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RECEIVED 07 May 2023

ACCEPTED 16 June 2023

PUBLISHED 30 June 2023

## CITATION

Peixoto RS and Voolstra CR (2023)

The baseline is already shifted:  
marine microbiome restoration  
and rehabilitation as essential tools  
to mitigate ecosystem decline.

*Front. Mar. Sci.* 10:1218531.

doi: 10.3389/fmars.2023.1218531

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# The baseline is already shifted: marine microbiome restoration and rehabilitation as essential tools to mitigate ecosystem decline

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Climate change is turning formerly pristine ecosystems into ever-changing states, causing major disturbance and biodiversity loss. Such impacted marine ecosystems and organisms exhibit clear microbiome shifts that alter their function. Microbiome-targeted interventions appear as feasible tools to support organismal and ecosystem resilience and recovery by restoring symbiotic interactions and thwarting dysbiotic processes. However, microbiome restoration and rehabilitation are perceived as drastic measures, since they alter 'natural relationships'. What is missing from this notion is that microbiomes already drastically differ from any pre-anthropogenic state. As such, our perception and definition of even 'pristine states' may in fact represent an already disturbed/derived condition. Following this, we argue that restoring and rehabilitating marine microbiomes are essential tools to mitigate ecosystem and organismal decline.

## KEYWORDS

microbiome restoration, rehabilitation, probiotics, microbial therapy, climate change, anthropogenic impacts, biodiversity loss

## Background

Microorganisms continue to shape our planet (Cavicholi et al., 2019; Lopez et al., 2019) and the biology of most living organisms (Bosch and McFall-Ngai, 2011; McFall-Ngai et al., 2013; Wilkins et al., 2019; Santoro et al., 2021). Consequently, microbiology thus far has focused on exploring microbial diversity, distribution, and response to environmental change (Lozupone and Knight, 2007; Rachid et al., 2012; Gilbert et al., 2014; Fonseca et al., 2018). In addition, current research explores to utilize microbial-based

capacities for restoration (de Jesus et al., 2015; Berg et al., 2021; Peixoto et al., 2021), biotechnological application (Cross et al., 2019; Modolon et al., 2020; Vilela et al., 2021), and promotion of organismal health and resilience (Sanders et al., 2019; Woodhams et al., 2020; Berg et al., 2021; Peixoto et al., 2021), predominantly from an anthropocentric point of view (Cavicchioli et al., 2019).

Probiotics and other microbial therapies (Daliri et al., 2018; Wegh et al., 2019; Peixoto et al., 2022), for example, have been administered to a variety of organisms, including humans (Liu et al., 2021), plants (do Carmo et al., 2011; Berg et al., 2020; Bziuk et al., 2022), and wildlife (D'Alvise et al., 2012; Küng et al., 2014; Hoyt et al., 2019; Rosado et al., 2019; Daisley et al., 2020), representing a growing industry currently worth ~USD15 billion per year (van den Nieuwboer et al., 2016).

Despite the favorable prospect of microbiome interventions, from an ecological rather than an economic perspective, we must consider that microbes themselves are threatened by global change. In particular host-associated beneficial microbial symbionts - the very agents to counter ecological decline (Peixoto et al., 2022) - may be as sensitive to environmental impact as animals and plants (Cavicchioli et al., 2019; Averill et al., 2022). Recent surveys have emphasized that Earth's microbial biodiversity is under threat and highlighted the urgency of conserving and restoring soil microbiomes (Averill et al., 2022), although these concepts are still poorly explored for marine conservation.

Notably, global change-related impacts, such as warmer temperatures, droughts, and weather extremes, have been causing the emergence and spread of new pathogens (Robert et al., 2015; Nnadi and Carter, 2021; Tiedje et al., 2022) as well as an overall increase of pathogens in ecosystems such as coral reefs (Haas et al., 2016). Decreased host-specificity and the increase of pathogens, hypermutators, and antimicrobial resistance genes were defined as signatures of declines of plant microbiomes in the Anthropocene (Berg and Cernava, 2022). Such microbiomes are termed 'pathobiomes' in contrast to 'beneficiomes', a term used to signify microbes that are members indicative of a healthy microbiome, where 'healthy' is defined as the absence of signs of disease and/or a dysbiotic process (Figure 1).

