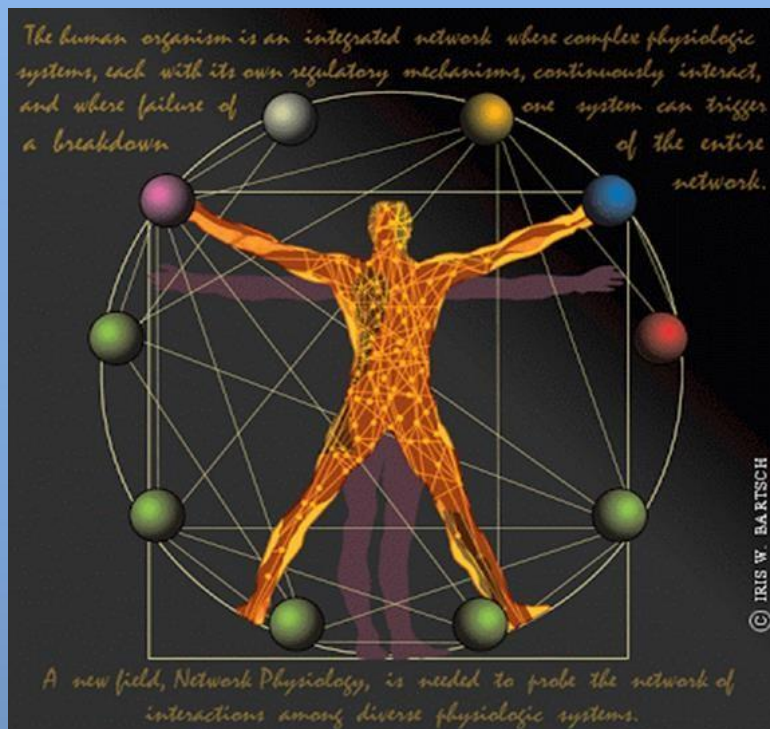




# Third International Summer Institute on Network Physiology (ISINP)

Lake Como School of Advanced Studies, 24 – 29 July, 2022



**Fondazione**  
**Alessandro Volta**

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# Welcome to ISINP 2022

The human organism is an integrated network, where multi-component organ systems, each with its own regulatory mechanism, continuously interact to coordinate their function. Physiological interactions occur at multiple levels and spatiotemporal scales to produce distinct physiologic states, e.g. wake and sleep, consciousness and unconsciousness. Disrupting organ communications can lead to dysfunction of individual systems or collapse of the entire organism, as observed under clinical conditions such as sepsis, coma and multiple organ failure. Yet, despite its importance to basic physiologic functions, the nature of interactions between diverse organ systems and sub-systems, and their collective role in maintaining health is not known. Further, there are no adequate analytic tools and theoretical framework to probe these interactions.

Despite the vast progress and achievements in systems biology and integrative physiology in the last decades, we do not know the basic principles and mechanisms through which diverse physiological systems and organs dynamically interact and integrate their functions to generate a variety of physiologic states at the organism level.

The emerging new interdisciplinary field of *Network Physiology* aims to address this fundamental question. In addition to defining health and disease through structural, dynamical and regulatory changes in individual physiological systems, the new conceptual framework of Network Physiology focuses on the coordination and network interactions among diverse organ systems and sub-systems as a hallmark of physiologic state and function.

Novel concepts and approaches derived from recent advances in network theory, coupled dynamical systems, statistical and computational physics, signal processing and biological engineering show promise to provide new insights into the complexity of physiological structure and function in health and disease, bridging sub-cellular level signaling with inter-cellular interactions and communications among integrated organ systems and sub-systems. These advances form first building blocks in the methodological formalism and theoretical framework necessary to address the problems and challenges in the field of Network Physiology.

This international summer institute will integrate empirical and theoretical knowledge across disciplines with the aim to understand in different contexts, from extensive data analysis and modeling approaches to clinical practice, how diverse physiological systems and sub-systems dynamically interact to produce health and disease.

This will be an interactive event with lectures ranging from physics and applied mathematics to neuroscience, physiology and medicine, covering a range of physiological systems from the cellular to the organ level, and will discuss the challenges, current frontiers and future developments in the emerging field of Network Physiology.

Presentations on basic research will be combined with lectures by leading physiologists and clinicians, working with large medical and ICU databases.

This International Summer Institute aims to provide a relaxed setting where lecturers and attendees interact throughout the course of the week. We have speakers, prominent leaders in their respective fields, who will present new directions in the theory of networks of dynamical systems, brain and neuronal dynamics, tissues and cell assemblies, pair-wise and network interactions of organ systems and sub-systems, and advanced methods from non-linear dynamics and synchronization phenomena.

The Summer Institute will address a diverse audience of graduate students, postdoctoral fellows, research scientists and faculty across a broad range of disciplines and fields from physics, applied mathematics and biomedical engineering to neuroscience, physiology and clinical medicine.

We look forward to a product meeting in Como!

A handwritten signature in blue ink, appearing to read 'Plamen Ch. Ivanov', with a stylized flourish at the end.

Plamen Ch. Ivanov, Ph.D., D.Sc.

Director, [Keck Laboratory for Network Physiology](#), Boston University

Director, [Third International Summer Institute on Network Physiology \(ISINP\)](#)

Field Chief Editor, [Frontiers in Network Physiology](#)

24 July 2022, Como, Italy

# Sponsors



Frontiers in **Network Physiology**

## [Frontiers in Network Physiology](#)

is the first journal publishing rigorously peer-reviewed research dedicated to furthering our understanding of network physiology. This multidisciplinary, open-access journal is at the forefront of communicating impactful scientific discoveries to academics and clinicians.



## [Frontiers Media SA](#)

is the 3<sup>rd</sup> most-cited and 9<sup>th</sup> largest research publisher. Frontiers publishes groundbreaking discoveries by the world's top experts. Frontiers Media SA places the researcher at the center of everything we do, and enables the research community to develop the solutions we need to live healthy lives on a healthy planet. Frontiers articles have been viewed and downloaded more than 1.9 billion times, reflecting the power of research that is open for all.



## [Fondazione Alessandro Volta](#)

"The Foundation makes available the energy of Alessandro Volta for the City of Como, to promote science and culture at all levels, to enhance human capital, to put man back at the center and create a useful foundation for the concrete development of the city."



## [W.M. Keck Foundation](#)

The ISINP international institute builds on groundbreaking research at the Boston University Keck Laboratory for Network Physiology that pioneered the new field of Network Physiology. This has been made possible by support from the W.M. Keck Foundation.

# School Director

## Plamen Ch. Ivanov

Professor Ivanov, PhD, DSc, is Director of the [Keck Laboratory for Network Physiology](#) at Boston University, Associate Physiologist at Brigham and Women's Hospital, and Lecturer in Medicine at Harvard Medical School.

He has introduced innovative ways to analyze and model physiological systems, adapting and developing concepts and methods from modern statistical physics, nonlinear dynamics and networks theory. He has investigated the complex dynamics and underlying control mechanisms of a range of physiological systems, including studies on cardiac and respiratory dynamics, sleep-stage transitions, circadian rhythms, locomotion and brain dynamics, and has uncovered basic laws of physiologic regulation.

Professor Ivanov has pioneered the study of dynamic network interactions of physiological and organ systems. He is the originator and founder of the interdisciplinary field of [Network Physiology](#). His current work focuses on developing methods of data analysis to investigate interactions among diverse organ systems and build a theoretical framework to understand how physiologic states and functions at the organism level emerge out of organ network interactions, and how diverse organ systems coordinate and integrate their functions to produce health or disease. His work lays the foundation of the [Human Physiome](#), a new type of BigData, containing streams of continuously recorded, high frequency, synchronized physiological signals under various states and clinical conditions, with an associated Atlas of network maps representing interactions among physiological systems at different levels in the human organism.

His discoveries have been broadly featured in the [Media](#), including Scientific American, Science News, Nature Science Update, New Scientist, Physics World, Nature Medicine Research Highlights, Washington Post, Futurity Magazine, The Boston Globe.

Professor Ivanov is the Field Chief Editor of the journal [Frontiers in Network Physiology](#). He is the founding Director of the [International Summer Institute on Network Physiology \(ISINP\)](#), Lake Como School of Advanced Study. Professor Ivanov is one of nine founding members of [PhysioNet](#) — the first NIH-sponsored data sharing research resource with millions of users and data downloads. He has served as editorial and advisory board member for several leading journals, including New Journal of Physics, EPL (Europhysics Letters), EPJ Nonlinear Biomedical Physics, Journal of Biological Physics (JOBP), Physiological Measurement and Frontiers in Physiology. His research has been funded by NIH, the W.M. Keck Foundation, the Office of Naval Research (ONR) and the US-Israel Binational Science Foundation (BSF).

For his pioneering applications of statistical physics and nonlinear dynamics to physiology and biomedicine, and for uncovering fundamental scaling and multifractal properties, self-organized criticality, sleep- and circadian-related phase transitions in physiologic dynamics, Professor Ivanov was elected Fellow of the American Physical Society in 2010. He is recipient of the Sustained Research Excellence Award of the Biomedical Research Institute, Brigham and Women's Hospital, Harvard Medical School (2009-2011); the Georgi Nadjakov Medal of the Bulgarian Academy of Sciences (2012), the Pythagoras (Pitagor) Prize for high achievements in interdisciplinary research bestowed by the President of Bulgaria (2014), and \$ 1 million W.M. Keck Foundation Award (2015).

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# Organizing Committee

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# Speakers

## **Natàlia Balagué**

Professor of Exercise Physiology at INEFC (University of Barcelona) and coordinator of the Complex Systems and Sport Research Group. She participates in education programs addressed to professional soccer coaches under the auspices of Football Club Barcelona and the Spanish Soccer Federation. Her research applies complex systems tools to biobehavioural sciences with particular focus on sport related phenomena. Her main aim is to understand the general principles of adaptive behavioral and experiential dynamics of human beings. She has published numerous works and is co-author of the first books applying complex systems science to sport. She founded the international conference Complex Systems in Sport, has been member of the scientific committee of the European College of Sport Science and is Editor-in-chief of Frontiers in Network Physiology of Exercise.

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## **Ronny P. Bartsch**

Dr. Bartsch studied physics in Konstanz, Germany where he received a M.Sc. degree in theoretical physics in July 2003, and at Bar-Ilan University, Israel where he received his PhD in June 2009. He was a post-doctoral fellow at the Division of Sleep Medicine, Harvard Medical School from 2008 till 2012, after which he joined the faculty at the same division as an Instructor in Medicine. In April 2014, Dr. Bartsch joined the Physics Department at Boston University as a Research Assistant Professor. Currently he is a Senior Lecturer at the Physics Department, Bar-Ilan University. Dr. Bartsch applies methods from statistical and computational physics and nonlinear dynamics to study physiologic systems, sleep regulation, circadian rhythms, and how physiologic transitions affect coupling between organ systems. He is recipient of the prestigious German DAAD Fellowship for the period 2010-2012. In 2012 he was awarded the Young Investigator of the Year Prize by the German Society of Sleep Medicine, and in 2014 he won a “Marie Curie” fellowship from the European Commission.

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## **Barbara E. Corkey**

Barbara E. Corkey has been the Zoltan Kohn Professor of Medicine and Vice Chair for Research in the Department of Medicine at Boston University. Dr. Corkey has been a leader in the fields of diabetes and obesity research for over 50 years with over 180 related publications and 40 years of continuous government research support. The Corkey laboratory is engaged in research on obesity and diabetes, with a particular focus on metabolic signal transduction in  $\beta$ -cells, adipocytes and hepatocytes, intercellular communication via circulating redox and the role of hyperinsulinemia in obesity and diabetes. Projects in metabolic regulation have been ongoing since 1981 using such techniques as single cell imaging, metabolic profiling, ionic fluxes and membrane potential, respiration, redox state, reactive oxygen species generation and diet-induced obesity and diabetes models. She does seminal work on the molecular basis of nutrient signaling that has a major impact on our current understanding of health and disease. Finally, Barbara has received



numerous honors including the NIH MERIT Award, National Honorary Membership in Iota Sigma Pi, the National Honor Society of Women in Chemistry, Women in Science Lecturer at the Boston Museum of Science, the George Bray Founders Award of the Obesity Society, the Charles H. Best Lectureship and Award, University of Toronto and the Banting Medal for Scientific Achievement from the American Diabetes Association. A current major focus is on developing clinical/basic collaborative multi-PI grants to explore novel approaches to understand and treat metabolic diseases.

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### **Marina de Tommaso**

Marina de Tommaso is Professor of Neurology at the Psychiatric and Neurologic Sciences Department of the Bari University, head of the Applied Neurophysiology and Pain Unit. She graduated in Medicine in 1982, specialised in Neurology in 1986 and in Physiotherapy in 1993 with full marks cum laude at Bari University. In 1994 she received the title of Research Doctor in Human Relational Sciences. From 1995 to 2005 she has been Researcher in Neurology. Since 2008 she is the coordinator of the diploma in neurophysiopathology techniques. She is the Head of the regional referral Center for Huntington's disease and Neuropathic Pain. She is Editor of BMC Neurology and Pain Research and treatment and Associate editor of Journal headache and Pain journals. She is the President of the Italian Psychophysiology and Cognitive Neuroscience Society. She is author of 170 publications in extenso, concerning the field of Clinical and Applied Neurophysiology, Clinical Neurology, Migraine, Fibromyalgia, Huntington's disease. She is responsible for more than 20 funded projects from private and public committees (European Commission, Italian Research Ministry, CHDI foundation)

Recent studies <http://www.ncbi.nlm.nih.gov/pubmed/?term=de+tommaso+m>

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### **Caterina Da Re**

Caterina joined Frontiers in 2017 after completing her PhD in Genetic and Molecular Biology of Development. She is currently Head of Publishing Program at the leading open access publisher Frontiers, she currently handles a group of journals within the Biosciences, Humanities & Social Sciences and Sustainability programs. She manages a portfolio of 33 journals, overseeing an editorial team of over 150 publishing, based at the different company's locations (Lausanne, London, Beijing and Seattle). She develops and coordinates projects, supervising cross-functional stakeholders through refined internal communication. Prior to this, Caterina was a geneticist primarily interested in mitochondrial disorders.

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### **Luca Faes**

Luca Faes is Professor of Biomedical Engineering at the University of Palermo, Italy. He obtained his MS and PhD in Electronic Engineering at the University of Padova (1998) and at the University of Trento (2003), Italy, respectively. He was with the Dept. of Physics (2004-2013) and the BIOtech Center (2008-2013) of the University of Trento, and with the Bruno Kessler Foundation (FBK, Trento, 2013-2017). He has been visiting scientist at the State University of New York (2007), Worcester Polytechnic Institute (MA, USA, 2010), University of Gent (Belgium, 2013), University of Minas Gerais (Brazil, 2015), and Boston University (MA, USA, 2016). He is Senior Member of the IEEE, and member of the IEEE Engineering in

Medicine and Biology Society (IEEE-EMBS), for which he serves in the Technical Committee of Biomedical Signal Processing and regularly organizes symposia and invited sessions at the Annual EMBC Conference. He is member of the European Study Group on Cardiovascular Oscillations (ESGCO), and was organizer and Program Chair of the 8th ESGCO conference (Trento, Italy, 2014). He is Specialty Chief Editor of the Section "Information Theory" of Frontiers in Network Physiology, and serves as editor at several peer-review journals, including Entropy, Frontiers in Physiology, and Computational and Mathematical Methods in Medicine. His teaching activity includes Biosensors, Biomedical Devices and Statistical Analysis of Biomedical Signals. His research activity is focused on the development of methods for multivariate time series analysis and system modeling, with applications to cardiovascular neuroscience, cardiac arrhythmias, brain connectivity and network physiology. Within these fields, he has authored eight book chapters and more than 200 peer-reviewed publications, receiving more than 5700 citations (h-index: 44; font: Scholar).

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### **Charles C. Hardin**

C. Corey Hardin M.D., Ph.D. is assistant professor of medicine at Harvard Medical School and staff physician in Pulmonary and Critical Care Medicine at Massachusetts General Hospital (MGH). Dr. Hardin completed his Ph.D. in Biophysics working in the laboratory of Prof. Peter Wolynes, studying the prediction of protein structure from sequence using Hopfield neural networks. He completed an internship and residency in internal medicine at MGH and did his clinical training in Pulmonary and Critical Care Medicine in the Harvard Combined Program. His current work centers around the physiology of critical illness and, in particular, the mathematical modeling of septic shock and the acute respiratory distress syndrome (ARDS). Dr. Hardin also serves as an editor at the New England Journal of Medicine and at NEJM Evidence.

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### **Shlomo Havlin**

Professor Shlomo Havlin made fundamental contributions to the physics of complex systems and statistical physics. These discoveries have impacted many other fields such as medicine, biology, geophysics, and more. He has over 60,000 citations on ISI Web of Science and over 100,000 in Google Scholar. His h-index is 111 (140) in Web of Science (Google Scholar). Havlin has been a Highly Cited Scientist in the last 3 years. He is a professor in the Physics Department at Bar-Ilan University. He received his Ph.D. in 1972 from Bar Ilan University and he has been a professor at BIU since 1984. Also, between the years of 1999 – 2001 he was the Dean of the Faculty of Exact Sciences and from 1996 to 1999 he was the President of the Israel Physical Society. Havlin won the Israel prize in Physics (2018), Order of the Star of Italy, President of Italy (2017), the Rothschild Prize for Physical and Chemical Sciences, Israel (2014), the Lilienfeld Prize for "a most outstanding contribution to physics", APS, USA (2010), the Humboldt Senior Award, Germany (2006), the Distinguished Scientist Award, Chinese Academy of Sciences (2017), the Weizmann Prize for Exact Sciences, Israel (2009), the Nicholson Medal, American Physical Society, USA (2006) and many others. His main research interests are in the field of statistical physics and complex networks, with a focus on

interdependent networks, cascading failures, networks of networks and their implications to real world problems. The real-world systems he studied include physiology, climate, infrastructures, finance, traffic, earthquakes and others.

