Applications of marine microbial community models in the nature-based economy

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Abstract:

Marine microorganisms are central to global ecological and biogeochemical systems, with their intricate interactions shaping community dynamics. While meta-omics datasets have revolutionized marine microbial ecology, they often provide fragmented insights, underscoring the need for advanced integrative modeling frameworks. In this perspective, we highlight the potential that metabolic models of microbial communities, in combination with meta-omics and environmental datasets, offer in advancing marine microbial ecology from identifying keystone species to predicting harmful algal blooms. Furthermore, we explore how these integrative methods can address challenges with significant economic impact such as the design of engineered microbial consortia and the assessment of ecosystem services in the context of the nature-based economy. As the marine domain transitions to a nature-based economic paradigm, the fusion of different modeling tools will be crucial in aligning economic frameworks with the invaluable services provided by marine ecosystems.

Introduction

Marine microorganisms tend to form intricate and evolving interaction networks which play pivotal roles in global ecological systems and biogeochemical cycles (underlined words are defined in Box 1) (Glibert and Mitra 2022). Their complex metabolic cross-feeding further shapes microbial community structure, biogeography, and diversification. Despite these insights, our understanding of marine microbial cross-feeding remains limited due to challenges in cultivating marine microorganisms and in discerning the vast array of molecules that are interchanged (Gralka et al. 2020).

The advent of meta-omics datasets has revolutionized marine microbial ecology. For instance, advancements in bioinformatic tools have further promoted this revolution by enabling rapid and precise annotation of sequences extracted directly from environmental samples and the reconstruction of metagenomic-assembled genomes (MAGs). In the latter case, MAGs often represent the only source of information to characterize marine microorganisms, offering a lens into their genomic and metabolic footprints, due to the difficulties obtaining cultured isolates.

However, while meta-omics datasets and MAGs have significantly advanced our understanding, they often provide a fragmented view of the microbial community's metabolic potential. This fragmented perspective can make it challenging to discern intricate metabolic interactions and ecological roles of marine microorganisms within their communities (Giordano et al. 2023). Furthermore, understanding the dynamics of community composition in relation to environmental parameters and recognizing the internal feedback mechanisms that shape these communities requires additional information beyond omics datasets (Fuhrman, Cram, and Needham 2015). The sheer volume and complexity of data generated from environmental samples can be overwhelming, leading to potential oversights in the interpretation of these datasets. In this regard, an integrative approach combining mathematical models with meta-omics datasets can address these complexities.

Mathematical models of microbial communities serve as frameworks to perform hypothesis testing and gain mechanistic insights, and, as such, have been instrumental in elucidating the complex interactions and dynamics of microbial communities. Traditionally, dynamic models, such as those based on generalized Lotka-Volterra equations and their extensions, have been employed to capture microbial dynamics including predator-prey and competitive interactions. However, while these models offer detailed dynamic predictions, they require profound knowledge of the model structure, particularly with respect to parameter values, which is not always possible. Additionally, interactions are typically evaluated pairwise, hence missing the opportunity to evaluate higher-order interactions among community members. In addition, the integration of environmental or meta-omics datasets is not straightforward (Succurro and Ebenhöh 2018).

Box 1. Glossary.

Biogeochemical cycles: The pathways by which chemicals or elements move through both the biotic (biosphere) and abiotic (lithosphere, atmosphere, and hydrosphere) components of Earth.

Biome: A large naturally occurring community of flora and fauna occupying a major habitat, e.g., forest or tundra.

Bioremediation: The use of living organisms, typically microorganisms, to remove or neutralize pollutants from a contaminated site.

Biostimulation: A remediation technique that enhances the growth of existing microorganisms in an environment to improve the degradation of contaminants.

Constraint-based metabolic modeling: A method to predict the metabolic fluxes and behavior of a cell or a community of cells under different environmental and genetic conditions, based on stoichiometric and physicochemical constraints.

Ecological firewalls: specialized strategies designed to regulate and contain the activities of engineered organisms within a specific ecological or microbial community.

Ecosystem services: Benefits provided by ecosystems to humans, including provisioning (e.g., food), regulating (e.g., climate regulation), and supporting (e.g., nutrient cycles) services.

Generalized Lotka-Volterra model: This model is a mathematical framework used in ecology to study interactions within microbial communities, including predator-prey and competitive dynamics.

Genome-scale metabolic models (GEMs): Detailed representations of an organism's metabolic network, based on its genomic information.

Marine microbial ecology: The study of microorganisms in marine environments, focusing on their roles in ecological and biogeochemical cycles.

Marine protected areas (MPAs): Regions of seas, oceans, or estuaries that restrict human activity for conservation purposes, to protect natural or cultural resources.

Metagenomic-assembled genomes (MAGs): Genomes assembled from metagenomic data, which is the collective genetic material obtained from environmental samples.

Meta-omics datasets: Collections of data derived from various 'omics' technologies, such as metagenomics, metatranscriptomics, metaproteomics, and meta-metabolomics, that provide insights into the collective genetic and metabolic potential of microbial communities.

Nature-based economy: An economic system that integrates ecological and environmental values and services into economic decision-making.

Genome-Scale Metabolic Models (GEMs) and constraint-based metabolic modeling have revolutionized the understanding of microbial metabolism. GEMs, using stoichiometric, biochemical, physicochemical, and environmental constraints like available nutrients, enable genome-scale predictions of metabolic fluxes, encompassing growth, metabolic capacities, and potential metabolite exchanges for individual organisms (Figure 1). By providing mappings between genes, proteins, and enzyme-catalyzed reactions, GEMs also serve as integrative frameworks for multi-omics datasets, providing insights into metabolic capabilities and environmental interactions (Gu et al. 2019). Additionally, GEMs can be reconstructed in a semi-automated manner from MAGs extracted from environmental DNA, thus offering predictions tailored to specific marine ecosystems (Machado et al. 2018; Zorrilla et al. 2021).

