MASTER IN BIOCHEMISTRY FOR HEALTH

CURRICULAR GUIDE 2018-2019

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* Students choose up to four curricular units corresponding to a total of 12 ECTS

** Classes take place between the 1st and 2nd semesters

DESCRIPTION OF CURRICULAR UNITS

Mandatory Curricular Units

ADVANCED TOPICS IN BIOINFORMATICS

TEACHING STAFF

João Aires de Sousa (FCT NOVA)
Cláudio Soares (ITQB NOVA)
António Baptista (ITQB NOVA)
José Pereira Leal (IGC)
Jorge Carneiro (IGC)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

This curricular unit aims at giving a general overview of the major areas of Bioinformatics and Chemoinformatics, providing the students with knowledge on the fundamentals as well as on practical applications in biosciences. The knowledge and skills acquired in this curricular unit will allow the students to have a general understanding of the scientific literature in the area, to be able to (individually) deepen their knowledge in selected areas in bioinformatics, and to use some computational tools to study real-life problems in biosciences.

SYLLABUS

The topics in this curricular unit are very varied, reflecting the large number of areas and methodologies present in the field. The topics below aim at covering this vast field. The depth of coverage will vary depending on the topic.

1) Computational genomics and evolution.
2) Computational systems biology.
3) An experimentalist survival guide in computational biology methods – Practical sessions, in a problem-solving context.
4) Representation and visualization of molecular structures.
5) Introduction to molecular mechanics/dynamics.
6) Molecular docking.
7) Protein structure prediction
8) Quantitative Structure-Activity Relationships (QSAR).
9) The role of Chemoinformatics in drug discovery and development.

TEACHING METHODOLOGIES AND EVALUATION

Classes will be Lectures/problem-solving with computers.

Some modules will adopt the Team-Based Learning (http://www.teambasedlearning.org, TBL) method. TBL is centered on permanent teams of 5-7 members, individual accountability for pre-class preparation, application activities and peer evaluation. The first phase of each

module assures the acquisition of the essential concepts – it includes an individual test, repetition of the test in teams and mini-lecture. In the second phase, teams perform application activities.

Evaluation consists of class evaluation (50%) and final exam (50%). In the TBL modules, class evaluation will be based on the TBL intrinsic deliveries (individual and team tests, application activities and peer evaluation). In other modules, class evaluation may be based on a computational work.

MAIN BIBLIOGRAPHY

1. Leach, A. R., *Molecular Modelling: Principles and Applications*, 2nd ed., Prentice Hall, 2001
2. Bioinformatics and Molecular Evolution by Paul G. Higgs and Teresa K. Attwood. Wiley-Blackwell (ISBN-13: 978-1405106832)
3. An introduction to systems biology. Design Principles of Biological Circuits. U. Alon. Chapman & Hall/CRC Mathematical & Computational Biology; 2006.
4. *Chemoinformatics - a Textbook*, Gasteiger, J. Engel, T., Eds.; Wiley-VCH: Weinheim, 2003.
5. Leach, A. R.; Gillet, V. J. *An Introduction to Chemoinformatics*, 2ª ed.; Springer: Dordrecht, 2007.
6. *Handbook of Chemoinformatics: from Data to Knowledge*, Gasteiger, J., Engel, T., Eds.; Wiley-VCH: Weinheim, 2003.
7. Selected papers from specialized international journals.

BIOANALYTICAL PROCEDURES

TEACHING STAFF

Ana Coelho (ITQB NOVA)
Marco Silva (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

- To acquire knowledge and skills in Analytical Biochemistry and related procedures
- To know the bioanalytical methods (spectrophotometry, mass spectrometry, chromatography, electrophoresis, enzymatic and immunologic methods) used to quantify and/or characterize drugs and compounds in biological matrices.
- To be able to implement and develop bioanalytical methods.
- To know the validation parameters, perform validation plans and conclude on the validity of bioanalytical methods.
- To be familiar with the basic aspects of regulation, quality control and quality systems.
- To be able to search and critically interpret the literature in this field.

SYLLABUS

1. Introduction to Analytical Biochemistry.
2. Bioanalytical methods relevant for the quantification and/or characterization of drugs, metabolites and other compounds in biological matrices.

3. Strategies for the development and implementation of bioanalytical methods.
4. Validation of bioanalytical methods.
5. Introduction to regulation, quality control and quality systems in the Clinical Biochemistry Laboratory

TEACHING METHODOLOGIES (INCLUDING EVALUATION)

This curricular unit includes lectures, tutorials and practical laboratory classes. The lectures classes will be given using "data show", together with complementary bibliography made available at the *Web* page of the curricular unit.
Tutorial classes: resolution of problems, literature search, study and discussion of clinical case studies.
Laboratory practical classes: experimental work following provided protocols and integrated in the curriculum of Integrated Laboratories I.
Attendance of the curricular unit: mandatory for 2/3 of the total tutorial and lab classes.
Evaluation: Continuous evaluation in the tutorial classes (40 %) and lab classes (30%).
Preparation of the validation plan for a bioanalytical method (30 %).

MAIN BIBLIOGRAPHY

- Thomas Devlin. Textbook of Biochemistry with Clinical Correlations. 6th Edition, Wiley-Liss, 2006.
- Allan Gaw, Michael J. Murphy, Robert A. Cowan, Denis St. J. O'Reilly, Michael J. Stewart, James Shepherd. Clinical Biochemistry: An Illustrated Colour Text. 4th Edition, Churchill Livingstone Elsevier, 2008.
- David Sheehan. Physical Biochemistry: Principles and Applications, 2nd Edition, Wiley, 2009
- Garofolo, F. (2004) Bioanalytical Method Validation, in Analytical Method Validation and Instrument Performance Verification (eds C. C. Chan, H. Lam, Y. C. Lee and X.-M. Zhang), John Wiley & Sons, Inc., Hoboken, NJ, USA

DISSERTATION

TEACHING STAFF

Maria Teresa Catarino (FCT NOVA)
Members of the teaching staff of the Master in Biochemistry for Health

LEARNING OUTCOMES OF THE CURRICULAR UNIT

The main aim of this unit is the development of a research project in biochemistry. Students will learn how to conduct a research project and how to interpret and present their results.

SYLLABUS

The curricular unit is fully dedicated to carrying out laboratory work and writing of the dissertation which will focus on topics addressed in previous semesters, or topics suggested by Teaching Staff and discussed with students.

TEACHING METHODOLOGIES AND EVALUATION

The unit includes research and development work with individual tutorial support from an advisor chosen by the student. The evaluation will be performed by public discussion of the Master's thesis with a jury.

