



UNIVERSITÄT HEIDELBERG ZUKUNFT SEIT 1386

COLLOQUIUM ENGINEERING MOLECULAR SYSTEMS

FLAGSHIP INITIATIVE

MOLECULAR SYSTEMS

ENGINEERING

- In person/hybrid -

EDWARD LEMKE will talk about **DECODING MOLECULAR PLASTICITY IN THE DARK PROTEOME** in the "Engineering Molecular Systems" colloquium on **December 12th 2022** at **12 pm** (CET) hosted by the Flagship Initiative Engineering Molecular Systems of Heidelberg University. The colloquium will be **in person** and **takes place at the IMSEAM** (Insitute for Molecular Systems Engineering and Advanced Materials, Im Neuenheimer Feld 225, seminar room 01.413). If you prefer online participation, please register <u>here</u>.

E. Lemke will be on the campus after the talk, K.Klingmann (k.klingmann@zmbh.uniheidelberg.de) will organize a schedule and a speakers dinner.



Edward Lemke

Department of Biology and Chemistry, Biocentre Johannes Gutenberg-University Mainz

December 12th 2022 12 pm CET

IMSEAM Im Neuenheimer Feld 225 seminar room 01.413



FLAGSHIP INITIATIVE Engineering Molecular systems



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ABSTRACT:

Intrinsically disordered proteins (IDPs) account for up to 30% of the eukaryotic proteome. Their polymer like nature makes them very hard to study by conventional approaches. I will show in my talk how we combine modern synthetic and chemical biology tools with advanced biophysical measurements to develop a path towards studying the protein conformations of IDPs in situ. In my talk I will focus on the function of IDPs that are central to nuclear pore complex (NPC) function. Nuclear transport receptors (NTRs) can move through the central channel of the NPC which is filled with hundreds of phenylalanine-glycine-rich and disordered nucleoporins (FG-Nups) reaching millimolar concentrations with elusive conformational plasticity. Since site-specific labeling of proteins with small but highly photostable fluorescent dyes inside cells remains the major bottleneck for directly studying protein dynamics in the cellular interior, we have now developed a semi-genetic strategy based on novel artificial amino acids that are easily and site-specifically introduced into any protein by the natural machinery of the living cell via a newly developed thin-film synthetic organelle. Our strategy basically equips the living cell with up to three genetic codes and shows the power of biological engineering for rewriting a process as complex as translation inside the living cell, without altering canonical host translation. This allowed us to develop an experimental approach combining site-specific fluorescent labeling of IDPs in non-fixed cells with fluorescent lifetime imaging microscopy (FLIM) to directly decipher the plasticity of FG-Nups via FRET. Our study enabled a conformational look on the densely packed IDPs in the sub-resolution cavity of the NPC and describe the conformations of FG-Nups at their functional status as well as the solvent quality in the inner NPC environment.

BRIEF CV:

After several years as group leader of an Emmy Noether and ERC consolidator research group at the European Molecular Biology Laboratory (EMBL), the biophysical chemist Edward A. Lemke has taken up a professorship for synthetic biophysics at Johannes Gutenberg University Mainz. He has also become Adjunct Director at the Institute of Molecular Biology (IMB) in Mainz. Combining new research methods and expertise in synthetic biology, chemistry, biophysics and cell biology, he has established himself as an innovative researcher in the field of intrinsically disordered proteins. He is speaker of the Priority Programme on molecular mechanisms of functional phase separation of the DFG and his current work is also funded by an ERC advanced grant.