Marine ecosystems have been heavily impacted by human activities (Jackson et al., 2001), and even the most remote deep-sea areas can be heavily contaminated with pollutants (Vilela et al., 2022). The impact can be at the organismal or at the ecosystem level. Most notably, coral reefs have been decimated by ongoing environmental impact over decades (Eddy et al., 2021), compounded by forecasts of massive future losses in the coming decades driven by global climate change and local anthropogenic impact (Knowlton et al., 2021) that threaten their very existence (Kleypas et al., 2021). Likewise, this has impacted and will further affect marine microbiomes (associated with marine organisms or ecosystems), including the possible extinction of an unknown diversity of obligate microbial symbionts that are yet to be discovered (Weinbauer and Rassoulzadegan, 2007). Microbiomes are characteristic microbial communities that shape or compose specific ecological niches, establishing dynamic interactions with

species, populations, and ecosystems at large, being crucial for their functioning and health (Berg et al., 2020).

## 'The shifting baseline trap' - pristine-like marine ecosystems and microbiomes no more

Dysbiotic processes, i.e., the breakdown of symbiotic interactions between a host and its associated microbiome (Petersen and Round, 2014), are frequently triggered by environmental disturbance (Egan and Gardiner, 2016). In such cases, beneficial or commensal microbes that are sensitive to shifts in environmental conditions are replaced by pathogens or opportunistic microbes (Sweet and Bulling, 2017). Microbiome restructuring towards a more pathobiomic assemblage is hypothesized to be the main cause of coral disease and is also apparent in coral bleaching caused by thermal stress (Boilard et al., 2020). The notion that microbiome deterioration underlies the deterioration of organismal and, by extension, ecosystem health, is prevalent to the point where diseases traditionally considered as non-communicable (non-transmittable), such as cardiovascular diseases, cancer, or certain lung diseases in humans, are now discussed to harbor a microbiome component, e.g. with regard to disease transmission or even the underlying cause of the disease (Finlay et al., 2020). Besides corals, other marine organisms such as kelps, seagrasses, fishes, and mangrove plants have also been highly affected by anthropogenically-driven dysbiotic processes (Harvell et al., 1999; Filbee-Dexter et al., 2016; Minich et al., 2018; Conte et al., 2021; Tye et al., 2022).

Mass mortality of marine organisms can cause severe shifts in ecosystem structure, prominent examples being the widespread lethal stony coral tissue loss disease (SCTLD) (Precht, 2021), the devastating (and anthropogenic impact-associated) sea star wasting disease (SSWD) decimating populations of asteroids (Echinodermata) (Hewson et al., 2019; Jaffe et al., 2019), or the climate change-associated spread of oyster diseases (Cook et al., 1998; Soniat et al., 2009; Epstein, 2010). All of these examples of marine die-offs are associated with microbiome changes (Aquino et al., 2020; Clark et al., 2021).

These marine organisms are critical for their respective marine ecosystems and "planetary homeostasis" (Dyke and Weaver, 2013). Consequently, altered microbiome states of these organisms are at the core of alarming losses of marine biodiversity (Peixoto et al., 2022), and microbiomes will continue to shift towards more pathogenic assemblages in pace with ongoing global change. Importantly, increasing rates of environmental change induced by human activity have been apparent for the better part of the last century for many anthropogenic actions considered (e.g., fertilizer consumption, transport, tourism, etc.) (Steffen et al., 2011). As such, we fall victim to the 'shifting baseline trap', i.e. the perception that the already altered state experienced by the previous generation is/was the pristine state, even though in reality it already represented a disturbed/derived condition (Soga and Gaston, 2018).

