Introduction to Protein Structure with Chimera

EMBO Practical Course on Computational analysis of protein-protein interactions: From sequences to networks

28 September - 3 October 2014, UCT, Cape Town, South Africa

Tuesday 30th September 2014

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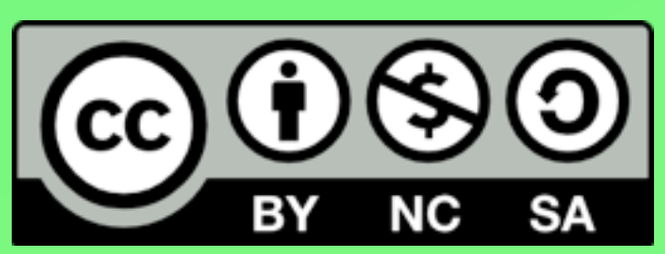

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Protein Structure Basics

will assume that the following ideas aren't new to you

- all proteins consist of one (or more) polypeptide chains
- some proteins are post-translationally chemically modified
- some proteins are made up of other non-peptide components e.g. haeme groups
- peptide units are planar

Protein Structure Basics

will assume that the following ideas aren't new to you

- peptide Calpha carbon is bound to C' and C' atoms by single bonds which can rotate, so orientaion of a pair of peptide units is characterised by two angles x and x
- *de novo* prediction of 3D protein structure (even just the peptide backbone) is extremely difficult to do accurately

Protein Structure Basics

will assume that the following ideas aren't new to you

- there are some commonly-observed patterns in protein structures
  - certain x/x angle combinations are observed much more frquently than others (ramachandran plot)
  - secondary structure elements (helices and sheets)
  - buried sidechains of proteins that function in aqueous solvents are mostly hydrophobic; exclusion of water from these protein cores seen as a strong driver of protein folding

Protein Structure Basics

will assume that the following ideas aren't new to you

- in physiological conditions, proteins have dynamic structures
- PDB files describe models of the 3D structure of biological macromolecules, in most cases the locations of atoms of polypeptide chains

Protein Structure Basics

look through the slides so far with your partner

- decide if you agree with/understand the statements
- can you think of exceptions to the statements?
- are there words/concenpts that are unclear in them?
- if you do have questions/problems, try and solve them together, or ask a trainer for help, or perhaps search the internet for more information
- any unresolved questions/problems, share with everyone after the partner discussions

Linking Protein Structure to PPIs

Interactions happen in 4D

- molecules in different 3D conformations form interact differently (different strengths, different kinetics) with a given entity (although chemistry also important too!)
- conformations change with time, unless at 0K, so characterising interactions also involves how they change with time
- looking at the structure and dynamics of protein interactions can provide insights into protein function (i.e. improve predictive accuracy of models)

Linking Protein Structure to PPIs

- Analysing PPI 3D structures helps predict residues/ regions important for the interaction e.g. residues contributing high energy to the interaction
- these are good candidates for residues that, if changed, would disrupt the interaction
- useful for guiding experiments
- more specifically, for example, useful for interpreting effects of mutations e.g. in genetic disease

Linking Protein Structure to PPIs

- thus: examining and analysing PPI 3D structures can yield useful insights i.e. help us build better i.e. more accurate predictive models of the system
- Chimera is a good **free** tool for such analyses
- We're lucky to have one of the Chimera developers teaching on this course (Scooter)
- Scooter will demo some features of Chimera useful for examining PPIs, then you'll try out Chimera yourself in some exercises