

BIOETHICS

Objectives

The course will introduce to the main historical and theoretical knowledge needed to understand the cultural and political relevance that in the western and democratic societies has taken the reflection on the ethical dimensions of biological and medical research.

The course objectives are to provide students with the cognitive tools to understand the terms of the discussions on the various controversial bioethical issues, and to enable him to develop a personal and critical view on the various issues addressed in the lessons.

Program

The origins of bioethics; The public perception of biotechnology; Natural foundations of the moral sense, moral philosophy and bioethics; Bioethics of agrifood biotechnology; Bioethics of genomic research; Bioethics of reproductive medicine; Bioethics of Regenerative Medicine, Bioethics of research integrity; Bioethics of animal experimentation; Neuroethics

Teaching materials

Slides used for lessons and review articles related to specific topics

Biochemistry 2 – (6 cfu)

This module provides an overview of the basic principles of metabolism with emphasis on the structural and regulative aspects. The course will be supported by practical sessions in the computer room available at the Department of Biochemical sciences.

Detailed list of topics:

Enzymes: Biological Catalysts. Kinetics, mechanisms, regulation, structure.

Carbohydrates: Sugars, Saccharides, Glycans

Lipids, Membranes, and Cellular Transport

Chemical Logic of Metabolism. Thermodynamics

Carbohydrate Metabolism: Glycolysis, Gluconeogenesis,

Glycogen Metabolism, and the Pentose Phosphate Pathway

The Citric Acid Cycle

Electron Transport, Oxidative Phosphorylation, and Oxygen Metabolism

Photosynthesis

Lipid Metabolism

Amino Acid and Nitrogen Metabolism

Mechanisms of Signal Transduction Metabolic Data Banks

Textbooks

C. I. Branden, J. Tooze. Introduction to protein structure. Garland science
Biochemistry: Concepts and Connections Plus Mastering Chemistry with eText,
Applying, Anthony-Cahill & Mathews , 2016 , Prentice Hall

Other learning material may be provided or suggested during lessons.

Elearning2 service available at Sapienza University will be used to communicate and share information with the students.

Biochemistry I

MAIN AIMS OF THE I MODULE

KNOWLEDGE AND UNDERSTANDING

The main goal of the module is to provide students with the necessary tools for a detailed analysis of the structure of proteins and their macromolecular complexes. The first part of the module is dedicated to the understanding of the physico-chemical properties of the amino acids and their interaction within a protein. During the second part of the module, students are challenged with practical sessions on the structural analysis of protein models, also by means of open source software. The module consists of lectures that cover the main topics of the program and practical exercises. Exercises are carried out in a computer room with the use of open source software for the visualization of the tridimensional structure of macromolecules. Beside textbooks, students have access to lectures' slides, scientific articles, and other teaching resources made available through this web site.

APPLYING KNOWLEDGE AND UNDERSTANDING

The educational objective of the module is to achieve the necessary knowledge for a critical analysis of the structure of proteins and their interactors. By the end of the module students will have acquired the skills necessary to deal with the analysis and experimental study of biological macromolecules. They will learn how to retrieve the coordinates of macromolecules from the PDB database, recognize the fold and use software for a detailed analysis of their structure.

MAKING JUDGEMENTS

The module is aimed at increasing the ability to critically analyze the structure of proteins and other macromolecules.

COMMUNICATION SKILLS

The module includes significant activity of classroom discussion aimed at developing the ability of students to transfer skills acquired in support of their arguments. In the final exam, students must take an oral presentation on the structure and function of an assigned protein.

LEARNING SKILLS

The many advancements of scientific research, particularly in the field of biochemistry and molecular biology, require a constant updating. For this reason, the module aims to provide the necessary tools to achieve a wider knowledge and to align skills to the advancement in biology and bioinformatics research.

TEXTBOOKS

C. I. Branden, J. Tooze. Introduction to protein structure. Garland science

David Whitford, PROTEINS STRUCTURE AND FUNCTION (Wiley)

<http://books.google.it/books?id=qbHLkxbXY4YC>

Voet D & Voet JG. Biochemistry (Wiley)

Slides of the module

Bioinformatics I

1. DESCRIPTORS

- 1.1 SSD: ING-INF/06
- 1.2 CFU: 6
- 1.3 Docente: Paola Paci
- 1.4 Calendarizzazione: secondo anno, secondo semestre
- 1.5 Offerto a: corso di laurea triennale di Bioinformatica
- 1.6 Tipologia di valutazione: esame con votazione in trentesimi

2. LEARNING OBJECTIVES

The course aims to provide some basic bioinformatic tools to retrieve biological information from public databses.

The attendee will be able to query primary biological databases to retrieve information to be analyzed using software environment like R and Matlab.

3. TEACHING PROGRAM

Biological databases (EntrezGene, Ensembl ...) – Biological Data Repository (GEO, SRA) – Bioinformatics Web-tools bioinformatici (Beagle, Fidea, David, TargetScan, MirTarBase,...) - Sequence and structure alignment – Phylogenetic analysis methods – International genomic projects (TCGA, ENCODE , Galaxy, CGP, ...) – Biological controlled vocabulary (GO, KEGG, gene and protein ID ...)

