CellPress
REVIEWS

Review

Biological Concepts for the Control of Aquatic Zoosporic Diseases

Thijs Frenken [iD],[1,*] Ramsy Agha,[1,5] Dirk S. Schmeller,[2,5] Pieter van West,[3,5] and Justyna Wolinska[1,4]

Aquatic zoosporic diseases are threatening global biodiversity and ecosystem services, as well as economic activities. Current means of controlling zoosporic diseases are restricted primarily to chemical treatments, which are usually harmful or likely to be ineffective in the long term. Furthermore, some of these chemicals have been banned due to adverse effects. As a result, there is a need for alternative methods with minimal side-effects on the ecosystem or environment. Here, we integrate existing knowledge of three poorly interconnected areas of disease research – amphibian conservation, aquaculture, and plankton ecology – and arrange it into seven biological concepts to control zoosporic diseases. These strategies may be less harmful and more sustainable than chemical approaches. However, more research is needed before safe application is possible.

Aquatic Zoosporic Diseases and Biological Control

Emerging infectious diseases (see Glossary) present a worldwide threat to food security and ecosystem health [1,2]. Amongst these are zoosporic diseases, caused by fungi or water molds (oomycetes) that require a wet or moist environment to survive and which are able to infect a diverse range of organisms, including prokaryotes, fungi, plants, arthropods, and vertebrates [3,4]. The infectious stages of zoosporic pathogens (i.e., zoospores) use flagella to actively swim and potentially navigate towards suitable hosts [5]. After location, they attach to and penetrate host cells, and extract nutrients from the host. The encysted zoospore then gradually develops into a sporangium, a reproductive structure that, once mature, releases new zoospores into the water [6,7]. Research has focused largely on the devastating impact of zoosporic diseases on crop yields, such as infection of potatoes by *Phytophthora* [8]. However, zoosporic diseases also represent a serious threat to **biodiversity** and **ecosystem services** in aquatic environments, and through that pose a substantial threat to human wellbeing [1].

Aquatic zoosporic diseases are caused by parasites or **sapronotic infectious agents** which are widely distributed in marine and freshwater habitats. They affect a broad range of organisms (Box 1) which are generally killed or severely weakened upon infection [4,9]. In fact, aquatic zoosporic diseases have drawn attention for posing a substantial risk to amphibian biodiversity [10] and dramatically reducing yields of fish farms and algal mass production facilities [11,12]. For example, in Korea alone, economic losses by oomycete infections in sea farms producing algae for human consumption are estimated to be well over US$10 million per year [13]. Losses in salmon production due to oomycete infections are at least $6.5 million per annum in Scotland [14]. Losses in key biological elements due to emerging diseases will also alter whole ecosystems, incurring an as yet unknown cost for society [15]. Current methods to control aquatic zoosporic diseases are mainly focused on the use of chemicals [11,16]. However, chemical treatments pose a high risk of toxicological side-effects on humans or wildlife [17–19]. For example, the use of the fungicide itraconazole can result in lethal side-effects on the very species targeted by conservation efforts [17,20] or may even lead indirectly to an increased incidence of fungal infections due to long-term adverse effects on amphibian defenses [21].

Highlights

Aquatic zoosporic diseases pose a threat to biodiversity, ecosystem services, and economic activities.

Current control methods are based on the use of chemicals that have large negative side-effects.

To support the development of alternative biological control strategies, we outline seven general biological concepts to control zoosporic diseases.

We discuss some of the research required to successfully apply biological control strategies in the future.

[1]Department of Ecosystem Research, Leibniz-Institute of Freshwater Ecology and Inland Fisheries, Berlin, Germany
[2]ECOLAB, Université de Toulouse, CNRS, INPT, UPS, Toulouse, France
[3]Aberdeen Oomycete Laboratory, College of Life Sciences and Medicine, Institute of Medical Sciences, University of Aberdeen, Aberdeen, UK
[4]Institute of Biology, Freie Universität Berlin, Berlin, Germany
[5]These authors contributed equally to this work

*Correspondence:
thijs.frenken@gmail.com (T. Frenken).

Box 1. Description of the Cases

Amphibians

Amphibians are critical components of both aquatic and terrestrial environments, acting as important indicators of environmental sensitivity [115]. For instance, amphibians can regulate mosquito recruitment or other potential pest species in wetlands, and also affect pollination through predation on arthropods [116]. Changes in amphibian community composition and abundance can thus impact overall ecosystem functioning [117]. Amphibians are facing an extinction crisis estimated to threaten over one-third of all species; this represents the greatest potential biodiversity loss of any vertebrate class since the Cretaceous mass extinction [118,119]. The zoosporic disease chytridiomycosis caused by chytrid fungi, for example *Batrachochytrium dendrobatidis* (*Bd*) and *B. salamandrivorans*, can eradicate over 50% of local amphibian species within 4–6 months after first infection establishment [119,120]. Moreover, *Bd* was able to spread rapidly over the entire South American continent in about 20 years at a rate of 25–282 km per year [121]. A global quantitative assessment of this panzootic demonstrates its role in the decline of at least 501 amphibian species over the past half-century, including 90 presumed extinctions [122].

Fish

Fish play an important role in top-down processes of aquatic ecosystems by controlling growth of underwater plants, plankton, and macroinvertebrates [123,124]. Currently, 80 million tons of global fish production comes from aquaculture [125], and its share in human protein diet is expected to increase [126,127]. Fish production is threatened by a variety of zoosporic diseases, including many species of oomycetes such as *Saprolegnia parasitica* and *Aphanomyces invadans* [3,14]. Diseases in fact constitute the largest cause of economic losses in aquaculture [128]. In catfish and trout production systems, diseases are responsible for about 40–50% of total fish death, and at least 10% of all hatched salmon in the aquaculture industry succumb to *Saprolegnia* infections [14,128]. Efficient and sustainable ways of controlling fish diseases are therefore paramount to the future success (and economic viability) of the aquaculture industry [11].

Plankton

Plankton are microscopic organisms that inhabit all aquatic ecosystems. Phytoplankton (eukaryotic algae and cyanobacteria) represent the base of most aquatic food webs, acting as the main primary producers in marine and freshwater ecosystems, accounting for about 50% of global carbon fixation [129]. Several phytoplankton taxa are used for the production of biofuels and other valuable compounds, such as polysaccharides, carotenoids, and lipids for commercial use [130,131]. Phytoplankton-based mass production systems are often infected by chytrids and oomycetes, with up to 64% reduction in yield potential [132].

Some of the applied chemicals have been banned by transnational regulations, as was the case with malachite green in 2002, the most commonly used chemical to treat zoosporic infections in aquaculture [18,22]. Also, some of the applied chemicals may not remain effective in the long term, due to the rapidly developing resistance of zoosporic pathogens towards fungicides [23]. As a result, there is an urgent need for alternative methods capable of controlling zoosporic diseases with minimal effects on the environment.

