

Trophic transfer of anticoagulant rodenticides while managing rodent pests: the fine line between predator-prey regulation and pesticide-pest regulation

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Running Title Bufferscapes to preserve Non-Target Organism / Ecosystem services

Abstract

1. Understanding pesticide impacts on populations of target/non-target species and communities is a challenge to applied ecology. When predators that otherwise regulate pest densities ingest prey contaminated with pesticides, this can suppress predator populations as contaminated prey act as a super-predator, with pesticides controlling both pest and predators. It is, however, unknown how species relationships and protocols of rodenticide treatments, i.e. farmer functional responses, interact to affect pest regulation.
2. Here we used linked differential equations to model a heuristic non-spatialized system including montane water voles, specialist vole predators (stoats, weasels), and a generalist predator (red fox) which consume voles, mustelids and other prey. By considering anticoagulant rodenticide toxicokinetic and toxicodynamic equations, we explored the impact of 5 farmer functional responses (defined by both rodenticide quantity and threshold vole density above which rodenticide spreading is prohibited) on predator-prey interactions, rodenticide transfer across the trophic chain and population effects.

3. Spreading low quantities of rodenticide while maintaining sufficient voles as prey resources led to less rodenticide being applied and extended periods without rodenticide in the environment, benefitting predators while avoiding episodes with high vole density. This may meet farm production interests while minimizing the impact on small mustelid and fox populations. Spreading rodenticide at low vole densities suppressed mustelid and fox populations, leading to vole population dynamics being entirely regulated by rodenticide use. This vole-eradication treatment regime inhibited predator ecosystem services and promoted pesticide dependence.
4. Farmer functional response with high or intermediate densities thresholds triggering treatment produced vole population fluctuations caused by rodenticide that could be followed by periods during which mustelids regulated vole populations. These alternative phases of mustelids and farmer regulation highlight the benefit of intraguild relationship where mustelids may rescue foxes from poisoning.

Synthesis and applications Different farmer functional responses lead to a rich variety of population dynamics in predator-prey systems. That such a pesticide-tri-trophic system may cause a variety of population dynamics responses to pesticide use in agro-ecosystems is a novel insight. Our model reveals the need for maintaining refuges with sufficient non-poisoned voles for specialist mustelids, to conserve predator community, given the super-predator role of rodenticides. We suggest that long periods without pesticide treatment are essential to maintain predator populations, and that practices of pesticides use that attempt to permanently eradicate a pest over a large scale are counterproductive.

Keywords Biodiversity conservation; bromadiolone transfer; cyclic fluctuations; pesticides impact; secondary poisoning; super-predation; cascade effects

1 Introduction

Since the “green revolution” following the 1950s, pesticides use has increased to control pests damaging properties, public health or crops [Tilman et al., 2002]. Pesticides usage is varyingly triggered by the perception/estimation of pest densities. Natural enemies (e.g., predators, parasites, competitors) also reduce pest densities and hence may preclude the need for using pesticides [Michalko and Pekár, 2017]. Natural enemies are, however, also affected by pesticides, either by direct exposure, through ingestion of contaminated prey [Berny, 2007] or indirectly by cascade effects of resource depletion [Halstead et al., 2014]. Thus, under some regimes of pesticides use, pest populations only become regulated by pesticides once predators have collapsed. To preserve ecosystem health and the services of predators through regulation of pest densities, we need to assess the feasibility and benefit of pesticide treatment regimes in their ability to control pest species with minimal damage on predators [Halstead et al., 2014]. It is however empirically challenging to assess the overall impact of pesticide treatments on the dynamics of species linked by trophic interactions. In this context, process-based models describing simplified scenarios are powerful tools to reveal hidden

70 patterns by disentangling processes emerging from pesticide impacts on predator-prey system (e.g.,
71 Baudrot et al. [2018]).

72 Voles and other grassland rodent species undergo multi-annual population cycles (e.g., Krebs
73 [2013]. At their peaks, they may attain extremely high densities, causing substantial damage to
74 grass/cultivated crops and forestry and conflicts with humans [Delattre and Giraudoux, 2009].
75 Farmers worldwide expand financial resources to purchase and spread anticoagulant rodenticides
76 (hereafter AR), hoping to reduce vole populations and damages and increase profits despite the
77 investment required [Stenseth et al., 2003]. They do so according to protocols, equivalent to farmer
78 functional responses (hereafter FFR), that involve varying amounts of AR spread in response to
79 different thresholds in vole densities.

80 Voles and many small rodents are perceived as pests, but they are also keystone species, cru-
81 cial to the functioning of grassland ecosystems, as well as being the prey of numerous predators,
82 including species of conservation concern [Delibes-Mateos et al., 2011, Coeurdassier et al., 2014].
83 Their population cycles create pulses of resources crucial to the viability of a wide range of resident
84 predators and the aggregation of mobile avian vole predators [Korpimäki and Norrdahl, 1991]. The
85 smallest mustelids (e.g. weasels *Mustela nivalis*) are specialist vole predators. Their numerical re-
86 sponse has been shown theoretically to be necessary for generating predator-prey cycles [Hanski
87 et al., 1991]. They are said to be responsible for driving 3-to-5-year vole cycles in Fennoscan-
88 dia (specialist predation hypothesis) Hanski et al. [1991]. Generalist resident predators like foxes
89 (*Vulpes vulpes*) are expected to have regulatory and limiting effects on voles, owing to dietary plas-
90 ticity that slows down vole population increase at low density Hanski et al. [1991]. Foxes do not
91 show numerical responses to vole abundance [Weber et al., 2002] but they influence the food chain
92 through occasional killing and consumption of bite-sized mustelids. Mustelids form a small pro-
93 portion of fox diet (0-10%) but their offtake could represent a significant portion of the population
94 (reviewed in ?).

95 Anticoagulant rodenticides are non-selective toxicants with deleterious effects on non-target
96 fauna (e.g. Coeurdassier et al. [2014]. Despite AR being exclusively licensed for rodent control,
97 a large number of predator species are secondarily exposed to AR [Sánchez-Barbudo et al., 2012].
98 Repeated consumption of dead and sub-lethally intoxicated voles reduced fox abundance in farm-
99 land in eastern France [Jacquot et al., 2013] and ARs caused short-term declines in stoats in New
100 Zealand [Alterio, 1996]. Rodent-eating mustelid populations are affected by ARs given the perva-
101 sive levels of contamination reported [McDonald et al., 1998]. Thus, there is little doubt ARs use
102 inadvertently depresses predator populations. As they likely limit vole populations, it is essential
103 to understand when AR use becomes counterproductive by altering the pest population dynamics,
104 producing more frequent outbreaks and high residual vole abundance.

