BCBP4870 Protein Structure Determination
Term Projects 2020

Several protein structures have been determined independently by solution NMR and Xray crystallography. By comparing the same protein solved in the crystalline state and in solution, we can answer some questions about the nature of protein in the aqueous and the crystalline state, and we can answer questions about the strengths and weaknesses of the two methods.

Study two structures
Select a protein whose structure has been solved by both methods. The sequence should be identical or nearly identical in the NMR structure and the crystal structure. Submit your choice for approval by sending us the PDB codes for both.

Use NCBI and RCSB to identify a protein to study.
http://www.ncbi.nlm.nih.gov/
http://www.rcsb.org/
In NCBI search the "structure" database.

Superpose structures in Coot.
Open two PDB files, the Xray structure and the NMR structure. In Coot, run Calculate/ SSM Superpose.

Use Coot to study the structural differences.

Report your findings
For the Xray structure, report the vital statistics: resolution, completeness, number of molecules in the asu, average B-factor, number of waters, R-factor, free R-factor.

For the NMR structure, report the number of structures determined in the NMR structural ensemble, RMSD of the backbone and heavy atoms, Ramanchandran statistics, statistics of NOE, dihedral, hydrogen bond and RDC (if used) constraints. Identify the strategy for isotope labeling for the production of NMR samples.

Find places in the structure where there are differences. Are they near crystal contacts? (You can use Coot to view crystal contacts). How precise is the NMR structure in the variable regions? How many NMR distance constraints were used in the variable region? How high are the B-factors in the Xray structure, variable region? Are the differences real? Or are they possible errors? What could have caused the errors? Or, what could have caused the real structural differences?

Comment on how the two methods provided <u>complementary information</u> about the structure. Were any special methods used?

Detailed Requirements:
1. Work in teams of two (BIOL 4870) or one (BCBP 6870).
2. Topic. Choose a protein whose 3D structure has been determined by both X-ray and solution NMR. Compare their structural differences and the functional relevance of such differences. Explore the origin of such differences in methodology.
3. The proposal for the project should include:
    a. Names of the team member(s).
    b. The title, journal, volume and pages number of the paper describing the X-ray structure and the corresponding PDB code.
    c. The title, journal, volume and pages number of the paper describing the solution NMR structure and the corresponding PDB code.
4. Deadline for proposal Nov. 23th, Monday. Email submission to both wangc5@rpi.edu and bystrc@rpi.edu .
5. For BCBP 6870, presentations will be Dec. 7th, Monday. For BCBP 4870, they will be Dec 10, thursday.
   Email slides (PDF) to both wangc5@rpi.edu and bystrc@rpi.edu .

Presentations:
1. Present solo (BCBP6870) or in a team of two (BCBP4870).
2. The presentation will be 12 minutes talk + 3 minutes of Q & A.
3. As a guideline, include about 1 slide/minute of talk.
4. You presentation should consist of four parts (1) a short introduction about the protein, (2) a segment each on the NMR methods, (3) a segment on the Xray methods, and (4) an analysis of the structural differences.
5. Each student is <u>required to ask at least one question</u> of another group. Students will be graded on the quality of the questions asked.
6. Your grade will be based on the quality (=content + clarity) of the slides, the quality of the presentation, and the quality of the answers to questions.
7. Please email slides to the professors on/before the due date.