**GML-7020 - Nanomatériaux pour l’imagerie médicale**

**Name in English : *Nanomedicine and nanomaterials for imaging***

**(Language of the course: English)**

**Résumé descriptif pour le cursus de l’université Laval:**

**Résumé (en français):** Plusieurs types de nanomatériaux sont maintenant utilisés pour des applications biomédicales et en particulier pour l’imagerie médicale. Ainsi, le développement de nanoparticules d’or comme agent de contraste pour la tomodensitométrie, ou les nanoparticules d’oxyde de fer pour le suivi de cellules en imagerie par résonance magnétique, nécessitent d’abord de maitriser la fabrication de ces matériaux de pointe. Ensuite, une formation dans ce domaine nécessite de développer des connaissances approfondies des techniques analytiques permettant de visualiser ces objets à de très forts grossissements, ainsi que de mesurer toute l’étendue de leurs propriétés physico-chimiques. Finalement, les experts en nanotechnologies biomédicales doivent maitriser principes de base des différentes modalités d’imagerie médicale, ainsi que des principes des traceurs et des agents de contraste qui leur sont associés. En empruntant la voie du développement des nanotechnologies biomédicales, le cours permet aux étudiants de se forger de solides connaissances dans le domaine de la synthèse des nanomatériaux, de la caractérisation de leur taille et de leurs propriétés physico-chimiques. Les principaux outils analytiques associés aux nanomatériaux sous forme colloïdale, sont présentés, décrits et expliqués. Le cours permet aussi de présenter aux étudiants gradués dans des domaines connexes au génie biomédical, les notions de base associées aux techniques d’imagerie médicale fondamentales que sont la résonance magnétique, la tomodensitométrie, et la tomographie par émission de positons. Finalement, les nouveaux nanomatériaux développés pour l’imagerie médicale et pour la livraison de produits thérapeutiques (ex. : médicamenteux, génétique, radioactif), sont analysés en fonction de leurs caractéristiques de biodistribution, de leur biodégradation, et de leur biocompatibilité relative. En résumé, ce cours vise à fournir aux futurs ingénieurs et scientifiques biomédicaux, une revue des connaissances fondamentales et pratiques de la synthèse des nanomatériaux, de leur caractérisation, et de leur utilisation dans le domaine de l’imagerie et de certaines thérapies ciblées.

**Summary (English):** Nanomaterials have entered the field of medicine. They are used in a variety of biomedical applications, in particular in biomedical imaging. For instance, gold nanoparticles generate contrast in computed X-ray tomography, whereas iron oxide nanoparticles are frequently used as contrast media in magnetic resonance imaging. Nanoparticles are also being developed to deliver therapeutic treatments (radiotherapy, drug or gene delivery, etc). This course (45 h) builds on the selection of the main classes of materials that are used as probes and contrast agents in biomedical imaging. A strong focus is put on the synthesis and characterisation of metal-based nanoparticles and inorganic/hybrid materials, in order to better understand their performance as contrast agents and imaging probes in MRI, CT, and nuclear medicine. The first modules (3 h) cover the main general aspects, concepts and descriptions of nanomedicine. The second series of modules cover principles of nanoparticle synthesis (gold, transition metals, silica, polymer-based micelles – 3.5 h), followed by modules on purification (centrifugation, filtration, chromatography) and particle size analysis (DLS, NTA, TEM - 5.5 h). The fourth series of modules is an overview of the main physico-chemical characterisation tools for nanomaterials (FTIR and Uv-Vis spectroscopy, XPS, EDS, TGA – 5h). The fifth and sixth series cover the concepts of nanoparticle functionalization for imaging applications, and in vitro/in vivo biological validation. The last series covers the fundamental concepts of the main translational biomedical imaging modalities (MRI, CT, nuclear imaging), with specific focus on the optimal design of nanomaterials. In resume, this course aims at providing biomedical engineers and scientists, a broad knowledge of the fundamental and practical aspects of nanoparticle synthesis and nanomaterials characterisation. It also covers the basis of several pre-clinical and clinical imaging modalities, and guidelines for the optimal development of imaging probes.

**Objectives:**

* To cover the fundamental aspects of nanoparticle synthesis, characterisation, and preparation for biomedical imaging applications;
* To provide an introduction to the field of biomedical imaging, for students in the field of chemistry, materials science and engineering, as well as biomedical engineering;
* To cover the essential physico-chemical analytical techniques and methodologies for the study of nanoparticles (particle size, chemistry, purity, surface functionalisation)
* To present a comprehensive and integrated overview of nanoparticle synthesis for bioimaging applications, from their synthesis, purification, characterization, functionalization, and in-vivo validation.

