Medical Imaging Alliance Siberia & UK

BOOK OF ABSTRACTS

RUSSIAN FOUNDATION FOR BASIC RESEARCH

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UNIVERSITY OF HULL

Novosibirsk, Russia,
22-25 November, 2018

Novosibirsk, Russia,
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Vladimir Fedin

Professor in Inorganic Chemistry, Director of the Nikolaev Institute of Inorganic Chemistry, Siberian Branch of Russian Academy of Sciences, Novosibirsk
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Vladimir Fedin received his M.Sc. degree in 1976, and PhD degree in 1980 from Department of Chemistry, Moscow State University. Since 1981 he holds permanent position at Nikolaev Institute of Inorganic Chemistry SB RAS, Novosibirsk, and since 2005 he is Director. He was visiting/invited professor at University of Versailles (France), University of La Laguna (Spain), University of Karlsruhe (Germany) and University of Bielefeld (Germany). Prof Fedin is an editor of Journal of Structural Chemistry and an advisory board member of Russian Journal of Inorganic Chemistry, Journal of Cluster Science, and Russian Chemical Bulletin. He also served as a Panel member for European Research Council Advanced Grants. His research interests include (1) Development of cluster and polyoxometalate chemistry; (2) Supramolecular chemistry of cucurbiturils, (2) Synthesis and functional properties of metal-organic framework based materials.

Carl Redshaw

Department of Chemistry & Biochemistry, University of Hull; College of Chemistry & Materials, Northwest University, Xi′an.

Current Positions

100 Plan Professor, Northwest University, Xi′an, China.
Chair of Inorganic Materials, University of Hull, UK.
Visiting Professor, National Institute of Technology, Akashi College, Hyogo, Japan.

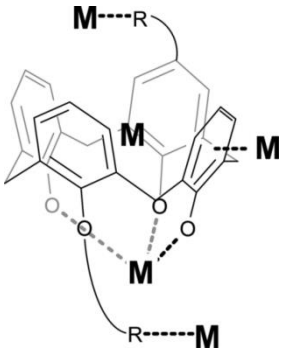
Metrics

Publications in the primary literature ~350.
h index 46.

Membership of Professional bodies

Fellow of the Royal Society of Chemistry (FRSC)
Fellow of the Higher Education Academy (FHEA)
Member of the American Chemical Society.

Using the coordination chemistry toolbox to tackle societal issues



By manipulating the versatile coordination chemistry of the calix[*n*]arene family (see figure on right), it is possible to isolate highly active catalysts for α-olefin homo (and co-)polymerizations [1] and for the ring opening polymerization (ROP) of cyclic esters. [2] This allows access to new polymers with useful properties including biodegradation. We can also use calixarenes to access MOFs for gas storage, [3] and employ them as scaffolds for metal complexes of interest as anti-cancer and imaging agents. [4] This talk will give an overview of our results to-date and will include synthetic and structural studies, together with results for the above-mentioned applications.

Our group has extensive international links with China (including a lab at Northwest University, Xi′an), Japan, USA, Canada and in Russia (Novosibirsk). The latter part of the talk will be a geography test!

References

[1] Vanadium(V) Oxo and Imido calix[8]arene complexes: Synthesis, structural studies and ethylene homo-(co-)polymerization capability. C. Redshaw, M. J. Walton, D. S. Lee, C. Jiang, and M. R. J. Elsegood and K. Michiue, *Chem. Eur. J.* **2015**, *21*, 5199-5210.

[2] Highly Selective and Immortal Magnesium Calixarene Complexes for Ring Opening Polymerization of *rac*-Lactide. M. J. Walton, S. J. Lancaster, and C. Redshaw. *Chem.Cat.Chem.*, **2014,** *6*, 1892-1898 (Front cover & VIP status).

[3] Pillared 2-D metal-organic frameworks based on a lower-rim acid appended calix[4]arene. C. Redshaw, O. Rowe, M. R. J. Elsegood, L. Horsburgh and S.J. Teat, *Cryst. Growth & Design*, **2014**, *14*, 270-277.

[4] D. M. Miller-Shakesby, S. Nigam, D. L. Hughes, E. Lopez-Estelles, M. R. J. Elsegood, C. J. Cawthorne, S. J. Archibald and C. Redshaw. *Dalton Trans*. **2018**, *47*, 8992 - 8999.

Prof. Steve Archibald

Positron Emission Tomography Research Centre, University of Hull, UK

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Steve Archibald is the Director of the Positron Emission Tomography (PET) Research Centre and a Professor in Molecular Imaging Chemistry at the University of Hull. He has interests in PET probe development, chelator synthesis and chemokine receptor binding molecules. He started his research into medical imaging and positron emission tomography on joining the University of Hull in 2000. Since 2011 he has led a research project to develop new lab-on-a-chip devices for integrated synthesis and quality control of radiopharmaceuticals (five patent applications). Current probe development includes chemokine receptor targeted agents, multimodal (PET/MR) imaging with coated nanoparticles, targeting fibrotic plaques, new bifinctional chelators for PET metalloradioisotopes, mitochondrial function reporting agents, PET/MR imaging of tissue engineering constructs and contrast agent encapsulation. Steve is also a company director of Daisy Medical Research Ltd.

Positron Emission Tomography Molecular Imaging of Receptor Targeted Radiopharmaceuticals

Positron emission tomography (PET) is a medical imaging technique using radioactive biomarkers to locate abnormalities within the body. Currently, fluorine-18 is the radionuclide 'gold standard' for PET imaging [1]. However, radiometals are becoming an attractive alternative due to their range of radioactive half-lives and decay characteristics but they have not yet been fully exploited. Gallium-68 ($t_{1/2}$ = 68 min) is quickly emerging as the main competitor to fluorine-18 for PET imaging due to its short half-life and on-site generator production.

Copper-64 ($t_{1/2}$ = 12.7 h) can be used to label high affinity CXCR4 chemokine receptor antagonists can be engineered through optimised coordination interactions and used in positron emission tomography imaging after radiolabelling. This class of molecules offer two key advantages in the receptor binding: high affinity and tunable residence time at the receptor. This indicates the potential for use of this class of molecules in therapy as well as imaging. Microreactor technology is a useful tool for radiolabelling as it offers the potential to greatly improve radiochemical yields, reduce shielding requirements and subsequently generate 'dose-on-demand' quantities of the radiotracer for patients within the clinical environment.[1]

[1] Tarn MD, Kizilyer NY, Esfahani MMN, Joshi P, Brown NJ, Pamme N, Jenkins DG, Archibald SJ: *Chem. Eur. J.* 2018, **24**(52):13749-13753.

Mark Green

Department of Physics, King's College London.

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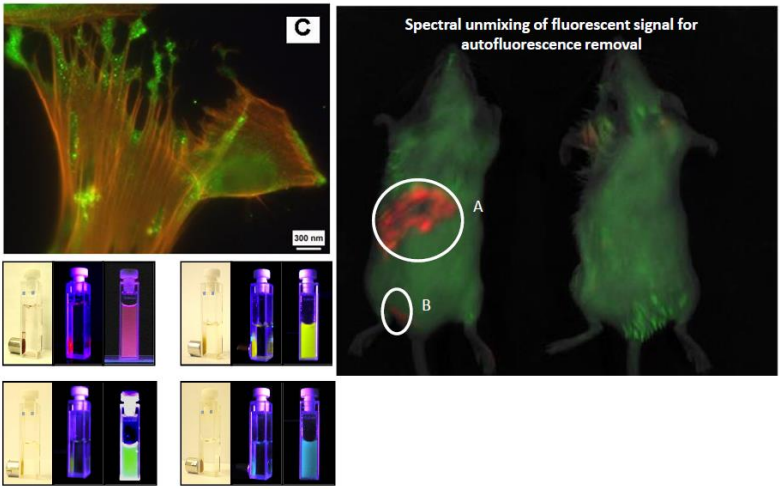
Professor Mark Green received his BSc from Manchester Metropolitan University in 1995 and his PhD from Imperial College London in 1998. He was a post-Doctoral fellow at Imperial College from 1998-99 and at the University of Oxford from 1999-2000. He worked as a Scientist at Oxonica Ltd from 2000-2004 and then joined King's College as a lecturer in Bio-nanotechnology in 2007. He became a Senior Lecturer in 2007, a Reader in 2009 and a Professor in 2014.

Nanomaterials for biology

The use of nanoparticles in imaging applications has become a mainstream discipline. Since the seminal use of quantum dots in simple imaging in 1997, the area has been the focus of a massive amount of research, despite the fact that these solid-state materials have obvious down falls – notably the toxicity associated with metals such as cadmium. The benefits, such as enhanced stability and tuneable, multicolour, narrow emission are desirable and in some cases outweigh the negative aspects. In this talk, we will describe the work undertaken in the last several years at KCL in the preparation of quantum dots, alternatives such as metal-free particles, and explain the more unusual results such as the biosynthesis of quantum dots inside living animals.



Olga I. Lavrik

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Olga Lavrik has completed her graduation from Novosibirsk State University. PhD and Dr. of Sciences degrees were from the Institute of Bioorganic Chemistry in Moscow. She is a director of Laboratory of Bioorganic Chemistry of enzymes in the Institute of Chemical Biology and Fundamental Medicine of Russian Academy of Sciences. Olga Lavrik is professor of Novosibirsk State University and head of the department of physicochemical biology and biotechnology of Altay State University. Olga Lavrik was a supervisor for 30 PhD thesis. She has worked as a Visiting Professor at The University of Texas, Texas, NIEHS(NIH), North Carolina, Institute Jacques Monod and University of Évry Val d'Essonne, France. She has published more than 350 papers and has been serving as a member of the Editorial Board of Journal of Molecular Biology. She is a Member of the Study Section of Russian Fund for Basic Research , Member of Federation of European Biochemical Societies and a Chancellor of European Environmental Mutagenesis and Genomics Society. She won a State prize and was awarded other decorations of Russia and France. She is a correspondent member of Russian Academy of Sciences.

Bioimaging of human protein complexes involved in repair of DNA damages

Multiprotein complexes play a central role in repair of DNA damages which appear under endogenous and exogenous stress. DNA structure can be damaged by oxidative stress, UV-light, oxidized aromatic compounds and ionizing radiation. Usually repair machines represent by complex protein assemblies and they are very effective in the removal of DNA lesions to keep the integrity of genomes. The various approaches based on imaging of these complex structures were developed to study protein–protein and DNA- protein interactions operating in DNA repair in vitro and in vivo. The lecture will be devoted to review of these methods. The efficiency of protein –protein interactions in the protein complexes responsible to repair damaged bases was studied by using fluorescence titration and FRET techniques and the most effective interactions were revealed. DNA repair machines are regulated by reaction of poly (ADP-ribosylation) catalysed with Poly(ADP-ribose)polymerases (PARP1 and PARP2). The specificity of PARP1 and PARP2 interaction with long DNA fragments and DNA plasmids containing single- and/or double-strand breaks (SSBs and DSBs) have been studied using atomic force microscopy (AFM) imaging in combination with biochemical approaches. The activity of DNA repair systems is preventing to action of anticancer therapy directed to DNA damage. Therefore one of the important directions of the modern medicinal chemistry is search of the inhibitors of DNA repair enzymes as potential anticancer drugs. In our studies we have developed rapid fluorescent methods for the real-time measurement of PARP1 and TDP1 activities which are the important targets to develop anticancer drugs. Some of the inhibitors of these enzymes were selected as leader compounds for the preclinical studies.

This study was supported by grants RNF 14-24-00038 and RFBR 17-04-00925.

References

Moor et al, NAR, 2015, Moor et al., Biochemistry, 2018, Sukhanova et al, NAR, 2016, Kurgina et al, Anal Biochem, 2018, Zakharenko et al., Bioorg. Med. Chem, 2015.

