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Synthetically Assisted Conservation and the Application of Emerging Biological Technologies for the Protection of Biodiversity

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ABSTRACT

New tools of synthetic biology that enable precise manipulation of genomes, metabolic pathways, and ecosystems present new opportunities, risks, ethical dilemmas, and responsibilities for stewards of biodiversity. We argue that the risks and benefits of synthetic biology for use in biodiversity conservation, which we term "synthetically assisted conservation," can be better understood, evaluated, and regulated by precisely defining the techniques in relation to well-established and regulated conservation frameworks: conservation translocation and integrated pest management. Synthetically assisted conservation translocation could include the release of genetically modified organisms for in situ conservation of genes or restoration of ecological functions, while a synthetically assisted application of integrated pest management could involve using genetic modifications propagated through gene drives to remove invasive species. Contextualizing the range of techniques as expansions of these frameworks clarifies how new approaches may impact conservation, facilitating risk assessment and responsible implementation. Decision-making may be informed by existing policy guidance in accordance with national and international regulations on conservation translocation and integrated pest management. Nevertheless, additional policy and evaluative guidelines are needed to keep pace with rapid technological growth and novel issues such as the release of genes (e.g., in pollen or marine-dispersed gametes) separate from live organisms.

1 | Introduction

Despite significant local successes, conservation efforts have not been able to halt the ongoing global loss of biodiversity. *Synthetic biology*—the use of engineering principles to design, modify, or create new biological organisms and systems—offers new opportunities to help abate biodiversity declines (Redford et al. 2013). While many synthetic biology techniques involve genetic modification, the term also includes constructing entire genomes, optimized metabolic pathways, artificial cells, and altering ecological functions. These approaches have largely been ignored or resisted by the mainstream conservation community because of the associated risks, both real and perceived (Redford and Adams 2021). Some proposed applications of synthetic biology for conservation include modifying invasive species to reduce or eliminate their populations (e.g., Leitschuh et al. 2018), augmenting populations of endangered species with lost gene variants (e.g., from cryopreservation) to increase genetic variability (Szuszwalak 2024), and creating proxies of extinct species that have not been in ecosystems for thousands of years (colloquially called "de-extinction") (Seddon et al. 2014; IUCN 2016). Despite risks, synthetic biology tools are increasingly used, often outpacing regulatory guidance (Redford et al. 2019; Schwartz et al. 2024). Synthetically altered organisms continue to be released around the world for agricultural purposes; incomplete understanding of the ecological consequences of these actions can render effective regulation difficult (Redford and Adams 2021). Conservation biologists need to understand both the potential benefits and dangers of using synthetic biology to further biodiversity conservation (Schwartz et al. 2024) so they can make informed decisions and help develop guidance and regulatory frameworks.

Here, we clarify and define applications of synthetic biology to conservation—which we term *synthetically assisted conservation* (see the glossary in Table 1)—and contextualize the techniques as extensions of existing conservation frameworks. We argue that this will help guide effective implementation and risk assessment. We do not advocate for or against the application of synthetic biology to conservation, but we highlight the need for vetting procedures to help evaluate risk and mitigate unintended ecological impacts from the release of synthetically altered organisms for intended conservation benefit. We also assert the importance of clearly distinguishing whether the novel genes or organisms released will be ephemeral or long-term components of the landscape (see "Applications" below) to facilitate decision-making. Careful planning using both Western and traditional ecological and ethical frameworks and clearly distinguishing whether the novel genes or organisms released will be ephemeral or long-term components of the landscape (see "Applications" below) will be required to evaluate risks and benefits and strengthen conservation tools.

Conservationists have long grappled with tools that may carry risks seemingly at odds with conservation goals or other societal concerns. Even the translocation of nongenetically modified organisms for conservation purposes has been opposed based on ethical, welfare, regulatory, socioeconomic, and ecological concerns (Ricciardi and Simberloff 2021; Moehrenschlager et al. 2022). Many of these concerns, however, have been addressed, and the risks have been at least partially mitigated through careful planning, risk assessment, and transparent decision-making, all facilitated by precise definitions (Gaywood et al. 2023).

