

Foreword



I am a mathematician and started my professorship at IST Austria two months ago. As is common for academics these days, I arrived here from a series of previous positions. I graduated from Eötvös Loránd University, received my PhD from Trinity College Cambridge, and worked as post-doctoral fellow at the Institute for Advanced Study in Princeton, and in the Miller Institute for Basic Research in Science at the University of California Berkeley. I was Assistant and Associate Professor at the University of Texas Austin and then became a Royal Society research fellow at the University of Oxford. I was Chair of Geometry at École Polytechnique Fédérale de Lausanne before I joined IST Austria in September 2016.

My research interests include geometric studies of spaces appearing in supersymmetric quantum field theories. I am particularly interested in their topology, arithmetic and representation theory. What I enjoy is when many different types of mathematics interact and yield surprising new results.

To me, IST Austria is an ideal work place to focus on fundamental research in science. The research institute educates young scientists in the tools of the trade, creates a discovering atmosphere for more advanced researchers and promises new breakthroughs in science. Located in Klosterneuburg on the outskirts of Vienna and linked by the Danube to my home-town Budapest, IST Austria provides optimal living conditions for me.

Tamas Hausel | Professor, IST Austria



ERC Starting Grants for professors

Five Assistant Professors at IST Austria are to receive Starting Grants from the European Research Council (ERC). Computer scientist Bernd Bickel, mathematician Jan Maas, evolutionary biologist Beatriz Vicoso, and neuroscientists Gaia Novarino and Sandra Siegert secured an award, each with a budget value of approximately EUR 1.5 million. IST Austria President Thomas Henzinger congratulates the awardees: "ERC Starting Grants recognize young talented scientists for their excellent research. With five more Starting Grants for IST Austria researchers, the total number of our ERC-funded projects has now risen to 28. This success strongly confirms our recruiting strategy."

In 2016, faculty members at IST Austria have secured eight ERC Grants so far. In addition to Bickel, Maas, Vicoso, Novarino and Siegert having been successful within the Starting Grant scheme, neuroscientists Peter Jonas and Ryuichi Shigemoto as well as physicist Robert Seiringer received ERC Advanced Grants this year.

Novarino receives SFARI award

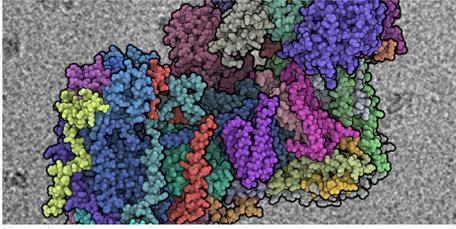
Professor Gaia Novarino has been granted a Pilot Award of the Simons Foundation Autism Research Initiative (SFARI) for her project on "Probing development and reversibility of autism spectrum disorders". Launched in 2003, SFARI is a scientific initiative within the Simons Foundation's suite of programs focusing on the science underlying a medical condition. Its mission is to improve the understanding, diagnosis and treatment of autism spectrum disorders by funding innovative research of the highest quality and relevance. To this end, SFARI grants annual awards to individual scientists who conduct particularly bold, imaginative, rigorous and relevant research.

The Simons Foundation also seeks to create strong collaborations and foster cross-pollination of ideas between investigators, as these interactions often lead to unexpected breakthroughs and new understanding. As the recipient of a Pilot Award, Gaia Novarino also becomes a member of the prestigious community of Simons Investigators.

Six new professors join IST Austria

President Thomas A. Henzinger announced the names of six new professors: the neuroscientist Maximilian Jösch, the mathematician Julian Fischer, the computer scientist Dan Alistarh, and the physicists Peter Krogstrup, Johann Georg Danzl and Maksym Serbyn will join IST Austria as Assistant Professors, bringing the number of the faculty to 46.

