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Extended Abstract

Journal of Computational Methods in Molecular Design, 2020, 10(1)
https://www.scholarsresearchlibrary.com/journals/journal-of-computational-methods-in-molecular-design/

ISSN 2231-3176

Water tracking as an alternative method for tunnels search in proteins core

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In past years, a number of tools for porous, tunnels and pathways identification in macromolecules were developed. The most current ones like CAVER 3.0 or Mole 2.0 can facilitate evaluation of molecular dynamic (MD) simulations and permit gathering unique records about the geometry of detected pathways and their prolongation in time. However, the noted strategies use a spherical probe for tunnels exploration, consequently presenting an approximation of tunnels to tubes with symmetrical diameter instead of a actual tunnel pictures. Moreover, the understanding of geometrical houses of existing tunnels can solely propose ways of solvent or ligands molecules entry/exits. It is challenging to estimate what are the principal elements controlling the solvent flow: tunnel diameter, the size of the tunnel, and the residences of amino acids that build the tunnel. It is additionally uncertain how lengthy the tunnel wants to be detected as an open one to grant access for the favored molecule. In principle, MD simulations supply such information. Simulated protein is immersed in the water container and for the duration of the complete simulation, water molecules penetrate the protein core. However, the identification and tracking of water molecules which enter areas essential for catalysis, require screening of the function of lots of dozens of single molecules alongside with numerous thousands of MD steps. To facilitate analysis of the conduct of water (and if critical other solvent molecules or ligands), we have developed aquaduct. Here we would like to furnish an example of its utilization for evaluation of water transportation in chosen enzymes, which lets in defining the water penetration pathways at once and in an effortless way distinct the substrate and water pathway. Enzymes grant their carrier immersed in a solvent that contributes to catalyst stability, activity, and selectivity. In enzymes with a buried active site and linked to the surrounding solvent by means of tunnels, the solvent flux can be managed much greater exactly via the molecular homes of amino acids constituting tunnels, or in greater sophisticated enzymes by gates controlling the opening and closing of the access pathways. Information involving the trade of solvent molecules between the protein core and a cumbersome solvent is embodied in the effects of molecular dynamic (MD) simulations. However, due to the requirements of the simultaneous tracking of many thousand interactions, the consequences for specific molecules are challenging to access. To the great of our knowledge, there is no universal software that should facilitate this type of analysis. Existing strategies grant solely visual information related to water site visitors or use an advanced approach to direct the water glide in a unique direction. Other current tools can provide records about the geometry of possible tunnels, however, considering there are disregarded chemical houses of amino acids, the detected pathways do not have to correspond to their genuine usage. AQUA-DUCT (AQ) is filling this hole and facilitates the evaluation of the movement of any small ligand(s) in the course of MD simulations.

AQ is a device for tracing, analyzing, and visualizing molecular trajectories at some stage in MD simulations. Calculations in AQ are divided into 6 stages, which include statistical analyses and subsequent visualization. During the first stage, a list of all the molecules to trace is created. This is performed via screening the complete trajectory for molecules that enter a user-defined region of interest, the so-called object region of the macromolecule. AQ then traces molecules only inside the second user-defined region, i.e. the scope region which typically encompasses the complete macromolecule. The second stage of calculations relates the list of all traceable molecules to summary coordinates at the middle of hundreds for each molecule in all frames of the MD simulation. This result, saved as a listing of raw paths, is used in the third stage of calculations to create a listing of separate paths. Each path involves facts for one molecule. A molecule may enter and depart the scope and the object areas many times over an whole MD simulation. Each event is considered via AQ to be a separate phenomenon and is thus represented via a distinct separate path. However, the ID and variety of occurrences are retained and can easily be retrieved.

Bottom Note: *This work is partly presented at 10th Edition of International Conference on Structural Biology* March 15-16 2018 Barcelona, Spain