MAIN BIBLIOGRAPHY

Specific scientific papers and other literature search to be carried out by the student.

INTEGRATED LABORATORY PRACTICALS I

TEACHING STAFF

Maria Teresa Catarino (FCT NOVA)
Margarida Frazão (ITQB NOVA)
Ana Coelho (ITQB NOVA)
Marco Silva (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

This course has the objective of endowing students with an extensive knowledge of the experimental techniques used in different areas of Biochemistry. The students will be exposed to a broad range of techniques available at the Department of Chemistry of FCT and at ITQB. It is intended that students improve their knowledge of the selected experimental techniques, and develop a critical approach to the analysis and interpretation of experimental data.

SYLLABUS

The students will have the opportunity to perform experimental work in different areas of Biochemistry, from molecular biology to biophysics. They will apply techniques used in the isolation and purification of biomolecules and their characterization at the biochemical and biophysical, kinetics, spectroscopic and structural levels. The experimental work will be integrated with the syllabus of other curricular units in the 1st semester of this Master's program.

TEACHING METHODOLOGIES AND EVALUATION

The students will be organized in groups with a maximum of 3 elements. The assessment will be continuous and will take into account the student’s laboratory work and his/her critical analysis of the data. The final grade will be given by a three-member panel including at least one examiner external to the teaching staff of this curricular unit, and will also be based on the presentation by the students of the scientific reports of their experimental work, followed by a discussion.

MAIN BIBLIOGRAPHY

Biochemistry textbooks of general interest:

LEHNINGER PRINCIPLES OF BIOCHEMISTRY
Nelson, D.L., & Cox, M.M.
W.H. Freeman and Company, San Francisco, 5th ed. 2008

PRINCIPLES OF BIOCHEMISTRY
Voet, D., Voet, J.G. & Pratt, C.W.
John Wiley & Sons, Inc., New York, 3rd ed. 2008

BIOCHEMISTRY
Lubert Stryer
W. H. Freeman and Company, San Francisco. 6th Ed. 2007

BIOANALYTICAL CHEMISTRY
Andrea Manz, Nicole Pamme and Dimitri Iossifidis
Imperial College Press, 2004

More specialized books, reviews and/or original papers will depend on the selected experimental techniques.

INTEGRATED LABORATORY PRACTICALS II

TEACHING STAFF
Lígia Martins (ITQB NOVA)
Cristina Costa (FCT NOVA)
Other members of the Teaching Staff of the Master in Biochemistry for Health.

LEARNING OUTCOMES OF THE CURRICULAR UNIT
This course follows up on Integrated Laboratory Practice I, where the students have acquired a knowledge of the multiple techniques used in biochemistry.
In this course, students will choose short research projects from a list presented by the instructor. Throughout the semester, students will have to plan and carry out experimental work to achieve the objectives of the project. The work will be undertaken in research laboratories at FCT or ITQB and each student will participate in up to 3 such projects during the semester. Each project will be a team work of up to 3 members in each team.
It is intended that students acquire an integrated view and practice of several methodologies used in biomolecular laboratorial research.

SYLLABUS
The students will plan and undertake experimental work to achieve the goals of the chosen research projects, making use of the different experimental techniques and methods available at FCT and ITQB.

TEACHING METHODOLOGIES AND EVALUATION
At the beginning of the semester, specific projects will be distributed to the student groups,

chosen from a list prepared by the instructor, with the collaboration of the other instructors of this Master's program.
The students must begin by preparing a feasible work plan. Upon approval of this plan, the students will execute the experimental work, in a research laboratory environment, using the several experimental techniques available at FCT and ITQB.
The execution of the project will be monitored by tutorials.
There will be a continuous evaluation system and at the end of the semester the students will write a short report and make an oral presentation with the results.

MAIN BIBLIOGRAPHY
The students will research specific literature for each assigned project.

METHODS FOR CHARACTERIZATION OF BIOMOLECULES

TEACHING STAFF
Miguel Teixeira (ITQB NOVA)
Maria João Romão (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT
This course aims at introducing the basic concepts and the potential of multiple methodologies for functional and structural characterization of biomolecules, in an integrated and complementary perspective.

SYLLABUS
Brief overview of basic concepts related to the different biomolecules, followed by a deeper introduction to the multiple methodologies for their functional and structural characterization, referring to the respective complementarities.

I-Biomolecules

Proteins; Lipids and Membranes; Nucleic Acids; Molecular Complexes and interaction of biomolecules.

II- Methodologies

1. Spectroscopic Techniques
   a) UV-Visible spectroscopy;
   b) Fluorescence spectroscopy;
   c) Spectroscopies with polarized light: Circular Dichroism (CD) and Magnetic Circular Dichroism (MCD). Surface Plasmon Resonance;
   d) Vibrational spectroscopies: Infra-red and FTIR. Raman and Resonance Raman;
   e) NMR spectroscopy;
   f) EPR spectroscopy.
2. Mass spectrometry
3. Determination of 3D structures of biological macromolecules by:
   a) NMR spectroscopy;

b) X-ray Crystallography (Crystallization; X-ray diffraction; calculation of electron density maps). Structural information by SAXS.
c) Electron Microscopy (EM).

TEACHING METHODOLOGIES AND EVALUATION

This curricular unit includes lectures, tutorials and practical laboratory classes. The lectures classes will be given using "data show", together with complementary bibliography made available at the *Web* page of the curricular unit.
Tutorial classes: resolution of problems, literature search, study and discussion of clinical case studies.
Laboratory practical classes: experimental work following provided protocols and integrated in the curriculum of Integrated Laboratories I.
Attendance of the curricular unit: mandatory for 2/3 of the total tutorial and lab classes.
Evaluation: Continuous evaluation in the tutorial classes (40 %)and lab classes (30%). Preparation of the validation plan for a bioanalytical method (30 %).

MAIN BIBLIOGRAPHY

Proteins: From Analytics to Structural Genomics (Hardcover) by Robert A. Meyers (Editor) , Vols. I and II, Wiley-VCH Verlag (2007)
Biophysical Chemistry: Part I,II e III (Paperback) by Charles R. Cantor (Author), Paul R. Schimmel (Author) W. H. Freeman; 1st edition (1980)

MOLECULAR BASES OF DISEASE

TEACHING STAFF

Paula Videira (FCT NOVA)
Lígia Saraiva (ITQB NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

- To acquire knowledge and skills about the biochemical mechanisms underlying human disease.
- To be able to relate biochemical mechanisms with associated pathologies
- To acquire knowledge and skills on a seminar context and to be able to develop critical analysis, using the scientific literature.