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### **Kathryn A. Hibbert**

Kathryn A. Hibbert is a Pulmonary and Critical Care physician at Massachusetts General Hospital(MGH), where she also serves as the director of the Medical Intensive Care Unit. She received her MD degree from Mount Sinai School of Medicine before residency training in Internal Medicine at MGH and serving as a Chief Resident in Medicine. She completed her fellowship in the Harvard Pulmonary and Critical Care Fellowship. Her early research focused on translational ARDS research using functional PET-CT imaging to better understand regional pathophysiology. She now runs a critical care clinical research program that includes serving as the site principal investigator for the PETAL network at MGH and a project that examines the novel use of metabolomics to identify drug resistant pneumonia. In addition, she is a course director for the Harvard Medical School Health Sciences & Technology curriculum, serves as the Critical Core Educator for the Department of Medicine at MGH and has developed a novel advanced physiology course for internal medicine residents. She has won multiple teaching awards and serves as the Associate Program Director for the Harvard Pulmonary and Critical Care Fellowship.

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### **Plamen Ch. Ivanov**

Professor Ivanov, PhD, DSc, is Director of the Keck Laboratory for Network Physiology at Boston University, Associate Physiologist at the Division of Sleep Medicine, Brigham and Women's Hospital, and Lecturer in Medicine at Harvard Medical School. He has introduced innovative ways of analyzing and modeling physiologic systems, adapting and developing concepts and methods from modern statistical physics and nonlinear dynamics. He has investigated the complex dynamics and underlying control mechanisms of a range of physiological systems, including studies on cardiac and respiratory dynamics, sleep-stage transitions, circadian rhythms, locomotion and brain dynamics, and has uncovered basic laws of physiologic regulation. He is the originator and founder of the new emerging field of Network Physiology, to address the fundamental question of how diverse organ systems and sub-systems in the human body interact as a network and continuously coordinate, synchronize and integrate their functions to produce health and disease. Dr. Ivanov is one of the nine founding members of PhysioNet, an NIH sponsored data sharing research resource. His research has been funded by the W. M. Keck Foundation, NIH, Office of Naval Research (ONR) and the US-Israel Binational Science Foundation (BSF). For his achievements, Dr. Ivanov was elected Fellow of the American Physical Society in 2010. He is recipient of the Sustained Research Excellence Award (2009-2011) of the Biomedical Research Institute, Brigham and Women's Hospital, Harvard Medical School; of the Georgi Nadjakov Medal, Bulgarian Academy of Sciences (2012), and of the Pythagoras Award for significant achievements in interdisciplinary research (2014). He served on several Editorial and Advisory Boards, including EPL (Europhysics Letters), EPJ Nonlinear Biomedical

Physics, Journal of Biological Physics (JOBP), Frontiers in Fractal Physiology, Physiological Measurement. Professor Ivanov is the Field Chief Editor of the journal Frontiers in Network Physiology. He is the founding Director of the International Summer Institute on Network Physiology (ISINP), Lake Como School of Advanced Study.

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### **Mohit Kumar Jolly**

Mohit Kumar Jolly is an Assistant Professor at Indian Institute of Science where he leads the Cancer Systems Biology research group. He obtained his Ph.D. from Rice University and was a Gulf Coast Consortia Postdoctoral Fellow jointly at Rice University and MD Anderson Cancer Center. He currently co-chairs the Mathematical Oncology subgroup at Society for Mathematical Biology (SMB) and serves as an Associate Editor at Computational and Systems Oncology (Wiley). His work in decoding the nonlinear dynamics of cancer metastasis and therapy resistance using mathematical modeling has elucidated fundamental design principles for underlying regulatory networks driving cancer progression as well as identified new therapeutic strategies to delay the emergence of drug resistance. His contributions to network physiology include decoding how large and complex regulatory networks converge to only a limited number of phenotypes/cell-states, as well as understanding how cellular networks driving various axes of metastatic fitness (drug resistance, immune evasion, tumor-initiation etc.) are coupled with one another to drive coordinate changes in cellular plasticity and heterogeneity. He won the iBiology 2016 Young Scientist Seminar Series – a prestigious award to communicate one's work to diverse audience, and was recently included in top 2% of systems biology researchers (Elsevier/Stanford Univ list 2021).

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### **Jürgen Kurths**

Jürgen Kurths studied mathematics at the University of Rostock and got his PhD in 1983 at the GDR Academy of Sciences and his Dr. habil. in 1990. He was full Professor at the University of Potsdam from 1994-2008 and has been Professor of Nonlinear Dynamics at the Humboldt University, Berlin and chair of the research domain Transdisciplinary Concepts of the Potsdam Institute for Climate Impact Research since 2008 and a 6<sup>th</sup> century chair at the Institute for Complex Systems and Mathematical Biology at Kings College of the Aberdeen University (UK) 2009-2017. He is a fellow of the American Physical Society and is a member of the Academia Europaea. He got an Alexander von Humboldt research award and a 1000 Talents award for foreign experts from China and was awarded the L.F. Richardson Medal of the European Geosciences Union. He got several Honorary Doctorates and Honorary Professors. He was a Burgers Visiting Professor at University of Maryland and is a Chapman Professor at the University of Alaska (Fairbanks). Jürgen has supervised more than 75 PhD students from about 20 countries; more than 40 of them have now tenured positions in various countries. He has published more than 650 papers in peer-reviewed journals and two monographs which are cited more than 35.000 times (H-index: 85). He is editor-in-chief of the AIP journal CHAOS and is in the editorial board of more than further 10 journals. His main research interests are complex synchronization phenomena, complex networks, time series analysis and their applications in neuroscience and physiology. He works on inferring complex networks from spatio-temporal data in neuroscience to

characterize the underlying dynamics and to get new kinds of predictions of extreme events, such as episodes of migraine. Moreover, he is developing multilayer neural networks with time delay to model brain activity, in particular cognitive processes. Another main direction is to develop measures of causality and their applications to physiological signals. He coordinated several large projects in EU and DFG and is now speaker of an International Research Training Group on complex networks (DFG and Brazil), of a Megagrant on inferring models from climate spatio-temporal data (Russia) and of a joint project on collective nonlinear dynamics of complex power grids (BMBF, Germany).

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### **Klaus Lehnertz**

Professor Lehnertz, PhD, is a Physicist and Director of the Neurophysics Group at the Department of Epileptology at Bonn University Medical Center. In addition, he is Co-Director of the Interdisciplinary Centre for Complex Systems and an affiliated member of the Helmholtz-Institute for Radiation and Nuclear Physics at Bonn University. He is Co-initiator of the International Seizure Prediction Group, which brings together researchers from a wide range of backgrounds including epileptology, neurosurgery, neurosciences, physics, mathematics, computer science, and engineering to deepen scientific and medical understanding of epilepsy and to develop new diagnosis, treatment and intervention options for patients with epilepsy. For more than two decades, his research group has been developing methods of data analysis and a theoretical framework to understand how brain sub-systems dynamically interact and coordinate functions under physiological and pathophysiological activities. His research interests include nonlinear dynamics, complex networks, statistical physics, neurophysics, computational physics, physics of imaging, medical physics, and epilepsy. He is the author of more than 200 original publications in international peer-reviewed journals, reviews, book chapters, and books.

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### **André Longtin**

André Longtin is Professor of Physics at the University of Ottawa, where he runs the Neurophysics and Nonlinear Dynamics Group. He is also co-founder and co-director of the uOttawa Centre for Neural Dynamics. His interests lie at the interface of nonlinear dynamics, statistical physics, biology and medicine. He seeks physical principles of brain function as well as the origin and role of randomness in neural and other physiological systems, and studies the properties of stochastic nonlinear systems, especially those with adaptation, memory, delays and plasticity. He received an honors B.Sc. Physics in 1983 and an M.Sc. Physics in 1985 from the Université de Montréal, and a Ph.D. Physics from McGill University in 1989 co-supervised by Michael Mackey and John Milton. He then joined Los Alamos National Laboratory for two years, both as a Natural Sciences and Engineering Research Council of Canada Postdoctoral Fellow and a Los Alamos Director's Funded Postdoctoral Fellow. He held a joint position in the Theoretical Division T13 (Complex Systems) and the Center for Nonlinear Studies. He began as assistant professor of Physics in 1992 at the University of Ottawa. He is now Professor since 2002, and cross-appointed to the Department of Cellular and Molecular Medicine in the Faculty of Medicine, and Mathematics and Statistics. He is on the

editorial board of Biological Cybernetics, Cognitive Neurodynamics, Bulletin of Mathematical Biology, Mathematical Neuroscience and Applications, Entropy, Frontiers in Computational Neuroscience, Frontiers in Applied Mathematics and Statistics, and Mathematical Biosciences and Engineering. He is a Fellow of the American Physical Society, was awarded a senior Humboldt Research Prize in Germany in 2010 as well as Canada's NSERC Brockhouse Prize for Interdisciplinary Research with Len Maler in 2017. He has been a visiting professor at Humboldt U. Berlin, EPFL and TU Munich. He collaborates very closely with neurobiologists and clinicians.

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### **Gorana Mijatovic**

Gorana Mijatovic received B.Sc. degree and M.Sc. degree in Electrical engineering in 2009, 2010, and the Ph.D. degree in Electrical Engineering in 2018, from the University of Novi Sad, Serbia. Her current position is Assistant Professor at Department of power, electronics and telecommunications of Faculty of Technical Sciences (FTS), University of Novi Sad (UNS), Serbia. Her teaching activity regards fundamentals of electrical engineering. Her research activity includes computational neuroscience, complex systems, non-linear dynamics, network dynamics, synchronization, and electromagnetic fields. Within this fields, she has authored more than 70 journal and conference publications. She was rewarded with the annual award of the Department of power, electronics and telecommunications (FTS, UNS) as the teacher with the highest number of journal scientific publications in 2021, as well as with the annual award "Dr Zoran Djindjic" for the best young scientist and researcher in 2021, autonomous province of Vojvodina, Serbia. In 2022, she received an award for the best-graded professor at the Faculty of Technical Sciences. She is review editor in Frontiers in Physiology (Fractal Physiology) and Frontiers in Network Physiology (Fractal Physiology). She is also member of the IEEE, and of the CEVAS (Centre of Excellence for Vibro-Acoustic Systems and Signal Processing) and ICONIC (Center for Intelligent Communications, Networking and Information Processing) centers associated to the FTS, UNS. She is currently participant of the project H2020 INCISIVE (A multimodal AI-based toolbox and an interoperable health imaging repository for the empowerment of imaging analysis related to the diagnosis, prediction and follow-up of cancer), and of the COST action (CA19136 NET4AGE friendly, international interdisciplinary network on smart healthy age-friendly environments).

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### **J. Randall Moorman**

Randall Moorman, M.D., is Professor of Medicine, Physiology, and Biomedical Engineering at the University of Virginia where he is a clinical cardiologist and founding Director of the UVa Center for Advanced Medical Analytics. He completed his undergraduate and medical degrees at the University of Mississippi, did clinical training at Duke Hospital where he was Chief Medical Resident, and undertook basic science research training at Baylor in molecular electrophysiology and membrane biophysics. His research focuses on bedside prediction of subacute, potentially catastrophic illnesses using advanced mathematical and statistical pattern recognition analyses of time series data from clinical monitors. His work initially centered on neonatal sepsis, a life-threatening infection of the bloodstream, and now on adult patient deterioration in ICUs and hospital

wards. He developed sample entropy for use in physiological time series, and he introduced coefficient of sample entropy for detection of atrial fibrillation. He is an inventor on 9 issued US patents, the 2014 UVA Innovator of the Year, and Chief Medical Officer of Advanced Medical Predictive Devices, Diagnostics, and Displays. He is vice-president of the Society for Complex Acute Illness and Editor-in-Chief of Physiological Measurement.

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### **Ulrich Parlitz**

Ulrich Parlitz is a research scientist at the Max Planck Institute for Dynamics and Self-Organization, Göttingen (Germany) and an adjunct professor of Physics at the University of Göttingen. He received his PhD in 1987 at the University of Göttingen. From 1989 to 1994 he was with the Institute for Applied Physics at the Technical University of Darmstadt, Germany, and in 1994 he became a scientific assistant at the Third Institute of Physics of the University of Göttingen where received his habilitation in 1997. His main research areas are nonlinear dynamics and data analysis with applications in life sciences, nonlinear oscillators, networks, cavitation, and laser dynamics. In 2010 Ulrich Parlitz joined the Research Group Biomedical Physics at the Max Planck Institute for Dynamics and Self-Organization. There he is involved in theoretical and experimental studies for understanding the nonlinear dynamics of the heart focusing on cardiac arrhythmias. This research includes numerical studies of (transient) spatio-temporal chaos in excitable media and the application of data assimilation methods for fusing experimental measurements (e.g., multichannel ECG time series) with mathematical models of electro-mechanical excitation waves in cardiac tissue. Ulrich Parlitz has published over 170 peer-review publications, including 13 papers in Physical Review Letters. He serves as a panel member of the German Science Foundation (DFG) for Statistical Physics, Soft Matter, Biological Physics and Nonlinear Dynamics, and he is member of the Editorial Board of Frontiers in Applied Mathematics and Statistics (Dynamical Systems) and the Editorial Advisory Board of Chaos: Int. J. of Nonlinear Science.

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### **Louis M. Pecora**

Dr. Pecora is currently a research physicist at the Naval Research Laboratory, Washington, DC, where he heads the section for Magnetic Materials and Nonlinear Dynamics in the Materials and Sensors branch. He received his B.S. degree in physics from Wilkes College and he then enrolled in the Syracuse University Solid State Science program from which he received a Ph.D. in 1977. In the same year, he was awarded an NRC postdoctoral fellowship at the Naval Research Laboratory where he worked on applications of positron annihilation techniques in determining electronic states in copper alloys. This led to a permanent position at NRL. In the mid-1980's Dr. Pecora moved into the field of nonlinear dynamics in solid state systems. Subsequent work has focused on the applications of chaotic behavior, especially the effects of driving systems with chaotic signals and coupling nonlinear dynamical systems in complex networks. This has resulted in the discovery of synchronization of chaotic systems, control and tracking, and dynamics of many coupled, nonlinear systems. Recently his research interests have turned to quantum chaos and collective behavior of oscillators in large complex networks, especially using the techniques of computational group theory. Dr. Pecora has published over 150 scientific papers and has 5 US patents for the applications of

chaos. His original paper on the synchronization of chaotic systems has over 7000 (ISI) citations and is the 10th most cited paper ever in Physical Review Letters. In 1995 he received the Sigma Xi award for Pure Science for the study of synchronization in chaotic systems. He is also a Fellow of the American Physical Society (APS) and of the American Association for the Advancement of Science (AAAS).

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### **Alberto Porta**

Professor Alberto Porta received MS degree in Electronic Engineering at Politecnico di Milano, Milan, Italy in 1989. He was a Research Fellow on Automatic Control and System Theory at the Department of Electronics for Automation, Università degli Studi di Brescia, Brescia, Italy until 1994. He received his PhD degree in Biomedical Engineering at Politecnico di Milano, Milan, Italy in 1999. Since 1999 he has been with Università degli Studi di Milano, Milan, Italy where he became Researcher in Biomedical Engineering in 2005, Associate Professor in 2011 and Full Professor in 2017. Since 2006 he has been teaching Medical Physics, since 2007 Applied Medical Statistics and since 2011 Bioengineering at Università degli Studi di Milano, Milan, Italy. He is referee of several international journals in the fields of Computational Biology, Biomedical Engineering, Biological Cybernetics, Bioinformatics, Applied Physics and Statistics, Physiology, Clinical Cardiology and Neurosciences. Since 2007 he has been Associate Editor of the International Conference of the IEEE Engineering in Medicine and Biology Society (Theme 1: Biomedical Signal Processing). He is Senior member of the IEEE since 2020. He is currently member of the board of American Journal of Physiology (Regulatory, Integrative and Comparative Physiology), Autonomic Neuroscience: Basic and Clinical, Clinical Autonomic Research, European Physical Journal Nonlinear Biomedical Physics, Physiological Measurement, Entropy, and Frontiers in Fractal Physiology and Associate Editor of Medical & Biomedical Engineering & Computing, Frontiers in Autonomic Neuroscience and Frontiers in Networks in the Cardiovascular System. Since 2012 he has been the President of the European Study Group on Cardiovascular Oscillations. His primary interests include time series analysis, biomedical signal processing, spectral analysis, quantification of complexity, entropy, causality, prediction, symbolic analysis, nonlinear dynamics, biological cybernetics, system identification and modeling. Applications are mainly focused on cardiovascular system, cardiovascular regulatory mechanisms, cerebrovascular autoregulation and autonomic neuroscience. He is author of 299 papers published on peer-review international journals. His current H-index is 61 (source: Scopus). Complete list of publications can be found at the Scopus ID: 7005322848.

