Roman Holomb

CURRICULUM VITAE

Personal data

Name:	Roman Holomb
Born:	January 24th, 1979, Dorobratovo, Ukraine
Marital status:	Single
Citizenship:	Ukraine
Address:	1122 Budapest, Maros utca 15
Affiliation:	Department of Applied and Nonlinear Optics, Institute for Solid State Physics and Optics, Wigner Research Centre for Physics, Budapest, Hungary e-mail: holomb.roman@wigner.hun-ren.hu

Education and qualifications

June 2021	**Assoc. Prof. (docent)**, Dept of Informative and Operating Systems and Technologies, Uzhhorod National University
March 2007	**Ph.D. in Physics of Semiconductors and Insulators**, Uzhhorod National University Thesis: “Photon energy dependent vibrational spectroscopy of $As(Ge)_xS_{100-x}$ glasses combined with first-principles calculations of $As(Ge)_nS_m$ clusters” Supervisor: Professor Volodymyr Mitsa
June 2001	**M.Sc. in Physics**, Uzhhorod National University, *diploma with honours*
June 2000	**B.Sc. in Physics**. Uzhhorod State University, *diploma with honours*
June 1996	Secondary school, v. Dorobratovo, *gold medal for special successes in education*

Professional career

Sept. 2020 – (till now) Wigner Postdoc, Dept. of Applied and Nonlinear Optics, Institute for Solid State Physics and Optics, Wigner Research Centre for Physics, Budapest, Hungary.

- Synthesis and characterization of novel functional chalcogenides;
- DNA recognition, single nucleotide polymorphism in RNA/DNA;
- Raman and surface-enhanced Raman spectroscopy;
- X-ray and synchrotron-radiation photoelectron spectroscopy;
- Electron- and atomic force microscopy;
- Molecular/DNA modelling and *ab initio*/DFT calculations.

July 2018 – Aug. 2020 Researcher at the Dept. of Applied and Nonlinear Optics, Institute for Solid State Physics and Optics, Wigner Research Centre for Physics, Budapest, Hungary.

Sept. 2014 – June 2018 Asst. Prof., Dept of Informative and Operating Systems and Technologies, Faculty of Information technologies, Uzhhorod National University.

Main special courses for BSc/MSc programs:

- Methodology of scientific research;
- Modellingof processes in heterogeneous environments;
- Broadband ultrahigh-speed optical methods of information transmission and processing;
- Management of scientific projects;
- System analysis;
- Presentations of scientific results;
- Information security and information protection methods;
- Mathematical economics;
- Information protection technologies;
- Models, technologies of design and management of information systems;
- Methods and tools of intelligent data analysis;
- Special topics in information technology (Ontology).

July 2007 – Aug. 2014 Researcher/Senior research scientist, Institute for Solid State Physics and Chemistry, Uzhhorod National University.

- Structure and properties of ionic liquids for Li-battery applications;
- Investigation of high optically nonlinear chalcogenide photonic media;
- Research projects at Elettra Sincrotrone Trieste (MSB);
- Scientific project management.

Nov. 2005 – June 2007 Research fellow, Condensed Matter Physics, Dept of Applied Physics, Chalmers University of Technology, Göteborg, Sweden.

- Vibrational and photon-correlation spectroscopy of ionic liquids;
- Absorption spectroscopy and Brillouin scattering;
- Differential scanning calorimetry;
- Molecular modelling and first-principles calculations;
- Classical and quantum mechanics (QM) MD simulations of ionic liquids.

Nov. 2001 – Apr. 2005 Post-graduate school, Dept of Solid State Electronics, Uzhhorod National University.

- Structure and properties of glassy and amorphous materials;
- *Ab initio* and DFT calculations of local atomic structures (clusters): geometry, energy, stability, electronic and vibrational properties;
- Vibrational (IR/Raman) and absorption edge spectroscopy;
- Low-frequency Raman and resonant Raman spectroscopy of binary and ternary glassy chalcogenides (As-S, As-Se, Ge-S, As-Ge-S).

Sept. 1996 – Jun. 2001 Graduate school, Department of Physics, Uzhhorod National University.

Teaching experience

2014-2018 Docent at the Department of Informative and Operating Systems and Technologies, Faculty of Information technologies, Uzhhorod National University.

2008-2018 Supervising Master students and co-supervising Ph.D. students; developing guidelines in using *ab initio* and DFT methods, Raman and XPS analysis for lab. of Spectroscopy of Thin Films, Dept of Solid State Physics, Uzhhorod National University.

2007 Teaching Electromagnetism and Optics, University of Augustine Voloshin (Uzhhorod).

2005 Teaching assistant; Laboratory exercises, Spectroscopy of glasses and thin films materials, Dept of Solid State Electronics, Uzhhorod National University.

