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Научном већу Математичког института САНУ
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ИЗВЕШТАЈ са конференције EURASIAN HEALTH & MEDICINE 2018, одржане од 03-04, новембра 2018, на Southern University of Science and Technology (SUSTech), Shenzhen, China

Поштовани,
Подносим вам кратак извештај са конференције EURASIAN HEALTH & MEDICINE 2018, одржане од 03-04, новембра 2018, на Southern University of Science and Technology (SUSTech), Shenzhen, Кина, на којој самимала 45-минутно предавање по позиву на тему: „*Sperm number, velocity and arrangement affect oscillatory behavior of mouse zona pelucida*“.

Организатори конференције су били:
Prof. dr Wang Guanyu (SUSTech, Shenzhen/Kanton, Kina)
Prof dr Mau Jochen (Düsseldorf, Nemačka)

А научни секретари конференције:
Lü Mo(SUSTech, Kina) i Jian (Medical School, Ludwig-Maximilians University-LUM Minhen, Nemačka)

Домаћин је био **Department of Biology, SUSTech, China & Guangdong Provincial Key Laboratory of Cell Microenvironment and Disease Research**. SUSTech ја релативно млад универзитет-7 година.

Конференција је једна у низу од три конференције са везаном тематиком које се баве неким аспектом здравља и медицине (биокибернетика, математички модели, молекуларна биологија, медицина...):

1. EURASIAN HEALTH & MEDICINE 2018, одржане од 03-04, новембра 2018, на Southern University of Science and Technology (SUSTech), Shenzhen, Кина, заједно са **jointly with 2nd Symposium Biodynamical Systems**
2. **БИОКИБЕРНЕТИКА 2018, 3rd Russo-German Conference MultiScale BioMathematics Coherent Modeling of Human Body System**,
Заједно са 2nd Russo-German “Young Talent” Workshop Mathematical Bio-systems Modeling. 07 - 09 November 2018., Москва, Русија
3. **1st Chinese-German Conference Comprehensive Understanding of Human Health with Impact from Person’s Surroundings**
заједно са 5th “Arbeitstreffen” German Initiative Biokybernetik Health Cybernetics - Coherent Control of Health Impacts, 10 - 12 December 2018, TRYP Dusseldorf Krefeld, Germany

Све три конференције имају четворојезични флајер: на енглеском, руском, кинеском и немачком језику.

Циљ ових конференција је покретање евроазијске интеграције у области науке на мултидисциплинарној и трансконтиненталној основи као и заједничким научним пројектима.

Предавачи су по свом основном образовању били: лекари-2, математичари-8 физичари-3, физико-хемичари-1, молекуларни биолог-1, наука о земљишту-1.

На конференцији је било 16 предавача из различитих земаља: Немачке-3 (од тога један Кнез), Русије-2, Индија-2, Кина-4, Сингапура-1, Јапана-1, Аризоне-1 и Србије-2.

Списак учесника, њихове афилијације и апстракти излагања дати су у прилогу извештаја.

У овој идеји заједничке евроазијске сарадње, мислим да би учешће требало да узме и Математички институт САНУ, наручито у области биокибернетике и математичким моделима биошких система у физиолошком стању као и патофизиолошким моделима. Уколико има заинтересованих проследићу контакте предавача са EURASIAN HEALTH & MEDICINE 2018. SUSTech, Shenzhen, Кина конференције.

У Прилогу вам достављам:

1. Позивно писмо
2. Сажетак радова са конференције
3. Пар фотографија

С Поштовањем,

Анђелка Хедрих
научни сарадник,
истраживач на пројекту ОИ174001

У Београду, 01.12. 2018.







南方科技大学
SOUTHERN UNIVERSITY OF SCIENCE AND TECHNOLOGY

July 29, 2018

To:

HEDRIH Andjelka, MD, PhD,
Department of Mechanics,
Mathematical Institute of Serbian Academy of Sciences and Arts (MI SANU),
Kneza Mihaila 3611000 Belgrade, Serbia
E-Mail: handjelka@turing.mi.sanu.ac.rs

Dear Dr. Hedrih,

EURASIAN HEALTH & MEDICINE 2018 will be held on November 03-04, 2018, at Southern University of Science and Technology (SUSTech), Shenzhen, China, with Profs. Jochen Mau (Univ of Duesseldorf, Germany) and Guanyu Wang (SUSTech, China) as Organizers, jointly with Dr. Jian Li (Univ of Munich, Germany) and Dr. Mo Lu (SUSTech, China) as Scientific Secretary to the Conference.

This conference is dedicated mainly to Theory, Computational Methods, and Experimentation in Systems Biology, but it will also reach out to other aspects of human life sphere.

The organizers enjoy the privilege to invite you to give a KEY NOTE LECTURE at EURASIAN HEALTH & MEDICINE 2018 international conference.

Topic of lecture: *Sperm number, velocity and arrangement affect oscillatory behavior of mouse zona pelucida.*

And they both sincerely hope that you will accept their invitation and share your latest insights from your field of expertise.

Your travel expenses from 02 to 05 Nov 2018 (economy class flights to and from Shenzhen) and 3 nights (Nov 02, 03, 04) accommodation during the conference will be covered, accordingly.

Looking forward to welcome you at the Conference,

Sincerely yours,

For the Organizers:
Dr. Lü(LV) Mo (吕沫)
Scientific Secretary
SUSTech

**EURASIAN HEALTH&MEDICINE 2018,
3-4 November 2018, Shenzhen, China
is hosted by
Department of Biology, SUSTech, China & Guangdong Provincial Key
Laboratory of Cell Microenvironment and Disease Research**

Contents

Eurasian Institutes visited 2008-2013	Inside (Front) Cover Page	II
Host's Welcome Address		2
Foreword		3
Conference Schedule		4
List of Abstracts		6
Speakers' Abstracts		7
TIME HAS COME since MEDICA 2008		25
BIOKYBERNETIKA 2018 07-09 Nov, Lomonosov MSU, Russia		26
BIG BRAIN 2018 10-12 Dec, Krefeld, Germany Preview		28
BIOKYBERNETIKA 2017 11-12 Dec, Krefeld, Germany		32
BIOKYBERNETIKA 2016 07-09 Nov, Lomonosov MSU, Russia		34
Site & Event Information		36
Initiative Biokybernetik 2014-2018	Inside (Back) Cover Page	III

Host's Welcome Address

It is a true pleasure for me to welcome you to **Eurasian Health & Medicine 2018**, here in Shenzhen, China. Thank you all for taking time off from your busy schedule to attend this important conference, at which I also welcome Professor Jochen Mau from Heinrich Heine University, Germany, who has the great vision of globalization in the fields of health and academic medicine and who has explored the possibility of Eurasian collaboration, since 2008. His philosophy does resonate with mine. For a long time, China advocates globalization and international collaboration to achieve all over the world higher productivity in industry and higher power of innovation in scientific research and technological development. It is thus highly significant to bring Prof. Mau from the West of the Eurasian continent to the East.

It is no surprise indeed that the first conference takes place here: Southern University of Science and Technology (SUSTech) is one of the most successful new universities in China, a platform to experiment Chinese higher education reform, with deepened internationalization and global collaboration as one major goal. As a famous Chinese saying goes: “a common belief brings people together a thousand miles away”. Today here gathers a spectrum of distinguished scientists from countries some close and some far away, for a comprehensive understanding of health and disease in human populations, with the ultimate goal of raising the health status of people to a high level and of fostering young talent to achieve highest merits in the sciences.

I am grateful to all of you who have turned the event from an idea into reality. Prof. Chuanyue Wu provided the prestigious Funds of Vice President, without which the conference could not have taken place. Drs. Chunhong Yu, Mo Lv, and Jian Li have put great efforts to help organize the conference; without their great works, particularly Dr Mo Lv’s diligent logistics contribution, the conference would not be so well-organized. My gratitude extends to all the speakers who, by delivering exciting lectures, serve as backbone of the conference. Last but not least, thanks to all the SUSTech teachers and students whose great help shaped the conference in many different ways: I can assure you that the rewards will also be great as you can learn so much about the state-of-art in academic medicine from our honorable guests during these two days.

Together, let’s now start to shape health in Eurasia. It is one continent, and health of its people is our common goal.

Guanyu WANG, PhD
Department of Biology
Southern University of Science and Technology
Shenzhen, China

Foreword Vorwort Предисловие 发刊词

EurAsian Collaboration in Health and Academic Medicine has two general objectives,

- raise the health status of the population to a high level,
- aim at highest achievement in the sciences in education of young talent.

Respective returns of investment are

- higher productivity in industry, and
 - higher power of innovation in scientific research and technological development,
- both of which are necessary for wealth and welfare of a society in global economic competition.

It is then vital to visibly occupy a key field in scientific research and to take a leading role there in international competition - and to keep this role for thirty years and more.

“*Comprehensive Understanding of Health and Disease in Human Populations*” is such a key field for which the most significant resource is a native population in its habitual space throughout the millenia, and the culture that has been molding it.

The variation on the landmass between the Yellow Sea in the East , Indian Ocean in the South, and the River Rhine in the West then make EurAsia first choice: abundant variation in territory, abundant size and variation in population (note that Russia, Central Asia, China, Pakistan and India alone account already for almost half the total world population), abundant raw material for almost all industries, abundant natural resources, abundant spread of ecosystems, cultures, and social embeddings in its uprising threshold economies.

This creates abundant options and opportunities for the young talented ambitious to reach out in the sciences for a synthesis of Western focused approaches and Eastern systems thinking towards implementation of control-engineering and mathematical systems dynamics theory in three fields that make *The Scope*,

- cellular systems biology,
- functional body-system physiology,
- human exposures and behavior in interactive cultural and economic context.

