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Marine infectious disease dynamics and outbreak thresholds: contact transmission, pandemic infection, and the potential role of filter feeders

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Abstract. Disease-causing organisms can have significant impacts on marine species and communities. However, the dynamics that underlie the emergence of disease outbreaks in marine ecosystems still lack the equivalent level of description, conceptual understanding, and modeling context routinely present in the terrestrial systems. Here, we propose a theoretical basis for modeling the transmission of marine infectious diseases (MIDs) developed from simple models of the spread of infectious disease. The models represent the dynamics of a variety of host–pathogen systems including those unique to marine systems where transmission of disease is by contact with waterborne pathogens both directly and through filter-feeding processes. Overall, the analysis of the epizootiological models focused on the most relevant processes that interact to drive the initiation and termination of epizootics. *A priori*, systems with multi-step disease infections (e.g., infection-death-particle release-filtration-transmission) reduced dependence on individual parameters resulting in inherently slower transmissions rates. This is demonstrably not the case; thus, these alternative transmission pathways must also considerably increase the rates of processes involved in transmission. Scavengers removing dead infected animals may inhibit disease spread in both contact-based and waterborne pathogen-based diseases. The capacity of highly infected animals, both alive and dead, to release a substantial number of infective elements into the water column, making them available to suspension feeders results in such diseases being highly infective with a very small "low-abundance refuge". In these systems, the body burden of pathogens and the relative importance between the release and the removal rate of pathogens in the host tissue or water column becomes paramount. Two processes are of potential consequence inhibiting epizootics. First, large water volumes above the benthic susceptible populations can function as a sink for pathogens. Second, unlike contact-based disease models in which an increase in the number of susceptible individuals in the population increases the likelihood of transmission and epizootic development, large populations of filter feeders can reduce this likelihood through the overfiltration of infective particles.

Key words: basic reproduction number; epizootiology; disease ecology; host–pathogen models; waterborne pathogens.

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Introduction

Proliferation of marine infectious diseases (MID) substantially impacts the structure and function of diverse ecosystems by causing significant mortalities in ecologically relevant populations of a wide range of marine organisms including mammals, corals, shellfish, finfish, and sea grass (Ward and Lafferty 2004, Burge et al. 2014, Lafferty et al. 2015). This, in turn, threatens ecologically valuable habitats such as coral reefs, oyster beds, sea grass beds, and the diversity of the rocky shore, and results in substantial economic losses in aquaculture (Walker and Winton 2010, Lafferty et al. 2015). Despite the increasing recognition of the importance of MIDs, in part due to the potential of climate change to extend the range and impact of parasites and pathogens (Harvell et al. 2002, Burge et al. 2014), the understanding of the dynamics that underlie the generation of outbreaks and associated epidemiological concepts lags behind that of terrestrial ecosystems (Harvell et al. 2004).

How epizootics are initiated and terminated in terrestrial organisms has been described and modeled extensively (e.g., Gill 1928, Ackerman et al. 1984, Anderson 1991). Typically, the contact-based and vector-borne infectious diseases of terrestrial vertebrates and their epidemiology are modeled using some adaptation of the Kermack and McKendrick (1927) (as reprinted in Kermack and McKendrick (1991*a*, *b*, *c*)) formulation. In these models, the initiation of an epidemic event begins with one or a few infected individuals and a large number of susceptible neighbors with whom contact is possible (Anderson and May 1991). Thus, it is assumed that relatively close contact between the infected individual, or the vector, and the host is required for transmission (Hassell 2000, Mundt et al. 2009).

Contact-based diseases also exist in the marine environment, most frequently in fishes (e.g., Lotz and Soto 2002, Løvdal and Enger 2002, Ogut et al. 2005), being common in the case of the transmission of multicellular parasites such as trematodes or cestodes (Huspeni and Lafferty 2004). Although some authors (Dobson and May 1987, Ogut et al. 2005, Krkošek 2010) formulated contact-based MID models based on the Kermack and McKendrick (1927) model, other MID transmission processes are different in nature from those on land, and adapting the Kermack–McKendrick models requires the appreciation and incorporation of these fundamental differences (Harvell et al. 2004, McCallum et al. 2004).

In MIDs, in addition to live infected animals, dead infected animals are an important source of pathogens. For instance, the pathogen body burden in dead oysters infected by Dermo disease and the potential release rate upon death is much higher than those of infected live animals (Bushek et al. 2002). Similarly, fish that died of disease can be a source of infection by releasing pathogen particles to the surrounding water (Soto and Lotz 2001, Lotz et al. 2003, Vike et al. 2014). In the terrestrial environment, this transmission route is less well represented, although one well known example is the microparasite *Bacillus anthracis*, which infects both humans and animals and where the infectious agent is spores that enter the environment soon after the death of a host (Getz 2011).

One of the most distinctive features of MIDs, particularly for marine invertebrates, is the importance of spatial factors in determining the spread of disease. The differences in physical properties between seawater and air, such as density, result in greater buoyancy, longer life spans, and long-distance dispersion for aquatic organisms including pathogens (Strathmann 1990). This, in turn, can result in important pathogen dispersion, concentration, and availability issues for some invertebrates such as sessile filter and suspension feeders (e.g., bivalves and corals). Such species can accumulate pathogens from a dilute solution that may have been released nearby or from many kilometers away, thus the number of neighboring infected individuals may be relatively unimportant in comparison with the number of infective pathogens being supplied by water transport. This suspension- or filter-feeder life style, highly vulnerable to disease transmission and widespread, is a rare condition in terrestrial animals, and apart from swallows who snag insects on the wings when flying, the nearest approach to this condition are the web-spinning spiders. No mechanism has evolved for concentrating particles from the atmosphere in sufficient quantity to provide an adequate food supply for a terrestrial filter feeder (Strathmann 1990).

Disease transmission in filter-feeders probably occurs via an infective dose (Bushek et al. 1997, Ford et al. 1999, Powell et al. 1999) rather than by

unique contact between pathogen and host. The phenomenon of the infective dose may be particularly important for filter-feeders because overfiltration (i.e., the water is filtered more than once as it passes through the population (Officer et al. 1982)) can occur when the density of animals is high enough, thereby reducing the pathogen concentration available sufficiently to permit the competition for pathogens and the internal inactivation mechanisms to limit body burden below the infective dose level.

Model adaptations to long-distance infection often assume that infected individuals cross distance barriers at some rate to make contact with susceptible hosts or define contact-based distance criteria [Rodríguez and Torres-Sorando (2001), but see also Hassell (2000) for alternative approaches]. Notwithstanding that the development of an airborne disease in, for instance, a plant metapopulation involves a process of dispersion as well as local dynamics, the transmission process itself can be modeled as a contact-based and point-source process (Brown and Hovmøller 2002). The effect of pathogen dilution on nonpoint-source marine diseases transmission common in suspension-feeders (Hofmann et al. 1995), has not yet been investigated theoretically.

The distinctive characteristics of MIDs together with the limited barriers to dispersal (McCallum et al. 2003) potentially makes oceans a much more favorable medium than land for nonpoint-source processes to control the transmission process and the generation of epizootics. These characteristics are a primary reason why adaptation of terrestrial epidemiological models to marine diseases remains one of the poorly addressed problems in MIDs, with little advance (e.g., McCallum et al. 2005, Sokolow et al. 2009, Yakob and Mumby 2011) as Harvell et al. (2004) stated it as a priority for future research. In contrast, proliferation-based disease models have received considerable attention as understanding of proliferation of infection was sufficient to describe the disease impact in populations characterized by rapid nonpoint-source transmission (Calvo et al. 2001, Powell et al. 2011, 2012).

This paper focuses on the formulation of a series of models exemplifying the dynamics of a variety of MIDs representative of a diversity of host, pathogen, and transmission processes present in marine ecosystems. Thus, we study disease transmission by either direct contact between susceptible and infective animals, by contact with waterborne pathogens released by live or dead infected animals through passive impingement of infective particles via water currents or through active filtration of infective particles during filter feeding. The formulation and description of each model is presented together with examples of marine host–pathogen systems which might be appropriate examples of the given transmission model. For each modeled MID system, we analyze the basic reproduction number R_0 and consider how changes in model parameters vary the outcome of the transmission process relative to the threshold condition of $R_0 = 1$.

Models and Basic Reproduction Numbers R_0

Theoretical basis for the models

A series of models (Fig. 1, Tables 1 and 2), adapting to a greater or lesser extent the mathematical theory of epidemics apropos Kermack and McKendrick (1927), are formulated to represent infectious disease transmission processes and dynamics in marine systems (*Results*). For this purpose, the more complex sessile invertebrate disease models, including contact with or filtration of waterborne pathogens and particle diffusion processes, are built up from those simpler contact-based SI models applied to fish and mammal diseases. The models presented here do not cover facultative bacterial parasites (Kazama and Fuller 1977) or complex life cycles of protozoan (Robertson 2007) or metazoan parasites (Gam et al. 2008) requiring intermediate hosts.