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### **Caterina A. M. La Porta**

Caterina La Porta is professor of General Pathology at the University of Milan where she coordinates the research group Oncolab and is member of the steering committee of the Center for Complexity and Biosystems. In 2018, she co-founded the startup ComplexData where she serves as CEO. During her scientific career, Prof. La Porta published more than 200 papers in international journals mainly on cancer and neurodegenerative diseases, receiving thousands of citations. In the past 15 years, she shifted her



interest to quantitative biology and digital health. The focus of her current research activity focuses on understanding cancer heterogeneity using tools from cell biology, biophysics and data science. Her interdisciplinary view of cancer is summarized in a book published by Cambridge University Press in 2017 entitled “The Physics of Cancer”. Prof. La Porta was selected as one of the 100 most important female scientists in Italy (<https://100esperte.it/>) and was visiting scientist in many universities around the world, including MIT, Cornell University, Aalto University, Rice University, the ENS Paris, the Weizmann Institute of Science and LMU in Germany. Prof. La Porta has a long track record of public outreach activities, including the organization of several editions of the EU Researcher’s night, and is involved in many other science dissemination activities.

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### **Rossella Rizzo**

Rossella Rizzo is a mathematician and assistant professor in Applied Mathematics at the Department of Engineering, University of Palermo, Italy, awarding a grant on European Funds. She currently works on Turing instability and pattern formation for reaction-diffusion (RD) systems in brain dynamics. Her primary research goal is to study chemotactic RD systems to model multiple sclerosis lesions formation and understand under which conditions the system evolves towards coherent structures corresponding to the lesions visible in the brain magnetic resonance images (MRI). Dr Rizzo completed her PhD in Science and Engineering (specialization in Applied Mathematics) at University of Calabria, Cosenza, Italy, with excellent grades in 2020, working on the identification of brain structures to improve the knowledge of cerebral morphometry and the processing capacity of software for brain imaging. In 2018 Rossella joined Prof. Robert Whelan’s group at the Trinity Institute of Neuroscience (TCIN) as Visiting Researcher to conduct research on unhealthy ageing within the BrainPAD project. Between 2018 and 2020 Rossella worked, and since then collaborates with Prof. Plamen Ivanov’s group at the Keck Laboratory for Network Physiology at Boston University, applying cross-correlation functions and statistical analysis to understand dynamical interactions between the brain and the locomotor system during different sleep stages in healthy and Parkinson’s subjects. Between 2020 and 2021 Dr Rizzo worked as a Postdoctoral Research Fellow in the FRAILMatics Research Group, under the direction of Prof. Roman Romero–Ortuno, at The Irish Longitudinal Study on Ageing (TILDA). There, she worked on cognitive data for older people, applying big data analysis, computational modeling and machine learning techniques to identify in a large population-based study participants who are at high risk of mobility and cognitive decline and consequential loss of independence. Dr Rizzo contributed to various conferences with talks, posters, and abstracts, organized conferences and summer schools, has received international awards, and has published on different high impact factor peer-reviewed journals. She is review editor in Frontiers in Network Physiology and Frontiers in Fractal Physiology, and referee for Physiological Measurements, Scientific Report and Physics in Medicine.

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### **Marianna La Rocca**

Dr. La Rocca is assistant professor in applied physics at the Physics Department of Bari University, Italy.

Currently, her research focuses on developing and applying complex network-based quantitative methods and machine learning techniques to analyze and relate multimodal neurophysiological data for the study of different neurological diseases. Dr. La Rocca received her doctorate in Physics applied to Neuroscience from Bari University. She devoted great effort in using multimodal neuroimaging techniques and computational methods to study neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. During her PhD, she developed an automatic and quantitative method based on multiplex networks to support the early diagnosis of Alzheimer's disease, this approach has generated a great scientific and media interest. From 2018-2021, Dr. La Rocca was a Postdoctoral Scholar – Research Associate in the Laboratory of Neuro Imaging at the University of Southern California (USC) where she applied computational and quantitative methods to electrophysiology and imaging data to identify validated biomarkers of epileptogenesis after traumatic brain injury. Dr. La Rocca is continuing to collaborate and be affiliated with USC and is member of different Editorial Boards: Frontiers in Network Physiology, Frontiers in Neurology and Frontiers in Fractal Physiology. Dr. La Rocca was invited as keynote speaker to various international scientific events and was awarded third place in the international challenge for automated prediction of Mild Cognitive Impairment from MRI data. Dr. La Rocca has received different international awards, has published on different high impact factor peer-reviewed journals, and has authored several abstracts, conference papers and book chapters.

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### **Michael G. Rosenblum**

Professor Rosenblum, PhD, has been a research scientist and Professor in the Department of Physics and Astronomy, University of Potsdam, Germany, since 1997. His main research areas are nonlinear dynamics, synchronization theory, and time series analysis, with application to biological systems. The most important results include description of phase synchronization of chaotic systems, analysis of complex collective dynamics in large networks of interacting oscillators, development of feedback techniques for control of collective synchrony in neuronal networks (as a model of deep brain stimulation of parkinsonian patients), methods for reconstruction of oscillatory networks from observations, application of these methods to analysis of cardio-respiratory interaction in humans. He studied physics at Moscow Pedagogical University, and went on to work in the Mechanical Engineering Research Institute of the USSR Academy of Sciences, where he was awarded a PhD in physics and mathematics. He was a Humboldt fellow in the Max-Planck research group on nonlinear dynamics, and a visiting scientist at Boston University. He is a co-author (with A. Pikovsky and J. Kurths) of the book "Synchronization: A Universal Concept in Nonlinear Sciences", Cambridge University Press, 2001 and has published over 100 peer-review publications, including 5 papers in the journals of the Nature Group and 11 papers in Physical Review Letters. Michael Rosenblum served as a member of the Editorial Board of Physical Review E. Since 2014 he is on the Editorial Board of Chaos: Int. J. of Nonlinear Science. He was named an American Physical Society Outstanding Referee for 2015.

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### **Olga Sosnovtseva**

Olga Sosnovtseva, PhD, is Professor with Special Duties at the Department of Biomedical Sciences,

University of Copenhagen, Denmark. She received her M.S. and PhD degree in physics from Saratov State University (Russia) and worked in the field of nonlinear dynamics and theory of chaos. She received her second PhD degree in Human Biology from the Faculty of Medicine, University of Marburg, German, and worked in the field of biophysics and mathematical physiology. The most important results include development of nano-sensors to study heme protein properties and signalling pathways in living cells, development of biophotonics tools to study blood flow regulation in microcirculation, introduction of the concept of synchronization to renal physiology, methods to study interaction of physiological oscillations, development of the first nephro-vascular dynamical model of renal autoregulation. She is a co-author of the book “Synchronization: From Simple to Complex” (Springer, 2009), co-editor of the book “Biosimulation in Biomedical Research, Health Care and Drug Development (Springer, 2012) and has published over 150 peer-review publications. She received Skou fellowship (Denmark) for development of mechanism-based models of intercellular interactions and became Edmund Optics Educational Award finalist. She serves as a panel member of Swedish Research Council for Basic disease mechanisms: Molecular, cellular and biochemical aspects, and for Consolidator Interdisciplinary Grants.

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### **Christopher R. Stephens**

Chris Stephens is Full Professor and Director of Data Science at the C3 – Center for Complexity Science at the National University of Mexico (UNAM), the oldest university in the Americas. He possesses a B.A. and an M.A. from The Queen’s College, Oxford and an M.S. and Ph.D in theoretical physics from the University of Maryland. After his doctoral work he was chosen by Nobel Laureate Gerard ‘t Hooft to work with him at the University of Utrecht and was later awarded a prestigious Marie Curie Fellowship by the European Union at the Dublin Institute for Advanced Studies. He has been invited to Visiting Professor positions at many universities, including the Universities of Birmingham, Essex, Limerick and Northumbria as well as being a Senior Visiting Fellow at the Dublin Institute for Advanced Studies. Among his honors are a Leverhulme Professorship from the Leverhulme Trust U.K. and the Jorge Lomnitz Prize of the Mexican Academy of Sciences. He is a member of the editorial boards of Genetic Programming and Evolvable Hardware and Theory in Biosciences. His work is highly interdisciplinary, with over 160 publications in international journals across a wide spectrum of fields, including statistical physics, artificial intelligence, ecology, finance, emerging diseases and medicine. He was a founding partner of Adaptive Technologies Inc. and is currently Founder and Director of Presage Research, both companies dedicated to the application of artificial intelligence research to predictive modelling and optimization in business and industry, including finance, energy, CPG, education, transport and healthcare. He has three patents awarded in predictive analytics/agent-based methodologies. Chris’ main current interest is in using big, deep data to predict the dynamic, adaptive nature of health risk, with a special emphasis on metabolic diseases, particularly obesity, and emerging diseases, such as SARS-Cov-2, with a focus on understanding and modelling them as Complex Adaptive Systems. He has received substantial government and private sector funding to lead large interdisciplinary teams in the development of cutting-edge solutions that make machine learning-based prediction platforms, such as SPECIES ([species.conabio.gob.mx](http://species.conabio.gob.mx)) – for the modelling of biodiversity and

zoonoses, and Epi-PUMA (covid.c3.unam.mx) for the SARS-Cov-2 pandemia, available to a wide variety of stakeholders and decision makers.

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### **Ruedi Stoop**

Professor Stoop studied mathematics at the University of Zurich and completed his PhD in computational physics at the same university in 1991. After obtaining grants from the Swiss National Science Foundation, he became a reader in computer science at the School of Life Sciences, University of Applied Science Northwest Switzerland, and worked in parallel as a scientific advisor and designer for several industrial companies. He became an Associate Professor in physics at the University of Berne in 1997, Adjunct Professor in mathematics at the University of Zurich in 2004 and soon after also in theoretical physics at the Swiss Federal Institute of Technology (ETH). In 2008 he obtained tenure in Neuroscience and Physics at the Institute of Neuroinformatics, run jointly by the University of Zurich and the Swiss Federal Institute of Technology (ETH). His main research directions lie along two related paths: Nonlinear dynamics of biological systems, and principles and applications of biocomputation, seen as domains of mathematics, physics and information science. Prof. Stoop has published a large number of peer reviewed papers documenting a true interdisciplinary approach, from physics over mathematics, engineering, biology to data science. He authored and co-authored books published by Springer, Birkhäuser and World Scientific.

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### **Sebastiano Stramaglia**

Dr. Stramaglia is an Associate Professor of Applied Physics at the University of Bari, Italy, and External Scientific Member of the Basque Center for Applied Mathematics, Bilbao, Spain. He received his Ph.D. in Statistical Mechanics of random surfaces from the University of Bari in 1995, and the Laurea degree in models of strongly correlated electronic systems in 1991. Since 2001 he is a member of the Center of Excellence “Innovative Technologies for Signal Detection and Processing”, funded by the Italian Ministry for Scientific Research; since 2002 he is a member of the V National Scientific Commission of INFN-Istituto Nazionale di Fisica Nucleare, Italy. He chaired several international events, including “Modeling Migraine: from nonlinear dynamics to clinical neurology” July 2009, Berlin, and “Nonlinear dynamics in electronic systems” July 2013, Bari. Editor of the books “Modelling Biomedical Signals”, World Scientific 2002, and “Emergent Complexity from Nonlinearity, in Physics, Engineering and the Life Sciences”, Springer 2017. He has been visiting scientist at the Institute for Theoretical Physics NORDITA and at the Department of Data Analysis of the University of Gent, Belgium, and visiting professor at Biocruces Health Institute, Bilbao, Spain. Since 2003 he is team leader of the INFN project “Biological applications of Theoretical Physics Methods”. His research focuses on dynamical networks and Granger causality approaches to physiological interactions, in particular he developed a kernel approach for the inference of nonlinear coupling among dynamical systems with applications to brain function and brain-heart interactions.

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### **Franca Tecchio**

Professor Franca Tecchio is a Senior Researcher at the National Research Council (CNR) in Italy, where

she is the Director of the Laboratory of Electrophysiology for Translational Neuroscience (Let's Laboratory). Her work focuses on methods of brain complexity analysis and therapeutic interventions via precision electroceuticals. Her laboratory utilizes magneto- and electroencephalography (MEG, EEG, EMG) and non-invasive neuromodulation techniques to investigate neuronal electrical activity (TMS, tES, tDCS, tIDS). Dr. Tecchio has seminal contributions to understanding brain function and dynamics through network approaches and to elucidating coupling forms and interactions with other peripheral systems and environment, including brain somatosensory activation and processing in response to body movement; sensory cortex activity in anesthesia; coupling of neural activation and local hemodynamics; cortical responses to auditory stimuli etc. Her work is presented in more than 250 publications. Dr. Tecchio is among the 10 most active Italian researchers in Clinical Neurology ('La Repubblica Salute', 2003), and her discoveries are broadly featured in the media, including in 'Il Venerdì di Repubblica' (2016), one of the most read weekly magazines in Italy. She appeared as a speaker at the TEDx lecture series in 2016 with more than 42,000 views. She served as the Primary investigator of 32 grant projects, expert evaluator of 18 European funding initiatives (including ERC), and was a Chairwoman of 10 scientific congresses and speaker at numerous international conferences. She is an Associate Editor of the journals Neuroscience and Restorative Neurology.

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### **Robert J. Thomas**

Robert Joseph Thomas, M.D., M.M.Sc, is Associate Professor of Medicine, Harvard Medical School & The Division of Pulmonary, Critical Care & Sleep, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA, His background includes Internal Medicine, Neurology and Sleep Medicine. His research spans mood, cognition (translational and epidemiology), sleep epidemiology, signal analysis in sleep medicine, and sleep-breathing outcomes, and functional imaging of cognition in sleep disorders. He has articulated a new approach to sleep physiology termed "sleep effectiveness", which is a cross-physiology, networked, integrative approach to characterizing sleep state using cardiopulmonary coupling estimates (patented). His laboratory generates novel approaches and analysis tools for probing several sleep signals – ECG, EEG, respiration and multi-signal integration approaches. He funding sources are the NHLBI, NINDS and the American Sleep Medicine Foundation. He was key in the development of a FDA approved wearable device, the M1/SleepImage system, for dynamic sleep quality tracking. He is an acknowledged expert in the area of treatment of central and complex sleep apnea and periodic breathing, utilizing CO<sub>2</sub> regulation approaches (patented). He studies brain health in the context of sleep disorders in the USA and South Korea. He directs the AASM accredited clinical sleep center and sleep laboratory, and the sleep medicine training program at the Beth Israel Deaconess Medical Center. I worked in the development and implementation (patented) of auto CPAP algorithms from concept through regulatory submission, which are now in FDA approved products.

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### **Alexey Zaikin**

Alexey Zaikin has a Chair in Applied Mathematics and Systems Medicine at UCL, holding a shared appointment between Department of Mathematics and Institute for Women's Health. Currently funded by

MRC and CR-UK, he has published more than 140 papers in multidisciplinary areas, especially in the field of complex systems and data analysis, and has long experience of collaboration with wet biologists and clinicians. He studied physics at Moscow State University, and received an MS in Physics with distinction and the Khoklov Award for Excellence in Research. He got his PhD in 1998 in Moscow and Habilitation in 2003 in Potsdam, Germany. In 2008 he joined UCL and worked on analysis of clinical data, to find new oncomarkers for ovarian cancer, to investigate new methods for the analysis of DNA methylation, to study association of sex-steroid hormones with breast cancer risk, to investigate sex-hormone system in BRCA1/2 mutation carriers, to study early detection of colorectal and pancreatic cancer or aberrant regulation of RANKL/OPG in developing breast cancer. In addition to data analysis, he devoted a significant amount of time to the development of new statistical and AI methodologies, including development of algorithms for the detection of network community oncomarkers, parameter estimation methods, Bayesian change point methods for the analysis of longitudinal oncomarkers, or new methods to analyse trends in longitudinal oncomarkers. These works confirmed the power of longitudinal algorithms over the analysis of single time points. Recently he started to utilize parenclitic and developed synolitic network analysis methodology. For the past 5 years, his research interests have included the study of intelligence and consciousness in genetic and neuron-astrocyte networks, investigating the role of astrocytes and a generation of Integrated Information.

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### **Stefano Zapperi**

Stefano Zapperi is currently professor of theoretical condensed matter physics at the University of Milano and coordinator of the Center for Complexity and Biosystems. He graduated in physics at the University of Rome “La Sapienza” and received his Ph. D. in physics from Boston University. After a postdoctoral position at ESPCI in Paris, he became tenured researcher at INFM at the University Rome and then at the University Modena and Reggio Emilia. He became then senior researcher at CNR-IENI in Milano. He has been invited as visiting scientist or visiting professor in many institutions worldwide, including Cornell University, Aalto University, ENS Paris and Lyon, LMU Munich, FAU Erlangen-Nuremberg, Boston College, Rice University and the Weizmann Institute of Science. Prof. Zapperi is an expert in the statistical physics of complex systems and has contributed to the fields of materials science, biophysics and systems biology. His most notable contributions include the theory of the Barkhausen noise in magnets, the statistical physics of plasticity and fracture, and recent work on the physics of cancer and protein aggregation. He published more than 200 scientific papers. In 2017, he co-authored with Caterina La Porta a book on the “Physics of Cancer” and in 2022 a book on “Crackling Noise”. Prof. Zapperi is the recipient of numerous awards including the Marie Curie Excellence Award, the Humboldt Research Award, the Advanced Grant from the European Research Council. He was elected fellow of the American Physical Society and named Finland Distinguished Professor by the Academy of Finland. He is member of the editorial boards of JSTAT.