EURASIAN HEALTH & MEDICINE 2018 is then the first conference that commences to bring together a spectrum of scientists from India, Singapore, Japan, China, Russia, Germany and Serbia, for interaction about that first field. BIOKYBERNETIKA 2018 in Moscow and GeneSEES Impact 2018 in Krefeld will soon follow suit in coverage of *The Scope* and in pursuit of a *Common Ambition: Shaping health in EurAsia 亚欧地区塑造健康 формирование здоровья в Евразии Gesundheit in EurAsien gestalten.*

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Department of Biology
Southern University of Science and Technology
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MAU Jochen
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LÜ Mo
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LI Jian
Medical School
Ludwig Maximilians University
Munich, Germany

Program on Saturday 03 November 2018

08:30-09:00 WELCOME BEGRÜSSUNG ПРИВЕТСТВИЕ 欢迎

09:00-09:15 Break for **Group Photo**

09:15-10:15 DISCUSSION OF EURASIAN COLLABORATION

MAU Jochen

Medical School, Heinrich Heine University, Düsseldorf, Germany

Eurasian Health and Medicine – rationale, goals, concepts, and theory

10:15-10:30 BREAK

10:30-11:30 THE LANDMARK LECTURE

HESCHELER Jürgen

Institute for Neurophysiology, University of Cologne, Cologne, Germany

Pluripotent stem cells: A novel tool to simulate embryonic development and understand tissue regeneration

11:30-13:00 LUNCH BREAK

13:00-13:45 KEY NOTE LECTURE

ZI Zhike

Max Planck Institute for Molecular Genetics, Berlin, Germany

To survive or to die: the balance of p53 and p21 dynamics determines apoptosis response to chemotherapy

13:45-14:00 After-lunch Break

— sorry, not present this time —

LI Jian

Medical School, Ludwig-Maximilians University, Munich, Germany

The discovery of telomere activity on predicting overall survival in acute myeloid leukemia

14:00-14:45 KEY NOTE LECTURE

VASSILEVSKI Yuri

Institute of Numerical Mathematics of Russian Academy of Science, Moscow, Russia

Finite element simulation of incompressible flows in time-dependent domains and hemodynamic applications

14:45-15:30 INVITED LECTURE

SHANGERGANESH Lingeshwaran

Department of Applied Sciences, National Institute of Technology Goa, India

Finite element computations of a cancer invasion mathematical model

15:30-15:45 Afternoon Break

15:45-16:30 KEY NOTE LECTURE

VASILYEVA Nadezda

V.V. Dokuchaev Soil Science Institute, Moscow, Russia

Soil structure formation in a plant-microbe-soil interaction model

16:30-17:15 KEY NOTE LECTURE

FENG Wenting

CAAS Chinese Academy of Agricultural Sciences, Beijing, China

Controls of soil organic carbon dynamics across Chinese cropland

18:00 BANQUET

Program on Sunday 04 November 2018

08:30-09:15 KEY NOTE LECTURE

CHEN Luonan

**CAS Key Laboratory of Systems Biology, Shanghai Institutes for Biological Sciences SIBS,
Chinese Academy of Sciences, Shanghai, China**

Making short time series predictable by randomly distributed embedding

09:15-10:00 KEY NOTE LECTURE

HEDRIH Andjelka

Mathematical Institute of Serbian Academy of Science and Arts, Belgrade, Serbia

Sperm number, velocity and arrangement affect oscillatory behavior of mouse zona pelucida

10:00-10:15 Morning Break

10:15-11:15 THE KEY NOTE LECTURE ON ENDOCRINE CONTROL

KOLAR-ANIĆ Ljiljana

Faculty of Physical Chemistry, University of Belgrade, Belgrade, Serbia

Modelling the influence of stress, cholesterol and alcohol on the neuroendocrine hypothalamic-pituitary-adrenal (HPA) system

11:15-12:00 KEY NOTE LECTURE

LAI Yingcheng

School of Electrical, Computer & Energy Engineering, Arizona State University, Tempe AZ

Controlling complex nonlinear dynamical networks

12:00-13:00 LUNCH BREAK

13:00-13:45 KEY NOTE LECTURE

ZHU Jun

Institute of Bioinformatics, Zhejiang University, Hangzhou, Zhejiang, China

Association mapping for complex diseases and precision molecular medicine

13:45-13:55 Brief After-Lunch Break

13:55-14:30 INVITED LECTURE

RASHEED SA Kabeer

Duke-NUS Medical School, Singapore

GNA13 is a theranostic target that drives drug resistance and cancer stem-like phenotypes in solid tumors

14:30-15:05 INVITED LECTURE

SONI Gautam

Raman Research Institute, Bangalore, India

Measuring molecular and cellular structures and the forces that control it

15:05-15:20 Afternoon Break

15:20-15:55 KEY NOTE LECTURE

SUGHIYAMA Yuki

Institute of Industrial Science, The University of Tokyo, Japan

Pathwise analysis for a multi-type age-structured population dynamics

15:55-16:40 THE HOST'S PERSPECTIVE

WANG Guanyu

Department of Biology, SUSTech, Shenzhen, Guangdong, China

Around singularity: A big bang theory of diseases

16:40-17:00 CLOSURE AND FAREWELL

Abstracts Section: List of Contents

Speakers in latin alphabetical order

1. **CHEN Luonan** CAS Key Laboratory of Systems Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China
Making short time series predictable by randomly distributed embedding
2. **FENG Wenting** Institute of Agricultural Resources and Regional Planning, CAAS Chinese Academy of Agricultural Sciences, Beijing, China
Controls of soil organic carbon dynamics across Chinese cropland
3. **HEDRIH Andjelka** Department of Mechanics, Mathematical Institute of Serbian Academy of Science and Arts- MI SANU, Belgrade, Serbia
Sperm number, velocity and arrangement affect oscillatory behavior of mouse zona pelucida
4. **HESCHELER Jürgen** Institute for Neurophysiology, University of Cologne, Germany
Pluripotent stem cells: A novel tool to simulate embryonic development and understand tissue regeneration
5. **KOLAR-ANIĆ Ljiljana** Faculty of Physical Chemistry, University of Belgrade, Belgrade, Serbia
Modelling the influence of stress, cholesterol and alcohol on the neuroendocrine hypothalamic-pituitary-adrenal (HPA) system
6. **LAI Yingcheng** School of Electrical, Computer, and Energy Engineering, Arizona State University, Tempe, AZ, USA
Controlling complex nonlinear dynamical networks
7. **LI Jian** Institute of Medical Information, Biometry and Epidemiology, Ludwig-Maximilians University, Munich, Germany
The discovery of telomere activity on predicting overall survival in acute myeloid leukemia
8. **MAU Jochen** Medical School, Heinrich Heine University, Düsseldorf, Germany
Eurasian Health and Medicine – rationale, goals, concepts, and theory
9. **RASHEED SA Kabeer** Duke-NUS Medical School, Singapore
GNA13 is a theranostic target that drives drug resistance and cancer stem-like phenotypes in solid tumors
10. **SHANGERGANESH Lingeswaran** Department of Applied Sciences, National Institute of Technology Goa, India
Finite element computations of a cancer invasion mathematical model
11. **SONI Gautam V Raman** Research Institute, Bangalore, India
Measuring molecular and cellular structures and the forces that control it
12. **SUGHIYAMA Yuki** Institute of Industrial Science, The University of Tokyo, Japan
Pathwise analysis for a multi-type age-structured population dynamics
13. **VASILYEVA Nadezda** Interdisciplinary Laboratory for Mathematical Modeling of Soil Systems, V.V. Dokuchaev Soil Science Institute, Moscow, Russia
Soil structure formation in a plant-microbe-soil interaction model
14. **VASSILEVSKI Yuri** Institute of Numerical Mathematics of Russian Academy of Science, Moscow, Russia
Finite element simulation of incompressible flows in time-dependent domains and hemodynamic applications
15. **WANG Guanyu** Department of Biology, SUSTech, Shenzhen, Guangdong, China
Around singularity: A big bang theory of diseases
16. **ZHU Jun** Institute of Bioinformatics, Zhejiang University, Hangzhou, Zhejiang, China
Association mapping for complex diseases and precision molecular medicine
17. **ZI Zhike** Max Planck Institute for Molecular Genetics, Berlin, Germany
To Survive or to die: the balance of p53 and p21 dynamics determines apoptosis response to chemotherapy

Making Short Time Series Predictable by Randomly Distributed Embedding

Luonan Chen

Key Laboratory of Systems Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China



Future state prediction for nonlinear dynamical systems is a challenging task, particularly when only a few time series samples for high-dimensional variables are available from real-world systems. In this work, we propose a model-free framework, named randomly distributed embedding (RDE), to achieve accurate future state prediction based on short-term high-dimensional data. Specifically, from the observed data of high-dimensional variables, the RDE framework randomly generates a sufficient number of low-dimensional “nondelay embeddings” and maps each of them to a “delay embedding,” which is constructed from the data of a to be predicted target variable. Any of these mappings can perform as a low-dimensional weak predictor for future state prediction, and all of such mappings generate a distribution of predicted future states. This distribution actually patches all pieces of association information from various embeddings unbiasedly or biasedly into the whole dynamics of the target variable, which after operated by appropriate estimation strategies, creates a stronger predictor for achieving prediction in a more reliable and robust form. Through applying the RDE framework to data from both representative models and real-world systems, we reveal that a high-dimension feature is no longer an obstacle but a source of information crucial to accurate prediction for short-term data, even under noise deterioration.

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Controls of Soil Organic Carbon Dynamics across Chinese Cropland

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²Key Laboratory of Poyang Lake Watershed Agricultural Resources and Ecology of Jiangxi Province, Academy of Land Resource and Environment, Jiangxi Agricultural University, Nanchang, China



Soil organic matter is key of soil quality and health and is widely quantified by soil organic carbon (SOC). Soil organic carbon dynamics is jointly controlled by the chemistry of organic matter, climate, soil properties, microbial community, and management [1]. Improving the prediction of SOC dynamics at the large scale lies in accurate estimate of carbon (C) inputs to soils and SOC turnover time [2]. Since C inputs to soils in cropland can be estimated due to well documented data of crop yields, SOC turnover rate becomes critical for accurate prediction of SOC dynamics. The laboratory incubation is widely used but cannot well represent the turnover of slow soil C that accounts for the majority of total SOC [3], while the long-term observation of temporal changes in SOC stock offers an opportunity to estimate the turnover of slow soil C [4].

