Ciel: Software for Visualizing Protein-Protein Interactions by Andrew Ban

**Background:** A key decision must be made in any study of protein-protein interactions at the molecular level -- the definition of the interfacial region of interest. Standard interfacial definitions using absolute distance or solvent excluded surface area incorporate a threshold set by the investigator. As a result, the interfacial region varies from study to study. These definitions can therefore be considered somewhat arbitrary in nature. In addition, interfaces defined in these ways may be fractured in a manner which is difficult to interpret. To address these issues we develop an alternative definition using concepts taken from computational geometry and topology. Through the use of a relative distance threshold, we define the interfacial region of a protein-protein complex by an interface surface which is symmetric, orientable, and has a defined decomposition [1].

**Implementation:** Ciel is a new software package for generating these interface surfaces from protein structural data. The package includes a core implementation written in pure Java and a visualizer (Bianca) written in Java3D. The software requires only modest computing resources and is robust & accurate, performing calculations in arbitrary precision when necessary. Modules implemented in Ciel to generate interface surfaces include Delaunay triangulation in 3D for balls and points, Alpha Shape generation, and topological persistence (as applied to Alpha Shapes). The only available facility in the current release (version 0.5) of Ciel is interface surface generation, but future versions will enable all of the individual modules to run standalone. Ciel is available in binary from the Biogeometry website. Source code will be forthcoming, with a planned release date around the end of May 2004.

**Usage:** Input to Ciel is by standard PDB file. Multimeric complexes are supported and an arbitrary number of chains may be included. Two VDW parameter sets for atoms are currently selectable -- AMBER99 [2] and Richmond [3]. Generation of an interface surface for a protein-protein complex also creates the Delaunay triangulation, Alpha Shape filtration, and retracted complex filtration (defined by topological persistence and the seal function). Following generation, interface surfaces may be visualized in Bianca and may also be exported in kinemage format or an arbitrary file format, which contains coordinate and topology information suitable to generate files for import into other programs.

**Visualization:** The Bianca visualizer included with Ciel is the easiest and most direct way to view interface surfaces in the context of protein structure. The interface surface & boundary, Delaunay edges dual to the interface surface, and retracted complexes may all be viewed in the context of the interface surface filtration, which is dynamically changeable by slider. The Alpha Shapes of the protein-protein complex may be viewed as well. A few representations of protein structure are available, though a selection language is currently not implemented, so user definable groups and coloring of protein structure is not yet possible. One feature of interest in Bianca is the interaction graph, which shows all interactions involved in the protein-protein interface at the residue level. The interaction graph dynamically changes with respect to the user's currently selected rank in the interface surface filtration, offering a useful visual aid to quickly focus in on the more critical, interior regions of the interface. Residues are also selectable within the interaction graph, which then highlight the chosen residue and its interaction in the main visualization window. Arbitrary numbers of interface surfaces may be simultaneously loaded into Bi-
anca, facilitating comparison between interface surfaces of different protein-protein complexes. Preliminary support for synchronous rotation of objects has been implemented, which is useful for viewing similar interface surfaces from the same angle.

**Planned Features:** Ciel is under heavy development. The current initial release is meant to familiarize the biology community with the new definition of interface surfaces and provide a means to visualize and think about the surfaces. Future versions will include "heavier" capabilities, such as complete support for measuring and analyzing interface surfaces in both geometric and physical terms. Software runtimes will also be improved.

User-defined coloring schemes and a selection language are planned for the Bianca visualizer. Since Bianca is not meant to be a replacement for a fully-featured protein structure visualizer, export filters for programs such as VMD [4] and PyMOL [5] are being added, and work on a plugin for the KING visualization system [3] has started.


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**Announcement**

**BioGeometry Meeting**

The first BioGeometry meeting of 2004 is scheduled for Saturday, June 12 in Brooklyn, New York, at Polytechnic University, in conjunction with the 20th Annual Symposium on Computational Geometry. Organizers are Jack Snoeyink and Pankaj Agarwal.

For details, please go to http://biogeometry.cs.duke.edu/meetings/ITR/04jun12

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Left: The interaction graph for barnase/barstar at rank 0 of the level-of-focus hierarchy. ASP 39, a critical residue for interaction on barstar is shown selected, along with its interaction partners on barnase.

Above: The corresponding view for ASP 39 in the main view of Bianca. The interface surface boundary is shown as a black polyline.

Ciel is available at http://biogeometry.cs.duke.edu/software/ciel