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DAS Workshop 2009

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ProteomeBinders

- Co-ordinate infrastructure for the generation of binding molecules for detection of the human proteome
- Create platform for the systematic development and quality control for these essential reagents
- Consistently characterised binders (QC), required to detect all the relevant human proteins in tissues and fluids in health and disease
- Protein State, modifications, splice variants etc.

Moving from Bench to Bioinformatics

Table 2. Protein epitope selection choices

Questions at the bench	Answered through epitope targeting for	Applications and technologies
Does the binding reagent need to recognise the native protein?	Full length expressed protein	Protein–protein interaction studies (coprecipitation), protein expression (capture arrays)
Will a binder targeted to a globular domain be sufficient?	Complex epitopes from folded globular domains	Binders for families of proteins sharing domains
Are binders to the unfolded (denatured) globular domains also needed?	Nonnative linear epitopes	Monitoring of unfolded protein; Western blotting, IHC
Would a linear epitope, from natively unstructured polypeptide regions, be desirable?	Linear, natively unstructured peptide epitope	Targeting of functional linear motifs
Are binders against posttranslationally modified variants (*e.g.* phosphoproteins) required?	Epitopes with and without PTMs	Tracking of signaling events influencing PTMs
Can the binder distinguish splice variants?	Epitope in modules alternatively spliced in or out	Detection of splice variants
Should the binder interfere (agonistically or antagonistically) with a function of the protein?	Functional site as epitope	Stimulatory/inhibitory binders for membrane receptors; competitive inhibition of protein–protein interactions; intrabodies

Proteomics. 2007 Jul 19; Affinity reagent resources for human proteome detection: Initiatives and perspectives.

Taussig. M.

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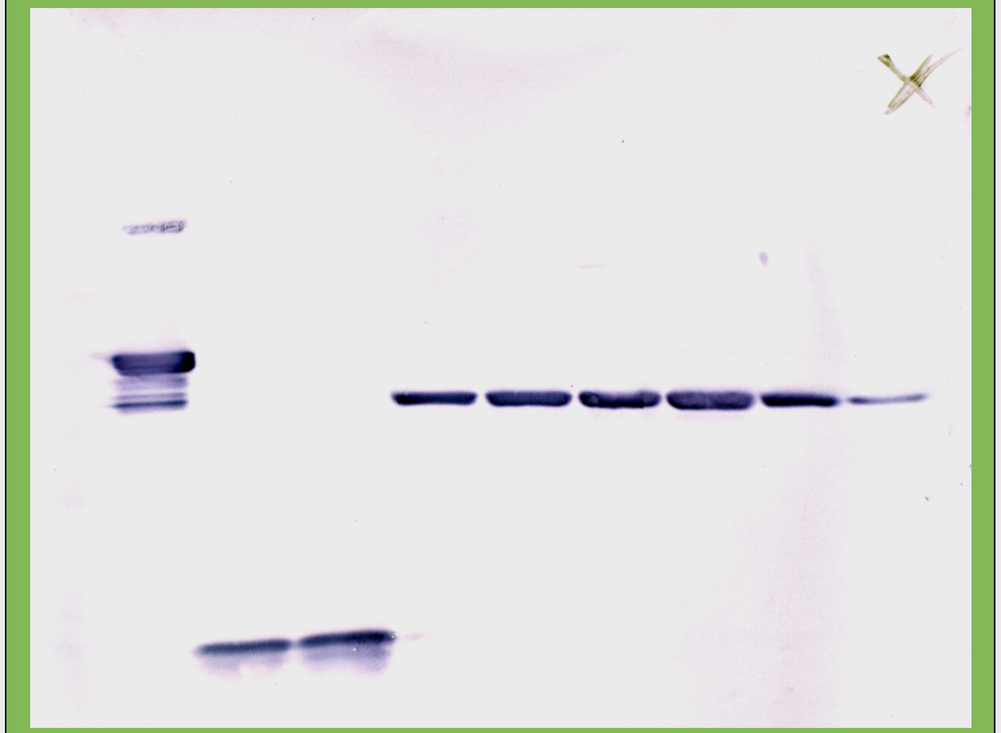
Move each question to a slide with pictures.

