Chapter 9

Conclusion and Further Work

9.1. Introduction

Based on the evaluation strategy and the recorded experimental results from previous Chapter; this Chapter discusses about the Conclusion of this thesis by interpreting the results derived from evaluation. The discussion continues further by describing the achievement of project objectives, solutions provided for the problems encountered along with possible further enhancements worth doing as a continuation of the project.

8.7. Conclusion

I have executed the molecular simulation 20 times for the known ligand-protein pairs and compared it to the actual time taken for the manual molecular docking. The experiment results derived based on two scenarios as follows:

- Time for the docking: By comparing the time taken for the manual docking process with the time taken for the automated molecular docking, it says the software tool can obtain 95% accuracy
- Accuracy: It has 80% accuracy by considering the prediction of the correct actual existence of the docked molecules according to the energy calculations

Unlike the established approaches following to develop molecular docking such as manual methods, the agent-based approach doesn't require developing algorithms to simulate the different steps of the molecular docking.

Further the information embedded in these rules for a given individual agent needs not to be completed. Each individual agent in the molecular docking simulation will always discover something which was earlier unidentified because of the knowledge sharing, with other individuals via message passing. The interesting thing is this tool can be used to discover new drugs for the selected protein targets. Some drugs can be effective for the selected proteins unexpected.

This tool could successfully exhibit multi-agent system characteristics such as autonomy, deliberation, communication and negotiation. Protein, Ligand, Shape

Determination and Energy Calculation agents are sharing their knowledge to come up with new docked molecule. NanoAgent system could exhibit self-organization as well as other control models and associated composite activities. The results suggest that the Multi-Agent Systems technology could be successfully applied to automate the manual molecular docking process, which is an inherently complex process.

8.8. Achievement of the Objectives

With respect to the aim and objectives listed for this project (under Section 1.2); core concepts behind the development of automated molecular docking tool and significant observations from real world scenarios related to manual molecular docking are discussed inside the literature review of this thesis (provided in Chapter 2).

The solution to the multi-agent system based automated molecular docking tool is described in detail under the design chapter of this thesis (refer to Chapter 5). Further implementing related details of the docking tool are discussed under the implementation chapter of this thesis (refer to Chapter 7). Results obtained from the simulation sessions of the molecular docking are validated against observations recorded from real world manual docking scenarios within the evaluation chapter (i.e. Chapter 8) of this thesis. Finally, Chapter 9 (i.e. the main Conclusion) managed to prove the hypothesis of this thesis (stated under section 5.2) while describing on how to use the proposed design of the multi-agent molecular docking system.

The results expressed that the Multi-Agent Systems technology can be successfully used to automate the manual molecular docking. So the aim of this research work could be successfully achieved with their mentioned objectives as follows:

1. Able to critically study the molecular docking domain with a view to identify current practices and the issues in molecular docking
2. Critically analyzed and did a comprehensive evaluation of the existing software solutions in molecular docking with a view to define the research problem and possible technology
3. Did in depth study about Multi-Agent Technology and its applications
4. Designed and implemented Multi-Agent System for Molecular Docking.

5. Evaluated the accuracy of the Multi-Agent System based molecular docking tool by entering known existing ligands and protein pairs

The results suggest that the Multi-Agent Systems technology could be successfully applied to automate the manual molecular docking. With this tool, it is better to have animated transition of the molecular docking process that associate with each step of the entire process. So this tool is lacking the presentation of the docking process step by step.

9.2. Further Work to Improve Molecular Docking Tool

The main focus throughout this thesis was about simulating automated molecular docking process by developing a computer simulation tool using multi-agent systems technology. Artificial Neural Network is amazing technology, which can be applied to improve this software tool. If we can implement this tool with a trained artificial neural network for the results of pre docking processes of known protein-ligand pairs, it will be helpful to improve the performance and the accuracy.

Even if it discovers the ligand-protein pairs it is essential to perform a test for identification of possible poisonous of drugs using experiments. But it is a not economically effective and not efficient procedure that needs actual living beigns testing. First, we can use this software tool and have to verify it by doing proper clinical trials.

The most significant types of docking systems are protein-ligand and protein-protein. In this research I have addressed only protein-ligand docking. But it can be improved for the other two categories too. However, the reduced efficacy of the existing scoring functions I have used for the docking tool, is the biggest barrier, which obstructs the improvement of the molecular docking method.

9.3. Summary

In this chapter presented the conclusion and the future work associated with this research work. There is clearly much work to be done in the area of automated molecular docking using multi-agent system technology to improve the quality and the accuracy of the software tool that I have developed for this research work.

This thesis addressed the application and benefits behind proposing a multi-agent based solution for automated molecular docking process. Further, it has been proven that the multi-agent based prototype is able to provide identical results during a simulation of ligand-protein binding process simulation, comparing with statistics recorded on real world manual molecular docking scenarios. The major advantage derived here over the conventional approaches is that the multi-agent based approach doesn't require waiting until complete one step in the docking process. Instead, through communication (i.e. passing messages) and unplanned knowledge sharing between the agents, the multi-agent based approach is able to emerge uncertain drug discoveries for the selected decease proteins.

