SAN RAFFAELE INTERNATIONAL MD PROGRAM

YEAR 1
Academic Year 2011/2012

- Statistics and Bioinformatics
- Medical Physics
- Medical Humanities
- Chemistry and Biochemistry
- Cell & Molecular Biology
- Genetics & Developmental
- Basic life Support

STATISTICS & BIOINFORMATICS

Total Credits: 6
Total hours: 100
Scientific Discipline Sector: MED/01 – INF/01

Course Coordinator: Prof. Clelia Di Serio
Email: diserio.clielia@hsr.it
60 hours

Teaching Assistant: Chiara Brombin, Ph.D
Email: Brombin.chiara@hsr.it
40 hours

Course Description
The course presents fundamental concepts in applied probability, exploratory data analysis, experimental design, statistical inference, focusing on probability and analysis of one and two samples. Fundamentals in informatics, data management and basic data analysis are also provided in the course. Topics are described in detail in the timetable.

Course Objectives
The goal of this course is to equip medical students with core applied statistical concepts and methods:

1) The course will refresh the mathematical, computational, statistical and probability background that students will need to take the course.
2) The course will introduce students to the display and communication of statistical data by means of descriptive statistics for univariate and bivariate variables.
3) Students will learn to recognize the experimental design to understand different types of studies arising in public health studies.
4) Students will learn to read epidemiological papers and interpret the statistical analyses.
5) Students will learn to understand basics in probabilities (Bayes theorem) to interpret screening tests and main topics in experimental design (e.g., studies type definition, sources of bias, etc..)
6) Students will learn to evaluate correlation, calculate regression coefficients and interpret confidence intervals for population means and proportions in order to build a hypothesis systems one and two tails;
7) Students will learn to perform a two-sample t-test and interpret the results; calculate a 95% confidence interval for the difference in population means and proportions
8) The course will also cover Analysis of Variance (ANOVA)

During the course lessons in information technology will be held in computer room. Excel and SPSS statistical software will be used for computer applications of theoretical issues.

Course Schedule:

Date	**TIME**	**Subject index**
11/10/2011	16-18	Opening
12/10/2011	9-11	Data description:Types of data and frequency distribution
13/10/2011	9-11	Data Description: Measure of central tendency
13/10/2011	11-13	Data Description:Measure of variability
17/10/2011	9-11	Exercises All
18/10/2011	9-11	SPSS (introduction)
18/10/2011	11-13	Exercises All
19/10/2011	9-11	Data Description:Bivariate analysis covariance
24/10/2011	9-11	Data Description: correlation
25/10/2011	9-11	Data Description: Regression and Goodness of fit
25/10/2011	11-13	Data Description: Regression and Goodness of fit
26/10/2011	9-11	exercises Group1 Tutorial 1
27/10/2011	9-11	Exercises Group 2 Tutorial 1
27/10/2011	11-13	Data Description: contingency tables, marginal and conditional frequency
02/11/2011	9-11	Data Description: association
03/11/2011	9-11	Exercises All
03/11/2011	11-13	SPSS
08/11/2011	9-11	SPSS
08/11/2011	11-13	exercises (All)
09/11/2011	9-11	Introduction to probability objective and subjective :main rules
10/11/2011	9-11	Introduction to probability objective and subjective :Bayes Theorem and screening test
10/11/2011	11-13	exercises Group1 Tutorial 2
14/11/2011	9-11	Exercises Group 2 Tutorial 2
15/11/2011	11-13	Experimental design, OR and RR
16/11/2011	9-11	SPSS: ROC CURVE
17/11/2011	9-11	exercises (All)
17/11/2011	11-13	Introduction to discrete distributions: binomial distribution
21/11/2011	9-11	exercises (All)
22/11/2011	11-13	Poisson distribution and exponential distribution
23/11/2011	9-11	Continuous distribution : Gaussian distribution
24/11/2011	9-11	exercises (All)
24/11/2011	11-13	Midterm
25/11/2011	9-11	SAMPLE DISTRIBUTION Student T distribution
28/11/2011	9-11	SPSS(confidence intervals)
01/12/2011	9-11	Introduction to inference: confidence intervals for mean (I)
01/12/2011	11-13	Introduction to inference: confidence intervals for mean (II)
02/12/2011	9-11	exercises Group1 Tutorial 3
05/12/2011	9-11	Exercises Group 2 Tutorial 3
06/12/2011	11-13	exercises Group1 Tutorial 4
12/12/2011	9-11	Exercises Group 2 Tutorial 4

13/12/2011	11-13	Hypothesis testing: main concept
14/12/2011	9-11	exercises (All)
15/12/2011	9-11	Hypothesis testing: mean (one samples)
15/12/2011	11-13	Hypothesis testing: p-value
16/12/2011	9-11	exercises (All)
19/12/2011	9-11	SPSS (hypothesis testing)
20/12/2011	11-13	SPSS (final)
21/12/2011	9-11	exercises Group1 Tutorial 5
09/01/2012	9-11	Exercises Group 2 Tutorial 5
11/01/2012	9-11	

Textbook:
Biostatistics. Basic Concepts and Methodology for the Health Sciences (9th edition). Author: Wayne W. Daniel. WILEY

Supplementary Online Material.

Additional material (one of the following):

- **Discovering Statistics Using SPSS (Introducing Statistical Methods),** 3rd edition, by Andy P. Field (2009)- Sage Publications
- **SPSS Survival Manual: A step by step guide to data analysis using SPSS,** 4th edition, by Julie Pallant (2010)-Allen & Unwin
- **SPSS Programming and Data Management, 4th Edition,** by Raynald Levesque; SPSS Inc.

Homework

Each lecture topic will be accompanied by a homework assignment. Homework completion will contribute to the final mark.

Prerequisites

Calculus and a moderate level of mathematical literacy are prerequisites for this class (set theory, concept of function, linear function, logarithm, exponential, concept of derivative and integral). Students are required to have good knowledge of Office package (Excel in particular). Upon entering the course, students are expected to have basic skills in Excel (e.g. reading in data, creating new variables, merging data sets, case selection, sub-setting, sorting, stratification

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MEDICAL PHYSICS

Total Credits: 5
Total Hours: 60
Scientific Discipline Sector: FIS/07 – MED/36

Course Coordinator: Prof. Monika Grothe
Email: grothe@mail.cern.ch
60 hours

Course Description

Mathematical review

Cartesian coordinates, functions and their graphical representation. Linear and logarithmic scales. Significant digits. Scientific notation. Vectors and operations with them: sum, difference, scalar and vector product.

Physics quantities and their measurement

Units. Statistical and systematic uncertainties.

Mechanics

Velocity, acceleration. Uniform straight motion. Constant-acceleration motion. Falling objects. Motion in two and three dimensions. Circular motion: angular and tangential velocity, centripetal acceleration; uniform circular motion.

Force, mass, Newton's laws; inertial and non-inertial reference frames. Gravitational forces. Friction.

Work, kinetic and potential energy. Total mechanical energy and its conservation. Conservative forces, dissipative forces. Power. Impulse and linear momentum. Momentum conservation; collisions.

Simple harmonic motion; pendulums and springs. Elastic forces, elastic potential energy. Damped and forced oscillations; resonance.

Torque; couples. Equilibrium of rigid bodies. Levers. Centre of gravity. Stability.

Motion of the centre of mass; Newton's law for particle systems. Motion of rigid bodies: angular speed and acceleration. Moment of inertia. Angular momentum and its conservation.

Elasticity. Stress and strain. Young's modulus; Poisson's ratio; shear modulus; bending; bulk modulus. Elastic limit, ultimate strength.

Fluids

Archimedes' principle. Flow rate. Equation of continuity. Conservation of energy and Bernoulli's equation. Viscosity; Hagen-Poiseuille's law; flow resistance; Stokes' law; sedimentation velocity; turbulent flow; Reynolds number.

Ideal gases; equation of state; kinetic theory. Real gases. Vapours and gases. Saturated vapour. Diffusion, diffusion coefficient, Fick's law. Surface tension; laws of Laplace and Jurin.

Thermodynamics

The first principle of thermodynamics. Specific heat capacity, heat capacity. Heat capacity of an ideal gas at constant pressure or constant volume. Metabolic rate. Second principle of thermodynamics; reversible and irreversible processes; entropy; thermodynamic cycles, Carnot's cycle, efficiency.

Electricity and Magnetism

Electric charge, Coulomb's law, electric field, electrostatic potential energy, potential; electron volt. Relation between field and potential difference. Electric dipole: field lines and behaviour in an electric field.

Conductors and insulators. Polarisation of a dielectric. Electric capacity; capacitor; effect of a dielectric. Relative dielectric constant. Energy stored in a capacitor. Capacitors in series and parallel.

Electric current. Drift velocity of the charge carriers. Electric resistance; resistivity. Ohm's law. Resistors in series and parallel. Electrical circuits. Kirchoff's rules. Power in electrical circuits, Joule's law. Ohmic and non-ohmic conductors. RC circuits.

Direct and alternating current circuits.