4. Course materials

- Class Slides
-

Bioinformatics II

1. DESCRIPTORS

- 1.1 SSD: ING-INF/06
- 1.2 CFU: 6
- 1.3 Docente: Paola Paci
- 1.4 Calendarizzazione: terzo anno, primo semestre
- 1.5 Offerto a: corso di laurea triennale di Bioinformatica
- 1.6 Tipologia di valutazione: esame con votazione in trentesimi

2. LEARNING OBJECTIVES

The course aims to provide some bioinformatics tools to analyze and visualize data produce from next generation sequencing technologies. In particular the attendee will be to perform differential expression analysis of RNA-sequencing data and then integrate the results with other data coming from high-throughput technologies

3. TEACHING PROGRAM

Next-generation sequencing (NGS) and software for NGS analysis (Tuxedo suite) – Methods and models for the analysis of differential expression – Functional Characterization of gene's list - High-throughput data visualization (USCS Genome Browser) – Software multi-levels integration of data (CIRCOS, Cytoscape, Aracne)

4. Course materials

- Class Slides
-

-
- **Bioinformatics in Plant Pathology: a key to food security & safety**
 - Recent advances in -omics technology, namely genomics, proteomics and metabolomics allow to go deeper into the understanding of the subtle mechanism underlying host-pathogen interactions. This is made possible by next generation sequencers that uncover entire genome or exome of host and pathogens while interacting, skipping complicate procedures for separating the two challengers. Moreover, we are moving faster in re-shaping plant pathology from the one disease-one pathogen dogma, as embodied in Koch's postulate, to the pathobiome concept. Meta-omic tools shed light on the inter-reign network originating the disease of the host in its complexity. The analysis and understanding of the huge amount of data generated by a single experiment represents currently the classical bottleneck. In relation to this, bioinformatics plays a crucial role in data capture, analysis and integration.
 - Plant pathologists have to answer to very concrete and problematic question, today, more, and more in the next future: food security, food safety and food quality. Actually, plant disease burden current food production, accounting for more than 40% of food losses. Climate change and globalization enhance pathogens ability and mobility worldwide. Nevertheless, for environmental as well as political reasons, pathogens cannot be controlled anymore by using pesticides and/or GMO plants. A more sustainable, "green" and integrated pest management is needed.
 - A modern plant pathologist has to face this complex reality, plan experiments at real scale, "sucks the marrow out of -omics" (par. Walt Whitman) by using bioinformatics tools, individuate biocontrol agents and stimulate plant self-defences. In relation to this, the main aim of this course is forming young scientists in managing plant diseases *tout court* by the mean of the -omics *plus* bioinformatics tools.
 -
 - *Course contents*
 - - Introduction to Plant Pathology: the concept of disease
 - - The Pathogens: from virus to fungi, different strategies for different pathogens
 - - The Pathobiome concept
 - - Integrated Pest Management: how to couple food security with food safety
 - - Pathogenomics; how genomics meets pathogen
 - - -omics sciences applied to plant-pathogen interaction
 - - metagenomics approaches to study plant pathogens
 - - Integration between genomics and metagenomics
 - - How Pathotranscriptomics helps to understand interaction host-pathogen
 - - New bioinformatics tools for pathogenomics
 - *Text books*
 - - Agrios G., Plant Pathology V edition
 - - Review on the major topics of the course provided by the teacher
 - - R & Bioconductor Manual
-

Biology of the cell

Educational Objectives:

Students acquire the knowledge and thinking skills necessary to understand biological problems in a evolutionary perspective. The course will provide students with understanding of the basic molecular mechanisms that operate in living cells, with a focus on the flow of genetic information.

Contents:

1. Definition of life. Darwinian evolution: variation, heritability and fitness. Origin of life: prebiotic chemistry, RNA world. Gene-centered view of evolution: replicators and vehicles. From molecules from the first cells. From single cells to multicellular organisms. The tree of life. The major transitions in evolution: mutualistic symbiosis and complexity
2. Proteins: structure and functions. Enzymes and biological reactions.
3. Bio-membranes: Structural Organization and Functions. Principles of membrane transport: active/passive transport, carrier proteins, ion channels, electrical properties of membranes.
4. Biological order and energy. Energy for cellular activities. Production of ATP. Structure and function of mitochondria. Glycolysis, Krebs cycle, electron transport chain. The mitochondrial ATP synthase.
5. RNA and DNA structures. DNA replication and repair. The cell nucleus: chromatin structure, epigenetic modifications.
6. Transcription and translation. RNA transcription in prokaryotes. RNA transcription and processing in eukaryotes: mRNA, tRNA, rRNA. The genetic code. Protein synthesis: initiation, elongation and termination .
7. Regulation of gene expression. Control of transcription in prokaryotes: bacterial operons. Control of transcription in eukaryotes. Post-transcriptional and translational regulation. Non-coding RNAs, microRNAs.
8. The genome organization in prokaryotic and eukaryotic organisms. Mobile elements. Genome evolution.
9. Endomembrane system: endoplasmic reticulum, Golgi. Protein sorting and glycosylation. Lysosomes. Phagocytosis and Endocytosis.
10. Principles of cell signaling: G Protein–Coupled Receptors. Effectors and second messengers. Receptor Tyrosine Kinases, MAP Kinase Pathways.
11. Eukaryotic cell cycle. Phases of cell cycle. Cyclin-dependent protein kinases (CdKs). Cell cycle checkpoints. S phase. Mitosis. Cytokinesis. Apoptosis.
12. Genetics of cancer. The hallmarks of cancer. Oncogenes and tumor suppressor genes. Somatic evolution in cancer.