Henzinger welcomed the new professors: "These appointments are an indicator for the great attraction that IST Austria has for extraordinarily promising young scientists. I am very happy that they will join us at this stage of their career because they will further broaden our research portfolio. At IST Austria they can expect an environment that will enable them to contribute outstanding results to their fields of research." Following the recent promotion of Eva Benkova and Krzysztof Pietrzak to tenured professors, this brings the number of faculty to 46, among them 21 tenured Professors and 25 Assistant Professors including the newcomers. The 46 members of the IST Austria faculty come from 22 countries.



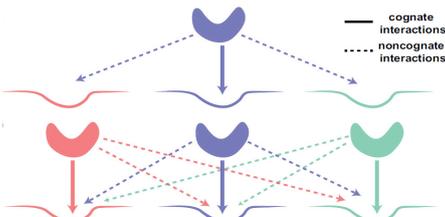
Structure of mammalian protein complex of respiratory chain solved

The mitochondrial Complex I plays a central role in cellular respiration and energy metabolism. The ~1 Megadalton L-shaped protein complex is the largest protein assembly of the respiratory chain and now the largest asymmetric membrane protein assembly solved to date. Professor Leonid Sazanov and his British collaborators published the nearly

complete atomic structure of the ovine (mammalian) mitochondrial complex I at 3.9 Å resolution, solved by cryo-electron microscopy aided by cross-linking/mass-spectrometry mapping in the scientific journal *Nature*.

The respiratory chain is responsible for most energy production in humans. Several large protein assemblies are embedded in the mitochondrial lipid membrane. The mitochondrial Complex I is the first and largest complex in this chain. Metabolites derived from food are processed by this enzyme complex in order to contribute to the electron transfer and proton translocation. So far, research groups were only able to reveal mostly poly-alanine models lacking necessary full atomic details due to the fact that huge and complex molecules are difficult to

examine with current methods. Cryo-electron microscopy made huge advances in recent years due to the development of new direct electron detectors, allowing high-resolution studies. The resolution of the structure at an atomic level now allows the understanding of the intricate arrangements and interactions of all 45 subunits (14 conserved core and 31 mitochondria-specific supernumerary subunits) with implications for the coupling mechanism and its regulation. The insight into mechanism, assembly, maturation, and dysfunction of Complex I allows a detailed molecular analysis of disease-causing mutations and affected enzyme activity. Therefore the publication in *Nature* is expected to serve as reference source of information in medicine, bioenergetics and other research areas.



Global crosstalk limits gene regulation

Molecular recognition is fundamental to transcriptional regulation. The specificity of this regulation originates in the binding interactions between special regulatory proteins, called transcription factors (TFs), and short regulatory sequences on the DNA, called binding sites. Although each type of TF preferentially binds certain regulatory DNA sequences, evidence shows that this binding specificity is lim-

ited, and that TFs bind other noncognate targets, too. If these sites happen to be regulatory elements of other genes, noncognate binding not only depletes TF molecules, but could also actively interfere with gene regulation.

In their *Nature Communications* paper, ISTFellow Tamar Friedlander, PhD student Roshan Prizak, and Professors Calin Guet, Nick Barton and Gasper Tkacik construct a biophysical model for crosstalk in transcriptional regulation. They identify the parameters that have a major influence on crosstalk severity. While some of these parameters are difficult to estimate, there exists a lower bound to crosstalk with respect to these parameters. This implies the existence of a “crosstalk floor,” which cannot be overcome even if TF concentrations were

optimally adjusted by the cell and compensated for sequestration at noncognate sites.

Although most biophysical constraints have been understood at the level of individual genetic regulatory elements, crosstalk is special: while it originates locally due to biophysical limits to molecular recognition, its cumulative effect only emerges globally. At the level of a single genetic regulatory element, crosstalk can always be avoided by increasing the concentration of cognate TFs or introducing multiple binding sites in the promoter. Only when these same cognate TFs act as noncognate TFs for other genes, or that new binding sites in the promoter drastically increase the number of noncognate binding configurations, that crosstalk constraints become clear.