Effects of current through the human body. Grounding.
Magnetic field. Lorentz's force; force on a current-carrying wire. Biot-Savart law. Field generated by a wire, field generated by a circular current loop. Solenoid. Magnetic dipoles; magnetic dipole moment; behaviour of a magnetic dipole in a magnetic field. Ferromagnetic materials, permanent magnets.
Magnetic field flux. Faraday's law. Electric generators, transformers.
Cathode-ray tube. Linac, cyclotron, synchrotron.
Nuclear magnetic resonance.
Periodic waves. Wave velocity; period and wavelength. Longitudinal and transverse waves. Fourier analysis. Electromagnetic waves and their spectrum. Antennas. Quantisation of energy in electromagnetic waves: the photon.
Generation of X rays: Bremsstrahlung and characteristic lines.

Sound Waves

Nature of sound. Intensity of sound waves. Intensity level; decibels. Doppler effect. Ultrasounds. Reflection and absorption of ultrasounds. Principles of sonography and Doppler sonography.

Geometrical Optics

Refraction index. Reflection, refraction, Snell's law. Total internal reflection. Lenses. Lensmaker equation; thin-lens formula. Accommodation; near and far points.

Modern Physics, Nuclear Physics

The main concepts of special relativity. The main concepts of quantum mechanics (energy quantization). Atomic structure; transitions between atomic orbitals.
Structure of the atomic nucleus. Stable and unstable nuclei. Alpha, beta and gamma decays. Activity; law of radioactive decay. The physics principles of PET.

Interaction of radiation with matter

Interaction of charged particles with matter: the Bethe-Bloch equation; the case of electrons and positrons. Interaction of X and gamma rays with matter: photoelectric effect, Compton effect, pair production. Biological effects of radiation. Applications to imaging.

Radioprotection

Dose; equivalent dose and the radiation-weighting factors; effective dose and the tissue-weighting factors. The three principles of Radioprotection. Dose limits (occupational and public). Typical doses in some diagnostic examinations.

The course covers the basic principles of Physics, with emphasis on subjects useful for understanding biological phenomena and biomedical instrumentation. Problem sessions are foreseen.

Prerequisites

Basic mathematics. Knowledge of calculus is not required.

COURSEBOOK:

Essentials of College Physics
Raymond A. Serway, Chris Vuille:
ED Brooks/Cole.

In addition any of the following:

- **General Physics 2nd Edition,**
  Morton Sternheim, Joseph Kane
  ED. Wiley & Sons
- **Physics 3rd Edition,**
  Morton Sternheim, Joseph Kane
  ED. Wiley & Sons
- **Fundamentals of Physics Extended, 9th Edition** (or preceding editions),
  David Halliday, Robert Resnick, Jearl Walker
  ED. Wiley & Son

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MEDICAL HUMANITIES

Total Credits: 13
Total Hours: 120
Scientific Discipline Sector: MED/02 – M-FIL/33 – M-FIL/03 – L-LIN/01 – L-LIN/12

Professors Teaching:
Course Coordinator Prof. Michael John john.michael@unisr.it
Prof. Donatella Lippi
Prof. Giuseppe Pantaleo
Dr. Michele Loi
Prof. William Cooke
Prof. Roberta De Monticelli
Prof. Andrea Moro
Prof. Massimo Reichlin

Aim:
The aim of the course is to help students understand that patients are people, and not just a mass of molecules, who have not only an illness, but are also suffering fear and anguish. Doctors must therefore strive to empathize with individuals and not simply distribute medication and drugs to faceless and nameless numbers.

Discussion and active student participation will be paramount to the overall success of the course.

Course objectives:
In today's frenetic, high-tech world, where medicine is evidence based and focuses on specialties of all possible kinds, doctors generally have little time to ponder the multifaceted problems of their patients. Indeed, there are innumerable horror stories told by sick people that stem from the uncaring attitudes and the lack of sensitivity shown by many health professionals. Yet medicine should be seen as a caring profession that requires doctors not only to provide valid clinical assistance but, above all, to empathize with patients and their families when they are at their most vulnerable and in need of understanding.
Nowadays, medical school students are encouraged to interact with patients virtually from the beginning of their training and an increasing amount of emphasis is being placed on the teaching of social sciences, ethics and communication skills to help create a new kind of doctor. One way of doing this is by introducing the study of the *Medical Humanities* (literature, music, visual arts, psychology, sociology, philosophy, ethics, history, language, religion etc.) into the medical curriculum. These subjects require imagination, close observation and understanding, which are all fundamental characteristics of a successful and caring doctor.
How otherwise might a 20-year-old medical or nursing student learn about the complexities of the human condition? How would they be able to understand the reactions and feelings of someone with a terminal illness or a crippling disability, let alone a parent who has just lost a child? They certainly will not learn these skills from standard clinical textbooks, where the words fear and anguish do not appear in the index. Yet fear and anguish are at the very center of how a patient faces up to and lives with an illness.

At the end of this course, students will have a greater understanding of:
- *empathy and patient-centered communication*
- *team work and the ability to interact with colleagues and other health professionals*
- *linguistics and use of language*
- *truth-telling and the delivery of bad news*
- *withdrawal of treatment*
- *euthanasia and assisted suicide*
- *treatment of violence and abuse*
- *ethical and legal problems linked to medical errors*

- *ethics committees*
- *conflict of interest and relationship with industries*
- *chronic illness*
- *old age, death and bereavement*
- *cross-cultural conflicts*
- *alternative and complementary health practices*
- *religion and spirituality*
- *ethical problems linked to stem cells, organ donation and transplantation*
- *re-pro ethics and new reproductive technologies*
- *history of medicine and medical education*

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MICHAEL JOHN - Coordinator *(20 hours)*
Email: john.michael@unisr.it
02.2643.3059
Scientific Discipline Sector: L-LIN/12
This is a two-semester course. There will be 10 hours of teaching in semester 1 and 20 hours in semester 2.

General aims and objectives

1. To develop the students' knowledge of basic doctor-patient-doctor communication skills
2. To focus on the language and communication skills that doctors need to make consultations more effective, focusing on five fundamentals: verbal communication, active listening, voice management, non-verbal communication, cultural awareness
3. DVD viewing to observe a range of doctor-patient encounters, exploring the importance of non-verbal communication.
4. Use of DVD movies and books to focus on empathy in the doctor-patient relationship
5. An introduction to peer-to-peer communication in the biomedical context: papers, posters, presentations.
6. The importance of publishing research papers and the need to attend international congresses.
7. How to prepare for and give an oral presentation before a peer audience.

Course Schedule:

Semester 1

7/11/2011 Introduction: *I am not a number…*
7/11/2011 The patient
9/11/2011 The aims of the consultation
11/11/2011 DVD 'The Doctor'
11/11/2011 Analysis of 'The Doctor' with discussion

Semester 2

5/3 2012 Introduction to peer-to-peer communication
8/3/2012 Planning the paper
9/3 2012 Paper structure
12/3/2012 The destiny of your paper
15/3/2012 The poster
16/3/2012 Once upon a time there was a congress
19/3/2012 The Q+A session
22/3/2012 IT room exercises: creating slides for presentations
23/4/2012 Student presentations
26/4/2012 Student presentations

Compulsory readings:

- The Diving Bell and the Butterfly – ISBN - 1-85702-794-9 Jean-Dominique Bauby
- English for the medical profession (Michael John: Masson 2006 ISBN 8821429105)

Recommended reading:

- Teaching and Learning Communication Skills in Medicine (second edition) - Suzanne Kurtz, Jonathan Silverman, Juliet Draper ISBN 1-85775-658-4
- Skills for Communicating with Patients (second edition) - Silverman, Kurtz, Draper ISBN 1-85775-640-1
- The Doctor's Communication Handbook - Peter Tate ISBN 978-1-84619-392-7

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DONATELLA LIPPI *(20 hours)*
E-mail: donatella.lippi@unifi.it
Scientific Discipline Sector: MED/02

History of the History of Medicine: trends, sources, aims (The concept and evolution of Medicine according to Classical Authors; the current situation; Iconodiagnosis, Paleopathology, History of Medicine); 2 hours
Mediterranean Medicine: heart, brain liver (Egypt, Greece, Italic cultures, Rome: Galen and the experimentalism; History of the clinical relationship: from teurgic Medicine to Natural Philosophy; Hippocrates; the so called Hippocratic oath; Incubatio and quackery); 4 hours
History of the concept of health-care (The notion of *hospitalitas* and the transformations of hospitals; a virtual trip in Florence); 2 hours
History of Anatomy and anatomical dissection (From Berengario da Carpi to Vesalio, passing through Michelangelo and Tiziano); 2 hours
Between Middle Age and Renaissance (Pathology, Therapy, Language); 2 hours
The collapse of Galenism (The Accademia del Cimento and the Experimentalism; new instruments for "new" diseases); 2 hours
The French revolution and the triumph of Surgery (From Ambroise Paré to Jospeh Lister); 2 hours
Starting to calculate (I. Semmelweis, P. A. Louis and F. Nightingale- Evidence Based Medicine and Evidence Based Nursing); 2 hours
Medicine and Art, liaisons dangereux (Medicine in Art and Art in Medicine; Medicine as an Art and Art as medicine); 2 hours

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GIUSEPPE PANTALEO *(20 hours)*
Email: pantaleo.giuseppe@hsr.it
Scientific Discipline Sector: L-LIN/12

Psychological aspects of social interaction in health-related contexts

Unique individuals or interchangeable group members? *Social identification*, *self-categorization* and the shape of social interaction

The intensity of positive/negative *emotions* and *motivations* in health-related and broader societal contexts

'Intensity' issues in compliance, health, and risky behaviors – the paradoxical role of *deterrents*

Perspective-taking and (mis-)communication: *Self-symbolizing* and the neglect of others' perspectives

'Physical/biological orienting' vs. *'multiple psychological perspectives'*

Consistency needs in doctor-patient communication

Static vs. *dynamic* thinking: Cognitive and motivational factors underlying doctor-patient communication

From "empathic resonance" to "empathic perspective-taking": The evolution of empathy.

