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

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

<sup>1</sup> 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,

<sup>2</sup> Epidémiologie des maladies animales et zoonotiques (UMR EPIA), Université Clermont Auvergne, INRAE, VetAgro Sup, Saint-Genès-Champanelle, France

<sup>3</sup> Epidémiologie des maladies animales et zoonotiques (UMR EPIA), Université de Lyon, INRAE, VetAgro Sup, Marcy l'Etoile, France

<sup>4</sup> Department of Entomology, Michigan State University, East Lansing, MI, USA

<sup>5</sup> Department of Biological Sciences, Mississippi State University, MS, USA

<sup>6</sup> Department of Wildlife, Fisheries, and Aquaculture, Mississippi State University, MS, USA

<sup>7</sup> Fish and Wildlife Research Center, Mississippi State University, MS, USA

<sup>8</sup> Department of Osteopathic Medical Specialties, Michigan State University, East Lansing, MI, USA, <sup>9</sup> Ecology, Evolution and Behavior Program, Michigan State University, East Lansing, MI, USA

<sup>10</sup> AgBioResearch, Michigan State University, East Lansing, MI, USA

\*Corresponding authors

Correspondence: [nando2014@hotmail.fr](mailto: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,

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

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

70 Human activities often cause environmental disturbances that affect biodiversity patterns across spatial  
71 scales (Dornelas et al., 2014). Characterizing how this may affect infectious disease risks has been challenging,  
72 notably because of the complexity of ecological interactions among biodiversity levels, ecosystem functioning  
73 and the transmission strategies that pathogens have evolved for persisting in time and space (Rohr *et al.* 2020).  
74 Also, pathogen transmission patterns arise from complex interactions of local transmission and the broader  
75 spatial and temporal scales of the system (Lanzas et al. 2020). Indeed, disease pathogens, by altering life-history  
76 traits of infected hosts, affect the relations between biodiversity and ecosystem functioning (Frainer *et al.* 2018).  
77 Reciprocally, studies have shown predator top-down control effects on parasite infection patterns (Clarke et al.  
78 2019). In analyzing environmental transmission of pathogens, linking host and non-host environment, and  
79 pathogen scales can be particularly challenging; and this can be made even more complex by taking into account  
80 human ecosystem disturbances. Trophic interactions are important to ecosystem functioning, energy transfer  
81 and biodiversity maintenance, and environmental disturbance can strongly impact trophic interactions in  
82 communities (Cuff et al. 2023). With environmental disturbances predicted to become increasingly more  
83 important, it is urgent to understand how changes may affect particular functional guild of communities and  
84 consequently influence spatial and temporal dynamics of environmental pathogen ecology (Ostfeld et al. 2008).  
85 Unfortunately, there is little disease ecology modeling work showing how environmental disturbances affecting  
86 particular trophic guilds can cascade into infectious disease transmission dynamics. This type of ecosystem-based  
87 research is crucial to more broadly understanding the effects of local to global environmental changes on animal  
88 and human health (Johnson et al. 2015). Most scientific research, both empirical and theoretical, has focused on  
89 understanding the ways disease pathogens affect the existing inter-relationships in food webs, or on studying  
90 changes in food-web properties, i.e., modifying nodes and links, and their consequences in disease agents  
91 (Lafferty et al. 2008, Selakovic et al. 2014). Other work has looked at the effects of pathogens on food webs by  
92 studying the impact on the demography of a particular trophic level (De Rossi et al. 2014). In general, the  
93 theoretical analysis of the cascading effects of environmental disturbances acting on trophic webs and impacting  
94 on the presence and population dynamics of an environmentally-borne pathogen, not affecting trophic layers but  
95 having consequences for riverine species and even humans, has not been carried out (Ostfeld et al. 2008,  
96 Rossberg 2013).