Two existing conservation frameworks can be expanded to incorporate synthetically assisted conservation. First, the *conservation translocation* framework can be expanded to include *synthetically assisted conservation translocation* of modified organisms (Figure 1). Second, the well-established techniques of *biocontrol* can be supplemented with emerging techniques of *synthetically assisted biocontrol* into an expanded *integrated pest management* framework. These and all frameworks rely on precise language to ensure understanding of complex concepts and transparency in decision-making (Herrando-Pérez et al. 2014). Linguistic precision shapes how we conceive problems, models, and regulatory provisions (Elnathan 2021). In the context of environmental biology and ecology, terminology and language can influence the interpretation of data, making it not just a matter of semantics but a fundamental aspect of scientific integrity, legality, and progress (Herrando-Pérez et al. 2014). While not sufficient for comprehensive governance of all synthetic biology tools and applications in conservation, expanding these two frameworks addresses many of the more immediate applications. Other applications of synthetic biology may not fit neatly into these frameworks and require new terms and guidelines.

2 | Synthetic Biology and Conservation

Although synthetic biology is typically thought of as genetically modifying organisms, the applications are broader: synthetic biology technologies have also been proposed as a means to restore ecological systems (NASM 2016). The establishment of populations of synthetically altered organisms can replace lost ecological functions or maintain genes or gene combinations that would otherwise have been lost from the landscape (Redford and Adams 2021). Introducing new genes into a population can recover threatened species (Barnhill-Dilling et al. 2020) and increase ecosystem resilience to climate change (Van Oppen et al. 2015). Importantly, synthetically assisted conservation is distinct from synthetic biology at large, which is used for a range of economic, aesthetic, medical, and other applications.

Given the complex, challenging, and potentially risk-fraught nature of introducing organisms into natural communities, the Conservation Translocation Specialist Group of the International Union for the Conservation of Nature (IUCN) Species Survival Commission developed guidelines for *conservation translocations* (IUCN 2013). Conservation translocation includes both the processes of moving species within their indigenous ranges (population restoration) and outside them (conservation introductions) for conservation purposes. The IUCN framework clarified the language used to describe different types of conservation translocations, contributing to more effective actions in this field (Gaywood et al. 2023). New techniques merit clarification that the framework can include synthetic biology to enhance conservation translocations.

The parallels between non-synthetic conservation translocations and synthetically assisted conservation actions are compelling.

TABLE 1 | Glossary of key terms.

Term	Definition
Biocontrol	The use of predators, parasitoids, or pathogens to control populations of pests or invasive species
Conservation translocation	The intentional movement and release of a living organism where the primary objective is a conservation benefit (IUCN 2013)
De-extinction	A colloquial term for the recreation of extinct species using genetic technologies; it is a misnomer because genes from other species are used to fill gaps in the target taxon's genetic scaffolding, so the resultant organism is not the same as the extinct model
Integrated pest management	An approach that uses a combination of techniques to control invasive or pest species while minimizing long-term environmental and health risks
Synthetically altered organism	An organism that, without human intervention, would have had a negligible probability of emerging over ecological timescales via spontaneous genetic recombination
Synthetically assisted biocontrol	The use of genetically modified predators, parasitoids, or pathogens to control populations of pests or invasive species
Synthetically assisted conservation translocation	The release or planting into the wild population of genetically modified individuals, or the movement of modified genes into populations that have undergone conservation translocation, for in situ conservation
Synthetic biology	The use of engineering principles to design, modify, or create new biological organisms and systems
Synthetically assisted conservation	The application of synthetic biology to biodiversity conservation

Non-synthetic conservation translocation involves moving organisms into indigenous ranges for population restoration or, in some cases, for conservation introductions to areas where they have not previously occurred (Brodie et al. 2021; Gaywood et al. 2023). Synthetically assisted conservation translocation would similarly involve moving living organisms that have been genetically modified by humans and/or genetically modifying individuals in populations that have been reinforced, reintroduced, or created through conservation translocations to improve population viability. For example, introducing transgenic organisms can help to repopulate parts of former host ranges from which species have been extirpated (Barnhill-Dilling et al. 2020). The techniques of synthetically assisted conservation are varied, and the degree of manipulation or "synthetic-ness" occurs on a continuum (Figure 2). Defining these techniques is critical for shared understanding among scientists, policymakers, and the public. We refer to the synthetic portion of the conservation translocation framework as *synthetically assisted conservation translocation*, which is characterized by the release or planting into the wild population of genetically modified individuals or the movement of modified genes into populations that have undergone conservation translocation for in situ conservation or the restoration of ecological function.

