Julius-Maximilians-
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ABSTRACTS

Indo-German Workshop-2023

ENABLING METHODOLOGIES FOR RATIONAL DESIGN OF COMPLEX SYSTEMS

11-13 October 2023. Würzburg Germany

Organizers: Prof. Dr. Jürgen Seibel, Prof. Dr. Bernd Engels, Prof. Dr. Sandeep Verma

Venue: Residenz Würzburg (Toscanasaal), Germany

PROF. DR. SIVAPRIYA KIRUBAKARAN

Indian Institute of Technology Gandhinagar
Gandhinagar, India

Wednesday, 11th October 2023 AT 9:00 HRS

Targeting one kinase and addressing two types of cancers: A new class of TLK (Tousled-like kinase) inhibitors

Targeting protein kinases is an attractive strategy in cancer therapy owing to their importance in cell signaling pathways. Tousled-like kinases (TLKs) are associated with chromosomal integrity, DNA replication, and repair. However, the dysregulation of these genes can give rise to different aberrations. An isoform of TLK, TLK1B activity is found to be attenuated in the case of prostate cancer and breast cancer, as it can phosphorylate many proteins of the DNA Damage Response (DDR) pathway, making TLK1B a druggable target. Our work focuses on the development of a new class of TLK1B inhibitors to broaden the spectrum of understanding TLK1B inhibition. As an approach, we designed, synthesized, and validated indole-based molecules with potent TLK1B inhibition via *in-silico* studies. We further explored the synthesized inhibitors to understand their inhibition against recombinantly purified TLK1B in the presence of its different substrates. We found that the inhibitors are more potent in prostate cancer cell lines, as observed by the lowered downstream phosphorylation levels in those cells as well in initial animal model studies. Recently the inhibitors have shown a great potency in Glioblastoma. We anticipate that our step towards exploring a new class of potent TLK1B inhibitors would aid in elevating the therapeutics in a combinatorial approach to existing prostate cancer therapy. The overall studies on prostate cancer and GBM will be discussed in the presentation.

References:

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2. Synthesis, Kinetics and Cellular studies of new phenothiazine analogs as potent human-TLK inhibitors: Delna Johnson, Javeena Hussain, † Siddhant Bhoir, † Vaishali Chandrasekaran, Parul Sahrawat, Tanya Hans, Md Imtiaz Khalil, Arrigo De Benedetti, Vijay Thiruvenkatam * [b] and **Sivapriya Kirubakaran** * [a], *Org. Biomol. Chem.*, **2023,** ***21****,* 1980- DOI: 10.1039/D2OB02191A

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PROF. DR. THIRUVANCHERIL G. GOPAKUMAR

Indian Institute of Technology Kanpur
Kanpur, India

Wednesday, 11th October 2023 AT 9:35 HRS

2D Molecular Materials for Electronics Applications

Thin films of semiconducting molecules have increased a lot of attention in modern electronic devices. The library of molecules offers different electronic functionalities like switches, diodes, memories, wires etc. The unique self-assembling property of molecules is an added advantage in fabricating devices using well-ordered array of these electronic functionalities. Though molecular self-assembled films are easy to prepare, they suffer from poor charge transport. This is due to the weak electronic coupling between the molecules and thus the transport occurs through hopping or tunneling of charge carriers. This can be improved by linking the molecules in the film by aromatic linkage or metal linkage. In this talk I will discuss the formation of two dimensional (2D) molecular materials on surfaces and interfaces. 2D molecular materials formed by both aromatic linkage and metal linkage will be discussed. We use a combination of atomic force microscopy (AFM), scanning tunneling microscopy (STM), tunneling spectroscopy and density functional calculations to address the above examples.

PROF. DR. THOMAS SCHRADER

Duisburg-Essen University
Essen, Germany

Wednesday, 11th October 2023 AT 10:10 HRS

Advanced Molecular Tweezers – Revolutionary Treatment of Neurodegenerative Diseases and Viral Infections

Alzheimer's and Parkinson's Disease, SARS-Cov-2 and HCMV infections are among the top scorers in the numbers of patients worldwide and very difficult to treat. Neurodegenerative diseases and respiratory viral infections do not only cost millions of lives annually, they are also progressing even in the Western world and produce enormous costs for the health system. Mild and effective ways of prophylaxis and treatment are highly desirable, in order to prevent, e.g., the next pandemic.

Supramolecular Chemistry offers a deeper understanding and computational prediction of noncovalent interactions even on protein surfaces and the repertoire of Organic Synthesis to create novel binding motifs not found in Nature. Our group has pursued the rational design of artificial ligands for proteins and membranes and discovered that molecular tweezers with a tailored electron-rich aromatic cavity are able to interfere with two pathologic processes of high relevance: the misfolding and uncontrolled aggregation of proteins and the infection and spreading of pathogenic viruses.

Both processes rely on highly specific molecular recognition and can be antagonized in a very mild way by advanced nontoxic tweezer derivatives. The lecture explains the underlying supramolecular mechanism, the design of greatly improved new derivatives and cell culture as well as advanced animal experiments. The unique features of this highly promising new class of drugs are discussed which is currently developed in the preclinical stage.