Suggested Textbooks:

Essential Cell Biology, Fourth Edition. Alberts B. et al. Garland Science.

Biologia Molecolare e Genomica

Indicative Syllabus

Introduction to Genomes and Transcriptomes:

Genome structure and organization; the Central Dogma of molecular biology; mechanisms of gene regulation at transcriptional and post-transcriptional levels; RNA factories; Human Genome Project; Post-Genomic Era; genome complexity, C-value paradox and non-coding potential; ENCODE and FANTOM5 Atlas; role of ncRNAs (e.g. miRNA, lncRNAs) in gene expression regulation and pathologies.

Studying Genomes:

Plasmids and high-capacity cloning vectors (Cosmids, YAC, BAC). Genetic and physical maps. Introduction to Genomic sequencing technologies; Gilbert and Sanger methods; Next Generation Sequencing (NGS) and platforms (e.g. Illumina, SOLiD, Helicos, Ion Torrent); *de-novo* pipelines for sequence analysis; major genome browsers: Ensembl, UCSC, NCBI Map Viewer; BLAT queries; publicly available databases for model organisms (*Saccharomyces cerevisiae*, *Drosophila melanogaster* and *Arabidopsis thaliana*).

High-Throughput analysis of gene expression:

Applications of NGS to measure

- RNA (e.g. RNA-seq)
- Epigenetics (e.g. DNA methylation, ChIP-seq, ChIRP-seq, RIP-seq, CLIP-seq)

Repositories of High-Throughput sequence and profiling (GEO, ArrayExpress); miRBase, TargetScan, PicTar, GENCODE, lncRNAdb, LNCipedia. Data mining and statistics (hierarchical clustering, Gene Ontology and GSEA).

Identification and study of sub-topological domains (TADs). 3C, 5C, Hi-C e ChIA-PET.

Texts

- Watson J.D, DNA Ricombinante. Zanichelli, 2008.
- Watson J.D *et al* Biologia Molecolare del gene. Zanichelli, VI Edizione
- Gibson G. & Muse S.V., Introduzione alla genomica. Zanichelli, 2004.
- Dale J.W. & von Schantz M., Dai geni ai genomi. EdiSES, 2008.
- Hartwell L.H. *et al* GENETICA dall'analisi formale alla genomica. McGraw-Hill, 2008.

Aim of the Course

The new generation of sequencing technologies offered extraordinary opportunities for high-throughput functional genomic studies. These tools have been applied in a variety of contexts, including whole-genome sequencing, discovery of transcription factor binding loci, mapping out DNA accessibility and RNA expression profiling. Intriguingly, recent efforts in annotation led to the discovery of novel noncoding RNA genes that control temporal and/or spatial gene expression along cell differentiation. Aim of the course is the integration of the knowledge of the modern molecular biology with high-throughput technologies. Besides RNA metabolism and noncoding content, the course will introduce NGS technologies, highlight different applications of these new tools and show ways to analyse data in the context of completed genome sequences of different model organisms. The course will also feature methods to assist the study and the prioritization of gene lists from large-scale gene expression data.

Organic and inorganic chemistry I

Objective of the course

This course is an introduction to chemistry fundamentals addressed to students with limited chemistry background. The purpose of the course is to provide students with the knowledge of general chemistry principles, and with the tools to solve simple chemistry problems. At the end of the course the students are expected to know how to apply the acquired chemical concepts to different fields, including pharmaceutical chemistry and biochemistry which are the subjects of further courses.

Syllabus

Atoms molecules and ions. The mole. Atomic weight and atomic number. Geometry of molecules. The chemical bond. The hybridization. Chemical reactions: precipitations, acid-base, and oxidation-reduction reactions. Gases. Chemical equilibrium. Thermodynamics of equilibrium. Thermochemistry. Spontaneity, entropy, and free energy. Homogeneous and heterogeneous equilibria. Colligative properties. Acid and bases. Hydrolysis and acid-base titrations. Buffered solutions. Chemical kinetics. Electrochemistry: galvanic cells.

