TEZĂ DE ABILITARE

Abordări inovatoare pentru noi metodologii de diagnostic și terapie

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florescum@unitbv.ro

Universitatea Transilvania din Brasov, Romania
Facultatea de Medicina

Cuprins

Principalele realizări ştiinţifice şi academice

I. Experiență didactică și științifică

I. Scurt CV – Educație

1988 -1993: Universitatea din București, Facultatea de Fizică.	
Specializare Biofizică	*(4 semestre)*

2000-2001: Universitatea Transilvania din Brașov, România,	
Curs postuniversitar de specializare. Subiect: "Monitorizarea calității mediului".	Diploma post universitară

2007: Universitatea din București, Facultatea de Fizica,	
Doctor în Fizică, *Summa cum laude*.	„Metode biofizice de detecție a compușilor biologic activi".

2020: Universitatea Transilvania din Brasov:	
Doctor în Medicină, *Summa cum laude*	„Contribuții la dezvoltarea bioinstrumentelor și aplicațiile acestora în medicină".

I. Scurt CV - Evoluție profesională

1994 - 1998: Liceul Nicolae Titulescu, Brașov

Poziția: Profesor titular, definitivat în învățământ

1998 - 2018:

Universitatea Transilvania din Brașov, Facultatea de Inginerie Tehnologică, Catedra de Fizică.

Poziția: *Asistent universitar*, *Sef de Lucrări*,

2018 - în prezent:

Universitatea Transilvania din Brașov, Facultatea de Medicină, Departamentul Disciplinelor Fundamentale, Profilactice și Clinice.

Poziția: *Conferențiar universitar*

I. Scurt CV - alte cursuri (activitate didactică)

2022: The Catholic University of Ávila, Spain.

- VI Online e-learning seminar for university professors,

2017: Transilvania University of Brasov, Romania

- **Training program** "Developing academic abilities of teaching staff - Conditions of academic success".

2007: Transilvania University of Brasov, Romania.

- **Training program** "Interactive methods for teaching-learning-evaluation process"

2004-2005: Transilvania University of Brasov, Romania:

- **Specialization Curs** „Web Based Trainers – Wide Open Resourse for Learning and Development".

2001: Aug. 2001, Mangalia, Romania.

- **International Summer School**, "Cultural and organizational change in university teaching"

I. Scurt CV - alte cursuri (activitate științifică)

2012: Carol Davila University of Medicine, Bucharest, Romanian Society of Pure and Applied Biophysics. October 25-27.

- **International Course** "Electroporation for Medicine: Basic Knowledge, Applications and Technologies"

2022; Innovation Labs program, Bucharest, Romania

- University research spin-off for effective technology transfer,

2005: Babes-Bolyai University, Sept. 2005, Cluj-Napoca, Romania.

- **International Summer School**, "NANOMA 2005" - Physics and Chemistry of NANO-Materials Preparation, Analytics, Theory, and Applications

2003: SRBPA, Oct. 2003, Gaiser, Romania.

- **International Autumn School of Biophysics**, "Non-invasive Biophysical Methods and their application in Biology and Medicine"

I. Scurt CV - Stagii de cercetare internațională și burse

Doctorat

2005-2006: **"Universidade de Coimbra",** Coimbra, Portugal. Prof. Dr. Christopher M.A. Brett.

- PhD Research Internship

2002-2003**: Universidade de Coimbra**", Coimbra, Portugal. Prof. Dr. Christopher M.A. Brett

- Erasmus PhD Scholarship

2002: PhD "**Institut für Chemo- und Biosensorik**", Münster, Germany.

- Short-term scholarship DAAD (German Academic Exchange Service)

I. Scurt CV - Stagii de cercetare internațională și burse

Stagiu postdoctoral

- 2007-2008**: University of Wisconsin-Milwaukee,** Department of Physics, Laborator of Biophysics, WI, USA.

Burse postdoctorale

2015: **University of Twente**, Institute for Nanotechnology (MESA+), Microfluidics for nanomedicine, Enschede, Olanda. Prof. Dr. Séverine Le Gac.

- Short-Term Scientific Mission, COST TD 1104 Action - EP4Bio2Med, European network for development of electroporation-based technologies and treatments.

2012: **University of Texas-Dallas**, Nanoscale Integration Lab, Dallas, USA. Prof. Dr. Walter Hu

- Research Internship: (Nano-biosensors development using SiNW-FET)

I. Scurt CV – prelegeri invitate (didactice)

Prelegeri invitate

- Programul ERASMUS:
  - International Seminars in Biosciences, 2024, University of Ljubljana, Slovenia
  - Școala de vară Bioanalitycal methods for life sciences, 2009-2010", Brașov, România.
  - Mobilități in Germania, Portugalia, Turcia, Portugalia, Slovenia
- Programul CEEPUS
  - Școala de vară în “Modern Analytical and Bioanalytical Methods”, 2010-2011", Pardubice, Cehia.
  - Scoala de Vara „Classic and modern methods for molecular diagnostics in human pathology„ 2010-2011", Brașov, România

I. Scurt CV – prelegeri invitate

Prelegeri invitate

Conferințe internaționale **(selecție)**

- 9th International Workshop on Materials Physics (IWMP), 14-16 May 2024, Magurele-Ilfov, Romania. **Invited Presentation**
- 6th International Symposium on Nanoparticles and Nanomaterials and Applications, ISN2A 2024, 22 – 25 January 2024, Caparica. Portugal. **Keynote Presentation**.
- 14th International Conference on Processes in Isotopes and Molecules, 19 - 22 September 2023, Cluj-Napoca, Romania. **Plenary Presentation**.
- The 8th Annual Conference of AnalytiX, July 12-14, 2023, Amsterdam, The Netherlands. **Invited Presentation.**
- 5th International Symposium on Nanoparticles and Nanomaterials and Applications, ISN2A 2022, 24 – 27 January 2022, Caparica. Portugal. **Invited Presentation**.
- 13th International Conference Processes in Isotopes and Molecules, 22-24 September 2021, Cluj-Napoca, Romania. **Invited Presentation.**
- 12th International Conference on Processes in Isotopes and Molecules, 25-27 September 2019, Cluj-Napoca, Romania. **Plenary Presentation**.
- International Conference on Analytical Chemistry 2014, Târgoviște Romania, **Prezentare keynote**.

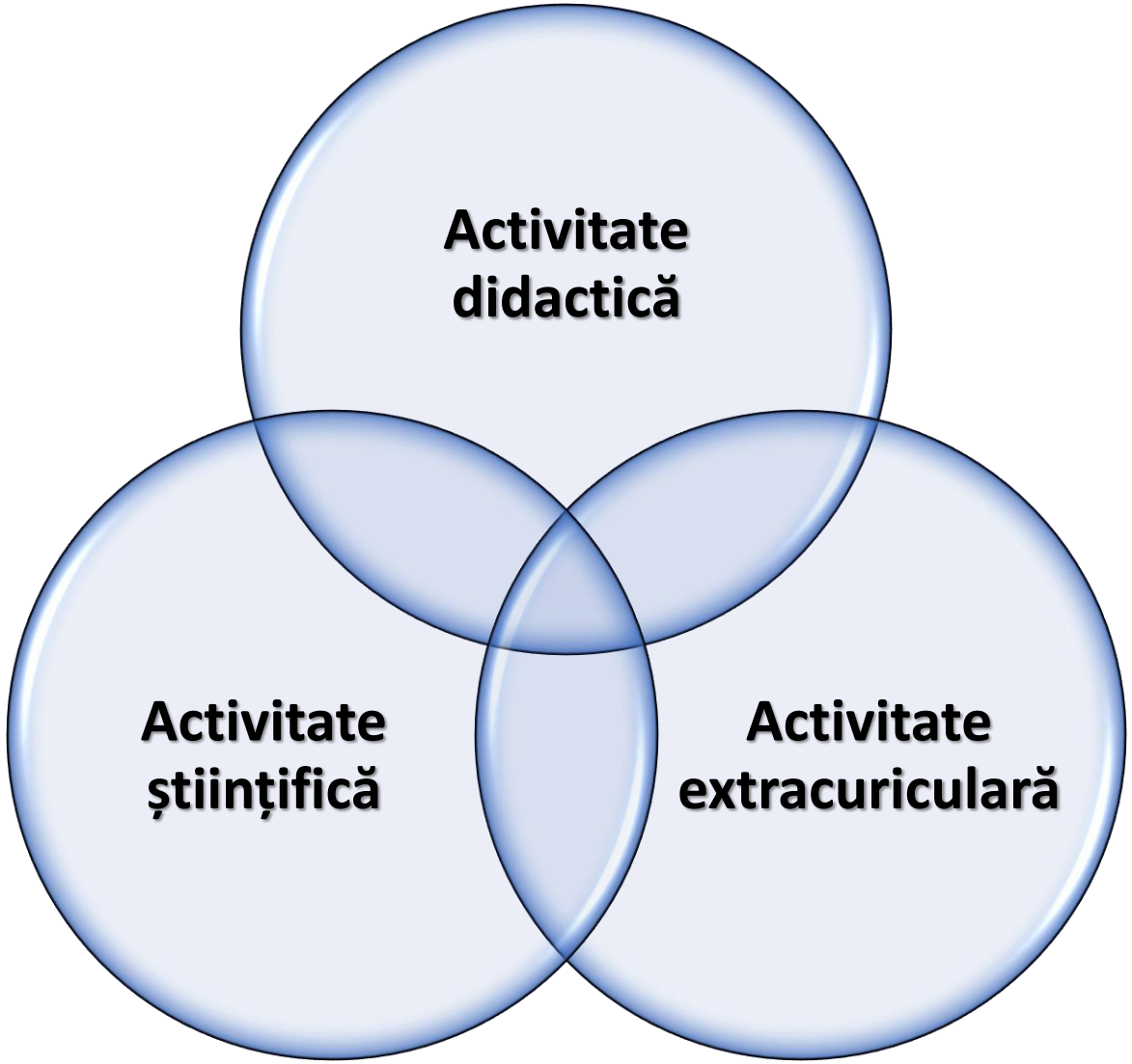
I. Scurt CV - Premii

- 2022: The best poster, 5th International Symposium on Nanoparticles, Nanomaterials and Applications, ISN2A 2022, Caparica, Portugal.
- 2016: Best Poster Award at IC-ANMBES 2016, Brasov, Romania
- 2015: Best paper awarded by Romanian Society of Pure and Applied.
- 2009: Award for outstanding publication in ISI journal, Transilvania University, Brasov, Romania.
- 2007: Best Oral Presentation Award at ICSAM Conference-2007, Patras, Grecia

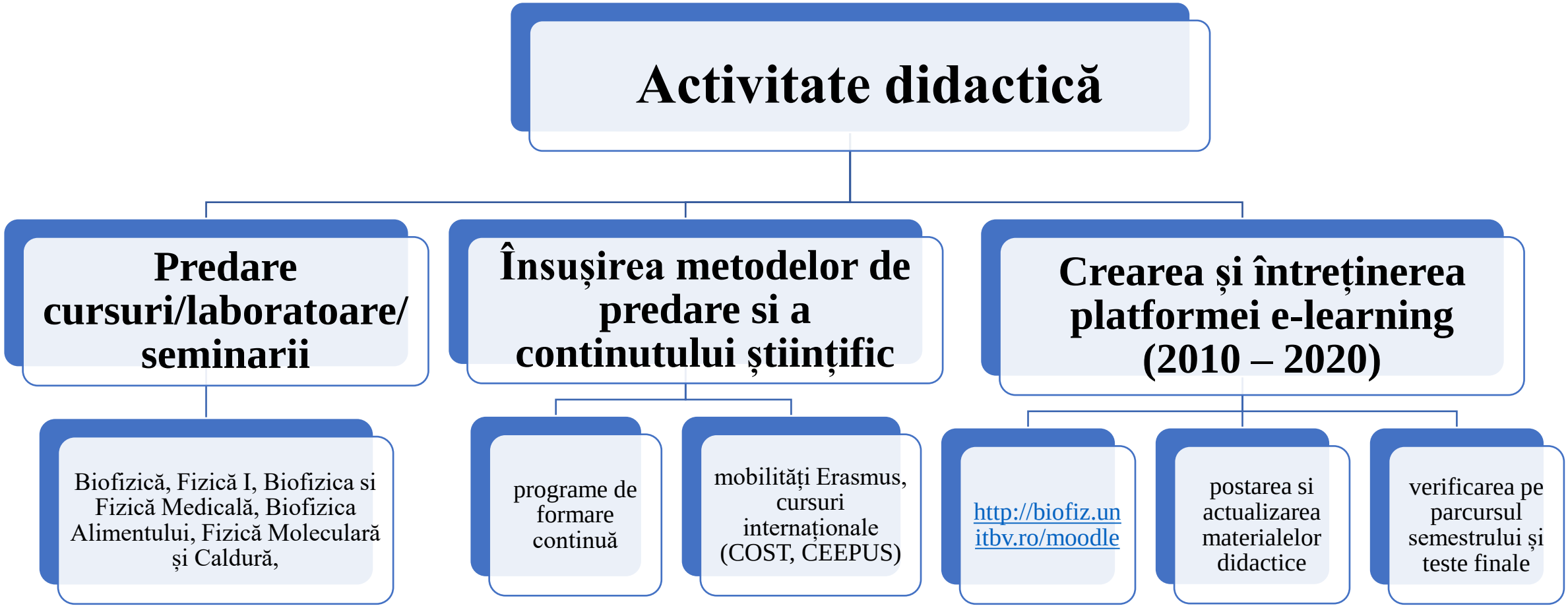
I. Scurt CV - Experiență managerială

Proiect Director/Responsabil proiect	Perioada:
PN-III-proiectului experimental demonstrativ, PN-III-P2-2.1-PED-2021-1323, nr. 582PED/2022	2022 – 2024
Joint research project with IUCN Dubna, Contract. no. 89 of IUCN Order no. 365/11.05.2021	2021
PN-III-Proiecte de cercetare complexe, PN-III-P1-1.2-PCCDI2017-0062, nr. 58/2018	2018-2020
Responsabil pentru România in cadrul comitetului de conducere al COST Action CA15126: *Between Atom and Cell: Integrating Molecular Biophysics Approaches for Biology and Healthcare* (MOBIEU)).	2018 -2020
PN-II –Tinere Echipe PN-II-RU-TE-2014-4-2801, nr 199 din 01/10/2015.	2015-2017
MCI Contracte (4) de finanţare a manifestărilor ştiinţifice şi evenimentelor asociate, IC-ANMBES, 48M/26.05.2010, 18M/08.05.2014, 48M/08.05.2016, nr. 10M/18.05.2018	2010-2018
Grant RO–JINR Dubna: Responsible person for Romania and Chairperson of the Organizing Committee of 8th International Student Summer School “Nuclear Physics – Science and Applications” (NUCPHYS-SC&APPL).	2017
PNCDI2-Parteneriate nr 72-172. 01.10.2008 - TIPSARMER”,	2008-2011

I. Realizări (2007 – 2024)



I. Realizări - Activitate didactică



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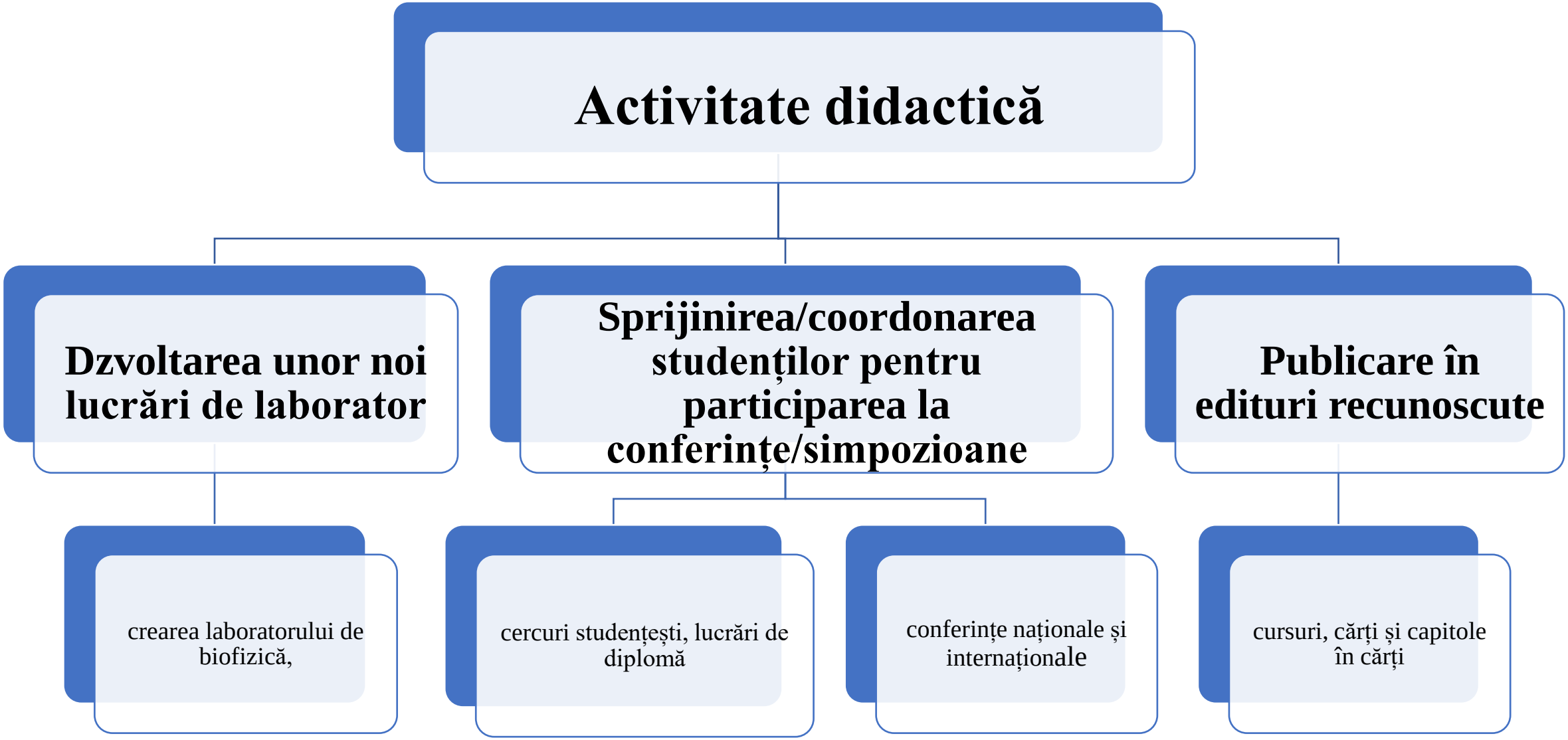