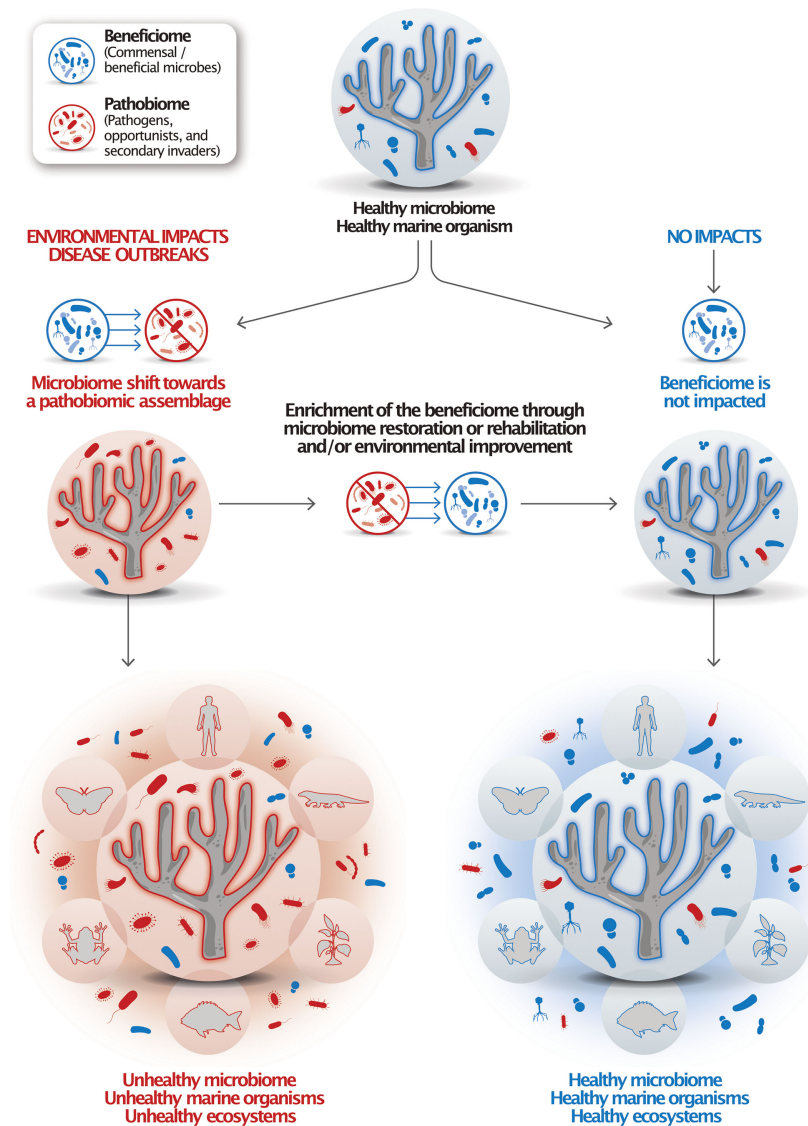


FIGURE 1

The ‘pathobiome’ and ‘benefiome’ as types of microbial assemblages to indicate deteriorated and healthy marine organisms. Healthy marine organisms harbor and rely on healthy microbiomes. When impacted by stressors, these microbiomes tend to shift towards a pathobiotic assemblage, which can cause disease and, ultimately, death. Microbiome rehabilitation is focused on through the use of retaining or restoring a healthy microbiome, the benefiome, which could be achieved through the application of probiotics, microbiome transplants, or other microbial therapies. Healthy organisms interact with other marine organisms and contribute to ecosystem health. Under the One Health concept, marine organismal and ecosystem health are connected to terrestrial organism and ecosystem health.

## Microbiome stewardship to attain rehabilitation

Even if current conditions are reversed immediately, in many cases, it is too late for “nature to heal itself” (Duarte et al., 2020; Knowlton et al., 2021), and significant losses are expected over the coming years before things (may) get better (Kleypas et al., 2021). Although any solution needs to incorporate reducing CO<sub>2</sub> emissions and mitigating local stressors eventually, active restoration efforts are equally important to buffer the gap and buy time (Knowlton et al., 2021; Voolstra et al., 2021). Our objective and obligation must ensure that sufficient foundational species and genetic diversity survive to assist in the long-term recovery of marine ecosystems once carbon neutrality is reached.

