Environmental Science and Ecotechnology 25 (2025) 100558

Contents lists available at ScienceDirect

Environmental Science and Ecotechnology

journal homepage: www.journals.elsevier.com/environmental-science-and-ecotechnology/

Commentary

Unlocking the potential of designed microbial consortia: A breakthrough for sustainable waste management and climate resilience

While the global waste crisis is intensifying, we are missing a crucial opportunity to address this challenge by embracing a transformative approach: engineered microbial consortia have the potential to revolutionize industrial waste management, reduce greenhouse gas emissions for climate mitigation, and promote a sustainable bioeconomy.

Greenhouse gas emissions (GHG) from industrial processes pose a notable threat to planetary health [1]. The need for biotechnological solutions specifically targeting CO_2 capture and recycling for bio-based compounds and energy production is clear but far from achieved [2]. There are one trillion microorganisms with a pangenome covering an unspeakable potential of processes. Microbes could provide a solution to many of the challenges our planet is currently facing, such as restoring environmental health, substituting fossil fuels-originating chemicals and products with biomass-originating ones, enabling regenerative agriculture, restoring eutrophic water recipients, reducing biodiversity losses, and mitigating pollution.

Traditional industrial fermentations, key processes in biotechnology, have limitations and cannot deal with complex environments and inhomogeneous substrates such as wastes and residues. Biowastes, often incinerated or used for biogas, contain valuable nutrients like nitrogen and phosphorus that are lost in the process. By upcycling wastes into valuable products such as biofuels and bioplastics, industries can cut costs and reduce environmental impact at the same time [3]. Nonetheless, organic waste streams tend to have an inherent complex nature, with considerable variations in the concentration of their constituents, making pure culture fermentations incompatible with residual bioresources utilization [4]. Indeed, single-strain fermentations struggle with fluctuating waste compositions, leading to inconsistent yields and costly process adjustments. As a result, industries are forced to invest in costly pretreatment processes or face substantial inefficiencies in waste valorization. For too long, we have relied on single-strain microbial systems, but these methods cannot compel with the heterogeneous characteristics of wastes, thus limiting our actions towards sustainability challenges [5]. Most importantly, turning organic waste into useful products requires the combined efforts of different microbial species. This teamwork among microorganisms leads to more stable fermentation processes, especially in environments without oxygen, where microbes produce valuable chemicals for industrial processes instead of just growing more cells [6]. Therefore, anaerobic microorganisms represent the most promising candidates for advancements in green biotechnology. Nonetheless, to address the raised challenges, it becomes essential to explore alternative strategies to reach a circular bioeconomy, mitigating environmental impact.

The status quo is untenable. With over two billion tons of waste generated annually and projected to increase [7], we are at a crossroads: either continue to rely on outdated systems or embrace the transformative potential of designed microbial consortia. What we need now is a shift in thinking: industry and policymakers should invest in developing microbial consortia technologies specifically tailored to handle the variability and complexity of biowaste streams, which single strains are ill-equipped to manage.

1. The need for tailored microbial consortia

The shift to designed microbial consortia is not just a technological upgrade; it is integral to achieving global sustainability goals. With the potential to considerably reduce GHG and transform industrial waste into high-value products like biofuels and bioplastics, engineered consortia could help industries worldwide meet climate targets while reducing reliance on finite resources [8]. Current mixed culture fermentations (MCFs) face challenges such as instability, metabolic competition, and limited control over interspecies interactions. Advancing strategies to design and monitor these communities will be key to their industrial scalability. Anaerobic microorganisms can process organic matter without oxygen, though they often rely on cooperative networks with other microbes to thrive. Such partnerships help them survive harsh conditions by sharing energy and resources [6]. It is especially for anaerobes that internal collaborations are imperatively important, as they only gain limited energy from their oxidative processes due to the lack of a strong electron acceptor such as oxygen. Therefore, sharing energy is necessary for adenosine triphosphate production [6]. The collaboration scheme provides resilience, enabling several cooperative microorganisms to perform the same reactions and compensate for the potential inhibition of individual species, resulting in robust processes based on MCFs [9]. Despite their immense potential, anaerobic microbes are still underused in biotechnology. Overcoming the challenges of managing these microbial communities could revolutionize waste management and drive the bioeconomy forward. Microbial communities are complex, with different species competing and sometimes reducing the process's efficiency, making it hard to get consistent results when turning waste into useful products [10]. Unwanted microbes can consume valuable materials or take over, preventing the desired outcomes. A key challenge is our limited understanding of how these microbial communities function, which makes it

