UC, IRVINE

FACILITIES AND OTHER RESOURCES

For conducting the proposed work, my main requirement is computers, in the form of both workstations for researchers to work at, and supercomputing or cluster facilities on which to run the calculations. We have ample resources on this front. I own a portion of the GreenPlanet shared cluster at the University of California, Irvine. We have ~1100 AMD processor cores along with another 200 Intel Xeon cores. We also recently added (with Tom Poulos) three GPU nodes from Exxact running NVIDIA Titan X cards (each node has 8 GPUs which have fast communication between blocks of 4). We also have close to 100 TB of storage for the group. On the GreenPlanet cluster we also have access to other processor cores contributed by other groups when on a reduced priority basis. Additionally, we have access to the HPC Cluster at UC Irvine, another shared computing facility, where we can use a reasonable portion of the several thousand nodes available depending on the usage of other groups, without cost. We also typically have supercomputing resources such as through NSF XSEDE. In addition to these facilities for running the simulations, we have ample resources in the lab in terms of workstations, with a number of desktop Macs and laptops on hand (more than enough for all lab personnel). Additionally, we recently purchased four more Exxact GPU nodes (identical to the above which are now housed in a shared GPU facility at UCSD with several other groups doing related research; this gives us access to another 32 GPUs plus spill-over access to ~100 more.

In addition to computational resources, my group has licenses to the software we need already. We use OpenEye software for helping to prepare our systems for simulations, and we have a license for that. Additionally, we have licenses for AMBER, MCCE, Modeller, Dock, PyMol, Desmond, the Schrödinger toolkits, and other common molecular modeling packages, and the majority of our simulations are done using GROMACS. So we are well equipped for performing the calculations proposed here.

Impact of the scientific environment on the probability of success

The scientific environment at UCI is excellent and will substantially impact the probability of success. We have regular molecular simulations meetings together with other groups at UCI (including the groups of Ray Luo, Ioan Andriciaoei, and Doug Tobias, among others), and we can benefit from their expertise. We also have collaborations (and are building others) with experimentalists at UCI, including Larry Overman, Tom Poulos, and Chris Vanderwal. I am also receiving both formal and informal mentoring from more senior faculty at UCI – formally from Tom Poulos in the Department of Pharmaceutical Sciences, and informally from other computational experts noted above.

UCI has invested substantially in the success of the Mobley lab. In addition to receiving roughly 20 nodes in the GreenPlanet cluster and various disk storage, furniture, etc., we received substantial financial resources to help expand the cluster, purchase additional software licenses, and support laboratory personnel.

SUBAWARDS:

SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH - CHODERA LABORATORY

FACILITIES AND OTHER RESOURCES

Computer: All lab members are equipped with laptop computers with integrated graphics processors (GPUs), and have access to high-performance development machines containing a range of modern GPU accelerators. The group has priority access to a high-performance computing cluster with 1920 total hyperthreads and 120 NVIDIA GTX-680, GTX-TITAN, or GTX-TITAN-X GPUs. Project storage is provided by a high-performance shared 1.5PB GPFS storage system. Dedicated servers provide access to Folding@Home, which currently provides ⇠19 PFLOP/s aggregate computational power in over 350,000 actively computing cores—equivalent computing facilities would cost tens of millions of dollars. Network connections are at least 1 Gbit/s throughout MSKCC, with HPC systems connected at 10 Gbit/s.

