Derivatives are considered to be interesting target chemicals for the further development of industrial processes. From a fundamental point of view, study of archaea has contributed to unravelling the mystery of the origin of life and complex biological systems we find in nature. In addition, study of extremophilic archaea allows us to understand how life at the borders of environmental extremes has adapted to not only survive but thrive in such environments. However, despite decades of research, many biological aspects of extremophilic archaea are still not well characterized. One such example is fatty acid metabolism. Unlike bacteria or eukarya that incorporate fatty acid-based lipids in their membranes, archaea employ isoprenoid-based phospholipids. Nevertheless, although the biological role of fatty acids in these organisms is unknown, archaean genomes typically encode a large relative fraction of genes involved in fatty acid metabolism. The abundance of archaea thriving in extreme conditions is interesting from a biotechnological viewpoint as well, given the potential development of more (cost-)efficient industrial processes using these organisms and their enzymes. Fatty acids and their derivatives are considered to be interesting target chemicals for biomanufacturing as a more sustainable alternative for petrochemical production. The consideration of extremophilic archaea and their biological parts as valuable components of biological production processes enforces the necessity to better characterise native mechanisms and metabolisms involving interesting target chemicals like fatty acids.

Abstract of the PhD research

Ever since their discovery, archaea and the many extremophiles belonging to this distinct domain of life have piqued interest. From a fundamental point of view, study of archaea has contributed to unraveling the mystery of the origin of life and complex biological systems we find in nature. In addition, study of extremophilic archaea allows us to understand how life at the borders of environmental extremes has adapted to not only survive but thrive in such environments. However, despite decades of research, many biological aspects of extremophilic archaea are still not well characterized. One such example is fatty acid metabolism. Unlike bacteria or eukarya that incorporate fatty acid-based lipids in their membranes, archaea employ isoprenoid-based phospholipids. Nevertheless, although the biological role of fatty acids in these organisms is unknown, archaean genomes typically encode a large relative fraction of genes involved in fatty acid metabolism.

The defense can also be followed through a live stream. Contact david.sybers@vub.be for more information.

Members of the jury

Prof. Dr. ir. Ronnie Willaert (VUB, chair)
Prof. Dr. Antonella Fioravanti (VUB, secretary)
Prof. Dr. Ulrich Hennecke (VUB)
Prof. Dr. Thomas Crispeels (VUB)
Prof. Dr. Bettina Siebers (University of Duisburg-Essen)
Prof. Dr. ir. Iris Corbet (UAntwerpen)

Curriculum vitae

David Sybers obtained his master’s degree in Bioengineering sciences: Cell and Gene Biotechnology in 2015 at the Vrije Universiteit Brussel. After graduating, he started his PhD in January 2016 at the research group of Microbiology at the VUB, supervised by Eveline Peeters. In 2016-2017, he obtained a FWO SB grant.

With his research, he took the first steps towards industrial applications of *Sulfolobus acidocaldarius*, a thermoacidophilic archaean, developing synthetic biology tools and approaches. Next to two peer-reviewed publications, several (international) conference posters and presentations, this work also led to further important insights leading to new project proposals for the development of *S. acidocaldarius* as an industrial host.

*Sulfolobus acidocaldarius* is a thermoacidophilic archaean that thrives at temperatures between 70-80°C and a pH between 2 and 3. It is an important model organism for the study of (cren)archaea. Its thermophilic and acidophilic characteristics render it an interesting host for industrial (bio)processes. In this PhD project, I aimed to generate a better understanding of fatty acid metabolism and its regulation in *S. acidocaldarius*, thereby opening perspectives for potential industrial applications. A first focus for the characterization of fatty acid metabolism is a fatty acid and lipid metabolism gene cluster (*sacI_1103-1126*). We investigated potential pathways and functions for these genes by in silico analysis, revealing the presence of esterases, lipases and ß-oxidation enzymes. Furthermore, a TetR transcriptional regulator, FadRSa, located in this gene cluster was extensively characterized. It has two modes of binding dependent on the recognition sequence (dimer or dimer-of-dimer stoichiometry) and is able to regulate the entire gene cluster by only binding a limited number of distinct binding sites in non-canonical positions relative to the operator sequences. Using the knowledge obtained from its characterization, several hybrid bacterial promoters regulated by the archaenal FadRsa were constructed and characterized. This allows us to better understand the regulatory mechanisms employed by FadRsa and takes the first steps towards expanding the available acyl-CoA responsive promoters. Finally, predicted ß-oxidation enzymes from members of the Sulfolobales were purified and characterized, taking the first steps towards better understanding of fatty acid metabolism in these organisms and simultaneously identifying interesting enzymes that could be used in engineering strategies.