Supervision/coaching of students

B.Sc.: Cheypes István (2016), Title: «*Associative memory systems based on Hopfield neural networks*» (supervision);
Tigly Borys (2016), Title: «*Development of an information system for solving the problem of data clustering using Kohonen networks*» (supervision);
Nagy István (2017), Title: «*Information system for one of the tasks of manufacturing process planning*» (supervision).

M.Sc.: Sekeresh Viktoriya (2017), Title: «*Software development and investigation of the dynamic modified Leontief-Ford model*» (supervision);
Petrishe Ivan (2017); Title: «*Software development and study the effect of dispersion on the spectral characteristics of optical filters*» (supervision).

Ph.D.: Markusson Henrik (2006), Title: «*New electrolyte materials for lithium batteries and fuel cells - an ab initio and vibrational spectroscopy study*» (coaching);
Martinelli Anna (2007), Title: «*Structure, interactions and functionality in novel electrolyte materials for fuel cell applications*» (coaching);
Lovas Gábor (2016), Title: «*Emission spectroscopy of germanium disulfide based chalcogenide glasses and surface degradation during natural aging*» (coaching);
Petretskyi Stepan (2017), Title: «*Low-temperature thermal conductivity of wide-bandgap chalcogenide glasses at changing the local coordination and characterization of high connectivity films for ray optic applications*» (coaching);
Mahmood Malik H. (2021), Title: «*Preparation and characterization of biopolymeric microparticles for surface-enhanced Raman spectroscopy and fluorescent spectroscopy imaging*» (coaching).

Presentations at scientific conferences

2023 The first 35 years of reverse Monte Carlo Modeling, RMC-8(+1) Conference, Budapest, Hungary.
IX Ukrainian Scientific Conference on Physics of Semiconductors, Uzhhorod, Ukraine (*Invited talk*).

III International Advanced Study Conference Condensed Matter and Low Temperature Physics, Kharkiv, Ukraine.

2022 International research and practice conference «Nanotechnology and nanomaterials», Lviv, Ukraine.

2021 X International seminar "Properties of ferroelectric and superionic systems", Uzhhorod, Ukraine (*Invited talk*).

2020 18th International Conference on Thin Films & 18th Joint Vacuum Conference, Budapest, Hungary.

2019 13th Pacific Rim Conference of Ceramic, Okinawa Convention Center, Japan.

2018 The 26th International Conference on Advanced Laser Technologies, Tarragona, Spain.

2017 International research and practice conference «Nanotechnology and nanomaterials», Chernivtsi, Ukraine (*Invited talk*).

2016 8th International conference on materials science and condensed matter physics, Chisinau, Moldova.

2015 7th International Conference on Amorphous and Nanostructured Chalcogenides, Cluj – Napoca, Romania.

2014 XXIV International Conference on Raman Spectroscopy, Jena, Germany.

2013 6th international Conference On Amorphous and Nanostructured Chalcogenides, Brasov, Romania (*Invited talk*).

2012 35th International Convention on Information and Communication Technology, Electronics and Microelectronics, Opatija, Croatia.

2011 X-th International Conference on Amorphous and Nanostructured Chalcogenides, Bucharest-Magurele, Romania.

2010 International Conference on Optical, Optoelectronic and Photonic Materials and Applications, Budapest, Hungary (*Invited talk*).

2009 23rd International conference on amorphous and nanocrystalline semiconductors, Utrecht, Netherlands.

2008 XXIX European Congress on Molecular Spectroscopy, Opatija, Croatia.

2007 IInd International Congress in Ionic Liquids, Yokohama, Japan.

2006 10th International conference on the structure of non-crystalline materials, Praha, Czech Republic.

2005 21st International conference on amorphous and nanocrystalline semiconductors Lisbon, Portugal.

2004 XI-th International conference on phonon scattering in condensed matter, St. Petersburg, Russia.

2003 IX International Conference of physics and technology of thin films, Ivano-Frankivsk, Ukraine (*Invited talk*).

2002 Ist Ukrainian conference on semiconductor physics, Odessa, Ukraine.

2001 XV International School-Seminar "Spectroscopy of molecules and crystals, Chernihiv, Ukraine.

Selected research projects

- Wigner Postdoc (2020-2023) "Experimental and theoretical investigation of hybridization of nucleobases, nucleosides and RNA/DNA sequences".