Textbook

Chemical Principles, Steven Zumdahl

Organic Chemistry

Structure and properties

Carbon compounds, Lewis structural formulas, types of bonds, functional groups, formal charge stereoisomer characteristics, identifies configuration of double bond cis (Z) /trans (E) identifies configuration of stereocenters (R)/(S), identifies rotation under plane-polarized light to determine whether molecule is (+) or (-), need to do laboratory tests where the molecule is put in plane-polarized light bonding and molecular structure atomic orbitals, covalent bond formation—molecular orbital (MO) method, hybridization of atomic orbitals, electronegativity and polarity, oxidation number, intermolecular forces, solvents, resonance and delocalized π electrons.

Chemical reactivity and organic reactions.

Reaction mechanism, carbon-containing intermediates, types of organic reactions, electrophilic and nucleophilic reagents, thermodynamics bond-dissociation energies, chemical equilibrium rates of reactions, transition-state theory and enthalpy diagrams, brønsted acids and bases basicity (acidity) and structure, Lewis acids and bases.

Alkanes and cyclic hydrocarbons

Definition, nomenclature of alkanes, preparation of alkanes, chemical properties of alkanes.

Nomenclature and structure, geometric isomerism and chirality, conformations of cycloalkanes and chemical properties.

Stereochemistry

Stereoisomerism, optical isomerism, relative and absolute configuration, molecules with more than one chiral centre, synthesis and optical activity.

Alkenes

Nomenclature and structure, geometric (cis-trans) isomerism, preparation of alkenes, chemical properties of alkenes, substitution reactions at the allylic position, summary of alkene chemistry

Alkyl halides

Introduction, synthesis of alkyl halides and chemical properties.

Alkynes and dienes

Alkynes, chemical properties of acetylenes, alkadienes, MO theory and delocalized π systems. Addition reactions of conjugated dienes, polymerization of dienes, cycloaddition.

Benzene and polynuclear aromatic compounds

Introduction, aromaticity and Hückel's rule, polynuclear aromatic compounds, nomenclature chemical reactions.

Alcohols and thiols

Alcohols, nomenclature and H-bonding, preparation and chemical properties. Thiols, nomenclature and chemical properties.

Ethers, epoxides, glycols, and thioethers

Ethers, introduction and nomenclature, preparation, chemical properties. Cyclic ethers. Epoxides, introduction, nomenclature, chemical properties and synthesis. Glycols, nomenclature and chemical properties. Preparation of 1,2-glycols, unique reactions of glycols.

Thioethers, introduction, nomenclature and chemical properties.

Carbonyl compounds: aldehydes and ketones

Introduction, nomenclature, preparation, and chemical properties. Oxidation and reduction of the carbonyl group.

Carboxylic acids and their derivatives

Introduction, nomenclature, preparation of carboxylic acids and carboxylic acid derivatives. Chemical properties of carboxylic acids and carboxylic acid derivatives.

Amines

Nomenclature and physical properties, preparation, chemical properties, reactions of quaternary ammonium salts, ring reactions of aromatic amines, spectral properties, reactions of aryl diazonium salts, summary of amine chemistry

Phenolic compounds

Introduction, Preparation, chemical properties, analytical detection of phenols, summary of phenolic chemistry, summary of phenolic ethers and esters

Aromatic heterocyclic compounds

Five-membered aromatic heterocycles with one heteroatom, six-membered, heterocycles with one heteroatom, compounds with two heteroatoms

Carbohydrates and nucleic acids

Introduction, classification of carbohydrates, the D and L notation, the configuration of aldoses and ketoses. The reactions of monosaccharides in basic solutions. The oxidation-reduction reactions of monosaccharides. Lengthening the chain: the Kiliani-Fischer synthesis. Shortening the chain: the Ruff degradation. Chemical properties of monosaccharides, evidence for hemiacetal formations as exemplified with glucose, stereochemistry and structure proof, disaccharides

Amino acids, peptides, proteins

Introduction, preparation of α -amino acids, chemical properties of amino acids, peptides

Reactivity and Reactions

Radicals

Radical stability. The reactivity-selectivity principle. The chlorination and bromination of alkanes.

Radical addition to alkenes. The stereochemistry of radical substitution and radical addition reactions.

Substitution and elimination reactions

Mechanism and factors that affect reactions S_N2 . Mechanism and factors that affect reactions S_N1 .

The stereochemistry of S_N2 and S_N1 reactions. Competition between S_N2 and S_N1 . The E_1 and E_2 reactions. Competition between E_1 and E_2 reactions, and between S_N2/E_2 and S_N1/E_1 reactions.

Reactions of benzene and of substituted benzenes

The general mechanism of electrophilic aromatic substitution reactions. Halogenation, nitration, sulfonation, Friedel-Crafts acylation and alkylation. The effect of substituents on reactivity and on

orientation. Nucleophilic aromatic substitution: addition-elimination mechanism and elimination-addition mechanism.

Carbonyl compounds: reaction of carboxylic acids and carboxylic acid derivatives

General mechanism for nucleophilic addition-elimination reactions. Reactions of acyl halides, acid anhydrides, esters. Acid and basic catalyzed hydrolyses of esters, amides and nitriles.