References

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2. Advanced Molecular Tweezers with Lipid Anchors against SARS-CoV-2 and Other Respiratory Viruses. E. Sanchez-Garcia, T. Schrader, J. Münch et al. *JACS Au* **2022**, *2*, 2187-2202. https://doi.org/10.1021/jacsau.2c00220.
3. Supramolecular mechanism of viral envelope disruption by molecular tweezers. T. Schrader, J. Shorter, E. Sanchez-Garcia, J Münch et al. *J. Am. Chem. Soc.* **2020**, *142*, 17024–17038. https://doi.org/10.1021/jacs.0c06400.
4. CLR01 protects dopaminergic neurons in vitro and in vivo in human neurons and mouse models of Parkinson's. N. Bengoa-Vergniory, E. Faggiani, P. Ramos, E. Kirkiz, N. Connor-Robson, S. Vingill, M. Cioroch, F. Cavaliere, S. Threlfell, B. Roberts, T. Schrader, F.-G. Klärner, S. Cragg, B. Dehay, G. Bitan, C. Matute-Almau, E. Bezard, R. Wade-Martins. *Nat. Commun.* **2020**, *11*, 4885. https://doi.org/10.1038/s41467-020-18689-x.

PROF. DR. FLORIAN BEUERLE

Eberhards Karls University Tübingen
Tübingen, Germany

Wednesday, 11th October 2023 AT 11:15 HRS

Functional Porous Boronate Ester Cage Materials

Shape-persistent covalent organic cage compounds[1)] are an emerging class of porous light-weight materials with high potential for applications in areas such as gas sorption and separation, catalysis, host-guest chemistry, or sensing. Typically, these complex nanostructures are synthesized by multiple bond formation between structurally defined subcomponents under reversible conditions. Molecular cage compounds can be considered as "soluble porous units"[2)] that allow solution processing and a well-defined alignment of connected pores in the bulk phase.

Previously, we reported on the implementation of rectangular tribenzotriquinacenes (TBTQs)[3)] as orthogonal vertices in cubic, tetrahedral or trigonal-bipyramidal cages[4),5)] and supramolecular structures assembled via B-N dative bonds.[6)] In this talk, I will present the synthesis and characterization of a series of TBTQ-based cage compounds that are obtained via boronate ester formation between hexahydroxy TBTQs and diboronic acids with varying bond angles. Depending on the substituents that are attached to the apical position of the TBTQs or the diboronic acid linkers, either soluble cage compounds or crystalline porous solids are obtained.[7)] Crystalline cage materials are analyzed by single-crystal X-ray diffraction and BET measurements revealed very high surface areas of more than 3500 $m^2\ g^{-1}$ for these porous molecular solids. Reticular design strategies allow for a precise control of pore size and shape for such modular porous materials. Cage materials with unprecedented stability under ambient conditions have been exploited for catalytic applications.[8)]

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PROF. DR. SATISH PATIL

Indian Institute of Technology Bengaluru
Bangalore, India

Wednesday, 11th October 2023 AT 11:50 HRS

Science of Triplet Excitons

Molecular triplet excitons are 'dark states' because of the forbidden nature of the electronic transitions. However, they can be harvested to enhance the efficiency of optoelectronic devices such as organic light-emitting diodes and solar cells. For example, multiexciton generation through singlet fission has the potential of exceeding the Shockley–Queisser limit in photovoltaic devices. However, only very few materials suitable for singlet fission are available at present, and the mechanism of inter- and intra-molecular singlet fission are not fully understood. Detailed knowledge regarding the processes is crucial for developing new materials. In this talk, I will present the molecular design and synthesis strategies to meet the exchange energy and morphology criteria for molecules to undergo singlet fission.

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PROF. DR. NADJA SIMETH

Georg-August-University of Göttingen
Göttingen, Germany

Wednesday, 11th October 2023 AT 12:25 HRS

Opto-Bioorganic Chemistry for Smart Biological Tools and Labeling Agents

In recent years, light has been employed as an external stimulus to photo-control diverse functional processes.[1] This approach relies on the use of small, light-responsive molecules that undergo a structural change upon irradiation, generating different functional states from a single molecule.[2] By attaching suitable substituents to such photoactuators, these molecules can be embedded in a system of choice to link their structural change to a change in the system's properties.[3] On the other hand, the sterical and electronic characteristics of the substituents influence the photophysical and photochemical properties of the core.[4] This mutual interaction needs to be finely balanced and studied in detail to rationally design probes and tools to study and modulate biological systems. Here, we show different strategies to employ light-responsive building blocks to interact with and control biomacromolecules focusing on the 3D-structure of peptides and their supramolecular interaction. In this context, we will highlight how optimizing the substituents on different photoactuators allows us to tune several of their properties, such as their UV-Vis absorption profile and photoconversion quantum yield. We will demonstrate how these properties can be employed in various model systems. [5,6] Eventually, we envision that deriving such design principles for an increasing number of light-responsive tools will pave the way to individually addressing a single photoactuator in a complex biologically relevant ensemble and thus, to the precise regulation of the biological machinery.

