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A new tool has been developed to aid in the visualization of electron density in crystals or from quantum chemistry calculations. It displays the fine details of the electron density on a plane and the three-dimensional model of the molecule at the same time. The program enables the user to examine the details of weak or irregular features. Such features frequently occur in low-resolution maps, where they determine the correct tracing of a protein backbone. In high-resolution maps, solvent regions are difficult or impossible to observe using isosurfaces. The tool has been integrated into an existing molecular visualization package (PyMol) making it possible to observe and interact both with a structure model and the electron density slices freely, simultaneously and independently. This visualization model fills a gap in the visualization methods available to crystallographers and others who work with electron density maps.

1. Introduction

The introduction of computer graphics into the field of macromolecular X-ray crystallography has probably made a more significant contribution to the development of this field than any other single experimental advance.

By representing an electron density map, obtained from X-ray crystallography experiments, as a surface by connecting points with identical electron density (ρ) at a user-defined density value, modeling programs like O (Jones et al., 1991) have made it relatively easy for crystallographers to fit structure models on top of experimental maps, even for very large maps. These representations of the electron density are known as isosurfaces or, colloquially, chicken-wire maps, and are the most popular and useful representation of the electron density when one wants to look for atoms in a map.

Although very useful for the crystallographer who is building the structure, isosurfaces have a serious limitation in that they make it extremely difficult to have any perception of how the electron density (ρ) changes throughout the map. This problem derives from the fact that electron density maps are naturally four-dimensional objects (x, y, z and ρ) and so not easily representable in our three-dimensional world, and even less so on a two-dimensional screen. The way isosurfaces solve the problem of the extra dimension is by keeping ρ at a constant level and only allowing x, y and z to change. This causes a problem when, for example, one wants to see how ρ changes as we move away from the center of an atom or to assess the amount of noise present in a seemingly ‘flat’ region.

To tackle these and similar problems, we have devised a tool that, instead of keeping ρ constant, keeps one of the spatial dimensions constant by drawing a slice through the electron density map and represents ρ as a function of the two coordinates in the plane.

2. Methods and results

PyMol 0.97 (Delano, 2002) was used as the vehicle for our tool. PyMol is a user-friendly tool for interactive visualization of molecular models, electron density and more. It contains tools to generate images, comparable in quality to e.g. the well known Molscript package (Kraulis, 1991; Esnouf, 1999). We added a new function that draws a slice representation of a map, stored in memory, between the two clipping planes.

First the viewing window is divided into a grid with a user-defined grid spacing. The spacing is relative only to the dimensions of the viewing window, and so is independent of the zooming level. Then for each point in the grid, the projection of that point onto the plane between the two clipping planes is calculated and the obtained coordinates are used to interpolate the electron density value from the electron density map using a simple trilinear interpolation method. If the coordinates fall outside the map, a special flag is set. A color is then assigned to each grid point that is inside the map.

Figure 1

Stick model of protein databank entry 1A0M (Hu et al., 1998) and color-map representation of the 1.1 Å electron density map.
according to a user-defined color function dependent on the value of the electron density. The grid points outside the map are made transparent. The color of the pixels other than the grid points is then computed by bilinear interpolation of the three color components (red, blue and green). An example is given in Fig. 1.

In addition to the color mapping, the density level can also be represented as a third spatial dimension yielding a mountainous landscape instead of a flat slice. In this mode the slice is not necessarily parallel to the screen. The user may first choose an orientation and fix the slice so that it becomes possible to rotate the slice along with the model; otherwise it would be impossible to see the relief.

3. Discussion
The ability to see both a molecular model of a structure and a representation of the electron density, at the same time, is of enormous value. This visualization tool fills a gap in the visualization methods available to crystallographers and others who work with electron density maps.

The slice representation has allowed us, for example, to see clearly deficiencies in an electron density model which were not apparent in the isosurface representation (Fig. 2). Another interesting application is to look at the profile of the variation of the electron density around an atom. It is nearly impossible to achieve this using an isosurface; however, it can easily be done using the height-map representation (Fig. 2) with a very thin clipping volume.

The new tool also allows one to visualize maps with arbitrary shapes and/or contents, like the maps resulting from the standard error of each electron density point. One can, for instance, visualize density difference maps in a rather quantitative manner (Fig. 3).

The fact that the grid used for interpolation is proportional to the viewing window and not to the zoom level is very useful, in that it effectively makes the grid coarser as one zooms out (and finer as one zooms in), such that the grid is always adapted to the zooming level. This technique is called dynamic map sampling (Emsley, 2004). The ability to select the slicing plane simply and interactively is one of the biggest advantages of this tool as the user-interface is often one of the biggest problems with this kind of visualization (Briggs, 2001). The disadvantage of these two features is that the slices have to be recomputed on each frame, which can make it slow on old computers although performance was acceptable on all the machines tested (e.g. a Linux PC, with NVIDIA GeForce 440MX graphics card).

Visualization methods are increasingly important for analyzing and solving increasingly difficult problems, in many fields of science and engineering. We believe that a powerful and easy-to-use tool like this one can be very helpful for the solution of a variety of problems related to X-ray crystallography and we hope that it encourages people think about electron density maps from a new perspective.

APPENDIX A
PyMol slices
The command to create the slices in PyMol is called ‘slice_map’. For more information simply issue ‘help slice_map’ within PyMol. The code will be available in the near future in a release of PyMol;

Figure 2
(a) Isomesh representation at 0.5 and 1.0 eÅ⁻³ of electron density, created using density functional theory, of Cisplatin [PtCl₂(NH₃)₂]. (b) Section through the electron density where bonding electrons are visualized. Some spherical shaped artifacts from the calculation are visible near the nucleus. The color levels in the electron density are made using a split scale: linear up until 1 eÅ⁻³, and logarithmic afterwards. (c) Molecular model of Cisplatin.
meanwhile the source code can be downloaded from http://xray.bmc.uu.se/~filipe/software/.

References