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THE SEVENTH GERMAN-RUSSIAN WEEK OF THE YOUNG RESEARCHER

"COMPUTATIONAL BIOLOGY AND BIOMEDICINE"

Moscow, September 11–14, 2017

Skoltech
Skolkovo Institute of Science and Technology

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Welcome to the Seventh German-Russian Week of the Young Researcher!

Dear colleagues from Russia and Germany,

We are very delighted to welcome you to our Seventh Week of the Young Researcher! When we convened the "German-Russian Year of Science", seven years ago, the idea was born to invite young researchers from both countries to come together to discuss current topics of mutual interest. The success of the first week in Kazan encouraged us to turn it into an annual event. The following years we met in Ekaterinburg (2012), Novosibirsk (2013), St. Petersburg (2014) and Moscow (2015, 2016). The main goal of these meetings is to foster collaboration among young scientists and researchers who will be setting the agenda of scientific cooperation between Russia and Germany in the near future.

Research organisations and institutions of higher education of both our countries will be presenting their funding programmes and describing the platforms that they can offer to both Russian and German PhD students as well as PostDoctoral researchers. The overarching principle behind these presentations is to facilitate collaboration and to broaden research networks. The brochure illustrates how young and experienced scientists can work across borders with local authorities, associations and industry in order to develop new approaches to global challenges.

This time we took an interdisciplinary approach and discussed various facets of the still growing field of computational biology and biomedicine. By now, almost every field in biology and medicine flourishes with the help of computational data analysis since the first attempt to apply algorithms for the interpretation of biological sequences such as proteins and genomes. Information and communication technologies enable the exploration of huge data spaces generated by various experimental –omics technologies. Computational biology has evolved as a discipline reaching beyond the investigation of individual parts of the cell using concepts borrowed from computer science such as networks and systems biology models.

This years' host location was the Skolkovo Institute of Science and Technology (Skoltech). Founded in 2011, Skoltech is an international graduate research university near Moscow that aims at educating students, advancing knowledge, and fostering innovation in order to address critical scientific, technological, and global challenges.

We thank all of you, the participants, for your involvement and cooperation in this conference.

DR. PETER HILLER

PROF. DR. RUPERT GERZER

DR. WILMA RETHAGE

Peter Hiller

German Academic Exchange Service
Head of DAAD Office Moscow
Managing Director of DWIH Moscow

Rupert Gerzer

Skolkovo Institute of Science and Technology
Provost

Wilma Rethage

Deutsche Forschungsgemeinschaft
Head of DFG Office Russia/CIS

PROFESSOR DR.
ALEXANDER KULESHOV

Member of RAS,

President of the Skolkovo Institute of Science and Technology

Dear colleagues, Dear participants!

It is widely believed that Russia had a fancy for French culture, while owing its scientific and engineering excellence to Germany. Back in the 18th century, Peter the Great invited German engineers, architects and scientists to Moscow which still has the historical German Quarter in one of its central districts.

Our nations have been very close for centuries. The 7th German-Russian Week of the Young Researcher that took place at Skoltech underscores our commitment to keep up the long-standing cooperation tradition. I would like to wish all the participants every success in their research endeavors.

Dear Professor Kuleshov, Dear Professor Allgöwer, Dear Professor Grothus, Dear Dr. Hiller, Ladies and gentlemen!

THOMAS GRAF

Head of the Department
of Economy and Science,
German Embassy Moscow

I am pleased to welcome you on behalf of the German Embassy in Moscow to the 7th German-Russian Week of the Young Researcher which is a cornerstone of the German-Russian science calendar.

Throughout this week new cooperation projects and partnerships will be developing, in particular between young scientists, thus making German-Russian science cooperation even more dynamic and intense.

More than ever Germany and Russia need each other in the fields of science and research. Because technologies are developing at a breathtaking speed. Only together we can develop synergies and achieve significant scientific and technological progress.

Germany and Russia are close and important partners in science and research. Our scientific-technological exchange continues to be successful, which is particularly important against the backdrop of the current political situation.

Our cooperation has a broad basis, ranging from exchanges of students and young scientists, through partner universities, joint research institutes and research groups, large research projects like XFEL near Hamburg and FAIR in Darmstadt to cooperation within the framework of vocational training.

The German House of Science and Innovation in Moscow bundles the expertise of the numerous German science organisations and actively promotes new cooperation. I would like to thank Dr. Hiller as DWIH Head, Mr. Rusakov as DWIH Coordinator, and Dr. Rethage as DFG Head and Deputy Head of DWIH in Moscow for their engagement.

For the DWIH the week of the young scientist is one of the key events. Since 2011, the event has been bringing together academics from Germany and Russia to exchange ideas in a changing science environment.

The topic of this particular week is as relevant as fascinating: Computational Biology and Biomedicine. The best example for processing large amounts of data in life sciences may be the sequencing of the human genome. It is to be hoped that similar scientific breakthroughs in bioinformatics will also be possible in cancer research.

The Skolkovo Institute of Science and Technology is without question the right place for new insights and findings. It has established itself in a short time as a center of scientific excellence in Russia, open to international exchange, with English as a working language. Last but not least, start-ups and the transfer of knowledge and technology play a prominent role in Skoltech's daily work. All these are excellent preconditions for an exciting week!

This week provides an opportunity to get to know new outstanding research results and approaches. It provides a platform for professional exchange of ideas between scientists – especially young researchers – from Germany and Russia. It is thus a source of possible new professional relationships and cooperation opportunities. On this note I wish you all an exciting week with many new encounters, stimulating conversations and new insights!

PROFESSOR DR. FRANK ALLGÖWER

Vice-President of the Deutsche Forschungsgemeinschaft;

Director of the Institute for Systems Theory and Automatic Control
University of Stuttgart

Dear Rector Kuleshov,
Dear Professor Gerzer,
Dear Mister Graf,
Dear Mister Grothus,
Уважаемые коллеги,
Dear participants,

I am very pleased that you have accepted the invitation of the joint initiative of the German Academic Exchange Service DAAD and the German Research Foundation DFG to the "Seventh Week of the Young Researcher" of the German House of Science and Innovation in Moscow and I would like to welcome you here on behalf of DFG!

Last year, I had the honour of representing the DFG at the opening of the previous Week of the Young Researcher held also in Moscow. My opening remarks ended with the words "and I very much hope that we can celebrate the seventh week together next year." Well, this year has passed by in no time, and I am very happy to be back in Russia and in Moscow – this bustling, vibrant and exciting European metropolis.

This year's Week of the Young Researcher explores new horizons in a number of ways – but without breaking with its tried-and-true traditions. Since its inception in the German-Russian Year of Science in 2011/2012, the event format has provided early career researchers with a forum for exchange on global research topics; with opportunities to network nationally and internationally – also with experienced colleagues; and – based on the interdisciplinary character of the event – to get ideas from a wider scientific community with regard to their own research questions.

This format has served us well over the past six years of organising this event and thus revived a very old tradition in German-Russian cooperation. Namely in the 1920s, the DFG's predecessor organisation (the "Notgemeinschaft der deutschen Wissenschaft"), together with the Soviet Academy of Sciences, organised joint science weeks. These bilateral research weeks, which were conducted in various disciplines including the natural sciences (1927), history (1928), the engineering sciences (1929), and the medical sciences (1932), proved to be a very successful instrument to foster cooperation between the two countries. And also in those days, special attention was paid to the next generation of researchers, like we do with the present day format.

After having focused on the topical issues of energy, health, aerospace, history, mathematics and urban studies during the last years, we are continuing the tradition of choosing exciting, current topics of global interest again this year. With "computational biology and biomedicine", we are delving into a highly relevant, complex and multidisciplinary field of research – a field that has been shaped in recent years by technological advances like few others and which is highly interdisciplinary by nature.

In my role as Vice President of the DFG, please allow me to emphasise that the DFG, being the most important self-governing organisation for fundamental research in Germany, finances and supports a large number of very interesting, and often interdisciplinary, projects in biology, bioinformatics, biophysics and computer science at German universities and research institutes with funding instruments ranging from individual grants to coordinated long-term programmes such as Research Training Groups, Col-

laborative Research Centers or Clusters of Excellence that were formed within the framework of the German Excellence Initiative. As an example, I want to mention the Graduate School of Quantitative Biosciences at the LMU in Munich, where various faculties – from applied mathematics, bioinformatics, organismic genetics, systems biology, biochemistry to molecular genetics – jointly launched a structured doctoral programme. Or the DFG Research Training Group entitled Computational Systems Biology at the Humboldt-University in Berlin, which, together with the Max Delbrück Center for Molecular Medicine and the Max Planck Institute of Molecular Genetics, contributes to the growing future need for qualified scientists at the interface between biology and mathematics. Or the DFG-funded Heidelberg Graduate School of Mathematical and Computational Methods for the Sciences that is dedicated to research on more effective methods of scientific computing with regard to various fields of application, such as environmental physics, medical science, the humanities and systems biology. This field of research has also become part of our international co-operations, like the DFG Research Training Group on Computational Methods for the Analysis of the Diversity and Dynamics of Genomes, launched in 2012/2013 at the University of Bielefeld together with Vancouver, Canada.

These are, of course, only a few current examples, but they show that DFG as a funding agency with a global view, has recognised the relevance of the topic and its knowledge-generating potential.

My own research that I am conducting as a professor for systems theory in the engineering sciences at the University of Stuttgart, is also connected to the topic of computational biology and biomedicine, and in particular to systems biology and synthetic biology. In fact, we have a fairly large center, the Stuttgart Research Centre Systems Biology, that was founded more than ten years ago and that brings together researchers from biology, chemistry, physics, mathematics and in particular from the engineering sciences. The latter aspect is the particularity of our Stuttgart center that gives it an interesting spin when compared to other, partly much larger centers in Germany. I will give a scientific talk on some of our research findings later today.

With regard to the venue and the choice of our Russian partner, we are venturing into new waters. In the past, we have traditionally held this event at universities with close ties to either the DFG or the DAAD and in which German-Russian collaborations had previously been set up. This year, we are embarking on a new path with the Skolkovo Institute of Science and Technology. Skoltech is a very young institution and probably a novelty in the Russian science landscape. It is positioning itself as a private research university with a clear-cut professional profile, combining basic research with strong practical applications. Additionally, it stresses its international focus. Taken together with its interesting origin and its cooperation with MIT, Skoltech stands out from the other institutions in the scientific landscape of Russia. Professor Kuleshov, I am very much looking forward to hearing and seeing more of your university during this week. I would like to especially express my gratitude to you as the rector of the university. We are very pleased to have the opportunity to get to know Skoltech both as a university and as a venue – but even more importantly as a potential scientific partner for future activities. These upcoming days will certainly provide numerous occasions to explore each other's potential for German-Russian research cooperation in the field of computational biology and biomedicine.

I also want to thank the German Embassy, represented today by Mr. Graf, Head of the Department of Science and Economy at the German Embassy in Moscow, for continuing to be a staunch supporter of this event. You have long recognised that the research cooperation between our two countries is an important, lively and productive component in the relationship between Russia and Germany and that scientific events like the present one make a valuable contribution to developing trust and partnerships among the early career researchers and future generations of scientists from both our countries. Thanks very much for your continuing support that is very important to us.

The DFG has been promoting German-Russian cooperation for many decades, since 2003 even with its own affiliation in Moscow. Since the 1970s, there has been an agreement with the Academy of Sciences on research exchanges between our nations. Together with each of our Russian partner organisations, the Russian Foundation for Basic Research and the Russian Science

Foundation, we publish annual calls for bilateral research projects that find great interest in the scientific communities here and in Germany. From 2014 to 2016, the DFG did invest around 60 million euros in projects with a reference to Russia. Over this two-year period, approximately 80 grants were awarded per year. And these grants, co-financed in part by our Russian partners, included not only research projects in the traditional sense, covering a wide range of subjects, but also projects aimed at initiating international cooperation with Russia. This also included German programmes for early career researchers and other programme formats such as Mercator Fellows with sustainable contributions by individual Russian scientists. And last but not least, this statistic also encompasses Germany-based research projects that focus on Russia as a subject of research.

With our joint German-Russian event, we are showing that wide areas of science, education and culture can be a bridge – and, I am convinced – a very valuable bridge between Germany and Russia. We will continue to foster this exchange in the future, extend it beyond the scientific discourse and leverage it to develop and facilitate new partnerships.

Now let's come back to our Week of the Young Researcher. I want to thank Dr. Rethage

and her team from the DFG office in Moscow and of course our friends from DAAD for the perfect organisation of this event. You have not only our thankfulness but also our admiration for the great work. I also want to thank Professor Werner Mewes from the Helmholtz Centre in Munich and the Technical University of Munich, who is the mastermind behind the scientific orientation and organisation of this week. Your vision, guidance and organisational help is much appreciated. Finally I want to thank all participants for being here. The senior and in particular junior scientists coming from Germany and of course the ones coming from various places in Russia, partly from as far away as Novosibirsk. We invite you all to actively participate in what promises to be a week characterised by lively and insightful discussions and dialogues. Let us use this week at Skoltech to foster bilateral German-Russian research collaboration.

I wish you and us all an interesting and fruitful seventh German-Russian "Week of the Young Researcher" and – to update my words from 2016: I very much hope that you keep the tradition alive and that we can celebrate the eighth week together next year.

Dear Rector Kuleshov, Dear Mr. Graf, Dear Prof. Allgöwer, Dear scientists and researchers,

ULRICH GROTHUS

Deputy Secretary General
of the German Academic Exchange
Service (DAAD)

It is a great pleasure for me to welcome all of you on behalf of the German House of Research and Innovation (DWIH) in Moscow and the German Academic Exchange Service (DAAD) to the German-Russian week of the young researcher. It's an established format, so we do it for the seventh time and the goals and objectives remain the same: we want to bring together junior and senior researchers on a hot scientific topic, to learn about the state of the art in research globally and in our two countries and to initiate new contacts and new cooperations. All of that is needed more than ever. In the current political situation it is even more important for people to talk to each other, to get to know each other, to understand other people's perspectives, to establish personal contact. And there is perhaps no better way than science to do that. No one is in a bigger responsibility to do it than academics and researches – younger or older.

There are probably only two goods, that grow by being shared. One is love and the other one is knowledge. There is no limit of the value of sharing these two areas of human life. And so we will all increase our knowledge and our insights by sharing them with each other.

This year we are talking about a very important subject, that has many different aspects "Computational biology and biomedicine". The topic is very significant for every one of us. New technologies give us huge opportunities but bring also new social and ethical challenges. New methods allow you to study and explore diseases in much more detail. But what we do with a huge amount of data on very intimate issues? How can the data be safely stored and used and how should we deal with so much information? All these important questions are part of the discussions that we will have this week.

The German-Russian week of the young researcher is an established format but it is also innovating itself. One of the innovative elements in this year's programme is an "innovation slot" that shows examples of good practice in German and Russian companies in translating scientific results into industrial applications through start-ups. And I am happy that a huge German company and a young Russian company will present good examples of initiating and growing start-ups.

We have to deal today with issues that need to be taken up globally by researchers and by networks of leading and innovative universities worldwide. In this context, we are very glad to be this year in this young and modern university Skoltech, which is teaching in English and is experimenting with new methods of learning. Thank you, Rector Kuleshov, thank you, Professor Gerzer,

thank you, the whole team at Skoltech, who were involved in the organisation of the event, for hosting us this year.

The Week of the young researcher is the flagship event of the German House of Research and Innovation. The purpose of this "House", that so far has no roof, is to showcase what German science and research innovation have to offer but also to have an open door for people to come in, to share their experience. It is a "one-stop-shop" for Russian researchers and young scientists, who want to develop their cooperation with German scientists and research institutions. We are happy this year again that this event is organized jointly by the German Research Foundation (DFG) and the German Academic Exchange Service (DAAD) under the banner of the German House of Research and Innovation (DWIH).

The German Houses of Research and Innovation are a network with so far five such houses across the globe. We started in 2009 and we are very happy that the German Parliament, the German Government and the German research organisations this year decided on the future institutional structure of this network. We at DAAD are proud to have a coordinating role for the DWIH network. It is a challenging task. But we are sure that, in close cooperation with other research and scientific organisations and universities, we will make that a success.

I am happy, that again a number of very prominent German universities and research institutions are represented in this event both of senior and of promising young researchers. Russia is an interesting and important partner for the DAAD. Russia is, like Germany, one of the few countries in Europe that have been investing more money into universities and research in recent years. In both countries, the structure of science and education is undergoing big changes. So I think we can learn from each other and share our experience not only in terms of research topics and results but also in the organisation of science and higher education. Russia is second only to the United States in terms of the amount of money we spend on any academic cooperation with an individual country. Russian students are the third group of international students in Germany after China and India. In spite of the demographic development, the number of Russian students in Germany continues to go up. We have the interesting experience of the German Institute for Advanced Technologies (GRIAT) in Kazan. An International Research Training Group in the humanities, that developed from a project funded by DAAD, is now supported by the DFG. We hope that additional Groups will develop over time. A German-Russian road map for our future academic and research cooperation will be worked out this year and should be finalized next year. Germany and Russia are working together at many projects and are developing a framework for joint research.

In conclusion, I would like to express my gratitude. First of all, to the academic contributors to the programme, because it is you who do the research and thus make our lives better. Let me repeat my sincere thanks to Skoltech for your academic hospitality and to the other German and Russian partner universities for your participation. The event would not be possible without the support of the Foreign Office and of the German Embassy, so, thank you very much, Mr. Graf. I wish to thank the organizers behind the scenes, Mr. Rusakov and his team, Wilma Rethage, Peter Hiller and the branch office of the DAAD. I wish you and all of us an exciting and fruitful week, interesting discussions, new partners and maybe new ideas for common German-Russian research projects!

"What will we be talking about?"

Introductory Remarks

Professor Dr. H. Werner Mewes, Technical University of Munich, Biomax Informatics AG

A scientific revolution has cracked the genetic code and translated the genetic information of any organism of choice into a representative sequence of letters. Novel technologies made cellular and subcellular structures visible down to atomic resolution and dramatically changed our understanding of life. Specific targeting of cancer cells as well as repair of inherited or somatic mutations became reality but was not even in sight only 30 years ago. Undeniable, this progress would have been impossible without massive computing and sophisticated use of information technologies by translating biological principles into algorithms and executable computer codes.