Using the time series data of SOC stock of more than thirty long-term agricultural trials that have initiated since 1990 in China, we estimated SOC turnover rates based on changes in soil C pool size and aimed to identify the dominant controls on SOC turnover rate across Chinese cropland. We used the two-pool first-order kinetic soil C model and the inverse modeling with Markov chain the Monte Carlo algorithm [5], and estimated humification coefficient (h) of C inputs to soils, turnover rates of the fast and slow soil C pools, and the transfer coefficient between these two soil C pools.

The preliminary results show that the turnover rate of slow soil C is positively correlated with climate (i.e. mean annual temperature and precipitation) but negatively correlated with the clay content, demonstrating that the clay content is important in regulating SOC turnover rates. The ratio of humification coefficient to C turnover rate (h/k), which indicates soil C sequestration efficiency, is negatively correlated with climate and positively correlated with the clay content. In addition, the quantity of C inputs is correlated with h/k and the turnover rate of slow soil C, suggesting that the quantity of C inputs plays an important role in mediating C sequestration efficiency. The results could inform us the drivers of SOC dynamics in Chinese cropland and provide guidance how management SOC in Chinese cropland properly.

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Sperm Number, Velocity and Arrangement Affect Oscillatory Behavior of Mouse Zona Pelucida

Andjelka Hedrih

Department of Mechanics, Mathematical Institute of Serbian Academy of Science and Arts- MI SANU, Belgrade, Serbia



The fertilization on cellular level could be considered as an oscillatory phenomenon [1]. During the process of fertilization many spermatozoa will influence the oocyte surface-zona pelucida (ZP). Spermatozoa are motile cells and in ejaculate there are with different velocities and morphological characteristics. Only 10% are functionally capable of fertilizing the oocyte. During the external impact of spermatozoa certain amount of kinetic energy is transfer to ZP. Numbers of progressively motile spermatozoa, as well as their kinetic characteristics are crucial for fertilization success [2]. Different distributions of spermatozoa with same/different kinetic parameters result in different distributions of external forces acting on the ZP surface [3].

To study interaction between ZP and sperm cell we create discreet continuum biomechanical oscillatory model of mouse zona pelucida (mZP) [4, 5]. According to this model, mZP is considered to be a spherical net consisting of crosslinked chains in meridian and circular directions. Knot molecules in the net correspond to mZP1 glycoproteins. The molar ratio and the masses of mZP glycoproteins are included into the model. If there is only an initial perturbation by kinetic and potential energy given to ZP oscillatory structures, the ZP oscillatory net starts to oscillate.

Using generalized Lussajous curves we analyzed the impact of sperm number, velocity and arrangement on resultant trajectories of knot molecules in mZP spherical net model. The influence of sperm number, velocity and its arrangement on resultant trajectory motion of corresponding mZP molecules are discussed in context for achieving favorable oscillatory state of mZP for successful fertilization. Component displacements in the meridian and circular directions of the knot molecules represent multi-frequency oscillations. The resultant trajectories of ZP knot molecules in the tangent plane to the sphere net are described by generalized Lissajous curves that could be of straight lines, periodic, non-periodic, or stochastic like curves. Determining the optimal spermatozoa impact parameters that will induce a ZP favorable oscillatory state opens the possibilities for more complete explanation of the fertilization process and application of bio-mechanical approach in male sub(in)fertility treatment.

Acknowledgements: Parts of this research is supported by the Ministry of Sciences and Technology of Republic of Serbia through Mathematical Institute SASA, Belgrade Grant ON174001 "Dynamics of hybrid systems with complex structures, Mechanics of materials."

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Pluripotent Stem Cells: A Novel Tool to Simulate Embryonic Development and Understand Tissue Regeneration

Jürgen Hescheler

Institute for Neurophysiology, University of Cologne, Cologne, Germany



It is our aim to provide a fundamental basis to the development of new medical treatments. This presentation will give an overview on our recent research work on human embryonic in comparison with induced pluripotent stem cells. Starting from basic investigations on the physiological properties of cardiomyocytes developed from pluripotent stem cells we have established *in vitro* and *in vivo* transplantation models enabling us to systematically investigate and optimize the physiological integration and regeneration of the diseased tissue. Our main focus is the cardiac infarction model. Induced pluripotent stem cell-derived cardiomyocytes (iPSCM) are regarded as the most promising cell type for cardiac cell replacement therapy. iPS cells are functionally highly similar to embryonic stem (ES) cells, but in addition have the advantage of being ethically uncontroversial and obtainable from readily accessible autologous sources. Moreover, iPSCMs also provide an interesting new tool to study the pathophysiology of monogenetic diseases of the cardiovascular system. A functional integration of iPSCMs is crucial for efficiency and safety, but has not been demonstrated, yet. Thus, we investigated the electrical integration of transplanted cardiomyocytes into host tissue.

Translation from the laboratory into the clinic is one of the key problems of stem cell research. After proof of principle for the therapeutic use of iPS cells in cardiac diseases has been shown both at the laboratory scale and in animal models, the methods used today for generation, cultivation, differentiation and selection are now adopted to the clinic enabling respective clinical trials. In this presentation I also will share our visions on the future of tissue regeneration with respect to interventional medicine in the three health sectors - prevention, clinical care and long-term nursing. Moreover, on a more fundamental level stem cells will be discussed as a novel tool to simulate and understand the basic biological mechanisms underlying the development of organs during embryogenesis and regeneration in our adult body.

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Modelling the Influence of Stress, Cholesterol and Alcohol on the Neuroendocrine Hypothalamic-Pituitary-Adrenal (HPA) System

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The state of the human body is above all defined by the state of the neuroendocrine systems, where the hypothalamic-pituitary-adrenal (HPA) axis has the main role. The HPA axis is a typical nonlinear biological system that is naturally in the oscillatory state. Oscillatory HPA axis dynamics is caused by internal self-organized phenomena but also by external periodic variations of, for example, temperature, light, food or seasonal changes. The HPA axis hormones, such as cortisol, aldosterone *etc.*, exhibit complex oscillatory behavior with two characteristic frequencies: ultradian oscillations, with a period between 20-120 min, superimposed on circadian oscillations, with a period of about 24 h.

HPA axis is sensitive to external and internal perturbations known as stress, exemplified here by variation of corticotropin-releasing hormone (CRH), cholesterol and alcohol concentration. To simulate the effect of stress on the HPA axis dynamics, mathematical modelling of the time evolution of essential HPA axis hormone concentrations based on the stoichiometric relations between them is used. [1] For this purpose, we present a low-dimensional model of the HPA axis [2,3] and show that the model can be easily expanded to account for additional reactions and additional species, such as internal and external cholesterol [4,5], which is the only precursor of steroid hormones and, also, ethanol, which in this model plays the role of a typical external species [6]

Besides, the advantage of stoichiometric approach to modelling complex nonlinear biochemical systems and their response to stress is demonstrated.

Acknowledgements: Support by the Ministry of Sciences and Technology of Republic of Serbia, Grants ON172015 and III45001, is gratefully acknowledged.

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Controlling Complex Nonlinear Dynamical Networks

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We discuss a framework to control nonlinear dynamical networks whereby we nudge the system from attractor to attractor through small perturbations to a set of experimentally feasible parameters [1]. This principle enables us to formulate a controllability framework for nonlinear dynamical networks, which we illustrate using a class of synthetic biological networks. We also discuss recent results on controlling tipping point dynamics in complex mutualistic networks and gene regulatory networks [2,3]. Time permitting, we will address the issue of whether linear controllability of complex networks is relevant to the real world [4].

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The Discovery of Telomere Activity on Predicting Overall Survival in Acute Myeloid Leukemia

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A telomere is a region of repetitive nucleotide sequences, which locates at the end of a chromosome. There are two main functions exerted by a telomere: stabilization of chromosomes by protecting chromosomes from recombination and end-to-end fusion [1]; and contribution to DNA replication by providing last RNA primers sequence attachments in the Okazaki fragments [2]. Based on this principle, a study developed a calculation formula for estimation of the age of human with the length of telomere [3]. Cawthon and colleagues showed that persons with shorter telomeres in blood DNA had poorer survival and immune systems, which contributed to high mortality rate from different diseases [4]. In order to prevent the critical loss of telomere for preserving pluripotent of stem cells as well as ability for tumorigenesis for the majority of cancer cells, the complex enzyme telomerase is expressed that uses TERC (telomerase RNA component) as template and catalyzes the addition of telomeric repetitive sequences to G-strand 3' end [5]. Diverse studies provide evidence that mutations in genes encoding components of the telomerase complex result in its dysfunctions, which predispose to different human disease including cancer [6]. In 2005, Huh and colleagues discovered the potential prognosis value of hTERT, the main component of the complex enzyme telomerase, regarding the development of acute myeloid leukemia (AML). This study proposes that serial and quantitative analysis of hTERT (human telomerase reverse transcriptase) mRNA may be a useful marker for prediction of prognosis and monitoring in AML patients [7]. A more recent study demonstrated that the telomerase inhibition effectively delays AML onset in murine AML cell line and prolongs overall survival of patient-driven xenograft in AML following chemotherapy. Furthermore, the authors discovered relevant molecular mechanisms related to telomerase deficiency in leukemic stem cells, which is highly associated with diverse pathways related to cell-cycle arrest, p53 activation and programmed cell death [8].