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# Scientific Program

**Registration** **12:00-14:00** **Sunday, 24 July, 2022**

**Opening** **Plamen Ch. Ivanov** **14:00-14:20** **Sunday, 24 July, 2022**

**Session Chair:** **Plamen Ch. Ivanov**

**Plamen Ch. Ivanov** **14:20-14:55** **Sunday, 24 July, 2022**

**Title:** *The new field of Network Physiology: Mapping the Human Physiome*

**Abstract:** The human organism is an integrated network where complex physiological systems, each with its own regulatory mechanism, continuously interact to optimize and coordinate their function. Organ-to-organ interactions occur at multiple levels and spatiotemporal scales to produce distinct physiologic states: wake and sleep; light and deep sleep; consciousness and unconsciousness. Disrupting organ communications can lead to dysfunction of individual systems or to collapse of the entire organism (coma, multiple organ failure). Yet, we know almost nothing about the nature of interactions among diverse organ systems and sub-systems, and their collective role as a network in maintaining health.

The emerging new field of Network Physiology aims to address these fundamental questions. In addition to defining health and disease through structural, dynamical and regulatory changes in individual systems, the network physiology approach focuses on the coordination and interactions among diverse organ systems as a hallmark of physiologic state and function.

Through the prism of concepts and approaches originating in statistical and computational physics and nonlinear dynamics, we will present basic characteristics of individual organ systems, distinct forms of pairwise coupling between systems, and a new framework to identify and quantify dynamic networks of organ interactions.

We will demonstrate how physiologic network topology and systems connectivity lead to integrated global behaviors representative of distinct states and functions. We will also show that universal laws govern physiological networks at different levels of integration in the human body (brain-brain, brain-organ and organ-organ), and that transitions across physiological states are associated with specific modules of hierarchical network reorganization.

We will outline implications for new theoretical developments, basic physiology and clinical medicine, novel platforms of integrated biomedical devices, robotics and cyborg technology.

The presented investigations are initial steps in building a first Atlas of dynamic interactions among organ systems and the Human Physiome, a new kind of BigData of blue-print reference maps that uniquely represent physiologic states and functions under health and disease.

**Kathryn A. Hibbert** **14:55-15:30** **Sunday, 24 July, 2022**

**Title:** *Heterogeneity in critical illness: Challenges and opportunities*

**Abstract:** A significant burden in critical illness is from two syndromes – sepsis and the acute respiratory distress syndrome (ARDS). Identified with broad reaching clinical definitions, both sepsis and ARDS are significantly heterogeneous and do not reflect a single disease process.<sup>1,2</sup> These definitions have both clinical and research utility, allowing for easy bedside identification and enrollment in trials. However, the innate heterogeneity in critical illness has also complicated both clinical care and research efforts. For example, a diagnosis of sepsis does not have adequate prognostic information to guide interventions and discussions with family. Additionally, we have failed to consistently identify therapeutic interventions, and most critical care trials have either been negative or have not been replicated with subsequent efforts. Many attempts have been made to identify both sub-phenotypes and endotypes, but this information is

rarely available in real time at the bedside. Critical care is therefore ripe for an approach that can leverage the data-rich environment of intensive care, and network physiology has the potential to answer significant unmet clinical needs including greater diagnostic and prognostic certainty, personalized therapy, and higher yield trial design.

**Coffee Break**

**15:30-16:00**

**Sunday, 24 July, 2022**

**Barbara Corkey**

**16:00-16:35**

**Sunday, 24 July, 2022**

**Title: *The redox communication network as a regulator of metabolism***

**Abstract:** Key tissues are dysfunctional in obesity, diabetes, cardiovascular disease, fatty liver and other metabolic diseases. Focus has centered on individual organs as though each was isolated. Attention has been paid to insulin resistance as the key relevant pathosis, particularly insulin receptor signaling. However, many tissues play important roles in synergistically regulating metabolic homeostasis and should be considered part of a network. Our approach identifies redox as an acute regulator of the greater metabolic network. Redox reactions involve the transfer of electrons between two molecules and in this work refer to commonly shared molecules, reflective of energy state, that can readily lose electrons to increase or gain electrons to decrease the oxidation state of molecules including NAD(P), NAD(P)H, and thiols. Metabolism alters such redox molecules to impact metabolic function in many tissues, thus, responding to anabolic and catabolic stimuli appropriately and synergistically. It is also important to consider environmental factors that have arisen or increased in recent decades as putative modifiers of redox and reactive oxygen species (ROS) and thus metabolic state. ROS are highly reactive, controlled by the thiol redox state and influence the function of thousands of proteins. Lactate (L) and pyruvate (P) in cells are present in a ratio of about 10 reflective of the cytosolic NADH to NAD ratio. Equilibrium is maintained in cells because lactate dehydrogenase is highly expressed and near equilibrium. The major source of circulating lactate and pyruvate is muscle, although other tissues also contribute. Acetoacetate (A) is produced primarily by liver mitochondria where  $\beta$ -hydroxybutyrate dehydrogenase is highly expressed, and maintains a ratio of  $\beta$ -hydroxybutyrate ( $\beta$ ) to A of about 2, reflective of the mitochondrial NADH to NAD ratio. All four metabolites as well as the thiols, cysteine and glutathione, are transported into and out of cells, due to high expression of relevant transporters. Our model supports regulation of all collaborating metabolic organs through changes in circulating redox metabolites, regardless of whether change was initiated exogenously or by a single organ. Validation of these predictions suggests novel ways to understand function by monitoring and impacting redox state.

**Caterina Da Re**

**16:35-17:10**

**Sunday, 24 July, 2022**

**Title: *Frontiers: where scientists empower society***

**Abstract:** Frontiers is the 3rd most-cited and 6th largest research publisher and open science platform.

One option for authors who wish to make their work openly accessible is to publish in a journal that makes their work immediately and permanently available online for everyone, worldwide. Open access (OA) is a step towards the democratization of scientific literature. By taking advantage of the digital revolution, OA exploits the interconnected world in order to provide free access and reuse of scientific literature for potentially everyone in the world. The "liberty of re-utilization" drastically promotes the spreading of scientific knowledge and its validation, making OA an efficient system for promoting scientific research.

Frontiers journals are community-driven and peer-reviewed by editorial boards of over 202,000 top researchers. Featuring pioneering technology, artificial intelligence, and rigorous quality standards, our research articles have been viewed more than 1.9 billion times, reflecting the power of open research. Our mission is to make science open – so that scientists can collaborate better and innovate faster to deliver the solutions that enable healthy lives on a healthy planet.

Frontiers was founded in 2007 by Henry Markram and Kamila Markram, two neuroscientists from the Swiss Federal Institute of Technology (EPFL) in Lausanne, Switzerland. Henry and Kamila launched Frontiers with a vision to make science open, peer-review rigorous, transparent, and efficient and harness the power of technology to truly serve researchers' needs. Initially starting in the field of neuroscience, Frontiers now spans hundreds of academic



disciplines and is one of the most cited and largest research publishers in the world.

As of today, Frontiers counts 163 journals. Frontiers in Network Physiology launched in 2020 and led by Doctor Plamen Ch. Ivanov, Field Chief Editor, is the first journal to focus on the mechanisms through which systems and organs interact and integrate to generate a variety of physiologic states. In addition to defining health and disease through structural, dynamical and regulatory changes in individual physiological systems, the new conceptual framework of Network Physiology focuses on the coordination and network interactions among diverse organ systems and sub-systems as a hallmark of physiologic state and function.

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**Registration** **8:00-9:00** **Monday, 25 July, 2022**

**Session Chair: Olga Sosnovtseva**

**Jürgen Kurths** **9:00-9:35** **Monday, 25 July, 2022**

**Title: *Synchronization and chimera phenomena in neural networks with time delay and noise***

**Abstract:** We study effects synchronization phenomena in neuronal networks. One focus is on systems with partial time delays and their resulting dynamics. Our research reveals that partial time delays significantly affect phase synchronization there. In particular, they can either enhance or decrease phase synchronization and induce synchronization transitions with changes in the mean firing rate of neurons, as well as induce switching between synchronized neurons. Moreover, in comparison to a network where all connections are delayed, we show that small partial time delay probabilities have especially different influences on phase synchronization of neuronal networks.

Another focus is on neural systems with excitatory and inhibitory synapses. We verify that the decrease in the influence of inhibition can generate synchronization originating from a pattern of desynchronized spikes. The transition from de-synchronous spikes to synchronous bursts, induced by varying the synaptic coupling, emerges in a hysteresis loop due to bistability where abnormal, excessively high synchronous regimes exist. Then, we show that it is possible to suppress such abnormal synchronization by applying a small-amplitude external current on about 10% of the neurons in the network, which opens an efficient way to control or treat epileptic seizures.

Next, we investigate the collective dynamical behaviors of a network of identical Hindmarsh-Rose neurons that are coupled under small-world schemes upon addition of alpha-stable Le´vy noise. According to the ring patterns of each neuron, we distinguish the neuronal network into spike state, burst state and spike-burst state coexistence of the neuron with both spike ring pattern and burst firing pattern. Furthermore, an interesting phenomenon is observed that the system presents coherence resonance in time and chimera states in space, namely coherence resonance chimeras.

**Caterina A. M. La Porta** **9:35-10:10** **Monday, 25 July, 2022**

**Title: *Classification of triple-negative breast cancers through a Boolean network model of the epithelial-mesenchymal transition***

**Abstract:** Predicting the metastasis risk in patients with a primary breast cancer tumor is of fundamental importance to decide the best therapeutic strategy in the framework of personalized medicine. We discuss ARIADNE, a general algorithmic strategy to assess the risk of metastasis from transcriptomic data of patients with triple-negative breast cancer, a subtype of breast cancer with poorer prognosis with respect to the other subtypes. Our method identifies hybrid epithelial/mesenchymal phenotypes by mapping gene expression data into the states of a Boolean network model of the epithelial-mesenchymal pathway. Using this mapping, it is possible to stratify patients according to their prognosis, as we show by validating the strategy with three independent cohorts of triple-negative breast cancer patients. Our strategy provides a prognostic tool that could be applied to other biologically relevant pathways, in order to estimate the metastatic risk for other breast cancer subtypes or other tumor types.

Coffee Break

10:10-10:40

Monday, 25 July, 2022

Shlomo Havlin

10:40-11:15

Monday, 25 July, 2022

**Title: *Network applications in physiology and biology***

**Abstract:** Complex systems—biological, ecological or technological—often experience perturbations and disturbances, from protein dysfunctions to species extinction in ecological networks. We identify the recoverable phase of a complex dynamical system, a state in which the system can be reignited by microscopic interventions, for instance, controlling just a single node. Multi-stability is a widely observed phenomenon in real complex networked systems, such as ecological systems and gene regulation. When a system functions normally but there exists also a potential state with abnormally low activity, although the system is at equilibrium it might make a transition into the low activity undesired state due to external disturbances and perturbations. Thus, such a system can be regarded as unsustainable, due to the danger of falling into the potential inactive state. Here we show, analytically and by simulations, how supporting the activity of a fraction of nodes can turn an unsustainable system to be sustainable one by eliminating the inactive potential stable state.

Freezing of gait (FoG), a gait disturbance commonly experienced by patients with Parkinson's disease (PD), is characterized by sudden episodes of inability to generate effective forward stepping. Here, by developing tools based on network science and non-linear dynamics, we analyze synchronization networks of electroencephalography (EEG) brain waves of three PD patient groups with different FoG severity. We find higher EEG amplitude synchronization (stronger network links) between different brain locations as PD and FoG severity increase. These results are consistent across frequency bands (theta, alpha, beta, gamma) and independent of the specific motor task (walking, still standing, hand tapping) suggesting that an increase in severity of PD and FoG is associated with stronger EEG networks over a broad range of brain frequencies. This observation of a direct relationship of PD/FoG severity with the overall EEG synchronization network may be used for evaluating FoG propensity and help to gain further insight into PD and the pathophysiology leading to FoG.

I will also discuss preliminary results on fMRI brain network during rest and show that each person has its own network features which might be related to personal performance.

Robert J. Thomas

11:15-11:50

Monday, 25 July, 2022

**Title: *Sleep as a network in health and disease***

**Abstract:** Sleep state is a complex network across the brain and body. Short and long-range communications, across neural, cardiac, motor, autonomic and respiratory systems are obvious, but sleep is much deeper network state, with classic cytokine, endocrine and immune mechanisms at play. The classic approach to sleep has a focus on the electroencephalogram, but "everything sleeps" during biological sleep, with measurable dynamics which at best partially correlates with conventional sleep states. Network interactions occur at each level (e.g., brain cortical, brain stem, peripheral hemodynamic) and across levels (e.g., ventilation-electrocortical, blood pressure-respiration, electrocortical-respiration) and can be measured. When network approaches or coupling across systems are mapped, sleep takes on a very different look from the conventional sleep stages. There are predictable and sometimes surprising patterns in both health and disease. Wearable or nearable technologies now allow dynamic tracking of signals from which network/coupling information can be extracted in ways impossible before. These aspects of the network biology of sleep will be presented with an eye to clinical utility and disease patterns which could be modified for benefit.

Ruedi Stoop

11:50-12:20

Monday, 25 July, 2022

**Title: *Network physiology, criticality and computation - facts and fiction***

**Abstract:** Collective dynamics of neurons is at the base of the cognitive functions and behavior of higher animals. Salient expressions are continued spontaneous activities that modulate neural responses to external

stimuli and are often thought to reflect expectations of future stimuli. An observation that has received widespread interest is spontaneous spatiotemporal patterns of neural activity, commonly termed 'neural avalanches', that have no characteristic scale, i.e., the distributions of avalanche size and lifetime follow power laws. If many—generally relatively simple—interacting elements generate system properties that exhibit power law distributions, this can be taken as a fingerprint of a neighboring critical (transition) point of the collective behavior. Consequently, it has been conjectured that biological and in particular cortical neural systems might operate in the close vicinity of a critical point and it has been suggested that, using such a state, the brain might optimize functional properties relevant for information processing (such as information transmission, information capacity and response flexibility and computation).

In physics, critical points are related to phase transitions. We shall discuss why and how the physics notion of critical states has been applied to biology and discuss existing or missing biological evidence for a number of prominent conjectures that have been made in the context of biological criticality. The biological system that provides the guideline for our analysis is the mammalian hearing system, an ancient prototype of a neural system embedded in the mammalian network physiology.

We will show that critical states of the hearing system (expressed by power-law activation distributions on the network), correspond to unbiased information uptake. In audition, this state roughly represents what we describe as "hearing". The process of "listening", in contrast, corresponds to a computational state, expressed by a "destruction" of parts of the available information complexity. In the latter state, the corresponding distributions no longer have the power-law form required by criticality. In this way, the working embedded hearing system exploits both critical and subcritical systems, a fact that has been, unfortunately, neglected in the construction of artificial hearing aid construction.

**Lunch Break**

**12:20-14:00**

**Monday, 25 July, 2022**

**Session Chair:**

**Ruedi Stoop**

**Olga Sosnovtseva**

**14:00-14:35**

**Monday, 25 July, 2022**

**Title: *Kidney function: Optimization of nephrovascular network***

**Abstract:** The kidney is an efficient filtering "device" whose microvasculature forms macroscopic networks that support communication between individual units called nephrons to optimize tissue perfusion and to fulfill overall function. Delicate structure of a nephron must be protected from episodes of high blood pressure that occur routinely in all of us. The kidney must be viewed as the champion among organs of the body when it comes to stability of organ blood flow. The regulation is normally attributed to highly efficient autoregulation mechanisms that interrelate reabsorption and filtration rate via regulation of renal vascular resistances. Current paradigm is that autoregulation at a nephron acts independently. However, there is evidence that neighboring nephrons exchange information and tend to work together. These interactions are important to the effectiveness of autoregulation but we know very little about them. What are the structural and anatomical features of the renal vascular network? Which techniques are available to access its structural and dynamical parameters? How can we relate structural and functional changes in health and disease? These fundamental questions will be discussed through the prism of structural and dynamic networks approaches to kidney function.

**Michael G. Rosenblum**

**14:35-15:10**

**Monday, 25 July, 2022**

**Title: *Controlling collective synchrony by pulsatile stimulation***

**Abstract:** The emergence of a collective mode in a strongly interconnected network of self-sustained oscillators has been studied theoretically and observed in various experiments. In particular, collective synchronization is frequently considered a mechanism of macroscopic rhythms' appearance in neuronal ensembles. For example, it is hypothesized that pathological brain rhythms observed in patients with Parkinson's disease result from the coherent activity of thousands of neuronal cells. This hypothesis helps

to model the effects of deep brain stimulation - the clinical procedure exploited to treat the disease. Here, we briefly review the mechanism of collective synchrony and then discuss a feedback scheme for synchrony control. Since the feedback control implies the processing of the brain signals, we discuss the relevant problem of real-time phase and amplitude estimation from measurements.

