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Environmental disturbances of trophic interactions and their impacts on a multi-host sapronotic pathogen

Ahmadou Sylla[1,2,3,4*], Christine Chevillon[1], Magdalene Dogbe[5], Kayla M. Fast[6], Jennifer L. Pechal[4], Alex Rakestraw[4], Matthew E. Scott[6], Michael W. Sandel[6,7], Heather Jordan[5], M. Eric Benbow[4,8,9,10], Jean-François Guégan[1,2,3]

[1] MIVEGEC, Université de Montpellier (UM), Centre National de la Recherche Scientifique (CNRS), Institut de Recherche pour le Développement (IRD), Institut national de recherche pour l'agriculture, l'alimentation et l'environnement (INRAE), Montpellier, France,
[2] Epidémiologie des maladies animales et zoonotiques (UMR EPIA), Université Clermont Auvergne, INRAE, VetAgro Sup, Saint-Genès-Champanelle, France
[3] Epidémiologie des maladies animales et zoonotiques (UMR EPIA), Université de Lyon, INRAE, VetAgro Sup, Marcy l'Etoile, France
[4] Department of Entomology, Michigan State University, East Lansing, MI, USA
[5] Department of Biological Sciences, Mississippi State University, MS, USA
[6] Department of Wildlife, Fisheries, and Aquaculture, Mississippi State University, MS, USA
[7] Fish and Wildlife Research Center, Mississippi State University, MS, USA
[8] Department of Osteopathic Medical Specialties, Michigan State University, East Lansing, MI, USA, **9** Ecology, Evolution and Behavior Program, Michigan State University, East Lansing, MI, USA
[10] AgBioResearch, Michigan State University, East Lansing, MI, USA

*Corresponding authors
Correspondence: nando2014@hotmail.fr (AS)

Authors' ORCID :
A. Sylla: 0009 0008 3111 0604
C. Chevillon: 0000-0002-1262-5839
M. Dogbe: 0000-0003-1533-6095
K.M. Fast: 0000-0001-5476-5330
J. Pechal: 0000-0002-2588-2519
A. Rakestraw: 0000-0002-8087-0780
M.W. Sandel: 0000-0001-9083-9202
H. Jordan: 0000-0002-4197-2194
M.E. Benbow: 0000-0003-2630-0282
J.-F. Guégan: 0000-0002-7218-107X

ABSTRACT

Sapronotic pathogens are constituents of complex trophic networks, such as those that structure aquatic and soil ecosystems. In such habitats, sapronotic pathogens live and reproduce among microbial consortia, and occasionally infect hosts and cause sapronotic disease (sapronosis). Sapronotic pathogens include almost all fungal microparasites and about a third of the bacterial pathogens infecting humans, including for instance non-tuberculous mycobacteria. Even though sapronotic agents are naturally present in the environment, their population dynamics are unknown. Despite growing rates of sapronotic disease incidence among humans and other animals, very few studies have examined sapronotic transmission and dynamics in the context of spatially explicit trophic networks. Patterns of sapronotic pathogen transmission arise from complex interactions,

including pathogen natural history, non-host and host environments, and spatial and temporal scales of the system. In order to infer and ultimately predict how environmental disturbances affect trophic interactions and influence sapronotic ecology, we analyzed host and non-host species interacting as prey and as micro- and macropredators within a metacommunity context. Using a set of differential equation models, we assessed responses of environmental load dynamics of a sapronotic disease agent, i.e., a mycobacterial pathogen, within a general framework of environmental disturbance. We show that variation in top-down and horizontal interactions mediated sapronotic pathogen abundance and dynamics in the environment. Our findings indicate that habitat change and trophic interactions within host-pathogen relationships may strongly affect sapronotic pathogen ecology through both synergistic and opposing mechanisms. This work provides for the first time an understanding of environmental disturbance consequences on trophic webs that include major sapronotic pathogens. In addition, the results provide a basis for interpreting the development of epidemics and epizootics in the context of ecosystem modifications, particularly that of agriculture. Further research of this type will provide a better understanding of the complex dynamics of sapronotic pathogens in animals and humans responding to global change.

Keywords: Infectious disease, sapronosis, environmental pathogen, trophic interactions, environmental disturbances, mathematical modeling, disease ecology

Introduction

Human activities often cause environmental disturbances that affect biodiversity patterns across spatial scales (Dornelas et al., 2014). Characterizing how this may affect infectious disease risks has been challenging, notably because of the complexity of ecological interactions among biodiversity levels, ecosystem functioning and the transmission strategies that pathogens have evolved for persisting in time and space (Rohr *et al.* 2020). Also, pathogen transmission patterns arise from complex interactions of local transmission and the broader spatial and temporal scales of the system (Lanzas et al. 2020). Indeed, disease pathogens, by altering life-history traits of infected hosts, affect the relations between biodiversity and ecosystem functioning (Frainer *et al.* 2018). Reciprocally, studies have shown predator top-down control effects on parasite infection patterns (Clarke et al. 2019). In analyzing environmental transmission of pathogens, linking host and non-host environment, and pathogen scales can be particularly challenging; and this can be made even more complex by taking into account human ecosystem disturbances. Trophic interactions are important to ecosystem functioning, energy transfer and biodiversity maintenance, and environmental disturbance can strongly impact trophic interactions in communities (Cuff et al. 2023). With environmental disturbances predicted to become increasingly more important, it is urgent to understand how changes may affect particular functional guild of communities and consequently influence spatial and temporal dynamics of environmental pathogen ecology (Ostfeld et al. 2008). Unfortunately, there is little disease ecology modeling work showing how environmental disturbances affecting particular trophic guilds can cascade into infectious disease transmission dynamics. This type of ecosystem-based research is crucial to more broadly understanding the effects of local to global environmental changes on animal and human health (Johnson et al. 2015). Most scientific research, both empirical and theoretical, has focused on understanding the ways disease pathogens affect the existing inter-relationships in food webs, or on studying changes in food-web properties, i.e., modifying nodes and links, and their consequences in disease agents (Lafferty et al. 2008, Selakovic et al. 2014). Other work has looked at the effects of pathogens on food webs by studying the impact on the demography of a particular trophic level (De Rossi et al. 2014). In general, the theoretical analysis of the cascading effects of environmental disturbances acting on trophic webs and impacting on the presence and population dynamics of an environmentally-borne pathogen, not affecting trophic layers but having consequences for riverine species and even humans, has not been carried out (Ostfeld et al. 2008, Rossberg 2013).