Computational biology has contributed to the translation of biological entities into symbols digital representations like biological networks. The transition from observation into digital recording of data has opened the door to a precise mechanistic understanding of biological processes. Genetic information including epigenetics as well as signalling driving cellular control functions are now represented in manifold, computable forms. Computational biology has steadily developed over more than 30 years and initiated multiple but not well separated sectors coined as "bioinformatics", "systems biology", and "synthetic biology".

Some fundamental questions in biology such as the evolutionary concept of protein and genome evolution or the genetic heterogeneity of human individuals can not be answered by experiments but successfully approached by computational methods. Using the repertoire of mathematics together with the tools from computer science have made computational biology an essential and scientifically indispensable discipline that is sometimes underestimated as the engineering part of data in life science.

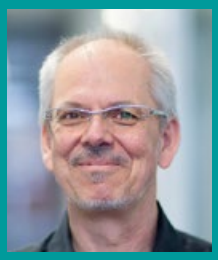
The historical coincidence of the rise of molecular biology and information technology has created a critical infrastructure starting with the compilation and maintenance of data and information resources, the design of powerful algorithms and data workflows, together with widespread applications and programmes used by the entire scientific community. Much wanted bioinformaticians must have a deep understanding of the entire research process starting with the biological question, followed by the experimental strategy and techniques, the capabilities and limitations of data transformation and analysis until the crucial interpretation of the results. Computational biology became instrumental for the progress of research but still still rather underestimated for its needs to support sustainable structures like databases and clinical expert groups.

It is a common misunderstanding of many biologists that truth has only to be found in the haystack of the data. The use of all -omics technologies and the application of some magic algorithm will not necessarily lead to immediate insight. Indeed, the reality of research in non-deterministic biological systems is like chasing a mystery: "…sometimes the information we've been given is inadequate, and sometimes we aren't very

smart about making sense of what we've been given, and sometimes the question itself cannot be answered." (Malcolm Gladwell writes about Puzzles and Mysteries; The New Yorker, 2007). If the question can be answered like the search for an inherited mutation of a rare disease or remains unsolved even after the collection of massive amounts of data (like in the hunt for the genetic component of depression) is often very hard to decide. But even more often this problem stays unreflected and therefore conclusions from large investigations remain vague and without practical consequences.

Computational biology has evolved as a discipline reaching beyond the investigation of individual parts of the cell. The idealized computational view to a human individual as an information source including all variables such as genome, proteome, metabolome, and cellular images seems to be out of sight. But how, with millions of cases and their data stored in the future, can we head for a better health care of all? Using "big data" in biology and medicine allows researchers to approach research questions in a new and a more complex way, but at the same time requires a deep and systematic understanding of the data, e.g. representing human biology, far beyond simple statistics. Together with experts and young scientists we will take an interdisciplinary approach and will discuss particular topics of interest such as: challenges of genotype/phenotype relations, impact of computational biology on health care systems and further applications, the challenges to educate researchers in using computational concepts and techniques to understand big data, and the impact of Big Data for future personalized health care. As elsewhere in the New Digital World we don't know what will happen and the future is more mysterious than predictable. But machine learning techniques and unbiased hypothesis-free approaches to large data need interdisciplinary thinking, intense scientific exchange and peaceful international collaboration.

PARTICIPANTS OF THE WEEK OF THE YOUNG RESEARCHER



Professor Dr.-Ing. Frank Allgöwer

Head of the Institute for Systems Theory and Automatic Control
University of Stuttgart

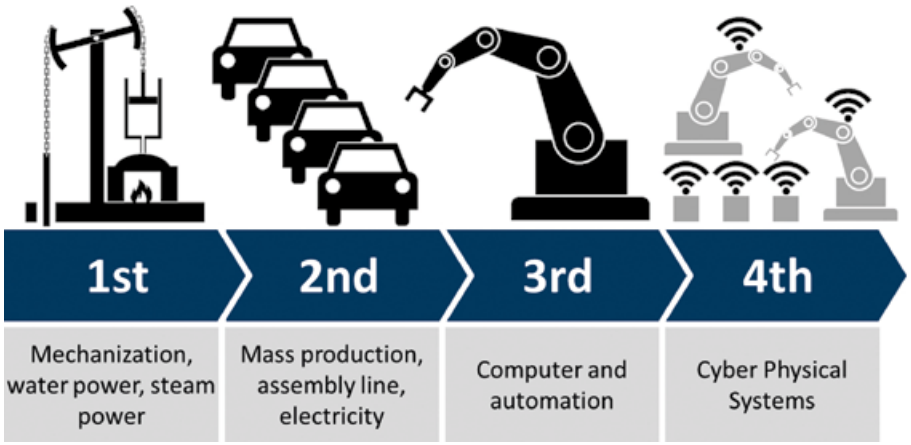
Vice-President of the DFG

RULING OVER CELL POPULATIONS – A SYSTEMS PERSPECTIVE ON SINGLE CELL ANALYSIS AND CONTROL

Karsten Kuritz and Frank Allgöwer, Institute for Systems Theory and Automatic Control, University of Stuttgart
Keywords: system biology, synthetic biology, systems and control theory

Frank Allgöwer, Vice-President of the Deutsche Forschungsgemeinschaft, is Director of the Institute for Systems Theory and Automatic Control and professor in the Mechanical Engineering Department at the University of Stuttgart in Germany. He studied Engineering Cybernetics and Applied Mathematics at the University of Stuttgart and the University of California at Los Angeles respectively. He received his PhD. degree in Chemical Engineering at the University of Stuttgart. Prior to his present appointment, he held a professorship in the Electrical Engineering Department at ETH Zurich. He also held visiting positions at the California Institute of Technology, the NASA Ames Research Center, the DuPont Company and the University of California at Santa Barbara. He serves among others the Scientific Council of the German Society for Measurement and Control (GMA), is on the Board of Governors of the IEEE Control System Society, Chairman of the IFAC Technical Committee on Nonlinear Systems, Member of the IFAC Policy Committee and Chairman of the International Affairs Committee of IEEE CSS and has been a Member of the Council of the European Union Control Association. Frank Allgöwer has arranged several international conferences and has published over 150 scientific articles. Frank Allgöwer received several recognitions for his work including the IEEE distinguished lectureship, the appointment as IFAC Fellow and the Leibniz Prize, which is the most prestigious prize in science and engineering awarded by the Deutsche Forschungsgemeinschaft (DFG).

At present engineering sees the 4th industrial revolution [1]. In a "smart factory" the ensemble of cyber-physical systems communicate and corporate with each other and with humans in real time thereby self-orchestrating the production process. Industry 4.0 is a transition from single machine control to automated interaction of a large number of constituents. The technology revolution in biology and medicine allows for a similar interpretation of biological



By Christoph Roser at AllAboutLean.com under the free CC-BY-SA 4.0 license.

function and the potential application of many of the systems tools that are being used in engineering. Omics technologies reaching single cell resolution allow the exploration of fundamental processes of live and death in great depth. Furthermore, manipulating these systems and controlling their behavior in almost any manner became possible with tools like genome editing or optogenetic switches.

Computational approaches taking systems level interactions and dynamics into account are crucial in retrieving the information hidden in these huge data spaces. Furthermore, integrating this information together with a systems level understanding of a disease to optimize the outcome of a treatment will and does already greatly improve personalized health care.

Systems and control theory deals with the analysis of dynamical systems and their control to achieve a desired behavior. Concepts of control theory can thus be used to tackle major challenges imposed by the revolutions in industry and biology. In this talk we demonstrate the usefulness of systems theoretical methods and tools and show their applicability by considering several examples for the analysis and control of cell populations on the single cell level [2], [3].

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MULTI REFERENCE SPECTRAL LIBRARY YIELDS ALMOST COMPLETE COVERAGE OF HETEROGENEOUS LC-MS/MS DATA SETS

Constantin Ammar[1,2], Evi Berchtold[1], Gergely Csaba[1], Andreas Schmidt[3], Axel Imhof[2,3], Ralf Zimmer[1,2]

[1] Institute of Bioinformatics, Department of Informatics, Ludwig-Maximilians-Universität München

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Keywords: Proteomics, Mass Spectrometry, Spectral Libraries

Spectral libraries play a central role in the analysis of data independent acquisition (DIA) proteomics experiments. DIA experiments require spectral libraries, as most current methods cannot apply traditional peptide identification via database searching on DIA data [1]. A central assumption in current spectral library tools is that a single characteristic intensity pattern (CIP) suffices to describe the fragmentation of an unmodified peptide in a particular parent ion charge state (peptide charge pair) [2][3]. However, we find that this is often not the case.

We analyze a heterogeneous dataset of 440.000 MaxQuant [4] – preprocessed peptide spectra from a QToF mass spectrometer, stemming from over 100 different LC-MS/MS runs. The dataset corresponds to 10.580 peptide charge pairs, which have each been measured and identified at least 20 times. We demonstrate that the same charged and unmodified peptide can fragment in multiple reproducible ways, even within the same LC-MS/MS run. We integrate multiple reference CIPs (MCIPs) in our model library and observe a >99% coverage of replicate fragmentation spectra

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for 95% of peptide charge pairs (using up to four CIPs). Using a single CIP (as in current spectral library approaches), we find >99% coverage for only 50% of the peptide charge pairs.

Our approach achieves substantially greater sensitivity in comparison to the popular SpectraST [2] library generation tool. Using randomized decoy spectra, we demonstrate that identification accuracy of the MCIP approach is improved by up to 12% compared to a single CIP approach. We test the MCIP approach on a SWATH data set and observe a ~30% increase in peptide recognition. We conclude that including MCIPs in spectral library approaches would yield increased sensitivity without compromising the false discovery rate.

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Dr. Maria Andrianova

Research Scientist

Center for Data-Intensive Biomedicine and Biotechnology
Skolkovo Institute of Science and Technology, Moscow

CHANGES IN MUTATIONAL PROCESSES DURING CANCER DEVELOPMENT

Mutations observed in cancer sample put together mutations accumulated in normal cells leading to cancer and mutations induced during cancer development by different exogenous and endogenous mutagenic processes. Accumulation of mutations and changes in cell properties during cancer development lead to clones differentiation and tumor heterogeneity and thus could influence the response to cancer therapy.

In this talk I will explain how to study cancer evolution using mutations data from bulk tumor sequencing. I will show how to track changes in known mutagenic processes during cancer development by comparing patterns of clonal (appear on the first steps of cancer development and are introduced in all cancer cells) and subclonal (appear later in cancer development and are introduced only in subpopulation of cells) mutations. I will also present our recent findings obtained using such methods.

READING THE FUTURE FROM A TREE: EVOLUTIONARY GENOMICS OF PATHOGENS

Georgii Bazykin graduated from the Department of Biology of the Moscow State University in 2001 and holds a PhD degree in Ecology and Evolutionary Biology from Princeton University (2007). He is also the Head of Sector of Molecular Evolution at the Institute for Information Transmission Problems of the RAS. He has published over 35 peer-reviewed papers on a wide range of topics in molecular evolution, and has presented over 50 invited talks and lectures on these topics.
Prof. Bazykin's research interests lie in the field of biological evolution at different levels. He focuses on disentangling the roles of natural selection and non-selective processes in evolution of genotypes, and on clarifying how genetic interactions shape the patterns of evolution and variation. He is particularly interested in evolution of immune system avoidance and drug resistance in pathogens, and in applications of evolutionary reasoning to medical genetics.

Pathogens are among the fastest evolving biological entities on Earth, and within pathogens, the most rapidly evolving systems are those involved in interactions with the host. We are now able to acquire nucleotide sequences of pathogens in near real time during a developing outbreak. The knowledge thus obtained can help trace the origin of the outbreak, elucidate transmission rate and pathways, and inform vaccine strain selection. I will describe how a novel discipline, phylodynamics, uses the concepts and methods of evolutionary biology and high-throughput sequencing data to inform public health decisions.

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IMPROVEMENT OF MECHANICAL PROPERTIES OF BIOCOMPATIBLE COLLAGEN MATERIALS USING THE LASER REINFORCEMENT BY METHODS STEREOLITHOGRAPHY

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Keywords: collagen, laser reinforcement, method of stereolithography

In this talk, we provide the experiment results of the mechanical properties on collagen materials modification by laser are given. It's shown that the laser reinforcement of the collagen films increases their mechanical strength. Films were coated with photosensitive composition based on tetrafunctional polylactide. The obtained materials with modified mechanical properties are promising for directed differentiation of the cells cultured on its surface.

The UV laser stereolithography [1] with bottom radiation feed were used for modifying the mechanical properties of the collagen materials. The experimental setup included a UV laser diode (405 nm, power 100 mW) and single-mirror galvanoscanner with a scanning frequency of 20 Hz. Laser pulses were focused by F-theta lens with a focal length of 160 mm, which gave the focal spot on the sample with a diameter of 100 μm. Samples were fixed in the supporting

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metal frame along the contour. The irradiation was carried out directly on the surface of the materials. The samples were: collagen sponge (a square of side 15 mm) and untanned collagen tape (a square of side 15 mm). The samples were impregnated with a photosensitive composition based on tetrafunctional polylactide synthesized according to [2]. We used 4,4'-bis(diethylamino) benzophenone 1 wt.% as the photoinitiator. Before the reinforcement procedure collagen films had irradiated to UV radiation for 15 minutes on each side (365 nm).

The experiments showed that the laser reinforcement by stereolithography method is a promising way to improve the properties of collagen materials and also to control the permeability inside the sample of cellular structures in growing. Mechanical properties of collagen films increased in 6 times after laser reinforcement with biocompatible photosensitive composition.

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Professor Dr. Maxim Fedorov

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COMPUTATIONAL METHODS FOR DISCOVERY AND DESIGN OF BIOACTIVE MOLECULES

Main areas of **Maxim Fedorov**'s research interests are high-performance computing (HPC) and Data Analytics with a focus on applications of HPC and Big Data in computational chemical physics, physical chemistry and molecular biophysics. A large part of this research focuses on energy-related applications covering a large range of topics from using molecular modeling methods for optimizing properties of ionic liquid-based super-capacitors to development of enhanced oil and gas recovery techniques. Another area of interest is in silico predicition of physical-chemical properties of bioactive molecules with use of modern HPC and chemical informatics techniques.

Maxim Fedorov holds a Ph.D. (Candidate of Science) degree in Physics and Mathematics and a D.Sc. (Doctor of Science) degree in Physical Chemistry from the Russian Academy of Sciences. He has significant experience in coordinating international projects in scientific computing, applications of modeling techniques to real-world tasks and development of sustainable large-scale e-infrastructure for computational science and engineering. Maxim's track-record includes leading the West of Scotland Academia-Industry Supercomputer Centre based in the University of Strathclyde in Glasgow. Under his strong leadership since 2012, the Centre has formed effective relations with the regional universities and local and international academic and industrial partners, underpinned a significant amount of the research base in the West of Scotland that resulted in some ~200 research publications and supported of ~100 postgraduate student projects. The Centre has established itself as a leading HPC centre in UK in terms of real-world applications of this emergent technology. Maxim's track-record includes other appointments in leading international research and academic organisations such as Full Professorship (Chair) in Physics in the Department of Physics, University of Strathclyde (Glasgow, UK), Research Group Leader at Max Planck Institute for Mathematics in the Sciences (Leipzig, Germany) and research positions at different levels at the Institute of Theoretical and Experimental Biophysics (Pushchino Biological Centre of RAS), National Research Centre "Kurchatovskyi Institute", University College Dublin and the Unilever Centre for Molecular Science Informatics of Chemistry Department at University of Cambridge (UK). To date, Dr Fedorov has published over 80 peer-reviewed publications and given over 100 invited talks and lectures. Several of these publications became top 1% cited papers in corresponding areas. Fedorov is an active member of several international research and scientific societies.

The talk will overview recent developments and applications of new computational methods for discovery and design of new bioactive molecules (drugs, agrochemical, fragrances etc). Modern automated systems for experimental screening and synthesis of new biomolecules provide new opportunities for development of new molecular compounds for medical, agricultural or food applications. However, while a vast number of bioactive molecules have been already found, these often result from trial and error rather than from a well-controlled design methodology. Another problem is the astronomically large number of potential candidates (estimates for the total number of molecules with potential bioactivity in 'chemical space' varies between 10^30 to 10^60).

The use of high-performance computing and state-of-the-art computational methods for rational design of bioactive molecules targeted for a particular application can help to speed up the process of development of new drugs and agrochemicals as well as food supplements, fragrances and cosmetics. The talk will discuss promising new hybrid approaches that combine molecular modelling methods with machine learning.

There will be discussed mathematical and numerical aspects of new computational tools that would allow to accurately describe many molecular properties of biomolecules. Development of such tools will lead to the predictive design of bioactive molecule with tailored functionality.

NEXT-GENERATION SEQUENCING: TECHNOLOGY AND BIOINFORMATICS

Professor Dr. Dmitrij Frishman

Professor for Bioinformatics
Life Science Center Weihenstephan
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Dmitrij Frishman received a M.S. in Biomedical Electronics from the Saint Petersburg Electrotechnical University in 1984 and a Ph.D. in Biochemistry from the Russian Academy of Sciences in 1991. He received an Alexander von Humboldt Research Fellowship at the end of 1991 that allowed him to join the Pat Argos group at the Biocomputing Department of EMBL in Heidelberg, where he pursued postdoctoral training in structural bioinformatics until 1996. He subsequently joined the Munich Information Center for Protein Sequences as a senior scientist and later became Deputy Director of the Institute for Bioinformatics at the German Research Center for Health and Environment. In 1997, he cofounded a bioinformatics company called Biomax Informatics AG, which provides computational solutions for better decision making and knowledge management in the life science industry. Since 2003, Dmitrij Frishman has been Professor for Bioinformatics at the Technical University of Munich. His current research interests focus on prediction and analysis of protein interactions, structural bioinformatics of transmembrane proteins, evolution of viruses, secondary structure of mRNAs, and cancer informatics.

I will start my talk by providing a brief overview of the modern DNA sequencing technologies and their application in the biomedical research. Next, I will explain the main problems in data quality and how it can be improved by simple pre-processing steps. Efficient algorithms for read mapping against a reference genome as well as for genome and transcriptome assembly will be briefly discussed. You will learn how the RNA-Seq approach has changed the way we study transcriptomes and conduct quantitative and differential gene expression analysis. Finally, I will describe some challenges in variation calling and present the overall framework for variation discovery and genotyping.

