Institut Européen de Chimie et Biologie

I E C B

Looking to the Future

8th workshop of candidates for group-leader positions at IECB

Thursday October 22nd, 2015

IECB Auditorium, free & open to all

2015 pre-selected candidates for group-leader positions at IECB

Dr. Nicolas Barry

Department of Chemistry, University of Warwick, UK

Combining Inorganic Medicinal Chemistry and Nanotechnology

Inorganic medicinal chemistry is in the early days of its development, although there are now a significant number of clinical trials involving metal compounds, or other agents which interfere with metabolic pathways for metals, both for therapy and for diagnosis. However, a number of challenges in inorganic medicinal chemistry remain to be overcome, such as for example, tumour-targeting and reduction of side effects. Nanotechnology, which has been defined as the engineering and manufacturing of materials at the atomic and molecular scale, offers unique tools for developing safer and more effective medicines, and provides several potential advantages for drug formulation and delivery. In this presentation, we will discuss the design of metallated particles combining unusual ligands (carboranes), precious metals and polymers, and their applications in medicine.

Dr. Christian Hoppmann

Department of Pharmaceutical Chemistry , University of California, San Francisco (UCSF),USA

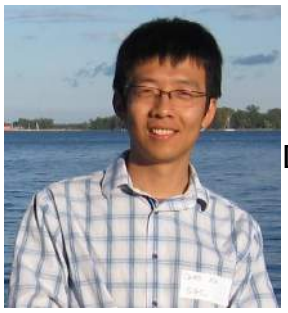
Photocontrol of Conformation and Bioactivity of Peptides and Proteins in Cells

Photoswitchable biomolecules are finding increasing utility for the in vivo investigation of biological processes, where they confer a minimally invasive means for precise spatiotemporal control. Of particular interest are photoisomerizable units, such as azobenzene photoswitches, which can drive reversible changes of conformation and activity of peptides and proteins. In my Ph.D., by incorporating azobenzene based ω-amino acids into peptides, I generated cyclic ligands the binding of which to the target protein was controllable by light, even in living cells. In order to install photo-responsiveness onto proteins, as a Postdoc, I developed PhotoSwitchable Click amino acids (PSCaa) that can be incorporated into proteins in E.coli and mammalian cells using an expanded genetic code. PSCaa's allow conformation and activity of proteins to be directed by light through a built-in photoswitchable bridge. These PSCaa's will prove valuable for optobiology and reversible optogenetic regulation.

Dr. Natàlia Carulla

Institute for Research in Biomedicine (IRB Barcelona), Barcelona, Spain

Novel molecular approaches to unravel the role of amyloid-β aggregation in Alzheimer´s disease. Amyloid-β (Aβ) aggregation is associated with Alzheimer´s disease (AD). However, this aggregation process is heterogeneous and dynamic, thus precluding the identification of the specific properties of Aβ that lead to neuronal dysfunction and death in AD. In this talk, I will describe novel molecular approaches that are allowing us to define the structures and properties of the various species formed during Aβ aggregation. Moreover, I will discuss the implications of this work for the development of much-needed diagnostic tools and novel therapies to treat AD.



Dr. Chao Xu

Structural Genomics Consortium (SGC) of the University of Toronto, Canada

Structural biology of the reader proteins in epigenetics and RNA epigenetics.

My research focused on the chromatin binding proteins and the methylated RNA binding proteins which play important roles in epigenetics and RNA epigenetics. Our past work put efforts into addressing the following questions in epigenetics: (1) How repressive epigenetic histone marks could be maintained during the cell cycle; (2) How chromatin binding modules of the transcriptional factor facilitates the eukaryotic gene expression and embryo development; (3) How the N6-methyladenosine could be recognized by its reader module—YTH domain.

Dr. Hesso Farhan

Department of Biology, University of Konstanz and Biotechnology institute Thurgau (BITg)

Signalling at the Golgi and its role in physiology and pathology.

The Golgi is emerging as a hub for cellular signaling and this is a central research area of my group. We are investigating the following aspects of Golgi biology:

(i) Signaling of the small GTPase Cdc42 at the Golgi and its role in polarity

(ii) The Golgi in cancer: systematic analysis in patient material. In addition, we investigate the role of the Golgi in invasion and migration and the consequences for tumor growth using a combination of experimentation and mathematical modelling.

(iii) Trafficking to and from the Golgi and its de-regulation in cancer.

(iv) Finally, a very new research area in the lab is the investigation of the effect of cellular stress on the Golgi. We have already performed computational modelling of protein-interaction networks of the Golgi-stress connection and identified signatures that point to a role in neurodegeneration. Our goal is primarily to study stress-signaling at the Golgi and to extend this in the future to test the relevance of our findings for neurodegeneration.

Pseudoenzymes in health and disease

We focus currently on the pseudophosphatase STYX which we showed previously to act as a nuclear anchored for the ERK1/2 kinases, which is in fact the first demonstration of a nuclear anchoring function. This was achieved using computational modeling together with molecular cell biology experiments. We reasoned that a pseudophosphatase like STYX might have evolved to regulate pathways beyond kinases. We therefore mapped the interactome of STYX and discovered that it interacts with several F-box proteins. Our data currently suggest that STYX acts as a rheostat for F-box proteins and thereby regulates their (mostly) tumor-suppresisve effects such as the control of proliferation and the sensitivity to pro-apoptotic stimuli.

Dr. Tanuj Sapra

University of Zürich, Biochemistry Institute, Switzerland

From synthetic organelles to synthetic organs: Engineering functional modules for bottom-up synthetic biology.