"Multiple perspectives" and the complexities of the human condition: fear, anxiety, and anguish as instigators of the *orienting* response

Beyond the Age of Empathy?

Articles and reading materials will be given to the students at the beginning of each lesson

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MICHELE LOI *(10 hours)*
Email: loi.michele@hsr.it
Scientific Discipline Sector: M-FIL/03

Lecture I – *Introduction*, the meaning and the history, ethics of research on human subjects.
Lecture II – *Bioethics in the global context* Clinical trials in third world countries. Sensitivity to cultural contexts.
Lecture III- *Justice* The relationship between social justice and health care The social determinants of health Measurement of health outcomes, quality of life and disability Accountability for reasonableness
Lecture IV – *Genetics* Genetic testing and screening Enhancement
Lecture V – *The end of life* Consent Quality end of life care Substitute decision-making

Compulsory readings:

Singer, Peter A., e Adrian M. Viens. The Cambridge textbook of bioethics. Cambridge University Press, 2008, chapters Ch. 2, 8, 11, 16, 22, 33, 25, 27, 29, 34, 43, 46 except sections on "law", "politics", "empirical studies".

Brock, Dan W. "Genetic Engineering". In R.G. Frey, C.H. Wellman (eds.), A Companion to Applied Ethics, cit., pp. 356-368, available in the student intranet.

Recommended readings:
The secontion on "law", "politics", "empirical studies" in each chapter of the book edited by Singer and Viens.

Useful Websites:
http://www.thehastingscenter.org/BioethicsForum/
http://blog.bioethics.net/
http://www.practicalethics.ox.ac.uk/
http://blog.practicalethics.ox.ac.uk/
http://ns.memberclicks.net/
http://moraliaontheweb.com

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WILLIAM COOKE *(22 hours)*
Email: William@maptraining.it
Scientific Discipline Sector: L-LIN/12

Can the pen be mightier than the scalpel?	
1	Why, How and What Doctors Write
2	Deductive Communication, from Roman Oratory to Quentin Tarantino
3	Mindset: (i) Writing is Writing, (ii) No Place for Narcissism, (iii) Content Expertise is not Enough
4	The Science of Science Writing: Five Golden Rules for Reader-Friendly prose
5	Clarity in the expression of Who (subject/actor) does What (verb/action). Practice and Peer Review

Materials consist in a pdf file + "The Science of Science Writing",
Gopen and Swan, American Scientist, Volume 78, 1990, a copy of which will be made available on intranet.

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ANDREA MORO *(10 hours)*
Email: andrea.moro@iusspavia.it
Scientific Discipline Sector: L-LIN/01

On the biological foundations of language: the linguistics perspective
1 &2. A short history of linguistics
3.The XX century: language(s), machines and children
4.The architecture of human language
5.Recursion or the specific differences with respect to other animals' codes
6.Grammar like a crystal: the universals of language (syntax)
7.Grammar like a crystal: the universal of language (semantics)
8.The brain and the mystery of impossible languages
9.Does the structure of the world influence the structure of language (and viceversa)?
10.Language, genetics and evolution

Coursebooks:

- The Generative Enterprise Rivisited, [selected parts]
  Noam Chompsky (2004) ,

- The Boundaries of Babel
  Andrea Moro (2010, paperback edition) [chapter 1 and 2]

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ROBERTA DE MONTICELLI *(10 hours)*
Email: demonticelli.roberta@hsr.it
Scientific Discipline Sector: L-LIN/12

Title: Outlines of a phenomenology of the doctor-patient relationship

1 Personal identity: theories of the self
2 The layers of the emotional life
3 The ways of empathy
4 Confidence and Suspicion
5 Dante's *Inferno*: Phenomenology of a strange passion

References:

Rudder Baker L. 2000, *Persons and Bodies – A Constitution View*, Cambridge Studies in Philosophy
Gallagher, S., Zahavi, D., 2008, *The Phenomenological Mind – An introduction to Philosophy of Mind and Cognitive Science*, Routledge
Ratcliffe, M. 2008. *Feelings of Being: Phenomenology, Psychiatry and the Sense of Reality*. Oxford University Press, International Perspectives in Philosophy and Psychiatry series.
Gallagher, S. & Schmicking, 2010, *Handbook of Phenomenology and Cognitive Science*. D. Springer.
Goldie, P. 2010, *Oxford Handbook of Philosophy of Emotion*. Oxford University Press.
Straus, E., 1966, *Phenomenological Psychology*, Tavistock, London
De Monticelli, R., 2006 *The Feeling of Values: for a Phenomenological Theory of Affectivity*, in: Bagnara, S., Crampton Smith, G., *Theories and Practice in Interaction Design*, Lawrence Erlbaum Associates, Mahwah, New Jersey, pp. 57-76

De Monticelli, R., (2007) *The Phenomenological Revolution,* Proceedings of the XXVII IHSRC, "Encyclopaideia", 22, July-December, pp. 9-30
De Monticelli, R. (2000) *Dante's Inferno: Phenomenology of a Strange Passion*, "Psychopathology" 2000, 33 182-190

Suggested reading:

1. Gallagher-Zahavi 2008, chapters 7 (The embodied mind); 8 (Action and agency); 9 (How we know others)
2. Dante, Inferno, Canti VII-VIII, (any English translation, for ex. *The Divine Comedy*, transl,. by Allen Mandelbaum, with an Introduction by E.Montale, New York, Everyman's Library, 199

Compulsory reading:

1. The Phenomenological Mind- An introduction to philosophy of Mind and Cognitive Science, 2008 Mylander Gallagher S. Zahavi D.

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REICHLIN MASSIMO *(10 hours)*
Email: reichlin.massimo@unisr.it
Scientific Discipline Sector: M-FIL/03

This course will deal with some of the main issue in a very important area of bioethics, *i.e.* end-of-life ethics. The problems that will be discussed include: a) those relative to the treatment of patients in a persistent vegetative state, also referring to the issue of advance directives; b) those relative to the definition of death and the present debate on the limits of total brain death, also with reference to the practice of organ transplantation; c) in relation to this, some reference will be made to the issue of the allocation of scarce resources. Lessons will start from the discussion of the suggested literature, and there will be much room for discussing the different approaches.

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CHEMISTRY AND BIOCHEMISTRY
Total Credits: 12
Total Hours: 118
Scientific Discipline Sector: BIO/13- BIO/10

Course Coordinator: Prof. Massimo Degano
Email: Degano.massimo@hsr.it
52 hours

Professors teaching:
Prof. Mauro Freccero
Email: mauro.freccero@unipv.it
40 hours

Prof. Angelo Corti
Email: corti.angelo@hsr.it
18 hours

Tutorials: 3 groups for 8 hrs tutorials each
Dr. Barbara Corsi - Dr. Annunziata Venuto - Dr. Nunzia Passaro

Type of subject: Traditional medical discipline
Field: General discipline for the preparation of a doctor: Structure, function and metabolism of molecules of medical interest.

Course objectives:
The Chemistry and Basic Biochemistry course is one of fundamental importance, in which students are presented with the notions of the chemical and biochemical mechanisms necessary to understand the regulation of biological processes of the cell and of the organism.
This course covers classical molecular and cellular biochemistry, cellular physiology, and molecular genetics. Metabolic interrelationships as they occur in the individual will be stressed and related to disturbances in disease states.
The knowledge and understandings provided by the course constitute the foundations for the following semesters both for the molecular analysis of physiological processes and those of pathogenetic mechanisms in disease. The specific field of Chemistry and Basic Biochemistry will focus on the principles of general and organic chemistry with a description of the fundamental chemical reactions for the understanding of biological processes, the structure and function of organic molecules that constitute the building blocks of living matter, and the analysis and structure and function of principle biological polymers, with particular emphasis on the processes of catalytic enzymes.

At the end of this course, students should be able to:
- Solve problems in diagnosis and treatment of human disease by application of biochemical principles.
- Use primary medical and scientific literature as a resource for learning and problem-solving.
- Define, describe and contrast functions of genes and macromolecules in normal and pathologic contexts.
- Define and describe systemic metabolic biochemistry in terms of genes and molecules.
- Deduce therapeutic mechanisms from established molecular mechanisms.
- Interpret new medical discoveries in terms of fundamental principles of biochemistry
- Explain the molecular basis of diseases that affect cellular function or development.

The course is a prerequisite for:
Foundation for "Cellular and Molecular Biology" and "Genetics and developmental Biology".

