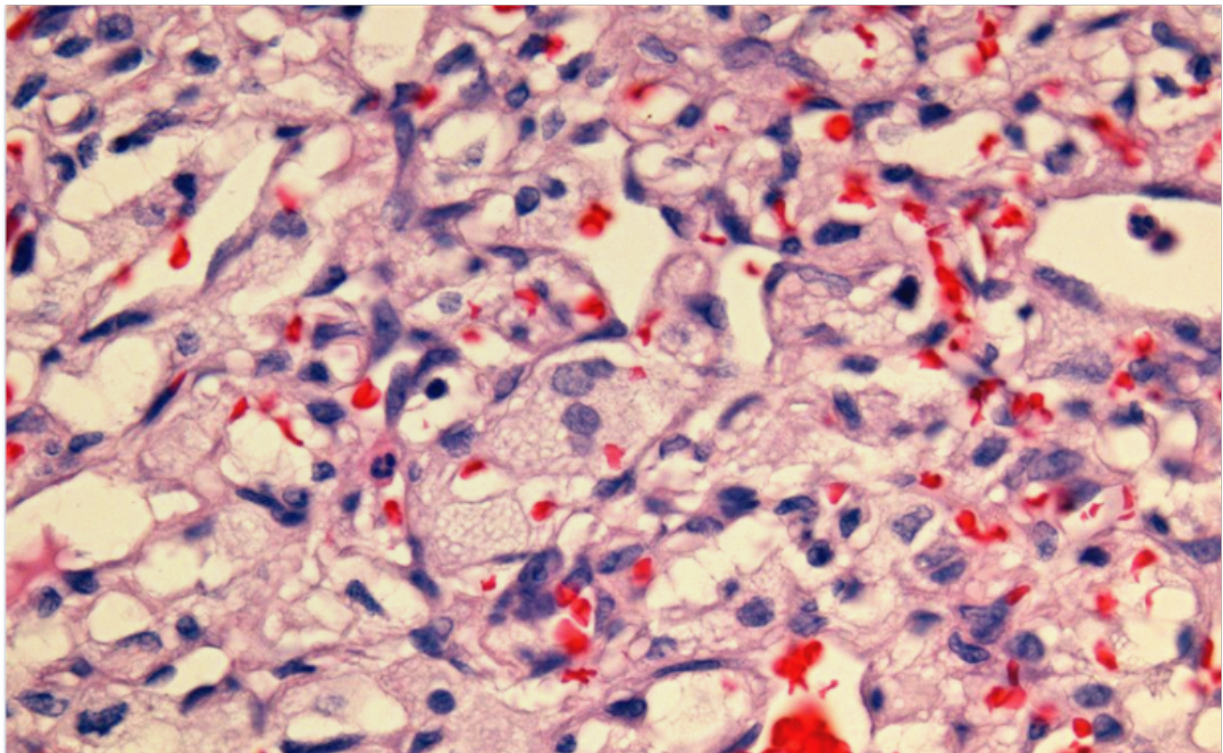




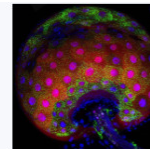
S8 Bioengineering

Detailed syllabus

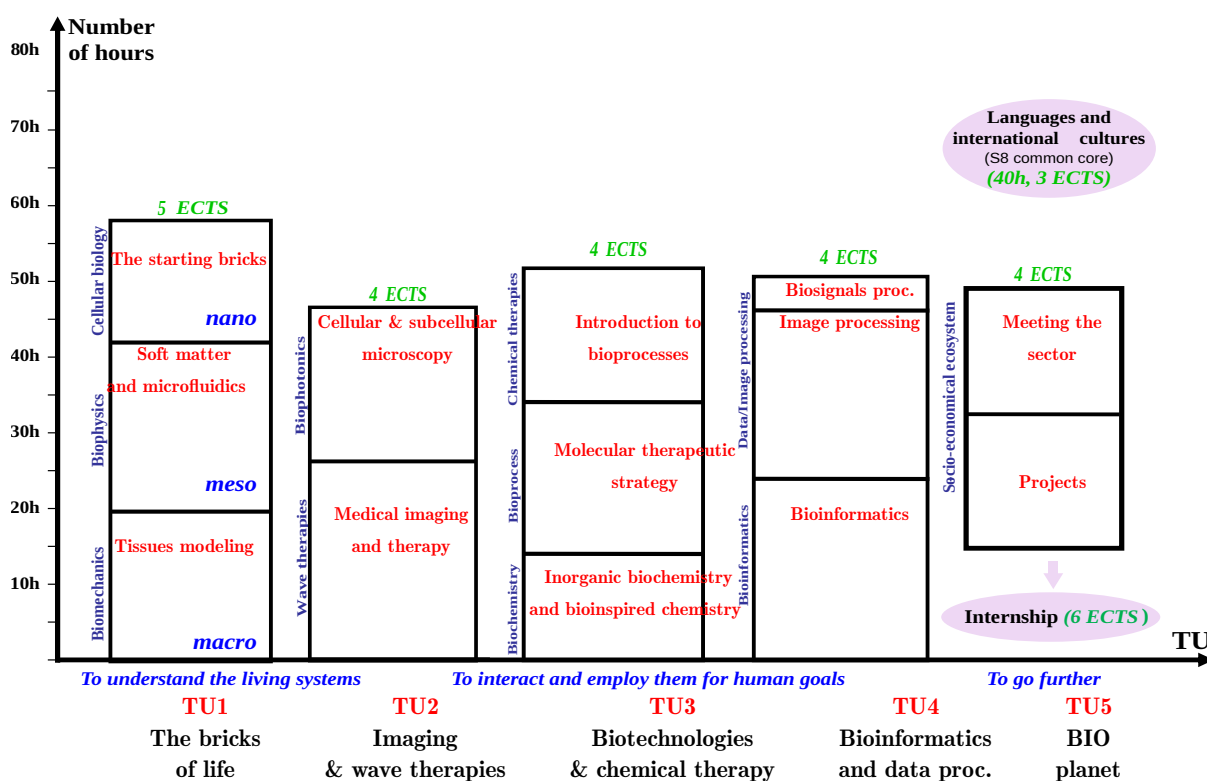
École Centrale Méditerranée - Engineering Initial Training 2A

MscT Complex Systems Engineering
Semester 2 - Biomedical Engineering

S8 BIOENGINEERING



Introduction - Objectives of the S8-BIO track

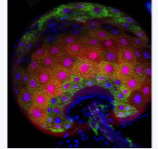


In a context of life expectancy's increase, climate change and exhaustion of fossil resources, biotechnologies represent hope to answer these crucial stakes. By combining engineering and life sciences, bioengineering brings a new paradigm as well as innovative solutions for issues on health, sustainable production, reduction of the ecological footprint, innovative modes of power production. **The one-semester bioengineering training program of École Centrale Méditerranée aims at broadening students' horizon by interdisciplinary teachings in order to be able to approach "life" all its main aspects.** Thus, the training's program is organized in four Teaching Units (TU, or UE, according to the french acronym for "Unité d'enseignement")¹.

The first TU covers the multiscale description of the living matter, going from the molecule up to the human's body. The two next ones focus on the ways of interacting with it, especially for diagnosis and therapeutic purposes. The

1. This document gives a description by TU and by subject. Scroll down the pages for a complete overview or **go directly to a TU or subject of your choice using the red hyperlinks in the table.** At the end of each part, an hyperlink will bring you back to this introductory page. The text written in pink corresponds to external hyperlinks (e-mail addresses, websites).

S8 BIOENGINEERING



fourth one is dedicated to image and data processing, comprising an introduction to the field of biostatistics and bioinformatics. The last one is an opening to the activity area with conferences and visits, and also comprises a project.

It is an introduction to bioengineering that gives the students the opportunity to pursue any type of engineering studies but which also allows to continue in this field, abroad within the **T.I.M.E.** network, or in France within the "Groupe des Ecoles Centrales". For instance, pursuing in biomechanics at Centrale Méditerranée is possible with the last year educational training program **Materials and Structures Mechanical Modeling**, in parallel with the "Tissues and Implants Bioengineering" program of the the Master in **Engineering and ergonomics of physical activities** of Aix-Marseille University. Moreover, Ecole Centrale Méditerranée is a founder member of the Turing Center for living systems "**CenTuri**", an ambitious interdisciplinary research project, gathering fifty research teams in Marseille in order to better understand the complexity of living systems. CenTuri offers to engineering students numerous perspectives of master internships and PhD offers within the various research laboratories involved, in varied disciplines : biology (neuroscience, immunology, biology of the development), physics, mathematics, biocomputing. In the biophotonics and medical imaging domains, opportunities of studies in third year of Centrale Méditerranée also exist, with co-habilitated Masters : **PICSEL 3A** specialization track, **Europhotonics Master**, **Signal and Image processing Master** among other examples... then in PhD in associate laboratories (Institut Fresnel, LMA,...)