**Pedagogical methodology, type of course:**

* Duration of the course: 10 weeks in total, between May 1st – July 15th); 3 hours of recorded powerpoint modules per week + a weekly journal club activity (on-line, through the University web-site and Adobe Connector).

**Course structure and activities:**

Introductory module (3h): Overview of nanomedicine and nanomaterials for imaging; functional applications of nanoparticles in medicine; principles of imaging probes and contrast media; biological barriers, biodistribution and fate of nanoparticles in vivo.

Nanoparticle synthesis segment (2.5h): Principles of nanoparticle nucleation and nanoparticle synthesis; Synthesis of high-Z nanoparticles: gold nanoparticles; Synthesis of magnetic nanoparticles: iron oxide; Production of polymer-based nanoparticles: PEG micelles.

Nanoparticle purification and size analysis segment (5 h): Purification of as-synthesized nanoparticles; Laboratory on purification of nanoparticles (3 techniques); Particle size analysis in situ: measurement of hydrodynamic diameter and nanoparticle concentration (DLS and NTA); Laboratory on DLS measurement: the concept of protein corona and surface charge; Transmission electron microscopy (TEM) for nanoparticle analysis; Particle size analysis: distribution, morphology, purity assessment etc.

Physico-chemical characterisation of nanoparticles segment (5.5 h): Introduction to spectroscopic techniques for nanoparticle analysis; Uv-Vis for nanoparticle analysis; X-ray induced spectroscopy techniques for elemental and molecular analysis (XPS, EDX); Fourier-transform infrared spectroscopy to measure molecular vibrations in nanoparticles; Thermogravimetric analysis to measure the organic/polymer contents of nanoparticles

**Assessment - 1 (40%): Nanoparticle synthesis and characterization exam (covers materials from the first 4 series of modules.**

Functionalization of nanoparticles and in vitro biological validation (3 h): Functionalization of nanoparticles for nanomedicine: molecules and functions; Chemical and biochemical routes for nanoparticle functionalization; Functionality assessment: physicochemical and biological assays; Cytotoxicity tests; Laboratory on cytotoxicity assays (+ demos); Genotoxicity, immunology and inflammatory tests.

Biomedical imaging segment I: MRI (5 h): Introduction to biomedical imaging; Introduction to MRI (4 h); Contrast media for MRI and relaxometric analysis; Virtual lab on MRI acquisition; Virtual lab on dynamic contrast-enhanced MRI: mouse anatomy, signal analysis;

Biomedical imaging segment II: CT and Nuclear imaging (5h): Introduction to X-ray computed tomography; Principles of contrast media for CT imaging; Nuclear imaging techniques (PET, SPECT); Radiolabeling, detection and imaging; Introduction to quantitative biodistribution of nanoparticles by nuclear imaging

Validation segment (2h): considerations for the validation of nanomedicine products by the health authorities: a perspective on contrast media for imaging

**Assessment 2 (40%):** Design of a biomedical imaging experiment involving preparation, dosage, in vivo administration of nanoparticles, followed by image acquisition and data analysis (15-p document including brief literature review, objectives and hypothesis, etc).

**Assessment 3 - Short Quizzes (20%):** 10 brief questions to be answered each week, during the discussion session.

**Relevance of the course to biomedical engineering, materials science, engineering physics and chemistry programs:** Biomedical imaging is a key tool for biomaterials scientists and biomedical engineers. By introducing the fundamentals of nanoparticle synthesis for contrast media applications, the course aims at providing graduate students in the fields of materials science and chemistry, the main guidelines allowing them to design optimal imaging products for a whole range of biomaterials applications. The students not yet familiar with the main spectroscopic and physico-chemical characterisation techniques in the field of nanotechnology will be instructed on the principles and on the complementarity of these techniques. The students will learn how to select and integrate adequate purification techniques into the flow-chart of nanoparticle development and validation; many of these techniques also apply to the development of biomaterials and pharmaceutical products. Finally, the course provides an overview of the most important pre-clinical and clinical imaging technologies relevant to the field of bionanomaterials. The course is oriented toward providing the materials scientist, chemist, or biomedical engineer, a good knowledge of the main imaging techniques that are key to demonstrating the functionality, efficacy, long-term retention, or body clearance of bionanomaterials.

**Evaluations:**

* Assessment 1 = intern exam (40%)
* Assessment 2 = design of imaging experiment (40%)
* Assessment 3 = short quizzes (8, for a total of 20%)

**General Breakdown of modules and schedules:**

PART 1:



**PART II:**