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

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

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

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

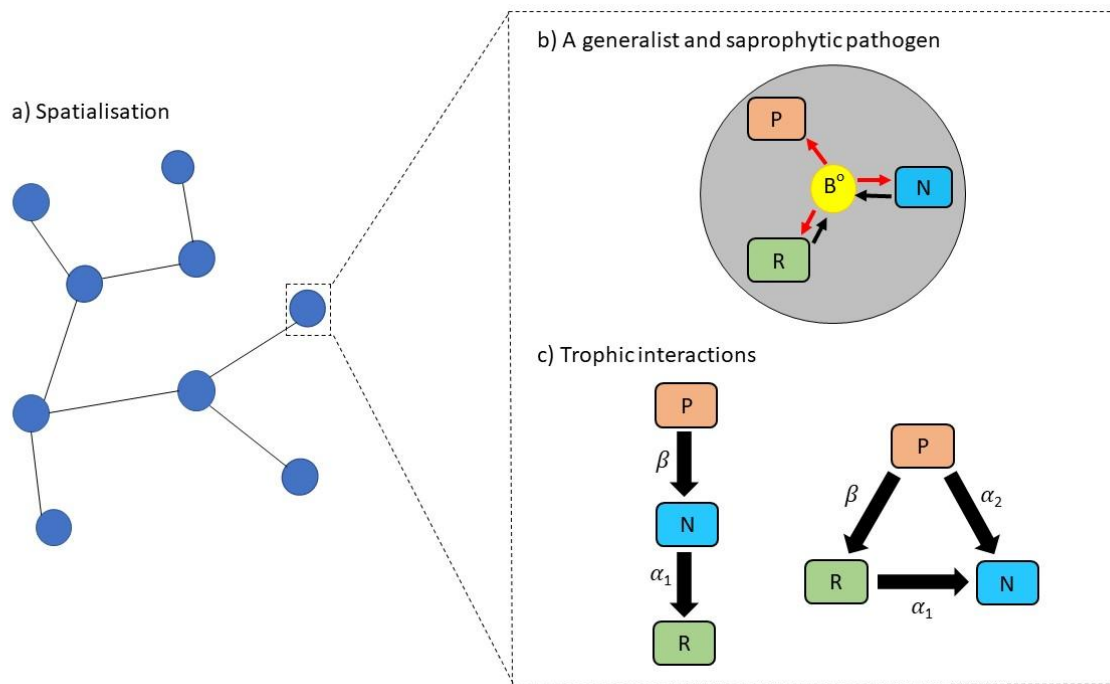
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## Materials and Methods

### 138 Model formulation

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



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**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 interspecific 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  $\alpha_1$  and  $\alpha_2$  as parameters describing the attack rates onto prey by micro- and macropredators, respectively, and by  $\beta$  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  $\alpha_2$  (null on the left and non-null on the right).

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**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
<b>State functions</b>		
$N_i$	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 $i$	
<b>Parameters</b>		
$r_i$	Intrinsic growth rate of prey species in patch $i$	-
$K_i$	Environmental carrying capacity of preys in patch $i$	1
$\mu$	Natural mortality of preys	0.05
$\alpha_1$	Maximal attack rate of micropredators onto preys	0.4
$\alpha_2$	Maximal attack rate of macropredators onto preys	0 or 0.25
$\beta$	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
$\xi$	Bacterial attachment rate on prey biomass	0.4
$\gamma$	Bacterial attachment rate on micropredator biomass	0.13
$\rho$	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
$\theta$	Growth rate of prey-associated bacteria	0.05
$\theta$	Growth rate of micropredator-associated bacteria	0.02
$\theta_1$	Natural mortality of prey-associated bacteria	0.03
$\theta_2$	Natural mortality rate of micropredator-associated bacteria	0.2
$\Lambda(t)$	Natural mortality rate of macropredator-associated bacteria	0.3
$\delta$	Time-dependence free-living bacteria growth rate	-
$\kappa$	Natural mortality rate of free-living bacteria	0.03
$\sigma$	Bacilli release rate from decomposing bodies of infected preys	3
	Bacilli release rate from decomposing bodies of infected micropredators	2

181 In patch  $i$ , we denoted by functions of time  $t$ :  $N_i$  the density of prey,  $R_i$  the density of micropredator species,  
182  $P_i$  the density of macropredator species,  $B_i^N$  the density of prey-associated bacteria,  $B_i^R$  the density of  
183 micropredator-associated bacteria,  $B_i^P$  the density of macropredator-associated bacteria, and by  $B_i^o$  the density  
184 of free-living bacteria in the aquatic environment. We assume that the prey population obeys a classical logistic  
185 growth, with  $r_i$  referring to the intrinsic growth rate and  $K_i$  to the environmental carrying capacity. Due to  
186 predation, the prey population size decreases by a quantity proportional to prey and predator populations. Here,  
187 the predator-prey interactions are modeled via Beddington–DeAngelis’ functional response (Beddington 1975,  
188 DeAngelis *et al.* 1975). This functional response is an enhancement of the well-known Holling’s type II functional  
189 response including a term representing interference among predators. Increasing the density of consumers (i.e.,  
190 predators) also reduces the consumption rate of the resource (i.e., preys). Several studies in the ecological  
191 literature have considered this type of response (Cantrell *et al.* 2004, Ghanbari and Kumar 2019, Ji and Wang  
192 2022, Tripathi *et al.* 2015).

