

PhD Program	MEDICINAL CHEMISTRY
Project title:	Organic-inorganic nanocomposite coatings for metal implants as drug delivery systems
Research field:	The proposed Ph D project is multidisciplinary including fields of physical and materials chemistry as well as biology. The research project includes finding the conditions of drug incorporation into the coatings, determining the drugs release kinetics and factors influencing it. Based on these findings coatings with different release kinetics will be developed and tested <i>in vitro</i> with different cell lines.
Institution where the experimental work will be performed	Ruđer Bošković Institute 10000 Zagreb, Bijenička 54 URL: http://www.irb.hr/en/str/zfk/labs/LSPSOM/LRK/
Supervision	The research will be supervised by dr. sc. Maja Dutour Sikirić.
Achievement	The candidate will acquire broad knowledge of bone implant materials and local drug delivery systems which should enable the candidate to either pursue academic career (in the field of medical chemistry, biomaterials research, development of drug delivery systems) or to find position in the related industries. In addition the candidate will be working in international research environment. The research will be performed in collaboration with Professor H. Füredi-Milhofer from the Hebrew University of Jerusalem, Israel, Professor F. Cuisinier, University of Montpellier I, France (preparation and physic-chemical characterization of the coatings) and Professor K. Leifeith, IBA, Germany (<i>in vitro</i> biological tests).
Abstract	<p>Many of the materials used for replacement and/or repair of bone and teeth, (metals, metal alloys, polymers) meet biomechanical requirements for load bearing applications, but are mainly bioinert or biotolerant and thus show poor or nonexistent interfacial bonding with the surrounding bone. To alleviate this problem, differently prepared surface coatings consisting of calcium phosphates have been applied for a long time. However, although it is known that the biological systems are organic-inorganic nanocomposites in which the inorganic phase is growing within the organic matrix, only recently have attempts been made to include organic molecules into surface coatings. Notably, inclusion of bioactive organic macromolecules (drugs, growth factor, etc.) has been attempted by co-precipitation with the inorganic phase. However, macromolecules in a crystallizing solution may profoundly influence crystallization of inorganic salts, including calcium phosphates. They may even exhibit a dual effect, inhibiting and/or inducing crystallization depending on the molecular structure, surface charge and solution concentration of the macromolecule. Consequently, although coprecipitation is possible, it is relatively far from controlled mineralization and therefore unpredictable. Learning from the mechanisms of biomineralization, our group in collaboration with colleagues from Israel and France has recently constructed novel organic – inorganic composite coatings for bioinert metal implants, by first depositing an organic matrix, then growing calcium phosphate crystals <i>in situ</i> within that matrix. It is the aim of this project, to demonstrate the suitability of our coatings for local drug delivery systems, i.e. to incorporate bioactive molecules without adversely affecting their bioactivity or the properties of the organic-inorganic coatings.</p> <p>It is proposed to study incorporation and controlled release of two types of drugs, an antibiotic, <i>vancomycin</i> (Vm) and an immunosuppressant, <i>cyclosporine A</i> (CsA) into the coatings. Drugs will be incorporated into the coatings by adsorbing the drug as a component at different depths during build-up of the PE ML or including it by diffusion into the coating. Developed coatings will be tested <i>in vitro</i> with different cell lines.</p> <p>The proposed research should introduce considerable improvements to the biomimetic coating methods, as they are known to date. The bioactivity of our novel organic-inorganic composite coatings will be considerably enhanced by immobilizing antibiotic and/or immunosuppressant drugs and it should be possible to chose the optimal location for immobilization as well as to optimize the release rates of the drugs, to ensure their maximum effectiveness, especially since the effect of most drugs might be dose dependent.</p>