VII Annual Conference RASA-USA

PROGRAM

Saturday, November 5, 2016
Carnesale Commons Palisades Room
251 Charles E. Young Drive West, Los Angeles, CA 90095

9:00 Opening of the First Day of the Conference

9:00 – 9:15 Opening remarks and review of RASA-USA activities – Nikolay Vasilyev, President of RASA-USA (Boston Children's Hospital, Harvard Medical School)

9:15 – 9:20 Welcoming remarks by Vyacheslav Turyshev, Department of Physics and Astronomy of UCLA, Jet Propulsion Laboratory

9:20 – 9:30 Welcoming address by the Consul General of the Russian Federation in San Francisco Sergey Petrov

9:30 – 11:15 Panel Discussion: Cooperation with Russian-Speaking Scientific Diaspora (Moderator – Igor Efimov, President of RASA International Coordinating Committee, George Washington University)

Evgeny Kuznetsov (Russian Venture Company, National Technological Initiative)

Alexey Sitnikov (Skolkovo Institute of Science and Technology)

Lev Zelenyi (Russian Academy of Sciences)

Vladimir Zelman (University of Southern California)

Oleg Zhiganov (Russian Cultural Centre in Washington D.C., Mission of Rossotrudnichestvo to the U.S.)

11:15 – 11:30 Coffee break

11:30 – 13:00 Scientific Session 1 (Moderator – Alexander Kabanov, University of North Carolina at Chapel Hill)

11:30 – 12:00 Mathematicians' Thoughts – Efim Zelmanov (University of California, San Diego)

12:00 – 12:30 How to Build a World-Class Research Center in Russia in Just 12 Months – Pavel Pevzner (University of California, San Diego)

12:30 – 13:00 A Brief History of Time in Chemistry – Gregory Yablonsky (Saint Louis University)

13:00 – 14:00 Lunch break

14:00 – 16:00 Honoring Sergei Korolev Session (Moderator – Vyacheslav Turyshev, UCLA, Jet Propulsion Laboratory)

14:00 – 14:15 Remembering My Father – Video address by Natalia S. Koroleva,

Introduction by Vladimir Zelman (University of Southern California)

14:15 – 14:45 Russian Program of Space Exploration – Lev Zelenyi (Space Research Institute of the Russian Academy of Sciences)

14:45– 15:15 Life on the International Space Station – Alexander Misurkin (ROSCOSMOS)

15:15 – 15:45 Human Spaceflight – Recent Past and Near Future – Garrett Reisman (SpaceX)

15:45 – 16:00 Q&A

16:00 – 16:15 Coffee break

16:15 – 18:15 Honoring Sergei Korolev Session - continued (Moderator – Vyacheslav Turyshev, UCLA, Jet Propulsion Laboratory)

16:15 – 16:30 Sergei Korolev and His Legacy – Video Lecture by Alexey Leonov

Introduction by Vyacheslav Turyshev (UCLA, Jet Propulsion Laboratory)

16:30 – 17:00 Studying Life on an Extra-Solar System Planet 500-1000 Years before Traveling There – Vyacheslav Turyshev (UCLA, Jet Propulsion Laboratory)

17:00 – 17:30 The Cultural Spaces of the Soviet Cosmos – Alexei Kojevnikov (University of British Columbia)

17:30 – 18:00 History of US-Russian Cooperation and the International Space Station – David Rousso (Docking Port Productions)

18:00 – 18:15 Honoring Sergei Korolev Session closeout

18:20 Summary of the First Day of the Conference

18:30 – 22:00 Gala Reception

Luskin Conference Center, Centennial Terrace

425 Westwood Plaza, Los Angeles, CA 90095

Sunday, November 6, 2016

Carnesale Commons Palisades Room

251 Charles E. Young Drive West, Los Angeles, CA 90095

9:00 – 9:15 Opening of the Second Day of the Conference

2016 RASA-USA George Gamow Awards Ceremony

Best Poster Presentation Award Ceremeony

9:15 – 11:15 Panel Discussion: Science and Education in Russia – National or International (Moderator – Artem Oganov, Skolkovo Institute of Science and Technology)

Elena Atochina-Vasserman (University of Pennsylvania)

Alexander Kabanov (University of North Carolina at Chapel Hill)

Evgeny Kuznetsov (Russian Venture Company, National Technological Initiative)

Mikhail Myagkov (University of Oregon)

Vladimir Shiltsev (Fermi National Accelerator Laboratory)

Alexey Sitnikov (Skolkovo Institute of Science and Technology)

Nargis Valamat-Zade (*New Development Technologies*, the nonprofit organization)

11:15 – 11:30 Coffee break

11:30 – 13:00 – Scientific Session 3 (Moderator – Vladimir Zelman, University of Southern California)

11:30 – 12:00 Soft Robotics in Cardiovascular Interventions – Nikolay Vasilyev (Boston Children's Hospital, Harvard Medical School)

12:00 – 12:30 Between Bleeding and Thrombosis: The Eternal Dilemma of Blood Clotting – Rustem Litvinov (University of Pennsylvania)

12:30 – 13:00 Nano Clinic for Brain Tumors: Imaging and Treatment – Julia Ljubimova (Cedars-Sinai Medical Center)

13:00 – 14:00 Lunch break

14:00 – 16:00 Scientific Session 4 (Moderator – Vadim Gladyshev, Brigham and Women's Hospital, Harvard Medical School)

14:00 – 14:30 Amphiphilic Copolymers Mediated Therapeutics in Cancer – Tatyana Bronich (University of Nebraska)

14:30 – 15:00 Russia Agricultural Science Heritage and Future – Sergey Nuzhdin (University of Southern California)

Best abstracts presentations:

15:00 – 15:15 Beyond Borders: Rochester Optics Meets Russian Optics – Svetlana Lukishova (University of Rochester)

15:15 – 15:30 American Students Travel to Russia for Project-Based Learning and Research – Oleg Pavlov (Worcester Polytechnic Institute)

15:30 – 15:45 Aerospace Russian: An Experiment in Teaching Content-Driven Introductory Language Course to Engineering Students at Cornell – Raissa Krivitsky (Cornell University)

15:45 – 16:00 Multilingualism and Education: Implementation of Advances in Humanities and Sciences into Educational Programs for Multilingual Speakers – Anna Kiryakova (Russian-American Community Center of Florida)

16:00 – 16:15 Coffee break

16:15 – 16:30 Presentation of the next President of RASA-USA, Passing of the Gavel ceremony

16:30 – 18:00 Open Panel Discussion: Development of RASA-USA and Future Projects of the Association (Moderator – Valery Fokin, University of Southern California)

RASA-USA Members, Partners and Guests

18:00 Summary of the Second Day of the Conference and Closing Ceremony

ABSTRACTS

Bacterial drug efflux pump MacAB as a new target for drug development

Matrosova L.E.[1], Khiyas I.V. [1], Shirshikova T.V. [1], Kamaletdinova L.Kh. [1], Danilova Y.V. [1], **Bogomolnaya L.M[1,2]**.

