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SaxsMDView: a three-dimensional graphics program for displaying force vectors

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A new three-dimensional graphics program, *SaxsMDView*, is described. The program performs a three-dimensional graphical representation for protein molecules along with the force vector (or vector potential) applying to each atom. The displayed object can be rotated and translated in arbitrary directions by interactive mouse manipulation. While *SaxsMDView* was originally intended to visualize the result of *SAXS_MD*, a previously developed program based on the restrained molecular dynamics with small-angle X-ray scattering constraints, it can also be useful for graphical representation of other objects such as coarse-grained molecular models reconstructed by *ab initio* modelling or solvent site-dipole field vectors induced around the protein molecule. Some examples of the application of the program including the graphical analyses of the results with *SAXS_MD* are also presented.

Keywords: three-dimensional graphics; constraint force vector; molecular structure; restrained molecular dynamics; vector potential.

1. Introduction

Various molecular graphics programs have been developed to visualize the three-dimensional structure of a biomolecule (Ferrin *et al.*, 1988; Sayle & Milner-White, 1995; Koradi *et al.*, 1996; Delano, 2002). Recent advances in hardware enable us to manipulate such macromolecules easily on personal computers. In order to understand the molecular properties in more detail, however, various physico-chemical quantities involved in the molecular structure should be considered. For example, if we are to understand the method of specific recognition between two molecules, we should consider not only the shape of the molecules but also the electrostatic properties of their surfaces. This property is a type of scalar potential, *i.e.* the function of the three-dimensional coordinate vectors and its own value are scalar. For better and intuitive comprehension of this quantity, several visualization tools such as *GRASP* (Gilson & Honig, 1987) have been developed. On the other hand, for field- or force-type properties derived from the molecule, we should consider vector potentials. Although their visualization is also effective for a profound comprehension, there is no convenient program available for that purpose.

We previously developed a new program, *SAXS_MD*, based on the restrained molecular dynamics algorithm with small-angle X-ray scattering (SAXS) constraints (Kojima *et al.*, 2004). The program rationally calculates the constraint force applied to each atom, and effectively changes the three-dimensional structure of the current model so that the calculated scattering curve matches well with the experimental SAXS data. It usually requires an iterative numerical integration to obtain the final structure. Actually the calculation does not always converge, owing to inappropriate initial structure and/or parameter settings. For example, if the constraint force applying to a certain atom is in conflict with the physical one, such as a van der Waals interaction, there may be strong steric hindrance or repulsion inside the molecule. In such cases it is of great help to visualize the orientation and magnitude of each force vector along with the atomic position in the molecule. The distribution of the constraint force field in the whole molecule can suggest which direction the current model should be changed to satisfy the constraints. For this purpose we have developed a new program, *SaxsMDView*, as the visualization tool for the results of *SAXS_MD*. In addition to the constraint force vectors, the program can generally visualize various vector potential quantities for molecules of interest.

2. Systems and methods

All the source codes were written in ANSI C, and the graphical user interface is based on the *OSF/Motif* toolkit (Heller & Ferguson, 1993). Three-dimensional graphics were implemented by the *OpenGL* library (Silicon Graphics, 1993). The program was designed to be used on the X-window system on a Unix or Linux platform with *OpenGL* environment. If some hardware-specific auxiliary libraries such as *GLX* (*OpenGL* extension to the X-window system) are not

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available, the compatible library *Mesa3D* (http://www.mesa3d.org/) can be used instead. In order to check the performance of our program, we created an executable file and ran it with a GNU GCC compiler on the RedHat 7.3 Linux platform with an Intel Pentium 4 processor (2 GHz) and NVIDIA GeForce2 graphics card (video memory: 32 MB).

3. Features of the program

The program is started simply by typing 'SaxsMDView <PDB file name>' on the Linux/Unix command prompt with appropriate options. If the file name is omitted, an on-line message for the command usage appears. The PDB file contains information about atomic coordinates according to the Protein Data Bank (PDB) nomenclatures (Bernstein *et al.*, 1977). It should be noted that the model treated in this program is expected to have a single conformation consisting of one polypeptide chain. If any rotamers exist in the model, the program outputs an appropriate message to stop. In the case of a molecule with multiple chains, the entity for the residue sequence number should be reassigned in an appropriate order. Fig. 1 shows the main window of *SaxsMDView*, which displays the protein structure by ball-and-stick representation and in atom-based colours. The background colour can be selected to be either black or white at the start of the program. When the molecule was read, its centre of gravity was shifted to the centre of the drawing area so that the whole structure can be displayed on an appropriate scale. The program implements a mouse-driven interface for manipulating the molecule currently displayed. Moving the mouse with its left-hand button pressed enables the user to rotate the molecule in the *xy* plane like a virtual trackball. Holding the middle mouse button allows translation of the molecule in the plane. The right-hand mouse button is used for scaling along the *z* axis perpendicular to the computer display. Rotation around each coordinate axis can also be attained using the 'rot-X', 'rot-Y' or 'rot-Z' sliding widget below the drawing area. A stereoview can be realised using the 'stereo' button. The program is terminated using the 'Quit' button.