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Director of N.N. Vorozhtsov Novosibirsk Institute of Organic Chemistry Siberian Branch Russian Academy of Sciences, Head of Department of Physical Organic Chemistry and Laboratory of Magnetic Resonance . A specialist in the field of physical chemistry, the development and application of new magnetic resonance methods for the study of mechanisms of chemical reactions, the structure and function of biopolymers, study the properties of molecular magnets. The author of over 180 scientific articles and 6 chapters in monographs, more than 400 abstracts. The main areas of r research interests: NMR and EPR application for studying the structure and function of biopolymers and new magnetic materials, research and application of the functional properties of the spin probes, spin labels based on nitroxyl radicals and trityl and supramolecular complexes; development of new highly sensitive time-resolved magnetic resonance methods for detecting short-lived radical species and their application to the study of radical reactions mechanisms of electron-nuclear spin polarization and electronic relaxation; radical polymerization controlled by nitroxides. A member of the Deputy Chief Editor of "Applied Magnetic Resonance", a member of ISMAR Committee, president of Asia Pacific EPR Society , President of the Russian EPR society. Scientific adviser of 15 PhD theses.

Spin probes and spin labels. Application in EPR tomography and structural biology

Spin probes and spin labels open various opportunities for application of EPR to study biological systems. Nitroxide and triarylmethyl radicals are the most widely used as spin labels and spin probes in EPR tomography and structural biology. In this presentation, we review (1) the application of nitroxides and triarylmethyl radical in EPR tomography to visualization of pH, oximetry and redox status *in vivo* and (2) highlights some recent achievements in pulsed dipolar EPR spectroscopy allowing for distance measurements in nanometer range and at room temperatures. A number of examples of spin traps and spin labels application in biology and medicine will be shown and discussed. General trends and focus on potential artifacts to be avoided in practical implementations will be discussed; we also address issues of persistence/protection of spin adducts (EPR reporters) against bioreduction and kinetic studies in this regard.

References

[1] E. G. Bagryanskaya, O. A. Krumkacheva, M. V. Fedin, S. R. A. Marque, Development and Application of Spin Traps, Spin Probes, and Spin Labels" *in Methods in Enzymology*, 2015, 563, 365.

[2] O. Krumkacheva, E. Bagryanskaya, Trityl radicals as spin labels, *Book EPR, From the book: Electron Paramagnetic Resonance:* 2016, **25**, 35-60.

Dr Olga Efremova

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email: o.efremova@hull.ac.uk

Olga Efremova (MSc in Chemistry, PhD in Inorganic Chemistry) is a lecturer at the University of Hull since 2015. Prior to that she held Marie-Curie Fellowship at Aston University (UK) and was a scientific researcher at Nikolaev Institute of Inorganic Chemistry, where she undertook her PhD study. In her research she integrates the best performing organic, inorganic compounds and polymers into bespoke materials to target specific biological or materials-based applications. Her particular interest is in the development of photoactive materials for such applications as bioimaging and optical sensing. Apart from that she is keen to develop smart materials for applications such as antibacterial surfaces and photocatalysis. She has published 40+ papers and secured £400K+ of research funding from the UK and international sources and has strong collaborative links with numerous institutions in both the UK and Russia.

Novosibirsk-Hull collaboration on photoluminescent octahedral metal clusters for biomedical research: the road so far

Photoluminescent octahedral cluster compounds of molybdenum and tungsten of general formula $[\{M_6X_8\}L_6]$ (where M is Mo or W; X is Cl, Br or I and L are organic or inorganic ligands) are a relatively novel class of compounds that have a unique set of properties such as luminescence in Red-Near-Infrared region, ability to generate singlet oxygen upon photoirradiation very efficiently (i.e. they act as photosensitisers) and high X-Ray attenuation ability. They also lack some draw-backs of other classes of photosensitisers, such as poor photostability or self-quenching. This ability of the metal clusters can, therefore, be employed in the development of materials for bioimaging, cancer therapy and photoinduced anti-bacterial activity. At the workshop I will present the results of our joint collaboration with Nikolaev institute of Inorganic Chemistry on development of materials based on octahedral metal cluster compounds to target applications such as above.

References:

[1]E.V. Svezhentsev et al, *Chemistry-A European Journal*, 2018, doi 10.1002/chem.201804663.

[2]D.V. Evtushok et al. *Dalton Trans.*, **2017**, 46, 11738-11747.

[3] A. O. Solovieva et al, *J. Mat. Chem. B*, **2016**, 4, 4839-4846.

Michael A. Shestopalov

Nikolaev Institute of Inorganic Chemistry SB RAS,
3 Acad. Lavrentiev ave, Novosibirsk, Russia

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Academic background:

9/2001 - 6/2007 Graduate Student, Novosibirsk State University;
7/2007-12/2010 – PhD student, Nikolaev Institute of Inorganic Chemistry SB RAS (Novosibirsk);
23.12.2010 Ph. D. In Chemistry: "Octahedral chalcogenide rhenium cluster complexes with organic ligands".

Current Positions

Senior Researcher in Nikolaev Institute of Inorganic Chemistry SB RAS
Senior Researcher in The Federal Research Center of Fundamental and Translational Medicine (1/2 position)
Senior Researcher in Meshalkin National Medical Research Center (1/4 position)
Senior Researcher in The Federal Research Center of Fundamental and Translational Medicine (1/4 position)
Senior Researcher in Novosibirsk State University (1/4 position)

Metrics: publications – 55, h index – 15.

Octahedral hexanuclear metal-cluster complexes as X-ray contrast agents

Radiocontrast agents are used in medicine to improve visibility of inner body structures in X-ray imaging techniques. To date, the most of radiocontrast agents are based on 1,3,5-triiodobenzene derivatives. Low toxicity and high solubility allowed these compounds to integrate into a medical field. However, their application has some drawbacks like cardiovascular, anaphylactic (allergic), painful effects, and probability of emergence contrast-induced nephropathy. We believe that octahedral chalcogenide rhenium cluster complexes with the general formula $[\{Re_6Q_8\}L_6]^n$ (Q = S, Se or Te; L = apical organic or inorganic ligands) may become alternative radiocontrast materials. In these compounds a cluster core $\{Re_6Q_8\}$ may potentially act as a radiocontrast component and the apical ligand environment similar to substituent in 1,3,5-triiodobenzene radiocontrast agents may provide biocompatibility.

Thus, the aim of our research was to study radiopacity, cytotoxicity, intracellular localization in vitro and acute intravenous toxicity in vivo of several octahedral rhenium cluster compounds with different inner (Q) and outer (L) ligands, namely, $Na_4[\{Re_6Q_8\}(CN)_6]$ and $Na_2H_8[\{Re_6Se_8\}(P(CH_2CH_2CONH_2)(CH_2CH_2COO)_2)_6]$, to evaluate which cluster complex is more promising for the application as X-ray contrast agent.

Elena Krivoshapkina

International Laboratory "Solution Chemistry of Advanced Materials and Technologies", Biochemistry Cluster, ITMO University, St. Petersburg, Russia

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Education and training

2006 Master of Science in Chemistry, with specialization in Physical Chemistry
2012 Ph.D. in Chemistry, Saint-Petersburg State Institute of Technology, Russia
Main field of study: formation mechanisms of supramolecular compounds between structural precursors of the proteins, peptides and polysaccharides with inorganic nanoparticles; the creation of functional organic-inorganic nanocomposites.

Internship

2011, 2012, 2013, 2016 Boreskov Institute of Catalysis SB RAS, Novosibirsk, Russia
2012 Helmholtz Zentrum Berlin (HZB), Berlin, Germany
Deutsches Elektronen-Synchrotron (DESY), Hamburg, Germany
2012 Institut Laue-Langevin (ILL), Grenoble, France
2015 Institute of General and Inorganic Chemistry National Academy of Sciences, Republic of Belarus

Work experience

2004-2016 – Senior Researcher, Institute of Chemistry, Komi SC RAS, Syktyvkar, Russia
2017 - Present time – Associate Professor, ITMO University, St. Petersburg, Russia

Nanobioarchitectonics: directed design of hybrid materials

Spider silk surpasses all the synthetic polymers in mechanical properties, due to its specific hierarchical structure. Nevertheless, there is no complete understanding of the structural organization of spider thread. When introducing metal oxides, nanoparticles into the silk structure, conformational rearrangements take place dramatically changing properties of the material. The goal of this research is the creation of interaction model of inorganic nanoparticles with polymer biomolecules with their subsequent testing. The obtained models can be used to create biocomposite materials based on scleroproteins of spider silk and inorganic nanoparticles for the needs of biomedical use and tissue engineering. Spider silk is supplied through an insectarium, in which more than 50 individuals of the funnel-web tarantulas and curtain-web spiders are represented. For instance, silk modified with TiO_2, Mo_2O_5 NPs showing enhanced antibacterial properties was performed for biomedical applications. Then, silk modification with optically active HfO_2 and ZrO_2 NPs was carried out for bio-visualization. Recently hafnium oxide nanoparticles were discovered to act as quantum dots. These NPs are advantageous with the respect to quantum dots due to their significantly lower toxicity towards the living systems. When doping hafnium oxide with rare earth elements, simultaneously electron transitions in rare earth elements allow observing upconversion luminescence. The development of highly efficient biocompatible agents for complex diagnostics and therapy of diseases is the main scientific challenge the project.

This work is supported by Russian Science Foundation, Grant No.18-79-00269.

Julio M. Rios de la Rosa

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Julio M. Rios de la Rosa obtained his BSc/MSc in Biotechnology at Universidad Pablo de Olavide in 2013. He completed his PhD in 2017 at the University of Manchester as part of the highly competitive North-West Nanoscience Doctoral Training Centre (NoWNano DTC), having enjoyed a funding from EPSRC to do part of his work at the University of Cambridge. Julio then became a Research Associate at the North-West Centre for Advanced Drug Delivery (NoWCADD), a translational centre funded through a collaboration with AstraZeneca's Pharmaceutical Sciences and Pharmaceutical Technology and Development departments. During his time in the UK, his research focused on the characterisation and biological evaluation of colloidal systems that promote selective accumulation of therapeutics in solid tumours. As an Honorary Research Fellow, he now contributes to the design of NoWCADD projects looking to develop next generation drug delivery systems. Julio is currently a Research Scientist at BiOncoTech Therapeutics, a VC-funded company with offices in Spain currently evaluating in the clinic several immune-oncology combinations with its lead nanomedicine product, BO-112.

Labelling of Colloidal Systems: A Cellular to Preclinical Perspective

Over the last few decades, nanomaterials have demonstrated huge potential to advance biomedical applications, providing researchers with valuable tools not only for understanding a myriad of processes at the molecular level, but also for evaluating/promoting the accumulation of therapeutics in specific tissues and even cell populations. However, the use of colloidal systems for such applications often requires of their surface 'decoration'/functionalization with (bio)molecules of interest, be it pharmacological drugs, tracking molecules (e.g. fluorophores, radioactive isotopes), or targeting ligands (e.g. antibodies, peptides). To this end, there is an increasing number of experimental strategies that can be used to functionalize colloids of different nature, from metallic nanoparticles to carbon nanomaterials to polymer polyplexes, in an easy and rapid manner. For example, several click chemistries have been readily applied to colloidal delivery systems by introducing or exploiting specific reactive groups present in these systems (e.g. azide-alkyne, amine-carboxylic acid).

During this talk, I will elaborate on my experience with the functionalization and biological evaluation of a number of nano-sized drug delivery systems in the context of cancer treatment. In particular, I will focus on the possibilities to make colloidal systems detectable, e.g. in order to evaluate their uptake by different cell types and subsequent intracellular processing, which may shed light about their *in vivo* behavior. Last, I will comment on the advantages and limitations of labelled colloids in assessing the translatability of clinical data and *in vivo* mechanism of action to *in vitro* models.

Mariya V. Edeleva

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Dr. Mariya Edeleva graduated from Novosibirsk State University in 2008. She obtained her PhD in 2011 at International Tomography centre SB RAS on the topic of controlled-living radical polymerization.

Since 2015 she's been working as research associate at Novosibirsk Institute of Organic Chemistry. Her scientific interests are synthesis of complex macromolecular structures by nitroxide mediated polymerization, kinetics of reaction, spectroscopic techniques like NMR, EPR and IR.