- Horizon 2020 NEURAM FET-Open project "Visual genetics: establishment of a new discipline to visualize neuronal nuclear functions in real-time in intact nervous system by 4D Raman spectroscopy", 2018-2020 (*Participant*).
- Project of Ministry of Science and Education (MSc.Ed.) of Ukraine DB-884 “Synchrotron-photoelectron, surface-enhanced Raman spectroscopy and stimulated mass transport processes in functional nonlinear-optical elements of ultrafast integral-optical circuits”, 2018-2020 (*Principal Investigator*).
- Project of MSc.Ed. of Ukraine DB-842 “The processes monolayers formation and nanophase structuring of two-dimensional graphene like arsenic and germanium chalcogenides in a glassy matrix”, 2015-2017 (*Principal Investigator*).
- Project of MSc.Ed. of Ukraine GP/F44 (grant of President of Ukraine) “Nanostructure formations and energy states in non-linear optical non-oxide photonic glasses for telecommunication”, 2012 (*Principal Investigator*).
- Project of MSc.Ed. of Ukraine of the program of Ukrainian-Turkish collaboration in science and technology (M/85-2010) “First principle calculations, IR and Raman investigation of high refractive index nanostructured amorphous layers formation for developing interference filters to control the content of gases polluting an atmosphere”, 2010-2011 (*Ukrainian co-director*).
- Stiftelsen FUTURA project “Future fuel cell and battery materials: Ionic Liquids”, 2005-2007 (*Participant*).
- Grant of President of Ukraine for young talent scientists: “Spectroscopic investigation and nano-structural modelling of structure and characteristics of homogeneous and inhomogeneous radiation strength optical coatings for high refractive and nanostructured materials”, 2005-2006 (*Responsible participant*).
- Project of MSc.Ed. of Ukraine M/467-2003 of the program of Ukrainian-Hungarian collaboration in science and technology (2003-2004) “Optical properties of optimized IR transparent glasses for detectors of gases polluting the atmosphere”, №0103U007898 (*Participant*).
- Project of MSc.Ed. of Ukraine DB-507 “Modeling and investigation of intercoupling between formation of nanostructures and physical properties of radiation strength non-crystalline systems and films on their base”, №0103U001682, 2000-2002 (*Participant*).

Additional skills

Languages: English (*advanced*), Ukrainian (*mother tongue*), Russian (*fluent*), Swedish (*intermediate*), Hungarian (*beginner*).

IT:

- Familiar with Windows, LINUX/UNIX systems, Clusters (PDC Center for High Performance Computing (Stockholm), National Supercomputer Centre (Linköping)).
- *Ab initio* quantum-chemical and semi empirical programs GAMESS (US), GAUSSIAN, MOPAC, HyperChem, Quantum Espresso, ChemOffice, Abinit, Gulp, MolDen, Molekel, *etc*.
- Classical and first principles (QM) molecular dynamics: GROMACS, CPMD.

- Programming in Ruby, Python, TP, experience in using Corel-Draw, Origin, MatLab, Data mining software, *etc*.

Honors/awards

- Scholarships of the Hungarian Government for young teachers outside Hungary (2014/15, 2015/16, 2016/17 acad. years).
- Support from CERIC-ERIC for experiments at Elettra Sincrotrone Trieste (2016, 2017).
- Grant from President of Ukraine for GP/F44 research project "Nanostructure formations and energy states in non-linear optical non-oxide photonic glasses for telecommunication" (2012).
- Support from International Centre for Theoretical Physics (ELETTRA-ICTP) (2010, 2011).
- Grants from Domus Hungarica for research projects (2011, 2013, 2014, 2015, 2016, 2017):

  Title: "*Raman and surface-enhanced Raman studies of amorphous As_2S_3, Sb_2S_3, and Bi_2S_3 thin films*" (2011);

  Title: "*Felületerősített Raman szórás és ab initio DFT-számítások ultragyors optikai adatfeldolgozásban használható $As_xS(Se)_{100-x}$ (x=40,50) amorf nanorétegekben*" (2013);

  Title: "*Gerjesztő fotonenergia-függő lumineszcencia és felületerősített Raman szórás ultragyors optikai adatfeldolgozó rendszerekben alkalmazható kalkogenideken*" (2014);

  Title: "*Germánium alapú kalkogenidek kísérleti és elméleti vizsgálata a jövő 3D elektronikai, fotonikai és napenergia technológiái számára*" (2015);

  Title: "*Kötésátrendeződés és lézersugárzás által okozott tömegtranszport vizsgálata fotonikus kalkogenid közeg felületén SERS és fotolumineszcencia spektroszkópiás kísérletekkel, és DFT számításokkal*" (2016);

  Title: "*Funkcionalizált kétdimenziós grafénszerű kalkogenid nanoszerkezetek előállítása és jellemzése*" (2017).
- Member of the public body of the Hungarian Academy of Sciences (2009).
- Grant from Stiftelsen FUTURA-project (research fellow, 2006).
- Granted by Swedish Institute three times (exchange Ph.D. student and research fellow).
- Award from Swedish Institute for participation on Nobel Prize Ceremony (2004).
- High school, Bachelor and Master Diplomas with honours.
- Secondary school, Gold medal for special successes in education.

Fields of activities

(i) Material science (chalcogenide photonic media; Ionic liquids, Li-ion batteries and energy related materials);
(ii) Biochemistry, genetics and molecular biology (molecular modeling, RNA/DNA analysis), DNA recognition;
(iii) Data mining, computational chemistry (molecular dynamics (MD) simulations, *ab initio*/DFT calculations).