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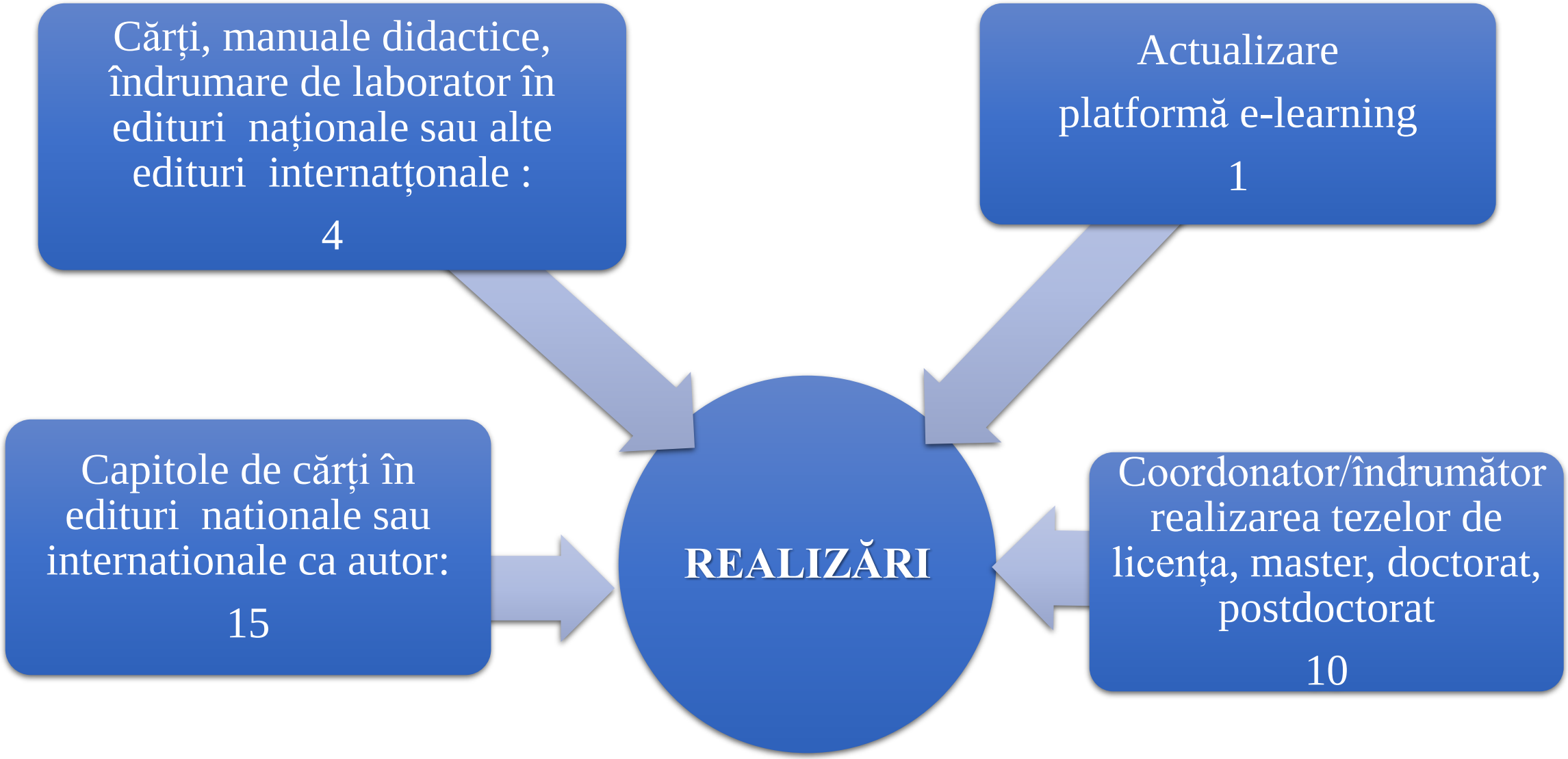
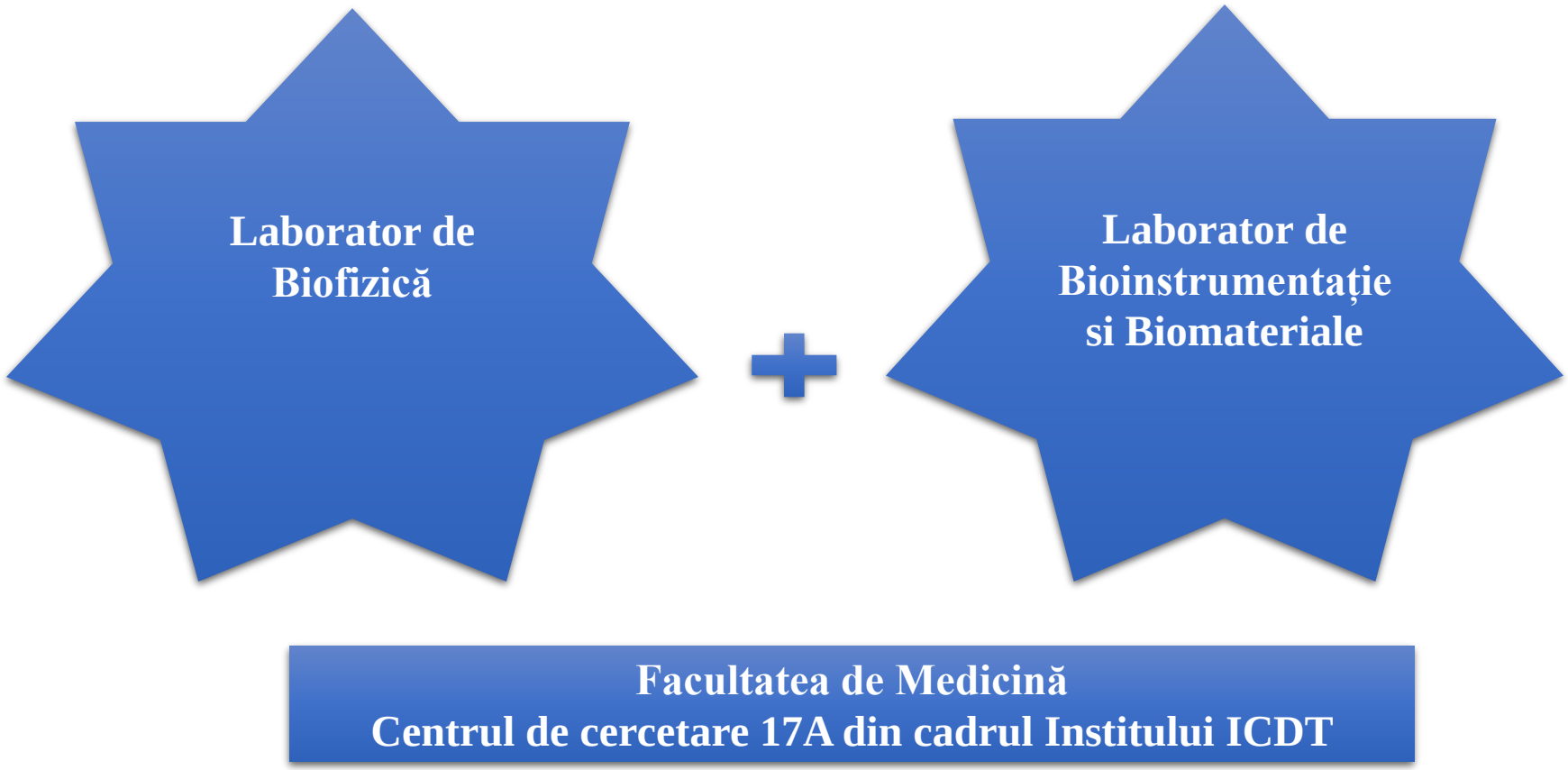
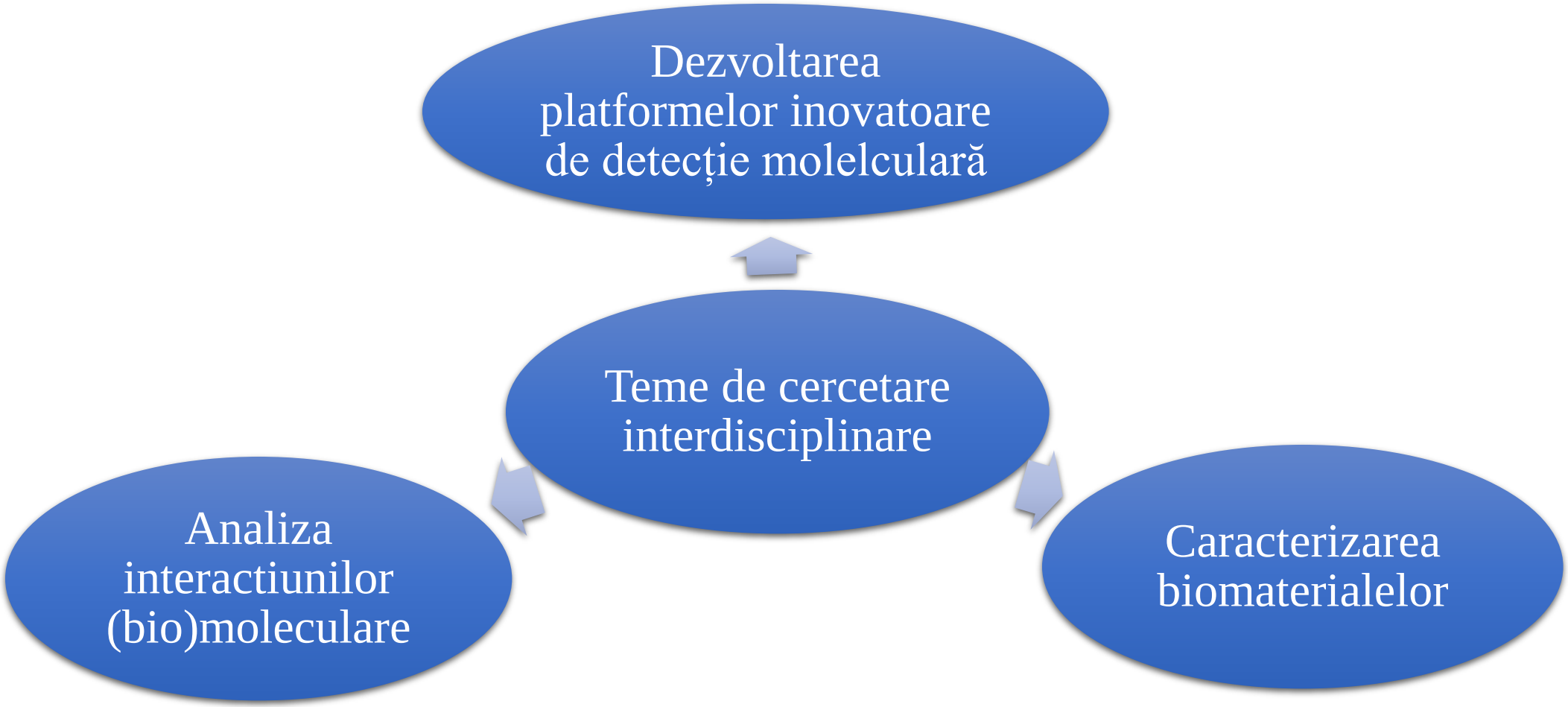


I. Realizări - Activitate de cercetare



I. Realizări - Activitate de cercetare
- biofizică, electrochimie, chimie analitică, biosenzori și bionanotehnologie -



I. Realizări - Activitate de cercetare

Membru în comitetul editorial al :

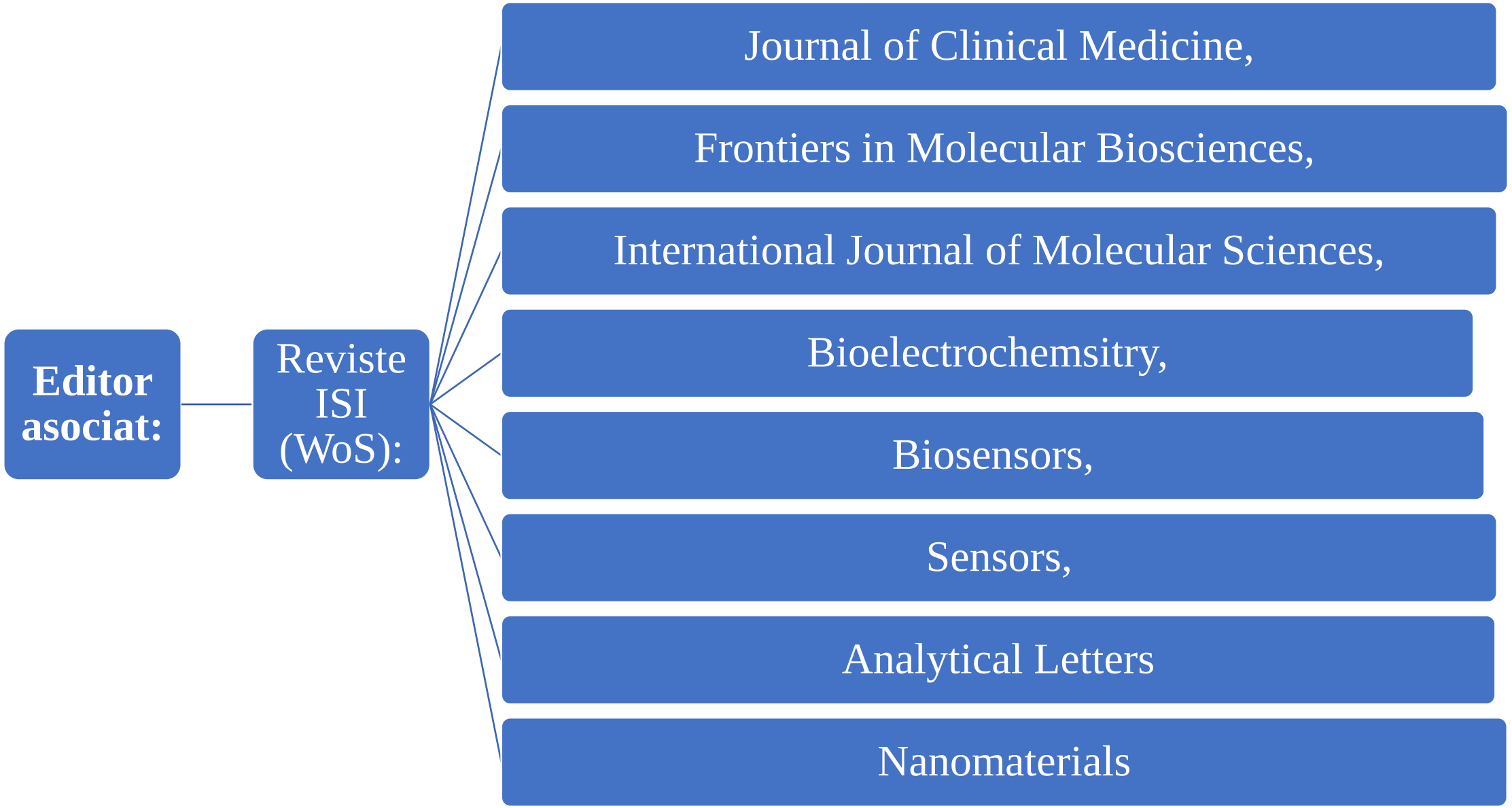
Reviste ISI (WoS):

- Frontiers In Molecular Biosciences
- Journal of Clinical Medicine
- Analytical Letters

Reviste BDI (PubMed)

- Medicines

I. Realizări - Activitate de cercetare



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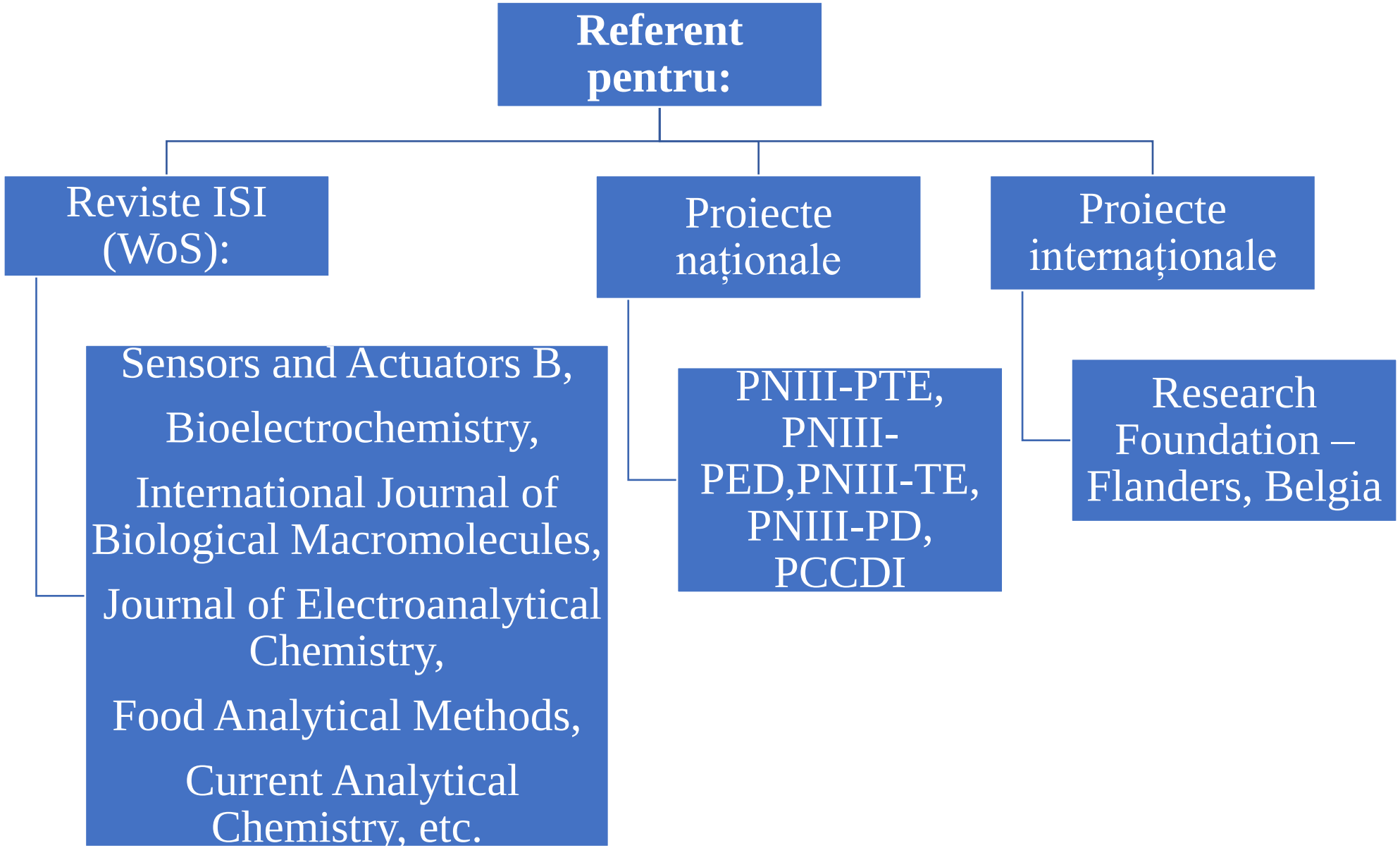

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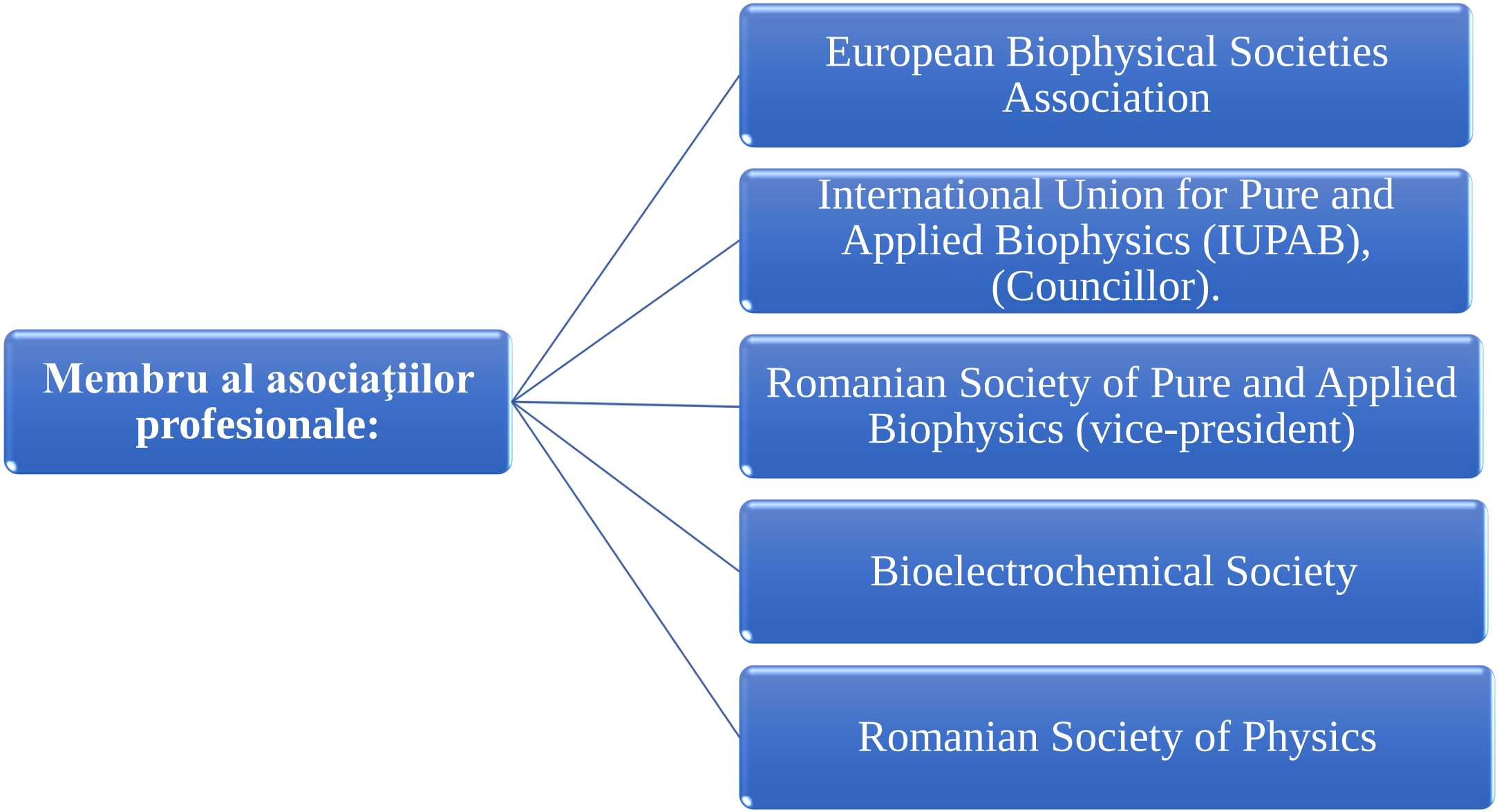


I. Realizări - Activitate de cercetare

Participare în proiecte

Coordonare a 10 proiecte de cercetare:		Membru al echipelor de cercetare in proiecte naționale și internaționale:
Director:	Responsabil din partea Universității Transilvania Brașov:	**11**
7	**3**	

I. Realizări – Activitate de cercetare

Proiecte de cercetare	**2022-2024: UTBv** Project responsible of **complex research project:** PN-III-P2-2.1-PED-2021-1323	Noi nanostructuri proteice hibride pentru direcționarea specifică în celulele tumorale ale colonului - **Prot-Col-Target.**
	2018-2020: UTBv Project responsible of **complex research project:** PNIII-P1-1.2-PCCDI-2017-0062	New diagnostic and treatment methodologies: current challenges and technological solutions based on nanomaterials and biomaterials – **SANOMAT.**
	2022: Joint research project with IUCN Dubna	Development and characterization of composite nanomaterials by means of Raman, SERS, CARS, AFM and electrochemistry to highlight their interaction with specific biomarkers
	2017: Grant RO–JINR Dubna: Responsible person for Romania and Chairperson of the Organizing Committee of	8th International Student Summer School "Nuclear Physics – Science and Applications" **(NUCPHYS-SC&APPL),** 2017, Brasov, Romania**.**
	2015 -2017: Director of **research project : PN-II-RU-TE-2014-4-2801.**	Cercetări privind detectarea substanțelor bioactive din extracte de resurse vegetale cu capacități antioxidante - **VEDETAX.**
	2010-2022: **Co-Chairperson and organizer**, Member of International Scientific Committee.	International Conference on Analytical and Nanoanalytical Methods for Biomedical and Environmental Sciences "**IC-ANMBES 2010-2022**" http://icanmbes.unitbv.ro/
	2008 -2011: Director of **research project:** No. 72-172/2008	Tehnici de înaltă precizie și sensibilitate aplicate în rețelele de biomonitorizare de poluare a mediului cu factori de poluare din regiunile de dezvoltare de sud, sud-est și centrale din România – TIPSARMER.