Conventional way for preparation of amphiphilic block-copolymers for metal-crosslinked micelles with enhanced stability

Hereafter we report synthesis of micelles based on two types of block-copolymers, i.e. ABA and AC, where block A is poly-(styrene-ran-4-vinyl pyridine), block B is polyethylene glycol, and block C is poly-(acetoxystyrene-ran-hydroxysturene). All block-copolymers were obtained by Nitroxide Medaited Polymerization with N-tert-butyl-N-[1-diethylphosphono-(2,2-dimethylpropyl) *nitroxide* as controlling agent. Two different strategies were used to synthesize block-copolymers: (a) 1,2 radical addition reaction of *N*-(2-methylpropyl)-*N*-(1-diethylposphono-2,2-dimethylpropyl)-*O*-(2-carboxylprop-2-yl) hydroxylamine (BlockBuilder, Arkema, BB) onto PEG-diacrylate dimonomer with subsequent formation of di-alkoxyamine based on SG1 which was used for initiation of styrene (Sty) and 4-vinyl pyridine (VP) copolymerization; (b) sequential polymerization of Sty with VP and acetoxyastyrene (AcOSty) with subsequent partial hydrolysis of second block. In both cases we obtained amphiphylic block-copolymers suitable for preparation of micelles in water. As one of the blocks contained VP units capable for formation of complexes with metal ions, we were able to cross-link the core of the micelles. We used $Zn(hfac)_2$ as a source of Zn ions and mimic conjunction with metal-based drug. Recently we showed that $Zn(hfac)_2$ enhances the initiation rate of NMP making it more efficient.[1] As we showed hereafter, complexation enhanced the stability of micelles in conditions similar to blood, i.e. high salt concentrations as shown by gel-filtration chromatography and dynamic light scattering. Furthermore due to reversibility of VP complexation micelles become unstable in acidic conditions that are typical for extracellular medium in tumors. Furthermore, we were able to synthesize micelles with stable organic radical substituents (triarylmethyl radicals) that make detection of drug delivery possible.

[1] Audran, G., Bagryanskaya, E., Edeleva, M., Marque, S. R., Parkhomenko, D., Tretyakov, E., & Zhivetyeva, S. Coordination-Initiated Nitroxide-Mediated Polymerization (CI-NMP). Australian Journal of Chemistry.

Masoomeh Bazzar

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Dr. Masoomeh Bazzar research interest encompass several areas of synthetic organic compounds, supramolecular and polymer chemistry and processing including electrospinning to prepare and characterization functional materials which have potential applications in the use of chemo and bio-sensors, molecular switches, extraction of metal ions from aqueous solutions and biomedical applications

PROFESSIONAL EXPERIENCE:

2014–2016 Post-doctoral research associate, Department of Chemistry, Bilkent University, Ankara, Turkey.

2016–2018 Post-Doctoral Research Fellow Department of Chemistry, University of Bologna, Bologna, Italy

01/06/2018–date Post-doctoral research associate, Faculty of Science and Engineering, School of Mathematics and Physical Sciences, University of Hull, United Kingdom. **09/10/2013–12/04/2014** Visiting researcher, Department of Chemistry, University of Waterloo, Waterloo, Canada

04/04/2016–27/05/2016 Visiting researcher, Department of Chemistry, University of Cambridge, Cambridge, United Kingdom

EDUCATION :

2010–2014 PhD in Polymer Chemistry, Faculty of Chemistry, University of Mazandaran, Babolsar, Iran.

MEMBERSHIP:

Member of Royal Society of Chemistry, **United Kingdom**

Near-infrared emitting polymer and oligomer nanoparticles conjugated polyrotexans and SPIONs

Near infrared emitting conjugated polymer and oligomer nanoparticles (NICNs) are highly appealing for various advanced applications such as in vivo imaging, cell labeling, and delivery of therapeutic agents, as well as nanophotonics, owing to their high quantum yields and molar absorptivity, tunable properties, easy functionalization, photostability, and so forth. To date, the use of NICNs has been demonstrated successfully in cell imaging, oxygen sensing, drug delivery, and nucleic acid delivery. When these nanostructures are judiciously designed, they can be utilized in theranostic applications by combining more than one functionality to deliver therapeutic and imaging agents. Cucurbiturils (CBs) are macrocycles with a rigid symmetrical structure that are composed of n glycoluril units (where n = 5, 6, 7, 8, 10, and 14) connected by methylene bridges and possess two identical hydrophilic portals with a hydrophobic cavity. A variety of nanostructured materials including nanoparticles, nanocomposites, vesicles, rods have been prepared by taking advantage of the varying cavity size of the CB homologues, their ability to accommodate more than one guests in their cavities, their rigid symmetrical structures. Moreover, they have been widely used to encapsulate and solubilize dyes. The high magnetic susceptibility of Superparamagnetic iron-oxide nanoparticles (SPIONs) makes them ideal for use in biotechnology in contexts such as biomagnetic separation, magnetic drug targeting, hyperthermia, and imaging. These particles are used in conjunction with magnetic resonance imaging (MRI) to identify infection and inflammation. Here we investigated the effect of cucurbit [7]uril (CB7) on the thermal and optical properties of fluorine-thiophene based conjugated polyelectrolytes and encapsulation of SPIONs with thiophene based conjucated polymers. For these purposes conjugated red emitting polymers were synthesized by threading the part of the conjugated backbone of these polymers with CB7 during their synthesis. The results show that CB7 containing fluorene–thiophene conjugated polymers exhibit considerably higher electroluminescence colour purity as compared to that of the pristine polymers thanks to the improved nanoscale morphology and photophysical properties in the CB7 threaded polymers. Also with TEM study we demonstrate that it is advantageous to precisely modify the SPION surface with aminosilane to encapsulate with thiophene based conjugated polymers.

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Evgeny K. Apartsin graduated from Novosibirsk State University in 2010. In 2014, he obtained his PhD degree in bioorganic chemistry from the Institute of Chemical Biology and Fundamental Medicine SB RAS. Currently, he is a research associate at the Laboratory of RNA Chemistry ICBFM SB RAS. His research interests cover the design of biomaterials for biomedical applications. Dr. Apartsin is a member of the international consortiums dealing with the design of nanomaterials for cancer treatment.

Highlighted publications:

1. E.K. Apartsin et al. *Hydrogels of polycationic acetohydrazone-modified phosphorus dendrimers for biomedical applications: gelation studies and nucleic acid loading*. Pharmaceutics. 2018. 10(3), Paper ID: 120 (13 pages).
2. Ju. Poletaeva et al. *Non-covalent associates of siRNAs and AuNPs enveloped with lipid layer and doped with amphiphilic peptide for efficient siRNA delivery*. Int. J. Mol. Sci. 2018. 19(7), Paper ID: 2096 (19 pages).
3. C. Gutiérrez Ulloa, et al. *Carbon nanotubes decorated with cationic carbosilane dendrons and their hybrids with nucleic acids.* ChemNanoMat. 2018. 4(2), pp. 220-230.
4. C.E. Gutierrez-Ulloa et al. *Amphiphilic carbosilane dendrons as a novel synthetic platform toward micelle formation.* Org. Biomol. Chem. 2017. 15 (35), pp. 7352-7364.
5. E. K Apartsin et al. *Novel multifunctional hybrids of single-walled carbon nanotubes with nucleic acids: synthesis and interactions with living cells*. ACS Appl. Mater. Interfaces 2014; 6(3), pp. 1454-1461.

Interaction of hydrophobic trinuclear tungsten clusters with phospholipid bilayers: a route towards functional hybrid materials

Nanoconstructions composed of lipid vesicles and inorganic nanoparticles arouse much interest across materials science and bionanotechnology as drug carriers, visualization or detection agents etc. Most potential applications of such composite nanoconstructions require nanometer-scale inorganic particles, either to achieve quantum effects or to avoid drastic changes of structure, physicochemical and biological properties of lipid vesicles. Ideally, however, a nanoparticle is not to be wrapped but rather to be embedded into a bilayer.

Herein, we report a spontaneous self-assembly of phospholipids and trinuclear W_3S_4 clusters bearing hydrophobic 4,4′-di-*tert*-butyl-2,2′-bipyridine (dbbpy)[29] and 4,4′-di-*n*-nonyl-2,2′-bipyridine ligands into novel cluster-lipid composite materials. Intact cluster molecules are embedded into the hydrophobic interior of the lipid bilayer, with hydrophobic interactions being the driving force for the embedding. The behaviour of clusters in the hydrophobic lipid environment is determined by the volume of the ligands and cluster-to-lipid ratio. The variation of these two parameters makes it possible to obtain different self-assembled associates such as cluster-doped liposomes or lipid-covered crystals. These cluster-lipid composites can be a platform for the design of new materials for nanotechnology.

The work was supported by the RFBR grants 17-03-00663 and 18-33-20056.

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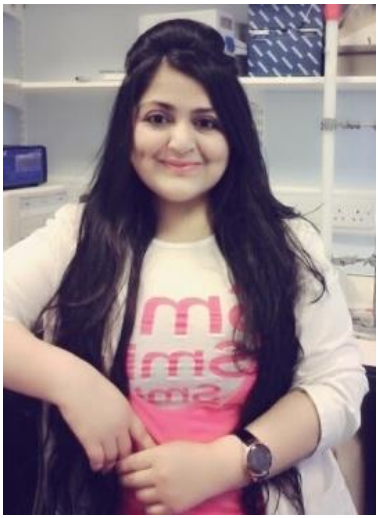

PhD in cell matrix and regenerative medicine

Stem cell research

2017-2021 at University of Manchester, Manchester, UK

President doctoral scholar Uom

Masters research: oral cancer

2015-2016 from university of Dundee, Scotland, UK.

BACHELORS IN DENTAL SURGERY B.D.S
2007-2011 from Altamash institute of dental medicine, Karachi, Pakistan.
Registered dental surgeon (Pakistan medical and dental council) since 2012.
Research interests : Gene editing, Crispr cas9 and stem cells.

Human Induced pluripotent stem cells imaging in detection of pluripotent surface and nuclear markers

My research project involves working on reprogrammed human induced pluripotent stem cells (hiPsc) acquired from patients suffering from rare genetic diseases.

Mesenchymal stem cells which closely resemble chondrocytes and ultimately forming a growth plate like cartilage structure. Pluripotency is a major step in detection of the authenticity of the stem cells regenerative capability and was checked through immunofluorescence. (Nakagawa, Lee et al. 2009)

Reference

Nakagawa, T., et al. (2009). "Induction of chondrogenesis from human embryonic stem cells without embryoid body formation by bone morphogenetic protein 7 and transforming growth factor beta1." Arthritis Rheum **60**(12): 3686-3692.

Peter Kozhin

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Peter received his PhD in 2016 in Federal research center of basic and translational medicine, Russia. His PhD research focused primarily on the investigation of role of redox-sensitive signal system Nrf2/Keap1/ARE in tuberculosis as a part of study of molecular-cellular mechanisms of mycobacterial granulomatous inflammation and study of pharmacological targets for its correction. A role of pharmacological activation of the redox-sensitive signaling system Keap1 /Nrf2/ARE in the development and resolution of mycobacterial inflammation was investigated. In his work he primarly focus on behavior of cellular compartments. His areas of particular interest include phagocytosis, autophagy, target delivery and pharmacokinetics of drugs with application of laser confocal microscopy.

Induction of redox sensitive signalling system to influence on processes of autophagy and lysosomal biogenesis in vitro

Autophagy should recognize an effective mechanism for elimination of mycobacterium tuberculosis from macrophages, even in the case when mycobacteria blocks phagosome-lysosomal fusion. The involvement of autophagy and Keap1/Nrf2/ARE redox-sensitive signaling system in regulating and eliminating effects of free radical oxidative processes is not in doubt, but at the moment very little is known about their mutual regulation and correction, and the data are often inconsistent.

The following drug combinations were investigated: control; isoniazid; rifampicin; TC-13 (Nrf2 inducer); isoniazid + TC-13; rifampicin + TC-13, isoniazid + rifampicin.

The combined effect of anti-tuberculosis drugs with TS-13 led to a significant increase in the number of autophagosomes compared with the mono-effects of anti-tuberculosis drugs.