In order to analyze overall survival (OS) of these AML patients, our study applied our implemented cancer hallmarks to created an univariate Cox-model with hallmarks for OS of each patient-cohort. For the study of AMLSG cohort, we found out that LRP ($p < 0.00001$), Sustained-Angiogenesis (SA) ($p = 0.0435$) and Cell-Cycle-Progression (CCP) ($p < 0.00001$) can significantly improve the accuracy of univariate Cox-model for OS. For the HOVON cohort, we found out that LRP ($p < 0.00001$) and Drug-Resistance (DR) ($p < 0.00001$) can significantly improve the univariate Cox-model for OS. For the TCGA cohort, LRP ($p < 0.00001$) and SA (0.0003) can significantly improve the univariate Cox-model for OS. Based on our results, we verified that the cancer hallmarks possess interesting predicting power regarding the OS of AML.

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Eurasian Health and Medicine – Rationale, Goals, Concepts, and Theory

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It is one piece of land, and while I cannot swim across the Atlantic, nor across the Pacific, I may follow the sun from Yellow Sea to River Rhine. It is one space of migrations throughout the millenia, then, and people are tied in suffering from common tragedies but left with the legacy to now jointly exploit the common opportunities that they share on their one piece of land.

While fundamental medicine establishes the scientific principles that doctors apply in prevention and care, the practice of medicine can manifest itself only in prevailing life-sphere context: “Statistical patients” lack reality for the practicing doctor: “klinisches Wissen ist die immer wieder überprüfte Erfahrung vieler Generationen von Ärzten” (S. Koller) [*clinical knowledge is the ever re-tested experience of many generations of medical doctors*] is just a paraphrase of this observation.

Really thrilling is that spectacular spread across Eurasian landmass – in terms of genetic dispositions, environmental exposures, economic opportunities and social embeddings within societal references: “Streuung gibt Erkenntnis” (S. Koller) [*discovery occurs with the study of variation*] makes a strong motivation for transdisciplinary scientific research into unknown etiology of disease and not understood variation in accuracy of diagnostics or in patient's response to medical treatment: To establish constants or gradients along pre-defined paths of life-shaping exposures are among the goals of collaborative research on transcontinental variants.

A first feasibility overview in selected regions along a 10 kms path from German North-Rhine Westphalia via Moscow and Samara (Volga) into West, Central and East China, with Chengdu (Sichuan), Zhengzhou (Henan), Beijing, Shanghai, and Hangzhou (Zhejiang), considered the infrastructure for clinical interventions (functional stimulation, immuno-competence strengthening, tissue reperfusion, regeneration, and replacement), for care in six cerebral diseases (epilepsy, multiple sclerosis, ischemic stroke, vascular and degenerative dementia, Parkinson disease), in three health-sectors (prevention, clinical management, long-term nursing); a second overview considered infrastructure for molecular research on *Human Genome-Proteome Environment Interaction* (HuGePEI) and resources for implied population studies.

Competences were found to be split into separate administrations – in different ways, between countries, but also between regions in the same country. Clinical structures and cultures, professional education and experience, seem more important issues than an often quite advanced equipment; motivation was the most impressive, though. Identified prerequisites are lasting mutual-benefit partnership within and between regional consortia, post-graduate qualification for transcontinental collaboration, harmonized methodology, and transnational supervision and control. Advance training for convergence shall promote collaboration readiness [1].

The theory challenge is to find a crystallization core for the talent and zeal in all involved sciences. A recent approach, *Biokybernetik*, separates material (cells) from function (physiology) towards a theory of multi-scale effectuation dynamics inside human-body system, the Whole [2], that also lends itself to model impact from Whole's life-sphere surroundings and thus to a rather comprehensive mathematical modeling of Whole's health in a future algorithmic medicine, but also as an entry point for coherent control of outside impact. It thus provides a challenge of last to an outreaching collaboration of Eurasia's young science – the “Big Brain”.

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GNA13 is a Theranostic Target that Drives Drug Resistance and Cancer Stem-like Phenotypes in Solid Tumors

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Despite considerable advancement in therapeutic strategies cancer-induced mortality and morbidity is still on the rise throughout the world. Drug resistance, tumor recurrence and metastasis are three major reasons for deaths due to cancers. Most of these aggressive traits are attributed to a small population of cells within the tumor called as cancer stem cells (CSCs) or tumor initiating cells (TICs). Interestingly, new emerging data points out that CSCs/TICs to survive longer also activate mechanisms to evade immune system mediated destruction of cancers. Identifying novel biomarkers and understanding the mechanisms that support TICs/CSCs is required to enhance therapeutic outcomes in the future.

G protein coupled receptors (GPCRs) are the largest class of cell surface receptors that play a major role in human development, physiology and disease states such as cancer. Recently, multiple GPCRs including CXCR4, CXCR1/2, LPAR1-4, PAR-1 are known to be upregulated in many solid tumors and mediate cancer cell invasion, metastasis and induction of Epithelial to Mesenchymal transition (EMT) and CSC/TIC-like phenotypes. Interestingly, most of these GPCRs mediate signalling through G12 proteins.

G12 proteins comprising two family members; G α 12 (encoded by GNA12) and G α 13 (encoded by GNA13) are heterotrimeric guanine nucleotide binding alpha proteins that mediate signalling through G protein coupled receptors (GPCRs). Most importantly both GNA12 and GNA13 are reported to be upregulated in breast, prostate, gastric and head and neck cancers. We and others have shown that blocking GNA12 and GNA13 expression or their activity suppresses cancer invasion and metastasis significantly in many solid tumors(1, 2). Recently, we have shown that GNA13 is a biomarker and drives multiple drug resistance by inducing CSC/TIC-like phenotypes in head and neck (HNSCC) and breast cancers(3). Currently, Dr. Rasheed's lab at Duke-NUS Medical School, Singapore, is focusing on two major questions; (1) What are the specific mechanisms that drive GNA13-induced CSC/TICs and drug resistance? and (2) Is targeting GNA13 a viable strategy to eliminate CSC/TICs mediated drug resistance in solid tumors.

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Finite Element Computations of a Cancer Invasion Mathematical Model

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Mathematical model is one of the useful and inexpensive approaches to determine and predict the stage, size and progression of tumors in realistic geometries. Moreover, these models can be used to get an insight into the cancer growth and invasion. Further, they can also be used to analyze the tumor size and shape for cancer treatment and surgical plannings. The invasion of cancer cells is modeled either by using a discrete cell-based approach that focus on individual cell behaviors [1] or by using a continuum approach [2] that deals with the evolution of the cancer cell densities. Under the assumption that the initial number of tumor cells are relatively small, one can get computationally reasonable results using the discrete cancer invasion model. However, the above assumption is too strong to identify clinically significant size of tumor with the current imaging techniques such as MRI, CT-Scan etc. Therefore, we consider the continuum tumor invasion mathematical model in this study.

In this talk, we consider a highly nonlinear coupled cancer invasion 3D model with density-dependent diffusion and haptotaxis functions. The interactions of cancer cell density with the ECM density and the degradation of the ECM by producing MDE concentration are modeled. Moreover, a nonlinear density-dependent diffusion and haptotactic sensitive functions are incorporated into the model. The considered mathematical model focuses on the spatial competition between cancer cells and host tissues. In addition, the considered model is capable of explaining the invasion of avascular tumors and metastasis behaviors of the cancer cells in a detailed manner. Further, the finite element scheme for solving a tumor model on realistic 3D domain is proposed as in [3]. In addition to the convergence study and the grid independence test, the proposed scheme is validated using an existing numerical results presented in the literature. The proposed finite element scheme is also implemented for the model with various density-dependent nonlinear diffusion and haptotactic sensitivity functions.

A sequence of computations are performed in order to understand the spatio-temporal behaviors of the cancer invasion process for different nonlinear density-dependent diffusion and haptotactic sensitive functions. Suppose the diffusion function is directly proportional to the MDE concentration, we observed that the migration cancer cells towards the ECM domain is not identical with the constant diffusion rate. However, the cancer cell migration in all other nonlinear diffusion cases is comparable with the constant diffusion. Similarly tumour invasion pattern morphologies formed by Michaelis- Menten kinetics and cooperative binding haptotactic functions are highly distinguishable with other haptotaxis models. Furthermore, an array of computations of cancer invasion in realistic breast geometry are performed. Grid independence test for the considered realistic geometry is performed with various mesh levels using millions of tetrahedral cells. To get an insight into the cancer invasion on realistic geometries, computational results are presented for different combinations of density-dependent diffusion and haptotactic sensitive functions. Since the boundary effects influence the cancer invasion significantly, it is important to consider a realistic geometry in practical applications. Finally, the proposed computational model can be used to predict the location and the shape of the tumor in realistic geometries at a particular instance during the cancer growth and invasion.

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Measuring Molecular and Cellular Structures and the Forces That Control It

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Structure and Function are deeply connected concepts in self-assembled biological systems. Interactions forces, crowding, shape and deformability, charge and active/passive motion are some of the biophysical parameters that shape and modulate biological structures and their function. This happens at both molecular scale, Chromatin is one excellent example of this, as well as at the cellular scale (cell shape and stiffness). Failure of any of these structural elements lead to various diseases and disorders. Main aim of our work is to precisely measure the molecular interactions that underlie these structures and then to understand the biophysical principles of disease causing changes therein. In this talk, I will introduce you to the various experimental approaches we build and employ to understand molecular and cellular structure. I will talk about high-resolution single molecule measurements on chromatin system using the nanopore and AFM platforms and a novel in-house developed electro-fluidic method to measure single-cell volume and stiffness [1-5].

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Pathwise Analysis for a Multi-type Age-structured Population Dynamics

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Control of the stationary population growth rate, which represents the averaged expansion rate of the total population size, is ubiquitous problem in many fields. In medical treatment, we attempt to diminish the growing speed of a population composed of cancer cells or pathogens by using antibiotics or some specific treatment. In the context of evolutionary biology, to survive in a fluctuating environment, cells maximize (optimize) their population growth by exploiting a bet-hedging strategy for adaptation to the environmental fluctuation. Theoretical studies to evaluate the stationary population growth rate and analyze its behavior have been often conducted by ordinary- or partial-differential equation approaches by focusing on the time-slice distribution of the population. In these approaches, the problems are mostly reduced to eigenvalue problem for a time evolution operator of a differential equation under an appropriate boundary condition.

