MANCHESTER 1824

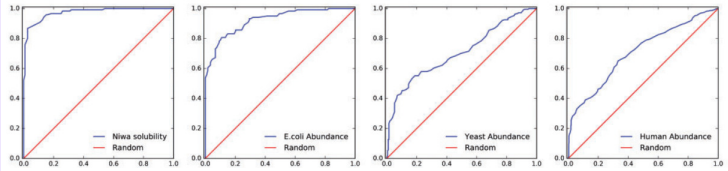
The University of Manchester

Computational Biology and Chemistry in Jim Warwicker's group at the MIB.

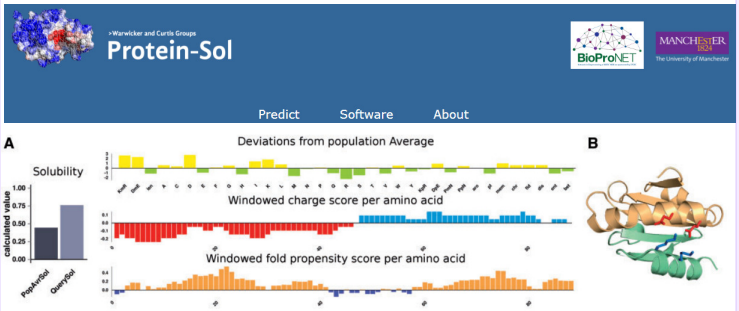
Structure/Function relationships in biological molecules, from algorithm development to genomic application and hypothesis discovery, in a collaborative environment with experimental colleagues. (jim.warwicker@manchester.ac.uk)

Algorithms: Protein Solubility and Bioinformatics

Develop sequence-based and structure-based methods for predicting protein solubility.



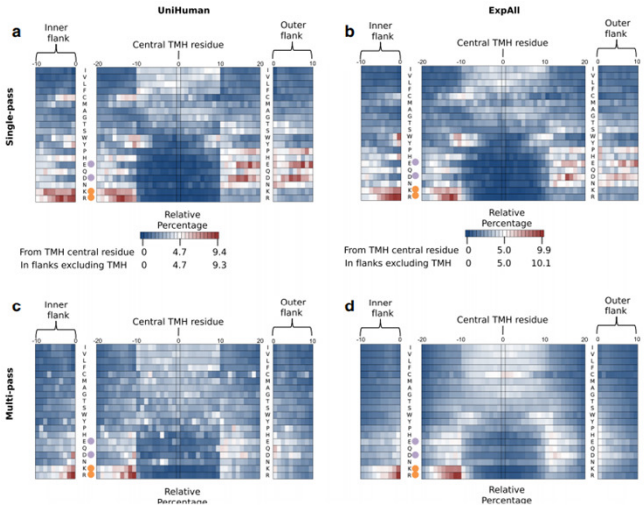
Make prediction schemes available as web tools for the community:
www.protein-sol.manchester.ac.uk,



Reference: Hebditch et al. (2017) Bioinformatics 33:3098.

Algorithms: Charges and Bioinformatics

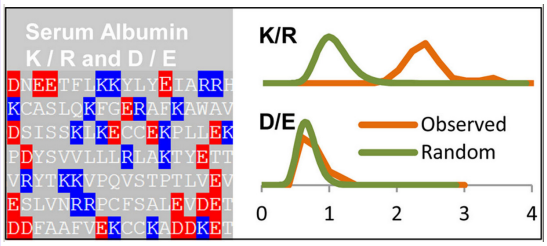
The "positive-inside rule" is an important tenet in the study of transmembrane proteins. We find that there is a complementary (although lower) signal for a "negative inside depletion/outside enrichment rule". This signal differs in importance for single and multi-pass membrane proteins.



Heatmaps for amino acid occurrence in transmembrane segments and flanking regions.