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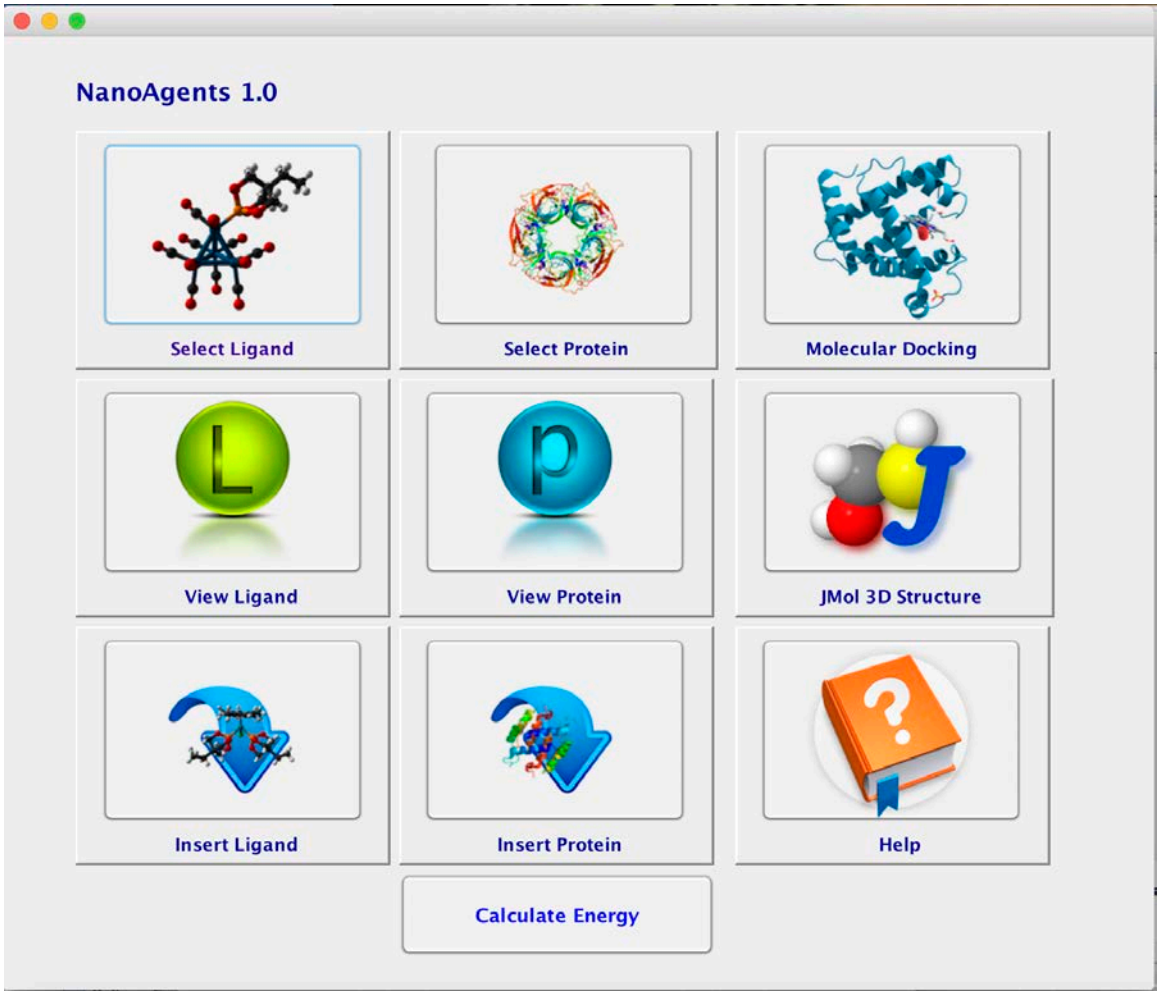
Appendix A

