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Meshing molecular surfaces based on analytical implicit representation

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ABSTRACT

We develop an algorithm for meshing molecular surfaces that is based on patch-wise meshing using an advancing-front method adapted to the particular case of molecular surfaces. We focus on the solvent accessible surface (SAS) and the solvent excluded surface (SES). The essential ingredient is a newly developed analysis of such surfaces in [18] that allows to describe all SES-singularities a priori and therefore a complete characterization of the SES. In addition, an algorithm for filling molecular inner holes is proposed based on the pre-computed data structures of molecular surfaces.

1. Introduction

Many fields of research like chemistry, biochemistry, physics and biomedicine work with molecular surfaces. For example, the majority of (bio-)chemically relevant reactions take place in the liquid phase and the effect of the environment (solvent) is important and should be considered in one way or the other in the model. As an alternative to the way of taking solvent molecules explicitly into account, various implicit solvation models have been proposed in which the molecular surface of the solute is a part of the model and constitutes the interface of the atomistic and the continuum model [1]. A second field where the notion of molecular surface is important is simply the visualization of molecules.

In the simplest model of a molecular surface of the solute or a molecule in general, each constituting atom is idealized by a simple sphere with its Van der Waals (VdW) radius. The boundary of the union of these VdW spheres is the so-called VdW-surface.

Besides the VdW-surface, two other kinds of molecular surfaces are commonly used in solvation models or in molecular visualization: the solvent accessible surface (SAS) and the solvent excluded surface (SES) [2]. Since the VdW-surface and the SAS are both the topological boundary of the union of spheres, their geometric features are therefore easier to understand. However, the SES, which sometimes performs better in a chemical calculation [3] or is more suitable for applications like docking [4], is more complicated.

1.1. Previous works

The definitions of the SAS and the SES were first introduced by Lee and Richards [5,6] in the 1970s. The SES is also called the "smooth molecular surfaces" or "Connolly's surfaces" due to Connolly's fundamental calculation on it [2]. Indeed, the SES can be considered to be the prototype for the computational study of molecular surfaces. This surface model has been applied to a very large variety of problems and has also been used to compute solvation energies with continuum solvation models [1,3,7].

Latter, Michel Sanner developed the reduced surfaces and proposed the MSMS (Michel Sanner's Molecular Surface) algorithm for computing an (in fact approximately) analytical representation of the SES [8]. The MSMS algorithm can also provide a triangulation

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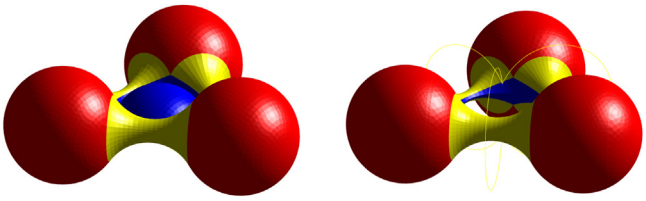

Fig. 1. The SES of a three atomic system with the self-intersection problem between two concave spherical patches (left, triangulation provided by the MSMS-algorithm) and the SES with a singular circle on the concave spherical patches (right, triangulation provided by our algorithm).

of the SES with a user-specified density of vertices. Although it can not deal with all self-intersections between different patches of the SES (see Fig. 1 for an example where self-intersection occurs), the MSMS algorithm is now one of the most widely-used packages of molecular surfaces.

Besides, there are many other contributions on the molecular visualization [9–13], high-quality meshing [14] or the calculation of molecular areas and volumes [15–17]. However, a computable analytical implicit representation of the SES and a complete characterization of all SES-singularities remained unsolved until a recently-published paper by us [18].

1.2. Contribution

We give a detailed strategy for constructing the data structures of molecular surfaces, based on the analytical characterization of the SES including its singularities presented in [18]. Then, a meshing algorithm for molecular surfaces, especially the SES, is developed, combining an advancing-front algorithm with the pre-computed data structures. The explicit characterization of all singularities resolves the issue of self-intersection that is experienced due to singularities as they can be computed prior to the meshing of the surface. This, in turn, allows the possibilities of meshing the SES exactly, in the sense that each vertex of the mesh lies exactly on the surface. We want to emphasize once again that this is only possible due to the newly developed analysis of the molecular surfaces and it is not the case for the existing meshing algorithms. In addition, we propose an algorithm for filling molecular inner holes with virtual atoms for the reason that the appearance of these inner holes is not always justified in the solute molecular cavity of the continuum solvation models, as this would mean that the solvent is present in these inner holes.