No.Theme

1 Introduction to the course. Chemistry and biochemistry in human physiology
2 Atomic Structure. Electron Configuration and the Aufbau Principle. Atomic and Molecular Orbitals. Chemical Bonding - Covalent, Ionic and Metallic Bonds.
3 Intermolecular Forces - Dipole-Dipole Forces, Hydrogen Bond, London Forces. Periodic System of Elements. Trends in the Periodic Table. Nomenclature of Inorganic Compounds. Characterization of sp-, d- and f-Elements and their Compounds.
4 Classification of Chemical Reactions. Chemical Thermodynamics -the Laws of Thermodynamics, Enthalpy, Entropy, Free Energy. Spontaneity of Chemical Change. Chemical Equilibrium. Equilibrium Constant. Le Chatelier´s Principle.
5 Chemical Kinetics. Reaction Rates and Factors that Influence them. Activation Energy and the Activated Complex. Catalysts and Mechanism of their Effect.
6 Solutions and their Properties. Solubility, Concentration of Solutions. Solutions of Electrolytes, Ionization Constant. Activity (effective concentration). Acids and Bases. The Dissociation of Water. The pH Scale. Salts, Hydrolysis of Salts, Solubility Product. Buffers, Characterization, pH, Capacity. Buffers of the Blood.
7 Oxidation-Reduction Processes. Hydrogen and Oxygen in these Processes. Standard Reduction Potentials. Osmosis. Osmotic Pressure. Colligative properties. Importance in Medicine.
8 Scope of Organic Chemistry. Formulas, Naming and Classification of Organic Compounds. Resonance, delocalization, conjugation, and aromaticity
9 Hydrocarbons and their Derivatives. Alkanes, Alkenes, Alkynes, Cycloalkanes.
10 Alcohols
11 Ethers, epoxides, and sulfides
12 Amines
13 Ketones and aldehydes
14 Carboxylic acids, esters, amides
15 Amino Acids and their Properties. Important Peptides.
16 Lactones, lactames and antibiotics
17 Phosphoric acids, inorganic and organic phosphates
18 Aromatic compounds
19 Alpha substitution and condensation of enols and enolate ions
20 Synthetic reactions in bioorganic chemistry
21 Proteins - Amino Acid Composition, Conformation of Proteins -
22 Monosaccharides - Classification, Configuration, Optical Activity, Anomers, Epimers. The Haworth Formulas. Reactions of Monosaccharides. Glycosidic Linkage, Reducing and non-Reducing Disaccharides. Polysaccharides and Glycosaminoglycans, Composition, Properties.
23 Types of Bonds and Interactions. Physical and Chemical Properties. Classification of Proteins.
24 Carbohydrates.
25 Myoglobin and Hemoglobin
26 Lipids and Steroids. Classification, Structure, Properties, Chemical Reactions.
27 Enzymatic catalysis
28 Introduction to the cell, compartments and cellular biochemistry.
29 Cell membranes. Introduction to metabolism.
30 Enzyme regulation
31 Overview of Intermediary Metabolism. Biological Oxidation and Bioenergetics. The Respiratory Chain and its Components. The Mechanism of Oxidative Phosphorylation. Oxygenases and Hydroperoxidases. Free Radicals.
32 The Citric Acid Cycle and its Regulation. The Pyruvate Dehydrogenase Complex.
33 Protein folding
34 Metabolism of Carbohydrates - Metabolism of Glucose and its Regulation. The Pentose Phosphate Pathway. Other Pathways of Hexose Metabolism. Gluconeogenesis. Metabolism of Glycogen and

its Regulation. Metabolism of Glycosaminoglycans.

35 Protein purification and characterization

36 Antibodies

37 Metabolism of Lipids and Steroids - Digestion, Resorption and Transport. Lipoproteins and their Metabolism. Biosynthesis and Degradation of Saturated and Unsaturated Fatty Acids. Ketogenesis. Eicosanoids. Metabolism of Acylglycerols and Sphingolipids. Metabolism of Cholesterol. Biosynthesis of Bile Acids and Steroid Hormones.

38 Metabolism of Proteins and Amino Acids -Digestion, Resorption and Transport. Transamination, Oxidative Deamination and Decarboxylation of Amino Acids. Catabolism of the Carbon Skeleton of Amino Acids. Ammonia Formation and its Removal. Biogenic Amines.

39 Nucleosides, Nucleotides and Nucleic Acids. DNA and RNA structure and properties. DNA sequencing.

40 Metabolism of Pyrimidine and Purine Nucleotides.

41 Protein Synthesis.

42 Metabolism of Porphyrins and Bile Pigments. Biosynthesis of Heme and Hemoglobin and their Catabolism. Jaundice.

43 Components of the Blood. Water and Ions Metabolism. Acid-Base Balance. The Lungs and the Kidney in Acid-Base Balance. Disorders of Acid-Base Balance.

44 Metabolism of Erythrocytes. Haemostasis and Blood Clotting.

45 Contractile and Structural Proteins. Mechanism of Muscle Contraction and its Energy Supply.

46 Metabolism of Connective Tissue. Connective Tissue Proteins, Proteoglycans. Process of Mineralization.

47 Metabolism of Adipose Tissue.

48 Metabolism of Liver.

49 Receptors. Hormones.

50 Extracellular and Intracellular Communication. Second Messengers, Protein Kinases.

Suggested textbooks

- Timberlake – General, Organic, & Biological Chemistry. Pearson ed.,
- Voet & Voet – Biochemistry. Wiley eds.

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CELL AND MOLECULAR BIOLOGY

Total Credits: 11
Total Hours: 103
Scientific Discipline Sector: BIO/11 – BIO/12 – INF/01

Course Coordinator: Prof. Roberto Sitia
Email: sitia.roberto@hsr.it
26 hours

Collaborators:
Prof. Marco Bianchi *MEB*
Email: bianchi.marco@hsr.it
10 hours
Prof. Anna Rubartelli
Email:
10 hours
Prof. Eelco Van Anken *EVA*
Email: vananken.eelco@hsr.it
30 hours
Prof. Simone Cenci *SC*
Email: cenci.simone@hsr.it
12 hours

Tutorials: 4 groups for 15 hrs tutorials each.
Tutors: Drs. Orsi Andrea, Celine Schaeffer, Jose Garcia Manteiga, Emilie Venereau

Students will be divided into 4 groups for about 15 hours of tutorials, including the 2 hours of presentation to the class.
Each group will be given a scientific paper to read, understand, put in context, summarize and present to the whole class.
The four interactive lectures are part of the programme. Student will be asked about their content and significance in the final exam.
This part of the programme is meant to show how scientific knowledge is created and disseminated, and to stimulate a critical attitude in our students.

Attending lectures

We *encourage students to attend to all lectures*, as teachers will cover aspects that are absent or hard to find in textbooks. However, attending a lecture means much more than the mere physical presence in the class.
Students are encouraged to read the topics that will be covered in class *before* attending lectures, so that they can raise questions and focus onto the most relevant or controversial issues. Topics are often tackled in a transversal, multidisciplinary manner.
Unfair behaviour will not be tolerated, such as clocking for others. Those found to do so will not be admitted to the exam.
Attending tutorials is mandatory. For those failing to do so, the maximal final grade will be 20/30.

RS 1 (5/03/12 h. 14-16)
Introduction to the Course of Molecular and Cell Biology
Structure of the Course, a voyage between Systematic teaching and Problem Based Learning
what are genes and how they work (MEB)
genetic and epigenetic mechanisms (MEB)
what are cells (RS, EvA)
how cells divide (MEB, SC)
how cells die (SC)
how cells know where they are and where to go (RS, AR, EvA)
how they interact with the environment (EvA, SC, MB, AR, RS)
how cells differentiate (MEB, AR)-molecular bases of disease (MB, EvA, RS)
What is life?
Where do we come from?
Introduction to our cells
Membranes, cytoskeleton, organelles.

RS 2 with Monica Fabbri (7/03/12 h. 11-13)
Cytoskeleton and adhesion molecules
Adhesion molecules
Integrins
Tissue organization

RS 3 with Tiziana Anelli (09/03/12 h. 11-13)
Intracellular transport and cell movements
Microtubules, microfilaments, molecular motors
Polarity
Axonal transport
Cytoskeleton
Muscular contraction
Cilia and flagella
Microvilli

RS 4 (12/03/12 h. 9-11)
Evolution, Darwin and the adaptable cell structure
Prokaryotes, eukaryotes, multicellular organisms.
The evolution of specialized tissues.
Homeostasis.

RS 5 (14/03/12 h. 11-13)
Intracellular transport
Three main mechanisms of macromolecular transport:
To and from the nucleus
Membrane translocation
Vesicular transport
Exo, endo, pino, phagocytosis
Transcytosis
Mechanisms of cell polarity

RS 6 (15/03/12 h. 11-13)
Cell compartmentalization
Specific signals target macromolecules to different organelles.

RS 7 (16/03/12 h. 11-13)
Protein folding, the second genetic code
Anfinsen's demonstration of the central dogma
Chaperones and protein evolution

RS 8 (19/03/12 h. 9-11)
Protein degradation
Proteasomes, lysosomes and autophagy

RS 9 (20/03/12 h. 11-13)
Protein quality control and homeostasis
Stress responses in development and disease

RS 10 (21/03/12 h 11-13)
Proteostasis as a signal and pathogenetic mechanism.
Mechanisms of proteotoxicity.
Molecular and cellular aging

RS 11 (22/03/12 h.11-13)
Conformational diseases
Prions, Amyloidoses, Alzheimer & Parkinson.