The force vector can be displayed with a '−v <file name>' option at the start of the program. The file contains information about the force vectors. The first column of each line represents the corresponding atom number in the PDB file, and the three subsequent columns represent the *x*, *y* and *z* components of the force vector. The magnitudes of the force vectors can be uniformly scaled using the arrow-labelled button below the drawing area. If the '−nobond' option is specified on the command input, only atoms without covalent bonds are drawn along with force vectors, which saves the required memory and simplifies the view. Space-filling representation is realised using the '−CPK' option. Hydrogen and water atoms can be omitted from the display using the '−noH' and '−noWAT' options, respectively.

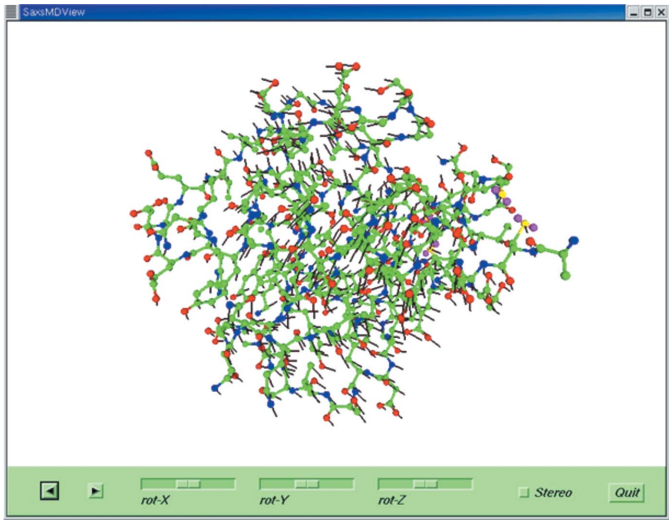

Figure 1
Main window of *SaxsMDView*. The three-dimensional structure of RNase T1 is displayed by ball-and-stick representation. Carbon atoms are coloured in green, nitrogen in blue, oxygen in red, sulfur in yellow and others in magenta. A force vector applied to each atom is drawn as a dark red line from the atom.

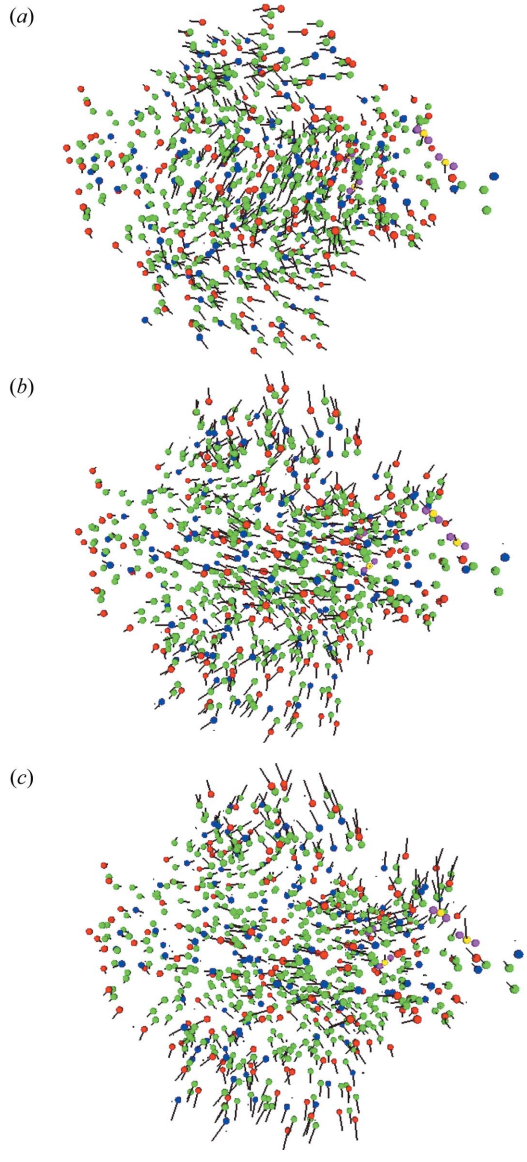

Figure 2
Time course of the molecular structure and the constraint force vectors during the refinement process with *SAXS_MD*. The transient structures after 50 fs (*a*), 100 fs (*b*) and 150 fs (*c*) are presented along with the corresponding constraint force vectors. Covalent bonds are omitted for simplicity, and the force vectors are drawn as dark red lines. The time course of overall constraint energy has been presented by Kojima *et al.* (2004).