1.3. Outline

In the next section, we give the definitions and the implicit representations of different molecular surfaces. In the third section, the construction of molecular surfaces, which is defined by different patches and their connectivity, is proposed. Based on this pre-computed data, an algorithm for filling molecular inner holes is proposed in the fourth section. Further, a meshing algorithm for molecular surfaces including two sub-algorithms for meshing respectively a (convex or concave) spherical patch and a toroidal patch is developed in the fifth section where we also present some illustrations of artificial as well as realistic molecular surfaces. Finally, a conclusion is presented in the last section.

2. Molecular surfaces

A mathematical analysis and calculation of the SAS and the SES has been presented in our recent work [18]. In this section, we recall some results including a mathematical definition of the surfaces, their implicit representations and the complete characterization of the SES.

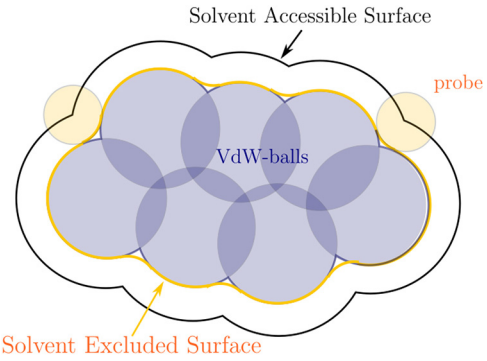

Fig. 2. 2-Dimension (2D) schematics of the solvent accessible surface and the solvent excluded surface, both defined by a spherical probe in orange rolling over the molecular VdW-atoms in dark blue. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

2.1. Definitions

As already emphasized, atoms of a molecule can be represented by VdW-balls with VdW-radii which are experimentally fitted, given the underlying chemical element [19]. In consequence, the VdW-surface is defined as the topological boundary of the union of all VdW-balls. Further, the SAS of a solute molecule is defined by rolling the center of an idealized spherical probe over the solute molecule, that is, the surface enclosing the region in which the center of a spherical probe can not enter. Finally, the SES is defined by the same spherical probe rolling over the molecule, but now we consider the surface enclosing the region in which a spherical probe can not access. In other words, the SES is the boundary of the union of all spherical probes that do not intersect the VdW-balls of the solute molecule, see Fig. 2 for a graphical illustration.

The definition of VdW-surface is based on the model that each atom has a specific radius around the atom center. However, the definition of the VdW-surface has ignored the size and shape of the surrounding solvent molecules in solvation models. The definition of SAS has taken this into account by modeling them by idealized spherical probes with a certain probe radius. The definition of the SES is different from the SAS in the sense that not the probe center traces out the desired surface, but the surface of the probe. In the application of the above-mentioned docking [4], the SES will not lead to the overlapping of neighboring surfaces since the SES does not inflate the atom radii but the SAS will.

Sometimes, the SAS can be non-connected: it can be composed of several separate surfaces. We call the outmost surface as the exterior solvent accessible surface (eSAS) and the union of all separated surfaces as the complete solvent accessible surface (cSAS), see Fig. 3 for an example and [18] for details. Correspondingly, we also propose the concept of the complete solvent excluded surface (cSES) and the exterior solvent excluded surface (eSES). We make a convention that the SAS refers to both the cSAS and the eSAS in a general context, and the SES refers in the same spirit to both the cSES and the eSES.

Both the VdW-surface and the SAS are composed of three parts: open spherical patches, open circular arcs (or circles) and intersection points (formed by the intersection of three or more spheres). The SES can be divided into three corresponding types of patches [2]: convex spherical patches, toroidal patches and concave spherical patches, see Fig. 4 for a 3D illustration. As showed in [18], any point on a convex spherical patch of the SES has a closest point to the SAS on a spherical patch. Similarly, any point on a toroidal patch of the SES has a closest point to the SAS on a circular arc, and any