We restrict this paper to compartmental models, the most frequently used class of models in epidemiology (Diekmann et al. 2013). The dynamics of the host–pathogen association is described by a system of ordinary differential equations (ODEs) which reproduce the change with time (in days) deterministically for all subpopulation components. More specifically, we implicitly assume a constant area (in m^{-2}) or volume (in m^{-3}) for the models, in order to describe the population in terms of density of individuals or concentration of pathogens instead of simply the number of individuals or particles. We assume the absence of migration or recruitment; we ignore nondisease mortality. In addition, infected individuals always

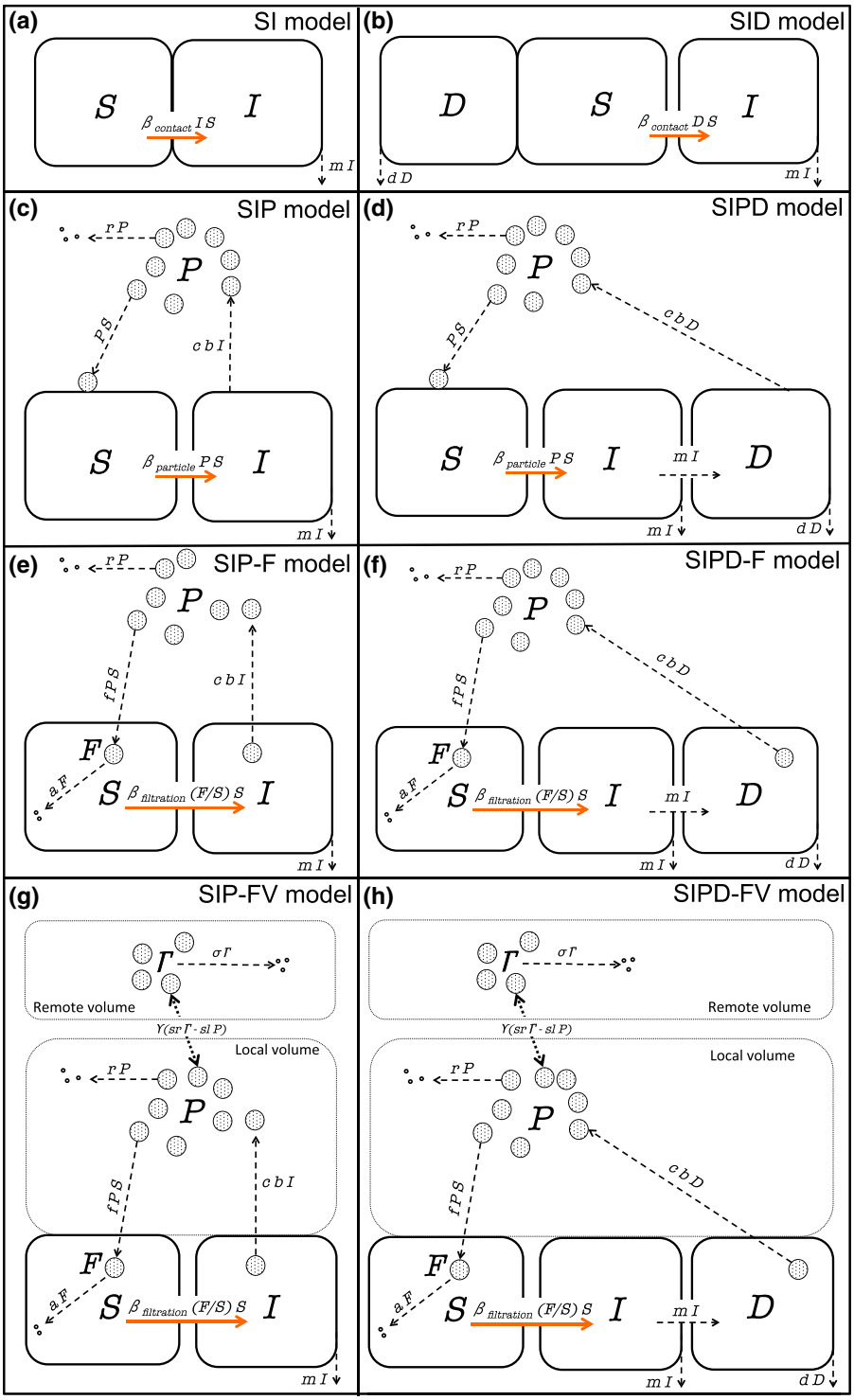

Fig. 1. Flow diagrams for the series of models (Table 1, *Results*). The variables (compartments) for each model are represented by upper letters (susceptible animals S), infected animals I, dead animals D, waterborne pathogens P, filtered pool of pathogens in the susceptible population F, remote pool of pathogens Γ). The model parameters are represented by lower letters described in Table 2. Orange solid arrows represent the transmission processes and dashed black arrows represent the other main processes in the models described in *Results*.

Table 1. Models, model characteristics, and example disease potentially applicable. The disease list is not meant to be comprehensive, nor does a unique mention of a disease imply restriction of the disease to that particular model.

Model	Transmission	Applicable systems
SI	Contact with infected individuals	Diseases in fish (e.g., salmons) (e.g., Løvdal and Enger 2002, Ogut et al. 2005) and mammals such as seals (Becher et al. 2002) where the disease is transmitted through rubbing. In corals, contact between sea fans when growing close together (Smith et al. 1996)
SID	Contact with dead infected individuals	Polar bears, fish, shrimps, and amphipods get infected by contacting or feeding on dead carcases (Lotz and Soto 2002, Lotz et al. 2003, Rudolf and Antonovics 2007)
SIP	Contact with infective particles or released by infected individuals	Black-band disease (Richardson 2004, Zvuloni et al. 2009) and Aspergillosis (Jolles et al. 2002) in corals; Withering syndrome (WS) in abalone (Moore , et al. , 2001, 2002); transmission of trematode cercariae (De Montaudouin et al. 1998)
SIPD	Contact with infective particles or fomites released by dead infected individuals	Black-band disease (Richardson 2004, Zvuloni et al. 2009) and Aspergillosis (Jolles et al. 2002) in corals through breakdown of decaying tissue; abalone with WS (Moore , et al. , 2001, 2002) and shrimp with White spot disease (Rudolf and Antonovics 2007) shed particles during decay and scavenging processes
SIP-F	Filtration of infective particles released by infected individuals; dose dependence	OsHV1 in pacific oysters (Schikorski et al. 2011); MSX (Haskin et al. 1966) and Dermo (Mackin et al. 1950) diseases in oysters; Perkinsosis in clams (Paillard 2004, Dang et al. 2010)
SIPD-F	Filtration of infective particles released by dead infected individuals; dose dependence	Oysters infected by Dermo disease (Perkinsus marinus) release pathogens into the water by natural decomposition or the action of scavengers, then to be filtered by the population (Choi et al. 1989, Bushek et al. 2002). This is a likely route for many other molluscan diseases
SIP-FV	Filtration of infective particles released by infected individuals; dose dependence; dilution via volume	Systems with nonpoint sources of pathogens and diffusion processes of waterborne pathogens, where a water volume can act as a reservoir of particles
SIPD-FV	Filtration of infective particles released by dead infected individuals; dose dependence; dilution via volume	Systems with nonpoint sources of pathogens and diffusion processes of waterborne pathogens, where a water volume can act as a reservoir of particles

die from disease. That is, individuals do not recover from the disease and, hence, also do not become immune to the disease. This is routinely the case for MIDs in invertebrates (Ford 1985, Powell et al. 1996, Curtis 2003) because invertebrates do not have adaptive immune systems (e.g., Chu and Lapeyre 1993, Ford and Tripp 1996, Allam and Paillard 1998) excepting some postepizootic coral populations with adaptive immunological resistance in surviving individuals (Mydlarz et al. 2010, Reed et al. 2010) and recuperation of aquaculture species after antibiotic treatment.

R_0 estimation and sensitivity analysis

R_0 represents the number of new cases of infection caused by one infected individual in a population of only susceptible individuals. Usually, the definition of R_0 in an epidemiological context includes the threshold value of 1, wherein, if $R_0 > 1$, the disease can invade and an epidemic can occur and if $R_0 < 1$, the disease cannot invade and an outbreak is not expected (Diekmann et al. 1990, Dietz 1993). The formulations for R_0 for the series of models presented here are obtained using the next-generation matrices (NGM) method (Diekmann et al. 2010, Diekmann et al. 2013).

We analyze the local sensitivity of R_0 for each model through the sensitivity index Ω (Cariboni et al. 2007). The normalized sensitivity index of R_0 with respect to any parameter p_i at a fixed value p^0 is

$$\Omega_{p_i}^{R_0} = \frac{\partial R_0}{\partial p_i} \times \frac{p_i}{R_0}\bigg|_{p_i = p^0} \quad (1)$$

The baseline parameter values (see caption in Fig. 3) were selected using as examples marine diseases described in each model introduction. We selected parameter values uniformly distributed (i.e., at increments of 10%) over the parameters full or at least wide range of feasible values.

Table 2. Description of variables and parameters. The last column identifies the models in which the variable or parameter is used. An asterisk identifies the use of the variable in the R_0 formulation for that model. Note that all models have an implicit surface area (m^{-2}) or volume (m^{-3}) for individuals and waterborne pathogens respectively.