The second major conservation framework that we propose can accommodate synthetic biology is integrated pest management via biological control (*biocontrol*) of invasive species. Integrated pest management seeks to control populations of agricultural pests or invasive species through a combination of methods designed to minimize environmental impacts. These methods include sterile insect techniques and the introduction of native or non-native predators, as well as cultural practices, trapping programs, and chemical controls (European Commission 2024). Such practices originated as a response to the inadequacy of other approaches and the ecological and human health risks of conventional pest management, including the widespread application of poisons. The integrated pest management framework can be expanded to include synthetically assisted biocontrol, offering an expanded range of tools (Figure 1). Some of these techniques offer benefits such as unprecedented ecological precision. For example, engineered population suppression of gene drives could remove populations of invasive species on islands (Leitschuh et al. 2018; Kelsey et al. 2020) with no effects on sympatric native taxa. This contrasts with many non-synthetically assisted biocontrol methods, such as the use of broad-spectrum poisons that can affect numerous nontarget species (Van den Brink et al. 2018). However, synthetic techniques are not risk-free. For example, engineered individuals that escaped from controlled invasive populations on islands could threaten mainland populations where the same species is native. And yet, standard biocontrol approaches also entail risk; the introduction of exotic weevils to control spotted knapweed in the western USA, for example, provided food subsidies to mice whose elevated populations threaten humans with zoonotic disease (Pearson and Callaway 2006). Thus, synthetically assisted biocontrol and standard biocontrol both present potential benefits and risks that must be weighed in the context of conservation and other societal goals.

3 | Novelty Versus Augmentation

When are synthetically altered species considered novel organisms versus augmentations of existing organisms, and when does it matter? This is an example of a classic philosophical quandary,