Advancing this approach, community Genome-Scale Metabolic Models (cGEMs) integrate these individual models together with environmental datasets to capture the collective metabolism and trophic interactions of diverse taxa within specific ecosystems (Dillard, Payne, and Papin 2021; Diener, Gibbons, and Resendis-Antonio 2020; Zampieri et al. 2023). cGEMs provide detailed insights into microbial community metabolism, uncovering aspects not evident from meta-omics data alone. Essential for predicting cross-feeding patterns, cGEMs elucidate metabolic dependencies and emergent behaviors, aiding in identifying keystone species vital for ecosystem robustness (Muller et al. 2018)

Moreover, cGEMs are adaptable, allowing for seamless integration with other modeling approaches or data-driven tools to refine predictions. For instance, Giordano et al. (2023) combined ecological interaction networks from Tara Oceans meta-omics data with cGEMs, enhancing understanding of trophic interactions in marine microbial communities and revealing significant metabolic cross-feedings in the euphotic zone, notably in the exchange of specific amino acids and group B vitamins. Additionally, the capability of cGEMs to provide a more nuanced view of potential auxotrophies and metabolic cross-feedings contributes valuable insights into community structure and dynamics. Furthermore, the adaptability of cGEMs extends to encapsulating community dynamics, moving beyond static, steady-state assumptions. Existing methodologies facilitate this expansion, enabling cGEMs to model temporal and spatial variations within microbial communities (Brunner and Chia 2020; Dukovski et al. 2021; Brunner, Gallegos-Graves, and Kroeger 2023; Bauer et al. 2017). This enhancement not only broadens the scope of cGEMs but also enriches their predictive accuracy and relevance in understanding complex marine ecosystems

Such comprehensive understanding renders cGEMs invaluable for hypothesis-driven research and experimental validation, potentially guiding the bioengineering of microbial communities for specific applications like the synthesis of compounds with commercial interests or environmental bioremediation (García-Jiménez, Torres-Bacete, and Nogales 2021). Furthermore, integrating cGEMs into broader biogeochemical or climate dynamic models offers a granular perspective on metabolic interactions within planktonic components, an aspect often oversimplified in current models (Tagliabue 2023), potentially enhancing predictive accuracy.

In addition to deepening our understanding of marine microbial ecology, cGEMs represent a powerful framework in the context of the nature-based economy. Enabling a comprehensive analysis of microbial communities and their metabolic interplays, cGEMs offer valuable insights for various applications with significant economic and ecological potential.

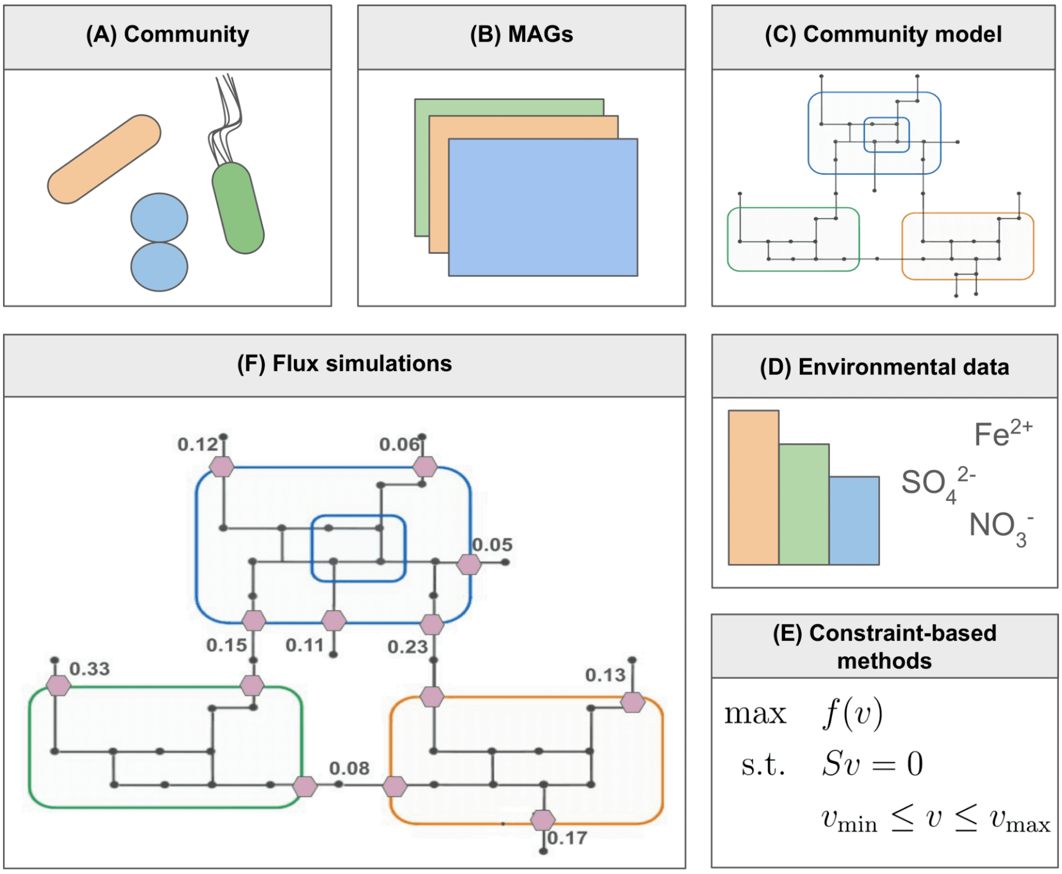

Figure 1. Elements of cGEMs and constraint-based modeling. Marine microbial communities, composed of diverse taxa, interact through trophic exchanges. (B) Metagenomic approaches facilitate the construction of MAGs for each community member. (C) These MAGs, supplemented with biochemical data, are used to reconstruct community genome-scale metabolic models (cGEMs), capturing both individual and collective metabolic processes, inclusive of trophic interactions. (D) Information on the relative abundances of community members and available environmental nutrients informs the application of constraint-based methods (E) such as Flux Balance Analysis (FBA), refining flux simulations for specific marine contexts. Panel (F) illustrates the results of cGEM simulations, emphasizing the exchange fluxes between community members on a simplified metabolic network, with salmon-colored hexagons denoting enzymes or transporters facilitating these exchanges. The inclusion of gene-protein-reaction associations for each enzyme in cGEMs permits the integration of metatranscriptomic or metaproteomic data, enhancing the model's predictive accuracy. This comprehensive approach yields insights into the metabolic interactions within marine microbial communities.

