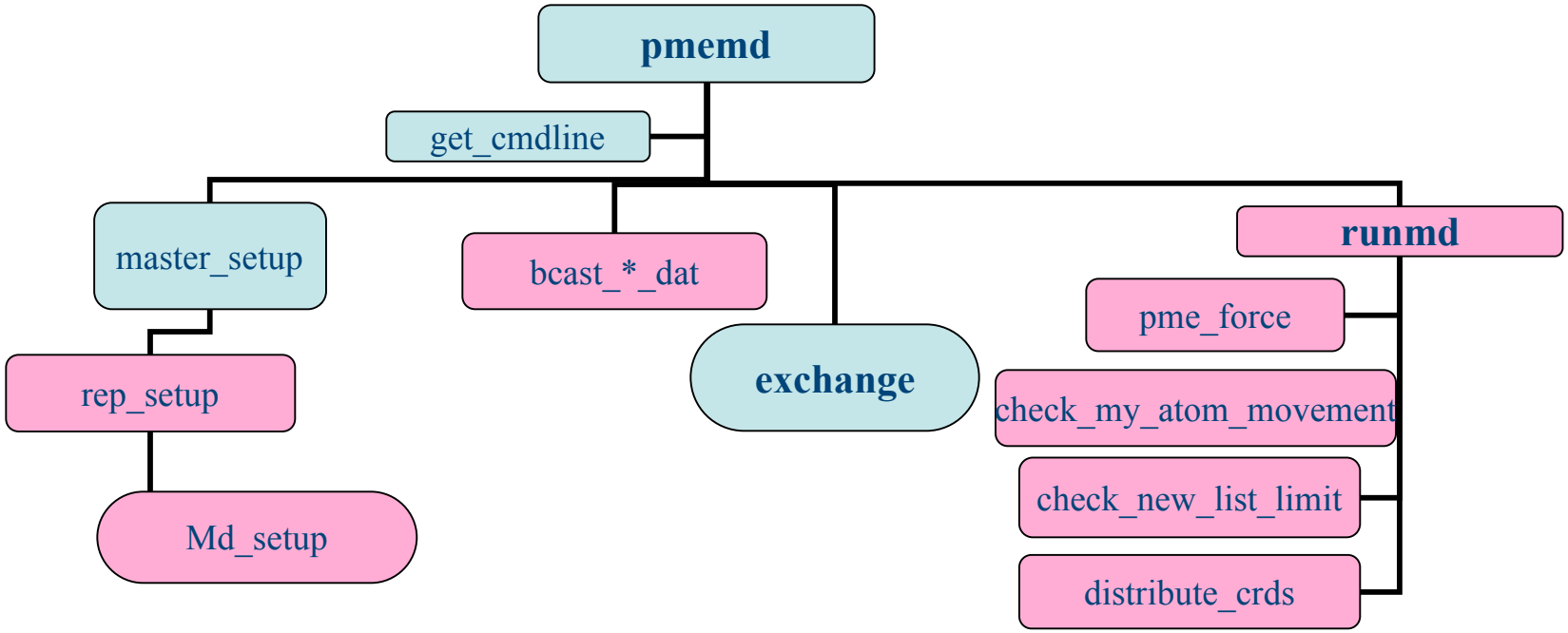
- On 16 processors, PMEMD takes 33 s to perform 1ps of simulation on one 25,000 atom system including setup, Sander takes 55 s. If exchanges and synchronization time are less than 22 s, my code will be faster than Sander REMD.

- Exchange criteria are monte-carlo criteria that depend only on replica temperatures and energies. Structure information does not need to be transferred between processors.



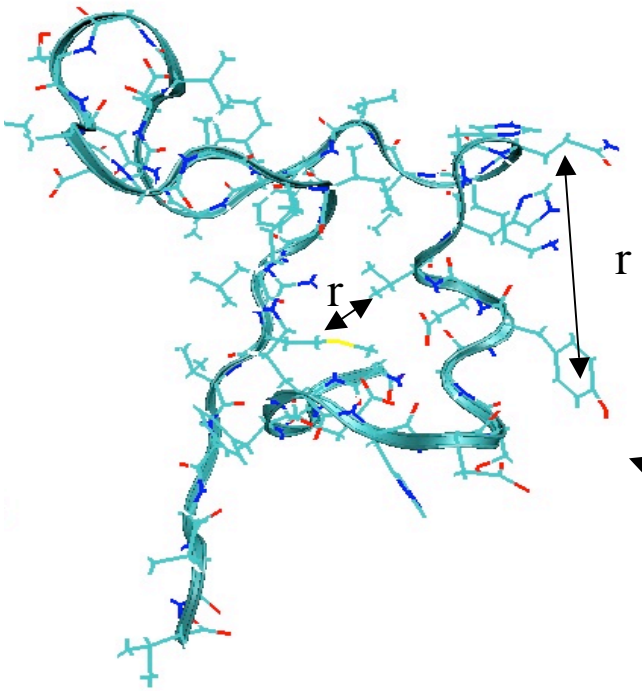
Subroutine Organization

Instead of one master task, I create a master for each replica that does everything that the master does in the original code. Each master has its own set of global variables that are never shared with the other replicas.

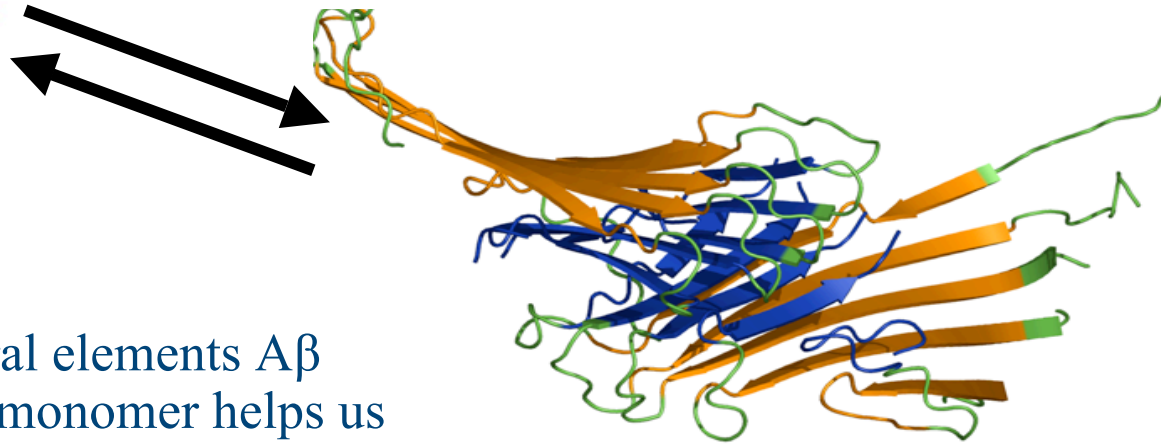


Light blue boxes indicate subroutines that I modified from the original code, but that are still only run once for the entire program. Pink subroutines are those that I modified and now separately for each replica.

Amyloid β peptide structural ensemble and Alzheimer's Disease



Computationally sampling the entire Aβ monomer conformational ensemble allows us to calculate average inter-hydrogen distances, which can be compared to NMR data.



Knowing what structural elements Aβ transiently adopts as a monomer helps us to understand how the Aβ oligomers that are believed to cause Alzheimer's disease are formed.

Fawzi, N. L. et al *J. of Mol. Biol.* 2007, **365** 535-550.