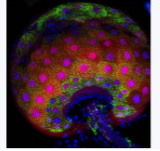
The members of the teaching staff of this one-semester bioengineering training program come from Centrale Méditerranée, Aix-Marseille University, CNRS and INSERM. Moreover, without directly intervening in teaching, several academic collaborators or economic actors take part in this educational program by proposing visits, conferences, internships and research projects.

Skills

- An awareness of the elementary structures and objects of living beings, their mode of assembly and their functions ;
- A sufficient theoretical/practical knowledge base to be able to model and anticipate the behavior of living organisms at different scales and different degrees of integration ;
- An introduction to physical/chemical methods of interaction with living organisms ;
- A general knowledge of technological devices and processes developed by man from or inspired by living organisms, or to interact with them, and the ability to use this knowledge to understand/use/design such devices ;
- A general knowledge of the sectors of activity related to this domain, and to be initiated to upstream research in the laboratory ;
- An awareness of risk management issues in the field of biology and health (procedure, legislation, organizations), and to know how to integrate these aspects in the management of a project in this field.

Responsible: Julien FADE (julien.fade@centrale-med.fr)

Intranet: Collaborative space for S8 BIOENGINEERING (Moodle: **S8 BIOENGINEERING**)



UE1 - THE BRICKS OF LIFE

The subject of this TU is the biological material in a multiscale vision, including the molecular and cellular nanoscale (The starting bricks), the biofluids flow mesoscale (Soft matter and Microfluidics) and tissues macroscale (Tissue modeling), up to the full human scale (Anatomy and pathology).

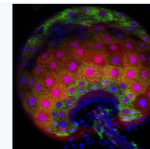
The complexity of the living matter comes from its multiscale organization. This TU gives a global vision of it through a multidisciplinary approach, which is believed to be essential for its understanding. Involved disciplines are chemistry, physics, mechanics, mathematics and numerical modeling. Studying a material or a system in a multidisciplinary vision shows the significance of a multidisciplinary education for new scientific, technological and social challenges.

This Teaching Unit completes others courses in material sciences provided at Ecole Centrale Marseille. Nowadays, the living matter is recognized as a promising source of inspiration in the fields of biomimicry and bioinspired materials.

Responsible: Marc JAEGER (marc.jaeger@centrale-med.fr)

Intranet: Collaborative space for TU1 (Moodle : [UE1 - THE BRICKS OF LIFE](#))

BACK



UE1 - THE BRICKS OF LIFE THE STARTING BRICKS

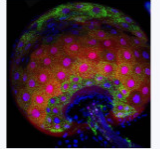
Karine ALVAREZ¹
Pierre SANTUCCI²
Stéphane BETZI³
Stéphane CANAAN⁴
Alexandre MARTINEZ⁵
Thien VU MANH⁶

Composition of matter has a crucial impact on structure (through elementary physical interactions), which itself dictates the function of the object (it is therefore indispensable to become familiar with the building blocks constituting DNA before looking at a DNA chip, with amphiphilic objects before considering a lipidic drug carrier or with proteins before designing antibiotics). Analyzing the constituents of living matter is the indispensable prerequisite to the design of systems interacting with living objects, imitating or overcoming their properties.

Thus, this section focuses on the micro- to nano-world. A preliminary introduction to the basics of structures and functions of cells is proposed in a first chapter. The molecular building blocks of life will then be explored starting from elemental monomeric constituents (nucleotides, aminoacids, carbohydrates, lipids) in order to understand how their assembling can lead to the corresponding polymers and aggregates (namely nucleic acids, proteins, polysaccharides, membranes). A structural physical analysis will be conducted in order to explain how these building blocks and their connecting mode can lead to objects of high molecular masses, displaying remarkable structures and universally equipping the living world.

As a second step, structure-function determinisms will be deciphered on these objects. This analysis will consist in elucidating how the structure of these macromolecular objects has been optimized through ages by nature leading to molecular machines with remarkable functions. Concerning deoxyribonucleic acids, the analysis of the structural properties of the architecture should explain why this polymer is universally used for information storage and transmission in living organisms. Similarly, a large panel of examples will illustrate the diversity of functions lead by proteins, the structural versatility of polysaccharides as molecular cellular fingerprints and the drug action of protein-target complexes.

-
1. karine.alvarez@univ-amu.fr, AFMB - CNRS UMR7257
 2. psantucci@imm.cnrs.fr, IMM, CNRS UMR7256
 3. stephane.betzi@inserm.fr, CRCM - INSERM UMR1068
 4. stephane.canaan@imm.cnrs.fr, LISM - CNRS UMR7255
 5. alexandre.martinez@centrale-med.fr, ISM2 - CNRS UMR7313
 6. vumanh@ciml.univ-mrs.fr, CIML - U1104



Cellular organization (S. Canaan)

Session 1 : The cell (2h)

Cells description and composition.

Function of all organites.

Session 2 : DNA and RNA (2h)

Properties of nucleic acids.

Transcription.

Traduction.

Genetics, heredity, evolution (T. Vu Manh) (2h)

Molecular bases : genes, RNA, proteins.

Heredity, mitosis, meiosis, reproduction, X-linked transmission, mitochondrial DNA.

Genetic variation, complex traits.

Mutations, natural selection, evolution, phylogenetic trees.

Carbohydrates and lipids (K. Alvarez) (2h)

Definition.

Importance and role in biology.

Classification.

Structure.

Properties.

Application : structure of biological membranes.

Amino acid and proteins (A. Martinez)

Session 1 : Amino acid (2h)

Amino acid's structure.

Physicochemical properties.

Reactivity.

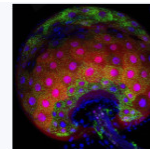
Peptic synthesis.

Session 2 : Proteins (2h)

Protein's structure (primary, secondary, tertiary, quaternary).

Interactions involved.

Examples of proteins.



From the structure of protein-target complexes to the drug (S. Betzi)

Session 1 : Study of the structure of proteins by crystallography (2h)

X rays.
Crystals.
Diffraction.

Session 2 : Study of the protein/ligand's molecular contacts (drug) (2h)

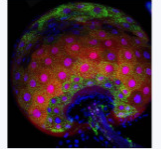
Electronic density.
PDB file.
Co-crystallization and soakings.
Analysis of the action's mode and of the molecular contacts.
Drug optimization on the basis of structures of protein/ligand complexes.

Assessment test: continuous assessment (written examinations, homework).

Reference textbooks

- B. Alberts, A. D. Johnson, J. Lewis, D. Morgan, M. Raff, K. Roberts, P. Walter** : "Molecular Biology of the Cell", Garland Science.
- D. Voet, J. G. Voet, C. W. Pratt** : "Fundamentals of Biochemistry : Life at the Molecular Level", Wiley.
- J. M. Berg, J. L. Tymoczko, L. Stryer** : "Biochemistry", New York : W. H. Freeman.

BACK



UE1 - THE BRICKS OF LIFE SOFT MATTER AND MICROFLUIDICS

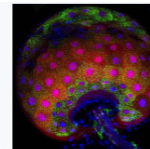
Marc JAEGER¹

The scale of observation corresponds to the mesoscopic one, between the molecular scale used by the chemist and the macroscopic one used by the mechanical engineer. So it is the physicist's one, which describes the structure of condensed matter in terms of physical bonds. It's the action of these cohesive forces that apply between two molecules and by addition between surfaces and colloids at the meso-scale, that is essential for micro-systems. These forces can explain a large number of specificities of the living matter, from self assembled systems (surfactants, micelles, liposomes) and self organized systems (cellular architecture) to the rheologic properties of complex fluids (as blood for example).