Among infectious disease agents, sapronotic pathogens form an important group constituted by fungi, protozoa and bacteria that can cause opportunistic infections in wild and domestic animals and humans through inhalation, ingestion and open wounds and trauma. They infect animal or human hosts by opportunity, and at least one third of human bacterial diseases are caused by sapronoses (Kuris, Lafferty and Sokolow 2014). Non-host environments such as freshwater, soils, decaying organic matter and abiotic or biotic surfaces are important components of the lifecycle of many sapronotic pathogens (Receveur et al. 2022). These environments provide microhabitats in which sapronotic microbes may replicate or survive, facilitating transmission and persistence in time and space (Garchitorena et al. 2015a,b). Expanding human habitat use and landscape change of natural ecosystems presents emerging opportunities for animal and human sapronotic pathogens (Guerra et al. 2021).

Mycobacterium ulcerans (MU), the causative agent of Buruli ulcer (BU), a skin neglected tropical disease, is a sapronotic pathogen (Lanzas et al. 2020) that has drawn considerable attention by disease ecologists during the last decade (see Douine et al. 2017, Receveur et al. 2022 for review). Environmental disturbances, notably those of human origins (e.g., deforestation, mining, dam construction, agricultural development), are known to be associated with increased BU disease risks in humans (Merritt *et al.* 2010, Guégan *et al.* 2020). Recent evidence indicates MU presence in aquatic habitats, e.g., soil, water column, macrophyte substrates, and in a wide diversity of aquatic and riverine macroorganisms, depending on seasonal periodicity (Garchitorena et al. 2015b, Morris et al. 2016a,b, Receveur et al. 2022). Since the MU DNA concentration in the water column is generally low due to the volume of water required for filtration, research has usually inferred MU presence and dynamics

from patterns in MU carriage among aquatic macroorganisms (Garchitorena et al. 2015b, Receveur et al. 2022). Widely diverse taxa up to 80-90 different taxonomic orders (e.g., fishes, annelids, mollusks, aquatic and terrestrial arthropods) naturally carry MU without necessarily promoting disease symptoms (Morris et al. 2016b, Receveur *et al.* 2022). Time-series analyses assessing seasonal variations in the distribution and carriage of MU among these aquatic and riverine species also showed that direct acquisition of MU from contaminated water bodies in Central Africa was the main mode of transmission to humans compared to alternative routes (Garchitorena *et al.* 2015a). Depending on weather conditions throughout the year, specifically increased rainfall patterns, MU load has been shown to increase in aquatic environments, having consequences on transmission risk to humans that occupy those areas (Garchitorena et al. 2015a).

In the present work, we focus on the MU sapronotic disease agent using a metapopulation approach and differential equations modeling to model host-parasitic dynamics the role of trophic chains and environmental disturbances on sapronotic disease ecology. Taking advantage of recent work on MU ecology and dynamics in aquatic ecosystems (Garchitorena et al. 2015a,b), we first explore the role of trophic levels on the persistence and population dynamics of this sapronotic system. We then analyze the effects of local and regional environmental disturbances on trophic chains and their cascading effects on MU distribution in aquatic ecosystems. We provide a theoretical framework through which other types of sapronotic systems can be analysed and used in a predictive manner in the assessment of environmental disturbance on natural ecosystems and their biodiversity. By understanding how disturbance impacts disease dynamics in ecological networks, we argue for more research on sapronotic disease agents in wild and domestic animals, and humans. We finally call for an explicit focus on developing mathematical modeling of sapronoses given their relative incidence and importance in animal and public health.

Materials and Methods

Model formulation

We propose a spatially explicit metacommunity model where a generalist and saprophytic bacterial pathogen, e.g., *M. ulcerans*, coexists and interacts with three functional groups of free-living species: prey, representing excellent habitats for pathogen survival and reproduction, and two groups of predators, hereafter referred to as micro- and macropredators. Figure 1 illustrates the interspecific interactions considered. Table 1 details the functions and parameters of the metacommunity model. Although micropredators exclusively feed on prey, we consider two scenarii depending on macropredator diet. The first is a simple trophic chain, with macropredators feeding on micropredators that in turn consume preys. The second, called intraguild predation (Arim and Marquet 2004), stipulates that micro- and macro-predators may share a common resource: under that scenario, macropredators are generalist feeding on both preys and micropredators with the diet changing when micropredators become locally rare. Trophic interactions allow pathogen transmission from infected species to their predators. We incorporated the fact that the pathogen is a saprophytic bacterium by considering its population dynamics as a free-living saprophyte and by explicitely formulating the exchanges between the environmental saprophytic state and infectious states. Free-living bacterial cells may directly attach to living organism surfaces (called biomass hereafter), and then can be released from infected organisms upon death (hereafter refer to as bacterial saprophytic transmission). Bacterial doubling times and carrying capacity of biomass-associated bacteria differed between the three functional groups (Table 1). We modeled a metacommunity model with nine different local patches differing in productivity level, i.e., in the nutriments available for prey survival and growth. We integrated this heterogeneity in the model by conserving among-patches differences in prey growth rate (r_i) and carrying capacity (K_i).

