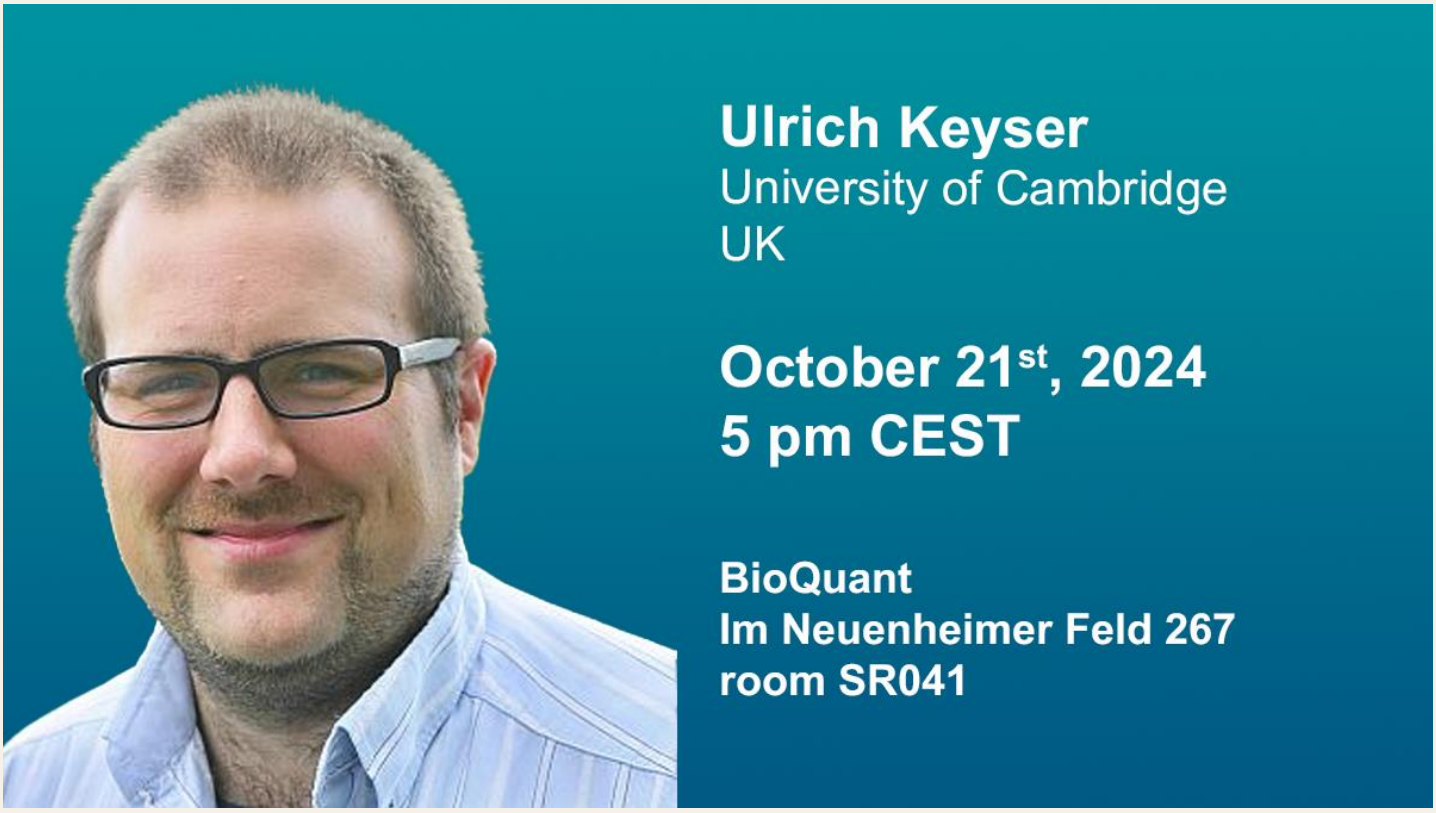
COLLOQUIUM
ENGINEERING MOLECULAR SYSTEMS

ULRICH KEYSER will talk about **NATIVE RNA DETECTION USING NANOPORES: ISOFORMS, RNA MODIFICATIONS AND DISEASE DIAGNOSTICS** in the “Engineering Molecular Systems” colloquium on **October 21st, 2024** at **5 p.m.** (CEST) hosted by the Flagship Initiative Engineering Molecular Systems of Heidelberg University. The colloquium will take place at the BioQuant (Im Neuenheimer Feld 267 room SR041).