Professor Dr. Mikhail Gelfand

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THREE-DIMENSIONAL STRUCTURE AND FUNCTIONAL STATES OF CHROMATIN

Mikhail Gelfand graduated from the Moscow State University (MSU) with a degree in mathematics. Since then he worked in the fields of bioinformatics and molecular evolution and obtained the Candidate of Sciences degree in Mathematics and Biophysics from Institute of Theoretical and Experimental Biophysics, Pushchino, and then the Doctor of Sciences degree in Biology and Molecular Biology from Research Institute for Genetics and Selection of Industrial Microorganisms (GosNIIGenetika). Mikhail Gelfand held research positions at Institute of Protein Research and at GosNIIGenetika, and the position of Director of Science at Integrated Genomics, Moscow. Today, he is Professor of Bioengineering and Bioinformatics at MSU, Vice-Director for Science at the Kharkevich Institute for Information Transmission Problems RAS (ITTP), and Head of IITP Research and Training Center of Bioinformatics.

Dr. Gelfand is a well-established bioinformatics specialist in the international scientific community. His research encompasses comparative genomics, systems biology, molecular evolution, transcriptomics, metagenomics. Currently he is studying co-evolution of transcription factors and their recognition sites, microevolution of bacterial genomes on the strain level, evolution of alternative splicing, three-dimensional structure of chromatin and epigenetics. He published the results of his research in major international scientific journals, such as Genome Research, Molecular Cell, Nature Communications, Molecular Systems Biology, Genome Biology, Trends in Genetics, Briefings in Bioinformatics, Proceedings of the National Academy of Science, Nucleic Acids Research, PLoS Genetics. His papers have been cited more than seven thousand times, and his Hirsch factor is 47.

Dr. Gelfand actively serves professional community: he is an elected member of Academia Europaea, Associate Editor of Journal of Computational Biology, member of editorial boards of peer-reviewed journals such as Journal of Bacteriology, Peer J, and Biology Direct, and referee for leading scientific journals. Dr. Gelfand also regularly serves on the Program Committees for international workshops and conferences on Genetics, Biophysics, and Bioinformatics.

Recent advances in experimental methods create the opportunity to integrate data about contacts between DNA regions, their epigenetic state, and gene expression. At the small scale, chromatin forms relatively tight globules, so called Topologically Associating Domains. In Drosophila, housekeeping and highly transcribed genes are enriched in inter-TAD regions, whereas tissue-specific and silent genes tend to be localized in TADs. Inter-TAD regions are enriched in active histone marks, whereas TADs are mainly formed by repressed chromatin. Moreover, differences in TAD structure between cell lines are accompanied by changes in expression of genes situated in such TADs. On the other hand, unlike mammals, TAD boundaries in Drosophila are not highly enriched in binding sites for insulator proteins such as CTCF. Similar trends are also observed in unicellular eukaryote Dictyostelium discoideum.

EVOLUTIONARY DYNAMICS OF PENELOPE RETROTRANSPOSONS IN FLATWORMS

Keywords: genomics, retrotransposons, penelope, evolution, flatworms

Retrotransposons are a group of mobile genetic elements capable to transposition through RNA intermediate. They are known to be a major part of eukaryotic genomes and drivers of genomic evolution. In this work I present genome-wide data on diversity, phylogeny, evolutionary dynamics and structure of Penelope-like elements (PLE) in flatworms – an enigmatic and ancient class of retrotransposons found in genomes of many eukaryotes. For this particular research I developed and automated a method for identification and extraction of PLE sequences from genome assemblies of 32 flatworm species (including those of medical and veterinary importance) available through WormBase. We found that the diversity of PLE in genomes of flatworms is underestimated: our data suggest that there are many previously unknown PLE families in the genomes of Trematoda and some Cestoda worms. On the contrary, some Cestoda genomes demonstrate full absence of nearly active PLE copies (genera Echinococcus and Hymenolepis). Moreover we found four species from different classes with a very high and therefore unusual level of PLE activity. Also the obtained data suggest that PLE do not fit "master copy" model of retrotransposition.

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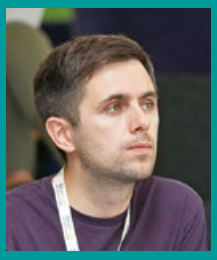

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INTEGRATIVE APPROACHES AND WORKFLOWS TO IDENTIFY DISEASE SPECIFIC BIOMARKERS AND THERAPEUTIC CANDIDATES

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Keywords: Integrative workflows, molecular signatures, tumor metastasis

Unravelling mechanisms underlying diseases for the prediction of disease markers have motivated the development of various systems biology approaches. Key challenges for the development of mathematical models to mimic the real biological scenario are (i) the size of interacting biological components, (ii) the nonlinear nature of spatio-temporal interactions and (iii) feedback loops in the structure of interaction networks. Exploring large scale networks is an art where several analytic tools are integrated in a computational workflow to identify disease in specific small regulatory modules. These small modules are subjected to a more detailed analysis using mathematical modeling for the prediction of disease signatures, i.e. set of network derived diagnostic/prognostic biomarkers.

Recently, we developed an integrative workflow by combining techniques from bioinformatics and systems biology to study large-scale biochemical disease network around E2F1

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transcription factor that switches duties from tumor suppressor to promotor during invasiveness and metastasis. In particular, we used an algorithm employing multi-objective optimization concepts to rank and select key regulatory motifs mainly responsible for network dynamics. A core regulatory network derived from key motifs enabled us formulating hypotheses on tumor type-specific molecular signatures which were further validated using invasive/non-invasive bladder and breast cancer cell lines and also in the patient data [1].

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LAMBDA: A LOCAL ALIGNER FOR METAGENOMICS AND OTHER LARGE DATABASE SEARCHES

Next-generation sequencing technologies produce unprecedented amounts of data, leading to novel research fields. A recent one to emerge is metagenomics, the study of large-size DNA samples containing a multitude of diverse organisms. A key problem in metagenomics is to functionally and taxonomically classify the sequenced DNA, to which end the well-known BLAST program is usually used. But BLAST has dramatic resource requirements at metagenomic scales of data, imposing a high financial or technical burden on the researcher. Multiple attempts have been made to overcome these limitations and present a viable alternative to BLAST.

LAMBDA is our alternative to BLAST, it is hundreds of times faster and provides additional features for taxonomic analysis not found in BLAST or other comparable tools.

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BIOINFORMATICS ANALYSIS OF ACTIN AND THE SEARCH FOR THE REGIONS INCLUDED IN THE CORE OF ACTIN FIBRILS

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Keywords: actin, multiple alignments, fibrillar actin, backbone of the fibrils, conservatism

The problem of amyloidosis occupies an important place in modern biology and medicine. The deposition of protein aggregates in tissues and organs can lead to an impaired functioning of the latter. Almost any cellular protein is able to form aggregates in the form of fibrils. However, a special study is required for the major proteins in various types of cells in the human body, one

of which is actin, the most important component of the cytoskeleton of eukaryotic cells.

There are six isoforms of actin that are grouped into 3 classes, depending on the localization in muscle fibers or other cells of mammalian organism. The paper presents the results of a study of fibrillogenesis of α-1-isoforms of actin from rabbit muscles. In the functionally active state actin is presented in a fibrillar form (F-actin) formed by the polymerization of globular monomers (G-actin). In this regard, the study of fibrillogenesis of this protein is an important task today.

In this work, we conducted a bioinformatics analysis of the set of 296 amino acid sequences of actin from representatives of various classes of Chordate type. Based on the results of the analysis, the degree of conservativeness of the primary structure of this protein among representatives of Chordate type was determined, the presence, length and localization of possible amyloidogenic fragments in the polypeptide chain of actin was established. Using the method of tandem mass spectrometry the actin regions included in the core of the actin fibril are determined. Bioinformatics analysis showed that these regions contain amyloidogenic amino acid residues located in the C-terminal part and the hinge region connecting the subdomains 1 and 3.

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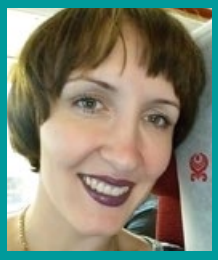

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CROSS-LINKING OF DECELLULARIZED BOVINE PERICARDIUM TISSUES TOWARDS TAILORING FUNCTIONAL PROPERTIES OF XENOPROSTHESES FOR SOFT TISSUE RECONSTRUCTION

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Keywords: bovine pericardium, xenoprostheses, cross-linking, personalized therapy

Decellularized bovine pericardium tissues are recognized as easily accessible and biocompatible xenoprostheses for soft tissue reconstruction [1–3]. In order to trigger their application in personalized tissue-engineering therapy we developed an approach to tailor their functional properties by means of cross-linking. Four different cross-linking agents were employed, namely, hexamethylene diisocyanate, ethylene glycol diglycidyl ether, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide and genipin. While preserving the cytotoxicity above the moderate level, these cross-linkers remarkably affected mechanical, functional and structural properties of decellularized pericardium tissues. Structural analysis was performed by means of scanning electron microscopy, two-photon microscopy, optical coherence tomography and histological study. The samples consisted of acellular eosinophilic septa organized in anisotropic structures. Picrosirius red staining and two-photon microscopy revealed collagenous fibers in all samples. However, these fibers appeared thicker and acquired more regular organisation following cross-linking, especially in the samples treated with ethylene glycol diglycidyl ether and genipin. Mechanical trials indicated that depending on the cross-linker nature mechanical properties of decellularized pericardium tissues, considering Young's modulus as the key parameter, varied significantly. The decrease in anisotropy degree was most clearly observed with the genipin-cross-linked sample. Optical properties of all samples were similar as showed by the optical coherence tomography study. Collagenase resistance varied dramatically with the highest value provided by ethylene glycol diglycidyl ether-assisted cross-linking. Thermal stability increased upon cross-linking as was indicated by the shrinkage temperature measurements with the lowest impact achieved with ethylene glycol diglycidyl ether-assisted cross-linking.

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HOW TO DETECT THE GENETIC CAUSES OF INHERITED RARE DISEASES IN CLINICS?

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Keywords: next-generation sequencing, rare diseases, clinical science

Inherited rare diseases challenge medical diagnosis for clinicians. Although each individual rare disease affects only very few people, they affect millions of patients worldwide due to the overall high number of different rare diseases, several thousands have been described in the literature. A fast and accurate treatment of each patient critically needs networks of specialists, fast diagnostic tools and efforts to understand the etiology of each rare disease.

Many rare diseases follow Mendelian inheritance patterns caused by mutations that disrupt the function of a single gene. Due to the rapid decline of the costs of next-generation sequencing (NGS), whole-exome sequencing became already a standard diagnostic procedure in clinics. Although the number of genes known to cause rare diseases grows continuously, there is still a considerable amount of patients with no clear genetic diagnosis. To identify the exact location of the mutation, to assign a molecular malfunction and to allow for a rational therapy, the application of additional NGS methods like whole-genome or RNA sequencing proved to be very promising. Another important key in this workflow are sophisticated bioinformatic analyses that complement the power of well-established analysis pipelines and integrate data of multiple patients as well as in vitro experiments.

Here, we present how we systematically apply NGS technologies and bioinformatics tools to unravel the genetic causes of rare diseases at the LMU Children's Hospital.

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EDGETIC PERTURBATION SIGNATURES AS CANCER BIOMARKERS

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Keywords: Cancer, protein-protein interactions, mutations, edgetic-perturbations, biomarkers

Even though great strides have been made in elucidating the main driver genes in cancer, determination of the complete set of cancer type and subtype specific as well as pan-cancer biomarkers is an ongoing challenge. Due to patient heterogeneity and cancer complexity as revealed by high throughput next generation sequencing, integrating multiple omic data has been suggested as a novel way of studying the cancer micro environment to reveal inherent biomarkers. In this experiment, we first used 639 paired (1239 in total) patient specific non-tumor (healthy) and tumor (cancer) mRNA expression data from TCGA to build patient specific protein-protein interaction networks, unlike the conventional use of differential gene expressions in current methods. Next, we compared the tumor network to the corresponding non-tumor network to identify molecular signatures (biomarkers) that are perturbed during tumorigenesis. Finally, we used 7121 known cancer specific significantly mutated (driver) genes to determine if somatic mutations

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play a role in edgetic perturbations in cancer. The obtained perturbed network biomarkers showed greater reproducibility across patient samples within a cancer type (and subtype) while some biomarkers were reproduced across multiple cancers (e.g KRAS, EGFR, MAGEA2, and LUZP4). In summary, we propose a framework to identify novel network biomarkers in cancer, and our results show that the approach is robust in the identification of known and novel pan-cancer, cancer type and subtype specific cancer biomarkers. The identified biomarkers should be of great significance in future biomarker experimental validation, targeted therapy and cancer monitoring.

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CONVOLUTIONAL NETWORK FOR BIOMEDICAL IMAGE INSTANCE SEGMENTATION

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Keywords: deep learning, U-net, instance segmentation

Instance segmentation is the problem of detecting and delineating each different object of interest appearing in the image. Instance segmentation is useful in a range of bio-medical tasks. For example counting healthy and infected cells in a tissue or blood sample [1, 2]. Moreover, instance level segmentation can be used to calculate properties of each detected object pixel wise.

We present a simple and flexible end-to-end framework for object instance segmentation of biomedical data. The model is based on semantic segmentation framework U-net [3], trained using a custom loss function in order to split neighboring objects into different feature maps.

The framework consist of four parts: training data preprocessing algorithm, semantic segmentation framework, custom loss function and a stochastic optimization process, which allows the training to converge.

The training data preprocessing algorithm produce a weight map for each instance in the training set. For each instance, we generate a margin using binary dilation. We used U-net model as the semantic segmentation framework. In order to increase depth of the neural network we have used additional convolutional layers in the encoding side. To train the model we designed a loss function that finds the best feature map for each instance that minimize the occlusion between instances margins.

In the experiments carried out, we found that our method is comparable to the state of the art methods on the Plant Phenotyping dataset [4] (standard instance segmentation benchmark). Moreover, once trained, our model can process images with a large number of objects, running at 7 fps on 512x512 picture with 100 objects, what makes it suitable for a large number of biomedical applications. We also show ours results for several biomedical datasets.

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THE IMPACT OF APOA1 AND LPA GENES POLYMORPHISM ON PREDISPOSITION TO ISCHEMIC STROKE DISEASE AND SUBCLINICAL ATHEROSCLEROSIS

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Keywords: APOA1, LPA, cardiovascular pathology

Cardiovascular pathology is one of the major death causes in many developed countries. During last decades the frequency of ischemic stroke disease (ISD) in people under 45 significantly increased. This and the fact that in more than 50% cases the disease manifestation debuts with acute myocardial infarction make the search of potential ISD risk markers extremely important. Apolipoprotein A1 is one of the major proteins from high density lipoproteins. APOA1 gene, encoding this protein, is located on the long arm of the 11th chromosome. G-75A (rs670) is the most frequently studied polymorphism within APOA1 gene. Some investigations show different effect of this locus on the high density lipoprotein blood concentration [1,2], which is an important biomarker of cardiovascular diseases susceptibility. Lipoprotein(a) (Lp(a)) is a complex compound containing apolipoprotein(a) encoded by LPA gene (6q27). KIV2 polymorphism of LPA gene (number of KIV2 repeats) is associated with Lp(a) blood concentration [3] and thus may play a significant role in predisposition to cardiovascular pathology.

APOA1 and LPA genes polymorphism was analyzed in 22 individuals with ISD, 44 individuals with subclinical atherosclerosis (SA) and 39 individuals without known cardiovascular pathology. Genotyping was performed using self-designed Taq-Man probes.

It was found that APOA1 genotypes distribution was significantly different in groups with ISD and SA (p=0,029). Both homozygote genotypes were found to be more frequent in the first group, while the frequency of the heterozygote genotype in the second group was more than twice higher (27,3% and 56,8% respectively). The differences between ISD and control group wasn't significant (p=0,097).

The average number of KIV2 repeats in LPA gene was significantly higher in patients with ISD compared to the controls (p=0,02). The difference in means between this two groups was 1,52, which proof the impact of the KIV2 polymorphism on ISD risk. The SA group doesn't significantly differ from two others.

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The upcoming enlargement of groups under investigation (especially with ISD) will give us an opportunity to ensure that the APOA1 and LPA genes polymorphism have an impact on ISD or SA development.

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AN OVERVIEW OF APSIM MODEL FOR CROP SIMULATION PREDICTIONS

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Keywords: yield prediction, crop modelling, biomass prediction

APSIM (Agricultural Production Systems sIMulator) [1] is an advanced tool for modelling in agriculture. It is based on use of complex mathematical model incorporating many communicating submodels including:

1. soil organic matter transformation cycle
2. nitrates and phosphates transformation cycle
3. water transport over soil profile
4. model of temperature distribution over soil profile
5. nutrients solvation
6. many models of potential crops.

On the output user gets prediction of crop yield, soil carbon and nitrates concentration time-series, soil water disctribution over profile. It also allows consideringpossible management and farm exploitation strategies such as

1. sowing time, depth and population density
2. tillage works and crop rotation cycles
3. type, amount and time of sowing fertilizer

In our numerical experiments we use experimental data from Kshen' fields including history of meteorological measurements and soil agrophysical and agrochemical properties (tons of time-consuming experimental data). As a result of numerical experiments, we obtain qualitative agreement of simulations results with historical yield of wheat on experiments fields. We also obtain correct response of the model output to change of sowing depth and change of sowing fertilizer strategy. We plan to continue exploitation of this software and validate it versus alternative decisions (e.g. DNDC [2] or DSSAT [3]). This work was supported by Skoltech/MIT NextGeneration programme.

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ADAPTAION OF GENE REGULATORY NETWORK TO EXTREME DESICCATION IN POLYPEDILUM VANDERPLANKI

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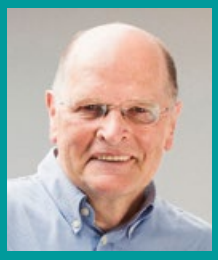
Polypedilum vanderplanki is a striking example of an insect that can survive almost a complete water loss. Desiccation is accompanied by massive transcriptome changes that are reversed just within 24 hours under rehydration. Here, using RNA-Seq data we found that the TCTAGAA DNA motif, which closely resembles the binding motif of the Drosophila melanogaster heat shock transcription activator (Hsf), is significantly enriched in promoter regions of desiccation-induced genes in P. vanderplanki but not in P. Nubifer (a congeneric desiccation-sensitive midge). Some of these genes, for example genes that encode late embryogenesis abundant proteins, was acquired by P. vanderplanki in course of adaptation to desiccation and not present in P. nubifer. Other genes, such as trehalose metabolism-related ones, are observed in P. nubifer but lack TCTAGAA DNA motif in their promoters. Unlike P. nubifer, P. vanderplanki has a double TCTAGAA sites upstream of the Hsf gene itself that is a likely explanation for the stronger activation of Hsf in P. vanderplanki compared to P. nubifer under desiccation. Thus, our results show that heat shock regulatory system has been co-opted in P. vanderplanki under adaptation to desiccation.



