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Recent changes to RasMol, recombining the variants

Roger Sayle's RasMol is one of the most popular molecular graphics programs. It has been used worldwide in structural biology research and education since 1993 and has spawned several variants, each with useful features. Because the source of the program is freely available, many people have been able to add useful features to RasMol, and the program has continued to evolve. Authors of several RasMol variants are cooperating in the creation of a new, common, open-source version.

RasMol*

RasMol is one of the most popular graphics programs for the display of macromolecules (proteins and nucleic acid structures) and small molecules, with many people throughout the world retrieving it daily. It is used routinely to assist in the processing of macromolecules for the Protein Data Bank (PDB)[1], which is operated by the Research Collaboratory for Structural Bioinformatics (RCSB)[2]. Its popularity stems from a combination of ease of use with power and flexibility. RasMol lets a novice bring up a 3D display of a macromolecule with minimal effort and allows an expert to prepare scripts to render different aspects of a macromolecule in whatever ways are most appropriate to understanding the structure. RasMol can be used directly to provide publication-quality 2D images for posters and presentations, or as a 'quick and dirty' tool to suggest approaches to be used in rendering the molecule with more powerful programs.

*Note from the editor. Owing to space restrictions some of the historical aspects concerning the development of RasMol could not be included in this article. However, these have been placed on the author's Web site: http://www.berstein-plus-sons.com/software/rasmol/history.html Please visit the site for the full background story and complete citation list.

RasMol reads the coordinate file for a molecule in one of several different formats, displays the molecule on the screen of a Macintosh, PC or X-windows Unix display in a variety of color schemes and molecular representations: wireframe, sticks, balls and sticks, spacefilling (CPK) spheres, ribbons and cartoons. Selected atom labels and dot surfaces can be added to images, and images can be scaled, rotated and translated, and displayed in stereo. In addition, depth cueing, cross-sections, shadows and specular reflections are available. The user can control the operation of RasMol from a command window or with pull-down menus. The molecule is displayed in a resizeable graphics window. Figure 1 shows the display for PDB entry 1CBN (crambin)[3].

The program is distributed free of charge as pre-compiled binaries for the most popular platforms, including Macintosh, PC, SGI and x86 Linux, as well as in the form of C source code. The overall program is called RasMol, the Windows version is called RasWin and the Macintosh version is called RasMac. The RasMol 2.7 releases are the latest versions.

New features in RasMol 2.7

The new RasMol 2.7 releases have a similar look and feel to the earlier versions of RasMol and can process scripts produced by those earlier versions. The new features are described below. Thanks to the cooperation of Roger Sayle and software developers throughout the community, RasMol remains under active development. To date, RasMol 2.7 has been built for Linuxppc, i386 RedHat 6.0 Linux, SGI, DEC OpenVMS, Mac, IBM PC under Windows, IBM RS/6000 under AIX 4.3.2 and Acorn RISC OS.

Handling CIF and mmCIF, alternate conformers and multiple models. The rendering of molecules by graphics programs has been complicated by a recent transition in the representation of coordinate files. The International Union of Crystallography (IUCr) adopted the Crystallographic Information File (CIF) format in the early 1990s for the representation of molecules. CIFs are becoming the standard for the presentation of small molecules[4], and the adoption of the macromolecular CIF (mmCIF) dictionary[5,6] by the IUCr encourages the increasing use of CIFs for macromolecules. The PDB at the RCSB now uses mmCIF internally for its processing