I. Realizări - Activitate de cercetare

Rezultate: articole stiintifice publicate in reviste de specialitate naționale si internaționale:

2004 – 2024: **57 articole** si rezumate publicate (53 in reviste cu cotatie ISI - Clarivate Web of Science (WoS)),

2007 – 2024: **46 lucrări** din care **33 în calitate de autor principal** (prim autor și autor de corespondență), **1 teză de doctorat**.

16 articole publicate în reviste cotate BDI,

11 lucrări publicate in extenso în volumele unor conferinţe ştiinţifice internaţionale si nationale cu editori, ISBN şi edituri internaţionale,

110 participari la conferinte internationale si nationale,

95 la conferinte internationale

15 la conferinte nationale,

publicare 30 carti/capitole de carti:

19 ca autor:

10 in edituri internationale si

9 in edituri nationale,

11 ca editor in edituri nationale

peste 900 de citari în reviste cotate ISI Clarivate Web of Science's (WoS)

I. Realizări - Activitate de cercetare

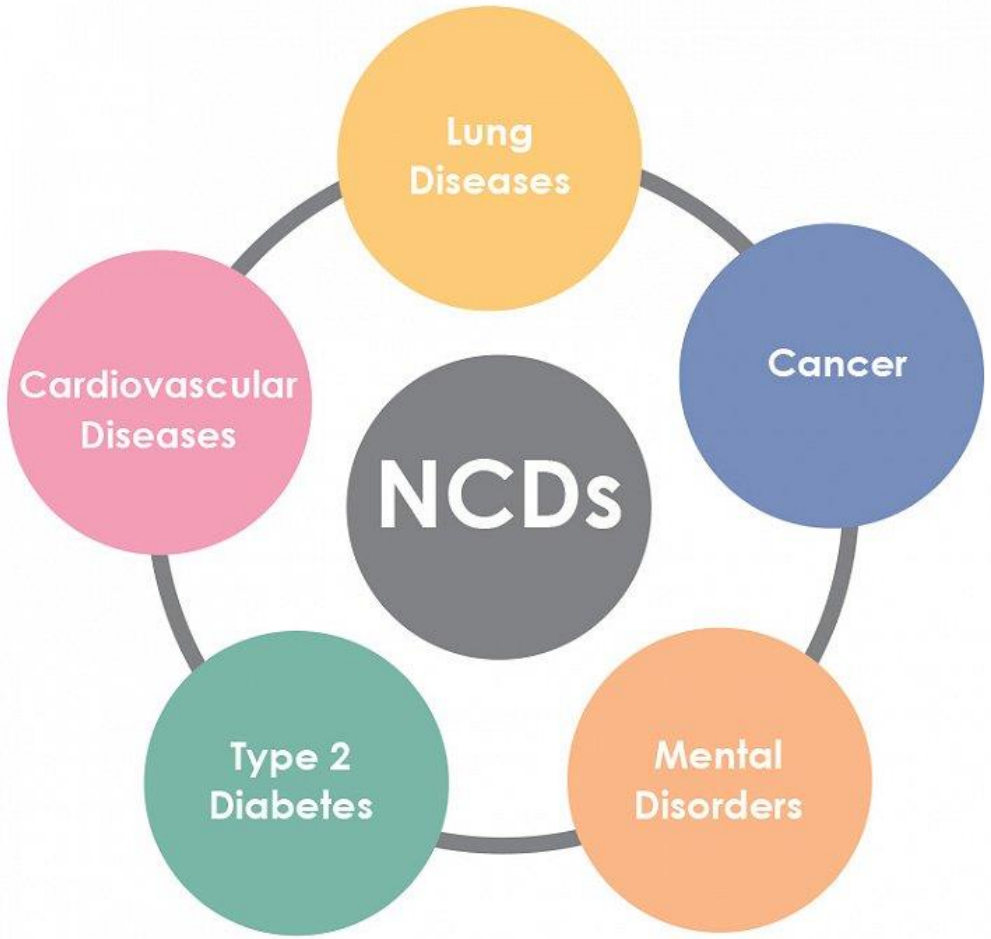
Dezvoltarea platformelor de detecție a biomoleculelor

Dezvoltarea nano(bio)senzorilor pentru diagnostic și monitorizarea terapiei

- Detecția și cuantificarea: biomarkerilor , medicamente, ionii metalelor grele, vitamine, capacitatea totală antioxidantă

Early diagnosis and screening

Chronic, non-communicable (NCD) diseases have a long duration and generally slow progression.



❖Selective **identification of biomarkers** will allow **early detection** of chronic diseases.

- ❖Neurodegenerative diseases
- ❖Diabetes
- ❖Thyroid diseases

❖**Easy** medication **monitoring** will enable personalized therapy.

❖The abnormal **oxidative status** assessed by circulating biomarkers was associated with patients with chronic diseases.

Early diagnosis and screening

Chronic diseases screening and monitoring

Currently,

- the diagnosis is mainly done through clinical observations, and expensive laboratory serum tests.
- The monitoring of treatment (medicine) intake is done through clinical observations !

It is done to a small extent:

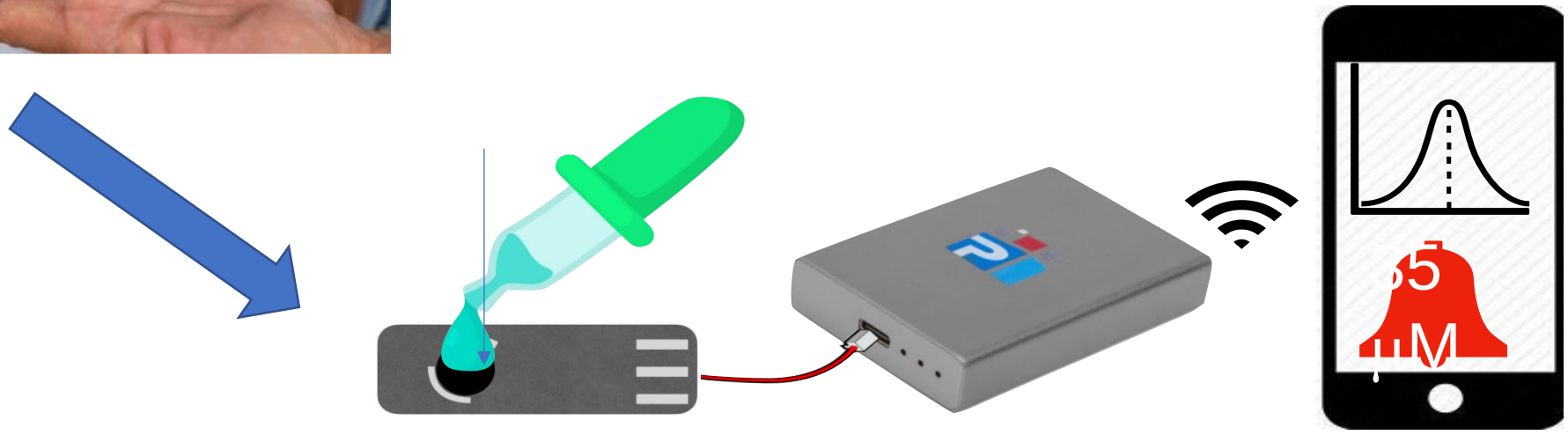
- early diagnosis of chronic diseases,
- monitoring the treatment of chronic diseases

Transilvania University of Brașov
FACULTY OF MEDICINE

Early diagnosis and monitorin

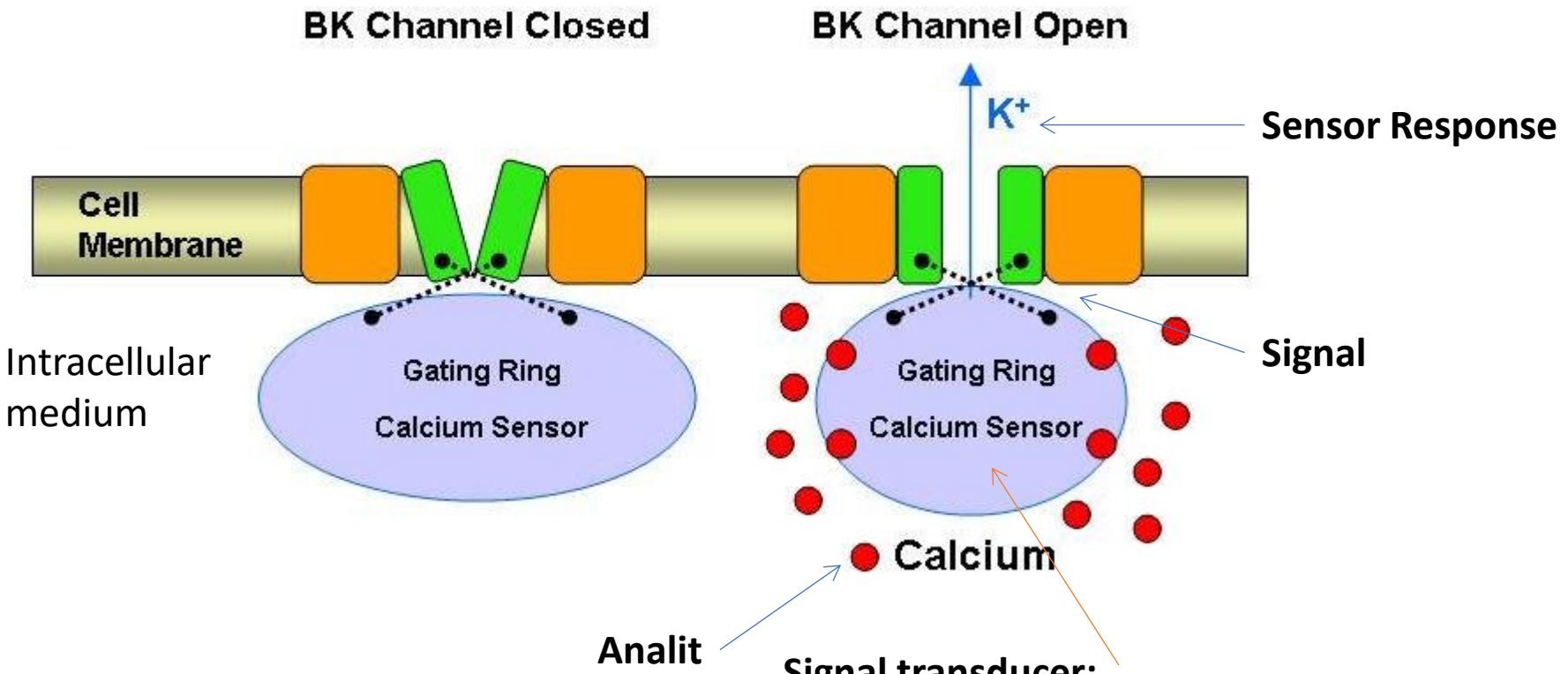
Our solution = ideas for sensing assays using integrated portable platform

Sample



Sensors

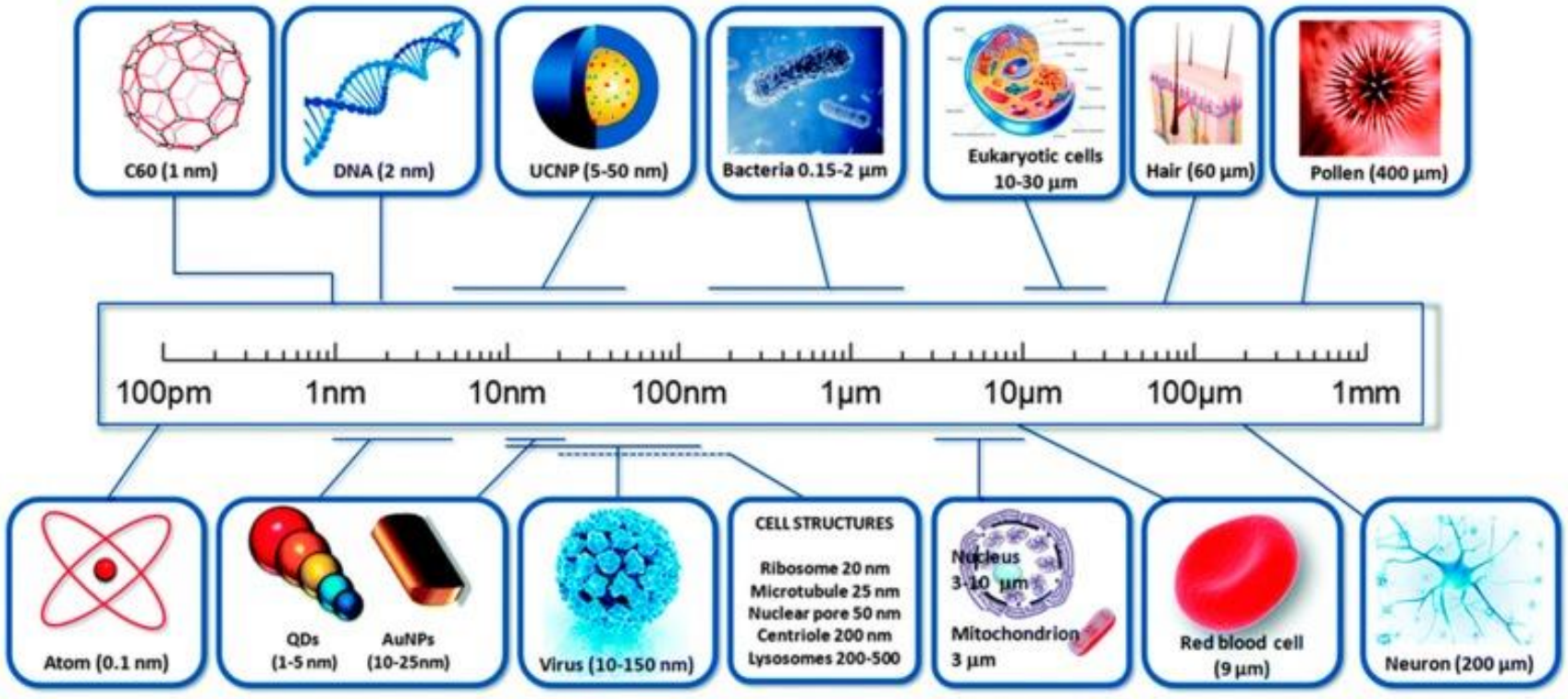
Biological sensors
Control of ion channels



https://news.softpedia.com/news/How-Major-Human-Biological-Sensors-Work-204628.shtml

Nanotechnology and nanomaterials

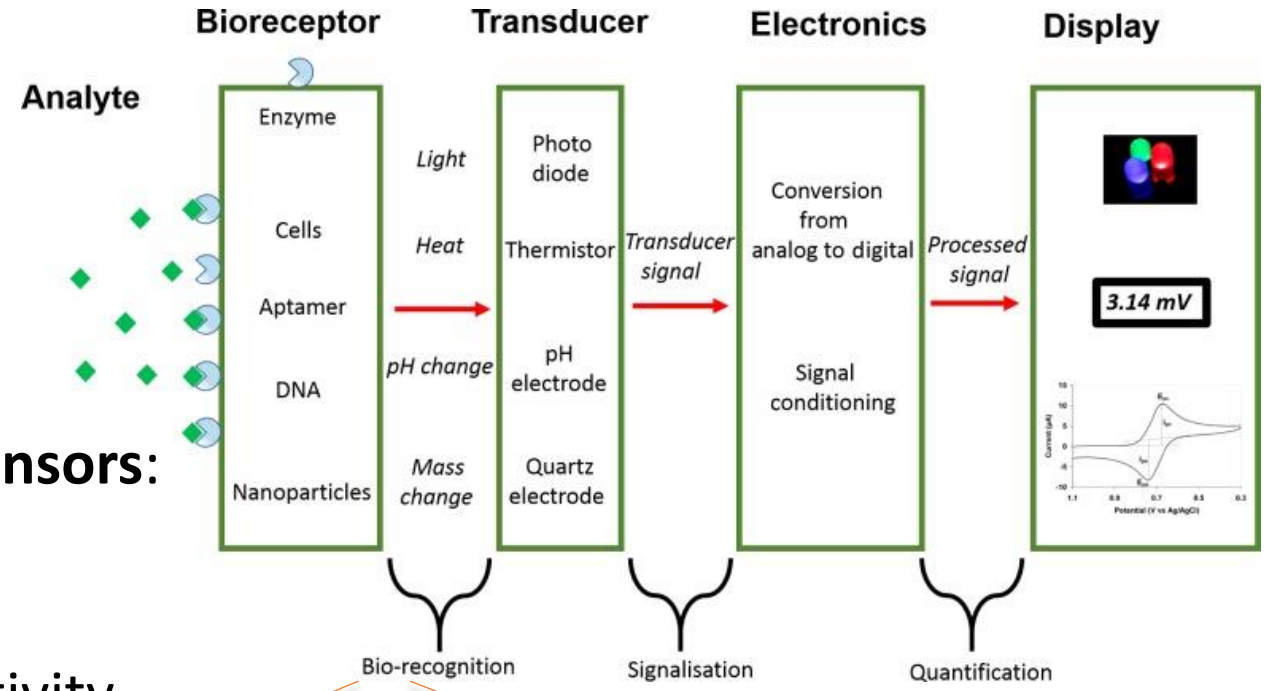
1959: Nobel Prize laureate Richard Feynman **introduce the concept of nanotechnology**. Feynman Hypothesis: "Why can't we write the entire 24 volumes of the Encyclopedia Britannica on the head of a pin?" and described a vision of using machines to construct smaller machines and down to the molecular level.



Chem. Soc. Rev. 2015;44:1561–1584

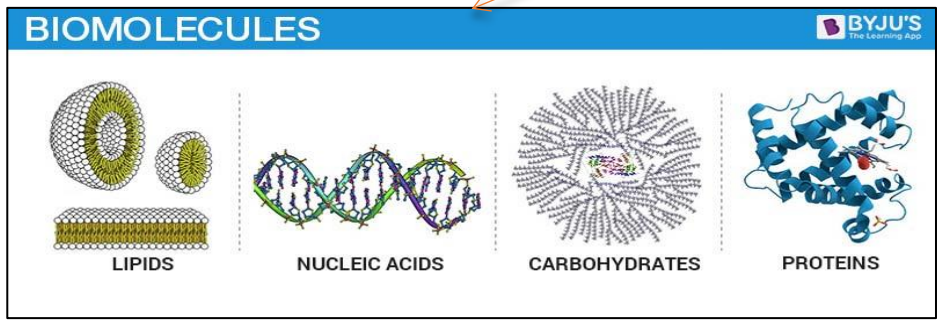
Sensors, Biosensors and Nanosensors

Nanosystems based on nanomaterials use the unicity of the properties **of biological (biomolecules) and physical (artificial) nanomaterials** in the **specific recognition** of a target molecule (analyte).

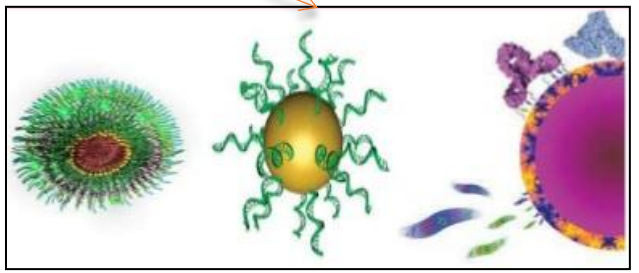


Advantages of nanomaterials-based (bio)sensors:

- can detect **low levels** of analytes,
- they responded **quickly in real time**,
- **very high** sensitivity, specificity and selectivity,
- **small** size, for **portable** devices.



NANOMATERIALS



Some of nanoparticles show *oxidase-, peroxidase- and catalase-like activity* = **nanozyme**

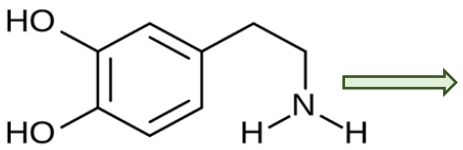
Biosensors and nanomaterials-based sensors and their applications

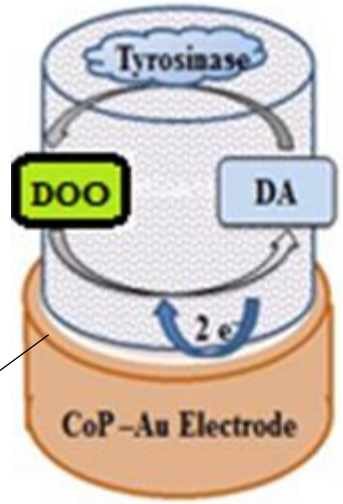
- How biophysical methods can help biomarker and drug detection-

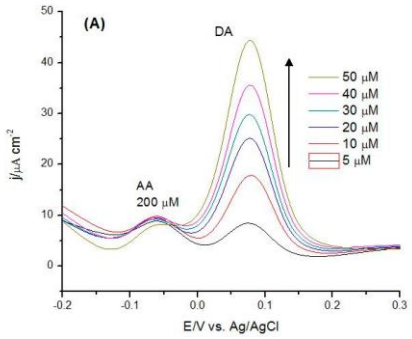
Enzyme based biosensors - Tyr

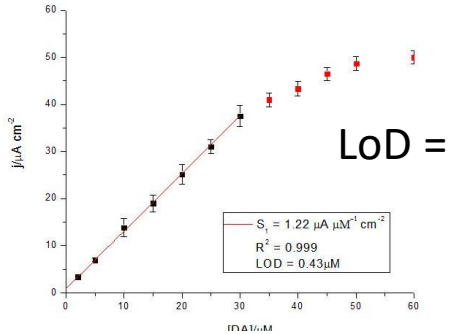
- **Tyrosinase** (Tyr) immobilization: on the surface of the cobalt (II) porphyrin (CoP) film-modified sensor by intermolecular cross-linking (GA).