105 With the aim of understanding the potentially complex interactions between prey that are per-
106 ceived as pest predators and farmers spreading rodenticide in response to vole abundance and their
107 functional responses, we studied a simplified system inspired by cyclically fluctuating montane wa-

108 ter voles (*Arvicola scherman*), small mustelids (stoats, weasels) that mostly eat voles (specialists),
 109 and foxes (generalists), with voles and mustelids as food items. We used a process-based model
 110 using differential equations to explore 5 FFR types of AR spread, combining population dynamics,
 111 predator-prey interactions and rodenticide transfer across the trophic chains. Model parameters
 112 and FFR were inspired by farming systems in the Jura Mountains, Franche-Comté (France), the
 113 region of Comté cheese production. In Franche-Comté, farmers shifted from polyculture to almost
 114 exclusively grass production for milk used to produce cheese from the early 1970s [Giraudoux et al.,
 115 1997]. Due to recurrent vole outbreaks and damages to grasslands, massive rodenticide treatments
 116 were implemented from the early 80s with consequences on non-target wildlife. Practices devel-
 117 oped technically under pressure from public opinion, farmer unions and farmer technical organiza-
 118 tions collaborating with researchers to find treatment regimes with less harmful consequences for
 119 biodiversity [Delattre and Giraudoux, 2009].

120 Hence, our main objective was to explore the properties of FFR in relation to varying vole
 121 density, to vole outbreak frequencies, to the guild of interacting predators and the effects on the
 122 global tri-trophic population dynamics. Additionally, we sought to establish under what regime of
 123 use the ARs deliver benefits to farmers without imposing damages to the ecosystem.

124 2 Methods

125 We specified and parameterized the tri-trophic system of voles-mustelids-foxes with use of AR by
 126 farmers in response to vole density. We considered different FFR to assess AR upward transfer
 127 through the trophic web, considering the coupled dynamics of pulsed of AR spread and population
 128 dynamics. In all cases, parameterization units are on hectare⁻¹ and day⁻¹.

129 2.1 Model for the tri-trophic dynamic

130 We considered a tri-trophic system described by Figure 1 and equations (1-5); parameterization is
 131 provided in Table 1. Voles, denoted V, were the primary prey, Mustelids, M, intermediate predators,
 132 and Foxes, F, were top predators, consuming voles and mustelids. For each species, the instanta-
 133 neous variation of population size over time is:

$$\left\{ \begin{array}{l} \frac{dV}{dt} = Vr_V \left(1 - \frac{V}{K_V} \right) - \Phi_{V,M}(V)M - \Phi_{V,F}(V, M)F \\ \frac{dM}{dt} = \varepsilon_M \Phi_{V,M}(V)M - m_M M - \Phi_{M,F}(V, M)F \\ \frac{dF}{dt} = Fr_F \left(1 - \frac{F}{K_F} \right) \end{array} \right. \quad (1)$$

134 The vole population followed a logistic growth rate, with r_V the maximal reproduction rate,
 135 fixed at $r_V = \ln(2 \times 600)/365$ per day, since montane water vole populations can increase from
 136 0 to 600 individuals ha⁻¹ or more [Giraudoux et al., 1997] resulting in the equilibrium density

being fixed at $K_V = 600$ individuals. The vole population was preyed upon by mustelid and fox populations. The vole consumption rate at different vole densities was described by functional responses ($\Phi_{V,M}$ for mustelids, $\Phi_{V,F}$ for foxes), see equations (2). We treated small mustelids as vole specialist predators [King and Powell, 2006], assuming a Holling Type 2 functional response with attack rate a_M and handling time h_M (equation (2)). We then represented foxes feeding on voles and mustelids by a multi-species functional response derived from Holling Type 3, referring to generalist feeding behaviour [Baudrot et al., 2016]. For that, we denoted a_{VF} and a_{MF} the fox attack rate on voles and mustelids respectively. The parameter h_F was the handling time for foxes.

$$\begin{aligned}\Phi_{V,M}(V)M &= \frac{a_M V}{1 + h_M a_M V} \\ \Phi_{V,F} &= \frac{a_{VF} V}{a_{VF} V + a_{MF} M} \times \frac{(a_{VF} V + a_{MF} M)^2}{1 + h_F (a_{VF} V + a_{MF} M)^2} \\ \Phi_{M,F}(V, M)F &= \frac{a_{MF} V}{a_{VF} V + a_{MF} M} \times \frac{(a_{VF} V + a_{MF} M)^2}{1 + h_F (a_{VF} V + a_{MF} M)^2}\end{aligned}\tag{2}$$

Parameterization of functional responses was estimated to fit the daily satiation level of predators for handling times, and the observed 5-6 year vole cycles for attack rates (Table 1). We assumed foxes spent longer searching for voles than mustelids, based on each species diet and daily number of individuals captured. Therefore, a_{VF} was considered larger than a_{MF} and selected to produce 6-year vole cycles without AR.

Since we assumed small mustelids behave as specialist predators, we considered a numerical response linearly dependent on the functional response with parameter ε_M (dimensionless) as conversion efficiency of prey into newborn predator (Supporting Information). The mustelid background mortality rate (i.e. all other reasons of death: ageing, disease, etc.) was m_M parameterized has the inverse of life expectancy (Table 1). We assumed foxes had a logistic growth rate function, parameterized with maximal growth rate $r_F = \ln(3)/365$ and equilibrium density $K_F = 0.03$ [individuals.ha⁻¹] [Ruelle et al., 2003] without numerical response [Weber et al., 2002].