Here, we review general methods of **biological control** that have the potential to limit or prevent aquatic zoosporic diseases. We use a broader definition of biological control than the more classical one, which focuses solely on the use of natural enemies to eliminate pests. Here, we use biological control to encompass all control strategies that involve a biological component, that is, approaches that apply understanding of organisms and their ecological interactions within an ecosystem, to eliminate or reduce unwanted organisms. Our conceptualization stems from existing knowledge of three poorly interconnected areas of aquatic zoosporic disease research: amphibian conservation, aquaculture, and plankton ecology (Box 1, Figure 1). These cases were chosen to cover the different biological control strategies (similar strategies might still apply to other zoosporic diseases, not covered in this review, infecting e.g., crustaceans, crayfish, and shellfish [14,24–26]). We also discuss some future challenges that are of immediate importance to safely implementing these biological control methods **in situ**. We thus aim to stimulate the development and application of new tools that offer alternatives to the use of chemicals while effectively controlling zoosporic diseases.

Glossary

Biodiversity: diversity of life forms, for example, indicated by the number of different species.

Biofuel: fuel produced from biological materials (in contrast to fossil fuels which are produced by geological processes), for example, from plants or plankton.

Biological control: an approach that applies understanding of organisms and their ecological interactions within an ecosystem to eliminate or reduce unwanted organisms.

Dilution effect: a phenomenon observed in communities comprised of species with different susceptibility to a pathogen, under which increased species diversity often leads to lower infection prevalence.

Disease reservoir: an organism on which a parasite can naturally live, often without causing disease.

Disease vector: any agent carrying and transmitting disease to a living organism.

Ecosystem services: the benefits humans gain from ecosystems, for example, pollination of plants and provisioning of drinking water.

Emerging infectious diseases: diseases that recently dramatically increased in their incidence, or are expected to increase in the near future.

ex situ: treatment of an organism taking place outside of its natural habitat (e.g., in laboratory or aquarium).

Fungicides: chemical compounds or organisms able to kill fungi or their spores.

in situ: inside its natural habitat.

in vitro: outside of a living organism in an artificial environment.

Oligopeptide: short-chain peptide containing few amino acids (oligo = a few).

Recirculating farming system: a farming system in which water exchange is limited, reducing the need for fresh and clean water.

Sapronotic infectious agent: a free-living organism that can, under specific circumstances, establish an infection and multiply within a host.

Serine protease: an enzyme that cleaves peptide bonds in proteins.

Trends in Parasitology

Figure 1. Examples of Hosts Infected with Zoosporic Disease. (A) Mass mortalities of an alpine (Pyrenees) population of the midwife toad (*Alytes obstetricans*) caused by a chytrid (*Batrachochytrium dendrobatidis*) epidemic. (B) Salmon parr (*Salmo salar*) infected with the oomycete *Saprolegnia parasitica*. (C) Filamentous phytoplankton (cyanobacterium *Planktothrix rubescens*) infected with the chytrid *Rhizophydium megarrhizum*. Pictures by Dirk S. Schmeller (A), Kostis Apostolakis (B), and Ramsy Agha (C).

Current Control Strategies

Amphibians

The development of methods to treat chytridiomycosis is currently focused either on reducing or eliminating the pathogen from the environment or on increasing the capacity of populations to persist despite increased mortality from disease, for example, by minimizing other sources of mortality [27]. Successfully tested *in situ* methods inhibiting fungal growth rely on the use of disinfectants or antifungal agents (**fungicides**) [28–30], or on temporarily modifying environmental conditions such as temperature or salinity, to alleviate disease [31,32]. Amphibian communities have also been successfully treated ***ex situ***. However, treatment can have negative effects on the very species targeted for conservation efforts, or may even lead indirectly to an increased incidence of zoosporic infections [20,21]. Disease symptoms can start to redevelop in some locations shortly after treatment, indicating that clearing site-level infection does not prevent pathogen reintroduction [16] and demonstrating the low effectivity of chemical treatments under natural conditions [33].

Fish

Control of oomycete infections in aquaculture relied traditionally on treatments with malachite green. However, in 2002 malachite green was banned globally due to its carcinogenic and toxic effects. Alternative prophylactic treatments are based on the use of disinfectants and fungicides [22,34], or on other biocidal chemicals such as boric acid and hydrogen peroxide [35,36]. Currently, the most commonly used chemical to control *Saprolegnia* infections in fish farms is formalin [14,36]. However, due to its high toxicity, formalin treatments pose a serious threat to both the environment and the people working with it [19,37]. Some less aggressive substances have also been applied to reduce infections. In **recirculating farming systems**, for instance, increased salinity can help to reduce the incidence of saprolegniasis [38].

Plankton

Potential control methods in plankton production systems include the use of chemicals such as the fungicide Headline [39]. However, a key limitation of these approaches is the negative collateral impact that chemicals may have on plankton growth and, if applied in natural systems, on other organisms therein [40]. For example, Headline application not only results in reduced yields of green algae but also has severe toxic effects on zooplankton, fish, and shrimp [39,41]. A safer method used in production facilities is to harvest the cultures immediately after detection of the parasite and prior to serious loss of biomass [12]. However, the optimal biomass for efficient harvesting may not yet have been achieved and, moreover, it may not solve the zoosporic problem
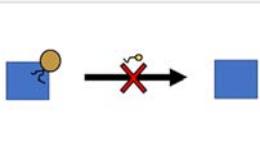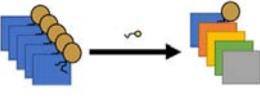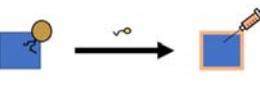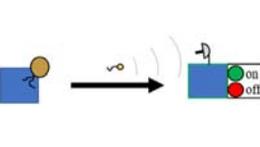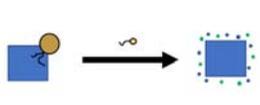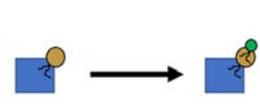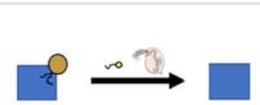
itself since the production system remains contaminated. Other control techniques include creating extreme environments (e.g., high pH or alkalinity) that limit the risk of contamination [39,40]. However, these approaches typically create environments that deviate from the physiological optima of the cultivated algae, which may substantially reduce yields and are therefore not aligned with the economics of **biofuel** production [39].

Biological Control Strategies: New Solutions to Old Problems?

