Proasis2®

Protein Structure Database and Visualization System

Industry's best protein structure database and visualization system for medicines research. It takes many years and iterations for a technology to become "stable". Proasis2's storage and retrieval of protein structure data, developed for over 12 years, has achieved this maturity and is ready for you to use today.

A superior relational database for storing, retrieving, and searching structures important to medicinal chemistry projects is combined with an intuitive desktop visualization system for exploring those structures. Proasis2 hides complexity behind a simple click and point format to allow all your scientists, not just the modeling and crystallography experts, make the best use of the data revolution changing drug discovery.

Improved productivity, efficiency and communication can be achieved throughout your pharmaceutical research units by the enhancing the sharing of data, methods, and ideas.

Seamless linkages exist between protein structure data, critically important in medicinal chemistry projects, and the tools needed for you to make the best use of the information.

Empowering medicinal chemists to explore ideas themselves; freeing up your crystallographers' and modelers' time to concentrate on sophisticated areas of drug discovery.

Up-to-date and innovative in-house research is championed. Using Proasis2 you can harness the power of the data revolution. McKinsey Global Institute in their report '*Big data: the next frontier for innovation, competition and productivity*' recognizes that it is critical that companies like yours become 'data competents' or risk being left behind.

Developed by a leading computational chemist, in collaboration with many global pharmaceutical companies, Proasis2 matches the real requirements of leading edge drug discovery and helps you innovate.

Customizable in every facet to make sure the system directly meets your needs. Proasis2 has been developed using the Python programming language. Coupled with its modular design, Proasis2 is easily customized to your specific requirements whilst remaining easy to maintain, extend and upgrade.

How Proasis2 Improves Your Research Capability

Proasis2 is designed to make your research easier by removing the burden associated with handling data and the diffucilties of using sophisticated modeling technologies.

Proasis2 specifically addresses and minimizes the challenges faced by you when dealing with complex protein structure data. These challenges include:

- Very large structures - poorly resolved relative to small molecules;
- Disparate information resources;
- Limitations of the PDB format;
- Accessing reliable chemical information;
- Understanding ligand binding modes;
- Using expert software always difficult and time consuming to learn
- Handling heterogeneous, oligomeric systems

Proasis2 solves these challenges for you.

Protein structures important to medicinal chemistry projects are stored in a relational database (Oracle or MySQL):

- existing structures (both in-house and public domain) can be deposited in batch mode;
- newly solved in-house structures can be entered using an advanced web interface;
- automated scripts regularly load newly solved public data

A hierarchical classification of research projects gives a distinct 'drug discovery' view of protein structure data.

Proasis2 has been designed to complement proven 'best practice' work methods within successful research companies.

For your medicinal chemists, Proasis2 enables:

- use of desktop PCs to search and retrieve structures, and launch a graphics package displaying a structure with the click of a button
- a deeper understanding of the factors determining tight binding through the automation of sophisticated modeling techniques

For your crystallographers, Proasis 2 enables:

- protein structures to be readily stored, annotated, and retrieved
- structure data to be published for all in-house colleagues
- database contents to be easily updated through the database administration interface

For your modelers, Proasis 2 enables:

- routine tasks to be automated
- seemless linkages between data and advanced modeling applications

Functions, Features and Benefits

BURDEN FREE STRUCTURE SUBMISSION

Proasis2 is a flexible relational database, with an intuitive web-based interface making structure submission, retrieval, and modification routine. Web-based structure deposition can be set up to maximize the information you store by enabling a large number and variety of data fields to be entered. The Proasis2 system is easily customized to meet your specific requirements.

Submitting a new protein structure to the database simply involves:

- uploading a file into web form and filling in a few text fields
- selecting the bound ligand from a pull-down menu
- clicking the submit button

This web-based structure deposition minimizes the burden on your crystallographers.

The database software completes the following tasks:

- parsing the pdb file, checking for format errors and extracting Header information
- identifying the class of protein using Blast
- determining ligand candidates
- characterizing the correct chemistry of the bound ligand
- storing data in database tables

Numerous methods are available for loading your structures including:

- web GUIs, customized to match in-house requirements
- command line scripts
- XML files
- Fully automatic structure deposition - enabling regular batch submission.

Deposition can be made even easier by copying data from previous submissions and fully automated methods are available to load the database – new pdb files can be simply 'dropped' into an upload directory.

CASE STUDY: Using Proasis2 in the monthly project meeting

Typically, teams from biochemistry, molecular biology, pharmacology, chemistry, and modeling, meet each month to update one another on recent progress in their project and discuss future plans.

To prepare for such a meeting, a modeler typically spends hours collating protein structure data for display and 'second guessing' the information to be requested at the meeting. With Proasis2, this information can be compiled at the click of a button, during the meeting.

For example using Proasis2 allows, in real time during the meeting, participants to:

- examine the key factors determining tight ligand binding
- view multiple targets
- immediately pose and have answered sophisticated questions about the project
- add additional structures to overlays
- explore new hypotheses

With its fast structure searching, retrieval, visualization, and overlay functionality, Proasis2 brings a new level of productivity into monthly project meetings.

