Proasis2

Protein Structure Database and Visualization System

It takes many years and many iterations for a technology to become ‘stable’.

Proasis2’s storage and retrieval of in-house protein structure data has attained this maturity.

Proasis2 Advantages

- Designed and developed for drug discovery by a leading computational chemist for all users, not just the experts.
- Crystallographers, modelers, and chemists can all make full use of protein structure data in drug discovery programs
- Developed for over 10 years in close collaboration with major pharmaceutical companies it is stable and mature, and satisfies user needs.
- Customizable to ensure it directly meets individual customer specifications
- Constantly evolving through direct feedback from multiple industry collaborators
- Performance optimized over the entire complex system of components to ensure maximum efficiency gains.
- Focuses on ligands in binding sites
- Minimizes the burden on crystallographers to deposit and publish their results
- Overlays multiple structures at the click of a button,
- Overlays can be based on sequences, binding site residues, ligand substructures or ligand similarity

Challenges of Protein Structure Data

- Protein structure data is complex - structures are very large and usually poorly resolved relative to small molecules
- Information resources are often disparate
- PDB format has many limitations
- Reliable chemical information is hard to access
- Oligomeric systems require special attention
- Ligand binding modes are challenging to comprehend
- Most of the software is designed only for expert users
- Graphics and modeling packages are time-consuming to learn

Proasis2 addresses and minimizes the burden of all of these issues

Structure Deposition

- Numerous methods are available for loading structures into the Proasis2 Database including:
  - using web GUI, customised to match inhouse requirements
  - using command line scripts
  - fully automatic structure submission, enabling regular batch submissions
  - from XML files

- Web based structure deposition minimizes the burden on crystallographers

- Web based structure deposition can be set up to maximise the information stored by enabling a large number and variety of data fields to be entered. It is easy to customize the system to match specific customer requirements

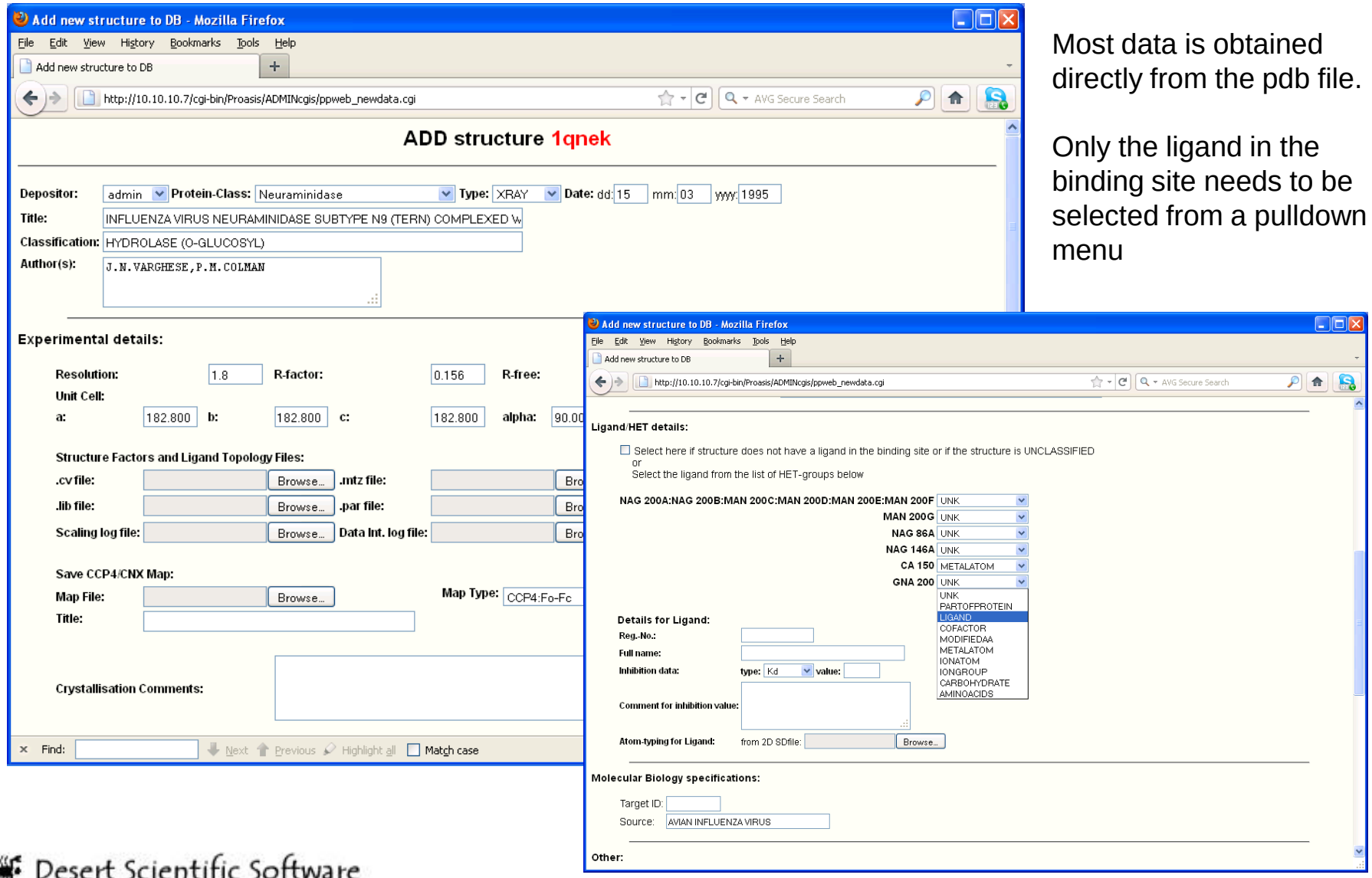
- Deposition can be made even easier by copying data from a previous submission

