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Direct and indirect effects of chemical contaminants on the behaviour, ecology and evolution of wildlife

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Abstract

Chemical contaminants (e.g. metals, pesticides, pharmaceuticals) are changing ecosystems via effects on wildlife. Indeed, recent work explicitly performed under environmentally realistic conditions reveals that chemical contaminants can have both direct and indirect effects at multiple levels of organisation by influencing animal behaviour. Altered behaviour reflects multiple physiological changes and links individual- to population-level processes, thereby representing a sensitive tool for holistically assessing impacts of environmentally relevant contaminant concentrations. Here, we show that even if direct effects of contaminants on behavioural responses are reasonably well-documented, there are significant knowledge gaps in understanding both the plasticity (i.e. individual variation) and evolution of contaminant-induced behavioural changes. We explore implications of multi-level processes by developing a conceptual framework that integrates direct and indirect effects on behaviour under environmentally realistic contexts. Our framework illustrates how sublethal behavioural effects of contaminants can be both negative and positive, varying dynamically within the same individuals and populations. This is because linkages within communities will act indirectly to alter and even magnify contaminant-induced effects. Given the increasing pressure on wildlife and ecosystems from chemical pollution, we argue there is a need to incorporate existing knowledge in ecology and evolution to improve ecological hazard and risk-assessments.

Keywords: behavioural ecology, chemical pollution, ecotoxicology, endocrine disrupting chemicals, evolution, indirect effects, sublethal

1. Introduction

Contamination of the environment with diverse inorganic and organic compounds, such as pesticides, pharmaceuticals, and metals, represent one of the main environmental challenges driven by anthropogenic activity. In 2010, the global chemical industry's value was US$4.12 trillion, having risen 54% over a decade [1]. In addition, the trend towards global urbanisation is concentrating chemical consumption in cities faster than environmental interventions and remediation systems can be implemented, including in developing countries near biodiversity hotspots [2]. The increasing production and release of chemicals means that wildlife, humans and ecosystems are continuously exposed to chemical contaminants. While large-scale mortality events of wildlife represent an obvious, if rare, sign of chemical releases, chemical contaminants can elicit more subtle but nevertheless important and harmful ecological impacts [3]. Further, chemical contamination of the environment is certainly not limited to short-term, acute exposures. Effects of long-term, low-level chronic exposures can be equally deleterious, though less obvious for human observers. In this review, we develop a conceptual framework that integrates concepts and approaches from multiple disciplines to investigate how chemical contaminants can alter animal behaviour, with resultant impacts on short- (e.g. individual and community) and long-term (e.g. evolutionary) responses, potentially leading to population declines.

Research on chemical contaminants conventionally recorded a limited range of endpoints, most commonly by studying mortality following exposure in the laboratory and/or by testing the impact of a single contaminant on a single species under standardised laboratory conditions ([4], but see [5]). These approaches are logistically tractable and repeatable but are criticised for their simplicity, particularly when such experiments neither take chemical nor biological complexity into account [6]. Behaviour, on the other hand, is the result of numerous complex developmental and physiological processes, and so connects physiological function and ecological processes [7]. Thus, behavioural change provides a comprehensive measure of both direct and indirect effects of chemical contaminants on individuals, linking to population-level processes [8-10] and, importantly, is often impacted at much lower contaminant concentrations than are traditional toxicological endpoints [11]. Here, we illustrate how behavioural responses can represent a powerful, highly quantifiable and biologically relevant indicator of environmental impacts.

Chemical contaminants can affect animal behaviour both directly and indirectly. Direct effects on behaviour in wildlife—here, we focus mostly on vertebrates—are caused by contaminants acting on the physiology of an animal (e.g. impaired sensory or cognitive abilities, altered endocrine/neural signalling, metabolic dysfunction). To date, research in behavioural ecotoxicology has largely focussed on direct effects of contaminants on individuals (e.g. activity) (see section 2). In contrast, indirect effects, when contaminant-induced changes to animal behaviour in one organism or species have cascading effects on other organisms and species in the exposed system, have received far less attention [12-15]. Indirect effects are most pronounced when a contaminant affects exposed organisms differentially, such as when one species is more sensitive and another more resistant (i.e. asymmetrical effects; [12,14,16]). While the importance of investigating both direct and indirect effects of contaminants is evident, this multi-directional approach has rarely been applied in ecotoxicology (but see [15,17]).

In this review, we focus exclusively on studies conducted under 'natural' conditions, specifically measuring behavioural responses following contaminant exposures in the wild or at environmentally relevant concentrations in the laboratory. We first critically examine existing literature on the role of chemical contaminants in mediating direct effects on individual behaviour (section 2). In contrast to previous reviews [14,17], our focus centres on sublethal effects, particularly those induced by emerging contaminants, such as pharmaceuticals. Moreover, as well as considering short-term, mean behavioural responses to exposure, we discuss how chemical contaminants can alter trait variance (i.e. plasticity) and act as potent evolutionary forces. Moving from effects on individuals, we investigate how chemical contaminants can alter inter-specific interactions indirectly via changes in behaviour of susceptible species (section 3). By integrating these collective effects, we develop a conceptual framework to identify ways in which animal behaviour can be affected by chemical contaminants (section 4). In doing so, we use predator-prey interactions as a case study to demonstrate how our conceptual framework has real-world impact. While we highlight the challenges of scale and complexity involved with predicting ecological effects of chemical contaminants (section 5), we also provide directions for future research (section 6). Finally, the overarching aim of this review is to improve research practices by increasing the ecological relevance of research approaches employed, in order to uncover global hazards and risks posed by chemical contaminants.

2. Direct effects on individual behaviour

Here, we discuss why, in a rapidly changing world, we need to expand our concept of direct effects—perhaps more accurately ‘mean behavioural responses’—to incorporate the potential for chemical contaminants to affect both plasticity in, and evolution of, behavioural responses.

2.1. Direct effects

Exposure to chemical contaminants can result in direct effects on a range of both ‘general’ behaviours (e.g. activity levels)—changes in which can have knock-on effects on multiple fitness-related traits—and specific mechanisms underpinning specific behaviours. Given that behaviour is the product of inter-connected physiological, anatomical, and neurological processes, and, in the wild, organisms are usually exposed to chemical cocktails rather than single contaminants, pinpointing mechanistic pathways between exposure to a contaminant and a behavioural change can be challenging. For example, round gobies (*Neogobius melanostomus*) collected from heavily contaminated industrial sites (e.g. PCBs, PAHs, metals) [18] or exposed to municipal wastewater effluent [19] both showed reduced aggression, even though the contaminant mixtures were very different.

Disruption of reproductive behaviours resulting from exposure to chemical contaminants has been increasingly studied in both laboratory and field settings because of the obvious population-level consequences [8]. Mechanisms underlying such behavioural changes include contaminant actions on endocrine and neural signalling, via changes to receptors, enzymes and/or transporters [20-22]. For instance, environmental exposures to organochlorine pesticides reduces parental care behaviour in predatory birds [23]. Studies on fish have demonstrated that exposure to municipal wastewater treatment plant effluent (e.g. [19]), and the active ingredients in (and metabolites of) the oral contraceptive pill, reduce nest building and courtship behaviours (reviewed in [20]). Furthermore, exposure to the insecticide endosulfan disrupts pheromonal communication between the sexes in red-spotted newts (*Notophthalmus viridescens*), leading to disrupted mate choice and depressed mating success [24]. Apparently subtle changes in reproductive behaviour could potentially be as devastating for fitness as major malformations of reproductive morphology, because an animal that fails to attract a mate or care for offspring appropriately will accrue zero fitness.