One particularly promising application is in the management and monitoring of Marine Protected Areas (MPAs), where cGEMs, combined with meta-omics datasets, can be instrumental in deriving metrics that quantify ecosystem services. These metrics could serve as the basis for robust economic valuation and the creation of financial instruments, offering a novel approach to economically sustain MPAs and help preserve vital marine ecosystems.

Beyond MPAs, these insights extend to optimizing bioremediation processes, enhancing sustainable aquaculture practices, and contributing to blue biotechnology innovations. Moreover, the ability of cGEMs to model complex interactions in marine environments informs strategies for maintaining ecosystem health and resilience which is crucial in the face of environmental change. This alignment of cGEMs with ecological and economic goals not only underscores their scientific significance but also highlights their role in shaping future bioeconomic strategies, where a fine-grained, mechanistic understanding of marine microbial dynamics becomes pivotal for the effective management and sustainable development of MPAs.

Harnessing community models for early detection of harmful algal blooms

Harmful Algal Blooms (HABs) are characterized by an excessive and rapid growth of microalgae, often resulting in the release of toxins that are harmful to wildlife, humans, and the environment. HABs result from a complex web of metabolic interactions between the causal microalgae, typically dinoflagellates and diatoms in marine environments, and the microbial community that strives within its *phycosphere*—the surrounding microenvironment characterized by algal exudates where most of the interactions between the microalgae and associated microorganisms occur. HABs have emerged as a significant threat to marine ecosystems and human economies, and are increasingly common due to ocean warming (Gobler et al. 2017). These blooms not only disrupt the natural balance of marine habitats but also impose substantial costs on aquaculture and fisheries, with a total estimated cost of $US 8 billion annually (Brown et al. 2020), healthcare, and tourism sectors worldwide (Berdalet et al. 2015). Thus, the prediction of HAB events is key to minimizing their impact on the nature-based economy and the bioeconomy, enabling more sustainable management of marine resources and more resilient economic sectors dependent on marine ecosystems.

The prediction of HAB events has traditionally relied on machine learning and correlative models. These models are effective in identifying patterns within extensive environmental datasets, enabling the forecasting of blooms based on historical data (Cruz et al. 2021). However, while excelling at processing large data volumes, they often lack depth in understanding the ecological processes and trophic interactions supporting microbial communities, such as those leading to HABs (Widder et al. 2016). Moreover, the predominantly data-driven nature of these models leads to challenges in interpretability and a limited ability to elucidate the complex biological and ecological mechanisms behind these patterns (Ghannam and Techtmann 2021). This highlights a significant gap, emphasizing the need for more integrative approaches that combine data-driven insights with a deeper ecological understanding of HAB events.

Seeking to enhance the accuracy of HAB predictions, Litchman (2023) proposed a novel trait-based approach, diverging from traditional models by focusing on the characterization of functional traits of HAB-forming taxa. This methodology delves into specific biological characteristics, such as cell size, nutrient utilization efficiency, and light adaptation strategies, to understand their influence on bloom dynamics. For example, variations in light utilization traits among different algal species can significantly impact their ability to form blooms under varying light conditions. Similarly, the study of temperature responses and buoyancy traits provides insights into how different HAB-forming species might respond to changing environmental conditions. By directly linking these ecological traits to bloom formation and progression, Litchman's approach offers a more nuanced and mechanistic understanding of HABs, moving beyond mere pattern recognition to revealing the underlying ecological processes.

Complementing this biological perspective, Ahn et al. (2021) have made significant strides with their revised Environmental Fluid Dynamics Code (EFDC) model, specifically tailored to target harmful cyanobacteria. This innovative model integrates both physical and biological processes in aquatic environments to simulate conditions conducive to cyanobacterial blooms. It incorporates physical parameters like water temperature, flow velocity, light penetration, and key environmental factors such as nutrient concentrations. The EFDC model is adept at simulating the dynamic and complex interplay between these factors, thereby providing a more realistic representation of the aquatic ecosystem. This allows for a more accurate prediction of the timing, location, and intensity of cyanobacterial blooms. Focussing on harmful cyanobacteria, Ahn et al.'s model presents a more direct method for predicting bloom events that pose risks to water quality and ecosystem health. Additionally, the model's comprehensive approach, encompassing a wide range of influential factors, marks a significant advancement in our ability to predict and manage the risks associated with these detrimental blooms in marine and freshwater systems.

While both Litchman’s trait-based approach and the EFDC model represent significant advances in understanding and predicting Harmful Algal Blooms (HABs), they present inherent limitations. Litchman's method, which focuses on trait analysis, confronts challenges such as data intensiveness and the difficulty in generalizing findings across diverse species and environments. Similarly, the EFDC model, though comprehensive, demands extensive data, is computationally intensive, and its effectiveness may vary in different aquatic environments. In this context, cGEMs emerge as a promising development for HAB prediction. Leveraging the biochemical information they encode, cGEMs provide a versatile framework capable of yielding mechanistic insights into the complex interplay among bloom-forming species, interacting organisms, available nutrients, and prevailing environmental conditions. Furthermore, cGEMs can be effectively combined with other predictive methods. For instance, cGEMs could enhance trait-based approaches by offering a more detailed dimension, thereby improving predictions and management strategies for HAB events.

A compelling example of this is the study of HABs caused by *Pseudo-Nitzschia*, notorious for its production of domoic acid. This neurotoxin, which accumulates in fish and shellfish, has been identified to cause Amnesic Shellfish Poisoning, with severe consequences to human health (Pulido 2008). The integration of cGEMs with metagenomic and environmental data can offer deeper insights into the intricate metabolic interactions that occur within the *Pseudo-Nitzschia*'s phycosphere, which are essential for the production of domoic acid (Kobayashi, Takata, and Kodama 2009). The economic impact of such blooms was starkly demonstrated in the 2015 toxic bloom on the U.S. West Coast, which led to substantial losses in fisheries and tourism with an estimated revenue loss of $US 97.5 million for the Dungeness crab fishery, the main fishery in the region (Moore et al. 2020). By modeling these complex interactions, cGEMs can help predict the conditions under which harmful blooms are likely to occur and inform strategies to mitigate their impact. For instance, altering nutrient concentrations in the environment could disrupt the phycospheric relations that favor toxin production, thereby reducing the frequency and severity of these harmful events.

