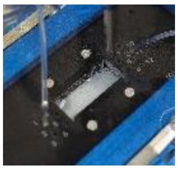

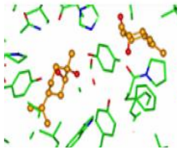
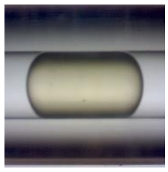

ESAB Webinar

BIOCATALYSTS FROM EXTREMOPHILES

Friday, 28th May 2021 at 14:00 – 16:00 CET
Welcome Address: Willi Meier, DECHEMA
Chairs: Jennifer Littlechild, University of Exeter, Vice-chair ESAB
Roland Wohlgemuth, Lodz University of Technology, Chair ESAB

PROGRAMME

14.00 Prof Michael Adams, Dept. of Biochemistry, University of Georgia, Athens, GA 30602, USA

Insights into the Evolution of the Mitochondrial Respiratory Chain from Sulfur-Reducing Hyperthermophilic Archaea

Hyperthermophilic archaea grow in volcanic vents at temperatures near, and even above, 100^{0}C. They are thought to represent an ancient life form. Many are strict anaerobes and obtain energy for growth by a respiratory process that lead to the production of H_2 gas or, if elemental sulfur is present in their growth media, H_2S. The production of H_2 is catalyzed by a membrane-bound NiFe-hydrogenase termed MBH that reduces protons to H_2 and generates a sodium ion gradient that is used for ATP synthesis. MBH contains fourteen different subunits, many of which are highly similar to those in proton-pumping Complex I of the aerobic respiratory chain. Elemental sulfur is reduced by a homologous 13-subunit membrane-bound complex termed sulfane sulfur reductase or MBS. MBS produces H_2S from polysulfide and also generates a sodium ion gradient. The structures of MBH and MBS, the first for relatives of Complex I, have now been determined by cryo-EM and are providing new perspectives on the mechanisms by which present day aerobic life forms convert electrochemical energy into chemical bond energy. Moreover, MBS is proposed to utilize a site-differentiated iron-sulfur cluster to catalyze polysulfide reduction and to represent the "missing link" in the evolution of the ubiquitous Complex I. Biochemical and genetic studies are revealing how a NiFe-containing catalytic site may have evolved from reducing protons to H_2 in MBH, to reducing polysulfide to H_2S in MBS, and ultimately to reducing quinone in Complex I.

Yu, H., Haja, D. K., Schut, G. J., Wu, C.-H., Meng, X., Zhao, G., Li, H., Adams, M. W. W., *Nature Commun.* 2020, **11**,5953.

14.30 Dr Daniela Monti Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC), Consiglio Nazionale delle Ricerche, Milano, Italy

Mining extremophiles (meta)genomes for novel and thermostable biocatalysts

Microorganisms living in extreme environments represent an important source for novel biocatalysts suitable for industrial processes. During the last few years, the evolution of high-throughput DNA sequencing has enabled the development and improvement of sequence-based metagenomic approaches that overcome the frequently observed limitations in the cultivation of extremophiles under laboratory conditions. We have exploited this approach in analyzing different high-temperature ecosystems like hot springs and we found novel enzymes with useful synthetic applications, such as epoxide hydrolases [1-3] and amine transferases [4]. More recently, the complementary use of activity-guided methods as an alternative discovery approach, such as enrichment cultures, led us to identification of a novel thermostable β-amino acid transaminase from a *Meiothermus* strain isolated in an Icelandic hot spring showing a broad substrate scope [5]. Additionally, we have recently discovered a library of novel hydroxysteroid dehydrogenases, enzymes so far described only from gut and soil bacteria, by mining extremophilic (meta)genomes. The results obtained in the study of the substrate promiscuity and synthetic application of these novel biocatalysts with non-steroidal substrates will be presented [6,7].