The usually amazing behavior of soft matter can only be understood by its bottom-up organization, starting at the molecular level. This organization is lead by the intermolecular forces, which playing together give the long-range interactions that organize the condensed matter. However, going from the molecular scale, where matter has a discrete nature, to the macroscopic one, where the matter can be seen as a continuous medium, implies a too huge number of particles to allow a deterministic description. Like for a perfect gas, these particles have a random motion induced by thermal agitation, which requires a statistical description. However, contrary to the perfect gas case, interaction potentials can no longer be ignored since they are responsible for the organization of condensed matter. We will start therefore by recalling the principles of statistical physics, applying them to the perfect gas case. We will then see how an interaction potential can be taken into account. We will speak from the origine of molecular interactions, leading finally to the Van Der Waals (VDW) interactions and to the Lennard-Jones' pair interaction model. The usefulness of the statistical approach to understand the living matter at the mesoscale will be shown on two examples of interest for biology : self-organization of amphiphilic molecules (fundamental for the organization of the living matter at the cell and subcell levels) and entropic elasticity.

In MEMS's (Micro Electro Mechanical Systems) capillaries, like in living matter, fluid flows presents typical small scale's properties. Mixing, omnipresent in the inertial regime, becomes a challenge. In contrast, the role of superficial forces becomes dominant. Therefore, the step towards the mesoscale will bring us to "DLVO" forces. We will introduce the Hamaker constant to characterize VDW forces between mesoscopic objects, like colloids. We will see Debye's theory to depict the influence of a charged surface and how a fluid may be conveyed in a micro-canal by electro-osmosis.

1. marc.jaeger@centrale-med.fr, M2P2 - CNRS UMR7340



Session 1 : Physics of liquids and soft matter (2h)

Place in material sciences of physics of liquid and soft matter.

Reminder of the structure of solids, atomic packing factor.

Necessity of a statistical description of fluids.

Increasing importance of intermolecular and superficial forces, from simple liquids to complex ones.

Session 2 : Reminders of the principles of statistical thermodynamics (self-paced study)

Session 3 : The ideal gas in the canonical ensemble (2h)

Session 4 : The ideal gas in the grand-canonical ensemble (2h)

Session 5 : Intermolecular forces modeling (2h)

The pair interaction.

The repulsive interaction and the structure of liquids.

The hard sphere's and Lennard-Jones models. Considering interactions in the statistical thermodynamic description of fluids.

Session 6 : Nature of intermolecular forces (2h)

The electro-statistical origin of intermolecular forces.

Van Der Waals forces in vacuum (London) and in a solvent (Mc Lachlan).

Session 7 : Chemical potential and self energy (2h)

Self energy in a crystalline solid : the rare gas example.

Self energy in a liquid : mean field approach.

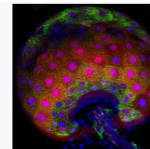
Relation with the molecular density.

Mixture characterization (solution).

Chemical potential and matter organization.

Matter distribution between phases.

Chemical potential and self energy.



Session 8 : Chemical potential and cohesive energy (2h)

Generalized chemical potential.
Cohesive energy for a liquid, Trouton's rule.
Thermal energy as the measure unit for interactions.
Chemical activity.
Diffusion.
Chemical reactions, affinity.
Osmotic pressure.

Session 9 : Entropic elasticity (2h)

Session 10 : Self-assembling, Critical Micellar Concentration (CMC) (2h)

Session 11 : Specificities of microfluidics (2h)

Stokes flows.
Importances of surface forces.

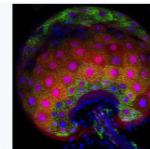
Session 12 : DLVO superficial forces (2h)

DLVO forces.
Van der Waals forces between macroscopic objects, the Hamaker constant.
Electrostatic forces between macroscopic objects, the Debye length.
Electro-osmosis.

Assessment test: continuous assessment (written examinations, homework).

Reference textbooks

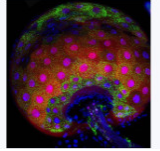
- R. Balian** : "From microphysics to macrophysics - Methods and application to statistical Physics", Vol.1 and 2, Study Edition, Springer.
- C. Ngo, H. Ngo** : "Physique statistique - Introduction", Dunod.
- I. Prigogine, D. Kondepudi** : "Thermodynamique", Odile Jacob.
- J. N. Israelachvili** : "Intermolecular and interface forces", Academic press.
- B. J. Birky** : "Micro- and Nanoscale Fluid Mechanics", Cambridge University Press.
- P. Tabeling** : "Introduction à la microfluidique", Belin.



Additional bibliographic sources

- C. Cohen-Tannoudji, B. Diu, F. Laloé** : "Quantum Mechanics", Wiley.
- J. P. Hansen, I. R. McDonald** : "Theory of simple liquids", Elsevier Academic press.
- J.-L. Barrat, J.-P. Hansen** : "Basic concept for simple and complex liquids", Cambridge University Press (chap. 2).
- J. Charvolin** : "Architectures de la matière molle : des films de savons aux membranes biologiques", Belin.
- P. G. DeGennes, D. Quere, F. Brochart-Wyart** : "Gouttes, bulles, perles et ondes", Belin.
- E. Guyon, L. Petit, J.-P. Hulin** : "Hydrodynamique physique", EDP Sciences.
- J. Happel, H. Brenner** : "Low Reynolds number hydrodynamics : with special applications to particulate media", Martinus Nijhoff publishers.
- D. D. Joseph, T. Funada, J. Wang** : "Potential flows of viscous and viscoelastic fluids", Cambridge University Press.
- J. Wolfe** : "Cellular Thermodynamics", in "Encyclopedia of Life sciences".
- E. Ben-Jacob, H. Levine** : "The artistry of nature", Nature, 409, 985-486 (2001).
- F. Huber et al.** : "Emergent complexity of the cytoskeleton : from single filament to tissue", Adv. Phys., 62, 1-112 (2013).
- D. J. Nicholson** "Is the cell really a machine ?", Journal of Theoretical Biology, 477, 108-126 (2019).
- J.-M. Di Meglio** "Colloïdes et nanosciences", Techniques de l'ingénieur, MM3200 V1, (2007).
- CNRS - Le journal** "Tous les cristaux liquides sont dans la nature", <https://lejournel.cnrs.fr/print/1811>
- CNRS - Le journal** "Cette matière molle qui défie les lois de la physique", <https://lejournel.cnrs.fr/print/1541>

BACK



UE1 - THE BRICKS OF LIFE TISSUES MODELLING

Jean-Marie ROSSI¹

Amal BECHIKH²

The scale of observation corresponds to the engineer's macroscopic scale who considers the biological material as a continuous medium. Tissues are considered as heterogeneous media with more or less organized microstructures and within which fluids may flow. It is then imperative to find methods to change scales that make it possible to obtain macroscopic average models of mechanical behavior.

Starting from a real clinical issue, the objective of this teaching is, through theoretical and numerical tools, mechanics and image analysis, to understand and model biological tissues at different scales : bones, tendons, cartilages, ligaments...

The following aspects are discussed :

- Homogenization of heterogeneous materials and structures in order to obtain mean models of mechanical behavior (rigidity, permeability...);
- Dynamic modeling of the evolution of living tissue (remodeling, cell differentiation, pathologies, treatments...);
- 3D reconstruction of anatomical finite element models at macro- or micro-scale from medical images (X-rays, micro-scan, MRI...);
- Design optimization of an implant or a biomaterial (dimensioning, link with 3D manufacturing, surgical practices...);
- Introduction to finite element modeling with software such as ABAQUS or COMSOL (practical exercises on machines).

Mechanical modeling of bone tissues (J.-M. ROSSI)

Session 1 : Introduction to Biomechanics (2h)

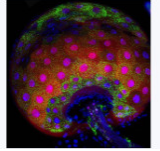
Main areas of analysis and application.

A short history of biomechanics.

Different approaches (in vivo, in vitro, in silico).

1. jean-marie.rossi@centrale-med.fr, ISM - CNRS UMR7287

2. amal.bechikh@centrale-med.fr, LMA - CNRS UMR7031



Session 2 : The bone tissue (2h)

- Bones function.
- Bones classification.
- Components of bone tissue.
- Bone tissues classification.
- Cortical bone versus trabecular bone.

Session 3 : Bone remodeling process (2h)

- Cellular mechanisms of bone remodeling.
- Adaptation to mechanical stresses.
- Adaptation to energy inputs.
- Some bone diseases.