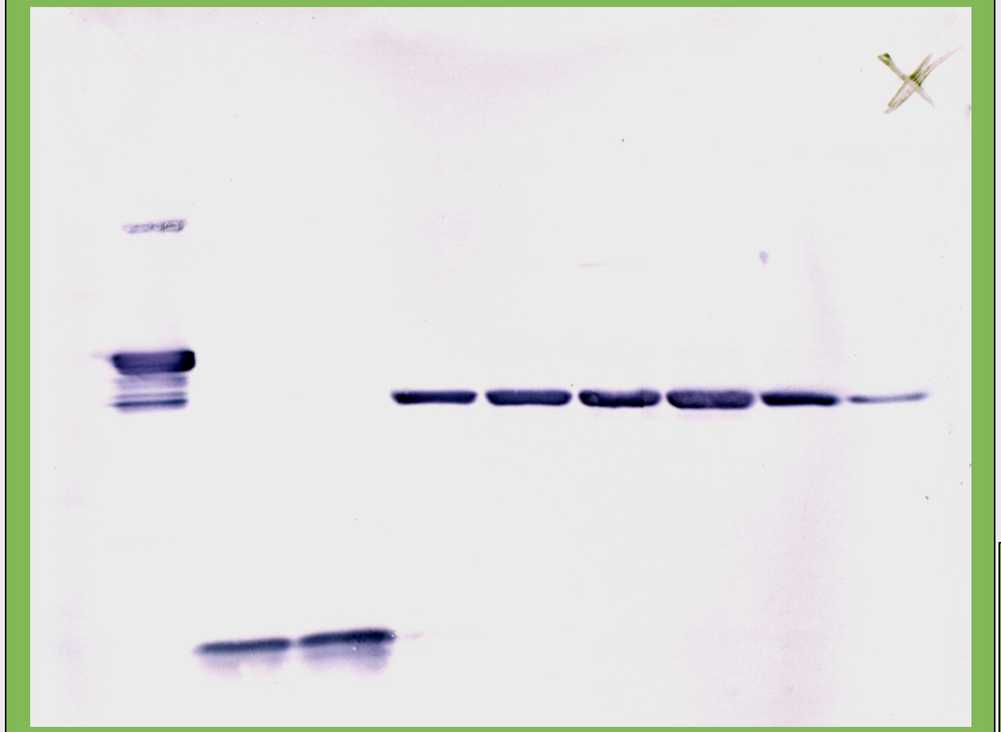
Mapping requirement to experiment

Western Blot

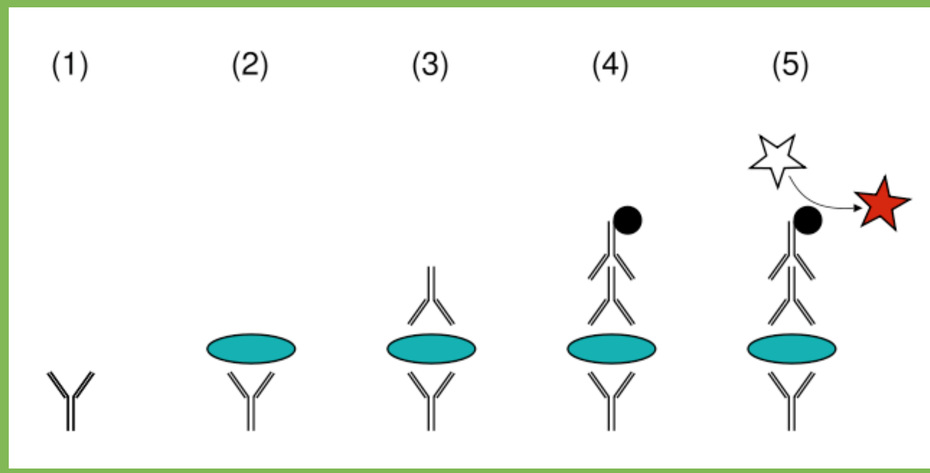


Mapping requirement to experiment

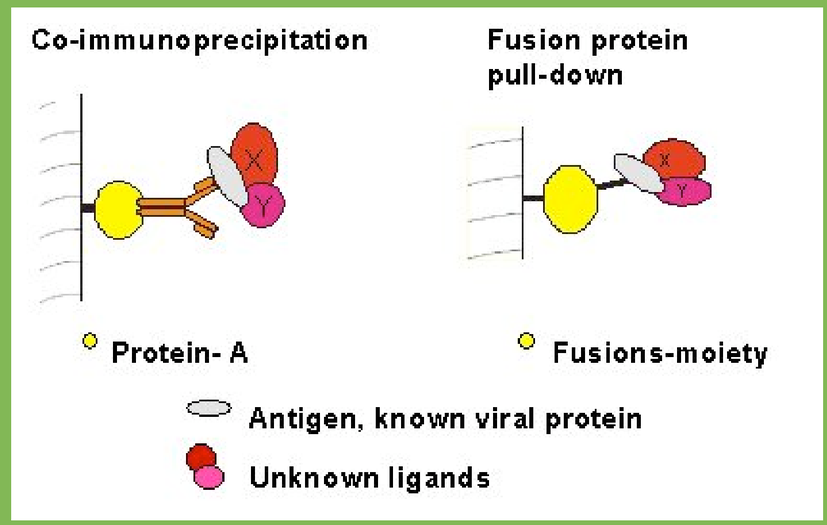