Experimental and theoretical methods

(i) Raman/SERS and infrared (IR) spectroscopy;
(ii) X-Ray and synchrotron radiation photoelectron spectroscopy (XPS/SRPES);
(iii) Photon energy dependent photoluminescence (PL);
(iv) Scanning electron microscopy (SEM);
(v) Energy dispersive X-Ray Spectroscopy (EDXS);
(vi) Differential Scanning Calorimetry;
(vi) MD simulations, *ab initio*/DFT calculations.

Recent collaborations

Dana Cialla-May, Leibniz Institute of Photonic Technology, Germany
James Tucker, University of Birmingham, UK
John S. Fossey, University of Birmingham, UK
Ferenc Mueller, University of Birmingham, UK
Attila Csik, Institute for Nuclear Research, Debrecen, Hungary
Kevin C. Prince, Elettra, Sincrotrone Trieste, Italy
Vladimír Matolín, Charles University in Prague, Czech Republic
Alexander Feher, P. J. Šafárik University in Košice, Slovakia
Miroslav Vlček, University of Pardubice, Czech Republic
Patrik Johansson, Chalmers University of Technology, Sweden
Wu Xu, Arizona State University, USA
Jean-Claude Lassègues, Université Bordeaux, France

References

Prof. Dr.Volodymyr Mitsa	Department of Solid State Physics, Uzhhorod National University, 88000 Uzhhorod, Ukraine, e-mail: mitsa@univ.uzghorod.ua Tel: +38(03122) 3-30-20
Prof. Dr. Patrik Johansson	Department of Applied Physics, Chalmers University of Technology, 41296 Göteborg, Sweden, e-mail: patrikj@fy.chalmers.se Tel: +46317723178
Prof. Dr. Kevin Charles Prince	Elettra-Sincrotrone Trieste S.c.p.A., 34149 Basovizza (Trieste), Italy, e-mail: prince@elettra.trieste.it Tel: (+39) 040-375-8642

Research skills

In my professional career, I have already demonstrated an excellent commitment to conduct independent and groundbreaking research. Among my >70 publications, 29 are with a "special" authorship (first, last and/or corresponding author). Several papers are published in journals with a high impact factor (IF>5) including leading specialized journals for non-crystalline materials, solid state physics, physical chemistry, Raman spectroscopy, surface science, such as of Non-Crystalline Materials (9 papers), Journal of Raman Spectroscopy (5 papers), Physica Status Solidi (5 papers), Journal of Physical Chemistry and Journal of Chemical Physics (3 papers), Journal Nanoscale Research Letter (2 papers), Applied Surface Science (2 papers), Philosophical Magazine (2 papers), Applied Physics (1 paper), Alloys and Compounds

(1 paper), Solid State Communication (1 paper), Scientific Report (1 paper), *etc*. [12 of them are as the first author]. The main area of research during my Ph.D. study was related with the structure-property relationship of chalcogenide materials. After a successful Ph.D. defence at the Uzhhorod National University (Ukraine), I conducted a postdoctoral research at the Chalmers University of Technology (Sweden) with world-class scientists in the field of energy related (mainly Li containing batteries) materials, namely P. Johansson (h-index 63 by Google Scholar), Wu Xu (h-index 103) and P. Jacobsson. I have developed an interdisciplinary vision in such areas as computational chemistry, Raman spectroscopy, surface science and light-matter interaction, including photo-induced phenomena in photosensitive chalcogenide media. Good research management skills can be demonstrated by the successful applications (six projects) for a beamtime at material science beamline (Synchrotron "Elettra"). The scientific leadership, team management skills and the ability to motivate of young researchers can be proven by our joint publications.

My research profile is characterized by a strong multidisciplinary character, covering a broad range of different types of materials and their states such as inorganic solids (crystalline, non-crystalline chalcogenides and functional thin films), mix of organic-inorganic liquids (ionic liquids) and recently - macromolecular systems (polymers, DNA and RNA strands). Being both experimental physicist and computational chemist, I acquired the mastery of various molecular/cluster modelling techniques, including *ab initio* HF/post-HF/DFT calculations and MD simulations in order to make predictions and to understand the structure-property relationship of different materials at the atomic scale in detail. These include, in particular, experimentally observed stimulated laser induced transformations occurring in the structure of photosensitive chalcogenide surface, Li-molecule coordination, cation-anion interaction in ionic liquids as well as hydrogen bonding formation and hybridization processes in DNA/RNA sequences. I distinguish myself for key achievements in the fields of non-crystalline and complex functional macromolecular materials, and for a highly motivated participant in various international collaborations. My research bridges the rigorous approaches of physico-chemical sciences, with the ambition to quantitatively describe the systems of high complexity from a structural and chemical point of view. From experimental side, I possess the expertise in different spectroscopic methods of material characterization starting from basic IR/Raman and XPS spectroscopy to highly surface sensitive techniques such as synchrotron radiation photoelectron spectroscopy and surface enhanced Raman spectroscopy.