Changes in animal movement (e.g. frequency and speed) following contaminant exposure are common behavioural endpoints in ecotoxicological studies [25, 26]. For example, small-scale activity, which is often measured in the laboratory, has high ecological importance because it increases encounter rates with both resources (e.g. food, potential mates) and risks (e.g. predators, diseases). Activity also underlies individual dispersal and migration tendencies [27,28], although smaller scale movements measured in the laboratory do not automatically reflect larger scale movements in the field. Chemical contaminants can alter these movement behaviours by disrupting either sensory capabilities used to locate suitable environments and resources (e.g. inability to detect chemical cues; [29-31]) or physiological pathways governing and supporting movement (e.g. neural/endocrine disruption, metabolic dysfunction; [32,33]). Contaminants can, for instance, directly impair movement, making animals less adept at capturing prey and/or escaping predators, as has been noted in vertebrates exposed to acetylcholinesterase-inhibiting pesticides [34]. So far, only a handful of studies have connected these measures to dispersal or migration in the wild. One such study showed that Atlantic salmon (*Salmo salar*) smolts exposed to the anxiolytic pharmaceutical oxazepam migrate faster both in laboratory migration pools and down a river [35]. In contrast, while round gobies collected from heavily contaminated environments dispersed more slowly in a laboratory maze, there was no evidence that dispersal was affected in the wild [36]. Recent work has also demonstrated that exposure of European starlings (*Sturnus vulgaris*) to a polychlorinated biphenyl (PCB) mixture in the laboratory resulted in reduced activity and incorrect orientation for migration [37], indicating that exposed birds might migrate later and less accurately in the wild. Overall, activity seems to be a sensitive and relatively easily measured endpoint but its potential to indicate individual fitness or population-level processes is assumed rather than proven, in most cases.

Chemical contaminants can also interfere with complex behaviours, such as predator-avoidance, grouping and aggression, which have direct implications for fitness and population dynamics. By acting on the sensory system, contaminants can affect an organism’s responses to conspecifics or predators by, for example, reducing their ability to detect stimuli, but also rendering them less active or motivated to respond [29]. If receivers are unable to detect prey, predators or signals from conspecifics, or alternatively if signallers emit altered signals, this could lead to ineffective communication [38]. The resulting disruption of group interactions and coordination could potentially reduce the anti-predator and food-location benefits of grouping [39]. By impacting conspecific detection pathways, chemical contaminants can also alter aggression and dominance hierarchies among individuals. For example, captive rainbow trout (*Oncorhynchus mykiss*) exposed to cadmium, which damages the olfactory epithelium, were less aggressive towards an unexposed rival and therefore, formed dominance hierarchies faster [40].

Interestingly, some chemicals, such as psychoactive pharmaceuticals, have actually been designed to modulate adaptive stress or fear responses. Thus, they have great potential to impact foraging and anti-predator responses of wild animals (e.g. [41-44]). Indeed, recent studies have shown that exposure of fish to environmentally relevant concentrations of the antidepressant fluoxetine can extend the duration of 'freezing' behaviour [44] after predatory attack and increase activity levels regardless of the presence of a predator [43]. Because natural selection favours individuals that can quickly and accurately detect and assess risk, any disruption of this fine-tuned system is likely to have important implications for individual fitness [45] (see electronic supplementary material for more on predator-prey effects).

2.2 Plasticity

Individuals can adjust their behaviour in response to chemical contaminants, i.e. they show phenotypic plasticity [7]. This ‘plasticity’ in behaviours has been the subject of much interest in behavioural ecology, because of its role in enabling species to cope with rapid environmental change [46, 47]. However, most studies so far have focused primarily on the mean behavioural responses of the contaminated population, with little to no mention of the variance in the trait. To date, we are unaware of any research explicitly investigating how contaminants can modulate behavioural plasticity or flexibility (i.e. how responsive individuals are to environmental variation) (but see [41]; section 5). Predictions as to how plasticity will be modulated by chemical contaminants are not straightforward. If a behaviour is attenuated by a contaminant by, for example, all individuals becoming inactive regardless of environmental conditions, this could erode plasticity. Thus, there would be no benefit to individuals having variable responses to environmental changes, because they would never be expressed. Consequently, over time this could decrease the intensity of selection for plasticity. In turn, this could reduce population variation in responsiveness to environmental change, reflecting a decrease in variance in behavioural responsiveness of all individuals. Conversely, one study found that exposure of jumping spiders (*Eris militaris*) to pesticides led to an increase in within-individual behavioural variability, whilst not changing the population's average level of predatory behaviour [48]. There is a clear need to integrate new experimental designs, technologies and statistical approaches (e.g. [35,47-50]) from behavioural ecology to measure individual behavioural responses under varying environmental conditions, such as, for example, multi-stressor studies, to better understand the consequences of contaminant exposure.

2.3 Chemical contamination drives evolution

There is growing interest in the long-term, multi-generational consequences of chemical contamination and how contaminants might modulate population persistence and evolutionary trajectories. Our current focus is on how selection can act directly on exposed organisms, although it is important to acknowledge that selection may also operate indirectly via impacts of chemical contaminants on, for example, a species' prey, or competitors (see section 4).

It is established that exposure to chemical contaminants can result in the evolution of physiological resistance, with perhaps the best-studied example being the micro-evolution of resistance in populations exposed to metal pollution (see [51,52]). By contrast, far less is known about how this resistance might affect the subsequent behavioural responses of exposed organisms. Adaptive physiological adjustments could reduce the likelihood that downstream behaviours are maladaptive. On the other hand, changes in physiology can also have negative effects on behaviour and life histories via the reallocation of resources required for growth and reproduction. For example, laboratory selection for cadmium resistance in least killifish (*Heterandria formosa*) resulted in decreased fecundity, female life expectancy, and brood size [53]. Whether such trade-offs also impinge on behaviour remains to be tested.

Even in the absence of physiological resistance, organisms can simply change their behaviour, for example altering their diet, to avoid contaminants. However, it is often unclear whether these behavioural changes reflect plasticity or evolved responses [54,55]. Studies have shown spatial avoidance of contaminated sediments and water by aquatic invertebrates [55] and vertebrates [54,55], as well as adjustment of migration routes by salmon in response to metal pollution [56]. Other species show temporal avoidance of potential contaminant exposure by employing a faster life history or changing reproductive timing [52]. An interesting hypothesis is that the adaptive potential of an organism to respond rapidly to strong selection favouring earlier maturation and reproduction could, in turn, facilitate adaptations to novel stressors, such as chemical contaminants [57].

If organisms have neither evolved physiological tolerance nor behavioural compensation, exposure to chemical contaminants can result in drastic population declines [58]. This potentially creates a destructive feedback loop where a reduction in population size leads to further loss of genetic diversity, thus restricting the adaptive potential of populations [59, 60], including adaptive behavioural responses. Chemical contaminants (e.g. persistent organic pollutants) can also affect mutation rate (e.g. [61]), which may either compensate for the loss of genetic diversity during population bottlenecks (e.g. marsh frogs, *Rana ridibunda*; [62]) or otherwise alter population responses to contaminants [63]. However, most contaminant-induced mutations are likely to be deleterious [64]. Thus, adaptive behaviour that shields genotypes from otherwise harsh selection imposed by chemical contaminants could allow for population persistence and the maintenance of adequate levels of standing genetic variation crucial for further adaptation [65].

Chemical contaminants can also impact the strength and targets of selection via their direct effects on behaviour. For example, since sexually selected behaviours can affect the rate and trajectory of evolution (e.g. [66]), contaminants that interfere with sexual selection (e.g. endocrine-disrupting chemicals, EDCs; [67]) have considerable potential to affect subsequent evolution. For example, in European starlings, treatment with an EDC mixture resulted in males producing longer and more complex songs that are preferred by females, despite exposed males also having suppressed immune responses [68]. Whereas, in guppies (*Poecilia reticulata*), exposure to the agricultural contaminant 17β-trenbolone increased the occurrence of coercive copulatory behaviour in males, thus circumventing female mate choice [69]. While such changes that weaken sexual selection could further contribute to population decline [70], some studies find the opposite effect, whereby sexual selection enhances the evolution of mechanisms to cope with contaminants, presumably resulting in population growth. For example, flour beetles (*Tribolium castaneum*) evolved resistance to a pyrethroid pesticide faster when sexual selection was allowed to occur compared to when it was experimentally precluded [71].

