Curriculum Vitae

Prof. Dr. Leonid Sazanov, FRS

Position in CoE: Member of the Board of Directors

Personal Details

Place of birth	Brest, Belarus
Nationality	British
Children	2 (1992, 2012)
Affiliation:	Institute of Science and Technology
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List of publications	ORCID: 0000-0002-0977-7989
Academic age	30 years since PhD

Research Institution

I am a **Professor of Structural Biology** at the *Institute of Science and Technology Austria*. The Institute is dedicated to fundamental cutting-edge research in the physical, mathematical, computer, and life sciences, with emphasis on **multidisciplinary research**. It was established only in 2009 but has already gained an international reputation for excellence. IST Austria has by far the highest success rate of **ERC Grants** in Europe, with more than 30 grants awarded so far. In 2019 IST Austria was ranked No. 3 among the **world's best research institutions**, surpassed only by the Cold Spring Harbor Laboratory and the Weizmann Institute. IST Austria invested in a wide range of state-of-the-art facilities, including the most advanced cryo-electron microscopy facility in Austria. Educating PhD students is a core mission of IST Austria, with a Graduate School offering an interdisciplinary PhD program.

Academic Career and Positions Held

I earned a Master's degree in Biophysics in **1982** from the B**elarusian State University**, Minsk, Belarus. Thesis – „Rheological properties of DNA-protein complexes." I received my **PhD** in Biophysics in **1990** from the **Moscow State University**, Moscow, Russia. Subsequently, I worked as **a PostDoc** with **Sergei Zaitsev** at Moscow State University and moved to the UK in **1992** to start a **PostDoc** with Baz Jackson at the **University of Birmingham**. In **1994**, I moved to the **Imperial College London** to work with Peter Nixon and in **1997** to the **MRC Laboratory of Molecular Biology Cambridge** to work with Nobel Laureate John Walker. In 2000, I accepted an offer to become a **group leader** at the newly reformed **MRC Mitochondrial Biology Unit** in Cambridge. **In 2015**, I moved to the **Institute of Science and Technology Austria** to accept a post of a **full professor** in **Structural Biology**.

Main Research Areas and Most Important Research Achievement

Since 1991, I have authored **65 publications**, mostly in leading journals. My work features in many basic biochemistry and biology textbooks. My discoveries transformed our knowledge about entire protein families, which are essential for life. My main research interests are in the study of the **structure and mechanism** of the large **membrane protein complexes (I-V) of the respiratory chain**, which work in series to produce ATP, with complex I being the entry point.

Scientific achievements. One of my main contributions to science is the **discovery of the atomic structures of respiratory complex I**. I determined the first atomic structure of any complex I using *T. thermophilus* enzyme.

This was a tour de force of structural biology, the largest membrane protein solved by X-ray crystallography at the time (14 subunits, 550 kDa). The structure allowed for interpretation of 40 years' worth of functional data, spawning new research directions. I then went on to solve the **first atomic structure** of a more elaborate **mammalian complex I** (45 subunits, ~1MDa), using novel cryo-EM methods. This discovery had **potential knock-on societal effects**, as mutations in complex I subunits lead to a wide range of devastating human diseases.

How the electron transfer events are coupled to proton translocation in complex I has long remained an enigma. Recently, we solved **cryo-EM structures of mammalian complex I** in **different redox** conditions. Analysis of all the structures allowed us to propose a first concrete functional mechanism of complex I, involving an unexpected combination of conformational changes and electrostatic interactions. This year, we **developed this mechanism further** using a bacterial enzyme and arrived at the universal "domino effect" coupling mechanism for the entire complex I family, a pinnacle of more than 20 years of our research.

Other major recent achievements include the determination of the structures and mechanisms of mammalian supercomplexes (respirasome and CIII2+CIV), MRP cation/proton antiporters, proton-translocating transhydrogenase, V/A-type ATPase and mammalian F1Fo ATP synthase.

General achievements. My international standing is reflected in the election as a **Fellow of the Royal Society** and as an **EMBO member**. I have acquired a wide range of competitive funding including an **ERC Advanced grant**. I receive regular invitations to deliver keynote lectures at major international conferences, invitations to write reviews and referee manuscripts for Nature, Science and other major journals, as well as invitations to nominate candidates for major scientific prizes.

Contribution to CoE. With my expertise, I will contribute to the structural (by cryo-EM) and functional analysis of novel membrane proteins from previously uncharacterised microbes. Such microbes contain many redox proteins of completely unknown structure, often catalysing unique reactions, so the insights from their characterisation will have far-reaching implications in microbiology.

10 Most Important Publications (*relevant for the CoE)

1. Vercellino, I.; **Sazanov, L. A.** Structure and Assembly of the Mammalian Mitochondrial Supercomplex CIII2CIV. *Nature* **2021**, *598* (7880), 364–367. *https://doi.org/10.1038/s41586-021-03927-z*.
2. *Kampjut, D.; **Sazanov, L. A**. The Coupling Mechanism of Mammalian Respiratory Complex I. *Science* **2020**, *370* (6516), eabc4209. *https://doi.org/10.1126/science.abc4209*.
3. *Kampjut, D.; **Sazanov, L. A.** Structure and Mechanism of Mitochondrial Proton-Translocating Transhydrogenase. *Nature* **2019**, *573* (7773), 291–295. *https://doi.org/10.1038/s41586-019-1519-2*.
4. *Zhou, L.; **Sazanov, L. A.** Structure and Conformational Plasticity of the Intact *Thermus Thermophilus* V/A-Type ATPase. *Science* **2019**, *365* (6455), eaaw9144. *https://doi.org/10.1126/science.aaw9144*.
5. *Fiedorczuk, K.; Letts, J. A.; Degliesposti, G.; Kaszuba, K.; Skehel, M.; **Sazanov, L. A.** Atomic Structure of the Entire Mammalian Mitochondrial Complex I. *Nature* **2016**, *538* (7625), 406–410. *https://doi.org/10.1038/nature19794*.
6. Letts, J. A.; Fiedorczuk, K.; **Sazanov, L. A.** The Architecture of Respiratory Supercomplexes. *Nature* **2016**, *537* (7622), 644–648. *https://doi.org/10.1038/nature19774*.
7. Baradaran, R.; Berrisford, J. M.; Minhas, G. S.; **Sazanov, L. A.** Crystal Structure of the Entire Respiratory Complex I. *Nature* **2013**, *494* (7438), 443–448. *https://doi.org/10.1038/nature11871*.
8. Efremov, R. G.; **Sazanov, L. A.** Structure of the Membrane Domain of Respiratory Complex I. *Nature* **2011**, *476* (7361), 414–420. *https://doi.org/10.1038/nature10330*.
9. **Sazanov, L. A.**; Hinchliffe, P. Structure of the Hydrophilic Domain of Respiratory Complex I from Thermus Thermophilus. Science **2006**, *311* (5766), 1430–1436. *https://doi.org/10.1126/science.1123809*.
10. Efremov, R. G.; Baradaran, R.; **Sazanov, L. A.** The Architecture of Respiratory Complex I. *Nature* **2010**, *465* (7297), 441–445. *https://doi.org/10.1038/nature09066*.