Variables, Parameters	Definition	Units
S	Susceptible hosts in the population	Number of individuals
I	Infected hosts in the population	Number of individuals
D	Dead infected hosts in the population	Number of individuals
P	Waterborne pathogens in the environment (i.e., local pool)	Number of particles
F	Total number of pathogens absorbed or filtered by the population	Number of particles
Γ	Waterborne pathogens in a remote pool	Number of particles
N	Susceptible hosts in the initial population	Number of individuals
R_0	Basic reproduction number	Nondimensional
β_{contact}	Disease transmission rate by direct contact between susceptible and infected individuals.	Individual $^{-1}$ day^{-1}
β_{particle}	Disease transmission rate by contact between susceptibles and waterborne pathogens.	Particle (water) $^{-1}$ day^{-1}
$\beta_{\text{filtration}}$	Disease transmission rate by filtration of waterborne pathogens by susceptibles.	Particle (internal) $^{-1}$ day^{-1}
m	Disease mortality rate	day^{-1}
d	Removal rate of dead individuals by scavengers or bacteria (decay)	day^{-1}
c	Release rate of pathogens from infected or dead animals	day^{-1}
b	Average body burden of pathogens in infected or dead animals	Number of particles
r	Loss rate of waterborne pathogens from the local pool	day^{-1}
f	Filtration or absorption rate of infective particles by hosts	Individual^{-1} day^{-1}
a	Reduction rate of pathogens inside hosts by diapedesis, phagocytosis, apoptosis, etc.	day^{-1}
γ	Exchange rate of waterborne pathogens between remote and local pools. Exchange is assumed to be diffusion-like and thus proportional to the difference in concentration between the two pools	day^{-1}
σ	Loss rate of waterborne pathogen from the remote pool	day^{-1}
$V_{l,sl}$	V_l, the local volume, and its reciprocal sl	m^{-3}
$V_{\Gamma,sr}$	V_Γ, the remote volume, and its reciprocal sr	m^{-3}

Results

SI model

We begin with the standard SI model (Susceptible–Infected) model in which contact with an infected individual spreads the infection. Transmission of the disease is controlled by the transmission rate β_{contact} (Eqs. 2 and 3). The number of infected individuals, $\beta_{\text{contact}}IS$, is linearly proportional to the product of the spatial densities of S and I. Besides transmission, the dynamics of the infected subpopulation I is controlled by disease mortality (mI), where m is the mortality rate (Eq. 3): thus,

$$\frac{dS}{dt} = -\beta_{\text{contact}}IS, \tag{2}$$

$$\frac{dI}{dt} = \beta_{\text{contact}}IS - mI. \tag{3}$$

The basic reproduction number is:

$$R_0 = \frac{\beta_{\text{contact}}N}{m}, \tag{4}$$

where N is the initial population of susceptible individuals S. R_0 increases linearly with respect to N (Fig. 2a). Relatively large populations are more likely to inhibit epizootics if disease mortality rate m is high (i.e., infected hosts remain in the system for a shorter time and are less likely to spread the disease) and transmission rate is relatively low (i.e., susceptible hosts are less easily infected). The sensitivity analysis demonstrates that all parameters have the same impact on R_0 (Fig. 3).

SID model

The distinctiveness of this second model, with respect to previous SI model, is that the SID

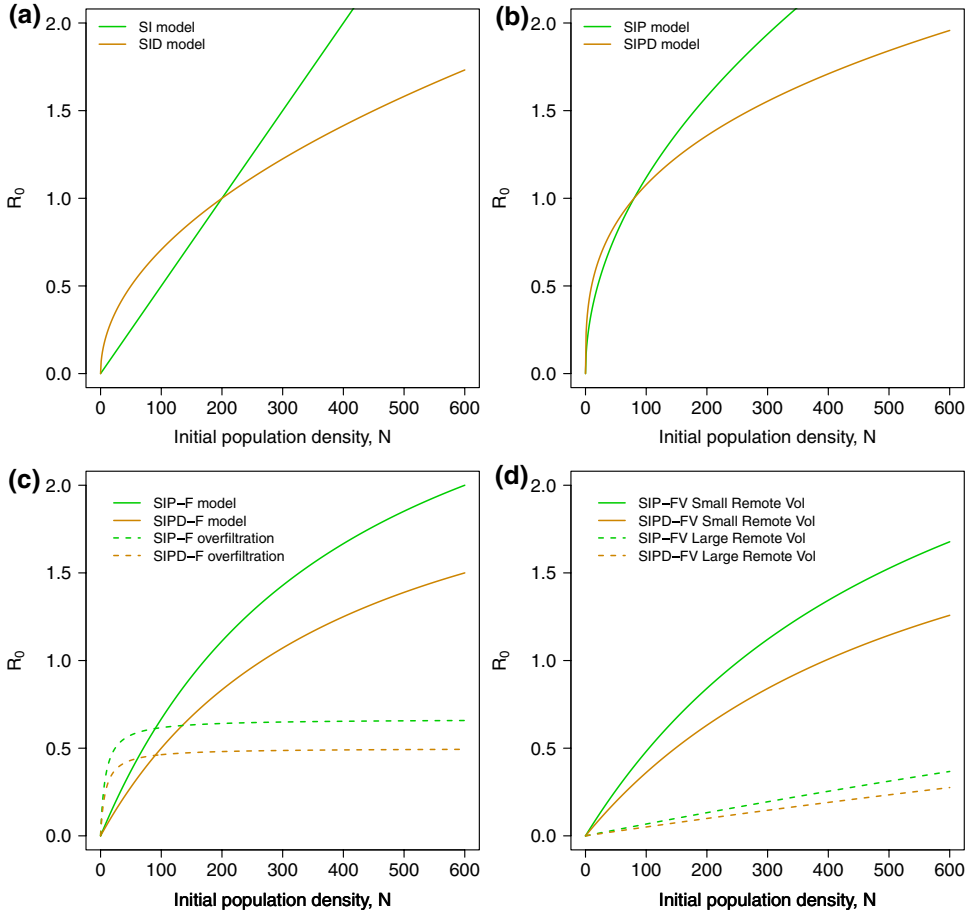

Fig. 2. Theoretical estimations of R_0 for a series of models, for increasing population density N. Using as examples marine host–pathogen systems described in Table 1, the following values of the parameters were used: SI and SID models ($\beta_{\text{contact}} = 1 \times 10^{-3}$, $m = d = 1 \times 10^{-1}$), SIP and SIPD models ($\beta_{\text{particle}} = 1 \times 10^{-5}$, $m = d = 1 \times 10^{-2}$, $c = 1 \times 10^{-3}$, $b = 1 \times 10^{4}$, $r = 8 \times 10^{-1}$), SIP-F and SIPD models ($\beta_{\text{filtration}} = 1 \times 10^{-5}$, $f = 2 \times 10^{-3}$, $a = 1 \times 10^{-3}$; for the overfiltration cases ($f = 5 \times 10^{-2}$, $a = 5 \times 10^{-3}$), SIP-FV and SIPD-FV models for reduced remote volume (V_Γ) cases ($\gamma = 1$, $\sigma = 0.8$, $sl = 10$ or $V_l = 0.1$, $sr = 20$ or $V_\Gamma = 0.05$) and for the large remote volume cases ($sr = 1$ or $V_\Gamma = 1$). Parameters are described and units are presented in Table 2. The orange dotted line at $R_0 = 1$ represents the critical value for the epizootic to occur.

model incorporates the dead infected individuals (D) as a source of infective particles. *SD* (Susceptibles–Deads) models arguably are less common in terrestrial habitats. The infection rate of the S population is controlled again by the transmission rate β_{contact}, and is linearly proportional to the spatial density of S and, in this case, D instead of I (Eqs 5 and 6). Eq. 7 describes the introduction of dead animals to the system after infected individuals die from infection (mI) and their disappearance by natural decay or consumption by scavengers including conspecifics (dD), where d represents the removal rate. Thus,

$$\frac{dS}{dt} = -\beta_{\text{contact}} DS, \tag{5}$$

$$\frac{dI}{dt} = \beta_{\text{contact}} DS - mI, \tag{6}$$

$$\frac{dD}{dt} = mI - dD, \tag{7}$$

which yields a basic reproduction number:

$$R_0 = \sqrt{\frac{\beta_{\text{contact}} N}{d}}. \tag{8}$$

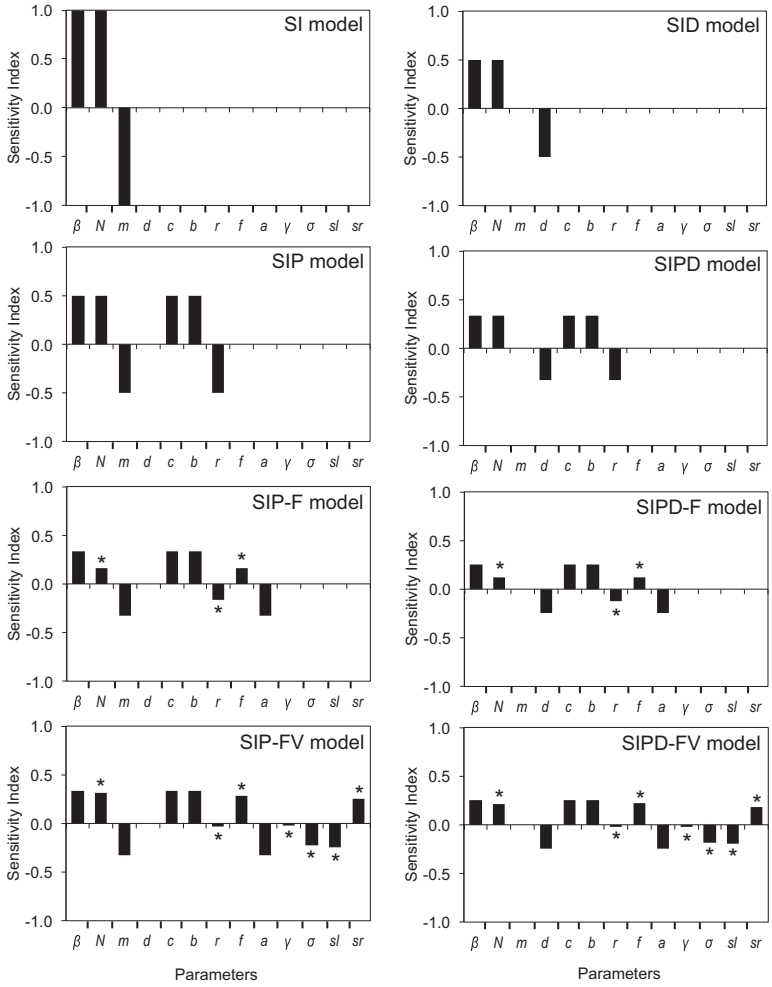

Fig. 3. Sensitivity analysis (SA) of R_0 to the parameters for a series of models. The sensitivity index represents the unit R_0 change per unit change in the given parameter. The analysis for each parameter was computed at a 0–1 parameter range for all parameters except for b (0–10,000), and N (0–200), while the rest of the parameters were held constant with these baseline values: $\beta = 0.001$, $m = 0.1$, $d = 0.1$, $c = 0.1$, $b = 10{,}000$, $r = 0.1$, $a = 0.1$, $f = 0.001$, $\gamma = 1$, $\sigma = 0.1$, $sl = 10$ ($V_I = 0.1$), $sr = 1$ ($V_\Gamma = 1$), $N = 100$. The asterisks mark parameters for which the sensitivity index was not constant over the evaluated range. For these parameters, the sensitivity index obtained for the baseline value of the parameter is shown. The variability of the sensitivity index for these parameters is presented in Fig. 6.

In this system, the generation of an epizootic, in addition to the initial population size and the disease transmission rate, is regulated by the removal or decay rate of dead animals d, not the mortality rate of infected animals m. The probability of an outbreak ($R_0 > 1$) is lower for the SID model at a given N than for the SI model (Fig. 2a) due to the extra step in the transmission process (i.e., infection via dead animals); the impact of parameters on R_0 is half that observed in the SI model (Fig. 3b). Moreover, commonly, in nature, scavenging rates (Veale et al. 2000, Morello et al. 2005) or decay rates (Smith 1953, Allison 1990, Lotz and Soto 2002) of dead infected animals are markedly higher than disease mortality rates. This, together with the fact that the process is inherently slower, make a susceptible population less vulnerable to an epizootic if transmission occurs via direct contact with dead infected individuals, assuming that the scavengers are not infected by the pathogen and become reservoirs for the disease (Hoese 1962).

SIP model

In this model, the disease is not transmitted from infected animals to susceptible animals by contact between individuals. Infected animals release infectious particles into the environment (P) and these waterborne pathogens can contact the susceptible animals thereby transmitting the disease. We consider a version of a model proposed to study the population dynamics of microparasitic infections (Anderson and May 1981). Thus, the model assumes that susceptibles are infected with a rate $\beta_{\text{particle}}PS$ (Eqs. 9 and 10). The release rate of infective particles by infected individuals occurs at rate c and the pathogens in the water are inactivated at a rate r (Eq. 11) by dilution, transport downstream, or by reduction of infectiousness by inactivation or death.

The model can be described by the following system:

$$\frac{dS}{dt} = -\beta_{\text{particle}}PS; \tag{9}$$

$$\frac{dI}{dt} = \beta_{\text{particle}}PS - mI; \tag{10}$$

$$\frac{dP}{dt} = cbI - rP. \tag{11}$$

The basic reproduction number is defined as:

$$R_0 = \sqrt{\frac{\beta_{\text{particle}}N}{m}\frac{cb}{r}}. \tag{12}$$

The response on R_0 due to changes in initial population N has a nonlinear increasing trend (Fig. 2b). All parameters have the same constant effect in R_0, regardless of the value of the parameters (Fig. 3). In this model (Eq. 12), large populations are less vulnerable to epizootics in conditions of relatively high r (i.e., a short pathogen life span in the water and/or rapid dilution) with respect to the particle release rate c (low r/c in Fig. 4). As the pathogen release rate rises with respect to the inactivation rate of infective particles in the water r, for a given m, the probability of a disease outbreak increases substantially even at low transmission rates for small populations. Hence, relatively small populations can support disease epizootics when particle inactivation rates are low

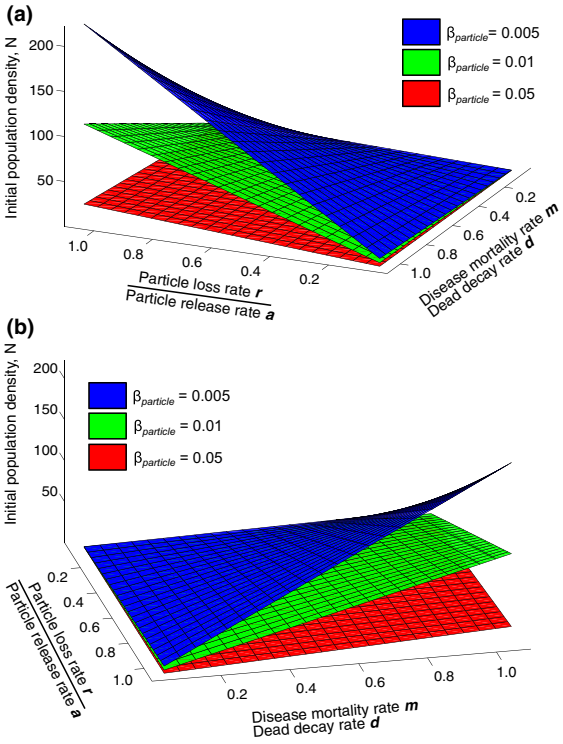

Fig. 4. Epizootic threshold values for the SIP model (mortality rate m on the y-axis) and the SIPD model (decay rate of dead infected animals d on the y-axis). 3-D surface plots represent the level surface for $R_0 = 1$, with $\beta_{\text{particle}} = 0.005$, 0.01 and 0.05, over a range of values of m, d, and the reciprocal ratio of pathogen release rate c and inactivation rate r. Above the surface, $R_0 > 1$ and the probability of an epizootic increases. Below the surface, $R_0 < 1$ and an epizootic cannot develop. For a better visualization and easier interpretation of the relative importance of the parameters, two different views of the same surfaces are presented.

enough that particles accumulate locally or when the particle release rate overwhelms the various modes of particle inactivation (Fig. 4). Death of infected individuals effectively terminates particle release; thus, a high mortality rate m can limit epizootic development even if the body burden of pathogens in the infected individuals is high.

SIPD model

Arguably, in marine systems, waterborne pathogens (P) are released more commonly by dead infected animals (D) instead of live infected individuals (I), and the disease is

transmitted by contact of susceptible animals (S) with the released free-living pathogens. When this occurs, a large number of infective particles may be released in a short time. The release of pathogens can occur during the natural decomposition process of dead animals or by the action of scavengers.

The SIPD model incorporates the dynamics of organisms (S, I, and D) and pathogens (P) in the environment. Pathogens infect hosts by contact with susceptible animals (Eqs. 13 and 14) and infected hosts die due to disease (Eq. 15). Internal or attached pathogens b are released from dead animals at rate c. Similar to the SIP model, pathogens in the water are inactivated at a rate r by natural death, or removed from the system by dilution or advection (Eq. 16). The governing equations are:

$$\frac{dS}{dt} = -\beta_{\text{particle}} PS; \tag{13}$$

$$\frac{dI}{dt} = \beta_{\text{particle}} PS - mI; \tag{14}$$

$$\frac{dD}{dt} = mI - dD; \tag{15}$$

$$\frac{dP}{dt} = cbD - rP. \tag{16}$$

The basic reproduction number is

$$R_0 = \sqrt[3]{\frac{\beta_{\text{particle}} N}{d} \frac{cb}{r}}. \tag{17}$$

In this model, the infection process is regulated by the removal of dead animals by the action of scavengers or natural decomposition d (Eq. 17), instead of the mortality of infected individuals m (Eq. 12), and cb refers to the body burden of infective particles in the dead animal tissue. The SIPD model is less sensitive than the SIP model to changes in parameter values (Fig. 3) resulting in an inherently slower transmission process (Fig. 2b). However, the release rate of pathogens from decaying tissue c is commonly much faster than from live infected animals, the body burden b of infective particles is higher in dead tissue than in the average living animal, and the removal rate of dead animals d is also much faster than the disease mortality rate m. The rapidity of tissue decay releasing particles means that the particle loss rate r must be high to limit epizootic development either through high flow and rapid water exchange rates or through the very rapid mortality of infective particles (Fig. 4).