EFFECTIVELY HANDLES DIFFICULT STRUCTURES

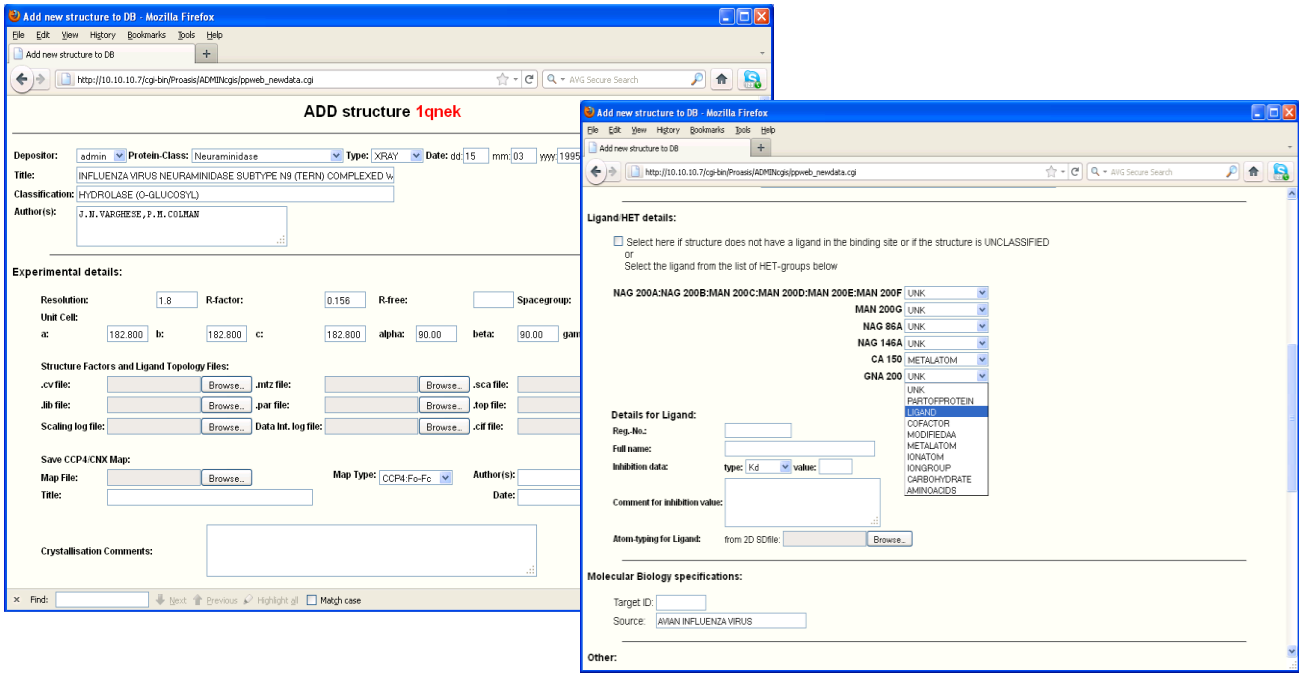
Proasis2's deposition tools effectively handle the harder problem of in-house protein crystal structure data.

- Binding site regions in both liganded and non-liganded structures can be located
- All monomers in homo-multimers automatically identified
- All proteins in hetero-multimers automatically identified
- Binding sites with multiple ligands carefully handled
- Protein chains with multiple binding sites carefully handled
- Binding sites at the interface of multiple chains managed
- All small molecules associated with a protein structure file comprehensively managed and ligands in binding sites differentiated from other small molecules
- All older and newer pdb formats supported
- Database contents easily updated using a wide range of database administration tools

INTUITIVE WEB SUBMISSION

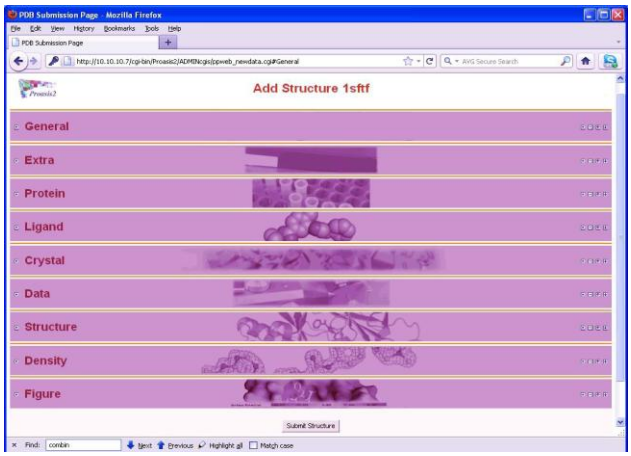
Web Submission Involving a Few Fields

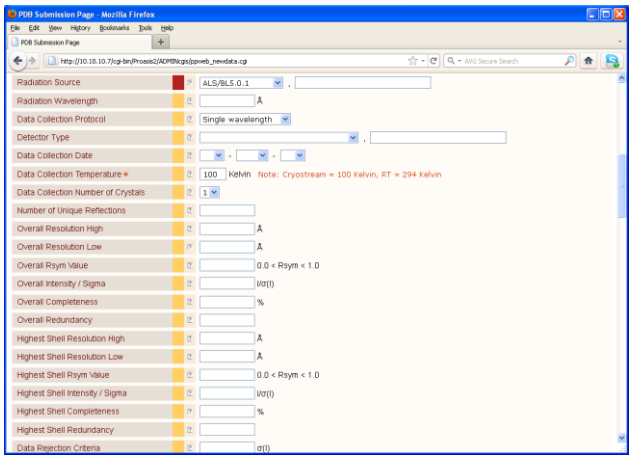
Most data is obtained directly from the pdb file. Only the ligand in the binding site needs to be selected from a pulldown menu. DesertSci can also assist with defining stardardized headers for in-house structures, making submission even easier.