Given the importance of evolution in facilitating population persistence, a key question is: what might limit the ability of organisms to evolve adaptive physiological or behavioural responses to contaminants? One possibility is that it may be difficult to adaptively respond simultaneously to multiple contaminants, or, more broadly, multiple stressors that exert conflicting selection pressures [72]. Resistance to a single class of contaminants, such as pesticides, can evolve very fast, but evolving resistance to cocktails of contaminants with different modes of action is likely to be much slower. Here, the ability to cope with a particular contaminant could make it more difficult to deal with another [63]. A complementary idea emphasises the role of evolutionary history—i.e., the notion that organisms often have greater difficulty coping with stressors that are truly 'novel', as opposed to those that are mechanistically similar to those that are familiar [73]. Clearly there is a need is for a deeper mechanistic understanding of when and why plastic or evolutionary responses to one contaminant should facilitate or conflict with responses to another.

3. Indirect effects of chemical contaminants on behaviour via interspecies interactions

Contaminants can, as outlined above, exert direct effects on the behaviour of species, which often results in decreases in organism abundance. However, species and their behaviours can also be altered *indirectly* because changes in behaviour (or abundance) of susceptible species will lead to cascading indirect effects—even on resistant species—at all trophic levels within a community. One of the most commonly documented indirect effects of contamination is predator responses to reduced prey abundance caused by contaminant-induced direct lethality or reproductive failure in their prey species. A population crash of fathead minnows (*Pimephales promelas)*, caused by experimental EE2-exposure of a whole lake, led to cascading indirect effects: zooplankton populations in the exposed lake increased without minnow predation, while the biomass of larger lake trout (*Salvelinus namaycush*) decreased without minnows as a prey item [14]. Indirect effects can also reduce the efficacy of ecosystem services provided by wildlife. For instance, population crashes of *Gyps* vultures in India due to diclofenac toxicity resulted in an increase in feral dogs scavenging on decaying carcasses and a consequent increase in human rabies infections from dog bites [74]. In contrast, examples of indirect effects caused specifically by changes to animal behaviour are rare in the literature [16]. For example, mummichog (*Fundulus heteroclitus*) from industrial sites were less active and less adept at capturing prey grass shrimp (*Palaemonetes paludosus*) than were fish at pristine sites, allowing these prey to grow larger and become more abundant [75]. We predict that contaminant-induced increases in boldness or aggression in one species, for example, will change the competition and predation pressures on, and thus alter the behaviour of, other species within a community (Figure 1). Contaminant-disrupted courtship leading to declines in abundance, are predicted to have cascading effects on the interspecies interactions across a community. Here, we use cascading effects as a tool to illustrate the importance of indirect effects in ecological risk-assessment, although other indirect effects such as keystone predator effects and exploitative competition can also be locally important [76]. The key point, here, is the need to understand the mechanism, i.e. the contaminant induced change in behaviour(s), initiating the cascade.

Given the complexity of studying multi-species responses to contaminants [12], it is not surprising that indirect community effects, particularly those acting via changed behaviours, have not yet been broadly studied and quantified. First, multiple organisms must be studied simultaneously in real time using environmentally realistic mesocosms or field-based studies. Second, the system often must be studied for longer durations than are typical of laboratory exposures (i.e. several months to years). One might argue that studying indirect effects is redundant since the net effect on the community is the ultimate endpoint. However, since species compositions differ between most environments and reactions to contaminants can be highly species-specific, the net effect on a mesocosm community will only provide the outcome for that particular community. Without a mechanistic understanding of which behaviours in which species are affected and how, the generality, and, as such, the predictive power of mesocosm studies for risk-assessment of particular contaminants is limited at best. Knowledge of indirect effects is also crucial for modelling ecological risk, a promising and cost-effective tool that will help to reduce the number of animals required for ecotoxicological testing.

4. Conceptual framework for understanding the ecological and evolutionary impacts of chemical contaminants

Here, we have developed a conceptual framework that can be used by researchers aiming to design experiments or research programmes that move away from the 'one chemical – one species – one (usually lethal) endpoint' style of ecotoxicology (but see [71]) towards a more holistic approach. Specifically, our framework demonstrates the direct and indirect effects of chemical contaminants on the behaviour of individuals within a population, and of species within communities. We draw upon knowledge and literature from ecology and lay out potential scenarios of community-level effects caused by chemical contaminants (Figure 1). Since communities are composed of interconnected populations overlapping in time and space, the effects of chemical contaminants on communities necessarily manifest in the interactions within and among populations [72]. For example, some of the most salient interactions shaping ecological communities worldwide are between prey and their predators [72,73]. All animals are either prey or predators at some point in their lives and this interaction often has considerable consequences on individual fitness and population size [74].

Imagine that a chemical contaminant is introduced into an ecosystem. This chemical does not change the behaviour of top predator 'species B', but does increase the boldness of a second top predator 'species A', resulting in 'species A' taking more risks, spending longer foraging and less time avoiding predators. 'Species C', the prey of species A, which is resistant to the contaminant, is indirectly affected because increased time and energy spent to anti-predator behaviours but it is still consumed at a higher rate than when the ecosystem was uncontaminated. Thus, prey species C decreases in numbers, which, in turn, causes its own plant prey 'species D' to proliferate, thereby shifting the nutrient cycling and changing the ecosystem for all species (Figure 1*a*). Notably, if the contaminant's action was conserved across taxa, such that species C also became bolder, its population would rapidly decline by predation-induced mortality from species A. Further, the decreased numbers of prey species C could potentially result in predator species B changing its foraging preference to alternative prey. The risky behaviour of species A will increase its own probability of being preyed upon, attacked by competitor species B and/or eating novel but toxic or infected foods. This would, in turn, decrease the predation pressure from predator species A on species C, and could potentially decrease competition between species A and B (Figure 1*b*) [72]. We have included dynamic feedback loops to magnify the actions of the chemical contaminant on both directly and indirectly affected species, which, in turn, have community-level consequences and can alter ecosystem functioning (Figure 1b).

Importantly, indirect effects due to contaminant-induced behavioural shifts could cause systems to respond far more strongly and quickly than an assessment of direct effects alone, or simply monitoring changes in the abundance of key predators, would predict [73]. Moreover, contaminant-mediated effects could yield novel forms of ecological interactions by, for example, inducing prey-switching due to changes in predatory behaviour and/or changes in prey abundance or quality, or by differentially altering the vulnerability of individuals or species to parasites [75]. Also, we have focused on the top-down effects, but some contaminants will affect primary productivity and so will have bottom-up impacts. These can be difficult to predict but, again, could have indirect, sublethal effects by increasing competition for food and/or necessitating greater foraging distances. Such a framework allows us to integrate and go beyond individual experiments and encourages researchers to assess behavioural change within its environmental context. By understanding the behavioural mechanism underpinning multi-level changes, modelling, for example, can be used to predict the impacts of contaminants with similar modes of action for enhanced environmental risk assessments [77]. As an implementation plan, we provide Figure 2, which directs researchers to consider which experimental design (laboratory, mesocosm or whole ecosystem manipulations) and level (individual, species or community), or modelling approaches are required, and which endpoints should or could be tested. Our basic framework can, therefore, be applied to specific behaviours and/or interspecific interactions, as well as to different levels of organisation, as required.