Western Blot



“Sandwich” ELISA Experiment



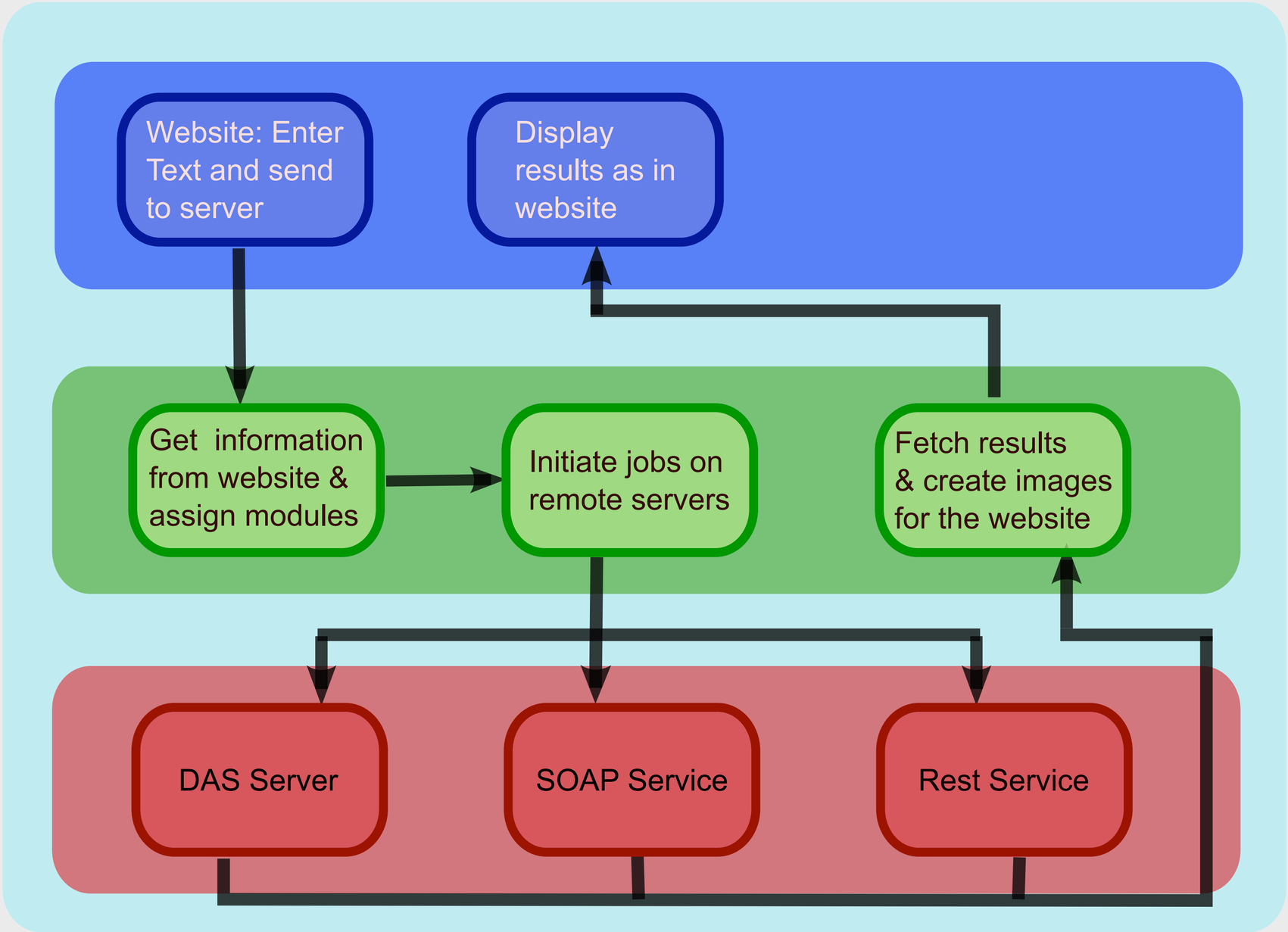
Pull-down



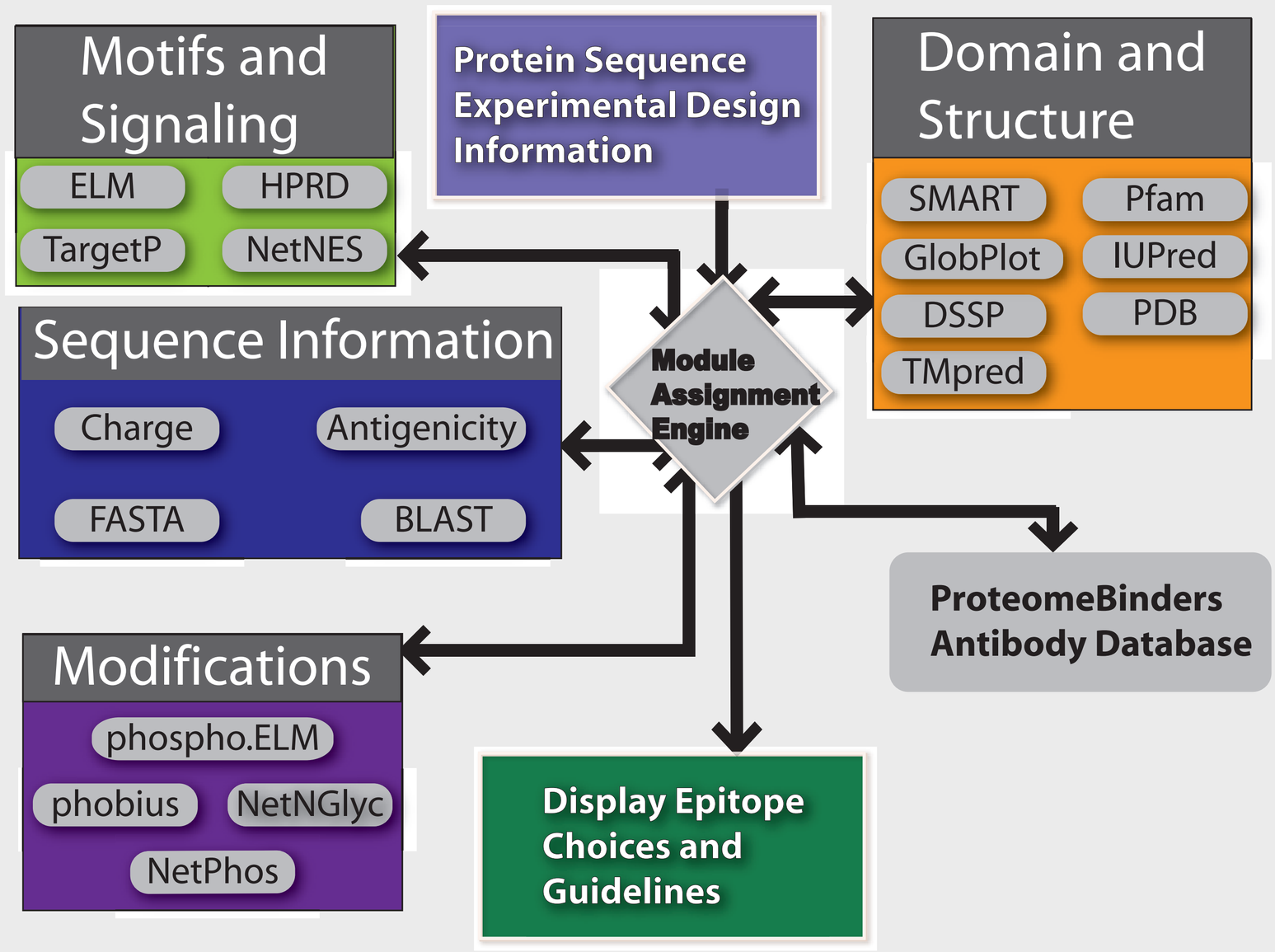
Why distributed collection of information