The above mentioned skills can be summarized as follows:

1. Experimental methods

1.1. Visible light spectroscopy

» Vibrational (Raman) spectroscopy. Low-frequency, photon-energy dependent, resonant, surface-enhanced and Fourier-transform Raman spectroscopy;
» Infrared (IR) absorption/edge-absorption spectroscopy. Attenuated total reflection IR spectroscopy;
» Brillouin scattering, photon-correlation spectroscopy. Photon energy dependent photoluminescence.

1.2. X-ray spectroscopy/electron diffraction

» X-ray and synchrotron-radiation photoelectron spectroscopy;
» Energy dispersive X-ray spectroscopy;

» Low-energy electron diffraction.

1.3. Microscopy

» Scanning electron microscopy;
» Atomic force microscopy.

1.4. Calorimetry and low-temperature physics

» Differential scanning calorimetry;
» Low-temperature thermal conductivityand heat capacity.

2. Molecular modeling and molecular dynamics simulations

2.1. Molecular and crystal modeling/calculations

» Molecular/macromolecular modelling and visualization (Avogadro, ChemOffice, ChemCraft, Gabedit, MolDen, Molekel);
» Crystal modeling, visualization and calculations (Diamond, Rasmol, Mercury, Abinit, Quantum Espresso);

2.2. Molecular dynamics simulations

» Classical and first-principles molecular dynamics simulations (Gromacs, Gulp, CPMD, SIESTA).

3. Computational chemistry and theoretical methods

3.1. Semiempirical and first principles calculations

» Semiempirical (CNDO, INDO, MNDO, AM1, PM3) calculations;
» First-principles calculations: Hartree-Fock and *ab-initio* correlation post-HF (configuration interaction (CI), Møller–Plesset perturbation (MP, MP2) theory and coupled cluster (CC) theory) methods.

3.2. Density functional theory calculations

» Density functional theory (DFT) calculations (pure and hybrid functionals);
» Software: MOPAC, HyperChem, Gamess (UK/US), Gaussian.

Five selected publications from the last five years

[1]. **R. Holomb**, O. Kondrat, V. Mitsa, A. Mitsa, D. Gevczy, D. Olashyn, L. Himics, I. Rigó, A.J. Sadeq, M.H. Mahmood, T. Váczi, A. Czitrovszky, A. Csík, V. Takáts, M. Veres. *Gold nanoparticle assisted synthesis and characterization of As-S crystallites: scanning electron microscopy, X-ray diffraction, energy-dispersive X-ray and Raman spectroscopy combined with DFT calculations.*
J. Alloys Compd. 894 (2022) 162467. https://doi.org/10.1016/j.jallcom.2021.162467

Short description: Using spherical gold nanoparticles and thermally initiated chemical vapor deposition we synthesized novel type of nanostructured chalcogenides. The surface morphology study showed a growth of As-S crystallites with well defined shape. The structural characterization (Raman spectroscopy, XRD, EDXRS and DFT calculations) indicated that these crystallites are built from As_4S_5 cage-line molecules.

My contribution: conceptualization, synthesis, DFT calculations and Raman study, drafting the paper.

[2]. **R. Holomb**, V. Tkáč, V. Mitsa, A. Feher, M. Veres. *Structural nature of Boson peak and low-temperature heat excess in* As_2S_3 *glass.*
Phys. Stat. Sol. B. 257 (2020) 1900525. https://doi.org/10.1002/pssb.201900525

Short description: we performed comparative analysis of experimental Raman spectra of crystalline, glassy and powdered As_2S_3 samples. Using density functional theory (DFT) study of $As_6S_{6+6/2}$ ring-like nanoclusters the additional super-low frequency modes of "soft" rings at wavenumbers being significantly lower than the "rigid" ring's vibrational band at 26 cm^{-1} were calculated. The shift of the super-low frequency Raman modes of "soft" nanoclusters and equivalent characteristic temperature are found to be nonlinearly dependent on the number of interconnections. It was determined that the main contribution of both the low-frequency Raman band intensity and the low-temperature anomaly of specific heat at 5.3 K originates from "soft" clusters with four and two interconnections.

My contribution: conception of the research, Raman measurements, DFT calculations, interpretation of the spectra, drafting the paper.