2.2 Model with rodenticide

Figure 1 represents the whole study system. Rodenticide is spread in grasslands during treatments, denoted $T_{Broma}(V)$, triggered by vole density V (FFR described in Table 2). Firstly, baits (50 mg.kg⁻¹ of bromadiolone, hereafter AR) were spread in grasslands at quantity 7.5 to 20 kg.ha⁻¹. Such quantity, C , was available for voles, and a proportion disappeared in the environment at rate k_0 (set at $k_0 = 0.0815$) [Sage et al., 2008]. The proportion consumed per vole, with rate $\kappa(C)$, was assumed to be an increasing function. The function $\kappa(C)$ was characterized by a maximum ingestion M_{in} , and a half-saturation constant for ingestion D_{in} in [mg.kg⁻¹]:

$$\kappa_C = \frac{M_{in} \times C}{D_{in} + C}\tag{3}$$

For the toxicokinetics of AR (i.e. internal compound dynamics) leading to AR concentrations

166 in animal body (voles, mustelids and foxes), we considered an uptake without biotransformation
 167 and time-regulated distribution, (i.e. AR concentration in the body of animals was instantly ho-
 168 mogeneous) and that the whole body was consumed or scavenged without selection/rejection of
 169 tissues-organs. We also assumed disappearance including excretion of the parent compound and
 170 metabolisation, and that metabolites were non-toxic and/or excreted in the scats. For the toxi-
 171 cokinetics of AR ingested by voles, a fraction C_V was assumed to remain active, stored mainly
 172 in vole livers and available to predators ingesting voles. The absorption rate of ARs (η) exceeds
 173 50% in less than 24h [Jacquot et al., 2013]. The excretion rate from voles, $k_{out, V}$ was 0.4 day^{-1}
 174 [Sage et al., 2008]. The mortality rate through ARs was $\mu(C_V)$. Death through poisoning created
 175 a dead vole population (V_d) with AR concentration C_V . Dead voles could either be scavenged by
 176 mustelids/foxes or decompose at rate d . We assumed AR in dead voles disappeared from the sys-
 177 tem when voles decomposed. Mustelids could feed on live voles V , or non-decomposed dead voles
 178 V_d and we assumed a Type 2 functional response adapted for a multi-species functional response
 179 [Baudrot et al., 2016]. Mustelids ingested AR with absorption rate η_M (ratio between biomasses of
 180 voles, B_V , and mustelids, B_M) and the total of ingested voles (alive V and dead V_d) was defined
 181 by function $\Theta_M(V, V_d)$ (Table 1), in equation (4) which provides the rate of AR ingested by a
 182 mustelid:

$$\text{Contaminant Intake Rate} = C_V \times \eta_M \times \Theta_M(V, V_d) \quad (4)$$

183 A fraction of AR ingested was accumulated in weasels while the rest was excreted with rate
 184 $k_{out, M}$. AR ingestion induced weasel lethal poisoning at rate $\mu_M(C_M)$, additive to natural mortality
 185 rate m_M . AR was ingested by foxes with a rate proportional to the functional response of foxes
 186 to voles, dead voles and mustelids. Foxes also accumulated AR available in their prey, resulting in
 187 upward AR transfer in the trophic chain. Foxes accumulated AR in concentration C_F . A fraction
 188 of AR was excreted by foxes at rate $k_{out, F}$ [Sage et al., 2008]. AR caused fox mortality at rate μ_F
 189 (C_F) [Sage et al., 2010]. We used log-logistic equations for describing dose-dependent mortality
 190 of animals exposed to AR. Vole and predator mortality rates due to AR $\mu_X(C_X)$ (X referring to the
 191 considered species) were expressed by equation (5):

$$\mu_X(C_X) = \frac{1}{\text{experiment duration}} \times \frac{1}{1 + (LD_{50}/C_X)^H} \quad (5)$$

192 where LD_{50} was the daily median lethal dose (50% of population dying) with different values
 193 for voles (2 mg kg^{-1}), mustelids (2.1 mg kg^{-1}) and foxes (0.5 mg kg^{-1} , Table 1). H is the Hill's
 194 coefficient, modulating the curve steepness and was estimated to fit the sparse data we have (Ta-
 195 ble 1). Mortality rates considered the duration of AR toxicity from experiments of up to 6 days
 196 [Sage et al., 2010].

197 2.3 The farmer functional responses explored through simulation

198 We considered a range of realistic FFR spanning treatments during vole outbreaks only as a pre-
199 cautionary approach; in which treatments only takes place at intermediate or low vole density
200 threshold. These scenarios are inspired by historic and contemporary protocols of bromadiolone
201 use to control montane water voles in Franche-Comté, but also representative of practice globally
202 (Table 2) [Delattre and Giraudoux, 2009]. To check the influence of foxes and intraguild predation
203 on the system's dynamics, we simulated scenarios with and without foxes.

204 Our simulations tracked the linked vole-mustelid-fox dynamics for 40 years, after a “burn-in”
205 period of 10 years to reduce dependency of results upon initial conditions, to observe several vole
206 cycles and to characterise AR effects on these species population dynamics. This burn-in period
207 also had AR treatment triggered at specific vole densities and with a given rodenticide quantity
208 for each FFR (see Table 2). The burn-in phase was selected according to a set of simulations with
209 different initial conditions. Those simulations showed that in a given FFR (i.e., same threshold of
210 vole density and amount of AR spread), the dynamics of the population were converging toward a
211 similar pattern. In order to assess the impact of FFR on both agriculture and conservation interests,
212 we estimated the following cost functions: (i) Number of treatment events per FFR ; (ii) Cumulative
213 amount of AR (kg) ; (iii) Proportion of time when the AR-induced mortality of mustelids higher than
214 50% (i.e. lethal exposure profile killing 50% of mustelid population) ; (iv) Proportion of time when
215 the mortality of mustelids was higher than 50% due to natural mortality; (v) Proportion of time
216 when the vole density was below 50 voles ha^{-1} , as a proxy for time when forage grass grows with
217 low herbivore influence; (vi) Mean vole, mustelid and fox densities.

218 3 Results

219 3.1 Population dynamics

220 Allowing for mortality by predators ingesting AR-poisoned voles changed the outcome of predator-
221 prey dynamics involving vole, mustelid and fox populations. Secondary poisoning led to a rich
222 spectrum of emergent dynamics according to the FFR to vole abundance. Without AR (FFR a),
223 vole dynamics were regulated by mustelid predation that gave rise to 6-year cycles (Figs. 2 and 3;
224 maximal vole and mustelid densities were around 600 ind.ha^{-1} and 2 ind.ha^{-1} respectively). The
225 fox population remained at its carrying capacity (i.e., 0.03 ind. ha^{-1} , see Table 1).

