Syllabus

STRUCTURE AND FUNCTION OF PROTEINS - 81817

Last update 24-04-2015

HU Credits: 2.5

Degree/Cycle: 2nd degree (Master)

Responsible Department: bio-medical sciences

Academic year: 4

Semester: 1st Semester

Teaching Languages: Hebrew

Campus: Ein Karem

Course/Module Coordinator: Ora Schueler-Furman

Coordinator Email: oraf@ekmd.huji.ac.il

Coordinator Office Hours: Tuesday 2-3pm

Teaching Staff:
Prof Ora Furman-Schueler
Course/Module description:
This course provides an introduction to the structure and function of proteins, proceeding from sequence to structure to function. The following subjects are covered:
* principles of protein folding
* the effect of mutations on protein stability and function
* evolution of protein sequences
* the structural basis for the recognition of biomolecules, for example protein-DNA binding
* principles of transmembrane proteins

The course also provides an introduction to the modeling of protein structure, and protein design.

Course/Module aims:
The aim of this course is to provide the student with a firm basis of protein structure. The lectures are accompanied by exercises (#81821)

Learning outcomes - On successful completion of this module, students should be able to:
- Characterize a protein based on its structure
- understand the structural basis of protein stability and function

Attendance requirements(%):
80

Teaching arrangement and method of instruction: lectures and exercises (#81821)

Course/Module Content:
Introduction to Protein Structure

- The chemical nature of polypeptides
- Forces that determine protein structure

Structural properties of proteins
- Secondary structure elements
- Classification of tertiary structure; Protein families
Databases for structure classification: SCOP & CATH

Analysis of structural determinants:
- Anfinsen’s principle: protein structure is determined by sequence
- Determinants of secondary structure: context or propensity? Conservation of tertiary structure during evolution
- Experimental evaluation of structural stability
- Large-scale saturation mutagenesis experiments

Protein folding: Theory and experiment

Protein structure prediction
- Introduction
- Secondary structure prediction
- Ab initio structure prediction
- Fold recognition (threading)
- Comparative modeling
- CASP
- Structural Genomics

Protein design
- The paracelsus challenge
- Switches (calmodulin)
- New proteins: top7
- New enzymes: enzyme design

The structural basis of protein function
- Evolution of new functions; Moonlighting
- Function prediction

Structural motifs in regulatory proteins: DNA-protein interactions
- The structure of DNA
- Principles of protein - DNA recognition

Transmembrane proteins

Required Reading:
none

Additional Reading Material:
References Lecture 1: Introduction
Biology 8:392-393

Protein basics:

Book Chapters:
* Chapter 1 in Branden & Tooze
* Chapter 1.1-1.3 in Proteins (Creighton)

Forces that determine protein structure

Book Chapters:
* Panel 2-3 in Molecular Biology of the Cell, 4th ed.

Lecture 2: Protein Secondary Structure & Protein Classification

Book Chapters:
* Chapter 2-5 in Branden & Tooze
* Chapter 5.1, 5.3 in Proteins (Creighton)

Databases of protein structure classification

(1) SCOP: http://scop.mrc-lmb.cam.ac.uk/scop/; http://scop.berkeley.edu


(2) CATH: http://www.cathdb.info/


(3) ECOD: http://prodata.swmed.edu/ECOD/ Grishin Lab, to be published

Lecture 3:

Anfinsen’s principle: Sequence determines structure


Determinants of secondary structure;


West MW and Hecht MH (1995). Binary patterning of polar and nonpolar amino
acids in the sequences and structures of native proteins. Protein Sci. 4:2032-2039


Effect of mutations on protein structure
Suppressor tRNA assays


Targeted mutation + measure of protein stability


He, Wood, Baase, Xiao and Matthews (2004). Alanine-scanning mutagenesis of the \(^2\)-sheet region of phage T4 lysozyme suggests that tertiary context has a dominant effect on \(^2\)-sheet formation. Protein Sci. 13:2716-2724

Deep mutational sequencing

Lecture 5: Protein Folding

Book Chapters:
* Chapter 6 in Branden & Tooze

Reviews:


Research Papers:

Lecture 6: Secondary structure prediction

Good short introduction to Artificial Neural Networks: ANN

Initial approaches for secondary structure prediction


PHD & PredictProtein PHD


PROFsec


PredictProtein


https://www.predictprotein.org

PSIPRED


Conformational Switches

Young, Kirshenbaum, Dill and Highsmith (1999). Predicting conformational switches in proteins Protein Sci 8:1752-64.

Lecture 7: Template-based modeling of protein structure

Sequence and structural similarities


Fold recognition


Homology modeling


Loop modeling


Rotamer libraries
Lecture 8: Ab initio modeling, CASP, structural genomics and phenomics

Rosetta

I-Tasser
homologous proteins on a genomic scale. PNAS 101(20), 7594–7599.
CASP
Casp 9 issue: Proteins special issue vol:79, S10
Casp 10 issue: Proteins special issue vol:82, S2
http://www.predictioncenter.org/casp10/meeting/talks.html
Structural genomics

Large-scale mapping of disease associated mutations (snps)

Lecture 9: Protein Design
Design of a novel globular protein fold with atomic-level accuracy. (2003). Design of


Lecture 10: Protein Function

Gene Ontology


Moonlighting Proteins


In vitro evolution of new functions


Lecture 11: Prediction of Protein Function


Lecture 12: Protein-DNA recognition and binding DNA Structure

* Chapter 7 in Branden & Tooze

* Review:


Helix-Turn-Helix

* Chapter 8 in Branden & Tooze

* Research Papers:


Zinc Fingers

* Chapter 10 in Branden & Tooze

Research Papers:

Leucine Zippers
* Chapter 10 in Branden & Tooze Reviews:

Research Papers:
* Konig and Richmond (1993). The X-ray structure of the GCN4-bZIP bound to ATF/CREB site DNA shows the complex depends on DNA flexibility. J Mol Biol 233:139-54.

Design of specific Leucine Zippers

TAL effectors
Review:

Research Papers:

Lecture 13: Outlook
Design of protein assemblies

Intrinsically Unstructured Proteins

**Course/Module evaluation:**
- End of year written/oral examination 67%
- Presentation 0%
- Participation in Tutorials 0%
- Project work 0%
- Assignments 33%
- Reports 0%
- Research project 0%
- Quizzes 0%
- Other 0%

**Additional information:**
- The exercises (#81821) are mandatory for this course

This course is also open to undergraduate students, upon evaluation of their background.