Marine probiotics have recently been introduced as a means to support conservation and restoration of marine wildlife (Peixoto et al., 2017; Peixoto et al., 2021; Voolstra et al., 2021; Peixoto et al., 2022). Such ‘enhanced restoration’ or rehabilitation (Voolstra et al., 2021, 2023) extends and clarifies the concept of restoration because i) it is unclear whether restoration to past (microbial) configurations under current environmental conditions is an actual remedy for stress susceptibility and also due to ii) uncertainties associated with the nature of past “pristine” microbial configurations (given our shifting baseline perception and ignorance what “pristine” actually means or signifies; see below). Although marine microbiome manipulation is still in its infancy (Blackall et al., 2020), integrated actions and global networks have been built to accelerate such research and development in the face of alarming marine

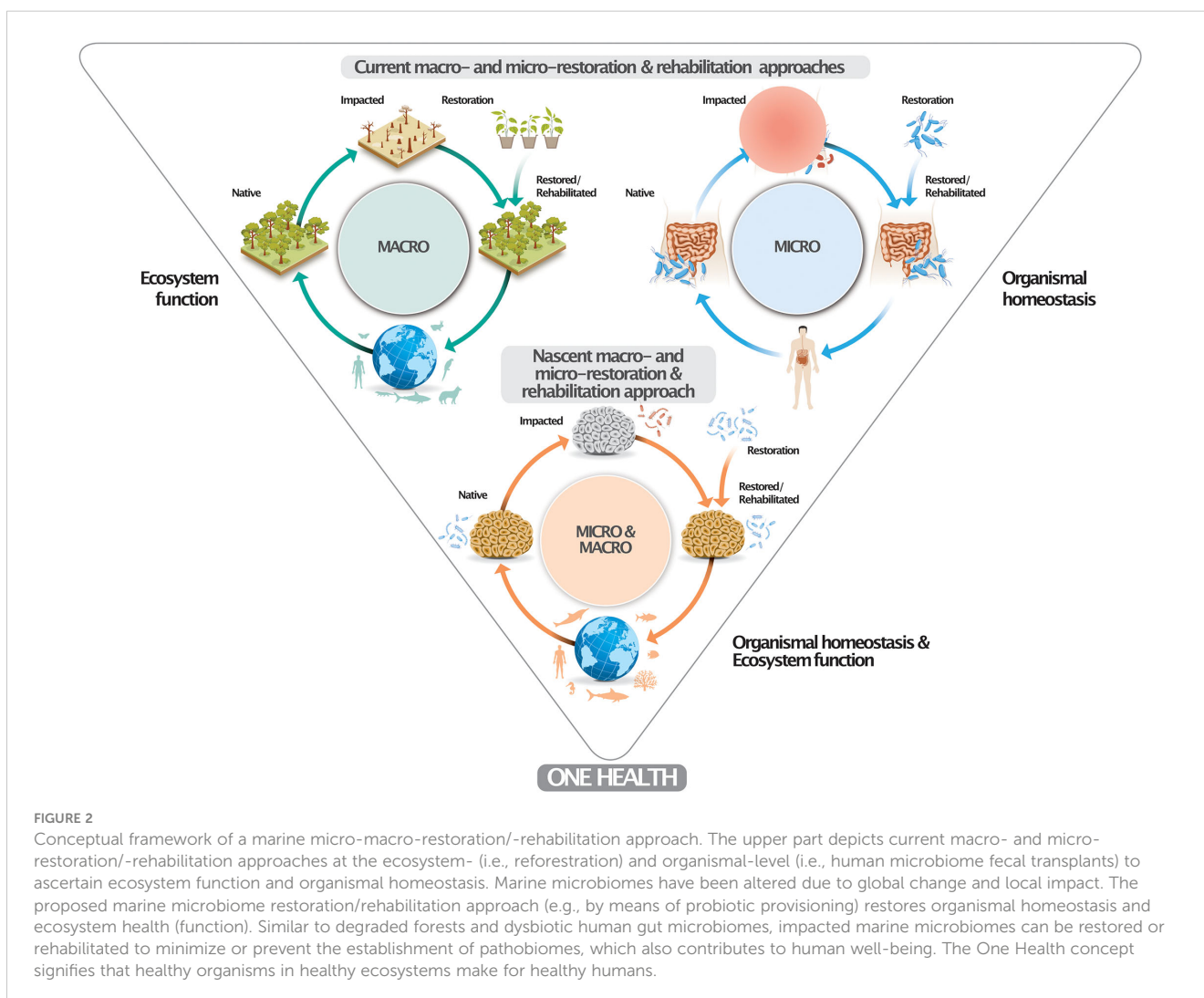
biodiversity losses (Allard et al., 2020). The high toll of inaction must be weighed against the potential caveats associated with microbial manipulation. A roadmap for the risk assessment and safe development of probiotics to protect wildlife has been recently proposed (Peixoto et al., 2022).