SYLLABUS

- Molecular aspects underlying neurological and immune disorders, cardiovascular diseases, infectious diseases, rare diseases, cancer and aging.
- Current molecular methodologies in the context of understanding human pathologies.

TEACHING METHODOLOGIES AND EVALUATION

The course includes theoretical, practical classes and seminars. The lectures will be taught using the "data show", accompanied by complementary bibliography previously available on the website of discipline.
The practical classes and seminars will focus on discussion of more specialized subjects. The seminars consist of lectures by invited speakers followed by discussions with active student participation.

Evaluation:

- Final examination on the subjects of theoretical classes: 60%
- Reports on practical classes: 40%
- Compulsory attendance of 70%

MAIN BIBLIOGRAPHY

Essential Concepts in Molecular Pathology. (2010) William B. Coleman and Gregory J. Tsongalis (Eds), Academic Press.
Molecular Basis of Health and Disease (2011) Undurti N. Das, Springer.

Optional Curricular Units

ACTIVE INGREDIENTS

TEACHING STAFF
Paula Cristina de Sério Branco (FCT NOVA)
Luísa Pinto Ferreira (FCT NOVA)
Maria Manuela Araújo Pereira (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT
It is intended that students understand the development process, the design strategy and the organic transformations used in the preparation of drugs.

SYLLABUS
- Drug Synthesis. Prime considerations in designing a synthesis. The retro-synthetic approach. New trends in synthetic medicinal chemistry.
- The chiral center. The methods for the preparation of enantiomerically pure drugs.
- Classical and bio-assisted organic synthesis
- Biocatalyzed reactions
- Peptides and peptidomimetic compounds
- Drugs based on a substituted benzene ring
- Opioid analgesics
- Five-membered heterocyclic based-drugs
- Rings that contain three or more heteroatoms

TEACHING METHODOLOGIES AND EVALUATION
Students have to attend lectures, where the theoretical concepts will be presented. There will be also a tutorial component in which the students analyze a theme in the form of a monograph which will be presented orally and discussed.
The evaluation consists of a written test on the lecture contents (60%) and an oral presentation and discussion of a written monograph (40%).

MAIN BIBLIOGRAPHY
New Trends in Synthetic Medicinal Chemistry, F. Gualtieri, Wiley 2000.
Advanced Practical Medicinal chemistry, Ashutosh Kar, New Age International Publishers, New Delhi (2004)

BASICS OF TOXICOLOGY

TEACHING STAFF

António Sebastião Rodrigues (NMS)
José Rueff (NMS)
Michel Kranendonk (NMS)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

- basic knowledge on pharmacokinetics, pharmacodynamics, metabolism and toxicology as well as the biological and chemical mechanisms of these phenomena.
- understanding the toxic biological effects due to exposure to environmental xenobiotics, food xenobiotics or pharmacological agents.
- understanding the toxicological consequences associated with inter-individual variations in biotransformation enzymes and membrane transporters, genetic polymorphisms and genetic variation in metabolism and drug transport.
- knowledge of practical examples of the application of these concepts in the clinics, research and industry
- skills concerning analytical methodologies applied in pharmacology and toxicology studies
- knowledge on the national, European and worldwide regulations, their differences, similarities and implications.

SYLLABUS

1. Principles of pharmaco/toxicodynamics and pharmaco/toxicokinetics.
2. Principles of toxicology.
3. Drug Metabolism.
4. Strategies for the improvement of the absorption and distribution of drugs: Prodrugs and drug delivery systems.
5. Membrane transporters and response to xenobiotics. Efflux and drug resistance.
6. Environmental Toxicology. Mechanisms of action of environmental toxic agents; Drugs in the environment and toxic effects; Endocrine disruptors; Metals; Organic industrial pollutants.
7. Pharmacogenomics and pharmacogenetics. Personalized medicine.
8. Methods in pharmacology and toxicology
9. Genetic Toxicology and cancer.
10. Risk evaluation
11. Regulation

TEACHING METHODOLOGIES AND EVALUATION

24 hours of lectures and 4 hours of problem-solving classes.
Evaluation will include a written examination and a group seminar (3 students) with weights of 70% and 30% respectively.

MAIN BIBLIOGRAPHY

Goodman & Gilman's The Pharmacological Basis of Therapeutics, 12th Edition, Laurence L. Brunton, ED

Pharmacology for chemists, ACS, Oxford University press, 1999, Joseph Cannon

Casarett & *Doull's Toxicology*: The Basic Science of Poisons, 6th Edition, Curtis D. Klaasen, Ed.

The bibliography will also consist of recent original scientific articles in specialized journals and review articles (e.g., Annual Review of Pharmacology and Toxicology).

BIOENERGETICS

TEACHING STAFF

Maria Teresa Catarino (FCT NOVA)
Ricardo Louro (ITQB NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

The course on Bioenergetics will focus on the various aspects of energy transduction performed by living organisms. By the end of the course the student should understand the thermodynamic and kinetic principles involved in energy transduction and be able to solve numerical application problems. He should know the components and organization of the respiratory chains and photosystems and understand the mechanisms of electron/proton coupling. He should be aware of the diversity of bacterial respiration and photosynthesis. It is also expected that the student develops skills in searching, understanding, and discussing the scientific literature in this field.

SYLLABUS

1. Introduction to Bioenergetics: Life, energy and metabolism.
2. Quantitative Bioenergetics: the measurement of driving forces. Gibbs free energy. Oxidation-reduction potencial. Electrochemical potential.
3. Chemiosmotic energy transduction. Electron transfer and electron/proton coupling. Proton motive force generation.
4. Mitocondrial respiratory chain.
5. ATPsynthase: structure, mechanism and regulation.
6. Light reactions of photosynthesis: organisation of the photosystems and proton motive force generation.
7. Bacteriorhodopsin and halorhodopsin: generation of ion gradients.
8. Diversity of bacterial respiration and its environmental relevance.
9. Oxidative stress and health. Mitocondria in the cell and its involvement in genetic and neurodegenerative diseases.

TEACHING METHODOLOGIES AND EVALUATION

The course is organized in lectures, workshops, journal club sessions and seminars. In the workshops, the students will solve numerical and computational problems of Bioenergetics. For the journal club sessions, the students have to read, present and discuss scientific articles

in the Bioenergetics field. For the seminars, the students have to prepare an oral presentation of a particular subject related to Bioenergetics. The presentation is followed by discussion. The final evaluation mark is the average of two theoretical examination papers (70%) plus the journal club discussions and seminar presentation (30%).