Session 4 : Mechanical behavior of bone tissues (2h+2h)

- At the macroscopic scale.
- At the microscopic scale.
- At the nanoscopic scale.
- Different techniques of characterization and influence of biological parameters on the tissue's mechanical behavior.

Tissue modeling with homogenization methods (S. BOURGEOIS, V. GALLICAN)

Session 1 : Principle of homogenization techniques (2h)

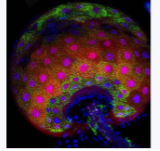
- Objectives.
- Notion of Representative Volume Element (RVE).
- Homogenizability conditions.
- Principle of mean stress and strains.

Session 2 : Methods in Elasticity (2h)

- Full-field methods (homogeneous stress boundary conditions, affine displacement boundary conditions, periodic homogenization).
- Computational homogenization.
- Mean field methods for isotropic media (Voigt, Reuss, Hashin and Shtrikman estimates, Mori-Tanaka, self-consistent method, Walpole bounds).
- Case of unidirectional long fiber tissues.
- Permeability of periodic porous media.

Session 3 : Numerical estimates of elastic moduli of heterogeneous media with the Abaqus software (4h)

- Periodic tissue made of unidirectional long fibers.
- Comparison of different methods applied to bone tissue from a sample whose microstructure is obtained by micro-tomography.



Assessment test: continuous assessment (written examinations, practical exercise report).

Reference textbooks

S. C. Cowin : "Tissue mechanics", Springer.

S. De : "Computational modeling in biomechanics", Springer.

C. Marcelli, J. L. Sebert : "Architecture et résistance mécanique osseuses", Masson.

Additional bibliographic sources

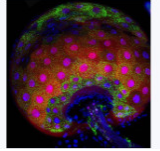
S. C. Cowin : "Bone Mechanics Handbook", second edition, CRC Press.

J. D. Knudson "Fundamentalsd of biomechanics", Springer.

R. Peterson, J. Bronzino "Biomechanics : principle and applications", second edition, CRC Press.

J. S. Khurana : "Bone pathology", Human Press.

BACK



UE1 - THE BRICKS OF LIFE ANATOMY AND PATHOLOGY

Didier BERTRAND¹

Bioengineering problematics, for instance the development of medical devices that can be implanted inside the body, raise problems that deal both with engineering and medical sciences. The ultimate goal is the improvement of the service provided to the patient with better functionalities, an improved durability and a reduction of secondary effects. These approaches imply the acquisition of knowledge on host tissues and a general insight on human anatomy. To achieve this goal, this course will provide scientific students with essential knowledge in that field.

Session 1 : General introduction to human anatomy (Arthrology, Myology, Kinesiology). (2h)

Sessions 2-4 : Practical and experimental anatomy (kinesiotherapy lab.) (3x2h)

Assessment test: work on audiovisual communication.

Reference textbooks

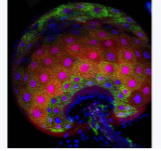
A. I. Kapandji : "Anatomie fonctionnelle", Maloine.

F. Netter : "Atlas d'anatomie humaine", Elsevier Masson.

M. Dufour : "Anatomie de l'appareil locomoteur", Elsevier Masson.

BACK

1. d.bertrand9@wanadoo.fr, MKDE



UE2 - IMAGING AND WAVE THERAPY

Medical imaging is the subject of multiple challenges. In the area of health, non-invasive observation of the body provides morphological, metabolic and functional information, leading to significant progress in terms of public care and health (screening). From an industrial point of view, the development of new modalities has resulted in the manufacture of increasingly sophisticated and highly specified equipment. Browsing a wide range of scales (from cellular to macroscopic), this TU will describe wave-tissue interaction and their use in imaging and therapy. The different imaging modalities, from the more conventional to the more advanced ones, and the associated therapies are put into perspective. The objective is to provide training on the most advanced imaging methods considering the physical foundations in order to be able to offer the best innovation potential in the medical care field.

This teaching deals with various aspects related to medical imaging and wave therapy. At the end of this Teaching Unit, students will have a good knowledge of fundamentals and potentiality of medical imaging :

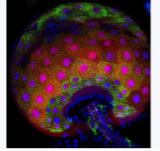
- Modern means of medical investigation and therapy using electromagnetic and mechanical waves as information carriers ;
- Physiological and metabolic properties targeted by the different imaging or therapy modalities ;

Therefore, different disciplines are involved : mechanics, physics and photonics. In physics, this teaching unit allows to address and complete the aspects related to imaging systems (microscopic and macroscopic) and interaction of electromagnetic or mechanical waves with living matter (modeling and practical applications for imaging and therapy).

This teaching allows to broaden the basic concepts of physics, optique or mechanics to imaging and wave therapy (applied to the living). These techniques involve the analysis of information resulting from the interaction between waves and matter in order to obtain an image and/or an effect on matter useful for therapy and then the information processing useful for diagnosis, reconstruction or follow-up. Students will be able to analyze the socio-economic context related to medical imaging and therapy through the presentation of the stakes associated with each technique and thus be able to measure the potential for innovation (emerging technologies in development in the laboratories). Practical exercises will also make it possible to give concrete expression to these different notions (in particular experiments on standardized ghosts).

This teaching essentially presents multidisciplinary notions applied to living systems. More precisely, it will enable the students to adopt a global vision of the complexity of imaging living matter, to use physical concepts to extract useful information for diagnosis or therapy, to recognize the specific elements related to the study of living beings for application to medical or biological imaging, to identify and understand the interactions between living matter and waves to derive morphological or functional information about matter, to draw from the interaction between living matter and waves an information to build and process an image, to take into account the uncertainty associated with all the complexity of the living being by taking, for example, into account the noises (electronic, acquisition ...), the movements of the human body, inhomogeneity between individuals... The methods of resolution will be illustrated in practical exercises

S8 BIOENGINEERING



and will highlight the contribution of the triptych biology/chemistry/physics for the development of optimal solutions (systems).

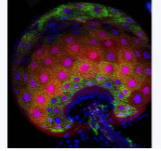
A large part of the scientific and technical dimensions related to the problem of imaging and therapy by going from the physical phenomenon to the image and then to the extraction of practical and useful information will be tackled. The goals of the imaging and image processing systems will be set according to the purpose (image contrast, information to be targeted...). Work methods in the specific field of the imaging life will be tackled (from acquisition to treatment, reflection on the adequacy of the means originating from physics research to medical needs, synthesis of the contribution of physics to medicine, measurement of potential for innovation (emerging technologies under development in laboratories)...).

At the end of this teaching unit, students will have a good knowledge of the foundations and possibilities offered by medical imaging (from waves-matter interaction to data processing). This skills portfolio will allow students to respond effectively to diagnostic and therapeutic needs, with an appreciation of the medical constraints.

Responsible: Julien FADE (julien.fade@centrale-med.fr)

Intranet: Collaborative space for TU2 (Moodle: [UE2 - IMAGING AND WAVE THERAPY](#))

BACK



UE2 - IMAGING AND WAVE THERAPY CELLULAR AND SUB-CELLULAR MICROSCOPY

Hervé RIGNEAULT¹

The subject at this course is high resolution imaging which aim at probing and observing cells or molecules. The goal here is to find approaches which allow to see structures that are as thin and small as possible. Optical microscopy is a technique often used to watch cellular mechanisms. Its main benefits are that it allows an imaging :

- that is non-invasive for living samples ;
- that has a good contrast, specific or not ;
- potentially eventually in three dimension of living specimens ;
- in real time of temporal phenomena.

Session 1 : basic techniques 1 (2h)

Introduction and history.

Structure of a simplified microscope.

Study of the components of an optical microscope.

Properties of microscope imaging (imaging under high numerical aperture)

Session 2 : basic techniques 2 (2h)

Properties of microscope imaging (resolution and coherence of lighting, depth of field).

Evolution of optical microscope.

Specific methods allowing to improve contrast or imaging properties.

Session 1 : advanced techniques 1 (2h)

Bioinformations (Cellular signaling and machinery).

Conventional contrast in optical imaging.

Fluorescence microscopy.

Session 2 : advanced techniques 2 (2h)

Non linear contrast in optical imaging.

Session 3 : advanced techniques 3 (2h)

Reduction of the observation volume

Session 4 : Biophotonics in practice (6h)²

Samples preparation.

