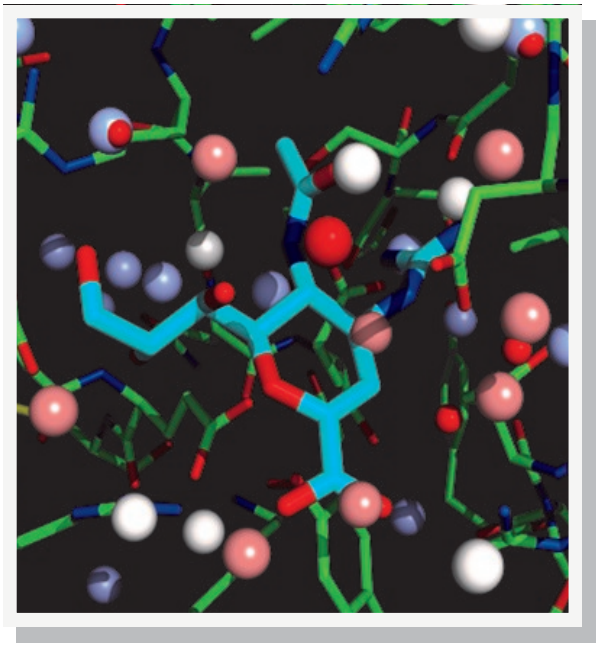
WATERVIEW

Water Clustering

WaterView identifies preferred locations for hydrogen bond donors and acceptors in a binding site based on real, experimentally derived data



An important question in structure based drug design is "*which water molecules in the binding site are located in regions that are highly favoured and which waters are in less favoured regions?"*

Significant gains in affinity and selectivity can be achieved by targeting the right waters

In today's fast-moving research environment there are regularly sufficient numbers of x-ray structures solved for a project, that enable us to answer this question using **real, experimentally obtained data.**

WaterView combines the power of DesertSci's Proasis3 and ProFusion software, to create a new tool to clearly highlight the favoured and less favoured waters, using real, experimental data, at the click of a button.

WATERVIEW

A **robust** method for better understanding the role of waters in ligand binding. Based on solid experimental data, both the preferred locations of binding site waters and their local distributions can be highlighted. Descriptors are derived from high quality overlays and a density based clustering approach. WaterView seamlessly links Proasis3 and Profusion functionality, improving the understanding of waters in the binding site.

PROASIS3

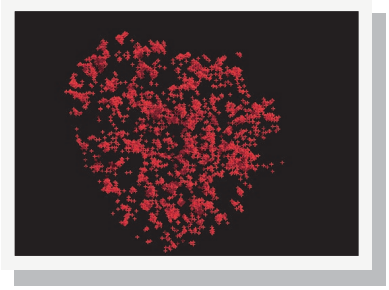
Proasis3 is a superior relational protein structure database and visualisation system designed for drug discovery research .

PROFUSION

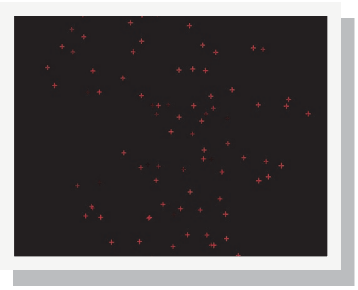
Fully automated project data files containing key target data, key ligand data, and state -of- the- art protein-ligand interaction data.

The Paradigm

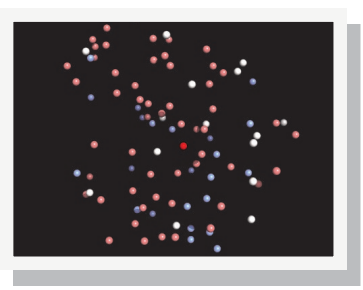
- Proasis3 is loaded with new structure(s) for a project
- Overnight, the automatic updating process begins: the new structure(s) is automatically added to ProFusion Session files and overlays are updated accordingly
- Water clusters are re-calculated using DBSCAN - Density Based Spatial Clustering of Applications with Noise
- When viewing any project structure in Proasis3 the template is retrieved and coordinates are transformed to the reference frame of the current structure
- Cluster centroids are colour coded according to degree of clustering AND occupancy in the binding site region



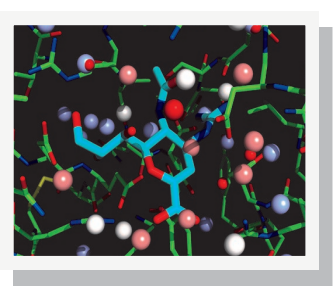
Overlayed waters →



Centroid positions →



Centroid positions showing degree of clustering AND occupancy →



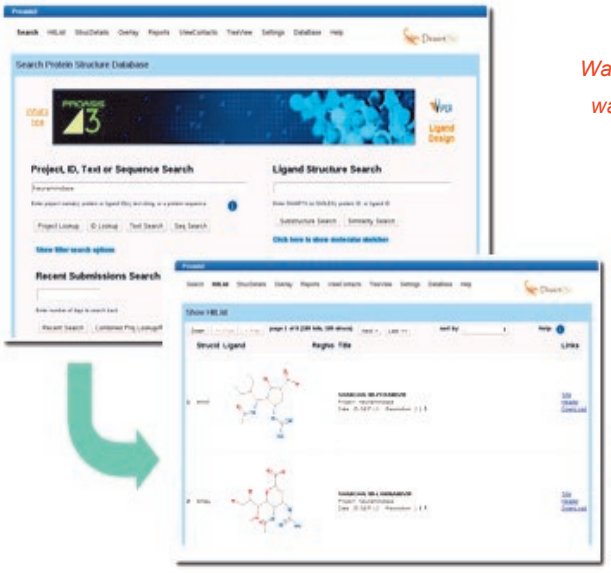
Coordinates transformed onto the reference frame of the current structure

DesertScientific Software

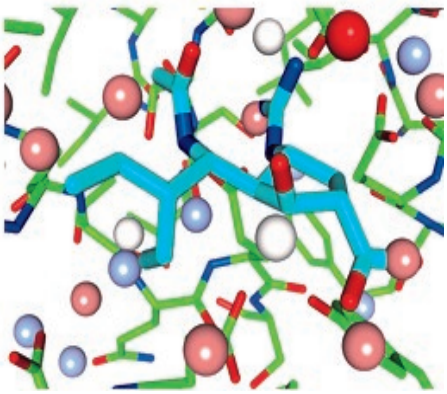
WATERVIEW

Features and Benefits

- WaterView is based on real, experimentally derived data providing better accuracy
- Different protein alignment schemes can be used allowing modelers to apply alignment and overlay methods best suited to their project
- Sequence similarity measures used to control which structures from a project should be included
- DBSCAN algorithm creates centroids with distributions that show close agreement with experimentally observed water networks
- Colour coding takes account of both degree of clustering and degree of occupancy of water clusters
- Automatic updating when new structures deposited to Proasis3
- Easy to explore water clusters overlayed with structures from a project
- Routinely available results on any desktop, daily
- Intuitive, fast, easily operated
- Designed for both expert modellers and medicinal chemists interested in ligand design



WaterView shows the highly favoured regions for water molecules and the less favoured regions … from just a couple of mouse clicks



Clustered water molecule positions, in aligned and overlayed experimentally solved structures, provide key information for drug discovery research

WATERVIEW

- Starts with alignments from ProFusion Session Files
- Uses DBSCAN (Density-based Spatial Clustering of Applications with Noise)
- Finds centroids for water clusters
- Stores centroid positions, degree of clustering AND degree of occupancy
- Transforms coordinates for each complex

CONTACT US

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