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

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

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

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

195

196 Parameters  $\alpha_1$  and  $\alpha_2$  denote, respectively, the attack rate of micro- and macropredators onto preys.  
 197 Parameter  $\beta$  represents the predation rate of macropredators onto micropredators. Predator growth clearly  
 198 depends on food consumption. We thus define  $c_1$ ,  $c_2$  and  $c_3$  as the respective food conversion efficiency of  
 199 predators, representing thus the number of newborn predators resulting from their consumption. In absence of  
 200 prey, micro- and macropredator densities decay exponentially at rate  $d_1$  and  $d_2$ , respectively. The term  $\mu N_i$   
 201 describes the prey loss due to natural mortality. Our model also incorporates macropredator migration events  
 202 across the different local communities. At each time  $t$ , a fraction of macropredators  $m_i(t)$  leaves patch  $i$  to other  
 203 patches. A part  $q_{ji}$  of these emigrants choose patch  $j$  as destination. Thus, the flux of biomass from patch  $i$  to  
 204 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  
 205 the last term figuring in equation (3).

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

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

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

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

208

209 The intrinsic growth rate of host-associated bacteria depends upon the density of predators and prey  
 210 biomasses as substrates for bacterial development. The parameters  $\eta$ ,  $\nu_1$  and  $\nu_2$  correspond, respectively, to the  
 211 natural mortality rate of prey-associated, micropredator-associated and macropredator-associated bacteria. Here,  
 212 we used Michaelis-Menten' type functional response to describe bacilli attachment to biomass, which is  
 213 proportional to both population biomass and free-living bacteria densities. We defined the maximum success  
 214 rates for bacilli attachment on prey, micropredators and macropredators as  $\xi$ ,  $\gamma_i$  and  $\rho$ , respectively. The  
 215 biomass-associated bacteria are able to replicate on alive biomass until surface saturation concentration is  
 216 reached. Focusing for instance on prey-associated bacteria, the Michaelis-Menten' type functional response is  
 217 thus given by  $\theta N_i / (N_i + s_N)$ , where  $\theta$  is the maximum production rate of prey-associated bacteria, and  $s_N$  is the  
 218 half-saturation constant in this type of micro-habitat. The same functional response was used for predator-  
 219 associated bacterial reproduction. Saprophytic bacilli growing on the surface of living biomass are released when  
 220 the bodies of dead infected organisms are decomposing, which thus produce free-living bacteria (Godfray *et al.*  
 221 1999, Kunttu *et al.* 2009, Merikanto *et al.* 2018). These phenomena, assumed to occur only in prey-and  
 222 micropredator guilds (i.e., macropredators are considered dead-ends for the pathogen), are here described by



223 parameters  $\kappa$  and  $\sigma$ . Note that, aside such releases, biomass mortality reduces the concentration of biomass-  
 224 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),  
 225 respectively. Similarly, while feeding on the prey present in patch  $i$ , predators locally decrease the number of  
 226 prey-associated bacteria. In our model, we further incorporated the changes in the local densities of biomass-  
 227 associated bacteria resulting from migration of macropredators among connected patches (see above).

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

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

229 where  $\Lambda(t)$  and  $\delta$  are the reproduction and natural mortality rates of free-living bacteria, respectively. The  
 230 body decomposition of infected organisms, either preys or micropredators, release saprophytic bacteria in the  
 231 environment, increasing thus the local density in free-living bacteria in the patch when these organisms died (see  
 232 terms  $\kappa \mu B_i^N$  and  $\sigma d_1 B_i^R$  in equation (7)).  
 233

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

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

238 where  $u$  is the maximal dispersal rate. In the alternative scenario considering macropredators as generalists  
 239 (Figure 1c, right), we have described the migration rate,  $m_i(t)$ , as a function inversely proportional to both local  
 240 densities of prey and micropredators:  
 241