Dopamine (DA)



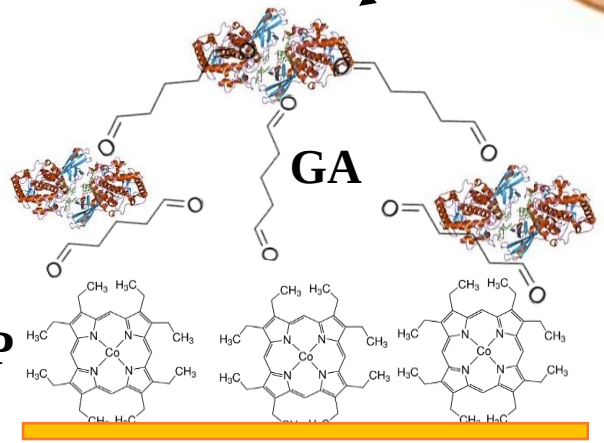






LoD = 0.43 μM

Sensor	DA Specified/μM	DA Found/μM	$\overline{\text{DA Found}}$/μM	Recovery (%)
CoP-Tyr	3.00	3.43	3.10 ± 0.32	114
	3.00	2.79		93
	3.00	3.09		103



Detection of DA in dopamine hydrochloride medication

sensors

MDPI

Article

Tyrosinase-Based Biosensors for Selective Dopamine Detection

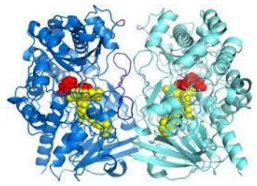
Monica Florescu * and Melinda David

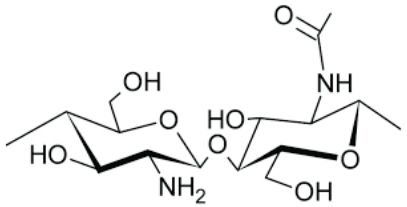
Faculty of Medicine, Transilvania University of Brasov, 500019 Brasov, Romania; melinda.dav@gmail.com
* Correspondence: florescum@unitbv.ro; Tel.: +4-0742-663-420

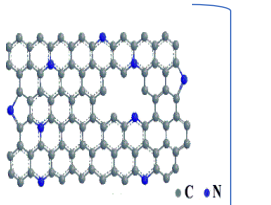
Academic Editor: Alexander Star
Received: 3 May 2017; Accepted: 1 June 2017; Published: 7 June 2017

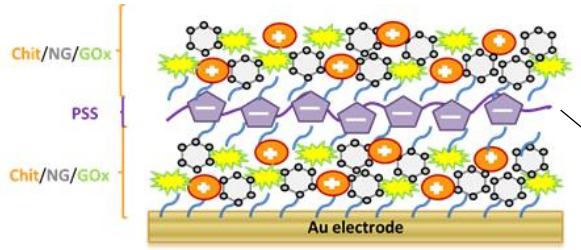
Enzyme based biosensors - GOx

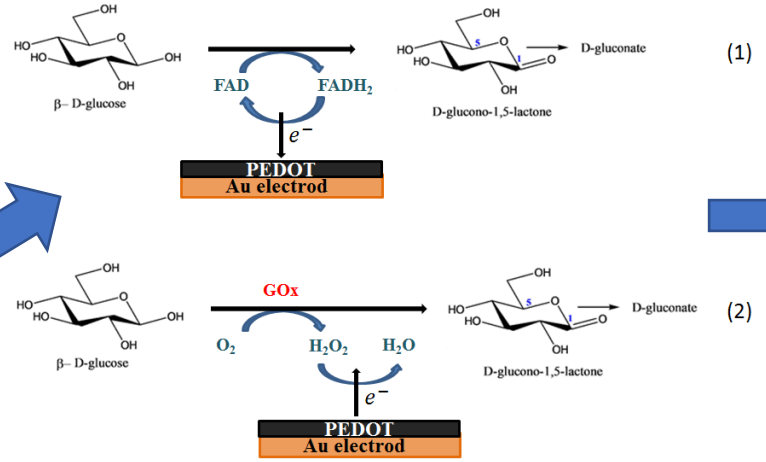
- **Glucose oxidase (GOx)** immobilization: on the surface of the PEDOT-modified sensor by Layer-by-Layer electrostatic adsorption (entrapment within **chitosan biopolymer (Chit)** and **nitrogen doped graphene (NG)).**

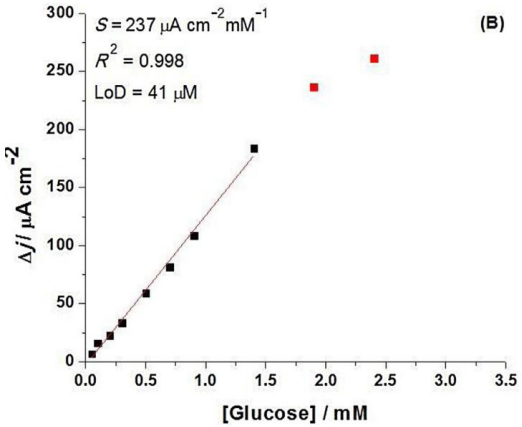

GOx


Chit


NG







Metoda	Au/PEDOT/{chit⁺(NG+GOX)}₂	Metoda spectrofotometrică Böhringer	Recuperarea (%)
Glucoză (g l⁻¹)	2,69± 0,30	2,83± 0,34	105
	2,35± 0,24	2,29 ± 0,17	97
	2,25± 0,14	2,27 ± 0,12	101

Detection of glucose in wine

ors B 255 (2018) 3227–3234

LoD = 41 μM

Contents lists available at ScienceDirect

Sensors and Actuators B: Chemical

journal homepage: www.elsevier.com/locate/snb

Research Paper

Improved glucose label-free biosensor with layer-by-layer architecture and conducting polymer poly(3,4-ethylenedioxythiophene)

Melinda David[a,b], Madalina M. Barsan[a], Christopher M.A. Brett[a], Monica Florescu[b,*]

[a] Department of Chemistry, Faculty of Sciences and Technology, University of Coimbra, 3004-535 Coimbra, Portugal
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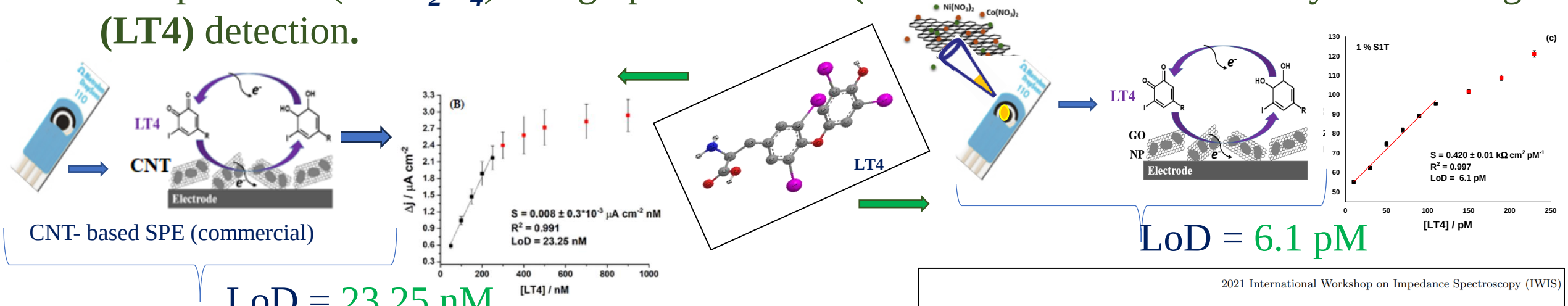
Carbon nanoparticle-sensors for LT4 detection

- **Sensors carbonic nanoparticles (**carbon nanotubes **(CN)** and bimetallic spinel oxide nanoparticles (***$NiCo_2O_4$***) on graphene oxide **(GO))** platforms for levothyroxine drug **(LT4)** detection**.**



CNT- based SPE (commercial)

LoD = 23.25 nM

LoD = 6.1 pM

Journal of Electroanalytical Chemistry 911 (2022) 116240

Contents lists available at ScienceDirect

Journal of Electroanalytical Chemistry

journal homepage: www.elsevier.com/locate/jelechem

Electrochemical quantification of levothyroxine at disposable screen-printed electrodes

Melinda David [a], Adrian Şerban [a], Teodor Adrian Enache [b], Monica Florescu [a,*]

[a] Transilvania University of Brasov, Faculty of Medicine, Universitatii Str. No. 1, Building C, Room CI30, Brasov 500068, Romania
[b] National Institute of Material Physics, Atomistilor 405A, Măgurele, 077125, Romania

Detection of LT4 in fetal bovine serum

2021 International Workshop on Impedance Spectroscopy (IWIS)

An Impedimetric Sensor for Levothyroxine Detection towards Point of Care Applications

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IEEExplore, *(IWIS)*, 2021, 99-103

Functional nanostructured materials and their applications

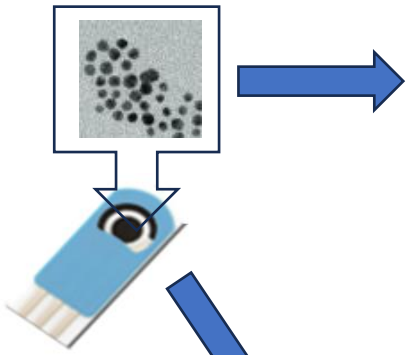
- Nanozyme-based sensors for total antioxidant capacity-

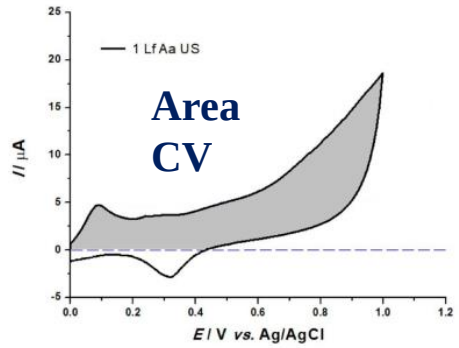
AuNPs-based sensors for total antioxidant capacity

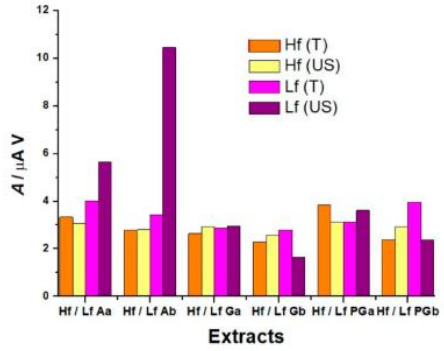
*Sensors with commercial gold nanoparticles (**AuNPs**) for **catalytic activity***

- **CV anodic areas** (A) of **antioxidants** can be corelated with the reducing power of the antioxidants,
- EI = quantification of the "total natural antioxidants" (samples with vitamine C) or "total polyphenols"

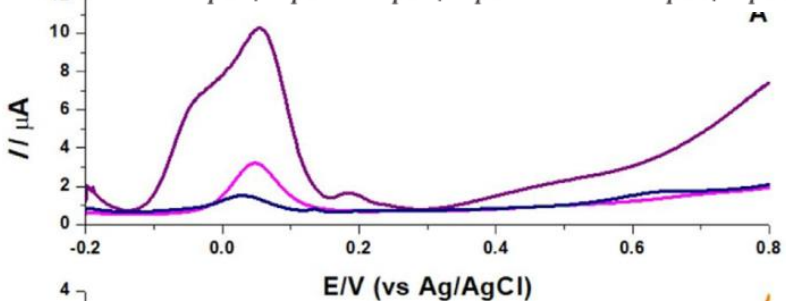
AuNPs-SPE

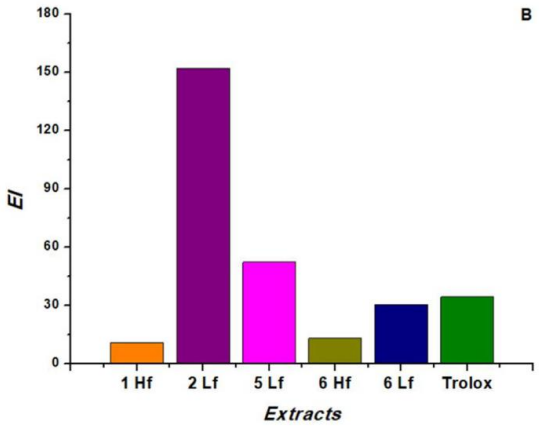






$$EI = I_{pa1}/E_{pa1} + I_{pa2}/E_{pa2} + ... + I_{pan}/E_{pan}$$





sensors
MDPI
Article

A Nanoparticle-Based Label-Free Sensor for Screening the Relative Antioxidant Capacity of Hydrosoluble Plant Extracts

Melinda David [1], Adrian Şerban [1], Claudia V. Popa [2] and Monica Florescu [1,*]

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2 Department of Organic Chemistry, Biochemistry and Catalysis, University of Bucharest, Sos. Panduri 90-92, 050657 Bucharest, Romania; popa_vali2006@yahoo.com
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Bioelectrochemistry 129 (2019) 124–134
Contents lists available at ScienceDirect
Bioelectrochemistry
journal homepage: www.elsevier.com/locate/bioelechem
ELSEVIER

Bioelectrochemical evaluation of plant extracts and gold nanozyme-based sensors for total antioxidant capacity determination

Melinda David [a], Adrian Serban [a], Cristiana Radulescu [b], Andrei Florin Danet [c], Monica Florescu [a,*]

[a] Faculty of Medicine, Transilvania University of Brasov, Colina Universitatii nr 1, Corp C, room CI30, Brasov 500068, Romania
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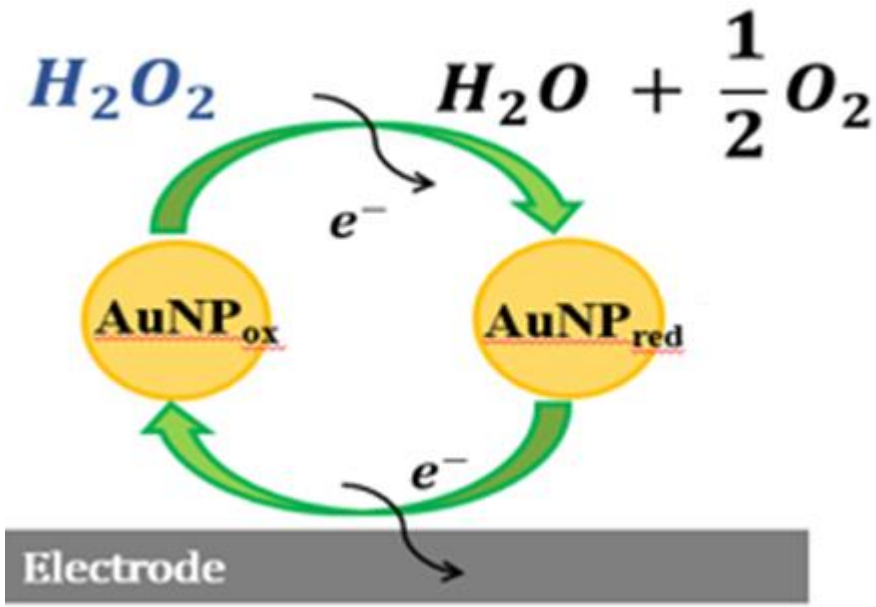
[c] Department of Analytical Chemistry, University of Bucharest, Şos. Panduri 90-92, Bucharest 050657, Romania

AuNPs-based sensors and their applications

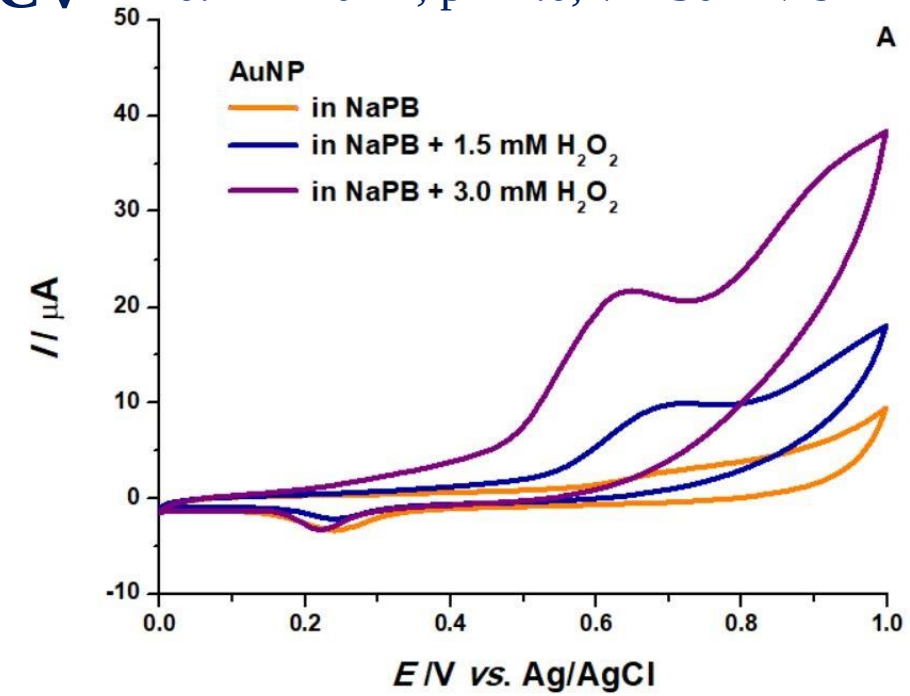
*Sensors with commercial gold nanoparticles (**AuNPs**) for **enzyme-like catalytic activity (nanozyme)***

Reactive oxygen species (ROS): **Hydrogen peroxide (H_2O_2)**



in 0.1 M NaPB, pH 7.0, v = 50 mV s^{-1}

CV in 0.1 M NaPB, pH 7.0, v = 50 mV s^{-1}

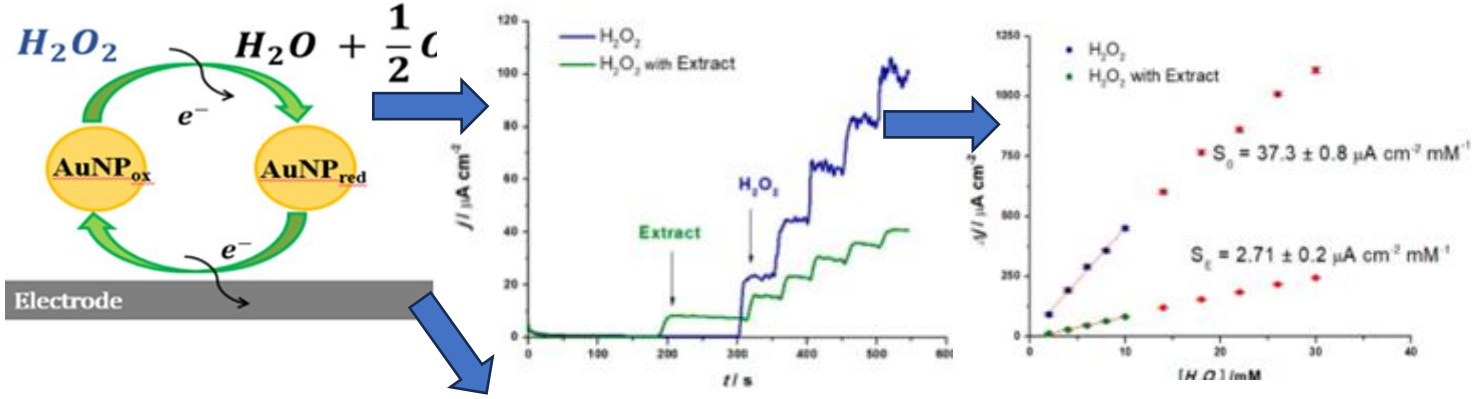


Sensors (2019) 19(3), 590;

Bioelectrochemistry (2019) 129, 124.

