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Nanotechnology for coral reefs in the

² Anthropocene

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18 Short abstract

- 19 The mounting pressure on coral reefs calls for a rapid push towards innovative actions.
- 20 Nanotechnology could help understand and protect present-day reefs to ensure their survival
- 21 for future generations.



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23 Fig. 1 | Overview of the coral holobiont partners (A), the existing nanotechnologies applied 24 to reef-building corals (B), and promising applications to develop in the near future (C). 25 Coral colonies are composed of clonal cnidarian polyps with a diverse microbiome and 26 engaged in a mutualistic symbiosis with dinoflagellate algae. Together, these organisms form 27 the coral holobiont (A). Among the nanotechnologies applied to coral today are gold 28 nanorods for cryopreservation of larvae, engineered larvae settlement surfaces, antioxidant 29 cerium dioxide nanoparticles, high resolution sensing and coral on a chip models (B). Some 30 of the advances that could benefit coral research and preservation in the future could consist 31 of nanocarriers for targeted drug delivery including lipid-based nanosupplements, 32 nanoparticle-enabled biobanking, small molecule and nanoparticle sensing microfluidics, 33 and 3D biofabrication of coral tissue (organ on a chip) for high throughput interrogations (C). 34 Graphic design credit: Hollie Putnam and Emma Strand

35 Coral reefs in the 21st century

36 Species richness and structural complexity have established coral reef ecosystems as one 37 of the most productive biomes on Earth. The ability of scleractinian corals, i.e. reef-38 building corals, to thrive in oligotrophic regions of our oceans hinges on a fragile equilibrium 39 between the coral polyp —the biological unit of coral colonies—, endosymbiotic 40 dinoflagellate algae (Symbiodiniaceae, housed in a tight intracellular compartment called 41 symbiosome) and a plethora of bacteria, archaea, viruses, endolithic algae and fungi with 42 mutualistic, commensal or pathogenic relationships (estimated between 100-1,000,000 43 cells/cm²). Cross-kingdom exchange of vital nutrients, including photosynthetic carbon, 44 nitrogen and trace metal elements¹ have allowed scleractinian corals to build the calcium 45 carbonate bedrock of tropical and subtropical coastal ecosystems over the last 25 million 46 vears.

47 The constant intensification of anthropogenic activities since the industrial revolution has 48 led to shifting baselines and the impossible task of returning to pristine conditions². Climate 49 change-induced thermal stress, ocean acidification and deoxygenation, combined with 50 coral diseases, eutrophication and pollution, are precipitating the destruction of coral reef 51 ecosystems across the globe. Under business-as-usual practices, coral reef surface area 52 is predicted to decrease by 90% in the next 30 years³. The loss of coral reefs would 53 have devastating consequences on biodiversity, food security, coastal protection, tourism, 54 trade and cultural heritage. Therefore, to rapidly catalyze transformative ocean solutions, 55 the United Nations launched the Decade of Ocean Science for Sustainable Development 56 (2021 - 2030).

Here, we argue that current interventions developed for coral reef conservation, restoration
and rehabilitation could be substantially transformed by leveraging the rapid progress
and multidisciplinarity of nanotechnology.

60

61 What has nanotechnology done for corals so far?

62 Understanding the ecophysiology of scleractinian corals in response to present-day and 63 future climate scenarios is of paramount importance to preserve coral reefs. The 64 foundational mechanisms driving the formation of coral reefs, photosynthesis and 65 biomineralization, take place in host-controlled intracellular spaces characterized by nm to 66 µm-scale gradients of O₂, pH and nutrients⁴. Such fine-scale variations of critical 67 environmental parameters present a grand challenge for coral ecophysiology as most 68 probes and sensors lack the required spatial and temporal resolution. Nanoparticle 69 technology should thus be exploited for improved coral health monitoring. For example, 70 platinum-based nanoparticles combined with ratiometric imaging has been successfully 71 developed to visualize O₂ concentration and flow across the coral tissue surface with nm 72 scale spatial resolution and rapid response time⁵. Dissolved oxygen levels in the coral 73 microhabitats are linked to photosynthesis and energy metabolism, and thus non-invasive 74 nanoparticle-based sensing can help to identify the onset and progression of physiological 75 stress across the coral landscape.

