EQUIPMENT - CHODERA LABORATORY

Computational

Local GPU cluster: The Chodera laboratory has priority access to a high-performance computing cluster with 2016 CPU cores (4320 hyperthreads) and 204 NVIDIA graphics processor-based accelerators (GPUs). Project storage is provided by a high-performance shared 2.2PB high-performance distributed storage system and 3.8PB of "warm" archival storage. Network connections are at least 1 Gbit/s throughout MSKCC facilities, and cluster, GPU, and storage systems are connected with at least 10 Gbit/s links.

Software development resources: All Chodera laboratory members are equipped with laptop computers with GPUs capable of GPU-accelerated software development. All members also have access to a pool of powerful GPU development machines containing an assortment of most available GPUs for software development and automated build testing/benchmarking.

Folding@home: The Chodera laboratory is a member of the Folding@home Consortium. Folding@home is a distributed computing infrastructure run by Vijay Pande at Stanford University with over 300,000 actively computing cores, making it the most powerful supercluster in the world in terms of aggregate performance, with ~100 PFLOP/s of aggregate computational power available for use at any time. The free availability of large quantities of computer time through this network---which would cost tens of millions of dollars in hardware and power---leverages funding provided for this proposal enormously. Access to the Folding@home network is provided via two dedicated servers at MSKCC connected to 180TB of usable storage housed in a high-availability datacenter.

Experimental

Integrated automation platform for accurate liquid handling and biophysical measurement: The experimental laboratory is equipped with an integrated automated system capable of carrying out a number of high-throughput automated plate-based biophysical assays (in 96- and 384-well plate formats) with a focus on measurement accuracy. The automated system integrates the following systems via a Thermo Fisher BenchTrak Orbitor plate-handling robot on a 3.2-meter track: a Tecan EVO200 liquid-handling robot with both liquid-displacement and high-precision air-displacement pipetting arms and stations for vacuum filtration, Peltier cooling/heating, heating/shaking, and septum piercing; an HP-D300 Digital Titration dispensing unit capable of accurately dispensing compounds in DMSO from picoliter to microliter volumes; four Inheco deep-well incubator/shaker stations for high-throughput bacterial culture; a Bionex HiG4 plate centrifuge capable of 4000g; a Tecan Infinite M1000PRO multifunction plate reader capable of absorbance, fluorescence, fluorescence polarization, and alpha-screen measurements with injectors for time-dependent measurements; a Roche LightCycler 480 qPCR machine also capable of ThermoFluor melts for protein quality control; an Agilent PlateLoc plate sealer; barcode tracking capabilities for all laboratory materials; a LabChip Caliper GXII microfluidic electrophoresis device for proteins and nucleic acids; a Thermo Fisher MultiDrop Combi reagent dispense; and a high-capacity automated plate carousel. A uPrint SE Plus 3D printer is available for fabricating custom SBS-format reagent or labware holders out of ABS plastic.

Gravimetric solution preparation: Biophysical measurements of protein-ligand binding affinities are fundamentally limited by the accuracy with which compound concentrations are known. High accuracies in affinity measurements are absolutely essential to validating and improving computational methodologies for probing and predicting binding affinities, so it is essential that these concentrations be well-determined.
Methods to *measure* concentrations are generally costly, inaccurate, time-consuming, and often not universally applicable. Precise preparation of initial compound solutions remains the best way to ensure accuracy.
Our laboratory is therefore equipped with a high-precision Mettler-Toledo Quantos balance for automated gravimetric solution preparation. Powder dosing heads dispense compound directly into vials on the analytical balance, while liquid dosing heads dispense solvent under argon (to prevent water uptake by hygroscopic solvents such as DMSO), ensuring accurate concentrations of compound solutions. Provenance, masses, concentrations, and uncertainties are tracked via barcodes and electronically within our ELN.

Additional biophysical characterization: Our laboratory also has access to instruments necessary to conduct automated isothermal titration calorimetry (ITC) experiments using a GE/MicroCal Auto-iTC200 and multiplexed surface plasmon resonance (SPR) experiments with a BioRad Proteon XPR36, both located in the adjacent Rockefeller HTSRC facility and available for our use at low cost. Both instruments accommodate sealed 96-well plates for fully automated measurement. Our laboratory automation platform allows numerous experiments to be set up automatically---including dilution, pipetting, plate sealing, and notification of laboratory members that the materials are ready to walk across the street to the HTSRC facility.

Electronic laboratory notebook: An electronic laboratory notebook (ELN) system manages all samples and data. 1D and 2D barcodes are used to track all materials received or generated within the laboratory.

Standard molecular biology equipment: The wet laboratory is also equipped with standard molecular biology equipment, including a wide array of multichannel and repeating pipettes for manually piloting robotic assays.

Proximity to pharmaceutical industry instrumentation: Our location in the Greater New York Area puts us in proximity to a number of pharmaceutical companies that have pledged to provide access to additional instrumentation, such as Sirius T3 instruments for measuring solubility, partition and distribution coefficients, and p*Ka*s (see Merck letter).