LESSON 12 friday 23 march, 11-13
MEB 1 *Nuclear structure*
Nuclear "organelles". Chromosome territories. Nuclear membrane and lamins. Nuclear pores and transport

LESSON 13 monday 26 march, 9-11
MEB 2 Chromatin
Nucleosomes. Histones and histone variants. Histone post-translational modifications, and enzymes that effect them.

LESSON 14 tuesday 27 march, 11-13
MEB 3 Transcription in eukaryotes
RNA polymerases. Promoters & enhancers. General transcription factors. Specific transcription factors. Coactivators and corepressors. How nucleosome position and histone modifications affect gene expression

LESSON 15 wednesday 28 march, 11-13
MEB 4 *Gene expression decisions:*
Examples of transcriptional regulation and signal transduction
The NF-kB system
Liver specification

LESSON 16 thursday 29 march, 14-16
MEB 5 Retroviruses, the genome and RNAi
Retroviruses
miRNA, siRNA, heterocromatin and centromeres

EvA 1 (2/04/12 h. 14-16)
Membrane Structure
Architecture, composition, membrane proteins .

EvA 2 (03/04/12 h. 14-16)
Energy conversion I
Mitochondria

EvA 3 (4/04/12 h. 11-13)
Energy conversion II
Chloroplasts, genetics of mitochondria & plastids, evolution of electron transport chains.

Eva 4 (4/04/12 h. 14-16)
Cell signaling I
Principles of cell communication

EvA 5 (16/04/12 h. 14-16)
Cell signaling II
G protein coupled cell surface receptors.

EvA 6 (17/04/12 h. 14-16)
Cell signaling III
Enzyme coupled cell surface receptors.

EvA 7 (18/04/12 h. 11-13)
Cell signaling IV
Unfolded Protein Response, determining cell shape.

EvA 8 (19/04/12 h. 14-16)
Manipulating proteins & DNA I
Cloning, cDNA libraries, tagging, PCR.

EvA 9 (20/04/12 h. 9-11)
Studying gene function & expression I
Function prediction, genetic screens, tagged libraries, reporter genes.

EvA 10 (23/04/12 h. 14-16)
Studying gene function & expression II
Reverse genetics, knock-out libraries, RNAi, complementation, epistasis & EMAP, microarray.

SC 1 24/04/2012 9-11
Cell cycle 1
Phases and logics of the cell cycle. Experimental approaches. The Cell Cycle Control System. Engineering checkpoints. Significance of G phases. Molecular players: cyclins, cyclin-dependent kinases, Cdk inhibitors.

EvA 11 (24/04/12 h. 14-16)
Visualizing cells I
Standard microscopy techniques.

SC 02 (Wednesday, 27/04/12 h 14-16)
Cell cycle 2
Regulatory strategies: cyclic degradation, post-translational modofocations, de novo synthesis. Checkpoints in G1 and G2. Preventing DNA re-replication. Cdc25 and regulation of M-Cdk activity. Rb and E2F: the restriction point and the Skp2 autoinduction loop. The DNA damage checkpoints. p53 and p14/19ARF. Cancer as a cell cycle disease.

SC 03 (Thursday, 2/05/12 h.11-13)
Mitosis
Phases and mechanics. Cohesins and condensins. Centrosome, microtubules and the mitotic spindle. Role of motor proteins. Mechanisms of high-fidelity segregation: centromere and kinetochore.

Mechanics of anaphase. Functions of chromokinesins. Cytokinesis. Drugs targeting mitosis and their clinical relevance.

AR 01 (3/05/12 h.14-16)
Intercellular communication

AR 02 (4/05/12 h.9-11)
Cytokines

AR 03 (7/05/12 h.14-16)
Unconventional secretion

AR 04 (8/05/12 h.9-11)
Inflammation

AR 05 (9/05/12 h.11-13)
Inflammation

EvA 12 (Tuesday, 10/05/12 h. 9-11)
Visualizing cells II
Advanced microscopy techniques
EvA 13 with Antonio Siccardi (Wednesday, 11/05/12 h. 11-13)
A historical perspective
The Luria-Delbruck experiment .

SC 04 (15/05/12 h. 9-11)
Apoptosis - I
Functional significance: apoptosis vs. necrosis. Methods to study and monitor apoptosis. Functions in physiology and disease. Mechanisms: extrinsic vs. intrinsic apoptosis. Caspases: redundancy, efficiency, velocity. Death receptors and the Death-Inducing Signaling Complex (DISC). Mitochondria as signal integrators and death executors. The Apoptosome. Mitochondrial Outer Membrane Permeabilization (MOMP). The Bcl2 family: sensors/transducers, brakes, and effectors. Inhibitors of Apoptosis (IAPs)..

SC 05 (16/05/12 h. 11-13)
Apoptosis - II
Apoptosis and the **i**ntegrated stress response. Stress specificity of BH3-onlies. The other functions of Bcl2 proteins: daily jobs of night killers. Mitochondria and ER cross-talk. ER calcium homeostasis and apoptosis. Regulation by the unfolded protein response and heat shock proteins. Proteotoxic apoptosis.

SC 06 (17/05/12 h. 14-16)
Apoptosis- III
Integrating Cell Cycle, Apoptosis, and Cancer. Apoptotic escapes from the cell cycle. Apoptosis from cytotoxic vs. genotoxic stress. Maladaptive thresholds: implications for cancer pathogenesis and therapy. Alternative forms of eukaryotic cell death: autophagy, paraptosis, pyroptosis. Autophagy in physiology and disease.

RS 12 (18/05/12 h. 11-13) with Domenico Cianflone
A DNA driven world

All tutorials must end before 20th May

EvA 14 22/05/2012 h9-11
S1 Group 1 Tutor: Jose Garcia Manteiga
EvA 15 23/05/2012 h 11-13
S2 Group 4 Tutor: Andrea Orsi
RS 13 24/05/2012 h 16-18
S3 Group 2 Tutor: Emilie Venereau
RS 14 25/05/2012 h 11-13
S4 Group 3 Tutor: Celine Schaeffer

COURSEBOOKS:

Textbooks

Alberts, Bray, et al. *Molecular biology of the cell*
Alberts, Bray, et al. *Essential cell biology* www.garlandscience.com/text**books**/081533480X.asp
Lewin, Cassimeris et al. *Cells*
Lodish et al. *Molecular cell biology* www.whfreeman.com/**lodish**4
Pollard & Earnshaw *Cell Biology* www.us.elsevierhealth.com/.../**book**/.../Cell-Biology/ -
The above books contain all the essential notions, differing primarily in the style of presentation.

Suggested readings

We encourage our students to read on science, medicine and society. Below are a few tips.
M. Perutz. *Is science necessary?* and/or *I wish I made you angry before.*
Two lovely series of essays on science and scientists.
J. Diamond. *Germs, guns and steel.*
A brief summary of the last 13000 years of humans… Why did some civilisations prevail?
J. Monod *Chance and necessity.*
A Nobel Prize winner in Medicine tackles fundamental philosophical issues
J.D. Watson. *The double helix.*
Watson tells the story of how the structure of DNA was solved, with the pace of a crime fiction novel.
P. Medawar. *Advice to a young scientist.*
A few useful tips, should you decide to become a physician scientist. A thoroughly enjoyable

USMLE REQUIREMENTS

Biology of cells
• adaptive cell responses and cellular homeostasis
• intracellular accumulations
• mechanisms of injury and necrosis
• apoptosis
• mechanisms of dysregulation
- cell biology of cancer, including genetics of cancer
- general principles of invasion and metastasis, including cancer staging
• cell/tissue structure, regulation, and function, including cytoskeleton, organelles, glycolipids, channels, gap junctions, extracellular matrix, and receptors

Molecular biology
• gene expression: DNA structure, replication, exchange, and epigenetics
• gene expression: transcription
• gene expression: translation, post-translational processing, modifications, and disposition of proteins (degradation), including protein/glycoprotein synthesis, intra/extracellular sorting, and processes/functions related to Golgi complex and rough endoplasmic reticulum
• structure and function of proteins and enzymes
• energy metabolis

GENETICS AND DEVELOPMENTAL BIOLOGY

Total Credits: 12
Total Hours: 120
Scientific Discipline Sector: BIO/13 – MED/03

Course Coordinator: Prof. Giorgio Casari
Email: casari.giorgio@hsr.it
40 hours

Collaborators:
Prof. Giangiacomo Consalez
Email: consalez.giangiacomo@hsr.it
40 hours

Prof. Luca Rampoldi
Email: rampoldi.luca@hsr.it
40 hours

Topics covered by the course

Mendelian and non-Mendelian genetics
Course introduction_ The Human Genome Project.
Mendelian Inheritance (I)_Definition of gene, locus, allele. The first Mendel's law.
Mendelian Inheritance (II)_The second and third Mendel's laws. Segregation and independent assortment.
Exceptions to Mendelian inheritance_Incomplete dominance, co-dominance. Penetrance and expressivity.
Exceptions to Mendelian inheritance_Sex-related effects. Pleiotropy. Pedigree design_2
Chromosomes/mitosis/meiosis_Chromosome structure (telomeres, centromere) and segregation during mitosis and meiosis. Crossing-over.
Chromosome structure. Chromatin structure and function. Histones and nucleosomes. Chromatin remodelling.
Recombination/mapping (I)_Molecular basis of recombination.
Recombination/mapping (II)_Recombination as a measure of genetic linkage. Mapping in bacteria and Drosophila.
Non-Mendelian inheritance (I)_Gene conversion.De-novo mutations.Mosaicism (X-inactivation).
Non-Mendelian inheritance (II)_Epigenetic control of gene expression. Imprinting.
Dynamic mutations (I)
Dynamic mutations (II)
Mitochondrial Inheritance
Chromosome mutations
Cytogenetics
CGH
DNA/RNA structure
Transcription/translation_Gene structure and transcription. The genetic code, structure of tRNA and ribosome.
Translation. Mechanisms of splicing
RNA interference_miRNA, siRNA, shRNA. Discovery and applications.
Point mutations and repair_Spontaneus and induced mutations. Repair of mutations and recombination.
Nonsense mediated decay
Complex mutations/polymorphisms/CNVs
Mutation detection techniques
Deep sequencing
Effect of mutations (gain/loss-of-function)_Gain-of-function and loss-of-function effect of mutations. Negative dominance.
Effect of mutations (ESE)
Genetic markers_DNA markers (microsatellites, SNPs). Genetic maps. Haplotype maps (the HaploMap project).
Genetic Mapping (I)_Linkage analysis in human pedigrees. LOD score calculation.