Currently, a variety of biological control strategies have been discussed across the three different areas of research, which we summarize here in seven general concepts (Table 1, Key Table).

Key Table

Table 1. Conceptual Depiction of the Seven Biological Zoosporic Disease-Control Concepts and Some of the References Supporting Their Potential

Biological control concept		Research area	Refs
Vector control and preventing spillover		Amphibians	[42,45]
Altering host diversity		Amphibians	[52,54,55]
		Plankton	[50,58,59]
Vaccination and immunization		Amphibians	[65]
		Fish	[62]
Inducible defense and production of antifungal peptides		Amphibians	[66,74,75]
		Fish	[73]
		Plankton	[70]
Probiotics		Amphibians	[76,77,83]
		Fish	[78,79,84–86]
Hyperparasitism		Fish	[133]
Parasites as food		Amphibians	[54,95–98]
		Fish	[99,100]
		Plankton	[93,94]

Vector Control and Preventing Spillover

Spillover occurs when a population carrying a high infection load comes into contact with an uninfected host population, after which the disease may be transmitted. This may, for instance, hamper the success of amphibian conservation efforts, as newly introduced species or populations might become infected when in contact with resident ones, or vice versa [42]. The same holds true for host or non-host individuals acting as a **disease vector** or **disease reservoir**. For example, not all amphibian species nor different life stages are equally susceptible to infection by a given pathogen strain. Specifically, long-lived tadpoles of several amphibian species are reservoirs of *Batrachochytrium dendrobatidis* (*Bd*) (Box 1); they act as a source of infectious zoospores in the habitat [43] and can spread the pathogen quickly in a cohort and population [44]. Additionally, non-host organisms, such as geese and crayfish, have the potential to act as disease vectors or environmental reservoirs of chytridiomycosis [45–47]. For fish-infecting oomycetes, a broad spectrum of these pathogens is also capable of infecting insects, amphipods, and cladocerans [48,49], which may thus act as a competent reservoir or vector. These reservoirs and vectors may facilitate the reintroduction and spread of chytrids and oomycetes into disease-free or previously treated locations. When planning disease mitigation measures, spillover as well as the possibility of disease spread by vector or reservoir species needs to be considered, for example, by eradicating invasive vector species, by creating unfavorable conditions for pathogen transfer, or by targeting sites at low risk of reinfection by vector or spillover species.

Altering Host Diversity

It is a commonly held view that genetically homogeneous host populations are more vulnerable to infection than genetically diverse ones [50]. Evidence originates from agricultural systems where diseases are observed to expand rapidly during monoclonal cropping strategies, also referred to as the 'monoculture effect'. Host diversity can be manipulated at two levels: at the community level, by diversifying *species* composition, or at the species (population) level, by increasing host (intraspecific) *genetic* diversity. The concept of diversifying species composition has been described as the **dilution effect** [51]. Although this concept has been observed, amongst others, in amphibian communities [52–55], it remains controversial since it may occur only under very specific conditions. For instance, when the parasite has a more generalist infection strategy, increased species diversity may also enhance disease risk (referred to as the amplification effect [56,57]). Parasite spread may also be affected by manipulating host genetic diversity [50]. For example, chytrid parasites that are challenged with novel monoclonal phytoplankton hosts undergo rapid adaptation towards their homogeneous host, whilst parasite fitness (and spread) is in turn reduced for chytrid populations exposed to multiclonal host mixtures. This indicates that host intraspecific diversity hampers parasite adaptation and thus results in increased resistance to disease on a population level [58,59]. The big advantage of applying the diversification strategy is that it can decrease or prevent pathogen spread at early stages of pathogen colonization and infection. However, although diversification may be achieved relatively easily under controlled conditions, its application in natural environments is challenging, especially when host species richness is naturally low, for example, in mountain environments. Introducing genetically diverse strains into plankton-production facilities may also be costly since growth conditions cannot be optimized to obtain maximum yield for all strains simultaneously [60]. Finally, as parasites might eventually evolve and adapt to their previously novel host, reintroduction events might need to be repeated.

Vaccination and Immunization

Exposing organisms to a small dose of a weakened pathogen (i.e., vaccine) can lead to immunization, and thus potentially provides long-term resistance to the specific pathogen upon re-exposure. Vaccinating fish is a common practice in modern aquaculture to prevent infection by

bacteria and viruses. However, only a few commercially available vaccines exist, and no vaccines against oomycetes or macroparasites are available [61]. Vaccination might provide a method for controlling saprolegniasis in aquaculture, but vaccine development will first require a better understanding of the pathology of the parasites [11]. Recently, a **serine protease** from *Saprolegnia parasitica* (Box 1) was found to be recognized by sera in trout and it is hoped that this protein might provide adequate protection in future vaccination trials [62]. Active immunization therapy in amphibians showed mixed results [63–66] and has not yet been tested for phytoplankton. However, plants can be systemically immunized against diseases caused by fungi, bacteria, and viruses [67]. Vaccination, in most cases, can grant protection against many strains of the same parasite. However, the inherently short generation times of zoosporic parasites make them able to evolve rapidly [58,59]. As a result, vaccination therapy may need to keep up with the evolvability of the targeted pathogens, and may be efficient over only short periods of time, demanding repetition and frequent adaptation [68]. Alternatively, vaccines that confer broad protection against heterovariant strains could be used [69]. This might be possible under controlled conditions, but it is difficult to achieve in natural environments harboring genetically diverse parasite populations.

Inducible Defense and Production of Antifungal Peptides

Inducible defenses are temporary defense mechanisms that are triggered under threat, for example, during attacks by predators or parasites. Increased **oligopeptide** production by cyanobacteria, which may inhibit enzymes used by chytrids to digest their host, may be part of such a defense mechanism [70]. After the parasite infects and kills, host cells lyse and peptides are released into the water. Cyanobacteria exposed to spent medium, in which cyanobacteria lysate was present, have been shown to display increased intracellular concentrations of oligopeptides, strongly suggesting upregulation of peptide production in the remaining host population [71]. Analogous processes are observed in fish defenses against viruses and bacteria [72], in which infected cells produced signaling proteins that triggered antiviral defenses in neighboring cells. Antimicrobial peptides may also play a crucial role in the defense of fish against oomycetes [73]. Skin peptides resulting from inducible synthesis that act to deter chytrid infections have also been described for amphibians [66,74,75]. Identifying stimuli that trigger inducible defenses in threatened hosts may aid the development of strategies based on providing conditions where host defenses are stimulated and grant temporarily increased resistance to disease. These strategies may be especially effective when applied in combination with (or after) other treatments aimed at reducing the abundance of infective agents from the water. Such combinations might increase the success of disease eradication in both closed systems (e.g., bioreactors) and natural setups.