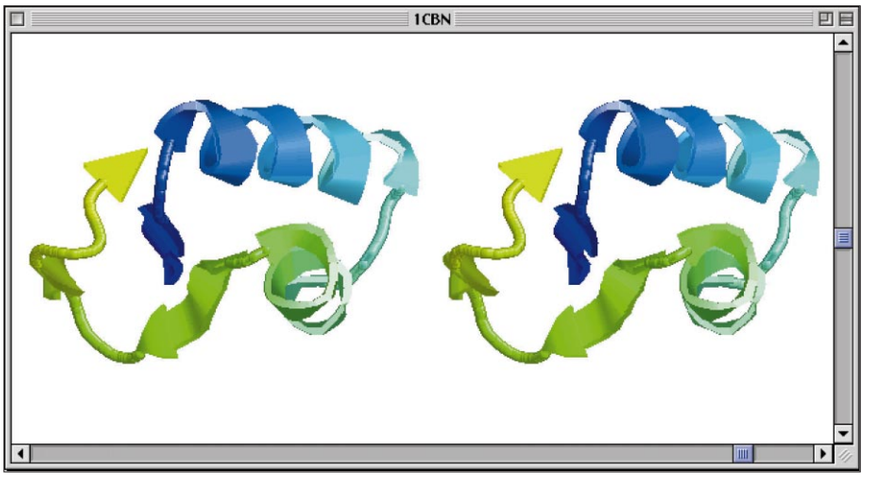

Figure 1
RasMol display window showing a cross-eyed stereo view of a cartoon with specular reflections, colored progressively from N to C terminus. The molecule shown is the PDB entry 1CBN (crambin).

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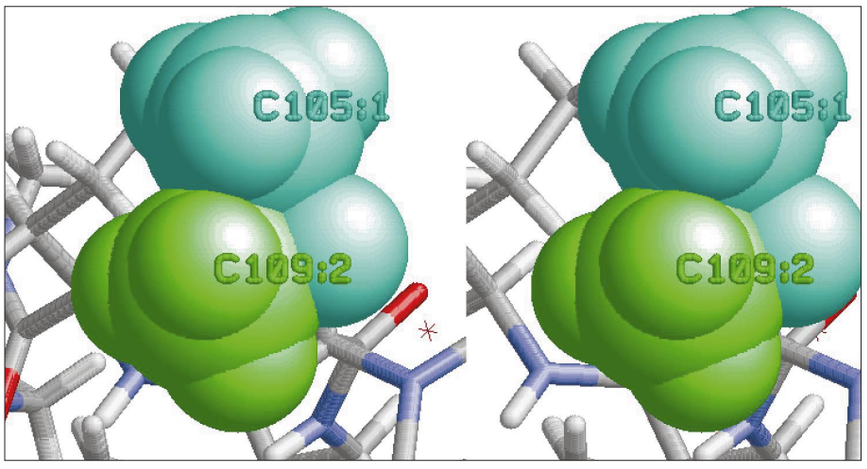

Figure 2

A cross-eyed stereo view of alternate conformers of a methyl group (with the two C atoms labelled) from core CIF SX1054 (a tridecapeptide lactone) downloaded from *Acta Crystallographica C*. The star in the lower right is a water molecule. The image was exported directly from RasMol without the use of any auxiliary rendering software.

Box 1. The history of RasMol

The source code of software used in experimental science and modelling is essential to a full understanding of the results obtained. The source code of RasMol has been freely available to the community and has proven to be a suitable platform for the development of new ideas for rendering in structural biology. There are many private variants of RasMol and several heavily used public variants available to the community.

In 1992, Roger Sayle described the program RasMol, which used a highly efficient rendering algorithm to allow high-quality interactive rendering of macromolecules on a wide variety of platforms[8]. The RasMol 2 series began with the release of RasMol 2.1 by Roger Sayle in 1993. The evolution of the program has continued with releases by Roger Sayle of the very popular version 2.6b2 in late 1996 and version 2.6.4 in late 1999. In 1995 and 1996, Marco Molinaro created the '-ucb' versions, which display multiple molecules simultaneously and allow rotation around bonds. Arne Mueller created a version that added the ability to calculate individual torsion angles and Ramachandran plot data, to show selected chains, groups and atoms, to select by CIS bond angles, and added POV-Ray 3 output capabilities. Herbert Bernstein made versions that accept CIF and mmCIF input and that manage alternate conformers and multiple models. Andreas Bohne created a version with automatic detection of pixel depth, extended menus and better scripting capabilities.