226 Under FFR b (high vole density threshold triggering treatment and high AR amount per treat-
227 ment) and FFR d (intermediate threshold and low AR amount), vole dynamics were sequentially
228 regulated by either AR treatments, which we refer to as farmer-regulated phase (FR in Figures 2 &
229 3), or by mustelids, mustelids-regulated phase (MR), alternately (MR in Figures 2 & 3). Farmer-
230 regulated periods started when densities of living voles triggered treatments. This produced sud-
231 den declines of live voles followed by increases of dead voles. However, the vole population re-grew

quickly which triggered frequent further treatments and pulses of availability of contaminated (both live and dead) voles. In FFR d (intermediate threshold and low AR), vole declines were not as deep as when pulses of AR amount were high (FFR b), owing to the reduced rodenticide amount per treatment. Mustelids and foxes also experienced AR-induced declines during this period. Under FFRs b (high threshold density, high AR) and d (intermediate threshold, low AR), mustelid-regulated periods started when mustelid numbers grew slowly to a peak, which depressed vole density, precluding rodenticide treatments and releasing the fox population from secondary poisoning, such that its abundance rebounded. Vole depletion by mustelids and subsequent mustelid declines allowed the vole population to grow again up to threshold densities and initiated a new period of regulation by farmers. Vole dynamics were permanently regulated by AR treatment under FFR c (intermediate threshold, high AR, Figs. 2c, 3c). Populations of live and dead voles experienced high frequency fluctuations (around 2 peaks every year) driven by AR. As AR treatments were frequent, being triggered by voles peaks, contaminated dead voles were always abundant (peaks at 90 ind. ha^{-1}), and mustelid and fox densities remained low (mustelids, converging to 0 ind. ha^{-1} ; foxes, $0.003\text{-}0.006 \text{ ind. ha}^{-1}$) with only short-term fluctuations (2 peaks every year, following vole cycles). With FFR e (low threshold, low AR), vole populations were maintained by farmers at around 50 voles ha^{-1} (Figs. 2e and 3e). The population of live voles was buffered by treatments. Additionally, whenever voles reached densities triggering treatment, predator populations experienced strong declines. However, fox densities ($0.01\text{-}0.015 \text{ ind. ha}^{-1}$) were higher compared to FFR c (intermediate threshold, high AR), reflecting the reduced amount of AR used (7.5 kg) and transferred to foxes as there were lower vole densities. The maximum numbers of dead voles under this FFR e was relatively low (highest around 15 ind. ha^{-1}) but, due to frequent treatments, there was a steady replenishment of contaminated dead voles. This, in turn, induced mustelid and fox mortality and population declines (Supporting Information). Additionally, low availability of live voles triggered small mustelids mortality through starvation down to abundances similar to those resulting from AR use (Supporting Information).

3.2 Comparison between farmer functional responses in terms of cost functions

As expected, spreading AR generally reduced vole densities (Table 2) but the extent to which it also affected predators and the costs and benefits for conservation and farmer's interests varied widely. The FFR b (high threshold, high AR) implied the lowest number of treatments (mean 0.87 year^{-1}), while FFR d (intermediate threshold, low AR) resulted in the lowest amount of AR used (mean $14.5 \text{ kg. ha}^{-1} \cdot \text{year}^{-1}$). The FFR e (low threshold, low AR) had the lowest mustelid mortality due to AR (no instance in 40 years) but maximised starvation-induced mortality of mustelids (Table 2). Additionally, FFR e (low threshold, low AR) had the highest proportion of time with $<50 \text{ voles ha}^{-1}$, (96% of study period). When considering the effectiveness in reducing mean vole densities, FFR e (low threshold, low AR) ranked highest followed by FFR c (intermediate threshold, high AR). The FFR d (intermediate threshold, low AR) and b (high threshold, high AR) allowed the highest mean

densities of mustelids and foxes respectively. Comparison of these protocols indicates that FFR d (intermediate threshold and low AR) delivered the best compromise between farm production and conservation interests (Table 2). It had the lowest AR quantity applied (mean 14.5 kg.ha⁻¹.year⁻¹) and the highest mean densities of mustelids (0.47 ha⁻¹) and foxes (0.02 ha⁻¹). The number of treatments was among the lowest values (1.6 treatment year⁻¹). Its drawback was that it only suppressed voles at low densities (<50 voles ha⁻¹ for 21% of time). Conversely, emergent mean vole densities were low to intermediate (122 voles ha⁻¹). Other FFR regimes were poorer compromises either because mustelids were kept at low densities (FFR c, intermediate threshold, high AR, and FFR e, low threshold, low AR) or had relatively high mean vole densities (229 voles ha⁻¹, FFR b, high threshold, high AR). In summary, FFR d (intermediate threshold, low AR) was the best compromise because it minimized the impact over predator populations contributing to the natural reduction of vole densities with the lowest quantity of AR applied for farm production interests.

3.3 Influence of intra-guild predation

Figure 3 shows the system dynamics under FFR d, where successive farmer-regulated and mustelids-regulated phases occurred. This simulation shows that the removal of foxes did not eliminate the successions of mustelids-regulated and farmer-regulated phases. However, the mustelid regulated period allowed short-term peaks of voles, suggesting the emergence of a classical one-predator - one-prey cycles interrupted by a farmer-regulated period. Without foxes, population dynamics of mustelids presented a more chaotic behaviour, while it presented regular cyclic pattern with fox occurrence. Therefore, this simple model suggests a stabilizing role of a generalist predator (foxes in this system) during the mustelid-regulated period. At the end of the mustelid-regulated period, foxes strongly contributed to vole mortality and, to a lesser degree, mustelid mortality. Consequently, the removal of foxes implied less predation over voles during the mustelid regulated period, and short-term vole releases from mustelid predation. The 2-year rolling mean of vole density (blue lines in Figure 3) illustrates the change of regime from farmer-regulated to mustelids-regulated phases. Indeed, the amplitude of averaged vole densities (i.e., the amplitude of vole cycles for the 2-year rolling mean) was relatively stable at the beginning of farmer regulation period and then suddenly decreased to become minimal before sharply increasing, announcing the regime change. These changes in density amplitude may be used as an early-warning signal of the regime transition.