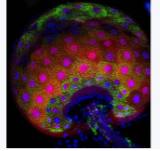
Hands-on techniques seen in class.

Report in group on the different handles.

1. hervé.rigneault@fresnel.fr, Institut FRESNEL - CNRS UMR7249

2. Biophotonics facility at the FRESNEL Institute in Saint Jérôme

S8 BIOENGINEERING

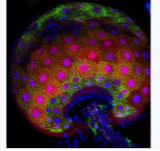


Assessment test: continuous assessment (written examinations, practical exercise report).

Reference textbooks

M. Locquin, M. Langeron : "Handbook of Microscopy", Butterworth-Heinemann.

BACK



UE2 - IMAGING AND WAVE THERAPY MEDICAL IMAGING AND THERAPY

Caroline FOSSATI¹, Pascal BERTO²
Emilie FRANCESCHINI³
Philippe LASAYGUES⁴, Carine GUIVIER-CURIEN⁵

The subject deals with the morphologic, therapeutic and functional imaging from distinct methods. In particular, it focuses on the modeling of the interactions between waves and tissues, in order to optimize the image quality and the therapeutic indices.

Optical imaging (Pascal BERTO)

This section first looks at the interaction between light waves and tissue, then at the propagation of these waves in biological tissue. The different modes of light transport depending on the type of medium are presented. Next, coherent imaging systems that allow probing at a scale greater than microscopy (OCT (optical coherence tomography), phase imaging, etc.) and the use of polarized light for functional imaging are discussed. Finally, the different laser therapies will be presented. The various imaging setups will potentially be presented during a lab tour.

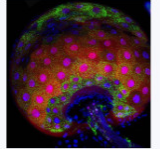
Session 1 : Light-matter interaction (2h)

Session 2 : Optical coherence tomography (2h)

Session 3 : Optical phase imaging techniques (2h)

Session 4 : Laser optics-wave therapies and/or demo-visit (2h)

-
1. caroline.fossati@centrale-med.fr, Institut FRESNEL - CNRS UMR7249
 2. pascal.berto@centrale-med.fr, Institut FRESNEL - CNRS UMR7249
 3. franceschini@lma.cnrs-mrs.fr, LMA - CNRS UPR7051
 4. lasaygues@lma.cnrs-mrs.fr, LMA - CNRS UPR7051
 5. carine.guivier@univ-amu.fr, IRPHE - CNRS UMR7342



Imaging and electromagnetic therapy (Caroline FOSSATI)

Session 1 : MRI imaging (2h)

Principle (T1 and T2 relaxation, chemical displacement).
Techniques (spin echo, selective impulse).
Imaging (field gradient, tomography).
Functional (BOLD) and diffusion (neurology) MRI.
Constraints and risks.

Session 2 : X-ray imaging and therapy (2h)

Differential absorption.
Tomodensitometry (CT scan) and angiography.
Radiotherapy.

Session 3 : Nuclear imaging and therapy (2h)

α , β , γ radiations.
Gamma camera.
PET (Positron emission tomography) scan.
Brachytherapy and Proton therapy.

Imaging and ultrasonic therapies (Émilie FRANCESCHINI)

Session 1 : Introduction (2h)

Specificity of ultrasonic imaging (real-time and non-ionizing imaging)
Evolution and miniaturization of ultrasound scanners.
Diagnostic and socio-economic issues.
Therapeutic potential (examples ; drug delivery, localized tissue destruction).

Session 2 : Ultrasounds physics (2h)

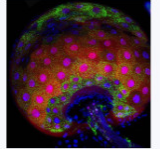
Compression and shear waves.
Piezoelectricity.
Specificity of compression and shear modulus for tissue characterization
Elastography principles.
Bandwidth and resolution.

Session 3 : Ultrasound modes A and B (2h)

Acoustical intensity (dosimetry) and impedance (reflectivity).
Time Gain Compensation (TGC).
Electronic focusing.

Session 4 : Ultrasonic semiology (2h)

Speckle (origins and reducing).
Artefacts (nuisance or information source ?).
Ultrasonic Semiology (application to senology).



Session 5 : Ultrasounds : Doppler and TM modes (2h)

Doppler effect.

Strain imaging.

Echocardiography.

Session 6 : Ultrasound-based therapy (2h)

HIFU (high intensity focused ultrasound) waves and extra-corporeal shock waves (lithotripsy, histotripsy).

Contrast agents for ultrasound (microbubbles).

Extravasation and sonoporation.

Session 7 : Practical work on ultrasonic imaging (Carine GUIVIER-CURIEN, Philippe LASAYGUES) (3h)⁶

Handling of a sonographic instrument.

Measures on calibrated phantoms.

Assessment test: continuous assessment (written examinations).

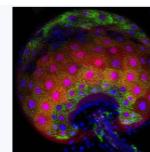
Reference textbooks

V. Tuchin : "Tissue optics : Light scattering methods and instruments for medical diagnosis", SPIE Press.

J. Beutel, R Van Metter, H. Kundel : "Handbook of Medical Imaging : Physics and Psychophysics", SPIE Press.

BACK

6. Technical facilities of the Licence Pro MTB of the IUT Aix-Marseille, Saint Jérôme.



UE3 - BIOTECHNOLOGIES AND CHEMICAL THERAPY

This teaching unit is about biotechnology and pharmacology. So it makes sense to study the strategies used in the development of bioinspired systems and in the production of biologically active compounds, both natural and synthetic ones. In pharmacology, the industrial technologies and process of the traditional pharmaceuticals are introduced, while in biotechnologies the progress based on basic modules of every living being (nucleic acids, proteins) are presented. Recently, the economic sector has developed new instruments (MEMS, DNA microarrays, bioinformatics etc.), which accelerate the research of new medication, to optimize their employment (vectorization), and revolutionize the process of biological analysis. In the past few years these promising technologies have boomed considerably, first in the academic world, then through the creation of a multiplicity of start-ups which are currently being integrated in the pharmaceutical industry. Today, the principles based on this new tools are sources of innovation in lots of other branches of industry.

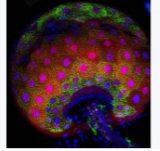
This class involves knowledge about process engineering and chemistry for the pharmaceutical aspects and the bioinorganic studies of living systems, leading to a biomimetic chemistry. It also entails skills in discrete mathematics and in computer science for bioinformatics. The skills gained in these lessons complete those already attained by the students. Observation of the development and life-cycle of pharmaceutical products illustrates the multidisciplinary education required in this sector and shows to our students the interest in a general education for new scientific, technological and social challenges in the field of biotechnologies and health.

The development of a medicament is a procedure with multiple parameters, involving regulatory, temporal and social conditions, as well as an innovative component. Multiple guidelines must be respected (regarding efficiency, availability, harmlessness etc.). Thus, it is a sector in which, par excellence, the solutions emerge from the capacity to mobilize complementary competences and to approach a complex problem with multiple parameters. These required complexity and multidisciplinary approach are illustrated by the continuity and the complementarity of the dispensed education, by the case studies and by the variety of suggested professional reports.

Thus, the heart of this Teaching Unit hence concerns the creation and the commercial launch of new active molecules and biotechnological devices. It is about stimulation of ingenuity to invent creative and original solutions with the help of what has been produced in the past and of what is developed today. In addition, a great part of the teaching is dedicated to bioinformatics and to biotechnologies, which aim for using genomes, biomolecules, cells and tissues in order to create innovative tools to face human challenges of the future. The sector itself is conducive to stimulate the imagination as it is in direct contact with life, which due to its long creativity of several millions of years of evolution is the richest of all sources of inspiration for humans.

Responsible: Alexandre MARTINEZ (alexandre.martinez@centrale-med.fr)

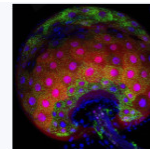
S8 BIOENGINEERING



Intranet: Collaborative space for TU3 (Moodle: [UE3 - BIOTECHNOLOGIES AND CHEMICAL THERAPY](#))

BACK





UE3 - BIOTECHNOLOGIES AND CHEMICAL THERAPY MOLECULAR THERAPEUTIC STRATEGY

Karine ALVAREZ¹

Stéphane CANAAN², Jean-François CAVALIER³,

Stéphane BETZI⁴, Philippe ROCHE⁵

Healthcare Regulatory Affairs (RA), the different scales of production, the targeted molecule choice and the strategy of quick synthesis (structure activity relationships, test with large family of compounds, shipping optimization, screening technologies, drugs major targets, product life cycle...) are introduced. Protein biotechnologies are overviewed : new diagnosis tools and new drugs obtained by genetic engineering. Case studies are discussed and supplemented with a visit of a high throughput screening platform and with a lab work session on biologic activity assays for active molecules.