Carbonyl compounds: reactions of aldehydes, ketones and α,β -unsaturated carbonyl compounds

Reactions of carbonyl compounds with: Grignard reagents, acetylide ions, hydride ions, hydrogen cyanide, amines and amines derivatives, water, alcohols, sulphur nucleophiles. The Wittig reaction. Nucleophilic addition to α,β -unsaturated aldehydes and ketones. α,β -unsaturated carboxylic acid derivatives.

Carbonyl compounds: reactions at the α -carbon

Keto-enol tautomerism. How enolate ions and enols react. Alkylating the α -carbon of carbonyl compounds. Alkylation of the α -carbon using an enamine intermediate. The Michael reaction. Aldol condensation and Claisen condensation. The Robinson annulation.

Testi:

Graham Solomons, Craig Fryhle: Organic Chemistry Ed. Wiley

Paula Bruice: Organic Chemistry Ed Pearson Chimica Organica: Bruno Botta Ed. Edi-Ermes

Obiettivi:

The course aims to provide a correct knowledge of the fundamental principles of organic chemistry, proposing the contents into two distinct phases that are closely and logically linked. In the first phase the teaching is addressed to provide basic knowledge about classification and nomenclature of organic compounds, about the symbolism used to represent both structures and reactions, as well as over the chemical-physics, acid-base, nucleophilic-electrophilic properties of the considered compounds. In the second phase the teaching is instead focused on the description of the different reactivity involved by different classes of compounds, rationalizing the study through the analysis of the relevant mechanisms. In the context of the described methodology the objectives to be achieved are: 1) attainment of a suitable degree of specialized knowledge, understood as the ability to invoke theories, rules, nomenclature etc.; 2) capacity to properly interpret and process the reaction schemes and propose alternatives to the encountered syntheses; 3) establish connections between different studied subjects.

Genetics and computational genomics (BIO/18, 6 CFU)

Aim of the course:

The purpose of the course is to provide students with a deep understanding of the theoretical and practical tools to solve genetic problems. Fundamentals concepts in genetics, functioning and evolution will be reconsidered in light of the sequencing and re-sequencing projects. Computational genetics has been an important area of science since the discovery of the first sequencing method and advances in tools and techniques for data generation are rapidly increasing the amount of data

available to researchers. During the course, students will learn to rely on computational and data science tools for the storage, management, analysis, and visualization of genetic data.

Course Program:

Formal Genetics

- Mendel's principles of heredity and extensions to Mendel's laws.
- The chromosome theory of inheritance.
- Anatomy and function of a gene.
- DNA mutations, chromosomal rearrangements and changes in chromosome number.
- Strategies of gene mapping.
- Bacterial genetic analysis.
- Genetics of sex determination.

Human population genetics

- Hardy-Weinberg equilibrium.
- Genetic effects of inbreeding, calculation of the inbreeding coefficient from pedigrees.
- Genetic drift and natural selection.

Human genetic diversity in health and disease:

- Classes of genetic variants/ polymorphisms. De novo mutation rates.
- International projects on the human genetic diversity: "1,000 genomes" and "UK10K" projects.

Genetics of multifactorial characters and complex pathologies:

- Decomposition of phenotypic variance: environmental and genetic variance; heritability.
- Polygenic theory of quantitative and discontinuous characters.
- The polygenic threshold model. The "infinitesimal" and the "rare allele" models.

Human gene mapping

- Linkage analysis, lod score calculation.
- Haplotypes and linkage disequilibrium, linkage disequilibrium-based mapping methods.

Storage, management, analysis, and visualization of data

- Use of genome browsers: theoretical aspects and practical exercises.
- Use of genome viewer programs: theoretical aspects and practical exercises on NGS data.
- Structure, feature and handling of the main files used in NGS analysis.
- Storage and analysis of genetic raw data.
- Mining information from databases

Suggested texts:

“Genetics: From Genes to Genomes” Hartwell

“Human Molecular Genetics” 4th Edition, Strachan & Read

MICROBIOLOGY

Aims

To introduce the microbial diversity, the structure/function relationship of prokaryotic cells and viruses, the microbial taxonomy and the basic principles of clinical, environmental and industrial microbiology.

Program

Introduction to microbiology, microbial growth *in vitro*, structural and physiological features of bacteria and viruses, differentiation, motility and formation of microbial communities, genetics and genomics of microorganisms, gene regulation and metabolism in bacteria, control of microbial growth, methods for the study of complex microbial communities, microbial phylogeny and taxonomy, basic principles of clinical and environmental microbiology.

Suggested Textbook

Brock Biology of Microorganisms

Madigan et al.

Pearson

Modelling and simulation of biomolecular

dynamical systems(6 CFU)

Outline:

- General principles of modeling bio-molecular systems.
- Modeling of gene regulatory systems with ODE: transcriptional regulation, self-repression, self-activation, cross-interaction. Sequential activation. Post-transcriptional regulation.
- Boolean functions.
- Regulatory network motifs.
- Bayesian and boolean networks.
- Stochastic master equation.
- Spatially distributed models (cellular Potts model) .

- Elements of synthetic biology.
- Matlab programming for simulation.