1 – Kazan Federal University, Kazan, Russia

2 – Texas A&M University Health Science Center, Bryan, Texas, USA

Bacterial drug efflux pumps are protein membrane complexes that function to actively expulse antimicrobials from the cells. They can be divided into several classes based on the energy source used for transport of the substrate. Genomes of many Gram-negative bacteria encode multiple efflux pumps with high redundancy in substrate specificity to antibiotics. Current data indicate that the role of drug efflux pumps is not limited to just antibiotic resistance. Macrolide-specific ABC-type drug efflux pump MacAB first identified in *E. coli* has been linked to virulence of *Salmonella enterica* serotype Typhimurium in mice.

We have recently showed that MacAB efflux pump is required for protection of *Salmonella* Typhimurium against oxidative stress both *in vitro* and *in vivo*. Moreover, the function of MacAB is conserved across other members of *Enerobacteriaceae* family. Here we show that MacAB is essential for survival of *Serratia marcescens* in the presence of hydrogen peroxide. We further show that *S. marcescens ΔmacAB* mutant cells could be protected against peroxide-mediated killing by low molecular weight metabolites present in the media used to grow wild type bacteria but not in the media conditioned by growth of *ΔmacAB* mutant strain. Protective effect of these metabolites was abolished by heat- or proteinase K treatment. These data indicate that the identified molecules are proteins or peptides. We are currently working on identification of MacAB substrates with anti-H_2O_2 properties.

Combined, our data strongly suggest that the drug efflux pump MacAB present in many Gram-negative bacteria represents an attractive target for development of new antimicrobials.

This work was supported in part by Russian Science Foundation project 16-14-10200.

NOTCH LIGAND-BASED REAGENTS AS THERAPEUTICS FOR IMMUNOMODULATION IN CANCER AND ORGAN TRANSPLANTATION

Elena E. Tchekneva, Anneliese Antonucci, Nicholas Long, Jason V Evans, Anwari Akhter, Thomas Magliery, **Mikhail M. Dikov**.
The Ohio State University, Columbus, OH, USA.
Corresponding author: Mikhail.Dikov@OSUMC.edu

Objectives of the study: To elucidate molecular mechanisms of the regulation of T cell-mediated in anti-tumor immunity by Notch system and to develop reagents for therapeutic modulation of Notch signaling. We have recently demonstrated in human and mouse studies that tumor-induced modulation of Notch ligand expression and Notch signaling in hematopoietic compartment contributes to tumor immune escape. Down-regulation of delta-like ligands (DLL) leads to defects in T cell development and T helper (Th1) cell differentiation with the prevalence of regulatory T cell (Treg) generation.

Methodology: To determine the role of Notch ligands in antigen-presenting dendritic cells on regulation of antitumor immune responses, we generated a set of lineage-specific knock-out mice lacking one of the Notch ligands in $CD11c^+$ dendritic cells (DC). We are and testing reagents for clinical application for ligand-specific Notch signaling to stimulate or inhibit various types of immune responses for applications in oncology and immune diseases.

Results: Mice with DLL1 insufficiency in DC demonstrated remarkably accelerated growth of Lewis lung carcinoma (LLC) tumor, and reduced survival compared to wild type animals. This associated with impaired anti-tumor immune responses indicated by the decreased tumor infiltration by interferon-γ (IFNγ)-producing T cells. In contrast, Jagged2 knockout did not cause any significant alterations. The data reveal that expression of Notch ligands by antigen-presenting cells is an important immune response specifying mechanism and that ligand-specific Notch signaling could be a valuable therapeutic target. Our cell-based *in vitro* study showed that pharmacological activation of Notch ligands required multivalent receptor-ligand interaction, whereas soluble ligands acted as competitive Notch inhibitors. We have generated reagents that comprise specific functional domains of the DLL1 in multivalent or monovalent form. Therapeutic inhibition of Notch by monovalent DLL1-based reagent accelerated LLC tumor growth and attenuated T cell-mediated anti-tumor immune response. In a heart transplantation mouse model, monovalent DLL1 reagent significantly prolonged allograft survival by inhibiting Th1 effector and memory T cell differentiation. Multivalent forms of DLL1 effectively stimulated Notch signaling in T cell cultures and enhanced IFNγ production, whereas monovalent reagent had opposite effects.

Conclusions: Pharmacological up-regulation of DLL1-mediated Notch signaling represents an efficient strategy for the enhancement of anti-tumor immunity and targeting multiple mechanisms of tumor growth. Monovalent DLL1 forms could be utilized for therapeutic inhibition of Th1 responses in autoimmune disease and organ transplantation. As Jagged1-mediated signaling was associated with regulatory Treg cell generation, therapeutic monovalent Jagged1 fragments have potential to reverse Treg-mediated immunosuppression in cancer. Reagents based on the mono- and multivalent forms of Notch ligands can be efficiently utilized for the therapeutic modulation of Notch signaling.

Significance: Novel molecular mechanisms of regulation of anti-tumor immunity by Notch system are revealed. Notch ligand expression in antigen-presenting cells was identified as a "checkpoint" regulating the type of immune response. A set of reagents for the pharmacological modulation of immune responses based on Notch ligand constructs is proposed.

Photionization/photodetachment spectroscopy and Dyson orbitals: Theoretical tools to aid experimental studies

Anastasia O. Gunina and Anna I. Krylov

Department of Chemistry, University of Southern California
Corresponding author: *gunina@usc.edu*

Various exotic species such as polyradicals and molecules in highly charged or highly excited states exist at non-terrestrial conditions. Unusual electronic structure of these species poses a challenge for both experimental and theoretical studies. Moreover, high-energy energy radiation in interstellar media facilitates all kinds of ionization processes, including core ionizations. Special attention is deserved by anions, both of valence and dipole-bound character, as well as by species in metastable states.

Theoretical tools for description of ionization process will be presented. The central object is the so-called Dyson orbital representing the difference between initial and final states of the system in the ionization process. Dyson orbitals enter the expression of the photoelectron matrix element [1] which is, in turn, a prerequisite for calculating experimental observables, such as photoionization cross-sections and photoelectron angular distributions [2].