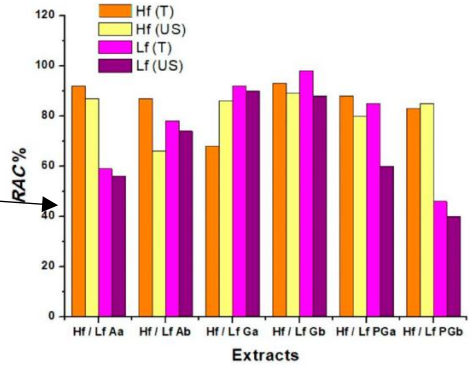
AuNPs-based sensor for antioxidant capacity and activity

Relative and Total Antioxidant Capacity (RAC and TAC)

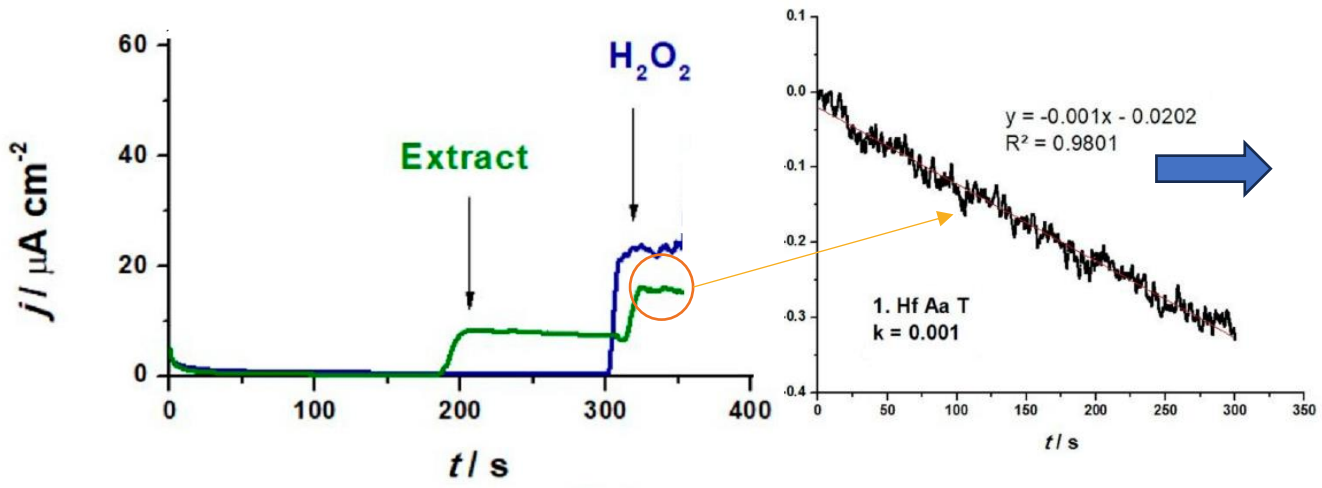


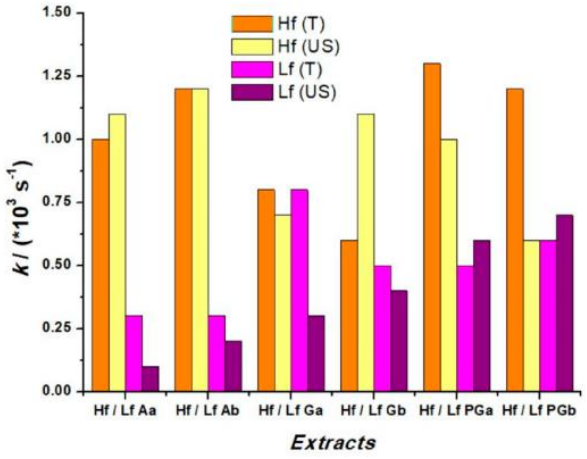
$$RAC(\%) = \frac{S_0 - S_E}{S_0} * 100$$

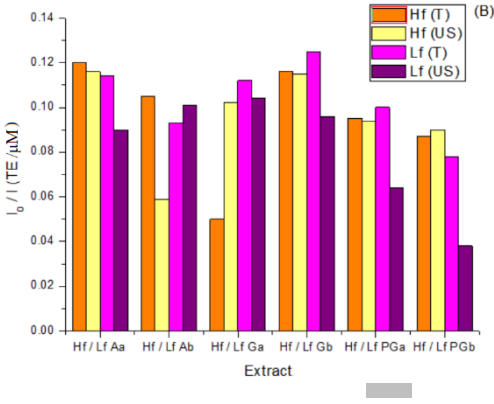
$$TAC(\%) = \frac{I_0}{I_E} * 100$$



Antioxidant activity (kinetic constant (k))







Sensors (2019) 19(3), 590; Bioelectrochemistry (2019) 129, 124, Patent No. RO 133102 B1 / 30.01.2024 (OSIM).

Transilvania University of Brașov

Antioxidant capacity
Comparison with spectroscopy

Pearson's correlation: (high) positive correlations among the two methods

Extracts	Electrochemical RAC (%)	Spectrophotometry RAC (%)
1.Lf Aa US	83.8 ± 0.04	77.6 ± 0.11
1.Hf Aa US	72.8 ± 0.22	79.0 ± 0.09
1.Js Aa US	30.9 ± 0.32	56.7 ± 0.92
1.Vp Aa US	47.6 ± 0.83	73.4 ± 1.08
1.Lf Aa T	78.5 ± 0.03	84.5 ± 0.07
1.Hf Aa T	69.6 ± 0.20	81.9 ± 0.24
1.Js Aa T	20.0 ± 0.44	33.3 ± 1.05
1.Vp Aa T	36.7 ± 0.23	58.2 ± 2.11

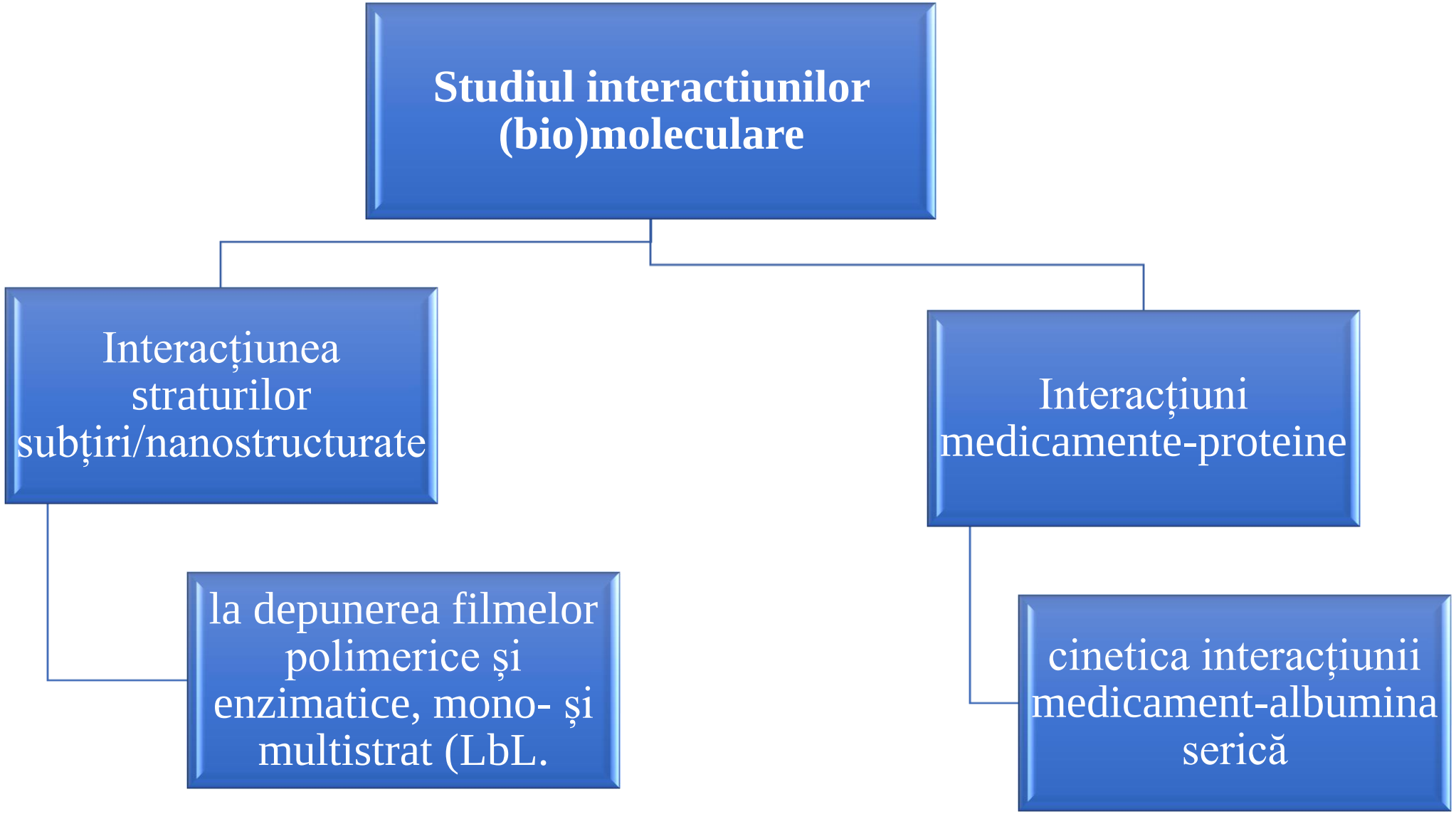
R = 0.907

Extracts	Electrochemistry TE (mg/100 mL extract)	Chemiluminescence TE (mg/100 mL extract)
1.Hf Aa US	45.1 ± 0.22	49.2 ± 0.90
2.Hf Ab T	42.0 ± 0.85	42.5 ± 1.40
3.Hf Ga T	22.0 ± 0.90	29.4 ± 1.00
3.Hf Ga US	47.8 ± 0.36	44.6 ± 0.82
4.Hf Gb US	53.5 ± 1.28	44.8 ± 3.90
5.Hf PGa T	42.3 ± 0.78	39.9 ± 1.50
5.Hf PGa US	48.4 ± 0.36	48.1 ± 0.80
6.Hf PGb T	35.0 ± 60	40.7 ± 1.50
3.Lf Ga T	54.2 ± 1.05	52.8 ± 4.60
4.Lf Gb US	31.7 ± 0.50	20.5 ± 0.84

R = 0.822

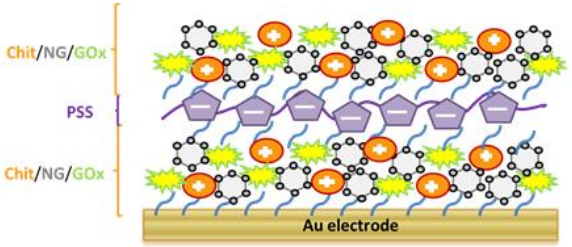
Sensors (2019) 19(3), 590

I. Realizări - Activitate de cercetare



Enzyme based biosensors - GOx

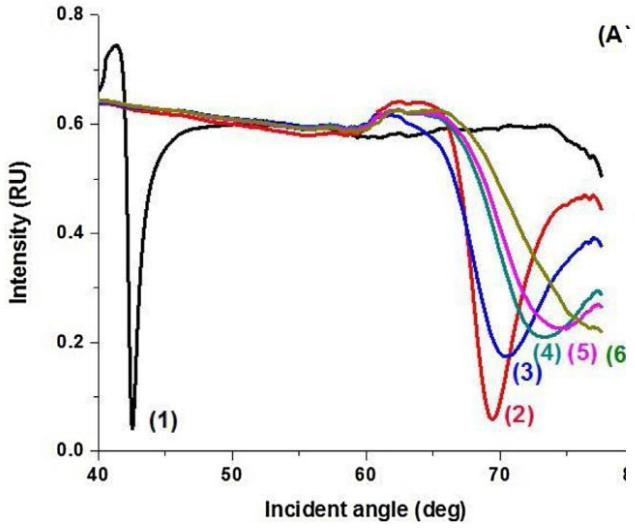
- **Glucose oxidase (GOx)** immobilization: characterization of the thin films interactions

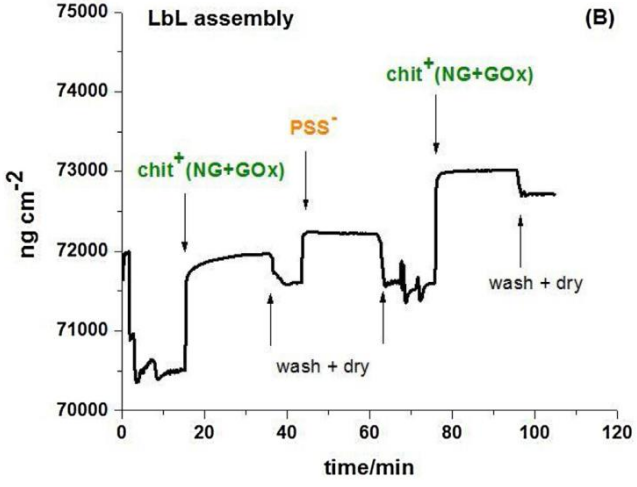


Mass coverage estimation and binding for each monolayer in hydrated and dry state on Au electrode modified with PEDOT thin layer.

Layer	$m/\mu g\,cm^{-2}$ (hydrated)	$m/\mu g\,cm^{-2}$ (dry)	Binding/% (dry)
$\{chit^{+}(GOx)\}_1$	1.43 ± 0.005	1.11 ± 0.004	75.1
PSS^{-}	0.50 ± 0.010	0.01 ± 0.005	1.61
$\{chit^{+}(GOx)\}_2$	1.14 ± 0.004	1.11 ± 0.002	79.1

LoD = 41 μM





Sensors and Actuators B 255 (2018) 3227–3234

Contents lists available at ScienceDirect

Sensors and Actuators B: Chemical

journal homepage: www.elsevier.com/locate/snb

Research Paper

Improved glucose label-free biosensor with layer-by-layer architecture and conducting polymer poly(3,4-ethylenedioxythiophene)

Melinda David[a,b], Madalina M. Barsan[a], Christopher M.A. Brett[a], Monica Florescu[b,*]

[a] Department of Chemistry, Faculty of Sciences and Technology, University of Coimbra, 3004-535 Coimbra, Portugal
[b] Faculty of Medicine, Transilvania University of Brasov, 500019 Brasov, Romania

Investigation of the binding of drugs to confined BSA

- Understanding the **pattern and mechanism of the interaction** is very important for the evaluation of the optimal dose and clearance of the drug in the body.

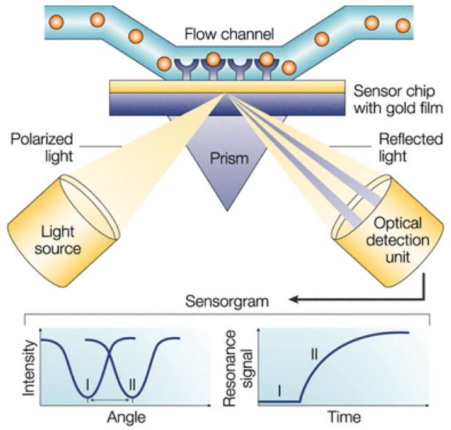
Binding follows the physical adsorption mechanism

Linearized form of Langmuir isotherm model reveals the *interaction mechanism*:

- *Intensity of the reflected light I or electrical parameters*

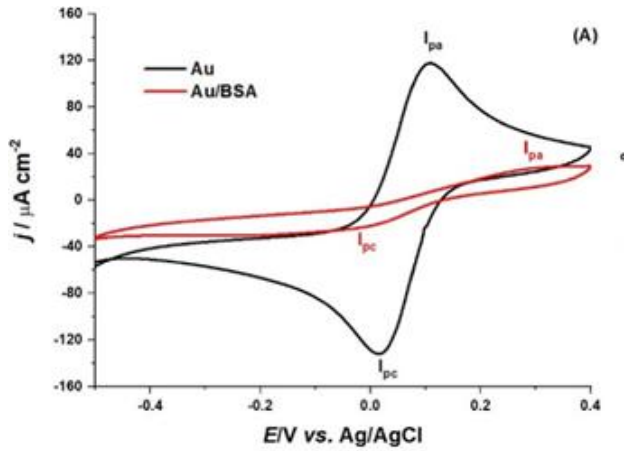
- Surface Plasmon Resonance (SPR) -

$$\frac{c}{I} = \frac{c}{I_e} + \frac{1}{Kb_{app}I_e}$$

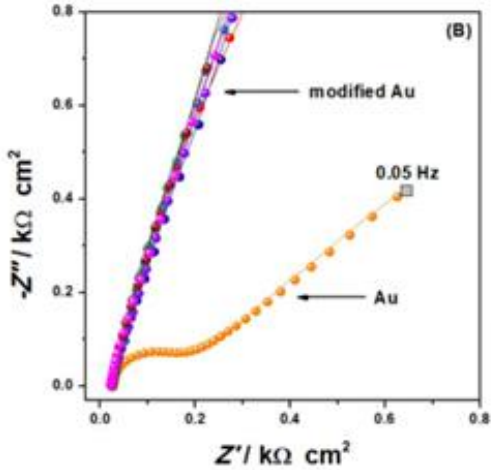


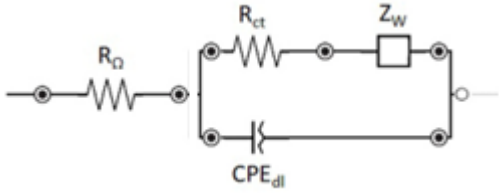
- Electrochemistry-

$$\frac{c}{C} = \frac{c}{C_e} + \frac{1}{Kb_{app}C_e}$$

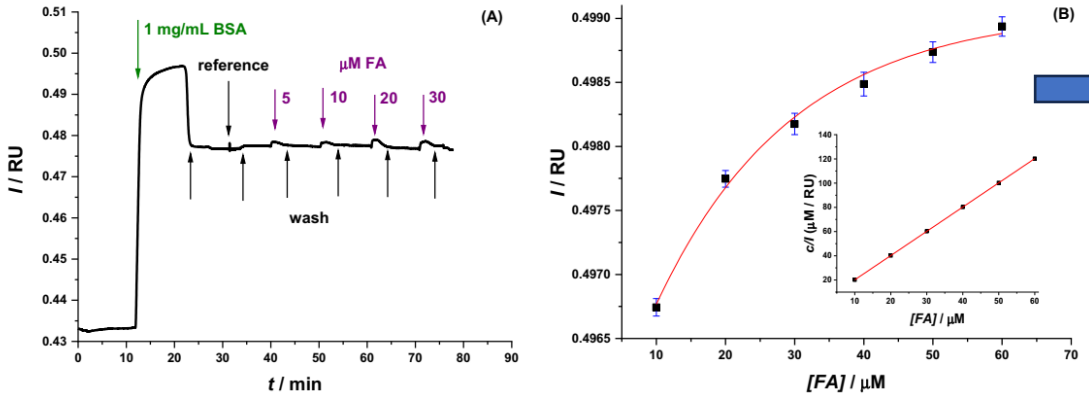


$$\frac{c}{CPE} = \frac{c}{CPE_e} + \frac{1}{Kb_{app}CPE_e}$$





Investigation of the binding of folic acid (FA) to confined BSA –SPR-



Linearized form of Langmuir isotherm model:

$$\frac{c}{I} = \frac{c}{I_e} + \frac{1}{K_{bapp} I_e}$$

Hydrodynamic immobilization of BSA:

Confined SPR_BSA-FA is characterized by a *strong interaction:*

$Kb_{app} = 19 \times 10^{6} M^{-1}$

$Kd_{app} = 0.526 \times 10^{-9} M$

$\mathbf{Kb_{app} \cong 200\ Kb}$ ***(for free BSA-FA)***

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 230 (2020) 118074

The **interaction of FA with free BSA**:

- mainly by a *static quenching mechanism (is initiated by FA-BSA complex formation),*
- **FA** affects *the protein conformation* at the binding site.
- **FA** *binds* **free BSA** (1:1) and binding process is characterized by a *moderate interaction* (K_d = *11.5 x* 10^{-6} *M, 25 ℃)*

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: www.elsevier.com/locate/saa

Monitoring biomolecular interaction between folic acid and bovine serum albumin

Claudia G. Chilom [a], Melinda David [b,*], Monica Florescu [b]

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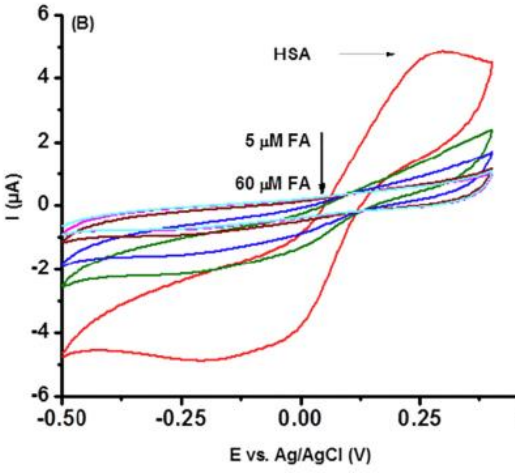
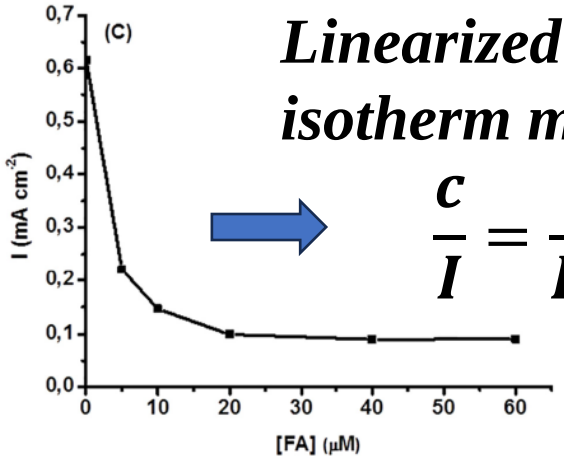
[b] Department of Fundamental, Prophylactic and Clinical Disciplines, Faculty of Medicine, Transilvania University of Brasov, Brasov, Romania, Colina Universitatii no. 1, Building C, room CI30, 500068, Brasov, Romania

BSA-FA = base for an efficient targeted drug delivery systems or cellular uptake of folic acid

Investigation of the binding of folic acid (FA) to confined HSA –electrochemistry-

In the literature, there **are not many studies** that use to electrochemical methods to investigate the binding properties of **ligand-binding proteins**, such as serum albumin.