5. Problems of scale and complexity: predicting effects in the wild from effects in the laboratory

Predicting the ecological effects and behavioural perturbations caused by chemical contaminants is valuable for guiding legislation and policy to protect wildlife but it is also challenging for many reasons. Behaviour is inherently variable—although so are many of the physiological endpoints currently measured—and how organisms respond to any given contaminant may vary across an individual's lifetime, between sexes, among individuals of the same species, and across species with different life-histories, habitat use, trophic position, and/or physiology [7,10,33,75,78].

Most earlier standardised ecotoxicological tests used model species that are easily cultured with simple, measurable endpoints [4], which allowed direct comparisons of toxicity among different compounds. This long-used approach has efficiently generated hazard and risk-assessments for many chemical contaminants under the premise that similar species are equally affected by the contaminant. Of course, the ‘all species are the same’ argument does not hold for the effects of many contaminants (e.g. pharmaceuticals [79]). Inter- and intra-species differences in physiology, behaviour and life history, when coupled with differential metabolism, generate substantial differences among species and individuals in susceptibility and responses to chemical contaminants. Unfortunately, our understanding of comparative mechanistic responses to contaminants still remains quite limited, even for model laboratory organisms.

Susceptibility differences between species are one of the key challenges in ecotoxicology. For example, studies have shown that small wild-caught prey fish are more sensitive to the anxiolytic effects of the pharmaceutical oxazepam than larger predatory fish or laboratory-reared fish [5,80,81]. This could be due to species differences in the rate and extent of pharmaceuticals being taken up, metabolised and concentrated. Indeed, bioconcentration of pharmaceuticals in fish tissues can differ by several orders of magnitude between species [82], and even across life-history stages [83]. Therefore, two species inhabiting the same polluted system can be exposed to very different internal concentrations of contaminants [81]. Moreover, tests including a less vulnerable life-stage might underestimate ecological risk [83]. Such differential exposures, and the associated effects, make it very difficult to predict the ecological effects of chemical contaminants in the environment [16].

Differential behavioural responses to chemical contaminants in laboratory-reared versus wild species have also been explained by the lack of predation risk or high competition in laboratory environments, which selects for inherited behavioural phenotypes that are often bolder, more aggressive and less responsive to predators than wild-type individuals [84]. For example, in assessing the risk of chemicals that potentially modify anti-predator behaviour, using a laboratory fish model that may exhibit a suppressed basal behavioural response to predators may greatly underestimate actual risk in the field (Figure 3). Also, the distribution of behavioural traits studied should be characterised within each test group [83]. This consideration is critically important because a contaminant that acts to increase activity and/or boldness will more likely generate behavioural change in individuals originating from a (wild-type) population of low competition/high predation, compared with a (lab-reared) high-competition/low-predation population that contains many active and bold individuals (Figure 3). Even in the wild, populations of the same species under different predation pressures are known to have evolved different physiology, morphology and behaviours [84]. In terms of our conceptual framework, such population-level differences in behavioural responses will alter both the state of a community prior to contamination, and the magnitude of feedback loops triggered by a contaminant. Such differences between populations, generated by differing selection regimes, have received very little attention despite clearly being important considerations when assessing contaminant vulnerability.

6. Future directions

The use of behavioural studies enables us to link the effects of contaminants at multiple levels of organisation, from individual to ecosystem. This is an invaluable asset, because chemical contaminants have a wide range of actions and effects. At the individual-level, the fields of behavioural ecology and so-called ‘personalised medicine’ are increasingly realising the need to analyse inter-individual variation in responses, not just population means [46]. Far from being ‘noise’, plasticity in responses in itself represents a trait that can shape the capacity of individuals and populations to cope with environmental change in the short term. In this review, we illustrate that chemical contaminants can impact the capacity of populations to persist into the future by altering the strength and targets of evolutionary selection, for example via direct effects of behaviour. To date, a mechanistic understanding of how evolutionary and plastic responses interact to facilitate population persistence is lacking. This also limits our ability to predict how populations respond if legislation succeeds in reducing concentrations of specific chemical contaminants. Consequently, we have identified avenues to fill the knowledge gaps and challenge the often simplistic assessment of direct effects of contaminants, specifically in terms of how behaviour and other endpoints should be measured, analysed and interpreted.

With the rise in emerging contaminants, many of which are designed to exert sublethal effects on evolutionarily conserved physiological systems at ecologically realistic concentrations, it is important to update existing frameworks for studying their short- and long- term consequences. Sublethal behavioural effects can be both ‘positive’ and ‘negative’ for individuals, populations and communities. As illustrated by our conceptual framework (Figure 1) effects can vary dynamically within the same individuals and populations. Indeed, this could be described as a key feature of emerging or dilute contaminants. Importantly, behavioural effects can lead to top-down and/or bottom-up effects. For example, changes at a lower trophic level could have sublethal effects by increasing competition for food and/or necessitating greater foraging distances. This is because linkages within communities will act indirectly to alter and even magnify contaminant-induced effects. Future work, integrating modelling, remote sensors and tracking technologies and statistical analyses should focus on quantifying changes on the individual level and how the linkages within these networks are affected by contaminants. We argue that understanding the behavioural and ecological mechanisms underpinning contaminant-induced population changes will greatly increase the accuracy and power of Environmental Risk Assessment to protect wildlife and ecosystems from disturbance by chemical contaminants.

Authors' contributions

MS, TB and KEA organised the symposia on which this paper is based, developed the conceptual framework, edited the manuscript and created figures. All authors contributed to publication writing. All authors gave final approval for publication.

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Figure legends

Figure 1. Outline of our conceptual framework modelling the direct and indirect effects of a chemical contaminant using predator-prey dynamics as a case study. Two predatory species (A and B) are exposed to a chemical contaminant. a) State 1 shows initial changes to species in the food web at the individual and community levels; b) State 2 includes feedback loops, which show dynamic interactions between species in time and space. Increases and decreases in population size for each species are indicated by arrows. The solid arrows indicate direct effects, dashed arrows indirect effects, dotted arrows nutrient cycling, and blue arrows species interactions.

Figure 2. Implementation plan suggesting methodological approaches for utilising our conceptual framework to identify the routes by which animal behaviour is affected by chemical contaminants. For each level of biological organisation (individual, species, community and ecosystem), we highlight some of the factors that should or could be quantified or experimentally manipulated.

Figure 3. The distribution of expressions of a trait (here, activity) in two populations from environments with different levels of predation risk. a) Population collected from the field (high predation); b) Laboratory-bred population (low predation). Black arrows illustrate the potential for contaminant-induced increases in activity in the populations (the longer the arrow, the greater the potential change).

References

[1] UNEP. 2013 Global Chemicals Outlook - Towards Sound Management of Chemicals. United Nations Environment Programme.

[2] Kookana, R.S., Williams, M., Boxall, A.B., Larsson, D.G., Gaw, S., Choi, K., Yamamoto, H., Thatikonda, S., Zhu, Y.G. & Carriquiriborde, P. 2014 Potential ecological footprints of active pharmaceutical ingredients: an examination of risk factors in low-, middle- and high-income countries. *Phil Trans R Soc B* **369**.

[3] Hellou, J. 2011 Behavioural ecotoxicology, an "early warning" signal to assess environmental quality. *Environ Sci Pollut Res* **18**, 1-11.

[4] OECD. 2012 *Test No. 229: Fish Short Term Reproduction Assay*, OECD Publishing.

[5] Klaminder, J., Hellström, G., Fahlman, J., Jonsson, M., Fick, J., Lagesson, A., Bergman, E. & Brodin, T. 2016 Drug-Induced Behavioral Changes: Using Laboratory Observations to Predict Field Observations. *Front Environ Sci* **4**.

[6] Levin, S.A., Harwell, M.A., Kelly, J.R. & Kimball, K.D. 1989 *Ecotoxicology: problems and approaches*. New York, Springer.

[7] Wong, B.B.M. & Candolin, U. 2015 Behavioral responses to changing environments. *Behav Ecol* **26**, 665-673.

