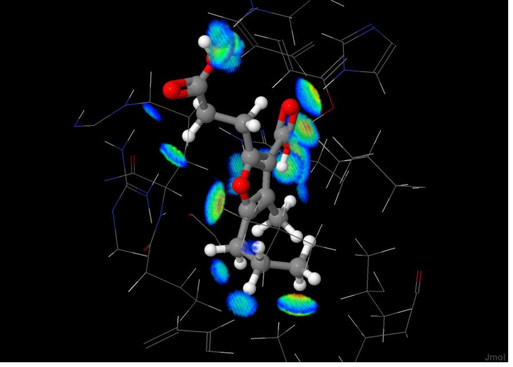
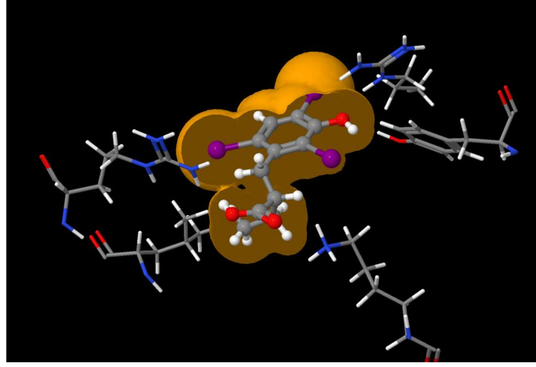


Interactive Visualization of Intermolecular Contacts



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Gordon Research Conference on Visualization In Science & Education

Bryant University, July 10-15, 2011

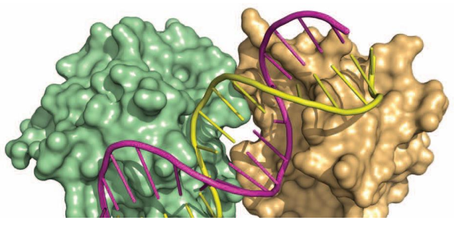
Abstract

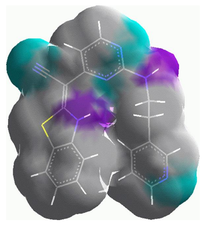
The visual depiction of protein-ligand interactions is often made difficult due to limitations inherent in popular programs such as PyMOL and VMD. Our goal in this project is to devise new and more effective ways of depicting interactions that will be vivid, concise, and -- most importantly -- simple enough to create that they could be generated easily by anyone wanting either a production-quality image or its underlying user-interactive model equivalent.

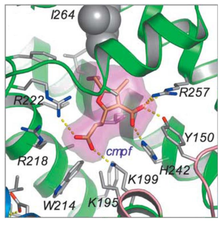
We describe here a method that allows depiction of protein-ligand interactions in a variety of ways. The method is based on linear combinations of van der Waals surfaces (intersection, difference, and sum). Jmol implements the method in the **contact** command, to be introduced in Jmol version 12.2 later this summer.

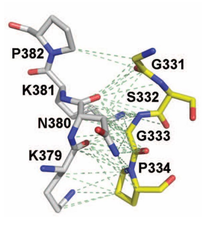
Two Problems

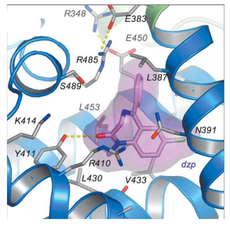
A cursory glance at recent journals relating to biomolecular structure or dynamics indicates that depiction of molecular surfaces has become an important method of communication of scientific results. Van der Waals, solvent-accessible and solvent-excluded (or "molecular") surfaces in particular have become ubiquitous.









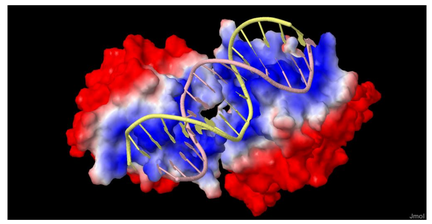


Surface depictions are particularly useful because they can provide focal points in a complex molecular picture. However, most currently popular production-quality image-producing software (for example, PyMOL and VMD) are limited in their surface-generating capabilities to just a few standard options. The result is that visualizations are needlessly complex or do not effectively convey the salient points described by the authors in the text.

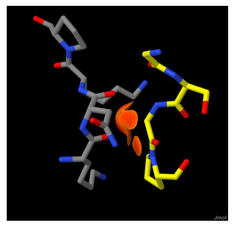
Further compounding this problem is the fact that visualizations such as these are not easily analyzed by the reader. Although the 2D images were produced by 3D modeling programs, reviewers and readers do not generally have access to the original 3D version of the image. Thus, viewers cannot readily explore the model interactively and convince themselves of the author's argument.

The Solution – Jmol CONTACT

The key is to relate one isosurface to another. In the case on the right, we have mapped the protein's solvent-excluded surface with the DNA's van der Waals surface data (the map data Jmol uses to create the van der Waals surface). Color is based on the distance between the two surfaces with blue (in this case) showing close proximity.

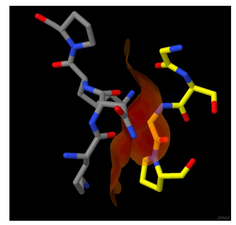


isosurface select {protein} only molecular map select {DNA} only VDW



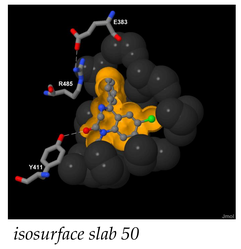
contact {c1} {c2} full 100%

It is not necessary to use molecular surfaces. By mapping the data from one van der Waals surface onto another and then trimming, we can create an object that specifically visualizes just the overlap between two van der Waals surfaces. Different extents of overlap can be visualized using different percentages of van der Waals radii.



contact {c2} {c1} plane 150%

Jmol 12.2 also allows extensive slabbing of isosurfaces. In this case we simplify the picture by adding a "backdrop" surface behind the inhibitor. The local receptor region is shown as a simple van der Waals surface, giving some indication of the fit between it and the inhibitor.