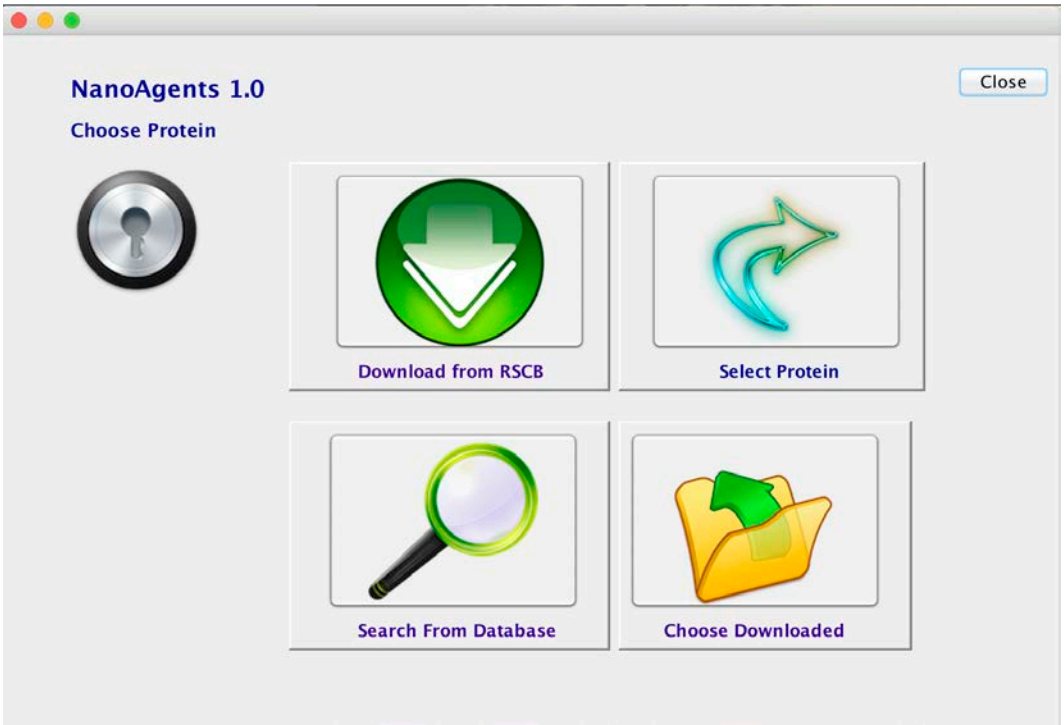
MAS Based Molecular Docking Tool

A.1 Screenshots

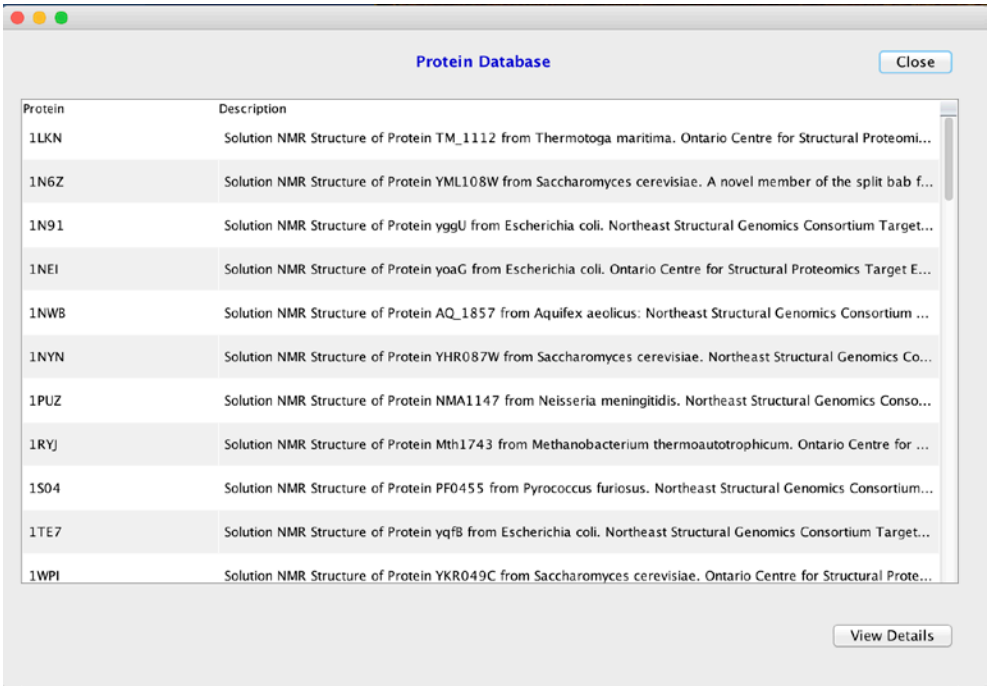
Following diagrams shows the main functions of the molecular docking tool.



Following diagram shows the dashboard for choosing the protein from the existing database, search protein if you know the name or download pdb files from the RCSB Protein Data Bank.

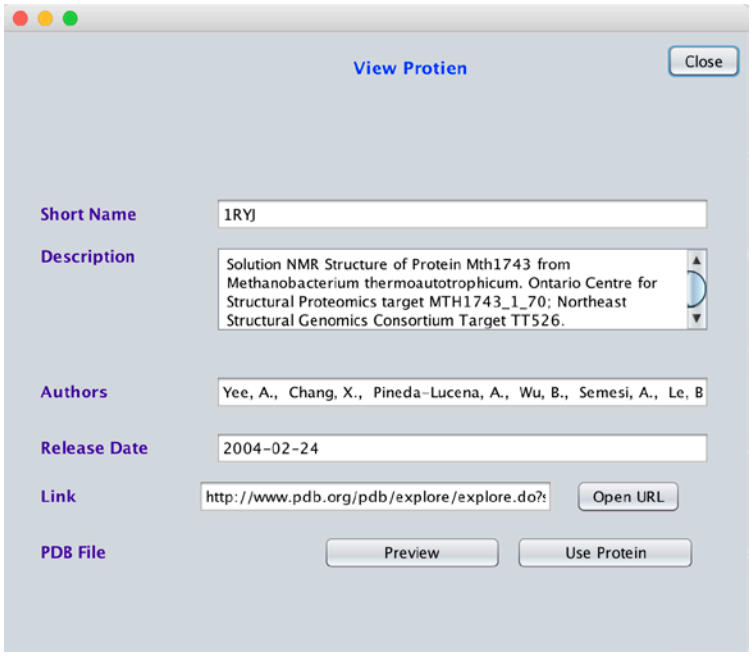


Following diagram shows the list of proteins retrieved from the local database.

