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Triangulation of molecular surfaces based on extracting surface atoms

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ABSTRACT

In this paper, we propose a novel surface atom extraction algorithm. By calculating the relative positions of the extended spheres, this algorithm detects all surface atoms reachable by the probe. Our algorithm overcomes the drawbacks of current methods and can be implemented in real time. This algorithm significantly improved the efficiency of calculating the solvent-excluded surface because only the values for the surface atoms are calculated instead of for all atoms. We also construct a triangular mesh model of the molecular solvent-excluded surface in terms of the surface atoms. By subdividing the saddle patches into more uniform triangular meshes, we improved the existing methods for triangulating a molecular surface composed of triangular concave spherical patches, saddle patches and convex patches. In addition, we introduce a new method that seamlessly joins saddle patches to convex patches.

1. Introduction

The three-dimensional structure of a molecule is one of the most important factors determining its function. The molecular surface is a primary part of the protein structure and is crucial to protein docking and visualization. Currently, most research has focused on three molecular surface models [1–6]: the *van der Waals surfaces*, *solvent-accessible surfaces* (SASs) and *solvent-excluded surfaces* (SESs). Solvent-excluded surfaces are also commonly known as *solvent contact surfaces* (SCSs), *Connolly surfaces* or *smooth molecular surfaces*. We consider the SES in this work.

The SES was first proposed by Richards [2] in 1977, and it considers a probe sphere representing a solvent molecule rolling over the atoms in a molecule. SESs, which have become a well-known definition for the molecular surface, consist of three types of patches according to Connolly [7], namely, convex spherical patches, saddle patches and triangular concave spherical patches, as shown in Fig. 1. Throughout the rest of this article the term molecular surface refers to SES unless otherwise indicated.

In [7,8], Connolly showed how to calculate the three types of patches as well as the molecular area and volume and briefly discussed triangulating the molecular surface. Varshney et al. [9,10] presented a parallelizable algorithm for computing the molecular surface, which needs $O(k \log k)$ over n processors, where n is the number of atoms in the molecule and k is the average number of neighbors per atom. Note that the extended sphere defined by Varshney et al. [9,10] is important to our algorithm for extracting molecular surface atoms.

In 1996, Sanner et al. [11] proposed a *reduced surface* consisting of a polyhedron with faces, edges and vertices that indicate whether the probe is in contact with more than two atoms, two atoms or only one atom. This reduced surface can be computed for a molecule from a binary spatial division tree, which provides an efficient algorithm for computing the molecular surface. Sanner et al. [11] claimed that the binary spatial division tree can be constructed using $O(n \log n)$ computations in the worst case and the reduced surface can be computed using $O(n \log n)$ computations on average, where n is the number of atoms in the molecule.

In 2006, Ryu et al. [12,13] introduced a β-shape, which is a generalization of the well-known α-shape [14,15] that can be used to efficiently calculate molecular surfaces. Later, Ryu et al. [16,17] discussed the uniform triangulation of the three patch types. However, constructing the β-shape is difficult. First, for a molecule with n atoms, the Voronoi diagram of atoms requires $O(n^3)$ calculations in the worst case (the average complexity is $O(n)$). Second, for a given Voronoi diagram, the β-shape can be computed in $O(\log n+k)$ calculations in the worst case, where k is the number of edges and faces in the resulting β-shape [13,18,19]. Nevertheless, the Voronoi diagram of the atoms and β-shape are powerful tools for other important applications such as protein docking problems. The reduced surface [11] is equivalent to one β-shape. In this paper, we improve Ryu's methods for triangulating saddle patches [17]. Our improved method generates a uniform mesh even though the saddle patch is narrow.

Several other researchers have studied the calculation and visualization of various molecular surface models in other ways [20–29].

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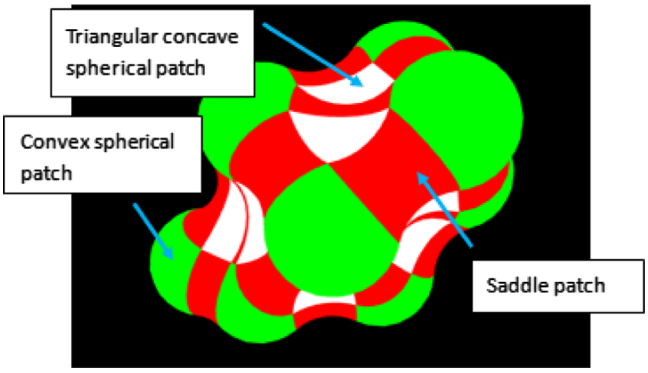

Fig. 1. The solvent-excluded surface.

Most previous works researched various molecular surface models based on all of the atoms in the molecule. However, if the surface atoms can be effectively extracted, the scale of the problem could decrease. Because the SES is constructed independently of the internal atoms, the calculation efficiency for SES can be improved by only accounting for the surface atoms. In this paper, we define *surface atoms* as those that can be reached by a probe rolling over the molecule and *internal atoms* as those that cannot be reached.