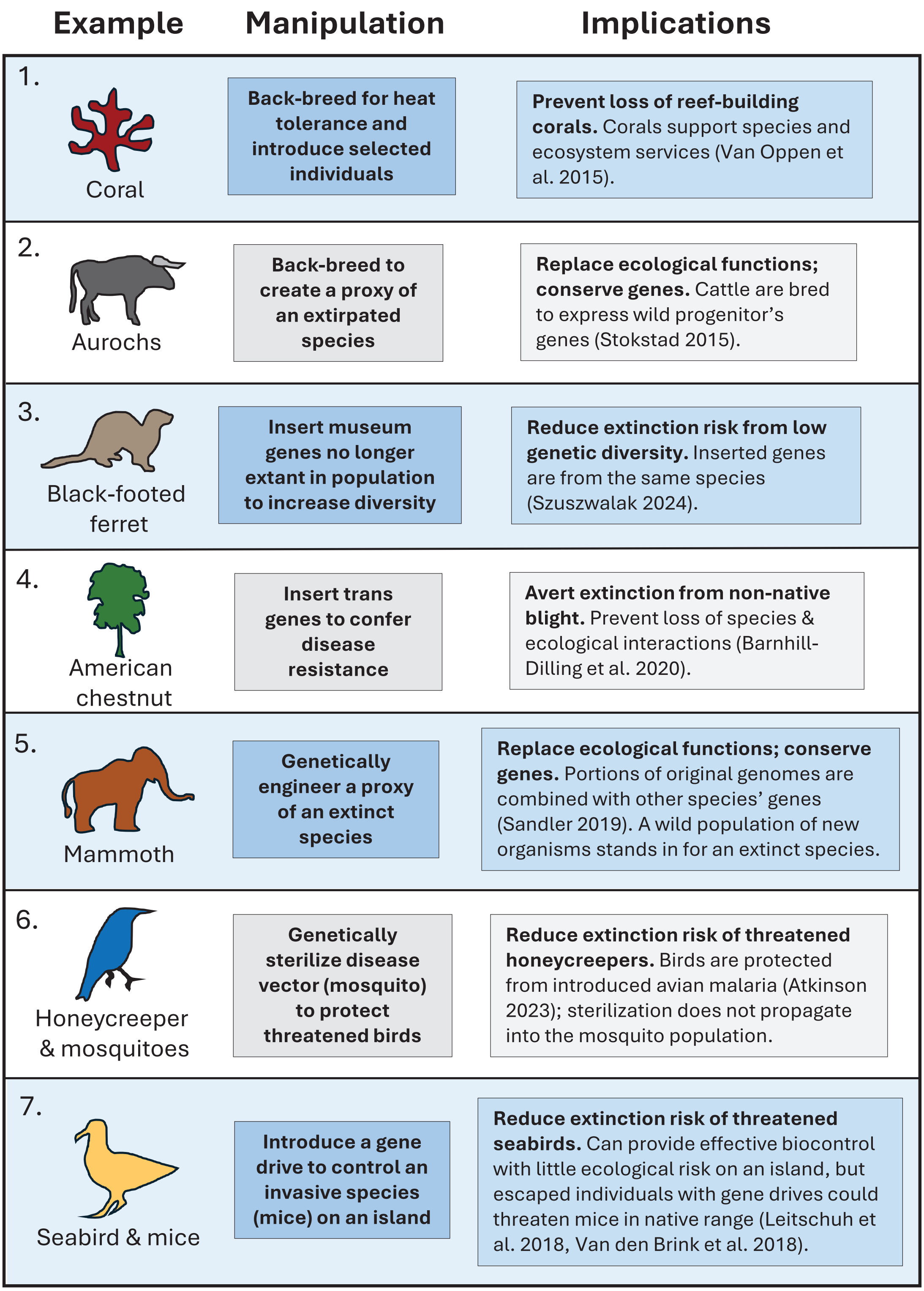

FIGURE 1 | Example scenarios illustrating the range of synthetically assisted conservation applications and their relationship to the conservation translocation and integrated pest management frameworks.

"The Sorites Paradox," describing the difficulty in determining the degree of manipulation beyond which a thing becomes a new kind of thing rather than an altered version of the original (Hyde and Raffman 2018). Recognizing that there are no simple or general solutions to this ancient paradox, we outline context-specific factors to support conceptually and empirically informed decisions about where an organism falls along the continuum between "natural" and synthetic.

As an operational definition, a *synthetically altered organism* is one that, without human intervention, would have had a negligible probability of emerging over ecological timescales via