[3]. O. Kondrat, **R. Holomb**, A. Mitsa, M. Veres, A. Csik, V. Takáts, T. Duchoň, K. Veltruská, M. Vondráček, N. Tsud, V. Mitsa, V. Matolín, K.C. Prince. *Reversible laser-assisted structural modification of the surface of As-rich As-Se nanolayers for active photonics media.*
Appl. Surf. Sci. 518 (2020) 146240. https://doi.org/10.1016/j.apsusc.2020.146240

Short description: using the synchrotron radiation photoelectron spectroscopy we studied the reversible structural changes of As-rich As–Se nanolayers occurring during *in situ* thermal annealing and above-bandgap laser illumination. It was found that the *in situ* green laser illumination of thermally annealed samples causes an increase in the concentration of homopolar As–As bonds associated with $As\text{-}Se_2As$ structural units, while the opposite effect was detected during further thermal treatment. These processes appeared to be fully reversible for many annealing and illumination cycles. The observed effect of the reversible photo-induced structural modification can be utilized as active optical medium for photonics.

My contribution: design of the research, sample preparation, *in-situ* synchrotron radiation photoelectron measurements, data analysis, drafting the paper.

[4].**R. Holomb**, P. Ihnatolia, O. Mitsa, V. Mitsa, L. Himics, M. Veres. *Modeling and first-principles calculation of low-frequency quasi-localized vibrations of soft and rigid As–S nanoclusters.*
Appl. Nanosci. 9 (2019) 975. https://doi.org/10.1007/s13204-018-00948-5

Short description: we conducted experimental and theoretical studies on Boson peak of binary As_xS_{100-x} glasses and As–S polycrystalline composites of different concentration. The low-frequency and Fourier-transform Raman spectra of As–S sampleswere measured in the ranges of 5–100 $cm^{-1}$and 50–600 cm^{-1}, respectively, in order to reveal the structure of the materials at nanoscale. Density functional theory calculations were also performed on different (branchy$As_{2+4/3}S_5$ and 12-membered ring-like $As_6S_{6+6/2}$) As–S nanoclusters for determination of their low-frequency vibrational modes. It was established that the vibrational mode frequencies of the clusters have a U-shaped dependence on the level of interconnection, which correlates with experimental findings on compositional dependence of the Boson peak position and features detected at low-energy sidein the low-frequency Raman spectra of As_xS_{100-x} glasses.

<u>My contribution</u>: main idea, Raman and low-frequency Raman measurements, modelling and first-principles calculations, drafting the paper.

[5]. O.B. Kondrat, **R.M. Holomb**, A. Csik, V. Takats, M. Veres, A. Feher, T. Duchon, K. Veltruska, M. Vondráček, N. Tsud, V. Matolin, K. C. Prince, V. M. Mitsa. *Reversible structural changes of in situ prepared $As_{40}Se_{60}$ nanolayers studied by XPS spectroscopy.* **Appl. Nanosci.** 9 (2019) 917. https://doi.org/10.1007/s13204-018-0771-3

<u>Short description</u>: we performed structural investigations of as-deposited, annealed and *in situ* irradiated (with 532 nm laser) $As_{40}Se_{60}$ nanolayers using synchrotron radiation photoelectron spectroscopy. Changes in composition and local atomic coordination occurring in the irradiated region of $As_{40}Se_{60}$ films were monitored by analysis of As 3*d* and Se 3*d* core levels. It was found that the thermal treatment causes a decrease of the concentration of homopolar (As–As and Se–Se) bonds. On the other hand, an increasing concentration of both As-rich and Se-rich structural units with homopolar As–As and Se–Se bonds was observed under *in situ* green laser illumination. The surface local structure of the $As_{40}Se_{60}$ nanolayers is discussed and the mechanism of photo-induced transformation is proposed.

<u>My contribution</u>: design of the work, material synthesis, XPS and valence band spectra measurements, data analysis and interpretation.

<u>Publications</u>

Total number of papers:	43
Number of papers as first/last/corresponding author:	21
Number of papers in the last 5 years (2019-2023):	22
Monographs/collective monograph:	4
Conferences/Meetings/Workshops:	~150

<u>Citations & related metrics</u>

Total number of citations:	912 (Scopus),	851 (WoS),	909 (MTMT),	1196 (Scholar)
h-index:	14 (Scopus),	13 (WoS),	14 (MTMT),	18 (Scholar)

Independent citations (MTMT): 688
Effective independent citations (MTMT): 602.75
Cumulative impact factor: ~116

Researcher profiles:

Scopus:	https://www.scopus.com/authid/detail.uri?authorId=6507694648
Web of Science:	https://www.webofscience.com/wos/author/record/299565
MTMT:	https://m2.mtmt.hu/gui2/?type=authors&mode=browse&sel=authors10044326
Google scholar:	https://scholar.google.com/citations?user=WGTqsNcAAAAJ&hl=en

Research plan for the next three years

DNA is the information repository of life. Nowadays the synthetic DNA and gene related technologies are of increasing demand across many research areas as well as commercial activities. The successes in next generation sequencing and gene editing technologies stimulated rapid development in gene engineering, chemistry and biology, medicine and therapy, data storage and nanotechnology. The ability to sequentially synthesize polynucleotides allows to control the composition and size of DNA sequences. The past two decades have witnessed a remarkable progress in generating and testing biological systems from synthetic genomes. On the other hand, there is still challenge in the development of fast, unambiguous and low cost detection of a particular DNA sequence, especially in a living organisms (*in vivo*).

