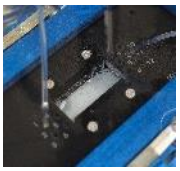
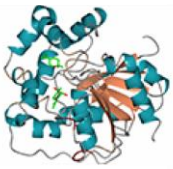
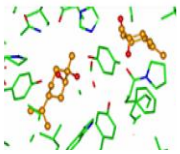
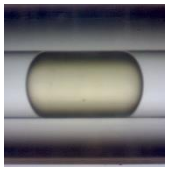

ESAB European Society of Applied Biocatalysis

ESAB Webinar

Enzymatic Reaction Mechanisms and their Biocatalytic Applications

November 18th 2022 **09.00-11.00 Greenwich Mean Time (GMT)**
10.00-12.00 Central European Time (CET)
16.00-18.00 China Standard Time (CST)
17.00-19.00 Japan Standard Time (JST)

Chairs: Jennifer Littlechild (University of Exeter)
Roland Wohlgemuth (Lodz University of Technology)

PROGRAMME

10.00 Em. Prof. G.M.Blackburn, M.A., Ph.D., C.Chem., FRSC, Krebs Institute, School of Biosciences, The University of Sheffield, Sheffield S10 2TN, United Kingdom

How Evolution Harnessed Phosphorus for its Dominant Roles in Biology

One of the most remarkable features of the chemistry of living organisms is the evolutionary development of phosphate esters: on the one hand they provide the extremely stable backbone for the biopolymers that encode the genetic information, RNA then DNA, on the other hand they deliver the temporal protein regulation that is largely under the control of kinases and phosphatases, and yet again they underpin the generation, distribution, and application of free energy throughout the cell by the manipulation of anhydrides of phosphoric acid and its esters, notably adenosine triphosphate. Over the last 6 decades, chemists have sought to understand how enzymes achieve remarkable acceleration of phosphoryl transfer, with remarkable insights from Todd [1] and Westheimer [2], on whose shoulders the present knowledge has been founded. They convert the spontaneous hydrolysis of ATP, k_{cat} from 10^{-6} s^{-1} in water, pH 8 at 37 ˚C [4] to ATP hydrolysis turnover numbers of ca. 1 μs [5], a rate acceleration of 10^{12}. I shall explore how our Planet acquired phosphorus [3], how it remarkably concentrated it in cellular Life on Earth, and how it has developed protein catalysts to overcome the remarkable stability of its mono- and di-esters and phosphate anhydrides to enable the development of life as we now understand it.

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10.30 Prof. Dr. Ming-Daw Tsai, Institute of Biological Chemistry, Academia Sinica, Taipei, Taiwan

Cryo-EM in enzymology and biocatalysis

While cryo-EM has been widely used to solve the structures of large protein complexes, this lecture will present two stories for its applications in enzymology and applied biocatalysis [1]. The first story involves ketol-acid reductoisomerase (KARI) from archaea Sulfolobus solfataricus. Structures of both the Mg^{2+}-form (KARI:2Mg^{2+}) and its ternary complex (KARI:2Mg^{2+}:NADH:inhibitor) were solved at six temperatures from 4-70 °C, leading to dissection of the induced-fit mechanism into ligand-induced and temperature-induced effects, and capturing of temperature-resolved intermediates of the temperature-induced conformational change [2]. In the second, unpublished story, we found that cyanobacterial phosphoketolase (XPK) in Synechococcus elongatus PCC7942 functions as a metabolic break to reduce the carbon fixation flux. Cryo-EM and kinetic analysis of XPK uncovered an allosteric regulatory mechanism involving two subunits jointly binding two ATP, which constantly suppresses the activity of XPK until an energy crisis occurs. A PDB search revealed uniqueness of the ATP binding mode. This sensitive ATP regulatory motif occurs in many species across all three domains of life. It may also serve as a useful tool for metabolic regulation in synthetic biology and metabolic engineering.

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11.00 Dr. Ben Schumann, Chemical Glycobiology Laboratory, The Francis Crick Institute, London, United Kingdom

Metabolic engineering to generate chemical precision tools for glycosylation

Carbohydrates (glycans) are the most abundant biomass on earth and decorate the surface of every single living cell. Cell surface glycans influence major physiological processes, and changes are strongly associated with the formation of cancer [1]. Unlike nucleic acids and proteins, the biosynthesis of glycans is not encoded in a template but instead mediated by the combinatorial interplay of >250 glycosyltransferase enzymes.