An important indicator is the number of LC3b / LAMP1-positive vesicles, reflecting the processes of autophagosomal-lysosomal fusion. It was greatest in the group of combined exposure of monophenol TC-13 with isoniazid or rifampicin (especially rifampicin), which reflects an increase in the autophagosomal-lysosomal fusion process necessary for the elimination of mycobacteria.

Experimental confirmation of effectiveness and specific mechanisms of action of the inducer of Keap1/Nrf2/ARE system monophenol TS-13 make possible to consider it a promising drug for use in treatment of tuberculosis.

Dr. Daria Novopashina

Senior researcher of the Laboratory of RNA Chemistry of the Institute of Chemical Biology and Fundamental Medicine of SB RAS, Russia

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Daria received her M.Sc. degree in Chemistry (2000) from Novosibirsk State University and Ph.D. in Bioorganic Chemistry (2009) from Institute of Chemical Biology and Fundamental Medicine SB RAS. Her Ph.D. research focused on the synthesis of conjugates of modified oligoribonucleotides and their application for the gene expression inhibition. Her research interests include nucleic acid chemistry, investigation of hybrid formation between carbon nanotubes, dendrimers and nucleic acids fragments and the synthesis and study of new types of fluorescent oligonucleotides probes for nucleic acids detection, and other applications of oligonucleotides as instruments of molecular biology and fundamental medicine. Currently, her work is devoted to the synthesis and application of functional RNA molecules for gene therapy and gene editing and fluorescent oligonucleotide probes for NA visualization. She has more than 30 peer-reviewed articles.

Sequence-specific Fluorescent Probes for Nucleic Acid Visualization

Design of sequence-specific fluorescent probes for intracellular RNA and DNA imaging in fixed and living cells is the issue of the day[1]. In the case of double-stranded DNA, sequence-specific polyamide oligo(N-methylpyrrole/N-methylimidazole) minor groove binders are promising as the basis for fluorescent probes. Synthetic minor groove-binding pyrrole-imidazole polyamides labelled by fluorophores and targeted to the repeated sequences from mouse major satellites were synthesized and tested[2].In the case of intracellular RNA, modified oligonucleotides provide sequence-specific imaging. Several types of fluorescent probes targeted to 28S ribosomal RNA were developed: linear fluorescent probes based on 2'-O-methyl RNA analogs, molecular beacons and binary fluorescent probes[3-5]. Pyrene that possesses a high quantum yield and able to form excimer with appearance of a new band in fluorescence spectrum was used as a fluorophore. The suitability of these probes for DNA and RNA visualization were demonstrated.

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Current Positions

FRC Institute of Cytology and Genetics of Siberian Branch of the Russian Academy of Sciences, senior researcher
FRC of Fundamental and Translataional Medicine of Siberian Branch of the Russian Academy of Sciences, senior researcher
Novosibirsk Institute of Organic Chemistry of Siberian Branch of the Russian Academy of Sciences, researcher
Novosibirsk State University, professor

Metrics

19 publications, top 3 articles:

1. Orientation-controlled, low-temperature plasma growth and applications of h-BN nanosheets // NanoResearch. 2018.
2. Preparation of curcumin self-micelle solid dispersion with enhanced bioavailability and cytotoxic activity by mechanochemistry // Drug Delivery. 2018.

Antioxidant and antitumor activity of trolox, trolox succinate, and α-tocopheryl succinate conjugates with nitroxides // European Journal of Medicinal Chemistry. 2016.

Fluorescent labeling of ursolic acid for investigation of its cytotoxicity

Fluorescent labeling is a widely-used approach in the study of intracellular processes. This method is becoming increasingly popular for studying small bioactive molecules of natural origin; it allows us to estimate the vital intracellular changes which occur under their influence. In this paper we propose a new approach for visualization of the intracellular distribution of triterpene acids, based on fluorescent labeling by fluoresceine isothiocyanate.

As a model compound, we took the most widely-used and best-studied acid in the ursane series – ursolic acid, as this enabled us to compare the results obtained during our research with the available data, in order to evaluate the validity of the proposed method. Using molecular modeling and microscopic analysis, we investigated possible targets for triterpene acids.

We investigated biological activity of obtained fluorescent labeled epimers. As predicted by molecular modeling, the cytotoxic and apoptotic properties were increased after inclusion of fluoresceine isothiocyanate. Using confocal microscopy we registered the distribution of fluorescent labeled ursolic acid first on the intracellular membranes, and then on the mitochondria.

Experimental tracing of the dynamics of penetration and distribution of the labeled ursolic acid has shown that when the acid enters the cell, it initially localizes on the inner membranes where the predicted target Akt1 – a protein that inhibits apoptosis – is located.

Dr Ruslan Cusnir

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Trained as analytical radiochemist, I obtained my PhD in Life Sciences from the University of Lausanne in Switzerland studying bioavailability and speciation of plutonium in aquatic environments. I then moved on to radiopharmaceutical chemistry, joining King's College London as a postdoctoral fellow. My interests encompass translational radiochemistry and radiopharmacy, and bringing new metallic radionuclides to the clinic.

Education:

2016-2018 Certificate of Advanced Studies in Radiopharmaceutical Chemistry / Radiopharmacy, ETH Zurich, Switzerland
2013-2016 PhD in Life Sciences, University of Lausanne, Switzerland
2010-2012 MSc in Molecular and Biological Chemistry, EPF Lausanne, Switzerland
2006-2010 BSc in Chemistry, State University of Moldova, Chisinau, Moldova

Experience:

August 2016 – current Postdoctoral research fellow, Department of Imaging Chemistry and Biology, King's College London, UK
October 2012 – March 2016 Research assistant, Institute of Radiation Physics, University Hospital of Lausanne, Switzerland

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Investigation of the effects of trace metal impurities on radiolabelling *tris*(3-hydroxy-4-pyridinone) with ^{68}Ga

Diagnostic and therapeutic radiopharmaceuticals that target cancer cell receptors have transformed healthcare practices in oncology. New metallic radioisotopes will have important applications in nuclear medicine, as long as they can be chemically incorporated into relevant biomolecules. The commercial availability of the ^{68}Ge/^{68}Ga generator together with radiolabelling kits enables clinics and hospitals on-site access to diagnostic radiopharmaceuticals for PET imaging, without expensive cyclotron facilities. This fosters broader applications of positron emission tomography (PET) for cancer diagnostics. Trace metals are found in generator-produced ^{68}Ga, and these interfere with radiolabelling reactions. Advanced chelator design as well as efficient and robust methods of purification of solutions of ^{68}Ga will improve radiosynthesis of kit-based radiopharmaceuticals. In my recent project I used a promising new chelator, *tris*(3-hydroxy-4-pyridinone) (THP) that has clinical utility in biomolecular imaging of cell receptors. I identified trace metal impurities that are present in solutions of generator-produced ^{68}Ga, investigated radiolabelling of THP chelator with ^{68}Ga in the presence of competing metal impurities, elucidated which metals interfere with radiolabelling, and defined purification methods for removing these competing metals.

Zabrodina Galina

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Educations:

2000-2005 Graduate student, Lobachevsky State University, Nizhny Novgorod, Russia.
2005-2008 Ph.D. student, G. A. Razuvaev Institute of Organometallic Chemistry of RAS, Nizhny Novgorod, Russia.
2009 Ph.D. in chemistry.
2009-current, scientific researcher of G. A. Razuvaev Institute of Organometallic Chemistry of RAS, Nizhny Novgorod, Russia.
Research interest: chemistry of coordination and organic complexes, water-soluble aminohydroximate complexes, gadolinium contrast agent, nanosized hybrid materials.

Water-soluble aminohydroximate 15-metallacrown-5 complexes towards potential MRI contrast agents for ultra-high magnetic field

The development of contrast agents specifically designed for high-field magnetic resonance imaging (MRI) is required because the relaxation efficiency of classic Gd(III) contrast agents significantly decreases with increasing magnetic field strengths. With an idea of exploring the unique structure of lanthanide 15-MC-5 metallacrowns, we developed a series of water-soluble Gd(III) aqua-complexes, bearing aminohydroxamate (glycine, α-alanine, α-phenylalanine and α-tyrosine) ligands, with increasing number of water molecules directly coordinated to the Gd(III) ion. The ability to increase the number of Ln(III) inner-sphere water molecules up to four, the planar metallacrown structure and the rich hydration shell due to strong hydrogen bonds between the [15-MC-5] moiety and bulk water molecules provide new opportunities for potential MRI applications.

References:

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[2] M.A. Katkova, G.S. Zabrodina, M.S. Muravyeva, A.A. Khrapichev, M.A. Samsonov, G.K. Fukina, S.Yu. Ketkov, Inorganic Chemistry Communications, 2015, 52, 31-33.

[3] M.S. Muravyeva, G.S. Zabrodina, M.A. Samsonov, E.A. Kluev, A.A. Khrapichev, M.A. Katkova, I.V. Mukhina, Polyhedron, 2016, 114, 165-171.

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Benjamin Burke

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Ben Burke earned his PhD in 2013, during which he developed methodologies for chelator-free radiolabelling of iron oxide nanoparticles to form PET/MR imaging agents. He is currently the principle translational radiochemist between the PET Research Centre at the University of Hull and the Molecular Imaging Research Centre at Castle Hill Hospital, where he is focussed on the development of novel imaging agents from bench-to-bedside. His research interests include using nuclear imaging to understand nanoparticle behaviour, chemokine receptor imaging for oncology, and improving radiochemical methodologies using both radiometals and fluorine-18.

Nuclear Imaging of Magnetic Nanoparticles

Successful translation of magnetic nanoparticles through to clinical use requires an extensive development and iterative design process to optimise a range of *in vivo* characteristics Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) are nuclear imaging techniques which offer unparalleled non-invasive imaging sensitivity. Tagging nanoparticles with a radioactive isotope which emits a positron or gamma photon allows for the collection of *in vivo* information including clearance properties and target tissue accumulation concentration. This information can be key to understanding how chemical modifications affect *in vivo* behavior, allowing for expedited design optimization and clinical translation. This talk will present both the advantages of using nuclear imaging for researchers designing magnetic nanoparticles for biomedical applications and offers a roadmap for developing and imaging radiolabeled nanoparticles.

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EMPLOYMENT:

2016 – current Postdoctoral Research Associate in Radiochemistry, King's College London
2010 – 2012 Scientific Editor, European Directorate for the Quality of Medicines, Council of Europe, Strasbourg

EDUCATION:

2012 – 2016 PhD in Chemical Biology, King's College London
2004 – 2010 Doctor of Pharmacy, Université de Strasbourg, France
2007 – 2010 Master's degree in chemistry and biology, Université de Strasbourg, France

PET Tracking of therapeutic Gamma-delta T-cells in a cancer model using ^{89}Zr-oxine

Introduction: The development of cellular immunotherapies against cancer would greatly benefit from *in vivo* cell tracking solutions. Vγ9Vδ2-T cells are a highly cytotoxic subset of T cells, used successfully in several clinical trials in cancer immunotherapy. Using the recently developed PET tracer [^{89}Zr]Zr(oxinate)$_4$ ($t_{1/2}$ = 78.4 h), human Vγ9Vδ2-T cells were tracked in a xenograft breast cancer model, using PEGylated liposomal alendronate (PLA) to attract Vγ9Vδ2-T cells towards tumour tissue.

Methods: MBA-MB-231.hNIS-GFP breast cancer cells were injected s.c. in female SCID/beige mice. In one group (*n*=9), tumours were sensitised by i.v. administration of PLA (5 mg/kg alendronate) 4 days prior to Vγ9Vδ2-T cell injection. Control groups received placebo liposomes (*n*=4), non-liposomal alendronate (*n*=3) or Vγ9Vδ2-T cells alone (*n*=5). γδ-T cells isolated from peripheral blood were radiolabelled with [^{89}Zr]Zr(oxinate)$_4$ and injected in the tail vein. Animals were imaged by PET/CT and by SPECT/CT (^{99m}Tc). The cancer-cell-killing ability of radiolabelled γδ-T cells was evaluated *in vitro*.

