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Computational Biology for Drug Discovery and Characterization

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Auspices Statement

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FY08 LDRD Final Report
Computational Biology for Drug Discovery and Characterization
LDRD Project Tracking Code: 08-FS-023
Felice C. Lightstone, Principal Investigator

Description

We proposed to determine the underpinnings of a high-throughput computational infrastructure that would support future efforts in therapeutics against biothreat pathogens. Existing modeling capabilities focus on pathogen detection, but extending such capabilities to high-throughput molecular docking would lead to a proactive method to guide the development of therapeutics. This project will focus on determining the feasibility of extending current databases to accommodate molecular docking. We will also examine the feasibility of massive parallelization of docking algorithms and the utility of docking libraries. Transferring this new technique to a high-performance computing (HPC) platform at LLNL would result in a unique capability not available elsewhere in government or industry.

Results

We have accomplished the proposed work defined in this LDRD FS study. 1. We successfully defined the feasibility of using three different small-molecule databases for high-throughput docking, the NCI diversity set, ZINC and the ACD. 2. We analyzed the accuracy and parallelization capabilities of six separate docking programs: DOCK, AutoDock, FlexX, Glide, and eHiTS. Each program is completely amenable to parallel execution. The fastest code was eHiTS, and Glide was the most accurate. 3. Customizing large libraries was cumbersome without the proper software, making the databases a bit difficult to tailor. The ZINC database has some prefiltered versions. 4. Scripts were created for quality and job control functions. Further development is needed for analysis and visualization needs.

FY2009 Proposed Work

The successful conclusion of this project enables LLNL to have a high-throughput computational docking capability where we have evaluated the codes to specific docking problems and utilized LLNL's HPC for significant gains in performance. We have established a CRADA with an industrial partner (funded by the Naitonal Institutes of Health) that will fully utilize this technology for biodefense therapeutic design and development.