KBDOCK Demo – Basic Operations

- KBDOCK web site: http://kbdock.loria.fr/

- Browsing domain-domain interactions
- Viewing DDI networks
- Structural superpositions in Jmol (or JsMol)
- Structure-based sequence alignments
- Looking at structural neighbours
- Downloading structural templates
- ...
- Using Kpax (again) to superpose targets onto templates
- ...
- Ask me!

Practical Activities – 1

Finding domain interactions involving API-A

- Download the API-A data from: http://hex.loria.fr/emmsb/t40.tgz
  - t40_c.fasta (sequence), t40_c.pdb (structure)
- Use KBDOCK to find the Pfam domain for this sequence
  - Tip: the Search page allows pasting a sequence or uploading a structure
- View some representative inter-chain hetero interactions
- Can you identify LEU-87 and LYS-145 on API-A?
  - Tip: In Jmol right-mouse for Menu; then: Set Picking → Identity

Downloading the template structures

- Download and uncompress all hetero interaction partners
  - (this should give a folder called PF00197)
- Delete the 3e8l structure – this is the solution structure!

Practical Activities – 2

Modeling API-A/Trypsin by structural homology

- Use Kpax to superpose one of the Trypsin complexes onto t40_c.pdb
  - Tip: in Kpax, the "query" never moves; only the "target(s)" move(s)
- (this should give a very good template for one of the binding modes)

- For the other mode, superpose Peptidase S8 complex (1bx1) onto t40_c.pdb
- Use Hex to identify the API-A loop that interacts with Peptidase S8
- Use Hex again to place a Trypsin active site around this loop...

- Refine your proposed docking pose using a focused docking search in Hex

Practical Activities – 3

Modeling a bi-enzyme complex using structural neighbours

In our paper (Ghoorah et al. 2014, NAR, 42, D389–D395), we proposed that a GATase/ImGP cyclase complex (PDB code 1GPW, Pfam codes PF00117, PF00977) could be modeled using a complex from structural neigbours found by Kpax (PDB code 2NV2, Pfam codes PF01174, PF01680). Here, your task is to verify that the proposed model is structurally reasonable.

- Download the data provided: http://hex.loria.fr/emmsb/gatase.tgz
- Look at Figure 3 of the paper (PDF file)
- Use KBDOCK to search for structural neighbours of 1GPW
- Verify that a proposed complex is indeed 2NV2

- Using the given PDBs, use Kpax to superpose one complex onto the other
- Tip: Kpax can move two structures with one superposition using:
  - kpax -ligand query.pdb target.pdb ligand.pdb
- Tip: You can put two structures into one file using a shell command:
  - cat file_a.pdb file_b.pdb >file_ab.pdb