SIP-F model

SIP-F model incorporates the filtration of infectious particles by, for example, bivalve filter-feeders. In this model, the waterborne pathogens are filtered by susceptible and infected individuals at a rate f (Eq. 20). Noteworthy in this case is the fact that infected individuals also filter out infective particles; this activity represents a debit to the waterborne infective particle pool without initiating any new infections. The specific particularities of the host and pathogens will determine if f is the same or not for S and I, that is, S and I individuals may filter at different rates.

At any point, some particles will have been filtered out by the susceptible population, but these particles may not be sufficient to initiate an infection. Thus, the SIP-F model also incorporates the concept of an infective dose which is considered to be important in the bivalve transmission process (Chu 1996, Chu and Volety 1997). F is the total number of particles inside the S population (Eq. 21). Considering that f is the portion of the local volume filtered per individual and time, the number of pathogens removed from the local volume by a susceptible individual per time is fP and the number of pathogens filtered by the population from the local volume is represented by fPS.

The internal pool of pathogens in the susceptible population is a balance between the rate of uptake by filtration and the rate a of inactivation by or loss from the animal, which might be due to pseudo-fecal rejection, defecation, digestion, deactivation by the immune system, or diapedesis. As the total number of filtered particles (F) increases, the average body burden in the susceptible population increases, which in turn increases the rate of infection. F/S represents the average pathogen body burden of the susceptibles. Consequently, disease transmission is linearly proportional to the average body burden per individual times the number of individuals, that is, $\beta_{\text{filtration}}(F/S)S$ (Eq. 17).

This model diverges from previous models in three important ways: (1) S no longer is present as a discrete variable in Eqs. 18 and 19: the variable F acts as a surrogate; (2) infective particles are lost due to mortality or dilution r, and also by filtration f: that is, the population is an active contributor to particle loss; and (3) the dose–response relationship is described by the new Eq. 21 that relates filtration f to particle loss a. The governing equations are:

$$\frac{dS}{dt} = -\beta_{\text{filtration}} \frac{F}{S} S; \tag{18}$$

$$\frac{dI}{dt} = \beta_{\text{filtration}} F - mI; \tag{19}$$

$$\frac{dP}{dt} = cbI - (r + f(S+I))P; \tag{20}$$

$$\frac{dF}{dt} = fPS - aF. \tag{21}$$

The basic reproduction number for this model is

$$R_0 = \sqrt[3]{\frac{\beta_{\text{filtration}}}{m} \frac{cb}{a} \left(\frac{fN}{r+fN} \right)}. \tag{22}$$

In this model, R_0 increases nonlinearly with increasing N (Fig. 2c). The generation of an epizootic is regulated by the same parameters as in the SIP model (Eq. 22), and also by the filtration rate f and the inactivation rate of pathogens inside the animal a. Large populations with a relatively high filtration rate are less vulnerable to epizootic development in conditions of relatively high disease mortality m and relatively high inactivation of pathogens inside the animal a with respect to the release of pathogens c (Fig. 5).

The initial population N and the removal of pathogens from the water, by filtration f, or by dilution or loss r, have varying influences on R_0 (Fig. 6). R_0 is less sensitive to changes in N particularly when the inactivation of pathogens in the environment r is slow (Fig. 6a) or filtration rate is relatively high (Fig. 6b). Similarly, the model is relatively less sensitive to changes in filtration rate beyond a certain f, and more drastically for low r (Fig. 6c).

The impact of the particle loss rate from the waterborne particle pool is determined by the ratio between the loss due to filtration of particles by the population and the total loss rate ($fN/(fN+r)$). When fN is relatively much smaller than r, due to the fact that filtration rate is very low or the initial population is small, the pathogen inactivation rate in the waterborne pool is an important limiter on epizootic development (Fig. 6d, green line). In contrast, when filtration rate is high, or the initial population N is large, both leading to high fN with respect to r, then $fN/(fN+r) \approx 1$ and R_0 becomes highly insensitive

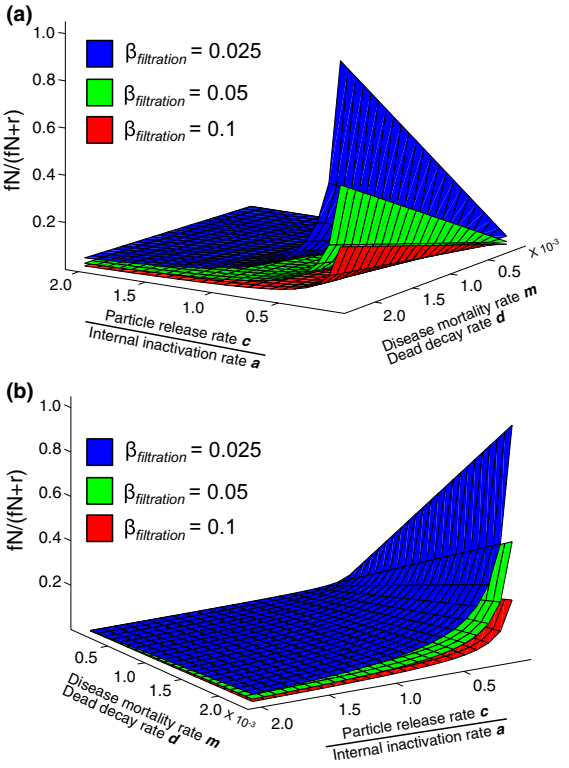

Fig. 5. Epizootic threshold values for the SIP-F model (mortality rate m on the y-axis) and the SIPD-F model (decay rate of dead infected animals d on the y-axis). The term $\frac{fN}{fN+r}$ on the z-axis represents the interaction between the removal of particles by the population through filtration fN and the inactivation or loss of particles in the water column r. 3-D surface plots show the level surface for $R_0 = 1$, with $\beta_{\text{filtration}} = 0.025$, 0.05 and 0.1, over a range of values of m, d, and the ratio between the pathogen release rate c and *in vivo* inactivation rate a. Above the surface, $R_0 > 1$ and the probability of an epizootic increases. Below the surface, $R_0 > 1$ and an epizootic is unlikely to develop. For a better visualization, two different views of the same surfaces are presented.