Therapeutic strategies (K. ALVAREZ)

Session 1 : Therapeutic strategies (2h)

Introduction to drugs.

Drug discovery and development.

Pharmaceutical Industry (some figures).

Concepts definition (epidemiology, epidemic, endemic, pandemic, prevalence).

Drugs contribution to mankind.

Dosage, indications, contraindications. The drug conception key steps are :

- Disease choice.
- Drug target choice.
- Structured biological activity development.
- Identification, isolation, purification, structure establishment of the "lead" molecule.
- Identification of the structure activity relationships and of the pharmacophore.
- Interactions with the target improvement.
- Pharmacokinetics properties study and improvement.
- Drug metabolism study and toxicity tests.
- Manufacturing processes development.
- Clinical trials.
- Commercialization.

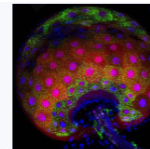
1. karine.alvarez@univ-amu.fr, AFMB - CNRS UMR7257

2. stephane.canaan@imm.cnrs.fr, LISM - CNRS UMR7255

3. jfcavalier@imm.cnrs.fr, LISM - CNRS UMR7255

4. stephane.betzi@inserm.fr, CRCM - INSERM UMR1068

5. philippe.roche@inserm.fr, CRCM - INSERM UMR1068



Session 2 : Pharmacokinetics (2h)

Study and improvement of pharmacokinetic properties in drug design.

Introduction to pharmacokinetics and pharmacodynamics for drugs.

Definition of the main concepts and issues.

Drug activity definition.

ADMETox (definitions).

Description of the different drug administration modes.

Concept definition (adsorption, distribution, metabolization, toxicity).

Chemical principles for the improvement of pharmacokinetics.

Session 3 : Therapeutic strategies in practice (1h30)¹

Screening and protein structure (S. BETZI)

Session 1 : Screening and experimental validation (2h)

Active compounds identification, chemical libraries, robotization.

Experimental tests design.

Enzymatic screening.

Z factor.

Non enzymatic screening (ELISA, Double Hybrid, FRET, HTRF, BRET).

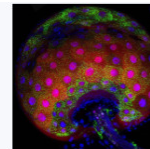
Screening development (miniaturization, screening for pharmaceutical industry, screening integration and robotization).

Orthogonal confirmation (micro-calorimetry, interferometry, various methods of co-purification, NMR confirmation).

Structure confirmation (NMR, crystallography).

Screening on cells and animals : High Content Screening (HCS).

1. AFMB lab on the campus of Luminy.



Session 2 : Structural methods for the study of protein/drug interactions and molecules optimization (2h)

Experimental structural method reminder (EM, Saxs, NMR, X-Ray).

Crystallographic structure of protein/small molecule complex (co-crystallization, soaking, electron density, solution, alternative conformations, B-factor).

RCSB data base : PDB, *.pdf files, *.sdf files, *.mol2 files.

Structure Based Drug-Design and guided SAR with crystallographic data.

Water molecule and protein structures.

NMR for protein structure solving and protein/ligand interaction study.

Interaction strength and speed.

Intrinsically disordered proteins.

Protein/protein interactions (notions).

Session 3 : Macromolecule visualization and manipulation with PyMol software (8h)

Protein Data Bank.

Crystallographic structure.

3D molecule imaging.

Helix, beta sheet, random coil.

Active site.

Inhibitors.

Water molecule.

Hydrogen bond.

“Van der Waals” contacts.

Electron density.

Therapeutic targets, molecular modeling and drug design (P. ROCHE)

Session 1 : Therapeutic targets (2h)

From the target to the drug.

Bioactive molecule conception strategies.

Therapeutic target large family.

Protein structure reminder.

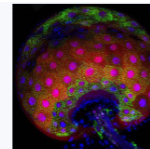
Receptors :

- Definition and functional principle
- Example : GPCR.

Protein recognition modes.

Enzymes :

- Definition and functional principle.
- Example : protein kinase.



Session 2 : Molecular modeling and drug design (2h)

Modeling contribution to drug discovery processes.

Introduction to molecular modeling.

Protein structure prediction (homology modeling, ab initio, docking...).

Modeling applications.

Introduction to molecular mechanic.

Force fields definition.

Molecular dynamic principle.

Molecular dynamic application for drug design.

Session 3 : Example of a biological target : protein-protein interaction (3h)

Protein-protein interactions as therapeutic targets.

Biologic concerns for protein-protein interactions.

Protein-protein interactions distinctive features.

Peptidomimetic compounds.

Example : Inhibitors development of the MDM2/P53 complex :

- Structure-based approach.
- Ligand-based approach.

Chemical library development for protein-protein interactions.

Study case (inhibitors development of the MDM2/P53 interaction).

Biological assay in practice (S. CANAAN, J.-F. CAVALIER)

Session 1 : Lab Work on biologic activity assays for active compounds (4h)²

Understanding of a lab protocol.

Calculation of test sample (dilution ratio, moles of enzymes, molar excess of inhibitor...).

Enzyme activity measurements using the pH-stat technique.

Interpretation of kinetic curves with determination of enzyme specific activity.

Inhibition tests using Orlistat as reference inhibitor.

Plot of obtained inhibition curves.

Interpretation of results. Writing a test report.

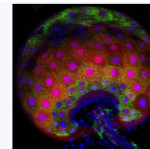
Assessment test: continuous assessment (written examinations, homework, practical exercise report).

Reference textbooks

Ng. Rick : "Drugs : from discovery to approval", Wiley-Liss.

BACK

2. LISM's technical facility on CNRS Joseph Aiguiller campus.



UE3 - BIOTECHNOLOGIES AND CHEMICAL THERAPY INTRODUCTION TO BIOPROCESSES

Pascal DENIS¹

Paul CHARBONNIERE²

This course introduces students to fundamental principles in bioprocesses engineering through four progressive stages, applied to the case study of bioethanol production. In Stage 1, students learn basic unit operations, creating Process Flow Diagrams, and work with key metrics like flow rates and conversion rates. Stage 2 covers bioreactors, emphasizing material balances with reaction kinetics. In Stage 3, students explore equilibrium curves, flash calculations, and apply energy balances with enthalpy changes. By Stage 4, they gain expertise in concentration changes, molar fractions, and energy optimization for process extrapolation.

Step 1 : (2h)

Understanding the function of some unit operations

From a description, know how to transfer them to a Process Flow Diagram

Handle the notions of flow rates, concentrations, conversions of volume/molar/mass flow rate, stoichiometry and yield of transformations and Heating Value.

Step 2 : (2h)

Understanding the particularities of bioreactors

Make material balances with reaction kinetics (make the relationship between transformation speed / process duration / volume).

Step 3 : (3h)

Understanding the equilibrium curve

Know how to use it to calculate one or two flashes

Mastering the changes in concentration/mass and molar fractions

Mastering the material and energy balance, know the enthalpy variations associated with a change in temperature or state.

Step 4 : (3h)

Mastering the changes in concentration/mass and molar fractions

Understanding the problems of extrapolation : energetic optimisation

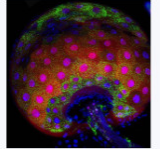
Assessment test: continuous assessment (written examinations).

Reference textbooks

1. pascal.denis@centrale-med.fr, M2P2 - CNRS UMR7340

2. paul.charbonniere@centrale-med.fr, M2P2 - CNRS UMR7340

S8 BIOENGINEERING



D. Ronze "Introduction au génie des procédés - Applications et développements", Tec et Doc, Lavoisier, 2013.

A.J. Hickey, D. Ganderton, Dekker "Pharmaceutical Process engineering", 2001.

B. Atkinson, F. Mavituna "Biochemical engineering & biotechnology handbook", Stockton Press, 1991.

J.E. Bailey, D.F. Ollis "Biochemical Engineering Fundamental", McGraw Hill, 1977.