More than 20 years ago, chemists have started modifying single monosaccharides – the most basic unit of glycans – with chemical tags and subsequently track how these are incorporated into proteins by bio-orthogonal or “click” chemistry. This technique, awarded the 2022 Nobel Prize in Chemistry [2,3], carries great potential for the generation of so-called “Precision Tools” that act as reporters for specific glycosyl-transferase enzymes. However, the use of these tools can be limited because some bioorthogonal tags are not accepted by cellular biosynthetic enzymes to activate sugars [4–6]. This talk will highlight how enzyme engineering is key to the development of next-generation chemical Precision Tools to unravel glycosylation in health and disease.

References

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11.30 Prof. Dr. Florian Seebeck, Department of Chemistry, University of Basel, 4002 Basel, Switzerland

On C-S bond making and breaking enzymes

The discovery and description of entirely novel mechanisms by which enzymes catalyze difficult reactions represents fundamental progress in chemical research. New enzymatic reaction types are evolutionarily validated solutions to chemical problems that may be explored for synthetic application. In this presentation I will discuss our recent progress in understanding the structures and mechanisms of enzymes that catalyze carbon-sulfur bond making and breaking reactions. Specifically, I will highlight a recently discovered molybdenum-dependent enzyme that catalyzes reversible C-S bond formation in the context of ergothioneine biosynthesis [1]. Secondly, I will detail our latest efforts in recruiting methyltransferases for biocatalytic applications. S-adenosylmethionine (SAM)-dependent methyltransferases constitute a large family of enzymes that can catalyze regio-, chemo- and stereospecific methylation of complex molecules. Until recently, preparative applications of methyltransferases in vitro were limited because of the requirement for SAM as a stoichiometric methyl donor. Introduction of a simple SAM-regeneration process based on the ability of halide methyltransferases to transfer methyl-groups from methyl iodide or methyl sulfonates to S-adenosylhomocysteine (SAH) has paved the way to harness enzyme-catalyzed alkylation in biocatalysis [2a,2b].

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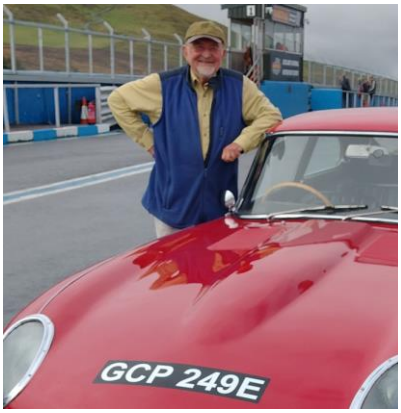
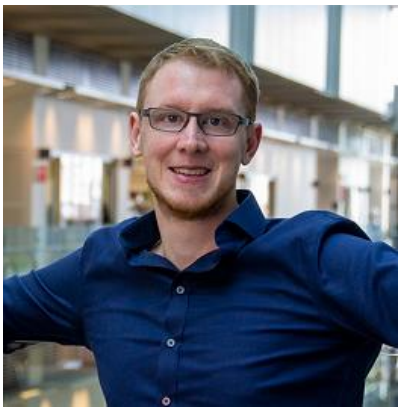
ABOUT THE SPEAKERS



George Michael Blackburn has been active in chemical biology research for over 50 years, beginning with chemical synthesis of a substrate analogue for ribosomal peptide synthesis (J. Mol. Biol., 1965, 13, 617). He studied enzyme mechanisms with W. P. Jencks (Brandeis University, 1966-7) and launched into the use of stable analogues of phosphate esters and anhydrides for studies on nucleotides and glycolysis intermediates from the late '70s. This has culminated in the current use of metal fluorides to generate transition state analogues for phosphoryl transfer reactions by kinases, mutases, and isomerases. He has authored some 300 research papers, several patents, one book ("Nucleic Acids in Chemistry and Biology, 4th Edition, RSC 2022), and is a co-author for more than 70 structures in the Protein Data Bank.