In early 1999, Roger Sayle, Arne Mueller and Herbert Bernstein agreed to work together on a new, common, open-source version of RasMol, the 2.7 series, which is managed and released by Herbert Bernstein. All of their modifications have been integrated into the 2.7 series, and agreement has been reached with Marco Molinaro and Andreas Bohne to integrate their modifications into the main line of development.

Additional information on the historical context of RasMol can be found at http://www.bernstein-plus-sons.com/software/rasmol/history.html

and makes both the older PDB format and the newer mmCIF format available for downloading from its website (http://www.rcsb.org). RasMol now allows display of those mmCIF datasets as easily as it has always allowed display of the older format. This should help to encourage wider adoption of the new mmCIF format.

RasMol 2.7 can read both core CIF and mmCIF datasets. The image in Fig. 2 was created by reading a core CIF (a tridecapeptide lactone)[7] from the IUCr journal *Acta Crystallographica C* (which accepts papers for publication as CIFs), rendering the bulk of the molecule as sticks and the alternate conformers as spacefilling spheres, using the default coloring scheme for alternate conformers. Stereo and specular reflections have been chosen. Bolded proportional spacing of the label font and the use of a star to mark a water molecule have been selected. The image was created interactively on the screen and then exported as a PICT image directly by RasMol for inclusion in this document. No auxiliary rendering program was used. RasMol 2.7 provides the capability of coloring structures with multiple models by model.

Torsion angle output and Ramachandran plots. In general, macromolecules are modelled as linear polymers of amino acids. For polypeptide chains, the relative position of two sequential residues is given by two angles, the so-called ϕ angle of rotation around the N–C^{α} bond, and the so-called ψ angle of rotation around the following C–C′ bond. Using software developed by Roger Sayle and Arne Mueller, RasMol will calculate and report this 'torsion angle' information for any chosen set of residues. Only certain ranges of torsion angles are sterically favourable; a Ramachandran plot of ϕ against ψ helps in finding scientifically interesting, unusual conformations or problems with the structure. RasMol will present the torsion angles of a molecule as a simple printer plot. The torsion angle calculation capabilities were extended to Ramachandran printer plot logic using logic and formats from Frances Bernstein's program fisipl (see ftp://bnlarchive.rcsb.org/pub/pdb_software/program_tape/fisipl.for).

Improved fonts. For most interactive studies, a simple, stroke-based font is adequate, but, when producing a rendering for publication, better quality fonts are desirable. RasMol 2.7 includes the ability to use a font with proportional spacing and to draw strokes as small cylinders highlighted with shading and specular reflections, as shown in Fig. 2.

Better in-line scripting. One of the most powerful techniques in the use of RasMol has been the practice of placing a short script to control the display of a PDB entry as a prologue to that entry. This is called in-line scripting. The new version extends this capability. It is forgiving of common scripting mistakes by automatically recognizing the beginning of a PDB entry or a CIF dataset and will accept a dataset without a prologue as a valid script.

Marking atoms as stars. When drawing a structure with many solvent atoms, it is common practice to use a simple marking for them, rather than using full spheres. The new version of RasMol has the ability to mark solvent atoms with stars, as suggested by Curt Haltiwanger, thereby reducing clutter while giving an indication of positions. Although intended for solvent atoms, any atom can be marked with a star of any desired size.

Other features of the latest release can be found by retrieving the program from the primary development site at http://www.bernstein-plus-sons.com/software/rasmol or from one of the many mirror sites provided by the IUCr.

RasMol 2.7 – an open-source version

The new RasMol 2.7 series differs from the earlier versions (see Box 1) by being a copyright-protected open-source version, in contrast to Roger Sayle's earlier versions, which were made freely available without restriction. Those distributing unmodified versions are required to either include the source and documentation or refer to it, and those making modified versions are required to make their changes to the source available (see the Notices with the RasMol release for details of the conditions).

RasMol 2.7 is not in the public domain, but it is given freely to the community in the hopes of advancing science. Those who make changes are expected to make them in a responsible manner and to offer the development team the opportunity to include those changes in future versions of RasMol.

