Institut Européen de Chimie et Biologie

I E C B

Looking to the Future

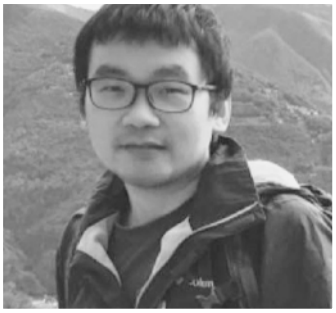
15th workshop of candidates

for group leader positions at IECB

Wednesday 13th November, 2024

IECB Auditorium

2024 pre-selected candidates for Group-leader positions at IECB



Dr. Dalu CHANG

EPFL, Lausanne, Switzerland / University of Oxford, UK

Spatiotemporal Control of Biological Events Using Photo-Uncaging Systems.

In the fields of chemical biology and biochemistry, the traditional approach to study endogenous or synthetic biomolecules typically involves introducing them directly into cells to observe downstream functional changes. However, this method has limitations such as off-target effects, a lack of precise subcellular delivery, and an inability to control the timing of molecule activation. Photo-uncaging systems have emerged as a powerful solution, allowing researchers to release active molecules at specific locations and times within cells and tissues. In this talk, I will mainly focus on 1) **Rational design of photo-uncaging systems**: I will briefly introduce the current State-of-the-art and limitations in the field, explain the innovative design approaches developed during my PhD and postdoctoral research; 2) **Development and Application of designed biochemical tools to reprogram mRNA processing under spatial and temporal manner.** In this project, we combined localized electrophile delivery with genetic-code-expansion-based translation reporter systems to investigate how subcellular stress affects protein translation. This approach allows us to control and study biological events with unparalleled precision, shedding light on the intricate relationships between mRNA processing and cellular stress responses.

Dr. Kyong T. FAM

Scripps Research, La Jolla, California, USA.

Chemical approaches for microbial modulation and drug discovery.

Increase of antibiotic resistance in hospitals requires development of new approaches to combat bacterial infections. In this talk, I will discuss the development of chemical tools to interrogate bacterial cell-wall remodeling enzymes and a new therapeutic modality to fight antibiotic-resistant bacteria.

Dr. Jianwei LI

MediCity Research Laboratory, University of Turku, Finland.

Functional Soft Materials from Complex Chemical Systems.
Biological systems are intricate soft materials, organised across scales from molecules to tissues. Their functionality emerges from structural and rheological assemblies sustained by numerous simultaneous chemical reactions, making them challenging to replicate in the laboratory. This challenge is approached by employing simpler synthetic systems, created through dynamic combinatorial chemistry (DCC). This talk will introduce the fundamental principles of DCC and demonstrate how this approach can be used to synthesise soft materials, ranging in size from nanometres to centimetres, with potential applications in drug delivery, degradable plastics, and soft robotics. Finally, an outlook on future directions will be offered to inspire further advancements in this exciting field.

Dr. Andrea BELLUATI

Darmstadt University of Technology, Darmstadt, Germany.

Polymer-Cell Interactions for Controlled Biological Systems.
Advancing the design of polymer-cell interactions is critical for applications ranging from tissue engineering to targeted therapeutics. Current strategies to interface synthetic materials with cells are limited by poor stability, uncontrolled interactions, and suboptimal functionality. My research focuses on leveraging *Single-Cell Nanoencapsulation* (SCNE) and *polymerisation-induced self-assembly* (PISA) to create polymer-based artificial cells that can interact with living systems in a controlled and predictable manner. These engineered cells encapsulate biological components, enabling the replication of key cellular processes like protein synthesis and metabolic activity and offer new possibilities in cell-based biomanufacturing and therapeutic applications.

Dr. Aurore DUPIN

Weizmann Institute of Science, Rehovot, Israel.

Surface-based cell-free platform to characterize host-pathogen interactions.

The immune system is one of the most complex systems of the human body. At its core, it uses protein-protein interactions to achieve the emergent property of differentiating self from other. Synthetic biology aims to implement biological functions in programmable environments. Here, we reconstitute immune protein-protein interactions on a cell-free surface-based approach. We use innovative silicon chips to parallelize antigen display and antibody epitope screening. Linear DNA sequences are immobilized in micrometer-sized carved compartments, where phenotype and genotype are linked by localized expression and capture of antigens. Binding to a panel of viral antigens is assessed with high specificity for monoclonal antibodies and for polyclonal antibodies in human serum, revealing a rich picture of epitopes and individual immune profiles. This platform mimics and extends the function of antigen-presenting cells, allowing us to interrogate protein-protein interaction between host receptor, pathogenic antigen and immune system.