Probiotics

Probiotics are products that contain living microorganisms that, when administered in an adequate dose, provide health benefits to hosts. Previous work has suggested that the use of probiotics may successfully inhibit growth of zoosporic pathogens infecting amphibians and fish [76–80], for example, via the production of surfactants that function as antagonists towards other (micro)organisms, affecting their motility and/or attachment to surfaces [78,80,81]. For amphibian hosts, probiotic treatments can be effective if infection is low at the time of treatment [82], but may provide only a temporary benefit [17] or even be metabolically costly [83]. Applied *in vitro* in fish aquaculture, probiotics show high potential as a zoosporic disease control method. Many bacterial isolates, for example, *Pseudomonas* and *Aeromonas*, display a high degree of inhibitory properties against saprolegniasis development [79,80,84–86] and may thus provide a new sustainable mitigation strategy in aquaculture. However, probiotics might be difficult and expensive to produce in large quantities. Also, before applying probiotics in natural settings, potential antagonistic side-effects on the ecosystem must be well thought out. Most work on the use of probiotics has focused only on the positive effects of treatment, while any detrimental side-effects have usually not yet been put forward. Whereas the

use of probiotics can help in alleviating the effects of zoosporic disease, other side-effects, such as the emergence of antibiotic resistance, need to be taken into account [87]. Prior to incorporating new bacterial isolates to fight zoosporic pathogens, new strains should be carefully assessed and evaluated for safety. Then, routine molecular screening should be employed to ensure that the species used as probiotics in aquaculture are correctly identified [88].

Hyperparasitism

Pathogen fitness may also be reduced by the presence of secondary parasites. Some of these hyperparasites (sometimes referred to as biofungicides) are already commercially available, for example, to control plant disease caused by the ascomycete powdery mildew [89]. Also, other plant pathogenic fungi, such as *Fusarium*, have been reported to be infected by viruses [90]. Similarly, zoosporic parasites have been reported to be infected by other zoosporic parasites, sometimes belonging to closely related taxonomic groups [5]. Hyperparasitism can have large effects on host–parasite dynamics and can even indirectly protect the primary host from disease [91]. Thus, using hyperparasites to biologically control aquatic zoosporic diseases is, in principle, an appealing possibility, but more work is necessary to unravel their functional role in natural populations first.

Parasites as Food

In addition to their role as pathogens, parasites commonly function as prey within ecosystems [92]. In the case of zoosporic diseases, parasites can be preyed upon during their free-living zoospore stage, or, alternatively, through the consumption of the entire host, including the parasite stages within host (i.e., concomitant predation). Regarding the first mechanism, zoospores of chytrids infecting phytoplankton and amphibians can be grazed by zooplankton and even amphibian tadpoles, which may reduce infection risk [54,93–98]. Earlier work also indicated that, in principle, macroinvertebrates can graze on mycelia of oomycetes infecting fish eggs, thereby reducing the infection rate of the eggs, but with potential collateral impact on the survival of live eggs [99,100]. The second mechanism, consumption of the entire host including its parasites via concomitant predation, has not yet been studied in depth. So, although grazing does reduce abundance of parasitic zoospores in the water [93,95], it is unclear if these 'grazing on parasite' mechanisms can really effectively be applied as a biocontrol.

Future Challenges

The Role of the (Changing) Environment

The outcome of host–parasite encounters is often modulated by the external environment [101], making it challenging to predict and control disease outbreak and spread, especially under rapidly changing or unpredictable conditions as caused by global change. For example, the pattern of temperature-dependent growth of *Bd* on frogs was opposite to the pattern of growth in culture (on broth), emphasizing the importance of the environment in which parasites are studied when predicting climate-dependent disease dynamics [102]. Thus, before applying biological control concepts in controlled conditions, or outdoors, we need a better understanding of the extent to which the outcome of zoosporic diseases is affected by changes in environmental conditions. Indeed, most of the biological control concepts tested thus far have only been assessed under single laboratory conditions or under undefined natural settings, which makes generalization of their outcome questionable, taking into account the crucial role of the environment [101].

The abiotic and biotic environments clearly have a direct effect on the outcome of host–parasite interactions and thus can determine which biological control concepts are appropriate for application in different habitats and the likelihood of their success. Therefore, it is important to first study any potential conservation location before deciding on the best possible biological control strategy. As an example, in the case of amphibian conservation, the presence of zooplanktivorous fish might hamper the effective use of zooplankton in a 'parasites as food'

biological control method, since these might quickly be consumed by fish [103]. In this case, fish removal would have to precede any zooplankton-related mitigation measure. Thereafter, biomanipulation using zooplankton may follow, either by translocations from nearby habitats or by producing zooplankton individuals found in the focal habitat under laboratory conditions to reintroduce them in large enough quantities into the depleted habitats. Moreover, before translocating novel or indigenous species into a natural context, we have to be very aware of potential side-effects on the rest of the ecosystem. This may affect choice of an appropriate biocontrol method and/or efficiency and concomitant costs. It is imperative to consider the ethical and legal issues associated with whatever strategies are proposed or adopted [33].

Feasibility of Biological Mitigation Strategies and Potential Side-Effects

Zoosporic disease-control strategies using a biological approach are only in their infancy. As the strategies conceptualized here have rarely, if at all, been tested in realistic settings, an accurate assessment of their feasibility and potential side-effects is needed. One of the biggest concerns, relevant for most of the biological-control concepts here proposed, relates to the introduction of alien species into novel environments with a lack of natural enemies, sometimes referred to as biological pollution [104]. These alien species might, besides having a positive contribution by controlling zoosporic disease, have a negative impact on native populations or on non-target organisms, or develop into pests. Additionally, the newly introduced species may potentially become invasive itself [105]. An infamous example is the introduction of the cane toad into Australia, an unsuccessful attempt to control the cane beetle, a damaging insect pest of sugarcane crops [106]. The toads quickly established and invaded large parts of Australia and, since they are very toxic, caused harm to predators attempting to ingest them [106]. Self-dispersing organisms can find their way to all suitable available habitats and may not stay within the prescribed area [107]. Hence, modern biological control of zoosporic diseases should rely on bioaugmentation and translocation of indigenous species and invest in understanding the natural processes supporting those species.