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SCIENCE THEORY AND MEDICAL REALITY

Retired professor for bioinformatics. Studying in chemistry at the Philipps University Marburg, **Hans-Werner Mewes** started with digital data analysis in the late 70s to monitor bioenergetics in brown fat mitochondria at the University of Heidelberg. After two years in protein chemistry at the EMBL, he moved to the Max-Planck-Institute for Biochemistry at Martinsried to achieve his dissertation on the identification of proteins using data analytics. In 1988 the Munich Institute for Protein Sequences (MIPS) was established; during the 1990s, the group was pioneering the field of genome annotation as part of the international consortia to sequence yeast (1996) and A. thaliana (2000). In 2001 Mewes was appointed as full professor at the Technical University of München and became the Head of the Institute for Bioinformatics and Systems Biology of the Helmholtz Zentrum München. He (co-)founded Biomax Informatics AG (1997) and Clueda AG (2012). Present interests of Professor Mewes are individual genetics, clinical patient stratification and the theory of life sciences.

Whenever the progress in science or technology is jumping from one level to the next instead of advancing slowly, exploration of a new potential resembles a gold rush. Reflection on the chances and their genuine limits are put behind, even if many washing mud instead of gold are left behind or the exploration of the claim is inefficient due to very fundamental reasons. J. Ioannides has recently questioned the vast majority of clinical trials as waste (BMJ 2014).

Several millions of publications are registered in Pubmed every year; the information flow from observations, studies, trials, and experiments is language and text based leaving room for analysis of data, interpretation, speculation, and opinion somehow creating the common state of knowledge and belief. Complex biology can not be reduced to simple laws and rules; it escapes deterministic algorithms. In clinical practice, doctors have an ever increasing amount of information to consider while taking life saving therapeutic decisions with in a short time. How can we escape the dilemma of finding the relevant information in a misty haystack of data generated by all kinds of devices gathering molecular, cellular, and image data? And how can we put this information in the context of the available knowledge buried as free text in millions of publications? How to deal with inescapable complexity? The human data space including individual genetic variance comprises hundreds of thousands of variables making it practically infinite.

The decision on the best possible treatment for therapeutic action was based on evidence and experience of the medical doctor in the past. Human diseases are extremely diverse for their symptoms, their underlying genetic or environmental causes and the individual response to treatment. Most drugs show the desired effect only in some patients treated, others are non-responders, and many unwanted side effects or adverse reactions are known. As long as we accept the cause and effect principle, we have to hunt for causes; however for complex diseases on a background of genetic variation and the individual medical history of a patient, we have to deal with uncertainty. These rather epistemological considerations have practical implications for the use of data in clinical practice.

Medical data gives straight advice for treatment in a few cases only. The information available from all diagnostic sources over time does not allow for intuitive interpretation, our cognitive capacity does not cope with large amount of data and confusing complexity. The risk to overlook some highly relevant information may cause fatal consequences.

The success of outcome oriented data analysis to solve complex challenges such as chess or go by machine learning techniques opens a new perspective for personalized and outcome oriented medicine. Using data integration technology provided by a flexible software platform (BioXM, Biomax, Germany), it was possible to develop a knowledge model to follow COPD (Chronic Obstructive Pneumological Disease) in all patients in a university hospital (CIRO, Maastricht, The Netherlands) from diagnosis through the course of therapy involving several medical disciplines and dozens of therapeutic interventions. By learn-

ing success or failure of treatment from every patient it was possible to deduce those critical parameters that allow for a reliable prediction of the outcome. The application of the system in clinical practice allowed for a measurable better treatment at lower cost for the benefit of the patient.

Keeping the basic but intrinsic problems of human health as the upmost complex challenge in mind has guided us to practical consequences. We have to cope with the flood of data without ignoring the quest for a better understanding of disease mechanisms.

FABRICATION OF MICROSTRUCTURED BIODEGRADABLE POLYLACTIDE SCAFFOLDS USING TWO-PHOTON MICROSTEREOLITHOGRAPHY POLYMERIZATION

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Keywords: polylactide, scaffolds, microstereolithography, 2PP, two-photon polymerization

Materials and 3D structures based on biostable or bioresorbable polymers are one of the most promising approach of modern biomedical materials science. Polymer composition, based on polylactide materials is one of the most perspective material for forming 3D scaffolds for tissue reconstruction. The report will present the newest results obtained on the original system, based on 3D Nano-Rapid-Protoryping System (Laser Zentrum Hannover, Germany) and TeMa–100 femtosecond ytterbium laser (OOO Avesta-Proekt, Russia) and it was created by grant of the Government of Russian Federation for the Support of Scientific Investigations under the Supervision of Leading Scientists (Contract no. 14.B25.31.0019). Several promising biocompatible photosensitive polymer compositions, based on polylactide [1] with various parameters, such as mechanical rigidity and bioresorption rate, have been developed. Three-dimensional structures were formed based on the polymer composition containing reactive capable polylactide derivative via two-photon polymerization method. The optimum ratio of the components, methods of preparation of photopolymerizable compositions, parameters of the laser structuring, method of washing out a non-crosslinked material were chosen.

The experiments have shown that the laser two-photon microstereolithography method is a promising way of formation of microstructures with complex architectonics. The mechanical properties of the formed samples can vary both with the design of the three-dimensional model and with the change in the composition of the photosensitive polymer composition

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COMPREHENSIVE BRAIN MAPS OF HUMAN AND PRIMATE BRAINS

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Keywords: primate, brain, lipidome

Adult human brain contains a large amount of lipids and displays the biggest diversity of lipid classes and lipid molecular species in the human body. It is speculated that each brain region or structure is different in lipid content and composition reflecting their distinct functions. At present, however, the analysis of the human and animal brain lipidomes remains limited to no more than three brain regions.

The aim of this study is to assemble a comprehensive lipidome atlas of the adult human brain, as well as of the brains of closely related non-human primate species: humans, chimpanzees, bonobos, and rhesus macaques. To this end up to 77 brain regions covering all major anatomical and functional brain structures were dissected from 14 brains of 4 species, resulting in a total of 706 brain specimens. In order to generate the comprehensive lipid maps, we perform a large-scale liquid chromatography coupled to mass spectrometry (LC-MS)-based analysis of the lipid composition of all brain specimens. The experimental procedures include optimization of lipid extraction, lipid fractionation using high-throughput ultra-performance liquid chromatography (UPLC), and high-resolution, high-mass-accuracy mass spectrometry in both polarities (ESI- and ESI+) to achieve highest coverage of lipid compounds (MS1 runs). Fragmentation spectra are acquired to validate identified lipid species (MS2 runs).

The construction of comprehensive lipidome maps of the human and non- human primate brains is unprecedented and is expected to help deciphering molecular mechanisms that underlie brain organisation and evolution of the human phenotype, including cognition and longevity. Furthermore, it holds a considerable promise for unraveling neuronal diversity and connectivity of different brain structures, and understanding mechanistic processes of brain aging as well as the identification of lipid markers for disease.

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ASSESSMENT OF TUMOR-SPECIFIC T CELL ANTIGENS AND EPITOPE CROSS-REACTIVITY FOR CANCER IMMUNOTHERAPY

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Keywords: cancer immunotherapy, tumor antigen, neoepitopes, antigen expression, cross-reactivity

Cancer immunotherapy has become a thriving field in life sciences, which already showed promising progress for cancer treatment of patients whose tumors were resistant to conventional therapies. One approach of curing cancer by enhancing patients' immune systems aims at modifying T cells to enable them to detect cancer cells throughout the entire body. Cytotoxic T cells that are able to destroy target cells possess a receptor (TCR) that binds to epitopes presented on cell surfaces by major histocompatibility complex I. These epitopes come from intracellularly processed proteins which need to be tumor-specific in order to ensure discrimination of tumor cells from cells belonging to healthy tissue. One potential source of such tumor-specific antigens is somatic cancer mutations that are used to predict so-called neoepitopes.

However, not all TCRs are specific for one single epitope, thus not only on-target off-tumor but also off-target cross-reactivity has to be considered. Therefore, a tool called Expitope has been created to assess cross-reactivity patterns of epitopes [1]. This tool has recently been developed further to incorporate results from protein abundance databases additionally to gene expression data. Furthermore, an index calculation has been introduced, which includes weighting tissues according to their importance for survival. We could retrace the findings of two studies of reported cross-reactivity by using Expitope 2, with one study discovering that the TCR targeting a nonamer also recognized an epitope with four mismatches [2, 3].

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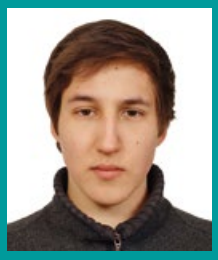

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LOCAL-SCALE SOIL MAPPING VIA PIVOTED CHOLESKY DECOMPOSITION

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Keywords: soil mapping, gaussian processes, low-rank approximation

A growing demand for detailed soil information lead to development of global-scale soil mapping tools, such as SoilGrids [2], which provides predictions for standard soil properties and soil types at moderate resolution (250 m). In order to provide soil mapping at better resolution, such tools require (i) high resolution remote sensing data, e.g., landform and lithology maps, climate and Digital Elevation Model (DEM) data; and (ii) accurate local-scale soil maps obtained from direct measurements. In [4] authors establish connection between water regime of chernozems (as a factor of soil formation) and lateral water flow formed by relief. To accomplish this goal, authors created accurate DEM (2.5 m resolution, cm accuracy), then, chose sampling points based on expert knowledge and, finally, measured the depth of occurrence of secondary carbonates at these locations. Collecting many soil samples may be ineffective and expensive. In order to overcome this limitation, we propose the following sampling scheme: (i) we model depth of occurrence of secondary carbonates using Gaussian Process Regression (GPR) with Radial Basis covariance Function (RBF); (ii) given DEM and its morphological derivatives, we calculate covariance matrix lazily (elements are evaluated on demand); (iii) driven by D-optimality design [3] approach, we select sampling points by searching for maximum-volume submatrix of covariance matrix using low-rank pivoted Cholesky decomposition [1]. We evaluate our approach on the dataset from [4] consisting of 157 sampling points and 57000 of DEM points over 38 ha field. Our experiments show, that 80% accuracy of prediction can be achieved by using only 10 samples. Moreover, our approach avoids calculation of the whole covariance matrix, which grows prohibitively for high-resolution DEMs. This sample selection technique can be also used when modeling other soil properties, e.g., microbial communities, if an appropriate set of soil covariates is provided.

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EXTACELLULAR PROTEASES OF MICROMYCETES AS NEW AGENTS FOR PROTEIN C AND FACTOR X DETERMINATION

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Keywords: protein C, factor X, diagnostic testing

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Determination of hemostatic proteins is important branch of diagnostic medicine. Diagnostic testing is often used for selecting appropriate and optimal therapies based on the context of a patient's genetic content or other molecular or cellular analysis. Some of the proteins in snake venom have very specific effects on protein C and X factor. But these diagnostic systems are expensive.

The aim of this work was a selection of optimal concentrations range of extracellular protease-activator of micromycete Aspergillus ochraceus. These proteases have protein C and factor X activator activity.

Efficiency of isolated protease for protein C and X factor determination was compared with commercial preparations – Protac® and RVV-X® from snakes' venom in different human plasmas.

It demonstrated the same results with specific activity proteinases of Aspergillus ochraceus and with Protac® and RVV-X®. Similar experiments were conducted in the presence of factor X deficient plasma and protein C deficient plasma. It was found that concentration of protein C is identical with Protac® (32,7% ± 5%) diagnostic system and specific activity proteinases of Aspergillus ochraceus (31,5% ± 5%). Uniform diagnostics interval was detected with RVV-X® diagnostic system (36,6% ± 4%) and proteinases of Aspergillus ochraceus (37,4% ± 4%).

To sum up, proteases produced by Aspergillus ochraceus are very perspective for protein C and X factor diagnostics. This method may be cheaper and easier than other methodics.

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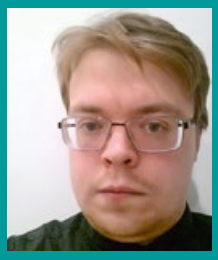

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OPTIMIZATION OF BIODEGRADABLE IMPLANTS

Biodegradable implants key advantage is that they provide only temporary support, dissolving at rates close to bone formation thus eliminating the need for secondary surgeries. Now with the ability to use the 3d print with biodegradable materials one can construct patient specific implants which would be easier for implantation (less muscles and ligaments removal needed, more convenient fixing points) [2] and a faster dissipation of implants, because of fewer materials being used. This patient specific design can be achieved automatically with process called topological optimization.

Topological optimization finds material density distribution minimizing functionallity of the solution of a partial differential equation (PDE), subject to a set of constraints (typically, a bound on the volume or mass of the material). Standard approaches to optimization of biodegradable implants usually leads to unrealistic solutions with checkerboard-like patterns [3]. It occurs because using finite elements discretization (FEM) of the PDE and functionalilty, we introduce some errors due to FEM discretization and underlying optimization problem becomes mesh-depended and possess false, physically inadequate optimums, while functional value heavily depends on fineness of discretization scheme used to compute it.

To alleviate this problem, we propose regularization of the given functionality by error estimate of FEM discretization [1]. This regularization provides robustness of solutions and improves obtained functional values as well.

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SEQUENCE AND STRUCTURE FEATURES OF GROE SUBSTRATE ORTHOLOGS IN MYCOPLASMA

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Keywords: molecular chaperones, protein folding, GroEL/ES, Mycoplasma

GroEL/ES chaperonin prevents its substrates from aggregation by shielding them in a large cage. The E.coli GroEL interactome contains 250 proteins, which are subdivided into three classes [1]: proteins that can fold correctly without GroEL, proteins that need GroEL under stress conditions, and obligate substrates. In spite of the importance of the GroEL/ES, the majority of the Mycoplasma genomes lack the groe operon (GroE- Mycoplasma). We identified four GroE+ Mycoplasma species and found orthologs of the E.coli GroEL substrates in both GroE+/- Mycoplasma. All GroEL substrate orthologs display a depletion in aromatic amino acid residues and enrichment in hydrophobic residues in comparison with cytoplasmic proteins.

We sought to identify the features that enable orthologs of obligate GroEL substrates to fold in the absence of GroE. In [2] authors compared the amino acid usage of the E.coli NanA protein (EcNanA), which is an obligate GroEL substrate, with the amino acid usage of its ortholog, the NanA from GroE- Mycoplasma synoviae (Ms-

NanA). This comparison revealed that MsNanA has two times more Lys and two times fewer Arg than EcNanA, and that its amino acid sequence is also strongly enriched in Phe and Tyr. Here we attempted to reproduce the results presented in [2] at a proteome-wide scale by extending amino acid usage comparison to include all orthologs of obligate GroEL substrates in GroE+ and GroE- Mycoplasma. The majority of the amino acid residues overrepresented in MsNanA are helix-promoting residues. This observation prompted us to test the hypothesis, originally formulated in [2], that it is the higher content of helix-formers that drives the folding of proteins in GroE-organisms. To test this hypothesis we obtained secondary structure assignments using the DSSP algorithm [3]. Our analysis of amino acid usage in the orthologs of GroEL obligate substrates in GroE- Mycoplasma only partially confirms the findings reported in [2], as we only detected a significant enrichment of Lys and Phe in the helical regions. Lys is known to be a strong helix-former, while Phe is a hydrophobic amino acid with a large side-chain, known to be favorable for secondary structure formation. Work is underway to determine other features of chaperons and protease systems in GroE- Mycoplasma that might compensate for the absence of GroEL.

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NOVEL INSIGHTS INTO RNA BIOLOGY FROM HIGH THROUGHPUT SEQUENCING DATA

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Dmitri Pervouchine is a skilled computational biologist, qualified statistician, and strong mathematician. He obtained the MSc in Mathematics (1996), MSc in Chemistry (1997) and PhD in Algebra, Logics, and Number Theory (1999) from the Moscow State University (MSU). In 2002, he received MSc in Bioinformatics from Boston University, where he stayed until 2005 with the group of Dr Nancy Kopell at the Center for BioDynamics and the Department of Mathematics and Statistics to conduct his postdoctoral research in computational neuroscience. Then Pervouchine returned to his alma mater to work with Dr. Mikhail Gelfand and Dr. Andrei Mironov on computational RNA structure prediction and comparative genomics, where he identified a group of ultra-conserved RNA structures that impact pre-mRNA splicing. In 2011, Pervouchine joined the group of Dr Roderic Guigo at the Center for Genomic Regulation, Pompeu Fabra University (Barcelona), as a research associate to do research in transcriptomics and big data analysis. He also worked in close collaboration with ENCODE consortium where together with the colleagues he identified a group of genes with constrained expression across mammalian evolution and described distinct properties of this group of genes.
Pervouchine's research career in computational biology encompasses computational neuroscience, structural bioinformatics of RNA, and the analysis of big transcriptomics data. One of the projects he is currently working on is the integrative analysis of transcription, alternative splicing, and chromatin modifications to shed some light on RNA-chromatin interactions and their role in post-transcriptional RNA processing.
Dmitri Pervouchine has considerable international experience in teaching: he taught many diverse classes including calculus, probability and statistics, linear algebra, discrete math, stochastic calculus, polymer chemistry, applied statistics for biologists at Boston University, MSU, and the National Research University Higher School of Economics, Moscow.

Eukaryotic RNAs undergo extensive processing at the post-transcriptional level, including capping, 3'-cleavage and polyadenylation, and splicing. These steps happen synergistically and at the same time concurrently with each other and with transcription, generating alternative transcript isoforms. While it was recently debated to what extent alternative transcripts actually diversify the protein repertoire of an organism, alterations in RNA processing are undoubtedly a potent force that contributes greatly not only to protein evolution but also to a large number of human diseases.