[1] E. E. Ferrandi *et al.*, *FEBS Journal*, 2015, 282, 2879-2894, DOI: 10.1111/febs.13328; [2] E. E. Ferrandi, *et al.*, *ChemCatChem*, 2015, 7, 3171-3178, DOI: 10.1002/cctc.201500608; [3] E. E. Ferrandi, *et al.*, *Front. Bioeng. Biotechnol.*, 2018, 6, 144, DOI: 10.3389/fbioe.2018.00144; [4] E. E. Ferrandi, *et al.*, *Appl. Microbiol. Biotechnol.*, 2017, 101, 4963-4979, DOI: 10.1007/s00253-017-8228-2; [5] E. E. Ferrandi, *et al.*, *Biotechnol. J.*, 2020, 15, 2000125, DOI: 10.1002/biot.202000125; [6] S. Bertuletti, *et al.*, *Adv. Synth. Catal.*, 2020, 362, 2474-2485, DOI: 10.1002/adsc.202000120; [7] S. Bertuletti, *et al.*, *Eur. J. Org. Chem.*, (2021) in press, DOI: 10.1002/ejoc.202100174.

15.00 Prof Bettina Siebers, Dept. Molecular Enzyme Technology and Biochemsitry, University of Duisburg-Essen, Germany

HotSolute – Thermophilic bacterial and archaeal chassis for extremolyte production

Thermophilic organisms are composed of both bacterial and archaeal species. The enzymes isolated from these species and from other extreme habitats are more robust to temperature, organic solvents and proteolysis. They often have unique substrate specificities and originate from novel metabolic pathways. Thermophiles as well as their stable enzymes (‘thermozymes’) are receiving increased attention for biotechnological applications. In HotSolute we established thermophilic *in vitro* enzyme cascades as well as two new chassis, the thermophilic bacterium *Thermus thermophilus* (*Tth*, 65-75°C, pH 7.0) and the thermoacidophilic archaeon *Sulfolobus acidocaldarius* (*Saci*, 75-80°C, pH 2-4), as new thermophilic, bacterial and archaeal platforms for the production of novel high added-value products, i.e. ‘extremolytes’. Extremolytes are small molecular compatible solutes found naturally in the cells of thermophilic species that accumulate in the cell in response to multiple environmental stresses and stabilize cellular components (including proteins, membranes). Extremolytes offer an amazing so far unexploited potential for industrial applications including food, health, consumer care and cosmetics. However, their production in common mesophilic organisms (i.e. yeast, *E. coli*) seems to be hampered by the hyperthermophilic origin of the respective metabolic pathways requiring a thermophilic cell factory. Here we developed two newly designed ‘cell factories’ for the production of two extremolytes, cyclic 2,3 di-phosphoglycerate (cDPG) and mannosyl-glycerate (MG) in *Tth* and *Saci*, respectively. These extremolytes (with few exceptions for MG) are exclusively found in hyperthermophiles, and have not been produced in a mesophilic host to date. Current insights into metabolism, involved enzymes as well as the effect of extremolyte production on the hosts will be presented.

Reference The ERA-CoBiotech HotSolute Project - Bettina Siebers, University of Duisburg-Essen, Essen, Germany; Jennifer Littlechild, University of Exeter, Exeter, United Kingdom; Daniela Monti, Istituto di Chimica del Riconoscimento Molecolare, Milano, Italy; Felix Müller, Evonik Industries AG, Essen, Germany; Elizaveta Bonch-Osmolovskaya, Academy of Sciences, Winogradsky Institute of Microbiology, Moscow, Russia; Jacky Snoep, Stellenbosch University, Stellenbosch, South Africa

15.30 Prof Garabed Antranikian, Hamburg University of Technology (TUHH), Germany

From Origin of life to Circular Bioeconomy

Bioeconomy is the production, utilization and conservation of biological resources, including related knowledge, science, technology, and innovation, to provide products, processes, and services across all economic sectors aiming towards a sustainable biobased technology. With its diverse possibilities, the bioeconomy can make an important contribution to solving global problems. Like digitization, the biologization of the economy will trigger a profound change in all areas of society and industry. This includes the health and nutrition of a growing world population, their sustainable supply of food, energy, water and raw materials as well as climate and environmental protection. The change to such a “greener economy, is not possible without innovations in life sciences including microbiology, enzymology, molecular biology, bioinformatics (metagenomics, transcriptomics) and process engineering. An interdisciplinary approach involving academia and industry from various branches will provide a smooth transition from crude oil-based industry to Sustainable Circular Bioeconomy taking into consideration the environmental issues.