- Impossible or impractical to maintain databases in-house
- Difficult to deploy a range of clients to each server
- Stability of APIs in web available sources
- Speed - server is relatively small and underpowered
- DAS and webservices make it possible for small server to achieve complex analysis in acceptable time

Overview of web and server interaction



Module Assignment Engine



Collecting the information

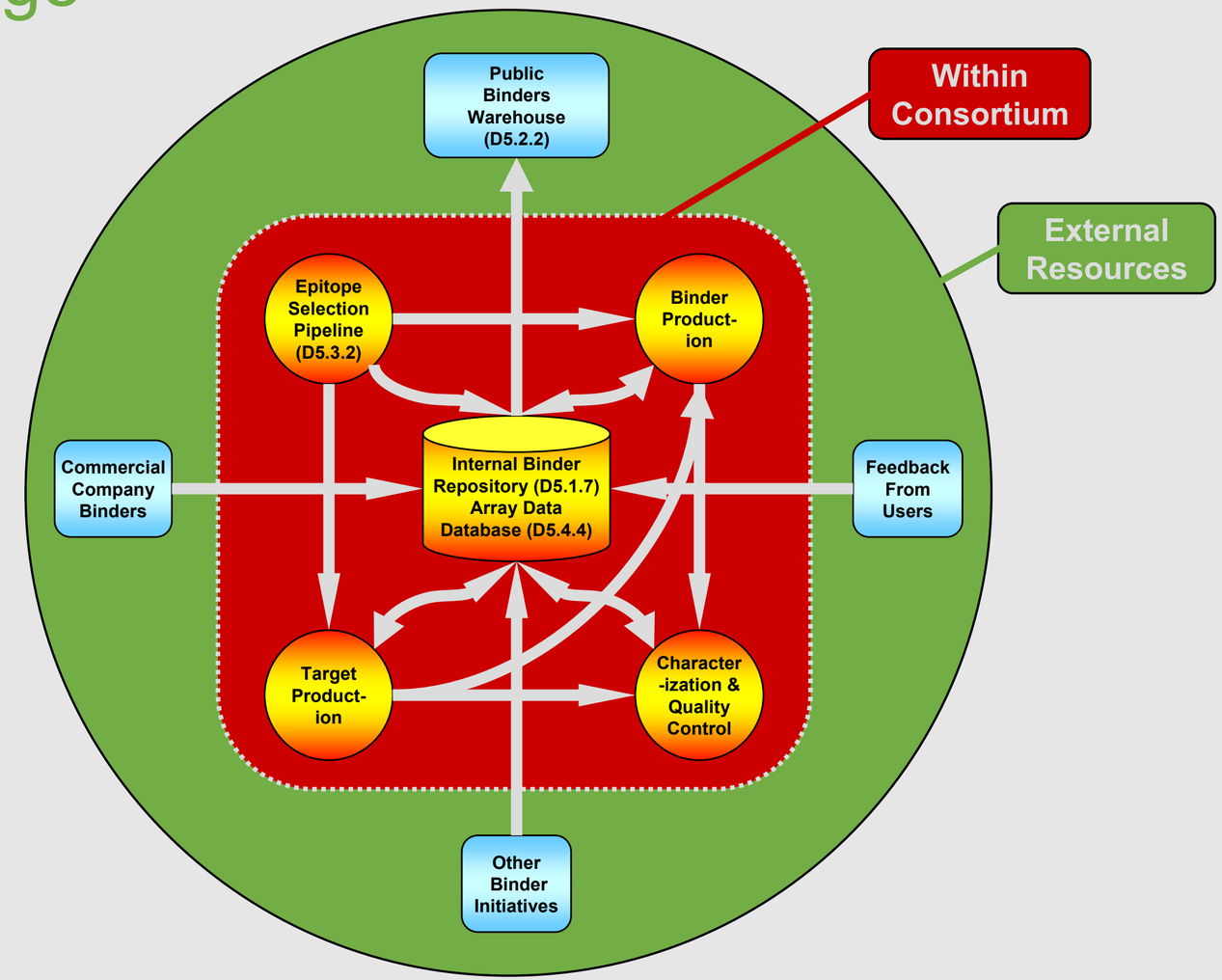
- Ajax interface to collect the results
- RPC Calls to a tomcat server
- Job creation/management by the server
- Parsing of results
- Send result objects back to GUI to be drawn there
- Responsive and interactive GUI