These conditions should help ensure the continued open-source development of RasMol for the indefinite future. There might have been some concern in the past that such open-source licensing might discourage commercial use of the new versions of RasMol, but the recent successes of other open-source based efforts would seem to indicate that such concerns are not to be taken as seriously as they might once have been, and users of RasMol in research and instruction can only benefit from access to source code of the full series.

Conclusion

RasMol will, no doubt, continue to evolve. Marco Molinaro's RasMol-ucb modifications for multiple molecules and bond rotation, and Andreas Bohne's automatic detection of pixel depth, extended menus and even better scripting capabilities need to be integrated into the common version (see Box 1). Further work on representation of alternate conformers is needed. It would be desirable to add electron-density and smooth-surface plotting capabilities to RasMol. These are certainly challenges, but they should be manageable in the collaborative open-source environment in which RasMol is being developed. By sharing the work among the members of the community and bringing the fruits of their labours back into a common open-source program, the community gains a program that continues to adapt to evolving scientific requirements in an upwards-compatible manner.

Acknowledgements

I would like to thank the many people who have contributed improvements, reported bugs and tested pre-releases of the RasMol 2.7 series releases. I also thank David Atkinson, Bob Sweet, Helen Berman, John Westbrook, Jan Boshoff, David Atkinson, Jon Bruno and Martin Wuerthner for providing computer access or pre-compiled binaries, to Brian McMahon for arranging the IUCr mirror sites for RasMol, and to Frances C. Bernstein for advice and consultation on PDB format and for our collaboration on CIF and the handling of alternate conformers and multiple models. Special thanks are due to Roger Sayle for creating RasMol and for his support and encouragement in the creation of the new common open-source version.

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The two faces of bioenergetics

Frontiers of Cellular Bioenergetics – Molecular Biology, Biochemistry and Physiopathology

*edited by **S. Papa**, **F. Guerrieri** and **J.M. Tager**, Kluwer Academic/Plenum Press, 1999. £126.75 (xxx + 801 pages) ISBN 0 306 45851 9*

For those of us who graduated in the late 1980s, the golden age of bioenergetics seemed a thing of the past. Following the universal acceptance of the chemiosmotic theory, my old departmental chairman even stated that the essential research in this area was complete. So it was with a wistful and jealous look over our shoulders that we studied for our PhDs at this time. Sure, there were still microdebates over how many protons were pumped by which members of the respiratory chain enzymes, but even these seemed rather half-hearted compared with former battles.

Fortunately, recent research has proved that the excitement and controversy in bioenergetics has been merely dormant, not extinct. On the one hand, the plethora of enzyme structures of proton translocating enzymes that were solved in the late 1990s has regenerated the mechanistic field; it is now possible to generate meaningful theories about how protons (and electrons) move through the protein structure, rather than being forced to focus on only those redox centres that are accessible to spectroscopic techniques. On the other hand, cellular bioenergetics has been revolutionized by the finding that mitochondria perform an essential signalling role in most forms of apoptotic cell death. The lonely band of 'mitochondriacs' who stressed the role of the mitochondria in disease through the 1980s were joined by rampaging legions of molecular and cell biologists in the late 1990s. It is clear that bioenergetics research is entering another golden age to match that of the 1960s and 1970s.

So, how well is this revolution charted by this book? *Frontiers of Cellular Bioenergetics* grew out of a FEBS Advanced Course on Oxidative Phosphorylation held in Bari, Italy, in 1996. The participant lecturers and others in the field have contributed 15–30 page chapters for this monograph. Two-thirds of the 30 chapters cover the mechanistic and structural end of bioenergetics and the remainder focus on mitochondrial pathology. Of the latter, most chapters relate to DNA defects, rather than the more recent interest in apoptosis. Thus, there are chapters on mitochondrial mutations, ageing and neurodegenerative diseases, but the role of the mitochondrial permeability transition in reperfusion injury and septic shock is much less extensively covered. The control of mitochondrial activity and the