Recent development of experimental devices has enabled us to observe a lineage tree data, which describes a growing cell population with hundreds of cells over hundreds generations. From the lineage data, we can obtain the information of mother-daughter relationship and inter-division interval (cell cycle), which can never be directly accessible in the time-slice observations. In order to analyze the lineage data, a pathwise approach have recently developed, instead of the conventional differential equation approaches. Main actors of this approach are two kinds of genealogical paths on a lineage tree: time-forward and time-backward (retrospective) paths. By using these two genealogical paths, we can evaluate the stationary population growth rate and selection strength that exists in the growing population. Furthermore, owing to this framework, a response relation of the stationary population growth rate is revealed. To be more precise, the response coefficients can be evaluated by a statistics on a retrospective path, which can be measured in an experiment.

In this talk, we see the pathwise structure introduced above, under a multi-type age-structured population dynamics (MTASP), which has an age-dependent cell replication and type transition. In analysis of the MTASP, the large deviation technique for semi-Markov processes plays an important role. As a result, we find that the response coefficients of the stationary growth rate with respect to environmental changes can be evaluated by retrospective tracking on cells lineage tree.

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Soil Structure Formation in a Plant-Microbe-Soil Interaction Model

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To tackle soil evolution mechanisms providing stability and resilience to climate and land-use changes we develop a model of soil carbon dynamics in granulo-densimetric fractions with a feedback to soil aggregation process. Turnover rates of microbially-driven soil organic matter (SOM) transformations are dynamic and affected by SOM localization and physical protection mechanisms and climatic factors. Aggregation process is a result of fast transformation cycle of labile SOM in rhizosphere.

In this study we continue to develop a multiscale model of SOM transformation with a self-organization of soil pore space as a result of microbial growth with effects of temperature, water and oxygen [1, 2, 3]. The concept comprises consideration of SOM in granulo-densimetric fractions (by particles size and density). SOM transformations between fractions occur due to microbial activity. Spatial patterns of microbial activity in turn define waterstable aggregate size distribution.

Objects. Model parametrization was based on experimental data of several long-term bare fallow (LTBF) experiments (network for isolation of stable SOM) and laboratory measurements of soil respiration in series of moisture and temperature for LTBF (stable SOM) and grassland (labile SOM) soils.

Results. Revealed are two driving parameters which together with climatic data were sufficient to describe the differences in C dynamics between experimental sites. The first one is the characteristic C concentration (an overall scaling parameter that adjusts to C input). The second is a SOM stabilization parameter representing concentration of “adsorption sites” (on mineral or black carbon particles) that affects SOM decomposition rates. Discussed are long-term dynamics at different scenarios of climate and land use changes.

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Finite Element Simulation of Incompressible Flows in Time-dependent Domains and Hemodynamic Applications

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We present a stable finite-element scheme for incompressible flows in time-dependent domains. The time step is independent of the mesh size, and only one linear system is solved on each time step. We consider fluid-structure interaction (FSI) and Navier-Stokes equations in time-dependent domains. The properties of the scheme are shown on several benchmarks and hemodynamic applications.

In particular, we address 2D and 3D flows in blood vessels with nonlinear hyperelastic models of wall, steady and periodic interactions between a viscous incompressible fluid and a nonlinear solid filament in a 3D setting for which experimental data are collected using phase-contrast magnetic resonance imaging. We also present simulation of a flow in a model of the left ventricle of a human heart, where the ventricle wall dynamics is reconstructed from a sequence of contrast enhanced Computed Tomography images.

This is the joint work with Maxim Olshanskii (University of Houston), Alexander Danilov, Alexander Lozovskiy and Victoria Salamatova (INM RAS, MIPT).

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Around Singularity: A Big Bang Theory of Diseases

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A complex disease involves many etiological and risk factors operating at multiple levels—molecular, cellular, organismal, and environmental. The incidence of such diseases as cancer, obesity, and diabetes are increasing in occurrence, urging us to think fundamentally and use a broader perspective to identify their connection and revolutionize treatments. The understanding of biological data derived from studying diseases can be enhanced by theories and mathematical models, which clarify the big picture and help to reveal the overarching mechanisms that govern complex biological phenomena.

Focusing on diseases related to aging, such as cancer, diabetes, and Alzheimer's disease, in this talk I present a holistic approach for illuminating the molecular mechanisms of these diseases and the evolutionary underpinning of their simultaneous epidemics. Using mathematics to identify patterns of deviation from normality, or the healthy state—spanning multiple levels from molecules to the organism—I identify a range of dynamical behaviors that correspond to either cellular physiology or pathology and use the information from multiple levels to present a unified theory, which includes the discovery that certain diseases may stem from well evolved, useful mechanisms activated in the wrong context.

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Association Mapping for Complex Diseases and Precision Molecular Medicine

Jun Zhu

Institute of Bioinformatics, Zhejiang University, Hangzhou, China



Many human diseases are complex diseases attributed by multiple genes with genetic effects and their environment interactions. We developed software QTXNetwork for association analyses of complex diseases with genetic variants and their ethnic specific effects. Quantitative Trait SNPs (QTSs) were detected for Total Cholesterol (TC) by three different models: 15 QTSs (13 individual loci and 3 epistases loci) by full model, 2 QTS by GCTA method and only one QTS by PLINK method. Influence of smoking on human BMI was analyzed, there were 11 QTSs detected for BMI, but 18 QTSs for BMI|Cig. When quite smoking, there were 6 female-specific loci will decrease

BMI, but one large epistasis effect can increase BMI for both man and woman. Calibrated Factor VIII was affected by human physical activities (10 QTSs and 14 epistatic QTSs). The identified FVIII-associated genetic variants were known to be linked to cardiovascular events. We detected 20 QTSs highly associated to Alcohol dependence, including four previously reported genes (ADH1C, PKNOX2, CPE and KCNB2). Highly significant association was also identified in variants within four novel genes (RGS6, FMN1, NRM and BPTF), two non-coding RNA and two epistasis loci. We identified 34 QTSs related to emotional social support index (ESSI), and found that smoking and other lifestyles could play important roles on genetic effects in the perturbation of human emotion. For analyzing startle responses in *Drosophila melanogaster*, we identified 33 quantitative trait SNPs (QTSs), and also 81 quantitative trait transcripts (QTTs) directly associated with phenotypic variation of startle response in, 20 transcripts controlled by QTSs (tQTSs), and 73 transcripts controlled by QTTs (tQTTs).

References

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- [2] Zhu J. Analysis of conditional genetic effects and variance components in developmental genetics. *Genetics*, **141(4)**: 1633-1639, 1995.
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To Survive or to Die: the Balance of p53 and p21 Dynamics Determines Apoptosis Response to Chemotherapy

Marijn TM van Jaarsveld¹, Difan Deng¹, Erik AC Wiemer², Zhike Zi^{1,*}

¹Max Planck Institute for Molecular Genetics, Otto Warburg Laboratory, Berlin, Germany

²Erasmus MC Cancer Institute, Department of Medical Oncology, Rotterdam, The Netherlands



The DNA damage response (DDR) protects cells against genomic instability. Surprisingly little is known about differences in DDR across tissues, which may affect cancer evolutionary trajectories and chemotherapy response. Using mathematical modeling and quantitative experiments, we found that the DDR is regulated differently in human breast and lung primary cells. Equal levels of cisplatin-DNA lesions caused stronger Chk1 activation in lung cells, leading to resistance. In contrast, breast cells were more resistant and showed more Chk2 activation in response to doxorubicin. Further analyses indicate that Chk1 activity played a regulatory role in p53 phosphorylation, whereas Chk2 activity was essential for p53 activation and p21 expression. We propose a novel “friction model”, in which the balance of p53 and p21 levels determines the apoptotic response in different tissues. Our results suggest that modulating the balance of p53 and p21 dynamics could optimize the response to chemotherapy.

References

[1] van Jaarsveld MT, Deng D, Wiemer EA, Zi Z. Tissue-specific Chk1 activation determines apoptosis by regulating the balance of p53 and p21. 2018 (submitted).

Notes

TIME HAS COME

since MEDICA2008 World Fair of Medicine, Düsseldorf Germany

“One Continent, One Mission – Health in Eurasia”

一洲、一志：亚欧地区健康

“Westwards, we cannot cross the Atlantic as fish do; it is to the East that we can walk – right to the Pacific.” The epidemiologist Jochen Mau considers Eurasia as a walkable landmass, in fact throughout the millennia. “People follow the sun to the West, whilst our dreams go with the winds to the East.” The professor likes to recall the shared history when looking at the current expansion of the Eastern economic powers to the West. ...The fascination, that the melancholy of the Russian landscape and the mystical exoticness of China evoke, explains Jochen Mau with the genetic traces left from the surviving wounded Huns and Mongols, which leads him to address his colleagues in China as “Brother” or “Sister”.

“Health in Eurasia” is the vision of *equivalent health care, equivalent medical service and equivalent nursing* for people from and across Eurasia.

Towards this goal, the Düsseldorf medical scientist is building a network with selected medical universities in North Rhine-Westphalia, Russia and China for long-term collaborations in public health and advanced clinical training, in research and development. The professor considers mutual acquaintance with local clinical practice, advanced training for concerted research, and research coaching as essential preparations for his large-scale transcontinental research programs. (Excerpt from MEDICA 2008 Press Release, 22 October 2008.)