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PROF. DR. MARKUS SAUER

University of Würzburg,
Würzburg, Germany

Wednesday, 11th October 2023 AT 14:30 HRS

Molecular Resolution Fluorescence Imaging

In the last decade, super-resolution microscopy has evolved as a very powerful method for sub-diffraction resolution fluorescence imaging of cells and structural investigations of cellular organelles. Super-resolution microscopy methods can now provide a spatial resolution that is well below the diffraction limit of light microscopy, enabling invaluable insights into the spatial organization of proteins in biological samples. However, current super-resolution measurements become error-prone below 25 nm. In addition, refined single-molecule localization microscopy methods achieved localization precisions of only a few nanometers, but here too, translation of such high localization precisions into sub-10 nm spatial resolution in biological samples remains challenging. In my contribution I will discuss two possibilities to bypass these limitations. One is based on physical expansion of the cellular structure by linking a protein of interest into a dense, cross-linked network of a swellable polyelectrolyte hydrogel. Since its first introduction by Boyden and co-workers in 2015, expansion microscopy (ExM) has shown impressive results including the magnified visualization of pre- or post-expansion labeled proteins and RNAs with fluorescent proteins, antibodies, and oligonucleotides, respectively, in cells, tissues, and human clinical specimen. By combining ExM with super-resolution microscopy it is potentially possible to enable multicolor molecular resolution fluorescence imaging. The other approach uses resonance energy transfer between fluorophores separated by less than 10 nm and reveals interfluorophore distance information from time-resolved fluorescence detection in combination with photoswitching fingerprint analysis. We will show how the method can be used advantageously to determine the number and distance even of spatially unresolvable fluorophores in the sub-10 nm range. In combination with genetic code expansion (GCE) with unnatural amino acids and bioorthogonal click-labeling with small fluorophores photoswitching fingerprint analysis thus brings us a step closer to molecular-resolution fluorescence imaging in fixed and living cells.

DR. WESTPHAL

DLR Project Management Agency

Bonn, Germany

Wednesday, 11th October 2023 AT 15:05 HRS

The Indo-German Science and Technology Centre (IGSTC): Mandate, Mission and Programme Portfolio

Hans Westphal is the Head of the German Office of IGSTC which is hosted by DLR Project Management Agency at Bonn. He joined the Asia Division of DLR Project Management Agency in 2012. Since then he was mainly involved in cooperation with India but also other countries and regions such as Southeast Asia, Japan, South Korea and Iran. His experience covers bilateral as well as multilateral cooperation (EU – partner country).

Hans holds a Master of Science in Public Policy and Human Development from the Maastricht Graduate School of Governance, Maastricht University/UNU-MERIT, The Netherlands and a Bachelor of Arts in Integrated European Studies from the University of Bremen, Germany. One of Hans' main research interests was the role biotechnology can play for poverty alleviation with a special focus on the impact on absolute and relative poverty.

PROF. DR. HOLGER BRAUNSCHWEIG

University of Würzburg
Würzburg, Germany

Thursday, 12th October 2023 AT 9:00 HRS

Activation of Small Molecules: Can Boron act as a Transition Metal?

The activation of small molecules is generally associated with transition metals (TM) and constitutes the basis of catalysis. It was believed that TM catalysts are required to facilitate processes such as the activation of H_2 and other unreactive substrates. However, recent exciting developments in main group element chemistry showed, that carbenes, FLPs and heavy main group species are capable of TM-like activation reactions.[1] Our ongoing studies on borylenes, diborenes, and diborynes have shown that these low-valent species exhibit a very rich chemistry, which is distinctly different from that of common compounds deriving from boron in oxidation state +3. Particularly interesting is the metal-like behavior of some borylenes and diborynes, which form CO complexes analogous to TMs, bind H_2 and unsaturated organic substrates under mild conditions and even activate N_2.[2].

References:

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PROF. DR. R. BOOMI SHANKAR

Indian Institute of Science Education and Research Pune
Pune, India

Thursday, 12th October 2023 AT 9:35 HRS

Molecular Ferroelectric Materials and their Piezoelectric Nanogenerators Supported by Amino-P(V) Cations

Ceramic oxides possessing noncentrosymmetric crystal symmetries are extensively probed for their ferro- and piezoelectric properties and for their potential utility in high-tech applications. In the domain of energy research, these materials are explored as piezoelectric nanogenerators (PENGs) in which electrical energy is harvested via external mechanical forces. Molecular ferroelectrics based on organic and Organic-inorganic hybrids are attractive alternatives for ceramics for their easy synthesis and flexibility.[1] Our group is involved in the development of molecular ferroelectrics supported by ammonium, phosphonium and the combined amino-P(V) cations and employs them as PENGs. These cations afford two-component ferroelectrics in the presence of multi-atomic or metal-containing anions, elucidated by their response to SHG, dielectric, P-E loop hysteresis, PFM and strain measurements. Subsequently, polymer composites of these materials and their 3D-printed porous scaffolds were prepared with commercial polymers, which showed sizable PENG output characteristics and promised their utility in next-generation wearable electronics. This presentation will highlight some of our key findings in this direction.[2-6]

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MARCEL BAMBERG

Goethe-Universität Frankfurt
Frankfurt, Germany

Thursday, 12th October 2023 AT 10:10 HRS

Chloride-Encapsulating [20]Silafulleranes: Making Use of the Endohedral Guest by ^{35}Cl NMR Spectroscopy