Laboratory: The Chodera wetlab occupies ⇠340 square feet of space. The central feature of the wetlab is an integrated platform for fully automated biophysical experiments instrumented for remote monitoring and operation. This system includes a Thermo BenchTrak Orbitor, a Tecan EVO200 with three dispensing technologies (including an HP D300), four Inheco incubators, a BioNex HiG4 centrifuge, Tecan Infinite M1000PRO plate reader (capable of absorbance, fluorescence and FP, luminescence, and AlphaScreen measurements, with injectors installed for kinetics measurements), Caliper GXII microfluidic electrophoresis platform, Roche LC480 qPCR machine, Agilent VCode barcode printer and PlateLoc plate sealer, Thermo MultiDrop Combi reagent dispenser, and Thermo automated Cytomat Hotel. This platform automates cloning, site-directed mutagenesis, recombinant bacterial protein expression and purification, cell-free transcription and translation, microfluidic gel electrophoresis, Thermofluor protein stability assays, and fluorescence measurements of binding affinities. It can also automate preparation of ITC and SPR experiments that can be conducted at the Rockefeller HTSRC across the street. There is bench space for one group member to work manually using standard molecular biology tools. A Mettler-Toledo Quantos automated gravimetric solution preparation system ensures compound concentrations are always accurately and traceably prepared. An electronic lab notebook tracks all materials and measurements in the laboratory using barcodes. Shared equipment space, standard laboratory refrigerators and freezers, and common shared equipment (centrifuges, incubators, etc.) is also provided. Both experimental and computational spaces are located in Memorial Sloan-Ketterings new Zuckerman Research Center (ZRC).

Animal: N/A

Office: All lab members have desks in a modern open-plan computational biology working space where the Chodera lab currently occupies ←400 ft2. Group members are equipped with monitors, backup storage, and other standard workstation accessories. Additional office space includes Dr. Chodera's office, office space for a shared administrative assistant, shared conference rooms, and meeting and library space.

Clinical: N/A

Other Resources:

The Rockefeller high-throughput screening resource center (HTSRC) is located across the street at the Rockefeller University. The HTSRC provides a number of high-throughput binding and biophysical measurement facilities at a minimal cost to us, most notably (1) a GE/MicroCal Auto-iTC200 automated isothermal titration calorimeter capable of processing up to 384 samples unattended, and (2) a Proteon XPR36 SPR instrument (capable of processing 96 samples), among others. The MSKCC Analytical NMR Core under the direction of Dr. George Sukenik allows for the unattended 1H-NMR characterization of compounds using an automated sample workflow. Numerous additional MSKCC core facilities are available to MSKCC researchers, including proteomics and mass spectroscopy, NMR, X-ray crystallography, high-throughput screening, analytical chemistry, DNA sequencing, and bioinformatics consulting. Many of these core facilities are highly automated. Over 30 core facilities are currently available, all directed by Ph.D.-level experts available for consultation.

FACILITIES AND OTHER RESOURCES (GIBB, DEPARTMENT OF CHEMISTRY, TULANE UNIVERSITY)

Laboratory: The group has two laboratories in Percival Stern Hall (each 900 sq. ft. and furnished with 4 fume hoods) located adjacent to the Gibb's office. In addition, Gibb has a laboratory in the new Donna and Paul Flower Hall for Research and Innovation adjacent to Stern Hall. This laboratory is approximately 1200 sq. ft. and is equipped with four fume hoods. All of these spaces are new (2012+), contemporary space for organic synthesis and physical organic studies. Major/specialized equipment for these laboratories include: two Isothermal Titration Calorimeters, Dynamic Light Scattering/Zeta-Sizer, a micro-well plate reader (UV-Vis/ Fluorescence), UV-visible spectrometer, an HPLC, and an osmometer. Minor/general equipment for the laboratories include: automated flash chromatographic system for organic mobile phases, refrigerators, drying ovens, rotary evaporators, balances, ultrasound baths, vacuum manifolds, glassware (for reactions and chromatography), and hot plates.

Computer: In his office Gibb has one portable MacBook Pro laptop with 15" Retina display (2.6 GHz Intel Core i7, with 16 GB RAM, and Mac OSX version 10.10.5 operating system) and related peripherals for: viewing (27 inch Apple LCD monitor), printing (color, HP Laserjet Pro), scanning and data backup. The computer has the requisite software installed (such as Microsoft Office (Word, Excel, PowerPoint), Key Note, ChemDraw, Adobe Acrobat Professional, Adobe Photoshop, and Adobe Illustrator. In addition to the five laboratory computers dedicated to instruments, the labs are also equipped with three high-end (Apple) desktop computers. The group uses an Electronic Laboratory Notebook (ELN) system (iLabber from Biovia) for data storage, and a DropBox folder for rapid movement of documents and files within the group. Gibb and Department of Chemistry pays for licenses for software (e.g., Mnova from Mestrelab Research). Additionally, the Department maintains a computer coordinator who assists with all information technology-related needs.