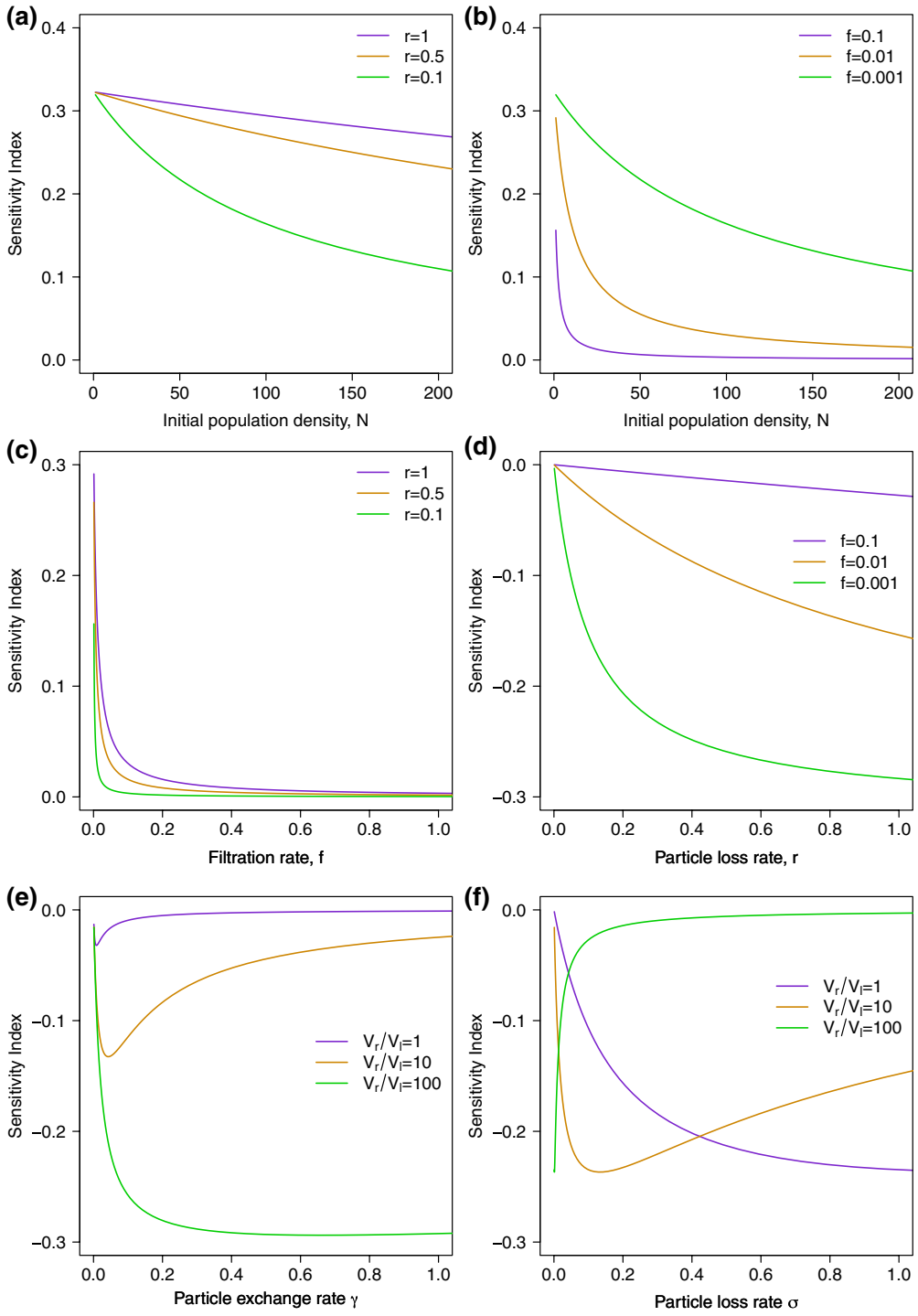

Fig. 6. Sensitivity analysis of R_0 for parameters with varying sensitivity index in the SIP-F and SIP-FV models. The values for the nonvarying parameters are identical to those of the analysis in Fig. 3. Note that results for the SIPD-F and SIPD-FV models are not presented as the sensitivity of R_0 to the parameters analyzed has the same pattern of variation although with lower maximum or minimum values of the sensitivity index due to the fourth root. For these two models, the maximum values of the sensitivity index for the plots presented in these figures would be 0.25 instead of 0.33.

to changes in r (Fig. 6d, solid purple line). This situation is the overfiltration scenario, wherein the population is filtering all the pathogens that are released. In this case, $P \approx 0$, so that once the population rises above a certain initial population, R_0 remains constant (Fig. 2c, dashed green line). Whether the epizootic develops depends on the balance between the *in vivo* inactivation of pathogens a and the rate of particle acquisition through filtering that determines whether the body burden of infective particles will exceed the infective dose.

SIPD-F model

SIPD-F model is very similar to the SIP-F model, but, in this case, dead infected animals (D) are responsible of releasing particles into the water (Eq. 26) instead of live infected animals. We suspect that this transmission process is common to many proliferative marine diseases that are accompanied by high mortality rates (see Table 1), but inadequate confirmatory data exist. This model consists of a system of five equations:

$$\frac{dS}{dt} = -\beta_{\text{filtration}} \frac{F}{S} S; \tag{23}$$

$$\frac{dI}{dt} = \beta_{\text{filtration}} \frac{F}{S} S - mI; \tag{24}$$

$$\frac{dD}{dt} = mI - dD; \tag{25}$$

$$\frac{dP}{dt} = cbD - (r + f(S+I))P; \tag{26}$$

$$\frac{dF}{dt} = fSP - aF; \tag{27}$$

The basic reproduction number is:

$$R_0 = \sqrt[4]{\frac{\beta_{\text{filtration}}}{d} \frac{cb}{a} \left(\frac{fN}{r + fN} \right)}. \tag{28}$$

R_0 is controlled by the removal of dead animals by the action of scavengers or natural decomposition d (Eq. 28), instead of the mortality of infected individuals m (Eq. 22; Fig. 5). As in the SID model, the nature of the process of organic matter destruction is decisive as it controls the release rate of pathogens to the water (see SIPD model).

The sensitivity analysis of R_0 for this model gives identical results to the SIP-F model in terms of the relative importance of the parameters and their sensitivity to variation (Figs. 3 and 6). However, the sensitivity of R_0 to the parameters is lower than for the SIP-F model due to the additional process involved. Although, the transmission process is inherently slower than that in the SIP-F model (Fig. 2b), the rate of infection is likely to be increased considerably by higher rates of some of the parameters, such as c, as in the SIPD model. The overfiltration scenario in this model also has a similar pattern to the SIP-F model (Fig. 2c, dashed orange line).

SIP-FV model

In the previous models with waterborne pathogens, we assume an unique "local volume" within which pathogens are released and remain free floating as they contact hosts, are consumed by the hosts, lose their infective properties after some time, or are otherwise lost. This volume may be large or small, but is inherently a single closed compartment. The SIP-FV model and the following SIPD-FV model consider a second volume of water contiguous with the local volume, wherein a remote reservoir of infectious particles can accumulate, without direct interaction with the hosts. Thus, a new variable, the remote pool of infectious particles (Γ), is specified (Eq. 32). Exchange between the local pathogen pool P and the remote pool Γ is a diffusion-like process proportional to the difference in concentration between the two pools times the diffusion coefficient or exchange rate γ (Eqs. 31 and 33). The parameters sl and sr are the reciprocals of the volumes of the two pools, $sl = 1/V_l$ and $sr = 1/V_\Gamma$ where V_l is the local volume and V_Γ is the remote volume. Otherwise, the SIP-FV and SIPD-FV models are similar to the SIP-F and SIPD-F models, respectively. The other process in this new equation σ represents the loss of particles from the remote pool either through mortality or loss from the system. The latter could be thought of as the loss of infective particles from an estuary via tidal exchange, death of the infective particle, sedimentation of the infective particle out of the water column, or any other loss mechanism that might occur in the remote pool.

The following equations represent this model for the specific case where the pathogens are

released to the water by infected individuals, and a diffusion-like transfer of pathogens between the local pool and the remote pool exists:

$$\frac{dS}{dt} = -\beta_{\text{filtration}} \frac{F}{S} S; \tag{29}$$

$$\frac{dI}{dt} = \beta_{\text{filtration}} \frac{F}{S} S - mI; \tag{30}$$

$$\frac{dP}{dt} = cbI - (r + f(S+I))P - \gamma(slP - sr\Gamma); \tag{31}$$

$$\frac{dF}{dt} = fSP - aF; \tag{32}$$

$$\frac{d\Gamma}{dt} = \gamma(slP - sr\Gamma) - \sigma\Gamma. \tag{33}$$

The basic reproduction number is:

$$R_0 = \sqrt[3]{\frac{\beta_{\text{filtration}}}{m} \frac{cb}{a} \frac{fN}{r + fN + \gamma sl\left(\frac{\sigma}{\sigma + \gamma sr}\right)}}. \tag{34}$$

A more cumbersome representation of Eq. 34 having volumes instead of reciprocals of the volumes is:

$$R_0 = \sqrt[3]{\frac{\beta_{\text{filtration}}}{m} \frac{cb}{a} \frac{fN}{r + fN + \frac{\gamma}{V_l}\left(\frac{1}{1 + \frac{\gamma}{\sigma V_\Gamma}}\right)}}. \tag{35}$$

The exchange of particles between pools formulated in Γ is a physical process and not part of the transmission process. Thus, R_0 is similar to that for the filtration SIP-F model, with the additional term in the denominator $\frac{\gamma}{V_l}\left(\frac{1}{1+\frac{\gamma}{\sigma V_\Gamma}}\right)$ representing the role of the exchange of particles between remote and local pools in regulating the probability of an epizootic.

R_0 increases nonlinearly with increasing population abundance N (Fig. 2d). This response is affected by the relative importance of the local (V_l) and remote (V_Γ) volumes. For most filter feeders, the volume directly influenced by filtration V_l will be small (e.g., a volume with a height of 0–15 cm for oyster populations (Wilson-Ormond et al. 1997)), thus the size of the remote volume becomes decisive.

An interesting outcome of the SIP-FV model occurs when a large V_Γ is combined with a high exchange rate of particles between pools ($\gamma \approx 1$) and a relatively high inactivation rate of pathogens in the remote pool σ results in a system with an effective mechanism to purge pathogens from the local pool. This configuration produces an outcome that is similar to the overfiltration effect discussed under the SIP-F model in that the average dose for the animals may be lower than the infective dose and accordingly the system may not be vulnerable to an epizootic ($R_0 < 1$) (Fig. 2d, dashed orange line). This situation is represented by Eq. 36 (modification of Eq. 35). When V_Γ is large and σ high, the additional term in the SIP-FV model $\frac{\gamma}{V_l}(\frac{1}{1+\frac{\gamma}{\sigma V_\Gamma}})$ can be simplified to $\frac{\gamma}{V_l}$. Here, the role of γ in determining the epizootic probability becomes paramount, as the exchange rate becomes the dominant process controlling the concentration of infective particles in the local pool and its influence is increased when the population filtration rate (fN) is low and the pathogen inactivation rate in the local volume r is inconsequential.

$$R_0 = \sqrt[3]{\frac{\beta_{\text{filtration}}}{m} \frac{cb}{a} \frac{V_l}{\gamma}}. \tag{36}$$

Consequently, a high pathogen exchange rate γ resulting in a low V_l/γ provides an important restraint on epizootic development (Fig. 7) over a large range of values of c/a and m, and particularly when the internal particle pool is maintained low by high a or when the release rate of pathogens to the water c is low (Note that the level defining $R_0 = 1$ rises sharply in Fig. 7, as it does in the overfiltration case). Under these conditions, the transfer of pathogens to the remote pool is similar to the effect of high population filtration fN (Figs. 5 vs. 7) and becomes an interesting arbiter of the fate of infective particles and an interesting modulator of the probability of epizootic development.