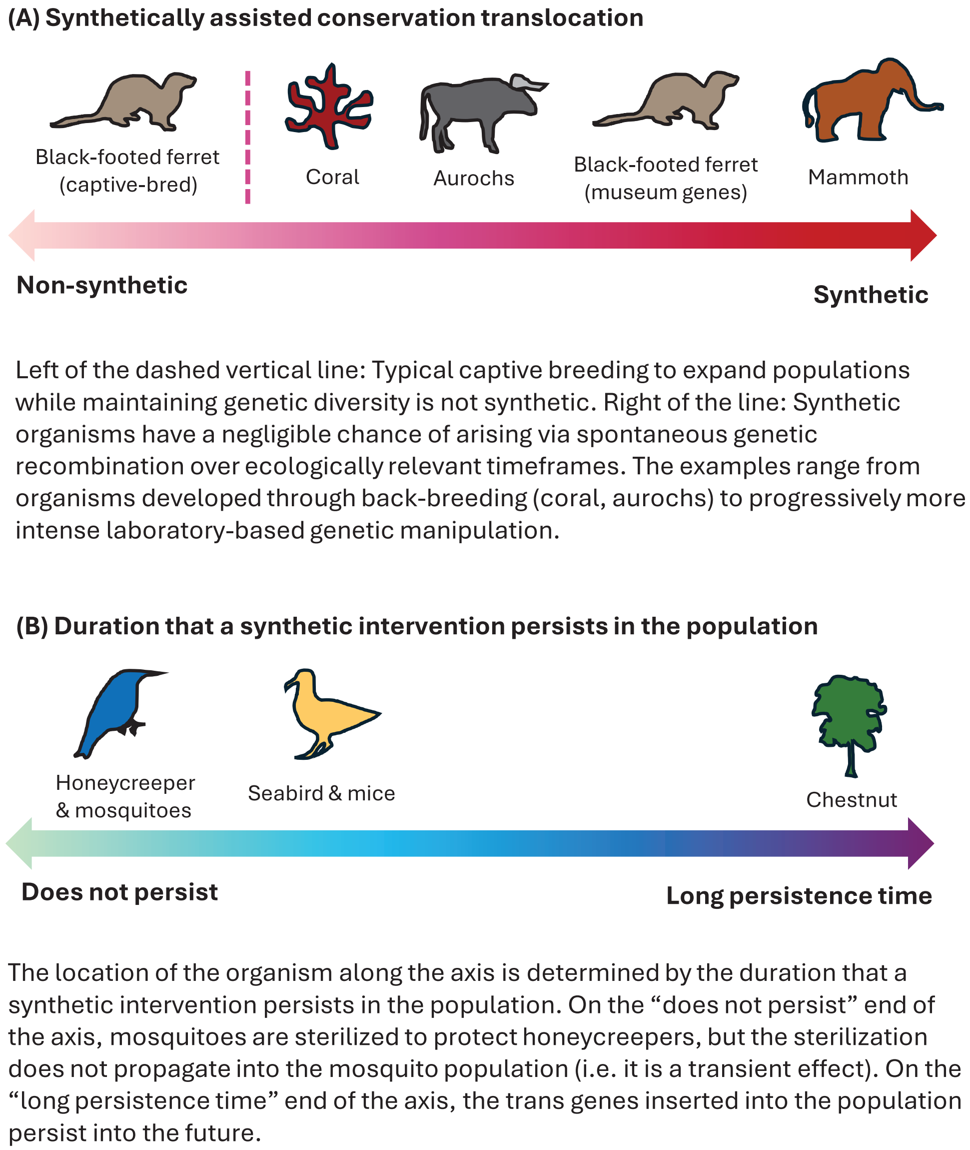

FIGURE 2 | Spectra of the degree of synthetic-ness in potential conservation applications (A) and the persistence time of the synthetic modifications on the landscape (B).

spontaneous genetic recombination. Considerations about the degree of synthetic alteration could include the process or mechanisms by which augmentation occurred and the outcomes, or how much those processes altered the organisms' phenotype and function. At the synthetic end of the continuum are organisms that have been heavily altered by laboratory-based manipulation, leading to very different phenotypes and functions that would not have arisen via unassisted evolution. At the other end of the continuum are organisms with only minor alterations that induce relatively little phenotypic or ecological change. Complicating the situation, however, is the fact that even small genetic changes can have large phenotypic influence.

The mechanism by which the augmentation occurred can be broadly divided into laboratory-based direct genetic manipulation versus artificial selection via back-breeding. Genetically modified organisms are typically considered more synthetic than those created by traditional breeding. Yet both laboratory-based genetic manipulation and back-breeding can induce changes, either large or small. Back-breeding generally involves artificial selection via traditional breeding (rather than laboratory-based genetic modification) over a few generations, typically leading to relatively small phenotypic changes and genotypes within the range of variability of the original species. Mutagenesis can also be employed to increase genetic diversity (Butler et al. 2015), potentially with large impacts on the organisms' function. Genetic engineering can produce organisms with novel phenotypes and functions, for example, creating proxies of extinct species that are, in fact, combinations of the extinct species and one or several extant relatives. Alternatively, more targeted genetic modifications can be employed, such as editing a single gene or base pair; these approaches might be considered more synthetic, but the departure from "naturalness" might, in fact, be more minor, especially given the prevalence in nature of horizontal gene transfer across even distantly related lineages (e.g., Irwin et al. 2022). In some cases, these changes even make the organisms more functionally similar to how they were before human intervention; for example, genetic modifications can make native trees resistant to human-introduced pathogens (Barnhill-Dilling et al. 2020) and therefore able to once again be functional participants of the forest community. Such organisms are synthetic if unlikely to arise via natural genetic recombination over ecological timeframes. In order for the release of such organisms into the wild to be considered synthetically assisted conservation translocation, they would need to be justified either by the restoration of ecological function or the in situ conservation of genes or gene combinations that are threatened on or lost from the landscape.

Overall, the complexity of such issues highlights the importance of developing international guidance and policy that can help ensure the standardization of definitions and approaches (Kelsey et al. 2020). We argue that the metric of interest should be, not the mechanism or process or alteration, but rather the "phenotypic functional change," or the degree to which the organisms' phenotypes have been altered in ways that affect their ecological function (cf. Brodie et al. 2018).

4 | Applications

As part of an interdisciplinary working group on the application of synthetic biology to conservation, we developed example scenarios to illustrate the range of synthetically assisted conservation applications (Figure 1). The first five scenarios constitute ways by which conservation translocation can be enhanced through *synthetically assisted conservation translocation* techniques when genetically modified individuals are translocated. This includes genetic manipulation via hybridization to promote traits that enhance resilience to anthropogenic changes (Scenario 1), both via back-breeding (Scenario 2) and via molecular techniques such as inserting genes from preserved conspecific specimens (Scenario 3) or other species entirely (Scenario 4). Synthetically assisted conservation translocation would also include more extreme scenarios (e.g., Scenario 5) where entirely new organisms have been created; this would be the farthest towards the synthetic end of the continuum (Figure 2).