Mechanistic Understanding of Infections

Recent progress in molecular and genomic methods opens up a wide suite of options to gain a better mechanistic understanding of host–parasite interactions. This will support the development of biological control concepts such as probiotics and vaccines. As an example, earlier work has characterized effector proteins crucial for the establishment of oomycete infections [108–110]. Understanding exactly how parasites infect their host will aid development of vaccines that can target more specific pathways during different stages of infection. Additionally, molecular approaches can be used to genetically manipulate hosts, for example, via CRISPR/Cas-9 technology [111], to enhance resistance against pathogens which, as an example, has already been applied successfully in rice, enhancing resistance against the rice blast fungus [112]. In plankton production systems this technology has also already been developed into an efficient genome-editing and selection tool for yield improvement [113], but not yet for disease resistance. Another research area that will greatly benefit from recent molecular and genomic methods is the field of environmental DNA (eDNA) monitoring approaches. eDNA approaches may allow for early detection of parasites, but may also elucidate existing complex interactions of parasites with viruses, bacteria, and fungi [15]. This may consequently benefit the development of probiotic treatments, which require a better understanding of environmental processes which determine the environmental microbiome as well as the skin microbiome of potential hosts [15].

The Role of Society in Mitigation Strategies

For successful mitigation of aquatic zoosporic diseases through biological control, several aspects of the socioecological system also have to be considered. Most importantly, stakeholders, decision-makers, and the general public need to be made aware of the ever-increasing threat of

emerging pathogens. The willingness of people to accept conservation actions that involve restrictions, for instance physical access to a nature area or disinfection before entering, increases when peers are adequately informed [114]. An outreach strategy to raise general awareness of the loss of biodiversity through parasites is also important for conservation practitioners; for many policy-makers and decision-makers wildlife disease impact on natural as well as captive populations remains a novel concept. Current legal frameworks are insufficient to capture this increasing threat, and administrative procedures may be too slow to react in a proper time frame. Mitigation through biocontrol needs to consider legal barriers and potential conflicts with other conservation priorities (e.g., manipulations in Natura2000 areas). Mitigation needs to be coordinated with authorities that not only understand the how and why, but are also able to (re)act quickly and efficiently. The important question remains of how to set priorities for different simultaneous conservation goals/actions (see Outstanding Questions). Procedures need to be put in place to considerably shorten the time from detection to action. Hence, legal frameworks may have to be challenged and modified to account for responses to this growing threat to biodiversity [33].

Concluding Remarks

In conclusion, we outline seven different biological-control concepts and propose immediate research needs that will help to progress their development. From our review it is apparent that we are only at the beginning of understanding what kind of biological zoosporic disease control strategies exist, and what potential they have. Much work still needs to be done to further advance our understanding of the interaction between hosts, pathogens, and the environment, to successfully implement biological-control applications in aquaculture or production facilities as well as in the natural environment (see Outstanding Questions). Moreover, we still need to gain a better understanding of potential side-effects before biological-control approaches can be implemented in natural habitats without incurring unforeseen risks.

References

1. Fisher, M.C. et al. (2012) Emerging fungal threats to animal, plant and ecosystem health. *Nature* 484, 186–194
2. Gurr, S. et al. (2011) The rise and rise of emerging infectious fungi challenges food security and ecosystem health. *Fungal Biol. Rev.* 25, 181–188
3. Derevnina, L. et al. (2016) Emerging oomycete threats to plants and animals. *Philos. Trans. R. Soc. B Biol. Sci.* 371, 20150459
4. Frenken, T. et al. (2017) Integrating chytrid fungal parasites into plankton ecology: research gaps and needs. *Environ. Microbiol.* 19, 3802–3822
5. Gleason, F.H. et al. (2014) Ecological functions of zoosporic hyperparasites. *Front. Microbiol.* 5, 244
6. Canter, H.M. (1967) Studies on British chytrids: XXVI. A critical examination of *Zygorhizidium melosirae* Canter and *Z. planktonicum* Canter. *J. Linn. Soc. Lond. Bot.* 60, 85–97
7. Kanouse, B.B. (1932) A physiological and morphological study of *Saprolegnia parasitica*. *Mycologia* 24, 431–452
8. Haas, B.J. et al. (2009) Genome sequence and analysis of the Irish potato famine pathogen *Phytophthora infestans*. *Nature* 461, 393
9. Kuris, A.M. et al. (2014) Sapronosis: a distinctive type of infectious agent. *Trends Parasitol.* 30, 386–393
10. Daszak, P. et al. (1999) Emerging infectious diseases and amphibian population declines. *Emerg. Infect. Dis.* 5, 735
11. van West, P. (2006) *Saprolegnia parasitica*, an oomycete pathogen with a fishy appetite: new challenges for an old problem. *Mycologist* 20, 99–104
12. Carney, L.T. and Lane, T.W. (2014) Parasites in algae mass culture. *Front. Microbiol.* 5, 8
13. Kim, G.H. et al. (2014) A revaluation of algal diseases in Korean *Pyropia* (*Porphyra*) sea farms and their economic impact. *Algae* 29, 249
14. Phillips, A.J. et al. (2008) New insights into animal pathogenic oomycetes. *Trends Microbiol.* 16, 13–19
15. Schmeller, D.S. et al. (2018) People, pollution and pathogens – global change impacts in mountain freshwater ecosystems. *Sci. Total Environ.* 622–623, 756–763
16. Bosch, J. et al. (2015) Successful elimination of a lethal wildlife infectious disease in nature. *Biol. Lett.* 11, 11
17. Woodhams, D.C. et al. (2012) Treatment of amphibians infected with chytrid fungus: learning from failed trials with itraconazole, antimicrobial peptides, bacteria, and heat therapy. *Dis. Aquat. Org.* 98, 11–25
18. Srivastava, S. et al. (2004) Toxicological effects of malachite green. *Aquat. Toxicol.* 66, 319–329
19. Wooster, G.A. et al. (2011) Human health risks associated with formalin treatments used in aquaculture: Initial study. *N. Am. J. Aquac.* 67, 111–113
20. Loyau, A. et al. (2016) Side effects of itraconazole on post-metamorphic *Alytes obstetricans* after a cold stress. *Amphib. Reptil.* 37, 345
21. Rohr, J.R. et al. (2017) A pesticide paradox: fungicides indirectly increase fungal infections. *Ecol. Appl.* 27, 2290–2302

22. Alderman, D. and Polglase, J.L. (1984) A comparative investigation of the effects of fungicides on *Saprolegnia parasitica* and *Aphanomyces astaci*. *Trans. Br. Mycol. Soc.* 83, 313–318

23. Delmas, C.E.L. *et al.* (2017) Soft selective sweeps in fungicide resistance evolution: recurrent mutations without fitness costs in grapevine downy mildew. *Mol. Ecol.* 26, 1936–1951

24. Gleason, F.H. *et al.* (2008) The ecology of chytrids in aquatic ecosystems: roles in food web dynamics. *Fungal Biol. Rev.* 22, 17–25

25. Sparrow, F.K. (1960) *Aquatic Phycomycetes*, University of Michigan Press

26. Sime-Ngando, T. *et al.* (2011) Hidden diversity among aquatic heterotrophic flagellates: ecological potentials of zoosporic fungi. *Hydrobiologia* 659, 5–22