Silafulleranes have been considered an attractive subject of numerous purely quantum-chemical studies over decades.[1] Only in recent years has the Wagner group found a synthetic approach to [20]silafulleranes, which allows reactivity studies in this novel area of inorganic chemistry. The one-step synthesis of the T_h-symmetric anion $[Cl@Si_{20}(SiCl_3)_{12}Cl_8]^-$ ([**1**]$^-$; isolated as [nBu$_4$N][**1**]) provides the starting point for different routes of regioselective derivatization.[2] Our synthesis protocols allow (i) the desilylation of [**1**]$^-$ leading to the parent, chloride-encapsulating siladodecahedrane $[Cl@Si_{20}H_{20}]^-$,[3] (ii) exhaustive substituent exchange on the Si_{32} framework to afford $[Cl@Si_{20}(SiH_3)_{12}H_8]^-$ ([**2**]$^-$),[4] (iii) regioselective partial Cl/H exchange on [**1**]$^-$ and H/Br exhange on [**2**]$^-$, respectively,[4,5] and (iv) the simultaneous introduction of different substituents on the silyl groups and the cluster core of [**1**]$^-$. The fourth pathway, leading to $[Cl@Si_{20}(SiH_3)_{12}Me_8]^-$, indicates a distinctly different reactivity of Si^{I} and Si^{III} centers in [**1**]$^-$.[4]

Our new silafulleranes bring together the fields of Si clusters and endohedral complexes: Due to their highly symmetric environments, the endohedral Cl$^-$ ions inside the Si_{20} cages give rise to unusually narrow ^{35}Cl NMR signals. A combined experimental and computational study rendered the $d(^{35}Cl)$ value a useful probe for the Cl$^-$→Si_{20} interaction. Consequently, synthetic modifications of the Si_{20} host can be supported by the NMR-spectroscopic investigation of its spectating Cl$^-$ guest.[3–5]

Refereces:

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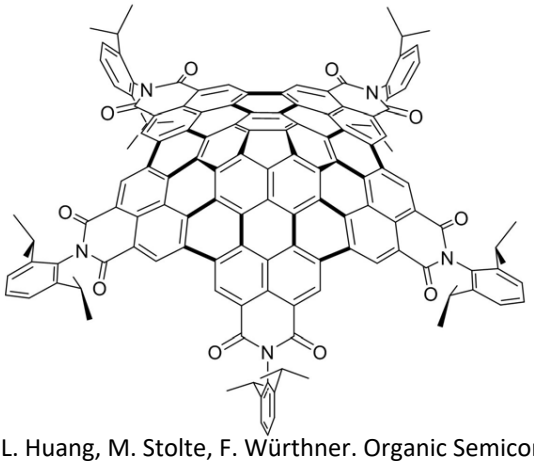
PROF. DR. FRANK WÜRTHNER

University of Würzburg
Würzburg, Germany

Thursday, 12th October 2023 AT 11:15 HRS

Nanographene Dicarboximides – New Horizons in Colorant Research

Despite of the fact that many functional properties of π-conjugated scaffolds only originate by the substitution of aromatic hydrocarbons with electron-donating and -withdrawing groups, research on larger π-scaffolds has so far been focused on the pristine subunits of graphene, carbon nanotubes or other polycyclic aromatic hydrocarbons. In contrast, driven by our ongoing interest in functional dyes and n-channel organic semiconductors,[1] we recently focused our attention on planar and bowl-shaped polycyclic aromatic hydrocarbons with low-lying LUMO levels that are realized by the functionalization with multiple dicarboximide units in the π-scaffold's periphery. Due to a lack of available synthetic methodologies towards such desirable molecules we first developed a new cross-coupling-annulation cascade reaction for the synthesis of large-sized planar and contorted electron-poor π-scaffolds.[2] In this talk I will discuss this new synthetic methodology and give insight into the supramolecular[3] and functional[4] properties for a new class of nanosized two-dimensional functional π- conjugated molecules.



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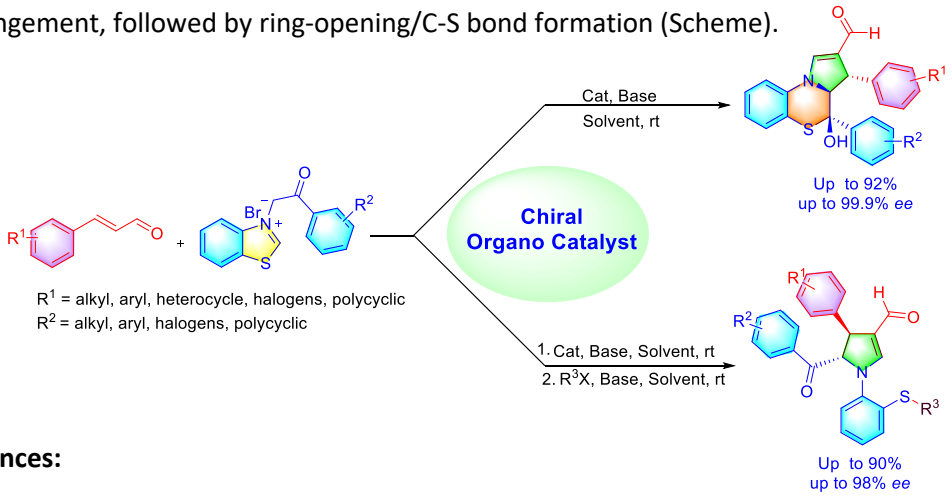
PROF. DR. GOVINDASAMY SEKAR

Indian Institute of Technology Madras
Chennai, INDIA

Thursday, 12th October 2023 AT 11:50 HRS

Asymmetric Synthesis of Chiral Pyrrolothiazine and Tetrasubstituted Dihydropyrrole using Domino Cycloaddition/Rearrangement