Ming-Daw Tsai is Professor and Distinguished Visiting Chair in Academia Sinica, Taiwan. He received B.S. degree from National Taiwan University (1972) and Ph.D. from Purdue University (1978), and served in the faculty of the Department of Chemistry and Biochemistry, The Ohio State University in 1981-2006. His research interests include mechanistic enzymology of phosphoryl transfer enzymes including DNA polymerases, kinases and phospholipases, and structure-function relationship of proteins in DNA damage response and cancer signaling, including ankyrin repeat proteins, FHA domain proteins, and recently photolyases. He probes mechanistic problems by applying emerging methodologies in structural biology, including NMR, X-ray crystallography, MS, and recently cryo-EM and X-ray free electron laser (XFEL), leading to 300 publications.
In 2018 he led the initiative to establish Academia Sinica Cryo-EM Center (ASCEM). He was elected to Fellow, American Association for the Advancement of Science (AAAS, 1992), Academician, Academia Sinica (2012), and Fellow, The World Academy of Science (TWAS, 2014).



Ben Schumann is a chemical biologist with a profound interest in the biology of carbohydrates (glycans). The advent of modern biology has brought about means to design and use new chemical tools.After completing his biochemistry undergraduate studies in Tübingen, Germany, he was trained in synthetic carbohydrate chemistry in the lab of Peter H. Seeberger at the Max Planck Institute of Colloids and Interfaces Potsdam and the FU Berlin. Developing vaccines against pathogenic bacteria based on synthetic glycans, Ben learnt to apply his compounds in biological settings in vivo and in vitro. For his achievements, he received the Award for Excellence in Glycosciences and, in 2017, the prestigious Otto Hahn Medal by the Max Planck Society. During his postdoctoral work in the lab of Carolyn R. Bertozzi at Stanford University as an Alexander von Humboldt foundation Feodor Lynen fellow, Ben developed an interest for "precision tools" to study glycosylation of human cells in great detail. He started as a Group Leader at the Francis Crick Institute and Imperial College London in 2018 to develop such tools, using a combination of organic and chemo-enzymatic synthesis, molecular and cell biology. His work routinely incorporates cutting-edge methods of metabolic and protein engineering as well as chemical glycoproteomics. The team has received the 2021 RSC Horizon Prize in Chemical Biology. Ben is an EMBO Young Investigator and has received an Imperial College Outstanding Early Career Researcher Award.

ABOUT THE SPEAKERS

Florian Seebeck received a Diploma in Chemistry from the University of Bern, and a PhD from the ETH Zürich for a thesis on enzyme engineering. After postdoctoral research at the Harvard Medical School he joined the Max Plank Institute in Dortmund as a group leader in the Department for Physical Bio-chemistry. There he initiated an independent research program on the bio-synthesis of sulfur-containing natural products. He is now Associate Professor for Molecular Bionics in the Department for Chemistry at the University of Base His group focusses on the discovery and characterization of enzymes that catalyze carbon-sulfur bond breaking and making with the goal to develop novel concepts in biocatalysis.

NEXT ESAB WEBINARS

ESAB aims to promote the development of Applied Biocatalysis and takes initiatives in areas of growing scientific & industrial interest in the field.

Schedule and Topics of the next ESAB webinars:

16th December 2022 14.00-16.00 CET	Biocatalytic Total Synthesis organized by Roland Wohlgemuth and Jennifer Littlechild
27th January 2023 10.00-12.00 CET	Advances in the Analysis of Enzymatic Reactions organized by Roland Wohlgemuth and Jennifer Littlechild
24th February 2023 14.00-16.00 CET	Biocatalysis and Molecular Medicine organized by Jennifer Littlechild, Antonio Ballesteros, Thomas Sauter & Roland Wohlgemuth
24th March 2023 10.00 -12.00 CET	Synthetic Biology and Metabolic Engineering Tools and Methodologies organized by Frangiskos Kolisis and Roland Wohlgemuth

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Personal membership is free.
Institutional membership is very much welcome and has been established as new membership category. Academic, governmental, research and other public Institutions as well as private companies based inside or outside Europe and whose activities are related to the field of applied biocatalysis, are welcome to apply for Institutional Membership.

ESAB has been founded in 1980 and has the mission of promoting the development of Applied Biocatalysis throughout Europe. The aims of ESAB are to promote initiatives in areas of growing scientific and industrial interest of importance within the field of Applied Biocatalysis.

Further information on ESAB Conferences and other activities can be found on the ESAB website www.esabweb.org
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