2021F_01_WAND

Research Development Fund – Fall 2021

Application Title: Implementation of state-of-the-art hydrogen exchange capability at Texas A&M University

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Key Participating Units: Biochemistry & Biophysics (BCBP-COALS); Chemistry (CHEM-COS); Institute for Biotechnology (IBT); Molecular & Cellular Medicine (MCM-COM)

RDF Amount Requested: $564,649

Executive Summary

Over the past half century, atomic-scale structure has brought into focus a breathtaking view of the structure-function relationships of proteins and nucleic acids. Yet it has become clear that this static picture is unable to capture important aspects of how proteins really work. In other words, insight into the natural structural fluctuations and transitions of biomacromolecules is critical to understanding their function. A powerful lens into the dynamics of proteins is the phenomenon of hydrogen exchange (HX), which is the exchange of amide hydrogens of proteins with hydrogens of water. HX occurs naturally all the time and its details provide unparalleled information about the dynamical fluctuations of a protein which, in turn, inform on critical aspects of its structure, structural stability and ultimately function. Recently, methods to monitor HX by mass spectrometry (HX-MS) have emerged and have led to an extremely powerful version of the HX technology that is impacting almost every aspect of protein centered research. Unfortunately, HX-MS is currently unavailable at Texas A&M University. Recent recruitments to TAMU have captured expertise in HX methods. However, the instrumentation to implement HX in the context of mass spectrometry is lacking. This is a huge opportunity cost that this proposal seeks to remedy. The purchase of a Thermo-Fisher Orbitrap Q Exactive Plus mass spectrometer will greatly leverage on-going sponsored research program studies of structure-function relationships in enzymes and macromolecular complexes, protein-drug interactions, virus assembly and disassembly, protein folding and refolding, allosteric phenomena, protein-protein interactions, and many other fundamental and applied research efforts. This proposal is promoted by over a dozen principal investigators from the Departments of Chemistry, Biochemistry & Biophysics and Molecular & Cellular Medicine as well as the Institute for Biosciences and Technology. The instrument will be placed within the long-standing Protein Chemistry Laboratory in the Department of Biochemistry & Biophysics. Over time, the availability of the HX-MS technology will develop an even broader user base through applications in biomedical engineering and biology and a strong synergy with the emerging cryoEM expansion at TAMU.