1,4-Thiazine, benzo[1,4]thiazine, pyrrolo[1.4]thiazine and their polyhydro derivatives are privileged heterocyclic core present in many bioactive molecules.[1-2] Over the past decades, several methods have been developed to construct achiral/racemic pyrrolo[1,4]thiazine derivatives.[3] Recently, Feng *et al*. reported the first synthesis of chiral hydropyrrolo-thiazoles and [1,4]thiazine derivatives using chiral *N,N´*-dioxide/metal catalysts.[4] Herein, we report a proline-derived organocatalytic enantioselective synthesis of pyrrolo[1,2-*d*][1,4]thiazine-2-carbaldehydes using domino 1,3-dipolar cycloaddition/rearrangement of benzothiazolium salt with α,β-unsaturated aldehyde. This domino process produced fluorescent emissive chiral molecules with three contiguous stereocenters, having one chiral quaternary center in a single step. This strategy was extended to the stereoselective one-pot synthesis of chiral *N*-phenyl thioether-tethered tetrasubstituted dihydropyrrole-3-carbaldehydes via 1,3-dipolar cycloaddition/ rearrangement, followed by ring-opening/C-S bond formation (Scheme).



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PROF. VISHAL RAI

Indian Institute of Science Education and Research Bhopal
Bhopal, India

Thursday, 12th October 2023 AT 12:25 HRS

Disintegrate theory for precision engineering of proteins and antibodies

The chemical toolbox for investigating biological systems or enabling biologics requires the precise covalent attachment of tags to the proteins. In this perspective, we have been leading the efforts toward chemical technologies to enable precise control over the site of bioconjugation. The critical barrier involves the simultaneous deconvolution of multiple challenges associated with reactivity and selectivity. In this perspective, the DisINtegrate or DIN theory creates new reactivity landscapes on a protein's surface.[1] As a result, it enabled the development of methods for targeting reactivity hotspots,[2] N-Gly residue-specific labelling (Gly-Tag®),[3] and modular Linchpin-Directed Modification (LDM®).[4] This comprehensive technological platform offers homogeneous antibody-drug conjugates (ADCs) for directed cancer chemotherapeutics and fluorophore conjugates (AFCs) for imaging-guided tumour surgery.[4,5] Besides, our findings create an opportunity to realize precision therapeutics with small molecules.

The presentation would highlight the principles that enabled chemical technologies to deliver precisely engineered protein and antibody conjugates.

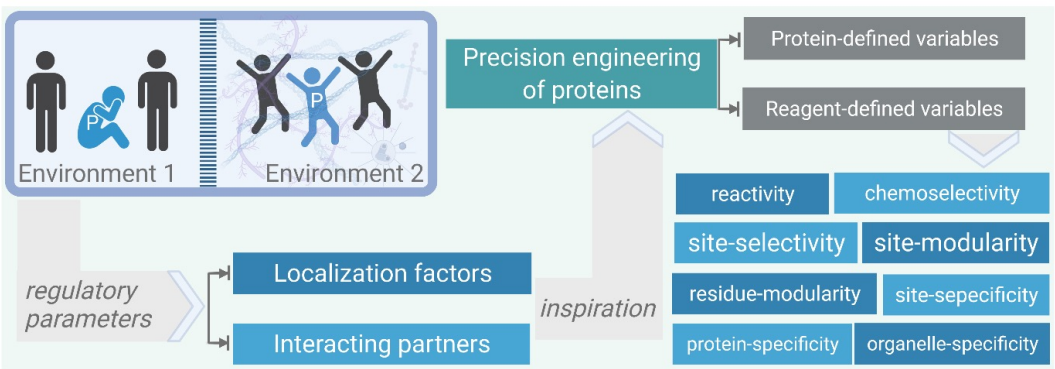

Figure. Human behavior-inspired Disintegrate (DIN) theory enables the precision engineering of proteins and antibodies.

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4. LDM® platform, AFC/ADC: (a) *Nat. Commun.* **2022**, *13*, 6038. (b) *Chem. Sci.* **2021**, *12*, 6732. (c) *Angew. Chem. Int. Ed.* **2020**, *59*, 10332. (d) *J. Am. Chem. Soc.* **2018**, *140*, 15114.
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PROF. DR. CLAUDIA HÖBARTHNER

University of Würzburg
Würzburg, Germany

Thursday, 12th October 2023 AT 14:30 HRS

Molecular architectures of functional nucleic acids

Functional nucleic acids are synthetic DNA or RNA molecules that fold into intricate three-dimensional structures and enable sophisticated functions beyond the natural roles of storing and transmitting genetic information. Ribozymes and aptamers generated by in vitro selection provide enabling tools for studying RNA labelling in vitro and in cells.

Modified nucleotides expand the chemical diversity of the four standard letters of the genetic alphabet. In nature, methylated nucleotides belong to the most abundant DNA and RNA modifications and have implications in the regulation of gene expression. Besides modulating the RNA modification landscape, synthetic RNA modifications for post-transcriptional RNA labelling and visualization are critical prerequisites for studying RNA localization, folding and structural dynamics.

This presentation will introduce recently developed ribozymes for site-specific RNA alkylation and discuss the underlying molecular architecture and catalytic mechanism. In addition, examples of synthetic DNA modifications for programmable photoactivated crosslinking will be discussed.