Combining cGEMs with metagenomic and environmental data offers a promising advancement in addressing HABs, such as those caused by *Pseudo-Nitzschia*. This approach, while still in its developmental stages, promises deeper insights into the intricate metabolic interactions within the phycosphere, as well as the key factors that influence the production of toxins like domoic acid. By better understanding the ecological relations supporting the onset of HABs, we could elaborate targeted mitigation strategies as well as more accurate and timely predictions of bloom events. Thus its successful implementation could enable industries, such as fisheries and tourism, to proactively manage and reduce the widespread damage caused by HABs, thereby safeguarding marine ecosystems and the economies that rely on them.

Designing microbial consortia for specialized metabolic activities

cGEMs serve as pivotal tools in the design of engineered microbial consortia tailored for specific objectives. Leveraging the insights derived from these models, we can conceptualize and subsequently cultivate minimal microbial communities optimized for distinct metabolic tasks such as environmental remediation or specialized compound synthesis.

A suite of available computational tools facilitates the bioengineering of microbial communities, each addressing different aspects of community optimization (García-Jiménez, Torres-Bacete, and Nogales 2021). Some of these tools adopt a combinatorial strategy, centering on the strategic alignment of metabolic reactions and the associated community members responsible for synthesizing target compounds (Eng and Borenstein 2016; Julien-Laferrière et al. 2016). Conversely, others implement constraint-based methodologies, focusing on the active optimization of metabolic fluxes and growth rates to determine the most effective arrangements (García-Jiménez, García, and Nogales 2018; Zomorrodi and Maranas 2012; Thommes et al. 2019). Collectively, these tools encompass a holistic approach, ranging from the initial conception of metabolic interactions to the meticulous fine-tuning of community behavior, ensuring optimal performance.

For instance, Zuñiga et al. (2020) effectively utilized OptCom (Zomorrodi and Maranas 2012) and cGEMs to design synthetic microbial communities, pairing phototrophic *Synechococcus elongatus* with several heterotrophic bacterial strains. Their models illuminated key metabolic exchanges, notably sustaining heterotrophs without external organic carbon. Among the communities, the *S. elongatus* - *Escherichia coli* K-12 consortium was highlighted for its metabolic vigor. Importantly, these model-derived insights were experimentally validated, emphasizing the pivotal role of cGEMs and community optimization tools, such as OptCom, in guiding synthetic microbial community design for biotechnological applications.

Beyond the design of individual consortia, cGEMs offer a broader perspective on the interplay of microbial interactions within a community. This holistic view allows for the identification of potential bottlenecks, competitive interactions, and synergistic relationships that can be harnessed or mitigated to achieve desired outcomes. In this line, cGEMs could be key players in the exploration of biostimulation—a process that fine-tunes environmental conditions to expedite the natural degradation capabilities of native microbes. By simulating different environmental scenarios, cGEMs could help identify the optimal concentration of nutrients that can catalyze microbial activity without causing eutrophication or other harmful side effects (Figure 2, Supplementary Notebook 1). Such targeted biostimulation could significantly enhance the breakdown of contaminants, as seen in marine oil spill events where adjusting nitrogen and phosphorus levels have been linked to improved biodegradation rates (Banet et al. 2021; Popoola et al. 2022).

Another essential facet of this design process is understanding and ensuring the dynamic stability of these consortia. Stability analysis not only provides insights into how microbial communities maintain their structure and function in the face of perturbations, ensuring that beneficial engineered communities can consistently perform their tasks in dynamic environments, but it also offers a lens to identify vulnerabilities in harmful communities (Coyte, Schluter, and Foster 2015). For instance, in the context of marine HABs, stability analysis can be instrumental in pinpointing specific species or interactions that, when targeted, can destabilize the harmful microalgal community and its supporting phycosphere consortium. This dual utility of stability analysis—both as a tool for reinforcement and disruption—underscores its significance in microbial community engineering.

Building on these insights, the concept of ecological firewalls presented in Vidiella and Solé (2022) emerges as a particularly intriguing avenue. Grounded in the nonlinear attractor dynamics of certain ecological network motifs, ecological firewalls are designed to perform specific functionalities while ensuring containment within the resident community, providing a form of self-regulating biocontainment. Such firewalls ensure that engineered organisms have a limited spread but also prevent their extinction when required, offering a promising avenue for the protection and restoration of ecosystems at risk of catastrophic transitions due to anthropogenic impacts. Additionally, the framework of ecological firewalls, rooted in ecological and trophic networks, aligns seamlessly with the capabilities of cGEMs. cGEMs can be easily integrated to describe the metabolism and predict the growth of each individual member within a community, thereby enhancing the precision and predictability of engineered ecological firewalls. This synergy between cGEMs and ecological firewalls underscores the potential of a unified approach in designing robust and efficient microbial consortia.