- Fully automated methods can be used to load the database - new pdb files can simply be ‘dropped’ into an upload directory

Proasis2 Manages Hard Structures

- Proasis2 deposition tools effectively handle the harder problem of in-house protein crystal structure data
- Binding site regions in both liganded and un-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 can be managed
- All small molecules associated with a protein structure file can be comprehensively managed, and ligands in binding sites differentiated from other small molecules
- Supports all older and newer pdb file formats
- Administration tools enable database contents to be updated easily

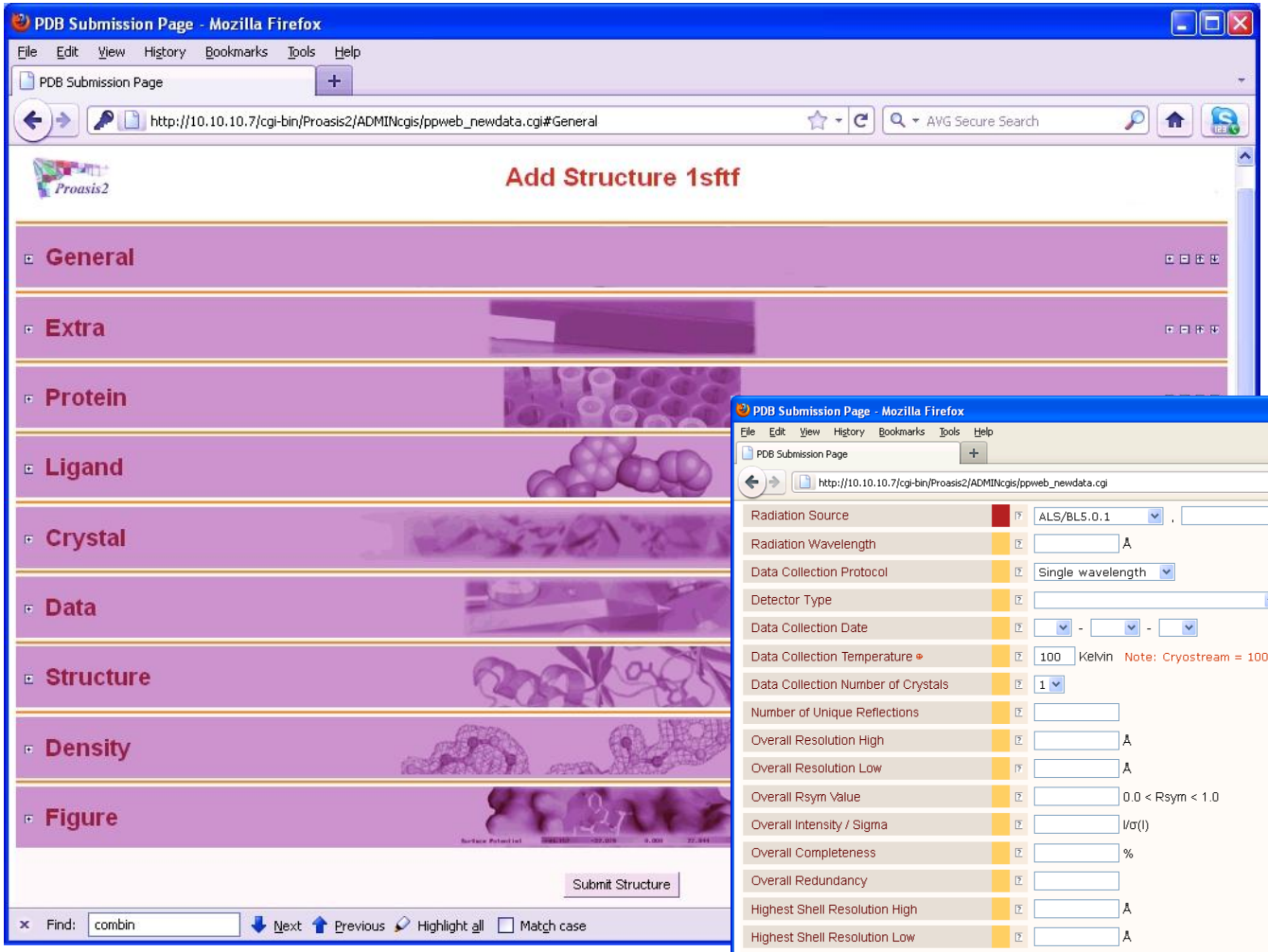
Web Submission Involving a Few Fields

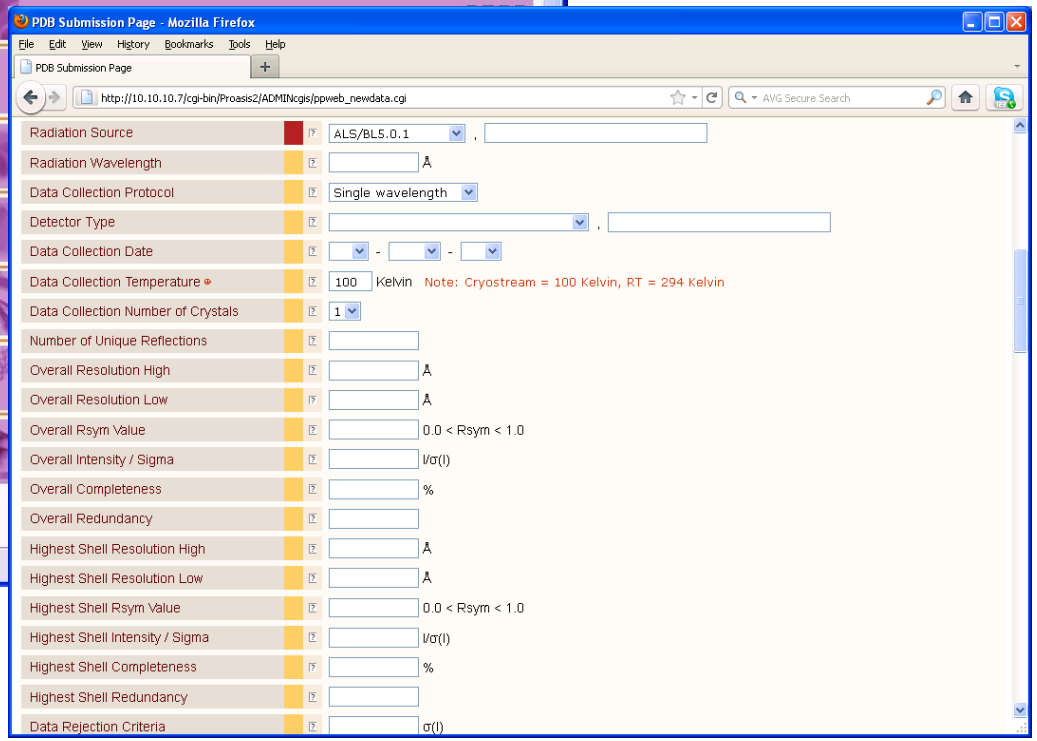


Most data is obtained directly from the pdb file.

Only the ligand in the binding site needs to be selected from a pulldown menu

Web Submission Involving Many Fields





Data can be obtained from a pdbfile; log file or previously submitted structure.

It is then loaded into a comprehensive web GUI for checking prior to submission

Structure Retrieval

- Searches available include:
  - Project Id lookup, structure Id lookup, ligand Id lookup
  - Full text based searching with advanced query logic
  - Sub-structure searching
  - Sequence searching using Blast
  - Recently submitted structures
  - Combined project/text/substructure/date searches

- Fully operational molecular graphics applications can be automatically launched on the desktop, showing curated structures as viewed by expert molecular modellers

- Flexibility in the layout and reporting of hitlists