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1) C.P.M. Scheitl, M. Ghaem Maghami, A.-K. Lenz, C. Höbartner. Site-specific RNA methylation by a methyltransferase ribozyme. *Nature* **2020**, *587*, 663–667. doi: 10.1038/s41586-020-2854-z

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PROF. DR. S. G. SRIVATSAN

Indian Institute of Science Education and Research (IISER)
Pune, India

Thursday, 12th October 2023 AT 15:05 HRS

Probing pathogenic nucleic acid motifs using functionalized nucleoside toolbox

Numerous biophysical tools have provided efficient systems to study nucleic acids. However, our current understanding on how nucleic acid structure complements its function, particularly in cellular environment, is limited. This general limitation is largely due to the lack of probes that can be used in both cell-free and cellular assays, and in more than one biophysical technique. In this context, moving away from the tradition approach of "one label one technique" we adopted an innovative approach to investigate the nucleic acid structure and function in cell-free and cellular environments by using conformation-sensitive multifunctional nucleoside analog probes. Based on this strategy, we develop nucleoside analogs equipped with two or more labels (eg., fluorophore, ^{19}F NMR isotope label and X-ray crystallography phasing atom), which serve as common probes for analyzing nucleic acid motifs simultaneously by using a combination of fluorescence, NMR and X-ray crystallography techniques.[1-5] In parallel, we also develop chemo-enzymatic labeling technologies to functionalize and image nucleic acids in vitro and live cells.[6,7] In this presentation, I will discuss the utility of our nucleoside probes in dissecting the population equilibrium of G-quadruplexes formed by HIV-1 long terminal repeat (LTR), which are implicated in viral propagation and latency. Structural analysis and ligand binding properties in *in vitro* and in cell models by using fluorescence and ^{19}F NMR techniques will be presented.

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PROF. DR. SONU GANDHI

DBT-National Institute of Animal Biotechnology (NIAB)
Hyderabad, India

Thursday, 12th October 2023 AT 16:00 HRS

Nanomaterials: major advancements in disease diagnostics

The field of nanotechnology relies on the ability to design, manipulate, and manufacture materials at the nanoscale. Nanomaterials are materials possessing, at least, one external dimension from 1-100 nm. They may either be found in nature or artificially synthesised in a lab and have very different physical and chemical properties as compared to their bulk counterparts. By making use of these properties, these nanomaterials, both metallic and non-metallic, can be used in the field of diagnostics and therapeutics. One of the most commonly used nanomaterials are carbon allotropes such as graphene and its nanocomposites, carbon nanotubes, and fullerenes due to their conductive properties. Another easy to synthesise nanomaterial often used for diagnostic purposes are gold-based nanomaterial such as nanoparticles, rods, and wires due to their surface plasmonic resonance property and ease of bioconjugation. They are especially useful in development of colorimetric based assays for detection of environmental contaminants, pesticides, and disease biomarkers. Another important class of nanomaterials are fluorescence property-based quantum dots made of carbon, cadmium telluride, and cadmium selenide. In this lecture, I will be discussing about various nanomaterials that led to major advancement in the field of disease diagnostics.

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2. D. Shahdeo, A. Roberts, G. J. Archana, S. Mahari, N. S. Shrikrishna, K. Nagamani, **S. Gandhi$**, Label free detection of SARS CoV-2 Receptor Binding Domain (RBD) Protein by Fabrication of Gold Nanorods deposited on Electrochemical Immunosensor (GDEI). Biosensors & Bioelectronics, 2022, 212, 114406. https://doi.org/10.1016/j.bios.2022.114406
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PROF. DR. C. EGGELING

Friedrich-Schiller-University & Leibniz Institute of Photonic Technology e.V.
Jena, Germany

Thursday, 12th October 2023 AT 16:35 HRS

Studying molecular membrane dynamics with advanced optical microscopy

Molecular interactions are key in cellular signalling. They are usually ruled by the organization and mobility of the involved molecules. For example, the direct and non-invasive observation of the interactions in the living cell membrane is often impeded by principle limitations of conventional far-field optical microscopes, for example with respect to limited spatio-temporal resolution and information content. Here, we present an advanced optical microscopy study involving tools such super-resolution STED microscopy in combination with spectral imaging and fluorescence correlation spectroscopy or single-molecule tracking on a MINFLUX and interferometric Scattering (iSCAT) microscope. We highlight how these approaches can reveal novel aspects of membrane bioactivity such as of the existence and function of potential lipid rafts and during pathogen invasion.

PROF. DR. AAMIR NAZIR

CSIR – Central Drug Research Institute
Lucknow, India

Thursday, 12th October 2023 AT 17:10 HRS

Understanding Neurological Resilience Employing C. elegans model: The Role of Glia-enriched PTR-10 in Neuronal Health

The progressive understanding of neurobiological systems opens new avenues in the study of neurodegenerative diseases. Within this realm, our study employs the C. elegans model to probe the role of PTR-10, a gene significantly enriched in glial cells, and its implications on neuronal protection and repair. This exploration provides a nuanced view of neurogenesis and neuronal repair, aligning with the quest for methodologies enabling the understanding of complex systems in the neurobiological domain. By utilizing novel methodology for creating a model for early neuronal damage, RNAi-induced silencing, expression assaying, and knockout studies, we analyzed ptr-10's contribution to the inherent neuronal repair mechanisms, delving deeper into its broader impact on conditions such as Parkinson's disease. Our findings reveal PTR-10's elevated expression during developmental stages, which declines with aging, affecting a suite of genes integral to axonal regeneration and uncovering novel modulators associated with protein quality control.