ABSTRACT

Rapid identification of RNA molecules is a major challenge in biotechnology. This is driven by the discovery of RNAs that control cellular function ranging in length from a few to 1000s of nucleotides. Here we design three-dimensional nucleic acid constructs that enable the identification of short and long RNA molecules and nanopore readout. [1]

First, we describe the identification of long transcript isoforms at the single-molecule level using solid-state nanopore microscopy. We refold target RNA into RNA identifiers (IDs) with designed sets of complementary DNA strands. Each reshaped molecule carries a unique sequence of structural (pseudo)colours. The sequence of structural colours of RNA identifiers enables simultaneous identification and relative quantification of multiple RNA targets without prior amplification. RNA IDs discriminate circular and linear transcript isoforms in a one-step, enzyme-free reaction in a complex human transcriptome using single-molecule read-out [1]. We will show recent results on detection of RNA modifications like 5mC, Inosine and MeC using RNA nanotechnology in ribosomal RNA (rRNA) from pathogenic bacteria like A. baumannii. The process is amenable for rapid sample extraction with an enzyme-free one-pot reaction.[2]

In the second part, we use designed DNA identifiers that allows the multiplexed identification of short RNA molecules. We demonstrate the power of the approach by identifying common viruses and their variants with a nanopores microscope [3]. Finally we show bacterial disease identification with single-base pair resolution with advanced RNA:DNA nanotechnology and solid-state nanopore sensing [4].

SELECTED REFERENCES

1. F. Bošković and U. F. Keyser. Nanopore microscope identifies RNA isoforms with structural colors. Nature Chemistry, 14:1258-1264, 2022.
2. F. Bošković, S. E. Sandler, S. Brauburger, Y. Shui, B. Kumar, J. Pereira Dias, P. Naydenova, J. Zhu, S. Baker, and U. F. Keyser. One pot RNA:DNA assembly for ribosomal RNA detection of pathogenic bacteria with single-molecule sensitivity. biorxiv, https://doi.org/10.1101/2024.08.15.608086, 2024.
3. F. Bošković, J. Zhu, R. Tivony, A. Ohmann, K. Chen, M. Alawami, M. Djordjevic, N. Ermann, J. Pereira Dias, M. Fairhead, M. Howarth, S. Baker, and U. F. Keyser. Simultaneous identification of viruses and viral variants with programmable DNA nanobait. Nature Nanotechnology, 18:290–298, 2023
4. J. Zhu, J. , R. Tivony, F. Bošković, J Pereira-Dias, S. E. Sandler, S. Baker, and U. F. Keyser*. Multiplexed Nanopore-Based Nucleic Acid Sensing and Bacterial Identification Using DNA Dumbbell Nanoswitches. JACS, 145:22, 12115–12123, 2023

BRIEF BIO

Ulrich Keyser was appointed as Assistant Professor in 2007 and is now Professor of Applied Physics at the Cavendish Laboratory, University of Cambridge. His research group consists of 10 members working on elucidating the physics of membrane transport, controlling molecules in nanopores, mimicking, and understanding protein channels. His experimental group uses single molecule techniques, nanopore sensing, DNA (origami) self-assembly, optical tweezers and microfluidics. He was awarded an ERC Starting Grant 2010-2015, ERC Consolidator Grant (2015-2021), two ERC Proof-of-Concept Grants, The Helmholtz Price for Metrology in 2016 and the Sam Edwards Medal of the Institute of Physics in 2023. Currently, his lab is working on integrating RNA:DNA nanotechnology with solid-state nanopore based single-molecule biosensing for DNA data storage, studies of RNA structure, and disease detection.

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