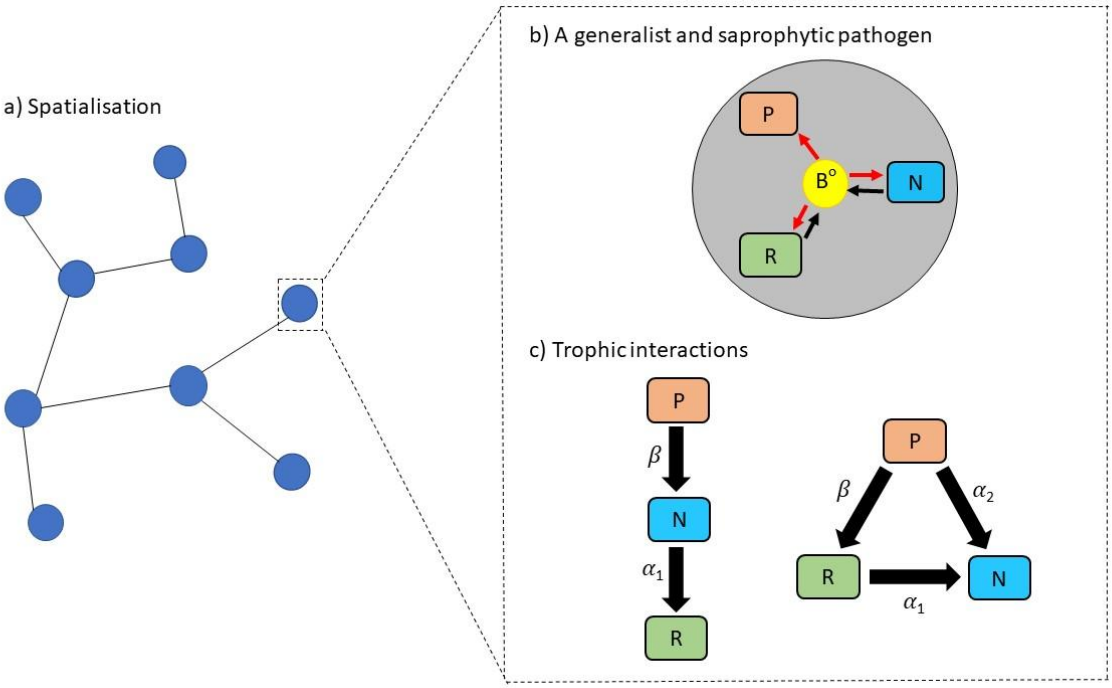

Figure 1. Schematic representation. State variables and parameters are defined in Table 1. Panel a illustrates the metacommunity in space: it includes nine habitat patches (represented by blue dots) that differ in productivity levels and are interconnected (connections represented by black lines), which allows macropredator migration across patches. Panels b and c describe the inter-specific interactions occurring within each local patch as illustrated on panel a. Panel b focuses on the characteristics of a bacterial pathogen that is both generalist and saprophytic, hence occurring within patches as both free-living bacteria (B^0) and in association with different organisms (i.e., P, N and R for macropredators, micropredators and prey, respectively). The red and black arrows respectively represent the attachment rates of free-living bacteria to living biomass and the releases of free-living bacteria from dead infected organisms when their bodies are decomposing. Panel c shows scenarios of trophic interactions considered depending on the diet of the macropredators when micropredators are only feeding on prey. Macropredators can be specialists feeding only on micropredators (on the left) or generalists feeding on micropredators and prey (on the right). We defined α_1 and α_2 as parameters describing the attack rates onto prey by micro- and macropredators, respectively, and by β the attack rate of macropredators onto micropredators. This allowed switching from the trophic chain scenario, illustrated on the left, to the intraguild predation scenario, figured on the right, simply by manipulating the value taken by α_2 (null on the left and non-null on the right).

Table 1. Functions and parameters of the metacommunity model. The third column indicates the values taken by default for the different parameters across experiments. When no value is illustrated, it means that parameter is either a vector or a function, and its value is specified in section 2.2.

Notations	Descriptions	Values
	State functions	
N_i	Density of prey species in patch i	
R_i	Density of micropredator species in patch i	
P_i	Density of macropredator species in patch i	
B_i^N	Density of prey-associated bacteria in patch i	
B_i^R	Density of micropredator-associated bacteria in patch i	
B_i^P	Density of macropredator-associated bacteria in patch i	
B_i^o	Density of free-living bacteria in patch i	
	Parameters	
r_i	Intrinsic growth rate of prey species in patch i	-
K_i	Environmental carrying capacity of preys in patch i	1
□	Natural mortality of preys	0.05
α_1	Maximal attack rate of micropredators onto preys	0.4
α_2	Maximal attack rate of macropredators onto preys	0 or 0.25
β	Maximal attack rate of macropredators onto micropredators	0.25 or 0.5
e_1,e_2,e_3	Constants of the Beddington–DeAngelis functional response	0.1
b	Constant of the Beddington–DeAngelis functional response	1
h	Constant of the Beddington–DeAngelis functional response	1
c_1	Food conversion efficiency of preys into micropredator births	0.7
c_2	Food conversion efficiency of preys into macropredator births	0.7
c_3	Food conversion efficiency of micropredators into macropredator births	0.7
d_1	Natural death rate of micropredators	0.05
d_2	Natural death rate of macropredators	0.05
$m_i(t)$	Migration rate of macropredator in patch i	-
q_{ji}	Probability that an individual from patch i migrates to patch j	1/8
ξ	Bacterial attachment rate on prey biomass	0.4
γ	Bacterial attachment rate on micropredator biomass	0.13
ρ	Bacterial attachment rate on macropredator biomass	0.06
s_N	Half-saturation constant of prey-associated substrate	1
s_1	Half-saturation constant of micropredator-associated substrate	1
s_2	Half-saturation constant of macropredator-associated substrate	1
θ	Growth rate of prey-associated bacteria	1
□	Growth rate of micropredator-associated bacteria	0.05
□	Natural mortality of prey-associated bacteria	0.02
□$_1$	Natural mortality rate of micropredator-associated bacteria	0.03
□$_2$	Natural mortality rate of macropredator-associated bacteria	0.2
$\Lambda(t)$	Time-dependence free-living bacteria growth rate	0.3
δ	Natural mortality rate of free-living bacteria	-
κ	Bacilli release rate from decomposing bodies of infected preys	0.03
σ	Bacilli release rate from decomposing bodies of infected micropredators	3
		2

In patch i, we denoted by functions of time t: N_i the density of prey, R_i the density of micropredator species, P_i the density of macropredator species, B_i^N the density of prey-associated bacteria, B_i^R the density of micropredator-associated bacteria, B_i^P the density of macropredator-associated bacteria, and by B_i^o the density of free-living bacteria in the aquatic environment. We assume that the prey population obeys a classical logistic growth, with r_i referring to the intrinsic growth rate and K_i to the environmental carrying capacity. Due to predation, the prey population size decreases by a quantity proportional to prey and predator populations. Here, the predator-prey interactions are modeled via Beddington–DeAngelis' functional response (Beddington 1975, DeAngelis *et al.* 1975). This functional response is an enhancement of the well-known Holling's type II functional response including a term representing interference among predators. Increasing the density of consumers (i.e., predators) also reduces the consumption rate of the resource (i.e., preys). Several studies in the ecological literature have considered this type of response (Cantrell *et al.* 2004, Ghanbari and Kumar 2019, Ji and Wang 2022, Tripathi *et al.* 2015).

Using the functions and parameters described in Table 1, we formulated the model as follows. The dynamics of biomass for the three functional groups in patch *i* are given by:

$$\frac{dN_i}{dt} = r_i N_i \left(1 - \frac{N_i}{K_i}\right) - \mu N_i - \frac{(\alpha_1 R_i + \alpha_2 P_i) N_i}{1 + e_1 R_i + e_2 P_i + b N_i} \quad (1)$$

$$\frac{dR_i}{dt} = \frac{c_1 \alpha_1 R_i N_i}{1 + e_1 R_i + e_2 P_i + b N_i} - d_1 R_i - \frac{\beta P_i R_i}{1 + e_3 P_i + h R_i} \quad (2)$$

$$\frac{dP_i}{dt} = \frac{c_2 \alpha_2 P_i N_i}{1 + e_1 R_i + e_2 P_i + b_1 N_i} - d_2 P_i + \frac{c_3 \beta P_i R_i}{1 + e_3 P_i + h R_i} - m_i P_i + \sum_{j \neq i} m_j q_{ij} P_j \quad (3)$$

Parameters α_1 and α_2 denote, respectively, the attack rate of micro- and macropredators onto preys. Parameter β represents the predation rate of macropredators onto micropredators. Predator growth clearly depends on food consumption. We thus define c_1, c_2 and c_3 as the respective food conversion efficiency of predators, representing thus the number of newborn predators resulting from their consumption. In absence of prey, micro- and macropredator densities decay exponentially at rate d_1 and d_2, respectively. The term μN_i describes the prey loss due to natural mortality. Our model also incorporates macropredator migration events across the different local communities. At each time *t*, a fraction of macropredators $m_i(t)$ leaves patch i to other patches. A part q_{ji} of these emigrants choose patch j as destination. Thus, the flux of biomass from patch i to patch j at time *t* is $m_i(t) q_{ji} P_i(t)$. Summing the immigrants coming from all the other patches to patch *i* provides the last term figuring in equation (3).

