The SRS 3D module: integrating structures, sequences and features

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ABSTRACT

Summary: In this paper we present SRS 3D, a new service that allows users to easily and rapidly find all related structures for a given target sequence; structures can then be viewed together with sequences, alignments and sequence features (currently from UniProt, InterPro and PDB). Extensive user feedback confirms that SRS 3D is intuitive and useful especially for those not expert in structures.

Availability: An SRS 3D server is provided at http://srs3d.ebi.ac.uk/

Contact: contact@lionbioscience.com

Supplementary information: Complete documentation is available (click the ‘Help’ button after login). Product information can be found at http://www.lionbioscience.com/SRS3D/products/srs/srs-3d

INTRODUCTION

For about half of all proteins, some three dimensional (3D) structural information is available since they are significantly similar to proteins with known 3D structure (Schafferhans et al., 2003). However, many scientists fail to benefit from this information because it is difficult to access and use. Here we describe SRS 3D, a module of SRS (Etzold et al., 1996) that extends the integration philosophy of SRS to 3D structures. SRS 3D enables scientists to more easily access structures and to gain insight into protein function.

SYSTEM ARCHITECTURE

SRS 3D has three components: first, the LION Structure Viewer, a Java 3D application (Fries and O’Donoghue, 2002). Second, the PSSH family of databases of sequence-to-structure alignments (Schafferhans et al., 2003) derived from the HSSP database (Sander and Schneider, 1991).

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Third, presented in this paper, a set of scripts to integrate structure-related databases into SRS (Fig. 1a) and to create the associated database entry views. These views make extensive use of SRS’s ability to create composite views from multiple databases, combining sequence alignments, structures and sequence features. Due to space limitations, the reader is referred to the online documentation for details.

NAVIGATING FROM SEQUENCES TO STRUCTURES

In SRS 3D, when a user searches the UniProt sequence database (the successor to SwissProt, TrEMBL and PIR; Apweiler et al., 2004), the results table shows an icon for proteins with structural information (Fig. 1b, Steps 1 and 2). Clicking on the icon opens the corresponding PSSH entry, which shows a graphical summary of all 3D structures with significant homology to the target protein (Fig. 1b, Step 3). It can be useful to bookmark PSSH pages for proteins of special interest.

VIEWING A SEQUENCE-TO-STRUCTURE ALIGNMENT

The PSSH entry view (Fig. 1b, Step 3) helps to identify the most relevant structures. Selecting a structure opens an HSSPalign entry (Fig. 1c), showing sequences, alignments, the PDB structure and features from UniProt, all displayed in the LION Structure Viewer (Fig. 1c). The initial colouring of the structure highlights where the sequences differ, giving an immediate impression of the likelihood that the sequences share the same structure. Features from UniProt, InterPro (Apweiler et al., 2001) and PDB (Berman et al., 2000) can be mapped onto the structure (Fig. 1c), giving insight into function. The LION Structure Viewer has many functions that help users to understand the relation between sequence and structure (e.g. search for sequence patterns, save selections, save view states; see SRS 3D documentation section 1).
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VIEWING PDB ENTRIES

SRS 3D considerably enhances the view of PDB entries. UniProt and PDB features can be mapped on to the structure, and the user can easily navigate to related sequences and structures (Section 2.5, SRS 3D documentation).

BLAST versus PDB

The PSSH database gives accurate alignments and fast look-up. However, users will sometimes have sequences not included in PSSH. In these cases, the user can BLAST against PDB, view matches in the same way as a PSSH page (Fig. 1b) and open a page like an HSSPalign entry showing the target sequence and matching PDB entries (Section 2.8, SRS 3D documentation).

DISCUSSION

Currently, SRS 3D provides structural information for 540,000 sequences, with 920,000 UniProt features and over 1.5 million InterPro domain annotations. SRS 3D is designed to enable new feature databases to be added easily, thus we hope the EBI site will be extended in the future to include further feature data (e.g. exons, SNPs). Several other sequence-to-structure databases are similar in scope to PSSH (discussed in Schafferhans et al., 2003). The NCBI site provides a similar system for accessing related 3D structures (Chen et al., 2003). However, SRS 3D is the only system we know that combines sequences, alignments, features and structures in an integrated and generic way. Feedback from users indicates that SRS 3D is intuitive and useful.

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REFERENCES