Genetic Mapping (II)_Linkage analysis in human pedigrees. Haplotype analysis.
Probability_Bayes' theorem, application for risk calculation in human pedigrees.
Examples of linkage/positional cloning
Examples of functional cloning
Quantitative Trait Loci
Population genetics_1
Population genetics_2
Molecular Evolution (I)
Non-parametric linkage analysis/association studies
Jolly

Embryology and developmental biology
This part of the course will cover the essentials of normal human development and of its main aberrations, providing information on some recognizable patterns of human malformation.

General Embryology
Gametogenesis: Conversion of Germ Cells into Male and female gametes
First Week of Development: ovulation to implantation
Second Week of Development: Bilaminar Germ Disc
Third Week of Development: Trilaminar, Germ Disc
Third to Eighth weeks: The Embryonic Period
Third Month to Birth: The Fetus and Placenta

Systems-based Embryology
Skeletal System
Muscular System
Body Cavities
Digestive System
Cardiovascular System
Respiratory System
Urogenital System
Head and Neck
Central Nervous System
Ear and eye development
Tegumentary System

COURSEBOOKS:

Langman's Medical Embryology / Edition11,
Thomas W.Sadler, ED. Lippincott Williams & Wilkins ISBN: -13: 9780781790697

Human Molecular Genetics 3rd Edition,
Tom Strachan, Andrew Read **-** ED: Garland Science - ISBN:0-8153-4184-9

USMLE REQUIREMENTS
Human development and genetics
• principles of pedigree analysis
- inheritance patterns
- occurrence and recurrence risk determination
• population genetics: Hardy-Weinberg law, founder effects, mutation-selection equilibrium
• principles of gene therapy
• genetic testing and counselling
• genetic mechanisms

SAN RAFFAELE INTERNATIONAL MD PROGRAM

YEAR 2
Academic Year 2011/2012

- Human Morphology
- Physiology
- Principles of Pharmacology
- Introduction to Surgery

HUMAN MORPHOLOGY

Total Credits: 30
Lessons: 224 hrs
Practicals:84 hrs

SSD BIO/16, BIO/17, MED/36, MED/37, MED/33

Course Coordinator: Ottavio Cremona
Email: ottavio.cremona@unisr.it

Professors Teaching:
Naldini Luigi
Marchisio Piercarlo
Rende Mario
De Palma Michele
Cerulli Giuliano
Peretti Giuseppe
Cappa Stefano
Consalez Giangiacomo
Falini Andrea

Goals

Aim of the course is to provide the morphological foundations of the various functions and pathologies affecting our organism. Approaches to morphological education include the acquisition of foundational knowledge in microscopic observation and in dissection with the aim of correlating structure with function and clinical relevance. The human morphology course of the "San Raffaele MD Program" puts a wide emphasis on clinical applications by means of integration of imaging techniques and interpretation, effective peer teaching and the use of electronic resources to facilitate the understanding and memorization of morphological data. The study of tissue and organ architecture by different microscopic techniques is organized to provide the structural basis for tissue and organ function; principles of tissue development and homeostasis, cellular turnover, isolation and properties of stem cells will be given as a priming for tissue pathology.

Pre-Requisites

Although there are no formal restrictions to the access to the final exam, we strongly advise students to have solid foundations in:

- Cell Biology and Cytology
- Developmental Biology

Knowledge of these disciplines was acquired during the 2nd semester of the past academic year.

Evaluation

The final score will be calculated as a results of a number of in-course and end-of-course exams, including:

- An oral histology exam including an observation test at the microscope
- A multiple-choice exam on "Dynamics of Movement"
- A final written exam covering the remaining part of the program

Program

1st semester:

INTRODUCTORY MORPHOLOGY

1. Introduction to Tissues
2. Epithelial Tissue .
3. Connective Tissues
4. Adhesion & Matrix
5. Cell Migration
6. Anatomical Position & Terminology

MORPHOLOGY OF ORGAN SYSTEMS

- *Support and Movement*
  - *i. Skin*
  - *ii. Skeletal Tissues*

1. Histology of the skeletal muscle
2. Histology of Muscle, Bone & Cartilage
3. Bone remodeling
4. Dynamics of Movement

   Upper limb

   Lower limb

   Thorax

   Rachis

- *Transportation & Defense*
  - *i. Blood*

1. Blood.
2. Hematopoiesis
   - *ii. Cardiovascular system*
3. Heart.
4. Structure of Vessels
5. Major Vessels. General Organization.
6. Major Vessels.

   Head and neck.

   Thorax.

   Abdomen.
   - *iii. Lymphatic system*
7. Overview and structure of the system
8. Major lymphatic vessels

iv. Immune system

9. General overview of the Immune system
10. Immune organs (MV)

- *Respiratory System*

1. Nasal Cavity & pharynx
2. Larynx, trachea & bronchi
3. Lung & Pleura

- *Digestive System*

1. Oral Cavity.
2. Teeth
3. Esophagus & topography of the mediastinus
4. Peritoneum
5. Stomach
6. Small Intestine
7. Large intestine & rectum
8. Gut stem cells
9. Liver
10. Gallbladder & Pancreas

- *Urinary System*

1. Kidney
2. Urinary tract
3. Topography of the abdomen.
4. Topography of the pelvis
5. Perineum

- *Endocrine System*

1. Pituitary gland
2. Thyroid & Parathyroid glands
3. Adrenal glands
4. Topography of head and neck

- *Reproductive Systems*

i. Male reproductive system

1. Testis
2. Reproductive tract
3. Accessory reproductive glands & Supporting structures

ii. Female reproductive system

4. Ovaries & Uterine tubes (OC)
5. Uterus & placenta (OC)
6. Vagina, Vulva & Breast (OC)

Human Morphology book list

One between:
Gray's Anatomy for Students by Richard L. Drake, A. Wayne Vogl and Adam W. M. MitchellISBN: **978-0443069529**
Atlas of Human Anatomy by Frank H. Netter ISBN: **978-1416059516**
Atlas of Anatomy (Thieme Anatomy) by Anne Gilroy, Brian MacPherson, Lawrence Ross and Michael Schuenke **ISBN:** 978-1604060621
Histology: A Text and Atlas by Michael H. Ross and Wojciech Pawlina **ISBN**: 978-0781772006
Junqueira's Basic Histology: Text & Atlas by A. Mescher ISBN: 978-0071630207
Neuroanatomy: Text and Atlas by John Martin **ISBN:** 978-0071381833
Neuroanatomy: An Atlas of Structures, Sections, and Systems by D.H. Haines. **ISBN**: 978-0781763288
Clinical Neuroanatomy and Neuroscience: M. J. T. FitzGerald, Gregory Gruener and Estomih Mtui. 978-0702037382

Gray's Anatomy: The Anatomical Basis of Clinical Practice by Susan Standring. ISBN: 978-0443066849
Clinically Oriented Anatomy by Keith L. Moore ISBN-13: 978-0781775250
THIEME: **The "Atlas of Anatomy" Series**
Neuroanatomy through Clinical Cases by Hal Blumenfeld **ISBN:** 978-0878930586

BIOPHYSICS AND PHYSIOLOGY

Total Credits: 17
Lessons: 180 hrs
Practicals: 130 hrs
SSD: BIO/09

Course Coordinator: Antonio Malgaroli
Email: malgaroli.antonio@hsr.it

Professors Teaching:
Alessandra Abenavoli
Carley Benton
Fausto Baldissera
Maddalena Ripamonti
Roberto Teggi
Vincenzo Zimarino

TUTORS
Alessandro Arena
Mattia Ferro
Gabriella Racchetti
Eugenio Rapisarda

COURSE INTRODUCTION

The purpose of this course is to provide a complete training in biophysics and human physiology. This course is designed to promote learning by practice, with a particular emphasis on stimulating student experimental creativity and interdisciplinary approaches. We all know that *Physiology* is the investigation of cell and body functions, hence the major goal is to understand and be able to predict the acute and adaptive responses of the body to external stimuli but also to understand how the body can maintain a stable set of internal conditions while the external environment is constantly changing. Physiology can be studied at many different levels including biophysics, cell physiology, organ physiology and systems physiology. In this course you will be exposed to all of these levels, initially to the biophysical and cellular physiology level, then quickly moving up to the organ and system levels. In the mainframe of this M.D. program, clearly Physiology and Anatomy must be closely related subjects. To fully appreciate the physiology of a given system it is necessary to first know its anatomy, therefore much coordination work has gone into ensuring that each topic will be presented sequentially, first in the Anatomy and then in the Physiology Course. Indeed, in most cases true understanding of physiology can only take place if structure and function are concurrently learned. A complete and in depth understanding of physiology would be essential to appreciate in subsequent courses how the human body might be functionally altered by diseases (pathophysiology) and also to predict the response of the body to pharmacological therapies or drugs.