https://doi.org/10.1016/j.ese.2025.100558

difficult to control or optimize them for industrial use. This lack of control can result in incomplete waste breakdown, leading to inconsistent results and lower efficiency in bioprocesses [11]. To unlock the full potential of microbial consortia, we need to overcome challenges in controlling their behavior. By developing tools to guide these complex communities, industries can turn waste into valuable products, helping meet climate targets while cutting down waste-related emissions. Governments and industries should invest in pilot projects to test and scale up microbial consortia for waste management. By accelerating research, developing infrastructure, and fostering collaboration between industry and academia, these projects will show how we can make this technology work on a larger scale, reducing waste and emissions.

2. A call to action

The anaerobic microcosm is a “treasure trove” representing a huge reservoir for discovering novel microorganisms, enzymes, or genetic information to novel ways to transform waste into valuable products, helping industries worldwide address waste and reduce emission [12]. Nonetheless, the design of anaerobic microbial consortia to develop a robust platform for upcycling and valorizing waste streams still has several unknowns. To develop effective microbial consortia, we need to identify key microbial partnerships and exploit their cooperative interactions to ensure efficient and stable performance [13]. One of the biggest challenges is our limited understanding of the complex metabolic networks that allow these microbial communities to function smoothly. However, mapping these metabolic activities and interdependencies remains one of the toughest obstacles, as in some cases, microbes have unique nutritional needs that can only be met by exchanging metabolites with other species [9]. Computational models play a crucial role in addressing these challenges by enabling the systematic analysis of microbial networks, resource allocation, and metabolic fluxes [14,15]. Approaches such as genome-scale metabolic models (GEMs), flux balance analysis (FBA), and machine learning provide valuable insights into microbial interactions, allowing researchers to predict community behavior under different conditions and design consortia with improved stability and efficiency [15]. Recent advances in artificial intelligence demonstrated the capability to predict microbial communities and key functional groups in activated sludge [16]. Computational modeling has been instrumental in identifying key metabolic exchanges that support cooperative growth, minimizing competition, and optimizing nutrient utilization in synthetic consortia. For instance, the combination of GEMs and FBA can predict how metabolic fluxes shift in response to environmental changes, guiding the design of consortia that are resilient to perturbations [15]. Moreover, machine learning algorithms are increasingly being applied to analyze large-scale microbial datasets, uncovering hidden patterns of cooperation that could be exploited for industrial applications [14]. Most of current research has focused on engineering microbial communication within *Escherichia coli* multiple-strains consortia by exploiting quorum sensing mechanisms [17,18]. The first study developed a set of synthetic acyl homoserine lactones-receiver devices for fine-tuned gene expression control in microbial consortia. A software tool was designed to pinpoint orthogonal communication channels to enhance consortia designs [17]. The second study developed a co-repressive microbial consortium, demonstrating tunable gene expression based on strain ratio and how QS signaling governs fluorescence patterns in fluctuating environments [18]. To design synthetic microbial communities by assembling naturally occurring microorganisms and exploiting their synergistic interactions, rather than engineering and combining single strains, future research needs to combine advanced computational models with experiments. Understanding microbial interactions enables developing efficient waste-to-product systems by identifying key exchanges, metabolic capabilities, and limitations [15]. However, computational predictions alone risk overlooking real-world variability, necessitating laboratory experiments to ensure reliability and guide future designs. This dual approach—combining computational insights with empirical testing—is essential for advancing synthetic microbial consortia from theory to real-world industrial applications.