4 Discussion

Considering that rodenticide kills not only voles but also their predators through secondary poisoning, our models show that AR profoundly changes the outcome of predator-prey dynamics involving vole, mustelid and fox populations beyond what mere intuition could elucidate. Our study reveals how the dual influences of the amount of pesticide spread and the vole density threshold trig-

gering AR spread drives (i) pesticide spreading frequency, (ii) predation ecosystem service, and subsequently (iii) the control of pest outbreaks. Two types of a rich spectrum of emergent dynamics, including farmer or mustelid regulation deviating from classical predator prey dynamics arose because poisoned voles acted as “super-predators”.

4.1 Modelling farmer regulation into a classical predator-prey system

The threshold functional response of farmers deciding when to apply varying amounts of rodenticides according to prevailing vole density was crucial in selecting the emergent ecosystem dynamics, resulting in much variability in ecosystem and conservation and farming production interests. In the ecosystem our models depict, farmers spreading rodenticide not only depleted vole prey exploited by specialist and generalist predators but also created pulses of lethally or sub-lethally poisoned voles that became super-predators by poisoning their predators. Arguably this set of ecological interactions has similarities with circumstances where a pathogen affecting prey species also infects predators, as in the case with the flea vectored plague (*Yersinia pestis*) infecting prairie dogs (*Cynomys* spp.) and black footed ferrets (*Mustela nigripes*) in central US [Matchett et al., 2010]. However, to our knowledge, the behaviour of such tri-trophic model with multiple reciprocal interactions has not been explored. This is despite the obvious relevance to the management of the globally widespread circumstances where keystone small mammals are poisoned and may secondarily poison their predators [Delibes-Mateos et al., 2011]. Under the “reference” scenario without AR spreading (FFR a), we assumed a predator-prey cycle which is a plausible pattern thoroughly explored theoretically [Hanski et al., 2001]. There is no controversy on the role of small mustelids tracking vole dynamics, though it is not yet well understood whether predation may drive steep declines [King and Powell, 2006]. Parameters of the reference scenario for our predator-prey model were realistic and tuned to generate population fluctuations similar to those observed in the studied cyclic system [Delattre and Giraudoux, 2009]. The addition of pulses of rodenticide and their toxicokinetics in vole and predators are based on previous experiments with bromadiolone, a widely used AR, ensuring biologically realistic functional forms and their parameterization. Irrespective of the FFR considered, the frequency of vole cycles dramatically increased compared to the reference scenario, except during mustelid-regulated phases emerging under some FFR scenarios.

4.2 How specialist predators may protect generalists from poisoning

An interesting model behaviour was seen with FFR b (high vole density threshold and high AR) and FFR d (intermediate vole density threshold and low AR) with farmer- and mustelid-regulated phases alternating with low frequency. Such flipping between alternative states in population dynamics has been previously described in predator-prey model where weasels rely on a primary prey and entrain the dynamics of secondary prey [Hanski and Henttonen, 1996] but not for the kind of indirect interaction we explore here. It further demonstrates that adding biological realistic complexity to simple models may drastically change the emergent properties of trophic interactions.

From these scenarios, we understand that the emergence of successive farmer and mustelid phases is neither driven by vole density threshold alone nor by AR amount, but instead by a subtle combination of both. The modelling description of these patterns uncovered the dual key roles of mustelids on fox dynamics, as intraguild competitors and as a vector for poisoning. This led to a surprising form of facilitation for foxes: mustelids protect foxes from collapses. The establishment of such a response can be described in 3 steps. Firstly, low mustelid densities inhibit their regulation of voles and contribute to farmer AR use. In line with empirical evidence, the latter directly impacts foxes by poisoning [Jacquot et al., 2013]. Secondly, fox predation on mustelids is reduced, and with an intermediate AR amount, this allows mustelids to slowly recover. Vole outbreaks and subsequently farmer treatments are then gradually delayed, benefitting mustelids recovery. This is the point of transition from farmer to mustelids regulation, starting the third step: mustelids increase faster, suppressing vole densities and precluding the need for AR treatments, and eventually indirectly allowing fox population growth. Our finding that complexities in trophic interaction, induced by the poisoning of predator by poisoned prey, may cause the system to flip between alternative states is novel and robust. However, given we only explored deterministic versions of our models, any inference on the frequency of flipping between states should be cautious given the inherent stochastic nature of natural and farmland environments. If such dynamics occur within real farming systems, flipping between states is unlikely to emerge with regularity (40 years) where many other factors impact population dynamics. Moreover, under our heuristic modelling framework, we have shown that the removal of fox population induced chaotic dynamics of voles and mustelids (Figure 3). While generalists are known to have stabilising effect [Hanski et al., 1991], the benefit of specialist predators imparted to generalist predator and resulting increase in the prevalence of intraguild predation would be difficult to detect in empirical studies. Nevertheless, other generalist predators such as the endangered red kite (*Milvus milvus*) which feed on voles opportunistically, occupy areas with bromadiolone treatments and are also affected by rodenticides [Coeurdassier et al., 2014] and may therefore also benefit from the presence of mustelids in the ecosystem.

4.3 How region-wide vole extirpation may inhibit ecosystem services

Under FFR c (intermediate vole density threshold and high AR) and FFR e (low vole density threshold and low AR), the whole system was solely driven by farmer regulation, whereby the chronic use of AR completely suppressed the pest-regulation ecosystem service of predators. It has previously been shown empirically that repeated rodenticide treatments are highly detrimental to the populations of predators and reduce their densities [Jacquot et al., 2013]. Secondary poisoning of predators is an established reality [Berny, 2007]. Through modelling, we formalised the insight that some poison deployment protocols, including those presently used in the empirical system which motivated our study, are counterproductive if employed on a large scale, suppressing natural predator regulation of pest rodents. It has been long known that poisoning rodents with AR permeates the food chain at peak abundance and achieves little in terms of protecting crops and

may have strong deleterious impact (FFR b and c) [Olea et al., 2009]. In Franche-Comté, a change in treatment protocols, from controlling voles at high densities to low-intermediate densities, has reduced the mortality of non-target species (including foxes) [Jacquot et al., 2013]. Nevertheless, deployment regimes of pesticides that can contaminate the food chain should also enable periods of time which allow predator populations to rebound and avoid extirpation from the ecosystem. We have shown that, over time, farmers who strictly maintain voles at low density thresholds would suppress predation services provided by vole predators and instigate pesticide dependence. In addition, small mammals like voles certainly have ecosystem functions. Our results also suggest that the presence of small mustelids in ecosystems is beneficial for biodiversity conservation (see above) and agriculture interests. Given the importance of vole cycles and their trophic interactions, it is desirable to maintain vole population fluctuations of sufficient amplitude to maintain ecosystem processes.