SPECIFIC GOALS AND OBJECTIVES

The goals of this M.D. Course in Physiology are to train students to:

1. be able to demonstrate comprehensive understanding of biophysics and physiology as well as the integration of these with basic and applied disciplines;
2. understand the molecular and cellular mechanisms of physiological processes, in order to provide a foundation for understanding pathophysiology and therapeutics in subsequent courses;
3. integrate knowledge and concepts from cellular physiology and organ physiology to understand the integrative body functions, e.g., maintenance of blood gas levels; responses to stresses; regulation of fluid volumes and compositions; digestion; reproduction, etc.;
4. use and develop adequate knowledge of the most current developments in basic and medical sciences as related to biophysics and physiology;
5. acquire skills in research methodologies used in biophysics and physiology to be able to understand experimental research more effectively;
6. plan and run simple biophysics and physiology experiments utilizing standard equipments, including the evaluation and interpretation of experimental results; demonstrate competence in basic concepts of research methodology; effectively use the statistical methods for data analysis;
7. develop communication skills by frequent in-class discussions;
8. understand scientific papers dealing with physiological results;
9. function as a productive member of a student team engaged in learning and designing experimental strategies to understand structure-function problems;

DETAILED PROGRAM SECTIONS

Biophysics and Cell Physiology (Prof. Alessandra Abenavoli; Prof. Antonio Malgaroli)

1. Historical grounds of physiology; Units and Scales in physiology; The concept of homeostasis
2. Cellular Membranes and Transmembrane Transport of Solutes and Water
3. Mechanisms of carrier-mediated transport: facilitated diffusion, cotransport, and countertransport. Sodium pump function, Na+ - Ca2+ exchange currents
4. Diffusion and permeability
5. Osmosis and regulation of cell volume
6. Ionic Equilibria and the concept of equilibrium potential.
7. Origin of resting membrane potentials. The driving force for ionic-fluxes.
8. Gibbs-Donnan equilibrium potentials. Intracellular chloride regulation
9. Patch-clamp techniques and analysis of cell currents and ion channels
10. Different families of Ion channels

11. Structure-function of voltage-gated ion channels
12. Electrogenesis of membrane excitability: the action potential
13. The concept of threshold, its nature and its modulation
14. Cable properties and propagation of action potentials
15. Derivation of the Cable Equation and the AC length constant
16. Toxins, drugs, genetic diseases, variation in extracellular ions concentration and their effects on resting membrane potential and membrane excitability
17. Introduction to synapses
18. Synaptic transmission and ligand-gated ion channels
19. Synaptic transmission and release of neurotransmitter molecules
20. Synaptic transmission and transporters for neurotransmitter molecules
21. Quantal analysis of synaptic transmission
22. Synapses as targets for toxins, drugs, and genetic diseases

Muscle Physiology (Prof. Carley Benton)

23. Introduction to Skeletal muscle physiology
24. Membrane excitability of skeletal muscle cells
25. Excitation-contraction coupling in skeletal muscle; regulation of Ca2+ release from sarcoplasmic reticulum
26. Muscle metabolism and energetics
27. Role of muscle mitochondria and regulation of ATP production
28. Response to exercise and muscle fatigue
29. Smooth Muscle and Cardiac Muscle Physiology

Renal Physiology (Prof. Carley Benton)

30. Elements of Renal Function
31. The Nephron; The ultrafiltration process
32. Solute and Water Transport Along the Nephron. Tubular Function
33. Feedback mechanisms and autoregulation of the kidney function
34. Control of Body Fluid Osmolality and Extracellular Fluid Volume
35. Potassium, Calcium, and Phosphate Homeostasis
36. Intracellular pH Regulation and role of the Kidneys in Acid-Base Balance

Physiology of the Respiratory System (Prof. Carley Benton)

37. Overview of the Respiratory System
38. Mechanical Properties of the Lung and Chest Wall
39. Ventilation, Perfusion, and Their Relationship
40. Oxygen and Carbon Dioxide Transport
41. Control of Respiration
42. Nonrespiratory Functions of the Lung

Physiology of the Cardiovascular System

43. Overview of the Circulation, Blood, and Hemostasis
44. Electrical Activity of the Heart
45. Natural Excitation of the Heart and the pacemaker ion channels
46. Cardiac Pump
47. Regulation of the Heartbeat
48. Hemodynamics
49. Arterial System
50. Microcirculation and Lymphatics
51. Peripheral Circulation and Its Control
52. Control of Cardiac Output. Coupling of the Heart and Blood Vessels
53. Special Circulations
54. Interplay of Central and Peripheral Factors in Control of the Circulation

Physiology of the Digestive System (Prof. Vincenzo Zimarino)

55. Introduction to the digestive system
56. Nutrition and energy metabolism
57. The enteric nervous system
58. Motility of the Gastrointestinal Tract
59. Gastrointestinal Secretions
60. Digestion and Absorption for lipids, carbohydrates, proteins

Physiology of the Nervous System (Dr. Maddalena Ripamonti)

61. Cellular and functional organization of the nervous system
62. The autonomic nervous system and its control
63. The structure and functional organization of cerebral cortex
64. Introduction to the sensory nervous system
65. Transduction of sensory information and the Perception process
66. Coding of sensory information
67. The perception of touch and pain
68. The visual system and the visual processing
69. The functional organization of the retina
70. Central visual pathways and the functional organization of visual cortex
71. The control of gaze
72. Perception of borders, color, motion, depth and forms
73. Introduction to the auditory system
74. Sensory transduction in the ear; the auditory pathways; the auditory cortex
75. The vestibular system; posture and equilibrium
76. The central organization of the motor system and the motor pathways
77. The spinal reflexes
78. The spinal cord and the control of movements; Locomotor activity centers

79. Motor function and the role of brainstem, basal nuclei and cerebellum
80. Activation of the brain, sleep and wakefulness
81. EEG recordings; Seizures and epilepsy
82. Brain Plasticity; Associative and non-associative forms of synaptic plasticity
83. The role of NMDA receptors; The Hebb rule and the BMC model;
84. Long-term synaptic plasticity; The concept of critical periods
85. Higher Functions of the Nervous System: memory, consciousness, language, emotions.

Physiology of the Endocrine System (Prof. Vincenzo Zimarino)

86. General Principles of Endocrine Physiology
87. Whole-Body Metabolism
88. Hormones of the Pancreatic Islets
89. Endocrine Regulation of the Metabolism of Calcium and Phosphate
90. Hypothalamus and Pituitary Gland
91. Thyroid Gland
92. Adrenal Cortex
93. Adrenal Medulla
94. Overview of Reproductive Function
95. Male Reproduction
96. Female Reproduction

PRACTICAL SESSIONS AND LABS

I. Review of electricity and circuit elements
II. Review of circuit properties
III. Review of electrical concepts applied to passive and active cellular responses
IV. Introduction to electrical signal acquisition and signal processing
V. Regulation of cell volume; techniques for the preparation of a solution including measurements of osmotic pressure and pH; Diffusion models and techniques to characterize diffusional properties
VI. Recording of the nerve and muscle evoked potential; The EMG recording and its analysis
VII. The H.H. model for action potential generation; Review of cable properties: propagation of action potentials in nerve, cardiac muscle and smooth muscles.
VIII. The ECG recording and its analysis
IX. Techniques to record electrical activity from nerve cells
X. Review of geometric optics and analysis of the functional organization of the eye.