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

242 These definitions ensure that the migration rate of macropredators will increase when local food abundance  
 243 decreases. For simplicity, we suppose that the pool of emigrants leaving the patch  $i$  has equal probability to  
 244 reach any other local habitats ( $q_{ij}=1/(n-1)$ ).  
 245

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

## 252 Simulation parameters

253 We simulated a metacommunity composed of nine interconnected local sites. We set the vector describing  
 254 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  
 255 bacteria reproduction as simple Weibull's distribution ( $t = 4 \times \text{Weibull}(t, 100, 4)$ ). Table 1 presents the values taken  
 256 by default across all simulations by other parameters. We conducted numerical analysis of the model using the  
 257 MATLAB software (MATLAB, ver. 8.6).

## 258 Results

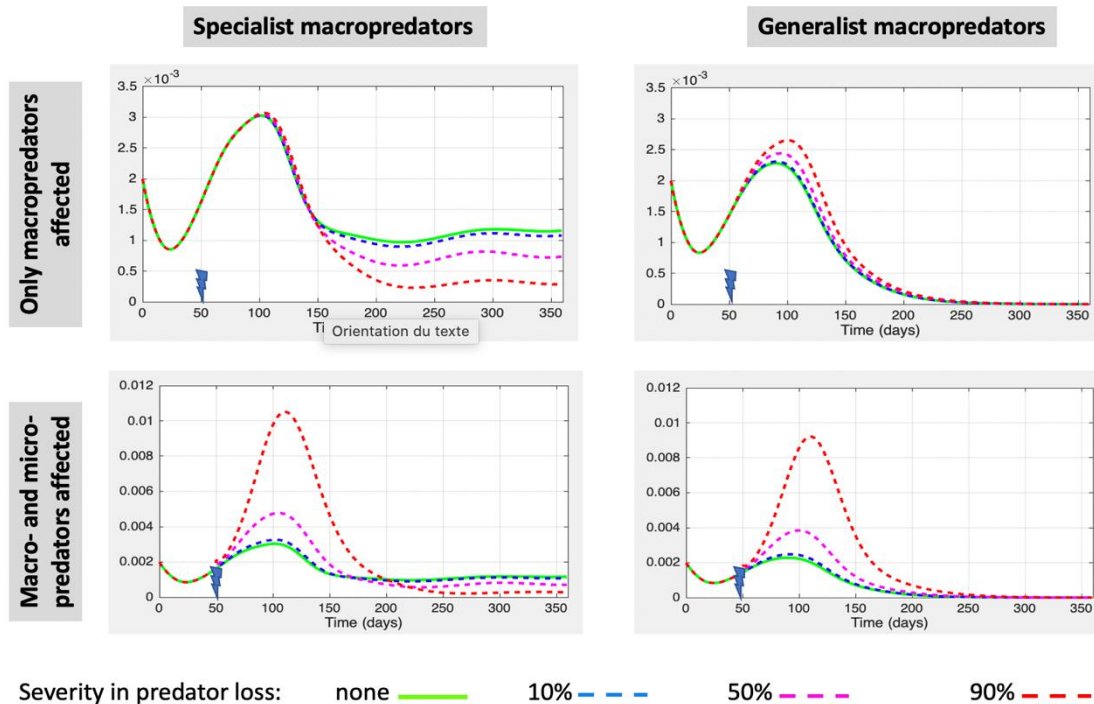
259 Numerical simulations are proposed with the aim of understanding how disturbing local communities affects,  
260 via their direct and indirect impacts on species communities, the infection risks by a bacterial pathogen that is  
261 both generalist and saprophytic. For each model scenario, we randomly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

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

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

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



296

297 **Figure 2: Effects of local disturbances onto the local dynamics in free-living bacteria density.** X-axes  
 298 represent time and Y-axes free-living bacteria density. In all panels, green curves represent the local density  
 299 in free-living bacteria in absence of perturbation. Other curves refer to the dynamics in free-living bacteria  
 300 for an instantaneous reduction in predator densities at  $t = 50$ , when disturbance occurs, ranging from 10% to  
 301 90%. The perturbations affect only macropredators in top panels but both micro- and macropredators in  
 302 bottom panels. Macropredators are specialists in left panels and generalists in right ones. Predation  
 303 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.

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### Experiment 2: Regional ecological disturbance affecting predators

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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.

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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.