Web Submission Involving Many Fields

Data can be obtained from a pdb file, log file, and a previously submitted structure. It is then loaded into a comprehensive web GUI for checking prior to submission





DATA ORGANIZATION FOR MEDICINAL CHEMISTRY

Unlike its competitors, Proasis2 provides you with a drug discovery/medicinal chemistry view of protein structure data. It allows structures to be classified so that any chemist can easily browse all protein-ligand complexes associated with their project(s).

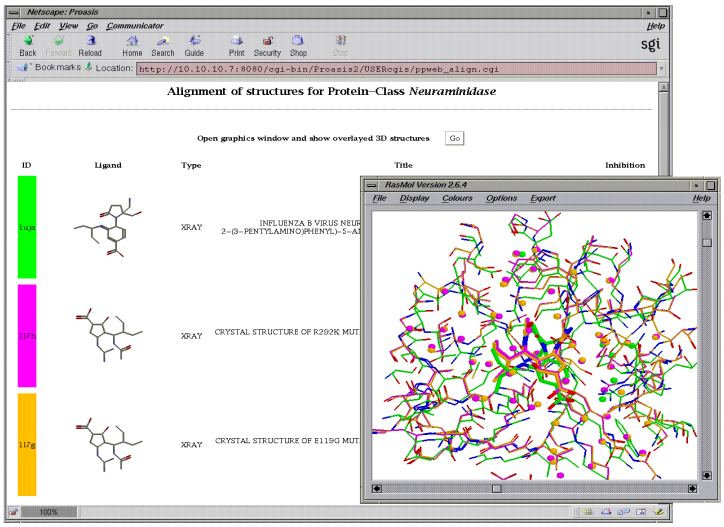
Proasis2 has developed a multiple hierarchical classification scheme to allow you to organize your data to suit specific requirements within a research company, regardless of size. The classification of protein structures is completely flexible enabling any subset to be grouped together.

FAST AND EFFECTIVE DATA RETRIEVAL

You can retrieve structures by searching:

- Project ID lookup, structure ID lookup, ligand ID lookup
- Full text based with advanced query logic
- Sub-structure and chemical similarity
- Sequences using Blast
- Recently submitted structures
- Combined project/text/substructure/date.

Fully operational molecular graphics applications, such as PyMol, can be automatically launched on the desktop showing you curated views. **It's like having an expert molecular modeler sitting by your side doing the work for you**. There is plenty offlexibility in the layout and reporting of hitlists so you can have the output to suit your organization. Structures can be downloaded in batches, overlayed onto a reference structure of choice.



Proasis2 works the same way as your brain – regular tasks are automated so that you can focus on the relevant information and put it to the best use.

SEAMLESS INTEGRATION OF ADVANCED TOOLS AND SOFTWARE LINKAGES

Proasis2 seamlessly integrates with DesertSci's other innovative software:

- Proasis3 – the Rich Internet Application (RIA) interface to the Proasis2 database tables
- ViewContacts – a superior tool for identifying and classifying non-covalent interactions
- Scorpion – state of the art molecular recognition software and scoring function

In addition, Proasis2 includes advanced tools for structure validation, including checking for missing atoms and residues, vdW clashes, contacts with symmetry molecules, and links with Molprobity. Advanced tools are now available for automatically generating comprehensive session files for any project.

OTHER FEATURES

Proasis2 is a comprehensive, robust system tested and used by many of the top ten global pharmaceutical companies. Other features include:

- ability to store structure factor files, topology files, parameter files, scaling log files, map files, supplementary data files, reports, presentations, images etc.
- creation of deposition reports for ELN systems
- storage and visualization of electron density maps and on-the-fly creation of maps from structure files
- symmetry module for building and displaying symmetry molecules, molecular assemblies and crystal packing arrangements
- robust backing up using xml
- comprehensive security features
- source code available (conditions apply)

HARDWARE AND SOFTWARE REQUIREMENTS

- server software runs on Linux
- clients can use Windows, Mac and Linux
- Proasis2 will work on an industry standard desktop PC without any specific configuration requirements
- protein structures are stored and retrieved as pdb files; indexed and annotated in Oracle or MySQL
- front-end HTML and JavaScript
- all major browsers and graphics packages are supported (PyMol, Jmol, AstexViewer, Chime, DS ViewerPro, Focus, MOE, Benchware 3D Explorer, Rasmol);

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www.desertsci.com
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