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<p style="text-align: center;">BIOKYBERNETIKA 2018 Lomonosov Moscow State University</p> <p style="text-align: center;">3rd Russo-German Conference MultiScale BioMathematics – Coherent Modeling of Human Body System and 2nd Russo-German “Young Talent” Workshop Mathematical Bio-systems Modeling</p> <p style="text-align: center;">07 - 09 November 2018 Lomonosov Moscow State University</p> <p style="text-align: center;">Organizers acad. prof. Boris N. Chetveryshkin prof. Jochen Mau prof. Sergey V. Bogomolov prof. Sergey I. Mukhin</p> <p><small>* Design: Prof. Dr. J. Mau, Buschstr. 9, 47800 Krefeld. © 2018, Institut für Quantitative Methodik - Privates Akademisches Beratungsbüro für Forschung und Entwicklung</small></p>	<p style="text-align: center;">Background and Objectives</p> <p>"Biokybernetik" is the "systematics of control for good cooperation of 'functional ensembles' in human body". As such cooperation expresses in energy transfers between components on and between several functional levels, biokybernetik is at the basis of "multi-scale biomathematical modelling of energy transfer dynamics in body system".</p> <p>Conferences BIOKYBERNETIKA aim to combine bio-systems modeling and clinical characterizations for a holistic understanding of human body's inside functional and person's outside-world operational management and control systems from an engineering science perspective.</p> <p>Supplemental Conferences GeneSEES Impact aim to assess variants in outside-world impact on body system's functioning and person's health in Eurasian populations from East to West.</p> <p>3rd Russian-German Conference on MultiScale Biomathematics - Coherent Modeling of Human Body System aims to address in particular, not exclusively,</p> <ul style="list-style-type: none">• mathematical topics in complex systems models,• modeling the human cardiovascular system,• modeling the human body immune system. <p>2nd Russian-German Young Talent Workshop / молодёжная школа / Nachwuchsachule on Mathematical Bio-systems Modeling aims to foster the next generation of scientists in mathematical bio-systems modeling for collaborative research.</p> <p style="text-align: center;">Venue Moscow State Univ., 2nd Educat¹ Bldg, CMC Fac., Leninskie Gory, GSP-1, 119991 Moscow, Russia. РФ 119991 Москва, ГСП-1, Ленинские горы, МГУ, 2-й учебный корпус, ф-т ВМК</p> <p style="text-align: center;">Organizers Acad. Prof. Boris N. Chetveryshkin (MSU Lomonosov) Prof. Jochen Mau (University Düsseldorf) Prof. Sergey V. Bogomolov (MSU Lomonosov) Prof. Sergey I. Mukhin (MSU Lomonosov)</p>
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Confirmed Foreign Speakers

HENRION René Dr Sc , Principal Investigator

Weierstrass Institute of Applied Analysis and Stochastics (WIAS), ResGrp Nonlinear Optimization and Inverse Problems, Berlin, DE

Optimization problems under probabilistic constraints

Проблемы оптимизации с вероятностными ограничениями

MAU Jochen Prof Dr rer nat habil

Heinrich Heine University, School of Medicine, Düsseldorf, DE

On Identification of Effectuation Dynamics in System Function Architecture

Zur Identifikation der Wirk-Dynamik in der System-Funktions-Architektur

YONG Wen-An Prof Dr rer nat habil

Tsinghua University, Zhou Pei-Yuan Center for Applied Mathematics, Beijing, China

TBA

БИОКИВЕРНЕТИКА 2018г

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Богомолв Сергей В. (МГУ)
Мухин Сергей И. (МГУ)**

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г Москва, МГУ, Россия**

EURASIAN COLLABORATION 2018

2018 年亚欧地区合作会议

Конференция по сотрудничеству в Евразии 2018г

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BIG BRAIN 2018
 Conference for Interdisciplinary Collaborations in Building Neuro-Body System
 Конференция по сотрудничеству в Евразии 2018г
 पूर्व-पश्चात्य जीवविज्ञानम्-2018

w/ TUTORIAL *Systems Theory for Collaboration in Eurasian Health & Medicine*

5th "Arbeitsreffen" of German Initiative Biocybernetik: Health Cybernetics - Coherent Control of Health Impacts
 Organizers: MAU, Leoben, HNU, Düsseldorf, Germany
 MIEBZHIN S.L., Lomonosov MSU, Russia

2nd Transcontinental Conference GeneSEES Impact 2018
 "Comprehensive Understanding of Human Health and Impact from Person's Life-Spheres Perspective in Populations across the Eurasian Landmass"
 CASL, Beijing

WANG Wang, HNU, HNU, Düsseldorf, Germany
 TIAN Wen-Hua, Tsinghua University, Beijing, China
 WANG Guangyao, SUSTech, Shenzhen, China

Aims & Scope

BIG BRAIN is the emblematic "umb-umb" to beliefs that "generating with data" can replace thoughtful scientific research.

BIOCYBERNETIK (engl. bio-cybernetik) aims to model the human-body management and control systems of physiological function from an engineering perspective, individually. **BIOCYBERNETIK** explains complex diseases of unknown origin as slowly intensifying disorders arising from compromised controls.

INTERPERSONAL BIOCYBERNETIK aims to restore regulation.

GeneSEES Impact captures such systems perspective to include essential-for-life interaction with person's surroundings, if it then addresses impact of life-spheres factors in families, systems medicine, environmental exposure, energetic support, health, social embedding including societal reference framing.

HEALTH CONSTITUTIONS aims of integrative views of vital factors in combination across all dimensions, and at concepts for coherent control of their impact on a person's body-system functional and operational control system. It then implies development of neuro-ecological and neuro-ecological concepts of "GeneSEES Impact" for which models of human-body efficiency questions, dealt with at the **Lomonosov Moscow State University** conferences **BIOCYBERNETIK**, **Arbeits-Treffen** Co-ventures or "Wissenschaftliche Zusammenkünfte - Coherent Modeling of Human Body System", are a prerequisite.

EURASIAN COLLABORATIONS aims to generate the required "big brain" from the most available and talented in Eurasia.

Joint Executives & Organizing Team

MAU Leoben, Leibniz Science University, Düsseldorf, DE (Chair)
 DAU Yang, Shanghai Hosp, Zhejiang Univ, Hangzhou, CN
 GERASIMOV Andrey, Sechenov First MSU, Moscow, RU
 MIEBZHIN Sergey, Lomonosov Moscow State University, RU
 TIAN Wen-Hua, Tsinghua University, Shanghai, China
 WANG Guang-Yu, Southern University of Science, Shenzhen, CN
 XU Shufu, SIBS CAS MPB Partner Institute, Shanghai, CN
 ZHANG Jianjun, East China Univ Science & Technology, Shanghai
 Li Jian 李剑, AMBE Meitich, LU Ma 吕沫, SUSTech Shenzhen

Registration for **BIG BRAIN 2018** includes

GeneSEES Impact 2018 1st Chinese German Co-venture "Comprehensive Understanding of Human Health with Impact from Person's Life-Spheres Standpoints"

5th "Arbeitsreffen" German Initiative Biocybernetik: Health Cybernetics - Coherent Control of Health Impacts

WORLDWIDE Systems Theory for Collaboration ...

Fee of 80€ includes attendance of all sessions w/ tutorials and without the Social Dinner on 11 Dec 2018, 7:10 a.m., and without extra charges 241€ (hotel + transport) or accommodation from 210€.

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ABOUT

Transcontinental Health

丝路科学合作

Purpose:

To achieve significant progress in transcontinental health, a broad spectrum of sciences must collaborate in research, and respective 'community' be built in order to generate inspirations from transdisciplinary insight and to create new opportunities from unattended connections.

General objectives:

To expand insights from empirical studies in regional populations to transcontinental comparisons in order to enhance the relevance of research to people in specific areas, and to establish 'population-response profiles' along transcontinental trajectories.

Specific objectives

To advance a systems understanding of disorders, of impact from exposures, and of effects and outcome from interventions - that applies to the variant populations between Yellow Sea and river Rhine, in every region.

First Medical Focus Suggestion

A better understanding of functional disorders from the control-theory viewpoint of patho-biokybernetik is in foreground. In particular, cerebral control disorders *epilepsy, multiple sclerosis, ischemic stroke, vascular dementia, degenerative dementia, Parkinson's disease*, endocrine control disorders *thyroid allostasis, metabolic syndrome, polycystic ovary syndrome*, and some nervous-hormone-immune systems-interaction disorders *chronic inflammation, autoimmune arthritis*, will be in focus for clinical medicine.

Health-factor Focus Suggestion

Human fitness in challenges from *environmental conditions, economic limitations, social stressing* - in particular, *abrupt trauma, natural "turn-over", vanishing financial options, human-relations crises*: their metrics, dynamics, and points-of-impact on human body system, and potentials for autonomous containment of impact by *balancing-out, functional repair* (compensation), or *coping* with persistent deficits.

Health-factor Scope

Topic 1: Foundations of Life, Health, and Medicine

- 1.1: Life Sciences e.g., biology, genetics, proteomics, bioinformatics, computational biology, systems biology
- 1.2: Molecular Medicine e.g., genomic translational medicine, genetic neurology, molecular neurobiology
- 1.3: Basic Medicine e.g., biochemistry, genetics, physiology, microbiology, parasitology, virology

Topic 2: Systems Medicine

- 2.1: Functional Control, Cognitive and Mood Disorders e.g., interactions with other body subsystems
- 2.2: System-level Disorders and Interventions e.g., rescue / intensive care medicine, multiple-organ failure, sepsis
- 2.3: Traditional Chinese Medical (TCM) comparison of concepts in prevention, diagnostics and intervention

Topic 3: Environmental Exposures

- 3.1: Living-nature cohabitation exposures e.g., transmission of pathogens from plants and animals
- 3.2: Civilization exposures e.g., pollution; sea, forest and farmland economy; exploitation of natural resources
- 3.3: Geographic setting e.g., air, radiation, climate; water, soil; sea, deserts, high-mountains

Topic 4: Economic Factors

- 4.1: Base resources access e.g., food, housing, mobility access
- 4.2: Self-supported living e.g., occupation, employment, welfare system participation
- 4.3: Health care access e.g., service access, health insurance, social security schemes

Topic 5: Social Factors

- 5.1: Family (close friends)-life embedding e.g., emotional bindings, legal obligations, adopted life-style
- 5.2: Neighborhood-life embedding e.g., mutual-benefit interaction: learning, substituting; rumors,
- 5.3: Community-life embedding e.g., cultural-life participation, 'distant' altruism: volunteerism, political activity