Results: Vγ9Vδ2-T cells radiolabelled with ^{89}Zr showed the expected biodistribution/pharmacokinetics. Radiolabelling did not affect their ability to kill tumour cells *in vitro*. Vγ9Vδ2-T *in vitro* proliferation was only affected by amounts of ^{89}Zr ≥50 mBq/cell. Accumulation of Vγ9Vδ2-T cells in tumours was demonstrated by PET/CT and confirmed by histology. Tumour uptake was higher in the PLA-treated group than in control groups (Vγ9Vδ2-T +PLA: 2.1 ± 0.8 %ID/g versus Vγ9Vδ2-T without PLA: 1.2 ± 0.3 %ID/g, *n*=9-12, p=0.0018). Radiolabelling of liposomes with ^{111}In demonstrated accumulation of PLA in the tumour. **Conclusion:** We demonstrated that [^{89}Zr]Zr(oxinate)$_4$ allows efficient delivery of ^{89}Zr to γδ-T cells and sufficient retention for *in vivo* tracking by PET over 7 days. *In vitro* studies showed no adverse effect of radiolabelling on γδ-T cell functionality. Accumulation of γδ-T cells in tumour tissue was enhanced by pretreatment with aminobisphosphonate-loaded liposomes.

Richard Edwards

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Research Experience

Since 2017 *The Institute of Cancer Research,* Sutton, UK Chemistry and Radiochemistry for application in Cancer Imaging

2016 - 2017 *Institut Européen de Chimie et Biologie (IECB)*, Bordeaux, France Synthesis of novel hypervalent iodine reagents for utility in new asymmetric transformations

2011 - 2015 *Cardiff University*, Cardiff, UK, (PhD) Synthesis of [^{18}F]F-DOPA using hypervalent iodine compounds

2010 - 2011 *Cardiff University*, Cardiff, UK, (Masters) Palladium catalysed hydrogen / deuterium exchange using microwave irradiation

Esteem Indicators

07. 2018 Oral Presentation, 22nd International Symposium on Fluorine Chemistry, Oxford, UK

02. 2015 Best poster award (1st prize) at RSC Organic Division South-West Meeting

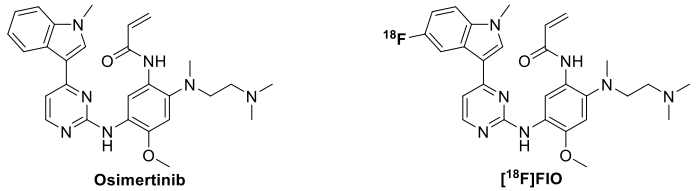
11. 2014 Selected as Cardiff University's participant at the 'Lilly Drug Discovery Workshop 2014'

05. 2014 Best student talk award (1st prize) at 13th Cardiff Chemistry Conference

Design and Synthesis of an ^{18}F-Labelled Osimertinib Derivative [^{18}F]FIO for PET Imaging of Mutant EGFR

Tyrosine kinase inhibitors (TKIs) such as Erlotinib and Gefitinib have been used effectively for the treatment of non-small cell lung cancer (NSCLC) patients bearing 'sensitising' mutations.[1,2] However, acquired resistance to these targeted therapies through an additional T790M mutation occurs in 50%-60% of patients.[3] Osimertinib is a third generation EGFR inhibitor which selectively and irreversibly binds to both 'EGFR sensitising' and double mutant (T790M) mutations and is currently the only globally approved TKI for EGFR T790M positive NSCLC patients.[4,5]

Radiolabelled Osimertinib analogues for PET imaging could potentially provide information on the tumour penetration of Osimertinib, tumour heterogeneity and serve as a means of patient stratification. Here, we report the design, realisation and biological assessment of an ^{18}F-labelled 5-fluoroindole analogue of Osimertinib (**[^{18}F]FIO**). Screening of both the biological and physicochemical properties of a variety of fluorinated analogues established **[^{18}F]FIO** as the most attractive target, with a profile similar to Osimertinib.



Scheme 1 – Osimertinib and 5-fluoroindole Osimertinib (**[^{18}F]FIO**)

Radiofluorination of a fully functionalised precursor using diverse radiochemistry strategies proved unsuccessful. However, a simple two-step synthesis has been developed to access the target compound. The approach utilises a copper catalysed radio fluorination[6] of boronic ester precursor **1** to produce intermediate **2** in excellent radiochemical yields (50-75% decay corrected RCY) before S_NAr with functionalised aniline **3** yields the target compound **[^{18}F]FIO** (9-12% decay corrected RCY over 2 steps).

Investigation into the use of **[^{18}F]FIO** as a PET radiotracer for the *in vivo* determination of EGFR mutation status in NSCLC cell lines is ongoing.

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Academic background:

9/2002 - 6/2005 Chemistry department student (Master Degree), Novosibirsk State University;
9/2005 - 6/2007 Graduate Student, Novosibirsk State University;
7/2007-5/2010 – Ph. D. student of A.V. Nikolaev Institute of Inorganic Chemistry (Novosibirsk);
19.05.2010 Ph. D. In Chemistry: "New approaches to synthesis of 6-9 group transition metal chalcogenide complexes";

3/2015 POM Group Leader

Research interests:

Chemistry of transition metal clusters, noble metal chalcogenide clusters, chemistry of non-innocent ligands, chemistry of polyoxometalates, luminescent materials, catalysis, small molecules activation.

Highlighted publications:

[1] M.A. Moussawi, N. Leclerc-Laronze, S. Floquet, P.A. Abramov, M.N. Sokolov, S. Cordier, A. Ponchel, E. Monflier, H. Bricout, D. Landy, M. Haouas, J. Marrot, E. Cadot, J. Am. Chem. Soc. 139 (2017) 12793–12803.

[2] M.A. Moussawi, M. Haouas, S. Floquet, W.E. Shepard, P.A. Abramov, M.N. Sokolov, V.P. Fedin, S. Cordier, A. Ponchel, E. Monflier, J. Marrot, E. Cadot, J. Am. Chem. Soc. 139 (2017) 14376–14379.

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[4] A.A. Ivanov, C. Falaise, P.A. Abramov, M.A. Shestopalov, K. Kirakci, K. Lang, M.A. Moussawi, M.N. Sokolov, N.G. Naumov, S. Floquet, D. Landy, M. Haouas, K.A. Brylev, Y. V. Mironov, Y. Molard, S. Cordier, E. Cadot, Chem. - A Eur. J. 24 (2018), 13467-13478.

New materials for MRI and angiography based on polyoxometalates

In this research we studied a system based on $SeO_3^{2-}/WO_4^{2-}/Mn^{2+}$ for the synthesis of Mn^{2+} containing selenotungstates. Dependently on a pH value and reagents ratio we isolated and characterized a set of complexes. At pH 2 formation of a sandwich type $(Me_4N)_8Na_2[\{SeW_9O_{33}\}_2\{WO(H_2O)\}\{Mn(H_2O)\}_2(H_2O)]$ has been observed. Increasing of the pH value and tungstate amount produces self-assembly of a cyclic complex $(Me_2NH)_{12}Na_2[\{Se_2W_{12}O_{44}\}_2\{Mn_2Cl(H_2O)_2\}\{Mn(H_2O)_2\}_2(SeO)_2]$. Decreasing of the tungstate amount gives a coordination polymer $Mn_{2.5}Na_5[H_2W_{12}O_{42}]\cdot 35H_2O$, while changing of the sodium cation to lithium produces a fully manganese containing polymer $Mn_5[H_2W_{12}O_{42}]\cdot 35H_2O$. All complexes were characterized by XRD, IR, EA and TGA.

The next step of this work is formation of a hybrid materials based on isolated complexes and cationic organic polymers. Stability, toxicity and relaxivity measurements for prepared materials are under investigation.

This work was partially supported by RSF (grant number 14-13-00645).

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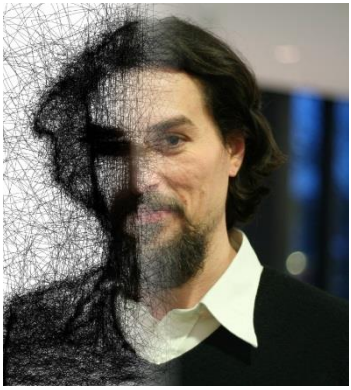

Mohammad Majid al-Rifaie is a lecturer in computing at the School of Computing & Mathematical Sciences, Old Royal Naval College, University of Greenwich as well as a visiting lecturer at Goldsmiths, University of London and a senior research fellow at the Faculty of Life Sciences & Medicine, King's College London. Mohammad holds a PhD in Artificial Intelligence and Computational Swarm Intelligence (CSI) from the Goldsmiths, University of London. He has published extensively, covering both the theoretical grounds and the applications of CSI and evolutionary computation (EC). His work in the area has featured multiple times in the media including the BBC (Persian). Over the past 10 years, his interdisciplinary research profile includes more than 65 publications on CSI, EC and their applications in medical imaging, data science and machine learning. In addition to organising and chairing several workshops, digital art exhibition and editing special issue journals, Mohammad's work has received more than 315 citations since 2011 with h-index 10 and i10-index 10.

Tomographic Reconstruction with Reduced Projection Angles Using Swarm Intelligence

Tomographic reconstruction is the process of inferring the internal structure of an object from a set of projected images. The projected images are records of the quantity of penetrating radiation that has passed through, or has been emitted from the interior of, the object in question. There are many applications, ranging from medical imaging (CT, SPECT, PET and MRI) to oceanography (seismic tomography) and quantum tomography (quantum state tomography).

In this talk, a swarm based tomographic reconstruction algorithm, particle aggregate reconstruction technique (PART), is presented where a focus is placed on reducing the number of projections and whether this impacts the reconstruction of images. There are several benefits stemming from reducing the number of projections, including but not limited to: shortening the data collection process as well as reducing the harmful impact of projections on subjects.

The proposed technique is also compared with some of the existing techniques, such as simultaneous algebraic reconstruction technique (SART), random search (RS) and filtered back projection (FBP).

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Dr. Andrei Gorodetsky received his M. Sc. degree in Physics from Saint-Petersburg State University, Russia, in 2006, and the Ph.D. degree in Optics from ITMO University, St. Petersburg, Russia, in 2010. He was with the same University as Senior Researcher and Assistant Professor till 2011. From 2011 to 2013, he was a Postdoctoral Researcher in the IESL FORTH, Heraklion, Greece, where he was engaged in THz metamaterial research and THz generation in laser filaments. From 2014 to 2016, he was a PostDoc in Aston Institute of Photonic Technologies, Aston University, Birmingham, U.K., where he worked on the development of quantum dot based compact THz sources and detectors, and their applications for biomedical imaging. In 2016-2017 he was a Senior PDRA in Lancaster University, and now he works in Ultrafast Optoelectronics group, Department of Chemistry, Imperial College London. His research interests include THz imaging, pump-probe THz studies, semiconductor and nonlinear THz sources.

Compact Room Temperature Sources for Terahertz Imaging

Terahertz (THz) imaging and spectroscopy have become an ultimate tool for detection and localisation of illicit substances[1], imaging of biological tissues[2], and biomedical imaging[3]. THz radiation is non-ionizing, as the photon energy is very low, yet it can penetrate non-metallic materials and provides sub-mm (and even sub-um! in some imaging approaches) spatial resolution. Numerous materials, including biological tissues, drugs, sugars and other have their THz fingerprints, and thus can be easily revealed remotely and in many cases non-invasively. THz waves are very sensitive to water content. There are numerous approaches to THz imaging, they are done either in time or frequency-domain and include holographic, raster scanned, compressed, near-field imaging, and other[4]. The main challenge that prevents THz imaging from becoming out-of-the lab technique is the absence of efficient yet compact room temperature operating coherent THz sources, For the past few decades, the generation of coherent THz waves remained a very challenging task. Here, we present most recent results on compact THz sources development, and we focus on hybrid THz photoconductive antennas (PCAs)[5] and room-temperature quantum-cascade laser (QCL) based photomixers[6]. While PCAs cover lower – frequency band (0.1-3 THz), and operate in both CW and pulsed regimes, QCL sources provide narrowband quasi-monochromatic radiation in 1-5 THz frequency range.