3. Innovation in action: roadmap for sustainable industrial fermentation

With growing environmental challenges and the urgent need for more sustainable industrial processes, designed microbial consortia offer a groundbreaking solution for improving fermentation methods. We urgently need to shift toward precision-engineered microbial communities that can transform waste into valuable resources, helping industries move toward a circular economy. To achieve this, we first need to identify the key members of a microbial community that are essential for carrying out the desired process. By using computational tools, we can better understand how these microbes work together and what they need from each other to function efficiently. The combination of omics technologies is used to discover the full potential of a microbial community by identifying which species are interacting and which metabolites are exchanged. This information can be used to predict how they will behave in different conditions, building GEMs and estimating metabolic fluxes exchanged with FBA, helping us fine-tune their interactions. From there, we can design microbial communities tailored for specific tasks, ensuring that the microbes cooperate effectively to maximize waste conversion. Using genetic information, techniques like live-fluorescence *in situ* hybridization (live-FISH) and FISH—Transcript Annealing Molecular Beacon (FISH—TAMB) can be applied to isolate the identified synergistic microorganisms for the specific process [19]. Once the consortium is established, effort needs to be put into its stabilization (e.g., 3D-printed gel matrix), which can ensure the proximity of symbiotic microbes and the stability of the process. The hydrogel-based printed filamentous structure substitutes the microbial filaments, known to give a template structure around which other microorganisms are entangled, and form granules (Fig. 1). Stabilization is a key challenge in the design of synthetic microbial consortia. Indeed, while reactor retention can be addressed through immobilization, maintaining the stability of the consortium's microbial composition requires careful consideration [20]. Although mutualistic relationships can be leveraged to regulate consortium dynamics, this strategy is insufficient for controlling mutations and horizontal gene transfer, which may lead to undesirable changes in both functional groups and the production of target biomolecules [20]. Overcoming this challenge would significantly enhance the application of engineered microbial consortia. While a detailed techno-economic analysis is not yet feasible due to limited commercialization, increased process specificity is known to enhance yield and economic viability, whereas the lack of process stability remains a key barrier to large-scale implementation. By adopting this roadmap, industries can shift from outdated, inefficient methods toward sustainable, precision-driven fermentation technologies. The broader implications are clear: designed microbial consortia enable the full exploitation of biowaste streams, transforming organic residues into high-value bio-based products such as biofuels, bioplastics, and biochemicals [21]. This shift will reduce reliance on finite fossil resources and advance a sustainable bioeconomy. By turning waste into useful products and reducing landfill use, anaerobic microbial communities can help lower GHG emissions and even capture carbon.

