Visualizing movements of protein tunnels in molecular dynamics simulations

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Abstract
Analysis and visualization of molecules and their structural features help biochemists and biologists to better understand protein behavior. Studying these structures in molecular dynamics simulations enhances this understanding. In this paper we introduce three approaches for animating specific inner pathways composed of an empty space between atoms, called tunnels. These tunnels facilitate the transport of small molecules, water solvent and ions in many proteins. They help researchers understand the structure-function relationships of proteins and the knowledge of tunnel properties improves the design of new inhibitors. Our methods are derived from selected tunnel representations when each stresses some of the important tunnel properties — width, shape, mapping of physico-chemical properties, etc. Our methods provide smooth animation of the movement of tunnels as they change their length and shape throughout the simulation.

Categories and Subject Descriptors (according to ACM CCS): I.3.7 [Computer Graphics]: Three-Dimensional Graphics and Realism—Animation

1. Introduction
Molecular analysis and visualization are currently two of the most interesting and important areas in biochemistry. Researchers more often analyze molecular dynamics (MD) simulations rather than static molecules, as the results are more biochemically relevant. This involves analyzing and displaying hundreds of thousands of atoms in order to reveal important features of protein molecules. While the analysis leading to the detection and categorization of the protein inner empty space can be very time and memory consuming, the visualization of results should be performed at interactive frame rates in order to make the visual analysis applicable.

The protein empty space can be categorized with respect to its shape and other properties. We distinguish between cavities, tunnels, channels, pores and pockets. Due to intrinsic protein dynamics, these specific inner void structures change their shape and properties over time [KM02, CPB∗12, KPK∗09]. The detection and visualization of these structures can facilitate the study of important biochemical phenomena as well as designing effective drugs or new catalysts [PGB∗12, PKC∗09, KCB∗13, GBD13]. The design is mostly based on the study of chemical reactions between proteins and small ligand molecules. These reactions take place in a specific cavity called an active site. Thus, studying the entrance pathways leading to the active site has been in the scope of researchers over the last years.

In this paper we concentrate on the description of our novel techniques for animating tunnels in molecular dynamics. We discuss three different tunnel representations emphasizing different tunnel properties, such as tunnel width, shape and physico-chemical properties.

2. Related Work
Several geometric solutions for the detection of protein pathways and inner cavities appear in literature. Numerous algorithms for detecting and visualizing molecular cavities appeared as far back as several decades ago, e.g., in [HM90, AW91, Del92]. Cavities can be detected using different approaches — a grid algorithm described, e.g., in [VG10], an approximation algorithm [SNW∗96] or a space partitioning structure, e.g., the Delaunay triangulation (DT) applying the alpha-shape [LWE98] or beta-complex [CKW∗11] theory. The existing visualization techniques presenting the computed inner structures primarily concentrate on cap-