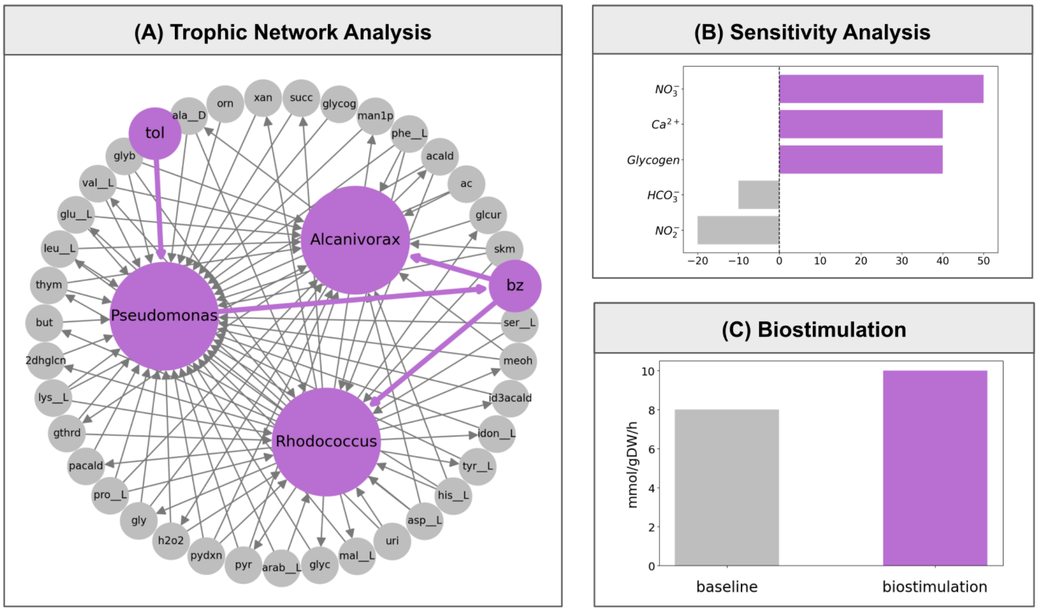

Figure 2. Designing a biostimulation strategy for a coastal oil spill. cGEMs together with environmental datasets can be employed to design a bioremediation strategy for a coastal oil spill. This figure summarizes a cGEM-informed biostimulation strategy demonstrated in the accompanying Supplementary Notebook 1, in which the capacity to uptake toluene from polluted waters by a community is increased through biostimulation. (A) a cGEM and constraint-based methods are employed to analyze the trophic interactions that support toluene uptake and degradation by the community, identifying *Pseudomonas* as the main genus uptaking toluene. (B) A sensitivity analysis is conducted to identify which environmental nutrients show the largest positive effects on toluene uptake by the community. (C) Community flux simulations are run at baseline and in a biostimulation scenario, where key nutrients for the enhancement of toluene uptake are added to the medium, resulting in an increase of the predicted toluene uptake rate by *Pseudomonas*. This case study demonstrates the potential of cGEMs for guiding intervention strategies, leveraging natural processes for environmental restoration. The full runnable example can be found in Supplementary Notebook 1 and in the GitHub repo: https://github.com/Robaina/oil_spill_example.

The economic implications of optimizing microbial consortia are profound, particularly within the context of the nature-based economy. By fine-tuning microbial communities to perform specific tasks, such as biodegradation, bioenergy production, or nutrient cycling, there is potential for significant advancements in sustainable practices. Furthermore, the ability to tailor microbial communities for specific ecological functions can play a pivotal role in ecosystem restoration projects, which are central to the nature-based economy. These applications not only offer economic benefits but also contribute to environmental conservation. As we continue to refine our tools and expand our understanding, the horizon looks promising for the development of microbial consortia that can address some of the most pressing challenges of our time, from sustainable bio-production to environmental conservation.

Community metabolic models to improve ecosystem and climate predictions

The integration of microbial community models with broader ecosystem and climate models presents a promising frontier in marine microbial ecology, aiming to decipher the complex interactions that define marine ecosystems and their interplay with the Earth system. Previous studies in this area have employed a range of methodologies to connect the genetic underpinnings of microbial communities with broader ecosystem processes. These methodologies range from gene-centric approaches, highlighting the roles of functional genes in ecosystem functions, to metabolic flux modeling that spans single-species to complex multi-species systems (Kreft et al. 2017). Each modeling strategy, whether environmentally coupled, directly linked, or aggregated, unveils unique insights into microbial interactions and their potential impacts on ecosystem functions.

For instance, Coles et al. (2017) demonstrate how genomic sequencing data can be utilized to simulate metagenomes and metatranscriptomes, providing a nuanced understanding of how microbial communities orchestrate ocean nutrient gradients. Specifically, their results show that the collective metabolic capabilities of microbial communities, rather than the specific functions of individual organisms, are instrumental in driving the assembly of microbial communities and biogeochemical gradients in the ocean. Similarly, Reed et al. (2014) used a gene-centric biogeochemical model to dissect the complexities of nitrogen cycling within oxygen minimum zones. Their research not only elucidates the relative contributions of denitrification and anammox processes but also explores the influences of cryptic sulfur cycling on biogeochemical cycles, offering a more comprehensive perspective on the biogeochemical implications of microbial activities.

Additionally, recent advancements underscore the urgent need to incorporate the biological complexity of marine microorganisms, including bacteria, archaea, fungi, algae, and viruses, into the ocean component of Earth System Models to accurately predict climate change impacts on ocean health. Specifically, traditional ocean models initially focused on physical processes, have gradually incorporated biogeochemical cycles and a limited range of phytoplankton types, but still struggle to accurately represent the full spectrum of microbial dynamics and responses to environmental changes. Technological advances, particularly in the omics domain, offer deeper insights into the molecular-level functioning of marine microbes. However, existing climate models often overlook these detailed datasets, opting instead to focus on bulk biological indicators. A more integrated approach, which combines biological information with biogeochemical modeling and utilizes both statistical techniques and mechanistic metabolic models like cGEMs, would more effectively represent the diverse interactions and responses of marine microorganisms to changing ocean conditions. This integrated approach holds promise for the development of more accurate and comprehensive climate models, which are crucial for predicting the future states of ocean ecosystems under the stress of climate change (Tagliabue 2023).

Following this groundwork, the specific integration of cGEMs into climate and ecological models holds significant promise. cGEMs offer a more granular perspective on the growth predictions of individual species, delving deeper into the mechanistic interactions through shared compounds between community members, as well as the effects of environmental factors. Some of these compounds play pivotal roles in global climate models. For instance, certain marine microbes emit dimethyl sulfide (DMS) into the atmosphere, a sulfur-containing gas that significantly influences the Earth's radiation budget. DMS emissions from marine sources have been identified as a major contributor to marine aerosol mass, which in turn affects cloud condensation nuclei over remote oceanic regions (Teng et al. 2021). Furthermore, cGEMs offer a powerful method to predict metabolic fluxes, which are key to understanding biogeochemical cycles and global climate patterns, such as those associated with carbon fixation and organic carbon utilization. Integrating satellite-derived data on phytoplankton biomass, quantified through chlorophyll measurements, with cGEMs can enhance the accuracy of these predictions (Tagliabue 2023). This integration allows for the correlation of satellite observations with the biomass predictions made by cGEMs, offering a more precise understanding of phytoplankton dynamics and their contribution to carbon cycles.

