

Editorial overview

Microbial community engineering

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Robbert Kleerebezem is associate professor at the Department of Biotechnology of Delft University of Technology. His research group focuses on the understanding and exploration of (open) microbial communities for development of processes for wastewater treatment and the production of chemicals from a wide range of feedstock. His specific interests are related to process thermodynamics, computation modelling of bioprocesses, and high resolution functional characterisation of bioprocesses in the laboratory. Experimental systems that Robbert works with include nitrogen cycle conversions, the role of storage polymers in microbial ecology, and anaerobic bioconversions. Robbert is a curiosity driven researcher that always aims for identifying new insights in microbial communities and enjoys exploring uncovered grounds in microbial community engineering with enthusiastic students.

Diana Z Sousa



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Environmental biotechnology is the branch of biotechnology that addresses environmental problems using biotechnological processes. Historically, environmental biotechnology uses open (undefined) microbial communities to achieve objectives related to wastewater treatment, soil remediation, or gas treatment, but in recent years the field has expanded to initiatives related to the production of chemicals and the recovery of resources from low value feedstock (e.g. [1–3]). Furthermore, besides open microbial communities, also defined microbial co-cultures are currently explored for bioprocess development as discussed by Diender et al. [3].

Due to the use of microbial communities, environmental biotechnology has a clear microbial ecology component. Microbial ecology is defined as the scientific study of interactions between microbial communities and their environment, and extends beyond the field of environmental biotechnology to global biogeochemical cycles, and human microbiome related health studies for example. Process development in environmental biotechnology requires a thorough insight in microbial ecology to select adequate communities and the conditions to drive them in a desired direction.

This issue reflects the link between microbial ecology and environmental biotechnology. It addresses ecological aspects of specific bioprocess development related topics [1–6], discusses experimental tools for investigating microbial communities [7–9], and theoretical (modelling) concepts for understanding and exploring microbial communities [10–13]. Given the extended scope of the research field of environmental biotechnology, we propose that it is more appropriate to define topics covered in this issue as microbial community engineering: the use of ecological principles for enrichment, design and exploration of microbial communities for the development of biotechnological processes.

Experimental tools for understanding microbial communities

Recent breakthroughs in culture-independent, high-throughput molecular tools, (16S rRNA gene, metagenomic sequencing) have revealed an enormous microbial diversity in numerous ecosystems. Taş et al. [7] makes a tour over the past 20 years metagenomic sequencing and, reflect on how metagenomics studies have impacted our knowledge on microbial diversity in a vastity of natural environments. Genome centric metagenomics approaches, in combination with metatranscriptomics and metaproteomics, open up routes for a better understanding of microbial function of individual clades in microbiomes, and how environmental parameters affect them. The continuous development of metagenomics analysis workflows allows for improved exploitation of metagenomic data, for example the recovery (binning) of high quality metagenome assembled genomes (MAGs). MAGs can also be very useful to get information on uncultured microbes, e.g. taxonomy, biochemical potential, cellular structure, biological evolution. Yet, a critical aspect in genomic analyses is still the

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Diana Z Sousa is professor at Wageningen University & Research where she heads the Microbial Physiology group within the Laboratory of Microbiology. Her research interests are in the study of the metabolic pathways, microbes and microbial networks that anaerobically convert one-carbon molecules such as carbon monoxide, carbon dioxide, methane and methanol, and their application to produce chemicals. An example is her research on the design and development of synthetic co-cultures for the conversion of syngas (produced from wastes or lignocellulosic materials) to medium-chain fatty acids, alcohols and other low solubility added-value products. Other topics researched at her group include, syntrophy, methanogenesis, the microbial sulfur cycle and, more recently, electromicrobiology. Diana studied Biological Engineering at the University of Minho and obtained her PhD from the same university, where she also worked as Assistant Professor in the field of Environmental Biotechnology before moving to Wageningen. Diana seeks for a better understanding of microbial communities and microbial interactions, while searching for biotechnological applications of these communities in circular economy approaches.

accuracy of functional gene predictions, as the function of many genes is still not known even in culturable model organisms. In addition, even when certain genes/pathways are present in a genome it does not signify per se that they are functional, or what other physiological properties the microorganisms have. To establish a more quantitative understanding of microbial ecosystems it is of crucial importance that steps are made to integrate metagenomic studies with functional characterisation, computational modelling of microbial communities, and their response to changes in environmental conditions. This is the central theme of the paper by Kleerebezem et al. [8], who propose that the developments in the microbial ecology research field should be based on (i), the integration of fields of expertise through collaboration, (ii), standardization of methods (including standards for findability, accessibility, interoperability, reuse of datasets), (iii), a scale increase in experimental procedures to enable comparative research, increase in experimental resolution, to ensure reproducibility. According to the authors these steps are a prerequisite for resolving important, complicated questions in microbial ecology, like the comprehensible understanding of the intricate ways microbes interact in microbial ecosystems.

Interdependencies in microbial communities

Metabolic cross-feeding (i.e. exchange of amino acids, vitamins, growth factors, etc.) is likely the most common interspecies relation in microbial communities. In environments with no external electron acceptors, the exchange of diffusible electron-carrying molecules, such as formate and hydrogen, between an electron-donating species (syntroph) and an electron-accepting partner allows microbial communities to overcome thermodynamic constraints. However, the actual mechanism of electron transfer is not limited to the production and consumption of electron carriers like formate and hydrogen, it can also be achieved by Direct Interspecies Electron Transfer (DIET) or via a Conductive Material Mediated IET (cMIET).

