

Structural Bioinformatics

Descriptive details concerning the subject:

• **Name of the subject:** Structural Bioinformatics

• **Code :** 30169

• **Type of subject:** Optativa

• **Module:** SBI

• **Credits:** 5

• **ECTS:** 5

• **Total hours:** 125.0

• **Scheduling:**

• **Curs:** 1r. curs

• **Període:** 2on. trimestre

• **Coordination:** Baldo oliva

• **Department:** Ciències Experimentals i de la Salut

• **Edifici:** Mar 60.119

• **Horari:** 11:00-13:00

Teaching staff:

• **Group:** 1

• **Language:** Anglès

• **Lecturer:** Baldo Oliva

• **Department:** Ciències Experimentals i de la Salut

Subject presentation:

• **Presentation:**

The main goal of the course is to learn the basic concepts on the structure of macromolecules, more specifically of proteins. Also the principles of crystallography are given in order to gain a deeper understanding on the 3-dimensional data. The main features relating sequence and protein fold will be used on the prediction of secondary and tertiary structure of proteins and on its evaluation. Finally, the relationship between sequence/structure and function of proteins will be analysed.

Prerequisites in order to follow the itinerary:

• **Prerequisites:**

1) Knowledge in Bioinformatics: alignment algorithms (Needleman-Wunsch and Smith-Watermann) and substitution matrices (PAM and BLOSUM); Hidden Markov Models and Neural Networks; Linux and windows operative systems; Perl programming

2) Knowledge in Mathematics: Derivatives and Integrals in n-dimensions; Taylor polinomia; Linear algebra and trigonometry; main concepts of statistics and probabilities: combinatorial analysis, permutations, Bayes theorem, Gaussian and Poisson distributions; numerical analysis, optimization and fitting of functions.

3) Knowledge in Physics: Newton classical mechanics; Thermodynamics, Gibbs energy, entropy, enthalpy and basic statistical mechanics.

4) Knowledge in Chemistry: Chemical structure, conformation, configuration and estereoisomers; Reactivity, transition state, electrophilic and nucleophilic attacks; Electronic densitty, molecular orbitals, quantum

numbers, Shroedingen function and wave function; Steady state and equilibrium.

5) Knowledge in Biochemistry: 20 aminoacids, peptide bond, hydrogen bond and hydrophobic/polar properties of residues; Michaelis-menten equation and enzyme kinetics and reactivity.

6) Knowledge in Molecular Biology: exonic structure and splicing; DNA duplication, transcription and translation; transcription factors; site directed mutagenesis; signalling pathways.

Competences to be attained in the subject

General competences:

Instrumentals:

1.

Competence to unveil the relationship between the three-dimensional structure of bio-molecules and their biological activity

2. Competence to unveil the relationship between molecular patterns of aminoacids and nucleotides and their functions

3. Proficiency on the main programs that handle macromolecular data of sequence and three-dimensional coordinates

Interpersonal:

1. Capacity to be integrated on a working multi-cultural team and split in milestones the analyse of biomolecules

Systemic:

1.

Leading capacity on a working team and motivation to finish on time the work

2. Creativity and motivation to increase the quality

Learning aims:

· Aims:

Avaluació

General assessment criteria:

The evaluation is performed in three parts: theoretical exam, practical exam and presentation of a working project.

The working project implies groups of 2/3 students to analyze a family of protein structures to identify the key residues implied on the activity of the protein. The aim of the work is to prove the relationship between structure, sequence and function, unveil the conservation of the most important residues and racionalize its structural role on the protein activity. The presentation has to be done using the programs learn during the course.

The practical exam is aimed to prove the ability of the student to solve problems on molecular modeling and to characterize the protein structure

The theoretical exam is aimed to validate the basic knowledge of the student on protein folds.

Avaluació de competències	Attainment indicator	Assessment procedure	Scheduling
Instrumentals: 1. Competence to unveil the relationship between the three-dimensional structure of bio-molecules and their biological activity	Rationalize the knowledge on protein structure, evolution and characterization of biological sequences	Project presentation on the analysis of a set of bio-macromolecules by a working group	1 month
	Use of chemico-physical concepts on the rational of protein structure	Practical exam	
	Three dimensional visualization of proteins and macromolecules		
5. Competence to unveil the relationship between molecular patterns of aminoacids and nucleotides and their functions	Comparison of proteins.		
	Identification of aminoacids in a protein sequence	Project presentation on the analysis of a set of bio-macromolecules by a working group	1 month
9. Proficiency on the main programs that handle macromolecular data of sequence and three-dimensional coordinates	Protein comparison	Practical exam	
	Main concepts on evolution sequence variability		
	Knowledge of biological databases	Practical exam	1 month
	Mathematical abstraction		
	Ability to use computers		
Interpersonal: 1. Capacity to be integrated on a working multi-cultural team and split in milestones the analyse of biomolecules	Project presentation on the analysis of a set of bio-macromolecules by a working group	presentation	1 month

Systemic:

1. Leading capacity on a working team and motivation to finish on time the work	Project presentation on the analysis of a set of bio-macromolecules by a working group	presentation	1 month
5. Creativity and motivation to increase the quality	Project presentation on the analysis of a set of bio-macromolecules by a working group	presentation	1 month

Contents

Contingut

Contents 1: Principles of Protein Structure

Conceptes	Procedures	Attitudes
Concepts of protein structure: primary, secondary and tertiary	Visualization of protein structures in the computer Using DSSP to calculate secondary structures	Organization of data
Classification of folds: all alpha, all beta, alpha/beta and alpha+beta	Identification of energetic terms involved in fold and folding pathway.	Visual abstraction

Contents 2: Sequence Comparison

Conceptes	Procedures	Attitudes
Definition to score alignments between residues		
Differences between local and global alignments	Use of the package HMMER and the PFAM database	
Methods of alignment: Needleman-Wunsch and Hidden Markov Models	Use of BLAST and PSI-BLAST	Criticism to modify computer based alignments
Definition of sequence domains by PFAM	Use of ClustalW	
Multiple alignment of sequences		

Contents 3: Structure Comparison

Conceptes	Procedures	Attitudes
Structure superposition: pairwise and multiple		
Calculation of backbone RMSD (root mean square deviation)	Pairwise and mutiple structural alignment with STAMP	Visual abstraction on three-dimensional space
Structure is more conserved than sequence		

Contents 4: Comparative Modeling

Conceptes	Procedures	Attitudes
Distance restraints based on evolution		
Application of energies to optimize protein structure	Use of MODELLER	Intuition to superpose structure and sequence conservation
Protein flexibility on loops		

Contents 5: Threading and fold recognition

Conceptes	Procedures	Attitudes
The Boltzmann Law and relationship between energy and probability	Use of PROSA, THREADER, LOOPP, FUGUE and 3D-PSSM	Criticism to accept the solutions from fold recognition programs
Pseudo-energies and statistical potentials		

Contents 6: Refinement and evaluation

Conceptes	Procedures	Attitudes
Detection of modeling errors with PROSA: missalignments, wrong target, secondary structure modification.	Use of secondary structure prediction programs: PSIPRED	Criticism to modify sequence alignments and refine a model.
Helix capping	Use of the structural classification of loops: ArchDB	

Structural classification of loops

Relationship between secondary structure conservation and model refinement.

Loop prediction:

ArchPred and

ModLoop.

Last updated 04-10-2006

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