Area and Volume of Molecular Skin Surfaces

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1 Introduction

In this paper, we propose a new method for computing the geometric measures of bio-molecules using skin surfaces to represent their shapes. Specifically, we give the formulas for measuring the total area A and volume V of the skin surface defined by n weighted points, as well as the contributions of the individual points to A and V.

Motivation. Bio-molecules interact and function according to their shapes: understanding of the latter is therefore crucial in life sciences. A common way to represent the shape of a bio-molecule is to use a union of balls in which each ball corresponds to an atom. Geometric measures of this union of balls (mainly surface area and volume) give access to energetics properties of the molecule, such as its stability in water (see [3] for a complete review). Among all analytical and numerical methods that have been proposed to compute these measures, the approach based on the Alpha Shape theory is the most promising [3]. Its applications for modeling however have been limited because of the discontinuous nature of the derivatives of the surface area and volume of a union of balls. As an alternative, the skin surface introduced by Edelsbrunner [2] has a number of desirable properties for molecular shape representation such as smoothness, free of self-intersection and deformation with smooth transitions. Cheng and Edelsbrunner [1] developed formulas for the area, perimeter and derivatives of skin curves. Here we generalize these formulas to skin surfaces in three dimensions.

Main Results. We give the formulas for measuring the total area A and volume V of the skin surface defined by n weighted points, as well as for measuring the contributions of the individual points to A and V. All the formulas except part of the area calculation can be evaluated analytically. We first introduce geometric structures defining skin surfaces. Then, we give the formulas for computing the area and volume as well as the formulas of the individual contributions of each point. We briefly discuss their applications and the calculation of the derivatives.

2 Geometric Structures

Given a set of weighted points $B = \{b_i = (z_i, w_i) \in \mathbb{R}^3 \times \mathbb{R} \mid i = 1..n\}$, the skin surface F_B is defined as the envelope of the convex hull of B after shrinking, namely, $F_B = \text{env}(\sqrt{\text{conv}(B)})$, in which the addition and the scalar multiplication operations of two weighted points follows the addition and multiplication of weighted distance functions $\pi(x) = \|x - z_i\|^2 - w_i$ in vector space, and the shrinking operation for a set of weighted points X is defined as $\sqrt{X} = \{\sqrt{b_i} = (z_i, w_i/2) | b_i \in X\}$.

We consider each weighted point as a sphere centered at z_i with a radius $\sqrt{w_i}$; the convex hull of B is then an infinite family of spheres. After shrinking these spheres by a factor of $1/\sqrt{2}$, the boundary of the union of spheres, namely, the skin surface, is a tangent continuous surface that blends adjacent spheres smoothly. A skin surface can be decomposed into a collection of simple quadratic patches based on the framework of the weighted Delaunay triangulation and Voronoi diagram.

Let D_B be the weighted Delaunay triangulation of B, V_B be its dual Voronoi diagram, and K_B the dual complex of B. For a simplex $\sigma_* \in D_B$, we denote its vertices $\sigma_i = z_i$, its edges $\sigma_{ij} = z_i z_j$, its triangles $\sigma_{ijk} = z_i z_j z_k$ and its tetrahedra $\sigma_{ijkl} = z_i z_j z_k z_l$. Similarly, the dual Voronoi cell v_* of σ_* are polytopes v_i, polygons v_{ij}, edges v_{ijk} and vertices v_{ijkl} respectively. The Minkowski sum of σ_* and its dual v_* scaled down by half is called the mixed cell μ_*, namely, $\mu_* = \frac{1}{2}(\sigma_* + v_*)$. The center f_* of μ_* is defined as $\text{aff}(\sigma_*) \bigcap \text{aff}(v_*)$, in which $\text{aff}(\sigma)$ is the affine hull of σ. The size R_* of μ_* is defined as the absolute value of the radius of the orthosphere of σ_* divided by $\sqrt{2}$. As proved in [2], the skin surface within a mixed cell, $S_* = F_B \bigcap \mu_*$, is a quadratic patch defined by f_* and R_*. Specifically, S_i and S_{ijkl} are the parts of spheres (f_i, R_i) and (f_{ijkl}, R_{ijkl}) within μ_i and μ_{ijkl}, respectively, and S_{ij} and S_{ijk} are the parts of hyperboloids with focus f_{ij} and f_{ijk}.