***Linearized form of Langmuir isotherm model*:**

$$\frac{c}{I} = \frac{c}{I_e} + \frac{1}{K_{bapp} I_e}$$

Static immobilization of HSA:

Confined HSA-FA is characterized by a *stronger interaction:*

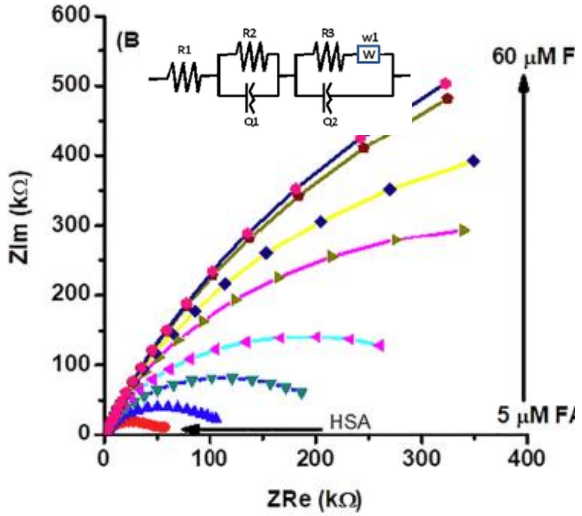
CV

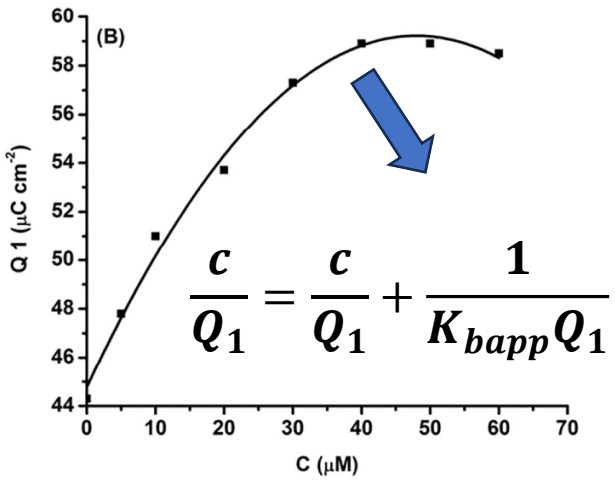
$Kb_{app} = 4{,}6 \times 10^5\, M^{-1}$

EIS

$Kb_{app} = 9{,}1 \times 10^5\, M^{-1}$

$Kb_{app} \cong 10$ Kb ($10^4 M^{-1}$)for free HSA-FA)





$$\frac{c}{Q_1} = \frac{c}{Q_1} + \frac{1}{K_{bapp} Q_1}$$

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 204 (2018) 648–656

https://doi.org/10.1016/j.saa.2018.06.093

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: www.elsevier.com/locate/saa

Insight into the interaction of human serum albumin with folic acid: A biophysical study

Claudia G. Chilom [a], Mihaela Bacalum [b], Mirela M. Stanescu [c], Monica Florescu [d,*]

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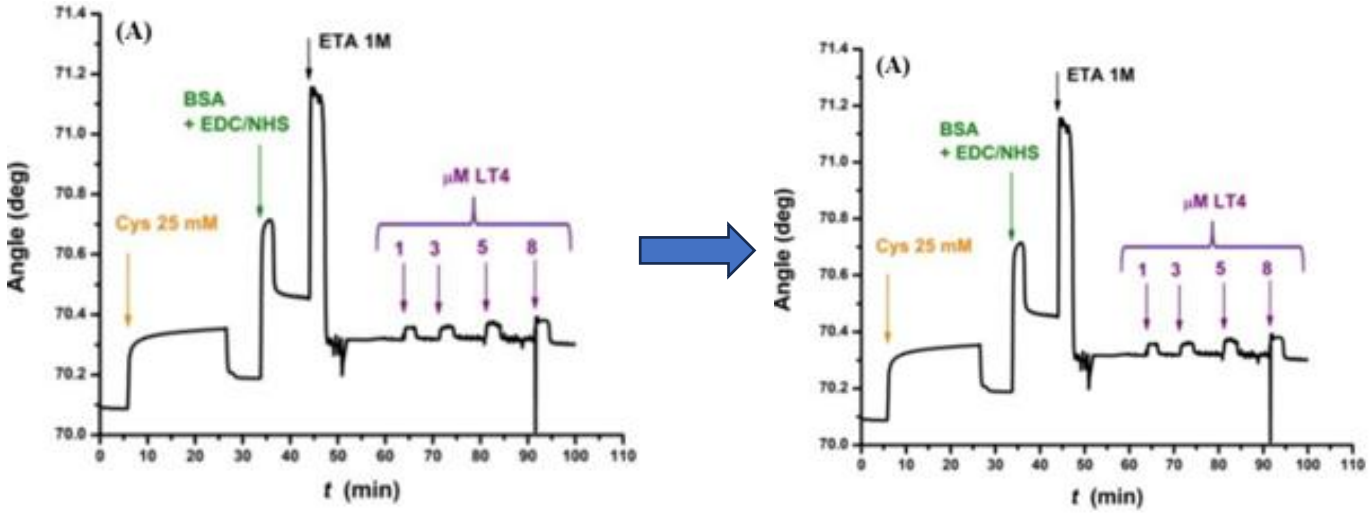
[b] Department of Life and Environmental Physics, "Horia Hulubei" National Institute of Physics and Nuclear Engineering, Str. Reactorului no. 30, P.O. BOX MG-6, Bucharest-Magurele, Romania
[c] Faculty of Applied Sciences, University Politehnica of Bucharest, Splaiul Independentei no. 313, sector 6, RO-060042 Bucharest, Romania
[d] Department of Fundamental, Prophylactic and Clinical Disciplines, Faculty of Medicine, Transilvania University of Brasov, Colina Universitatii no. 1, Building C, room CI30, 500068, Brasov, Romania

Investigation of the binding of LT4 to confined BSA - SPR



Linearized form of Hill-Langmuir model:

$$\log\left(\frac{\theta}{1-\theta}\right) = n\log\,[LT4] - \log Kd_{app}$$

Confined BSA-FA is characterized by:

- $\boldsymbol{Kb_{app} = 0.015 \times 10^{6}\ M^{-1}}$
  $Kb_{app} < Kb$ *(free BSA-LT4)*
- a *moderate interaction*:
  $\boldsymbol{Kd_{app} = 67.6 \times 10^{-6}\ M}$
- ***Confined-BSA*** *exhibits competitive binding characteristics.*

The **interaction of LT4 with free BSA**:

- mainly by a *static quenching mechanism*, and
- **LT4** affects *the protein conformation* at the binding site.
- **LT4** *binds* **free BSA** (1:1) and binding process is characterized by a *strong interaction (Kd = 0.195 x 10^{-6} M)*.

JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS
https://doi.org/10.1080/07391102.2020.1822919

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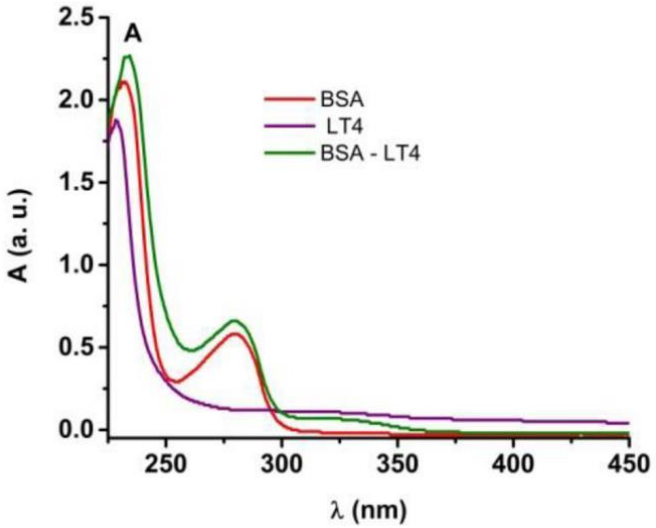
Check for updates

Evaluation of the interaction of levothyroxine with bovine serum albumin using spectroscopic and molecular docking studies

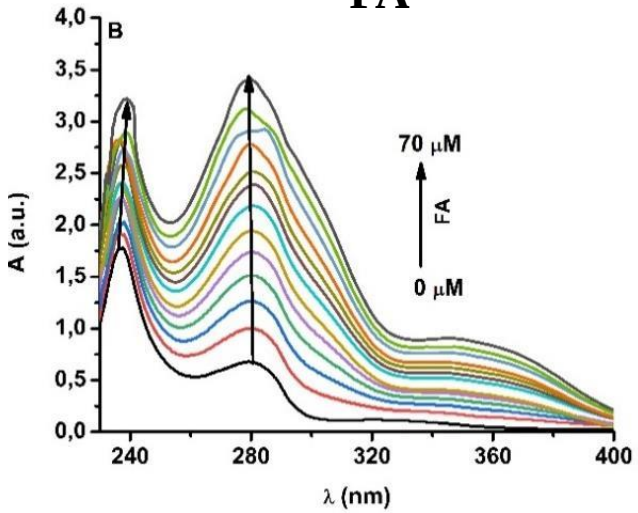
Nicoleta Sandu[a], Claudia G. Chilom[a], Melinda David[b] and Monica Florescu[b]

[a]Department of Electricity, Solid Physics and Biophysics, Faculty of Physics, University of Bucharest, Măgurele, Romania; [b]Department of Fundamental, Prophylactic and Clinical Disciplines, Faculty of Medicine, Transilvania University of Brasov, Brasov, Romania

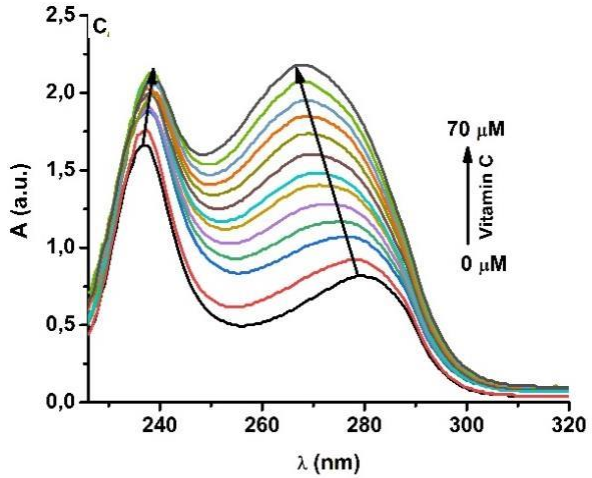
Effect of vitamins on the BSA - LT4 complex – UV-Vis spectroscopy -



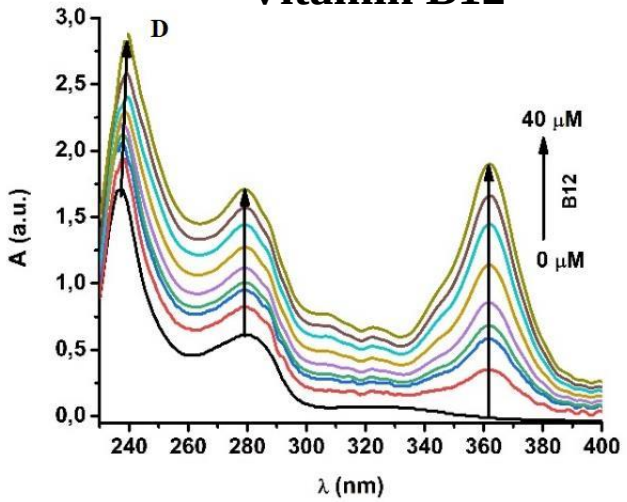
FA



Vitamin C



Vitamin B12



Folic acid (FA)

- No shift for the BSA absorption peak.
- LT4 absorption peak shifts bathochromically

Vitamin C

-BSA absorption peak shifts hypsochromic,

- LT4 absorption peak shifts bathochromically

Vitamin B12

- No shift for the BSA absorption peak
- LT4 absorption peak shifts bathochromically

The results provide important information about the complex behavior of BSA-LT4 in a biological environment.

International Journal of *Molecular Sciences*

MDPI

Article

Conformational Changes in the BSA-LT4 Complex Induced by the Presence of Vitamins: Spectroscopic Approach and Molecular Docking

Nicoleta Cazacu [1], Claudia G. Chilom [1], Melinda David [2] and Monica Florescu [2,*]

II. Îndeplinirea standardelor naționale

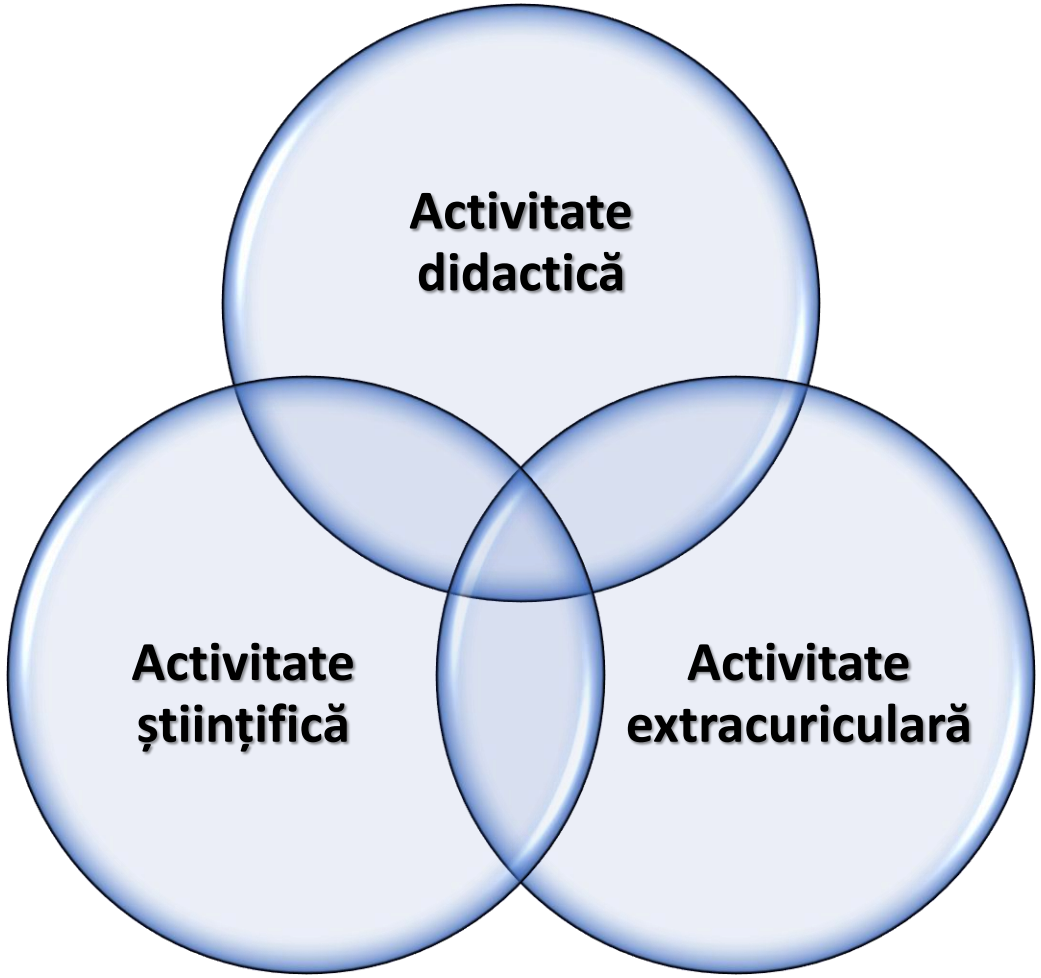
Îndeplinirea standardelor naționale -Medicină

Post didactic	Realizări conform standardelor proprii ale universității
Conferențiar Universitar	(i) Nr. Articole ISI Autor Principal: 28 (ii) Nr. Articole ISI Coautor: 15 (iii)Index Hirsch: 17 (ISI) (iv)Factor cumulat de impact autor principal (FCIAP): >58,875

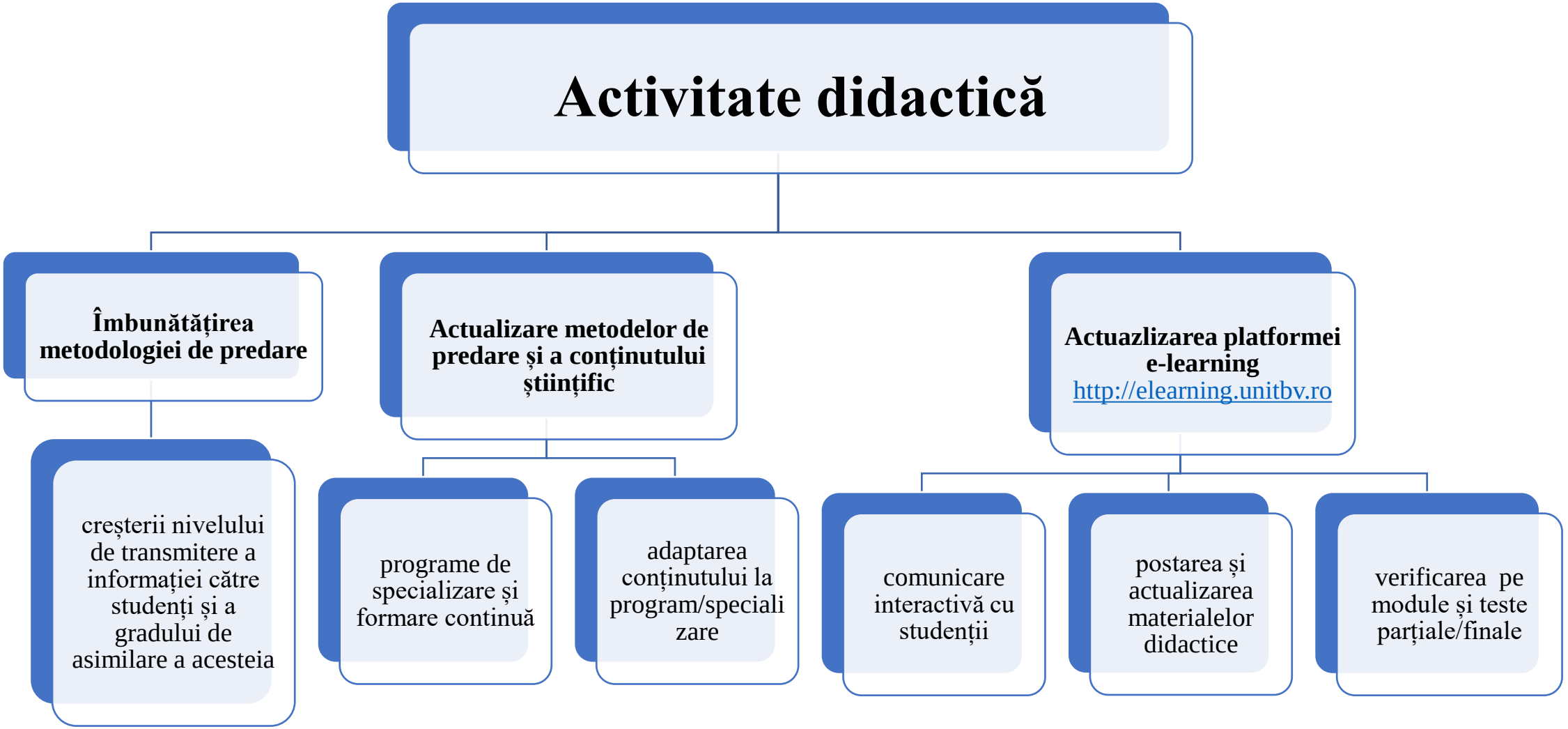
Condiții minimale CNATDCU			
Nr. Crt.	Categoria		
	Domeniul de activitate	Condiții Abilitare de îndeplinit	Condiții Abilitare realizate
1	Nr. Articole ISI Autor Principal	10	28
2	Nr. Articole ISI Coautor	5	15
3	Index Hirsch	6	17
4	FCIAP	10	>58,875

III. PLANURI DE EVOLUȚIE ȘI DEZVOLTARE A CARIEREI

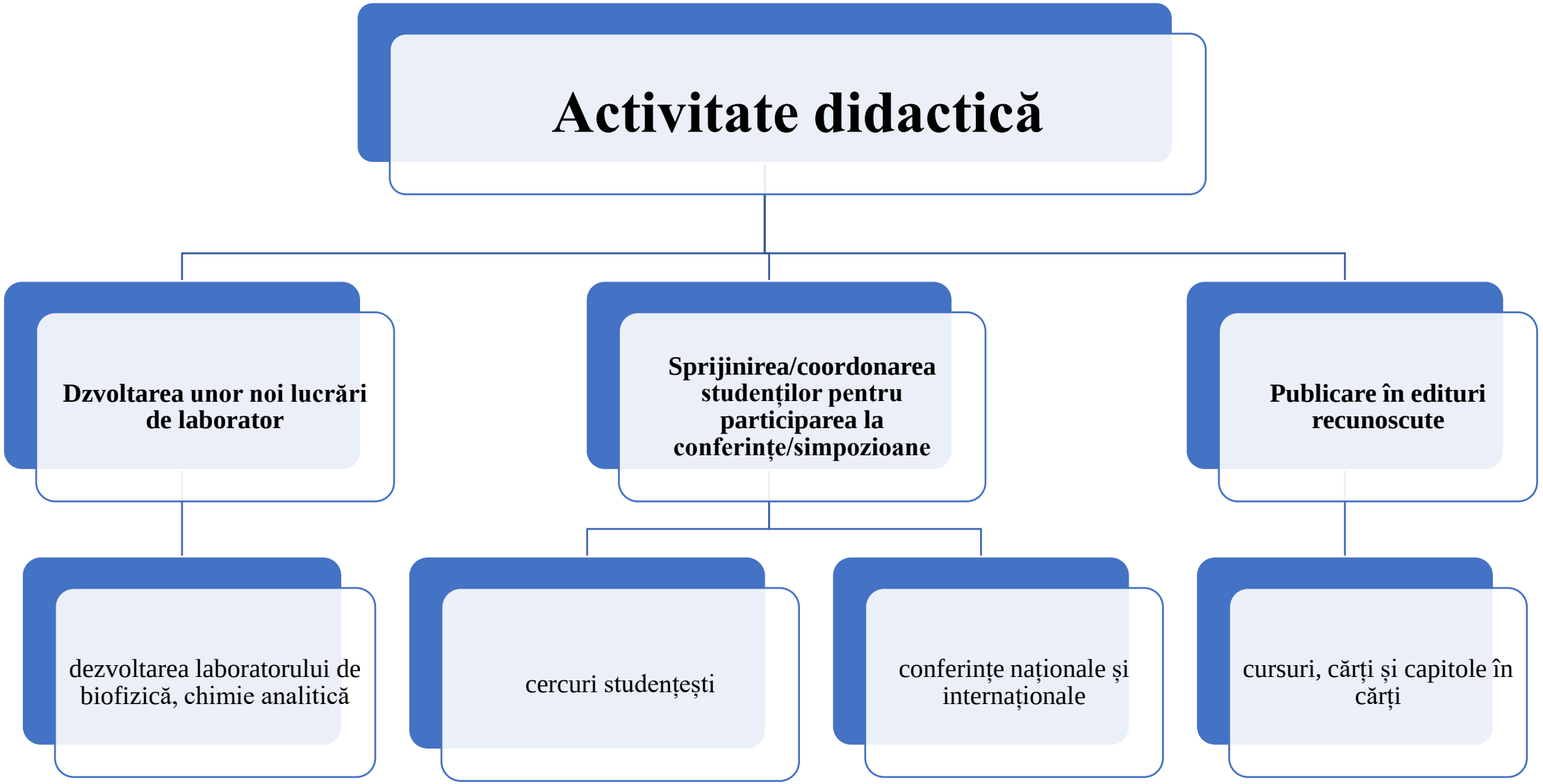
III. Dezvoltare



III. Dezvoltare



III. Dezvoltare



III. Dezvoltare

Cercetare științifică interdisciplinară în **domeniul științelor nano- și biomedicale** și **translatarea rezultatelor cercetării** în medicină.