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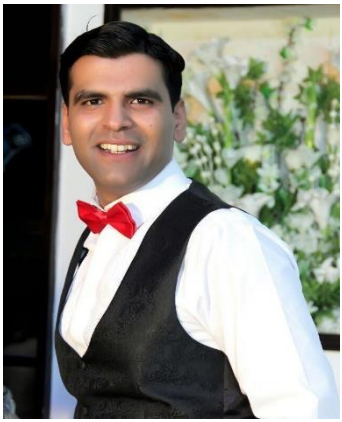
[1] M. Massaouti, et. al., Appl. Spectrosc. 67, 1264 (2013), [2] L. Rong, et. al., Opt. Express 22, 17236 (2014), [3] L. Rong, et. al., Sci. Rep. 5, 8445 (2015), [4] N. V. Petrov, et. al., IEEE Trans. Terahertz Sci. Technol. 6, (2016), [5] S. Lepeshov et. al., Laser Photon. Rev. 11, 1600199 (2017). [6]M. A. Belkin and F. Capasso, Phys. Scr. 90, 118002 (2015).

Dr Saim Memon



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Dr Saim is a Senior Lecturer in Electrical Engineering at London South Bank University, UK. He studied BEng(hons) in Electrical Engineering, MSc in Mechatronics (Staffordshire University, UK), PhD in Electronic and Electrical Engineering (Solar Thermal Vacuum Systems Engineering) (Loughborough University, UK) and PGCert in Teaching Qualification (University of Aberdeen, UK). He is a Fellow of Higher Education Academy. He has extensive multi-disciplinary research and academic experiences in Electrical, Electronic, Solar Thermal and Solar Energy Materials Engineering. His research area lies in the area of Mechatronics, solar energy materials for sustainable low-carbon economy, automation technologies in wastewater treatment and imaging with sensors. In this workshop on medical imaging alliance, his intention is to contribute with novel ideas on sensor imaging technologies and automation in detecting and capturing under-water microplastic debris. His research interests are also on improving the energy-efficiency of thermo-electric materials with vacuum insulation for electrical power generation.

Developing Under-Water Microscopic Imaging for Microplastic Debris and Capture with Automated Integrated Technology Powered by Renewable Energy

A global challenge of increasing under-water microplastic debris (less than 1 mm in diameter), are by now reached at an alarming rate, polluting ocean water and impacting marine vertebrates. This increases the potential danger to human health risks due to the presence of micro polymers in seafood and shows a pressing need for adequate imaging for detection and capture methods but also sustainable standalone system for on-site cleaning. Indeed, the current global initiatives and research reported in the literature have already disenthralled the abundance of microplastics. This research proposes under-water microscopic imaging system to identify and imaging the presence of micro plastic/polymer composites in ocean water with capture and cleaning using automated integrated technology powered by renewable energy on-site. The automated IR and Ultrasonic sensors allow higher precision of detecting under-water objects and avoid obstacle detection by providing input control signal to the main process, bi-directional pumping unit that allows the flow of water bidirectionally. A protecting valve controlled by the input signal from the sensors and the monitoring control unit providing greater control of flow. The water flow from the inlet, including microplastics, may undergo through the layer of 1μm mesh sieve and then 40 μm mesh screen as a filtration of the microplastic debris and capturing in the sieve. To make the whole plant sustainable, the photovoltaic panels, made of monocrystalline material, were proposed and turbine based electric generator using permanent magnet, coils and turbine rotor run by the water discharge flow that cut the magnetic flux and generates the electrical power to be stored in the energy storage device to feed power to the pump and control system stand-alone. This system will enable to allow collecting live microscopic images of ocean water samples for the detection of microplastics without sacrificing the marine biota and where human approach is difficult whilst cleaning the under-water targeted area.

Dmitry Bagrov

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Current positions

- Lead researcher at the Faculty of Biology, MSU (Moscow)
- Senior researcher at FRCC PCM (Moscow)
- CEO and co-founder at “Photonic-NT” LLC (Moscow)

Research areas: application of high-resolution microscopy (AFM, TEM, SEM) in biological research and polymer science; structure-property relationship in bidegradable polyesters; polymer scaffolds for tissue engineering; properties of electrospun polymer films.

Activities beyond research: project management; administration of scientific projects.

Key achevements:

- Published more than 35 articles
- Mentored 8 students in the fields of microscopy and polymer science

Established a startup company “Photonic-NT” LLC which specializes in development of electronic and optical equipment

Visualization of extracellular vesicles by transmission electron microscopy

Extracellular vesicles are small membrane particles which are produced by the cells and released into the surrounding space. They can transfer biomolecules into recipient cells. The typical vesicle size is 100-1000 nm, so transmission electron microscopy (TEM) is a suitable tool for their visualization. This is especially true for the smallest vesicles – the exosomes with the size below 200 nm. We used TEM to visualize vesicles extracted from cancer cells MCF-7 and two drug-resistant MCF-7 sublines [1]. The exosomes produced by the three studied cell lines had equal size. We used immunogold labelling to verify that the exosomes carry the CD9 marker on them. We achieved the labelling specificity in the range of 8-10. We hope that the sample preparation and imaging procedures that we used could be useful for the investigation of other extracellular vesicles.

Reference:

[1] S. Semina, A. Scherbakov, A. Vnukova, D. Bagrov, E. Evtushenko, V. Safronova, D. Golovina, L. Lyubchenko, M. Gudkova, and M. Krasil'nikov, "Exosome-Mediated Transfer of Cancer Cell Resistance to Antiestrogen Drugs," Molecules, vol. 23, no. 4, p. 829, 2018.

Dr. Tanveer Tabish

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Tanveer received his PhD in early 2018 from the University of Exeter, UK. His PhD research focused primarily on the development of graphene-based anti-cancer nanomedicine. Through his association with the EPSRC CDT in Metamaterials, he investigated the efficacy of nanotechnology for developing the next generation of image based therapeutic and diagnostic tools in nanomedicine. He has also pioneered an anti-metastatic enzyme cancer therapy for both diagnosis and treatment of breast and ovarian cancers that are currently being pursued for clinical translation. He has authored or co-authored more than 20 peer-reviewed articles on basic and applied research topics, with a primary focus on nanomedicine and medical physics. His areas of particular interest include, but are not exclusive to, nanostructured biomaterials, image-guided light-triggered theranostic options for the diagnosis and treatment of cancer and infectious diseases in a single modality. He is currently working with the internationally-leading team of multidisciplinary UK-based scientists from University of Exeter, University of Cambridge and University College London.

Nanostructured graphene for medical imaging and cell response

Nanostructured graphene is a versatile two-dimensional carbon-based nanomaterial for medical applications since the structure, molecular weight, size-dependent luminescent features and chemical composition as well as bioconjugation/functionalization can be precisely controlled. This talk will provide an overview of our recent developments in the design of graphene nanostructures to interface with cells, tissues and living systems for cancer diagnosis and treatment in a safe and targeted single procedure [1-2]. We have recently reported graphene nanopores capable of efficiently inducing apoptosis in lung cancer cells while remaining non-toxic to surrounding cells [3]. Graphene quantum dots being accumulated within tumors directly, due to nanoscale dimensions, are not inducing any toxic effects in the dark environment [4]. Their accumulation, uptake and cellular localization have been monitored by fluorescent imaging. This work further builds upon our expertise in designing graphene-based technologies for medical imaging and for application in anti-cancer nanomedicine. This talk will also describe how different derivatives of graphene (such as reduced graphene oxide, graphene nanopores, graphene quantum dots, three dimensional graphene foam) can be used to generate reactive oxygen and nitrogen species with innovative synthesis strategies, structures and properties enabling first-in-field multimodal imaging and therapeutic options.

References:

[1] Tabish, T. A., Scotton, C. J., J Ferguson, D. C., Lin, L., der Veen, A. V., Lowry, S. & Zhang, S. (2018). Biocompatibility and toxicity of graphene quantum dots for potential application in photodynamic therapy. *Nanomedicine*, *13*(15).

[2] Tabish, T. A., Lin, L., Ali, M., Jabeen, F., Iqbal, R., Horsell, D. & Zhang, S. (2018). Investigating the bioavailability of graphene quantum dots in lung tissues via Fourier transform infrared spectroscopy. *Interface focus*, *8*(3), 20170054.

[3] Tabish, T. A., Pranjol, M. Z. I., Jabeen, F., Abdullah, T., Latif, A., Khalid, A., & Zhang, S. (2018). Investigation into the toxic effects of graphene nanopores on lung cancer cells and biological tissues. *Applied Materials Today*, *12*, 389-401.

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Patrick Bergstrom Mann

Department of Physics, King's College London,

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2015 – Present: PhD, Department of Physics, King's College London

- PhD as part of the EPSRC Medical Imaging Centre for Doctoral Training.
- Project title: The Development of Copper Chalcogenide Nanocrystals for Imaging and Therapy
- Summary: Development of Cu-In-S quantum dots for near-infrared fluorescent imaging in vivo and plasmonic CuS nanocrystals synthesised via a novel route, with demonstration of their photothermal therapeutic potential.

2014 – 2015: MRes, Department of Biomedical Engineering, King's College London

- Master of Research in Medical Imaging with Distinction, as part of the EPSRC Medical Imaging Centre for Doctoral Training.
- Project title: Near-Infrared Emitting $CuInS_2$/ZnS Quantum Dots for Fluorescence Imaging.

2010 – 2014: MChem, Department of Chemistry, Cardiff University

- Master of Chemistry.
- Project title: Dual-Modal Superparamagnetic Iron Oxide Nanoparticles for PET/MR Imaging via a Facile Co-Precipitation Synthesis.

Near Infrared Fluorescent Quantum Dots for Biomedical Imaging

Near-infrared (NIR) fluorescence imaging promises to be a valuable modality for the rapid and inexpensive diagnosis of early-stage cancer. The use of NIR-emitting probes allows for greater imaging depth through tissue than visible light. Investigation into quantum dots (QDs), colloidal semiconductor nanocrystals, as fluorescent imaging probes has been gaining popularity given their favourable optical properties over organic fluorophores. These include narrower emission bands, larger Stokes shifts and increased photostability. However, there are concerns regarding the toxicity of these nanoparticles, which often contain toxic elements (Cd, Pb, Se, etc.) and feature residual organic molecules on their surface.

Our research has focused on the development of Cd-free, NIR-emitting QDs for use as minimally toxic in vivo imaging agents. In particular, we have focused on the preparation of $CuInS_2$-based nanomaterials as they have shown significant promise as biocompatible NIR-emitters. CuInZnS/ZnSe/ZnS core/multishell structures were found to offer favourable optical properties, with an emission maximum above 750 nm and quantum yield around 30%. These QDs were encapsulated within a PEG-functionalised, amphiphilic polymer to impart colloidal stability in water and increase biocompatibility.

The direct synthesis of similar $CuInS_2$ QDs in water has also been explored as an alternative approach to bright fluorophores. Aqueous synthesis circumvents the need for ligand exchange or encapsulation steps that can result in reduced quantum yield. Core/shell Cu-In-S/ZnS QDs could be prepared in water with NIR emission and exhibited high biocompatibility in HeLa cells. In vivo assessment of the QDs indicated sufficient brightness and wavelength for penetration through tissue.

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Ekaterina Grayfer is a research scientist at Nikolaev Institute of Inorganic Chemistry (NIIC). Her PhD thesis focused on the chemistry of graphene and related layered materials was defended in 2013. One of the main fundamental achievements of Ekaterina and colleagues consists in the demonstration of the generality of approaches that can be used to produce thin sheets of layered materials of various natures. Currently, Ekaterina and her colleagues actively research various chalcogenide-based materials (MoS_2, Mo_2S_3, NbS_3, VS_4, etc.). Ekaterina is the co-author of over 20 articles in high-ranking journals, including 3 reviews (h = 10, according to Web of Science). She received a number of prestigious prizes, such as L'Oréal-UNESCO National Fellowship (2017), Scholarship of the President of the Russian Federation for Young Scientists (2018), and others. She is the leader and participant of many scientific projects.