Activity-dependent processes govern place representation in hippocampus

The hippocampal CA3 region plays a key role in learning and memory. One of its most remarkable properties is its ability to retrieve previously stored memories from incomplete or degraded versions, a phenomenon widely known as pattern completion. It is generally accepted that the synapses between CA3 pyramidal cells, the recurrent CA3–CA3 syn-

apses, play a key role in pattern completion, but how this exactly works has remained enigmatic. In their *Science* paper, Jose Guzman, Alois Schlögl, Michael Frotscher, and Peter Jonas have investigated these mechanisms by combining functional connectivity analysis and network modeling. Their findings suggest that the rules of synaptic connectivity between CA3 pyramidal cells contribute to the remarkable efficiency of pattern completion.

Previous theories of the hippocampal formation often depicted the CA3 region as a network of highly interconnected cells. The neuroscientists tested this hypothesis using a technique that allows monitoring the connection between electrical signals in up to eight neurons at the same time. Using this octuple recording technique, they made several highly

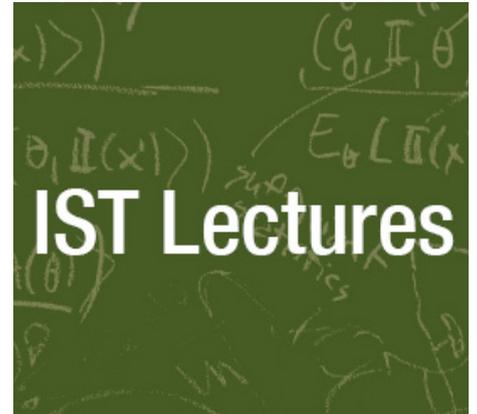
surprising observations. First, they found that connectivity was sparse, with an average connection probability of approximately 1%. This massively challenges the dogma of a network of highly connected cells. Even more surprisingly, they discovered that connectivity in the network is not random, but exhibits connectivity motifs that occur much more frequently than expected for a random network. Thus, the structure of the hippocampal CA3 network may be somewhat reminiscent of a “small world” architecture as found in social networks. Finally, the authors revealed that synaptic connections between two cells are mediated by only one or two synaptic contacts. This is also remarkable because much higher numbers have been found for excitatory synaptic connections in the neocortex.

Upcoming IST Lecture / IST Science and Society Lecture

On November 30, the American physicist Steven Chu will be giving an IST Lecture on “Climate change, clean energy and nanotechnology for energy”. He is William R. Kenan, Jr., Professor of Physics and Professor of Molecular and Cellular Physiology in the Medical School at Stanford University. He has been granted numerous awards including the 1997 Nobel Prize in Physics for laser cooling and atom trapping.

On December 14, the Austrian demographer Wolfgang Lutz will be delivering the IST Science and Society Lecture titled “Human capital as the root cause of development and policy priority for the 21st century”. He is Founding Director of the Wittgenstein Centre for Demography and Global Human Capital, and has published extensively on international population trends.

For further information on the talks and registration visit the [IST Austria website](http://www.ist.ac.at).



Student Open Day 2016



IST Austria will hold this year’s Student Open Day on November 25. Talented students who are interested in performing their doctoral studies in biology, neuroscience, computer science, mathematics, or physics at IST Austria will be invited to a varied program on campus, ranging from information talks, lab and campus tours and research group sessions. Dean Nick Barton and PhD Program Chair Gasper Tkacik will provide them with information on the PhD program and internship opportunities available at IST Austria. The prospective PhD students will also get the opportunity to meet professors, postdocs, and PhD students and ask them about their research. In addition, they will also take campus tours to learn more about the founding principles of IST Austria as well as its past and future development. A think&drink event will conclude the Student Open Day 2016, with IST Austria scientists presenting their ongoing research.

For detailed information on the program and registration see the [IST Austria website](http://www.ist.ac.at).