1. **continuarea** activității științifice desfășurată până acum, dar și
2. **deschiderea** unor noi direcții de cercetare

A. Dezvoltarea sistemelor de biodetecție non-invazivă

B. Dezvoltarea sistemelor de administrare țintită a factorilor terapeutici (nanoterapii)

C. Evidențierea interacțiunilor care implică proteine și nanoparticule

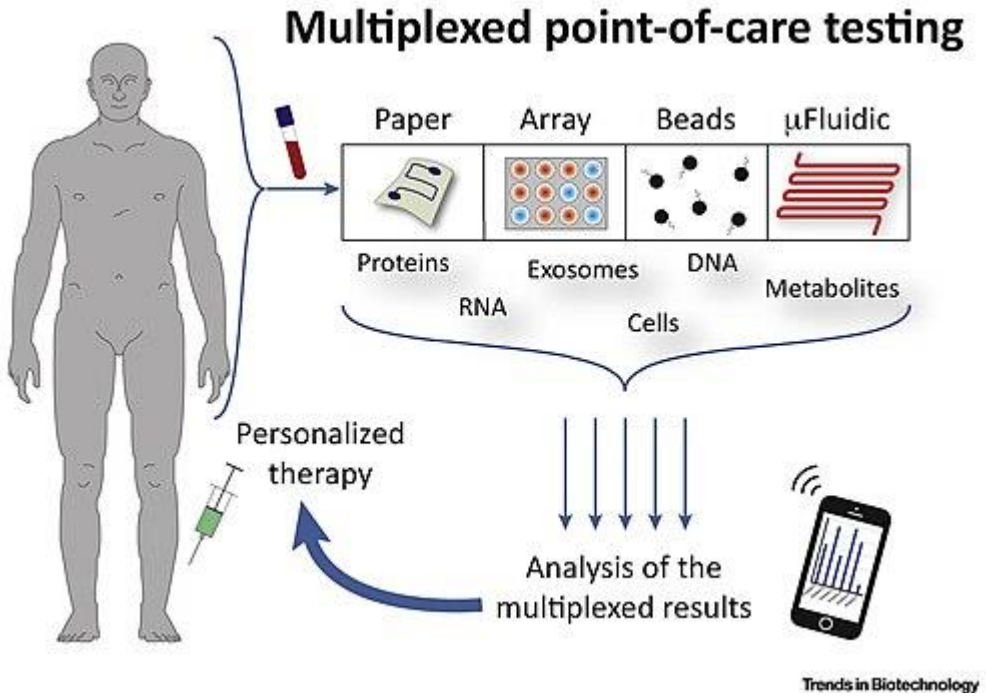
A. Dezvoltarea sistemelor de biodetecție non-invazivă

Point-of-Care testing (POCT) = bedside testing
Wearable bandage = continuos monitoring

Point-of-care testing (POCT)

Point-of-care testing (POCT) is designed to provide:

- diagnostic tests at or near the time and place that the patient is admitted, outside of the clinical laboratory.
- help in emergency triage or surgery room
- for early detection and personalized therapy adjustment



Main objective:

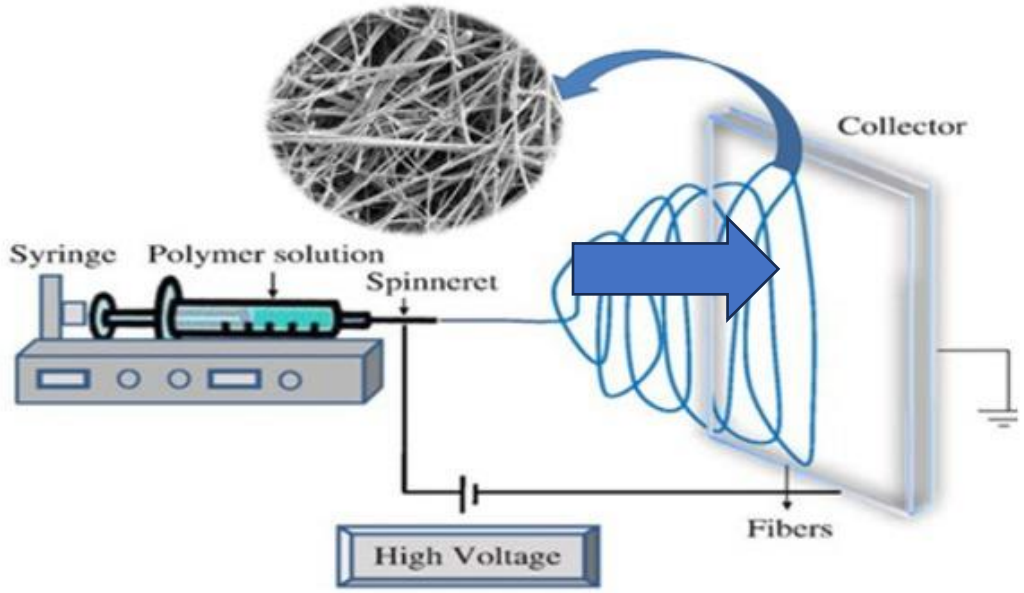
- **the integration of sensors in inovative platforms for POC detection, but also wearables.**

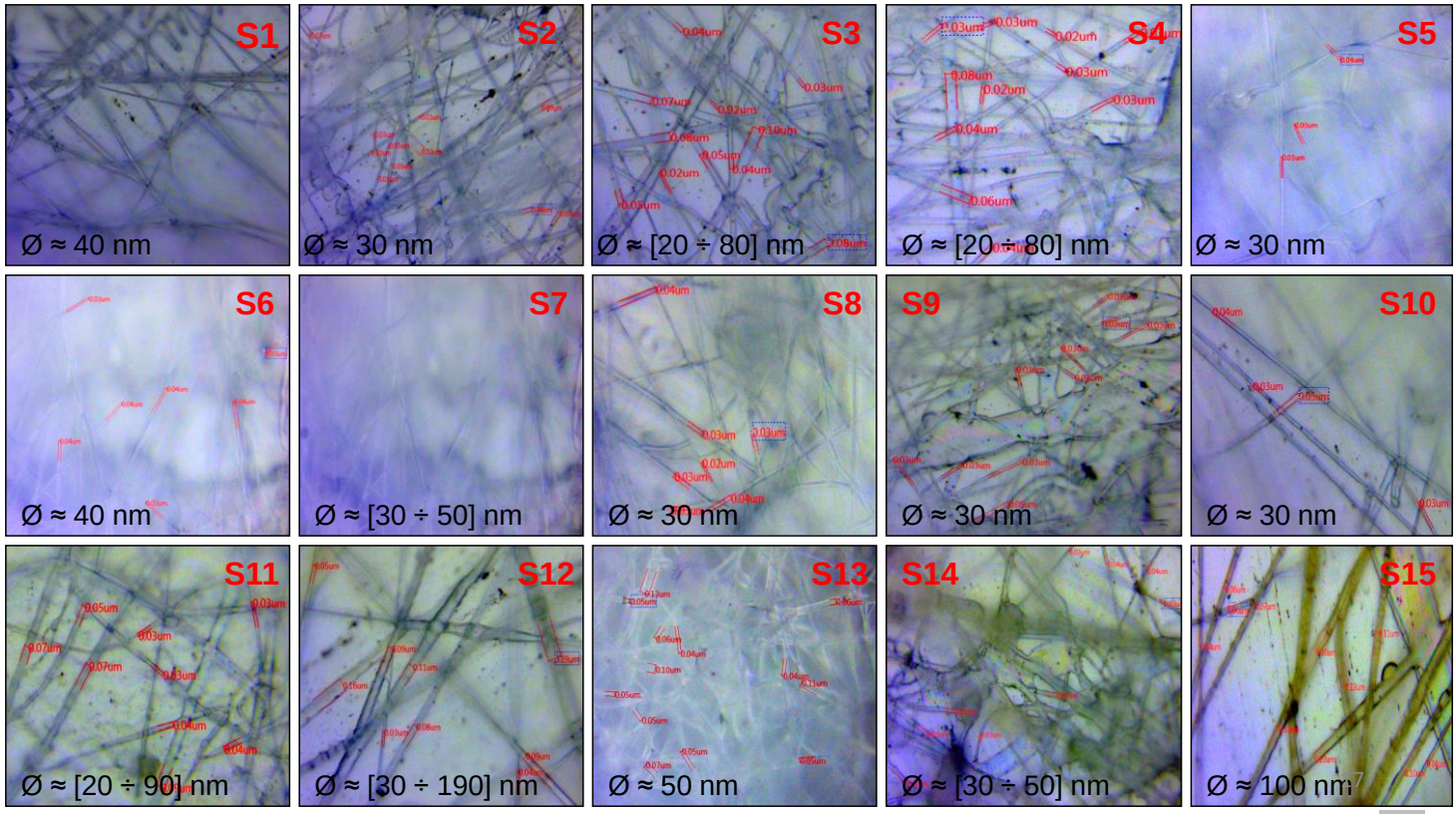
https://en.wikipedia.org/wiki/Multiplexed_point-of-care_testing

Bio-AuNP-based sensors for glycoproteins

Green composite nanomaterials (GCM) based on:

- electrospun fibers (NF) based on aqueous polymer solutions (PVA, PEI, chitosan), and
- biologically synthesized gold nanoparticles (Bio-AuNPs)





Bio-AuNP-based sensors for glycoprotein

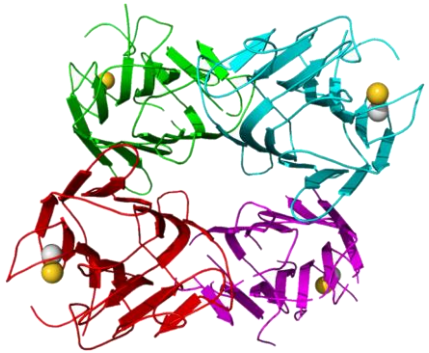
- **Lectins**
  - class of proteins able to bind to **soluble carbohydrate** or to a **carbohydrate moiety** from glycoproteins or glycolipids.
- interaction between sugars and lectins has:
  - **low affinity** ($K_b \sim 10^4\ M^{-1}$) for animal lectins.
  - **strong affinity** ($K_b = 10^6–10^7\ M^{-1}$) for plant lectins

- Standard methodologies (e.g. ELISA) fail to detect weak interactions!

Bio-AuNP-based sensors for glycoprotein

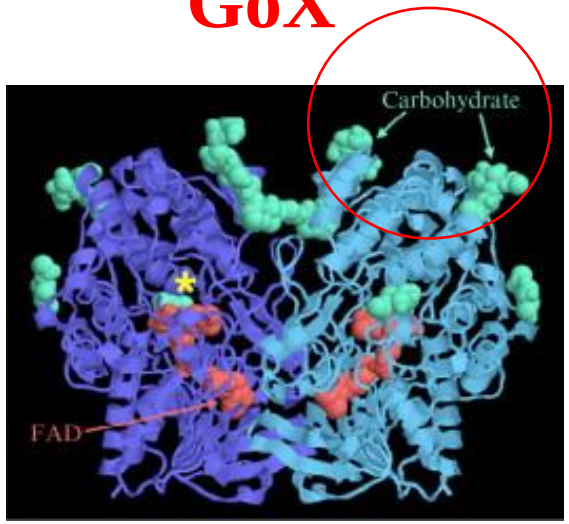
- Modification of a gold surface with electrospun nanofibers decorated with Bio-AuNPs.
- **Receptor: lectin = protein (Con A)** (affinity for the sugars mannose and glucose).
- **Ligand: glycoprotein (Glucose oxidase, GoX).**

ConA

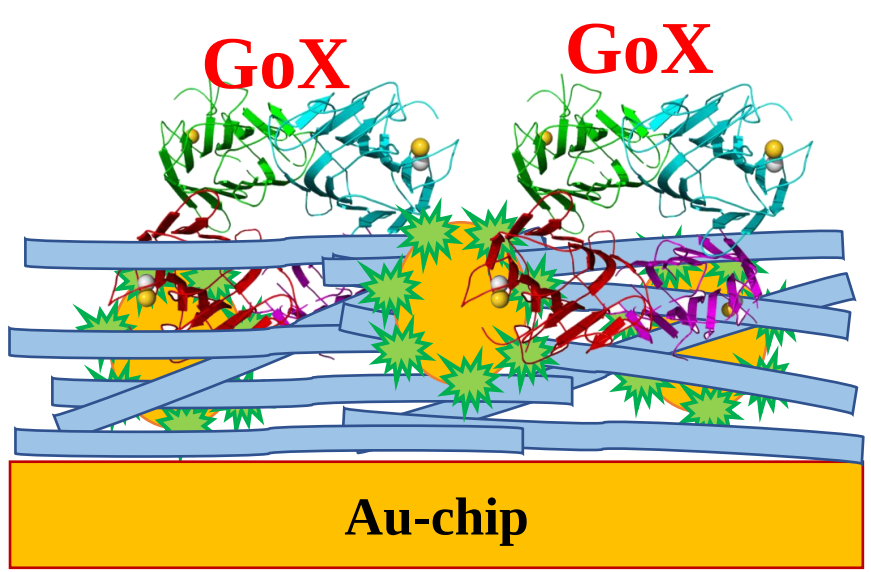


104-112kDa

GoX



160 kDa

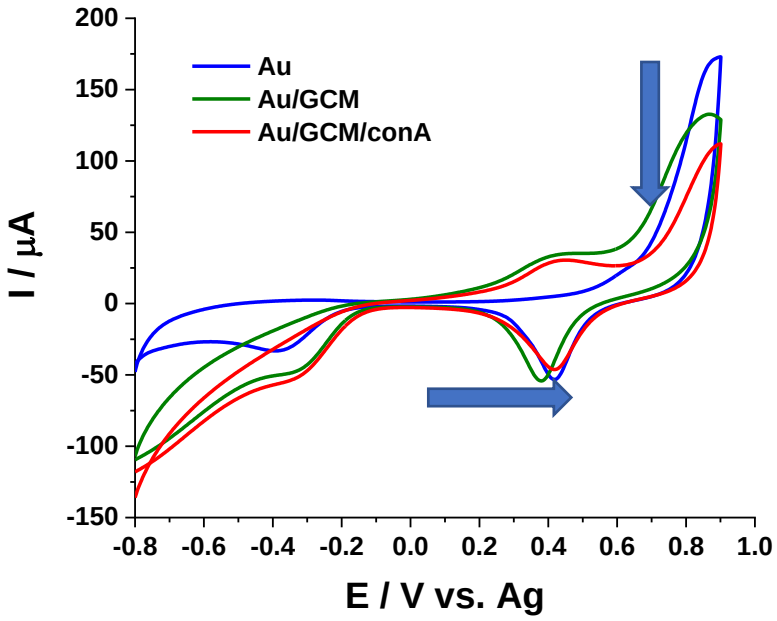


Methods in Enzymology Volume 509, 2012, Pages 165-194

Bio-AuNP-based sensors for glycoprotein

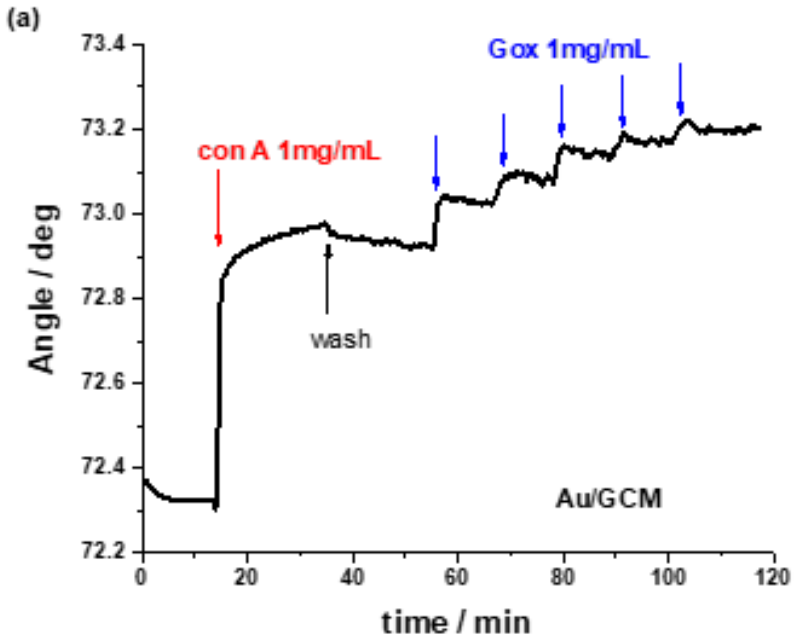
- **CV (ν = 50 mV s^{-1})**

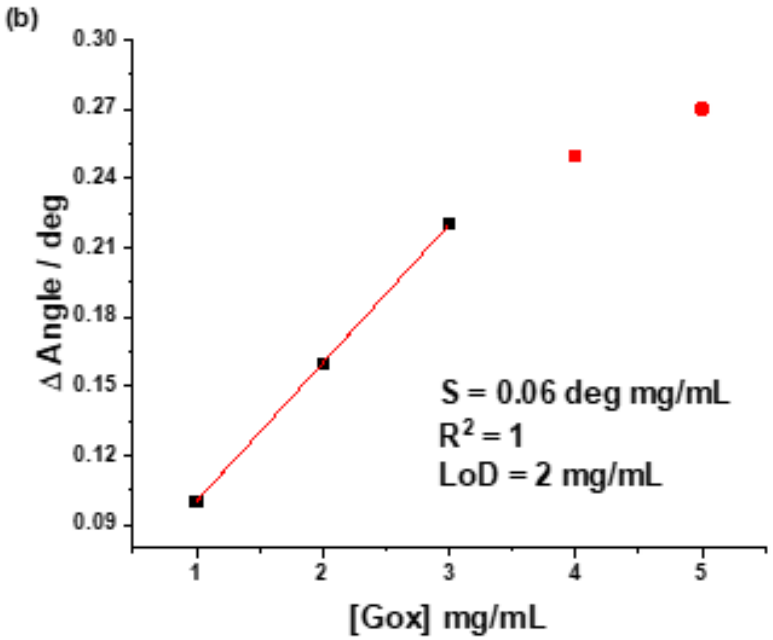
  - GCM modification



- **Surface Plasmon Resonance (SPR)**

  - Gox sensing





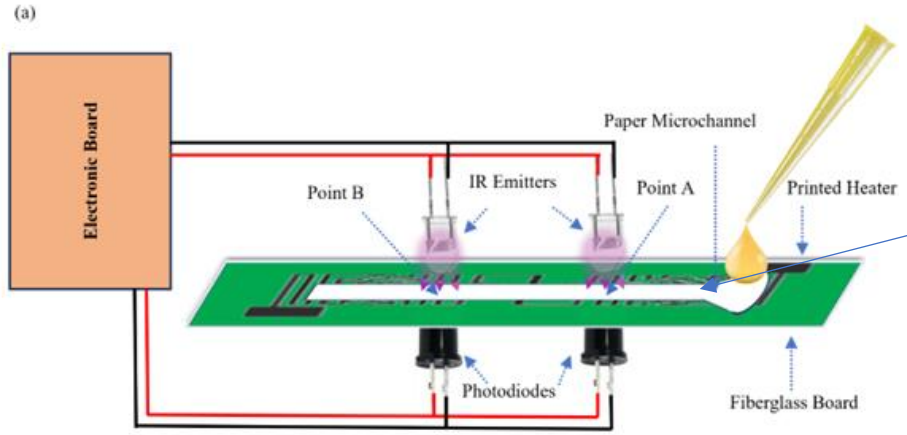
in 0.1 M NaPB, pH 7.4

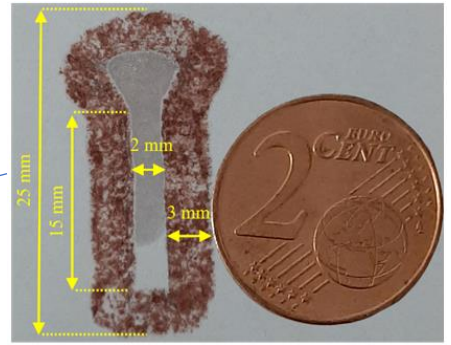
Unpublished results

Optoelectronic Microfluidic Device for Point-of-Care Blood Plasma Viscosity Measurement