MAIN BIBLIOGRAPHY

1. "Bioenergetics 3", David G. Nicholls and Stuart J. Ferguson (2002) Academic Press.
2. "Energy and Life", John M. Wrigglesworth (1997) Taylor and Francis.
3. "Bioenergetics at a Glance", David A. Harris (1995) Blackwell Science.

BIOETHICS

TEACHING STAFF

Isabel Maria da Silva Pereira Amaral (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

- To contextualize the ethical dimension of the life sciences and their applications;
- To promote an informed debate on the increasing importance of the life sciences and biotechnology in society;
- To develop the ability of students to debate scientific and ethical problems;
- To reflect about the neutrality of science and the social responsibility of scientists and engineers.

SYLLABUS

1. The Social responsibility of scientists and engineers in society.
2. The creation of Bioethics as a discipline - history amd principles
3. Bioethics and Technology - Landmarks in the history of Biotechnology
    a. Access to genetic information;
    b. Cloning and steam cells;
    c. Gene therapy;
    d. Genetically Modified Organisms and biotechnological agriculture
4. Bioethics and medicine
    a. Genetics and prenatal diagnosis
    b. Sexuality and humane procreation
    c. Experimentation in animals and humans
5. The bioethics committees - codes of conduct and scientific research at national and international level

TEACHING METHODOLOGIES AND EVALUATION

The classes involve a combination of theory and practice. The lecturer will provide introductions to the main themes of the course and questions for debate as well as case studies for discussion by the students. All the materials (articles, books, PowerPoint slides) will be available online to the students in the course page in Moodle.

Evaluation includes:

- Participation in classes (15%);
- Group presentation of an article (4 members) concerning a specific subject of the course (30%);
- An individual essay on a course topic (45%).

MAIN BIBLIOGRAPHY

- Cristina Beckert (2012), Ética. Lisboa: CFUL.
- Fukuyama, Francis, (2002), Our Posthuman Future: Consequences of the Biotechnology Revolution, Profile Books.
- Elio Screccia (1999), Manual de Bioética – fundamentos e ética biomédica, Edições Loyola, S. Paulo, Brasil.
- Gehring, Verna V. (ed. 2003), Genetic Prospects: Essays on Biotechnology, Ethics, and Public Policy, Rowman & Littlefield Publishers.
- Singer, P. (2000), Ética Prática. Gradiva.
- Guy Durand, (2ª ed. 2007), Introdução Geral à Bioética, Edições Loyola, S. Paulo, Brasil.
- Walter, L. (1999), Contemporary Issues in Bioethics, Wadsworth Publishing.
- Warren, T. R. (ed.) (1995), Encyclopedia of Bioethics, 5 vols., Macmillan Library.

BIOLOGICAL EFFECTS OF RADIATION

TEACHING STAFF

Pedro António de Brito Tavares (FCT NOVA)
Maria Alice Santos Pereira (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

This curricular unit aims to provide a basic understanding of the effects of ionizing radiation in biological systems. Mainly, it seeks to provide understanding of the interaction of ionizing radiation with matter on the molecular level and how molecular-level effects lead to damage at the cell and tissue levels. At the end of this curricular unit, students should be able to:

1. Understand the effect of radiation on atoms and molecules;
2. Distinguish between different mechanisms of damage at the molecular level;
3. Understand the biological mechanisms of defense and repair against radiation damage;
4. Critically review the pertinent scientific literature in this field.

SYLLABUS

1. Introduction and Historical Perspective
2. Sources and types of Ionizing Radiation
    a. Particulate vs. Electromagnetic
    b. Atomic structure, origin and nature of ionizing radiation
    c. Radiation dose and units

   d. Principles of radiation dosimetry
   e. Interaction of radiation with matter
3. Introduction to Radiation Chemistry
   a. Water radiolysis
   b. Free radical formation
   c. Direct vs. indirect effects
4. Radiation-induced cell death
   a. Survival curves *in vivo* and *in vitro*
   b. Damage repair at the cellular level
   c. Dose rate effects
5. Radiation effects on cell cycle
6. Antioxidants
7. Radiation Effects on DNA
   a. Types of damage caused by ionizing radiation
   b. DNA repair mechanisms
8. Genetic Effects of Radiation
   a. Chromosome and chromatid aberrations
   b. Radiation-induced mutations
9. Radiation effects on proteins and lipids

TEACHING METHODOLOGIES AND EVALUATION

The contents of the curricular unit will be presented in two types of class: i) lectures, illustrated whenever possible with practical cases; and ii) seminar classes, that will include presentation and group discussion of articles published in international journals. The students will also be asked to prepare an individual essay in specific chosen themes. Evaluation will consider the presentation (40%) and the essay (60%).

MAIN BIBLIOGRAPHY

"Radiation Biology: A Handbook for Teachers and Students", training course series no. 42, International Atomic Energy Agency, Vienna, 2010.
"Essentials of Radiation, Biology and Protection", Steve Forshire, Delmar Cengage Learning; 2nd edition, 2008.
Selected papers from international scientific journals.

BIONANOTECHNOLOGY

TEACHING STAFF

José Ricardo Ramos Franco Tavares (FCT NOVA)
Pedro Miguel Ribeiro Viana Baptista (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

The main objective of this course is to raise awareness towards the increasing relevance of nanosciences and nanotechnology, with emphasis on nanotechnology for biomedical

applications.
Specific objectives are:

- To stimulate the students' understanding of concepts and underlying mechanisms of nanotechnology applications in biodiagnostics and construction of biosensors, within a broader field of developments in clinical diagnostics and biomedicine research.
- To develop basic laboratory skills in synthesis and characterization of nanostructures;
- Knowledge transfer from theory into practical application of nanoscale properties of materials in a biodiagnostics context;
- Critical evaluation and discussion of scientific work.

SYLLABUS

1. Historic perspective on the origin of Nanotechnology
2. Scale effect and properties of nanomaterials.
3. Nanofabrication: bottom-up vs. top-down approach
4. Microscopy for nanomaterials characterisation (TEM, SEM, SPR)
5. Bionanotechnology and Bionanomachines
6. Nanoparticles for clinical applications
7. Nanotechnology and Green Chemistry
8. Nanotoxicology
9. Construction of nanostructures
    - 9.1. Surface functionalisation
        - 9.1.1. Self-assembling
        - 9.1.2. Bio-polymerisation
        - 9.1.3. Cross-linking
    - 9.2. DNA based nanostructures
        - 9.2.1. Electronics
        - 9.2.2. Bio-mimetizing
    - 9.3. Protein based nanostructures
10. Bionanodetection applications
    - 10.1. DNA & RNA (cross-linking vs. non-cross-linking)
11. Nanoparticles for drug delivery and nanovectors for gene therapy.