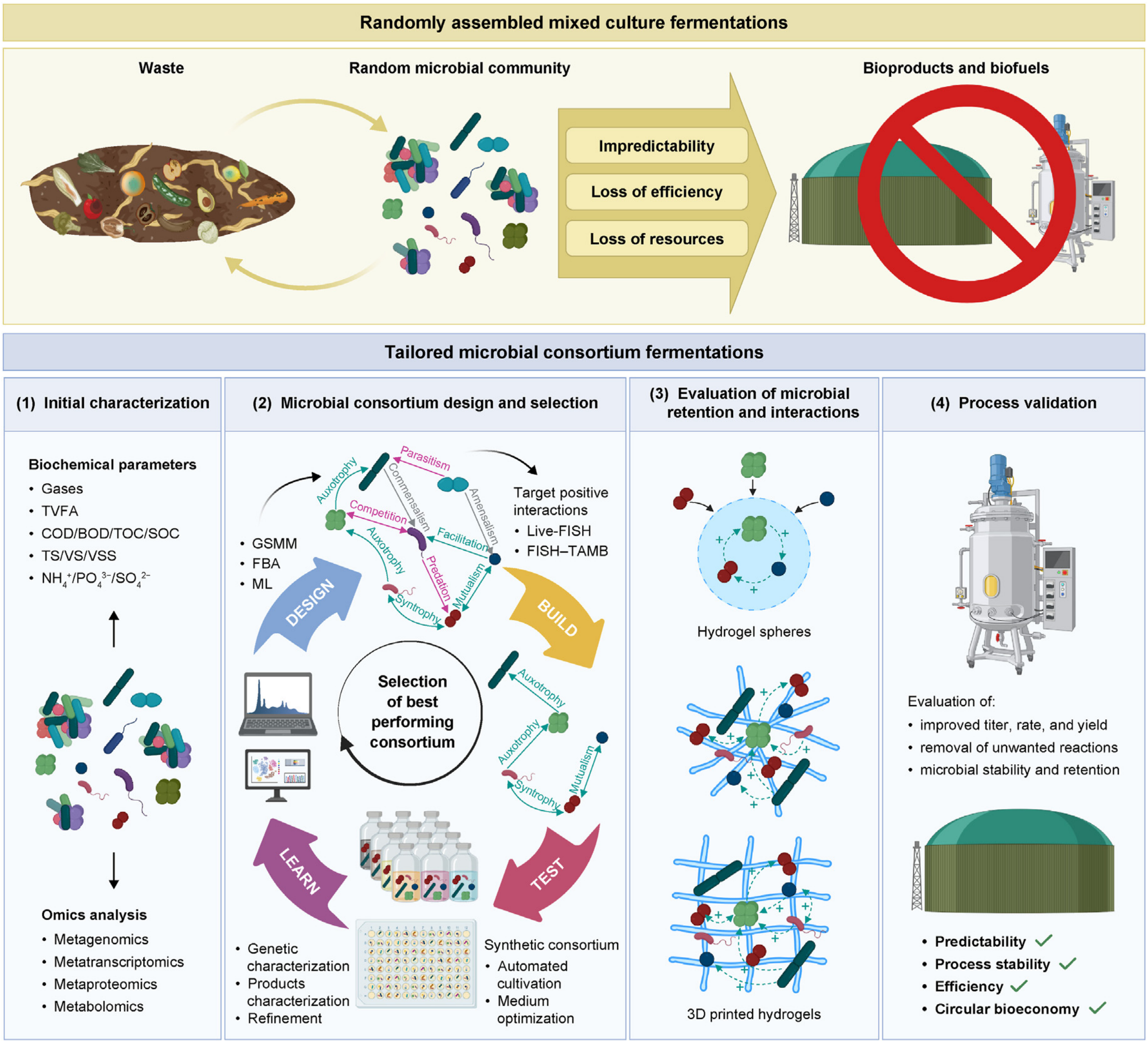

Fig. 1. The transition from randomly assembled mixed culture fermentations to tailored microbial consortium fermentations. On the top part, the figure displays the main drawbacks related to randomly assembled MCFs. At the bottom, the novel approach proposed is depicted. Starting from the characterization of the whole microbial community considering both biochemical parameters (total volatile fatty acids – TVFA –,chemical and biological oxygen demand – COD and BOD –, total and soluble organic carbon – TOC and SOC –, total, volatile, and volatile suspended solids – TS, VS, and VSS –, ammonia, phosphates, and sulfates – NH_4^+, PO_4^{3-}, SO_4^{2-} –, and omics analyses (1), computational tools like genome-scale metabolic modeling – GSMM –, flux balance analysis – FBA –, machine learning – ML – are employed to select the species of interest to perform the desired process. Afterwards, the genetic information is used for isolation by using fluorescence *in situ* hybridization techniques like live-FISH and FISH transcript annealing molecular beacon –FISH-TAMB –, retaining the microbial cells alive, and the interacting microorganisms are put together to select the best-performing consortium in a design-build-test-lean cycle (2). The microbial consortium is then immobilized in a hydrogel matrix (3). Finally, the designed microbial consortium is tested to improve the process's predictability, stability, and efficiency (4).