At the moment, fluorescent microscopy has become a dominant research tool to study and visualize complex biological systems containing lipids, proteins, RNA/DNA, drug molecules, *etc*. Being a very useful technique to monitor the biological processes, this method have some shortcomings connected mainly with the basic working principles. For example, fluorescent probes (dye molecules, proteins, quantum dots) may effect on cell and/or tissue due to toxicity, mutations or alteration of biological function limiting their *in vivo* applications. The other disadvantage is connected to the limitations of spatial and temporal resolution. The size of fluorescent probe and interaction time for luminescence emission being hundreds of picoseconds. However, at the moment there is a high interest in the development of new imaging modalities that use intrinsic sample contrast to generate images, including fast imaging techniques based on infrared/Raman spectroscopy or coherent anti-Stokes and stimulated Raman scattering (the interaction time for Raman process is less than one picosecond) in which the imaging contrast is generated by probing thevibrational transitions of chemical bonds.

Nowadays, stimulated Raman scattering (SRS) is preferred as a highly sensitive and very fast imaging method allowing to study even the dynamics of different biological processes. The sensitivity and selectivity of such system can be enhanced remarkably by using very small molecular tags (alkynes, azides, deuterium, nitrile, *etc.*), which demonstrate specific and large Raman band intensities. Preliminary results indicate that the sensitivity, selectivity and performance of this method can additionally be expanded and thus successfully used for different areas of bioimaging and genetics. Theoretical and experimental study performed by me in the frame of the NEURAM EU H2020 project at the Wigner Research Centre for Physics showed that the sensitivity of the SRS for bioimaging can further be enhanced by factor of ~6-7 by using double alkyne (bis-alkyne) tagging of the nucleotide molecule (hereafter denoted as reporter molecule) instead of the single alkyne one. Also, theoretical predictions indicated that one of the fundamental features of biological molecules, namely hydrogen bonding interaction, can be used to extend the specificity of vibrational spectroscopy based imaging techniques.

It was discovered that the hydrogen bonding interactions of the reporter molecule (alkyne-tagged nucleotide containing alkyne group (C≡C bond)) in the DNA sequence affects the Raman frequency of the alkyne stretching vibrations. This phenomenon opens the way towards novel applications of bioimaging, especially if the structural origin of the Raman mode shift is known. Moreover, this possibility can bring new insights into the understanding of underlying processes allowing the detection of the hybridization of DNA and to find damaged regions in the DNA/RNA. In addition to the research on biological systems, identification of damaged genes is very promising for histopathological diagnosis, allowing identification of different diseases (cancer, mutations) at early stage. Recently we have successfully used alkyne labelled test DNA sequences to detect single nucleotide polymorphism (genetic mutation) by Raman spectroscopy. Such technique allowed us to detect the BRAF 600E cancerous mutant which is a single point variation (difference between TA match and TT mis-match nucleobase pairs) for prostate cancer. Together with the University of Birmingham and University of Pécs we already filed an international patent for using of this method ("Single point variant detection", EP4237582A1, WO2022090747A1). Also, the manuscript describing the details of the method is ready for submission. It should also be mentioned that similar methodology can potentially be used for the detection of different DNA/RNA viruses and we have recently proved it for the SARS-CoV-2 (COVID-19) virus.

Summarizing the above, the main goal of my research is to establish new directions of using Raman spectroscopy/SRS for a fast and easy DNA recognition which is very important for practical applications in different areas, such as engineering biology, genetics and medicine, including *in vivo* experiments on living cells. My future work will contain two main parts - theoretical studies (related with the improvement and predictions) and experiments (practical realization). Therefore, the research plan is as follows:

First year: *Improving the sensitivity of reporter nucleotide molecule.* In addition to the simplest (single alkyne labelled) reporter molecule (5-ethynyl-2'-deoxyuridine, EdU), I will consider other reporters such as C_8-Alkyne-dT and C_8-Alkyne-dC. Both are available in phosphoramidite form ready for solid-phase oligonucleotide synthesis. In addition, the nucleotides containing two C≡C bonds (bis-alkynes) will be considered for future application. *Ab initio* calculations will be performed on single nucleobases and different nucleobase pairs in order to understand the effect of frequency shift of C≡C stretching vibrations of these molecules upon conformational change and base pairing (DNA hybridization). The Raman activities of different molecules will also be calculated in order to increase the sensitivity of Raman detection. In addition, the HOMO-LUMO gap modified reporter molecules (containing Au and/or Ag atom) will be tested theoretically in order to achieve the resonant Raman condition in the visible photon energy range. Such approach will allow to increase the Raman signal up to several orders of magnitude, decreasing the detection time to seconds. To improve the spectral resolution (higher frequency shift due to hydrogen bonding interaction), the effect of selective hydrogen-to-deuterium substitution in the reporter molecules will also be calculated. For better predictions, I will also adapt the hybrid QM/MM (quantum mechanics/molecular mechanics) approach to simulate 15-20 nucleobase long oligos using "Our own N-layered Integrated molecular Orbital and Molecular mechanics" (ONIOM) method developed by Morokuma and co-workers, considering the nucleobase pair containing the reporter as a high ONIOM layer (the region is treated using QM) and the remaining part of the oligo will be treated empirically (semi-empirically) using the novel force field developed for nucleic acids (Amber OL15 and OL3 for DNA and RNA, respectively).