The dynamics of prey-associated, micropredator-associated and macropredator-associated bacteria in patch *i* are respectively given by:

$$\frac{dB_i^N}{dt} = \frac{\xi N_i B_i^o}{s_N + N_i} + \frac{\theta N_i}{s_N + N_i} B_i^N - (\eta + \mu) B_i^N - \frac{(\alpha_1 R_i + \alpha_2 P_i) B_i^N}{1 + e_1 R_i + e_2 P_i + b B_i^N} \quad (4)$$

$$\frac{dB_i^R}{dt} = \frac{\gamma_i R_i B_i^o}{s_1 + R_i} + \frac{\lambda R_i B_i^R}{s_1 + R_i} - (\nu_1 + d_1) B_i^R + \frac{\alpha_1 R_i B_i^N}{1 + e_1 R_i + e_2 P_i + b B_i^N} - \frac{\beta P_i B_i^R}{1 + e_3 P_i + h B_i^R} \quad (5)$$

$$\frac{dB_i^P}{dt} = \frac{\rho P_i B_i^o}{s_2 + P_i} - (\nu_2 + d_2) B_i^P + \frac{\alpha_2 P_i B_i^N}{1 + e_1 R_i + e_2 P_i + b B_i^N} + \frac{\beta P_i B_i^R}{1 + e_3 P_i + h B_i^R} - m_i B_i^P + \sum_{j \neq i} m_j q_{ij} B_j^P \quad (6)$$

The intrinsic growth rate of host-associated bacteria depends upon the density of predators and prey biomasses as substrates for bacterial development. The parameters η, ν_1 and ν_2 correspond, respectively, to the natural mortality rate of prey-associated, micropredator-associated and macropredator-associated bacteria. Here, we used Michaelis-Menten' type functional response to describe bacilli attachment to biomass, which is proportional to both population biomass and free-living bacteria densities. We defined the maximum success rates for bacilli attachment on prey, micropredators and macropredators as ξ, γ_i and ρ, respectively. The biomass-associated bacteria are able to replicate on alive biomass until surface saturation concentration is reached. Focusing for instance on prey-associated bacteria, the Michaelis-Menten' type functional response is thus given by $\theta N_i/(N_i + s_N)$, where θ is the maximum production rate of prey-associated bacteria, and s_N is the half-saturation constant in this type of micro-habitat. The same functional response was used for predator-associated bacterial reproduction. Saprophytic bacilli growing on the surface of living biomass are released when the bodies of dead infected organisms are decomposing, which thus produce free-living bacteria (Godfray *et al.* 1999, Kunttu *et al.* 2009, Merikanto *et al.* 2018). These phenomena, assumed to occur only in prey-and micropredator guilds (i.e., macropredators are considered dead-ends for the pathogen), are here described by

parameters κ and σ. Note that, aside such releases, biomass mortality reduces the concentration of biomass-associated bacteria that are respectively described by terms $-\mu B_i^N$, $-d_1 B_i^R$ and $-d_2 B_i^P$ in equations (4), (5) and (6), respectively. Similarly, while feeding on the prey present in patch *i*, predators locally decrease the number of prey-associated bacteria. In our model, we further incorporated the changes in the local densities of biomass-associated bacteria resulting from migration of macropredators among connected patches (see above).

The dynamics of free-living bacteria in patch *i* is given by:

$$\frac{dB_i^o}{dt} = (\Lambda - \delta)B_i^o - \frac{\xi N_i B_i^o}{s_N + N_i} - \frac{\gamma_i R_i B_i^o}{s_1 + R_i} - \frac{\rho P_i B_i^o}{s_2 + P_i} + \kappa\mu B_i^N + \sigma d_1 B_i^R \quad (7)$$

where □(t) and □ are the reproduction and natural mortality rates of free-living bacteria, respectively. The body decomposition of infected organisms, either preys or micropredators, release saprophytic bacteria in the environment, increasing thus the local density in free-living bacteria in the patch when these organisms died (see terms $\kappa\mu B_i^N$ and $\sigma d_1 B_i^R$ in equation (7).

The metacommunity dynamics result from macropredators dispersal among-patches. We considered this dispersal to be active, depending on the local availability of resources. In the trophic chain scenario (Figure 1c, left), we have described the migration rate, $m_i(t)$, as a function inversely proportional to the local density of micropredators:

$$m_i(t) = \frac{u}{1 + R_i(t)} \quad (8)$$

where *u* is the maximal dispersal rate. In the alternative scenario considering macropredators as generalists (Figure 1c, right), we have described the migration rate, m_i(t), as a function inversely proportional to both local densities of prey and micropredators:

$$m_i(t) = \frac{u}{1 + R_i(t) + N_i(t)} \quad (9)$$

These definitions ensure that the migration rate of macropredators will increase when local food abundance decreases. For simplicity, we suppose that the pool of emigrants leaving the patch *i* has equal probability to reach any other local habitats (q_{ji}=1/(n-1)).

Regarding environmental disturbances, we focused on cases where they promote sudden increases in predator mortality, hence instantaneous decreases in predator densities (P_i and/or R_i). We also considered perturbations that, in addition to their sudden and direct impact on predator mortality, reduce the growth rate in preys, r_i, relatively to the value determined by the primary productivity level of the affected patch (see below, the third simulating experiment). Given differences among simulation experiments considered in the present paper, the modeling methodology is further developed within each section referring to a particular experiment.

Simulation parameters

We simulated a metacommunity composed of nine interconnected local sites. We set the vector describing prey growth rate among sites as *r* = [0.15, 0.17, 0.2, 0.23, 0.25, 0.28, 0.31, 0.35, 0.38]. We simulated free-living bacteria reproduction as simple Weibull's distribution (t) = 4×Weibull(*t*,100,4). Table 1 presents the values taken by default across all simulations by other parameters. We conducted numerical analysis of the model using the MATLAB software (MATLAB, ver. 8.6).