3 Surface Area and Volume of a skin surface

Let A_* and V_* be the surface area and volume of S_* respectively. We denote A_*^i and V_*^i the portions of A_* and V_* that belong to the sphere b_i if $z_i \subset \sigma_*$. The surface area A^i and volume V^i of a sphere b_i is defined as follows,

$$A^i = A_i^i + \sum_{\sigma_{ij} \in D_B} A_{ij}^i + \sum_{\sigma_{ijk} \in D_B} A_{ijk}^i + \sum_{\sigma_{ijkl} \in D_B} A_{ijkl}^i,$$

$$V^i = V_i^i + \sum_{\sigma_{ij} \in D_B} V_{ij}^i + \sum_{\sigma_{ijk} \in D_B} V_{ijk}^i + \sum_{\sigma_{ijkl} \in D_B} V_{ijkl}^i.$$

The total surface area of the skin surface F_B is $A = \sum_{b_i \in B} A^i$ and the total volume is $V = \sum_{b_i \in B} V^i$. They can be expressed as:

$$A = \sum_{\sigma_i \in D_B} A_i + \sum_{\sigma_{ij} \in D_B} A_{ij} + \sum_{\sigma_{ijk} \in D_B} A_{ijk} + \sum_{\sigma_{ijkl} \in D_B} A_{ijkl},$$
$$V = \sum_{\sigma_i \in D_B} V_i + \sum_{\sigma_{ij} \in D_B} V_{ij} + \sum_{\sigma_{ijk} \in D_B} V_{ijk} + \sum_{\sigma_{ijkl} \in D_B} V_{ijkl}.$$

Next, we give the formula A_*, V_*, A^i_* and V^i_* in terms of the centers, sizes and boundaries of the mixed cells.

Mixed Cells μ_i and μ_{ijkl}. There is only one sphere b_i that specifies the mixed cell μ_i; we have $A_i = A^i_i$ and $V_i = V^i_i$. The area and volume of S_i is equal to those of sphere b_i clipped by its Voronoi cell v_i and scaled down by a proper factor,

$$A_i = \frac{1}{2}\Big(2\pi R_i^2 - \sum_{\sigma_{ij} \in K_B} C^a_j + \sum_{\sigma_{ijk} \in K_B} C^a_{jk} - \sum_{\sigma_{ijkl} \in K_B} C^a_{jkl}\Big),$$

$$V_i = \frac{\sqrt{2}}{4}\Big(\frac{4}{3}\pi R_i^3 - \sum_{\sigma_{ij} \in K_B} C^v_j + \sum_{\sigma_{ijk} \in K_B} C^v_{jk} - \sum_{\sigma_{ijkl} \in K_B} C^v_{jkl}\Big),$$

in which C^a_j is the area of the cap C_j formed by the sphere b_i and the Voronoi plane of edge σ_{ij}, C^a_{jk} is the area of $C_j \bigcap C_k$, and C^a_{jkl} is the area of $C_j \bigcap C_k \bigcap C_l$. Similarly, C^v_* are the volumes of the cap and its intersections. The formula of C^a_* and C^v_* will be given in the extended version of this paper.

For the case of mixed cell μ_{ijkl}, we can use similar inclusion-exclusion formulas for calculating A_{ijkl} and V_{ijkl}. We use the Voronoi planes of the six edges of σ_{ijkl} to divide A_{ijkl} into four parts that belongs to b_i, b_j, b_k and b_l respectively. There are no dual complex that gives the combinatorial intersections among these six planes; we therefore set up four figure sphereS and calculate the dual complex of five spheres so that we can apply the inclusion-exclusion formula to compute A^i_{ijkl} and V^i_{ijkl}.