27. Scheele, B.C. *et al.* (2014) Interventions for reducing extinction risk in chytridiomycosis-threatened amphibians. *Conserv. Biol.* 28, 1195–1205

28. Blooi, M. *et al.* (2015) Successful treatment of *Batrachochytrium salamandrivorans* infections in salamanders requires synergy between voriconazole, polymyxin E and temperature. *Sci. Rep.* 5, 11788

29. Van Rooij, P. *et al.* (2017) Efficacy of chemical disinfectants for the containment of the salamander chytrid fungus *Batrachochytrium salamandrivorans*. *PLoS One* 12, e0186269

30. Garner, T.W.J. *et al.* (2009) Using itraconazole to clear *Batrachochytrium dendrobatidis* infection, and subsequent depigmentation of *Alytes muletensis* tadpoles. *Dis. Aquat. Org.* 83, 257–260

31. Chatfield, M.W.H. and Richards-Zawacki, C.L. (2011) Elevated temperature as a treatment for *Batrachochytrium dendrobatidis* infection in captive frogs. *Dis. Aquat. Org.* 94, 235–238

32. Stockwell, M.P. *et al.* (2015) Effects of pond salinization on survival rate of amphibian hosts infected with the chytrid fungus. *Conserv. Biol.* 29, 391–399

33. Garner, T.W.J. *et al.* (2016) Mitigating amphibian chytridiomycoses in nature. *Philos. Trans. R. Soc. B Biol. Sci.* 371, 1709

34. Lilley, J.H. and Inglis, V. (2008) Comparative effects of various antibiotics, fungicides and disinfectants on *Aphanomyces invaderis* and other saprolegniaceous fungi. *Aquac. Res.* 28, 461–469

35. Barnes, M.E. *et al.* (1998) Observations on hydrogen peroxide control of *Saprolegnia* spp. during rainbow trout egg incubation. *Progress. Fish-Cultur.* 60, 67–70

36. Waterstrat, P.R. and Marking, L.L. (1995) Communications: Clinical evaluation of formalin, hydrogen peroxide, and sodium chloride for the treatment of *Saprolegnia parasitica* on fall chinook salmon eggs. *Progress. Fish-Cultur.* 57, 287–291

37. Leal, J.F. *et al.* (2016) Use of formalin in intensive aquaculture: properties, application and effects on fish and water quality. *Rev. Aquacult.* 10, 281–295

38. Ali, E.H. (2005) Morphological and biochemical alterations of oomycete fish pathogen *Saprolegnia parasitica* as affected by salinity, ascorbic acid and their synergistic action. *Mycopathologia* 159, 231–243

39. McBride, R.C. *et al.* (2014) Contamination management in low cost open algae ponds for biofuels production. *Ind. Biotechnol.* 10, 221–227

40. McBride, R. *et al.* (2016) Crop protection in open ponds. In *Micro-Algal Production for Biomass and High-Value Products* (Slocombe, S.P. and Benemann, J.R., eds), pp. 165–182, Taylor & Francis

41. Pest-Management-Regulatory-Agency (Ottawa, Canada) (2003) Regulatory Note REG2003-06

42. Brannelly, L. *et al.* (2017) Non-declining amphibians can be important reservoir hosts for amphibian chytrid fungus. *Anim. Conserv.* 21, 91–101

43. Catenazzi, A. *et al.* (2013) High prevalence of infection in tadpoles increases vulnerability to fungal pathogen in high-Andean amphibians. *Biol. Conserv.* 159, 413–421

44. Courtois, E.A. *et al.* (2016) Initiation of *Batrachochytrium dendrobatidis* infection in the absence of physical contact with infected hosts – a field study in a high altitude lake. *Oikos* 126, 843–851

45. Garmyn, A. *et al.* (2012) Waterfowl: Potential environmental reservoirs of the chytrid fungus *Batrachochytrium dendrobatidis*. *PLoS One* 7, e35038

46. Brannelly, L.A. *et al.* (2015) *Batrachochytrium dendrobatidis* in natural and farmed Louisiana crayfish populations: prevalence and implications. *Dis. Aquat. Org.* 112, 229–235

47. McMahon, T.A. *et al.* (2013) Chytrid fungus *Batrachochytrium dendrobatidis* has nonamphibian hosts and releases chemicals that cause pathology in the absence of infection. *Proc. Natl. Acad. Sci. U. S. A.* 110, 210–215

48. Sarowar, M.N. *et al.* (2014) *Saprolegnia* strains isolated from river insects and amphipods are broad spectrum pathogens. *Fungal Biol.* 118, 579–590

49. Wolinska, J. *et al.* (2009) Molecular identification and hidden diversity of novel *Daphnia* parasites from European lakes. *Appl. Environ. Microbiol.* 75, 7051–7059

50. King, K.C. and Lively, C.M. (2012) Does genetic diversity limit disease spread in natural host populations? *Heredity* 109, 199

51. Schmidt, K.A. and Ostfeld, R.S. (2001) Biodiversity and the dilution effect in disease ecology. *Ecology* 82, 609–619

52. Searle, C.L. *et al.* (2011) A dilution effect in the emerging amphibian pathogen *Batrachochytrium dendrobatidis*. *Proc. Natl. Acad. Sci. U. S. A.* 108, 16322–16326

53. Civitello, D.J. *et al.* (2015) Biodiversity inhibits parasites: Broad evidence for the dilution effect. *Proc. Natl. Acad. Sci. U. S. A.* 112, 8667

54. Venesky, M.D. *et al.* (2014) Linking manipulative experiments to field data to test the dilution effect. *J. Anim. Ecol.* 83, 557–565

55. Becker, C.G. *et al.* (2014) Partitioning the net effect of host diversity on an emerging amphibian pathogen. *Proc. R. Soc. B Biol. Sci.* 281, 20141796

56. Keesing, F. *et al.* (2006) Effects of species diversity on disease risk. *Ecol. Lett.* 9, 485–498

57. Begon, M. (2008) Effects of host diversity on disease dynamics. In *Infectious Disease Ecology: Effects of Ecosystems on Disease and of Disease on Ecosystems* (Ostfeld, R.S. *et al.*, eds), pp. 12–29, Princeton University Press

58. Agha, R. *et al.* (2018) Adaptation of a chytrid parasite to Its cyanobacterial host is hampered by host intraspecific diversity. *Front. Microbiol.* 9, 921

59. De Bruin, A. *et al.* (2008) Adaptation of the fungal parasite *Zygorhizidium planktonicum* during 200 generations of growth on homogeneous and heterogeneous populations of its host, the diatom *Asterionella formosa*. *J. Eukaryot. Microbiol.* 55, 69–74