Results

Numerical simulations are proposed with the aim of understanding how disturbing local communities affects, via their direct and indirect impacts on species communties, the infection risks by a bacterial pathogen that is both generalist and saprophytic. For each model scenario, we randomly chose the timing of disturbances, and repeated simulations with different starting dates of disturbances and variable severity impacts on local communities. We explored the properties of the model by investigating how such variations in timing, spatial scale and/or severity of disturbances affect free-living bacteria density. For each model scenario, we run the simulations long enough for encompassing the two phases that follow the occurrences of perturbations; i.e., a first phase along which the food web remains destabilized, and a second where it reaches a new dynamic equilibrium. In the two first experiments, local or regional environmental perturbations are instantaneous events that only affect predatory guilds: predator densities in disturbed patch(es) are recovering just after the environmental disturbance as function of the local resources. In the third experiment, environmental disturbances reduce the densities of predator but also affects prey growth, with this latter effect lasting for several days or weeks, promoting delays in both prey and predator recoveries relatively to expectations for undisturbed habitats. Hereafter, for the sake of brevity, we have selected the most interesting and informative findings.

Experiment 1: Local ecological disturbance (i.e., affecting a single patch)

The Figure 2 illustrates cases of local environmental disturbance that occurs when the fluctuating density in saprophytic bacteria was naturally rising. For a same species assemblage at $t = 0$, four possibilities exist. The environmental disturbance may affect only macropredators (Fig. 2, top panels) or both macro- and micropredators (Fig. 2, bottom panels). Macropredators may be specialist (left panels) or generalist (right panels). In each panel, the green curve represents the temporal dynamics in free-living bacteria density that one would have observed in absence of disturbance. Green curves are thus identical in the two right panels (left panels, respectively) but obviously different between left and right panels. Other lines represent the dynamics in free-living density observed after disturbance.

In all panels, the most obvious impact of disturbance onto the dynamics in free-living bacteria density relies to the period along which the local food-web remains destabilized. There is a temporary increase in sapronotic bacteria along that period, which results from a temporary excess of the inputs from the decomposing bodies of previously infected organisms relatively to the observations in absence of disturbance. For a given food-web structure (i.e., for panels within the same column in Figure 2), such an excess is much higher when the disturbance affects both predatory guilds, enriching thus the community in unconsumed preys (bottom panels) relatively to the case where disturbance only affect macropredators (top panels). For a given impact of disturbance (i.e., for panels within the same raw), the food-web structure matters on the long-term response to local disturbance. Indeed, in trophic chain scenarios (i.e., involving only specialist predators), the post-disturbance equilibrium translates in a reduction in free-living bacteria density relatively to the pre-disturbance equilibrium. This is not the case for food webs involving generalist macropredators: there, the pre- and post-disturbance equilibria of the system result in similar dynamics in free-living bacteria density.

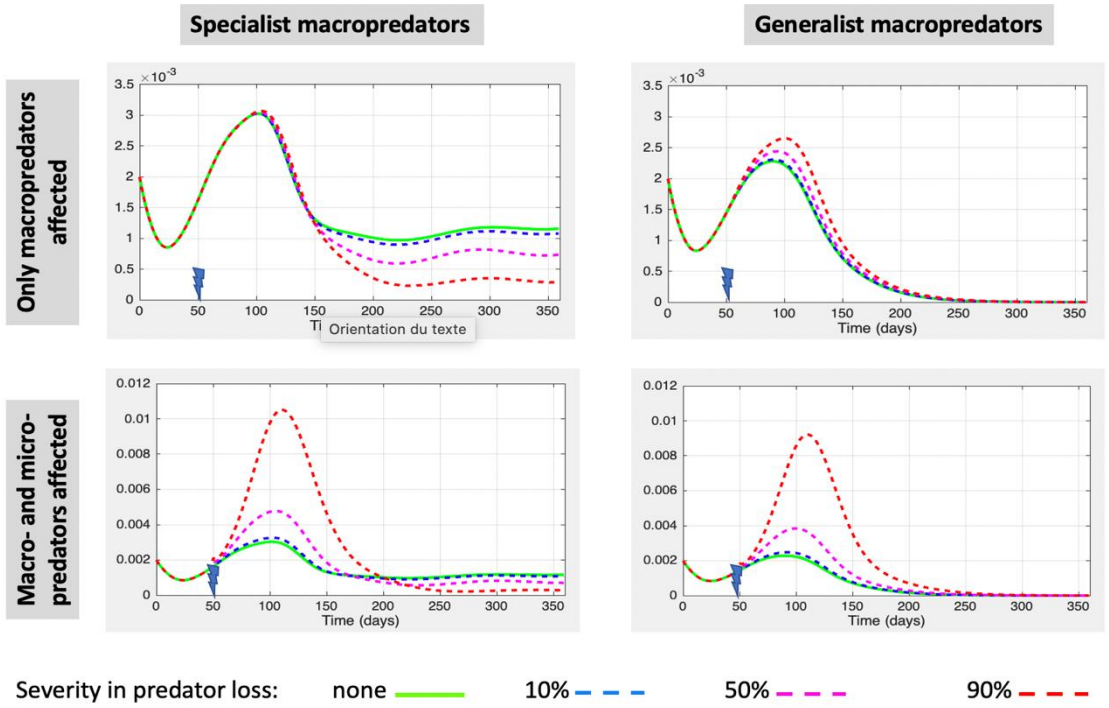

Figure 2: Effects of local disturbances onto the local dynamics in free-living bacteria density. X-axes represent time and Y-axes free-living bacteria density. In all panels, green curves represent the local density in free-living bacteria in absence of perturbation. Other curves refer to the dynamics in free-living bacteria for an instantaneous reduction in predator densities at t = 50, when disturbance occurs, ranging from 10% to 90%. The perturbations affect only macropredators in top panels but both micro- and macropredators in bottom panels. Macropredators are specialists in left panels and generalists in right ones. Predation parameters used in trophic chain scenarios are $\alpha_2 = 0$ and $\beta = 0.5$; they are $\alpha_2 = 0.25$ and $\beta = 0.25$ otherwise.

Experiment 2: Regional ecological disturbance affecting predators

Here, we consider the case of regional ecological disturbance so that (i) every patch is the subject of local disturbance once a year and (ii) within-patches disturbances evenly affect micro- and macropredators. Patches still differ from one another in primary productivity (hence in prey logistic growth). Local disturbances can occur as synchronous events across all patches or as asynchronous events that include time lags between disturbances affecting distinct patches. In addition, disturbances may differ in the severity of predator reductions they induced. We thus simulated synchronous and asynchronous events with homogeneous (i.e., all local communities suffer the same reduction in both micro- and macropredator densities) and heterogeneous effects across patches.

Figure 3 shows the simulation results obtained for specialist macropredators. Panels a-d are evidence of the importance of time lags between successive disturbances affecting distinct patches with homogenous severity. Specifically, synchronous events (panel a) or short delays (panel c) between successive disturbances events lead to larger temporary increases in regional average in free-living bacteria density.