COLLOQUIUM SPEAKERS

PAST SPEAKERS (September - October): Garret Stuber, The University of North Carolina at Chapel Hill (Sep 5) | James Briscoe, The Francis Crick Institute (Sep 12) | David Nelson, Harvard University (Sep 26) | Kenneth S. Suslick, University of Illinois at Urbana-Champaign (Oct 10) | Ryohei Yasuda, Max Planck Florida Institute for Neuroscience (Oct 17) | Erik Jorgensen, The University of Utah (Oct 24) | Marcel Salathé, École polytechnique fédérale de Lausanne (Nov 7)

FUTURE SPEAKERS (November - January): Alfonso Martinez Arias, University of Cambridge (Nov 21) | Frank Morgan, Williams College (Nov 21) | Felix Otto, Max Planck Institute for Mathematics in the Sciences (Dec 5) | Tanya Zelevinsky, Columbia University (Dec 12) | Matthias Troyer, ETH Zurich and Microsoft Research (Dec 19) | Laure Saint-Raymond, École Normale Supérieure (Jan 16) | Christian Schönenerberger, University of Basel (Jan 23) | Patricia Wittkopp, University of Michigan (Jan 30)

SELECTED RECENT PUBLICATIONS

Akopyan A., Balitskiy Alexey, Karasev R., and Sharipova Anastasia, “Elementary approach to closed billiard trajectories in asymmetric normed spaces”, *Proceedings of the American Mathematical Society*, vol. 144, Jan. 2016, 4501-4513.

Avni G., Henzinger T.A., and Kupferman O., “Dynamic resource allocation games”, *SAGT: Symposium on Algorithmic Game Theory*, vol. 9928, Sep. 2016, 153-166.

Baym M., Lieberman T.D., Kelsic E.D., Chait R., Gross R., Yelin I., and Kishony R.K., “Spatiotemporal microbial evolution on antibiotic landscapes”, *Science*, vol. 353, Sep. 2016, 1147-1151.

Dieterle P.B., Kalaee M., Fink J.M., and Painter O.J., “Superconducting cavity electromechanics on a

silicon-on-insulator platform”, *Physical Review Applied*, vol. 6, Jul. 2016, Article number: 014013.

Fendrych M., Leung Jeffrey, and Friml J., “TIR1 AFB Aux IAA auxin perception mediates rapid cell wall acidification and growth of Arabidopsis hypocotyls”, *eLife*, vol. 5, Sep. 2016, e19048.

Fulek R., “Bounded embeddings of graphs in the plane”, *IWOCA: International Workshop on Combinatorial Algorithms*, vol. 9843, Aug. 2016, 31-42.

Giacobbe M., Guet C.C., Gupta A.K., Henzinger T.A., Paixão T., and Petrov T.P., “Model checking the evolution of gene regulatory networks”, *Acta Informatica*, Aug. 2016, epub ahead of print.

Hansen K.A., Ibsen-Jensen R., and Koucký M., “The big match in small space”, *SAGT: Symposium on Algorithmic Game Theory*, vol. 9928, Sep. 2016,

64-76.

Kaczmarczyk J., Weimer H., and Lemeshko M., “Dissipative preparation of antiferromagnetic order in the Fermi-Hubbard model”, *New Journal of Physics*, vol. 18, Sep. 2016, Article number: 093042.

Maas J., and Matthes D., “Long-time behavior of a finite volume discretization for a fourth order diffusion equation”, *Nonlinearity*, vol. 29, Jun. 2016, 1992-2023.

Oliveto P.S., Paixão T., Heredia J.P., Sudholt D., and Trubenová B., “When non-elitism outperforms elitism for crossing fitness valleys”, *GECCO: Genetic and Evolutionary Computation Conference*, Jul. 2016, 1163-1170.

A full list of publications from IST Austria can be found at publist.ist.ac.at.