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Domain: Medicine

ABSTRACT

The thesis of habilitation "**Innovative approaches for new diagnostic and therapy methodologies**" is structured in three parts. In **the first part** I presented the results of the research activities carried out after obtaining the title of **Doctor in Physics** with the ***Summa cum laude*** distinction in 2007. In **the second part** I presented the future research plans, after defending the thesis, and in **the third part** are presented the bibliographic references used in the first part of the thesis.

The first part is divided into 3 sections. Thus, in **the first section of thesis (I.1)** I described the main professional and academic achievements, detailing my course within the Transylvania University of Brasov in **1998, as a university assistant** for the disciplines of general biophysics and physics, and until now when I am an associate professor of general biophysics and physics courses. **Between 2007-2008 (1 year)** I also worked as an **associated researcher** at the **University of Wisconsin-Milwaukee, the biophysical laboratory, Wi, USA**, in a **post-doctoral internship** where we did scientific research to correlate the biophysical properties of the rat brain and the state of consciousness when it was under the action of different anaesthetic substances.

In **the second section (I.2)** I detailed the **main scientific achievements** focused on two main fields, interconnected, with a strong inter- and transdisciplinary character, obtained after the PhD in Physics, which also led to the title of **doctor in medicine with the *Summa cum laude*** distinction in 2020: 1.Study of interactions and (bio) molecular reactions 2.Development of sensory platforms for detection of biomolecules.

I have published 54 publications published in journals included in the **Web of Science's (WOS) (ISI)**, with **over 100** participations in international and national conferences (of which 10 were **invited, Keynote or plenary)**, **30** books/chapters of books, of which **10** as an author in international publishers and 9 in national publishers, **11** as an editor in national publishers.

Between **2007-2023,** I published **45 publications** indexed on the Web of Science's (WOS) (ISI), of which **33 as the main author** (first author and correspondence author) and **1 doctoral thesis**. **Index h = 16 (WoS)**, and the articles received **835 cities without self- citations** (27.07.2023), cumulative factor of the main author **FCIAP of 58,875**. The results of the research activities also materialized in the submission of two **patent applications.**

The publications were obtained, both as a result of **my own research topics**, as well as within the **research projects obtained through competition** as a director, but also as a **member of the research teams** in other national and international projects.

I am a **member of the Editorial of WoS Journals**, **Reviewer (Peer Reviewer) for WoS Journals** (verified on Publons, with WOS Impact Factor between 2.0 and 7,392) *and* ***reviewer for competitions of national and international projects****.*

My didactic and research activity has been completed by **coordination and organization** of scientific events:

1. **International Conference** "*Analytical and Nanoanalytical Methods for Biomedical and Environmental Sciences - IC-ANMBES*" (**co-president and chairman** of the Committee for organizing 6 editions during 2010 - 2022) (icanmbes.unitbv.ro).
2. **Summer School** "*8th International Student Summer School*" *Nuclear Physics-Science and Applications "(NUCPHYS-SC & APPL)*, 2017, Brasov, Romania (**responsible for Romania and chairman of the Organization Committee)**.

I am currently I am a **member of the professional associations**: Romanian Society of Pure and Applied Biophysics (Vice-President), European Biophytes Societies Association, Biophysical Society, Bioelectrochemical Society, Romanian Society of Physics.

In the third section (I.3) I presented, in the current scientific context, **the results of my research** within the biophysical laboratory for **the study of biomolecular interactions and the development of new diagnostic and therapy methodologies**. Below I will briefly present the topics addressed in this section.

I started from **studies published at national and international level** related to the **early detection** of important pathologies and the **monitoring of therapies**. **New methods of detection** are taken to be considered, as ***in vitro*** **molecular diagnosis,** with which to obtain it in an **easy, but more sensitive and precise way, identifying, quantifying, and monitoring biomolecules (biomarkers or drugs)**. **E*asy monitoring or self-monitoring*** of any administered drug is a **valuable tool for both early diagnoses**, but it can also provide real-time information to **adjust the therapy, nutrition, and physical activity** to achieve the highest bioavailability.