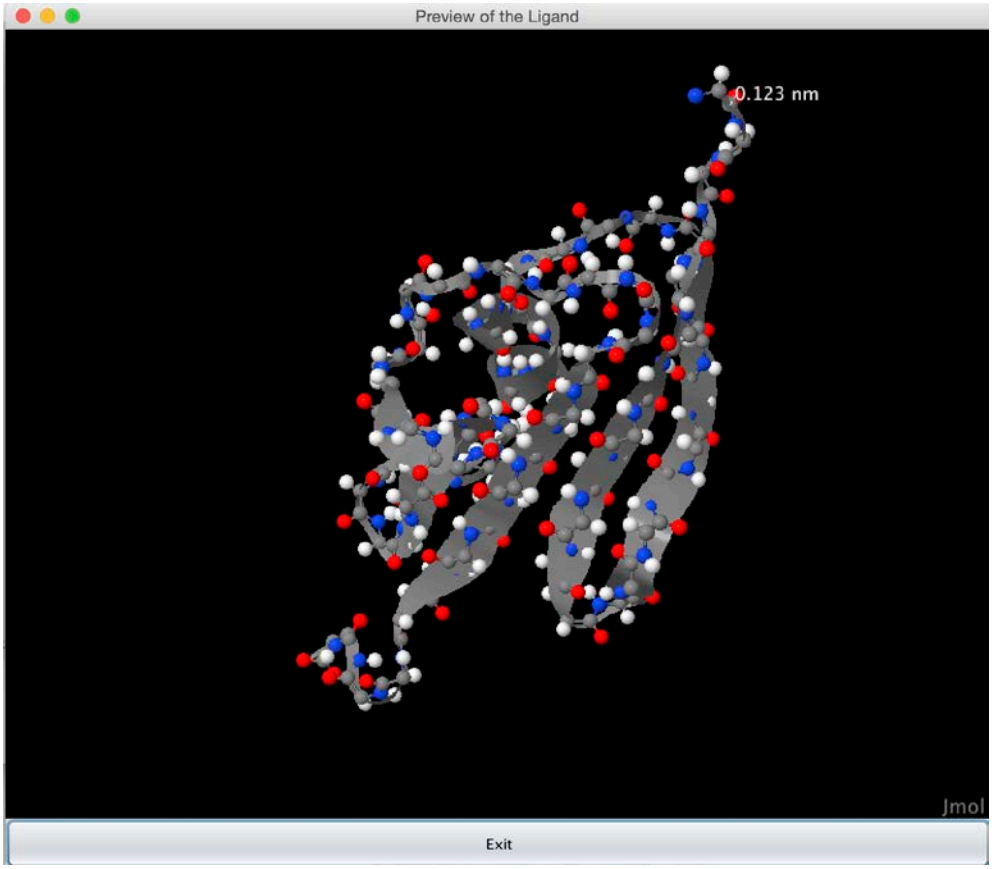


User can select one from the list and view the details and also can use it for the docking. It has the feature to preview the 3D structure before applying it for the docking.

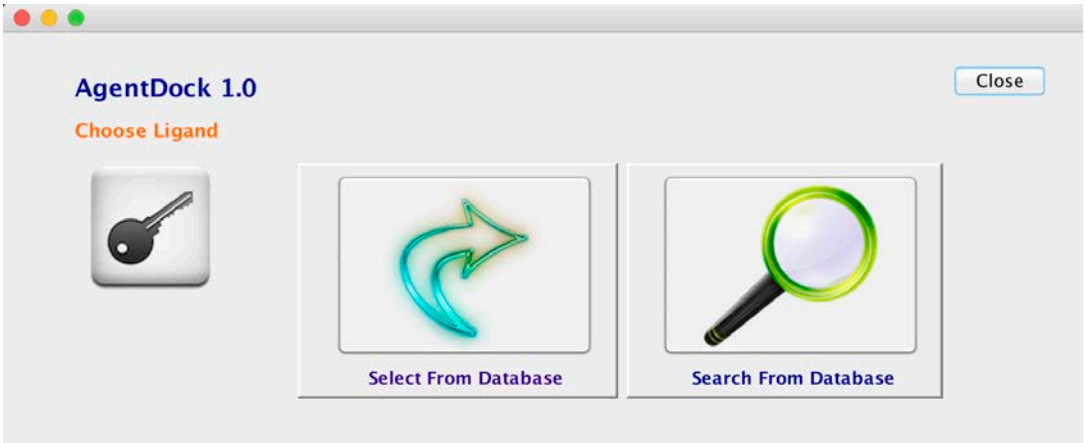
User can see more details from the PDB online database by clicking on the “Open URL” button.