Objectives:

This course aims to provide students with a practical and hands-on experience with common modeling and simulation tools in molecular biology. It would be expected that after completing this course a student would be able to model and simulate using Matlab a biomolecular systems like, for example, a gene regulatory network using the appropriate methodology. Further, students will understand the basic theory behind these modeling techniques and critically analyze the results of their analysis.

Teaching material:

Handouts provided by the teacher.

Molecular Biology

Integrated course

Crediti/Valenza 12

Main goal of the course is to give to the students a general view of the molecular mechanisms which are at the base of the biological processes. For each argument a methodological section will introduce the students to the main technical approaches used at the state of the art. Practical training (2 CFU) will make the students to breath the atmosphere of a molecular biology laboratory. Particular attention will be given to the high throughput methods utilized in "Omic" approaches to the comprehension of biological processes which will be further illustrated in the course of Molecular Biology and Genomics.

PROGRAM

The polymorphic DNA – Chemical components of DNA: bases, sugars and phosphodiesteric backbone (0.1 cfu). DNA B basic structure (0.2). Alternative DNA conformations, unusual structures (cruciforms, triple helix) (0.2) – Conformational variability of structural parameters, curvature and bendability (0.2). DNA topology, winding and unwinding; linking number; DNA topoisomerases (0.2). **The Genetic Code** - the code decrypting; the structure and function of the code (0.2). **DNA replication**: machinery and mechanisms in prokaryotes and eukaryotes (0.3). Replicons organization; topological and end-replication problems (0.1). **DNA mutability and repair**; damage checkpoints (0.4). **DNA transcription**: transcription in bacteria and bacteriophages; transcriptional machinery and RNA polymerase positioning signals (0.2). Methodological approach to the study of transcription: in vitro transcription systems (0.2). Transcription regulation in prokaryotic systems: activation and repressions; operon structures and function (0.2). Transcription in eukaryotic systems (0.3); transcriptional machinery and RNA polymerase positioning signals (0.2). Methodological approaches to the study of transcription: eukaryotic in vitro transcription systems (0.1). Coordinate regulation of the three eukaryotic RNA polymerases (0.1). Transcription factors and transcription regulation in eukaryotes (0.2). **The RNA molecule** (chemical and structural features) (0.2); structure and function of tRNA, rRNA, pre- and mRNA, snRNA e snoRNA (0.3); mRNA capping and

polyadenylation and their regulative role (0.2). **RNA Splicing (0.4)**: role of small nuclear RNAs; RNA/RNA interactions and structural modifications in active spliceosome formation; protein/protein interactions and the role of SR proteins; alternative splicing regulation; **mRNA transport**; **RNA stability and its regulation (0.3)**; self-splicing; ribozymes and their applications (0.2); RNAi (interference) and its applications, synthesis and regulative role of miRNA and other classes of noncoding RNAs (0.3). **Protein biosynthesis (0.6)**: general principles; structure and functions of the ribosome; comparison between prokaryotic and eukaryotic protein biosynthetic systems; translation initiation, elongation and termination. Protein biosynthesis inhibitors; protein folding and stability; role of molecular chaperones; protein transport and targeting. **Control of protein homeostasis (0.4)**: ubiquitin and proteasome systems. **Principles of protein engineering (0.2)**.

Genome structure. Instruments to approach genomic studies (application of “omic” techniques) (0.3). The structure of the genomes: coding and non coding DNA (0.3), transposable elements and genome variability (0.2); the evolution of the genomes the paradox of DNA content (0.2). Necessity of information compaction in the genomes. Chromatin basic structure in eukaryotes and prokaryotes (0.2). The structure of nucleosomes and further organization levels (0.2). Histone modifications and their regulatory effects; the histone code. (0.3). DNA methylation and its regulatory role (0.2). Histone variants and their regulatory role (0.2). Chromatin structure and chromatin remodelling at promoters (0.2). Chromosomes structure: centromeres, telomeres and origin of replication (0.2). **Basic methods in Molecular Biology** (3 CFU with 2 CFU of practical lab training): nucleic acids purification and quantitation methods; DNA cloning techniques; methods for sequencing nucleic acids; PCR amplification and its uses; techniques for analyzing gene expression; the multiple uses of reporter genes.

Testi consigliati:

James D. Watson, Tania A. Baker, Stephen P. Bell, Alexander Gann, Michael Levine, Richard Losick:
Molecular Biology of the Gene

Optimization methods for computational biology

Settore: MAT09

Crediti: 6

Obiettivi formativi

We aim to introduce students to the analysis of decision problems that arise in bioinformatics and health management. Students would be able to: model as mathematical programming problem to be used as a support to the decision maker, use algorithm suitable to each model for the solution, make post-optimality analysis.

Program

1. Mathematical programming Models
(decision variables, constraints, objectives)
2. Linear Programming, Integer Linear Programming, Nonlinear Programming, Integer nonlinear programming: an overview of theory and algorithms

3. Bioinformatics applications that can be modelled as LP, ILP, NLP, MINLP
4. Black-box models (deriving complex models from observing data)
5. Machine Learning: an overview on different class of learning machines
6. Bioinformatics applications that can be modelled using Machine Learning

References

Notes of the teacher

Introduction to biomedical statistics I

OBIETTIVI FORMATIVI:

This course provides an introduction to basic concepts of Statistics and Probability for students in the biosciences.