Scenarios 2 and 5 show situations colloquially referred to as "de-extinction." Contrary to what this vernacular term implies, extinct species are not resurrected; instead, related species' genomes support inserted genes from the target taxon (Scenario 5). The resulting organisms are putative ecological and genetic proxies rather than exact recreations. Alternatively, genetic manipulation could be done by back-breeding—using crosses and back-crosses to try to express particular gene combinations to approximate ancient phenotypes (e.g., Scenario 4). For example, there have been efforts to back-breed European cows to create something akin to their extinct wild progenitor, the aurochs (*Bos primigenius*) (Stokstad 2015).

The remaining scenarios (6 and 7) expand the integrated pest management framework. They fall into the category of synthetically assisted biocontrol rather than synthetically assisted conservation translocations because the organisms of conservation concern are not the ones being translocated or genetically altered but rather are the ones that will benefit from such interventions. For example, introducing genetically modified mosquitos or mosquitos inoculated with parasitic bacteria to Hawai'i (where mosquitos are not native) could reduce populations and protect endemic birds from avian malaria (also not native) (Atkinson 2023) (Scenario 6). Gene drives for eliminating invasive mice from islands where they threaten native seabirds (Scenario 7) represent an even more intensive level of genetic manipulation, one where the invasive population could feasibly be completely eliminated (Leitschuh et al. 2018).

These biocontrol scenarios raise the question of whether *process* or *product* should define synthetic-ness. Biocontrol is intended to eradicate invasive species or disease vectors; the transgenes or introduced microbes are not intended to become permanent residents of the landscape. So, if synthetic-ness is measured in part by the degree of genetic manipulation (Figure 2), then Scenarios 6 and 7 would indeed be considered synthetic, as discussed above. However, if synthetic-ness is measured in terms of whether transgenes will be present in the ecosystem at the conclusion of the biocontrol effort, then neither of the techniques would be synthetic. This distinction between process and product is already manifest in legal systems pertaining to the genetic modification of organisms. Existing European Union laws, for example, emphasize the techniques used in genetic modification, requiring approval for any organism created through specific genetic engineering processes regardless of their final characteristics (Runge et al. 2001). The United States, however, regulates organisms based on the traits they exhibit or the risks they might pose, regardless of whether synthetic biology or conventional techniques were used in their development (Runge et al. 2001).

5 | Conclusions

The tools of synthetic biology are powerful, and their use continues to expand, particularly in human medicine and agriculture. Only by understanding and engaging with the technologies of synthetic biology can conservationists hope to develop and shape applications to biodiversity conservation. The definitions we present show how human-induced movements of genes and genetically engineered organisms for conservation purposes can be viewed as extensions of existing frameworks for conservation translocation and integrated pest management. We propose that expanding existing frameworks in this way is useful to clarify communication and improve understanding (Herrando-Pérez et al. 2014, Elnathan 2021) both within the conservation community and among stakeholders, scientists, policymakers, and the public.

Such clarity will be essential as regulatory policies surrounding synthetically assisted conservation develop. Though several international treaties and protocols relate to the transfer (including release into the wild) of genetically modified organisms, these tend to predate recent technical advances such that many synthetically assisted conservation techniques could face policy and regulatory ambiguity (Redford et al. 2019). The Cartagena Protocol, for example, regulates the release of "living [genetically] modified organisms," focusing on risks to human health and biodiversity (CBD 2000). But the agreement is now more than a quarter century old and does not cover technologies such as synthetic metabolic pathways or the release of modified gametes (e.g., in pollen or marine-dispersed gametes) separate from living organisms (which would also not fit into the frameworks described here). Moreover, the protocol addresses potential threats to biodiversity from modified organisms without an accompanying assessment of potential benefits to conservation, which is critical when threats to conservation are so extensive that we must consider all possible strategies for conservation against the risks of nonaction. Treating synthetically assisted conservation translocation as an enhancement of traditional forms of conservation translocation and synthetic-assisted biocontrol as a tool of integrated pest management provides some policy guidance for the use of these strategies. The IUCN Conservation Translocation guidelines inform the usage of that set of techniques (IUCN 2013), while several national (Peshin et al. 2014) and international (European Commission 2024) policies guide or coordinate the application of integrated pest management.

Synthetically assisted conservation should not replace existing ecological and in situ conservation guidelines. Synthetically assisted conservation offers tools that could help prevent the extinctions of some of the myriad species that will not be able to adapt quickly enough to keep pace with global change. Land managers and conservationists navigate complex dilemmas involving conflicting values, duties, and consequences that make it challenging to determine the most effective and morally appropriate courses of action. By clarifying the concepts and techniques of synthetically assisted conservation, this paper intends to help maximize their potential benefits for biodiversity.

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Data Availability Statement

The authors have nothing to report.

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