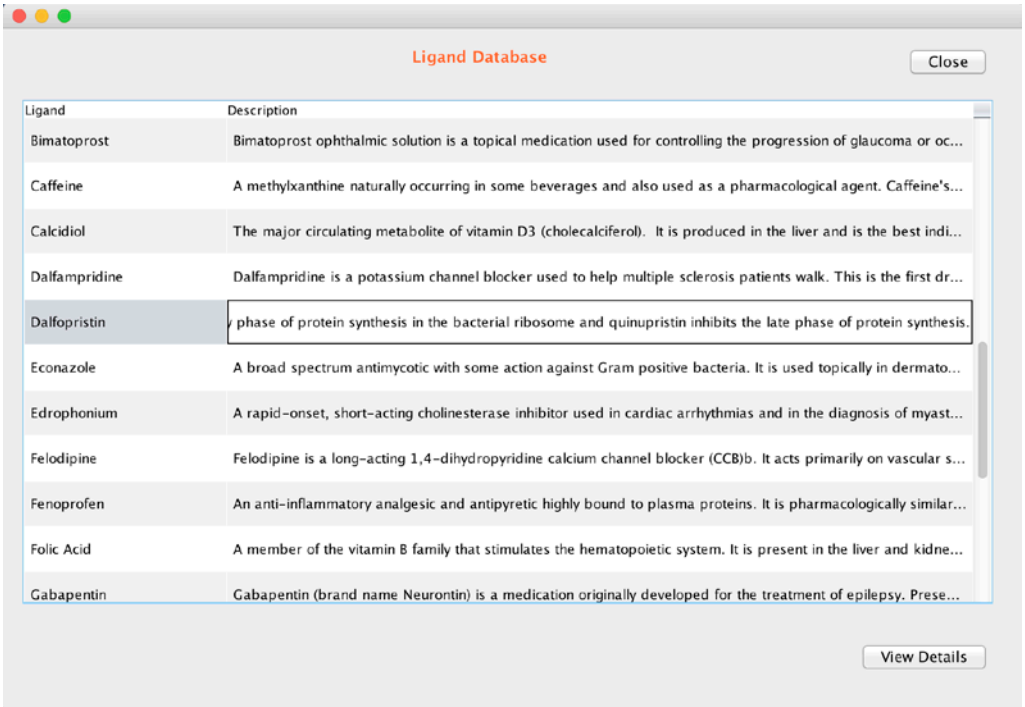
Following diagram shows the 3D preview of selected protein.



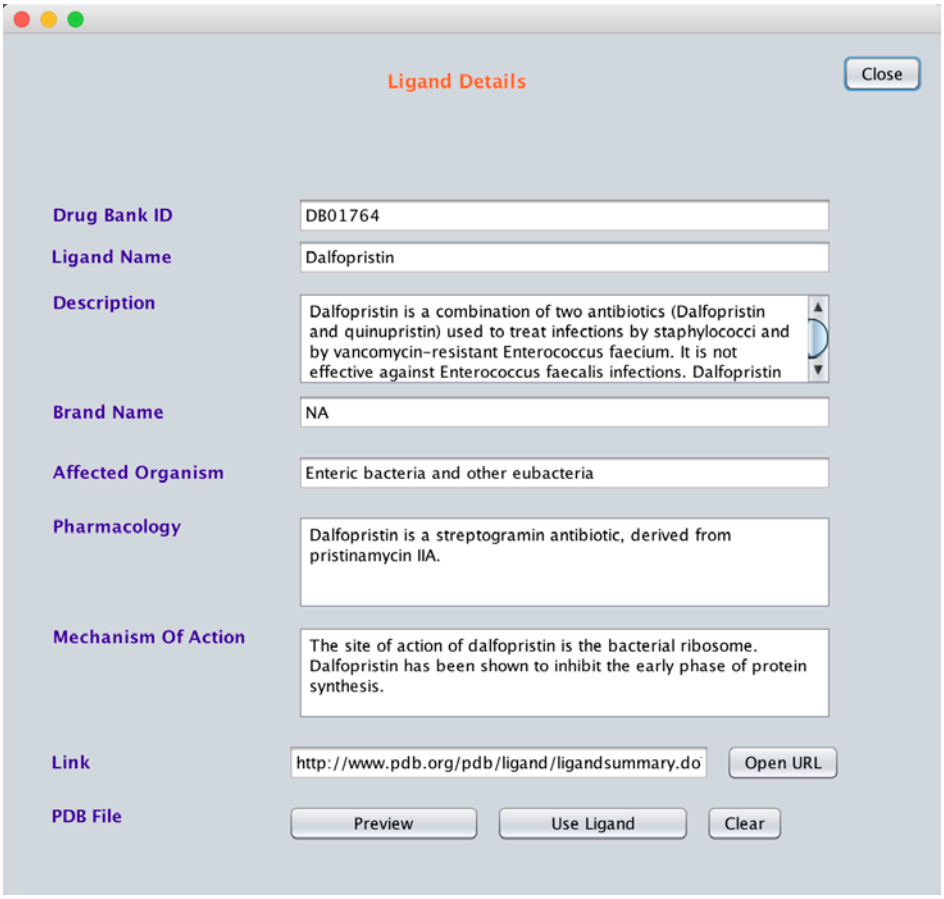
AgentDock has a dashboard to select a ligand from the database that the tool has.