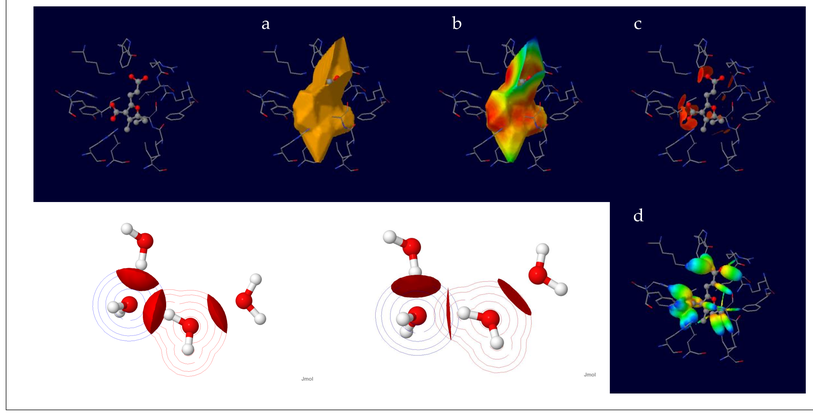


isosurface slab 50

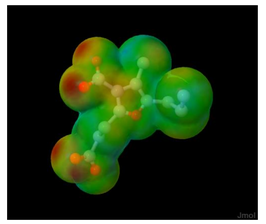
As the model is rotated, the isosurface slabbing plane rotates as well. This allows the surface to remain a backdrop and never obscure the inhibitor.

Isosurface Sums and Differences

Jmol's **contact** command can create novel contact surfaces. The angular-shaped surface shown in (a) is from data representing the *difference* between the van der Waals surface maps of the inhibitor and receptor. The pseudoplanar "faces" of the surface effectively mark the dividing points between the atoms. By mapping this data with the van der Waals surface data of the inhibitor (b) and then trimming based on that mapped value (c), we can visualize just the points of contact. Using the *sum* of the two van der Waals fields instead of the difference, we get (d), where specific point-to-point interactions are highlighted. Jmol implements these sums as **contact connect.**



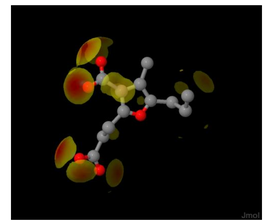
Gallery of Results



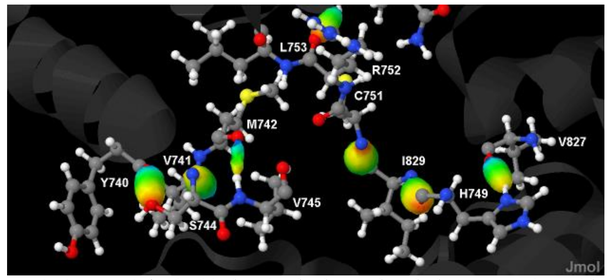
contact {2001:A} vdw

On the left, the VDW surface of the bound ligand in 2bxa is mapped by the VDW function of protein.

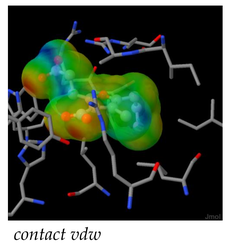
On the right, the same thing, but trimmed so that only areas of VDW overlap are visible.



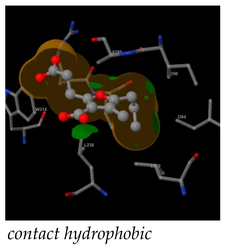
contact {2001:A} trim



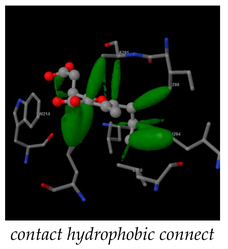
contact connect for 1m14, showing hydrogen bonds between amino acid residues of a single chain.



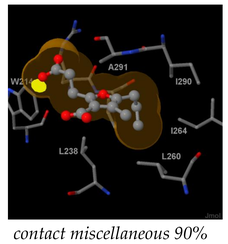
contact vdw



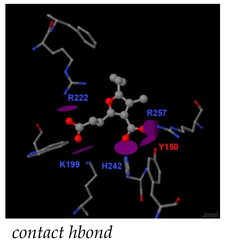
contact hydrophobic



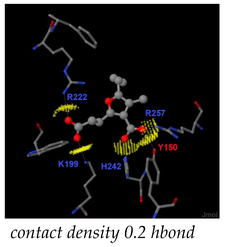
contact hydrophobic connect



contact miscellaneous 90%



contact hbond



contact density 0.2 hbond

Conclusions

Standard van der Waals, solvent-accessible, and solvent-excluded surfaces are just the beginning of the possibilities for using surface representations in describing intermolecular interactions. The Jmol **contact**, **isosurface intersection** , and surface **slab** methods offer several additional options. These methods should be relatively easy to implement in PyMOL, VMD, and other popular visualization programs. A secondary goal of this project, to allow for the inclusion of 3D modeling data in publication supplementary or hyper-linked material, has been achieved. Thus, any image created by Jmol is accompanied by enough information to reproduce that exact view in Jmol from the image file itself. Models for this poster are available at http://stolaf.edu/people/hansonr/jmol/contact/gordon.htm.