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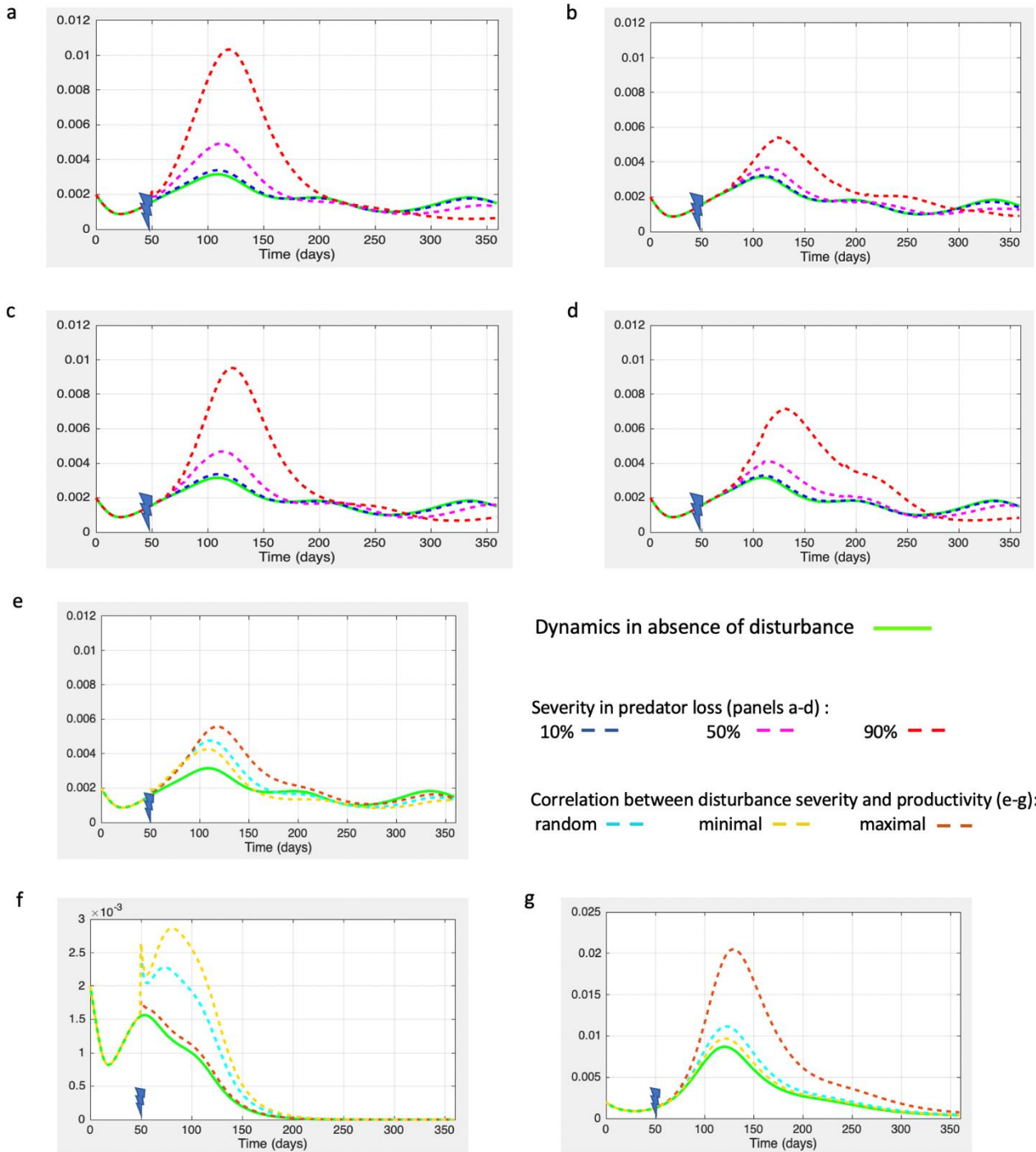
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Next, we assessed the importance of heterogeneity in predator losses resulting from synchronous regional disturbance on free-living bacteria density. Here, there are two sources of heterogeneity among patches: differences in primary productivity  $r$  (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).