TESTO DI RIFERIMENTO:

Daniel and Cross: Biostatistics. Wiley

PROGRAMMA:

Descriptive statistics; basic concepts of probability and main probability distributions; statistical inference.

Pharmaceutical Chemistry (Drug Design) Program
Prof Rino Ragno

The course is twofold: a theoretical part and practical section.

1) Theoretical Part Topics

- The basis of drug design
 - The process of drug discovery.
 - Main types of drug targets and drug-receptor interactions.
 - Methods of hit-finding: high-throughput screening.
 - Criteria for a good hit compound; concept of ligand efficiency.
 - Isostery
 - Vinilogy
 - Scaffold Hopping
 - Lipinsky rule of five and related approach
- Ligand Based Drug Design
 - 1-D and 2-D Quantitative Structure Activity Relationships
 - History of QSAR
 - Hansch Method and examples
 - Molecular descriptors
 - Statistical Methods: MLR and PLS
 - Coefficients (r^2 and q^2 , SDEP)
 - How to build and assess a QSAR model
 - 3-D QSAR and related approaches
 - History of 3-D QSAR
 - Comparative Molecular Field Analysis
 - GRID and Molecular Fields
 - The 3-D QSAutogrid/R Method

- Molecular Alignment in 3-D QSAR
 - Validation of a 3-D QSAR model
 - Steps to build a 3-D QSAR model: a tutorial
 - Pharmacophoric Approach
 - Definition of Pharmacophore
 - Examples of a pharmacophores
- Structure Based Drug Design
 - Analysis of drug/target interactions (use of UCSF Chimera)
 - Molecular Docking
 - Type of Dockings
 - Scoring Functions
 - Example of dockings
 - Step to make a molecular docking: a tutorial

2) Practical Part

- Analysis of Drug-Target interactions by means of a Molecular Graphic Program
- Building of QSAR model
- Building of 3-D QSAR model
- Molecular Docking

Objectives

During the course the student will learn the basics to design a drug through computational methods.

The aim of the course is to impart an understanding of what medicinal chemists consider when attempting to design new pharmaceuticals. The course is twofold: a theoretical part and practical section. In the first part the course will describe the principles involved in modern drug design and drug discovery, usually with reference to compounds in current clinical usage. In the second part practical sections will be set up to teach the student some computational methods to apply in the drug design process.

Medicinal Chemistry (Drug Design) Program

Prof Rino Ragno

The course is twofold: a theoretical part and practical section.

1) Theoretical Part Topics

- The basis of drug design
 - The process of drug discovery.
 - Main types of drug targets and drug-receptor interactions.
 - Methods of hit-finding: high-throughput screening.
 - Criteria for a good hit compound; concept of ligand efficiency.
 - Isostery
 - Vinilogy
 - Scaffold Hopping
 - Lipinsky rule of five and related approach
- Ligand Based Drug Design
 - 1-D and 2-D Quantitative Structure Activity Relationships
 - History of QSAR
 - Hansch Method and examples
 - Molecular descriptors
 - Statistical Methods: MLR and PLS

- Coefficients (r^2 and q^2 , SDEP)
 - How to build and assess a QSAR model
 - o 3-D QSAR and related approaches
 - History of 3-D QSAR
 - Comparative Molecular Field Analysis
 - GRID and Molecular Fields
 - The 3-D QSAutogrid/R Method
 - Molecular Alignment in 3-D QSAR
 - Validation of a 3-D QSAR model
 - Steps to build a 3-D QSAR model: a tutorial
 - o Pharmacophoric Approach
 - Definition of Pharmacophore
 - Examples of a pharmacophores
 - Structure Based Drug Design
 - o Analysis of drug/target interactions (use of UCSF Chimera)
 - o Molecular Docking
 - Type of Dockings
 - Scoring Functions
 - Example of dockings
 - Step to make a molecular docking: a tutorial
 - 2) Practical Part
 - Analysis of Drug-Target interactions by means of a Molecular Graphic Program
 - Building of QSAR model
 - Building of 3-D QSAR model
 - Molecular Docking
-

Principles of Physics

Formative Aims

The Physics course has several distinct aims. First, it aims to fill the gap between school and university level physics. Second, it aims to provide a much logical and analytical framework for classical physics, which will be essential for the course. Third, it includes bio-medical themes generally underestimated in basic physics courses. Such topics will be selected among those that will be developed in the subsequent years of the course. Fourth, single lectures aim to broaden the student's perspectives, so that he can begin to appreciate the great flexibility and generality of the laws of physics and their application in emerging biomedical fields of research.

Course Programme

- Physical Quantities and Basic Vector Operations.
- Kinematics and its Implications in Drug Delivery.
- Mechanics with elements of Bio-Mechanics.
- Work, Energy and Power.
- Dynamics of Fluids.
- Physics of the Cardiovascular System.
- Elements of Thermology.
- Electricity and Magnetism.
- Waves and radiation-matter interaction.

