CAVER Viewer - the explorer of behaviour of tunnels in proteins

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Abstract

Protein exploration in order to discover new medication has been the principal aim of biochemists. In combination with informatics the solution of this task can be faster, more accurate and also more intuitive and straightforward in comparison with traditional methods. Our CAVER Viewer application allows the exploration of protein structures and the visualization of results. It enables to find certain paths from the outer space around the molecule to the specific site inside the protein called the active site. The existence of these important paths (also called tunnels or channels) is crucial in the process of transferring some small molecule of substrate into this active site. Namely, the substrate enters the active site via these precomputed tunnels. There the chemical reaction between the substrate and protein can undergo. The product of this reaction can form the basis of a new medication.
This poster describes the key aim of our research in the field of protein visualization, when we have to visualize the protein dynamics - movements of the molecule as well as the behaviour of its tunnels in time space.

Categories and Subject Descriptors (according to ACM CCS): I.3.7 [Computer Graphics]: Three-Dimensional Graphics and Realism—Visible line/surface algorithms

1. Introduction

Exploration of protein behaviour has been one of the main scopes of interest of biochemists. This process is usually very tedious. However, some parts of the whole process can be facilitated using some precomputations. The involvement of computational power can shorten the time of the whole analysis from months to hours.

Our task is to precompute potential paths leading from the outside of protein molecule into its active site (see Fig. 1). These paths called tunnels are subsequently used for transportation of a small molecule (substrate) into the active site, where the chemical reaction between protein and substrate can undergo.

Nowadays there are many applications concerned with various chemical problems. But none of them is suitable for visualization of molecular dynamics in connection with tunnels. For example, PyMOL application [DeL02] is very powerful tool for molecular visualization and using the PyMOL plugin of the CAVER algorithm we are able to visualize tunnels using various methods.

However, PyMOL is not suitable for visualization and analysis of large sequences of molecular dynamics (thousands of snapshots). Another application, VMD [HDS96], can handle with many snapshots, but it is not prepared for tunnel computation.

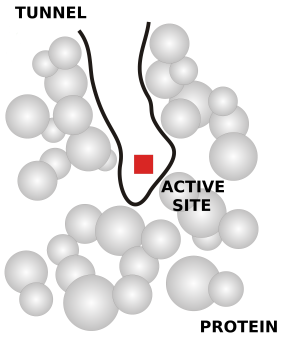

Figure 1: *Tunnel leading to active site.*

2. Tunnels

In the first phase the analysis leading to tunnel computation was performed on the static molecule. Tunnels were computed using the CAVER algorithm described in [DPBO07]. Its improved version [MBS07] uses Voronoi diagrams for computation and the main criterion for the evaluation of tunnel quality is its minimal width (see Fig. 2). In the subsequent research several new evaluation techniques were invented, involved and tested (see [MBS08]). Using these new

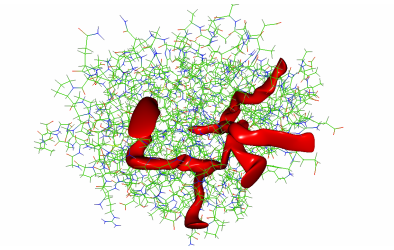

Figure 2: *Static molecule of DHaa protein with five best tunnels.*

algorithms we are able to compute any number of tunnels in various static molecules. Thus, we can compute tunnels in the sequence of snapshots, which represents the dynamic movement of protein molecule (see Fig. 3).

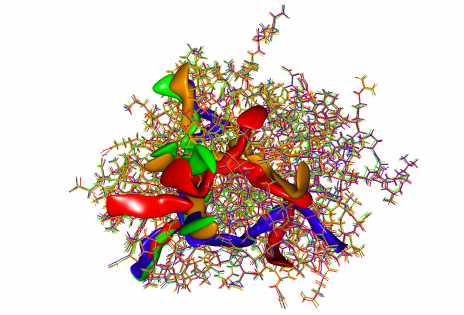

Figure 3: *Sequence of four snapshots, in each of them five best tunnels are computed (for illustration all the snapshots are visualized at once).*

3. Protein Dynamics

In molecular dynamics the computation of tunnels is not so straightforward as in the static case. The correspondence between tunnels in all snapshots must be taken into consideration. The algorithm solving this problem is described in [BMS09]. Our next task is to visualize this information.

In the current version of CAVER Viewer application the evolution of one tunnel in time space is visualized without any interpolation, just as the sequence of independent tunnels. In the Figure 4 you can observe one tunnel computed in four subsequent snapshots. All four configurations of the tunnel are displayed at once so we are able to see that three of them are quite similar but the fourth (red one) has slightly different shape in the region near to the molecular surface.

So our next challenge is to find methods for the continuous visualization of one tunnel in the time space. We also have to deal with the fact that many tunnels are closing and reopening during the simulation. This information has to be plausibly presented to the user via the CAVER Viewer application.

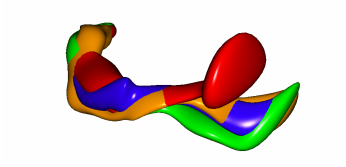

Figure 4: *One tunnel computed in four successive snapshots.*

3.1. Summary and Acknowledgments

The whole process of tunnel visualization in protein dynamics includes the following tasks:

- For each protein snapshot compute tunnels with required properties.
- Find the correspondece between tunnels throughout the whole sequence of snapshots.
- Visualize the tunnel evolution and reveal interesting properties and statistics.

Currently we are working on methods for the third task.

This work was supported by Ministry of Education of The Czech Republic, Contract No. LC06008 and by The Grant Agency of The Czech Republic, Contract No. P202/10/1435.

References

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