Next, we assessed the importance of heterogeneity in predator losses resulting from synchronous regional disturbance on free-living bacteria density. Here, there are two sources of heterogeneity among patches: differences in primary productivity r (ranging from 0.15 to 0.38) and differences in predator losses (randomly selected from 0% to 100%). In order to examine the interplay between the two sources of heterogeneity, we explored the dynamics in the regional average in free-living bacteria density when the correlation between them was random, minimal or maximal (Figure 3, panel e-f). At local scale, the impact of the heterogeneity in disturbance severity exceeds that of the heterogeneity in productivity (see the yellow curve in f panel and/or the red curve in g panel). Unsurprisingly, at the regional scale, the highest rebound in free-living bacteria density occurs when the correlation between both sources of among-patches heterogeneity is maximal (Figure 3e).

Results obtained for generalist macropredators are similar and presented in supplementary materials (Figure S1). It is nevertheless noteworthy that, as previously observed at local scale (Figure 2), the diet of the macropredators affects the long-term response of the metapopulation to a succession of local disturbances. On the one hand, when both predator guilds are specialist, the main difference between pre- and post-disturbances equilibria at metapopulation scale translates into a reduction in in free-living bacteria density (Figure 3). On the other hand, when macropredator are generalist, the long-term response of the metapopulation to a succession of local disturbances tend to be the same as that observed in absence of disturbance (Figure S1).

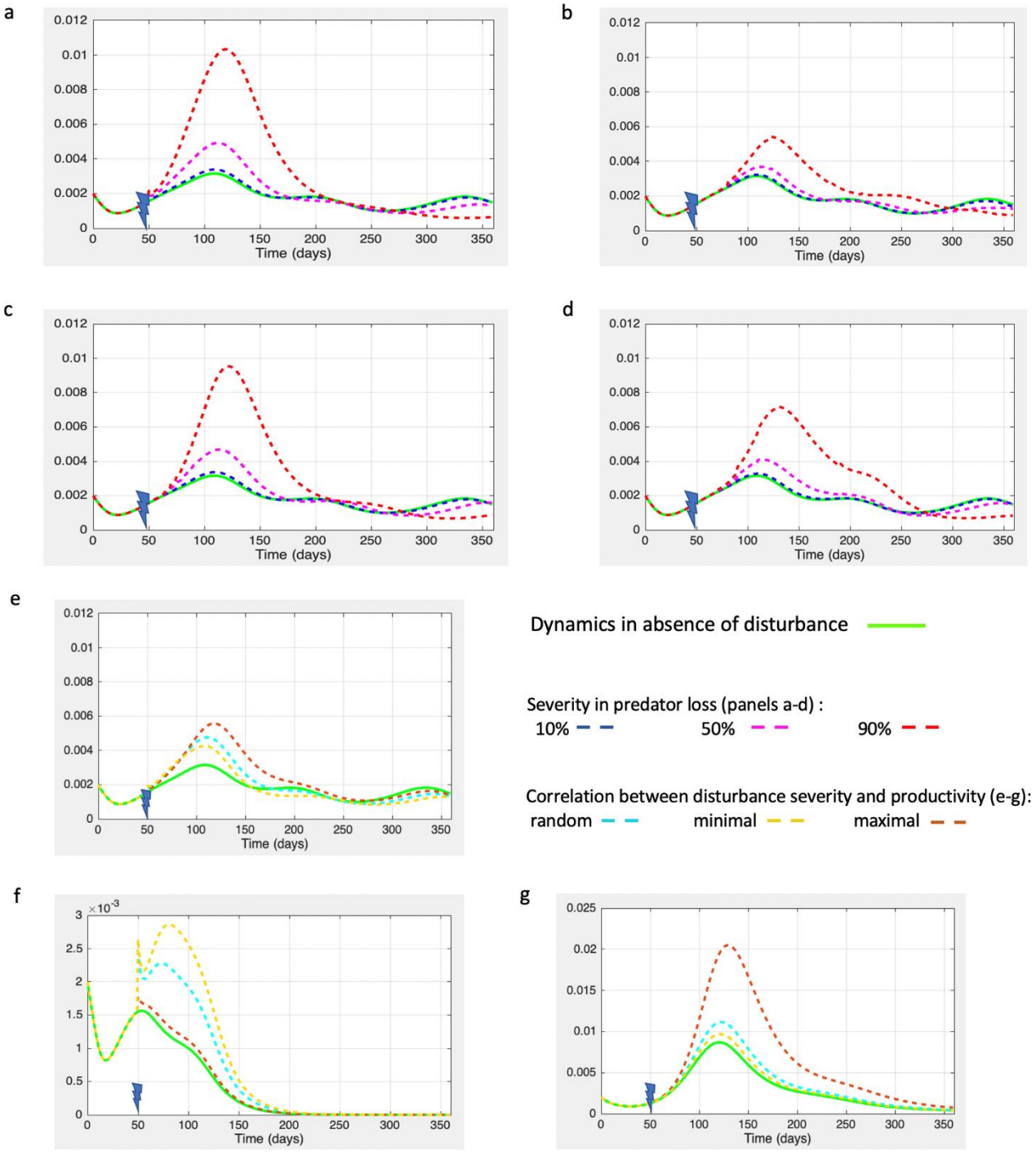

Figure 3. Impact of a succession of within-patches disturbances (trophic chain scenario). The diet of specialist macropredators is described by $\alpha_2 = 0$ and $\beta = 0.5$. First local disturbance occurs at $t = 50$ days. Panels a-e consider the regional scale of the entire metapopulation. Green curves refer to the regional dynamics in free-living density observed in absence of disturbances and others to those observed after successions of within-patches disturbances. In a-d panels, all local disturbances have homogeneous impact on within-patches predator densities. These local events are synchronized across patches in panel a. In panel b, the vector describing random timing of local disturbances across patches is t = [50, 123, 180, 346, 50, 211, 81, 271, 92, 183]. Time lags between successive disturbances last 5 and 20 days in panels c and d, respectively. In panel e, local disturbances are synchronized events with heterogeneous impacts on predator densities across patches. Panels f and g focus on the within-patches responses observed in the least and most productive patches, respectively.

Experiment 3: Regional ecological disturbance also affecting preys

The results presented so far concern disturbance with instantaneous effects that only affect predator guilds. However, some perturbations, such as pollution resulting from gold mining, may affect all species present in aquatic ecosystems. Here, we explore cases where disturbances affect all functional groups although differently. Disturbances instantaneously reduce predator densities, but promote a temporary or lasting reduction in prey population growth.

We carried out a sensitivity analysis on the duration of the blockage period of prey growth after disturbance for different impacts of local reproduction rate r_i. Figure 4 shows the results of simulations in cases where r_i is reduced either by 50% (top panels) or by 100% (bottom panels), and where macropredators are either specialist (left panels) or generalist (right panels). We found that the regional average in free-living bacterial density depends on how long and to which extent disturbances affects prey growth. It is noteworthy that the extent in the reduction in prey growth (here, 50% *versus* 100%) have larger impacts on metapopulation responses relatively to the period duration of such effects on prey (here, 15 days *versus* 60 days).

