DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Currently, there is great interest in the application of nanometallic particles for the creation and design of extremely sensitive and specific biochemical nanosensors and protective layers on implants (laryngology, cardiology, orthopedics, or stomatology), which when inserted into the patient's body will interact with body fluids (i.e., blood plasma). By the proper selection of the nano- and micro-structures of the surface layers (coatings and films) and the composition of the implemented chemical elements in these layers, it is possible to obtain not only biocompatible layers but also layers showing selective biological activity (chemical) with respect to the selected compounds, which interact (via adsorption and desorption processes) with a surface of interest (reaction at the solid/liquid interface). The interactions between biological, organic, and inorganic molecules and a metal surface are a key issue in biotechnology and biochemistry. Because biotechnology research relate to the processes at the molecular and cellular scales, the structure and properties of the interface must be designed and controlled at these scales. Thus, commonly used biosensors take the form of metallic nanoparticles obtained under controlled conditions in an aqueous medium by chemical and laser ablation methods and homogenously porous metallic surfaces. The nanoscale properties of the interface between biological and physical systems are a common theme in a large number of diverse devices.

This theme is an integral part of the presented research proposal, and proposed in this project studies intend to fill the existing gap in the systematic investigations of adsorption occurring at the metal/liquid interface for molecules playing an important physiological role. This gap includes the lack of information on how the adsorption process of a molecule is affected by structural factors (e.g., influence of the secondary structure, steric constraints, acidity/basicity, hydrophobicity/hydrophilicity, and aromaticity of the amino acids); constitutional isomerism (*o*–, *m*–, and *p*–)), environmental factors (e.g., solution ionic strength and pH), molecular concentration, and biosensor type (e.g., metal type, metal particle shape and size, roughness, implantation by different metals, corrosion).

The scientific aim of the proposed research project is to demonstrate the structure-activity relationship between the molecular structure of the biologically active compound and its activity in the process of adsorption on the solid/solution interface.

The peptides under investigation are small receptor-avid endogenous neurotransmitters that affects a broad range of physiological responses through the metabotropic seven transmembrane G protein-coupled superfamily receptors (GPCRs). A number of malignant tumors over-express certain types of GPCRs receptors on their surface (i.e., small cell lung cancer (SCLC) (85 – 100%), glioblastoma (85%), stomach/pancreatic (75%), prostate (62 – 100%)). This process renders these receptors accessible as potential receptor-positive cancer markers for imaging and therapy with synthetic antagonists and agonists in early diagnosis and as a molecular target for the detection of lesions in which they are expressed. Several peptide's agonists are considered to be growth factors involved in the carcinogenesis and progression of the neoplasm cells. The mechanism of tumor growth-stimulating effect still remains unclear and importantly can be blocked by the GPCRs antagonists. Therefore, the use of GPCRs receptor antagonists is an efficient chemotherapeutic and diagnostic drug design approach. In this respect, various investigations have focused on the development of mutated analogs that exhibit both substantially higher affinity and antagonistic properties or weaker agonistic properties for these receptors. Because of these properties, specifically modified neurotransmitters may effectively compete with the native peptides; when they preferentially bind to GPCRs, they block these receptors from triggering their action. Therefore, knowledge of effects caused by replacement of naturally occurring amino acids by unnatural ones on the peptide structure and in the processes occurring at the solid/solution interface is crucial for explanation and determination of each amino acid role on the peptides actions.

In this regard, several series of selected neurotransmitters analogues will be synthetized and tested, including analogues resulting from side-chain modification strategies (amino acid deletions or the retro-inverso modification), analogues with modified peptide bonds, and derivatives with a modified *C*-terminal region. Then, the analogues will be adsorbed onto the surface of different metallic biosensors. Surface-enhanced Raman spectroscopy (SERS), tip-enhanced Raman spectroscopy (TERS), and surface-enhanced infrared spectroscopy (SEIRA) will be used for description of the adsorption processes. Atomic force microscope (AFM), scanning electron microscope (SEM), and/or X-ray diffraction (XRD) will be used for the characterization of the surface morphology of the metallic substrates. For selected analogues the biological activity will be determined.

The scientific investigation proposed in this project reflects the priority areas in the basic research of "Diseases of civilization, new drugs and regenerative medicine" and "Advanced materials technologies" (The National Program for Research (PSC), adopted by the Council of Ministers on 16 August 2011, Annex to Resolution no. 164/2011).