D. J. Amende "Chemical Engineering in the Pharmaceutical Industry. R&D to Manufacturing".

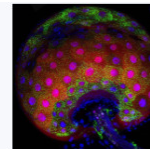
H.-H. Tung, E. L. Paul, M. Midler, J.A. McCauley "Crystallization of Organic Compounds. An Industrial Perspective".

Additional bibliographic sources

J. W. Mullin "Crystallization".

A. S. Myerson "Handbook of Industrial Crystallization".

BACK



UE3 - BIOTECHNOLOGIES AND CHEMICAL THERAPY INORGANIC BIOCHEMISTRY AND BIOINSPIRED CHEMISTRY

Jalila SIMAAN¹

This course deals with complex biological systems. Dioxygen transport, electron transfer in living system, photosynthesis or catalases are presented in detail. This helps understanding how nature finds elegant answers to crucial problems. Biologically inspired strategies are also discussed in order to illustrate how and why chemistry mimics this type of systems. For instance, the advantage of such an approach will be illustrated with the study of the mechanism of action of cis-platinum, a powerful anticancer drug. The mechanism of action of an anti malaria drug and fighting strategies against Alzheimer disease are also studied.

Session 1 : Transition elements in biological systems (2h)

- Transition elements properties.
- Biological ligands.
- Structure/properties relation.

Session 2 : the special case of Iron (2h)

- Iron's role.
- Siderophores.
- Ferritin.
- Hemoglobin.

Session 3 : Breathing and dioxygen transport (2h)

- Hemoglobin and myoglobin.
- Transport mechanism.
- Hemocyanin and "blue blood".

Session 4 : Photosynthesis (2h)

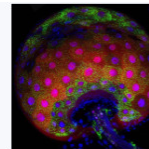
- Antenn.
- Photosystem I.
- Photosystem II.

Session 5 : Enzymatic catalysis (2h)

- Principle.
- CO₂ Transport : carbonic anhydrase.
- Methane mono-oxygenase.

1. jalila.simaan@univ-amu.fr, ISM2 - CNRS UMR7313

S8 BIOENGINEERING



Session 6 : Study of cytochrome P-450 (2h)

Role in living systems : oxydation and detoxifying of the cell.

Structure.

Mechanism.

Session 7 : Transition metals in medicine (2h)

Anticancer therapy (cis-platinum).

Antimalaria drug (artemisinin and quinine).

Strategies to fight against Alzheimer disease.

Assessment test: continuous assessment (written examinations).

Reference textbooks

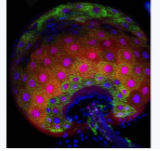
D. Voet, J.G. Voet : "Biochimie", De Boeck.

D.F. Shriver, P. W. Atkins : "Chimie inorganique", De Boeck.

J. E. Huhey, E. A. Keiter, R. L. Keiter : "Inorganique Chemistry", De Boeck.

S. J. Lippard, J. M. Berg : "Principe of bioinorganic chemistry", Wiley.

BACK



UE4 - BIOINFORMATICS AND DATA PROCESSING

The objective of this teaching unit is to enable students to familiarize themselves with the basics of processing data from the biomedical sector (images, gene sequences, etc.), including conventional image processing techniques, reconstruction methods, statistical methods, and deep learning. This field is becoming increasingly crucial in research and industrial developments in the bioengineering sector.

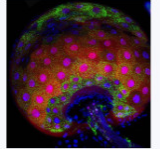
This course focuses on digital image processing, which is essential for medical diagnosis and therapeutic monitoring. It begins by covering fundamental concepts such as image acquisition, enhancement, filtering, and denoising. Students will learn to use classical methods such as Wiener filtering and frequency filtering. A large part of the course is devoted to deep learning, with an introduction to convolutional networks, deep architectures, and optimization techniques. The emphasis is on practical applications of deep learning in medical imaging. The course also covers image reconstruction, including tomographic and backprojection techniques. Finally, a significant portion is dedicated to image detection, classification, and segmentation, using region, contour, and histogram approaches. Practical sessions reinforce theoretical knowledge.

This teaching unit also aims to introduce students to the basics of bioinformatics through three main areas. The first section presents the technological evolution of modern biology, particularly sequencing and “omics” technologies, and their impact on biomedical research. It also addresses scientific integrity and statistical pitfalls. The second area deals with the modeling of biological regulatory networks, using mathematical and computational tools to better understand the complex interactions between genes. The final module explores artificial intelligence, with a focus on deep learning and its applications in biomedicine. Students will learn about supervised and unsupervised machine learning as well as dimensionality reduction. This multidisciplinary course highlights the current challenges in computational biology research.

Responsible: Caroline FOSSATI (caroline.fossati@centrale-med.fr)

Intranet: Collaborative space for TU4 (Moodle: [UE4 - BIOINFORMATICS AND DATA PROCESSING](#))

BACK



UE4 - BIOINFORMATICS AND DATA PROCESSING BIOSIGNALS PROC.

Adrien SARRADE¹, Julien FADE²

The acquisition and processing of biomedical signals is at the heart of many bioengineering-related technologies. This short module consists of two practical sessions allowing students, through an 8-hour practical activity in pairs, to acquire the basics of data acquisition, implement classic signal processing algorithms, and perform real measurements on human subjects. Depending on the equipment available, various types of biosignal acquisition may be covered : brain electrical activity, muscle activity, heart rate, respiratory rate, oximetry, force sensors, etc.

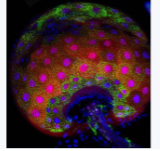
Acquisition of biosignals on Bitalino platform (Adrien SARRADE)

Biomedical signals processing (Adrien SARRADE)

Assessment test: continuous assessment (practical exercise report).

BACK

1. adrien.sarrade@centrale-med.fr, Institut FRESNEL - CNRS UMR7249
2. julien.fade@centrale-med.fr, Institut FRESNEL - CNRS UMR7249



UE4 - BIOINFORMATICS AND DATA PROCESSING IMAGE PROCESSING

Salah BOURENNANE¹, Caroline FOSSATI², Thierry GAIDON³

Digital image processing of images is a key step for diagnostic support and therapeutic control. In particular the subjects of image quality, data analysis, objects tracking in sequences and decision helping will be discussed. This course also introduces deep-learning and shows how it differs from usual machine-learning algorithms. The main methods used by the artificial intelligence community will be presented, as well as the key families of models (convolutive networks, recurrent networks and generative models). Finally, examples in image processing will be considered in practice.

Basic of image processing (Salah BOURENNANE)

Session 1 : Introduction (1h)

Session 2 : Basic methods (2h)

Organization of an image processing line.

Acquisition, sampling and quantization.

Pixels, neighborhood and connectedness.

Image enhancement.

Convolution filters.

Session 3 : Optimal method of image denoising (2h)

Inverse filter.

Frequency filtering.

Wiener's filter.

Deep-learning in image processing (Salah BOURENNANE)

Session 1 : Introduction to deep-learning (2h)

Fondamentals.

Relevance of deep-learning.

Big-data and deep-learning.

Session 2 : Learning optimization by deep-learning (2h)

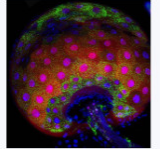
Optimization techniques for deep-learning.

Different models (deep architecture).

1. salah.bourennane@centrale-med.fr, Institut FRESNEL - CNRS UMR7249

2. caroline.fossati@centrale-med.fr, Institut FRESNEL - CNRS UMR7249

3. thierry.gaidon@centrale-med.fr, Institut FRESNEL - CNRS UMR7249



Session 3 : Deep-learning in image processing (2h)

Activation function and their use.

Application in image processing.

Basics of image reconstruction (Caroline FOSSATI)

Session 1 : Notions of image reconstruction (2h)

Tomographic reconstruction.

Session 2 : Methods of image reconstruction (2h)

Filtered backprojection method.

Detection, classification and segmentation in image processing (Thierry GAIDON)⁴

Session 1 : Methods of image segmentation (2h)

Region-growing methods.

Histogram thresholding methods.

Clustering methods.

Edge detection methods.

Session 10 : Using the main techniques of image denoising (4h)

Session 11 : Using image segmentation algorithms (4h)

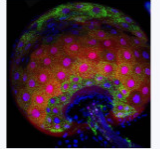
Assessment test: continuous assessment (written examinations, practical exercise report).

Reference textbooks

I.N. Bankman : "Handbook of Medical Image Processing and Analysis", Academic Press.