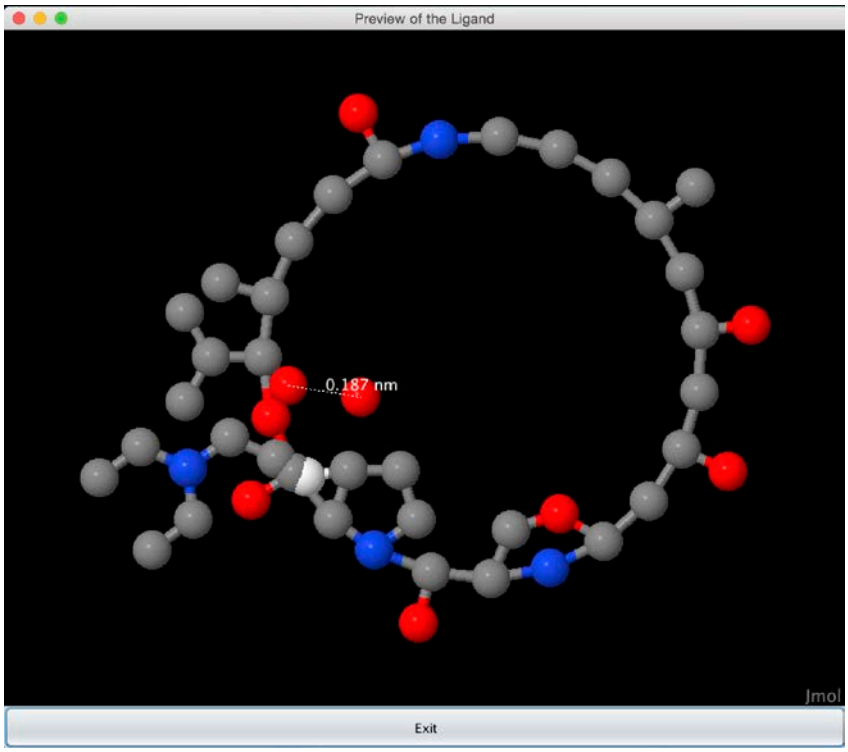
Following diagram shows the list of available ligands in the database.



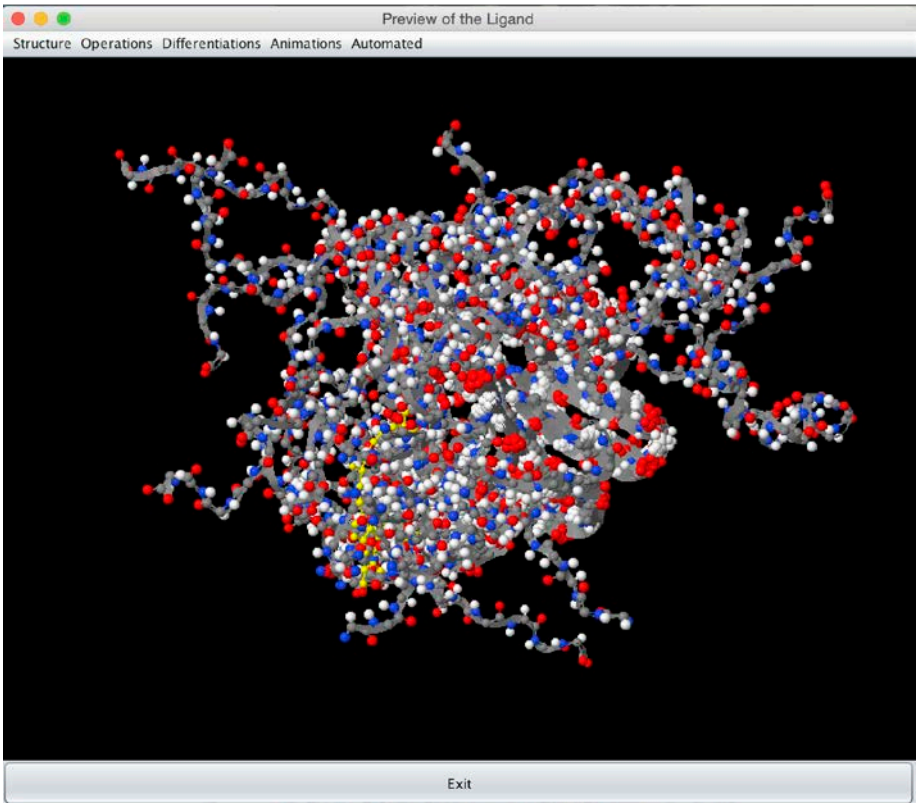
User can view more details by selecting the required ligand and also can preview it before apply it for the docking.



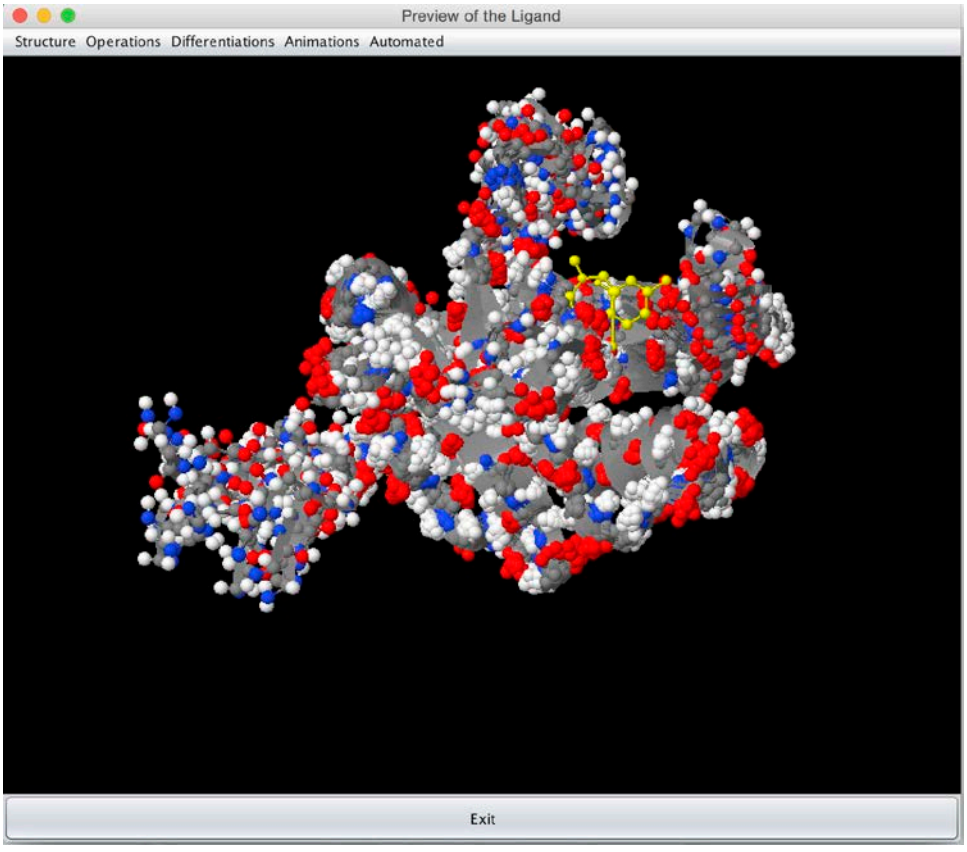
Following figure shows the selected ligand 3d structure preview.