Synthesis of photoluminescent nanographitic shells and their potential for biological applications

Nano-structured and few-layer graphitic materials (graphene oxide and others) have been shown to be promising for bio-applications, such as chemo/biosensing and cell imaging.[1-3] In this work, we have synthesized water-dispersible graphitic hollow spheres following a soft chemical route under hydrothermal conditions from glucose and a magnetite/silica-encapsulated core–shell sphere as a template. We have also produced nitrogen doped counterparts. Both samples demonstrate wavelength dependent photoluminescence in 300–600 nm range. Cellular uptake experiment show carbon sphere localization in the cytoplasm and their fluorescence signals in the cell. Their main features are rich surfaces with multiple functionalities, photoluminescence in the blue-green range, voids covered by multilayered graphite oxide, cell penetration capacity and low toxicity.

These materials may hold future promise for cellular photo-imaging and targeted drug delivery.

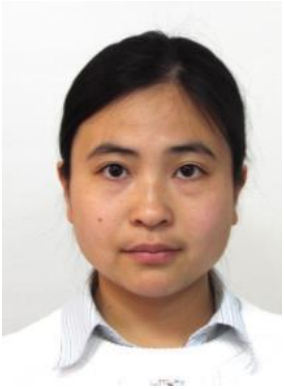
References:

[1] J. Lin, X. Chen, P. Huang, Adv. Drug Deliv. Rev., 2018, 105 (Part B), 242–254.

[2] J. Park, E.D. Grayfer, Y. Jung, K. Kim, K.K. Wang, Y.R. Kim, D. Yoon, H. Cheong, J. Mat. Chem. B, 2013, 1 (9), 1229-1234.

[3] F.-R. F. Fan, S. Park, Y. Zhu, R. S. Ruoff and A. J. Bard, J. Am. Chem. Soc., 2009, 131(3), 937–939.

Sunjie Ye



University of Leeds

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* **Oct. 2014 – Present** Postdoctoral Research Fellow

Research Projects: Developing gold nanomaterials for applications in bio-sensing, imaging or advanced therapeutic modalities, with clinical and industrial collaborators.

Jointly between School of Physics and Astronomy/School of Medicine, University of Leeds

* **Oct. 2012-Sept. 2014** Wellcome Trust ISSF Junior Investigator Development Fellow

Jointly between School of Physics and Astronomy/School of Medicine, University of Leeds

* **2011 PhD in Polymer Physics and Chemistry** Nanjing University (China)

Engineering novel gold nanostructures as probes for medical imaging

The fields of biomedicine and nanomedicine have recently witnessed an explosion of interest and progress in the design and study of plasmonic Au nanostructures (AuNSs) towards a broad range of biological and biomedical applications. Owing to their tunable and versatile optical properties, such artificially engineered AuNSs have the potential for enabling new bio-imaging modalities and new therapeutic techniques revolutionize the diagnosis and treatment of many diseases.

In this presentation, I will be talking about on my research on engineering a library of anisotropic AuNSs (e.g., Au nanotubes[1], hollow Au nanoflowers, and 2D Au nanoplatelets. etc.), with respect to the novel fabrication approaches, optical properties and the applications as nanoprobes for medical imaging (e.g. photoacoustic and SERS imaging).

References:

[1] Ye S et al, (2015) Engineering gold nanotubes with controlled length and near-infrared absorption for theranostic applications. Advanced Functional Materials, 25 (14) 2117

[2] Ye S et al (2016) One-step fabrication of hollow-channel gold nanoflowers with excellent catalytic performance and large single-particle SERS activity. Nanoscale, 8 (32) 14932

[3]Ye S et al (2018) Developing Hollow-Channel Gold Nanoflowers as Trimodal Intracellular Nanoprobes. International Journal of Molecular Sciences, 19(8), 2327

Dr Graeme J. Stasiuk

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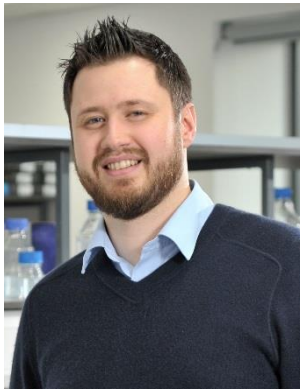
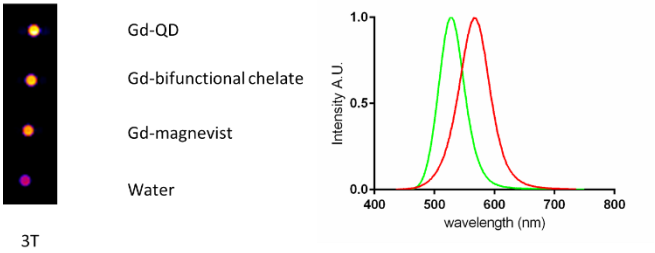


Graeme J Stasiuk (GJS) is an early career academic appointed as a non-clinical Lecturer in Molecular Imaging at the University of Hull in June 2014. GJS has 12 years of research experience (including PhD) into the design, synthesis and development of molecular imaging agents for all modalities. He obtained his MChem in Biological Chemistry from the University of Leicester in 2006 and his PhD entitled, "Design and Synthesis of Novel Lanthanide Chelates for use in Magnetic Resonance Imaging" from the University of Leicester in July 2010. Following a year at the le Commissariat à l'énergie atomique (CEA), in Grenoble, developing multimodal MR/Fluorescent contrast agents, he joined Professor Nicholas Long's group at Imperial College London in 2011 as a PDRA. This research was focused on the synthesis of agents for MRI, SPECT and Multimodal imaging. GJS research is multidisciplinary, from synthetic chemistry to translation into in vivo studies with 22 publications in high quality international journals with an H index of 12. GJS work was nominated for the early career research series in the international journal ChemPlusChem (Wiley), which resulted in a publication accepted 2017 and interview in the May 2017 edition. Furthermore GJS has been shortlisted for the ChemPubSoc Europe Early Career Award 2018.

Development of High Contrast Multimodal Imaging Agents.

Magnetic Resonance (MR) imaging compared with other imaging modalities has excellent anatomical resolution; however, it suffers at the molecular scale due to its intrinsic low sensitivity. To produce a detectable change in water signal intensity, a relatively high concentration of contrast agent (0.01 - 0.1 mM) is required.[1] This creates problems when imaging at the molecular level, as the most interesting targets are present at much lower concentrations, typically in the nano- or pico-molar range. In order to overcome the inherent sensitivity problem of the NMR phenomenon,[2] multimeric systems and/or dual modal nanoparticle contrast agents is an area of research that shows great promise.

In this study we have synthesised Gd(III) DOTA based bifunctional chelates for attachment to InP/ZnS quantum dots, upon attachment the r_1 is enhanced from 6.5 mM^{-1} s^{-1} to 17 mM^{-1} s^{-1} per Gd(III) complex (9.4T). The quantum dots have tuneable emission profiles from 525 -625 nm. Thus providing a platform for a dual-modal fluorescence/MRI probes. This enhancement in signal is significantly greater in comparison to the clinical used contrast agents.



References:

[1] P. J. Endres, K. W. MacRenaris, S. Vogt, and T. J. Meade, Biocon. Chem. 2008, 19, 2049.

[2] P. Caravan, Chem. Soc. Rev., 2006, 35, 512

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Education: Kazan Federal University, Alexander Butlerov Institute of Chemistry, Specialist's degree in chemistry (2007–2012); Kazan Federal University, Alexander Butlerov Institute of Chemistry, PhD in chemistry (2012–2016).

Work experience: Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of RAS, 2016 – present, Researcher.

Metrics: publications – 12, h index – 5.

Luminescent nanoparticles for monitoring of endogenous acetylcholine hydrolysis

The present work for the first time presents nanosensors for luminescent monitoring of acetylcholinesterase-catalyzed hydrolysis of endogenous acetylcholine released in neuromuscular junctions of isolated muscles. Silica nanoparticles (d=20nm) doped by luminescent Tb(III) complexes with p-sulfonatothiacalix[4]arene were applied as the nanosensors. The sensing function of the nanosensors results from the decreased of Tb(III)-centered luminescence due to the quenching effect of acetic acid derived from acetylcholinesterase-catalyzed hydrolysis of acetylcholine. Sensitivity of the SNs in monitoring acetylcholine hydrolysis was confirmed by *in vitro* experiments. The selective staining of the synaptic space in the isolated muscles by an optimal targeted nanosensor was revealed. The measuring of the Tb(III)-centered luminescence intensity of the targeted silica nanoparticles by fluorescent microscopy enables us to sense a release of endogenous acetylcholine in neuromuscular junctions of the isolated muscles under their stimulation by a high-frequency train (20Hz, for 3min).[1,2]

References:

[1] A.R. Mukhametshina, S.V. Fedorenko, A.M. Petrov, G.F. Zakyrjanova, K.A. Petrov, L.F. Nurullin, I.R. Nizameev, A.R. Mustafina, O.G. Sinyashin. Targeted Nanoparticles for Selective Marking of Neuromuscular Junctions and ex Vivo Monitoring of Endogenous Acetylcholine Hydrolysis. ACS Applied Materials & Interfaces 2018, 10, 14948-14955.

[2] A. Mukhametshina, A. Petrov, S. Fedorenko, K. Petrov, I. Nizameev, A. Mustafina, O. Sinyashin. Luminescent nanoparticles for rapid monitoring of endogenous acetylcholine release in mice atria. Luminescence 2018, 33, 588-593.

Dr. Julia R. Shakirova*, Anastasia I. Solomatina

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Current Position

Researcher, *Department of Chemistry, St. Petersburg State University, St. Petersburg, Russia.*

Education

2011-2014: PhD, Inorganic Chemistry, *Department of Chemistry, St. Petersburg State University, St. Petersburg, Russia.* Advisor: Professor Sergey P. Tunik. Thesis title: *Homo- and heterometallic luminescent copper subgroup metal complexes: Synthesis and study of photophysical properties.*

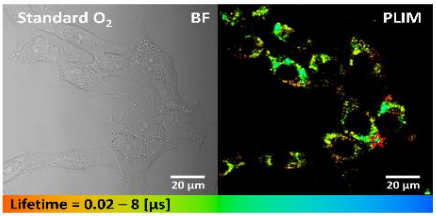
2005-2010: MS, Chemistry, *Department of Chemistry, St. Petersburg State University, St. Petersburg, Russia.* Advisors: Professor Sergey P. Tunik, Elena V. Grachova. Thesis title: *Synthesis and photophysical studies of polynuclear alkynyl-phosphine Au-Cu complexes.*

Awards

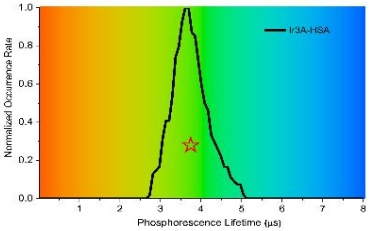
Grant recipient (PI) from the St. Petersburg Government (2012), the Russian Foundation for Basic Research (2014-2015; 2016-2018), Stipendiat of Russian Presidential scholarship (2016-2018).

Phosphorescent organometallic Ir(III) and Pt(II) compounds as prospective probes for the phosphorescence lifetime imaging

Oxygen is one of the critical components of biological systems that determines their physiological status both under norm and in pathology. It is well known that hypoxia is typical for tumors [1]. That is why mapping the spatial oxygen distribution in tumors, and in various model systems is of great interest. The most reliable method for determining the oxygen concentration is the phosphorescence lifetime imaging (PLIM). The application of this technique is based on the measurement of the lifetime of the phosphorescent oxygen-sensitive probes after their incubation into biological sample.



Excitation 800 nm, Monitor 550~750 nm



We have synthesized few types of phosphorescent cyclometalated iridium(III) and platinum(II) complexes, that demonstrate variable emission depending on the ligand environment. The most prospective candidates were applied as phosphorescent probes to study their internalization into cancer cells and to image molecular oxygen distribution using PLIM technique with two-photon laser excitation. This talk will give the overview of different types of complexes and prospective of their application as oxygen sensors.

The authors greatly appreciate financial support from the RFBR grant 18-33-00954.

[1] Höckel, M. & Vaupel, P.. *J. Natl. Cancer Inst.* **93,** 266–276 (2001).