Webservices integration to DAS objects

- Return results of webservices run analysis into DAS Objects
- These can be displayed in the Ajax GUI easily too
- Object in Ajax coded behaves like DAS Object
- Has properties like co-ordinates, description, name, id, version, notes
- Specifically - the objects sent/recieved are List<DasObject> or List<String> or String - whatever

Protein Standards Initiative Ontology: PSI - Protein Affinity Reagents (PAR)

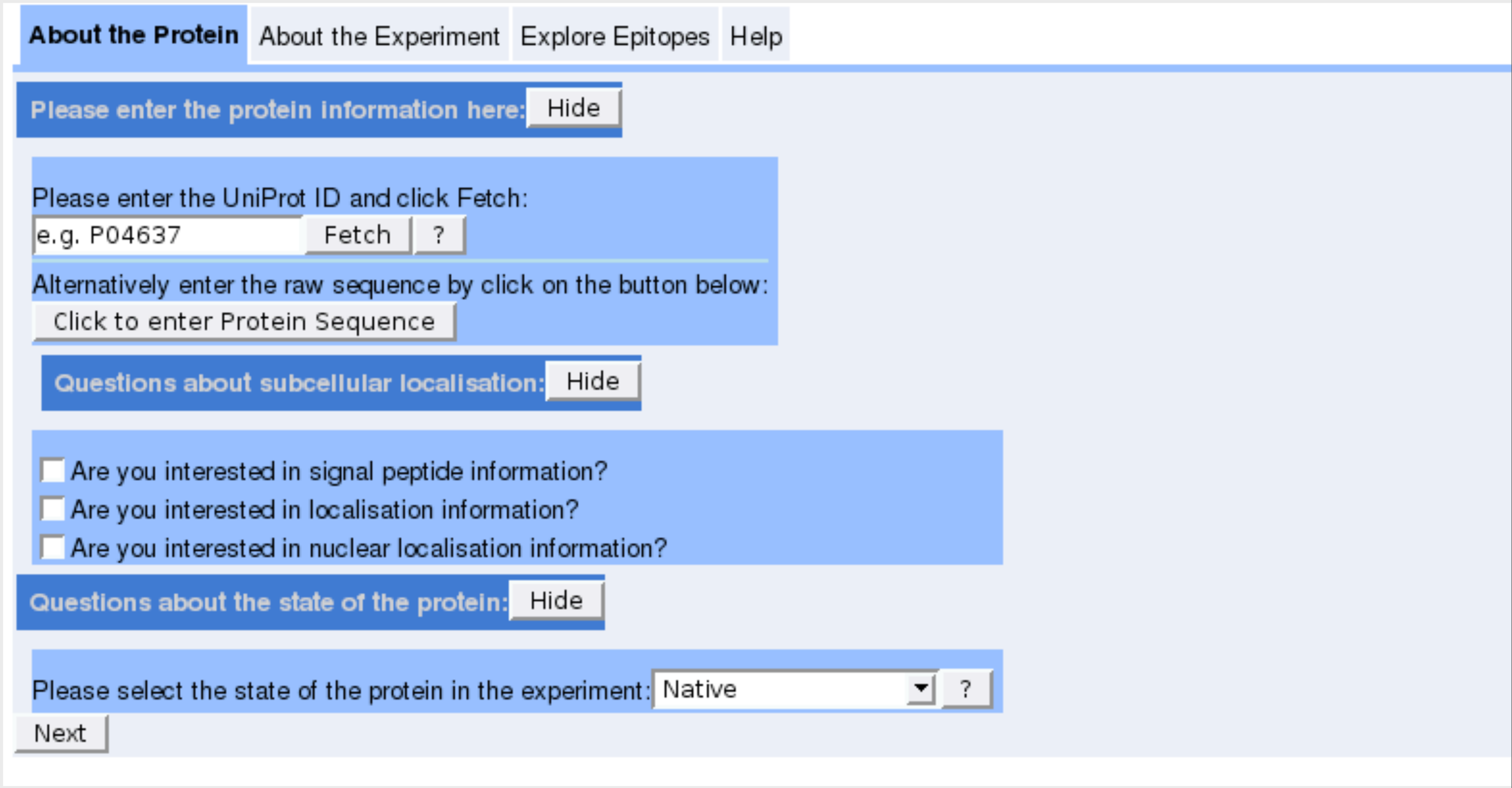
Exchange /Share Events



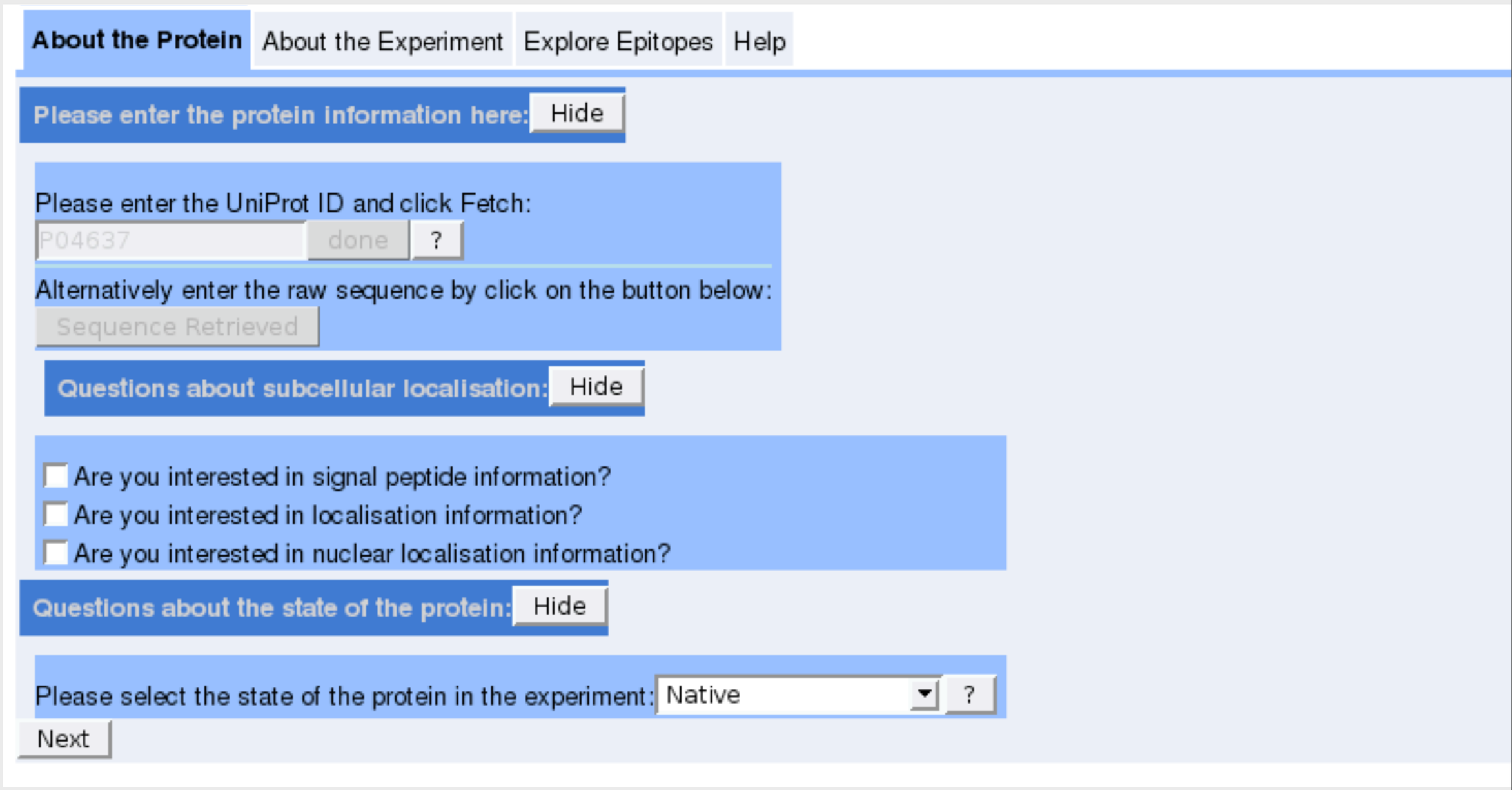
- David Gloriam
- Louisa and Sandra
- Sandrine Palcy
- EBI and Uni of Bordeaux