TEACHING METHODOLOGIES AND EVALUATION

Lectures will have a duration of 2 h, and will include problem solving. Practical classes with 3 h duration will take place in a laboratory, and will consist of a prior protocol preparation, its implementation and a written report by the students.
Evaluation: Reports and discussion of the practical sessions (25% of the final grade); Presentation and discussion of papers (10% of the final grade); Monograph on a selected theme (45% of the final grade) and its oral presentation (20% of the final grade).

MAIN BIBLIOGRAPHY

"Nanobiotechnology: Concepts, Applications and Perspectives" C.M. Niemeyer, C.A. Mirkin (Eds.), 2004, Wiley-VCH, Weinhein, Germany.
"Materials Chemistry" B.D. Fahlman, 2007, Springer, Dordrecht, the Netherlands.
"Bionanotechnology", D.S. Goodsell, 2004, Wiley-Liss, Hoboken, NJ, USA.

BIOPHARMACEUTICALS

TEACHING STAFF

Paula Marques Alves (ITQB NOVA)
Catarina Brito (IiBET)
Margarida Serra (iBET)
Ana Sofia Coroadinha (iBET)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

- Establishment of Animal Cell Technology as a key area in the discovery and development of complex biopharmaceuticals, including recombinant proteins (*e.g.*, monoclonal antibodies), vaccines and viral vectors for gene therapy.
- Relevance of stem cells as products of high therapeutic potential.
- Development of skills in cell culture technologies as *in vitro* models for basic research and preclinical trials (*e.g.*, primary cultures of brain cells and hepatocytes for toxicology testing).
- Case studies and examples of biotechnological applications of Animal Cell Technology.
- Impact of Animal Cell Technology in Pharma and Small Biotech companies.
- Commercial exploitation of the areas of animal technology and its contextualization in the biotechnology market.

SYLLABUS

- Basic principles of animal cell culture techniques, cellular immortalization and development of production cell lines.
- Culture of animal cells in bioreactors, upstream, downstream and product characterization.
- Production of biopharmaceuticals, vaccines, VLP's (Virus-Like Particles) and gene therapy vectors.
- Introduction to GMP (Good Manufacturing Practices).
- Animal cells as models in preclinical research.
- Aspects of stem cell bioengineering and applications in cell therapy and as tools for biopharmaceuticals screening.

TEACHING METHODOLOGIES AND EVALUATION

- This course includes lectures, theoretical/practical and laboratory classes. In the lectures, subjects are presented and in the tutorial sessions case studies are presented (analysis of scientific papers). These will allow the consolidation of knowledge that will later be put into practice in the laboratory sessions.
- The evaluation has three components that contribute to the final grade: a written examination on the themes explored in lectures (60 %); student presentations and discussions during the tutorial sessions and workshops on issues previously suggested by the lecturers (20 %); and the reports from the laboratory practical work (20%).

MAIN BIBLIOGRAPHY

- "Culture of Animal Cells: A Manual of Basic Technique and Specialized Applications", R. Ian Freshney, Wiley-Blackwell, 6th edition, 2010.
- "Animal Cell Technology: From Biopharmaceuticals to Gene Therapy", Castilho, Morais, Augusto e Butler (Ed), Taylor and Francis Group (Pub).
- "Tecnologia do Cultivo de Células Animais de Biofármacos e Terapia Gênica", Morais AM, Castilho L, Augustos EP (Eds), Editora Roca (Pub).
- Scientific articles published in specialized international journals with high impact factor, such as Nature Biotechnology, Trends in Biotechnology, Biotechnology and Bioengineering, Tissue Engineering, Journal of Biotechnology, Gene Therapy.

DRUG DISCOVERY, DESIGN AND DEVELOPMENT

TEACHING STAFF

Rita Ventura (ITQB NOVA)
Carlos José Rodrigues Crispim Romão (ITQB NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

The objective of this curricular unit (CU) is to contribute to the formation of future researchers or pharmaceutical industry professionals, equipped to understand and act upon the several stages of the creation of an active principle, its transformation into a drug and its introduction to the market as an efficient and safe medicine.
At the end of this CU the student must grasp and be able to articulate the following topics:

1. Processes of identification and discovery of new active principles;
2. Methodologies for the design and optimization of the active principles relative to their therapeutic target;
3. Methods to optimize administration, distribution and delivery of the active principle *in vivo*;
4. Stages and requirements of the process of bringing a drug to the market.

SYLLABUS

Drugs and drug targets: Introduction
Drug targets
  Proteins as drug targets
  Enzymes as drug targets
  Receptors as drug targets
  Nucleic Acids as drug targets
  Other molecular drug targets: lipids, carbohydrates, etc...
Drug discovery, Design and Development
  Finding a lead compound
  Develop a bioassay
Design of the Lead compound
  optimize interactions with the Target: (SAR; pharmacophore)
    optimizing the drug

optimizing access to the target
drug targeting
prodrugs

Problems of Formulation and Drug Delivery
methods to prepare water soluble compounds
solubilizing drugs in organic solventes, micelles or coloidal dispersions
solubilization with cyclodextrins

Bringing Drugs to the Market

Selected Topics (e.g. antibacterials, anti-cancer drugs) and Case Studies.

TEACHING METHODOLOGIES AND EVALUATION

Presential teaching will be made through regular lectures and tutorials as well as through seminars on selected topics or relevant Case Studies. The final evaluation will comprise two written tests to be done during the semester, and a final seminar (with public discussion) on a theme to be selected from a previously announced set. Each type of evaluation (written and oral) will contribute 50% to the final grade.

MAIN BIBLIOGRAPHY

- Graham L. Patrick, An Introduction to Medicinal Chemistry
- Gareth Thomas, Fundamentals of Medicinal Chemistry
- The Practice of Medicinal Chemistry
- Camille G. Wermuth, (Ed) The Practice of Medicinal Chemistry
- B. Silverman, The Organic Chemistry of Drug Design and Drug Action
- Drug Discovery Today, Elsevier periodical with extensive discussions, updates and case studies in Drug Discovery and Development.

FUNCTIONAL ORGANIZATION OF THE CELL

TEACHING STAFF

Júlia Carvalho Costa (ITQB NOVA)
Rita Abranches (ITQB NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

1. To acquire knowledge about the organization and functional dynamics of proteins, membranes and organelles in the eukaryotic cell, more specifically, in sorting and processing of proteins, vesicular transport, cytoskeleton organization and dynamics, cell cycle, interactions between cells and their environment.
2. To be able to characterize specific types of cells, for example, cancer cells and neural cells.
3. To acquire knowledge about deregulated molecular and cellular mechanisms associated with disease, for example, cancer and neurodegenerative diseases.
4. To perform bibliographic search and to develop critical reading of scientific literature to acquire knowledge about a specific theme for the elaboration of a monograph.