4.4 Managing rodents and ecosystems

Presently, in Franche-Comté, farmers relying on bromadiolone alone can only treat pre-emptively when voles are at low densities (FFR e) whereas those using alternative methods without pesticide are allowed to spread AR in low quantity up to intermediate vole densities (FFR d). Spreading AR in low quantity seems superficially desirable, but our heuristic model, assuming an idealised homogenous landscape, show this is associated with frequent treatments. Consequently, it would induce a near permanent availability of a small number of intoxicated voles which, combined with low availability of non-contaminated voles, would reduce predator populations. Therefore, the extreme situation of using a low vole density threshold (FFR e) at a large scale is undesirable because it depletes the prey resources of foxes and mustelids and their populations. Triggering treatment at intermediate vole density with a low amount of AR (FFR d) allowed for temporal refuges, i.e. longer periods free of rodenticide necessary for predator densities to rebound while simultaneously avoiding episodes with high vole density, as required by farm production interests. Under a landscape management approach, such temporal refuges could be spatial refuges, with parts of the landscape free of pesticides where predator populations can recover.

Our key result and the basis for management prescriptions is that allowing for refuges where voles are not poisoned and allowed to persist at medium-high densities such that they can be exploited by mustelids is crucial for predator population recovery and preserving the ecosystem services mustelids deliver. Treatment regimes allowing refuges seems compatible with both conservation and farming interests. A critical insight is to avoid potential side effects of chronic low-dose AR prescription (e.g., depletion of community services, stimulation of resistances), as is well known with antibiotics, by demanding regularly long-term period without treatment. However, combining chronic treatments and long periods free of AR may be difficult to achieve in real systems. Our model only considers temporal refuges, and the conceptualization of untreated areas as equivalent to triggering treatment at intermediate vole density cannot provide guidance on the size of these

414 spatial refuges. Nevertheless, while management of voles is implemented at the scale of fields,
415 mustelids and foxes roams over much larger areas [King and Powell, 2006], such that large refuges
416 with medium-high vole densities voles would be required while allowing to maintain low-voles
417 density at very local scale.

418 **4.5 Conclusion and perspectives**

419 Our process-based model revealed pesticides that permeate the food chain upward can lead to
420 diverse population dynamics with alternative states regulated by predators and farmers. It also
421 shows that the practice currently promoted to use low-dose AR treatments at low vole density
422 could be limited by the undesirable side-effects of leading to chronic application of AR on a large
423 scale and the depletion of the vole predator community. This emerging question would benefit
424 from a landscape modelling approach to characterize spatial refuges. We have also uncovered a
425 counterintuitive mechanism whereby, owing to intraguild predation, mustelids could rescue foxes
426 from poisoning. This suggest that contemporary Environmental Risk Assessment of pesticides that
427 mostly consider one-species - one-compound experiments fail to capture the impact of pesticides on
428 trophic links. Assessing risk at the ecosystem level is empirically challenging such that process-based
429 modelling can play a critical role.

430 **Authors' contributions**

431 XL conceived the initial idea; all authors developed the concept; VB and JF developed the models
432 and led manuscript writing; VB implemented the model and ran simulations. GC contributed treat-
433 ment protocols; JF, VB and MC explored model parameters; XL, PG and MC contributed critically
434 to drafts; all authors gave final approval for publication.

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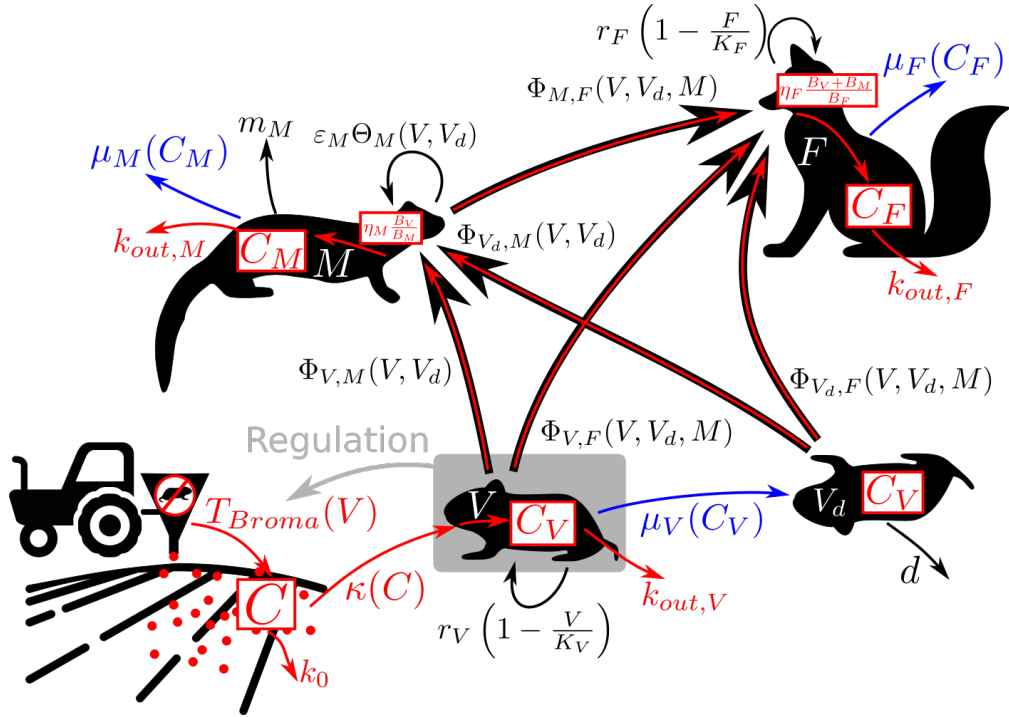


Figure 1 – Dynamics of mustelids (bold grey line) and red foxes (bold black line) after 50 years of simulation (10 years of burn-in period, shaded area, and 40 years considered here for the compute of results, estimation of cost functions, etc.). Letters at the top-right part of each sub-graph corresponds to the results obtained from each farmer functional response. FR (dashed line) and MR (dotted line) indicate the farmer-regulated and mustelid-regulated periods of vole population dynamics.