[8] Clotfelter, E.D., Bell, A.M. & Levering, K.R. 2004 The role of animal behaviour in the study of endocrine-disrupting chemicals. *Anim Behav* **68**, 665-676.

[9] Zala, S.M. & Penn, D.J. 2004 Abnormal behaviours induced by chemical pollution: A review of the evidence and new challenges. *Anim Behav* **68**, 649-664.

[10] Melvin, S.D. & Wilson, S.P. 2013 The utility of behavioral studies for aquatic toxicology testing: A meta-analysis. *Chemosphere* **93**, 2217-2223.

[11] Arnold, K.E., Brown, A.R., Ankley, G.T. & Sumpter, J.P. 2014 Medicating the environment: assessing risks of pharmaceuticals to wildlife and ecosystems. *Phil Trans R Soc Lond B* **369**, 20130569.

[12] Fleeger, J.W., Carman, K.R. & Nisbet, R.M. 2003 Indirect effects of contaminants in aquatic ecosystems. *Science of the Total Environment* **317**, 207-233.

[13] Clements, W.H. & Rohr, J.R. 2009 Community responses to contaminants: Using basic ecological principles to predit ecotoxicological effects. *Environ Toxicol Chem* **28**, 1789-1800.

[14] Kidd, K.A., Paterson, M.J., Rennie, M.D., Podemski, C.L., Findlay, D.L., Blanchfield, P.J. & Liber, K. 2014 Direct and indirect responses of a freshwater food web to a potent synthetic oestrogen. *Phil Trans R Soc Lond B* **369**.

[15] Rohr, J.R., Kerby, J.L. & Sih, A. 2006 Community ecology as a framework for predicting contaminant effects. *Trends Ecol Evol* **21**, 606-613.

[16] Brodin, T., Heynen, M., Fick, J., Klaminder, J., Piovano, S. & Jonsson, M. 2014 Inconspicuous effects of pharmaceuticals in aquatic systems – ecological impacts through behavioural modifications at dilute concentrations. *Phil Trans R Soc Lond B* **369**, 20130580.

[17] Halstead N, McMahon T., Johnson S., Raffel T., Romansic J., Crumrine P., Rohr J. & Fussmann, G. 2014 Community ecology theory predicts the effects of agrochemical mixtures on aquatic biodiversity and ecosystem properties. *Ecol Lett* **17**, 932-941.

[18] Sopinka, N., Marentette, J. & Balshine, S. 2010 Impact of contaminant exposure on resource contests in an invasive fish. *Behav Ecol Sociobiol* **64**, 1947-1958.

[19] McCallum, E.S., Krutzelmann, E., Brodin, T., Fick, J., Sundelin, A. & Balshine, S. 2017 Exposure to wastewater effluent affects fish behaviour and tissue-specific uptake of pharmaceuticals. *Sci Total Environ* **605-606**, 578-588.

[20] Soeffker, M. & Tyler, C.R. 2012 Endocrine disrupting chemicals and sexual behaviors in fish - a critical review on effects and possible consequences. *Crit Rev Toxicol* **42**, 653-668.

[21] Hotchkiss, A.K., Rider, C.V., Blystone, C.R., Wilson, V.S., Hartig, P.C., Ankley, G.T., Foster, P.M., Gray, C.L. & Gray, L.E. 2008 Fifteen years after "Wingspread"-Environmental endocrine disrupters and human and wildlife health: Where we are today and where we need to go. *Toxicol Sci* **105**, 235-259.

[22] Lopez-Antia, A., Ortiz-Santaliestra, M.E., Mougeot, F. & Mateo, R. 2013 Experimental exposure of red-legged partridges (*Alectoris rufa*) to seeds coated with imidacloprid, thiram and difenoconazole. *Ecotoxicology* **22**, 125-138.

[23] Grue, C.E., Gibert, P.L. & Seeley, M.E. 1997 Neurophysiological and behavioral changes in non-target wildlife exposed to organophosphate and carbamate pesticides: Thermoregulation, food consumption, and reproduction. *Amer Zool* **37**, 369-388.

[24] Park, D., Hempleman, S.C. & Propper, C.R. 2001 Endosulfan exposure disrupts pheromonal systems in the red-spotted newt: A mechanism for subtle effects of environmental chemicals. *Environ Health Perspect* **109**, 669-673.

[25] Little, E.E. & Finger, S.E. 1990 Swimming behavior as an indicator of sublethal toxicity in fish. *Environ Toxicol Chem* **9**, 13-19.

[26] Robinson, P.D. 2009 Behavioural toxicity of organic chemical contaminants in fish: application to ecological risk assessments (ERAs). *Can J Fish Aquat Sci* **66**, 1179-1188.

[27] Cote, J., Clobert, J., Brodin, T., Fogarty, S. & Sih, A. 2010 Personality-dependent dispersal: characterization, ontogeny and consequences for spatially structured populations. *Phil Trans R Soc Lond B* **365**, 4065-4076.

[28] Herborn, K.A., Macleod, R., Miles, W.T.S., Schofield, A.N.B., Alexander, L. & Arnold, K.E. 2010 Personality in captivity reflects personality in the wild. *Anim Behav* **79**, 835-843.

[29] Lürling, M. & Scheffer, M. 2007 Info-disruption: pollution and the transfer of chemical information between organisms. *Trend Ecol Evol* **22**, 374-379.

[30] Scholz, N.L., Truelove, N.K., French, B.L., Berejikian, B.A., Quinn, T.P., Casillas, E. & Collier, T.K. 2000 Diazinon disrupts antipredator and homing behaviors in chinook salmon (*Oncorhynchus tshawytscha*). *Can J Fish Aquat Sci* **57**, 1911-1918.

[31] van der Sluijs, I., Gray, S.M., Amorim, M.C.P., Barber, I., Candolin, U., , et al. 2011 Communication in troubled waters:responses of fish communication systems to changing environments. *Evol Ecol* **25**, 623-640.

[32] Sloman, K.A., Lepage, O., Rogers, J.T., Wood, C.M. & Winberg, S. 2005 Socially-mediated differences in brain monoamines in rainbow trout:effects of trace metal contaminants. *Aquat Toxicol* **71**, 237-247.

[33] Scott, G.R. & Sloman, K.a. 2004 The effects of environmental pollutants on complex fish behaviour: integrating behavioural and physiological indicators of toxicity. *Aquat Toxicol* **68**, 369-392.

[34] DuRant, S.E., Hopkins, W.A. & Talent, L.G. 2007 Impaired terrestrial and arboreal locomotor performance in the western fence lizard (*Sceloporus occidentalis*) after exposure to an AChE-inhibiting pesticide. *Environ Pollut* **149**, 18-24.

[35] Hellström, G., Klaminder, J., Finn, F., Persson, L., Alanärä, A., Jonsson, M., Fick, J. & Brodin, T. 2016 GABAergic anxiolytic drug in water increases migration behaviour in salmon. *Nature Comm* **7**, 13460.

[36] Marentette, J.R., Tong, S., Wang, G., Sopinka, N.M., Taves, M.D., Koops, M.A. & Balshine, S. 2012 Behavior as biomarker? Laboratory versus field movement in round goby (*Neogobius melanostomus*) from highly contaminated habitats. *Ecotoxicology* **21**, 1003-1012.

[37] Flahr, L.M., Michel, N.L., Zahara, A.R.D., Jones, P.D. & Morrissey, C.A. 2015 Developmental Exposure to Aroclor 1254 Alters Migratory Behavior in Juvenile European Starlings (*Sturnus vulgaris*). *Environ Sci Technol* **49**, 6274-6283.

[38] Ward, A.J.W., Duff, A.J., Horsfall, J.S. & Currie, S. 2008 Scents and scents-ability: pollution disrupts chemical social recognition and shoaling in fish. *Proc R Soc Lond B* **275**, 101-105.

[39] Dew, W.A., Azizishirazi, A. & Pyle, G.G. 2014 Contaminant-specific targeting of olfactory sensory neuron classes:Connecting neuron class impairment with behavioural deficits. *Chemosphere* **112**, 519-525.

[40] Sloman, K.A. 2007 Effects of trace metals on salmonid fish: The role of social hierarchies. *App Anim Behav Sci* **104**, 326-345.

[41] Bean, T.G., Boxall, A.B.A., Lane, J., Herborn, K.A., Pietravalle, S. & Arnold, K.E. 2014 Behavioural and physiological responses of birds to environmentally relevant concentrations of an antidepressant. *Phil Trans R Soc B* **369**, 20130575.

[42] Brodin, T., Fick, J., Jonsson, M. & Klaminder, J. 2013 Dilute concentrations of a psychiatric drug alter behavior of fish from natural populations. *Science* **339**, 814-815.

[43] Martin, J.M., Saaristo, M., Bertram, M.G., Lewis, P.J., Coggan, T.L., Clarke, B.O. & Wong, B.B.M. 2017 The psychoactive pollutant fluoxetine compromises antipredator behaviour in fish. *Environ Pollut* **222**, 592-599.

[44] Saaristo, M., McLennan, A., Johnstone, C.P., Clarke, B.O. & Wong, B.B.M. 2017 Impacts of the antidepressant fluoxetine on the anti-predator behaviours of wild guppies (*Poecilia reticulata*). *Aquat Toxicol* **183**, 38-45.

[45] Cresswell, W. 2008 Non-lethal effects of predation in birds. *Ibis* **150**, 3-17.

[46] Dingemanse, N.J., Kazem, A.J.N., Reale, D. & Wright, J. 2010 Behavioural reaction norms:animal personality meets individual plasticity. *Trends Ecol Evol* **25**, 81-89.

[47] Herborn, K.A., Heidinger, B.J., Alexander, L. & Arnold, K.E. 2014 Personality predicts behavioral flexibility in a fluctuating, natural environment. *Behav Ecol* **25**, 1374-1379.

[48] Royauté, R., Buddle, C.M. & Vincent, C. 2015 Under the influence:sublethal exposure to an insecticide affects personality expression in a jumping spider. *Funct Ecol* **29**, 962-970.

[49] Cleasby, I.R., Nakagawa, S., Schielzeth, H. & Hadfield, J. 2015 Quantifying the predictability of behaviour: statistical approaches for the study of between-individual variation in the within-individual variance. *Methods Ecol Evolut* **6**, 27-37.

[50] Snijders, L., Blumstein, D.T., Stanley, C.R. & Franks, D.W. Animal Social Network Theory Can Help Wildlife Conservation. *Trends Ecol Evol* **32**, 567-577.

[51] Medina, M.H., Correa, J.A. & Barata, C. 2007 Micro-evolution due to pollution: Possible consequences for ecosystem responses to toxic stress. *Chemosphere* **67**, 2105-2114.

[52] Hamilton, P.B., Rolshausen, G., Webster, T.M.U. & Tyler, C.R. 2017 Adaptive capabilities and fitness consequences associated with pollution exposure in fish. *Phil Trans R Soc Lond B* **372**.

[53] Xie, L.T. & Klerks, P.L. 2004 Changes in cadmium accumulation as a mechanism for cadmium resistance in the least killifish *Heterandria formosa*. *Aquat Toxicol* **66**, 73-81.

[54] Silva, D., Araujo, C.V.M., Lopez-Doval, J.C., Neto, M.B., Silva, F.T., Paiva, T.C.B. & Pompeo, M.L.M. 2017 Potential effects of triclosan on spatial displacement and local population decline of the fish Poecilia reticulata using a non-forced system. *Chemosphere* **184**, 329-336.

[55] Araujo, C.V.M., Moreira-Santos, M. & Ribeiro, R. 2016 Active and passive spatial avoidance by aquatic organisms from environmental stressors: A complementary perspective and a critical review. *Environ Internat* **92-93**, 405-415.

[56] Saunders, R.L. & Sprague, J.B. 1967 Effects of copper-zinc mining pollution on a spawning migration of Atlantic salmon *Water Res* **1**, 419-&.

[57] Rolshausen, G., Phillip, D.A.T., Beckles, D.M., Akbari, A., Ghoshal, S., Hamilton, P.B., Tyler, C.R., Scarlett, A.G., Ramnarine, I., Bentzen, P., et al. 2015 Do stressful conditions

make adaptation difficult? Guppies in the oil-polluted environments of southern Trinidad. *Evol App* **8**, 854-870.

[58] Oaks, J.L., Gilbert, M., Virani, M.Z., Watson, R.T., Meteyer, C.U., Rideout, B.A., Shivaprasad, H.L. et al. 2004 Diclofenac residues as the cause of vulture population decline in Pakistan. *Nature* **427**, 630-633.

[59] Willi, Y., Van Buskirk, J. & Hoffmann, A.A. 2006 Limits to the adaptive potential of small populations. *Ann Rev Ecol Evol System* **37**, 433-458.

[60] Blanquart, F., Gandon, S. & Nuismer, S.L. 2012 The effects of migration and drift on local adaptation to a heterogeneous environment. *J Evol Biol* **25**, 1351-1363.

[61] Cachot, J., Law, M., Pottier, D., Peluhet, L., Norris, M., Budzinski, H. & Winn, R. 2007 Characterization of toxic effects of sediment-associated organic pollutants using the lambda transgenic medaka. *Environ Sci Technol* **41**, 7830-7836.

[62] Matson, C.W., Lambert, M.M., McDonald, T.J., Autenrieth, R.L., Donnelly, K.C., Islamzadeh, A., Politov, D.I. & Bickham, J.W. 2006 Evolutionary toxicology: Population-level effects of chronic contaminant exposure on the marsh frogs (*Rana ridibunda*) of Azerbaijan. *Environ Health Perspect* **114**, 547-552.

[63] Oziolor, E.M., De Schamphelaere, K. & Matson, C.W. 2016 Evolutionary toxicology: Meta-analysis of evolutionary events in response to chemical stressors. *Ecotoxicology* **25**, 1858-1866.

[64] Loewe, L. & Hill, W.G. 2010 The population genetics of mutations: good, bad and indifferent. *Phil Trans R Soc Lond B* **365**, 1153-1167.

[65] Chevin, L.M. & Lande, R. 2010 When do adaptive plasticity and genetic evolution prevent extinction of a density-regulated population? *Evolution* **64**, 1143-1150.

[66] Maan, M.E. & Seehausen, O. 2011 Ecology, sexual selection and speciation. *Ecol Lett* **14**, 591-602.

[67] Gore, A.C., Holley, A.M. & Crews, D. 2017 Mate choice, sexual selection, and endocrine-disrupting chemicals. *Horm Behav* **101**, 3-12.

[68] Markman, S., Leitner, S., Catchpole, C., Barnsley, S., Muller, C.T., Pascoe, D. & Buchanan, K.L. 2008 Pollutants increase song complexity and the volume of the brain area HVC in a songbird. *Plos One* **3**.

[69] Bertram, M.G., Saaristo, M., Baumgartner, J.B., Johnstone, C.P., Allinson, M., Allinson, G. & Wong, B.B.M. 2015 Sex in troubled waters: Widespread agricultural contaminant disrupts reproductive behaviour in fish. *Horm Behav* **70**, 85-91.

[70] Martinez-Ruiz, C. & Knell, R.J. 2017 Sexual selection can both increase and decrease extinction probability: reconciling demographic and evolutionary factors. *J Anim Ecol* **86**, 117-127.

[71] Jacomb, F., Marsh, J. & Holman, L. 2016 Sexual selection expedites the evolution of pesticide resistance. *Evolution* **70**, 2746-2751.

[72] Whitehead, A., Clark, B.W., Reid, N.M., Hahn, M.E. & Nacci, D. 2017 When evolution is the solution to pollution: Key principles, and lessons from rapid repeated adaptation of killifish (*Fundulus heteroclitus*) populations. *Evol App* **10**, 762-783.

[73] Sih, A., Trimmer, P.C. & Ehlman, S.M. 2016 A conceptual framework for understanding behavioral responses to HIREC. *Curr Opin Behav Sci* **12**, 109-114.

[74] Markandya, A., Taylor, T., Longo, A., Murty, M.N., Murty, S. & Dhavala, K. 2008 Counting the cost of vulture decline - An appraisal of the human health and other benefits of vultures in India. *Ecol Econ* **67**, 194-204.

[75] Weis, J. & Candelmo, A. 2012 Pollutants and fish predator / prey behavior : A review of laboratory and field approaches. *Curr Zool* **58**, 9-20.

[76] Oksanen, L., Fretwell, S.D., Arruda, J. & Niemela, P. 1981 Exploitation Ecosystems in Gradients of Primary Productivity. *Am Nat* **118**, 240-261.

[77] Ankley, G.T., Bennett, R.S., Erickson, R.J., Hoff, D.J., Hornung, M.W., Johnson, R.D., Mount, D.R., Nichols, J.W., Russom, C.L., Schmieder, P.K., et al. 2010 Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment. *Environ Toxicol Chem* **29**, 730-741.

[78] Windsor, F.M., Ormerod, S.J. & Tyler, C.R. 2017 Endocrine disruption in aquatic systems: up-scaling research to address ecological consequences. *Biol Rev* **93**, 626-641.

[79] Brown, A.R., Gunnarsson, L., Kristiansson, E. & Tyler, C. 2014 Assessing variation in the potential susceptibility of fish to pharmaceuticals, considering evolutionary differences in their physiology and ecology. *Phil Trans R Soc Lond B* **369**, 20130576.

[80] Huerta, B., Rodriguez-Mozaz, S. & Barcelo, D. 2012 Pharmaceuticals in biota in the aquatic environment: analytical methods and environmental implications. *Anal Bioanal Chem* **404**, 2611-2624.

[81] Brodin, T., Nordling, J., Lagesson, A., Klaminder, J., Hellstrom, G., Christensen, B. & Fick, J. 2017 Environmental relevant levels of a benzodiazepine (oxazepam) alters important behavioral traits in a common planktivorous fish, (*Rutilus rutilus*). *J Toxicol Environ Health A* **80**, 963-970.

[82] Lagesson, A., Fahlman, J., Brodin, T., Fick, J., Jonsson, M., Bystrom, P. & Klaminder, J. 2016 Bioaccumulation of five pharmaceuticals at multiple trophic levels in an aquatic food web - Insights from a field experiment. *Sci Tot Environ* **568**, 208-215.

[83] Kristofco, L.A., Cruz, L.C., Haddad, S.P., Behra, M.L., Chambliss, C.K. & Brooks, B.W. 2016 Age matters: Developmental stage of *Danio rerio* larvae influences photomotor response thresholds to diazinion or diphenhydramine. *Aquat Toxicol* **170**, 344-354.

[84] Huntingford, F.A. 2004 Implications of domestication and rearing conditions for the behaviour of cultivated fishes. *J Fish Biol* **65**, 122-142.

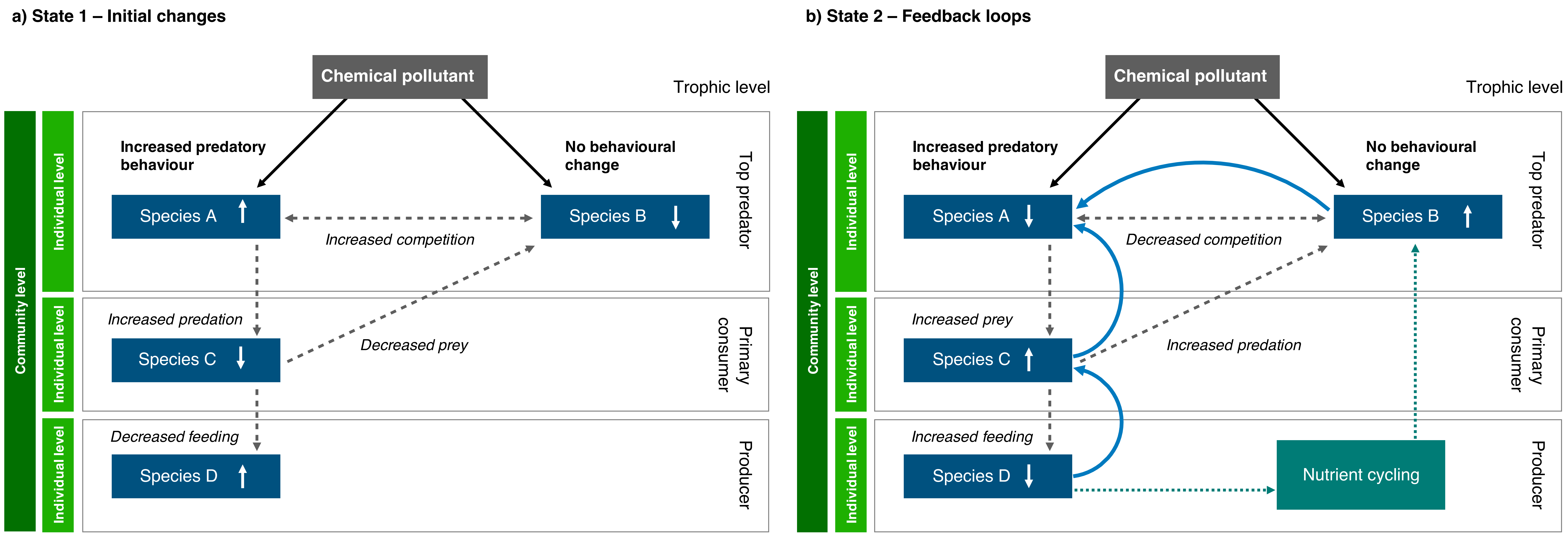
a) State 1 – Initial changes
Chemical pollutant
Trophic level
Community level
Individual level
Individual level
Individual level
Increased predatory behaviour
No behavioural change
Species A
Species B
Increased competition
Top predator
Increased predation
Species C
Decreased prey
Primary consumer
Decreased feeding
Species D
Producer
b) State 2 – Feedback loops
Chemical pollutant
Trophic level
Community level
Individual level
Individual level
Individual level
Increased predatory behaviour
No behavioural change
Species A
Species B
Decreased competition
Top predator
Increased prey
Species C
Increased predation
Primary consumer
Increased feeding
Species D
Nutrient cycling
Producer

