Structural Modelling and Molecular Docking Services

1) Protein structure modelling:

Moleculomics offers a bespoke protein structure modelling service for individual or smaller sets of proteins. Using our world-leading protein modelling platform that underpins the Human3DProteome platform, based on homology modelling and threading, that has been developed over the last 15 years and featured in more than 60 research publications, we are able to model any protein of interest, wild type or single nucleotide polymorphism variant forms.

2) Addition of cofactors and prosthetic groups

If the protein of interest is known to contain a cofactor or a prosthetic group, we are able to add them within the structure, such as metals or heme groups which are essential for protein function.

3) Active site definition

We have developed unique tools which can predict the location of the active site(s) of a protein, an essential step for accurate molecular docking and structural binding site analysis.

4) Molecular docking

We are able to undertake molecular docking at any scale, using our methodology that combines Empirical (Affinity) and Force field (Energy) methods within an in-house consensus (metascore) method, which has achieved 88%-90% hit-miss accuracy in validation with industrial partners involving “blind” testing by comparison with in vitro analysis of new compounds, and more extensively validated with in vitro databases. We provide specialist client-specified analysis of specific
protein-compound interactions, reporting how a ligand binds with a protein, key interacting residues, bound orientation and chemical and physical binding properties.

5) Peptide / antibody design and docking

Moleculomics has extensive capabilities in peptide and antibody design, characterisation and docking.

6) Structural modelling and analysis of variants:

The structural modelling pipeline developed by Moleculomics is also able to model and assess the functional and phenotypic impacts of single nucleotide polymorphisms of a particular protein. We can view the structural impact the mutations have upon the protein and changes in the positions of individual amino acid residues which can impact upon ligand metabolism. Molecular docking studies can then be carried out to assess the impact the mutation has on ligand binding and metabolism. This approach can be applied to understanding molecular mechanisms underpinning disease, and for predicting impaired metabolic or binding function synonymous with non-responses and adverse drug reactions that occur for particular compounds due to natural polymorphic variation in human populations.

6) Assembly of oligomers

We can construct multi-subunit proteins composed of multiple monomers. Biologically relevant ligand docking or protein-protein docking can then be carried out.

Figure 1. GlyR (right)
7) Pathway analysis and disease

Annotated Protein-Protein Interaction data pertaining to link Molecular Initiation Events with understanding of Modes of Action and tissue specific pathway analysis. Moleculomics offers in silico pathway analysis to facilitate the understanding of molecular mechanisms and modes of action from the Molecular Initiation Event (the first interaction of a chemical with a biological system) through a series of pathway events to the given outcome; efficacious or toxic (Adverse Outcome Pathway). This approach advances compound development processes from assessment of traditional endpoints to mechanistic understanding of chemical interactions at a molecular level.

8) Ligand interaction profiling and machine learning

AI approaches involving the construction and application of classification models which profile candidate drugs into “good” (approved drug-like) or “bad” (toxin-like) profiles based on prediction of protein-compound interactions and comparison with known in vitro interactions. AI approaches are also used in hit to lead work for similarity clustering in biological and chemical space, to identify hot spots of protein-compound interaction. Moleculomics offers this approach on a per compound or per target basis too.
9) Protein-protein interactions

Protein-protein docking or macromolecular docking involves computational docking of two or more proteins. It predicts the 3D structure of the macromolecular protein complex and outputs a score of how likely the structure will form in nature. It is very useful for investigation of protein therapeutics and for protein pathway analysis and assessing downstream protein events. Moleculomics provides a comprehensive service for protein docking that has been proven to be highly accurate in numerous studies, publications and work with industry.

![Image of protein-protein interaction](image)

**Figure 2.** Complex 2VIS, of influenza hemagglutinin (purple) and murine IgG1, λHC19 antibody in the bound (green) and unbound (red) crystal structures, superimposed on the binding domain.

References


**Publication List** - [https://scholar.google.co.uk/citations?user=e5sOfe0AAAAJ&hl=en](https://scholar.google.co.uk/citations?user=e5sOfe0AAAAJ&hl=en)