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



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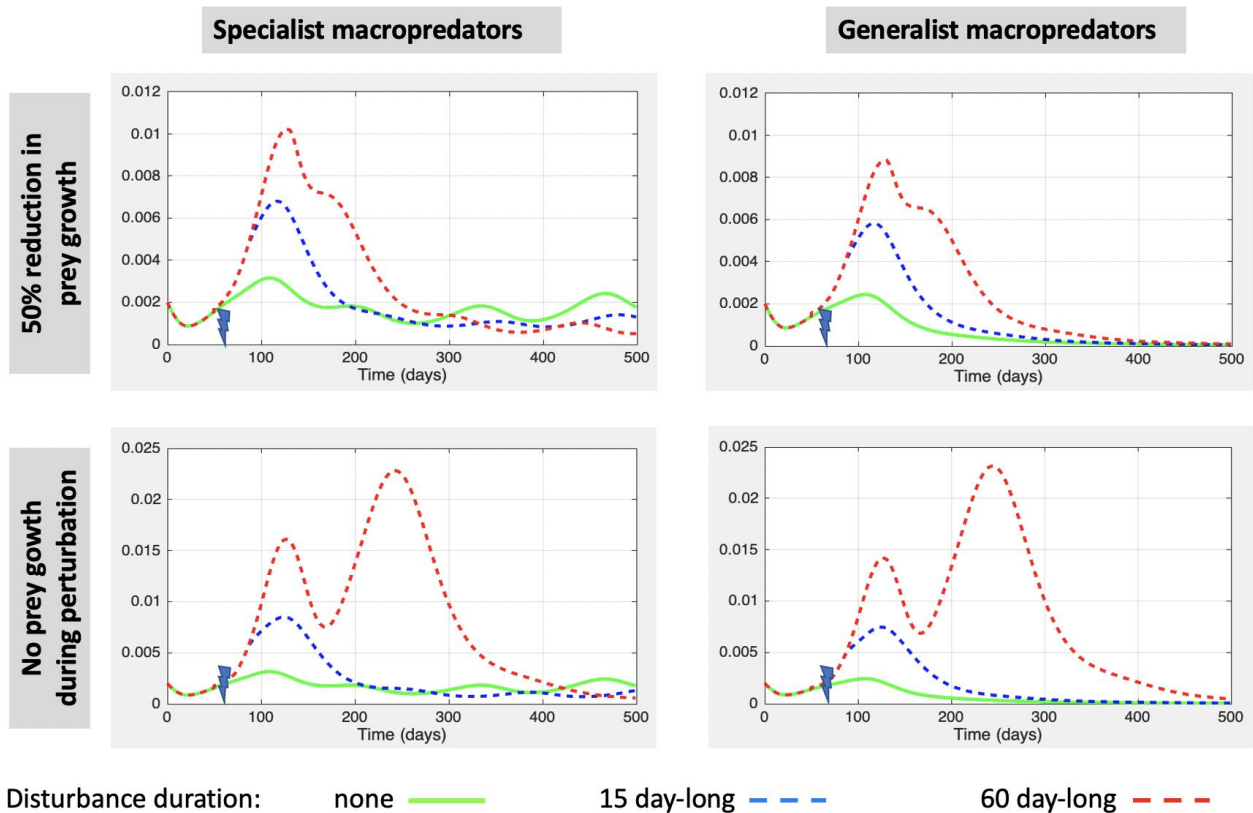
**Experiment 3: Regional ecological disturbance also affecting preys**

**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.

347

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

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



360

361 **Figure 4. Regional disturbance effects on prey and predators that impact density of free-living bacteria**  
362 **over the metacommunity.** X-axes represent time; disturbances occur at  $t = 69$  days. Y-axes refer to the  
363 regional averages in free-living bacteria density. Macropredators are specialist ( $\alpha_2 = 0$  and  $\beta = 0.5$ ) in left  
364 panels and generalist ( $\alpha_2 = 0.25$  and  $\beta = 0.25$ ) in right panels. Green curves refer to the regional average  
365 dynamics in saprophyte density observed in absence of disturbances. Those are identical in both left panels  
366 (right panels, respectively) but differ between right and left panels. Disturbances promote instantaneous  
367 reductions in predators. The vector describing the heterogeneity across patches in predator losses is [0.6663,  
368 0.5391, 0.6981, 0.6665, 0.1781, 0.1280, 0.9991, 0.1711, 0.0326]. The blue and red curves refer to the  
369 regional responses in free-living bacteria density to disturbances blocking prey growth for 15 and 60 days,  
370 respectively. The reduction in prey growth during disturbances is 50% and 100% in top and bottom panels,  
371 respectively. Please note that the scale of the Y-axes in bottom panels exceeds those referring to regional  
372 average in bacterial loads in Figures 2 and 3.