An additional, often overlooked factor that greatly influences ecosystem and biogeochemical cycle dynamics is the effect of marine viruses. Viruses can significantly alter host metabolic flux and population sizes through viral lysis. This process, known as the viral shunt, releases organic compounds into the environment, enriching it and impacting community growth (Roux et al. 2016). Representing this in cGEMs involves adjusting environmental compound exchange rates to mirror the effects of viral activities, such as increased organic compound production due to heightened cellular lysis, or the direct effect on relative abundances of host taxa. Including these viral impacts could allow cGEMs to offer a more complete representation of microbial interactions and their consequences on climate.

Integrating cGEMs into ecosystem and climate models opens new avenues for understanding the interplay between marine ecosystems and global climate dynamics. Prior studies, such as those by Coles et al. (2017), Reed et al. (2014), and Teng et al. (2021), have advanced our knowledge of biogeochemical cycles using other modeling approaches. However, the application of cGEMs in biogeochemical and climate models, while still in its nascent stages, has tremendous potential to improve model predictions by providing detailed insights into microbial interactions and processes, particularly when augmented by *omics* datasets and satellite-based phytoplankton biomass estimations.

Toward a quantitative assessment of marine ecosystem services

The nature-based economy emphasizes the intrinsic value of nature, advocating for its conservation and regeneration as essential to sustainable economic growth. This paradigm challenges traditional economic models that prioritize growth at nature's expense, recognizing instead the interdependence between economic prosperity and healthy ecosystems, and assigning an economic value to ecosystems and the diverse services they provide. Placing nature at the core of economic decisions, the nature-based economy seeks a harmonious balance between human development and environmental conservation, ensuring shared prosperity while respecting ecological boundaries (Chami et al. 2022).

Within the marine domain, microbial communities are central to maintaining the equilibrium and vitality of oceanic ecosystems. Their complex metabolic interactions and biogeochemical functions position them as indispensable contributors, whose roles are gaining increased attention as essential components in the context of Sustainable Development Goals (Abreu et al. 2022), but remain to be quantified and fully integrated into the economic paradigm of the nature-based economy. cGEMs in combination with environmental datasets offer a comprehensive framework to develop quantitative indices of microbial ecosystem services provided by specific biomes or ocean regions. Notably, we can leverage cGEMs to compute metabolic fluxes and maximum capacities of a community under specific environmental conditions. These models simulate different community compositions and abundances, as well as varying environmental factors, to assess how these changes impact key metabolic processes like nutrient cycling, carbon sequestration, or pollutant degradation. The resulting indices provide a nuanced view of ecosystem service capacity, reflecting the dynamic interplay between microbial communities and their environment, essential for informed decision-making in ecosystem management and conservation strategies (Samhouri, Levin, and Harvey 2009; Okada et al. 2019).

MPAs could greatly benefit from this system-level approach. For instance, cGEM-informed biodiversity metrics or ecological indices could add to the development of financial instruments or market-based solutions that recognize the value of pivotal marine ecosystem functions and services. In particular, , metrics based on carbon sequestration capacity could inform blue carbon credits (Mengis, Paul, and Fernández-Méndez 2023; Hilmi et al. 2021). Likewise, indices measuring nutrient cycling efficiency or bioremediation capacity for toxin breakdown could translate into actionable insights for ecosystem management and the creation of financial products such as water quality credits or nutrient cycling-based instruments (Figure 3). This scientific approach to the economic valuation of natural capital may not only aid in the maintenance and sustainability of MPAs but also align with broader objectives of the nature-based economy (Box 2). This system-level approach could ensure that conservation efforts are not only ecologically effective but also economically viable, creating a self-sustaining model that supports the preservation of marine ecosystems while contributing to sustainable economic growth (Chami et al. 2022; Berzaghi et al. 2022; Directorate-General for Research and Innovation (European Commission) 2022).

Moreover, shifting the focus from direct financial instruments to broader applications in risk management represents an interesting addition to the concept of economic valuation in MPAs. Here, the metrics and indices developed through the application of cGEMs gain new significance in environmental risk assessment and the insurance market, bridging ecological insights with economic resilience. Specifically, sensitivity analyses of cGEMs can be employed to investigate how robust the ecosystem services provided by microbial communities are to compositional perturbations (Diener, Gibbons, and Resendis-Antonio 2020). These analyses hold great promise to develop indices meant to quantify the metabolic robustness of microbial ecosystems, which are key for environmental risk assessment in the insurance market, informing the likelihood and impact of ecological disturbances like pollution or climate-induced changes (Holsman et al. 2017; Andersen et al. 2022). These data could enable insurance companies to develop precise, risk-reflective policies, assessing potential ecosystem service disruptions and the ensuing economic losses. The integration of cGEM-based indices into environmental insurance models could also spur innovative financial products like insurance-linked securities tied to marine ecosystem health. This represents a novel fusion of ecological science and financial markets, advancing environmental risk management strategies in the nature-based economy.

By facilitating the translation of complex metabolic and ecological insights into concrete economic value, we advocate for a nature-aligned economic system that truly values the irreplaceable services provided by marine ecosystems. These sophisticated tools and models herald a transformative approach to marine conservation, integrating ecological function into the growing paradigm of blue natural capital markets. Moreover, ecosystem-derived financial products offer an economically viable way to sustain MPAs, in which local and indigenous communities should be involved as key stakeholders. Ensuring that the financial benefits from ecosystem services are responsibly managed and reinvested in both the ecosystems and the local communities, and fostering a model of development that is ecologically responsible, economically beneficial, and inclusive (Cisneros-Montemayor et al. 2021).

As we progress towards a nature-based economy, the synergy of advanced scientific tools and economic innovation will be instrumental. This union ensures that our economic systems not only reflect but actively promote the stewardship of the natural world upon which all prosperity depends.

Box 2: Financial products anchored in marine ecosystem services

Economic Incentives for Marine Conservation

In the evolving landscape of a nature-based economy, financial products tied to ecosystem services are becoming increasingly crucial for marine conservation, aligning economic and environmental interests (Chami et al., 2022).

Carbon Credits in Marine Protected Areas (MPAs): The development of carbon credits based on the carbon sequestration capacities of MPAs exemplifies how ecosystem services can be monetized. Such initiatives offer economic incentives for preserving these vital ecosystems (Dasgupta Review, 2020).

Water Quality Credits: Metrics for nutrient cycling efficiency or bioremediation capacity in marine environments can be translated into water quality credits, incentivizing practices that maintain or enhance water quality (Handbook for Nature-related Financial Risks, CISL).