For this surface atom extraction, Wang et al. [30] proposed a geometric algorithm named the Protein Surface Atom Geometrical Algorithm (PSAGA) in 2007 to determine the molecular surface atoms according to a molecule's 3D geometric characteristics. However, the results extracted by this algorithm are not exact. Moreover, it requires the radii of all the atoms to be the same. In 2011, Zhang et al. [31] introduced a new extraction algorithm called the Molecular Surface Atom Rolling Algorithm (MSARA), which is more accurate than the PSAGA while being effective for atoms with differing radius. However, this algorithm cannot find certain surface atoms, and its efficiency is not ideal. Here, we present a new, real-time extraction algorithm that overcomes the drawbacks of the existing methods.

Our algorithm consists of three steps: (1) extract the surface atoms; (2) calculate and triangulate the three molecule surface patch types; and (3) connect these patches seamlessly. This paper is organized as follows. Section 2 introduces the new extraction algorithm. Section 3 provides the calculations for the SES based on the extracted surface atoms and discusses the triangulation and connection of the three SES patches. The time complexity is analyzed in Section 4. We test our algorithms in Section 5. Conclusions and future work are presented in Section 6.

2. Surface Atom Extraction based on Extended Spheres (SAEES)

In the rest of this article, we denote r_p as the radius of the probe.

Definition 1. Let $A(c, r)$ be an atom, where $\boldsymbol{c}$ is the center of the atom and r is the radius of the atom. The extended sphere of an atom is a sphere $S(c, r+r_p)$ with the center at $\boldsymbol{c}$ and of the radius $(r+r_p)$.

The definition of an extended sphere indicates that the center of the probe cannot be inside of an atom's extended sphere; otherwise a collision would occur between the probe and the atom.

Definition 2. Given two atoms, $A_i(\boldsymbol{c_i}, r_i)$ and $A_j(\boldsymbol{c_j}, r_j)$, let D be the Euclidean distance between $\boldsymbol{c_i}$ and $\boldsymbol{c_j}$ and $L = r_i + r_j + 2r_p$. A_i and A_j are neighbors to each other if $D < L$.

Theorem 1. *The extended spheres of two atoms intersect (except when tangent) if and only if the two atoms are neighbors.*

Proof. The extended spheres for two given atoms, $A_i(\boldsymbol{c_i}, r_i)$ and $A_j(\boldsymbol{c_j}, r_j)$, are $S_i(\boldsymbol{c_i}, r_i + r_p)$ and $S_j(\boldsymbol{c_j}, r_j + r_p)$, respectively, and the distance between their center is D. If these two extended spheres intersect (except when tangent), we obtain $D < L = r_i + r_p + r_j + r_p$. According to Definition 2, A_i and A_j are neighboring atoms. In contrast, two neighbor atoms have $D < L = r_i + r_p + r_j + r_p$; namely, their extended spheres intersect (except when tangent).

Theorem 2. *If the surface of an extended sphere for one atom in a molecule is completely covered by the interior of other atoms' extended spheres, it is an internal atom; otherwise, it is a surface atom.*

Proof. If the surface of an atom's extended sphere is not completely covered, the probe can reach this atom without colliding with other atoms whenever the probe's center lies on the uncovered portion of the atom's extended sphere surface. Thus, the atom is a surface atom. In contrast, if the probe cannot reach this atom without colliding with other atoms, it is an internal atom.

Theorem 2 provides a method for determining whether an atom is a surface atom. Fig. 2(a) and (b) shows a molecule and the extended spheres of its atoms, respectively. Because the extended sphere surface illustrated by the red dashed circle in Fig. 2(c) is completely covered, the corresponding atom in Fig. 2(d) is internal. On the other hand, because the extended sphere surfaces, which are illustrated by the black solid circles in Fig. 2(c), are not completely covered, their corresponding atoms in Fig. 2(d) are surface atoms. Moreover, according to Theorem 1, whether an atom is a surface atom only depends on it and its neighbors instead of all atoms.

We propose the following method to simplify determining whether the surface of an extended sphere is completely covered.

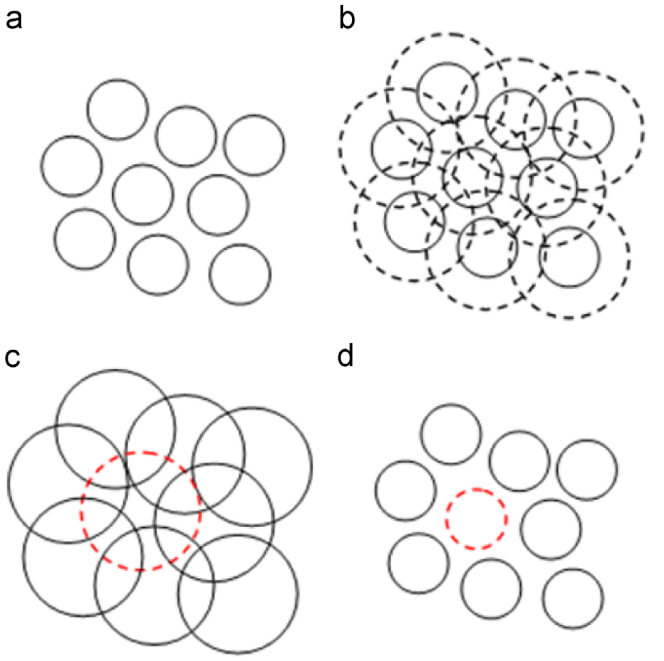

Fig. 2. Determine whether an atom is a surface atom based on the extended spheres. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.). (a) A molecule, (b) The molecule and the extended spheres of all the atoms, (c) All the extended spheres and (d) Surface atoms and an internal atom.