To create a sustainable future, industries must embrace microbial consortia to unlock new levels of efficiency, resilience, and environmental sustainability—helping us address the global waste crisis and meet climate goals. Microbial consortia offer a clear path toward a greener, more sustainable bioeconomy. The time to act is now—before we lose the chance to revolutionize the way we manage waste and protect our planet.

CRediT authorship contribution statement

Ginevra Giangeri: Writing – original draft, Visualization, Conceptualization. **Stefano Campanaro:** Writing – original draft, Supervision, Conceptualization. **Nikos C. Kyrpides:** Writing – original draft, Conceptualization. **Irini Angelidaki:** Writing – original draft, Supervision, Funding acquisition, Conceptualization.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

I.A. was supported by the ERC-advanced grant 101098064 – ANAEROB. The authors thank Antonio Grimalt-Alemany for the graphical support.

References

[1] W. Xu, G. Wang, S. Liu, J. Wang, W.H. McDowell, K. Huang, P.A. Raymond, Z. Yang, X. Xia, Globally elevated greenhouse gas emissions from polluted urban rivers, Nat. Sustain. (2024), https://doi.org/10.1038/s41893-024-01358-y.

[2] Z. Liu, K. Wang, Y. Chen, T. Tan, J. Nielsen, Third-generation biorefineries as the means to produce fuels and chemicals from CO2, Nat. Catal. 3 (3) (2020) 274—288, https://doi.org/10.1038/s41929-019-0421-5.

[3] U. Javourez, M. O'Donohue, L. Hamelin, Waste-to-Nutrition: a review of current and emerging conversion pathways, Biotechnol. Adv. 53 (2021) 107857, https://doi.org/10.1016/j.biotechadv.2021.107857.

[4] Y. Li, E.O. Mensah, E. Fordjour, J. Bai, Y. Yang, Z. Bai, Recent advances in high-throughput metabolic engineering: generation of oligonucleotide-mediated genetic libraries, Biotechnol. Adv. 59 (2022) 107970, https://doi.org/10.1016/j.biotechadv.2022.107970.

[5] N. Aggarwal, H.L. Pham, B. Ranjan, M. Saini, Y. Liang, G.S. Hossain, H. Ling, J.L. Foo, M.W. Chang, Microbial engineering strategies to utilize waste feedstock for sustainable bioproduction, Nat. Rev. Bioeng. 2 (2) (2023) 155—174, https://doi.org/10.1038/s44222-023-00129-2.

[6] B.E. Jackson, M.J. McInerney, Anaerobic microbial metabolism can proceed close to thermodynamic limits, Nature 415 (6870) (2002) 454—456, https://doi.org/10.1038/415454a.

[7] C.C. Ndiribe, The nature fit concept of waste reduction: prospects for engineering a clean future, Resour. Environ. Sustain. 14 (2023) 100127, https://doi.org/10.1016/j.resenv.2023.100127.

[8] B. Chatterjee, D. Mazumder, A critical review of the advances in valorizing agro-industrial wastes through mixed culture fermentation, J. Environ. Chem. Eng. 12 (1) (2024) 111838, https://doi.org/10.1016/j.jece.2023.111838.

[9] X. Zhu, S. Campanaro, L. Treu, R. Seshadri, N. Ivanova, P.G. Kougias, N. Kyrpides, I. Angelidaki, Metabolic dependencies govern microbial syntrophies during methanogenesis in an anaerobic digestion ecosystem, Microbiome 8 (1) (2020) 22, https://doi.org/10.1186/s40168-019-0780-9.

[10] G. Giangeri, P. Tsapekos, M. Gaspari, P. Ghofrani-Isfahani, M.K.T. Hong Lin, L. Treu, P. Kougias, S. Campanaro, I. Angelidaki, Magnetite alters the metabolic interaction between methanogens and sulfate-reducing bacteria, Environ. Sci. Technol. (2023), https://doi.org/10.1021/acs.est.3c05948 acs.est.3c05948.