**Coffee Break**

**15:10-15:40**

**Monday, 25 July, 2022**

**Christopher R. Stephens**

**15:40-16:15**

**Monday, 25 July, 2022**

**Title: *From the Physiome to the Conductome and back: A Conceptual Framework***

**Abstract:** Omic perspectives are intended to be comprehensive, holistic and integrative. Most omes - genomes, proteomes etc. - have been associated with developing a comprehensive understanding of the interactions between particular molecular structures, such as genes and proteins. The Physiome, in contrast, considers more macroscopic structures, such as tissues and organs, where information about the structure is often encoded in time series data from certain observables associated to those structures, with a natural representation for the ome being as a network, as at least this captures, in a more integrative manner, the simultaneous interactions between multiple systems. In general, however, current omes tend to be "closed-system" concepts, where interaction with the external world is not accounted for. At a certain level of understanding, and over a certain timescale, considering independence from the environment can be a reasonable approximation. However, if we consider, for example, the aetiology and progression of disease across a human lifetime then it is clear that, generally, the causes of disease are a result of our evolving and adaptable conduct in an equally evolving and adaptable environment. Indeed, conduct – what an organism does - is the very means by which it interacts with the external world. In this case, physiology, such as hunger state, affects conduct – for example, foraging – and conduct, in turn, affects physiology, as in changed levels of hormones such as ghrelin and leptin. The dynamical relations between physiology and conduct can be short term, such as in this example, or long term, such as in the case of energy imbalance over extended time periods leading to obesity and other metabolic disorders. We discuss the Conductome as a framework within which we may consider a wide range of drivers of human behaviour - from the "micro" to the "macro" – particularly across extended time horizons, in order to understand and predict those behaviours which have a consequent cumulative impact on our physiology.

**André Longtin**

**16:15-16:50**

**Monday, 25 July, 2022**

**Title: *Non-monotonic complexity in multi-delay physiological feedback systems.***

**Abstract:** Single delays in nonlinear systems can bring on complex behaviours including chaos, hyperchaos and multistability between chaotic attractors. Delays may be responsible for fluctuations seen in physiological control systems, and in the nervous system these delays are constantly prone to vary due to activity-dependent myelination of axons. The inclusion of more delays will generally - but not always - lead to more complex behaviour, measured e.g. with dynamical entropy. This talk will describe how the complexity first increases as more delays are added, and eventually can decrease past a certain threshold number of delays. The transition to the large number of delay limit also brings surprising bifurcations that depend on the distribution of delays. I will also show how the combination of local and global delays in neural networks can give rise to novel kind of spatio-temporal patterns, and say a few words about the reservoir computing potential of multi-delay systems.

**Poster Session I**

**17:00-18:30**

**Monday, 25 July, 2022**

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Session Chair: Christopher R. Stephens

Shlomo Havlin

9:00-9:35

Tuesday, 26 July, 2022

**Title:** *Network science and applications*

**Abstract:** Network science has been applied in many worldwide systems and processes in different disciplines. These include social systems, physiology, traffic, climate, epidemics, and very recently physics. I will show some examples of how network tools can mitigate pandemics, how switching between topics of scientists affects their scientific impact, and how fresh teams can be associated with original and interdisciplinary research. I will also show how network tools can help to improve urban traffic, identify novel features in interdependent networks, and can identify novel physical processes.

Barbara Corkey

9:35-10:10

Tuesday, 26 July, 2022

**Title:** *The mitochondrial redox network as a regulator of body weight and obesity*

**Abstract:** The increasing incidence of obesity correlates with insulin resistance, hyperlipidemia, fasting hyperinsulinemia, increasing consumption of highly processed food and potential environmental toxins such as plastics and air pollution. The sequence of appearance and causal relationship between the appearance of each of these potential causes of obesity and the onset of obesity has not been determined. The cause must precede obesity, the consequence, and temporally relate to its rising incidence in different populations. It is unlikely that macronutrients such as carbohydrates or fats cause obesity since these have long been constituents of the human diet. High carbohydrate diets have been common in warm to moderate climates, where agriculture thrives, and high fat diets, in cold climates. Furthermore, food consumption and body weight have been well-regulated in most humans and other species until recent times. Thus, our attention must focus on changes that have occurred in the last half-century and the relationship between such changes and specific populations that are impacted. The hypothesis presented here is that substances that have entered our environment recently, cause obesity through redox changes that generate false and misleading information about energy status throughout the entire body. Thus, an increase in mitochondrial redox or reactive oxygen species (ROS), is normally encountered when fuel supplies exceed energy needs. ROS generates important signals such as insulin secretion and triglyceride synthesis to store fuel and then rapidly converts mitochondrial ROS to water in a process that wastes energy via a mitochondrial proton leak in the presence of fuel beyond the storage needs of the body. Inappropriate signals will, thus, lead to excess insulin secretion and excess fat storage ultimately leading to metabolic dysfunction and obesity. Such signals may also stress the cellular ROS scavenging capacity leading to oxidative damage to proteins with sensitive thiols. Examples will be provided of common food additives that generate ROS and thereby elicit tissue specific functional changes that are inappropriate. Reversal requires the identification and removal of these compounds or preventions of their effects. Interestingly, very few of the new agents that may be consumed or inhaled have been tested.

Coffee Break

10:10-10:40

Tuesday, 26 July, 2022

Plamen Ch. Ivanov

10:40-11:15

Tuesday, 26 July, 2022

**Title:** *Physiologic network interactions: Novel hallmark of physiological state and function*

**Abstract:** The new framework of Network Physiology aims to understand states and functions at the organism level as emergent coordination among physiological sub-systems and systems, each of which exhibits unique dynamics characterized by non-stationary, noisy and even scale-invariant output. In this framework, transitions across physiologic states involve hierarchical reorganization of the networks of physiologic interactions. Despite the rapid development of Network Physiology as a new field, the specific question of how key physiologic systems continuously interact and collectively behave as a dynamic network to generate distinct functions remains elusive. I will discuss a general strategy to approach this fundamental question. I will outline the typical challenges encountered in probing physiologic interaction and present some recently developed techniques suitable to address these challenges. By applying these new methods to empirical physiologic recordings, I will

present some new findings regarding communications among distinct brain cortical rhythms as well as their feedback control on key organ systems with focus on plasticity of brain wave network interactions and brain-heart regulation.

**Kathryn A. Hibbert**

**11:15-11:50**

**Tuesday, 26 July, 2022**

**Title: *COVID-19: A case for Network Physiology***

**Abstract:** The COVID-19 pandemic has been a pandemic of both critical illness and chronic recovery, and has vividly demonstrated the shortcomings of our current approaches to identifying and understanding multisystem disease. COVID-19, likely many critical illnesses, is a multisystem and multidimensional disease with far reaching effects of multiple organ systems on different timelines – in addition to the acute manifestations of primary ARDS, there are long lasting and thus far poorly understood sequelae of disease, termed the post-acute sequelae of SARS-CoV-2 (PASC). The cumulative and heterogeneous experience of the millions of people who have been infected with SARS-CoV-2 also demonstrates that pathogen diversity may not be the primary source of heterogeneity in critical illness, and is similar to the diversity of experience seen in non-COVID critical illness. Moving through the next phase of the pandemic, what is urgently needed are network approaches that better identify vulnerable sub-phenotypes for targeted intervention and better predict post-acute sequelae of SARS-CoV-2 infection (PASC).

**Charles C. Hardin**

**11:50-12:20**

**Tuesday, 26 July, 2022**

**Title: *Physiologic modeling of respiratory, immune and coagulation dynamics in critical COVID-19***

**Abstract:** Respiratory failure in the setting of COVID-19 manifests as the acute respiratory distress syndrome (ARDS). ARDS results from complex and incompletely understood interactions between lung infection or injury, alveolar stability, the coagulation cascade, and multiple patient immune pathways. Further complicating the pathophysiology are multi-system interactions in which inflammatory mediators and thrombosis originating in the lung circulate and result in subsequent non-pulmonary organ failures. In this complex and dynamic environment, clinical trials, a traditional method of assessing novel treatment protocols, can be of limited utility. Trial populations may inadequately sample the entire parameter space of possible key variables. Moreover, clinical trials have limited ability to explore multi-variate interactions and or to test network effects in a controlled way. Mathematical modeling is ideally suited to these tasks, however. Here we describe the development of a systems biology model of COVID-19 ARDS which includes viral infection and replication, innate and adaptive immunity, microthrombosis and the systemic transport of virus, thrombi and immune mediators to non-pulmonary organs. We use this model to explore mechanisms of response to immune modulators and antiviral agents and to predict optimum treatment protocols.

**Lunch Break**

**12:20-14:00**

**Tuesday, 26 July, 2022**

**Session Chair:**

**Rhonny Bartsch**

**Klaus Lehnertz**

**14:00-14:35**

**Tuesday, 26 July, 2022**

**Title: *Biological rhythms and evolving functional brain networks***

**Abstract:** There are many examples of (not strictly periodic) oscillations in the human organism, ranging from microscopic oscillations of e.g. genes, cells, and neurons to macroscopic oscillations of e.g. heartbeats, brainwaves, and bowel movements. Oscillations can be associated with various endogenous and exogenous biological rhythms of which the circadian rhythm – a roughly 24-h cycle – is probably the best investigated rhythm. Biological rhythms typically arise via synchronization of self-oscillatory systems (cell and organs) and often play important functional roles in the human organism, both for physiological and pathophysiological conditions. Investigating the impact of biological rhythms typically begins with recording appropriate observables over an extended period of time (ideally years). For the brain and the

heart, this can be conveniently carried out with electroencephalography (EEG) and electrocardiography (ECG). Then, spectral analysis is often used to identify footprints of biological rhythms in the respective time series. Studies on how biological rhythms impact on interactions within and between pairs of organ systems are rare and this is even more true when it comes to networks of interacting organ systems. At the example of evolving functional brain networks, derived from continuous multiday, multichannel EEG recordings using commonly employed analyses techniques, I will showcase the impact of biological rhythms on various characteristics of functional brain networks. I will also discuss current limitations of and potential challenges for studies on evolving functional brain networks.

**Sebastiano Stramaglia**

**14:35-15:10**

**Tuesday, 26 July, 2022**

**Title: *Modelling high-order behaviors in Network Physiology with Information Theory***

**Abstract:** Two recent lines of research suggest that complex systems should take into account interactions of more than two elements. High-order mechanisms can be modelled by hypergraphs and studied via topological data analysis. In parallel, effective information-theoretic tools have been developed to characterize high-order interdependencies from observed data, i.e. high-order behaviors referring to emergent properties of the resulting multivariate statistics. Mechanisms and behaviors address fundamentally different questions: the former address how the system is structured, while the latter focus on emergent properties related to what it “does”; a complete account of higher-order phenomena needs to embrace both.

Two main concepts arise in the study of high-order behaviors, synergy and redundancy. In broad terms, synergy arises from statistical interactions that can be found collectively in a network but not in parts of it considered separately, while redundancy refers to group interactions that can be explained by the communication of sub-groups of variables. Here we will describe approaches for high-order behaviors based on partial information decomposition and O-information, a metric capable to reveal synergy- and redundancy-dominated interactions in a network of multiple interacting variables. Applications related to networked physiological systems will be reported.

**Coffee Break**

**15:10-15:40**

**Tuesday, 26 July, 2022**

**Olga Sosnovtseva**

**15:40-16:15**

**Tuesday, 26 July, 2022**

**Title: *Network Physiology aspects of diabetic kidney disease***

**Abstract:** The kidney links cardiovascular, nervous and metabolic systems providing regulation of blood pressure and release of hormones. Type 2 diabetes mellitus is affecting an increasing number of patients. It is one of the most urgent public health problems world-wide and one of the primary reasons for development of chronic kidney disease. Numerous drug classes are available for treatment, however, their efficacy with regard to diabetes-induced renal and cardiovascular complications remains limited. Can the kidney be a new target for new therapeutic strategies? Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are new anti-hyperglycemic drugs, which act directly on the kidney. Recent clinical trials have revealed their significant cardiovascular and kidney protective effects. We will focus on the effects of SGLT2i on the renal autoregulation and microcirculation to elucidate their immense potential as a new therapeutic measure in kidney disease and to discuss the utility of novel network physiology approaches.

**Ronny P. Bartsch**

**16:15-16:50**

**Tuesday, 26 July, 2022**

**Title: *EEG synchronization networks of Parkinson's disease patients with freezing of gait***

**Abstract:** Freezing of gait (FoG), a gait disturbance commonly experienced by patients with Parkinson's disease (PD), is characterized by sudden episodes of inability to generate effective forward stepping. Recent studies have shown an increase in certain brain frequencies during FoG, however, comprehensive research on the synchronization between different brain locations and frequency bands in PD patients is scarce. Here, we analyze synchronization networks of electroencephalography (EEG) brain waves of three PD patient groups with different FoG severity. We find higher EEG amplitude synchronization (stronger

network links) between different brain locations as PD and FoG severity increase. These results are consistent across frequency bands (theta, alpha, beta, gamma) indicating that an increase in severity of PD and FoG is associated with stronger EEG networks over a broad range of brain frequencies.

Poster Session II

17:00-18:30

Tuesday, 26 July, 2022

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Session Chair: Sebastiano Stramaglia

Ulrich Parlitz

9:00-9:35

Wednesday, 27 July, 2022

**Title:** *The nonlinear dynamics of the heart: collective excitation in networks of cardiac cell*

**Abstract:** The cardiac muscle is an excitable medium that exhibits complex dynamics, including spatiotemporal chaos associated with (life-threatening) cardiac arrhythmias. On a small scale, cardiac tissue consists of interacting cardiomyocytes embedded in an extracellular matrix. The beating cardiomyocytes form a dynamic network of electromechanically coupled oscillators that exhibit synchronized motion and support the propagation of excitation waves. These waves may transform into spiral or scroll waves (also called rotors), resulting in tachycardia with impaired pumping. In a further transition, the excitation waves may become even more complex, with spatiotemporal chaos leading to complete loss of pumping function. This condition is life-threatening in ventricular fibrillation if not treated and terminated immediately by electrical defibrillation shocks. In the lecture, we will discuss dynamic properties of the network of cardiomyocytes that constitute the myocardium and theoretical concepts to characterize complex cardiac dynamics such as phase singularities and complexity measures. We will also introduce different measurement methods, such as optical mapping or 4D ultrasound, to study the complex dynamics of the heart ex-vivo and in-vivo.

Christopher R. Stephens

9:35-10:10

Wednesday, 27 July, 2022

**Title:** *Applications to Obesity and Metabolic Disease of the Physiome and Conductome*

**Abstract:** In the talk "From the Physiome to the Conductome and back: A Conceptual Framework", the Conductome was introduced as a unifying concept that can link other omes, such as the genome and physiome, to the environment. In this talk we will use both "omic" concepts to illustrate how they can complement one another in promoting a better and deeper understanding of disease. In particular, we will consider those diseases that are particularly "lifestyle" dependent, such as obesity and chronic metabolic disorders. We will use obesity and metabolic disease data from our group, that covers more than 4000 participants and several thousand variables, from the genetic to the sociological and psychological, to illustrate both the Physiome and the Conductome in the context of obesity and other metabolic disorders and then show how the two may be linked to disentangle causal relations between environment, behaviour and physiology. We will also present evidence of how some simple public health interventions may be used to promote better metabolic health.

Coffee Break

10:10-10:40

Wednesday, 27 July, 2022

J. Randall Moorman

10:40-11:15

Wednesday, 27 July, 2022

**Title:** *Challenges: applying network physiology to predictive analytics monitoring for early detection of illness*

**Abstract:** Doctors will look to discoveries in the new field of network physiology to help them take care of patients. Many subscribe to the notion that we can detect some subacute potentially catastrophic illnesses early in their course by mathematical analysis of continuous cardiorespiratory monitoring where we are looking for signatures of illness. By that term, I mean the kinds of phenomena that applications of network physiology seek



to discover and quantify. Here are examples - rising heart rate and falling blood pressure, disrupted sinus arrhythmia, or bradycardia and oxygen desaturation in the newborn. These are signatures that present differently depending on clinical circumstances but are similar in that the abnormality may not lie in the measured value of one parameter, but in the way that two or more time-series interact, or fail to, over time. As we progress in the field and look to apply the principles of network physiology to the real world, we can stop to think about new challenges that, if met, would alter the trajectory of the field. Challenge 1: What are the anatomical substrates of network physiology? We accept, for example, that the autonomic nervous system couples the heart and the lungs via the brain stem. What are other substrates? One approach: The immune system may play a central role in signaling among organs. An example is the cholinergic anti-inflammatory pathway that tempers cytokine release when microorganisms enter the otherwise sterile peritoneum. Challenge 2: What new physiological networks can be monitored? One approach: In addition to the original scheme of monitoring EKG, EMG, and EEG, we might return to the analysis of breathing dynamics measured from the motion of the chest. I will show new results of an analysis of respiratory kinematics using a novel system. Challenge 3: What new measures can be used to measure network physiology? One approach: In another talk, I will discuss highly comparative time-series analysis that allows testing of very wide ranges of analytics. Challenge 4: How do we isolate the physiological network of the hospitalized patient from the external networks? The hospital is a complex network of care providers, tests, medications, and the time they are administered. It is an important challenge to separate the dynamics of the patient's illness from the distractions and decisions of the clinicians. Physiology should change first, but we base much of our hope for early detection of illness on information in the Electronic Health Record. One approach: We should quantify the impact of continuous cardiorespiratory monitoring, a window into the patient, to understand the improvement in detection that network physiology brings to EHR models. Challenge 5: How do we define the time scales over which we characterize dynamics? One approach: We might begin by thinking about the physiological and pathophysiological processes. The time scales of physiology are constant and short - beat-to-beat, breath-to-breath, thought-to-thought. The time scales of illness vary greatly - from moment-to-moment, as in acute myocardial infarction, to decade-to-decade, as in cancer. Network physiology might manifest itself over both. The new knowledge uncovered in pursuit of these or other challenges will surely advance acceptance and utilization of the fundamental precepts of network physiology at the bedside.