60. Shurin, J.B. *et al.* (2013) Industrial-strength ecology: trade-offs and opportunities in algal biofuel production. *Ecol. Lett.* 16, 1393–1404

61. Sommerset, I. *et al.* (2005) Vaccines for fish in aquaculture. *Expert Rev. Vaccines* 4, 89–101

62. Minor, K.L. *et al.* (2014) A putative serine protease, SpSsp1, from *Saprolegnia parasitica* is recognised by sera of rainbow trout, *Oncorhynchus mykiss*. *Fungal Biol.* 118, 630–639

63. Stice, M.J. and Briggs, C.J. (2010) Immunization is ineffective at preventing infection and mortality due to the amphibian chytrid fungus *Batrachochytrium dendrobatidis*. *J. Wildl. Dis.* 46, 70–77

64. Cashins, S.D. *et al.* (2013) Prior infection does not improve survival against the amphibian disease Chytridiomycosis. *PLoS One* 8, e56747

65. McMahon, T.A. *et al.* (2014) Amphibians acquire resistance to live and dead fungus overcoming fungal immunosuppression. *Nature* 511, 224

66. Ramsey, J.P. *et al.* (2010) Immune defenses against *Batrachochytrium dendrobatidis*, a fungus linked to global amphibian declines, in the South African clawed frog, Xenopus laevis. *Infect. Immun.* 78, 3981–3992

67. Kuć, J. (1982) Induced immunity to plant disease. *BioScience* 32, 854–860

68. Read, A.F. and Mackinnon, M.J. (2008) Pathogen evolution in a vaccinated world. *Evol. Health Dis.* 2, 139–152

69. Carrat, F. and Flahault, A. (2007) Influenza vaccine: The challenge of antigenic drift. *Vaccine* 25, 6852–6862

70. Rohrlack, T. *et al.* (2013) Putative antiparasite defensive system involving ribosomal and nonribosomal oligopeptides in

cyanobacteria of the genus *Planktothrix*. *Appl. Environ. Microbiol.* 79, 2642–2647

71. Schatz, D. *et al.* (2007) Towards clarification of the biological role of microcystins, a family of cyanobacterial toxins. *Environ. Microbiol.* 9, 965–970

72. Ellis, A. (2001) Innate host defense mechanisms of fish against viruses and bacteria. *Dev. Comp. Immunol.* 25, 827–839

73. de Bruijn, I. *et al.* (2012) Immune gene expression in trout cell lines infected with the fish pathogenic oomycete *Saprolegnia parasitica*. *Dev. Comp. Immunol.* 38, 44–54

74. Rollins-Smith, L.A. *et al.* (2002) Activity of antimicrobial skin peptides from ranid frogs against *Batrachochytrium dendrobatidis*, the chytrid fungus associated with global amphibian declines. *Dev. Comp. Immunol.* 26, 471–479

75. Rollins-Smith, L.A. *et al.* (2002) Antimicrobial peptide defenses against pathogens associated with global amphibian declines. *Dev. Comp. Immunol.* 26, 63–72

76. Bletz, M.C. *et al.* (2013) Mitigating amphibian chytridiomycosis with bioaugmentation: characteristics of effective probiotics and strategies for their selection and use. *Ecol. Lett.* 16, 807–820

77. Muletz-Wolz, C.R. *et al.* (2017) Inhibition of fungal pathogens across genotypes and temperatures by amphibian skin bacteria. *Front. Microbiol.* 8, 1551

78. Liu, Y. *et al.* (2015) Diversity of aquatic *Pseudomonas* species and their activity against the fish pathogenic oomycete *Saprolegnia*. *PLoS One* 10, e0136241

79. Carbajal-González, M.T. *et al.* (2011) Bacterial skin flora variation and *in vitro* inhibitory activity against *Saprolegnia parasitica* in brown and rainbow trout. *Dis. Aquat. Org.* 96, 125–135

80. de Souza, J.T. *et al.* (2003) Biochemical, genetic, and zoosporicidal properties of cyclic lipopeptide surfactants produced by *Pseudomonas fluorescens*. *Appl. Environ. Microbiol.* 69, 7161–7172

81. Raaijmakers, J.M. *et al.* (2010) Natural functions of lipopeptides from *Bacillus* and *Pseudomonas*: more than surfactants and antibiotics. *FEMS Microbiol. Rev.* 34, 1037–1062

82. Vredenburg, V.T. *et al.* (2011) *Host–Pathogen Dynamics of Amphibian Chytridiomycosis: The Role of the Skin Microbiome in Health and Disease*, National Academies Press

83. Küng, D. *et al.* (2014) Stability of microbiota facilitated by host immune regulation: informing probiotic strategies to manage amphibian disease. *PLoS One* 9, e87101

84. Bly, J.E. *et al.* (1997) Inhibition of *Saprolegnia* pathogenic for fish by *Pseudomonas fluorescens*. *J. Fish Dis.* 20, 35–40

85. Lategan, M.J. *et al.* (2004) Control of saprolegniosis in the eel *Anguilla australis* Richardson, by *Aeromonas media* strain A199. *Aquaculture* 240, 19–27

86. Lategan, M.J. *et al.* (2004) Biocontrol of saprolegniosis in silver perch *Bidyanus bidyanus* (Mitchell) by *Aeromonas media* strain A199. *Aquaculture* 235, 77–88

87. Zorriehzahra, M.J. *et al.* (2016) Probiotics as beneficial microbes in aquaculture: an update on their multiple modes of action: a review. *Vet. Q.* 36, 228–241

88. Wang, Y.-B. *et al.* (2008) Probiotics in aquaculture: challenges and outlook. *Aquaculture* 281, 1–4

89. Kiss, L. *et al.* (2004) Biology and biocontrol potential of *Ampelomyces* mycoparasites, natural antagonists of powdery mildew fungi. *Biocontrol Sci. Tech.* 14, 635–651

90. Chu, Y.-M. *et al.* (2002) Double-stranded RNA mycovirus from *Fusarium graminearum*. *Appl. Environ. Microbiol.* 68, 2529–2534

91. Parratt, S.R. and Laine, A.-L. (2016) The role of hyperparasitism in microbial pathogen ecology and evolution. *ISME J.* 10, 1815

92. Johnson, P.T. *et al.* (2010) When parasites become prey: ecological and epidemiological significance of eating parasites. *Trends Ecol. Evol.* 25, 362–371

93. Frenken, T. *et al.* (2018) Fungal parasites of a toxic inedible cyanobacterium provide food to zooplankton. *Limnol. Oceanogr.* 63, 2384–2393