ABOUT THE SPEAKERS

Michael W. W. Adams is the Georgia Power Professor of Biotechnology and a Distinguished Research Professor in Biochemistry, Molecular Biology and Microbiology at the University of Georgia, USA. He obtained both his B.S. and Ph.D. degrees in Biochemistry from the University of London, UK. He carried out post-doctoral studies at Purdue University and was a Research Scientist at Exxon Research and Engineering Company in New Jersey before becoming a faculty member at the University of Georgia in 1987. Dr. Adams has pioneered biochemical, genetic and microbiological research with so-called hyperthermophilic microorganisms that grow at 90°C and above. His studies have led to the discovery and characterization of many new oxidoreductase-type enzymes and redox proteins and of new metabolic pathways involved in sugar and peptide fermentation. He has also pioneered the development of genetic systems in hyperthermophiles and these have been used to engineered some of these organisms to produce a variety of fuels and chemicals from renewable resources. Dr. Adams has over 450 publications in the fields of metalloenzymes, anaerobic metabolism and hyperthermophilic microorganisms. He is a member of the American Academy of Microbiology.

Daniela Monti is Senior Researcher at the Institute of Chemical Sciences and Technologies “Giulio Natta” (SCITEC) of the Italian National Research Council (CNR). She received her MSc degree in Biological Science at the University of Milano in 1991 and Specialization degree in Biotechnological Applications from the same institution in 1995 studying in the field of synthetic applications of carbohydrate-active enzymes. From 1996 to 2000 she worked at CNR on the development of new biocatalytic processes for the preparation of semisynthetic antibiotics as research fellow in collaboration with pharmaceutical industries. She started her independent scientific career as CNR research scientist in 2001. She has published more than 90 scientific papers, patents and book chapters, mainly in the field of biocatalysis. Her research interests lie in the discovery of new enzymes and their application as biocatalysts in organic synthesis.

Bettina Siebers studied Biology at the University of Münster, Osnabrück and Bochum (Germany) and performed her diploma in plant physiology. In 1991 she started her PhD and at the University of Essen with Professor R. Hensel and continued her work as postdoctoral research assistant and independent junior group leader. In-between she spent one year (1998-1999) as postdoctoral guest scientist at the Virginia Polytechnic Institute and State University (VA, USA) with Professor P. J. Kennelly. She has been appointed Professor of Molecular Enzyme Technology and Biochemistry (Faculty of Chemistry) at the University of Duisburg-Essen (Germany) in 2008.
Bettina has long time experience in studying the central carbohydrate metabolism of (hyper)thermophilic Archaea and its regulation. The aim is to unravel the metabolic complexity and regulation by combination of “classical” biochemical/genetic approaches with modern high-throughput technologies and modeling (genomics, functional genomics as well as systems biology). In addition, her work focusses on the application of extremozymes, enzyme cascades as well as synthetic biology and metabolic engineering approaches for process optimization in (bio)economy using the thermoacidophilie *Sulfolobus acidocaldarius* as novel, archaeal platform organisms.

Garabed Antranikian studied Biology at the American University in Beirut. At the University of Goettingen he completed his PhD in Microbiology in 1980 in laboratory of Gerhard Gottschalk and since 1989 he was appointed to a professorship in Microbiology at the Hamburg University of Technology (TUHH). He coordinated EU, BMBF and DBU network projects on extremophiles and industrial biotechnology. In 2004 he was awarded the most prestigious prize for environment protection by the president of the Federal Republic of Germany. From 2011 to 2018 he was appointed as president of TUHH. Since February 2018 he is CEO of the “Center for Biobased Solutions” focusing on interdisciplinary projects on bioeconomy and Chair of the Board of Advisors of Foundation for Armenian Science and Technology (FAST).

NEXT ESAB WEBINARS

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

Schedule and Topics of next ESAB webinars:

June	2021,	Synthetic Biology and Metabolic Engineering Tools and Methodologies
July	2021,	Biocatalysis and Functional Genomics
August	2021,	Joint US-European Webinar on Biocatalysis and Bioeconomy Education
3 Sept. 14.00-16.00 CET	2021,	Standards for Reporting Biocatalysis Experiments, organized by Peter Halling

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