**Marina de Tommaso**

**11:15-11:50**

**Wednesday, 27 July, 2022**

**Title: *The cortical networks revised: motor nociceptive network and neuro limbic occipital networks in chronic pain and migraine, a fNIRS and EEG study***

**Abstract:** Migraine is a neurovascular disorder affecting around the 20% of general population. Understanding its pathophysiology could improve therapeutic management and prevention of chronic evolution. In the last years there was a remarkable advance in the knowledge of main mechanism of migraine pain and Calcitonin Gene Related Peptide (CGRP) fundamental role. Our group gave a contribution in the understanding of basal dysfunction in sensory stimuli processing, including visual and nociceptive inputs and related abnormal EEG rhythm oscillations and connectivity patterns. Our lecture will focus on recent results about the effects of novel preventive treatments on brain bioelectrical and metabolic signals, presenting integrated analysis on high density EEG and Functional Near Infrared Spectroscopy. Application of innovative methods of bioelectrical and metabolic cortical networks detection will be showed and discussed.

**Marianna La Rocca**

**11:50-12:20**

**Wednesday, 27 July, 2022**

**Title: *Network physiology to study neurological diseases and chronic pain investigating different brain scales and data.***

**Abstract:** Technological advances have been leading to a progressive increase of information and data in different fields. This is especially true in the context of neuroscience where the creation of large repositories of

medical images and metadata is making ever more pressing the necessity to produce quantitative methods and physical models to manage and analyze the great amount of data of complex matter (Big Data). The development of most of these tools is aimed at studying chronic pain and early diagnosis of neurodegenerative diseases such as Alzheimer and Parkinson. Network-based models of the brain have shown that both local and global topological properties can reveal patterns of disease propagation. However, these intra-subject descriptions do not exploit the whole information context, accessible through inter-subject comparisons. In this lecture, novel approaches, which model inter-subject similarities with a multiplex network was implemented. Direct comparisons to conventional methods on the same datasets showed that the multiplex network approach is more accurate. It also exhibits a higher sensitivity in terms of region number connected to the disease. The strong point of these complex network-based models is their great versatility. Indeed, they, in principle, can be applied, without any restriction, to various contexts, various pathologies and different types of data such as imaging and time series data (EEG and functional near-infrared spectroscopy or fNIRS data).

**Lunch Break**

**12:20-14:00**

**Wednesday, 27 July, 2022**

**Session Chair: Luca Faes**

**Randall Moorman**

**14:00-14:35**

**Wednesday, 27 July, 2022**

**Title: *Applied network physiology: new hammers, new nails***

**Abstract:** In the work ahead to understand the basic properties and mechanisms of network physiology, we should be on the lookout for new tools to use, and new places to apply the tools we have. Ivanov and coworkers developed the Time Delay Stability method to identify synchronized bursts of activity across systems, an approach that was very well-suited to detect networked physiology because it is independent of autocorrelations, nonlinearities, and nonstationarities. It has been a very effective tool and was forged in the context of other fundamental works from the Ivanov group on, for example, correlations in stochastic systems, entropy estimation in non-stationary systems, and phase synchronization in coupled nonlinear oscillators. The method is an excellent example of the success of how we pick numerical methods. We begin with a reason (and sometimes hope is the reason) to think they ought to work. When they don't, we figure out why not and move along, or change them so that they will. In this approach, though, we are limited by our imagination. In 2013, Fulcher and Jones suggested an entirely different one, a wholesale trial of all known families of numerical algorithms on a host of different kinds of time series data. They call this approach highly comparative time-series analysis. We applied it to the early detection of sepsis in premature infants with good results, and I offer it as an example of a way to find new tools for applied network physiology research. As an example of a new job for an old tool, I describe the use of familiar information entropy measures to look for the impact of the COVID-19 pandemic on the networking of healthcare professionals and their healthcare system. The notion is that a hospital is a network, too, not of organs but of human agents organized around the goal of taking care of sick people. The actions of one agent are coupled to those of other agents - for example, the sudden illness of a patient might lead to a flurry of actions by one more clinicians, coupled in that one might order a test but another sees the result and acts upon it. Or the extreme illness of one patient might distract clinicians from the other patients, whose standard tests and actions are delayed and disorganized as a result. We approach the problem by quantifying the surprisal of blood tests in our hospital over the years before and during the pandemic.

**Louis M. Pecora**

**14:35-15:10**

**Wednesday, 27 July, 2022**

**Title: *Statistics of attractor embeddings in Reservoir Computing***

**Abstract:** A recent branch of AI or Neural Networks that can handle time-varying signals often in real time has emerged as a new direction for signal analysis. These dynamical systems are usually referred to as

reservoir computers. A central question in the operation of these systems is why a reservoir computer (RC), driven by only one time series from a driving or source system of many time-dependent components, can be trained to recreate all dynamical time series signals from the drive leads to the idea that the RC must be internally recreating the drive dynamics or attractor. This has led to the possibility that the RC is creating an embedding of the drive attractor in the RC dynamics. There have been some mathematical advances that move that argument closer to a general theorem. However, for RCs constructed from actual physical systems like interacting lasers or analog circuits, the RC dynamics may not be known well or known at all. And many of the existing embedding theorems have restrictive assumptions on the dynamics. We first show that the best way to analyze RC behavior is to first treat it properly like a dynamical system, which it is. This will lead to some conflict with existing ideas about RCs, but also a clarification of those ideas. Secondly, in the absence of complete theories on RCs and attractor embeddings, we show several ways to analyze the RC behavior to help understand what underlying processes are in place, especially regarding if there are good embeddings of the drive system in the RC. We show that a statistic we developed for other uses can help test for homeomorphisms between a drive system and the RC by using the time series from both systems. This statistic is called the continuity statistic and it is modeled on the mathematical definition of a continuous function. We show the interplay of dynamical quantities (e.g. Lyapunov exponents, Kaplan-Yorke dimensions, generalized synchronization, etc.) and embeddings as exposed by the continuity statistic and other statistics based on ideas from nonlinear dynamical systems theory. These viewpoints and results lead to a clarification of various currently vague concepts about RCs, such as fading memory, stability, and types of dynamics that are useful.

**Coffee Break**

**15:10-15:40**

**Wednesday, 27 July, 2022**

**Sebastiano Stramaglia**

**15:40-16:15**

**Wednesday, 27 July, 2022**

**Title: *Localizing high order effects in time and across a complex system***

**Abstract:** High-order dynamical interactions, based on information-theory, help to dissect groups of variables sharing common information (redundant or synergistic) in a multivariate system.

In particular, O-information is an information-theoretic metric that captures the overall balance between redundant and synergistic information shared by groups of three or more variables.

The questions we address here are: how are high-order effects localized in time? How are they localized across a system of interest?

**Natàlia Balagué**

**16:15-16:50**

**Wednesday, 27 July, 2022**

**Title: *Percolation processes in network physiology of exercise: Understanding injuries and task disengagement***

**Abstract:** Macroscopic action variables reflect the coordination and control of the vast number of multilayer physiological network components and the competition between inhibitory and excitatory processes acting over different time scales during exercise. Previous work has shown the existence of critical phenomena in the vicinity of the task disengagement phenomena. Close to critical points, long-range spatial correlations enhance. This is a characteristic hallmark of a vast number of condensed matter and complex systems. Hence, under the framework of network physiology of exercise, we hypothesise that the previously mentioned critical phenomena reflect inhibitory percolation processes taking place at multilayered physiological networks. In particular, the emergence of macroscopic musculo-skeletal injuries and task disengagement are hypothesized as consequences of phase transitions of first order (abrupt shift of the order parameter value). This suggests analogies with critical processes in networked systems.

**Round Table Discussion**

**17:00-18:30**

**Wednesday, 27 July, 2022**

Session Chair: Klaus Lehnertz

Alexey Zaikin

9:00-9:35

Thursday, 28 July, 2022

**Title: *Longitudinal, deep, and network biomarkers: Parenclitic and synolitic network analysis***

**Abstract:** Representing high-dimensional biological data in the form of a graph and linking features by biological and thermodynamic laws seems to be a very promising approach to deal with overwhelming complexity of biological systems. However, one can utilise this approach only if we have information about how features and attributes are connected biologically. Here we would like to draw attention to alternative methods to represent high dimensional data in the form of the graph if a-priori we do not have established connections. First of all, correlation-prediction graphs can be used as a marker of survival and have been constructed to represent the gene methylation profiles of individuals. Secondly, there is an algorithm, first described by Zanin and Bocaletti, able to establish links between parameters/nodes without any a-priori knowledge of their interactions using residual distances from linear regression models constructed between every pair of analytes to construct a graph. They termed this approach a "parenclitic" network representation, from the Greek term for "deviation". Parenclitic networks have been successfully applied to problems of the detection of key genes and metabolites in different diseases. In we have applied this methodology to implement machine learning classification to identify signatures of cancer development from human DNA methylation data. Thirdly, based on the understanding that the interactions of two features (at least in biological systems) often cannot be described by a linear model, we proposed to use 2-dimensional kernel density estimation (2DKDE) to model the control distribution. Finally, we have introduced a variation of parenclitic networks, that can be called synolitic from the Greek word for "ensemble". In principle, these networks can be considered an ensemble of classifiers in a graph form and thus are a kind of correlation network where the correlation is in the changes between two classes (e.g. disease and non-disease). These networks have been successfully used to detect age related trajectories in Down's syndrome and for prediction of survival for severely ill Covid-19 patients.

Franca Tecchio

9:35-10:10

Thursday, 28 July, 2022

**Title: *Cortico-muscular synchronization dependence on age, body side and visual feedback***

**Abstract:** Human behaviour is formed and emerges from the coordinated communication between the activity of central networks and transmission to muscle effectors. Progressive fine-tuning of frequency coding and stabilisation of dynamic properties within and between corticospinal networks occurs during adolescence, refining the capacity for efficient dynamic communication in adulthood. In later life, there is an attenuation of tuning between networks and a breakdown in their integration (Graziadio et al., 2010). The fine-tuning of central networks, which depends on the continuous integration of sensory influxes with programming and executive activities within feedback circuits, supports all behavioural expressions, and in particular the control of hand movement (Tecchio et al., 2020), which are modified by the levels of fatigue (Tecchio et al., 2006; Tomasevic et al., 2013; Padalino et al., 2021). Given the crucial role of hemicorporeal dominance, we studied the synchronisation between brain and muscle electrical activities, depending on the side of the body performing the movement (Tecchio et al., 2006). Furthermore, we manipulated visual feedback during an elementary isometric handgrip to investigate the effects on brain-muscle synchronisations (L'Abbate et al., 2022). We approached this study through the most widely used measure, cortico-muscular spectral coherence (CMC), and a new measure that takes into account the complex nature of the signals involved (the normalised compression distance, CMncd).

Modulation of visual information modified the cortico-muscular synchronisations assessed by the two measures and cortical involvement, reflecting the crucial role of gaze in human behaviour. Dominance-dependent features were captured by CMncd more than by CMC, suggesting that signal representation by sinusoids misses an important aspect of neural network communication.

Coffee Break

10:10-10:40

Thursday, 28 July, 2022

Jürgen Kurths

10:40-11:15

Thursday, 28 July, 2022

**Title:** *Quantifying stability in deterministic and stochastic complex networks and its application*

**Abstract:** Power grids, the human brain, arrays of coupled lasers, genetic networks, or the Amazon rainforest are all characterized by multistability. For power grids, the strongly ongoing transition to distributed renewable energy sources leads to a proliferation of dynamical actors. The desynchronization of a few or even one of those would likely result in a substantial blackout. Thus, the dynamical stability of the synchronous state has become a leading topic in power grid research.

The likelihood that such systems will remain in the most desirable of their many stable states depends on their stability against significant perturbations, particularly in a state space populated by undesirable states. Here we claim that the traditional linearization-based approach to stability is in several cases too local to adequately assess how stable a state is. Instead, we quantify it in terms of basin stability, a new measure related to the volume of the basin of attraction. Basin stability is non-local, nonlinear and easily applicable, even to high-dimensional systems. It provides a long-sought-after explanation for the surprisingly regular topologies of neural networks and power grids, which have eluded theoretical description based solely on linear stability.

Alberto Porta

11:15-11:50

Thursday, 28 July, 2022

**Title:** *A network physiology approach to cardiovascular, cardiorespiratory and cerebrovascular dynamic interactions*

**Abstract:** Control mechanisms are responsible for the homeostasis of physiological variables in humans. The health of the entire organism depends on the correct functioning of regulatory reflexes. The intricate nature of these neurovegetative regulations requires approaches operating at systemic level capable to describe the dynamic interactions among several subsystems concurring to the realization of the final function. The network physiology (NP) provides a framework that could lead to significant advancements in the comprehension on how neurovegetative regulations work and in shaping new concepts redefining monitoring of the health and prevention of disease. The possibilities offered by NP are mainly grounded on the exploitation of techniques: i) disentangling closed loop relationships; ii) accommodating multivariate recordings; iii) accounting for the exogenous disturbances; iv) classifying the type of influences according to their effect on the function. In the lecture the possibility offered by NP in describing physiological control mechanisms, such as cardiovascular, cardiorespiratory and cerebrovascular regulations, will be made evident in several experimental situations in which homeostasis has been challenged by a stimulus. The resulting spontaneous fluctuations of the physiological variables will be considered expression of the activity of physiological control mechanisms, analyzed via Wiener-Granger causality tools and interpreted to gauge information about the status of the overall organism and capability of subsystems to interact with each other.

Rossella Rizzo

11:50-12:20

Thursday, 28 July, 2022

**Title:** *Network physiology of cortico-muscular interactions: reorganization with sleep-stages transitions and neurodegenerative disorders*

**Abstract:** The brain plays a central role in regulating physiological and organ systems, including the skeleto-muscular and locomotor system. However, the brain-muscle communication network remains not understood. Traditional approaches to cortico-muscular coordination focus on associations between movement tasks or exercises and the activation of particular brain waves at specific cortical areas. However, neural control of the muscular system is continuously present even at rest. Moreover, the possibility to treat movement disorders has recently met with considerable interest in medical research. Specifically, a deep understanding of Parkinson's Disease (PD), the second most common progressive neurodegenerative disorder affecting older adults, is strictly correlated to a deep comprehension of brain control on locomotor system. Besides, changes in sleep regulation and rapid-eye-movement (REM) sleep behavior disorder (RBD) can appear in the early stage of disease and even prior to the onset of motor symptoms, and can serve, then, as a biomarker for PD. We hypothesize that

network interactions between brain waves and rhythms embedded in muscle activity may also reflect changes in physiologic regulation as a function of physiological states. Moreover, we study the reorganization of brain-muscle networks with PD across sleep stages, developing useful biomarkers and providing a deeper understanding on the impact of PD on human organism networks.

We investigate the coupling between physiologically relevant brain waves at distinct cortical locations with peripheral EMG activity in different frequency bands across four major, well defined physiological states — Wake, REM, Light Sleep (LS), Deep Sleep (DS). Particularly, in the first part we analyze cortical EEG signals and surface chin and leg muscle tone EMG signals from 36 healthy young subjects; secondly, we consider data from 97 healthy subjects and 33 PD sub age matched. Utilizing a novel approach based on the Network Physiology framework and the concept of time delay stability (TDS) we find that for each physiologic state the network of cortico-muscular interactions is characterized by a specific hierarchical organization of network links strength, where particular brain waves are main mediators of interaction and control of muscular activity rhythms. We discover a hierarchical reorganization in network structure across physiologic states, with high connectivity and network link strength during wake, intermediate during REM and LS, and low during DS, a sleep-stage stratification that demonstrates a unique association between physiologic states and cortico-muscular network structure. However, we notice some differences between healthy older subjects and PD subjects: the formers have stronger network connectivity during wake and LS, while the latter manifest a gradual decline in link strength from wake to DS. Indeed, the network connectivity and link strength are lower for PD than for healthy subjects during all sleep stages, but REM, when the PD subjects show a stronger brain-muscle interaction. Moreover, within each sleep stage, also the profile of network links strength as function of cortical rhythms frequency breaks down with PD, showing different relations between brain waves in link strength. Our findings demonstrate previously unrecognized basic principles of brain-muscle communication, network integration and control, with potential clinical implications for neurodegenerative, movement and sleep disorders, and for developing efficient treatment strategies. Further, our studies could finally shed light on the connection between sleep behavior disorder and PD, and allow PD diagnosis in early course of the disease.

**Lunch Break**

**12:20-14:00**

**Thursday, 28 July, 2022**

**Session Chair: Alexey Zaikin**

**Klaus Lehnertz**

**14:00-14:35**

**Thursday, 28 July, 2022**

**Title: *Controlling brain networks: Insights from epilepsy***

**Abstract:** Epilepsy is one of the most common serious neurological disorders, affecting approximately 70 million people worldwide. Epilepsy is nowadays conceptualized as a network disease with functionally and/or structurally aberrant vertices and edges on virtually all spatial scales. All constituents of the large-scale epileptic brain network can contribute to the generation, maintenance, spread, and termination of even focal seizures as well as to the many pathophysiologic phenomena seen during the seizure-free interval. Commonly employed therapeutic procedures such as drug treatment and brain surgery that aim at controlling epilepsy (or more specifically: seizures) are accompanied by severe side effects or even fail in a high number of cases. Alternative therapies are based on neuromodulation, which uses e.g. direct or induced electrical currents to modulate network activity. In terms of control of complex networks, most neuromodulation-based therapies target at modifying structure and/or function of specific vertices and/or edges. Such local approaches are (minimally) invasive and their efficiency is critically discussed. In this talk, I will address control of an epileptic brain network taking into account more recent, particularly non-invasive approaches and will critically discuss pro and cons of network-centric neuromodulation techniques.