High-throughput sequencing revolutionized our ability to study transcription and post-transcriptional RNA processing. In this talk I will go over a large array of novel sequencing assays generated by ENCODE Consortium and comment on the perspective use of these data in the context of human wellness and disease. I will also mention the results obtained in my group which suggest a common structural mechanism of alternative splicing, alternative polyadenylation, and alternative transcription start site choice, which also indicate that different RNA processing pathways comprise a highly interconnected net of workstations in a giant assembly line rather than sequentially operating machines.

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CONSTANT-TIME AND SPACE-EFFICIENT UNIDIRECTIONAL AND BIDIRECTIONAL FM-INDICES USING EPR-DICTIONARIES

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Keywords: FM index, bidirectional, BWT, read mapping

We introduce a new method for conducting an exact search in a unidirectional and bidirectional FM index [1, 2] in O(1) time per step while using O(log σ * n) + o(log σ * σ * n) bits of space where σ is the number of characters in the alphabet and n the length of the indexed text. This is done by replacing the wavelet tree with a running time of O(log σ) [4] by a new data structure, the Enhanced Prefixsum Rank dictionary (EPR-dictionary) [3]. This is the first practical implementation of a constant time method for a search step in 2FM indices and a space improvement for FM indices.

Especially bidirectional indices are of great importance for approximate string searches in general and for applications in bioinformatics such as finding long non-coding RNA (lncRna). These indices allow extending a pattern by a character to the left as well as to the right in an arbitrary order, while using unidirectional indices one can only search into one direction. They not only allow reducing the exponentially large search space for approximate string matching but also support enumerating RNA sequences with a known secondary structure in a natural fashion by starting with the hairpin region and extending the stem on both sides by complementary characters. This enables searching for lncRna with a known well-conserved structure but a rather low sequence-similarity.

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ENGINEERING MEETS BIOMEDICINE

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Knut Reinert holds the chair of the Algorithms in Bioinformatics group at the Institute of Bioinformatics at Freie Universität Berlin. In addition, he is a Max Planck fellow at the Max Planck Institute for Molecular Genetics. He and his team focus on the development of novel algorithms and data structures for practical problems arising in the analysis of biomedical mass data and the efficient implementation of the algorithms in software libraries like SeqAn or OpenMS. Previously, Knut did his PhD at the Max-Planck-Institute for Computer Science in the group of Kurt Mehlhorn. After receiving his PhD he joint Gene Myers in the Informatics Research team at Celera Genomics, where he worked on bioinformatics algorithms and software for genome assembly and mass spectrometry. In 2002 he became full professor at the Freie Universtät Berlin and since then graduated numerous PhD and MSc students and coauthored around 100 research papers. He served on numerous PC committees as a committee member and (co)chair.

Keywords: Next Generation sequencing, parallel computing, vectorization, string indices

Bioinformatics has matured during the last 10 years now and combines many aspects of algorithmics, combinatorics, and computer science. At the same time, biomedical research is becoming more and more data driven and many analysis need timely analysis of genomic data. In addition, it is quite apparent that the available compute infrastructure evolves towards the use of hardware acceleration in form of many-core systems that have large vector units. Consequently, we have to adapt our algorithms and implementations so that they are able to take advantage of this development and provide the tools for the new precision medicine.

I will first introduce the research focus of my group, which is to bridge the gap between biomedical, experimental researchers and the computer science community. Then I will talk about the engineering aspects. Here, the main focus lies in the development of the C++ algorithms library SeqAn [1]. I will talk about its design and our roadmap to support vectorization and multicore processing. I will then exemplify the benefits using one well-known bioinformatics algorithm, pairwise sequence alignment, and a novel work of my group introducing an efficient method and implementation for constant time bidirectional search using FM-indices [2] requiring only the BWT and some small support data structures and point out what tools for biomedical research can benefit from this like [3], [4].

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FEATURES OF BLOOD AND URINE IN ALPORT SYNDROME PATIENTS: NOVEL GENOTYPE-PHENOTYPE CORRELATIONS

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Keywords: Alport syndrome, NGS, genotype-phenotype correlations, blood biochemical features

Alport syndrome (AS) is a hereditary hematuria usually associated with hearing loss and/or vision abnormalities [1]. Its frequency in Russia is estimated as 1:6 000 [2]. Most of the AS cases (~85%) are caused by COL4A5 gene mutations on X chromosome, ~15% are due to mutations in autosomal genes COL4A3 or COL4A4 [3]. Males with X-linked AS harboring missense mutations are known to have milder phenotype than those with splice site, nonsense, frameshift mutations or deletions covering at least 1 exon [4].

Multiplex amplification of coding sequence of COL4A3, COL4A4 and COL4A5 genes and subsequent NGS sequencing on Ion torrent platform has revealed pathogenic and likely pathogenic (according to [5]) COL4A5 mutations in 43 patients, 26 males and 17 females. Blood and urine characteristics were assessed at each hospitalization of the research participants aged 1 to 17 (average age at last examination: 11).

Here we show that start codon, splice site, nonsense, frameshift mutations and deletions covering at least 1 exon are characterized by earlier age at onset of hematuria ($p=0.012$ according to Mann-Whitney U test for both sexes taken together) and lower age-adjusted blood creatinine level in females ($p=0.042$ according to Mann-Whitney U test) compared to missense mutations. In patients of both sexes with glycine substitutions, position of the mutation was shown to negatively correlate with age-adjusted serum albumin level (i.e., C-terminal mutations tend to lead to lower albumin level than N-terminal) with Pearson correlation coefficient of –0,46 and Spearman correlation coefficient of –0,45 ($p<0,05$). These findings expand the knowledge on phenotypic characteristics typical for carriers of different COL4A5 mutation types.

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INDUCTION OF BONE FORMATION BY SURFACE MICROMORPHOLOGY OF CROSS-LINKED TETRAFUNCTIONAL POLYLACTIDE SCAFFOLDS

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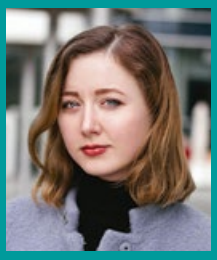
Keywords: scaffolds, two-photon polymerization, bone formation, tissue engineering, polylactide



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To date, scientists have showed that mechanical and surface properties of a substrate, where stem cells are cultured, can significantly influence their differentiation. Therefore, these physical cues can determine new approaches in scaffold design and tissue engineering [1–3]. In our study, we sought to assess how the surface micromorphology of polylactide scaffolds formed via two-photon polymerization (2PP) influence osteogenic differentiation of stem cells. We developed a synthetic strategy allowing a gradual variation of a polylactide arms' length, which influences the micromorphology of a 2PP scaffold surface. We showed that the highest number of cells was present on the scaffolds with the roughest surface fabricated from polylactide with longer arms (PLA760), and osteogenic differentiation of mesenchymal stem cells was most pronounced on such scaffolds. The PLA760 scaffolds were implanted into a created cranial defect in a mouse for an in vivo assessment of the bone tissue formation. The in vivo experiments revealed that, by week 10, deposition of calcium phosphate particles occurred in the scaffold at the defect site, as well as, the formation of a new bone and ingrowth of blood vessels from the surrounding tissues. These results show that the scaffolds from cross-linked microstructured tetrafunctional polylactides, which have a rough surface, are promising for bone tissue engineering

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THE GENOMES OF WESTERN CIVILISATION

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Keywords: wheat genome, barley genome, cereal genomics

Bread wheat (Triticum aestivum) has strongly shaped human civilization since its domestication at the Neolithic revolution. Today, wheat is one of the top three crops in agriculture and provides ~20% of all calories of the world's population. Another cereal of major importance for brewing and animal feed is barley (Hordeum vulgare). Whole genome sequencing projects have shown to provide invaluable tool boxes both for academic research as well as for agricultural and applied sciences for many plant species before. In contrast to two other major crops – maize and rice, whole genome projects have been impeded by several notoriously difficult properties of both the wheat and barley genome. With 17 Gigabases in size, the hexaploid wheat genome (three subgenomes) is more than five times larger than the human genome and the high repeat content of cereal genomes complicates whole genome assembly from short sequence reads.

While earlier whole genome sequencing attempts for wheat (1,2) and barley (3) mainly resolved the gene space and allowed first insights into the genome organisation and structure (4), recent technology improvements and novel strategies brought a breakthrough in cereal genomics. HiC chromosome capture as well as novel assembly algorithms allowed the generation of both a barley and wild emmer wheat reference genome sequence recently (5, 6), enabling access to 39,000 high-confidence barley gene models ordered on highly contiguous pseudochromosomes. In the framework of the IWGSC (International Wheat Genome Sequencing Consortium) (7), a highly improved genome assembly of bread wheat has been generated using a large array of technologies. These new resources will greatly assist targeted breeding and contribute to food security in a changing environment.

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DECIPHERING THE REGULATION OF ALTERNATIVE PRE-MRNA SPLICING BY COUPLING RBP BINDING PROFILES WITH LONG-RANGE RNA STRUCTURE

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Alternative splicing is an important mechanism for generating the diversity of protein products by expanding the repertoire of mRNA isoforms. The regulation of splicing is controlled by cis-acting RNA elements represented by two classes: splicing signals (the 5' splice site, the branch point, and the 3' splice site) and splicing enhancers/silencers, in which a number of RNA-binding proteins (RBP) operate. Splicing outcome is highly cell/tissue specific and regulated by many factors. We used the results of the ENCODE project, in which genome-wide profiling of nearly 80 RBPs has been performed using eCLIP method for two cancer cell lines (K562 and HepG2), in order to build a machine learning model that integrates the spatial signal of RBPs around splice sites and RNA secondary structures. Importantly, our model of the secondary structures involves long-range base pairing interactions, hence creating a more realistic distance metric compared to that of the unfolded RNA. Using only spatial signal of various RBPs our model achieves high performance for prediction inclusion of an exon in a transcript. We also trained a model to predict the difference in percent exon inclusion between pairs cell lines. Surprisingly, both models showed high and comparable performance. Also, we introduced to the model information about secondary RNA structures. To this end, we coupled long-range RNA secondary structure with the distant eCLIP peaks. This model allows to taking into account the possibility when distally bound RBPs are brought in proximity to splice sites. Overall, our model predicts splicing outcome and supports the hypothesis that secondary RNA structures, including long-range interactions, plays an important regulatory role performing localization of RPBs to the proximity of splice sites. Performance of the model with RNA structure is ~10% better than that of a control model. This mode of regulation has been recently shown for structures called RNA bridges which bring RBFOX2 binding sites to the site of action. We found that exon inclusion is strongly associated with the strength of the RBP signal. Additionally, several RBPs we predicted to be master splicing regulators. Moreover, RBPs signals exactly in the vicinity of splice sites (up to 200 bp) have the highest controlling impact.

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HILBERT SPACES AND COMPUTATIONAL BIOINFORMATICS

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Keywords: huge approximate genetic repeats, spectral analysis

Here we are offering a new method to find huge approximate tandem and dispersed repeats in DNAs. A number of discrete methods have been developed and successfully applied to that problem with only comparatively small tandem repeats considered. Many of them are based on k-tuple match detection [1] or edit distances [2], but they all are not applicable for finding really inexact huge tandem repeats with a period over 1000 bp [3]. Apparently this size seems to be a serious limitation for all of the earlier approaches.

Since the methods of bioinformatics are often 'ported' from other fields of Computer Science (e.g. text/image data analysis) our main idea was to 'borrow' the solution for the same problem that has already been faced when image and audio data starts growing fast. To address this specific issue they created a joint technical committee that decided to switch from discrete methods to the spectral ones (i.e. switching from GIF/Tiff formats to JPEG, switching from WAV to MP3, etc.). In other words, all the matrices of discrete data should be now approximately represented as vectors of a Hilbert space.

Thus we were to develop a novel spectral-based approach for comparative analysis of genomic sequences, which was mainly devoted to finding huge and highly inexact repeats in DNAs. The novelty of our approach consisted in using specific 'spectral invariants' for genetic regions, which were based on spectral decomposition of DNA's profiles, for instance, GC-content. Those spectral invariants are actually vectors of Hilbert spaces, so they obey to all the basic rules for those vectors, which still could be easily interpreted in terms of our comparative analysis (inverted repeats, complement repeats, etc.). Altogether, all these mathematical facts are extremely useful while comparing DNAs and they could make it much easier to find similar genetic chunks across highly divergent species (and still in a little amount of time/space) [4,5,6].

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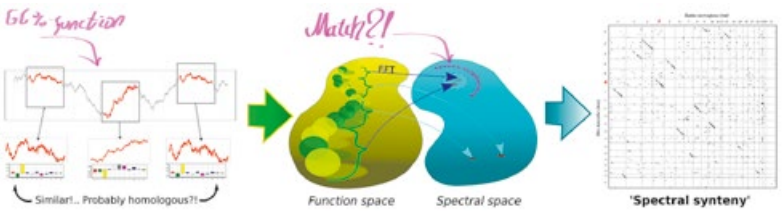

Figure 1. Understanding of 'Spectral Indexing' for lengthy genomic sequences and genome-wide visualization of local spectral similarity.

SBML VIEWER IS A VISUALIZATION TOOL FOR SYSTEMS BIOLOGY MODELING

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Keywords: SBML, systems biology, mathematical modeling

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Background: Nowadays computational biology is a popular approach for biomedical and pharmacological research. It allows maximizing therapeutic benefit minimizing toxicity and implement a "precision medicine" approach to improving the health of individual patients (1). Complexity of the biological systems results in complex mathematical models and requires specific software tools. One of the most important challenges in the area is the tools for visualization and annotation of the structural and numerical data.

Systems Biology Markup Language (SBML) is a free and open interchange format for computer models of biological processes (2). SBML is XML based format and designed basically for machine reading and writing, for transformations from SBML files into human readable format you need a 3rd-party software.

The software allows reading and editing SBML files directly, but all of them require installation and some experience, for example SBMLeditor (3). It is not convenient for the demonstration on a computer without preinstalled software.

Methods: For the development of visualization tool we used the following technologies:

XSLT transforms SBML structure into HTML file with tables, formulas, etc. which can be displayed by any web-browser. We develop three options of the transformation of SBML file to human readable formats: sbml2table, sbml2element and sbml2math.

To use interactivity, we use JavaScript language. This allows reading and displaying onloaded models in a browser.

MathJax library was used to translate MathML object from SBML into nice representation of mathematical equations.

Results: We have developed the tool for a fast and easy reading of biological models written in SBML format. SbmlViewer allows reading and checking SBML file without installation, readiing specific SBML versions or elements like event, constraint or functionDefinition.

SbmlViewer is an open project, distributed under Apache 2.0 license and can be tested online on page http://sv.insysbio.ru

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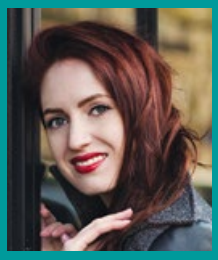

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ACCURATE NGS SEQUENCING WITH PRIMERID APPROACH DATA ANALYSIS USING THE CASE OF HIV-1 POPULATION DIVERSITY STUDYING

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Keywords: NGS, molecular barcode, PrimerID, HIV, sequencing errors

In 2010 the group of Prof. Kozlov began studying the transmission of HIV-1 in longitudinal blood samples of injection drug users (IDUs) [1]. In order to shed light on the viral dynamics the full-length env gene sequences of HIV were obtained for each sample (using SGA approach). Phylogenetic analysis of these sequences revealed the transmission of a single viral variant in 70% of cases. This phenomenon is called genetic bottleneck.

SGA is low-throughput approach, which may miss minor viral variants, resulting in observed genetic uniformity. We therefore resorted to NGS sequencing to confirm the HIV genetic bottleneck phenomenon for IDUs.

Due to its high resolution NGS sequencing allows for a more accurate detection of minor variants, but it suffers from high rate of sequencing errors. One approach to alleviating the sequencing errors is the use of specific molecular barcodes (PrimerIDs [2]) to tag each viral cDNA. Following cDNA amplification and sequencing, the reads with the same PrimerIDs are considered to be copies of the same original cDNA and are used to create a consensus sequence in order to reconstruct the original cDNA sequence while eliminating sequencing errors.

The PrimerID approach also has certain drawbacks. For example, sequencing errors may affect PrimerID sequences themselves. To solve this problem, the reads are subjected to stringent filtering, with all reads not beginning with the exact primer sequence being removed [3]. This procedure can result in the loss of a large number of otherwise high-quality reads.

In order to address this challenge, we have developed an improved computational pipeline to analyze PrimerID sequencing data with avoiding loss of data. The pipeline relies on a combination of publicly available tools and several in-house algorithms (developed in Python). At the moment some steps of created pipeline are to be improved.

Our results will be benchmarked against synthetic sequencing data.

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CUSTOMIZED WORKFLOW DEVELOPMENT AND OMICS DATA INTEGRATION CONCEPTS IN SYSTEMS MEDICINE

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Application of computer science in the life science plays an increasingly important role. A key challenge is to adapt, compare, benchmark and integrate the most appropriate computational tools into data analysis workflows. In my research, I focus on the needs of experimental researchers and develop flexible workflows for the analysis of low and high throughput data such as blood measurements, protein expression, RNA sequencing data and environmental information [1]. I am combining state-of-the-art tools including R, Galaxy and Docker as well as further downstream analysis approaches such as network analyses or machine learning. We have already applied and validated our developed methodologies in interdisciplinary collaborations. Exemplarily, pre-clinical and clinical data of stem cell derived cardiac cell types have been investigated to demonstrate the value of such integrative data analysis workflows, contributing towards a better understanding within the field of cardio vascular diseases and cardiac repair [2]. This work facilitates the use of Systems Medicine approaches in a clinical setting and thus supporting improved diagnosis, prevention and therapy.

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OPPORTUNITIES AND CHALLENGES FOR MODELLING IN THE LIFE SCIENCES

My research focusses on understanding intra and inter-cellular dynamics for biotechnological and biomedical applications. Technological advances allow us to identify and characterise cellular components but the mechanisms by which cells realise their function, remain poorly understood. My approach combines data-driven modelling with model-driven experimentation, using a wide range of computational and mathematical tools. My interest in uncertainty arising from the complexity of multilevel and multiscale nonlinear spatio-temporal systems has also led to interactions with philosophers of science. My work supports basic and clinical research. I received my first degrees in control engineering from the University of Applied Sciences in Hamburg, Germany and the University of Portsmouth in 1994, followed by a PhD from the Control Systems Centre at the University of Manchester, Institute of Science & Technology (UMIST) in the UK in 1997. In 1999 and 2000 I was an invited research fellowship at the Technical University Delft in the Netherlands, I spent almost eleven years of my academic life in England and had one of the first joint interdisciplinary appointments between a Dept. of Electrical Engineering and a Dept. of Biomolecular Sciences in the UK. Since 2005, I hold an adjunct professorship at Case Western Reserve University, Cleveland, USA, which was initiated by Mihaijlo Mesarovic, the founding father of the general systems theory. In 2005, I became a fellow of the Stellenbosch Institute for Advanced Study (STIAS) and in 2015, I was elected as a member of the Foundations in Medicine and Biology review panel of the German Research Foundation (DFG).
A summary of my research projects and publications can be found on our website at www.sbi.uni-rostock.de . When I am not thinking about maths, biomedicine or the philosophy of science, I am a keen kitesurfer, DJ and enjoy the production of electronic music.