In **subsection (1)** I presented an **assessment** of *interactions and (bio) molecular reactions* that allowed **the *optimization of*** both ***the modification of the surfaces*** and ***the detection parameters*** for the subsequent development of *new sensory platforms* (for specific molecular detection), as well as ***studying the mechanism of binding of drugs to carriers*** (serum albumin) and the **stability of the albumin-drug complex** for **innovative therapeutic approaches**. Different sensory surfaces have been modified with thin layers of **polymers, enzymes** and **gold nanoparticles** that **mimic the activity of biological enzymes** (*gold nanozyme*).

In the case of developing the **systems of transport and delivery of drugs based on serum albumin**, studying their interaction mechanism with each drug is very important. The way of **achieving the immobilization of protein molecules** (*hydrodynamic vs. static*) **influenced** both the **conformation** of the protein and **the exposure of the binding sites to the drug**, unlike the molecules are free in the solution. **Other compounds** in circulation can also **influence the stability of the transporting protein – drug complex**. A **strong interaction** is **beneficial for the**

transport of the complex in the systemic circulation, but **the concentration of the free drug** (the active form of the drug in the cell) **decreases**, therefore these studies should be correlated with studies of controlled release and delivery of drugs in a targeted manner.

In **subsection (2)** I presented **the development and optimization of sensing methods** using the surface-modified sensor platforms optimized in subsection (1) and **the validation of sensor platforms** for substance detection. Gold **sensors** surface modified with **thin polymeric films** and enzyme, were used for **the detection and quantification of dopamine (DA)** ***in vitro***. Surface-modified electrochemical **biosensors** with **enzyme structures** have been optimized and used for ***in vitro*** **glucose detection**. Electrochemical **sensors** with **gold nanoparticles (AuNPs)** highlighted the catalytic role of AuNPs for the reactive species H_2O_2, by **mimicking the activity of the peroxidase enzyme**, thus acting as an **artificial enzyme, named gold nanozyme**. Thus, these nanosensors offered **a faster and simpler alternative** for H_2O_2 dosing, compared to classical methods, but also **the evaluation of the total antioxidant capacity** of some biological samples (exemplified by plant extracts obtained by us). **Validation of sensory platforms was done *in vitro* on real samples** (drug solutions). The research shows that the development of **electrochemical sensors and biosensors with nanomaterials as detection and quantification platforms** for biomarkers and/or drugs can open the possibility of **developing new and innovative devices** that allow **the detection and monitoring of therapy at the point of care** (POC).

In **the second part** of the thesis, I presented **the plans for the evolution and development of the professional and scientific career**. The development **plan** of my university career aims at the **successful interweaving of didactic activities and interdisciplinary scientific research in the field of biomedical research and the translation of research results into medicine**. I propose to achieve as many of the didactic and scientific objectives that fall to me both from the role of teacher and researcher, and to **promote the maintenance and increase of standards** of academic and professional excellence, as well as **collaboration** with colleagues and students.

For the future, I propose the **continuation** of the scientific activity carried out so far, but also **the opening of new research directions**. **The main goal** of future research is in **the field of nano- and biomedical science research,** which involves **combining the knowledge of *biophysics, bionanotechnology, nanomedicine and preclinical medicine***, considering the current national and international state of research and the achievable goals in the near and long future. As **biological interactions occur at the nanoscale**, nanotechnology opens numerous opportunities. **Nanomedicine** is the medical application of nanotechnology. This ranges from ***medical applications of nanomaterials and biological devices*** to possible future applications of ***molecular nanotechnology*** such as ***molecular machines = nanomachines*** (molecular motors, switches, and logic gates).

The proposed research plan will be divided into ***three main, interdisciplinary directions***, considering previous experience and expertise, but also ongoing projects:

A. Development of non-invasive biodetection systems.

B. Development of systems for targeted administration of therapeutic factors (nanotherapeutics) and
C. Highlighting of interactions involving proteins and nanoparticles.

In **the third part** of the thesis, the bibliographic references used in the first part are presented.