94. Kagami, M. *et al.* (2004) *Daphnia* can protect diatoms from fungal parasitism. *Limnol. Oceanogr.* 49, 680–685

95. Schmeller, D.S. *et al.* (2014) Microscopic aquatic predators strongly affect infection dynamics of a globally emerged pathogen. *Curr. Biol.* 24, 176–180

96. Buck, J. *et al.* (2011) Predation by zooplankton on *Batrachochytrium dendrobatidis* biological control of the deadly amphibian chytrid fungus? *Biodivers. Conserv.* 20, 3549–3553

97. Hamilton, P.T. *et al.* (2012) *Daphnia* in tadpole mesocosms: trophic links and interactions with *Batrachochytrium dendrobatidis*. *Freshw. Biol.* 57, 676–683

98. Searle, C.L. *et al.* (2013) *Daphnia* predation on the amphibian chytrid fungus and its impacts on disease risk in tadpoles. *Ecol. Evol.* 3, 4129–4138

99. Oseid, D.M. (1977) Control of fungus growth on fish eggs by *Asellus militaris* and *Gammarus pseudolimnaeus*. *Trans. Am. Fish. Soc.* 106, 192–195

100. Bärlocher, F. and Kendrick, B. (1975) Assimilation efficiency of *Gammarus pseudolimnaeus* (Amphipoda) feeding on fungal mycelium or autumn-shed leaves. *Oikos* 26, 55–59

101. Wolinska, J. and King, K.C. (2009) Environment can alter selection in host–parasite interactions. *Trends Parasitol.* 25, 236–244

102. Raffel, T.R. *et al.* (2012) Disease and thermal acclimation in a more variable and unpredictable climate. *Nat. Climate Change* 3, 146

103. Parker, B.R. *et al.* (2001) The effects of stocking and removal of a nonnative salmonid on the plankton of an alpine Lake. *Ecosystems* 4, 334–345

104. Howarth, F.G. (1983) Classical biocontrol: panacea or Pandora's box. *Proc. Hawaiian Entomol. Soc.* 24, 239–244

105. Howarth, F.G. (1991) Environmental impacts of classical biological control. *Annu. Rev. Entomol.* 36, 485–509

106. Shanmuganathan, T. *et al.* (2010) Biological control of the cane toad in Australia: a review. *Anim. Conserv.* 13, 16–23

107. Pearson, D.E. and Callaway, R.M. (2003) Indirect effects of host-specific biological control agents. *Trends Ecol. Evol.* 18, 456–461

108. van West, P. *et al.* (2010) The putative RxLR effector protein SpHtp1 from the fish pathogenic oomycete *Saprolegnia parasitica* is translocated into fish cells. *FEMS Microbiol. Lett.* 310, 127–137

109. Trusch, F. *et al.* (2018) Cell entry of a host-targeting protein of oomycetes requires gp96. *Nat. Commun.* 9, 2347

110. Torto-Alalibo, T. *et al.* (2005) Expressed sequence tags from the oomycete fish pathogen *Saprolegnia parasitica* reveal putative virulence factors. *BMC Microbiol.* 5, 46

111. Doudna, J.A. and Charpentier, E. (2014) The new frontier of genome engineering with CRISPR-Cas9. *Science* 346, 1258096

112. Wang, F. *et al.* (2016) Enhanced rice blast resistance by CRISPR/Cas9-targeted mutagenesis of the ERF transcription factor gene OsERF922. *PLoS One* 11, e0154027

113. Nymark, M. *et al.* (2016) A CRISPR/Cas9 system adapted for gene editing in marine algae. *Sci. Rep.* 6, 24951

114. Loyau, A. and Schmeller, D.S. (2017) Positive sentiment and knowledge increases tolerance towards conservation actions. *Biodivers. Conserv.* 26, 461–478

115. Hopkins, W.A. (2007) Amphibians as models for studying environmental change. *ILAR J.* 48, 270–277

116. Hocking, D.J. and Babbitt, K.J. (2014) Amphibian contributions to ecosystem services. *Herpetol. Conserv. Biol.* 9, 1–17

117. Whiles, M.R. *et al.* (2006) The effects of amphibian population declines on the structure and function of Neotropical stream ecosystems. *Front. Ecol. Environ.* 4, 27–34

118. Stuart, S. *et al.* (2004) Status and trends of amphibian declines and extinctions worldwide. *Science* 306, 1783

119. Wake, D.B. and Vredenburg, V.T. (2008) Are we in the midst of the sixth mass extinction? A view from the world of amphibians. *Proc. Natl. Acad. Sci. U. S. A.* 105, 11466–11473

120. Olson, D.H. *et al.* (2013) Mapping the global emergence of *Batrachochytrium dendrobatidis*, the amphibian chytrid fungus. *PLoS One* 8, e56802

121. Lips, K.R. *et al.* (2008) Riding the wave: reconciling the roles of disease and climate change in amphibian declines. *PLoS Biol.* 6, e72

122. Scheele, B.C. *et al.* (2019) Amphibian fungal panzootic causes catastrophic and ongoing loss of biodiversity. *Science* 363, 1459–1463

123. Gilinsky, E. (1984) The role of fish predation and spatial heterogeneity in determining benthic community structure. *Ecology* 65, 455–468

124. Van Donk, E. and Otte, A. (1996) Effects of grazing by fish and waterfowl on the biomass and species composition of submerged macrophytes. *Hydrobiologia* 340, 285–290

125. FAO (2018) *The State of World Fisheries and Aquaculture 2018 – Meeting the Sustainable Development Goals*, Rome

126. Bostock, J. *et al.* (2010) Aquaculture: global status and trends. *Philos. Trans. R. Soc. B Biol. Sci.* 365, 2897–2912

127. Tidwell, J.H. and Allan, G.L. (2001) Fish as food: aquaculture's contribution. Ecological and economic impacts and contributions of fish farming and capture fisheries. *EMBO Rep.* 2, 958–963

128. Meyer, F.P. (1991) Aquaculture disease and health management. *J. Anim. Sci.* 69, 4201–4208

129. Falkowski, P. (2012) Ocean science: the power of plankton. *Nature* 483, S17

130. Mata, T.M. *et al.* (2010) Microalgae for biodiesel production and other applications: a review. *Renew. Sust. Energ. Rev.* 14, 217–232

131. Pulz, O. and Gross, W. (2004) Valuable products from biotechnology of microalgae. *Appl. Microbiol. Biotechnol.* 65, 635–648

132. Gachon, C.M.M. *et al.* (2010) Algal diseases: spotlight on a black box. *Trends Plant Sci.* 15, 633–640

133. Ayers, W. and Lumsden, R. (1977) Mycoparasitism of oospores of *Pythium* and *Aphanomyces* species by *Hyphochytrium catenoides*. *Can. J. Microbiol.* 23, 38–44