The insights obtained emphasize the pivotal role and enrichment of PTR-10 in glial cells, shedding light on potential avenues to harness its protective and reparative functionalities. This offers a foundation for developing innovative therapeutic strategies for neurodegenerative ailments and contributes substantially to the rational design and understanding of resilient and efficient neurobiological systems, ultimately enhancing our comprehension of neurological resilience and health.

PROF. DR. THOMAS BASCHÉ

Johannes Gutenberg University Mainz
Mainz, Germany

Friday, 12th October 2023 AT 09:00 HRS

The energy gap law at work: Emission yield and rate fluctuations of single NIR emitters

Internal conversion (IC) often is the dominating relaxation pathway in organic NIR emitters, limiting their fluorescence quantum yield. In this context, we have investigated Dibenzoterrylene (DBT) by bulk and single molecule spectroscopy. In stark contrast to Terrylene, DBT – an unsubstituted aromatic hydrocarbon - shows an unexpectedly strong fluorescence solvatochromism. With increasing solvent polarity, the S_1-S_0 energy gap decreases leading to a decrease of the fluorescence quantum yield and an increase of the IC rate in full accordance with the energy gap law.[1] Making use of the fluorescence solvatochromism of DBT, the validity of the energy gap law was also demonstrated at the single molecule level. By controlling the fluorescence lifetime and quantum yield of single DBT molecules, the S_1-S_0 energy gap dictates how these quantities develop during spectral fluctuations (Figure).

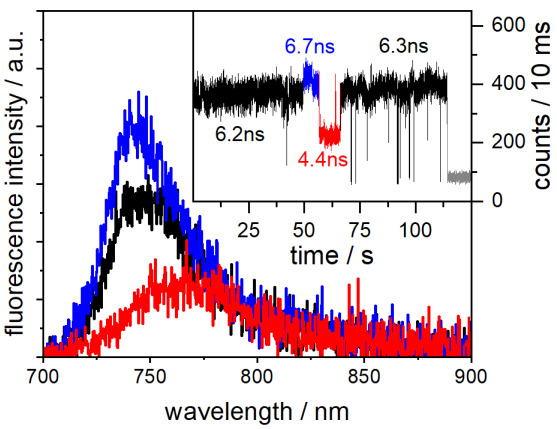

Figure: Fluorescence spectra and intensity time trace (inset) of a single DBT molecule as a function of time. Fluorescence lifetimes during the different phases are given in the inset.

Our results open new avenues into unexplored single molecule photophysics. Along these lines, we will discuss first attempts to improve the fluorescence quantum yield of DBT to obtain a truly bright single quantum emitter in the NIR.

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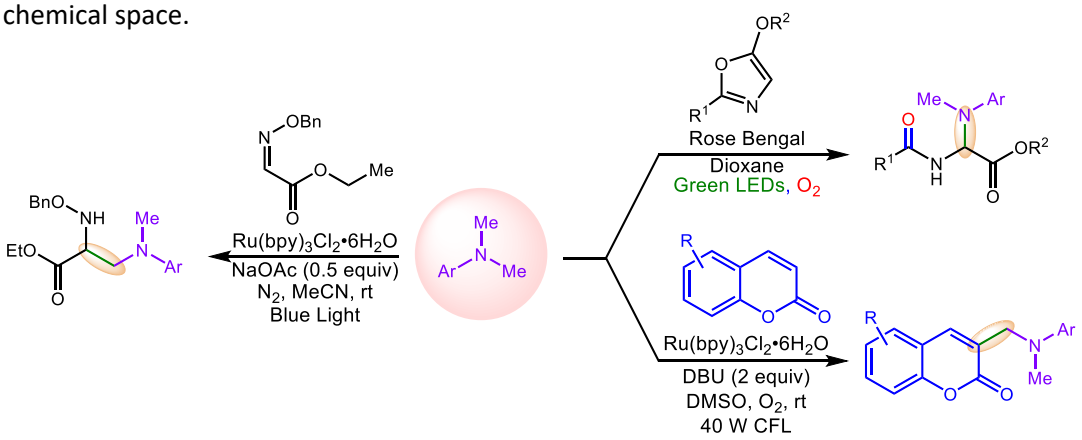
PROF. DR. ANAND SINGH

Indian Institute of Technology Kanpur
Kanpur, India

Friday, 12th October 2023 AT 09:35 HRS

Photochemical Functionalization of π-Systems: New Synthetic Strategies

This talk illustrates our ongoing research efforts in the area of photoredox catalysis as it relates to the development of novel synthetic pathways utilizing amine activation. The versatile nature of the intermediates resulting from the SET oxidation of amines enables a variety of transformations including amination, aminomethylation, and halogen atom transfer mediated haloalkylations. The diversification and control of the amine radical cation, α-aminoalkyl radicals and iminium ion intermediates are outlined which enabled the design of new chemical reactions and access to novel halogenated and deuterated chemical space.