**Louis M. Pecora**

**14:35-15:10**

**Thursday, 28 July, 2022**

**Title: *Choosing optimal Reservoir Computers***

**Abstract:** A reservoir computer is a high dimensional dynamical system used for computation. Typically a reservoir computer is created by connecting a large number of nonlinear nodes in a network. There can be hundreds to thousands of nodes, so optimizing the structure of the reservoir computer is difficult. There are a

number of conventional rules for optimizing a reservoir computer based on experience with simulations, but these rules are based on observations of a limited number of node nonlinearities. One feature of reservoir computers is that they may be built from connecting together analog nodes such as lasers, quantum dots, memristors, or other devices. There is a great range of possible nonlinear functions describing these nodes, so design rules beyond the conventional wisdom are required.

One conventional design rule that I show is not always true is that reservoir computers function best at the edge of stability, or the “edge of chaos”. There are dynamical reasons why this rule is not always true. I have found that the parameters for optimal performance of a reservoir computer depend on the task being considered, so for example maximizing entropy may be useful for classifications tasks but it may degrade the performance for transfer function, prediction or observer tasks.

**Coffee Break**

**15:10-15:40**

**Thursday, 28 July, 2022**

**Michael G. Rosenblum**

**15:40-16:15**

**Thursday, 28 July, 2022**

**Title: Inferring phase and amplitude response of oscillatory systems from observations**

**Abstract:** The phase sensitivity curve or phase response curve (PRC) quantifies the oscillator's reaction to stimulation at a specific phase and is a primary characteristic of a self-sustained unit. Knowledge of this curve yields a phase dynamics description of the oscillator for arbitrary weak forcing. Here, we discuss the problem of the PRC inference from observations using test stimulation. Though PRC inference for noise-free neuronal-like oscillators perturbed by narrow pulses is a well-known task, the general case is challenging. Here, we compare the performance of different techniques suitable for PRC inference for macroscopic neuronal oscillators. We suggest a technique based on the direct reconstruction of the Winfree phase dynamics equation. We consider a relevant case of charge-balanced pulses and suggest an error measure that can be computed solely from data. Moreover, we discuss different definitions of the amplitude response and provide an algorithm for its inference. We discuss the relevance of our results for the modulation of neuronal rhythms.

**Luca Faes**

**16:15-16:50**

**Thursday, 28 July, 2022**

**Title: *A new information-theoretic approach to analyze physiological networks of oscillatory and spike train processes***

**Abstract:** The framework of information dynamics offers a set of tools, grounded within the solid basis of information theory, to quantify several aspects of the dynamic interactions observed at the nodes of complex network systems. These tools, including measures of information storage, Granger causality and higher-order interactions, are extensively used to assess regulatory mechanisms, coupled activity and emergent behaviors in physiological networks studied from multiple simultaneously measured biosignals. Nevertheless, the framework of information dynamics has been developed mostly to assess interactions from discrete-time processes studied in the time domain, and this constitutes a limitation for the analysis of physiological systems where interactions occur at different levels of horizontal and vertical integration within the human body. For instance, the standard formulation of information dynamics is inappropriate to study the frequency-specific interactions occurring among the physiological rhythms of different organ systems.

This contribution illustrates some developments of the framework of information dynamics whereby we move from the analysis of pairwise interactions between coupled processes to the study of higher-order interactions involving more than two processes, and from the time-domain to the frequency-domain analysis of physiological time series. Our developments exploit the spectral representation of linear vector autoregressive models to quantify pairwise and higher-order interactions for multivariate rhythmic processes interacting in distinct frequency bands. The new framework will be first formulated theoretically and implemented through data-efficient estimators. Then, its performance and peculiarities will be illustrated on simulations of stochastic oscillatory processes. Finally, applications to physiological networks explored at different levels of vertical and horizontal integration will be reported, including human cardiovascular, cardiorespiratory and cerebrovascular

oscillations studied in different physio-pathological states, electrocorticographic signals acquired in an animal experiment during anesthesia, and multichannel EEG recordings acquired during a motor execution task.

**Social Event  
Dinner**

**Ristorante Sociale**

**20:30-22:30**

**Thursday, 28 July, 2022**

<https://www.ristorantesociale.it/>

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**Session Chair: Michael G. Rosenblum**

**Ulrich Parlitz**

**9:00-9:35**

**Friday, 29 July, 2022**

**Title: *Modelling and controlling complex dynamics in cardiac networks***

**Abstract:** The dynamics in networks of cardiomyocytes is determined by an interaction of electrical and mechanical processes for which several measurement techniques exist. However, despite significant advances in measurement technology, not all quantities of interest can be directly observed. For example, while mechanical motion in the myocardium can be observed with ultrasound, there are no noninvasive techniques (to date) to measure the electrical state in the tissue. To fill this gap and estimate or reconstruct quantities that are difficult to measure directly, nonlinear modeling, data assimilation, and machine learning techniques can be used. Methods and examples of this type of data-driven modeling in Network Physiology will be presented and their potential applications in research, diagnostics, and therapeutics will be discussed.

The second part of the talk will be devoted to new approaches to control and termination of cardiac arrhythmias. We will first discuss the possible role of transient chaos in excitable media and related consequences for control strategies aimed at terminating the chaotic fibrillation state as soon as possible. Other aspects include proper timing of defibrillation pulses and improvements in low-energy defibrillation methods using sequences of weak pulses instead of a single strong shock.

**Stefano Zapperi**

**9:35-10:10**

**Friday, 29 July, 2022**

**Title: *Information optimized multilayer network representation of high density electroencephalogram recordings***

**Abstract:** High-density electroencephalography (hd-EEG) provides an accessible indirect method to record spatio-temporal brain activity with potential for disease diagnosis and monitoring. Due to their highly multidimensional nature, extracting useful information from hd-EEG recordings is a complex task. Network representations have been shown to provide an intuitive picture of the spatial connectivity underlying an electroencephalogram recording, although some information is lost in the projection. Here, we propose a method to construct multilayer network representations of hd-EEG recordings that maximize their information content and test it on sleep data recorded in individuals with mental health issues. We perform a series of statistical measurements on the multilayer networks obtained from patients and control subjects and detect significant differences between the groups in clustering coefficient, betweenness centrality, average shortest path length and parieto occipital edge presence. In particular, patients with a mood disorder display a increased edge presence in the parieto-occipital region with respect to healthy control subjects, indicating a highly correlated electrical activity in that region of the brain. We also show that multilayer networks at constant edge density perform better, since most network properties are correlated with the edge density itself which can act as a confounding factor. Our results show that it is possible to stratify patients through statistical measurements on a multilayer network representation of hd-EEG recordings. The analysis reveals that individuals with mental health issues display strongly correlated signals in the parieto-occipital region. Our methodology could be useful as a visualization and analysis tool for hd-EEG recordings in a variety of pathological conditions.



Coffee Break

10:10-10:40

Friday, 29 July, 2022

Robert J. Thomas

10:40 -11:15

Friday, 29 July, 2022

**Title:** *Sleep transition networks – onset, offset, arousals and awakenings*

**Abstract:** Transitions of wake to sleep is a complex process with multi-system interactions across neural, respiratory, motor and autonomic cardiac systems. While sleep onset has seen much of the available research, sleep offset remains somewhat mysterious. Normally a mildly unstable process, disease states markedly amplify these transitions and cause classic disease manifestations – including amplified wake-sleep transitional instability (AWSTI), insomnia, and the prolonged sleep inertia and fog of idiopathic hypersomnia. Cardiovascular transients on awakening can increase risk of adverse cardiovascular outcomes. Sleep transients are relevant to epilepsy on awakening and strokes. Disorders of, and testing of, impaired vigilance focus on sleep onset mechanisms and markers. The neural circuits, neurotransmitters and networks mediating transitions will be presented. The phenomena at each of these transients will be discussed, with multi-modality data and their interactions, to provide a comprehensive “transition theory” which can then provide targets for manipulation for clinical benefit.

André Longtin

11:15–11:50

Friday, 29 July, 2022

**Title:** *Noise-induced and noise-perturbed physiological rhythms*

**Abstract:** Brain rhythms are usually studied in the framework of neural oscillators, and these oscillators can be driven by noise to reflect the typically strong fluctuations exhibited by these rhythms. This talk will present recent results on a framework that allows the rhythms to be either noise-perturbed or noise-induced, the latter case being called the quasi-cycle case. In other words, I will present an amplitude phase description that works on both sides of the Hopf bifurcation - a formalism based on the stochastic averaging method and which can be applied to physiological rhythms in general. I will also show how the envelope fluctuations display large excursions or “bursts” whose magnitude, duration and frequency content are thought to be under physiological control - and disrupted in diseases like Parkinson’s. I will finally discuss how such rhythms could “communicate” with one another through delayed long range connections by investigating the mutual information properties of rhythms in different brain areas.

Gorana Mijatovic

11:50-12:20

Friday, 29 July, 2022

**Title:** *A new information-theoretic framework to analyze neural spike trains and physiological point processes*

**Abstract:** The field of Network Physiology is witnessing a continuous development of different methodological approaches, often employing information-theoretic measures, aimed at recovering quantitative information on the joint dynamics of different organ systems or different units of the same system. These approaches are typically designed to treat discrete-time processes mapping the time course of different physiological variables such as the amplitude of biopotentials or the values of arterial pressure, heart rate or respiratory time series. However, in physiological systems where interactions occur at different levels of integration, information is often gathered in other forms which require specific treatment and ad-hoc developed analysis techniques. This is the case of point process data such as neural spike trains or heartbeat timings, for which the information to be analyzed resides in the times of occurrence of a given event and thus cannot be processed with the information-theoretic measures developed for the analysis of physiological time series.

The present work introduces a new information-theoretic framework for the model-free computation of both directed (causal) and undirected (symmetric) measures of interaction between physiological point processes. The framework defines the transfer entropy rate (TER) and the mutual information rate (MIR) for coupled point processes, showing that the MIR between the processes X and Y can be decomposed as the sum of the TER along the directions from X to Y and from Y to X. An estimation strategy to efficiently

compute the two measures from short realizations of point process data, based on nearest neighbor statistics and on bias compensation through the use of surrogate data, is then illustrated and tested on simulations of independent and coupled point processes. Finally, the method is applied to two types of point processes often studied in Network Physiology. First, analyzing in-vitro preparations of spontaneously-growing cultures of cortical neurons, we show that MIR and TER describe the emergence of functional networks of coupled firing activity over the course of maturation of the cultures. Then, considering heartbeat and pressure propagation times in a group of healthy subjects undergoing a protocol of postural stress and mental stress, we document that MIR measures reflect the physiological mechanisms of cardiovascular variability related to the joint neural autonomic modulation of heart rate and arterial compliance.

**Lunch Break**

**12:20-14:00**

**Friday, 29 July, 2022**

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**Session Chair:**

**Ulrich Parlitz**

**Ruedi Stoop**

**14:00-14:35**

**Friday, 29 July, 2022**

**Title: *What compiler-type computations are performed by biological neural networks?***

**Abstract:** The assessment of whether the dynamics of a system composed of many components is correctly described by a model, is facilitated if the dynamics is of an inherently simple nature. The latter may be the case if specific simplifying features, such as criticality or synchronization are present. It has been argued that biological neural networks host such beneficial properties, but whenever this fails to dominate the behavior, such an assessment turns into a difficult task. Choosing biological and artificial neural networks as the showcase, we demonstrate how symbolic dynamics-founded 'excess entropies' 1) measure how much simulations differ from the target processes, 2) uncover model inadequacies and 3) provide guidelines for model set-up and improvement. This opens a new gateway for the analysis and description of complex dynamical processes that the traditionally used measures do not offer.

In the neuronal culture experiments that we use to validate our measure, the role of the observational states is played by activated multi-electrode array (=MEA) electrodes. Symbols recorded from the MEA can be seen as generated according to a set of rules imposed by a grammar from one of the Chomsky language classes t-0-t-3, ordered by the ease of capturing complex relations among the language elements.

We demonstrate that the developed excess entropy measure is a general tool that directly assesses the distance between symbolic dynamics of simulations to those of the real-world example. By measuring how much simulation-generated symbol substring distributions deviate from distributions generated by the experimental example, also temporally variable patterns of transitions (that are generally difficult to extract from experimental systems) are included, which reaches beyond classical transition-matrix based methods. Strongly positive deviations indicate increased temporal clustering of subsets of symbols, whereas strongly negative deviations indicate that symbols occur in a too regular fashion. Such information exhibits weak points in the modeling and, as a consequence, can be used as a guideline for improving the modeling approach. As one application, our approach highlights that our most advanced neuron modeling is much closer to the MEA experiment than the branching model and suggests biological modifications of the latter model that bring the model closer to the targeted biological data.

**Mohit Kumar Jolly**

**14:35-15:10**

**Friday, 29 July, 2022**

**Title: *Network dynamics driving cancer metastasis: from design principles to therapeutic approaches***

**Abstract:** Cancer metastasis and drug resistance cause over 90% of cancer-related deaths. Despite extensive ongoing efforts, no unique genetic or mutational signature has emerged for metastasis. Instead, the ability of genetically identical cells to adapt reversibly by exhibiting multiple phenotypes (non-genetic heterogeneity) and switch among them (phenotypic plasticity) is proposed as a hallmark of metastasis. Also, drug resistance can emerge from such non-genetic adaptive cellular changes, and heterogeneity

remains a barrier in effective treatment. Such adaptive changes and heterogeneity is mediated by the emergent dynamics of underlying intracellular and intercellular regulatory networks.

We have simulated the dynamics of these regulatory networks using both discrete and continuous models, and validated our model predictions using high-throughput omics data at single-cell and bulk levels. Many of these networks are multistable in nature, consequently enabling cell-cell variability and stochastic state-switching as well (Hari et al. NPJ Sys Bio & Appln 2020; Chauhan et al. eLife 2021; Subbalakshmi et al. Cancers 2021), thus increasing 'fitness' of a population by facilitating bet-hedging. Importantly, our mechanistic models for melanoma and breast cancer reveal how drug treatment can also induce cell-state switching (Sahoo et al. NAR Cancer 2021; Pillai et al. iScience 2021), thereby revealing the complex adaptive nature of tumor progression.

I will present our findings on a) how these networks drive non-genetic heterogeneity in a cancer cell population, b) what design principles underlie these regulatory networks that enable only a limited number of phenotypes despite their size and complexity, and c) how can we design better therapeutic strategies based on a better network-level understanding of dynamics at single-cell and population levels. Our results unravel how systems-level approaches can integrate mechanistic mathematical modeling with in vitro and in vivo data to prevent and/or delay cancer metastasis and drug resistance.

**Coffee Break**

**15:10-15:40**

**Friday, 29 July, 2022**

**Alexey Zaikin**

**15:40-16:15**

**Friday, 29 July, 2022**

**Title: *Intelligence and consciousness in genetic-neuron astrocyte networks***

**Abstract:** Human brain has a very specific design as a result of a long evolution: a network of neurons linked in a very complex way is overlapped with a network of coupled astrocytes which are also linked to neurons. Additionally, inside each cell we have a very complicated network with ability to demonstrate intelligence properties. Naturally the research question arises how this design is related to the main feature of human brain, namely, ability to maintain a certain level of consciousness and awareness. To answer the question how quantify level of consciousness, recently the Integrated Information Theory of Consciousness has been developed, controversially claimed not only as a way to measure the complexity of brain but also its level of consciousness. Here I will report our results on a simple but realistic model of neuro-glial network and show that presence of astrocyte could contribute to the generation of positive Integrated Information and, hence, its evolutionary appearance was important to develop consciousness. Hence, astrocytes and genetic networks may contribute not only to the appearance of intelligence, but also consciousness.