Office: The research space in Percival Stern Hall includes two offices (160 sq. ft. each), group conference room (350 sq. ft.), and a student workroom (140 sq. ft.) directly adjacent to the laboratories.

General: The general support structure of the Department of Chemistry includes an electronic shop, machine shop, as well as electronic and NMR technicians. Comprehensive secretarial services are also available. A comprehensive library is available for the group, the facility of which includes on-line access to SciFinder and other science search engines.

Equipment: Major/specialized equipment for the laboratory includes: two Isothermal Titration Calorimeters, a Dynamic Light Scattering/Zeta-Sizer, a micro-well plate reader (UV/Vis/Fluorescence), UV-visible spectrometer, an HPLC, and an osmometer. Minor/general equipment for the laboratories include: an automated flash chromatography system (organic mobile phase), refrigerators, a lyophilizer, drying ovens, rotary evaporators, balances, ultrasound baths, vacuum manifolds, glassware (for reactions and chromatography), and hot plates.

Department Equipment: The group has access to Departmental equipment including: NMR spectrometers (400, 300 MHz, and 300 MHz solid-state), mass spectrometers (MALDI-TOF-MS, MicroTOF ESI-MS and high res. MALDI-TOF), GC-MS (2), X-ray diffractometers (2), HPLCs (3), gas chromatogram (semi-preparative), UV-vis spectrophotometers (3), spectrofluorometers (2), IR spectrometers (3, including 1 FT Raman), and inert atmosphere equipment (3 glove boxes).

Coordinated Instrument Center of Tulane University: The group also has access to the Tulane Coordinated Instrumentation Facility (CIF). Instruments at the CIF pertinent to this proposal include: NMR spectrometer (500 MHz), elemental analyzer, Inductively Coupled Plasma MS, and Gas Chromatography MS.

UNIVERSITY OF MARYLAND (ISAACS)

FACILITIES & OTHER RESOURCES

Laboratory: The Isaacs group laboratories (≈ 1400 sq. ft.) are housed in the newest wing of the chemistry building and comprise bench and hood space for 8 students. This space is fully equipped for the synthetic (e.g. vacuum lines and pumps, rotary evaporators, centrifuge, hotplate stirrers, microwave synthesizer, freezers, lyophilizer, common glassware, etc.) and analytical (Isothermal Titration Microcalorimetry, UV/Vis spectrometer, fluorescence spectrometer, HPLC, thermomixer, capillary electrophoresis) aspects of the proposed research. Adjacent to the synthetic laboratories are two instrument rooms (≈ 600 sq. ft.) for group use.

Clinical: Not applicable.

Animal: Not applicable.

Computer: The Isaacs group computer resources include an iMac and HP Laserjet for PI use. For student use we have an iMac, a MacBook, and an HP printer. The labs are outfitted with wireless internet. These computers run standard word processing, scientific data analysis, graphics creation, and molecular modeling software packages.

Office: Dr. Isaacs' office space is located across the hall from the synthetic labs and instrumentation rooms. Students have desk space adjacent to their respective benches and fume hoods.

Other: Dr. Isaacs research group has access to all of the shared instrumentation facilities within the Department of Chemistry and Biochemistry at the University of Maryland. Most relevant to the work proposed herein are the NMR (800, 3 x 600, 500, 4 x 400 MHz, directed by Dr. Fu Chen), x-ray (single crystal and powder diffraction capability, directed by Dr. Peter Zavalij), and mass spectrometry (ESI, MALDI, FAB, EI, high resolution, directed by Dr. Yue Li) facilities which are directed by Ph.D. level staff members.