Dr. Loïc BROIX

RIKEN Center for Biosystems Dynamics Research Kobe, Japan.

Crosstalk between membrane-bound organelles, mRNA and the cytoskeleton in neurons.

Neurons are highly polarized cells that rely extensively on long-range bidirectional transport between the cell body and synapses to ensure their homeostasis and proper activity. The microtubules provide long tracks in the axon along which a broad range of organelles, vesicles and mRNAs are transported by kinesin and dynein molecular motors. In the first part of my talk, I will demonstrate that moving axonal membrane-bound vesicles have on-board enzymatic machinery that can modulate their own transport by changing their local microtubule environment. In the second part, I will describe how the interplay between epitranscriptomics, mRNA trafficking and cytoskeletal dynamics is required for axon development in neurons. These works emphasize the importance of the crosstalk between membrane-bound organelles, mRNA and the cytoskeleton in the control of neuronal development and function.

Dr. Markel MARTINEZ
Pasteur Institute, Paris, France.

The archaeal core replisome: many ways to look at it.
Many of the replication factors that help replicate DNA act in concert in a dynamic protein complex referred to as the replisome. Using an integrative structural biology approach, combining NMR, X-ray crystallography and cryo-EM with DNA polymerization assays, our aim is to decipher the molecular mechanisms required for the assembly of the archaeal replisome, which possesses an intriguing blend of bacterial and eukaryotic replication machinery features. Our latest work focused on the essential replisome component Replication Protein A (RPA), which plays a pivotal role in DNA replication, avidly coating exposed single-stranded DNA as soon as the double-helix is unwound. We unveiled how RPA uses a conserved C-terminal winged-helix domain to interact with two key actors of the replisome regulating their activity: the DNA primase (PriSL) and the replicative DNA polymerase (PolD). We present multiple structures explaining a conserved mechanism for RPA-mediated interactions, which shares its ancestor with eukaryotic RPA and the CST telomere maintenance complex.

Dr. Harry M. Williams
Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany.

Structurally characterising the phenuivirus replication machinery.
Severe fever with thrombocytopenia syndrome (SFTS) is a tick-borne infection caused by SFTS virus (SFTSV) which has a case fatality rate of up to 30%. There is currently no specific treatment available for SFTS or any phenuivirus infection. There is therefore an urgent need to develop eEective countermeasures e.g. antivirals. A key target for the development of antivirals is the large (L) protein as this includes the viral RdRp. Unfortunately, eEorts in this area are hampered by significant gaps in our knowledge relating to how these viruses replicate. The aim of my current work is therefore to determine the structural mechanisms enabling both viral genome replication and transcription in phenuiviruses using SFTSV as a model system. I do this using a combination of in vitro biochemistry cell-based assays and single particle cryo-EM. Thus far this approach has allowed me to characterise several key steps in both viral genome replication and transcription. This data has also led to the identification of several highly-specific RNA binding pockets which represent tantalizing targets when designing broad-spectrum antivirals.

Looking to the Future Workshop Program

Wednesday 13th November, 2024

09.45 – 10.00 Introduction

10.00 – 10.40 Spatiotemporal Control of Biological Events Using Photo-Uncaging Systems.

Dr. Dalu CHANG

EPFL, Lausanne, Switzerland / University of Oxford, UK.

10.40 – 11.10 Chemical approaches for microbial modulation and drug discovery.

Dr. Kyong T. FAM

Scripps Research, La Jolla, California, USA.

11.10 – 11.50 Functional Soft Materials from Complex Chemical Systems.

Dr. Jianwei LI

MediCity Research Laboratory, University of Turku, Finland.

11.50 – 13.30 ***Cocktail lunch***

13.30 – 14.10 Polymer-Cell Interactions for Controlled Biological Systems.

Dr. Andrea BELLUATI

Darmstadt University of Technology, Darmstadt, Germany.

14.10 – 14.50 Surface-based cell-free platform to characterize host-pathogen interactions.

Dr. Aurore DUPIN

Weizmann Institute of Science, Rehovot Israel.

14.50 – 15.30 Crosstalk between membrane-bound organelles mRNA and the cytoskeleton in neurons.

Dr. Loïc BROIX

RIKEN Center for Biosystems Dynamics Research, Kobe, Japan.

15.30 – 16.00 ***Coffee break***

16.00 – 16.40 The archaeal core replisome: many ways to look at it

Dr. Markel MARTINEZ

Pasteur Institute, Paris, France.

16.40 – 17.20 Structurally characterising the phenuivirus replication machinery.

Dr. Harry M. WILLIAMS

Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany.