

Title: COVID-19 Drug Repurposing Guidance using Fragment Molecular Orbital (FMO) Calculations.

Abstract: In this talk, we share our experiences and updates of a COVID-19 HPC Consortium project (<https://covid19-hpc-consortium.org/projects/5eb5c8784c0571007b307650>). Motivated by the need to rapidly identify drugs that are likely to bind to targets implicated in SARS-CoV-2, the virus that causes COVID-19, we present a framework for Fragment Molecular Orbital (FMO) calculations to speed up quantum mechanical calculations that can be used to explore structure-energy relationships in large and complex biomolecular systems. These calculations are still onerous, especially when applied to large sets of molecules..

We will share our XSEDE ECSS collaboration in assisting with cyberinfrastructure aspects, mechanisms and user interfaces that manage job submissions, data retrieval, and data storage for the FMO calculations. The talk will summarize how we used the Apache Airavata science gateway platform to apply FMO calculations to complexes formed between SARS-CoV-2 Mpro (the main protease in SARS-CoV-2) and 2820 approved and experimental drugs in a drug-repurposing library. The talk will highlight Airavata's job submission and monitoring enhancements to support static and parallel parameter sweeping capability on remote compute clusters across a batch of input data. We will discuss integration of a data parsing workflow to capture, filter out, and validate the enriched metadata from the outputs. Finally, we will discuss generalization of the extensions made in support of large-scale FMO calculations for SARS-CoV-2 Mpro-drug complexes and potential use in other biomolecular systems.

Speaker Bio's

Aaron Frank is originally from Grenada, a small island in the Caribbean. After moving to the US in 2001, Aaron received his BA in chemistry from Brooklyn College in 2006. There he carried out research in the groups of Professors Charlene Forest, Shaneen Singh, and Alexander Greer. He then moved to Michigan to attend graduate school at the University of Michigan and then, with his Ph.D. advisor Professor Ioan Andricioaei, moved to UC Irvine in 2008. Aaron received his Ph.D. in chemistry in 2011. Following a two-year stint at Nymirum Inc. — a small biotech company in Ann Arbor founded by a close collaborator, Professor Hashimi Al-Hashimi — he returned to the University of Michigan as a Presidential Postdoctoral Fellow where he was mentored by Professor Charles L. Brooks, III. Aaron is now an Assistant Professor at the University of Michigan in the Biophysics Department. His research group uses integrative modeling to elucidate structure-function relationships in RNA and guide the discovery and design of RNA-targeting small molecules.

Dimuthu Wannipurage is a Research Software Engineer at Cyberinfrastructure Integration Research Center (CIRC) at the Indiana University Pervasive Technology Institute in Bloomington. He moved to the United States in 2018 from Sri Lanka to work as a full time employee at IU. Before joining CIRC, Dimuthu was involved in designing and developing mission critical middleware systems that are being used by stock exchanges, supermarket chains and transactional reservation systems. He completed his Masters degree at IU in

Intelligent Systems Engineering in 2020. In CIRC, Dimuthu is working as a backend systems architect of the Apache Airavata science gateway framework and SciGaP science gateway platform. In addition to that, he is researching optimized ways to transparently transfer and manage large amounts of data generated by science gateway systems across legacy and cloud storage resources.

Suresh Marru is a Science Gateways Architect within the Cyberinfrastructure Integration Research Center, Pervasive Technology Institute, Indiana University. Suresh is an XSEDE ECSS consultant and a member of the Apache Airavata Science Gateway framework.

Outline

- Problem motivation
 - Pandemic, the impact of COVID
 - Drug discovery for COVID
- FMO Calculations
 - Motivate the computational journey
- Results
 - Current analysis done
 - Future plans
- XSEDE resources
 - Started out on Jetstream
 - Resource estimation & Time estimation
- Stampede2 - covid queue
 - GAMESS code building on Jetstream & Stampede2 (acknowledgement to Kent)
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- Why a gateway is needed
 - PI's stayed focused on the data preparation and inputs
 - Motivate fault tolerance, automated submissions, monitoring
- Needed extensions to Airavata
 - Plans on generalization and merging into airavata master/production
- Summarize experiences
 - What did we learn in support of this project