FORMATIVE ASSESSMENT AND EXAMS

The assessment is continuous as well as end-of-term. The former is based on the feedback from teachers and tutors and a series of theory exams (eight written section tests on theory, one at the end of each section of the course). End-of-term assessments are held at the end of each semester. The performance of students during theoretical lectures and experimental sessions will monitored throughout the course and duly recorded in log books as evidence of the ability and daily work of the student. Final marks should be allotted out of 100 as follows:

Continuous Formative Assessment (30):

1. Personal Attributes (10)

   Behavior and emotional stability, motivation and initiative, honesty and integrity, interpersonal skills in the class and leadership quality.
2. Homeworks (10)

   Punctual and prompt response to home assignments, dedicated, hardworking, competent in practical work.
3. Practical Work (10)

   Proficient in experimental and lab sessions and when required in short presentations (paper and case discussions) during lectures

Section tests and end of term theory examinations (70)

The eight section tests and the end of term examinations will consist of written tests. The exams may consist of multiple choice, multiple-multiple choice (keyed questions), short answers, open or essay questions, numerical questions, small exercises (a pocket calculator with log and exp is needed). The students are expected to know the proper names and spelling of channels, transporters, receptors, reactions, structures, cells, currents, etc. as presented in class or in textbooks. Regarding the exercises, not only the procedures but also the final results should be accurate. For written tests 70 marks out of 100 will be allotted as follows:

Biophysics and cellular physiology (15)
Muscle physiology (6)
Kidney physiology (5)
Respiratory physiology (10)
Cardiovascular physiology (10)
GI physiology (5)
Physiology of the Nervous System (12)
Endocrine Physiology (7)

SUGGESTED BOOKS AND READINGS

-Course Syllabus and other reading material provided on the intranet (course page)
-E. R. Kandel,J.H.Schwartz e T.M. essel:Principles of neural science IV ed. McGrawHill, 2000
-Berne & Levy Physiology, Bruce M. Koeppen and Bruce A. Stanton , Mosby-Elsevier VI edition, 2010

ADDITIONAL BOOKS

-Aidley D.J. The Physiology of Excitable Cells. Cambridge Univ Press,, IV ed., 1998.
-Ashcroft, F. , Ion channels and disease, Elsevier eds
-Griffin, J.E. and Ojeda, S.R. , Textbook of Endocrine Physiology, 5th Edition, Oxford Univ Press ed
-Hille,B. Ionic channels of excitable membranes. III Edition, Sinauer, Sunderland, 2001
-Johnston D., S. Miao_Sin Wu, S. Maio_Sin Wu. Foundations of Cellular Neurophysiology. MIT, 1995.
-Katz, A.M., Physiology of the Heart, 5th ed, Lippincott Williams & Wilkins
-Sperelakis N. Cell Physiology Source Book: Essentials of Membrane Biophysics. III edition, Academic Press 2001
-Sheperd G.M. The synaptic organization of the brain. Oxford, V edition, 2004
-Vander, A., Renal Physiology, 5th ed, McGraw Hill ed
-West,J. Respiratory physiology: the essentials, 8th edition, Lippincott ed

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PRINCIPLES OF PHARMACOLOGY

Total Credits: 9
Lessons: 80 hrs
Practicals: 52 hrs
Semester II

Scientific Discipline Sector: BIO/14

Course Coordinator: Prof. Daniele Zacchetti
Email: zacchetti.daniele@hsr.it
Telephone: 02-2643.4817

Professors Teaching:
Daniele Zacchetti
Riccardo Fesce
Maria Pennuto
Addis Antonio

Tutors:
Sestina Falcone
Romina Macco
Ilaria Pelizzoni
Ilaria Prada

The course of Principles of Pharmacology, offered to the students already at the IV semester, is one of the unique features of our MD course. Pharmacology is the science that studies the effects of the exogenous substances to the physiology and pathology of the organism.
Within the traditional Italian MD curriculum, pharmacology is proposed after the other basic science disciplines, being thought to introduce concepts and instruments not emendable to the practical use of drugs (in diagnostics, anesthesia and, most importantly, therapy). For this reason this course in the other Italian Universities is still offered at the IV year, being addressed to the students already being exposed to Clinics and that have already acquired topics such as General Pathology and Microbiology. In the last years, however, this way of teaching has started to show its limitations. On one side the comprehension of the mechanisms of drug actions and the new therapeutic perspectives have been developed in an extraordinary way thanks to the knowledge at the molecular, cellular, genetic and physiological levels; on the other side the relationship between pharmacology and the clinics has tightened, due to the fact that drugs are not anymore "magic bullets", rather disease-modifying instruments and tools to understand pathology. The aim of our discipline has now widened in both operative and didactic-cultural terms. Teaching pharmacology at the boundary between basic topics and clinical courses is not anymore suitable for a modern School of Medicine. For this reason at the "Vita-Salute" San Raffaele University Pharmacology has been divided in two parts. This course, Principles of Pharmacology (coordinator Prof. Daniele Zacchetti), is offered together the other basic science courses and allows to recall and highlight, under a different point of view, information and basic biological concepts, opening them to problems that lead to clinics and therapeutics. The specific

pharmacological issues known as Therapeutics (responsible Prof. Flavia Valtorta) is now integrated within the clinical courses and allows to put the pharmacological topics in the specific issues as a fundamental tool for the approach to the patient. This is an important example of the integration, between basic and clinical teaching, that is a specific feature of our MD course. The two aspects of Pharmacology are so tethered that they make use to the same textbook, i.e. the Goodman and Gilman's, the classical compendium, known to all the physicians and that, not by chance, is entitled 'The Pharmacological Basis of Therapeutics'.

How is the course organized?

The aim of the course on Principles of Pharmacology is to provide the tools to understand drugs and their effects, answering a long list of questions such as 'why a drug has got one (or several) effect(s) and another molecule, possibly almost identical at the molecular level, has got a completely different profile of action?' up to "How a new drug is being developed?". Most of the concepts that will be provided are somehow new for the students of the second year, in the sense that they will be proposed from a different perspective; moreover, the topic of drugs is by itself comprehensive since it involves the entire organism. For this as well as several other reasons academic lessons are being held aimed to the explanation of concepts and issues. Presentation from groups of students might be also organized on specific topics. Last, the course is implemented with an experimental part represented by tutorials in which the techniques employed in pharmacological research are presented and explained. Pharmacology does not have its own techniques but, rather, employs the methods of the other disciplines. The point of view of Pharmacology is anyway often specific and there is always a lot to discuss, to critically analyze and to understand.

DIDACTIC MATERIAL

The textbook of reference is the Goodman e Gilman's, XII edition, published in English at the end of 2010 (mind! Of this book there are obviously 11 editions before this one, published every 5 years, approximately; Pharmacology is a discipline in fast development!).

Goodman & Gilman's
The Pharmacological Basis of Therapeutics, XII Edition
Ed. McGraw Hill, 2010

Meetings with students

Meetings with the coordinator of the course on Principles of Pharmacology can be organized by appointment organized by email (zacchetti.daniele@hsr.it) or calling the 02-2643.4817

Evaluation procedures

The exam is based on two steps: a test with 8-10 open questions, to be completed within 30 min and aimed to highlight students still far from an adequate knowledge of the discipline; then, an oral exam based on the critical discussion of wide and important topics, all included in then teaching program, on the basis of which the final grade will be established.

Program of the course

The Course is organized in the following topics. In details we will deal with
1. Introduction to the course, definitions, drugs and their molecular and biological properties.
2. Pharmacokinetics, i.e. the journey of the drug within the organism, the time-dependence of drug effects and the process that are responsible for them:
- Absorption and distribution of drugs: way of administration, proteins of the plasma;
- Drug elimination: drug metabolism, excretion, kinetic aspects.
3. Pharmacodynamics, i.e. the features and the quantification of the drug effects:
- Drug effects, dose-dependency
- Dose-effect curves.
4. Pharmacogenetics, pharmacogenomics and mechanisms of resistance.
5. Molecular targets of drugs – the receptors and their transduction mechanisms:
- Surface receptors;
- Circulation of receptors;
- Intracellular receptors.
6. Effects of drugs on cellular signaling:
- Second messengers – spatial coordination;
- Cross-talk among transduction pathways.
7. Pharmacology of the peripheral nervous system as a paradigm for the drug action:
- Sympathetic system; α and β adrenergic receptors;
- Direct and indirect agonists, receptor antagonists;
- Parasympathetic system and neuromuscular transmission;
- Muscarinic e nicotinic receptors;
- Cholinergic agonists; cholinesterase blockers;
- Antagonists: gangliоplegics and curare.
8. Autacoids, specific endogenous factors that act locally, and their pharmacology:
- the arachidonic acid cascade;
- the nitric oxide;
- histamine, serotonin, bradykinin, cytokines;
- ATP; adenosin.
9. General pharmacology of the central nervous system:
- neurons and glia, the synaptic signalling;
- excitatory and inhibitory transmissions; drugs of abuse;
- neurodegeneration.
10. Introduction to chemotherapy (bacteria, viruses, tumors):
- introduction to antibacterial drugs;
- introduction to antiviral drugs;
- growth and death of cells. antitumoral drugs.
11. Principles of pharmacognosy, toxicology and biologic therapy.
12. Development of new drugs: history, rules and future of pharmacology.

INTRODUCTION TO SURGERY

Total Credits: 3
Lessons: 24 hrs
Practicals: 30 hrs

Semester II

Scientific Discipline Sector: MED/18 – MED/19

Course Coordinator: Prof. Braga Marco
Email: braga.marco@hsr.it

Professors Teaching:
Braga Marco
Gianotti Luca

Tutors:
Stratta Gregorio
Pecorellii Nicolò
Capretti Giovanni

Course aims

Many surgical skills – except operating skills – are part of general medicine. A doctor has to deal with health problems on a daily basis, for which the solution implies the knowledge of illnesses pertaining to surgical subjects, but also the ability to carry out diagnostic and treatment procedures.
The course represents an approach to these issues, which will be followed consistently and completed in the other surgery courses.
The aim of the course is to learn about some pathological situations, know about some simple surgical procedures and know about performance and hospital issues in the surgical field.

Introduction to Surgery book list:

Texbook of Surgery - Sabiston