SYLLABUS

1. Protein sorting and processing in the eukaryotic cell: mechanisms of vesicular transport; secretory pathways; protein folding and glycosylation; endocytic pathways; deregulation in human diseases.
2. Organization and dynamics of the cytoskeleton: intermediate filaments; microtubules; actin filaments.
3. The cell cycle: overview of the cell cycle; mechanisms of control of the cell cycle; S phase; M phase; mitosis.
4. Interactions between cells and with their environment: cell junctions; cell adhesion; extracellular matrix.
5. Cancer: characteristics of cancer cells.
6. Nervous system: cellular components of the nervous system and their characteristics; neuroregeneration.
7. Deregulated mechanisms in neurodegenerative diseases: protein misfolding; protein degradation; axonal transport; mitochondrial dysfunction; apoptosis; excitotoxicity.

TEACHING METHODOLOGIES AND EVALUATION

The curricular unit is constituted by lectures and tutorials.
The lectures will address the theoretical aspects of the syllabus.
The tutorial component consists of a monograph written by the students about a specific theme which is presented orally and discussed with the lecturer and the colleagues. The theme is selected from a set of themes supplied by the lecturer.
The evaluation consists of a final exam about the theoretical component (60%) and the written monograph with oral presentation and discussion (40%).

MAIN BIBLIOGRAPHY

- Alberts, B., Bray, D., Hopkin, K., Johnson, A., Lewis, J., Raff, M., Roberts, K., Walter, P. (2010) Essential Cell Biology. 3rd Edition. Garland Science, Taylor & Francis Group, New York, USA. ISBN 978-0-8153-4129-1.
- Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., Walter, P. (2008) Molecular Biology of the Cell. 5th Edition. Ed. Garland Science, Taylor & Francis Group, New York, USA. ISBN 978-0-8153-4106-2.
- Lodish, H., Berk, A., Kaiser, C.A., Krieger, M., Scott, M.P., Bretscher, A., Ploegh, H., Matsudaira, P. (2007) Molecular Cell Biology. 6th ed., W. H. Freeman. ISBN-10: 0716776014.
- Siegel, G.J., Agranoff, B.W., Albers, R.W., Fisher, S.K., Uhler, M.D. (1999) Basic Neurochemistry. Molecular, cellular and medical aspects. 6th Ed. Lippincott Williams &Wilkins. ISBN 0-397-51820
- Papers published in international journals with high impact factor.

GLYCOBIOLOGY AND DISEASE

TEACHING STAFF

Paula Videira (FCT NOVA)
Angelina Palma (FCT NOVA)
Filipa Marcelo (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

All living cells express at their surface a complex network of glycoconjugates (glycoproteins, glycolipids, glycosaminoglycans and proteoglycans), which mediate functions as diverse as the construction of the extracellular matrix, immune and inflammatory responses, pathogen-host interactions and many others. This glycosylation is dramatically influenced by disease mechanisms such as the development of cancer.

This course aims to develop and apply basic concepts in Glycobiology to understand the role of glycans in physiology and disease mechanisms with a focus on cancer, pathogen-host interaction, congenital disorders of glycosylation and infection. Its programmatic content presents a wide range of topics. It will be given with a critical perspective, but also with an integrative view of Glycobiology in several areas of health.

At the end of the course, the student should have the ability to:

- Refer diseases whose mechanisms involve glycans and associate structure and the biological function of the glycans and of proteins (lectins) involved in their recognition.
- -Refer state-of-the-art methodologies in Glycobiology for the study of glycans.
- Relate diagnostic methods / technologies for Congenital Diseases of Glycosylation and cancer.
- List therapeutics based on glycans or glycoconjugates and vaccine development, correlating with clinical application.
- Formulate issues related to diversity and function of glycans and its importance in pathology.

SYLLABUS

Theoretical classes

1) Introduction to Glycobiology: basic concepts of the structural diversity of glycans and their biosynthesis; Advanced methodologies in glycobiology for the study of glycans
2) Recognition of glycans by the immune system and immunomodulation
3) Lectins and bacterial infection: functional and structural analysis
4) Inflammation and cell migration
5) Congenital disorders of Glycosylation
6) Changes in glycan expression in cancer
7) Complex gangliosides and aberrantly glycosylated mucins and role in tumor progression
8) Human therapies based on glycans

Practical classes:

1) Identification of aberrant glycosylation in tumor cells through lectin (microscopy / flow cytometry)

2) Glycan-arrays to identify glycans binding specificity and ligand discovery
3) NMR for protein-glycan interactions.

TEACHING METHODOLOGIES AND EVALUATION

The curricular unit is organized into eight themes, each comprising theoretical, theoretical/practical and practical classes. This course will be in b-learning format, i.e. it contains face-to-face classes with teachers and, in addition, part of teaching is online (videos, documents, forums), making use of computers and the internet as teaching tools. There will be two thirds of theoretical classes (b-learning) and one third of practical classes. Theoretical classes include distance-learning classes, online content with resources and videos of teachers. The curricular unit covers tutorial strategies with distance learning sessions and discussion forums on topics of interest. The practical classes include innovative technology and allow students to work hands-on in a variety of laboratory techniques.

The teaching will be in Portuguese and English. In this way, the student will update and expand his knowledge in glycobiology and develop critical thinking for application in glycosylation-related diseases. With these teaching methodologies, the aim is to captivate the student from the beginning of the curricular unit, to foster an active and collaborative participation, to foment discussion and criticism, allowing the students to interrelate the various themes among themselves and create bases for eventual application of Glycobiology in their future work.

The final grade will be a weighted average of:

1) A written test to evaluate the acquired knowledge (50%);
2) Participation in practical classes and mini-test or report (40%);
3) Discussion forum (e-learning format) (10%).