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Work experience:

2010-2015: Russian Research Anti-Plague Institute «Microbe», Laboratory of Molecular Microbiology, Junior researcher

2015-2018: Saint-Petersburg State University, Department of Cytology and Histology, Post-doc

2018-present: ITMO University, Chemistry and Molecular Biology Department, Associate Professor

Scientific degree: Candidate of Biological Sciences (Ph.D.), 2014

Number of publications for the last 5 years – 51,

of these, indexed in the Web of Science or Scopus – 18.

New phosphorescent probes based on transition metals complexes for bioimaging

In this study, we present investigation of new phosphorescent probes based on transition metals complexes for phosphorescence lifetime imaging microscopy (PLIM): homoleptic alkynyl gold(I) cluster [1] and cyclometalated platinum complex [2].

Cyclometalated platinum complex (Pt(phpy)(PPh3)Cl (phpy – 2-phenylpyridine; PPh3 – triphenylphosphine) is nonemissive in solution, but substitution of chloride ligand for imidazole ring in this complex switches on the resulting compound phosphorescence. The luminescence is switched on as a result of coordination bond formation with imidazole ring or with biomolecules, which contain this group in the structure, that is, histidine and histidine-containing peptides. This binding is highly selective and dominates over interaction with any other amino acid residues presented in proteins. This unique feature provides a novel route to sitespecific labeling of peptides and proteins. As an example, we have analyzed nonaggregated Pt complexes conjugated with human serum albumin. This probe was easily internalized into live HeLa and CHO cells and was displayed lifetime in the 6.8 to 7.8 μs range across the image depending on the microenvironment. Results of simultaneous fluorescence and phosphorescence lifetime imaging (FLIM/PLIM) displayed high potential of Pt complex as a metabolism sensor for live bio-objects.

The results of this study have shown that new phosphorescent probes retain its long lifetime in biological microenvironment and are amenable for different timeresolved imaging applications, particularly for phosphorescence lifetime imaging microscopy.

[1] E. I. Koshel, P. S. Chelushkin, A. S. Melnikov, P. Yu. Serdobintsev, A. Yu. Stolbovaia, A. F. Saifitdinova, V. I. Shcheslavskiy, O. Chernyavskiy, E. R. Gaginskaya, I. O. Koshevoy, S. P. Tunik (2017) Lipophilic phosphorescent gold(I) clusters as selective probes for visualization of lipid droplets by two-photon microscopy. Journal of Photochemistry and Photobiology A: Chemistry. 332: 122–130.

[2] A.I. Solomatina, P. S. Chelushkin, D. V. Krupenya, I. S. Podkorytov, T. O. Artamonova, V. V. Sizov, A. S. Melnikov, V. V. Gurzhiy, E. I. Koshel, V. I. Scheslavskiy, S. P. Tunik. (2016) Coordination to Imidazole Ring Switches On Phosphorescence of Platinum Cyclometalated Complexes: The Route to Selective Labeling of Peptides and Proteins via Histidine Residues. Bioconjugate chemistry. 28(2):426-437.

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Dr. Romanov obtained a double master's degree in chemistry from D. Mendeleev University of Chemical Technology of Russia in Moscow and New Mexico Highlands University, USA. He received his PhD degree in the group of Prof. Alexander Kudinov (A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences). He developed efficient synthetic procedures towards triple- and tetra-decker sandwich complexes based on boron heterocycles while being a PI on the grant from the Russian Foundation for Basic Research. Now he is on a postdoctoral position with Prof. Manfred Bochmann at the University of East Anglia, UK. His work on "High-performance coinage metal emitters for the Organic Light Emitting Diode (OLED) technology" was selected for the highly prestigious event "STEM for Britain" (the House of Commons, UK by Parliamentary and Scientific Committee). He was a finalist and "One to Watch" prize winner from the Royal Society of Chemistry, Emerging Technologies Competition in London. In 2019, he is starting his independent research carrier as a Royal Society University Research Fellow working on the design of new energy materials for various applications.

Carbene Metal Amides as a New Class of Highly Emissive Materials

We have recently designed numerous linear coinage metal complexes with efficient photo- and electroluminescent properties. Our materials are composed of the donor and acceptor ligands which are linked by a coinage metal atom.[1] Linear geometry enables rotational flexibility for the coinage metal complexes. Rotation about the metal-ligand bond allowed us to tune the energy gap between singlet and triplet excited states to be effectively zero. This enabled efficient harvesting both singlet and triplet excited state while realizing efficient reversed intersystem crossing process. We have designed various functional materials with either phosphorescent or thermally activated delayed fluorescence (TADF) properties. As a proof of concept, we fabricated Organic Light Emitting Diodes (OLED) with exceptionally high external quantum efficiencies (>28% EQE) in both solution- and vacuum-processed OLEDs.[2,3,4] Power and current efficiency are comparable to or exceeding state-of-the-art phosphorescent OLEDs and quantum dot LEDs. Our materials possess short excited state lifetime (300-500 ns) for the delayed emission which is highly important for the fabrication of the long-lived OLEDs. Bright phosphorescent and TADF materials with widely tuneable emission spectra and excited state lifetimes will be presented and discussed towards bioimaging applications.

[1] A.S. Romanov et al. *Chem. Eur. J.*, **2017**, 23(19), 4625–4637; [2] *Science*, **2017**, 356, 159–163; [3] *Adv. Mater.*, **2018**, 1802285; [4] *Adv. Opt. Mater.*, **2018**, 1801347

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Luminescent silica microparticles doped by $\{Mo_6I_8\}^{4+}$ metal clusters for protein transduction

In this work we examine the potential of luminescent (namely, octahedral molybdenum cluster doped) silica microparticles (SMPs) synthesized by a simple one-pot reaction for the labelling of cells and for protein transduction into larynx carcinoma (Hep-2) cells using Green Fluorescent Protein (GFP) as a model protein. Our data demonstrate that the SMPs internalize well in the cells within half an hour producing cells with luminescence detectable by conventional methods (CLSM). In addition, the particles are non-toxic neither in darkness and upon photoirradiation. The SMPs were modified to allow functionalization by a protein and have delivered the protein (GFP) efficiently into the cells. (Figure) Thus, the luminescent SMPs offer a cheap and trackable alternative to existing materials for cellular internalization of proteins, such as HIV TAT protein and commercial protein delivery agents (eg Pierce™).

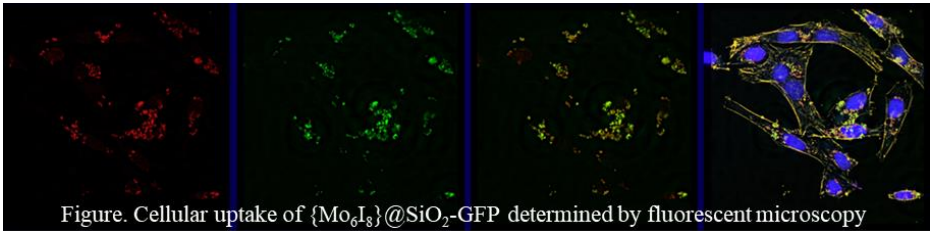

Figure. Cellular uptake of $\{Mo_6I_8\}@SiO_2$-GFP determined by fluorescent microscopy

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14.12.2016 PhD in Chemistry "*Synthesis and Physicochemical Properties of Tri- and Tetranuclear Molybdenum and Tungsten Sulphide Clusters with Heterocyclic Diimine Ligands"*

Research interests:

Chemistry of transition metal clusters, chemistry of non-innocent ligands, heterogeneous catalysis, homogeneous catalysis, quantum chemical calculations.

Highlighted publications:

1. D. Recatala, R. Llusar, R.; A.L. Gushchin, E.A. Kozlova, Yu.A. Laricheva, P.A. Abramov, M.N. Sokolov, R. Gomez, T. Lana-Villarreal. Photogeneration of Hydrogen from Water by Hybrid Molybdenum Sulphide Clusters Immobilized on Titania. *ChemSusChem*, 2015, 8 (1), 148-157;

2. J.A. Pino-Chamorro, Yu.A. Laricheva, E. Guillamon, M.J. Fernandez-Trujillo, A.G. Algarra, A.L. Gushchin, P.A. Abramov, E. Bustelo, R. Llusar, M.N. Sokolov, M.G. Basallote. Kinetics Aspects of the Reversible Assembly of Copper in Heterometallic Mo_3CuS_4 Clusters with 4,4'-Di-tert-butyl-2,2'-bipyridine. *Inorg. Chem*., 2016, 55 (19), 9912-9922;

3. E. Pedrajas, I. Sorribes, A.L. Gushchin, Yu.A. Laricheva, K. Junge, M. Beller, R. Llusar. Chemoselective Hydrogenation of Nitroarenes Catalyzed by Molybdenum Sulphide Clusters. *ChemCatChem*, 2017, 9 (6), 1128-1134;

4. A.L. Gushchin, Yu.A. Laricheva, M.N. Sokolov, R. Llusar. Tri- and tetranuclear molybdenum and tungsten chalcogenide clusters: on the way to new materials and catalysts. *Russ. Chem. Rev*., 2018, 87 (7), 670–706.

New hybrid materials based on trinuclear tungsten clusters with a phospholipid bilayer

A large variety of trinuclear M_3S_4 (M = Mo, W) clusters was prepared in last 30 years, and their relevance in bioinorganic chemistry and organic catalysis has been demonstrated[1-4]. Functionalization of these systems by using electro- and photochemically active ligands such as substituted bipyridines (bipy) to form the $[M_3S_4Cl_3(bipy)_3]^+$ compounds is very promising[5]. The non-innocent behaviour of bipy and the lability of chloride ligands towards further substitution (on a wide variety of ligands including biological molecules or bio-mimetic fragments) allows us to prepare new hybrid nano-scaled constructions.

Our preliminary data shows the incorporation of an electron-dense clusters $[W_3S_4Cl_3(bipy)_3]^+$ into a lipid bilayer makes it possible to study the structure of the latter using conventional TEM. This feature can be used to study the structure of artificial and natural lipid membranes. Moreover, by embedding clusters with desired properties into a bilayer, we can impart these properties to the entire lipid nanoparticle to form soft functional nanomaterials.

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Optical coherence tomography (OCT) imaging assistant for stenting long coronary artery lesions

Aim. The 48 mm long biodegradable polymer everolimus eluting SYNERGY stent (BP-EES) is a novel very thin strut device, designed to overcome necessity of stent overlapping while stenting long coronary lesions or CTOs. However, stent length is known to be an independent predictor of restenosis. We sought to study the stent coverage and neointima progression within 3 and 6 month follow-up in CAD patients who underwent PCI.

RESULTS

We present an interim analysis of OCT imaging data at post stenting follow-up on a total of 20 patients (10 - 3 month FU and 10 - 6 month FU). There were no significant differences between groups regarding clinical, angiographic measurements, and procedural data. Stent implantation was followed by NC-balloon postdilation in all cases. The analyzed average stent length was 47.03±0.46 mm and diameter 3.53±0.3 mm. Total number of 943 frames were assessed , with a total of 8297 visible struts. Overall strut coverage per stent was 82.96%±5.23 and 94.25%±3.4 (P=0.0001) in 3mFU and 6mFU groups, incidence of malapposed and uncovered struts was 0.3%±0.04 and 17.04%±5.23 versus 0.25%±0.03 (P=0.005)and 5.75%±3.4 (P=0.0001) in study groups, consequently. Cross-section level analysis revealed mean lumen area 9.64±2.01 and 8.73±1.46 mm^2 (P=0.0001), stent area 10.34±2.05 and 10.2±1.39 mm2 (P=0.219) and neointimal area 0.7±0.05 and 1.47±0.17 mm^2 (P=0.0001). The NIH score per stent was 34.86±9.8 and 10.23±3.76 (P=0.0001), while neointimal thickness per strut was 60±53 μm and 108±84 μm (P=0.0001) in study groups.

Safety analysis demonstrated no signs of stent thrombosis or restenosis in both groups.

CONCLUSION

The 48mm long everolimus-eluting stent is associated to a good intimal coverage at 3 months after implantation with significant increase at 6 months. Incidence of strut malapposition was extremely low, due to adequate postdilation. Synergy 48 mm, despite the stent length, showed favourable healing profile.