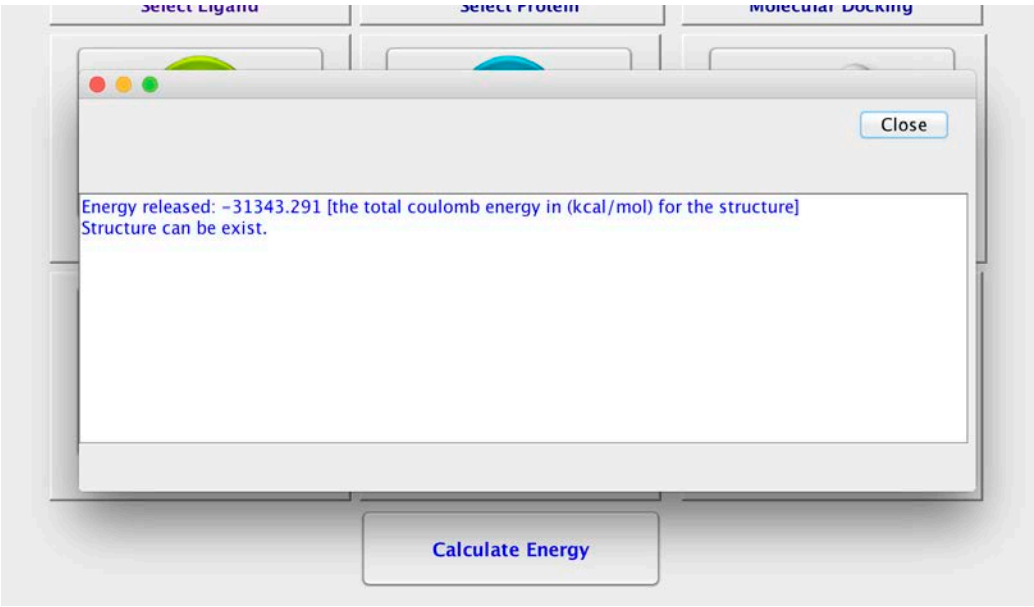
Following diagram shows the result after the molecular docking.



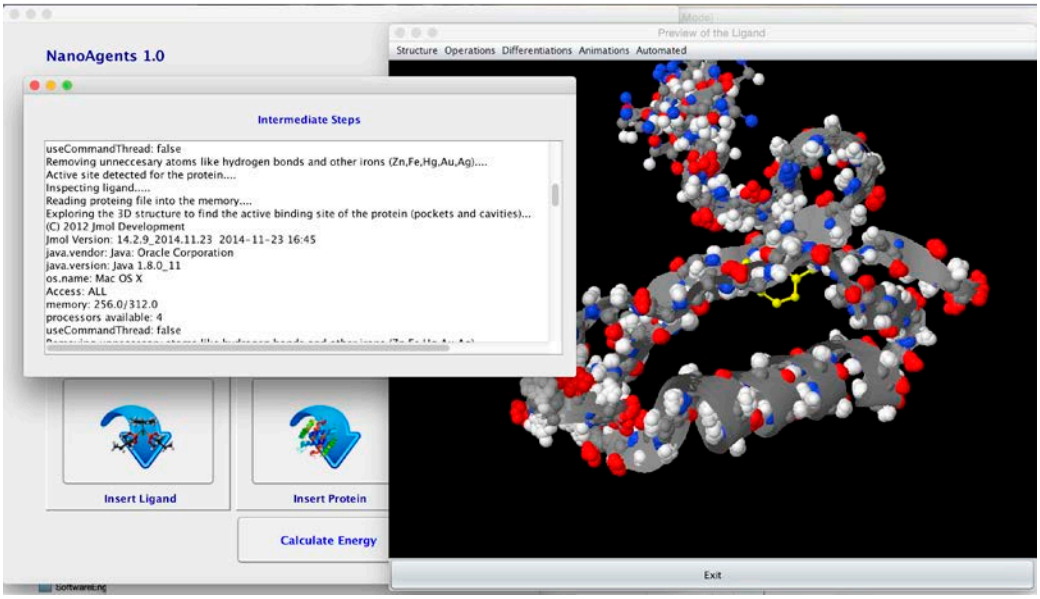
Another docked molecular result shows as follows (yellow color molecule represents the ligand)



Energy calculation feature shows the actual existence of the docked molecule using Python component for the energy calculations.