FIGURE 1

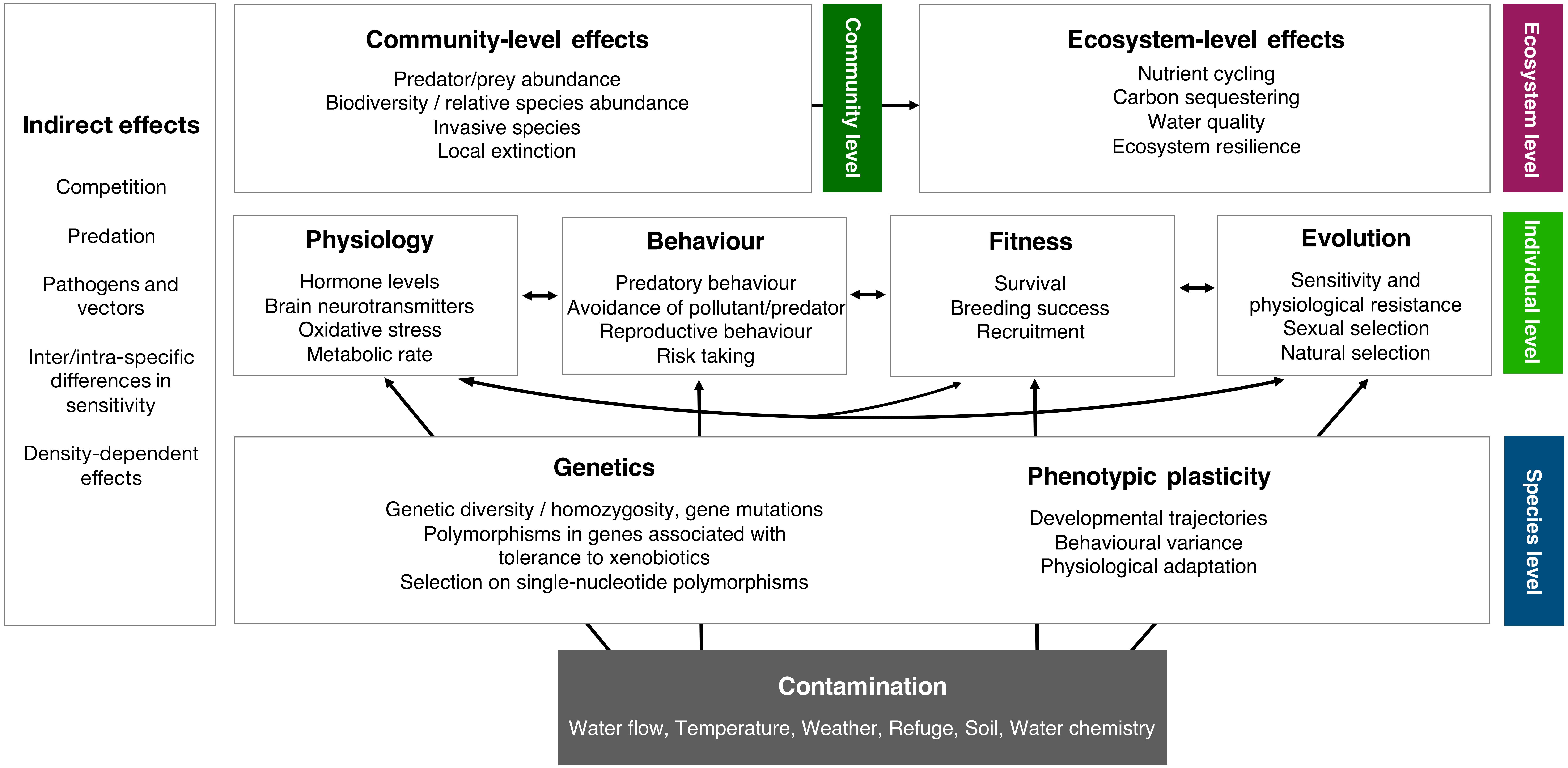
Indirect effects
Competition
Predation
Pathogens and vectors
Inter/intra-specific differences in sensitivity
Density-dependent effects
Community-level effects
Predator/prey abundance
Biodiversity / relative species abundance
Invasive species
Local extinction
Community level
Ecosystem-level effects
Nutrient cycling
Carbon sequestering
Water quality
Ecosystem resilience
Ecosystem level
Physiology
Hormone levels
Brain neurotransmitters
Oxidative stress
Metabolic rate
Behaviour
Predatory behaviour
Avoidance of pollutant/predator
Reproductive behaviour
Risk taking
Fitness
Survival
Breeding success
Recruitment
Evolution
Sensitivity and physiological resistance
Sexual selection
Natural selection
Individual level
Genetics
Genetic diversity / homozygosity, gene mutations
Polymorphisms in genes associated with tolerance to xenobiotics
Selection on single-nucleotide polymorphisms
Phenotypic plasticity
Developmental trajectories
Behavioural variance
Physiological adaptation
Species level
Contamination
Water flow, Temperature, Weather, Refuge, Soil, Water chemistry

FIGURE 2

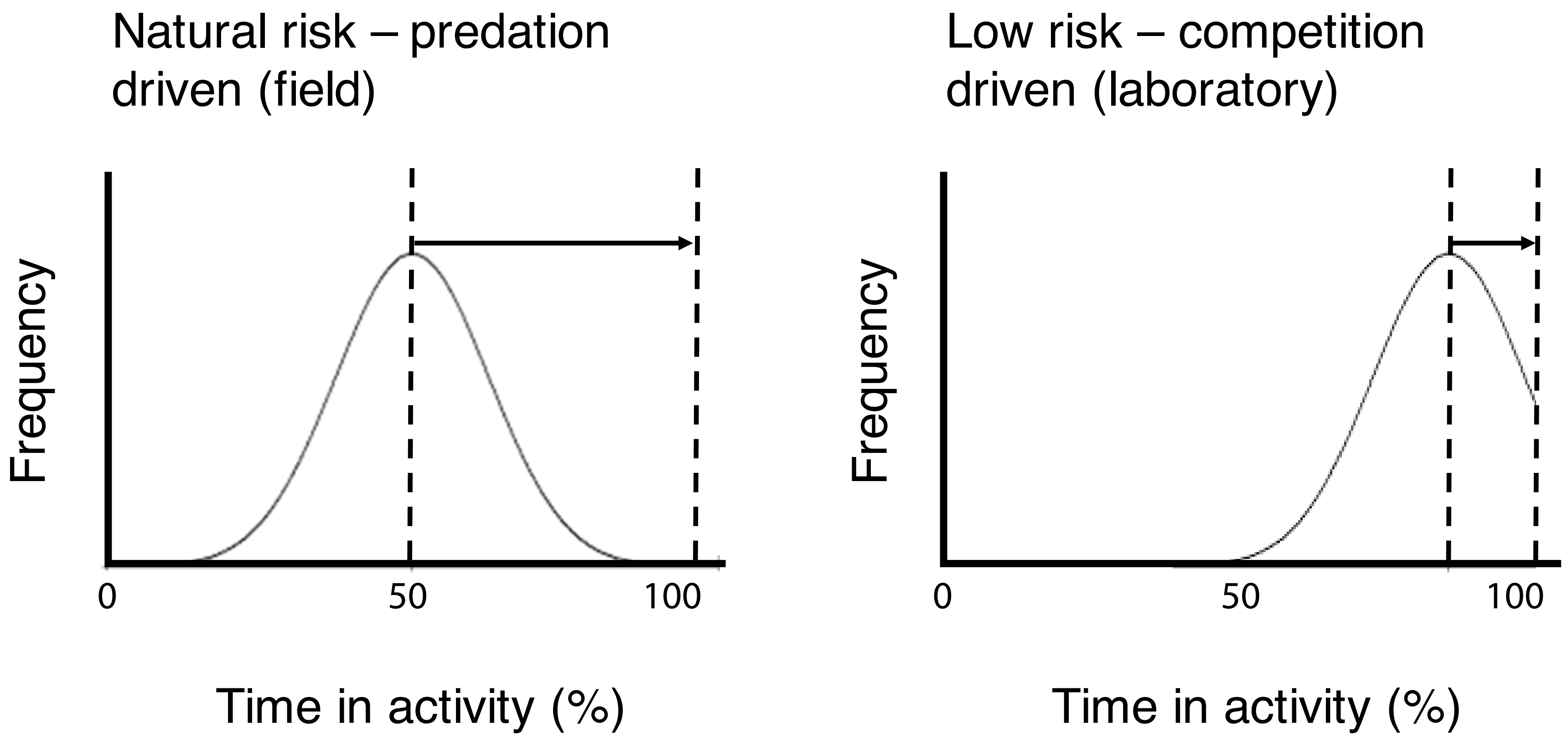
Natural risk – predation driven (field)
Frequency
0
50
100
Time in activity (%)
Low risk – competition driven (laboratory)
Frequency
0
50
100
Time in activity (%)

FIGURE 3