MAIN BIBLIOGRAPHY

- Essentials of Glycobiology, Third Edition. Edited by Varki A, Cummings RD, Esko JD, et al. Cold Spring Harbor Laboratory Press; 2017, ISBN 978-1-62-182132-8. Available from: https://www.bookdepository.com/Essentials-Glycobiology-Third-Edition-Ajit-Varki/9781621821328 or http://www.cshlpress.org/essenglycobio3
- Introduction to Glycobiology, Third Edition. Maureen E. Taylor and Kurt Drickamer, Oxford University Press, Inc., New York. 2011, ISBN 978-0-19-956911-3
- Selected scientific papers made available by the teaching staff on the MOODLE page of this Curricular Unit

HUMAN GENETICS

TEACHING STAFF

José Rueff (NMS)
Aldina Brás (NMS)
António Sebastião Rodrigues (NMS)
Helena Borba (NMS)
Michel Kranendonk (NMS)
Joaquim Calado (NMS)
Susana Silva (NMS)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

General Outcomes

Curiosity	the desire to discover the potential of genetics in medicine (... Wonderful and full of wonder).
Comprehension	To understand and grasp the genetic mechanisms and their role in pathology.
Competence	To know how to apply the genetic models and methods to new problems.
Capabilities	To be able to carry out experimental work and information search.
Creativity	To know how to criticize hypotheses and how to justify new hypotheses explaining genetic phenomena.

Specific Outcomes

- understanding and mastering of the genetic language and mechanisms, and their role in pathology - from genetic variability to disease specificity,
- training to collect clinical data to draft a genealogic tree aimed at inferring the heredity type associated to a given pathology,
- ability to recognize the most common genetic diseases, to understand their physiopathology and potential prognosis,
- ability to estimate the risk associated with the offspring transmission of mendelian pathology and its application to genetic counseling,
- selection and interpretation of genetic exams complementary to elucidate a specific genetic pathology,
- training to criticize hypotheses and to justify new hypotheses explanatory of genetic phenomena and their role in etiopathogeny, up to clinical application in translational medicine,
- awareness of the unique genetic nature of each individual and its relevance, in conjugation with environmental factors, in the individual susceptibility towards multifactorial disease,
- training to bridge Genetics research with therapeutical advances,

- stimulus to discover the potential of Genetics in Medicine.

Cross-contents Outcomes

- training for knowledge beyond textbooks - the textbook is not a closed, circular and finished genetics trajectory,
- training for permanent self-learning, and awareness development of the need to undergo learning activities throughout life,
- training for the evolution of knowledge,
- acceptance of the uncertainties of science,
- acceptance of multidisciplinary approaches,
- training for group work.

SYLLABUS

Gene structure and organization of the human genome

1. Gene organization. Coding and non-coding regions.
2. Regulation of gene expression. Regulation mechanisms. Chromatin structure. Epigenetics.
3. Role of mRNA processing.
4. Gene function variation in embryo/fetogenesis and pathology. Stress genes.
5. Usage and limitations of information obtained from gene sequencing.
6. Usage of the information obtained from RNAs and polypeptides.
7. Gene duplication and divergence. Paralogue genes. Translocatable elements.

Genes and disease

1. Transmission patterns of autosomal recessive and dominant situations, connected with chromosome X.
2. Modifying factors of phenotype expression. Penetrance, expressivity, abiotrophy, pleiotropy.
3. Clinical framework of the more frequent mendelian situations. From mutations to phenotype.
4. Innate metabolic errors and pharmacogenetic variations.
5. Mitochondrial pathology and mitochondrial heredity pattern.
6. Nature of mutations and pre-mutations; trinucleotide expansion.
7. Concepts and clinical importance of imprinting and uniparental disomy.
8. Medical uses of polymorphisms, genic mapping, linkage unbalance and association studies.
9. Multifactorial nature of many normal and pathologic characteristics. Multifactorial heredity.
10. Gene interactions with other genes and environmental factors, and their role in pathology. Epistasy.

Chromosomes and chromosomic pathology

1. Gene organization in chromosomes. Chromosome transmission.
2. Causal mechanisms in chromosome alterations.
3. Chromosomic anomalies: numerical, structural and mosaic. From cytogenetics to phenotype.

Population genetics

1. Basics of population genetics and frequencies in specific populations. Allelic frequency and genetic drift. Effects of consanguinity and neomutations in genic frequencies. Medical intervention and genic frequencies.
2. Evolutive principles in the understanding of human biology and pathology.

TEACHING METHODOLOGIES AND EVALUATION

Teaching is organized into:

1) Theoretical Lectures where the main syllabus topics in this curricular unit are critically presented;
2) Theoretical Thematic classes for analysis and discussion of specific relevant topics;

The evaluation of this curricular unit consists of a Written Exam (WE) and a Seminar (S). The Final Grade (FG) is the weighted average FG = 0.8 * WE + 0.2 * S, where both WE and S must be ≥9,50.

The Written Exam is without consultation and consists of multiple-choice questions covering all the topics presented in the Lectures and Thematic classes.

The Seminar consists on a 10-minute presentation followed by a 5-minute discussion of one of the proposed themes, by 4-5 student groups formed within the class.

Evaluation Criteria (S):

- Critical analysis of the theme
- Synthesis ability
- Bibliographic research
- Duration of presentation within the allotted limit

MAIN BIBLIOGRAPHY

Genetics:

- Speicher M, Antonarakis SE, Motulsky AG (Eds.) "Vogel and Motulsky's Human Genetics. Problems and Approaches" Springer Verlag, 4th ed., 2010.
- Strachan T, Goodship J., Chinnery P. "Genetics and Genomics in Medicine". ISBN 978-0-8153-4480-3; Garland Science, 2015.
- Strachan T, Read A.P. "Human Molecular Genetics", 4th edition. Garland Science, 2010.
- "Preventive and Predictive Genetics: Towards Personalised Medicine" Editors: Grech, Godfrey, Grossman, Iris (Eds.); Springer; Series: Advances in Predictive, Preventive and Personalised Medicine, Vol. 9. ISBN 978-3-319-15343-8
- Feuk L (Ed.) "Genomic Structural Variants". Series: Methods in Molecular Biology, Vol. 838. Springer Protocols. Humana Press, 2012
- Nussbaum RL, McInnes RR, Willard HF. "Thompson & Thompson Genetics in Medicine", 7th edition. Saunders, 2007.
- Korf BR, Irons MB "Human Genetics and Genomics", 4th edition. Wiley-Blackwell, 2013.
- Lewis R. "Human Genetics: Concepts and Applications". 9th edition. McGraw-Hill Companies Incorporated. 2009.
- Ellard S, Turnpenny P. "Emery's Elements of Medical Genetics". 14th edition. Churchill Livingstone, 2011.
- Passarge E. "Color Atlas of Genetics". 3rd edition. Thieme Medical Publishers, 2007.

- Regateiro FJ. “Manual de Genética Médica”. Imprensa da Universidade, Coimbra, 2007.
- Emery A, Rimoin D. “Principles and Practice of Medical Genetics" - 3 vols. 5th edition. Churchill Livingstone, 2007. (mainly the 1st volume)
- “Encyclopedia of the Human Genome” 5 vols. John Wiley & Sons, Ltd. 2003.