Besides synthesizing new forms of life, an ambitious challenge posed in synthetic biology is the bottom-up construction of a biological cell. Recently, a droplet-based lipid bilayer system termed droplet interface bilayer (DIB) was developed. Nanoliter-sized lipid-encased water droplets can be arranged in networks of desired patterns, forming electrical connections mer at all biological scales (nanometer, nm – millimeter, mm). To this end, I am studying the structural mechanics of protein assemblies using the atomic force microscopy and cryo-electron tomography. I believe that using state-of-the-art techniques to answer pertinent questions will pave the way to rationally designing synthetic systems for bio-nanotechnology.

Dr. Guillermo Acuna

Institute of Physical and Theoretical Chemistry, Braunschweig, Germany

DNA Origami for plasmonics and fluorescence applications

This contribution will focus on different applications of the DNA-Origami technique [1] in the fields of plasmonics and fluorescence enhancement. In particular, we employ DNA-Origami as a platform where metallic nanoparticles as well as single organic fluorophores can be organized with nanometer precision in three dimensions. With these hybrid structures we initially study the nanoparticle-fluorophore interaction in terms of the distance-dependent fluorescence quenching [2] and angular dependence around the nanoparticle [3]. Based on these findings, we build highly efficient nano-antennas (figure a) based on 100 nm gold dimers [4-5] which are able to strongly focus light into the sub-wavelength region where the fluorophore is positioned and produce a fluorescence enhancement of more than three orders of magnitude. Using this highly confined excitation field we were able to perform single molecule measurements in solution at concentrations as high as 25 µM in the biologically relevant range (>1µM). Additionally, we report on a controlled increment of the radiative rate of organic dyes in the vicinity of gold nanoparticles with the consequent increment in the number of total emitted photons [6,7]. We also employ the nanoantennas to mediate the fluorophore emission and thus to shift the apparent emission origin. Finally we will discuss how DNA-Origami can also improve the occupation of other photonic structures, the zeromode waveguides (ZMWs). These structures, which consist of small holes in aluminum films can serve as ultra-small observation volumes for single-molecule spectroscopy at high, biologically relevant concentrations and are commercially used for real-time DNA sequencing [8]. To benefit from the single-molecule approach, each ZMW should be filled with one target molecule which is not possible with stochastic immobilization schemes by adapting the concentration and incubation time. We present DNA origami nano-adapters that by size exclusion allow placing of exactly one molecule per ZMW (figure b). The DNA origami nano-adapters thus overcome Poissonian statistics of molecule positioning [9] and furthermore improve the photophysical homogeneity of the immobilized fluorescent dyes [10]

Dr. Anton Kuzyk

Max Planck Institute for Intelligent Systems, Stuttgart, Germany

DNA-based artificial dynamic molecular systems

DNA has proven to be one of the most versatile construction materials for building artificial molecular assemblies and devices1–3. Specificity of Watson-Crick base pair interactions allows for unprecedented control of both spatial and temporal distribution of matter. This control is in the heart of the research field of DNA Nanotechnology, which uses DNA as a construction rather than a genetic material1. With the invention of the DNA origami technique in 20064, DNA Nanotechnology has reached a new level of sophistication. DNA can now be used to arrange molecules and other nanoscale components, e.g., protein and nanoparticles5, with nanometer precision into almost arbitrary geometries. Moreover, dynamic DNA Nanotechnology6 allows for making such assemblies reconfigurable, i.e., dynamically controlled in time. Combination of precise spatial and temporal manipulation of matter on the nanometre scale is expected lead to important technological and scientific developments in various fields, e.g., in active plasmonics7,8, metamaterials, (bio)sensing, stimuli responsive smart materials, drug delivery etc.

Looking to the Future Workshop Program

Thursday October 22nd, 2015

11.00 – 11.30 Combining inorganic medicinal chemistry and nanotechnology

Dr. Nicolas Barry
Department of Chemistry, University of Warwick, UK

11.30 – 12.00 Photocontrol of conformation and bioactivity of peptides and proteins in cells

Dr. Christian Hoppmann
Department of Pharmaceutical Chemistry, (UCSF), USA

12.00 – 14.00 Cocktail lunch

14.00 – 14.30 Novel molecular approaches to unravel the role of amyloid-β aggregation in Alzheimer's disease

Dr. Natàlia Carulla
Institute for Research in Biomedicine (IRB Barcelona), Barcelona, Spain

14.30– 15.00 Structural biology of the reader proteins in epigenetics and RNA epigenetics

Dr. Chao Xu
Structural Genomics Consortium (SGC) of the University of Toronto, Canada

15.00 – 15.30 Signalling at the Golgi and its role in physiology and pathology / Pseudoenzymes in health and disease

Dr. Hesso Farhan
Department of Biology, University of Konstanz and BITg, Germany

15.30– 16.15 Coffee break

16.15– 16.45 From synthetic organelles to synthetic organs : engineering fuctional modules for bottom-up synthetic biology

Dr. Tanuj Sapra
University of Zürich, Biochemistry Institute, Switzerland

16.45 -17.15 DNA origami for plasmonics and fluorescence applications

Dr. Guillermo Acuna
Institute of Physical and Theoretical Chemistry, Braunschweig, Germany

17.15 – 17.45 DNA-based artifical dynamic molecular systems

Dr. Anton Kuzyk
Max Planck Institute for Intelligent Systems, Stuttgart, Germany

17.45 – 18.15 IGEM presentation

18.15 IECB Happy Hour