We compute high level Dyson orbitals within equation-of-motion coupled cluster (EOM-CC) formalism. This makes them applicable to cationic, anionic, open-shell or excited states, as well as extendable to metastable states. Several illustrative examples of EOM Dyson orbitals and photoionization cross-sections will be presented, with an emphasis on astrochemically relevant species.

1. C.M. Oana, A.I. Krylov. J. Chem. Phys. 127, 234106 (2007)
2. S. Gozem, A.O. Gunina, T. Ichino, D.L. Osborn, J.F. Stanton, A.I. Krylov. J. Phys. Chem. Lett. 6, 4532 (2015)

Multilingualism and Education: Implementation of Advances in Humanities and Sciences into Educational Programs for Multilingual Speakers (based on educational centers).

Anna Kiryakova

Educational Center "PriZm" at Russian-American Community Center of Florida, Orlando, Florida.

It is becoming a truth universally acknowledged, that neither scientific progress nor mineral reserves/resources will soon be able to measure the advancement of civilization. Sakharov, A.D. once wrote, that "Technological Revolution will bring happiness only if it is enhanced by deep changes in social, moral, and cultural aspects of the life of Humanity. A person's spiritual life, and internal motivation are very hard to predict; however, it is they that ultimately determine whether civilization will end or continue to exist." A human being becomes a true and unique asset of any socio-cultural paradigm.

On the other hand, the continuing tendency of scientific interdisciplinary collaboration, as well as deep cultural globalization with promising results present certain challenges in preserving identity and traditions, cultivating unity of individualities; meanwhile, posing a threat of falling victim to ersatzculture. The existing socio-cultural environment dictates the necessity to reexamine educational goals and education systems, redefine schools and learning programs, and reconceptualize the role of the teacher. While the whole world is fascinated by Finland's constant experiments with its education system, there are isolated attempts to create new approaches to help children to adapt to the ever-changing challenges of the world.

During the presentation the following questions will be offered for discussion: the problem of knowledge management and continuity (in the light of multiculturalism), collaborative work of humanities and science scholars as basis for developing educational programs for multilingual speakers, teacher competence development programs (in the light of multilingualism and multiculturalism), partnering with existing educational centers and creating educational labs on their basis (in the light of multiculturalism).

Aerospace Russian: an Experiment in Teaching Content-Driven Introductory Language Course to Engineering Students at Cornell Univesity

Raissa Krivitsky
Russian Language Program, Department of Comparative Literature, Cornell University

It has been an established norm in the language teaching community, that the study of a language with regard to scientifically, scholarly or professionally charged discourse should begin at the advanced or at least an intermediate stage of students' language proficiency.

However, with the raise in the Global economy and limitless possibilities of International communications, the growing number of people have become interested in learning the basics of a foreign language with focus on certain lexical domains. This interest is often driven by highly utilitarian purposes, such as ability to read manuals and instructions, or follow on-line information in the appropriate field. For this category of potential language learners, the phrase books or commercial teach-yourself textbooks are not helpful. At the same time, a commitment to spending 10-12 hours a week that a beginner foreign language course at college level usually requires, may not be seen as a justifiable option.

This proved to be true for a number of undergraduate and graduate students who were enrolled in the Sibley School of Mechanical and Aerospace Engineering at Cornell (MAE), a prominent center of space research and education. In response to their initiative, in the summer 2012, I designed and taught a pilot course "*Russian for Space Enthusiasts",* with the assumption that at least some knowledge of space-related Russian language would be helpful for their future collaborations with Russian colleagues.

The project greatly relied on the input and the feedback from six volunteer students who took the course. The exit test results indicated that the developed portion of the material (approximately 20%, covered in 8 hours of classroom instruction and varied amounts of independent study for each student), have not only provided students with the basic vocabulary and structures, but also with the gist of how the language works, which enabled them to read and partially interpret the content of specialized charts and simple texts selected from the Russian Space Agency website. The overwhelmingly positive student responses to the exit survey confirmed the initial hypothesis that such course should be useful for a sizable segment of engineering students who otherwise would not take a language course.

The presentation will contain a brief description of the course curriculum, classroom activities, and a review of the outcomes, such as the results of the course exit tests and students' responses to the blind survey. I would argue that early focus on a particular content and early introduction to the field specific vocabulary, combined with traditionally structured presentation of grammar, help form a useful and productive model of language instruction. In addition to that, my presentation aims at soliciting opinions from Russian-speaking experts in Space exploration and research on the value and feasibility of this approach. I am particularly interested in exploring the possibility of collaborative efforts with those who might be willing to engage in developing a full-fledged course of this nature.

Beyond Borders: Rochester Optics meets Russian Optics

Svetlana G. Lukishova[1], Sergei A. Kozlov[2], Irina N. Zavestovskaya[3]

[1]The Institute of Optics, University of Rochester, Rochester NY, 14627 USA; e-mail: sluk@lle.rochester.edu [2]ITMO University, 14, Birzhevaya liniya, St-Petersburg, Russia, [3]National Research Nuclear University MEPhI, Kashirskoye shosse 31, Moscow, Russia

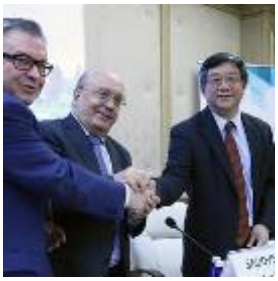
Since 2014, the oldest and one of the most comprehensive optics, photonics and laser schools in the United States, the Institute of Optics (IO) at the University of Rochester (UR), N.Y., and two leading Russian optics and photonics institutions—ITMO University of St. Petersburg and the National Research Nuclear University MEPhI (Moscow Engineering Physics Institute) in Moscow—have engaged in a growing collaboration in research and education.

ITMO reached out to the UR two years ago to initiate the first partnership—one of the early outcomes of which was the creation of the International Institute of Photonics and Optical Information Technologies, led by Sergei Kozlov of ITMO and Xi-Cheng Zhang of Rochester. On the educational front, the two universities also created a double Master's-degree program in optics in 2014, and five ITMO students have been awarded degrees from Rochester.