Embryology:

- Alberts, Bruce *et al.*; *Molecular Biology of the Cell*; Garland Publ. Inc.; New York.
- Carlson, Bruce M.; *Human Embryology and Developmental Biology*; Mosby.
- Larsen’s Human Embryology (2009)

General Bibliographic Research
MEDLINE
IARC
National Library of Medicine

Genetics databases
p53 mutations database
BioGPS
National Center for Biotechnology Information
Tools of Genetics and Molecular Biology
OMIM - Online Mendelian Inheritance in Man
Human Genome Resources
Martindale's Health Science Guide
Généthon
Information for Genetic Professionals
Clinical Genetics Homepage
Cytogenetics Gallery

Genetic Diseases
GeneClinics

Laboratory tests of genetic diagnosis
GeneTests

Database of genetic diseases for the public at large
NORD

DNA and Protein database
Genbank

DNA database
EMBL

Evidence-based Medicine
Cochrane Collaboration

MOLECULAR IMMUNOLOGY

PROFESSOR

Paula Videira (FCT NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

- Acquisition of knowledge about the constitution and function of the Immune System.
- Acquisition of basic knowledge about the mechanisms of immune response, in the different steps of the immune response.
- Learning the molecular basis and mechanisms of antigen recognition and leukocyte activation
- Introduction of knowledge on the role of immune dysfunction in autoimmune diseases and immunodeficiencies.
- Development of skills on the applicability of methodologies / technologies used in the study of Immunology in different areas, such as, basic research, diagnosis and new therapies.
- Understanding the dynamics of knowledge contained in a rapidly developing science that integrates in all other biomedical sciences.

SYLLABUS

- The human immune response in action: general concepts
- Elements and mechanisms of innate response
- Adaptive response and T and B cell cooperation
- Bases of the diversity of antigen recognition (antibodies and T cell receptors)
- Th1/Th2 balance
- Immunologic memory
- Adhesion molecules and leukocyte migration
- Cytokines
- Immune signaling pathways
- MHC and antigen presentation
- HLA immunogenetics and its relevance in the context of clinical histocompatibility.
- Immunotherapy
- Elementary techniques and animal models in Immunology
- Diagnostic techniques in Immunology
- Hypersensitivity and autoimmunity
- Immunodeficiencies
- Immunity in health and disease

EVALUATION

The student will be evaluated according to the weighted average of: 1) a written examination (50% weighting) which will include the themes explored in all classes, themes from the student's presentations and the discussions on research seminars; 2) presentation and discussion of high impact papers which will be supplied by responsible of the course (40% weighting); and 3) participation and attitude in all course (weighting 10%).

MAIN BIBLIOGRAPHY

- Cellular and Molecular Immunology, Saunders/Elsevier, 2011 by Abbas, Lichtman, and Pillai
- Janeway's Immunobiology; Garland Science, 7th edition, by Murphy, Travers, Walport
- Kuby Immunology; Kindt, Goldsby, Osborne
- Fundamentos de Imunologia, Lidel 2007, Fernando A. Arosa, Elsa M. Cardoso, Francisco C. Pacheco
- Scientific papers published in specialized international journals with high impact factor, such as
- Nature Immunology, Nature Reviews Immunology, Journal of Immunology, Molecular Immunology, European Journal of Immunology.

STRUCTURAL BIOCHEMISTRY A

TEACHING STAFF

Maria João Romão (FCT NOVA)
Maria dos Anjos Macedo (FCT NOVA)
Pedro Manuel Matias (ITQB NOVA)
Pedro Miguel Lamosa (ITQB NOVA)

LEARNING OUTCOMES OF THE CURRICULAR UNIT

This curricular unit will provide the students with theoretical and practical skills to:

- plan, execute and analyze protein crystallization assays;
- carry out a crystallographic characterization of the crystals obtained;
- collect and process diffraction data from a protein crystal;
- plan and execute the 3D structure determination of a protein;
- build, refine and critically analyze the 3D structural model of a protein;
- perform the structural analysis of the model obtained, compare it with models obtained by other methods and find similar structures in databases;
- carry out a basic interpretation of 1D and 2D NMR spectra of proteins;
- collect and process 1D and 2D NMR spectra of proteins;
- determine by NMR the structure of a protein with MW < 15 kDa.

SYLLABUS

- Crystal symmetry; crystallization methods; characterization of crystals;
- sources of X-rays, diffraction by single crystals, instruments and methods for diffraction data collection;
- The structure factor, electron density maps, the "phase problem" and methods for its solution;
- Methods for building and refining a crystallographic structural model; convergence criteria;
- Electron Crystallography and Electron Microscopy for 3D structure analysis;

- Validation methods for crystallographic protein 3D structures; structural comparison; crystallographic databases. Comparison with other methods of 3D structural analysis. *On-line* computational tools;
- Basic theory of 1D and 2D NMR. Structural information: angles, distances, chemical environment.
- Pulse sequences for data acquisition and spectral assignment. 2D and 3D methods.
- Protein structure determination methods by NMR: Proteins with MW <15kDa vs. proteins with MW >15kDa.

TEACHING METHODOLOGIES AND EVALUATION

- Theoretical classes - direct contact with the teaching staff in a classroom for presentation and discussion of the theoretical and theoretical-practical concepts included in the syllabus.
- Practical classes - direct contact with the teaching staff in classroom or laboratory for application of the concepts presented in the theoretical classes. The students will be divided into groups and each group will choose a project dealing with the structural characterization of a protein by X-ray crystallography and/or NMR. The work progress will follow as closely as possible the contents of the theoretical classes so as to allow the students a better assimilation of the concepts presented.
- Independent study - time used by the students to prepare project reports and study for the final examination.
- Evaluation - will consist of a written examination (45% of the final grade) and an oral presentation and discussion of the project(s) executed by the student (55% of the final grade).

MAIN BIBLIOGRAPHY

"Crystallography made Crystal Clear - A Guide for users of Macromolecular Models" G. Rhodes, 2nd Ed., Academic Press: San Diego, London (2000)
"Introduction to Protein Structure" Branden, C.-I. & Tooze, J. Garland Pub. (1999)
"Structural Biology; Practical NMR applications" Q. Teng, Springer Science +Business Media, Inc, NY (2005)
Wlodawer, A., Minor, W., Dauter, Z., and Jaskolski, M. (2008) "Protein crystallography for non-crystallographers, or how to get the best (but not more) from published macromolecular structures", *FEBS J 275*, 1-21. doi:10.1111/j.1742-4658.2007.06178.x