Table 1 – Populations dynamics and toxicological parameters used in the model simulations. Notation ppm stands for parts-per-million [mg.kg^{-1}] and n.d denotes a dimensionless parameter. See description in Methods.

Parameters	Definitions	Units	Value
Population dynamics parameters			
r_V	Maximal growth rate of voles	ind.day^{-1}	$\ln(2 \times 600)/365$
K_V	Carrying capacity of voles	ind.ha^{-1}	600
a_M	Attack rate of mustelids on voles	day^{-1}	1/30
h_M	Handling time of mustelids on voles	day	1/3.5
a_{VF}	Attack rate of foxes on voles	day^{-1}	1/10
a_{MF}	Attack rate of foxes on mustelids	day^{-1}	$1/10 \times 80/300$
h_F	Handling time of foxes on voles	day	1/6
ε_M	Conversion efficiency of ingested food		0.0025
m_M	Natural mortality rate of mustelids	day^{-1}	$1/(0.8 \times 365)$
r_F	Maximal growth rate of foxes	ind.day^{-1}	$\ln(3)/365$
K_F	Carrying capacity of foxes	ind.ha^{-1}	0.03
B_V	Mean biomass of a vole individual	g	80
B_M	Mean biomass of a mustelid individual	g	300
B_F	Mean biomass of a fox individual	g	5800
d	Degradation rate of dead vole	ind.day^{-1}	1/7
Toxicological parameters			
$T_{broma}(V)$	Farmer input AR function of vole density	kg.ha^{-1}	Scenarios
k_0	Persistence of AR in the field	day^{-1}	$(0.106 + 0.057)/2$
M_{in}	Maximal intake rate of vole	day^{-1}	$6 \times 1/5$
D_{in}	Half saturation intake rate of vole		100
$LD_{50,V}$	Lethal Dose for 50% of voles	ppm	2
H_V	Hill's coefficient dose-response curve	n.d.	4
$LD_{50,M}$	Lethal Dose for 50% of mustelids	ppm	2.1
H_M	Hill's coefficient dose-response curve	n.d.	4
$LD_{50,F}$	Lethal Dose for 50% of foxes	ppm	0.5
H_F	Hill's coefficient dose-response curve	n.d.	2
η_M	AR uptake rate in mustelids	n.d.	0.5
η_F	AR uptake rate in foxes	n.d.	0.5
$k_{out,V}$	Excretion rate of AR by voles	day^{-1}	0.4
$k_{out,M}$	Excretion rate of AR by mutelids	day^{-1}	0.6
$k_{out,F}$	Excretion rate of AR by foxes	day^{-1}	0.6

Table 2 – Results on the cost functions for the comparison of treatment protocols. Column "FFR" (farmer functional response) refers to the protocol denotation (a to e) and in brackets respectively: the vole density threshold, and the amount of AR/treatment in kg. The column "Nbr Treat." refers to the number of treatment in simulation over the 40 years after the burn-in phase. "Total AR" is the total use of anticoagulant rodenticides (bromadiolone in kg). "M, 50% AR death" is the proportion of time with mortality by AR over 50% in mustelids population. "M, 50% Nat. death" is the proportion of time with mortality by natural reason (i.e., all except AR) over 50% in mustelids population. " $V < 50 \text{ ha}^{-1}$ " is the proportion of time with less than 50 voles ha^{-1} . Finally, "Mean V density", "Mean M density" and "Mean F density" are mean densities of voles, mustelids and foxes respectively.

FFR (dose, thresh.)	Nbr. Treat.	Total AR	M, 50% AR death	M, 50% Nat. death	$V < 50 \text{ ha}^{-1}$	Mean V density	Mean M density	Mean F density
a (0,0)	0	0	0	1	0.48	211.27	0.61	0.03
b (500,20)	35	700	0.06	0.94	0.14	229.1	0.33	0.02
c (250, 20)	81	1620	0.11	0.89	0.28	105.49	<0.01	<0.01
d (250, 7.5)	64	480	0.06	0.94	0.21	122.35	0.47	0.02
e (50,7.5)	169	1267.5	0	1	0.96	31.42	<0.01	0.01