**Closing**

**16:20-16:40**

**Friday, 29 July, 2022**

**Plamen Ch. Ivanov**

**Panel participants:**

**Klaus Lehnertz, PhD**

Department of Epileptology at Bonn University Medical Center, Germany

**Barbara E. Corkey, MD**

Department of Medicine, Boston University, USA

**Ulrich Parlitz, PhD**

Max Planck Research Group Biomedical Physics,  
Max Planck Institute for Dynamics and Self-Organization, Germany

**J. Randall Moorman, MD**

Department of Medicine, Physiology, Biomedical Engineering, University of Virginia, USA

**Olga Sosnovtseva, PhD**

Department of Biomedical Sciences, University of Copenhagen, Denmark

**Robert J. Thomas, MD**

Harvard Medical School; Division of Pulmonary, Critical Care & Sleep,  
Beth Israel Deaconess Medical Center, USA

**Marina de Tommaso, MD**

Neurology, Department of Psychiatric and Neurologic Sciences, Bari University, Italy

**Jürgen Kurts, PhD**

Department of Physics, Humboldt University Berlin, Germany  
Potsdam Institute for Climate Impact Research, Germany

**Luca Faes, PhD**

Department of Engineering, University of Palermo, Italy

**Kathryn A. Hibbert, MD**

Department of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, USA

**Christopher R. Stephens, PhD**

Centro de Ciencias de la Complejidad, Instituto de Ciencias Nucleares,  
Universidad Nacional Autónoma de México

# Poster Session I

17:15-18:30

Monday, 25 July, 2022

## 1. Effects of SGLT2 inhibitor on renal tubuloglomerular feedback assessed with multi-scale laser speckle contrast imaging

Blaire Lee<sup>1</sup>, Dmitry D Postnov<sup>2</sup>, Charlotte M. Sørensen<sup>1</sup>, Olga Sosnovtseva<sup>1</sup>

*1 University of Copenhagen, Department of Biomedicine, Denmark*

*2 Aarhus University, Department of Clinical Medicine, Denmark*

## 2. Investigating the Heartbeat-evoked cortical response by means of Local information Measures

Chiara Barà<sup>1</sup>, Riccardo Pernice<sup>1</sup>, Yuri Antonacci<sup>1</sup>, Laura Sparacino<sup>1</sup>, Andrea Zaccaro<sup>2</sup>, Francesca Ferri<sup>2</sup>, and Luca Faes<sup>1</sup>

*1 Department of Engineering, University of Palermo, Palermo, Italy*

*2 Institute for Advanced Biomedical Technologies, ITAB, "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy*

## 3. Multiscale biological rhythm modulation as a network parameter for aging and disease detection: animal application and human potential

Benjamin Smarr<sup>1</sup>, and Joseph Natale<sup>2</sup>

*1 Department of Bioengineering, University of California, San Diego, USA*

*2 Halicioğlu Data Science Institute, University of California, San Diego, USA*

## 4. An AI-assisted and expert-supervised prediction and network analysis: novel integrated procedures for fastening, deepening, and leading topical research. A first application on human muscle secretome

Danilo Bondi<sup>1</sup>, Michele Bevere<sup>1</sup>, Valentina di Felice<sup>2</sup>, Guglielmo Sorci<sup>3</sup>, Rosanna Piccirillo<sup>4</sup>, Andrea David Re Cecconi<sup>4</sup>, Tiziana Pierangelo<sup>1</sup>, and Stefania Fulle<sup>1</sup>

*1 University "G. d'Annunzio" of Chieti - Pescara, Chieti, Italy*

*2 University of Palermo, Palermo, Italy*

*3 University of Perugia, Perugia, Italy*

*4 Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan, Italy*

## 5. Optimizing charge-balanced pulse stimulation for desynchronization

Erik T. K. Mau<sup>1</sup>, and Michael Rosenblum<sup>1</sup>

*1 Institute of Physics and Astronomy, University of Postdam, Germany*

## 6. The Amount of Redundancy of Respiration to Cerebrovascular Control Depends on the Type of Respiratory Signal

Francesca Gelpi, Vlasta Bari, *Member, IEEE*, Beatrice Cairo, *Member, IEEE*, Beatrice De Maria, Rachel Wells, Mathias Baumert, Alberto Porta, *Senior Member, IEEE*

## 7. Multiscale Partial Information Decomposition Under Long-Range Correlations: Application to Cardiovascular and Respiratory Control

Hélder Pinto<sup>1</sup>, Michal Javorka<sup>2</sup>, LucaFaes<sup>3</sup>, and Ana Paula Rocha<sup>1</sup>

*1 Porto University & CMUP, Portugal*

*2 Comenius University, Slovakia*

*3 Palermo University, Italy*

## 8. Analysis of multimodal Ca<sup>2+</sup> activity in beta cell networks: The semi-automated open-source multicellular Ca<sup>2+</sup> imaging and network analyzer

Jan Zmazek<sup>1</sup>, Marko Šterk<sup>1,2</sup>, Marko Marhl<sup>1,2,3</sup>, Andraž Stožer<sup>2</sup>, and Marko Gosak<sup>1,2</sup>

*1 University of Maribor, Faculty of Natural Sciences and Mathematics, Maribor, Slovenia*

*2 University of Maribor, Faculty of Medicine, Maribor, Slovenia*

*3 University of Maribor, Faculty of Education, Maribor, Slovenia, Maribor, Slovenia*

**9. A method to assess Granger causality and Granger autonomy in the time and frequency domains: theory and application to cerebrovascular variability**

Laura Sparacino<sup>1</sup>, Yuri Antonacci<sup>1</sup>, Chiara Barà<sup>1</sup>, and Luca Faes<sup>1</sup>

*1 Department of Engineering, University of Palermo, Palermo, Italy*

**10. Tracking the evolution and interrelations between frequency-specific multiplex EEG brain networks and heart rate dynamics during the onset of epileptic seizures**

Marko Šterk<sup>1,2</sup>, Rene Markovič<sup>1,3</sup>, Eva Paradiž Leitgeb<sup>2</sup>, Matjaž Perc<sup>1,4,5,6</sup>, Andraž Stožer<sup>2</sup>, Natalija Krajnc<sup>7</sup>, and Marko Gosak<sup>1,2</sup>

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*6 Complexity Science Hub Vienna, Vienna, Austria*

*7 General hospital Slovenj Gradec, Slovenj Gradec, Slovenia*

**11. Using multilayer network analysis to unveil how propagating intercellular signals shape the collective dynamics in the pancreatic islets of Langerhans**

Marko Šterk<sup>1,2</sup>, Jurij Dolensšek<sup>1,2</sup>, Maša Skelin Klemen<sup>2</sup>, Lidija Križančič Bombek<sup>2</sup>, Eva Paradiž Leitgeb<sup>2</sup>, Jasmina Kerčmar<sup>2</sup>, Marjan Slak Rupnik<sup>2,3</sup>, Matjaž Perc<sup>1,4,5,6</sup>, Andraž Stožer<sup>2</sup>, and Marko Gosak<sup>1,2</sup>

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**12. Analyzing EEG networks throughout the lifespan**

Nicolai Spicher<sup>1</sup>, Theresa Bender<sup>1</sup>, Ennio H. Idrobo-Ávila<sup>1</sup>, Niels K. Focke<sup>2</sup>, Dagmar Krefting<sup>1</sup>

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# Poster Session II

17:00-18:30

Tuesday, 26 July, 2022

## 1. Mechanisms of Disease Progression in Critically Ill COVID-19 Patients during Intensive Care Unit Stay

Moein E. Samadi<sup>1</sup>, and Andreas Schuppert<sup>1</sup>

*1 Institute for Computational Biomedicine, RWTH Aachen University, Aachen, Germany*

## 2. Network data analysis of sepsis patients

Moritz Alkofer<sup>1,2</sup>, Fenja Drauschke<sup>1,2</sup>, Rico Berner<sup>2</sup>, Jakub Sawicki<sup>1,2</sup>, Thomas Löser<sup>1,2</sup>, and Eckehard Schöll<sup>1,2</sup>

*1 Institut für Theoretische Physik, Technische Universität Berlin, Berlin, Germany*

*2 Institut LOESER, Leipzig, Germany*

## 3. The Role of Synchronization in Epileptic Seizures

Moritz Gerster<sup>1,2</sup>, Rico Berner<sup>2</sup>, Jakub Sawicki<sup>1,2</sup>, Anna Zakharova<sup>1,2</sup>, Antonín Škoch<sup>1,2</sup>, Jaroslav Hlinka<sup>1,2</sup>, Klaus Lehnertz<sup>1,2</sup>, and Eckehard Schöll<sup>1,2</sup>

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## 4. Optogenetics Control of Cardiac Arrhythmias

S. Hussaini<sup>1</sup>, S. L. Lädke<sup>1</sup>, J. S. Schetelig<sup>1</sup>, A. M. Kzyz<sup>1</sup>, L. N. Diaz-Maue<sup>1</sup>, V. Biasci<sup>3</sup>, A. Witt<sup>1</sup>, G. Bub<sup>2</sup>, L. Sacconi<sup>3</sup>, C. Richter<sup>4</sup>, U. Parlitz<sup>1</sup>, V. Biktashev<sup>6</sup>, R. Majumder<sup>1</sup>, V. Krinski<sup>1,5</sup>, and S. Luther<sup>1</sup>

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*3 Department of Experimental and Clinical Medicine, University of Florence, Italy*

*4 German Primate Center, Göttingen, Germany*

*5 INPHYNI, CNRS, SOPHIA Antipolis, France*

*6 Exeter University, Exeter, England*

## 5. Vertices and edges of time-dependent functional brain networks under the influence of biological rhythms disorders

Timo Bröhl, and Klaus Lehnertz

*Department of Epileptology, University of Bonn, Germany*

## 6. Quantifying Dynamical High-Order Interdependencies From the O-Information: An Application to Neural Spiking Dynamics

Sebastiano Stramaglia<sup>1,2</sup>, Tomas Scagliarini<sup>1</sup>, Bryan C. Daniels<sup>3</sup>, and Daniele Marinazzo<sup>4</sup>

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*2 Center of Innovative Technologies for Signal Detection and Processing (TIRES), Università degli Studi Aldo Moro, Bari, Italy,*

*3 Arizona State University and Santa Fe Institute Center for Biosocial Complex Systems, Arizona State University, Tempe, AZ, United States,*

*4 Department of Data Analysis, Ghent University, Ghent, Belgium*

## 7. Disruption, recovery, and modification of the physiological network during COVID-19

Antonio Barajas-Martínez, Paola V. Olguín-Rodríguez, Elizabeth Ibarra-Coronado, Ruben Fossion, Ana Leonor Rivera

*Center for Complexity Sciences, Universidad Nacional Autónoma de México, México*

## 8. Healthy behaviors and circadian patterns determined by actigraphy in researchers and administrative personnel as protective factors against metabolic disease and obesity

Estefania Espitia-Bautista<sup>1</sup>, and Christopher Stephens<sup>1,2</sup>

*1 Centro de Ciencias de la Complejidad (C3), Universidad Nacional Autónoma de México, México*

*2 Instituto de Ciencias Nucleares, Universidad Nacional Autónoma de México, México*

### **9. Effects of Guided Relaxation on Symptoms of Anxiety and Depression**

Aleš Oblak, Teja Rebolj, Klemen Rebolj, Jurij Bon

*Laboratory for Cognitive Neuroscience and Psychopathology, University Psychiatric Clinic Ljubljana, Slovenia*

### **10. Ordinal Patterns as Robust Biomarkers in Multichannel EEG Time Series**

Inga Kottlarz, Sebastian Berg, Diana Toscano-Tejeida, Iris Steinmann, Mathias Bähr, Stefan Luther, Melanie Wilke, Ulrich Parlitz and Alexander Schlemmer

*Biomedical Physics, Max-Planck-Institute for Dynamics and Self-Organization, Germany*

### **11. Influence of Cardiovascular Diseases on the Coupling Behavior between Central and Autonomic Nervous System**

Richard Hohmuth<sup>1</sup>, Alexander Hammer<sup>1</sup>, Niklas Hahn<sup>1</sup>, Hagen Malberg<sup>1</sup>, and Martin Schmidt<sup>1</sup>

*<sup>1</sup>Institute of Biomedical Engineering, TU Dresden, Dresden, Germany*

### **12. Prediction of neurological complications in the acute phase of ischemic stroke**

Joanna Aftyka<sup>1</sup>, Jacek Staszewski<sup>2</sup>, Jan Żebrowski<sup>1</sup>, Aleksander Dębiec<sup>2</sup>, Aleksandra Pogoda-Wesołowska<sup>2</sup>, Agata Kowalska<sup>2</sup>, Anna Jankowska<sup>2</sup>

*1 Faculty of Physics, Warsaw University of Technology, Warsaw, Poland*

*2 Military Institute of Medicine, Warsaw, Poland*

### **13. Personalized network approach to modeling effective TBI pre-interventions and treatments**

Thomas, GA; Lee, EC; Arent, SM

*Department of Kinesiology, Penn State University, USA Poland*



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# Announcements

## Special Issues in the journal *Frontiers in Network Physiology*

In parallel with the ISINP-2022 meeting, we organize several special issues in the journal [\*Frontiers in Network Physiology\*](#), published by Frontiers Media SA:

["Kidney Structure and Function: Interdisciplinary Approaches in Basic and Translational Research"](#),

["https://www.frontiersin.org/research-topics/41703/network-physiology-approaches-to-natural-and-data-driven-multi-omics-and-high-frequency-networks-met"](https://www.frontiersin.org/research-topics/41703/network-physiology-approaches-to-natural-and-data-driven-multi-omics-and-high-frequency-networks-met)

["Astrocytes in the Brain Active Milieu"](#)

["Brain-Heart Interaction: Recent Insights in Methods"](#)

Despite the vast progress and achievements in systems biology and integrative physiology in the last decades, we do not know the basic principles and mechanisms through which diverse physiological systems and organs dynamically interact as a network and integrate their functions to generate a variety of physiologic states and pathological conditions at the organism level.

This special issue will focus on both empirical and theoretical interdisciplinary work with contributions ranging from applied math, statistical physics, nonlinear dynamics and complex networks to biomedical engineering, neuroscience, physiology and clinical medicine, and is now open for manuscript submissions.

More information is available on the journal website:

<https://www.frontiersin.org/research-topics/10298/the-new-frontier-of-network-physiology-from-temporal-dynamics-to-the-synchronization-and-principles>

We invite all ISINP attendees and speakers to contribute work related to *Network Physiology*.

## Social Event

### Dinner

Ristorante Sociale

20:30-22:30

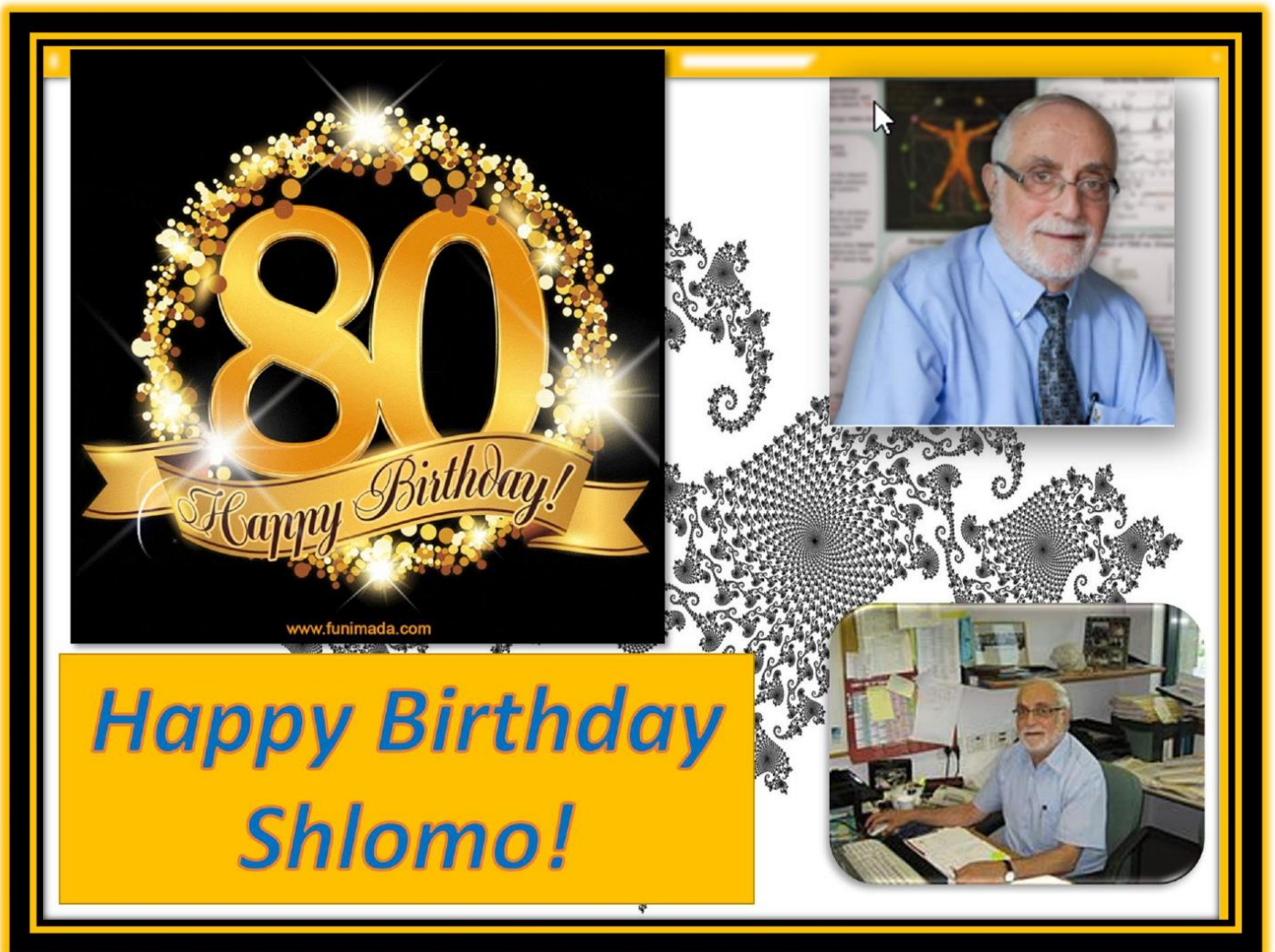
Thursday, 28 July, 2022

<https://www.ristorantesociale.it/>



Address: Via Rodari, 6, 22100 Como CO, Italy

**We celebrate  
the 80th birthday of  
Professor Schlomo Havlin!**



Thank you for joining this third international event on Network Physiology, and for being part of a growing society of scholars, clinicians and biomedical engineers working in this new field.

We look forward to meeting you again in 2024!