In 2015, the UR signed a similar agreement with MEPhI. Six Nobel Prize Winners were MEPhI faculty members. In 1964 Nikolaj Basov was a former MEPhI student who, as a director of the Lebedev Physical Institute (LPI) of the Russian Academy of Sciences (RAS), organized a Special MEPhI department (SD). In 2014, SD evolved to the Magistratura with its leaders having joint appointments in two leading laser and photonic institutions of RAS – LPI and the Prokhorov General Physics Institute (GPI). In the summer 2016, nine UR students participated in two events, both in Moscow and St-Petersburg. UR group leader Svetlana Lukishova organized this trip from the UR side. Firstly, in Moscow UR and MEPhI students during five days were immersed into the world of cutting edge research, technologies and ideas that Russian, European and US scientists offered them at the International School on Optics and Laser Physics in MEPhI. This School also included tours of MEPhI Nanotechnologies and Lasers Centers and Nano-bioengineering Laboratory as well as LPI and GPI laboratories of RAS. Last summer, for a second year, Rochester students participated in ITMO research summer camps in St. Petersburg. For two weeks the students carried out research projects under the supervision of the ITMO Department of Photonics and Optical Information Technologies.

The IO of UR also has close relations with Lomonosov Moscow State University (LMSU), where an International Consortium of THz Photonics and Optoelectronics, including 71 partners from 15 countries, was established on December 2015. Vladislav Panchenko, president of the Russian Foundation for Basic Research; Victor Sadovnichy, LMSU rector; and Xi-Cheng Zhang, director of the IO at UR signed the Memorandum of Understanding (MOU) in Moscow. In April 2015, Zhang and Panchenko had a meeting at the U.S. National Science Foundation (NSF) with NSF program directors about U.S.-Russia joint projects on photonics and THz research.

We hope that such collaborations will continue earlier traditions established by previous generations of optical and laser researchers—when, according John Marburger, the director of the U.S. Office of Science and Technology Policy and science advisor to President GW Bush, "contacts between Russian and American workers accelerated the rate of progress" in the field.



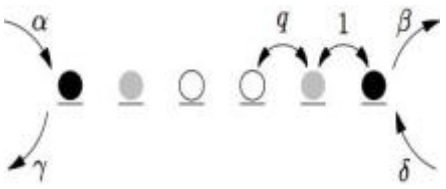
LEFT: A student-made mural a wall at ITMO depicts leaders from both ITMO and the UR; CENTER: Some UR and MEPhI student participants in the 2016 International School on Optics and Laser Physics, along with selected faculty; RIGHT: Vladislav Panchenko, Victor Sadovnichy and Xi-Cheng Zhang after signing MOU in Moscow.

REFERENCE: S.G. Lukishova, S.A. Kozlov, I.N. Zavestovskaya, Optics & Phot. News, pp. 20-21, Nov. 2016.

Combinatorics of the Two-Species ASEP and Orthogonal Polynomials

Olya Mandelshtam, PhD; UCLA Mathematics Department, olya@math.ucla.edu

Background: The Asymmetric Simple Exclusion Process (ASEP) is a process that is used in statistical analysis in physics that describes the dynamic interaction of particles hopping left and right on a 1D finite lattice with open boundaries. This is a non-equilibrium process that exhibits phase transitions, and is well-studied for many reasons, including a model for traffic flow or translation in protein synthesis. The ASEP is a Markov chain with 5 hopping parameters: particles may enter and exit at the left with rates α and γ and at the right with rates β and δ, and in the bulk the rate of hopping left is q times that of hopping right. The two-species ASEP is a generalization in which there are two species of particles, *heavy* and *light*, with transitions as in the figure above on the right.



Remarkably, one can compute the probabilities of the ASEP as sums over combinatorial objects such as tableaux [e.g. the alternative tableaux of Figure 1 (a), which were introduced in the last decade]. Consequently, our focus has been on finding combinatorial objects that provide formulae for the two-species ASEP to expand upon the results obtained for the single-species case.

Methods: We use the Matrix Ansatz of Uchiyama et. al. in order to reverse and engineer a Markov chain on tableaux that satisfy this Ansatz. Our proofs involve explicit construction of the matrices that represent the weight generating function of adding a new column to our tableaux, and then prove algebraically that these matrices satisfy the Matrix Ansatz.

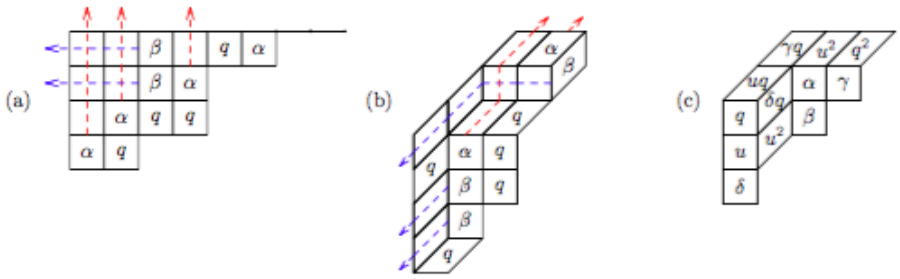


Figure 1: (a) alternative tableau, (b) rhombic tableau, (c) rhombic staircase tableau.

Results: We defined the rhombic alternative tableaux of Figure 1 (b) (joint with Viennot), giving combinatorial formulae of stationary probabilities for two-species ASEP at $\gamma = \delta = 0$. In subsequent work with Corteel and Williams, we generalized our tableaux to obtain rhombic staircase tableaux (see Figure 1 (c)) to obtain tableaux formulae for the two-species ASEP with all parameters general.

Conclusions: In recent work, a fascinating connection has been found between the two-species ASEP and Koornwinder polynomials, an important class of multivariate orthogonal polynomials that specialize or limit many other orthogonal polynomials. There is a *positive conjecture* that Koornwinder moments are polynomials with positive integer coefficients. As a result of our data, we are the first to obtain combinatorial formulae for a class of Koornwinder moments and we also proved a special case of the positivity conjecture.

Kinetic Study of Reactivity of para-phenyl substituted 1-iodo-alkynes and phenyl-azides in the Copper (I)-catalyzed Azide-Alkyne Cycloaddition Reaction.

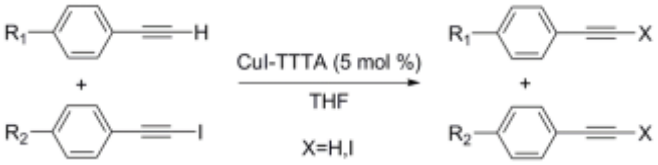
Antonina L. Nazarova, Heley A. Rossiter, Valery V. Fokin*
The Bridge at USC and Loker Hydrocarbon Research Institute, Department of Chemistry, University of Southern California, 837 Bloom Walk, Los Angeles, California 90089, United States. e-mail: *nazarova@usc.edu*; *fokin@usc.edu*

As it was recently discovered, the reactivity of 1-iodoalkynes exceeds the reactivity of terminal ones in copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC)[1,2]. Moreover, the product 5-iodo-1,2,3- triazole is an intermediate that can undergo further functionalization[2]. However, different functional groups in para-position of phenyl substituted alkynes and azides affect the rate and reactivity of triazole formation.