Looking further at the effect of changes in the exchange rate γ on R_0 in relation to the ratio between the remote and the local volume (V_Γ/V_l), R_0 is insensitive to changes in γ, when the remote volume is small relative to the local

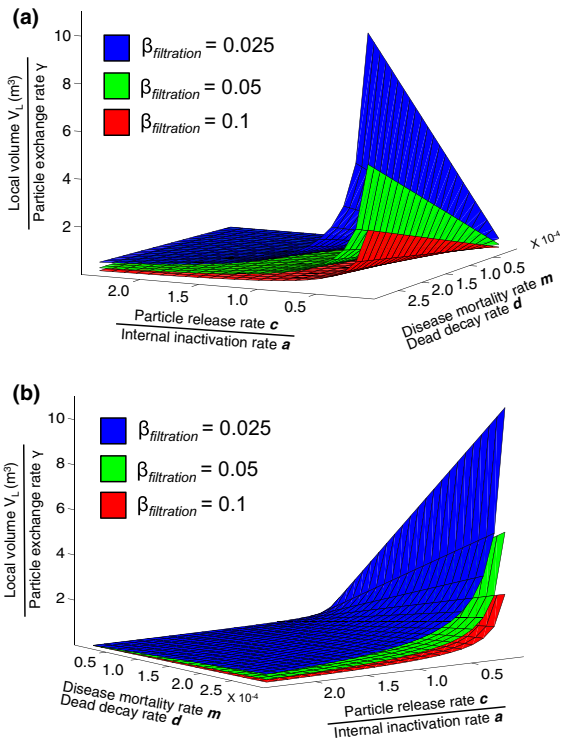

Fig. 7. Epizootic threshold values for the SIP-FV model (mortality rate m on the y-axis) and the SIPD-FV model (decay rate of dead infected animals d on the y-axis). 3-D surface plots represent the level surface for $R_0 = 1$, with $\beta_{\text{filtration}} = 0.025$, 0.05 and 0.1, over a range of values of m, d, and the ratio between the pathogen release rate c and inactivation rate inside the animal a. The considered local volume is small ($V_\Gamma = 0.1$) so that the value range for γ is 0.01 to 1. The population filtration is considered very low ($fN = 0.01$) reproducing the situation formulated in Eq. 36. Above the surface, $R_0 > 1$ and the probability of an epizootic increases. Below the surface, $R_0 < 1$ and the probability decreases. For a better visualization and easier interpretation of the relative importance of the parameters, two different views of the same surfaces are presented.

volume (Fig. 6e). However, when V_Γ is relatively large with respect to V_l, the sensitivity of R_0 to γ increases, particularly for values beyond $\gamma = 0.1$. On the other hand, when the ratio between the local and remote volume is relatively small, the removal of pathogens in the remote pool σ becomes relatively more important in determining the probability of an epizootic (Fig. 6f). Thus, as the remote volume increases in capacity relative to the local volume, the importance of the exchange rate increases and the importance of the inactivation or loss rate in the remote pool declines. Consequently, systems where the remote volume is small, are characterized by having the removal rate of pathogens in the remote pool σ imposing an uniquely important effect on R_0 (Fig. 6f). In contrast, when the remote volume is relatively large, as would be the case when the remote volume was, for example, the upper part of the water column overlying a bed of filter feeders, R_0 is more sensitive to the exchange rate between the two volumetric pools γ (Fig. 6e).

SIPD-FV model

The SIP-FV model represents the specific case where the particles are released by dead infected animals D instead of living infected animals I, and transfer of pathogens occur between the local and the remote pools. The model consists of a system of six coupled nonlinear ODEs:

$$\frac{dS}{dt} = -\beta_{\text{filtration}} \frac{F}{S} S; \tag{1}$$

$$\frac{dI}{dt} = \beta_{\text{filtration}} \frac{F}{S} S - mI; \tag{2}$$

$$\frac{dD}{dt} = mI - dD; \tag{3}$$

$$\frac{dP}{dt} = cbD - (r + f(S+I))P - \gamma(slP - sr\Gamma); \tag{4}$$

$$\frac{dF}{dt} = fPS - aF; \tag{5"}$$

$$\frac{d\Gamma}{dt} = \gamma(slP - sr\Gamma) - \sigma\Gamma; \tag{42}$$

The more cumbersome formulation of the basic reproduction number, specified in volume terms becomes:

$$R_0 = \sqrt[4]{\frac{\beta_{\text{filtration}}}{d} \frac{cb}{a} \frac{fN}{r + fN + \frac{\gamma}{V_l}\left(\frac{1}{1+\frac{\gamma}{\sigma V_\Gamma}}\right)}}. \tag{43}$$

R_0 for this model is identical to that of the SIP-FV model with the exception of including the

removal of dead animals d in the denominator, instead of the disease mortality rate m, and being specified as the fourth root instead of the third root. The sensitivity of R_0 to the parameters is identical to the SIP-FV model with the exception that for the SIPD-FV model, the maximum values of the sensitivity index for varying parameters is slightly lower due to the inherently slower infection process implied by the addition of one additional process in Eq. 39 (Fig. 3).

Discussion

This contribution covers the mathematical basis for the dynamics and epizootiology of a diverse array of marine infectious diseases, specifically focusing on the most relevant processes that interact to drive the initiation and termination of epizootics. We adapted the Kermack and McKendrick (1927) epidemiological theory and the model proposed by Anderson and May (1981) to comprehensively build disease dynamics models for sessile marine invertebrates that contact or filter waterborne pathogens.

Transmission of marine diseases includes a number of processes either rarely or never observed in the terrestrial world. Thus, the formulations proposed include transmission by direct contact not only between live animals (SI model) but also between dead animals and living susceptible hosts (SID model). We also explore cases where transmission occurs by environmental contact, that is, via particle transport through the water column and uptake by contact or filtration of waterborne infective pathogens released to the water column by live or dead infected animals. We finally explore the influence of a dose–response mechanism known to be present in filter-feeding mollusks and the potential of a remote volume to modulate the infection process through diffusive exchange of particles with the local pool (Table 1). In each case, we consider the epizootic thresholds of the studied systems by formulating their specific basic reproduction numbers R_0.

Some relationships exemplified by the basic reproduction number formulations for the models presented here deserve particular attention. In marine diseases transmitted by close contact between susceptible and dead infected individuals (Rudolf and Antonovics 2007) (SID model) rather than contact between susceptible and live infected individuals (standard SI model), transmission is regulated by the decay or removal by scavengers of dead animals. True scavengers do not exist in the marine world; however, many predators scavenge adventitiously (Hoese 1962, Veale et al. 2000, Morello et al. 2005). Particular attention has been paid to this process for white spot syndrome in crustaceans in which transmission involves infected carcasses which have died from infection but remain infectious (Soto and Lotz 2001, Lotz and Soto 2002, Lotz et al. 2003). Certain adventitious scavengers remove the carcasses without becoming infected; such activity may limit the spread of disease; an increase in scavengers or in temperature and oxygen conditions (Allison 1988, Kidwell and Baumiller 1990, Parsons-Hubbard et al. 2008) decreases the infectious period and hence, the number of secondary infections caused by a dead animal. Rates of scavenging are probably most readily modified by the number of scavengers. An increase in scavengers is proposed as an important outcome of commercial fishing (Collie et al. 1997, Veale et al. 2000), but whether this influences any marine disease is unknown.

Be that as it may, most marine diseases that frequently generate epizootics are proliferative diseases (e.g., Powell et al. 1996, Ford et al. 1999, Kleeman et al. 2002), that is, the pathogen multiplies within the host, frequently reaching high cell counts per gram of host tissue. Highly infected animals can release many infective elements and this capacity is exacerbated upon the animal's death (Bushek et al. 2002). Thus here, we focus on the theory of transmission of proliferative diseases in the marine world, emphasizing the cases of transmission via waterborne infective particles in populations of sessile hosts or hosts with limited mobility, dominantly invertebrates such as bivalves, corals, abalone, or some crustaceans (see particle-based models, Table 1 and sections *SIP model*, *SIPD model*, *SIP-F model*, *SIPD-F model*, *SIP-FV model*, and *SIPD-FV model*). Within the host, the possibility that b, the host body burden, is high, and thus, that cb, the number of particles released by live or dead animals is high, would result in such diseases being highly infective even at vanishingly low host abundance, that is, the low-abundance refuge of

Kermack and McKendrick (1927) may be very low for such diseases.

