Examplar Lonestar6 Allocation Request
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Title: Statistical Mechanics in Extreme Scales for Biological Systems

Project Description: Physics is simple fundamental laws that govern all the complex phenomena of the unadulterated nature and all the sophisticated behaviors of the engineered systems. Physics has always been and should always be a quantitatively predictive science. The study of biological systems should not be an exception. The bridge from the simple physics laws governing individual atoms to the simple biological functions such as metabolic activity indicating cell viability, however, can be extremely complex. It involves stochastic dynamics of trillions of atoms constituting a cell governed by the simple laws of Statistical Thermodynamics. Whole cell simulations are still out of our reach today or tomorrow but, with Lonestar6 (LS6), simulations may reach closer to the critical size that will not be too small to extract the science of whole cells, piece by piece, beyond the fluctuations/uncertainties that are inevitable in any simulations. The current state of the art of atomistic simulations of a biological system (or any physical/chemical systems) is that the pressure fluctuations in a typical model system (consisting of ~100K atoms) are >100 bar for NPT ensemble runs under a constant pressure of 1.0 bar (see, e.g. NAMD User's Guide https://www.ks.uiuc.edu/Research/namd/2.14/ug/node39.html).
The PI's lab recently found that this large artifactitious fluctuation caused the computed values of aquaglyceroporin-glycerol affinity appear low. This is a fundamental issue in computational physics that begs for reexamination: are the computed values of binding affinities or some other characteristics sensitive to the large pressure fluctuations of small model systems?
To investigate this, we propose: (1) We have to test whether or not a computed characteristic is sensitive to the artifactual fluctuations in pressure and, if yes, how sensitive it is. This test can be done straightforwardly, if sufficient computing resources are available, by increasing the size of the model system because the pressure fluctuations of a given system is inversely proportional to the system size (the number of atoms, in particular) as dictated by a fundamental law of statistical thermodynamics. (2) We can also look for ways to circumvent this law of statistical thermodynamics with AI tricks, which are still to be found. LS6 enables us to simulate the statistical thermodynamics of systems ranging in size from the typical ~100 K atoms to ~1 M atoms to ~10 M atoms or even larger. The root mean squared pressure fluctuations would range from ~100 bar to ~30 bar to ~10 bar or even smaller. LS6 A100 subsystem enables us to efficiently conduct analyses of the big-data sets generated by the compute nodes and to quickly test various AI tricks. Supercomputing powers like LS6 will greatly enhance our ability to pursue quantitatively predictive studies of complex systems, moving one step closer to the atomistic studies of whole cells.

Resource Justification/Computational Plan: The main scientific objective is to elucidate physics undergirding the insect olfactory receptor OR5 by searching for the EOL diffusion pathways and quantifying the EOL-OR5 interactions. This study will be used as a preliminary study for a proposal in collaboration with Robert Renthal, PhD in Biochemistry. We plan to use NAMD to

conduct molecular dynamics (MD) simulations of all-atom model systems of the following sizes: SysI consisting of ~200 K atoms (which is typical in today's literature), SysII consisting of ~1.6 M atoms, and SysIII consisting of ~12.8 M atoms.

The requested SUs (totaling 100,048 SUs) will be used for:
1. Running SysI, 40 jobs, each on 20 nodes for 48 hours, altogether 38,400 SUs.
2. Running SysII, 10 jobs, each on 100 nodes for 48 hours, altogether 48,000 SUs.
3. Running SysIII, 2 jobs, each on 200 nodes for 10 hours, altogether 4,000 SUs.
4. Running SysI and analytics, 67 jobs, each on 1 GPU-A100 node for 48 hours, altogether 9,648 SUs.