BRAGI: linking and visualization of database information in a 3D viewer and modeling tool

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ABSTRACT
Summary: BRAGI is a well-established package for viewing and mod-
eling of three-dimensional (3D) structures of biological macromolec-
ules. A new version of BRAGI has been developed that is supported
on Windows, Linux and SGI. The user interface has been rewritten
to give the standard ‘look and feel’ of the chosen operating system
and to provide a more intuitive, easier usage. A large number of new
features have been added. Information from public databases such as
SWISS-PROT, InterPro, DALI and OMIM can be displayed in the 3D
viewer. Structures can be searched for homologous sequences using
the NCBI BLAST server.

Availability: Freeware, licensed: http://bragi.gbf.de/
Contact: Reichelt@gbf.de
Supplementary Information: http://bragi.gbf.de/gallery

INTRODUCTION
BRAGI (Schomburg and Reichelt, 1988) is one of the first computer
programs optimized for the display and modification of protein and
nucleic acid structures. Combined with force field analysis it is a
highly valuable tool for the design of new proteins based on known
structures. Linking information of public databases, such as SWISS-
PROT, InterPro, DALI and OMIM can be displayed in the 3D
viewer. Among these functional annotations can be loaded, features selected and
viewed in the 3D viewer.

BRAGI offers all necessary tools to predict protein structures based
on known 3D structures, to replace as well as to insert and
delete residues in a protein structure (Desmet et al., 1997). The
insertion of residues is supported by the use of an internal loop-
database (Lessel and Schomburg, 1999; Wohlfahrt et al., 2002;
Fechteler et al., 1995). Furthermore, BRAGI allows a sequence-
based BLAST search on all sequences deposited in the PDB
default search database) via the NCBI BLAST server. The visu-
ization of conserved regions between proteins in a separate
‘alignment’ window optimizes the process of modelling of protein
structures.

The fold analysis of new structures is supported by the DALI
database. DALI (Heger and Holm, 2000) provides a multiple align-
ment of structural homologues of a query structure. BRAGI submits
the coordinates to the DALI server, receives the response and
then offers all alignments for seamless download and automatic
3D alignment.

REFERENCES
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Fig. 1. Screenshot of a session with BRAGI. The protein structure ‘Hemoglobin (1CBM)’ is entered by the user. In the ‘Tree View’ listing some atoms and residues are selected – orange lines – and highlighted in the 3D viewer in yellow ball and sticks respectively wireframe.

To closely follow an ongoing molecular dynamics run, BRAGI reads atomic coordinates from an AMBER force field analysis. To watch an active run, BRAGI will read in the trajectories of a running AMBER job and visualize them all or show one snapshot after another.

DISCUSSION AND CONCLUSION

BRAGI includes several novel additions that are useful in the structural analysis of macromolecules. Although some of the newly included features are not original, the integration of public databases in a tool for visualization, animation and editing of macromolecules is unique. A short comparison follows.

Cn3D is a helper application for web browsers that allows the viewing of 3D structures from NCBI’s Entrez retrieval service. SRS3D (O’Donoghue et al., 2004) is a viewer for annotations found in the SRS system. Both are limited in their graphic capabilities and are not suited for modification of biomolecules and use only their own databases. Links to public databases are available, e.g. in DeepView—The Swiss-PdbViewer (Schwede et al., 2003). Searches in SWISS-PROT and ExPDB, BLAST or a local database of PROSITE are implemented, but not integrated in a comparable way.

Other publicly available powerful 3D tools such as PyMOL (DeLano, 2002, http://www.pymol.org), UCSF Chimera (Huang et al., 1996), VMD (Humphrey et al., 1996) or YASARA (Krieger et al., 2003) currently do not provide the visualization of information available from various public databases, a precondition for a better understanding of protein function. The visualization possibilities are comparable to those of BRAGI. One can use lines, solid bonds (sticks), CPK, cartoons tubes, ribbons and many more to highlight interesting parts of molecules. RASMOL (Bernstein, 2000) is a frequently used viewer for all kinds of molecules included in nearly all Linux distributions. RASMOL does not use modern hardware for graphics display. In contrast to these programs BRAGI is fully menu driven, hence there is no need to use a command language to select parts of the molecule for a special display mode. Even movies are created using the graphic interface. For advanced users BRAGI provides a built-in command language.

The combination of a proven modelling and visualization tool, as established in BRAGI, and the linkage and integration of information
Fig. 2. Screenshot of a session with BRAGI. The protein structure ‘Hemoglobin (1CBM)’ is entered by the user. In the ‘Human Mutation Databases’ window containing all known mutation of this structure from OMIM one mutation PHE122LEU (No. 317) – jointly responsible for sickle cell anemia – is selected. This PHE residue in highlighted in the 3D viewer and marked with an arrow.

From public databases harbours an enormous simplification for the analysis of protein structures and rational protein design.

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