Insurance Products Based on Ecosystem Health: Evaluating the robustness of ecosystem services through cGEMs can inform the creation of insurance products that reflect the health of marine ecosystems, directing investments toward their conservation (World Economic Forum, 2020).

Innovative Financial Products: The potential for novel products, such as insurance-linked securities tied to marine ecosystem health, illustrates the innovative fusion of ecological science with financial markets (Directive of the European Parliament and of the Council on Corporate Sustainability Due Diligence, 2021).

Biocredit Market as a Future Development: The concept of a biocredit market, wherein companies could buy credits to offset their impacts on biodiversity, carbon, and ecosystem services, represents a promising future development. Emerging law proposals that require large companies to compensate for their environmental footprint through bioremediation, carbon, biodiversity, or ecosystem service offsets could be a catalyst for this market (“Proposal for a Directive on Corporate Sustainability Due Diligence and Annex” 2022; “Biodiversity Credit Markets: The Role of Law, Regulation and Policy | Taskforce on Nature Markets,” n.d.). Such legislation would not only enforce corporate responsibility for environmental impacts but also foster a market-driven approach to conservation and restoration efforts.

Community Involvement: Involving local and indigenous communities in the development and benefits of these financial instruments ensures responsible management and reinvestment of the financial benefits derived from ecosystem services (Chami et al., 2022).

These financial mechanisms provide a pathway to sustainably finance MPAs, aligning marine ecosystem preservation with sustainable economic growth. The advancement of such instruments in a nature-based economy will be key in promoting the stewardship of marine ecosystems, thereby safeguarding both their intrinsic and economic values.

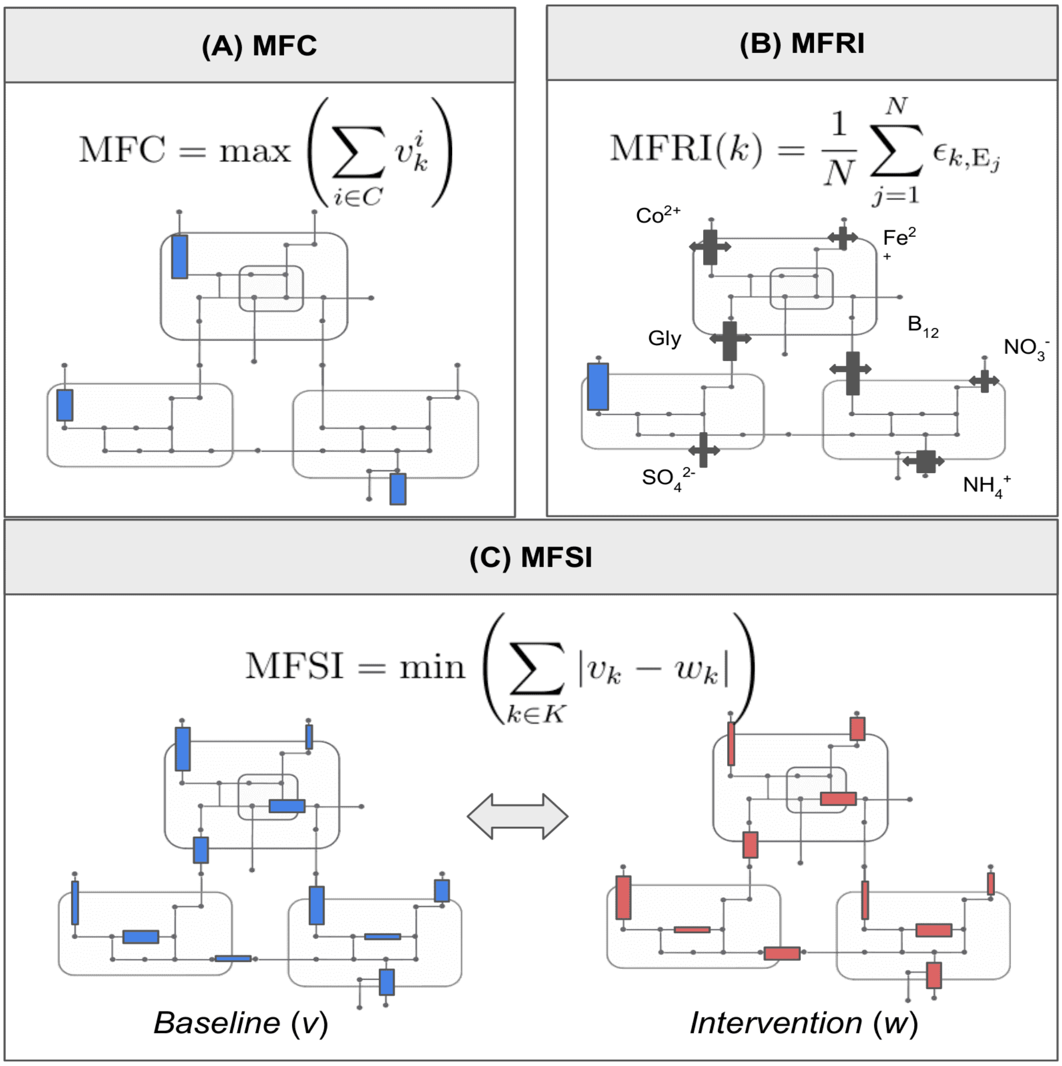

Figure 3. Examples of cGEM-derived indices quantifying ecosystem services. Illustration of three quantitative indices derived from cGEMs and constraint-based approaches to assess different aspects of microbial ecosystem services. (A) Depiction of the Maximum Flux Capacity (MFC) index, which quantifies the maximum potential of a specific metabolic function across a microbial community. Here, blue rectangles represent the target reaction whose flux is maximized across the community. (B) The Metabolic Functional Robustness Index (MFRI) quantifies the resilience of key metabolic reactions for ecosystem services against perturbations in nutrient exchange rates. To this end, it computes the average elasticity value across all perturbed nutrient uptake rates. Here, the flux through a key reaction is represented in blue, while the perturbed nutrient uptake rates are represented in gray. (C) The Metabolic Flux Shift Index (MFSI) measures the shift in metabolic state of a community from a baseline to an intervention scenario. To this end, it minimizes the sum of absolute differences in flux values, v, w, between both conditions over a set of selected key reactions, K. Here, key reaction fluxes between the two conditions are highlighted in blue and red, respectively. Quantitative indices such as the ones displayed in this figure could inform the sustainable management and economic valuation strategies in MPAs, ultimately facilitating the integration of ecological function into economic decision-making frameworks. A more detailed description of these indices can be found in Supplementary File 1.

