

The Minimal Molecular Surface

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Introduction

The structure and function of macromolecules depend on the features of their molecule-solvent interfaces. The commonly used Molecular Surface (MS) is an important model to describe such interfaces, and has had many applications in biosciences. However, the MS typically has singularities and is inconsistent with free energy minimization.

In this work, we introduce the concept of Minimal Molecular Surface (MMS) as a new paradigm for the theoretical modeling of molecule-solvent interfaces. When a less polar macromolecule is immersed in a polar environment, surface free energy minimization occurs naturally to stabilize the system, and leads to an MMS.

Theoretical modeling and algorithm

For a given set of atomic constraints (as obstacles), the Minimal Molecular Surface (MMS) is defined as one whose mean curvature

$$H = \frac{1}{3} \nabla \cdot \left(\frac{\nabla S}{\sqrt{g}} \right) \quad (1)$$

vanishes away from the obstacles. Here S is the hypersurface function and $g = 1 + S_x^2 + S_y^2 + S_z^2$ is the Gram determinant. The MMS is minimized via the mean curvature flow

$$\frac{\partial S}{\partial t} = \sqrt{g} \nabla \cdot \left(\frac{\nabla S}{\sqrt{g}} \right) \quad (2)$$

Our procedure involves iterating Eq. (2) until $H \sim 0$ everywhere except for certain protected boundary points where H takes constant value.



Figure 1: MMS generation. Left chart: initial influence domain of $S(x,y,z,0)$ at a cross section $z=0$; Center chart: steady state solution $S(x,y,z,0,t=10)$; Right chart: the extracted isosurface $S(x,y,z,t=10)=C$.

Numerical results



Figure 2: Surface area minimization of a diatomic molecular with $r_1=1$ and $r_2=0.6$. From left to right, separation distance $L=1.6, 1.8, 1.9,$ and 1.95 .

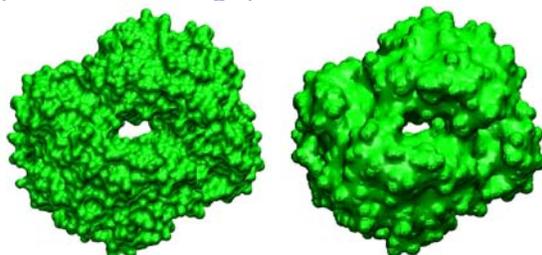


Figure 3: Cavity.

Left: MS;
Right: MMS.

Cavity constraints in terms of a probe are introduced in the MMS in order to capture cavities of the hemoglobin.

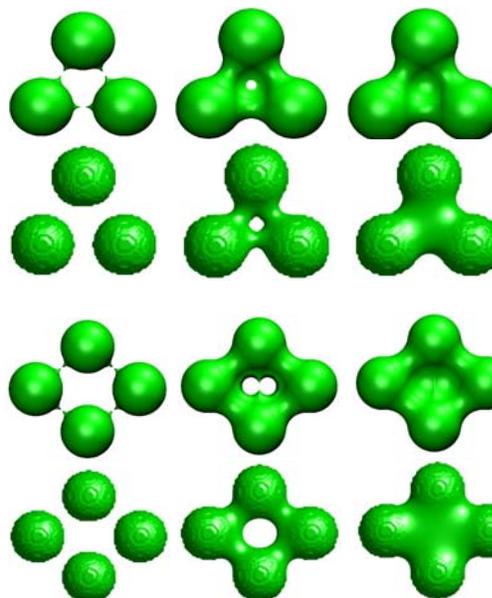


Figure 4: Singularity in a three-atom system.

The same centers and radius $r=1.5$ are used in all cases.

Top: the MS with $r_p=0.5, r_p=0.9,$ and $r_p=1.0$;
Bottom: the MMS with $r_p=0.5, r_p=0.6,$ and without probe constraint.

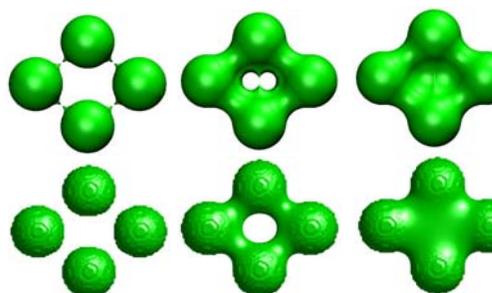


Figure 5: Singularity in a four-atom system.

The same centers and radius $r=1.5$ are used in all cases.

Top: the MS with $r_p=0.4, r_p=1.1,$ and $r_p=1.2$;
Bottom: the MMS with $r_p=0.4, r_p=0.8,$ and without probe constraint.

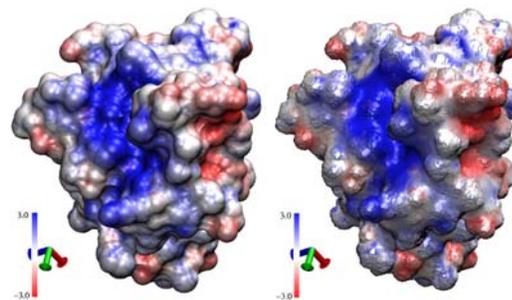


Figure 6: Surface electrostatic potentials of the Cu/Zn Superoxide dismutase.

Left: MS; Right: MMS.
A very good agreement between two potentials can be seen. Differences between the solvation energies computed using the MMS and MS are usually less than 3%.

Conclusion

The proposed Molecular Minimal Surface (MMS) is typically free of singularity and is consistent with surface free energy minimization. It provides a new paradigm for the analysis of stability, solubility, solvation energy, and interaction of macromolecules.

References

1. P.W. Bates, G.W. Wei and S. Zhao, Minimal molecular surfaces and their applications, J Comput Chem, in press, (2006).

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