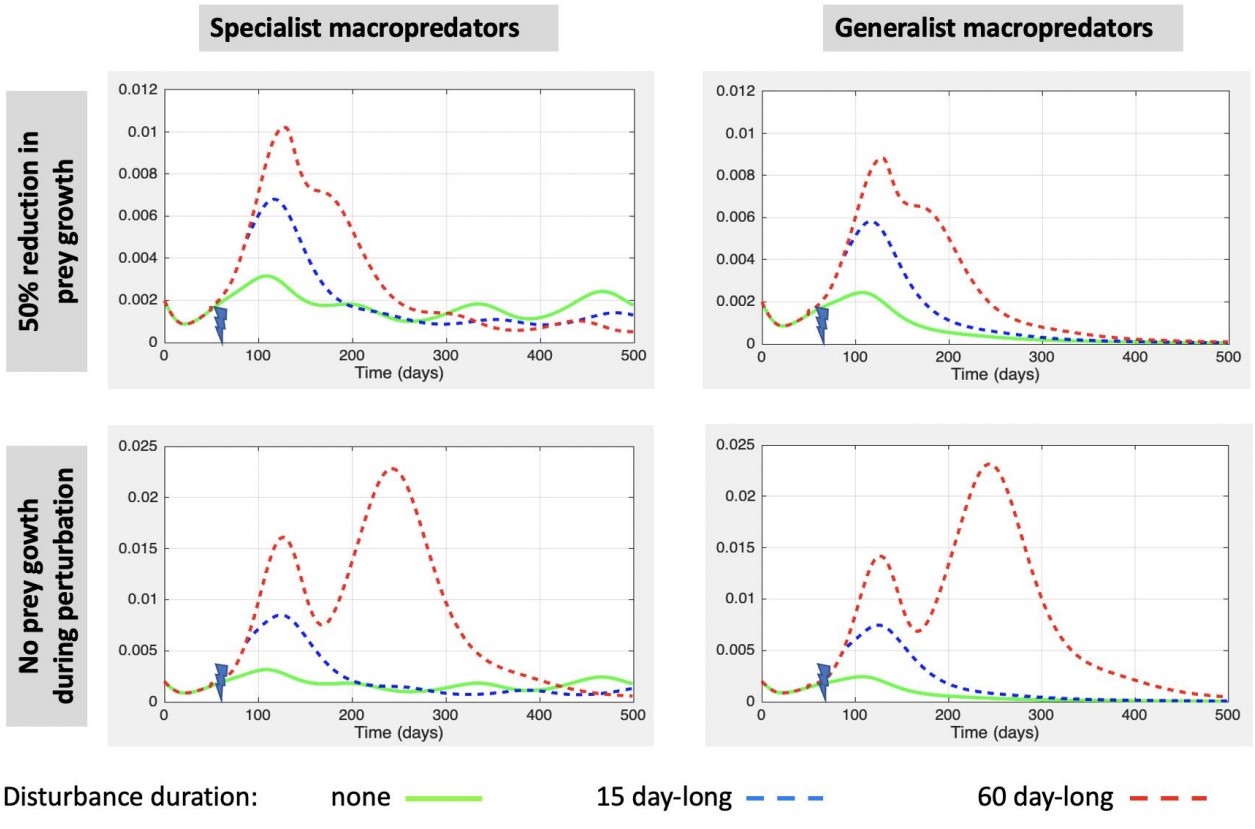

Figure 4. Regional disturbance effects on prey and predators that impact density of free-living bacteria over the metacommunity. X-axes represent time; disturbances occur at t = 69 days. Y-axes refer to the regional averages in free-living bacteria density. Macropredators are specialist (α_2 = 0 and β = 0.5) in left panels and generalist (α_2 = 0.25 and β = 0.25) in right panels. Green curves refer to the regional average dynamics in saprophyte density observed in absence of disturbances. Those are identical in both left panels (right panels, respectively) but differ between right and left panels. Disturbances promote instantaneous reductions in predators. The vector describing the heterogeneity across patches in predator losses is [0.6663, 0.5391, 0.6981, 0.6665, 0.1781, 0.1280, 0.9991, 0.1711, 0.0326]. The blue and red curves refer to the regional responses in free-living bacteria density to disturbances blocking prey growth for 15 and 60 days, respectively. The reduction in prey growth during disturbances is 50% and 100% in top and bottom panels, respectively. Please note that the scale of the Y-axes in bottom panels exceeds those referring to regional average in bacterial loads in Figures 2 and 3.

Experiment 4: Relaxing dispersal constraints on functional groups including species competent for the pathogen survival and growth

The first three experiments focused on cases where macropredators, which are dead-end hosts for the bacterial pathogen, constitute the only functional ecological group that include species dispersing across the metacommunity. We tested the dependency of the results withdrawn under this hypothesis by re-computing simulations for each experiment while assuming that species from the three tropic levels disperse across the metacommunity (everything else remaining unchanged). We assumed passive and non-oriented dispersal for preys, so that a fixed percentage of preys emigrate from each local site and evenly distribute among the other local sites. For micropredators, we assumed active migration that depends on the local resources in preys (i.e., obeying to the same rules than those defined for specialist macropredators; see equation #8 above).

Figures S3-S6 detail results for experiments 1-3 under two dispersal hypotheses for preys and micropredators (cases A and B). In case A, we fixed prey dispersal at 1% and maximal dispersal rates of micro- and macro-predators at 5% and 70%, respectively. In case B, we fixed prey dispersal at 6% and maximal dispersal rates of micro- and macropredators at 10% and 70% for micro- and macropredators, respectively. Comparing those to figures 2-3 and S1 evidence that the signals observed when only macropredator disperse remain if species from all functional groups disperse. Introducing dispersal of prey and micropredator nonetheless tend to make perturbations promoting lower and delayed peaks in the abundance of free-living bacteria relatively to cases where only macropredator disperse.

Discussion

Empirical studies show that predators affect animal and human pathogen emergence and spread, even though they reduce prey and vector abundances (Cohen *et al.* 1990). Despite evidence that interactions among predators, prey and other species might affect environmental pathogen abundance, few empirical or modeling studies have examined such interactions in a food-web context (see Clark *et al.* 2019). This is problematic since a better assessment of multitrophic interactions affecting pathogen dynamics in complex species communities could greatly increase our understanding of disease ecology. Here, we assessed, using a mathematical approach, how local and regional disturbances of micropredator - macropredator - prey trophic interactions affect the environmental load of a sapronotic and generalist pathogen, i.e., *Mycobacterium ulcerans* causing cutaneous infections in animals and humans, and responsible for Buruli ulcer in humans. Interestingly, our models are sufficiently flexible and adaptable to other types of sapronotic and generalist pathogens, assuming some basic modifications of equations (e.g., suppression of the parasite life cycle).