BACK

4. Image processing facilities of Centrale Marseille.



UE4 - BIOINFORMATICS AND DATA PROCESSING BIOINFORMATICS

Elisabeth REMY¹
Paul VILLOUTREIX²
Thien-Phong VU MANH³

The goal of the education in bioinformatics is to provide the students with general knowledge on what is commonly called bioinformatics, giving fundamentals on three distinct themes.

Introduction to Bioinformatics (T. VU MANH)

The aim is to give an overview of the different technologies used today in genomics and functional genomics, as well as to present some of their applications. Biology has indeed undergone a significant evolution with the production of large-scale data and the resulting changes in approach. This section aims at presenting the technological developments (sequencing, biomic technologies) that have led to this evolution, as well as the different challenges that biologists are currently facing.

Session 1 : History (1h)

History of applied bioinformatics.

History of biology in the big data era.

Session 2 : Genome sequencing (2h)

Session 3 : Biomic technologies and their applications in health (2h)

Session 4 : Scientific integrity, statistical pitfalls and case studies (2h)

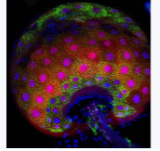
Modeling and analysis of biological regulation networks (E. REMY)

At the heart of every living organism, genes play an essential role. Besides their existence and their capacity for expression or inhibition, it is more precisely their interactions over time which make organisms have a certain number of phenotypic properties, follow a certain morphogenetic process... These interactions are difficult to define experimentally and, even if we were able to explicate them point by point, their global effect would remain an impossible mystery to characterize with molecular biology methods, because of the inherent complexity of the studied systems. In this context, we will present computer and mathematical methods related to discrete dynamical systems and control networks, which allow us to abstract the biological reality in order to apprehend the essence of the interactions and their influence over real biological systems.

1. elisabeth.remy@univ-amu.fr, I2M - CNRS UMR7373

2. paul.villoutreix@univ-amu.fr, Marseille Medical Genetics - LIS - CNRS UMR7020

3. vumanh@ciml.univ-mrs.fr, CIML - U1104



Session 1 : Introduction to modeling of complex systems (2h)

Session 2 : Dynamical systems (2h)

Discret dynamical systems.

Attractors.

Pools of attraction.

Updating modes.

Concrete applications to biology (2h)

Artificial intelligence and deep learning (P. VILLOUTREIX)

Artificial intelligence (AI) future seems full of promise. As the Russian President V. Poutine said, the leader in artificial intelligence will rule the world. It seems that AI is an area of strategic interest for industrialized countries and it is also ubiquitous given how it conquers all the fields of society and science (medicine, physics, intelligent robotics, connected objects, administration, etc...).

In this course, we will present a large view on AI through its concrete results, intelligent (cognitive) robotics and the nascent field of artificial general intelligence (AGI). We will show the links with neuroscience (when they exist). We will study more particularly a sub-domain of statistical learning : the deep learning. We will decipher its algorithms and will precise the interests and limits of this field. Finally, we will examine the applications of deep learning in biomedicine.

Session 1 : Introduction to Machine learning in biology and health (2h)

Historical perspective, which data for which questions.

Supervised learning : Regression, Classification (SVM, decision tree, random forest).

Examples.

Session 2 : Deep Learning (2h)

Deep learning, auto-encoder.

Applications (classification, data integration).

Session 3 : Unsupervised learning (2h)

Clustering.

Dimension reduction.

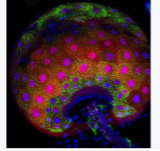
Applications (transcriptomics, genomics).

Assessment test: continuous assessment (homework).

Reference textbooks

O. Papini, H. Prade : "L'intelligence artificielle : frontières et applications", Cépaduès.

BACK



UE5 - BIO PLANET

The objective of this Teaching Unit is to allow the students to go out of the school's context in order to embrace more widely the biotechnological sector. The S8 BIOengineering offers them a large overview by meeting the Aix-Marseille's biology and health community. Conducting a project in the domain of the semester is also a part of this teaching unit, and the organization of which is left to the initiative of the students themselves. ¹.

The object of this Teaching Unit is the opening to the socio-economic sector by giving students the possibility to interact with the professional environment. This is why its position is out of the regular academic borders. Nevertheless, the multidisciplinary training of our students is the basis to build more complex competences of interpersonal skills.

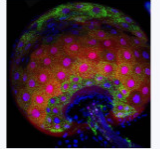
The TU assessment method is based on attendance at visits, active participation in organizing them, and individual behavior during these activities. The other part of the assessment is based on a project grade, the presentation format for which will be specified during the semester (oral, poster, video, etc.).

Responsible: Julien FADE (julien.fade@centrale-med.fr)

Intranet: Collaborative space for TU5 (Moodle: [UE5 - BIO PLANET](#))

BACK

1. The project activity requires that students applying to the S8BIO get ready in advance with the subject to start it readily at the beginning of the S8.



UE5 - BIO PLANET MEETING THE BIO-HEALTH SECTOR

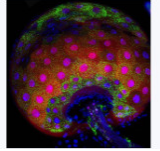
Julien FADE²

Bioengineering is the ultimate example of an emergent booming business sector, which increases continuously thanks to scientific and technological discoveries from public and private research laboratories. With an exceptionally large number of researchers and hospital practitioners and an impressive quantity of laboratories, covering a broad-spectrum of bioengineering research, the Aix-Marseille site offers an interesting opportunity to understand the challenges of this sector. In order to invite the students to this trip, to this open-mindedness, about one training day per week is decentralized in the Luminy site (in the south of Marseille, at the heart of the national park of the Calanques). This site offers an environment recognized for its research activity in Biology, Biochemistry, Biophysics, Biomechanics, Bioinformatics, and generally Biotechnologies. Its economic business park dedicated to the establishment of biotechnological start-ups and companies has already attracted an important number of investors (see [Grand Luminy Technopôle](#)). Other Marseilles places offer many opportunities to meet the community as well, like the hospitals center of Sainte Marguerite, of the Timone or of North hospitals. Many other opportunities to interact with the bioengineering sector are offered in the frame of this TU. A list of all the activities proposed each year is available on intranet (Moodle: [UE5 - BIO PLANET](#)). This list can be elaborated in concertation with students to consider at best their interests, at the condition that they tell us largely before the start of the S8.

Exemples of visits : plateaux techniques (imagerie médicale CERIMED, NeurotechCenter, INP La Timone, Ciphe, centre kinésithérapie/re-éducation CryoKiné . . .), laboratoires de recherche (Institut Fresnel, LISM, Institut des Sciences du Mouvement, IMM, CIML, . . .), conférences d'entreprises (Siemens, Avicenna.AI, Idmed, Veracyte, Deneb Medical, Sanofi, Vygon, Articares, . . .)

[BACK](#)

2. julien.fade@centrale-med.fr, Institut FRESNEL - CNRS UMR7249



UE5 - BIO PLANET PROJECT

Julien FADE¹

The recommended procedure for the project activity results from a double analysis :

1. The second year Internship is the golden opportunity to complete the discovery of the bioengineering sector thanks to a direct observation in the field.
2. The 8th semester lasts 4 months, which give a very comfortable timeframe to mature an internship subject with the following actions (non-exhaustive list) :
 - To make contact with the internship team, and if possible to get familiar with them ;
 - To gather information on the problematic via a bibliographic study ;
 - To get accustomed to the useful tools/techniques for the internship.

It is the mission that is proposed to our students within the scope of their project activity. It also offers a guarantee for the potential internship supplier to have a student who is more operational from the first day of internship, which makes the 2nd year internship more attractive. However, it implies to be already decided on the internship subject before starting the semester and to be able to propose a project, that is in relation to Bioengineering, even if the internship subject can differ. A database of our partners is available for the interested students to help them in their search (Moodle: [UE5 - BIO PLANET](#)), contact data upon request.

A project activity, which is de-correlated of the second year internship, is also possible under the same conditions of tackling the issue before the start of the semester. Students can propose themselves a subject on Bioengineering, which matter to them, and find a teacher/researcher, who agrees to supervise and validate the project. They can also solicit them for a subject proposition.

In every instance, it is suitable to contact early the teaching team to validate the proposed project/subject (content, assessment, supervisor).

BACK

1. julien.fade@centrale-med.fr, Institut Fresnel - CNRS UMR7249