Here we extend such reasoning and propose that marine conservation should generally consider microbiomes as one of its key components. Such efforts should not be defined as microbial manipulation since the eventual aim is the reversal of deteriorated states of organisms and ecosystems to more pristine states by means of the restoration/rehabilitation of associated/underlying microbiomes (Figure 2). It is crucial to highlight that already degraded ecosystems are unlikely to harbor “pristine-like” microbiomes (Leite et al., 2018) and that there is no certainty of what such pristine microbiomes would look like. Consequentially, an altered (in a sense manipulated) microbiome is already present in many marine ecosystems, often enriched with potential pathogens. We are witnessing a continuous alteration of microbiomes, in line with the pace and magnitude of environmental change. Accordingly, microbiome restoration/rehabilitation is a way to minimize impacts caused by ongoing

changes, rather than it being the cause of these changes. If we accept microbiome change as a consequence of continuous environmental change, our obligation should ensure such changes are towards a less pathogenic, neutral or, ideally, beneficial assemblage. The correct use of these terms and concepts is key for the development and public acceptance of the nascent field of microbiome stewardship (Peixoto et al., 2022) with parallels to terrestrial restoration/rehabilitation (e.g., reforestation) (Nave et al., 2018; Bziuk et al., 2022) and medical approaches (e.g., fecal transplants) (Daliri et al., 2018) (Figure 2). Microbes are a key factor connecting and supporting humans, animals, and ecosystem functioning under the ‘One Health’ concept (Trinh et al., 2018), representing a docile target for restoration/rehabilitation (Peixoto et al., 2022).

### In a nutshell

Innovative efforts to conserve, restore, and rehabilitate marine microbiomes can contribute to the protection of marine ecosystems and increase the adaptive capacity of marine





organisms and ecosystems to survive climate change (Woolstra et al., 2021; Peixoto et al., 2022). Impacted microbiomes, on the other hand, offer a clear path for opportunistic pathogens to thrive and spread, which may lead to pandemics and wildlife die-offs (Averill et al., 2022; Peixoto et al., 2022; Tiedje et al., 2022). Associated management approaches to rehabilitate degraded/impacted marine microbiomes range from improvement of environmental conditions to probiotic or other microbial-based interventions (Peixoto et al., 2019). Despite the promise of microbiome manipulation, it is often perceived as unnatural and overly intervening. Here we lay out the need to consider (i) how the 'shifting baseline trap', the notion that the previous ecosystem state was pristine, may obscure our sight of long-term ongoing deterioration; (ii) the need to adopt a terminology of 'microbiome restoration', or more accurately 'microbiome rehabilitation', as opposed to the term 'microbiome manipulation'; (iii) the notion that most marine microbiomes are already altered (and potentially damaged). The ongoing debate on whether microbial therapies will cause damage should be replaced by a discussion on how (and whether it is possible) to safely restore them. This notion is still very incipient (or null) for marine ecosystems and not even fully scrutinized for terrestrial systems.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding authors.

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## Author contributions

Both authors contributed equally to this work.

## Acknowledgments

RSP acknowledges funding from King Abdullah University of Science and Technology (KAUST) (grants FCC/1/1973-51-01 and BAS/1/1095-01-01). CRV acknowledges support by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) project number 15951622. CRV and RSP acknowledge funding from KAUST (OSR-2021-NTGC-4984).

## Conflict of interest

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