

Interactive poster: visualizing the interaction between two proteins

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Introduction

Protein docking is a fundamental biological process that links two proteins in order to change their properties. The link is defined by a set of forces between two large areas of the protein boundaries. These forces can be classified in two categories:

- The Van der Waals (VdW) forces, corresponding to the geometrical matching of the molecular surfaces [1].
- Other forces, including hydrogen bounds, induction, hydrophobic effects, dielectric effects, *etc.*

Two docked proteins are very close to each other due to the VdW forces. This makes the understanding of the phenomenon difficult using classical molecular visualization. We present a way to focus on the most interesting area: the interface between the proteins.

Visualizing the interface is useful both to understand the process thanks to co-crystallized proteins and to estimate the quality of docking simulation result. The interface may be defined by a surface that separates the two proteins. The geometry of the surface is induced by the VdW forces, while other forces can be represented by attributes mapped onto the surface. We present a very fast algorithm that extracts the interface surface.

Moreover, the result of a rigid docking simulation can be improved using the flexibility of the residues. We show how the interface surface geometry and attributes can be updated in real-time when the user interactively moves the residues. This way, we allow expert knowledge to be intuitively introduced in the process to enhance the quality of the docking.

Interface extraction

The interface can be defined as the iso-0 of a 'distance to molecule' function defined as follows :

$$dist(X) = dist_to_protein_A(X) - dist_to_protein_B(X)$$

While classical approaches extract this iso-surface using a greedy algorithm [2], we propose to speed-up the process using a Delaunay tetrahedrization.

The Delaunay tetrahedrization is computed by CGAL [3] using all atoms as vertices (see figure 1). The

interface is then extracted using a marching tetrahedra algorithm (see figure 2).

As illustrated in figure 3, slicing the surface along the tetrahedrization edges enables to interactively move the interface between the molecular surfaces of the proteins.

Mapping attributes

It is possible to map on the interface several attributes characterizing the potential interactions both qualitatively and quantitatively.

Remember that each vertex of the interface is on an edge of the tetrahedrization, joining a pair of atoms belonging to each protein. The Delaunay tetrahedrization ensures that these atoms are the closest ones to the interface vertex. This property makes it very easy to extract local information about docking possibilities around each vertex of the interface.

In our experiments (see figure 4), a quantitative attribute and a qualitative attribute have been tested :

- The distance to the proteins.
- The kind of potential residues interaction: hydrogen link, hydrophobia link, $\text{Pi}\dots\text{X}$, $\text{Pi}\dots\text{Pi}$, same charge and opposite charge are represented by symbolic colors.

As in the MolSurfer application, electrostatic potential and hydrophobia can also be used as attributes.

Interactive modifications

The interface extraction presented above is very fast (about 1 second), but not enough to enable interactive surface extraction. The most time consuming step is the tetrahedrization algorithm, whose complexity is $O(n.\log(n))$. Fortunately, it is possible to dynamically remove and insert vertices from such a tetrahedrization.

The interface can be updated in real-time when a small part of the protein (like a residue) is moved. At each frame, each vertex of the residue is removed from the tetrahedrization and inserted back with its new position; the new interface is then extracted. The whole process takes less than 0.1 second.

Acknowledgments

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References

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[3] A. Fabri, G.-J. Giezeman, L. Kettner, S. Schirra, S. Schönherr. On the design of CGAL, the computational geometry algorithms library. *Software - Practice and Experience*, Vol. 30, 1167-1202, 2000.

[4] <http://www.embl-heidelberg.de/~gabdoull/ads/imap/>

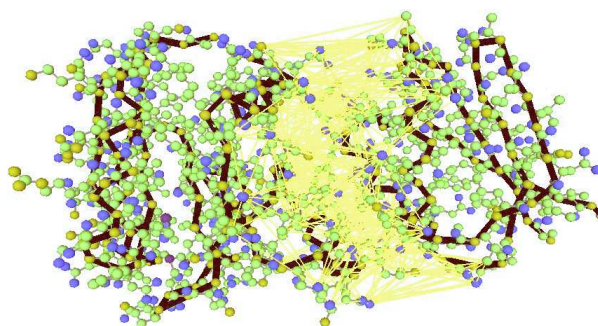


Figure 1: Delaunay tetrahedrization.