Second year: *Raman tests of DNA probes containing different reporter molecules.* Based on the theoretical predictions, I will test the DNA probes containing different reporter molecules and use complementary and non-complementary target sequences with different types of mis-match base pairs. At this stage, I will also develop the methodology to achieve the best sensitivity and spectral resolution, allowing future SRS imaging of DNA hybridization processes *in vivo* in real-time. Also, the SRS imaging will be performed on different biological objects (cells, tissues, *etc.*) in order to verify the sensitivity, specificity and reproducibility of the results obtained by this method. Unfortunately, more complicated structural modification is not possible for a small reporter molecule involved in the hydrogen bonding interactions because of the alteration their biological functionality and possible DNA hybridization problem. However, there is an alternative way to read out the information from DNA. The charge distribution at the phosphate backbone of a single stranded DNA is different from that of the double stranded DNA containing Watson-Crick or wrong base pairs. Therefore, both hybridization processes and single point variants can be distinguished by incorporation of a reporter molecule into the phosphate backbone. Also, this method will extremely be useful because the detection can be realized without the limitation of the modified reporter molecule's size. In collaboration with University of Birmingham, I have preliminary tested the reporter molecules containing phenyl alkyne part attached to the phosphate backbone of DNA. The results show that this is highly sensitive and very promising regarding the Raman mode intensity and spectral resolution. Therefore, I am planning to continue with the development of this method too.

Third year: *Surface-enhanced Raman spectroscopy of different oligo probes*. At present, the field of surface-enhanced Raman spectroscopy (SERS) obtains enormous interest for the detection of various molecules at extremely low concentrations. Using different types of SERS substrates this method is already in use for many practical applications, such as single molecule detection, identification of microplastics in water, *etc*. However, the use of this method for macromolecules is somehow limited due to complexity of the systems. As far as I know, there are no well developed and unambiguous techniques for DNA (or oligo) recognition using SERS. Several attempts, known from the literature, claiming for a DNA identification using SERS method limit their conclusion to the guanine-rich (or adenine-rich, *etc*.) region determination after the Raman bands interpretation. I am planning to eliminate this shortcoming by using alkyne-tagged nucleotides. Here, the already established alkyne Raman mode frequency shift upon oligo hybridization will be a unique and unambiguous identifier of the target strand structure when the complementary probe strand with alkyne-labelled nucleobase is used (a non-complementary strand will not hybridize). The surface enhancement will be achieved using different approaches: (i) by creation of self-assembled probe oligo-structures (*i.e.* by attaching one of the oligo end (3' or 5') to the gold/silver surface by using thiol bond while the second end will be connected to corresponding (Au/Ag) nanoparticle (NP). The variation with NPs at both 3'- and 5' ends of probe is also possible. (ii) By using π-bonding of gold and/or silver atom with the C≡C bond of the reporter nucleotide (direct interaction) or *via* the thiol group. (iii) By using different (spherical, dendrite-, star- and needle-like) nanostructured gold and silver-based SERS substrates. The one case of the latter approach I am testing together with the surface-enhanced vibrational spectroscopy group of Prof. Cialla-May (Leibniz Institute of Photonic Technology, Germany).

Funding acquisition plans

In the future, I am planning to setup an international network for collaboration in the field of DNA recognition and fast bioimaging using optical spectroscopy. Our group has already submitted new HORIZON-EIC-2023-TRANSITION project proposal (section: Full Scale Micro-Nano-Bio devices for medical and medical research applications), entitled "Easy detection of single nucleotide variants (SNV) using Raman spectroscopy" with the participants from Italy (University of Padova), Hungary (Wigner RCP, NEURON SzoftverKft., University of Pécs), UK (University of Birmingham) and Germany (Oncotherm Gmbh). In addition, my preliminary results indicate that the DNA recognition method can further be improved if the surface-enhancement is used. Therefore, I am planning to make close collaboration with University of Szeged (synthetic DNA) and Leibniz Institute of Photonic Technology (surface-enhanced spectroscopy) and, subsequently, apply for a grant supporting our common international research project in the future. I will also apply for the title of Doctor of the Hungarian Academy of Sciences in the next years.