DAS Sources Used

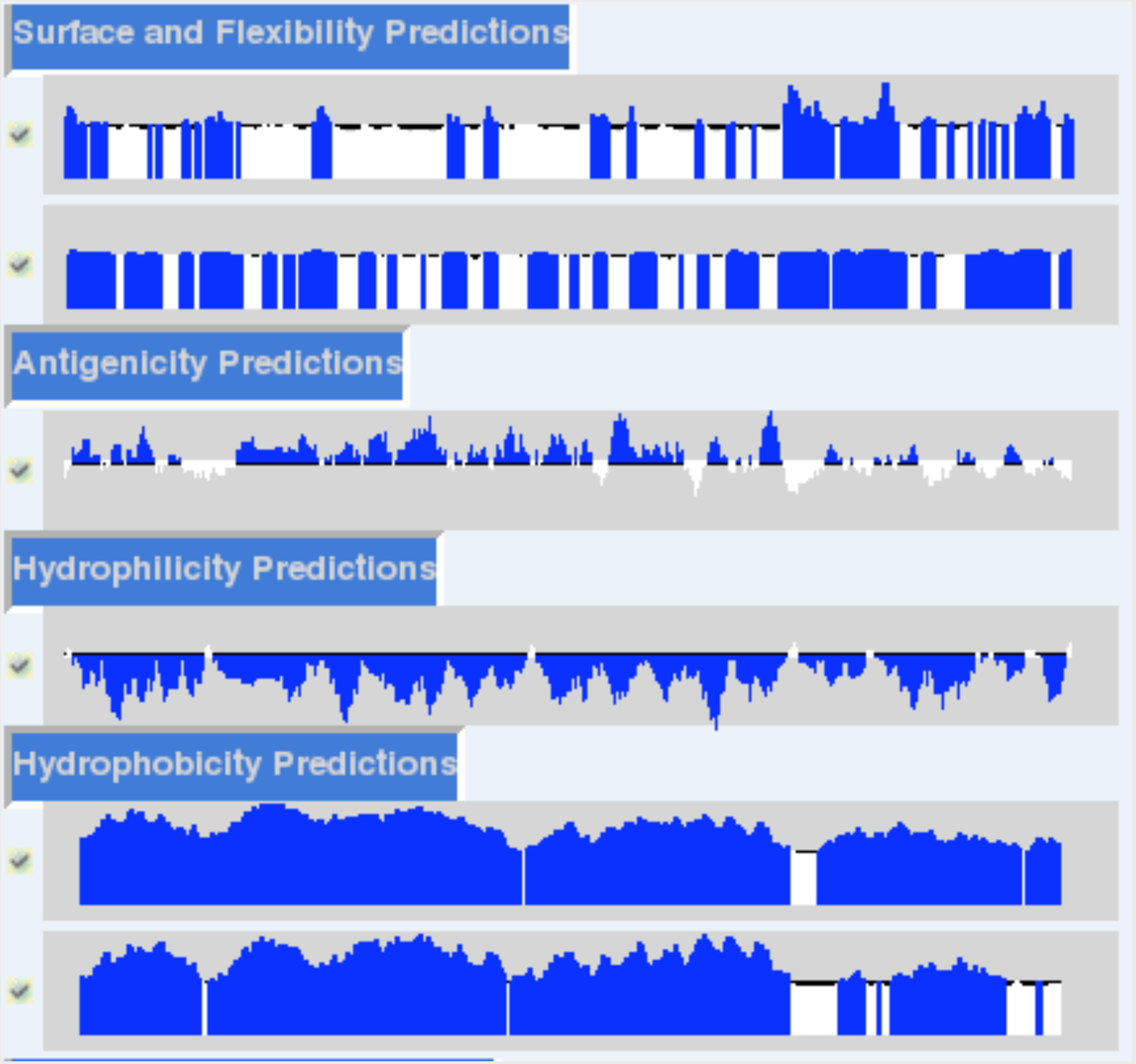
User Interface



User Interface



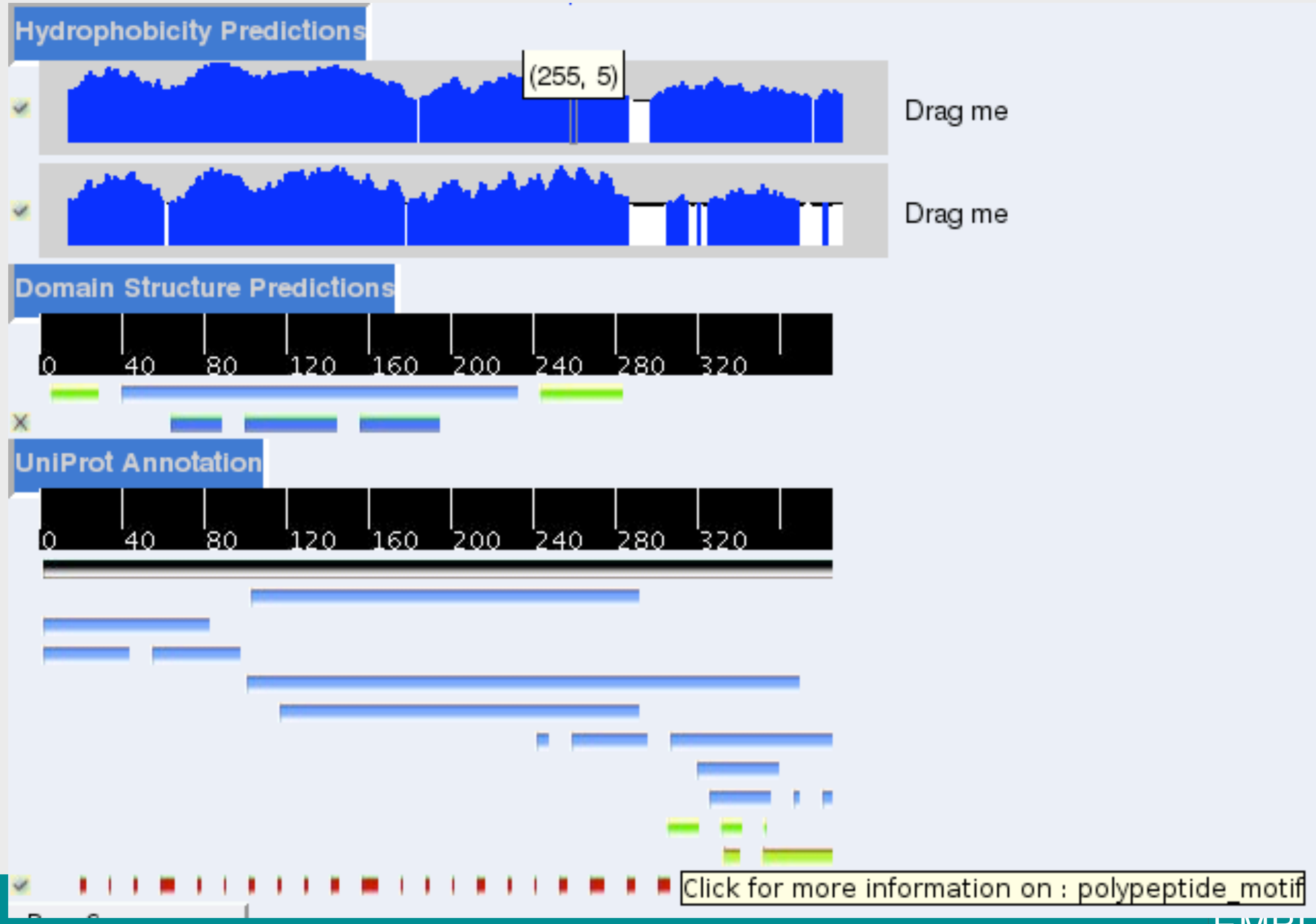
Results Page



Highlighting graphs

Highlighting graphs

Diagrams on the block objects below



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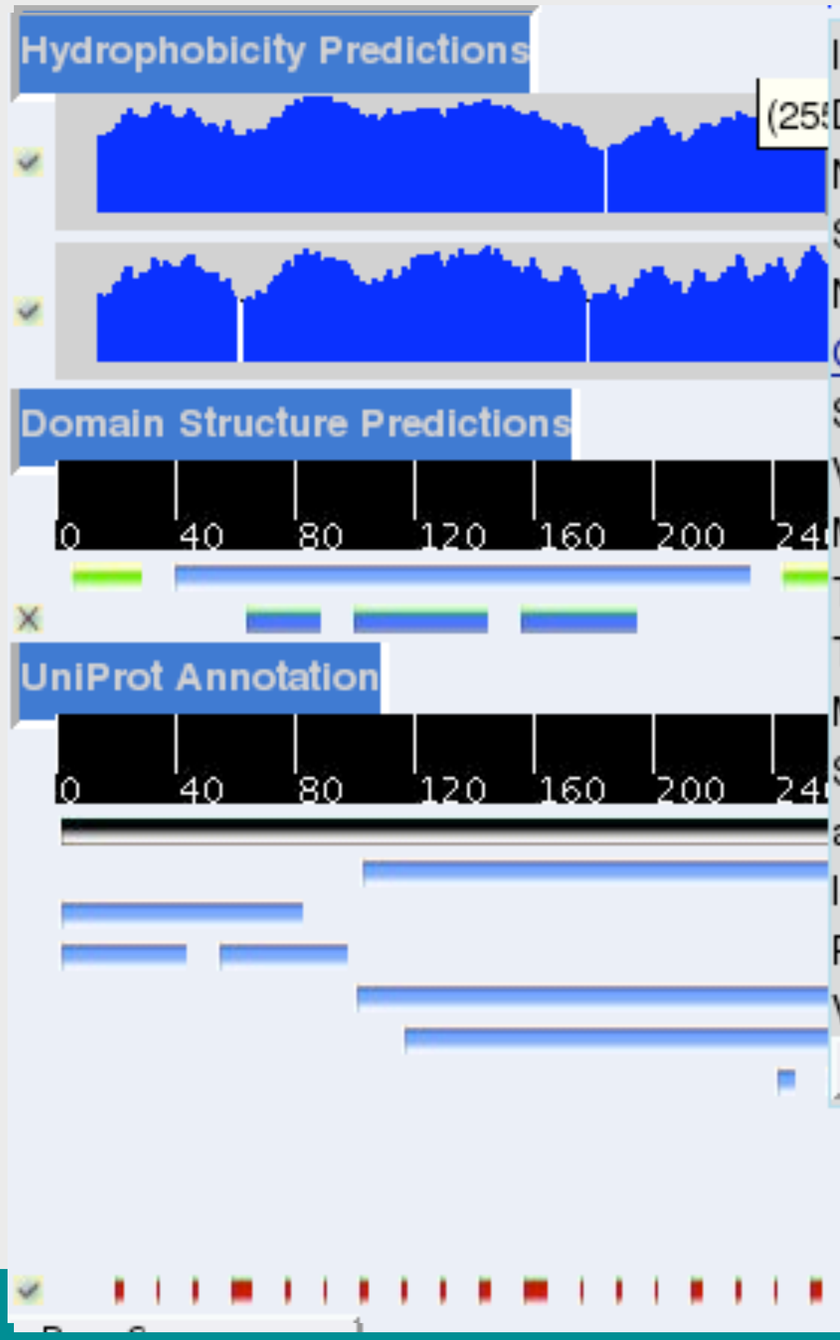
Diagrams on the block objects below



Id:
Description: polypeptide_motif
Note: Bipartite nuclear localization signal
Score: 0.0
No link available
Original DAS Server Response
Start: 305 End: 321
Version: a4339fbbe40c69e28b37c4eb4c4fad74
Method: UniProt
Type ID: SO:0001067
Type Category: inferred by curator (ECO:0000001)
Method OLS Def: A sequence motif is a short (up to 20 amino acids) region of biological
Such motifs, although they are too short to constitute functional domains, share sequenc
and are conserved in different proteins. They display a common function (protein-binding
location etc.).
Feature Sequence: KRALPNNTSSSP QPKK
Version Status:
X B

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Diagram on the pop ups.

- Mention that this controls the blast interface
- Version check from md5checksum
- Ontology lookup for Experimental Code and definitions of features

Conclusions

- DAS Sources speed up the delivery of information
- Alignment of objects in GUI much easier
- Ability to check provenance of information available in DAS
- Webservices require one client per app - DAS One client - many apps
- Wealth of information on there
- Would be nice to have updates on newly added DAS Sources
- facebook app as well.

Acknowledgements

- ProteomeBinders - EU Framework 6 Programme
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- SPICE, Dasobert, GoogleWebToolkit, biojava, tomcat

Acknowledgements

Comments or Questions