The applications of nanotechnology go well beyond sensors, and new approaches are being developed to actively manipulate processes relevant to coral ecophysiology. For example, reactive oxygen species (ROS) are a key trigger of bleaching and ROS scavengers hold the potential to enhance coral health. As recently shown in experimental trials, redox nanoparticles composed of a ROS-scavenging polymer (Methoxy-poly(ethylene glycol)-b-poly[4-(2,2,6,6-tetramethylpiperidine-1-oxyl)oxymethylstyrene], MeO-PEG-b-PMOT) 82 and antioxidant drugs increased survival of aposymbiotic coral larvae exposed to thermal 83 stress⁶. Moreover, engineered nanoceria (cerium dioxide nanoparticles coated with 84 poly(acrylic acid), PAA-CeO₂) delivered intracellularly to free-living symbiotic algae 85 typically associated with reef-building corals reduced the concentration of ROS when 86 cultures were exposed to thermal stress⁷. Antioxidant treatments could be coupled with 87 "stress-training", i.e. pre-exposure to thermal stress to increase the thermal tolerance of 88 coral genotypes⁸, in coral farm settings to boost acclimatory capacity ahead of reef 89 restoration.

90

91 Another approach to reef restoration consists of fabricating larval settlement and metamorphosis-92 inducing nanoengineered substrates with antifouling characteristics. Coral larval settlement is a 93 complicated process affected by a variety of biotic and abiotic cues, including substrate 94 biochemistry and microbial community dynamics, as well as substrate architecture and 95 light availability. A number of relevant biocompatible nano-substrates and coatings have 96 been designed, such as porous ceramics for larval settlement⁹, self-healing coral cell 97 adhesion promoting coatings^{10.11}, and CeO₂ nanoparticle-based antifouling coating¹². While 98 these success-stories are currently only laboratory-based, they bode well for field 99 deployments and the rapid development of the field promises further innovative 100 approaches. Beyond restoration efforts, recent advances in coral genetic material 101 cryopreservation now enable the preservation of fertilized coral larvae using gold nanorods 102 to absorb laser radiation progressively melting the cryoprotectant medium without 103 damaging the larvae¹³.

104

105 What potential does nanotechnology still hold for corals?

106 Undoubtedly, we are just beginning to exploit the vast potential that nanotechnology holds 107 for coral reef science and conservation. Two decades after the creation of the 108 National Nanotechnology Initiative in 2000, medicine, agriculture and energy sciences have 109 seen a burst in innovations. Now, with the recent kick-off of the Climate Change National 110 Nanotechnology Challenge (January 2023, https://www.nano.gov/nano4EARTH), coral reef 111 research could leverage these exciting developments towards new coral-specific 112 diagnostic tools, rapid testing, high-resolution health monitoring, coral nanomedicines/ 113 pharmacology, novel bio-nano-fabrication and, more generally, to improve the coral 114 research toolkit. We suggest that combining the known beneficial effects of ROS 115 scavenging with lipid-based supplements or liposome encapsulation is a viable way forward to protect corals during periods of stress^{6,7,14,15}. Likewise, the encapsulation of coral probiotic 116 and antibiotic treatments^{16.17} in highly modular, target-specific nanocarriers is an important 117 118 development that will reduce the severity of coral disease outbreaks. Biohybrid 119 nanoengineered materials (biochemistry, geochemistry, architecture, assembly, coating) 120 designed to release biochemical cues could radically improve recruitment success and coral 121 growth. Recent advances in coral cell culture methods^{18,19}, new coral-based applications of 122 microfluidics²⁰ and 3D biofabrication are paving the way towards biohybrid coral models and 123 high throughput systems^{22,22}. Nanotechnology should be integrated with such systems to 124 improve our understanding of molecular trafficking between holobiont partners in relation to 125 environmental change. The successful fusion of nanotechnology and coral science holds the 126 potential for cutting-edge transformative research across the different scales of the coral 127 holobiont. We call for a critical dialogue between the nanotechnology and coral research 128 communities to facilitate fundamental discoveries, and breakthroughs in coral conservation, 129 reef restoration and rehabilitation. True organ-on-a-chip models of coral systems combined 130 with CRISPR/Cas9 gene-editing techniques²³ have the potential to unlock high

throughput interrogations at the molecular level, while nano-enabled biobanking could preserve coral genetic material for future generations. Nanotechnological applications have far reaching consequences for coral research and should be driven by transdisciplinary collaborations to broaden the scope of coral sciences, address the critical issue of reef degradation, and promote innovations needed to safeguard coral reefs for future generations.

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205 Competing interests

206 The authors declare no competing interests.