Book

Physics: Principles with Applications (Author: D.C. Giancoli)

Plant Functional Genomics (BIO/04, 6 CFU)

Objectives

The aim of the course is to provide a theoretical knowledge of plant genomes, and practical explanation of the techniques used in plant functional genomics, i.e. a large-scale analysis of the function of the different gene products to understand how the genome generates the phenotype of the plant. Insights will be given into the new information that will be generated from whole genome-/proteome-/metabolome analysis. The course will cover the following concepts: array and sequencing based methods; reverse and forward genetics; comparison of plant genomes; epigenomics; proteomics and metabolomics. Also covered are robotization, miniaturization (single-cell studies) and high-throughput-screenings. Finally, the course will introduce methods for visualization and analysis of high-density data.

A textbook is not required for this course. Material will be presented in lectures and selected reviews and research papers.

Programme

Structure of plant genomes. Nuclear and plastid genomes. Approaches and specificities of plant genomes with relation to sequencing projects. Comparison of plant genomes: evolutionary and biotechnological implications.

Global transcript profiling in plants: microarrays and other approaches. Analysis of transcriptomic datasets. Cluster analysis of plant gene families. Gene expression correlation networks. Public databases and resources for the analysis of plant transcriptomes.

Functional genomics of plants: forward vs reverse genetics. Public databases and resources for the functional analysis of plant genes.

Epigenetic modifications in plants: mechanisms and methods of analysis. Gene silencing.

Use of genomic data to improve crops. Molecular markers. Marker-assisted selection and genetic transformation.

Introduction to plant specialized metabolism. Structure and biosynthesis of plant secondary metabolites. Overview of their applications in biotechnology and biomedicine.

Omics technologies for the study of plant metabolic networks. Metabolomics workflows and sources of experimental error, difference between targeted and un-targeted approaches.

Metabolomics data processing tools and data analysis using open source programs.

Quantitative proteomics and phosphoproteomics to investigate complex cellular networks.

Integration of high-throughput experimental data with mathematical modelling. Examples of integration of transcriptomic, proteomic and metabolomics data to elucidate how the plants cope with various biotic and abiotic stresses.

Metabolomics and proteomics downstream analyses: KEGG, BioCyc and Cytoscape for metabolic pathway and network analysis with visualization of differential expression, understanding metabolomics flux analysis.

Introduction to Computer Science I (INF/01):

MAIN GOALS: The goal of this course is to empower students with those basic programming skills needed to deal with bioinformatics data. More specifically, at the end of the course the students will be able to:

- model problems of medium difficulty and solve them by programming;
- decompose complex programming problems into simpler problems;
- implement well-designed and well-coded software
- test and debug programs
- analyse programs with respect to their correctness and efficiency
- use Python and its libraries

These skills are essential in order to analyse bioinformatics data using software libraries and scripts

SYLLABUS: Introduction to algorithms and programming with Python. Data types, variables, assignments, flow control, functions, classes, modules, input/output.

Data structures: arrays, strings, lists, dictionaries. Design and implementation of object-oriented programs. Python libraries for graphics, file management (text, HTML), internet access, biological data. Debugging and testing.

Introduction to computer architectures, and to privacy and security.

Introduction to Computer Science I – Practicum (INF/01): Implementation of various algorithms and data structures explained in the course, with special emphasis given to examples coming from bioinformatics.

Algorithms (INF/01):

MAIN GOALS: this course is an introduction to algorithms with special emphasis given to those algorithmic problems and techniques that have the greatest impact for bioinformatics.

SYLLABUS: Asymptotic analysis. Graphs and visits. Programming methodologies: greedy, dynamic programming, divide and conquer. Brief introduction to computational complexity: tractable and intractable problems. Introduction to data mining and machine learning: clustering, nearest neighbors, regression and classification, support vector machines, bayesian classifiers, neural networks.

These techniques, problems and algorithms will be exemplified by means of examples of special significance for bioinformatics such as sequencing, sequence alignment, clustering of genes and of proteins, analysis of genes and representation of evolutionary processes, phylogenetic trees

Kleinberg-Tardos "Algorithm Design"

Principles of Mathematics (12 cfu)

Syllabus

Sequences and Limits

Functions of one real variable: basic definitions and properties, limits, derivatives, and integrals.

Vectors and Matrices: linear independence, dot product, linear system of equations, solution of a linear system, vector spaces and their basic properties

Functions of several variables: partial derivatives, gradient, Taylor formula

(Systems of) Linear Differential Equations: qualitative analysis and basic properties

Optimization of functions of one or several variables

Elements of graph theory

Course Material

James Stewart and Troy Day

Biocalculus

Cengage Learning

Obiettivi Formativi

The aim of this course is to give the student sound mathematical basis in calculus of one or several variables, optimization and elementary graph theory in a way appropriate for a student bioinformatics. An emphasis will be given to applications and intuitive understanding of the underlying concepts.