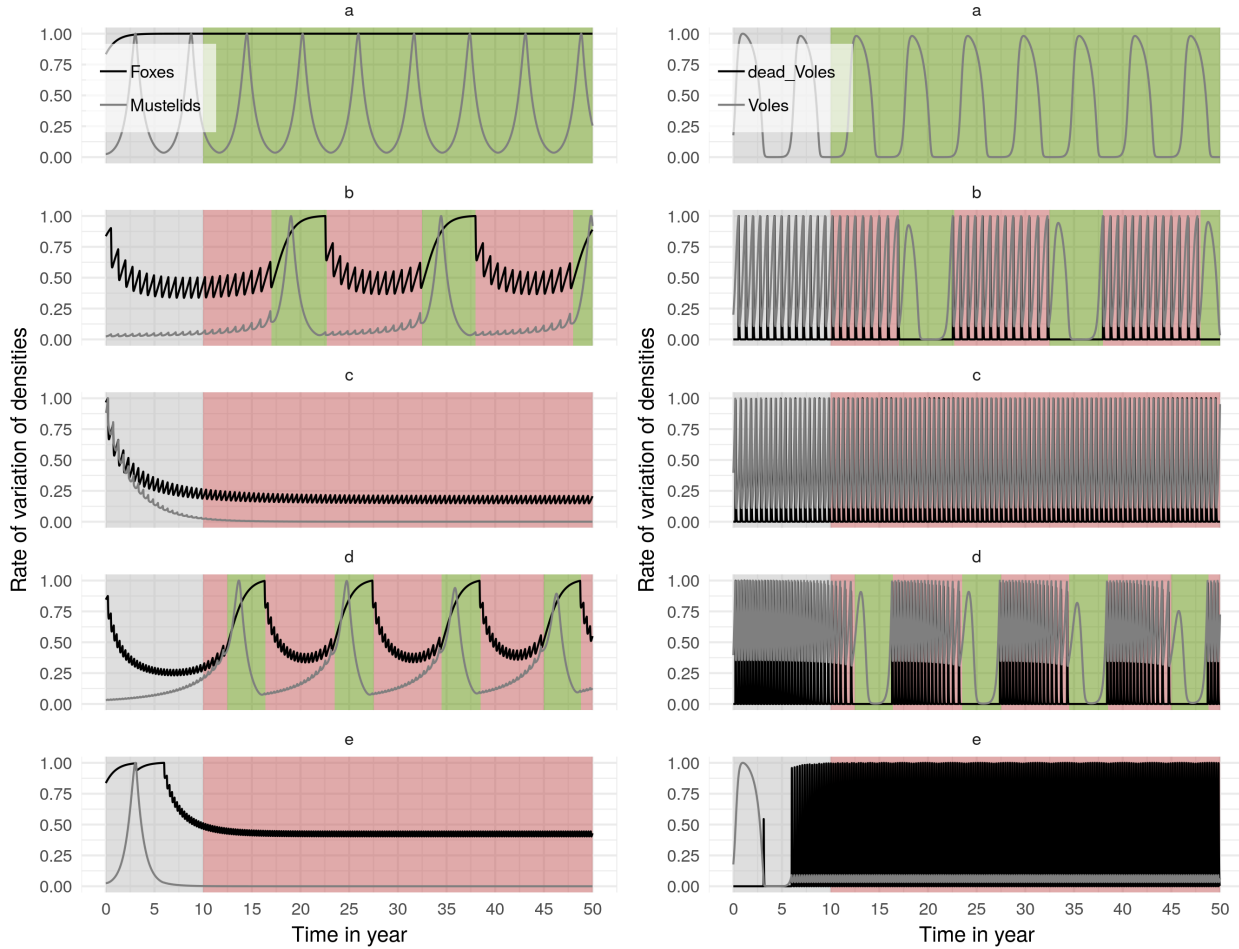


Figure 2 – Rate of variation of population densities simulated over 50 years (10 years of burn-in period in grey area): (Left) Dynamics of mustelids (grey line) and red foxes (black line), (Right) Dynamics of live (grey line) and dead (black line) voles. Letters at the top-center part of each sub-graph corresponds to the results obtained from each farmer functional response. Red area and Green area indicate the farmer-regulated (FR) and mustelid-regulated (MR) periods of vole population dynamics respectively.

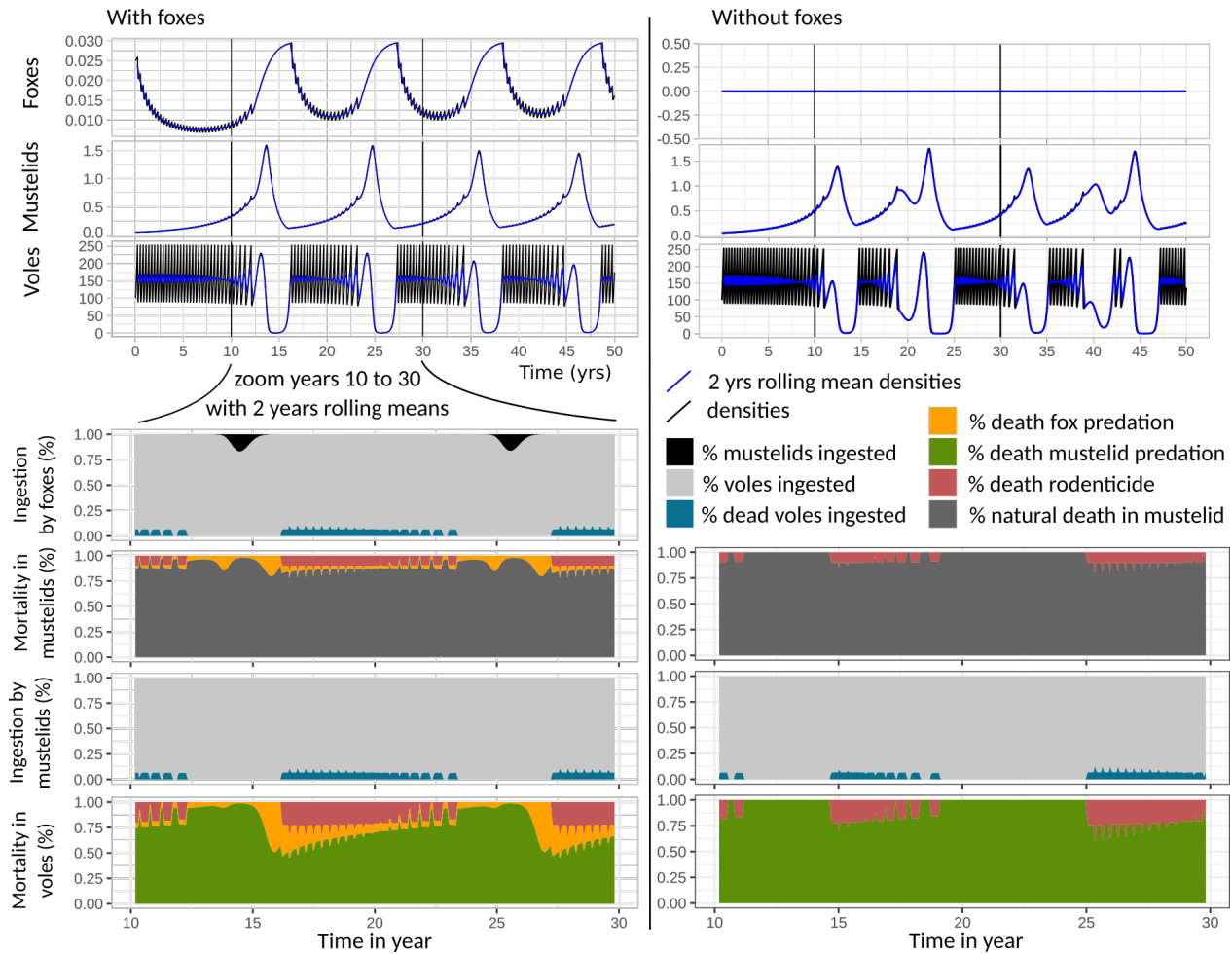


Figure 3 – Effects of intraguild predation. Top graphics: daily densities of voles (in black) and 2-years rolling means of densities (in blue) for the farmer functional response d (i.e., 7.5kg of rodenticide at threshold density of 250 voles) with and without foxes (left and right respectively). Bottom graphics: stacked charts of ingestion and mortality proportion.