Somayyeh Bakhtiaridoost,[a] Cristian Musuroi,[b] Marius Volmer,*[b] and Monica Florescu*[a]

Accepted for publication in:





Accepted results

Sample	Health status	Plasma viscosity (mPa.s)	Serum viscosity (mPa.s)	SD (mPa.s)	Average Time (s)
S1	Normal	1.26	-	0.038	27.73 ± 0.85
S2	Normal	-	1.16	0.074	25.42 ± 1.63
S3	High fibrinogen	1.95	-	0.110	42.9 ± 2.3
S4	Inflammation	-	1.62	0. 091	35.06 ± 2
S5	Waldenstrom	2.96	-	0. 160	65.23 ± 3.5

B. Dezvoltarea sistemelor de administrare țintită a factorilor terapeutici (nanoterapii)

C. Evidențierea interacțiunilor care implică proteine și nanoparticule

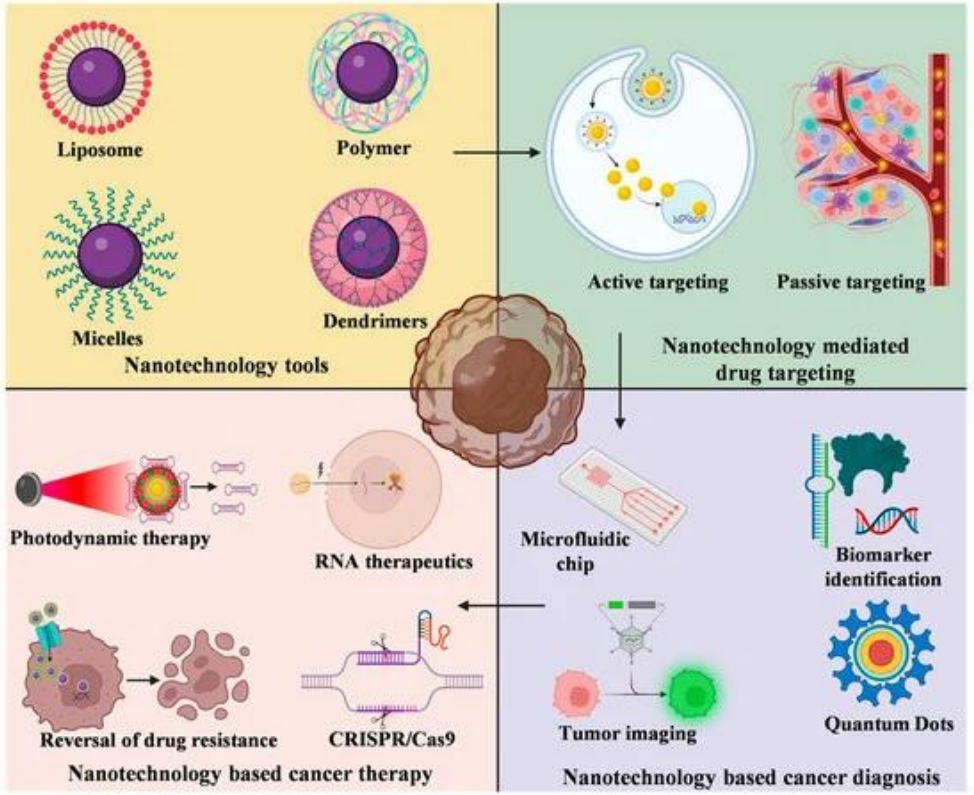
Point-of-care testing (POCT)

Nanoparticles are being widely investigated for **drug delivery** more and more lately.

NPs have the ability to **increase intracellular drug accumulation** due to their ability to **specifically target and deliver various drugs** (eg anti-cancer).

Main objective:

- **integration of NPs into functional composite materials for controlled wearable drug delivery systems.**



Nanotechnology tools-based cancer targeting diagnosis and treatment

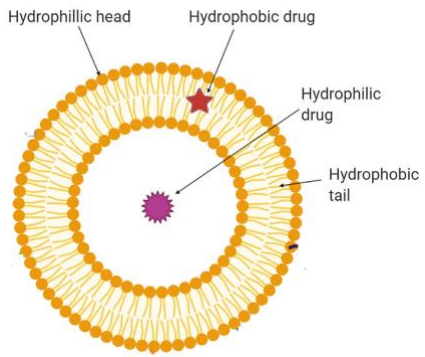
Bioengineering **2023**, *10*(7), 760

Functional nanostructured materials for delivery systems

Drug delivery vehicles represent different ways that medications can be *packaged so that the drug can safely travel within the body*.

Some common examples of drug delivery vehicles include *micelles, liposomes, or nanoparticles*. Different drug delivery vehicles can improve the targeting of the drug by helping the *medication travel exactly where it needs to go.*

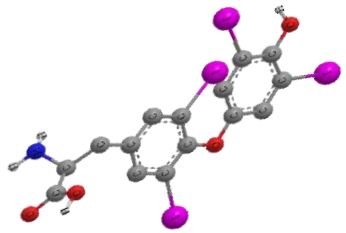
- **Delivery Vehicles = Receptor**
  - Liposomes
  - Nanoparticles



R

- **Pharmaceutical compound = Ligand**

L



$$R + L \rightleftharpoons RL$$

Investigation of the binding of ligand to receptor

- **Binding affinity** is a measure of how tightly the **drug** molecules (L) **bind** to the **transport vehicle** (R).
- The **binding affinity** should **not be too low** or **too high**.
  - If the **binding affinity is very low**, the **drug will be released** into the surrounding tissues in an uncontrolled manner, which eventually produces toxic effects.
  - If **binding affinity is very high**, then an **insufficient amount of drug will be released** from the vehicle within a requisite time.
- The **binding** (**affinity/association**) **constant, K_b** (M^{-1}), is a special case of the equilibrium constant K, and is the **inverse of the dissociation constant, K_d** (M) .
  - It is associated with the *binding and unbinding reaction* of receptor (R) and ligand (L) molecules:

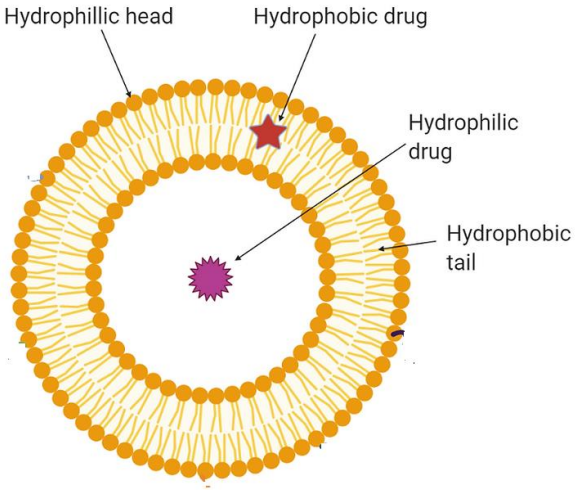
$$R + nL \rightleftharpoons RLn$$

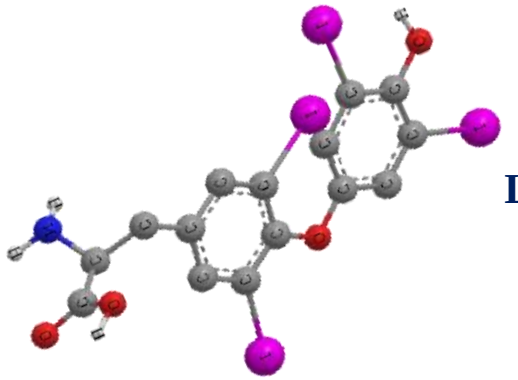
  - n is the *number of binding sites* on the protein (R = P) for the ligand.
- **High affinity**: K_b **=** typically 10^8 - 10^{10} M^{-1} (K_d = 0.1–10 nM).

Liposomes-based delivery system for drugs

- are non-toxic, biocompatible, and biodegradable *phospholipid vesicles* = **bio-inspired lipid membranes**.

- can ***deliver drugs*** (*inserted into* the *hydrophobic part* of the bilayer or *aqueous interior* of the liposomes) with improved cellular uptake.

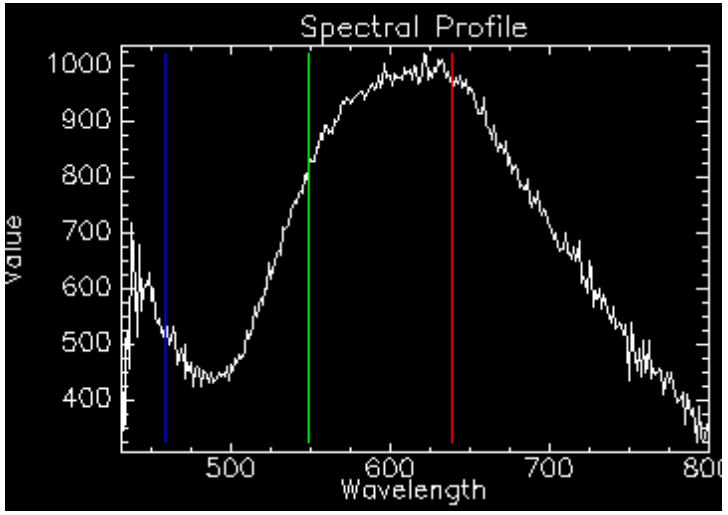




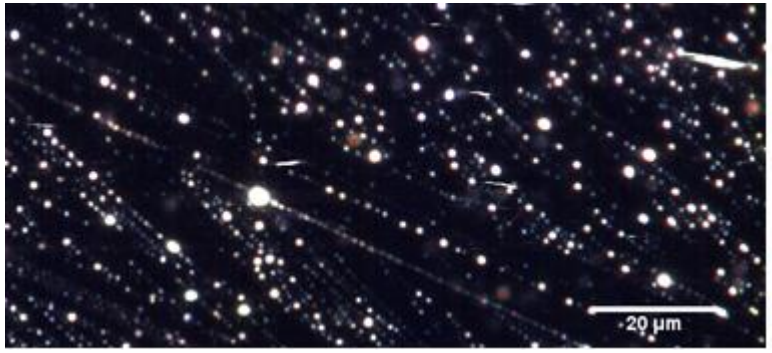
LT4

Transilvania University of Brașov

Bio-AuNPs liposomes nanohybrids
- CytoViva hyperspectral imaging-

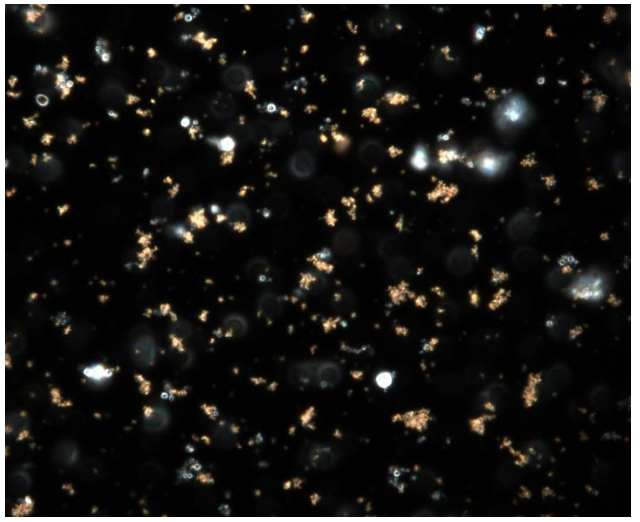


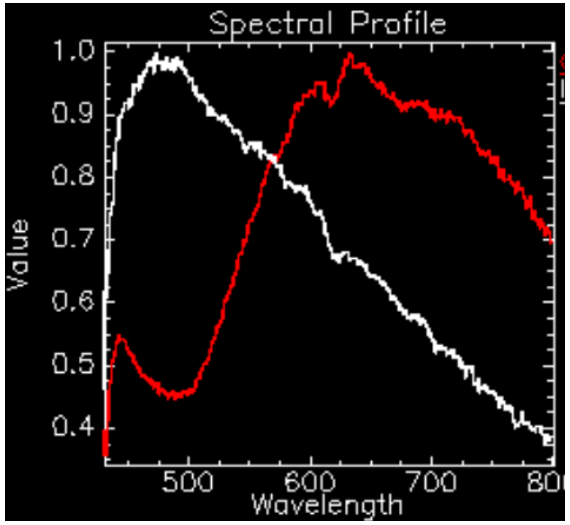
AuNPs Isolated



Liposomes Isolated

bio-AuNPs: d = 30 nm
Liposomes: 50 nm





AuNPs and Liposomes

Liposomes - based nanohybrids as delivery systems

Nanohybrids (liposomes drug carriers) = drug + *liposome*

The **lipid coating of drug** could be a *useful strategy to build effective drug delivery nanosystems*, which can improve the cellular uptake.

Studies on interaction between the **DPPC nanoliposomes** and the **LT4** for highlighting:

- detailed description of the **biomolecular interactions** occurring in the membrane model system.
- correlation between **changes in the model liposomal membrane's fluidity**.

European Biophysics Journal (2021) 50:1083–1101
https://doi.org/10.1007/s00249-021-01569-7

EBSA Biophysics in Europe

ORIGINAL ARTICLE

Check for updates

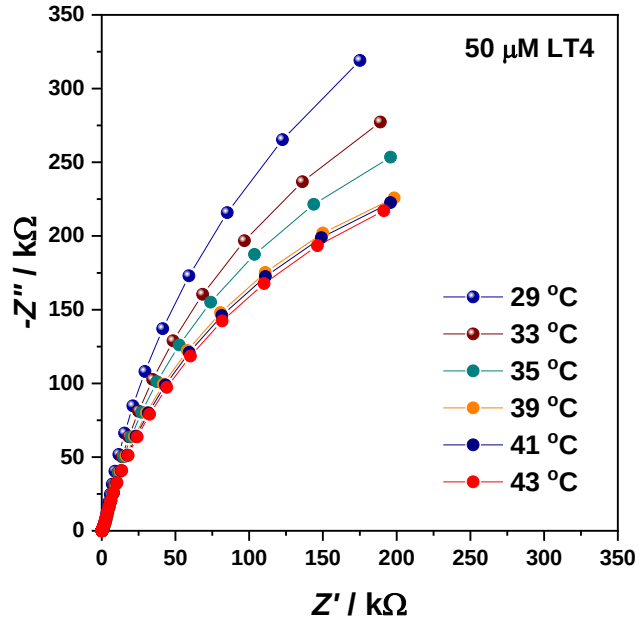
Insight into dual fluorescence effects induced by molecular aggregation occurring in membrane model systems containing 1,3,4-thiadiazole derivatives

Melinda David[1] · Iwona Budziak-Wieczorek[2] · Dariusz Karcz[3] · Monica Florescu[1] · Arkadiusz Matwijczuk[4]

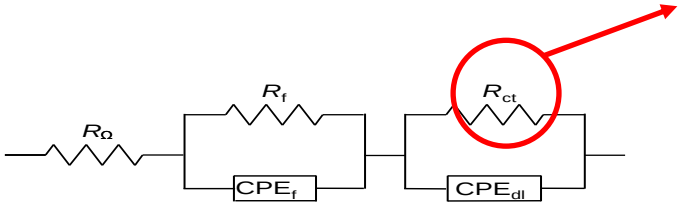
Liposomes-based nanohybrids
- thermal stability -

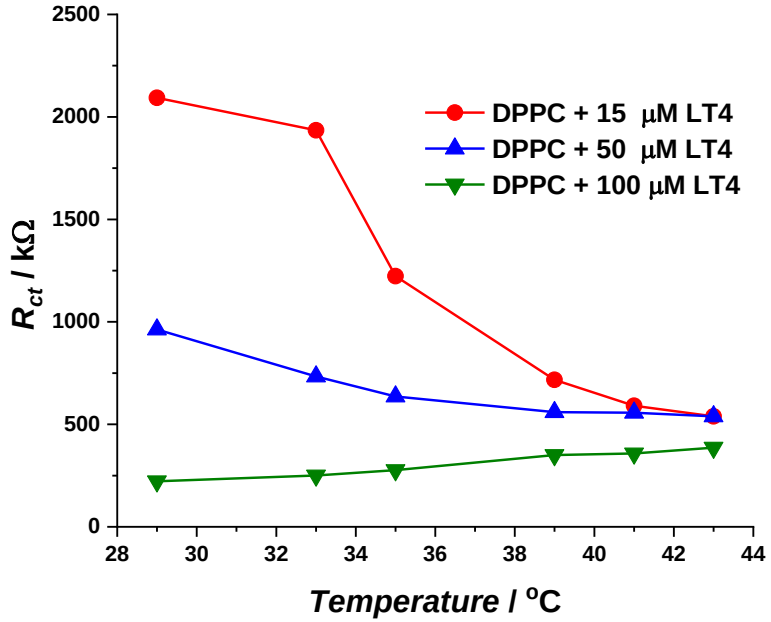
Electrochemical Impedance (EIS)

- at -0.2 V vs. Ag/AgCl for **LT4** with **DPPC** on **Au surface**



Electrical equivalent circuit:





R_{ct} decreases with T:

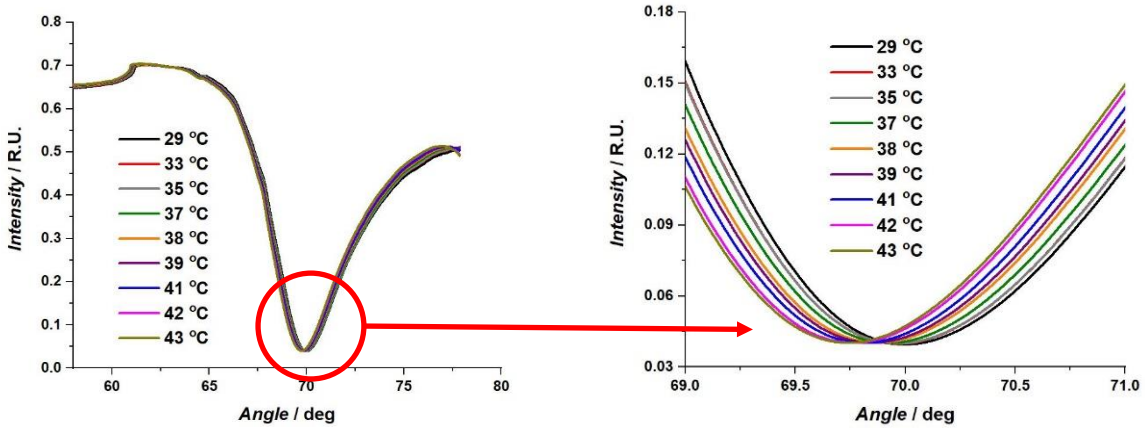
- *the conductance increases* suggesting the **interaction** of LT4 with the liposome's membrane and an **increase in membrane fluidity**, depending on LT4 concentration.

Liposomes-based nanohybrids
- thermal stability -

Surface Plasmon Resonance (SPR)

- Angular scan for 15 µM **LT4** with **DPPC** on **Au surface**

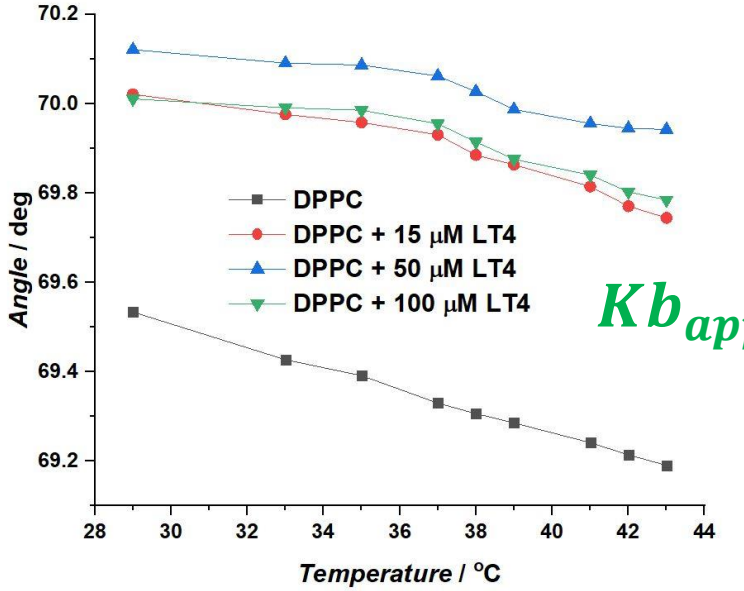
$$\frac{c}{ang} = \frac{c}{ang_e} + \frac{1}{Kb_{app} I_e}$$



SPR angle **decreases** with **T**:

- the *optical thickness decreases* suggesting the **interaction** of LT4 with the liposome's membrane and an **increase in membrane fluidity** (small dependence on LT4 concentration).

Linearized form of Langmuir isotherm model reveals a **strong interaction**:



Kb_{app} = 71.5 * 10^6 M^{-1}

Mulțumesc pentru atenție!