Mixed Cell μ_{ij} and μ_{ijk}. Mixed cell μ_{ij} is a n sided prism with their vertical edges parallel to the edge σ_{ij} where n is the number of Delaunay triangles shared the edge σ_{ij} in D_B. We can translate and rotate the system so that f_{ij} is the origin and the Z axis is parallel to line $z_i z_j$. In this configuration, the equation of the hyperboloids are $X^2 + Y^2 - Z^2 = \pm R^2_{ij}$; the sign of the right hand side determines if the hyperboloid is one sheeted or two sheeted. The area A_{ij} and volume of V_{ij} are those of this standard hyperboloid clipped by n side planes, a top plane $Z = Z_t$ and a bottom plane $Z = Z_b$. The Voronoi plane v_{ij},that is, $Z = Z_{ij}$, divides A_{ij} to A^i_{ij} and A^j_{ij}, in which Z_{ij} is the Z coordinate of f_{ij}. We take each side plane of μ_{ij} and form a triangular prism with the Z axis and calculate the area and volume in this prism by parts. The assembly of these parts give the complete formulas:

$$A^i_{ij} = \sum_{\sigma_{ijk} \in D_B} \mathrm{Sign}\big((f_{ij} - p_k)\cdot n_k\big) \times \big(\beta_k H^a(Z_b, Z_{ij}) + I^a(d_k, Z_{k_1}, Z_{k_2}) + I^a(d_k, Z_{k_1}, Z_{k_3})\big),$$
$$V^i_{ij} = \sum_{\sigma_{ijk} \in D_B} \mathrm{Sign}\big((f_{ij} - p_k)\cdot n_k\big) \times \big(\beta_k H^v(Z_b, Z_{ij}) + I^v(d_k, Z_{k_1}, Zz_{k_2}) + I^v(d_k, Z_{k_1}, Z_{k_3})\big),$$
$$A_{ij} = A^i_{ij} + A^j_{ij},$$
$$V_{ij} = V^i_{ij} + V^j_{ij},$$

in which n_k is the normal of a side plane determined by σ_{ijk} and p_k is a point on this plane, β_k is the ratio of the dihedral angle of the triangular prism to 2π, and the function $H^a(Z_1, Z_2)$ calculates the total surface area of a hyperboloid between two planes $Z = Z_1$ and $Z = Z_2$, the function $I^a(d_k, Z_{k_1}, Z_{k_2})$ calculates the partial surface between planes $Z = Z_{k_1}$ and $Z = Z_{k_2}$ after it has been clipped by the plane (p_k, n_k). All the parameters used in these equations can be derived using the center and size of μ_{ij} and its neighboring mixed cell μ_i, μ_j and μ_{ijk}. We note that the function $I^a(d_k, Z_{k_1}, Z_{k_2})$ includes a term of $\int_{Z_{k_1}}^{Z_{k_2}} \Big(\arccos \frac{d_k}{\sqrt{Z^2 + R^2_{ij}}}\Big) \sqrt{R^2_{ij} + 2Z^2} dZ$, which cannot be evaluated analytically. Efficient numerical integral using Lagrange polynomials can be used. We use a similar approach for the mixed cell μ_{ijk}.

4 Discussion

We have given formulas for computing the area and volume as well as the weighted area and volume for molecular skin surfaces. We will apply these results to estimate the solvation energies of small molecules as well as of proteins and nucleic acids. We are currently working on computing the derivatives of the area and volume of molecular skin surfaces with respect to the coordinates of the centers of the atoms. These derivatives are expected to be continuous, making them attractive for simulations such as energy minimization and molecular dynamics.

References

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