GPU-Accelerated Generation of the Molecular Surface

M. Alhazzazi[1], S. Hayward[1] and S.D. Laycock[1]

[1] School of Computing Sciences, University of East Anglia, Norwich, United Kingdom

Abstract

A variety of visualisation methods have been developed for displaying molecular structures. The solvent-excluded surface (SES) or molecular surface is one of the most popular and useful depictions as it helps to identify binding-site cavities. The molecular surface is particularly useful therefore for interactive molecular docking tools. Docking tools that incorporate molecular flexibility bring new challenges as the molecular surface must be recomputed in real time as the molecule changes shape in interaction with a ligand. Here we compute the SES by using a GPU-accelerated Marching Cubes algorithm which promises to lead to real-time surface generation for small- to medium-sized biomolecules undergoing conformational change.

CCS Concepts

• ***Human-centered computing*** → ***Visualisation application domains;*** • ***Computing methodologies*** → *Scientific Visualisation;*

1. Introduction

A variety of methods have been developed to visualise molecular structures such as the space-filling representation, backbone and cartoon rendering. They help us understand the complex molecular world by indicating structural features that may relate to function. In molecular docking applications the Solvent Excluded Surface (SES), which is also known as the Connolly Surface [Con83] or molecular surface, is particularly useful for highlighting those surface features such as pockets and cavities which indicate potential docking sites.

A variety of different molecular surface representations have been created. The Solvent Accessible Surface (SAS) [LR71] is defined by rolling a probe sphere over the van der Waals surface of a molecule. The center of the probe depicts the surface that is directly accessible to the solvent. The SES is defined similarly except that a point on the surface of the probe sphere traces the surface as opposed to the sphere centre. Sanner et al. [SOS96] developed an approach for computing the SES with high-quality triangulation. More recently Hermosilla et al. [HKV*17] developed a technique to compute SES with a progressive refinement approach.

The approach we present follows from Kim et al. [KKS12]. Their method generates a sampling of points on the SAS. The volume encompassing the molecule is then voxelised and the corners of each voxel are assigned values based on their distance to the closest SAS sample point. Data structures were used in the approach presented by Kim et al. which do not lend themselves well to a GPU implementation. Our contribution is the replacement of the data structures by regular grids for the development of a GPU implementation using CUDA.

2. Our Approach

Our approach takes the same initial approach as Kim et al. [KKS12] by creating points on the surface of the spherical atoms with radii corresponding to their van der Waals radii plus the radius of the probe, which is the radius of an oxygen atom corresponding to the water solvent, set to 1.4 Å. The green points in Figure 1 illustrate these sample points offset from the surface of the atoms.

Sample points located inside other spheres will not be part of the SAS and so these need to be removed. This step can be accelerated by creating a regular grid. The sample points of each sphere in a given grid cell are checked with spheres in the current cell and their immediate neighbours.

To construct a triangulated surface of the SES, the Marching Cubes algorithm by Lorensen and Cline is used [LC87]. A voxel grid is created enclosing the atoms of the molecule. The next stage of the algorithm requires values to be set at the voxel corners based on the distance to the closest sample points. Kim et al [KKS12], used a KD-tree to reduce the time to find the nearest sample points to the voxel corners. Here we utilise a regular grid implemented in CUDA, to store all of the sample points. To determine the nearest point to a given voxel corner requires only the regular grid cell containing the voxel corner or the 27 neighbouring cells to it to be tested. Once the values are set, the corners can be determined as interior or exterior to the SES by comparing against the probe radius. A CUDA-based Marching Cubes algorithm was implemented to create the triangulated mesh that represents the SES. Figure 2 illustrates the complete approach on a molecule comprising ten atoms.

DOI: 10.2312/egp.20201038

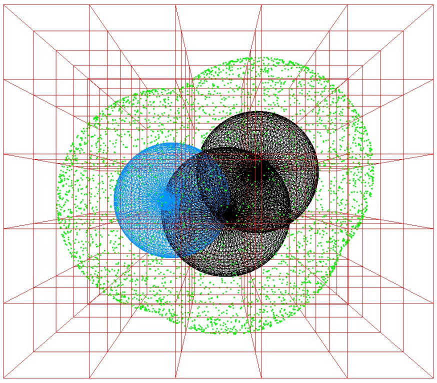

Figure 1: *The* ***green*** *points are the sample points offset by 1.4 Å from the surface of the atoms. These points lie on the SAS. A test example of three atoms is shown. The spherical wireframe represents the atoms in space-filling model. The* ***red*** *boxes represent the regular grid containing the sample points.*

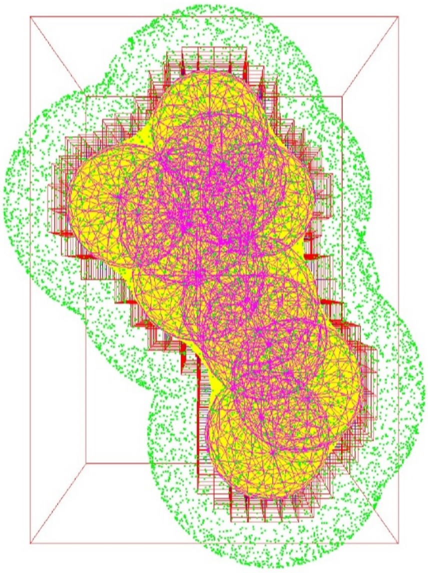

Figure 2: *Illustration of structures used to calculate the SES for an example molecule with 10 atoms. The* ***pink*** *spheres are the atoms in space-filling representation, the* ***green*** *dots are the sample points sampling the SAS, the* ***red*** *boxes are the Marching Cubes and the* ***yellow*** *is the mesh generated as a result of running the Marching Cubes algorithm.*

2.1. RESULTS

Table 1 shows the timings for computing the sample points for the SAS and the Marching Cubes for the SES. Figure 3 shows the SES for the small protein Crambin (Protein Data Bank (PDB) ID: 1CRN).

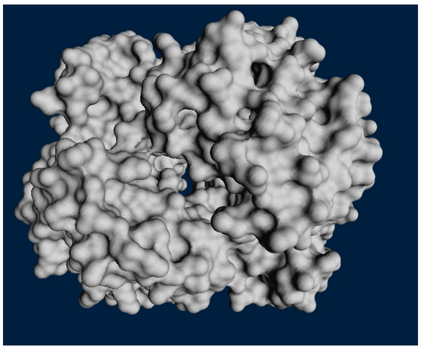

Figure 3: *The Solvent Excluded Surface generated for Haemoglobin (PDB ID: 1BIJ) comprising 4384 atoms.*

	Performance time (ms)			
PDB-ID	Number of Atoms	Calculate Sample Points (CPU)	Regular Grid (GPU)	Marching Cube Algorithm (GPU)
1BK2	468	32.0	1.31	5.17
2INS	778	47.0	2.27	9.80
1IZH	1521	91.0	3.13	30.15
1GT0	2746	170.0	6.18	112.10
1BIJ	4384	280.0	6.18	191.90
1VPN	11134	690.0	16.73	1545.80
1AON	58674	3610.0	29.83	4478.96

Table 1: *Results for computing the SES on several PDB structures.*

3. Conclusion

A GPU-accelerated approach is presented which computes the SES or molecular surface of a biomolecule loaded from a PDB file. However, only the Marching Cubes algorithm and the regular grid to assist in computing the values for the voxel corners has currently been accelerated on the GPU. Implementation in CUDA of the complete approach should enable real-time display of the deforming molecular surface of a medium-sized biomolecule undergoing conformational change.

References

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