Our study shows that interactive effects of the aquatic environment and multi-host and non-host local communities affected over space and time the abundance of an environmental pathogen under a range of scenarios. Notably, the effects of environmental disturbances were strongly context-dependent and had differential effects on the population dynamics of the environmental pathogen, and thus on potential transmissibility to animals and humans. In this system, we found that the magnitude of predator effects on prey abundance, which impacted environmental pathogen prevalence, were considerably stronger when both micro- and macropredators were affected by local and regional environmental disturbance regimes. In general, the role of disease pathogens and parasites in ecological webs is critical in shaping communities of populations (Dobson et al. 2008). Based on these considerations, then, in this work we wanted to consider the influence of environmental perturbations on a food system composed of three trophic levels, and their effects on population dynamics of a sapronotic disease agent. We assumed that the disease did not affect any trophic levels in the food web, but impacted on terrestrial animals and humans, using the example of *Mycobacterium ulcerans,* a neglected tropical skin disease in human. Several modeling studies exist that analysed the effect of pathogens on di-trophic systems, e.g., phytoplankton species and grazers (Beltrami and Carroll 1994, see also Rossi et al. 2014), and many

others have empirically studied the prey-predator interactions and their impacts on parasite population dynamics (Tian and Stenseth 2019 for hantavirus disease, Levi et al. 2012 for Lyme disease as two illustrative examples; see Ostfeld et al. 2008 for a more general overview). In this work, we were interested in considering disease agents in a larger ecosystem, namely a trophic chain composed of three trophic layers, and mathematically analyse the impacts of environmental disturbance on prey-predator-pathogen relationships. At least to our knowledge, this is the first time that a research work is identifying how habitat perturbation impacts the identity and frequency of a disease agent through mediated effects on trophic interactions.

First, our results demonstrate that, in a situation of local disturbance, density and diet regime, i.e., specialist *versus* generalist, are important factors in driving top-down effects of macropredators on environmental pathogen population dynamics. This effect is much greater when macropredators are specialised on feeding upon a particular micropredator species (Figure 2, top left panel) than when being generalists (Figure 2, top right panel). In fact, specific predation on a micropredator species leads to a relaxation of the pressure exerted on prey, and therefore leads to an increase in their abundance in the environment, and thus, providing favorable ecological conditions for sapronotic agents (Figure 2, top left panel). However, when macropredators are generalists, the consequences on the pathogen are less important due to a dual effect of intraguild competition. In this situation, there is a threshold effect of macropredator density on environmental pathogen abundance (Figure 2, top right row) depending on both macropredator diet strategy and local species diversity. In a situation where the local environmental disturbance affects both micro- and macropredator compartments, there is a significant impact on the population dynamics of the bacteria, whatever the type of macropredator diet. However, the increase in environmental pathogen abundance is slightly greater when macropredators are generalists. These results are consistent with studies showing top-down effects of local environmental disturbances on plant vector-borne pathogen dynamics through consumptive and non-consumptive effects (Finke 2012, Clarke *et al.* 2019).

Second, regional environmental disturbances affect local food-webs through both micro- and macropredator guilds, where synchronous or high-frequency disturbance events lead to higher pathogen abundance in the environment (Figure 3a-d). In addition, disturbance severity is more important to pathogen load than local biomass productivity and spatial heterogeneity (Figure 3e). We also found that regional disturbance did not influence how predator diet regime, i.e., generalist or specialist, affected pathogen dynamics (Figure S1).

Third, in the case of more extreme environmental disturbance in which prey guilds are also affected, we observed that local food-web effects on pathogen dynamics were mediated by impacts on prey population growth (Figure 4). Also, stronger impacts were observed for important reduction in prey reproduction rate relatively to perturbation duration, which did not significantly affect pathogen load.

Our modeling work has focused on analyzing the dynamic behavior of a sapronotic agent over a period of one year, for which we currently have sufficient empirical knowledge. Based on the knowledge gradually acquired, it will be necessary to study their complex and non-linear dynamics over multi-decadal time steps, which are more in tune with the tempo of local and more global changes currently taking place all over the planet.

Our theoretical study supports recent reviews and models that posit food-web theory provides important insights to understanding direct and indirect effects of ecological interactions involving disturbances, environmental heterogeneity and multi-host dynamics on pathogen transmission and disease ecology (Roche *et al.* 2013, Seabloom *et al.* 2015, Crowder *et al.* 2019). Notably, at local scales the strength and magnitude of disturbance on macropredators mediated the population dynamics of environmental pathogens in the case of specialized macropredators only. More broadly, regional environmental perturbations may affect pathogen dynamics when severe, long-term or successive disturbance events occur in a short period of time. This simulation study that integrates multitrophic frameworks to assess human (or other animal)-biodiversity-environmental pathogen communities will help us better understand and interpret why epidemics or epizootics of environmental pathogens can suddenly develop and spread. Further, it can promote better control and management of these harmful animal and human infectious diseases.

Conclusion

Since sapronotic disease agents have one or multiple reservoir hosts in the environment, their control is rendered impossible or ineffective if this origin is not taken into account. Control of such animal and human diseases therefore requires a thorough understanding of the host-parasite dynamics and pathogen ecology in their environment, which is very rarely the case. Sapronotic diseases may become a problem for wild and domestic animals, e.g., livestock, and humans when exposure increases or spillovers to other animal species of human concern, e.g., contacts between wildlife and livestock, happen. Models of sapronotic pathogen transmission are extremely rare in the current scientific literature. Our modeling study show that sapronoses may be highly dependent on the environmental conditions prevailing in species communities, and regulated by prey-predator relationships in trophic chains. In addition, these sapronoses are themselves highly sensitive to local and large-scale environmental disturbances impacting species communities in a cascade of effects' process. It is important for human and veterinary medicine, but also more generally, to recognize that the control of these sapronoses requires a better understanding of their ecology and environmental dynamics. Too few epidemiological studies have examined the influence of environmental change and species community structure on disease transmission, and this should constitute a priority for subsequent investigation. Mathematical modeling, combined with new experimental studies, represents highly valuable tool to better understand environmental transmitted pathogens and their population biology, and to project possible scenarios for future sapronotic outbreaks in the current international context of global change.

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Conflict of interest disclosure

Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the view of the institutions and funding agencies quoted above. The authors declare that they comply with the PCI rule of having no financial conflicts of interest in relation to the content of the article.

Scripts, code, and supplementary information availability

Script and codes are available online (https://doi.org/10.5281/zenodo.11085318; Sylla et al., 2024a); Supplementary figures are available online (https://zenodo.org/records/11083413; Sylla et al. 2024b).

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