Challenges and future directions

Applying cGEMs in marine microbial ecology presents inherent challenges and uncertainties. A significant challenge stems from prediction uncertainties, which are caused by knowledge gaps in microbial genomes, particularly MAGs, and by limitations within existing biochemical databases. The reliance on MAGs, predominantly due to the difficulty of isolating organisms from marine samples, leads to incomplete gene sets and functional annotations. Additionally, most marine microbes are not adequately represented in curated biochemical databases, which primarily focus on cultured organisms. This lack of representation exacerbates the uncertainty in cGEMs, particularly affecting the model's structure, which is contingent on different model reconstruction approaches and the databases used. Despite these challenges, efforts to reconstruct consensus GEMs from varied drafts and to unify biochemical databases have shown promise in reducing these structural uncertainties and enhancing the robustness of cGEMs in marine microbial ecology (Biggs and Papin 2017; Bernstein et al. 2021; Hsieh et al. 2023).

The choice of objective function and constraints during GEM optimization also significantly influences predictions. This is particularly challenging for uncultured organisms, where biomass component stoichiometry cannot be measured, necessitating alternative objective functions and generic biomass pseudo-reactions (Bernstein et al. 2021). Additionally, defining trophic or metabolic interactions within community models adds further complexity. These interactions, influenced by factors such as metabolite leakage and community composition, can lead to biases in predicted auxotrophies and exports, which are being addressed by new gap-filling approaches like COMMIT (Wendering and Nikoloski 2022).

Model validation in cGEMs faces the challenge of limited comprehensive experimental data, especially in metabolomics. The complexity of microbial community interactions complicates the validation process. Strategies to enhance validation include using parallel techniques like co-occurrence or co-activity networks, comparing cGEM-predicted community structures with actual abundances from metabarcoding or metagenomic datasets, and employing sensitivity analyses. These methods, coupled with comprehensive environmental measurements in recent studies (Muratore et al. 2022), offer insights into the accuracy of metabolic interactions within microbial communities. Furthermore, the validation of engineered microbial communities derived from cGEMs can be effectively conducted in controlled experimental setups, as demonstrated in the work by Zuñiga et al. (2020). In this context, mesocosm experiments, which closely mimic natural environmental conditions, are ideal for assessing the viability and impact of engineered communities in a realistic setting. These experiments provide critical insights into the practical application and ecological implications of engineered systems, substantiating the predictions and designs derived from cGEMs.

Lastly, it is crucial to recognize the ethical implications of subjecting natural ecosystems to bioremediation practices, such as those achieved through the application of biostimulation or bioaugmentation techniques.. Interventions in microbial communities, while beneficial for bioremediation, can potentially disrupt ecosystem balance and biodiversity. Recognizing this, ecological firewalls, as previously discussed, become essential. They ensure that any alterations to natural ecosystems, particularly through engineered microbial communities, are monitored and controlled to prevent unintended ecological consequences

As the field progresses, access to more comprehensive datasets and the development of innovative computational methods will be key to addressing these challenges. This advancement is crucial for enhancing the accuracy of cGEMs and fully realizing their potential in understanding the dynamics of microbial communities in marine ecosystems.

Conclusion

The advent of meta-omics datasets and computational modeling has catalyzed an unprecedented understanding of marine microbial ecology. cGEMs have played a pivotal role in this advancement by elucidating microbial community dynamics. They provide vital insights into metabolic cross-feeding, community stability, and the interplay between microbial activities and broader ecological processes.

The integration of cGEMs with meta-omics datasets and environmental variables offers a nuanced view of marine microbial communities. This enhances our capacity to predict and develop rational intervention strategies for improving ecological health, safeguarding ecosystems, as well as informing science-based economic valuation models of natural capital . The nature-based economy, which seeks a sustainable balance between economic development and ecological conservation, can greatly benefit from the application of cGEMs on the growing corpus of publicly available sequencing data. By quantifying and elucidating the intricate metabolic interactions within marine microbial communities, cGEMs contribute to a deeper understanding of ecosystem services and their economic valuation. This is particularly relevant in the management of MPAs, where cGEM-derived metrics can inform both the design of financial instruments and conservation strategies.

Furthermore, cGEMs offer a mechanistic framework that could significantly enhance the prediction of ecological threats, such as HAB events. This enables informed mitigation strategies to safeguard marine ecosystems and the industries dependent on them. Looking forward, integrating cGEMs into broader biogeochemical and climate models holds substantial promise for enhancing our understanding of global ecological dynamics. These models can provide a detailed perspective on the metabolic contributions of marine microorganisms to biogeochemical cycles and climate patterns, offering a more accurate representation of the complex interplay between marine ecosystems and the Earth system.

Despite significant advancements facilitated by cGEMs, challenges remain in their application. The inherent complexities of marine microbial communities, coupled with limitations in current datasets and computational tools, present obstacles to accurate modeling and prediction. Continuous efforts to refine cGEM methodologies, enhance data quality, and develop innovative computational strategies are crucial for overcoming these challenges. Collaboration between ecologists, bioinformaticians, and economists is imperative to translate the insights derived from cGEMs into actionable strategies within the nature-based economy.

In conclusion, the applications of marine microbial community models, as exemplified by cGEMs, represent a critical intersection of scientific discovery and innovation in economic valuation methods for natural capital. These models offer unprecedented insights into the complex dynamics of marine microbial communities, contributing significantly to our understanding of ecological processes and their economic implications. As we move towards a more sustainable and nature-centric economic model, the integration of scientific insights with economic frameworks becomes increasingly vital. We believe that the ongoing advancement and application of cGEMs will play a crucial role in shaping a sustainable future that integrally links the health of marine ecosystems with our economic prosperity and ecological well-being.

Code availability

Supplementary Notebook 1 and all the python code employed within can be found in the following repository: https://github.com/Robaina/oil_spill_example

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