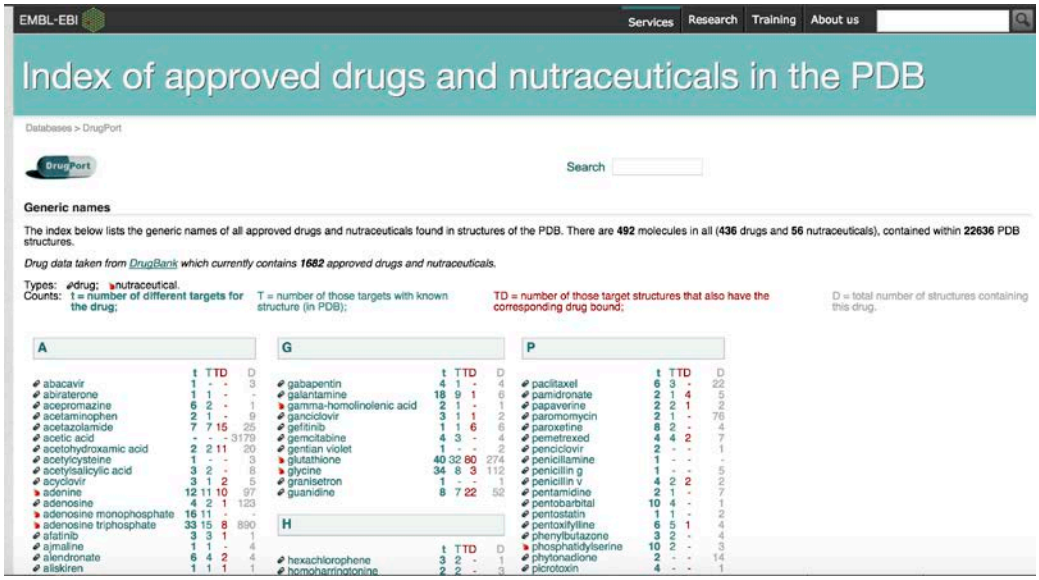
Intermediate steps can be viewed in a separate window as logs.



Appendix B

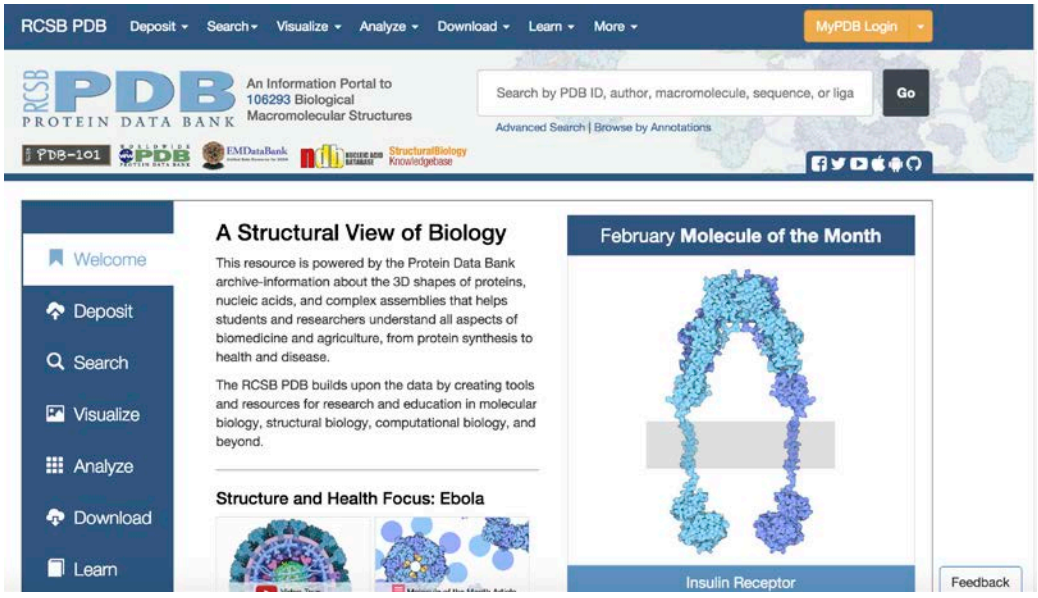
Free Databases and Ontologies

B.1 Ligand Database



The index below lists the generic names of all approved drugs and Nutraceuticals found in the structures of the PDB. There are 493 molecules in all (437 drugs and 56 Nutraceuticals), contained within 22935 PDB structures. Drug data taken from DrugBank [34], which currently contains 1682 approved drugs and Nutraceuticals.

B.2 Protein Database



This resource, is powered by the Protein Data Bank archive-information about the 3D shapes of proteins, nucleic acids, and complex assemblies that helps students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease.

B.3 Atom Ontology

Dumontier Lab provides free chemistry ontologies. Their research has significant implications for basic science, drug discovery, and health care. Their investigations into the dynamics of biochemical transformations will lead to improved identification of drug leads, thereby reducing the time and cost of drug discovery [83]. Following diagram shows the ontology in Protégé.