Rotaru et al. [6] describes the discovery timeline of 'electric' syntrophy, presenting examples in natural and man-made environments. Evidence for 'electric' syntrophy is discussed in several processes, including the anaerobic oxidation of methane (AOM) and, more recently, the anaerobic oxidation of butane and ethane. Besides, authors expose their view on the necessary approaches to validate DIET and cMIET, emphasizing the need to consistently exclude other ways of indirect electron exchange (via formate/hydrogen, but also via other redox-active compounds as flavins or cysteine).

Computational modelling of microbial communities

Computational models are indispensable tools for capturing the essence of microbial ecosystems in a limited set of mathematical expressions. Besides aiding understanding of the observed behaviour of microbial systems, a computational model also helps to identify and predict unknown properties of microbial communities and therewith contributes to defining new research directions.

The work of Regueira et al. [10] aims to provide insight in the different competitive strategies developed by microorganisms to inhabit a specific ecological niche. Microbial fitness models based on the concept of resource allocation propose that optimization of microbial metabolism (i.e. the growth rate) can be based on distribution of cellular resources for optimization of the metabolic efficiency (biomass yield) or maximization of the electron transfer capacity (flux). Based on their analysis of anaerobic lactate production, the authors demonstrate that apparently ineffective strategies are actually very competitive in specific cultivation conditions.

Also the work of González-Cabaleiro et al. [11] aims for providing insights in the competitive properties of microorganisms in specific environments. Using considerations related to the (i) flux-force trade off, also elaborated by Regueira et al, (ii) spatial organization of microorganisms in cellular conglomerates (see also Borer & Or [12]), and (iii) the division of labour between different types of microorganisms, the authors identify ecological niches for specific metabolic strategies. Both examples related to nitrification and storage polymer production by aerobic heterotrophic bacteria are elaborated. Spatial organization of microbial species in a microbial community is also the central theme of the review by Borer & Or [12]. This later review offers a consistent discussion on the potential of spatiotemporal metabolic network models, constructed by adding a layer of spatial information of microbial habitats to genome-scale metabolic models of microbial communities. As opposed to the models discussed by González-Cabaleiro et al. [11] that are based on simple (Monod) based kinetic description of the microorganisms involved, Borer & Or [12] use high-detail metabolic network models. The authors convincingly show that both approaches have their specific value.

Whereas Rotaru et al. [6] focus on experimental and mechanistic aspects of IET, Desmond-Le Quémener et al. [13] discuss recent computational modeling efforts of both DIET and MIET. The authors demonstrate that bioenergetic calculations only allow to make good predictions on possible DIET/MIET mechanisms in microbial communities, but the identification of the kinetic properties of these processes need further research.

Applications of microbial community engineering

Our increased understanding of competitive strategies in microbial ecosystems has resulted in the development of a wide range of bioprocesses that rely on specific groups of microorganisms with smart competitive strategies. The challenge is to integrate all the fundamental knowledge on ecophysiology of natural and man-made systems to efficiently engineer mixed microbial communities. This can be done using ‘open culture’ approaches (i.e. non-sterile mixed cultures composed of a naturally-developed network of microbes) or ‘synthetic culture’ approaches (defined mixtures of microorganisms set together for a specific purpose/application).

An excellent example of a smart ecological strategy to deal with the alternating absence and presence of electron acceptor and carbon substrate forms the basis of the biological phosphorous removal process as discussed by Roy et al. [5]. As so often, the authors demonstrate that the actual metabolic diversity in nature is significantly bigger than previously anticipated, and that boundaries between different competitive strategies are diffuse.

Studies on the nitrogen cycle have provided exciting findings, such as the recent discovery of complete ammonia oxidizers (commamox) – microorganisms able to oxidize ammonia to nitrite and then to nitrate (nitrification, previously thought to be dependent on the activity of two separate groups of bacteria). The potential of application of commamox for wastewater treatment is an example of the subjects covered by Garrido Amador et al. [4]. Another important aspect treated in this review, is the role/applications of microbes in the production/prevention of emissions of climate active gases such as NO and N₂O.

Shifting to the production of chemicals from waste materials we introduce three reviews. Rombouts et al. [1] explain their view on how to produce ethanol using open mixed cultures, whereas Candry & Ganigué [2] show an overview of studies dealing with the production of elongated carboxylates (e.g. caproate) using open mixed communities. An alternative approach to open mixed cultures is finally presented by Diender et al. [3], who discuss the potential of using synthetic mixed communities for biotechnology. Although synthetic mixed communities are not yet applied in environmental biotechnology at industrial scale, there are several examples showing that these synthetic mixtures can act as efficient and selective biocatalysts for the conversion of e.g. synthesis gas, cellulose, or other compounds to added-value products. In addition, synthetic co-cultures can be used as an important platform to discover new ways of microbial interactions, as also pointed out in the review by Zamarela et al. [9]. Synthetic co-cultures provide a simplified study model for microbial interactions, and very importantly allow for better standardization and reproducibility of results compared to open mixed cultures. Integration of experimental and computational methods to study these defined microbial communities can aid to our understanding of microbe-microbe interactions in complex biological systems.

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