Topic 6: Population-health Factors

- 6.1: Burden of disease e.g., epidemiology, epidemic threats, and preventive measures (e.g. vaccination)
- 6.2: Disaster response e.g., rescue-service & emergency-medicine care system; quarantine and evacuation
- 6.3: Health-policy systems e.g., health care, consumer (product, traffic) safety, occupational health

CONFIRMED INVITED SPEAKERS

1. BINKOFSKI Ferdinand Dr med, Professor, Chair
ognitive Clinical Sciences, Neurology Clinic, University Medicine of RWTH, Aachen, Germany
2. DAI Yiyang MD, Dr. med.(Charité), Director
Internal Medicine, Fourth Affiliated Hospital of Zhejiang University Medical School, Yiwu, Zhejiang Province, China
3. DIETRICH Johannes W. MD, Dr med, Dr Sci, Head
Endocrine Research Lab, Bergmannsheil Hospital of Ruhr University Bochum, Bochum, Germany
4. GERASIMOV Andrey PhD, Professor, Chair
Institute of Medical Informatics and Statistics, Sechenov First Moscow State Medical University, Moscow, Russia
5. HESCHELER Jürgen Dr.med. Professor, Chair, Director
Institute for Neurophysiology, Medical School, University of Cologne, Cologne, Germany
6. KHALYAVKIN Alexander PhD Acad Secret'y Gerontol Soc RAS, Moscow Branch
Institute Biochemical Physics of Russian Academy of Science, Moscow, Russia
7. LEONHARDT Steffen Dr.-Ing. Dr. med., Professor, Chair, Director
Dept. Medical Information Technology, Helmholtz Center of Biomedical Engineering of RWTH, Aachen, Germany
8. MICHALSKI Anatoli PhD, Professor, Head
Lab. Population Studies, Trapeznikov Institute of Control Science of Russian Academy of Science, Moscow, Russia
9. MÜLLER Matthias Dr.-Ing.,
Institute of Systems Theory & Automatic Control, Stuttgart University, Stuttgart, Germany
10. PONGRATZ Georg MD, Dr med Professor,
Hiller Research Institute, Heinrich Heine University Hospital Düsseldorf, Düsseldorf, Germany
11. ROZHNOVA Kseniya MD, PhD, Assistant Professor
Dept. General Practice Medicine, Sechenov First Moscow State Medical University, Moscow, Russia
12. ROZHNOVA Tatiana MD, PhD, Assistant Professor
Dept. Medical Genetics, Sechenov First Moscow State Medical University, Moscow, Russia
13. SIBBEL Rainer Dr. Professor, Chair
International Health Management, Frankfurt School of Finance & Management, Frankfurt-on-the-Main, Germany
14. TIAN Wenhua PhD, Professor
School of Social Development & Public Policy, Fudan University, Shanghai, China
15. TRETTER Felix Dr phil, Dr rer pol, Dr med, Vice-President (confirmation pending)
Bertalanffy Center for the Study of Systems Science, Vienna, Austria
16. VILLA Alessandro PhD, Prof Neuroeconomics and Informations Systems
Neuroheuristic Research Group, Faculté Business and Economics, Université de Lausanne (Unil), Switzerland
17. VUKOJEVIĆ Vladana PhD, Associate Professor
Dept. Clinical Neuroscience, Center for Molecular Medicine, Karolinska Institutet, Solna, Sweden
18. WAGENPFEIL Stefan Dr oec publ, Professor, Chair, Director
Institute of Medical Biometry, Epidemiology and Medical Informatics, Saarland University, Homburg/Saar, Germany
19. XU Shuhua PhD, Distinguished Adjunct Professor (ShanghaiTech)
CAS MPG Partner Institute of Computational Biology, Chinese Academy of Sciences, Shanghai, China
20. ZHANG Jianhua Dr.-Ing., Professor,
Applied Artificial Intelligence Research Group, Department of Computer Science, Oslo Metropolitan University (OsloMet), Oslo, Norway

TUTORIAL

Systems Theory for Collaboration in Eurasian Health & Medicine

Aims & Scope

Shall discuss and set reference-frame systems concepts for holistic modeling of human-body system and system's interaction with its life-sphere surroundings.

Tutorial Lectures

Sessions are interspersed into Conference main sessions

EURASIAN HEALTH & MEDICINE: Rationale, Goals, and Base Concepts for Realization of Collaboration
Jochen MAU

NEURO-PHYSIOLOGY: Control Theory Concepts (tentative)
Jürgen HESCHELER

NEURO-HEURISTIC Perspectives on Brain Dynamics
Alessandro VILLA

ARTIFICIAL INTELLIGENCE Perspective on Cognitive Functional Components
Jian-Hua ZHANG (invited, not confirmed)

SYSTEM FUNCTION ARCHITECTURE "SFA": A Holistic Standard Structure for Analysis and Modeling of Human-Body System
Jochen MAU

DYNAMICS IN SFA: Mathematical Theory of Multi-Scale Effectuation Dynamics in System Function Architecture
Jochen MAU

IDENTIFICATION: Theory for Statistical Estimation of Wirkgefüge Dynamics in System Function Architecture
Jochen MAU

"ROBOTIC SOCIETY": Systems-Theory Concepts of Human Behavior in Body-System's Socio-Sphere - an Industry 7.0+?
Jochen MAU

BIOKYBERNETIKA 2017

**4th Annual “Arbeitstreffen” of
German Initiative Biokybernetik
Patho-Biokybernetik -
Disorders of MultiScale Control
in Complex Diseases**

**Convenor: Jochen Mau
Heinrich Heine University Düsseldorf**

and

**2nd Russo-German Conference
MultiScale BioMathematics –
Coherent Modeling of Human
Body System**

**Convenors: Sergey I. Mukhin, Jochen Mau
Lomonosov Moscow State University,
Heinrich Heine University Düsseldorf**

**11 - 12 December 2017
TRYP Duesseldorf Krefeld
Europapark A1, Krefeld-Fichtenhain**



BIOKYBERNETIKA 2017, 11-12 Dec 2017, TRYP Düsseldorf Krefeld, Germany

List of Talks in sequence of presentation

Tatiana MOISEEVA Мусеева Татьяна, PhD(Econ), Scientific Secretary, Lecturer,
Institute for Control of Complex Systems of Russian Academy of Sciences (ICCS RAS), Samara, Russia:
Evergetics: Orientation on persons and their values.

Theodor KALVERAM, DrSc, Professor (em) Psychology Heinrich Heine University Düsseldorf, and Scientific
Collaborator, Institute of Sports Sciences, Darmstadt University of Technology, Darmstadt, Germany:
**'Self'-'Other' differentiation - a prerequisite for 'human'-'robot' cooperation? A contribution to behavioral
cybernetics.**

Dmitry FEDOSOV Федосов Дмитрий, DrSc, Research Staff Member, Group of Theoretical Soft Matter and
Biophysics, Institute of Complex Systems, Research Center Jülich, Jülich, Germany:
Modeling blood flow.

Alexander CHURILOV Чурилов Александр, Dr.Sc., Professor
Faculty of Mathematics and Mechanics, Saint Petersburg State University, Saint Petersburg, Russia:
Pulse modulation and its application to modeling hormonal homeostasis.

Stefan WAGENPFEIL, DrSc, Professor & Chair, Director of Institute of Medical Biometry, Epidemiology and
Medical Informatics, Saarland University Hospital, Homburg / Saar, Germany:
Parameter estimation considering uncertainty in model selection.

Caspar KRAMPE, MSc./Laurea Magistrale, Research Staff Member
Chair of Business Management, in particular Marketing, Heinrich Heine University, Düsseldorf, Germany:
Human behavior on markets - Insight from 'shopper neuroscience'.

Jian LI 李剑, PhD, Researcher
Institute for Medical Informatics, Biometry & Epidemiology (IBE), Ludwig-Maximilians Univ, Munich, Germany:
**Computational modeling of methionine cycle-based metabolism and DNA methylation and the implications for
anti-cancer drug response prediction.**

Chuong NGO NGUYEN, Dipl.-Ing., DrEng student (Prof. Dr.-Ing. Dr.med. S. Leonhardt)
Medical Information Technology, Helmholtz Institute for Biomedical Engineering of RWTH, Aachen, Germany:
Object-oriented cardiorespiratory modeling.

Berno J. E. MISGELD, DrEng., Senior Scientific Engineer,
Medical Information Technology, Helmholtz-Institute for Biomedical Engineering of RWTH, Aachen, Germany:
Type 1 diabetes-glucose metabolism modelling and optimal online model selection

Johannes DIETRICH, DrSc, Dr. med., MD, Lecturer, Senior Physician, Head of Laboratory of Endocrine Research
Medical Hospital I, Bergmannsheil University Hospital of Ruhr University Bochum, Bochum, Germany:
The concept of allostasis: A new paradigm at the frontier between health and disease.

Guanyu WANG 王冠宇, Associate Professor of Biology, DrEng, Dr rer medic (Cologne, Germany)
Department of Biology, South China University of Science and Technology (SUSTC), Shenzhen, China:
TUTORIAL: Disorders of multi-scale control.

Nicole RADDE, DrSc, Professor,
Institute of Systems Theory and Automatic Control (IST), Stuttgart University, Stuttgart, Germany:
From heterogeneous data of biological systems to quantitative predictive models.

Olga PANINA Панина Ольга, Professor, DrSc, MD, Head
Faculty of Fundamental Medicine, Lomonosov Moscow State University, Moscow, Russia:
Female reproduction failure: Biological, social and management factors.

Jochen MAU, DrSc, Full Professor (em) Statistics and Biomathematics in Medicine, Heinrich Heine University
Hospital, Düsseldorf, Germany
From macro to micro: On dynamics of the holistic function-level concept of human body system.

Sergey BOGOMOLOV Богомолов Сергей Professor, DrSc,
Faculty of Computational Mathematics and Cybernetics, Lomonosov Moscow State University, Moscow, Russia:
From micro to macro. Computational point of view.