- Structures can be downloaded in batches, and may be overlayed onto a reference structure

- Proasis2 works the same way as the brain – regular tasks are automated and the focus is on the relevant information.

Latest Features

- Proasis3 – the new Rich Internet Application (RIA) interface to the Proasis2 database Tables
- Provides the basis for the seamless integration of ViewContacts – DesertSci's state of the art software for identifying and classifying non-covalent interactions
- Provides the basis for the seamless integration of Scorpion - DesertSci's start of the art molecular recognition software and scoring function
- Advanced tools for structure validation, including checks for missing atoms and missing residues, vdW clashes, contacts with symmetry molecules, and links with Molprobity
- Advanced tools now available for automatically generating comprehensive session files for any project

Other Features

- Stores in-house, public domain, X-Ray, NMR and modelled structures in a RDMS, which can be Oracle or MySQL
- Projects can be viewed as a hierarchical tree, giving a medchem view of the data
- A wide range of browsers and graphics packages (PyMol, Jmol, AstexViewer, Chime, Rasmol, DSViewer Pro, Focus, MOE) supported
- Creates deposition reports for ELN systems
- Able to store structure factor files, topology files, parameter files, scaling log files, map files, supplementary data files, reports, presentations, images, etc.
- Storage and visualisation of electron density maps, and on-the-fly creation of maps from structure factor 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