Keywords: Systems approaches, Biomedicine, Complexity, Living Systems

A basic understanding of the (mal)functioning of cells provides the basis for numerous biomedical and biotechnological applications. Advances in these areas depend therefore on our ability to describe complex, that is, multilevel, nonlinear spatio-temporal processes.

While systems approaches have found their way into biomedical research over the last 30 years, their success in the physical and engineering sciences has not translated well into the life sciences. The complexity of living systems forces us to rethink our strategies by which we generate knowledge and how we make inferences when dealing with truly complex/living systems.

While technologies have made it possible to "zoom in" with ever more details, I believe we are lacking methodologies to "zoom out", to generalize results we obtain in a narrowly defined experimental context. Many biomedical research questions are formulated at higher levels of structural and functional organisation but experimentally investigated at the molecular and cellular level. So, while we are good at building "microscopes" to zoom in, what we indeed require are "macroscopes" that allow us to "zoom out", from molecular properties, to physiological processes.

It seems that we have no clue how to go about this. The complexity of molecular and cellular systems limits us and creates uncertainty. As one consequence, we are "integrating" information, models and conventional analyses in computational 'workflows' that support experimental scientists with the interpretation of their data. While these efforts have been proven successful in many interdisciplinary collaborations, I find it personally unsatisfactory that there is not a more honest discussion about the current limitations.

In our desire to provide useful, practical support for experimental scientists, we have forgotten our original interest in the development of methodologies and theoretical concepts. Maybe it is practically impossible to create abstract concepts that have clinical impact, but why are we not even trying?

OPENEHR METHODOLOGY FOR MULTIDISCIPLINARY CLINICAL DATA STORAGE AND RESEARCH

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Keywords: openehr, clinical data, health informatics

Gaining insights from multidisciplinary clinical data is hard. Among many possible ways to improve this situation – changing the way we store data is the most obvious one.

OpenEHR has sprung into existence as methodology in 1992 aiming to radically simplify the process of clinical data storage and exchange. Gaining momentum over time by 2010 it has reached a level of maturity that would allow it to compete with well-established industry solutions of clinical data storage in the world.

The concept of openEHR focuses on systems and tools necessary to the computation of complex and constantly evolving health information at a semantic level, according to the following three paradigms: separation of information models, domain content models, and terminologies; separation of responsibilities; and separation of viewpoints. Among these three paradigms, the separation of information models, domain content models and terminologies promotes a significant shift from the single-level modelling approach of information system development to a two-level modelling approach. In the single-level modelling approach, domain concepts that are processed by the electronic health records (EHR) system are hard-coded directly into the application and database models. In two-level modelling, the semantics of information and knowledge are separated into a small, comprehensible, non-volatile reference model (RM), which is used to build information systems and knowledge models; archetypes are used as formalisms and structures to express numerous and volatile domain concepts [6].

This approach promotes data interoperability between laboratories and clinical institutions while abstracting away the differences in processes, protocols and EMR implementations.

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Andrey Zaika

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Professor Dr. Ralf Zimmer

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BIOINFORMATICS OF A COMPLEX HUMAN DISEASE ATHEROSCLEROSIS – MECHANISMS AND NETWORKS OF NOVEL THERAPEUTIC TARGETS

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Keywords: Analysis of High-Throughput Data, Bioinformatics, Textmining, Network Analysis, Systems Biology Modeling

Ralf Zimmer is Professor of Informatics at the Ludwig-Maximilians-Universität München (LMU). He graduated from the Rheinische Friedrich-Wilhelms-Universität Bonn in 1986 and then joined the Institute for Scientific Computing and Algorithms (Sankt Augustin) first as a PhD student, then as project leader and group leader. After obtaining the doctoral degree at the University of Kiel in 1990 he held research at Stanford University. In 2001 he got professorship at the LMU München. He was elected Member of the senate of the LMU and member of the board. Professor Zimmer is involved in a wide range of national and international projects funded by the DFG, including DFG SFB 1035 "Conformational switching" (2011–2016), DFG SFB 1123 "Atherosclerosis" (2014–2018). He was a speaker of the Joint German Russian International Research Training Group (IRTG) "Regulation and Evolution of Cellular Systems" held from 2008 till 2013 together with TUM and Moscow State Lomonosov University.
His research focuses on the field of bioinformatics, gene expression analysis, protein sequence and structure analysis, Systems biology etc.

Atherosclerosis is a complex human disease with major impact on human health and health care costs. It is responsible for many health complications and a major cause of death and disabilities (heart failure, infarct, stroke) for humans in the modern society.

In the DFG funded CRC 1123 Atherosclerosis – Mechanisms and Networks of Novel Therapeutic Targets about 20 projects at the clinics of the LMU and cooperation partners we study the disease in humans and several animal models (mouse, rat, pig). A particular focus is on understanding the molecular mechanisms and networks involved in early stages of the disease in order to come up with preventive measures.

Towards this goal many models and experimental techniques are used to identify both novel mechanism and novel targets such as transcription factors, miRNAs, circular RNAs, and lncRNAs. Many experimental techniques are employed in particular in animal models including high-throughput measurements from expression profiling, various next generation sequencing protocols, mass spectrometry, and high resolution imaging.

We apply a wide range of bioinformatics approaches, both state-of-the-art and custom developed algorithms, to the challenges and data generated in the CRC. As various experimental measurements, several species, but also several cell types and complex interaction and communication are involved in the disease, we employ specialized high-throughput data analysis methods, methods to make the data comparable and several data integration methods to build as comprehensive systems models as possible. Bioinformatics methods also include text and figure mining approaches to generate network models, cross-species analysis to compare and transfer models across species, and regulatory networks including miRNAs and long non-coding RNAs.

SCIENCE – BUSINESS – INNOVATION

FROM A SURVIVING STARTUP TO AN ESTABLISHED COMPANY: LESSONS LEARNED OVER 20 YEARS

Professor Dr.
Hans-Werner Mewes

Co-Founder, Chairman
of the Board of Directors
Biomax Informatics AG

In 1997, together with my colleagues Klaus Heumann and Dmitrij Frishman, I founded Biomax Informatics to translate our experience in the early days of genome bioinformatics into the commercial world. Although startups were not very common in the field, we were not the only ones believing that there is a need for a professional support to manage, analyze and understand biological data. Nevertheless, only very few of the companies founded 20 years ago survived. Some were funded with substantial investment from venture capital firms, others started small as experts in specialized areas. In retrospective one may ask, why startups fail and if there is a promising perspective for young scientists to jump from an academic career into a pool crowded with piranhas. Starting with a lot of enthusiasm, founders often have brilliant and convincing ideas but forget to get readyfor the laws of commercial success that are very much different from the way to academic glory. Scientists are not well prepared to be good managers and sometimes they are poor communicators or fail to lead a team. Furthermore, the conflict overdiverging interest between venture capital and the founders bears ample chances for a conflict. Founders want to be independent entrepreneurs, implement ideas, and be good employers for ambitious experts that do not like to work in large companies or academic research institutes. Investors aim for a quick return of investment. Sometimes too much funding at the start appears to be rather a burden than an advantage. Both parties need each other, but not in all casesthe relationship remains a lovely one. Their governance needs control, not by building up pressure but in the way good coaches back up their team. Startups require support from experts for legal and contract issues, marketand management. Biomax has found its way by combining advanced technology with strict market orientation. Starting as a bootstrap with little capital and continuously developing a core technology for knowledge management based on data integration, the company moves toward another step on its way. Patient's stratification, personalized medicine and outcome-oriented therapies are in focus to overcome some of the obvious limitations of current health care systems. We have proven that digitalization is not a burden but anenormous potential to bring just the best, individually tailored therapy to the patient. Therefore, we are optimistic to enter the next decade from a not so small to a medium size company. And I am proud to say that one but certainly not the only building brick of success was the lasting trust and friendship between the founders.

BIOSOFT

Daria Stelmashenko

Creative Director
Biosoft

Our research is devoted to identification of new drug targets and biomarkers for various diseases. The approaches which we use allow identification of molecular processes, undergoing in a single cell. Knowing these processes, we are able to reconstruct and model the dynamic process of the diseases molecular mechanisms.

Our algorithms perform a multi-step analysis of DNA's non-coding regions and identify the complexes of transcription factors, which are responsible for regulation of differentially expressed genes that can be seen in the pathological state. This search is performed by using TRANSFAC database of transcriptions factor binding sites and a genetic algorithm for identification of transcription factors, which work together in one group (complex). After the complexes of transcription factors are identified, a graph search analysis it performed, aiming to find common regulators of the revealed factors. This part of our approach for identification of drug targets and biomarkers is called upstream analysis and it is performed with the use of the TRANSPATH database. Once the common regulators of the identified transcription factors are found, these regulators are referred to as potential drug targets and biomarkers depending on their drugability and experimental identification prospects. We call these regulators "Master regulators" and we always highlight their important role in the cell regulation processes. For instance, those master-regulators allow us to understand the molecular principles of cell's functioning and play a key role in such processes as cancer development and emergence of therapeutic resistance.

Prediction of possible changes in intracellular signal cascades, responsible for cell regulation, allows us to build hypothesis about "pathway rewiring", which is an experimentally proven for certain diseases theory of changes undergoing in a cell during the development of a studied pathological process. Prediction of new master-regulators, which would come to power after the transformation of cell's signaling pathways in response to a therapeutic agent or any other external interference in the cell's functioning system, is a key to treatment of such complex diseases as cancer, diabetes, etc. Thus this very first step of patient treatment or drug and biomarker development process, consisting of identification of master-regulators being in charge of the studied pathological process on a molecular level, plays a key role for the further success of such complex procedures as drug development, patient diagnosis and treatment, drug repurposing and health maintenance of human beings.

Willing to share our algorithms and analysis approaches with other scientists, we have developed a special ready-to-use workflow named "Upstream analysis", implemented in the geneXplain platform tool long with other important parts of integrated omics data analysis that is used for various biomedical studies.

OPEN INNOVATIONS PROGRAMMES OF BAYER: GRANTS4APPS, COLABORATOR

Igor Orshanskiy

External Innovation & Alliances Manager, Russia & CIS

CoLaborator

At Bayer, we believe collaboration is an essential way to bring new therapies to the patient. This philosophy led us to open the CoLaborator, a unique incubator space for start-up companies next door to our West Coast Innovation Center in the Mission Bay neighborhood of San Francisco and Berlin in 2012 and in Moscow in 2017. Bayer with the biological faculty of Moscow state University launched the third in the world "CoLaborator", aiming to support Russian scientific and technological companies in their early stages of development. The purpose of "CoLaborator" in Russia is joint with MSU research activities in the field of biology and biotechnology, chemistry, pharmacology, and related fields of knowledge, the results of which can be brought to the stage of local production and shown on Russian and international markets. MSU provides for startups – residents of "Collaborator" access to modern research infrastructure necessary to create new developments. Bayer provides for startups international expertise in the field of research and development and commercialization and helps to bring to market innovative solutions. Leading experts from Bayer will advise project participants in all phases of activities, including research, development, positioning for the future product on the market. This will help startups to Refine their designs based on the needs of the industry and, ultimately, to bring your solutions to the stage ready and commercially viable projects.

Participants of "CoLaborator" may be the company, formed by students, postgraduates, lecturers and researchers of the faculty of biology, Lomonosov Moscow state University in General, and from other scientific institutions.

Grigory Kolesnikov

IT Business Partner,
Pharmaceuticals Division,
Bayer

Head of Grants4Apps
in Russia

Grants4Apps (G4A) is a web-based crowdsourcing initiative, launched in 2013. It provides financial support to developers and start-ups for their software, hardware and technology projects which contribute to improve health outcomes or pharmaceutical processes. The crowdsourcing programme was expanded with the Accelerator as a new model of open innovation in the digital health field in 2014. The G4A Accelerator offers dedicated office space for up to 5 digital health start-ups with concepts for innovative technology solutions to healthcare problems at the headquarters of the company's pharmaceutical division in Berlin, and supports them in further advancing their products and business models. Each start-up receives 50,000 Euro as a financial support. They stay on the G4A Accelerator premises for about 100 days. During that time, the start-ups are coached by experienced Bayer senior managers, in addition to intensive mentoring by external entrepreneurs. Thereby, the Accelerator creates an ideal environment in which to advance cutting-edge technologies in healthcare and underlines Bayer's engagement in collaboration with young entrepreneurs.

Grants4Apps Coworking Moscow is a Russian acceleration programme for digital start-ups, implemented in partnership of Bayer and The Internet Initiatives Development Fund (IIDF). Digital Health and Digital Farming start-ups are involved in the selection of G4A. Teams have the opportunity to integrate into the international innovation ecosystem of Bayer, refine their projects and to expand its network of contacts and an audience that may be interested in the product. In the first year after launch Grants4Apps in Russia collected 150 applications. Three of the most promising projects were selected for acceleration in the Moscow office of the company. This year the contest received 220 applications. 5 digital health start-ups Apteki+, BestDoctor, MediSensum, Semantic Hub, TeleMD and one digital farming startup – Grow Tech were selected to Grants4Apps Coworking Moscow. During the 3-month of the accelerator operation in the Moscow office of the company, the start-ups have access to required work equipment. Teams get the expertise from leading industry players, business advice from IIDF, Bayer employees provide training and meetings to find ways to interact. This helps the start-ups to adjust their projects to the needs of the industry and to improve them. The most promising startups take part in the selection process of the global accelerator "Grants4Apps" in the headquarters of the pharmaceutical division of Bayer in Berlin. This year`s the graduate G4A 2017 Coworking Moscow, the project TeleMD entered the top 10 of global competition, the Semantic Hub and Qapsula – the top 30.

SCIENTIFIC ORGANISATIONS

SKOLKOVO INSTITUTE OF SCIENCE AND TECHNOLOGY (SKOLTECH)

Skoltech
Skolkovo Institute of Science and Technology

The Skolkovo Institute of Science and Technology (Skoltech) is a private graduate research institution. Established in 2011 in collaboration with the Massachusetts Institute of Technology, Skoltech educates global leaders in innovation, advances scientific knowledge, and fosters new technologies to address critical issues facing Russia and the world. Applying international research and educational models, the University integrates the best Russian scientific traditions with twenty-first century entrepreneurship and innovation.

With English as its official language, Skoltech serves as a gateway for international partnerships, students, scientists and organisations in Russia, bridging gaps in the international scientific community.

"Skoltech provides an entry point for western universities into Russia," said Provost Rupert Gerzer. "Our faculty includes professors from the West who know the ins and outs of the academic systems in their own countries, and are now sharing those nuances with their colleagues and students, and vice versa for our Russian professors."

Skoltech's local students also have the opportunity to immerse themselves in international research opportunities.

"We offer our students academic mobility programmes that have led them to prestigious academic institutions and companies all over the world," said Gerzer. "These programmes have taken students as far afield as Antarctica and Los Angeles, where they've had opportunities to conduct advanced research with leading international teams."

As an academic institution, Skoltech's primary mission is academic excellence in target domains. This includes performing cutting-edge basic- & applied research, and educating the next generation of international and Russian science, technology and business leaders.

Six target domains have been identified based on global technology priorities and experience: Cutting-edge engineering & advanced materials; Data Science & Artificial Intelligence (AI); Life sciences & Biomedicine; Energy efficiency; Quantum technologies; and Advanced studies.

Skoltech has six primary education programmes, corresponding to target domains. Each of these programmes provides Master's and Ph.D.

Over the next few years, Skoltech will endeavour to be the first university prepared to educate Digital Natives. The "digitally-born" incoming student body exhibits new behaviours and needs. To meet these needs, Skoltech will be based on full immersion ("living-learning-teaching").

Ten Centers for Research, Education and Innovation (CREIs) are associated with Skoltech, each residing under one or more of the target domains. Each CREI has a thematic research mission carried out through a distributed collaborative research programme between Skoltech and international and Russian institutions, and has both physical and virtual components. Skoltech faculty, staff, and students conduct their research under each CREI in new physical laboratories at Skoltech.

Professor Dr.
Alexander Kuleshov

President of Skoltech

Professor Dr.
Rupert Gerzer

Provost of Skoltech

Deutsches Wissenschafts- und Innovationshaus – Moskau

Deutschland
Land der Ideen

THE GERMAN HOUSE FOR RESEARCH AND INNOVATION (DWIH) MOSCOW

Dr. Peter Hiller

Managing Director
of the DWIH Moscow

Mikhail Rusakov

Coordinator
DWIH Moscow

The German Houses of Research and Innovation (DWIH) provide a platform for the German research and innovation landscape, showcasing the accomplishments of German science, research, and research-based companies and promoting collaboration with Germany and innovative German organisations. They are part of the Internationalization Strategy of the German Federal Government and the Federal Foreign Office's Research and Academic Relations Initiative. The Federal Foreign Office is implementing this project in cooperation with the Federal Ministry of Education and Research and in close collaboration with the Alliance of German Science Organisations, which includes the Alexander von Humboldt Foundation, Fraunhofer-Gesellschaft, German Academic Exchange Service (DAAD), German Council of Science and Humanities, German National Academy of Sciences Leopoldina, German Rectors' Conference (HRK), German Research Foundation (DFG), Helmholtz Association, Leibniz Association, Max-Planck-Gesellschaft – as well as the Association of German Chambers of Industry and Commerce (DIHK).