Igor YADYKIN Ядыкин Игорь Professor, DrSc,
Trapeznikov Institute of Control Sciences of Russian Academy of Science, Moscow, Russia:
**On the usage of energy functionals for the detection of the anomalies in the energy balance of human body
organs.**

BIOKYBERNETIKA 2016, 7-9 Nov 2016, Moscow, Russia

BIOKYBERNETIKA 2016
Lomonosov Moscow State University
Faculty of Computational Mathematics
and Cybernetics
Dean: Acad. Prof. Dr. E. I. Moise'ev

**1st Russo-German Conference
MultiScale BioMathematics –
Coherent Modeling of Human
Body System**

**1st Russo-German
“Young Talent” Workshop
Mathematical Bio-systems
Modeling**

07 - 09 November 2016

**Lomonosov
Moscow State University**

Short Report

**Convenors
Sergey I. Mukhin
Jochen Mau**

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Akademisches Beratungsbüro für Forschung und Entwicklung

БИОКИБЕРНЕТИКА 2016
Московский государственный
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Факультет вычислительной математики и
кибернетики
Декан: акад. РАН Е.И. Моисеев

**Первая российско-немецкая
конференция
МультиМасштабные
БиоМатематические науки –
Конвергентное моделирование
системы организма человека**

**Первая российско-немецкая
молодежная школа
«молодых дарований»
Математическое моделирование
биосистем**

**07 - 09 ноября 2016г
Московский государственный
университет имени М.В. Ломоносова**

Краткое Сообщения

**Устроители
Мухин С.И. (МГУ)
Май Й. (ДУТТ)**

¹Design: проф. д-р. Й. Май,
ул. Буша д. 9, Германия, 47800 г. Крафельд,
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академических консультаций в области исследования и развития

Young Talent

Gudimchuk Nikita B.

Center of Theoretical Problems of Physico-chemical Pharmacology of Russian Academy of Sciences, Moscow, Russia; Faculty of Physics, Lomonosov Moscow State University, Moscow, Russia
Modeling microtubule dynamic instability: from kinetic models to Brownian dynamics

Krauz Ilya E.

Faculty of Physics, Lomonosov Moscow State University, Moscow, Russia
Stochastic modeling of von-Willebrand factor dynamics in the bloodstream

Kuzina Ekaterina A.

V. A. Trapeznikov Institute of Control Sciences of Russian Academy of Sciences, Moscow, Russia
A method of approximation of the simulation curves describing effectiveness of immune response to the administration of the antitumor viral vaccines using the mathematical model of vaccine therapy

Mozokhina Anastasia S.

Fac. Computational Mathematics and Cybernetics, Lomonosov Moscow State University, Moscow, Russia
Quasi-onedimensional view on the lymph flow

Seifullaev Ruslan E.

Institute of Problems of Mechanical Engineering of Russian Academy of Sciences, Saint Petersburg, Russia;
Energy-based control of bipedal walk

Ustinov Vladimir D.

Fac. Computational Mathematics and Cybernetics, Lomonosov Moscow State University, Moscow, Russia
Inverse problem of cells' shape deformability distribution reconstruction using laser diffractometry data

**BIOKYBERNETIKA 2016, 7-9 Nov 2016, Moscow, Russia
Young Talent (ct'd)**

Yamalova Diana R.

Faculty of Mathematics and Mechanics, Saint Petersburg State University, Saint Petersburg, Russia;
Faculty of Information Technologies, University of Uppsala, Uppsala, Sweden
Hybrid observers for an impulsive model of testosterone regulation

Faculty

Bocharov Gennadin A.

Institute of Numerical Mathematics of Russian Academy of Sciences, Moscow, Russia
Mathematical modeling in immunology

Bogomolov Sergey V.

Professor, Faculty of Computational Mathematics and Cybernetics, Lomonosov Moscow State University, Moscow, Russia
Method of particles in micro and macro models

Chen Han-Fu

Academician CAS, Professor, Institute of Systems Sciences, Academy of Mathematics and Systems Sciences of China Academy of Sciences, Beijing, China
Recursive system identification

Chetverushkin Boris N.

Academician RAS, Scientific Advisor, Keldysh Institute of Applied Mathematics of Russian Academy of Sciences, Moscow, Russia
Parallel computing in applied problems

Churilov Aleksandr N.

Professor, Faculty of Mathematics and Mechanics, Saint Petersburg State University, Saint Petersburg, Russia
Impulsive Goodwin oscillator in hormonal regulation of testosterone

Dobroserdova Tatiana K.

Institute of Numerical Mathematics of Russian Academy of Sciences, Moscow, Russia;
Coupling of 1D and 3D blood flow models

Michalski Anatoli I.

Professor, V. A. Trapeznikov Institute of Control Sciences of Russian Academy of Sciences, Moscow, Russia
Mathematics for population health

Pongratz Georg

Professor, Hiller Forschungszentrum, University Hospital Düsseldorf, Düsseldorf, Germany
Interplay between autonomous nervous system and hormones in inflammation

Simakov Sergey S.

Lecturer, Moscow Institute of Physics and Technology, Moscow, Russia; Senior Scientific Researcher, Institute of Numerical Mathematics of Russian Academy of Sciences, Moscow, Russia
Computer modeling of endovascular surgery

Ustinin Mikhail N.

Professor, Deputy of Scientific Advisor, Institute of Mathematical Biology of Russian Academy of Sciences, Moscow, Russia
Functional structure of the human body reconstructed from the multichannel magnetic measurements

Vasilyeva Nadezda A.

Dokuchaev Soil Science Institute, a Federal State Budget Scientific Institute, Moscow, Russia;
Joint Institute for Nuclear Research, Dubna, Russia
Modelling microbiologically driven soil structure formation from a human-environment perspective

Volpert Vitali A.

Professor, Centre National de la Recherche Scientifique (CNRS); Université de Lyon 1, Lyon, France
Reaction-diffusion equations in biological applications

Zhao Wen-Xiao

Associate Professor, Key Laboratory of Systems and Control, Academy of Mathematics and Systems Sciences of China Academy of Sciences, Beijing, China
Recursive identification of nonparametric nonlinear systems with binary-valued output observations

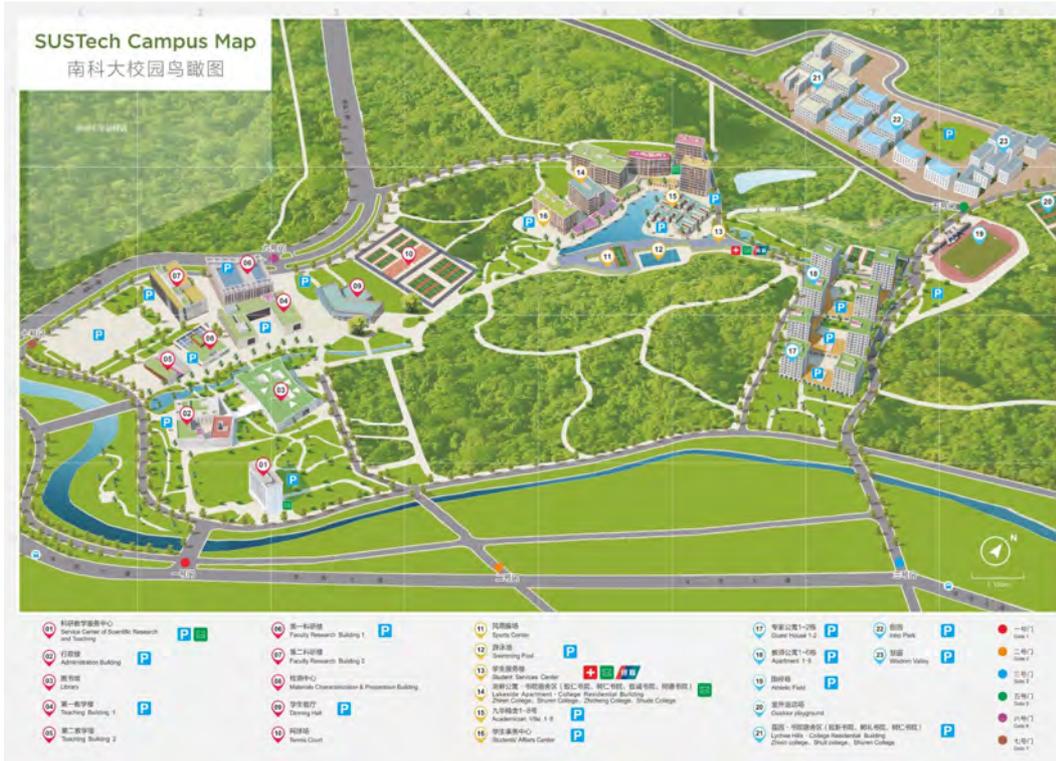
Site & Event Information

Venue

Southern University of Science and Technology SUSTech 南方科技大学

1088 Xueyuan Blvd., Nanshan District
ShenZhen, Guang Dong, P.R. China , 518055

深圳市南山区西丽学苑大道 1088 号
邮编：518055



Location of Hotel: Guest House No. 2 / 专家公寓 2 栋 (map no.17)
Location of Lecture Hall : Lecture Hall 111 in Library / 图书馆 (map no.3)
Location of Dining Hall : Staff Cafeteria, on 1st floor of Apartment No. 2
教师公寓 2 栋 1 楼 (map no.18)
Location of Banquet: Chinese restaurant, on 1st floor of Guest House No.1
专家公寓 1 栋 1 楼 (map no.17)
Tel. No. in case of Emergency: (local) 186-6595-5633
Tel. No. and Name of Contact Person: internat'l +86-136-3160-6720 Dr LÜ Mo 吕沫 博士

Department of Biology 生物系

Teaching Building No. 1 第一教学楼 230

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Buschstr. 9, 47800 Krefeld, Germany
Redaktion: Univ.-Prof. Dr. rer. nat. habil. Jochen Mau



Prepared for
Southern University of Science and Technology, Department of Biology
Printed in China