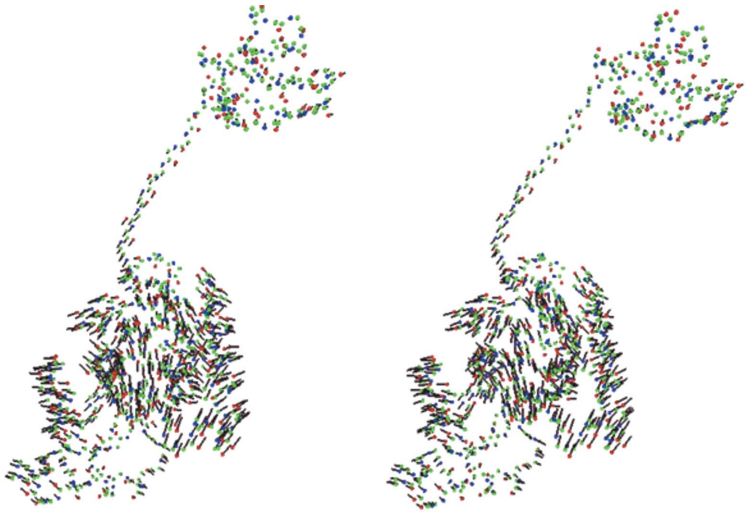

Figure 3
Stereoview of the molecular structure and the constraint force vectors for chitinase C. The SAXS-derived constraint force vectors are drawn as dark red lines. Only main-chain atoms are presented, and covalent bonds are omitted for simplicity. The catalytic domain and chitin-binding domain are located in the bottom-left and the top-right portions, respectively.

4. Examples

The first example is a trajectory analysis of RNase T1 during the refinement process using *SAXS_MD* (Kojima *et al.*, 2004). Since the crystal structure of the protein did not satisfy the experimental SAXS data, the rational structure satisfying the experimental data was calculated by restrained molecular dynamics algorithm. In the calculation the constraint energy was defined as the squared sum of differences between the observed and calculated SAXS intensities. At an early stage, constraint forces were widely distributed over the molecule (Fig. 2*a*). This may mainly be due to a tendency to expand the molecule. In the process of the calculation, the pattern of their distribution changed so that the total constraint energy could be decreased (Fig. 2*b*). At 200 fs, most of the atoms in the molecule, except for those in the peripheral area, had little constraints so as to be fully relaxed (Fig. 2*c*). Although the time courses for the total constraint energy and *R*-factor have already been presented by Kojima *et al.* (2004), the visualization using *SaxsMDView* is synergistically helpful for the comprehension of the results by *SAXS_MD* calculation.

The second example is an indication of the appropriate direction to change the modelled structure of chitinase C (Fig. 3). Chitinase C from *Streptomyces griseus* consists of a catalytic domain (bottom-left in the figure) and a chitin-binding domain (top-right in the figure), which are linked by ten residues. In the crystallized form (Kezuka *et al.*, 2006) the portion of this linker peptide was not able to be traced owing to low electron densities. The modelled structure obtained by the constructed linker peptide did not satisfy the experimental SAXS data, and non-coincidence between both curves on a dimensionless scale suggested that the current model should be expanded further. There are various possible ways to expand the whole molecule so that its radius of gyration can increase. One way is to expand the individual domains, and another is to change the distance between the two domains while fixing the structure of each domain. Fig. 3 shows the distribution of the constraint forces calculated using *SAXS_MD* along with the atomic position of the current model. Most constraint forces are concentrated in the catalytic domain, which indicates that the SAXS-derived constraints are mainly due to the structure of the catalytic domain. It is suggested from the figure that the most effective way of improving the current model is to change the catalytic domain exclusively.

5. Discussion

The *SaxsMDView* program was originally developed to facilitate the structural refinement process with *SAXS_MD* by providing a graphical representation of the SAXS-derived constraint forces. It can be used to check the transient results during the calculation or to estimate the desired direction for the current model. In the field of SAXS, there exist several graphics programs to visualize the *ab initio* model restored from SAXS data (Walther *et al.*, 2000; Konarev *et al.*, 2001). The current program can also display this type of model, if the coordinate information for each bead is provided according to the PDB format. *SaxsMDView* is also useful for the visualization of other vector potentials such as the solvent site-dipole field induced around protein molecules (Hamasaki *et al.*, 2006).

6. Program availability

All the source codes, the manual document and a precompiled executable file on the Linux platform of the program can be downloaded freely at the website http://www.dokkyomed.ac.jp/users/saxs/.

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