The houses were created for various goals:

- Promote Germany as a research location
- Provide a forum for international dialogue and scientific exchange
- Provide support and services (advising for international researchers; organizing educational events; facilitating collaboration)

The German House for Research and Innovation in Moscow goes back to a June 2009 meeting between Germany's then Foreign Minister Frank Walter Steinmeier and his Russian counterpart Sergey Lavrov, when both agreed with expanding the institute under the leadership of the DAAD. In 2011 a joint declaration between Dr. Guido Westerwelle and Sergey Lavrov on the establishment of a German House of Research and Innovation in Moscow was signed. Currently the DWIH project in Moscow is lead jointly by the German Academic Exchange Service (DAAD) and the German Research Foundation (DFG) and comprises partners with a representation/representative in Moscow like the Helmholtz Association of German Research Centres, Alexander von Humboldt-Foundation, the Freie Universität Berlin and the German Historical Institute (DHI) Moscow. The German Russian Chamber of Foreign Commerce (AHK), the Ministry of Innovation, Science and Research of Northrine-Westfalia and the Federal States of Thuringia and Lower Saxonia are also members of the DWIH. DWIH Moscow´s current director is Dr. Peter Hiller (DAAD).

In its various activities the DWIH Moscow focuses mainly on the topics of the German-Russian Modernization Partnership, i.e. climate, energy, health care, resource management, logistics and legal cooperation. Beside these, it has established an event portfolio on additional fields of German Russian scientific interest as aviation and space, energy saving technologies, bioenergy and many more.

The DWIH regularly organizes and supports German-Russian events like e.g.:

- Science Lectures of outstanding German scientists
- Science Talks with high-ranked representatives of German and Russian
- The „German-Russian Week of the Young Researcher", once a year on varying subjects in the Russian regions
- Regular meetings with rectors of leading Russian universities
- Symposia/Conferences on current scientific topics
- Information seminars in centres of scientific and innovative research in Russia
- Economy and innovation: participation in economic conferences on innovative topics
- Participation in fairs in the field of German research marketing

In 2015, the German House of Research and Innovation in Moscow participated in more than 40 events and organized itself several high-ranked scientific events.

DEUTSCHE FORSCHUNGSGEMEINSCHAFT (DFG)

DFG Deutsche Forschungsgemeinschaft

Dr. Wilma Rethage

Director

DFG Office Russia/CIS

The Deutsche Forschungsgemeinschaft (German Research Foundation) is the biggest funding agency in Europe for the development of fundamental research with an annual budget of approximately 3 billion Euro. Its membership consists of German research universities, non-university research institutions, scientific associations and the Academies of Science and the Humanities. The DFG has expanded its presence in other research regions around the world with its 7 liaison offices. The office Russia/CIS was opened in Moscow in 2003. Framework agreements on the co-funding of research projects and researcher mobility exist with the Russian Foundation for Basic Research (RFBR), the Russian Science Foundation (RSF).

How does the DFG promote young researchers?

Creative and intelligent minds are the key to successful science and research. That is why the Deutsche Forschungsgemeinschaft (German Research Foundation) places a special focus on promoting young researchers. We are committed to helping young talents pursue cutting-edge investigations in top-level settings and help them to become independent early on in their careers.

Flexible individual funding and customised excellence programmes give young researchers the opportunity to advance in their careers and undertake projects from all branches of science and the humanities. The DFG accepts funding proposals from researchers with a doctoral degree (PhD) who live and work in Germany or plan to do so in the future. PhD students are not supported individually, but can be, indirectly through the funding of programmes and projects.

Project-based doctoral and post-doctoral qualifications

For doctoral researchers, who like working in a team and value a well-designed framework, a **Research Training Group** (RTG) may be the right choice. It combines an ambitious research programme with target-oriented supervision and academic freedom to form an ideal environment for a successful doctorate. Post-docs help design the research and qualification programmes of an existing RTG and explore new research topics for your future career.

Following completion of the doctorate there is the possibility to assume responsibility as an **investigator in an existent DFG-funded project**. This will give young researchers the opportunity to advance their qualifications and improve their career prospects by gaining experience and by building new networks.

The **Temporary Position** is a funding mechanism that provides young researchers with funding for a temporary post-doctoral position in conjunction with a proposal for a research grant. Researchers may select the scientific setting in Germany that they think will provide the best conditions for their project.

Excellence programmes

The **Emmy Noether Programme** is aimed at outstanding scientists and academics with at least two and no more than four years of post-doctoral research experience (or up to six years for licensed medical doctors). It allows young researchers to head their own independent junior research group that will work on a project for five or, in exceptional cases, six years. It offers a fast-track opportunity to qualify for a leading position in research.

For young researchers, who have all the qualifications for a professorship, the **Heisenberg Programme** may be the right option. This programme provides them with funding for up to five years so they can distinguish themselves further academically. There are two variations of the programme: the portable Heisenberg fellowship, which also allows one to go abroad for some time; and the Heisenberg professorship, which offers the prospect of acquiring a tenured position at a German university, provided the candidate receives a positive review.

DAAD Deutscher Akademischer Austauschdienst
German Academic Exchange Service

THE GERMAN ACADEMIC EXCHANGE SERVICE (DAAD)

Dr. Peter Hiller

Head of DAAD Office
Moscow

The German Academic Exchange Service (DAAD) is the largest funding organisation in the world supporting the international exchange of students and scholars. Since it was founded in 1925, around 2 million scholars in Germany and abroad have received DAAD funding. It is a registered association and its members are German institutions of higher education and student bodies. Its activities go far beyond simply awarding grants and scholarships. The DAAD supports the internationalisation of German universities, promotes German studies and the German language abroad, assists developing countries in establishing effective universities and advises decision makers on matters of cultural, education and development policy.

Its budget is derived mainly from the federal funding for various ministries, primarily the German Federal Foreign Office, but also from the European Union and a number of enterprises and organisations. Its head office is in Bonn, but the DAAD also has an office in the German capital, Berlin, to which the famous Berlin Artists-in-Residence Programme (Berliner Künstlerprogramm) is closely affiliated. It maintains contact with and provides advice to its main partner countries on every continent via a network of regional offices and information centres.

In 2016, the DAAD funded more than 131.000 German and international scholars worldwide. The funding offers range from a year abroad for undergraduates to doctoral programmes, from internships to visiting lectureships, and from information gathering visits to assisting with the establishment of new universities abroad. Voluntary, independent selection committees decide on the funding. The selection committee members are appointed by the DAAD's Executive Committee according to certain appointment principles. The DAAD supports the international activities of German institutions of higher education through marketing services, publications, the staging of events and training courses.

The DAAD has three strategic fields of activity:

- Scholarships for the best: preparing students and researchers to take their place as responsible professionals and business leaders of tomorrow and encourage them to foster long-term contacts throughout the world;
- Structures for internationalization: encouraging cooperation between universities, improving the quality of research and teaching, enabling more people to study and conduct research abroad, ensuring that German remains an important language of culture and science;
- Expertise for academic collaboration: providing information and advisory services to institutions of higher education and other academic exchange stakeholders, both in Germany and abroad.

THE HELMHOLTZ ASSOCIATION OF GERMAN RESEARCH CENTRES

HELMHOLTZ SPITZENFORSCHUNG FÜR GROSSE HERAUSFORDERUNGEN

The Helmholtz Association researches major challenges to secure the future of our society. With almost 39,000 staff and an annual budget of almost €4 billion, the Helmholtz Association is Germany's largest scientific organisation. The Helmholtz Association brings together 18 scientific-technical and biological-medical research centers.

The Helmholtz Association contributes to solving large-scale challenges which face society, science and industry – by undertaking top-rate research in strategic programmes in the fields of Aeronautics, Space and Transport, Earth and Environment, Energy, Health, Matter as well as Key Technologies. We research systems of great complexity with our large-scale facilities and scientific infrastructure, cooperating closely with national and international partners. As Germany's largest scientific research community we contribute to shaping our future by combining research and technology development with perspectives for innovative applications and provisions for tomorrow's world.

To answer these challenges, the Association combines knowledge and resources from various disciplines and centers and creates strategic international alliances. Cooperation and networking with national and international partners from science and research, and especially from the universities and industry, are its key to producing outstanding research findings – more efficiently and quickly.

An excellent research infrastructure – in some cases with unique major scientific facilities and instrumentation – clearly demonstrates the strength which has made the Helmholtz Association a much sought-after research partner. Each year, several thousand visiting scientists from all around the world use the research opportunities which the Helmholtz Centers offer. The Association acts as a core focal point for worldwide research project – whether in the observation and study of the global climate or in the field of basic research in physics.

The Helmholtz Association aims to be an active and driving force in establishing the research area worldwide. This is why Helmholtz opened branch offices in Brussels, Moscow and Beijing. The Helmholtz Association chose Russia to be one of its key strategic partners to jointly face the challenges of the future through scientific cooperation. Partners in Germany looking for specific information about Russia and Russian seeking contacts in Germany have an excellent starting point in identifying the right people for their special interests. The transfer of new technologies and the exchange of promising young research talent hold great potential for the future development of both Germany and Russia.

The Moscow Office represents the interests of Helmholtz Association as a whole in Russia. It serves both Helmholtz scientists and Russian researchers interested in mutual cooperation. Its main tasks are to provide help for scientific partners to establish contacts, to promote joint projects and to foster the exchange of scientists, with the goal of helping initiate and establish new strategic networks of scientific excellence between Russia and Germany.

Dr. Elena Eremenko

Head of Helmholtz
Moscow Office

Russian Science Foundation

RUSSIAN SCIENCE FOUNDATION (RSF)

Dr. Alexander Khlunov

General Director of the RSF

With an annual budget of about 260 million euro (fiscal year 2016), RSF is the premier research funder in Russia providing sufficient financial support for the cutting-edge research projects in all branches of frontier science, including humanities. Scientists and scholars of any nationality and in any discipline can apply to the RSF for a grant to undertake research at the frontiers of knowledge.

Since 2014, about 35,000 project proposals have been submitted to the RSF, with, some 3,200 that have been selected to date for funding, which represents an investment of 650 million euro and 33,000 researchers, including approximately 20,000 young scientists, from more than 500 host organisations nationwide. Over 7,500 articles acknowledging RSF support were published in international peer reviewed scientific journals in 2016. At least half of each research team funded by the RSF are the young scientists aged under 39, which contributes to the training of a new generation of excellent researchers in Russia.

Through peer-reviewed competitions the most promising research projects, the best scientists are funded to perform their research in Russia. In a multi-layered decision-making process, each proposal is evaluated by 2 to 5 external reviewers from Russia and abroad exclusively according to scientific criteria; on the basis of this expert review, it is assessed by the members of an expert panel, and the final decision is made by the interdisciplinary expert council consisting of 63 members that are regularly rotated by research community on the basis of the voting process.

A new ambitious presidential programme to support early-career researchers was launched by the RSF in the spring 2017. This programme resulted in awards for 504 young scientists under the age of 33 (20,000–30,000 euros annually for 2 years with a special relocation bonus) and for 239 youth research groups (40,000–80,000 euros annually for 3–5 years). These youth-support programmes will become regular grant opportunity provided by the RSF on the yearly basis.

The RSF actively encourages international research cooperation. The Foundation participates in a number of bilateral funding schemes that provide assistance to the best Russian researchers for their participation in collaborative research projects with foreign researchers based on the principles of excellence, parity funding, credible independent peer-review and mutual trust.

The RSF secured a diversified portfolio of the bilateral collaborations with funders from Germany (DFG, Helmholtz Association), Austria (FWF), Japan (MAFF), India (DST) and Taiwan (MOST). As a result in 2017 36 international collaborative projects were co-funded by RSF in the amount of 3.6 million euro.

BERLIN – WHERE COMPUTER SCIENCE MEETS BIOLOGY

Freie Universität Berlin

Tobias Stüdemann

Liaison Office
of Freie Universität Berlin
in Moscow

The 7th Week of the Young Researcher stands in an already long line of conferences dedicated to bringing together young academics from Russia and Germany. Fostering careers in science by developing professional networks is one of the key elements of Freie Universität Berlin's career path model. Career development of young researchers is a cornerstone of the "International Network University" concept, successful in the German Excellence Initiative in 2007 and 2012. It is therefore no surprise that Freie Universität Berlin has been present at all prior weeks and has actively taken part with about half a dozen keynote speakers and more than a dozen doctoral students and young scientists. Interdisciplinary topics such as "Men and Energy", "Global History", "Discrete Geometry", and "Computational Biology and Biomedicine" are core research fields of Freie Universität, and the conference weeks have therefore been actively supported by the Moscow liaison office from the very outset.

Computational Biology and Biomedicine – the topic of the 2017 week of the young researchers – as part of the interdisciplinary area of computer science, biology, and medicine, represents a focus of the Berlin-Brandenburg region, including several Berlin-based universities and scientific institutions.

The three main formats of the Week – opening session, keynote lectures by experienced German and Russian scientists, and young researchers giving short presentation or participating in poster sessions – are open to all interested specialists and even students of the hosting institution. Early career researchers are actively involved in the conference and get a first impression on how conferences conducted entirely in English "feel." Especially in light of the rising demand to integrate oneself internationally into the scientific community, the weeks of the young researcher offer a great possibility to gain first experience. Many opportunities – not only during the lectures and scientific sessions, but also during excursions, evening receptions, and coffee breaks – are available for socializing and networking.

This year's conference location at SkolTech allowed young researchers and students to join for one or another session, which they actively did throughout the week. SkolTech was an excellent place to organize the week – close enough to Moscow to enjoy the vibrant capital of Russia, but far away to allow participants to network and intensively discuss scientific ideas.

The role of Freie Universität Berlin's liaison offices, in seven countries around the globe, is not only to attract highly talented young researchers to the exciting scientific environment in Berlin, but also to support scientists in Berlin who are interested in foreign experience to learn more about the respective regions, to motivate them to pursue a research stay abroad, and to connect with (young) colleagues, e.g., in Russia. High-level conferences, like the Week on Computational Biology and Biomedicine are ideal for fostering networks between the next generations of scientists. Although it is still a major challenge to plan scientific careers, Freie Universität Berlin offers excellent opportunities for career advancement, including structured doctorate programmes with its professional development programme and postdoc fellowships offered within the Dahlem Research School.

100K20 AND SPRINGER NATURE

Matthias Aicher

Springer Represenative Russia&CIS

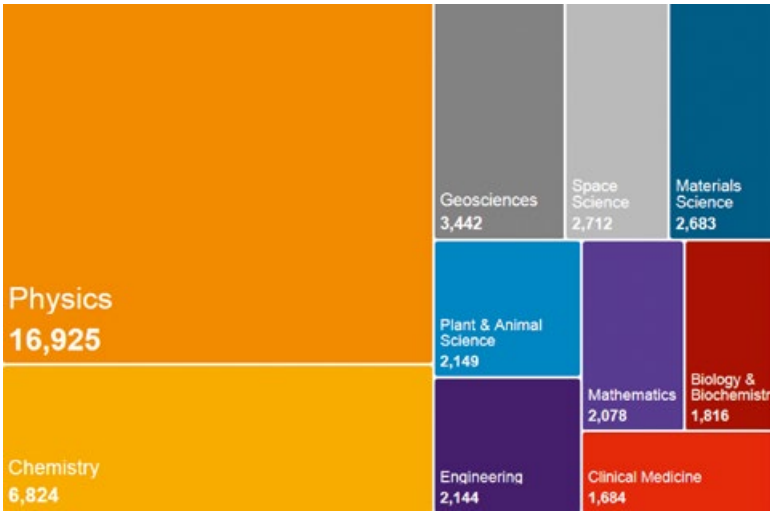
Daria Iovcheva

Senior Licensing Manager Springer Nature

Russia/Ukraine/Belarus/ Armenia/Georgia

100K20 LLC was founded as a part of the initiative which is directly reflected in the name of our company – 100 000 scientific publications by 2020. Our mission is to support Russian scientific community spreading the knowledge developed by the leaders of global science which enables researchers to communicate and promote their achievements more efficiently. We organize various seminars, master classes, consultations reaching different audiences, support authors submitting their papers for international journals, help researchers at international conferences, provide language and scientific audit.

Following one of the most important goals – providing Russian researchers with the access to world's leading scienti¬fic databases – 100K20 became the official Russian representative of Springer Nature – the largest scientific publisher of the world's most influential journals and a pioneer in the field of open research. Each year Springer Nature publishes around 2,400 English language journals and more than 9,000 books. Springer Link is one of the leading internet science portals offering over 9 million documents. Springer Nature counts more than 200 Nobel Prize laureates among its authors of books and journal articles and is presented in 25 countries worldwide, including Russia. Today more than half of all Russian articles in international journals are published by Springer Nature.



Articles published

Russia's integrity in the global research arena

The number of publications of Russian researchers in high-profile international journals has been significantly increasing during the past few years.

One of the most important drivers of the Russian growing research output is, undoubtedly, an increase in R&D expenditures. Russia ranks #10 globally by R&D spending, annual growth of which is at healthy 4% and higher than the global average (3%). Moreover, today Russia is in top 20 countries in a global rating of annual articles growth which is very much in line with R&D growth rate.

Russia's research and its article output are traditionally strong in Physics and Chemistry. This tendency is applicable to the number of published articles as well to citations of these articles.

Apart from Physics and Chemistry there are fields where Russian research output has shown significant growth in the period from 2006 to 2016. These are mostly Applied Sciences such as Materials Science (9, 5% of annual growth) and Engineering (4, 7 % of annual growth).

Talking about Russian researchers' growing success at the global scientific arena it should be noted that it also results from collaboration with their colleagues from all over the world. This collaboration is the strongest with German and American researchers. 8 other countries which make up this rating are France, England, Italy, Spain, China, Poland Switzerland and Netherlands.

Russian researchers and Springer Nature

Annual growth of articles published by Springer Nature is again in line with the overall growth of articles published by researchers from Russia – 4%. Having a quick look at the top Springer journals which publish the articles of Russian researchers is enough to see that the same fields are

in trend – Physics and Chemistry: Physics of the Solid State, Russian Journal of General Chemistry, Physical review, JETP letters etc.