373 **Experiment 4: Relaxing dispersal constraints on functional groups including species competent for the**  
374 **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 trophic 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).

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

383 **Discussion**

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

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

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

416 First, our results demonstrate that, in a situation of local disturbance, density and diet regime, i.e.,  
417 specialist *versus* generalist, are important factors in driving top-down effects of macropredators on  
418 environmental pathogen population dynamics. This effect is much greater when macropredators are specialised  
419 on feeding upon a particular micropredator species (Figure 2, top left panel) than when being generalists (Figure  
420 2, top right panel). In fact, specific predation on a micropredator species leads to a relaxation of the pressure  
421 exerted on prey, and therefore leads to an increase in their abundance in the environment, and thus, providing  
422 favorable ecological conditions for sapronotic agents (Figure 2, top left panel). However, when macropredators  
423 are generalists, the consequences on the pathogen are less important due to a dual effect of intraguild  
424 competition. In this situation, there is a threshold effect of macropredator density on environmental pathogen  
425 abundance (Figure 2, top right row) depending on both macropredator diet strategy and local species diversity. In  
426 a situation where the local environmental disturbance affects both micro- and macropredator compartments,  
427 there is a significant impact on the population dynamics of the bacteria, whatever the type of macropredator  
428 diet. However, the increase in environmental pathogen abundance is slightly greater when macropredators are  
429 generalists. These results are consistent with studies showing top-down effects of local environmental  
430 disturbances on plant vector-borne pathogen dynamics through consumptive and non-consumptive effects  
431 (Finke 2012, Clarke *et al.* 2019).

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

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

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

446 Our theoretical study supports recent reviews and models that posit food-web theory provides im-  
447 portant insights to understanding direct and indirect effects of ecological interactions involving disturbances,  
448 environmental heterogeneity and multi-host dynamics on pathogen transmission and disease ecology (Roche *et al.*  
449 2013, Seabloom *et al.* 2015, Crowder *et al.* 2019). Notably, at local scales the strength and magnitude of dis-  
450 turbance on macropredators mediated the population dynamics of environmental pathogens in the case of spe-  
451 cialized macropredators only. More broadly, regional environmental perturbations may affect pathogen dynam-  
452 ics when severe, long-term or successive disturbance events occur in a short period of time. This simulation  
453 study that integrates multitrophic frameworks to assess human (or other animal)-biodiversity-environmental  
454 pathogen communities will help us better understand and interpret why epidemics or epizootics of environmen-  
455 tal pathogens can suddenly develop and spread. Further, it can promote better control and management of  
456 these harmful animal and human infectious diseases.

457



## 458 **Conclusion**

459

460 Since sapronotic disease agents have one or multiple reservoir hosts in the environment, their control is  
461 rendered impossible or ineffective if this origin is not taken into account. Control of such animal and human  
462 diseases therefore requires a thorough understanding of the host-parasite dynamics and pathogen ecology in  
463 their environment, which is very rarely the case. Sapronotic diseases may become a problem for wild and  
464 domestic animals, e.g., livestock, and humans when exposure increases or spillovers to other animal species of  
465 human concern, e.g., contacts between wildlife and livestock, happen. Models of sapronotic pathogen  
466 transmission are extremely rare in the current scientific literature. Our modeling study show that sapronoses  
467 may be highly dependent on the environmental conditions prevailing in species communities, and regulated by  
468 prey-predator relationships in trophic chains. In addition, these sapronoses are themselves highly sensitive to  
469 local and large-scale environmental disturbances impacting species communities in a cascade of effects' process.  
470 It is important for human and veterinary medicine, but also more generally, to recognize that the control of these  
471 sapronoses requires a better understanding of their ecology and environmental dynamics. Too few  
472 epidemiological studies have examined the influence of environmental change and species community structure  
473 on disease transmission, and this should constitute a priority for subsequent investigation. Mathematical  
474 modeling, combined with new experimental studies, represents highly valuable tool to better understand  
475 environmental transmitted pathogens and their population biology, and to project possible scenarios for future  
476 sapronotic outbreaks in the current international context of global change.  
477

478

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486

## **Conflict of interest disclosure**

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

491

## **Scripts, code, and supplementary information availability**

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

494

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