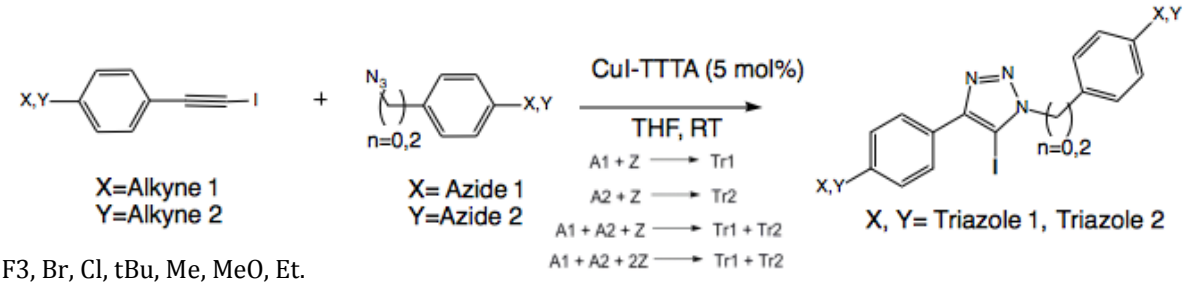
In this work, HPLC analysis was used for performing kinetic competition experiments with different para-phenyl substituted acetylenes and azides in the presence of catalyst system CuI-TTTA (tris((1-*tert*-butyl-1H-1,2,3-triazolyl)methyl)amine). Also, activity of the para-phenyl substituted acetylenes in pairwise iodo- and proto- exchange reactions was investigated.

The results support that the formation of iodo-triazoles satisfy the Hammett sigma values trend for electron withdrawing/donating functional groups of respective diverse iodo-alkyne and azide substrates. As we expected, kinetic competition reactions revealed that electron withdrawing capabilities accelerate the rate of the 5-iodo-1,2,3-triazole formation while electron donating groups slow down rate of the reaction. In addition, in pairwise iodo- and proto- exchange reactions, electron poor iodo-alkynes were discovered to be stabilized more than the electron rich or proto- derivatives. Results from kinetic and exchange reaction experiments favor pathway B in the proposed mechanism of copper(I)-catalyzed azide-iodoalkyne cycloaddition[1,3].

Exchange reactions



Competition reactions



X= H, CF3, Br, Cl, tBu, Me, MeO, Et.

(1) Hein, Jason E.; Tripp, Jonathan C.; Krasnova, Larissa B.; Sharpless, K. Barry; Fokin, Valery V. Copper(I)-Catalyzed Cycloaddition of Organic Azides and 1-Iodoalkynes. *Angew. Chem. Int. Ed.* **2009**, *48*, 8018–8021

(2) Worrel, B. T.; Malik, J. A.; Fokin, V. V. Direct Evidence of a Dinuclear Copper Intermediate in Cu(I)-Catalyzed Azide-Alkyne Cycloadditions. *Science* **2013**, *340*, 457–460.

(3) F. Himo, T. Lovell, R. Hilgraf, V.V. Rostovtsev, L. noodleman, K. B. Sharpless, V.V. Fokin, J. Am. Chem. Soc. 2005, 127, 210.

American Students Travel to Russia for Project-Based Learning and Research

Oleg V. Pavlov* and Svetlana Nikitina, *Worcester Polytechnic Institute, Worcester, MA, USA*
A. Ilyinsky, K. Kovnat, A. Didenko, J. Petrova, and E. Kameneva *Financial U under the Government of the Russian Federation, Moscow, Russia;* I. Akhunzhanova, *Astrakhan State U, Astrakhan, Russia* * WPI, 100 Institute Rd. Worcester, MA 01609, opavlov@wpi.edu

Worcester Polytechnic Institute (WPI) is a mid-sized private technological university in central Massachusetts. In collaboration with the Financial University in Moscow and more recently the Astrakhan State University, WPI has been organizing and sending groups of its students for 7-week projects in Russia. Students work on projects in teams of 3-5 students under the supervision of academic advisors, who travel with them to Russia from WPI. Each project answers a practice-inspired question that is formulated jointly with a Russian partner-organization. Partner-organizations included a major hotel in Moscow, universities in Moscow and Astrakhan, the Big Four consulting firms and a rail car leasing company.

The projects in Russia are part of a university-wide curriculum that uses project-based learning (PBL) approach. About 60 percent of the undergraduate students at WPI travels to nearly 40 project centers located around the globe, including one in Moscow. WPI has been following the PBL model since the mid-1970s. Every undergraduate student at WPI is required to complete three large projects before graduating. Each global project center hosts 3 to 8 teams at a time. All projects involve local partner-organizations.

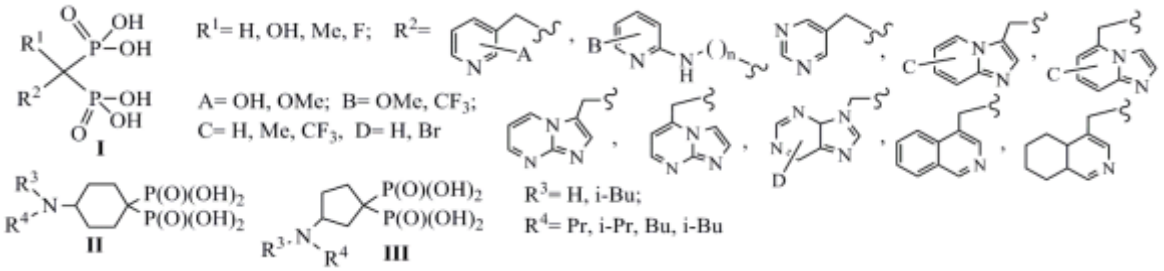
Our experience shows that a successful global PBL program requires three major components: (i) champions among the faculty; (ii) support of university administrators; and (iii) a considerable infrastructure of professional staff who support on a daily basis multiple activities in PBL. WPI maintains an entire academic division that prepares students and arranges their trips. Student teams preppare for seven weeks prior to their departure. They learn research methods, culture and language, and start working on projects. The need for significant resources from the sending and hosting universities is a major challenge. While PBL programs at WPI are self-sustaining, an infusion of funds from donors can boost administration's commitment to the PBL program and to a particular geographic project center, such as in Russia. The WPI project center in Moscow started with a generous financial contribution to the university by a donor. The donor wanted to create opportunities for students to travel to Russia as part of their regular academic work. The first student teams traveled to Russia in 2013; more WPI students have gone to Russia every year. In 2016, six teams of American and Russian students work on projects in Moscow, Astrakhan and Tuapse.

PBL has the following components: (i) a project addresses a problem or a question; (ii) students are involved in a variety of activities; (iii) there is an end product (e.g. a report); (iv) the project takes a considerable amount of time to complete; (v) students are supervised by academic advisors. Typical objectives of project-based learning are educational. Project-based curricula has been developed and used in a variety of courses. As an example of an educational project completed in Russia, we will present a student study on career trends among Russian students. The Financial University in Moscow and Deloitte CIS were partner-organizations. The project identified the career preferences of students at several elite universities in Moscow. Through interviews and a survey, the study determined how Russian students choose their academic majors, career paths and places of employment. The report found that work environment, advancement opportunities, salary and benefits, travel opportunities, and company reputation were the most important factors for Moscow-based students in making decisions about the choice of the employer.

Developments in the Synthesis of New Functionalized Bisphosphonates Drug Candidates such as Cyclic Prodrugs

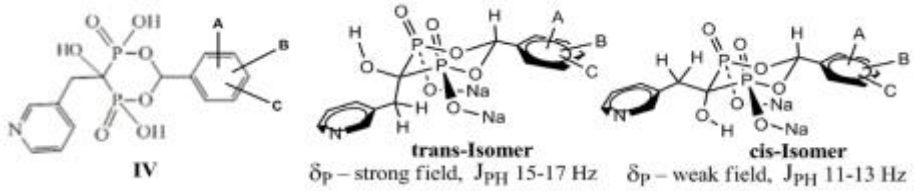
Valery A.Pavlov[a,b]*, F.H.Ebetino[c,d], M.W. Lundy[c], J. Joly[e], Roy Dobson[f], A.W.Mazur[a,g]
a) Worcester Polytechnic Institute, Department of Chemistry and Biochemistry, Worcester, MA, USA, b) Girindus America Inc., Cincinnati, OH, USA, c) BioVinc LLC, Culver City, CA, USA, d) Chemistry Dept. U. of Rochester, Rochester, NY, USA, e) Pharma-GPS, Dayton, OH, USA, f) Procter & Gamble, Mason, OH, USA, g) TWI Chem LLC, Cincinnati, OH, USA. Presenting Author: *e-mail: vpavlov@wpi.edu

The heterocyclic nitrogen bisphosphonates (BPs) such as risedronate, ibandronate, zoledronate, minodronate, and others, act by directly and selectively inhibiting the activity of osteoclasts, cells responsible for bone resorption. The synthesis and screening of more than 200 BPs led to the selection and development of risedronate as the prescription medication Actonel® for prevention and treatment of osteoporosis[1]. The clinical success of this drug stimulated further research. We report here the synthesis of new series of nitrogen containing heterocyclic and carbocyclic BP prodrugs (**I** – **III**).



BP medications such as alendronate and ibandronate suffer from side effects and pharmacological disadvantages as orally administered agents. For example, these drugs can cause esophageal irritation and ulceration. The high polarity and charged nature of BPs also result in very low oral bioavailability (ca. 1%), resulting in highly variable absorption which is further reduced when taken with food. This "food effect" can be explained by formation of insoluble calcium salts of bisphosphonic acids with calcium-ions contained in food. The currently described BP circumvent these side effects and absorption issues while maintaining the BP pharmacological activity.

We developed the synthesis of novel compounds-cyclic esters of bisphosphonic acids (**IV**)[2] where bisphosphonic acid functionality is "masked" as a cyclic ester moiety which results in increase of lipophilicity of the molecule, thus improving the absorption profile. Moreover, the ester moiety prevents the chelation of the BPs with metal ions in food by blocking two hydroxy groups of the phosphoryl fragments. Therefore, the described compounds (**IV**) have a decreased "food effect" which allow these drugs to be taken without restrictions with meals. Such protected BPs are also hydrolytically labile under enzymatic conditions *in vivo* after absorption into the bloodstream, thereby releasing the tetra-acid functionality of the bisphosphonates after their oral administration.



The cyclic bisphosphonate compounds (**IV**) exist in two isomeric cis- and trans-forms.

1. US Patent 5,583,122, **1996**; 6,165,513, **2000**; 6,096,342, **2006**
2. US Patent 8,822,435 B2, **2014**

Changes in the redox state during aging as a major factor in deregulation of the immune system

Svetlana N. Radyuk, PhD

Research Associate Professor, Southern Methodist University, Dallas, Texas

A theme uniting research in our group is the role of redox and redox-sensitive pathways in normal human physiology, aging and diseases. Our current research is centered around the study of antioxidant and immune defenses and redox aspects of the organismal systems in maintaining a healthy lifespan.

One of important directions is investigation of the interaction between immunity and aging. There are two major stresses that we experience throughout our lifetime, oxidative and immune, and the response and resistance to these stresses can be costly. Oxidative stress increases during aging, as has been supported by data from our research group and others. There is an exponential increase in concentrations of reactive oxygen species (ROS) as well as a shift to a more pro-oxidizing state, as defined by the ratio of redox couples such as GSH:GSSG. Concurrent with these changes, there is an activation of the effectors of humoral immunity, and the most dramatic changes in the redox state and activation of immunity occur in middle-aged organisms, coincident with the exponential increase in mortality rate. The hyperactive pro-inflammatory responses not only associate with aging but may also contribute to the aging process and be responsible for some age-related abnormalities in normal physiology. Using experimental models, we have shown that life span could be shortened by overexpression of the immunity factors, such as antimicrobial peptides.

Based on these observations, I developed a hypothesis that the changes in the redox state during aging is a major factor in deregulation of the immune system. This hypothesis was strengthened by the remarkable finding that the 'switch' governing this transition appeared to be controlled at least in part by antioxidant enzymes called peroxiredoxins, which are also known to serve as redox sensors and regulators of redox signaling. Furthermore, manipulating redox state by modulating levels of either peroxiredoxins or the GSH biosynthetic enzymes, was found to impact both the chronic overactivation of the immune response that accompanies aging, as well as longevity. Consequently, current focus of our work is to determine the window in which peroxiredoxin can have beneficial effects on survivorship by combatting oxidative stress, but without weakening the immune response and resistance to infection.