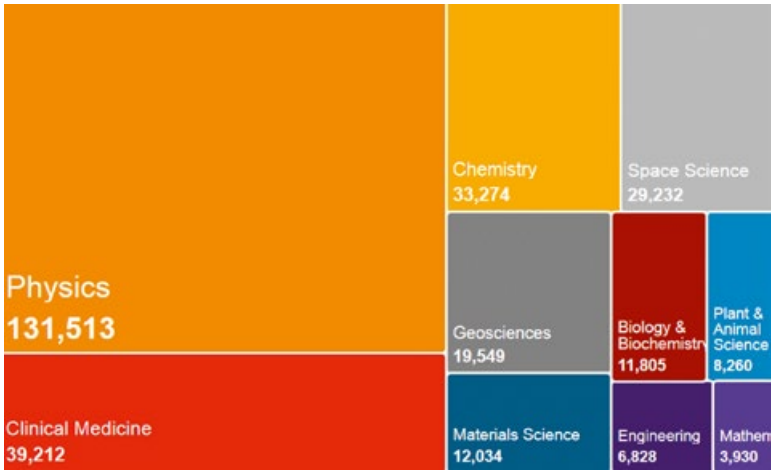
The success of Russian researchers with the journals of Nature Publishing Group is worth special mentioning. All Nature journals have exceptionally high rejection rates. The Nature journal alone receives around 12,000 papers a year, out of which about 60% are rejected without review. Around 40% of papers submitted to Nature are sent out for peer-review. At the end of the process, only 8-9% of submitted papers are published. Thus the total 1000 Russian articles published by NPG journals from 2006 to 2016 seem to be quite a high achievement, taking into account the difficulties mentioned above.

Access to global knowledge

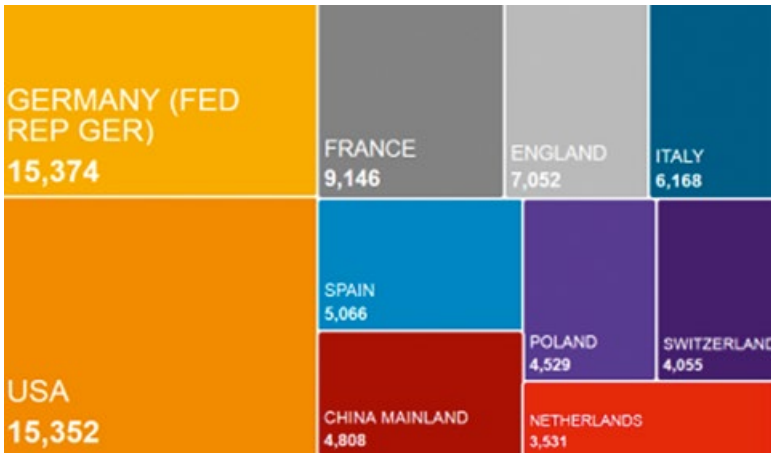
Apart from R&D expenditures, there exists yet another significant driver which results in Russia's ever growing research output. There is a direct relationship between the number of articles downloaded by a researcher or institution and the number of articles published. The access to high quality content leads to more and better research output.

Springer Nature and 100K20 share a mission to facilitate access to scientific knowledge for Russian researchers, to enable the advance of research and to help the Russian research community to improve outcomes. Today Springer Nature resources are free to access for almost 350 scientific institutions, which means that researchers can easily read and download articles and book chapters about the latest achievements, draw on them when preparing theses and dissertations, search for journals in their research area, submit articles online.

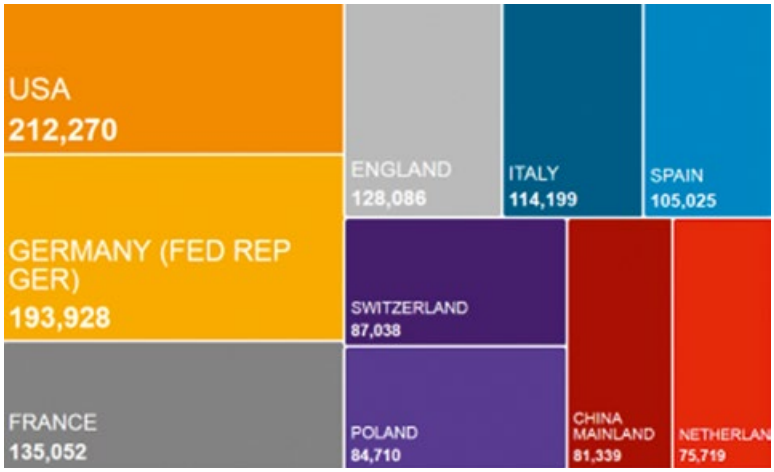
In case of any questions, please, feel free to contact 100K20 Moscow office.



Citations of the published articles



Articles published in international cooperation



Citations of these articles

LIST OF PARTICIPANTS

THE SEVENTH GERMAN RUSSIAN WEEK OF THE YOUNG RESEARCHER: COMPUTATIONAL BIOLOGY AND BIOMEDICINE

Moscow, September 11–14, 2017

TITLE	LAST NAME	FIRST NAME	STATUS / INSTITUTION
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Mr.	AMMAR	Constantin	PhD student, Institute of Bioinformatics; Graduate School of Quantitative Biosciences; Ludwig-Maximilian University of Munich
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Ms.	BARINOVA	Elena	Event Manager, Skoltech, Moscow
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Mr.	DOBIS	Michael	Head of Division for Science and Research, Embassy of the Federal Republic of Germany to the Russian Federation, Moscow
Ms.	DOBROWOLSKAYA	Natalya	Project Manager, DFG Office Russia/CIS, Moscow
Ms.	DUDOVA	Daria	Institute of Photon Technologies, Federal Scientific Research Centre "Crystallography and Photonics", RAS, Moscow
Dr.	EREMENKO	Elena	Head of Moscow Office, Helmholtz Association of German Research Centres
Prof. Dr.	FEDOROV	Maxim	Director, Center for Computational and Data-Intensive Science and Engineering, Skoltech, Moscow
Prof. Dr.	FRISHMAN	Dmitrij	Professor for Bioinformatics, Life Science Center Weihenstephan, Technical University of Munich
Prof. Dr.	GELFAND	Mikhail	Professor, Skoltech, Moscow
Prof. Dr.	GERZER	Rupert	Provost, Skolkovo Institute of Science and Technology, Moscow
Mr.	GRAF	Thomas	Head of Economic and Science Department, Embassy of the Federal Republic of Germany to the Russian Federation, Moscow

TITLE	LAST NAME	FIRST NAME	STATUS / INSTITUTION
Mr.	GROTHUS	Ulrich	Deputy Secretary General, DAAD, Bonn
Mr.	GRUBER	Markus	PhD student, Institute of Informatics, Ludwig-Maximilian University of Munich
Mr.	GULIAEV	Andrei	Research Associate, Institute of Gene Biology, RAS, Moscow
Dr.	GUPTA	Shailendra	Postdoctoral Fellow, Systems Biology and Bioinformatics, University of Rostock
Mr.	HAUSWEDELL	Hannes	PhD student, Inistute of Informatics, Freie Universität Berlin; Max Planck Inistute for Molecular Genetics
Dr.	HILLER	Peter	Head of DAAD Office Moscow, Director of DWIH Moscow
Mr.	IEVLEV	Roman	Institute of Protein Research, RAS, Pushchino
Ms.	ILINA	Julia	Project Manager, DFG Office Russia/CIS, Moscow
Ms.	IOVCHEVA	Daria	Senior Licensing Manager, Springer Nature, Russia, Ukraine, Belarus, Georgia & Armenia
Dr.	IVUKINA (GREBENIK)	Ekaterina	Leading Researcher, Institute for Regenerative Medicine, Sechenov State Medical University, Moscow
Mr.	JESKE	Tim	PhD student, Department of Pediatrics, Ludwig-Maximilian University of Munich
Ms.	KADANTSEVA	Maria	Project Coordinator, DFG Office Russia/CIS, Moscow
Mr.	KATAKA	Evans	PhD student, Genome Oriented Bioinformatics, Technical University of Munich
Mr.	KOLESNIKOV	Grigory	Project Manager, Grants4Apps, Bayer in Russia
Mr.	KONOVALOV	Sergey	Senior Expert, International Relations, Russian Science Foundation, Moscow
Dr.	KOPELEVICH	Grigory	Executive Officer for Academic Domain, Skoltech, Moscow
Mr.	KRUGLOV	Denis	Project Assistant, DWIH Office Moscow
Prof. Dr.	KULESHOV	Aleksandr	President, Skolkovo Institute of Science and Technology, Moscow
Dr.	KULIKOV	Victor	Research Scientist, Skoltech, Moscow
Dr.	LIAUDANSKI	Aleh	Institute of Genetics and Cytology National Academy of Sciences of Belarus, Minsk
Mr.	MATVEEV	Sergey	Junior Research Fellow, Skoltech, Moscow
Dr.	MAZIN	Pavel	Research Fellow, Skoltech, Moscow

TITLE	LAST NAME	FIRST NAME	STATUS / INSTITUTION
Prof. Dr.	MEWES	Werner	Technical University of Munich; Biomax Informatics AG
Mr.	MINAEV	Nikita	Institute of Photon Technologies, Federal Scientific Research Centre "Crystallography and Photonics", RAS, Moscow
Mrs.	MITINA	Aleksandra	PhD student, Skoltech, Moscow
Ms.	MÖSCH	Anja	PhD student, Graduate School of Life Sciences Weihenstephan, Technical University of Munich; Medigene Immunotherapies GmbH
Mr.	NIKITIN	Artyom	PhD student, Skoltech, Moscow
Prof. Dr.	NIKOLAEV	Evgeny	Professor, Space Center, Skoltech, Moscow
Ms.	OREKHOVA	Anastasia	Student, Lomonosov Moscow State University
Mr.	ORSHANSKY	Igor	Bayer Pharmaceuticals, Bayer, Moscow
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Ms.	PARR	Marina	Research Fellow, Lab of Bioinformatics, Peter the Great Saint Petersburg Polytechnic University; PhD student, Technical University of Munich
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Mr.	POCKRANDT	Christopher	PhD student, Research Fellow, Freie Universität Berlin
Prof. Dr.	REINERT	Knut	Institute for Informatics, Freie Universität Berlin; Max Planck Institute of Molecular Genetics
Dr.	RETHAGE	Wilma	Director, DFG Office Russia/CIS, Moscow
Mr.	RUSAKOV	Mikhail	Coordinator, DWIH Office Moscow
Ms.	SACHENKO	Victoria	Event Manager, Skoltech, Moscow
Ms.	SAVOSTINA	Anna	Project Coordination and Public Relations, DWIH Office Moscow
Mr.	SHADRIN	Dmitry	PhD student, Skoltech, Moscow
Mr.	SHAGAM	Lev	PhD student, Institute of Pediatrics, Pirogov Russian Medical University, Moscow
Mr.	SHIPILOV	Aleksey	Project Coordination and Public Relations, Helmholtz Association of German Research Centres, Moscow Office
Dr.	SHPICHKA	Anastasia	Senior Research Fellow, Sechenov First State Medical University, Moscow

TITLE	LAST NAME	FIRST NAME	STATUS / INSTITUTION
Dr.	SPANNANGL	Manuel	Group Leader, Plant Genome and Systems Biology, Helmholtz Zentrum München
Ms.	STELMASHENKO	Daria	Researcher, LLC Biosoft
Mr.	STÜDEMANN	Tobias	Head of the Liaison Office of Freie Universität Berlin in Moscow
Dr.	SVETLICHNYY	Dmitry	PhD student, Center for Data-Intensive Biomedicine and Biotechnology, Skoltech, Moscow
Dr.	TETUEV	Ruslan	Institute of Mathematical Problems of Biology – Branch of Keldysh Institute of Applied Mathematics of RAS, Pushchino, Moscow Region
Ms.	TKACHENKO	Victoria	Programmer, Institute of Systems Biology LLC, Moscow
Ms.	TSYGANKOVA	Varvara	Event Manager, Skoltech, Moscow
Mrs.	VASILIEVA	Aleksandra	Research Fellow, Lab of Bioinformatics, Peter the Great Saint Petersburg Polytechnic University; PhD student, Technical University of Munich
Mr.	WOLFIEN	Markus	PhD student, Research Fellow, Systems Biology and Bioinformatics, University of Rostock
Prof. Dr.	WOLKENHAUER	Olaf	Systems Biology and Bioinformatics, University of Rostock
Mr.	ZAIKA	Andrey	Head of Platform Development, Skoltech, Moscow
Prof. Dr.	ZIMMER	Ralf	Institute of Bioinformatics, Department of Informatics, Ludwig-Maximilian University of Munich
Mr.	ZOLOTAREV	Aleksandr	Skoltech, Moscow

PROGRAMME

SEPTEMBER 11, MONDAY

Welcome Party

19:00 **Words of Welcome** to the participants of the week by
- Dr. Peter Hiller, DWIH/DAAD Moscow
- Dr. Wilma Rethage, DFG Russia/CIS
- Professor Dr. Rupert Gerzer, Skoltech

& Introduction of the participants

SEPTEMBER 12, TUESDAY

10:00 **Registration of Participants**

10:30 **Official Opening of the Week** with welcome addresses by
- Professor Dr. Aleksandr Kuleshov, President of Skoltech
- Thomas Graf, Head of the Department for Economy and Science, Embassy of the Federal Republic of Germany in Moscow
- Professor Dr. Frank Allgöwer, Vice President of the DFG
- Ulrich Grothus, Deputy Secretary General of the DAAD

11:15 **Opening Lecture**
"Ruling over Cell Populations – a Systems Perspective on Single Cell Analysis and Control"
Professor Dr. Frank Allgöwer,
Vice-President of DFG,
University of Stuttgart, Institute for Systems Theory and Automatic Control
– Discussion –

12:40 **Lunch Break**

13:30 **Presentation of Skoltech**
Professor Dr. Rupert Gerzer,
Provost, Skoltech

14:00 **Lecture**
"Computational Methods for Discovery and Design of Bioactive Molecules"
Professor Dr. Maxim Fedorov,
Skoltech, Moscow
– Discussion –

15:00 **Coffee Break**

15:30–17:30 **Short Lectures of Young Researchers**
Chair:
- Professor Dr. Werner Mewes, Technical University of Munich; Biomax Informatics AG

15:30 **Dr. Maria Andrianova** (Skoltech, Moscow):
"Changes in Mutational Processes during Cancer Development"

15:50 **Dr. Manuel Spannagl** (Helmholtz Zentrum München,
German Research Center for Environmental Health):
"The Genoms of Western Civilization"

16:10 **Dr. Pavel Mazin** (Skoltech, Moscow):
"Adaptation of Gene Regulatory Network to Extreme Desiccation in Polypedilum vanderplanki"

16:30 **Anja Moesch** (Technical University of Munich):
"Assessment of Tumor-specific T Cell Antigens and Epitope Cross-reactivity for Cancer Immunotherapy"

16:50 **Dr. Dmitry Svetlichny** (Skoltech, Moscow):
"Deciphering the Regulation of Alternative Pre-mRNA Splicing by Coupling RBP Binding Profiles with Long-range RNA Structure"

17:10 **Tim Jeske** (Helmholtz Zentrum München):
"How to Detect the Genetic Causes of Inherited Rare Diseases in Clinics?"

19:30 **Evening Reception by the DWIH Moscow**
(German House for Research and Innovation)

SEPTEMBER 13, WEDNESDAY

09:00 **Lecture**
"Engineering Meets Biomedicine"
Professor Dr. Knut Reinert,
Freie Universität Berlin
– Discussion –

10:00 **Presentations of the Member Organisations of the DWIH**
(Deutsches Wissenschafts- und Innovationhaus / German House for Research and Innovation)
Dr. Peter Hiller,
Managing Director of the DWIH Moscow

10:30 **Science Café with the Members of the DWIH Moscow**

11:30 **Lecture**
"Three-dimensional Structure and Functional States of Chromatin"
Professor Dr. Mikhail Gelfand,
Skoltech, Moscow
– Discussion –

12:30–14:30 **Poster Session I and Lunch Break**
Chair:
• Professor Dr. Ralf Zimmer, Ludwig-Maximilian University of Munich

14:30 **Lecture**
"Reading the Future from a Tree: Evolutionary Genomics of Pathogens"
Dr. Georgy Bazykin,
Skoltech, Moscow
– Discussion –

15:30 **Lecture**
"Next-generation Sequencing: Technology and Bioinformatics"
Professor Dr. Dmitry Frishman,
Technical University of Munich
– Discussion –

16:30 **Coffee Break**

17:00 **Lecture**
"Science Theory and Medical Reality"
Professor Dr. Werner Mewes,
Technical University of Munich; Biomax Informatics AG
– Discussion –

SEPTEMBER 14, THURSDAY

09:00	**Science – Business – Innovation** **Start up and later: 20 Years' Experience** Professor Dr. Werner Mewes, Technical University of Munich; Biomax Informatics AG **Grants4Apps – Digital Health Startup Accelerator** Grigory Kolesnikov, Grants4Apps, Bayer **CoLaborator Moscow – R&D Partnering in Pharma** Igor Orshansky, Bayer Pharmaceuticals, Bayer **My-genome-enhancer: Pipeline to Find Drug Targets from Non-coding DNA** Daria Stelmashenko, Biosoft
10:30–12:00	**Poster Session II and Coffee Break** Chair: • Professor Dr. Dmitri Pervouchine, Skoltech, Moscow
12:00	**Lecture** **"Genomic Research in the Pushchino Scientific Center"** Dr. Nafisa Nazipova, Institute of Mathematical Problems of Biology RAS – the Branch of Keldysh Institute of Applied Mathematics RAS *– Discussion –*
13:00	**Lunch Break**
14:00	**Lecture** **"Opportunities for and Limitations of Modelling in the Life Sciences"** Professor Dr. Olaf Wolkenhauer, University of Rostock *– Discussion –*
15:00	**Lecture** **"Bioinformatics of a Complex Human Disease Atherosclerosis – Mechanisms and Networks of Novel Therapeutic Targets"** Professor Dr. Ralf Zimmer, Ludwig Maximilian University of Munich *– Discussion –*
16:00	**Coffee Break**
16:30	**Lecture** **"Novel Insights into RNA Biology from High Throughput Sequencing Data"** Professor Dr. Dmitri Pervouchine, Skoltech, Moscow *– Discussion –*
17:30	**Closing Remarks**


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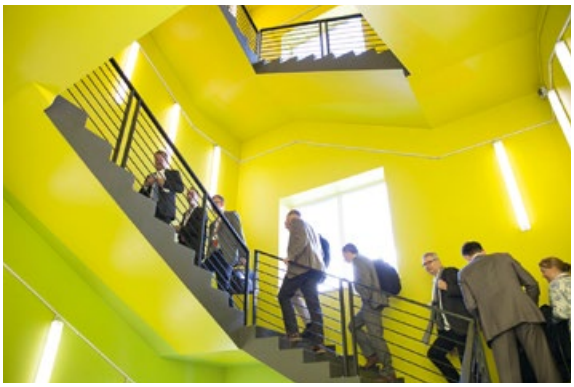


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