The Hebrew University of Jerusalem

Syllabus

Structure And Function of Proteins + Lab - 81817

Last update 03-10-2023

HU Credits: 4

Degree/Cycle: 2nd degree (Master)

Responsible Department: Bio-Medical Sciences

Academic year: 0

Semester: 1st Semester

Teaching Languages: Hebrew

Campus: Ein Karem

Course/Module Coordinator: Ora Schueler-Furman

Coordinator Email: ora.furman-schueler@mail.huji.ac.il

Coordinator Office Hours: Thursday 3-4pm

Teaching Staff:

Prof. Ora Furman-Schueler,
Ms. Nirit Trabelsi,
Ms. Sarah Knapp

Course/Module description:

This course provides an introduction to the structure and function of proteins, proceeding from sequence to structure to function.
The course also provides an introduction to the modeling of protein structure, and protein design.
The course includes both lectures and hands-on exercises.

The following subjects are covered:
** principles of protein folding*
** the effect of mutations on protein stability and function*
** evolution of protein sequences*
** protein structure prediction and protein design*
** the revolution of deep learning in protein structure prediction and design*
** protein function*
** Unstructured proteins*

The exercises provide experience in:
** visualization and inspection of protein structures*

Course/Module aims:

The aim of this course is to provide the student with a firm basis of protein structure, design and protein function. It includes both lectures and hands-on exercises.

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

Understand the revolution of Deep Learning in computational structure biology and use advanced methodologies to predict structure and functions of proteins of interest

Attendance requirements(%):

80

Teaching arrangement and method of instruction: lectures and exercises; group projects and short presentations by students

mandatory submission of 10/11 exercises

Course/Module Content:

Lectures:

Structural properties of proteins I

- *The chemical nature of polypeptides*
- *Forces that determine protein structure*
- *Secondary structure elements*
- *Classification of tertiary structure; Protein families*
- *Experimental ways to determine protein structure*
- *Prepare presentations on amino acids*

Sequence → structure

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*

Effects mutations on protein structure

- *Experimental measure of structural stability; effects of point mutations*
- *Large-scale mutagenesis experiments*

Protein folding: Theory and experiment

Protein structure prediction & design

Protein structure prediction

- *Introduction:*

o Challenges, approaches & CASP

- *How to optimize a protocol*
- *The revolution of Deep Learning (DL) in protein structure prediction*

o Basic concepts

o Examples of implementations

Protein design

- *Design of stable folds in Nature, in the computer and in the lab*
- *Design of novel proteins (Top7)*

Design with AI

- *Basic concepts*
- *Advanced design*

Structure → function

The structural basis of protein function

- *Evolution of new functions*
- *Function prediction*

Unstructured proteins

Unstructured proteins

- *Characteristic features of intrinsically disordered proteins (IDPs) and their*

functional roles
● *Phase separation in biology*

Exercises:
Ex1 (2 weeks):
● *Databases of protein sequence and structure (uniprot; pdb; alphafold uniprot)*
● *Structural visualization:*
o Introduction to Pymol
o “Personal encounter” with protein structure; amino acids
o Pymol example: HLA-peptide binding

Sequence → structure
Ex2: Helices & sheets

Ex3: Evolutionary conservation of protein structure: the hemoglobin family
Ex4: Measure of similarity and quality of protein structures: RMSD; xray, cryo-EM & NMR; plDDT
o Alphafold (AF) coloring: pLDDT (inverse coloring)
Protein structure prediction & design
Ex5-7: Alphafold (AF)
Ex5: The basics of AF (1): MSA, PSSM & PSIBLAST
Ex6: The basics of AF (2): Pairwise matrices Modeling with information from co-variation in evolution
Ex7: AF colab
Ex8: Effect of mutations on protein stability;
Effect of genomic variations in coding regions
Ex9: Protein design
● *Basics of protein design*
● *MPNN*
Ex10: Structural inspection of recent design applications
Structure → function
Ex11: DL for function prediction
Unstructured proteins
Ex12: Characterization of IDPs
● *IUPRED + Alphafold*
● *Globular domains vs linkers and tails*
● *Recognition motifs, posttranslational modifications*

<u>Required Reading:</u>
none

Additional Reading Material:

TBA

Grading Scheme:

Written / Oral / Practical Exam 67 %

Submission assignments during the semester: Exercises / Essays / Audits / Reports / Forum / Simulation / others 33 %

Additional information:

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

In case of online teaching, the written exam will be replaced by a home exam