Aberrant immune responses and chronic inflammation can also impose significant health risks and accompany the development of various diseases, including neurodegenerative disorders, such as Alzheimer's disease. Pro-inflammatory responses are largely mediated via ROS, key signaling molecules that play an important role in pathogenesis of diseases. A versatile control mechanism to deal with overproduction of ROS and pro-inflammatory effects are the various antioxidant and redox-regulating factors. Confirmed targets may then be used to develop strategies to control inflammatory response. Thus, we are testing the role of peroxiredoxins in modulating inflammatory response in the models of Alzheimer's disease. Together, these studies should help to define the mechanistic link between chronic inflammation, peroxiredoxin function, and progression of Alzheimer's disease. A positive outcome in this research would lead to discovery of potential targets for translational research in order to develop proper interventions.

Structure Based Screening for P2Y2 Receptor Antagonists

***Anastasiia Sadybekov*[1]**, *Nilkanth Patel*[2], *Kenneth Jacobson*[4], *Vsevolod Katritch*[2,3]

Corresponding author: asadybek@usc.edu

[1]*Department of Chemistry,* [2]*Department of Biological Sciences, Molecular & Computational Biology,* [3]*The Bridge Institute, University of Southern California, USA,* [4]*NIDDK, National Institutes of Health, USA*

P2Y2 receptor belongs to the purinergic receptor family P2Y of class A GPCR, which holds a promising potential as a drug targets for treatment of broad range of chronic disorders [1]. Agonists of P2Y2 receptors are in clinical trials for treatment of cystic fibrosis and dry eye syndrome [2, 3]. Another perspective application of P2Y2 receptor is treatment of metastatic cancer. Activation of P2Y2R is responsible for tumor cell migration and metastasis to other tissues, while silencing of P2Y2 receptor with shRNA in mice dramatically reduces tumor growth and metastatic cancer [3]. Further clinical validation of P2Y2 receptor as a clinical target is limited due to the lack of selective and potent antagonists. Standard medicinal chemistry approaches for ligand discovery such as derivatization of endogenous ligands are limiting here because known P2Y2R agonists are negatively charged nucleotide-like molecules with low stability in vivo. A handful of available P2Y2R antagonists are non-selective compounds with low affinity, usually dyes. To facilitate the development of high-affinity ligands, the model of P2Y2R receptor based on recently solved structure of closely related P2Y1R was built. The available mutagenesis data and SAR studies for P2Y2R were used to refine the initial row model and predict interactions between P2Y2 receptor and ligand. Refined P2Y2R model was used to design ligands for allosteric binding site and perform virtual ligand screening to find potential ligands for orthosteric pocket.

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Study of N_5^- excited states: influence of electronic structure on stability.

Arman Sadybekov, Karl Christe, and Anna Krylov

Department of Chemistry, University of Southern California, USA
Corresponding author: sadybeko@usc.edu

Polynitrogen species are hot topic in material sciences through the XX century. It was motivated by expectation that these materials will release large amounts of energy when decomposing to N_2 and will replace existing rocket fuel and explosives as green and very effective alternative. Nearly 100 years of search for N_5^- species finally led to success in 2002, when cyclopentazole was observed in gas phase by mass-spectroscopy. However, every attempt to prepare cyclo-N_5^- in solution failed. We decided to rationalize this phenomenon from electronic structure point of view. Excited states calculations of N_5^- were carried out; complex degenerate states structure was revealed. Jahn-Teller distortions were analyzed. Results predict stable structure of this compound. According to existing literature, N_5^*, product of ionization of cyclopentazole anion, is not a local minimum on PES and simultaneously decomposes to N_2 and N_3^*. Thus, source of instability was sought in ionization of N_5^-. Gas phase electronic rate transition was predicted and some results on condensed phase calculations will be presented.

Polynitrogen species attract attention as potential high energy density materials that release large amounts of energy when decomposing to N_2. They are also interesting from a fundamental point of view. N_5^- has been observed in 2002, however, attempts to prepare cyclo-N_5^- in macroscopic quantities were not successful. We investigate electronic structure of N_5^- to (i) understand its stability in solution and in bulk phase; (ii) predict its spectroscopic signatures for future experimental studies. Detailed characterization of electronically excited and ionized states will be presented. Jahn-Teller effects and a possible role of charge transfer on the stability of bulk species will be discussed.

QTL ANALYSIS IN ARABIDOPSIS THALIANA IDENTIFIES OLI2 AS A MAJOR REGULATOR OF TELOMERE LENGTH AND CELL PROLIFERATION

Liliia R. Nigmatullina[1], Inna B. Chastukhina[1], John T. Lovell[2], Callie Kobayashi[3], Liia R. Valeeva[1], Chuluuntsetseg Nyamsuren[1], Dorothy E. Shippen[3,*], Thomas E. Juenger[2,*] and **Eugene V. Shakirov[1,2,*]**

[1]Institute of Fundamental Medicine and Biology, Kazan (Volga Region) Federal University, Kazan, Republic of Tatarstan, 420008, Russia; [2]Department of Integrative Biology, University of Texas at Austin, Texas 78712, USA; [3]Department of Biochemistry and Biophysics, Texas A&M University, 2128 TAMU, College Station, Texas 77843-2128; *Corresponding authors

While each eukaryotic species is characterized by a specific size range of telomere tracts, mean telomere length in many species shows considerable inter-individual variation. This telomere length variation is known to be under strong genetic control, but the factors establishing telomere length set point within natural populations are largely unknown. We took advantage of natural telomere length variation in the model plant *Arabidopsis thaliana* to identify novel genes and genetic variants with large effects on telomere length set point.

Because of its superior biological and genomic resources and the availability of hundreds of genetically distinct natural populations and recombinant inbred lines, the model plant *Arabidopsis thaliana* offers a unique opportunity for the analysis of natural telomere length variation in a model multicellular eukaryote. Using quantitative trail analysis (QTL) approach we identified OLI2 gene as a major regulator of telomere length in natural Arabidopsis populations. Expression of OLI2 homologues in humans and mice have previously been correlated with tumor progression, indicating that these genes can be considered prognostic markers of cancer.

Our data indicate that identification of casual QTLs is a promising route to understanding genetic diversity controlling telomere length polymorphism, cell proliferation and tumor development.