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PROF. DR. CAROLINE KISKER

University of Würzburg
Würzburg, Germany

Friday, 12th October 2023 AT 10:10 HRS

The other side of XPD: the crucial role of the Arch domain for helicase action

The super family 2 (SF2) helicase XPD is a central component of the general transcription factor II H (TFIIH) which is essential for transcription and nucleotide excision DNA repair (NER). Within these two processes, XPDs helicase function is vital for NER but not in transcription initiation, where XPD only acts as a scaffold. We deciphered one of the most enigmatic steps in XPD helicase action: the separation of dsDNA. We solved a cryo EM structure of XPD at 3.2 Å in the presence of a forked DNA substrate containing an interstrand crosslink revealing how XPD approaches the dsDNA junction during 5'-3' translocation. Our structure clearly shows how dsDNA is separated and the intricate involvement of the Arch domain in dsDNA separation. Combined with mutagenesis and biochemistry data we define functional areas that modulate the helicase activity. Surprisingly, those areas also affect TFIIH translocase, revealing a yet unencountered function of XPD within the TFIIH scaffold.

PROF. DR. SIVAPRIYA KIRUBAKARAN

Johannes Gutenberg University Mainz
Mainz, Germany

Wednesday, 11th October 2023 AT 11:15 HRS

Inhibitors and tool compounds for methyltransferases and TME proteases

What do transfer-RNA methyltransferases (tRNA MTases) and proteases of the tumor microenvironment (TME) have in common and why may similar approaches be followed to develop inhibitors and biochemical tool compounds? Many enzymes in both types possess a catalytically active cysteine residue, which can be addressed by inhibitors with electrophilic groups, so-called warheads. In this talk, two relevant enzymes, DNMT2, a $tRNA^{Asp}$ MTase and cathepsin S, a TME cysteine protease, and their roles in various (patho)physiological processes as well as the development and optimization of reversible- and irreversible-covalent inhibitors for both enzyme classes will be covered.

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2. Covalent *S*-adenosylhomocysteine-based DNA-methyltransferase 2 inhibitors with a new type of aryl warhead. M. Schwickert, R. A. Zimmermann, T. Habeck, S. N. Hoba, Z. Nidoieva, T. R. Fischer, M. M. Stark, F. Lermyte, C. Kersten, M. Helm*, T. Schirmeister*, *ACS Med. Chem. Lett.* **2023**, 14, 777-787; https://doi.org/10.1021/acsmedchemlett.3c00062.

3. An optimized microscale thermophoresis method for high-throughput screening of DNMT2 ligands. R. A. Zimmermann, J. L. Meidner, M. Schwickert, Z. Nidoieva, M. Helm, T. Schirmeister, *J. Pharmacol. Transl. Sci.* **2022**, 5, 1079-1085; https://doi.org/10.1021/acsptsci.2c00175.

4. Discovery of potent inhibitors of DNA methyltransferase 2, an epigenetic modulator and potential target for cancer treatment. M. Schwickert, T. R. Fischer, R. A. Zimmermann, S. N. Hoba, J. L. Meidner, M. Weber, M. M. Stark, C. Kersten, M. Helm*, T. Schirmeister*, *J. Med. Chem.* **2022**, 65, 9750–9788, https://doi.org/10.1021/acs.jmedchem.2c00388.

5. New cysteine protease inhibitors: Electrophilic (het)arenes and unexpected prodrug identification for the *Trypanosoma* protease rhodesain. P. Klein, P. Johe, A. Wagner, S. Jung, J. Kühlborn, F. Barthels, S. Tenzer, U. Distler, W. Waigel, B. Engels, U. A. Hellmich, T. Opatz,* T. Schirmeister*, *Molecules* **2020**, 25(6), E1451. https://doi.org/10.3390/molecules25061451.

PROF. DR. TAPASYA SRIVASTAVA

University of Delhi,
New Delhi, India

Wednesday, 11th October 2023 AT 11:50 HRS

Epigenetic modulations in the hypoxic tumour microenvironment

In recent years, epigenetic changes have expanded to integrate DNA, proteins and RNA modifications. Increasing evidence suggests that perturbations in these epigenetic marks are associated with cancer onset and progression, and present as a viable target for therapeutic interventions. Epi-drugs such as DNA methylation inhibitors, histone deacetylase inhibitors and BET inhibitors, among others ,have generated considerable interest as they are positioned to target the readers, writers and erasers of the epigenome. Our lab studies epigenetic changes in the hypoxic tumour microenvironment (TME) in relation with biology of tumour onset and progression. This provides us an opportunity to identify new druggable targets and study efficacy of known drugs, in the chemo resistant tumour interiors.

In this lecture we will share our approach in studying Ten-eleven translocation (TET) enzyme mediated changes in the DNA, non-coding and protein-coding gene expression, specific for different isoforms of the TET enzyme. A large number of genes are regulated through these epigenetic mechanisms, often through multiprotein complexes. We find that TET proteins engage with different proteins in the hypoxic TME as compared to those in normoxia affirming the molecular heterogeneity associated with cancer. The outcome of modulation in the golgi accessory protein, CNIH1, in the hypoxic microenvironment in the prognosis of glioma and gastric cancer will be discussed in more detail.

References:

1. *Gandhi S[1], Bhushan A[1], Shukla U, Pundir A, Singh S*, **Srivastava T***. Downregulation of lncRNA SNHG1 in hypoxia and stem cells is associated with poor disease prognosis in gliomas. **Cell Cycle. 2023** May;22(9):1135-1153. doi: 10.1080/15384101.2023.2191411. PMID: 36945177.*
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