Reference: Baker et al. (2017) BMC Biology 15:66

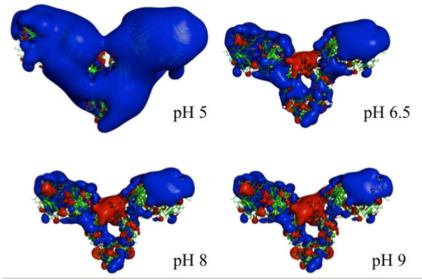
Biotechnology and Bioprocessing



Left: Proteins at high concentrations inside or outside of cells tend towards a higher content of lysine relative to arginine. This observation could be the basis for a conservative modification to improve solubility.
Mol Pharm (2014) 11:294-303.

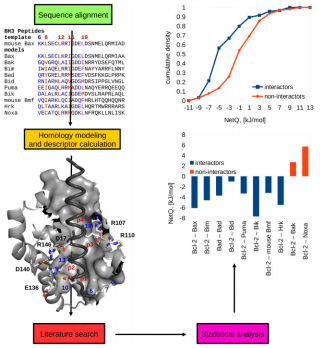
Right: Electrostatic interactions play a key role in the properties of monoclonal antibody solutions at high concentration (and thus in the bioprocessing, formulation, storage and delivery of mAb biologics). Charge calculations allow us to visualise transition between isotropic and anisotropic potential fields.

Mol Pharm (2014) 11:2475-2489.



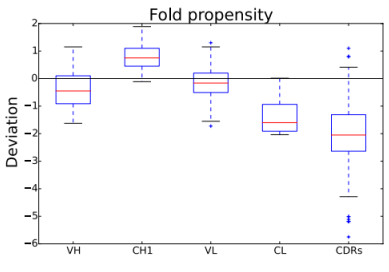
Other Work

Specificity in protein-protein interactions.



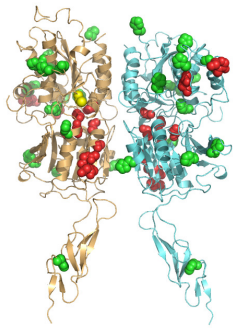
Ivanov et al. (2017) PLoS One 12:e0185928

Antibody CH1 domains are atypical IDPs, the signature for which is shared by other domains in the Immunoglobulin Superfamily.



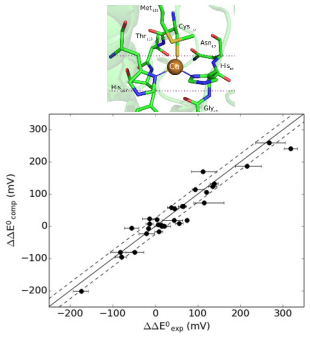
Hebditch et al. (2017) Sci Rep 7:12404.

pH-dependence of channels and receptors. Examples: Calcium Sensing Receptor, ASIC.



Campion et al. (2015) J Am Soc Nephrol 26:2163.

Model for protein reduction potentials.



Fowler et al. (2017) Chemistry 23:15436.

Current Group

Lorena Zuzic	PhD student	Modelling pH-dependence in endosomal processes (joint with BII, Singapore, Peter Bond Co-Supervisor)
Stefan Ivanov	PhD student	Modelling specificity in protein-protein interactions (joint with BII, Singapore, Peter Bond Co-Supervisor)
Max Hebditch	PDRA	Developing models for protein solubility and the effects of excipients (EPSRC, joint project with UCL)
James Baker	PhD student	Sequence analysis of transmembrane helices (joint with BII, Singapore, Frank and Birgit Eisenhaber Co-Supervisors)
Nick Fowler	PhD student	Computational and experimental investigation of redox potential (joint with Sam DeVisser and Chris Blanford)
Luke Holloway	PhD student	iCASE funding with MedImmune partner, Co-Supervisor in Manchester, Robin Curtis
		PDRA Grants with collaborators: Steve High – protein quality control ; Jeremy Derrick and others – protein solubility
		Joint PhD students in several other areas