The scenarios explored in this paper demonstrate that, theoretically, under similar conditions of initial population density, transmission rate, or disease mortality, the more processes involved in transmission the less likely that a marine disease will generate an epizootic (Figs. 2 and 3). This is likely one reason why multicellular parasites rarely produce epizootics, as most of them have complex life cycles and thus have many steps in the transmission process. Consequently, *a priori*, in systems where transmission involves a variety of processes, such as the death of infected animals, dead animals releasing pathogens in the water, or filter feeders accumulating them (i.e., SIPD-F model), an epizootic should be less probable than for contact-based diseases (SI or SID models) for the same population density. This is demonstrably not the case; thus, the rates of processes must also be increased considerably by these alternative transmission pathways. Thus, a system with a high release rate of pathogens from animals upon death and a limited inactivation rate of infective particles either in the water column or in the susceptible host, could easily be highly transmissible and be characterized by a high incidence of epizootics. This is the case, for instance, for oysters and the pathogen *Perkinsus marinus*.

The particle-based models proposed explicitly decouple the fate of the infected animal from the fate of the infective particles. The rate of release of infective particles c is inherently decoupled from disease mortality rate m and the rate of decay of tissue d, such that if $m > c$ or $d > c$, respectively, then some infective particles are never released into the water to infect other hosts. Thus, in these scenarios, the probability of an epizootic can be limited when disease mortality rate m is high (SIP model) or the removal rate of dead animals d is fast (SIPD model) and the release of pathogens from live or dead animals c is slow compared to the particle loss in the environment r (Fig. 4). Regarding mortality in the SIP model, for instance, coral species with high population turnover rates are naturally more resistant to epizootics because of the direct proportionality between the initial population N or coverage necessary for an outbreak and the mortality rate m (Yakob and Mumby 2011). For an epizootic to occur, populations with a high turnover require higher N to balance the fact that individuals do not to exist long enough to become infected and to spread the infection (Yakob and Mumby 2011). The unique aspect of the SIPD model is the nature of the process of organic matter destruction as it controls the release rate of pathogens to the water. A "clean" and fast removal of dead animals by scavengers (i.e., pathogens are not released into the water during the process and are inactivated inside scavengers) leads to a decrease in the particle release rate c and an increase in the decay rate of dead animals d, restraining the probability of an epizootic, whereas rapid decomposition may release a substantial number of particles to the water facilitating epizootic development.

This is a particularly important issue for certain diseases in filter feeders involving a much larger number of infective pathogens released by dead animals than by infected live animals (SIPD-F model). For some molluscan diseases such as Dermo (pathogen *Perkinsus marinus*), the inference from observation is that the release of particles from dead animals occurs rapidly during the decay process, that is, $c \geq d$ (Bushek et al. 2002). In these systems, the body burden of pathogens in infected or dead animals and the relative importance between the release and the removal rate of pathogens in the tissue or water column becomes paramount (Fig. 5). The filtration-based models proposed (SIP-F and SIPD-F) assume a dose–response mechanism. Although some models of disease in filter feeders assume infection by a single infective element for convenience (e.g., Powell et al. 1996), the concept of an infective dose has received attention, particularly for molluscan diseases (Chu 1996, Chu and Volety 1997) because these hosts do have some, albeit often inadequate, ability to discharge or inactivate accumulated pathogens. Diapedesis and apoptosis are obvious examples (Kleeman et al. 2002, Sunila and LaBanca 2003). What seems clear is that the ability of most filter feeders to accumulate infective elements often far exceeds the ability to deactivate them at the concentrations typically observed in the field (e.g., Audemard et al. 2006). Thus, filtration rate may be a dominant determinant of transmissivity. Nonetheless, the albeit limited ability to inactivate filtered infective particles may be consequential under

certain circumstances when the concentration of infective elements is low and, therefore, the acquisition rate is slow (Fig. 5).

A dense assemblage of filter feeders can effectively reduce the concentration of particles in the water column. Once abundance rises above a certain level, each animal acquires on average a reduced number of particles from the water (Peterson and Black 1987, Frechette et al. 1992, Wilson-Ormond et al. 1997). That filter feeders can be sufficiently dense as to compete for food is well described (e.g., Frechette et al. 1992, Wilson-Ormond et al. 1997, Widdows et al. 2002). Such dense assemblages may reduce the concentration of infective particles sufficiently to permit the internal inactivation mechanisms to limit body burden below the infective dose level. This is the case in the SIP-F model (Eq. 22) where high filtration rate reduces the basic reproduction number R_0 to the formula of the SIP model, that is, the controlling parameter becomes internal particle inactivation rate a. This situation is the overfiltration scenario, where all the pathogens in the water are filtered. Here, once the population density rises sufficiently, the probability of epizootic development remains low even with increasing N providing that the number of particles filtered by each animal is lower than the infective dose (Fig. 2c, dashed lines). Unlike most disease models in which increasing N increases the likelihood of transmission and epizootic development, for filter feeders, the probability of an epizootic is low at very low N and also can be low at intermediate to high N, the exact probability distribution being a function of filtration rate and *in vivo* inactivation rate. This case is shown in Fig. 5: at low c/a and high population filtration, there is essentially no scenario exists for which R_0 is above 1.

The SIP-FV and SIPD-FV models emphasize other important mechanisms controlling the concentration of infective particles in the water column. On the addition side is the buffering capacity of a remote pool replete with infective particles. On the dilutive side is a remote pool that operates as an infective particle sink. A large remote volume in the SIP-FV and SIPD-FV models together with a high exchange rate of particles between pools and a relatively high inactivation rate of pathogens in the remote pool is an effective mechanism to reduce particle concentration in the local pool. Although water flow has been considered in the context of parasite transmission (De Montaudouin et al. 1998), the effect of dilution is best demonstrated by the literature on fertilization efficiency (Levitan 1991, Babcock et al. 1994, Thomas 1994). Particle concentration drops rapidly with distance from a point source due to both diffusive and advective processes. In the case of infective particles, the exchange rate γ becomes the controlling parameter (Eq. 36). Given a sufficient exchange rate to maintain low particle concentration locally, a modest internal inactivation rate (a in Eq. 36) may be sufficient to prevent transmission. This case is shown in Fig. 7, where few particles are retained in the local pool due to a rapid transfer of pathogens to a large remote pool with a high particle loss rate.

One application of transmission models is the use of the basic reproduction number to estimate the host density leading to effective local extinction of the pathogen. Certainly, this process must be effective both in the terrestrial world, where it is well described (e.g., Bartlett 1960, Hasibeder et al. 1992, Hufnagel et al. 2004), and the marine world. Certain marine diseases are characterized by widespread high prevalence and rapid infection of newly recruited hosts. Dermo in oysters is an exemplar. Such diseases can be termed pandemic in the sense that their infection dynamics is little influenced by the local source of infective particles. The SIP-FV and SIPD-FV models offer insight into these diseases. A disease can become pandemic only if a remote pool harbors a concentration of infective particles that continuously buffers the local removal of pathogens. Such an outcome requires either continual replacement from source populations with high mixing such as might occur in tidally dominated estuaries or limited loss from the remote pool such as might occur in estuaries with long water residence times. Regardless, if the remote pool does not operate as a sink, that is if the inactivation or loss rate σ in the remote pool is small, the final term in Eq. 35 becomes $\frac{\sigma V_\Gamma}{V_l}$ and, consequently, the volume V_Γ becomes the buffering agent assuring a continual concentration of infective particles locally that can be expected to override any particle sink or loss process in the local pool under most circumstances. A question arises as to the mechanism by which a process dominated by a local

source becomes pandemic, as must have happened in the early 1990s in Delaware Bay (Ford 1996, Bushek et al. 2012). The SIP-FV and SIPD-FV models may provide the context to evaluate the probability of pandemic disease in a given estuary or marine waterbody.

Conclusions

The relevance of these results lies in the fact that they support research regarding the relative importance of the factors involved in the initiation and termination of marine epizootics. The parameter space leading to the local demise of marine diseases or their expansion depends on the specific parameters of primary importance that define the transmission process and their relative values. Here, the normalized sensitivity index of R_0 with respect to parameters was used to determine how sensitive model results are to each parameter, over a parameter's full or at least wide range of feasible values. The formulations we present identify a number of peculiarities that are relatively unique to marine diseases. Of importance is the fact that high abundance does not always enable epizootic development. Rather, for filter feeders, the effect of abundance is bimodal, with both low and high abundances mitigating against disease development. The degree to which the remote pool acts as a sink or buffer represents a second example. Pandemic disease depends on a remote pool that buffers the local pool, whereas a remote pool that operates as a sink limits the progression of disease. In both of these cases, in a sense, the local population dynamics is circumvented in that the potential for epizootic development depends upon factors beyond the transmission, mortality, and particle release rates within the local population. These unique features require a different appreciation of the disease process in marine systems for many marine diseases relative to the classic terrestrial model exemplified by the Kermak–McKendrick formulation.

Acknowledgments

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