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Cheminformatics platform for drug discovery application on Grid

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Overview

To extend the e-Science applications to public health, especially in Asia countries, the EUAsiaGrid in the past two years has establish in-silico high throughput drug screening platform, GAP Virtual Screening Service (GVSS). Providing intensive computing power and effective data management, the production e-infrastructure (such as EGEE and EUAsiaGrid) enables opportunities for in-silico drug discovery on the neglected and emerging diseases, for instance, Avian Influenza and Dengue Fever.
To extend compound 3-D structure database and compound information management. We will created 3D structure conformers of known compounds for in-silico screening and post structure-activity relation analysis.

Impact

We introduce GVSS which is a user-friendly graphical user interface desktop application for using this Grid-enabled virtual screening service. Through the GUI, the end-users can easily take the advantage of GRID computing resources for large-scale virtual screening. Furthermore, they can even upload their own target and ligands, and do the same docking process, visualization and analysis with this GUI, of course including the advanced refinement docking simulations. The end-users can finally have a real GRID-enabled desktop utility for the virtual screening service for their daily research.

To improve the application domain and bridge the gap between experimental and in-silico endeavor, firstly, we will focus on common interest and also the most impact issues of public health. The activity, therefore, can be two approaches aiming to accelerate and optimize the drug discovery process by computing method: firstly, to increase the collection of compound library, so as to extend the present compound structure database; secondly, to execute in-silico to disease target, such as critical proteins in cell wall formation and viral replication pathway. Examples are: penicillin-binding proteins (PbP) for antibiotics development and Non-structure protein (eg. NS3 and NS5) in anti-flavivirus drug development. Validation the computer work with experimental assay is also the focus of this activity. It bridge between e-Science activity and bioscience.

Description of the work

Cheminformatics is able to come into its own as a discipline and as an enabling science. The structured based molecular docking simulation is a common method for predicting potential interacting complexes of small molecules in protein binding site By promoting the integration of data, applications and workflows, it is providing scientists with broad access to information and methods. As cheminformatics systems become more prevalent, we can expect them to appreciably enhance our use of previous knowledge and our ability to generate new knowledge –significantly improving the drug discovery and development process.

However, Massive molecular docking required intensive computing power and effective data management. A GRID computing framework was established for AutoDock 3.0.5 and evaluated for its ability to process large-scale molecular docking. GRID is an ideal environment, which can provide large-scale and on-demand resources, including computing and storage resources.

Inspired by the successful experiences on Avian Flu Data Challenges, ASGC developed the GVSS application package that incorporates the EGEE gLite middleware DIANE2 and AMGA. Therefore, ASGC coordinated the Dengue Fever Data Challenge via EUAsiaGrid VO in June 2009. The objective is to utilize the grid enabled high throughput screening for structure–based computational methods to identify small molecule protease inhibitors. In addition to ZINC CDI 300,000 compounds library we used, we establish the new ZINC 800,000 ligands and Chembridge 300,000 ligands, the free database of available compounds library, were selected for virtual screening.

Conclusions

Molecular docking simulation is a time consuming process to search exhaustively all correct conformations of a compound. However, the massive in silico processes benefit from the high throughput computing grid technology. Providing intensive computing power and effective data management, the production e-infrastructure (EUAsia VO) enables opportunities for in silico drug discovery platform. We deployed this high throughput in-silico massive molecular docking service benefits from state-of-the-art Grid technology to the activities for designing the cheminformatics platform on EUAsiaGrid infrastructure since 2010. Furthermore, these activities also facilitates more biomedical e-Science applications, such as other diseases and compounds profiling.

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