A BRIEF HISTORY OF TIME IN CHEMISTRY

Prof. **Gregory S. Yablonsky**

Parks College of Engineering, Aviation and Technology, Department of Chemistry, Saint Louis University (St. Louis, USA)

An evolution of the concept of "chemical time" will be presented. Different milestones in introducing this concept into chemistry will be described, in particular a special role of the discovery of catalysis and development of chemical kinetics. Three meanings of "chemical time" will be explained: (1) "external time" of the chemical system, i.e. temporal scale of our observations; (2) "internal", or "intrinsic" time; (3) "residence" time. It will be doing an attempt to distinguish time as a framework for demonstrating the chemical transformations and time as a manifestation of the chemical complexity. State-of-the-art in studies of chemical temporal behavior will be shown using recent results on complex chemical dynamics (oscillatory and chaotic behavior) and "chemical calculus".

A special attention will be paid to two approaches:

I. Temporal Analysis of Products (TAP) -approach in which the advanced millisecond pulse-response technique is used for studying the complex catalytic reactions [1-3]

II. Joint Kinetics – approach which focuses on the analysis of special kinetic trends and invariants [4-6]

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Attendee name	University/Affiliation
Andriasyan, Annie	University of California, Riverside
Atochina-Vasserman, Elena	University of Pennsylvania
Bodrova, Alexandra	abodrova@caltech.edu
Bogomolnaya, Lydia	Texas A&M University Health Science Center
Bragin, Anatol	UCLA
Bronich, Tatyana	University of Nebraska
Chasovskikh, Sergey	Georgetown University
Chertkov, Michael	
Choumiline, Konstantin	University of California Riverside
Dikov, Mikhail M.	Ohia State University
Efimov, Igor	George Washington University
Ermolaev, Alexander	Russian Embassy
Falaleyev, Andrei	Interpreter
Figueroa, Leon	UCLA
Fokin, Valery	University of Southern Caifornia
Friedman, Louis	Planetary Society
Gassan-Djalalov, Anouchvan	non-profit organizatiob
Gerchikov, Vladimir	n/a
Giem, Elisabeth	University of California Riverside
Giem, Joshua	UCR
Gladyshev, Vadim N.	Brigham and Women's Hospital, Harvard Medical
Goudarzi, Persia Fatemeh	UCLA
Grigoriev, Maksim	фонд «Вольное дело» , Russia
Gunina, Anastasia	University of Southern California
Hekimyan, Richard	University of California, Riverside
Howe, Jacob	University of Central Florida
Ilchenko, Yuriy	UT/Austin
Isayev, Olexandr	University of North Carolina
Ivanova (Kudinova), Daria	University of Southern California
Kabanov, Alexander	University of North Carolina Chapel Hill
Kalashnikova, Olga	«Базовый Элемент», Russia
Karabut, Stanislav	«Базовый Элемент», Russia
Kelly, Carson	University of Central Florida
Kerimbayeva, Sultanat	University of Southern California
Khalatiyan, Vladimir	
Kim, Oleg	University of California Riverside
Kiryakova, Anna	UCF
Klichko, Vladimir	Southern Methodist University
Kojevnikov, Alexei	University of British Columbia
Konstantin, Kudinov	
Korkhin, Yakov	SciTech Legal P.C..
Korovina, Nadezhda	University of Southern California

Kriukova, Kseniia	I.M. Sechenov Moscow State Medical University
Krivitsky, Raissa	Cornell University
Kurilovich, Nadezhda	NY non-profit organization
Kutsaev, Sergey V	RadiaBeam Systems, LLC
Kuznetsov, Evgeny	Russian Venture Company, National Technological Initiative
Lavrinenko, Dmytro	n/a
Lebedev, Vladimir	Moscow House of Compatriots
Litvinov, Rustem	University of Pennsylvania
Ljubimov, Alexander	Cedars-Sinai Medical Center/UCLA
Ljubimova, Julia Y.	Cedars-Sinai Medical Center
Lukishova, Svetlana	University of Rochester
Mandelshtam, Olya	UCLA
Manko, Mikita	BSUIR
Mardanov, Sergey	Russian Venture Company
Mendoza, Eric James	University of California Los Angeles
Merinov, Boris V.	California Institute of Technology
Misurkin, Alexander	ROSCOSMOS
Muhin, Sergey	University of Southern California
Murokh, Alexander	
Myagkov, Mikhail	University of Oregon
Nadtochiy, Anna	University of Southern California
Nazarova, Antonina	University of Southern California
Nuzhdin, Sergey	University of Southern California
Odnokoz, Olena	Southern Methodist University
Oganov, Artem	Stony Brook University
Orms, Natalie	University of Southern California
Pavlov, Oleg	Worcester Polytechnic Institute
Pavlov, Valeriy	Worcester Polytechnic Institute
Petrov, Sergey	Consul General of the RF in San Francisco
Pevzner, Pavel	University of California, San Diego
Phelan, Jay	UCLA
Ponomareva, Larissa	University of Kentucky
Popov, Yury	BIDMC, Harvard Medical School
Popov, Damir	University of Southern California
Radyuk, Svetlana	Southern Methodist University
Reisman, Garrett	SpaceX
Rodchenko, Natalia	University of Southern California
Rousso, David	Docking Port Productions
Russell, Jonathan	University of California Riverside
Sadybekov, Anastasiia	University of Southern California
Sadybekov, Arman	University of Southern California
Sergeeva, Masha	DMPK4BIOTECH, Inc
Sergey Simeniv	sergey.simeniv@gmail.com
Shakirov, Eugene	University of Texas at Austin

Shiltsev, Vladimir	Fermilab
Shokhov, Oleg	GE Capital
Shuvalova, Ludmilla	Northwestern University
Sitnikov, Alexey	Skolkovo Institute of Science and Technology
Turyshev, Slava G	UCLA
Ufimtsev, Pyotr	UCLA
Valamat-Zade, Nargis	ANO New development technologies
Vasilyev, Nikolay	Boston Children's Hospital, Harvard Medical School
Vasserman, Sasha	Lower Moreland High School, PA
Vaughn, James Michael	University of California, Riverside
Vlasenko, Nikita	University of Southern California
Vlasov, Leonid	University of Southern California
Yablonsky, Gregory	Saint Louis University
Zelenyi, Lev	Space Research Institute of the Russian Academy of Sciences
Zelman, Vladimir	University of Southern California
Zelmanov, Efim	University of California, San Diego
Zhiganov, Oleg	Russian culture center, Washingdon, DC
Zoubko, Igor	Interpreter