[11] V.B. Centurion, A. Rossi, E. Orellana, G. Ghiotto, B. Kakuk, M.S. Morlino, A. Basile, G. Zampieri, L. Treu, S. Campanaro, A unified compendium of prokaryotic and viral genomes from over 300 anaerobic digestion microbiomes, Environ. Microbiome 19 (1) (2024) 1, https://doi.org/10.1186/s40793-023-00545-2.

[12] L.J. Rajakovich, B. Fu, M. Bollenbach, E.P. Balskus, Elucidation of an anaerobic pathway for metabolism of l -Carnitine—Derived γ-butyrobetaine to trimethylamine in human gut bacteria, Proc. Natl. Acad. Sci. 118 (32) (2021) e2101498118, https://doi.org/10.1073/pnas.2101498118.

[13] S. Saha, B. Basak, J.-H. Hwang, E.-S. Salama, P.K. Chatterjee, B.-H. Jeon, Microbial symbiosis: a network towards biomethanation, Trends Microbiol. 28 (12) (2020) 968—984, https://doi.org/10.1016/j.tim.2020.03.012.

[14] X.-W. Wang, Z. Sun, H. Jia, S. Michel-Mata, M.T. Angulo, L. Dai, X. He, S.T. Weiss, Y.-Y. Liu, Identifying keystone species in microbial communities using deep learning, Nat. Ecol. Evol. 8 (1) (2023) 22—31, https://doi.org/10.1038/s41559-023-02250-2.

[15] A. Basile, G. Zampieri, A. Kovalovszki, B. Karkaria, L. Treu, K.R. Patil, S. Campanaro, Modelling of microbial interactions in anaerobic digestion: from black to glass box, Curr. Opin. Microbiol. 75 (2023) 102363, https://doi.org/10.1016/j.mib.2023.102363.

[16] X. Liu, Y. Nie, X.-L. Wu, Predicting microbial community compositions in wastewater treatment plants using artificial neural networks, Microbiome 11 (1) (2023) 93, https://doi.org/10.1186/s40168-023-01519-9.

[17] N. Kylilis, Z.A. Tuza, G.-B. Stan, K.M. Polizzi, Tools for engineering coordinated system behaviour in synthetic microbial consortia, Nat. Commun. 9 (1) (2018) 2677, https://doi.org/10.1038/s41467-018-05046-2.

[18] R.N. Alnahhas, M. Sadeghpour, Y. Chen, A.A. Frey, W. Ott, K. Josić, M.R. Bennett, Majority sensing in synthetic microbial consortia, Nat. Commun. 11 (1) (2020) 3659, https://doi.org/10.1038/s41467-020-17475-z.

[19] R.L. Harris, M.C.Y.L. Vetter, E. van Heerden, E. Cason, J.-G. Vermeulen, A. Taneja, T.L. Kieft, C.J. DeCoste, G.S. Laevsky, T.C. Onstott, FISH-TAMB, a fixation-free mRNA fluorescent labeling technique to target transcriptionally active members in microbial communities, Microb. Ecol. 84 (1) (2022) 182—197, https://doi.org/10.1007/s00248-021-01809-5.

[20] N.E. Grandel, K. Reyes Gamas, M.R. Bennett, Control of synthetic microbial consortia in time, space, and composition, Trends Microbiol. 29 (12) (2021) 1095—1105, https://doi.org/10.1016/j.tim.2021.04.001.

[21] J.-Y. Lee, S.-E. Lee, D.-W. Lee, Current status and future prospects of biological routes to bio-based products using raw materials, wastes, and residues as renewable resources, Crit. Rev. Environ. Sci. Technol. 52 (14) (2022) 2453—2509, https://doi.org/10.1080/10643389.2021.1880259.

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