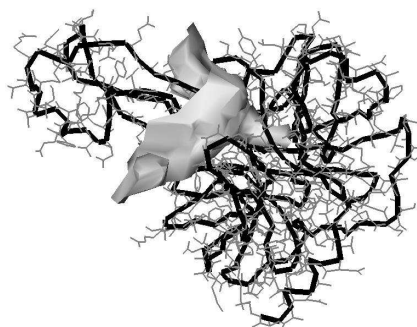


Figure 2: Interface extraction.

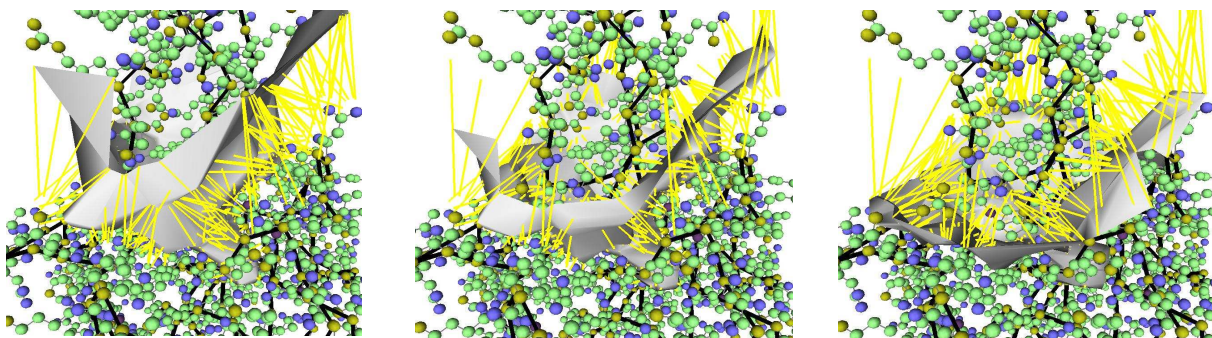


Figure 3: Slicing the interface. Left : the interface is snapped to the first protein. Middle : the interface is equidistant to both proteins surfaces. Right : the interface is snapped to the first protein.

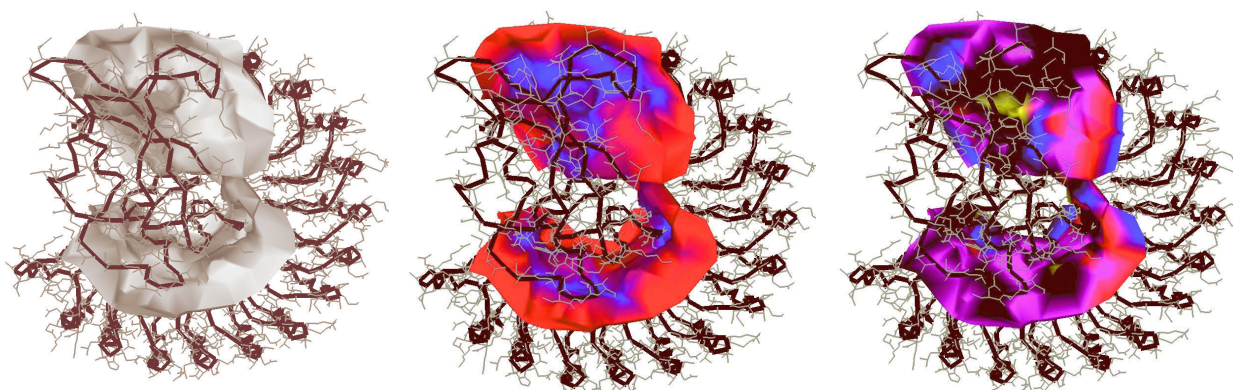


Figure 4: Mapping attributes. Left: interface. Middle: distance map. Right: kind of residue interaction.