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Neglected impacts of plant protection products on invertebrate aquatic biodiversity: a focus on eco-evolutionary processes

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Abstract :

The application of plant protection products (PPPs) may have delayed and long-term non-intentional impacts on aquatic invertebrates inhabiting agricultural landscapes. Such effects may induce population responses based on developmental and transgenerational plasticity, selection of genetic resistance, as well as increased extirpation risks associated with random genetic drift. While the current knowledge on such effects of PPPs is still scarce in non-target aquatic invertebrate species, evidences are accumulating that support the need for consideration of evolutionary components of the population response to PPPs in standard procedures of risk assessment. This mini-review, as part of a contribution to the collective scientific assessment on PPP impacts on biodiversity and ecosystem services performed in the period 2020–2022, presents a brief survey of the current results published on the subject, mainly in freshwater crustaceans, and proposes some research avenues and strategies that we feel relevant to fill this gap.

Keywords : Phytopharmaceuticals, Ecotoxicology, Evolutionary toxicology, Aquatic invertebrates

Introduction

One of the ultimate goals of ecotoxicology is to estimate non-intentional effects of anthropogenic pollution on biodiversity and ecosystem functioning, in order to provide decision-makers with tools to alleviate such effects and to maintain ecosystem sustainability and services. In the European framework of chemicals regulation (REACH), ecological risk assessment (ERA) targets this overarching objective by evaluating new substances upstream from placing them on the market. However, this assessment is most often based on short-term standard toxicity tests centered on the organism level (e.g., the great majority of OECD test guidelines) which lack ecological realism, especially regarding the protection goals targeted by the EU (e.g. population level assessment, see WDF for aquatic ecosystems ; see Hommen et al. 2010). While the statement of this regulatory hiatus is no news (e.g., Chapman 2002), it has been more recently extended to the *evolutionary impact* (Van Straalen and Feder 2012 ; Straub et al. 2020), as a consequence of an ever-growing corpus of evidences reported for the three last decades and which covers the tree of life [see e.g. special issues on genetic and evolutionary toxicology in journals such as Environmental Health Perspectives (Anderson et al. 1994), Ecotoxicology (Coutellec and Barata 2011, 2013) or Evolutionary Applications (Brady et al. 2017a)]. Nowadays, the issue of human-induced evolutionary impact finds a particular echo in the current context of Anthropocene (Earth's most recent geologic period during which humanity became the most influential driver of environmental change) and its trail of long term impacts on biodiversity. In the light of earlier findings on the development of resistance to pests targeted by agricultural treatments, the question of the eco-evolutionary effects of chemical contaminants is becoming increasingly important for biodiversity species, particularly in view of the ever-increasing toxic pressure on various components of ecosystem communities caused by the use of agricultural chemical inputs (e.g. Schulz et al 2021).

This mini-review focuses on evolutionary impacts of plant protection products (PPPs) on aquatic invertebrates and was performed as a contribution to the collective scientific assessment to which this special issue is devoted. More precisely, this work was part of a broader analysis of PPP ecotoxicological impacts on aquatic invertebrates, including studies addressing effects at organism, population, and community levels (see chapter 10 of the full report, Mamy et al. 2022). The literature encompassed in the present survey covers the period 2000-2020 (with a punctual addition of more recent, complementary studies), and includes both experimental and field approaches, which address microevolutionary and transgenerational changes triggered by PPPs (see Table 1). In terms of biodiversity, these studies typically lie at the level of intraspecies diversity- (genetic diversity within and between conspecific populations). Intraspecific diversity is one of the three pillars of biodiversity, upon which population adaptive potential towards environmental change is based (Lande and Shannon

1996). Genetic improvement programs have resorted for decades on the exploitation of genetic diversity (Falconer and Mackay 1996), and the positive relationship between genetic diversity and fitness, which is nicely illustrated by the experimental concept of heterosis (hybrid vigor), is today largely documented in numerous non resource species (DeWoody et al. 2021). Likewise, genetic diversity and extinction risks associated with its reduction are at the heart of conservation programs (Frankham, 2010). The central role played by genetic diversity in the maintain of populations exposed to PPPs has been recently demonstrated in a study on daphnids, showing that genetically more diverse populations are able to persist longer in environments contaminated with copper (Loria et al. 2022). This result takes on particular importance regarding previous works, which have revealed loss of genetic diversity within daphnid populations in agricultural landscapes (Coors et al 2009).

Table 1. Summary information on evolutionary impacts of PPPs to aquatic invertebrates

Organisms	Delayed effects, Phenotypic plasticity	Genetic adaptation (resistance)	Maladaptation, Cost of resistance
gammarids (arthropods)	• Tolerance induced by pre-exposure (clothianidine ; Siddique et al. 2021)		• Increased susceptibility to various PPPs (Schneeweiss et an 2023) • Fitness cost and increased susceptibility to thermal stress (Siddique et al. 2020 ; 2021)
daphnids (arthropods)	• Morphological defenses (carbaryl and endosulfan ; Barry 2000)	• Evolutionary rescue (copper ; Loria et al. 2022) • Resistance (carbaryl ; Jenssen et al. 2015)	• Loss of genetic diversity (various PPPs ; Coors et al. 2009) • Increased susceptibility to parasite (Jenssen et al. 2011)
H. azteca (arthropod)	• Plasticity of enzymatic systems of detoxification (pyrethroids ; Fung et al. 2021)	• Selection of point mutations in target proteins (pyrethrinoids, organophosphates and carbamates ; Weston et al. 2013 ; Major et al. 2018) • Gene duplication (chlorpyrifos ; Major et al. 2020)	• Fitness cost of resistance, lower thermal tolerance, increased sensitivity to additional contaminants (Heim et al. 2018) • Reduced thermal tolerance in interaction with increasing salinity conditions (Fulton et al. 2021)
ephemeropteran (insect)		• Selection of genes involved in cuticular resistance (Gouin et al. 2019)	
mosquitoes (insects)		• Resistance to various insecticides used in vector control, involving target site mutation, increased metabolic capacities, gene overexpression / amplificaion (see recent review by Liu 2015)	• Fitness cost of resistance (chlorpyrifos ; Delnat et al. 2019)
L. stagnalis (mollusc)			• Increased random genetic drift induced by PPP cocktails (Coutellec et al. 2013) • Increase of susceptibility in inbred lines (diquat ; Duval et al. 2016)

Aquatic invertebrates as non-intentional targets of PPPs

As representative of the main part of animal diversity and biomass, invertebrates do not form a monophyletic group (Lecointre and Le Guyader 2017). Indeed, this grouping covers all metazoan phyla (ctenophora, porifera, placozoa, cnidaria, and all bilaterian sub-phyla). Their biological traits (morphology, body size, development, reproduction, etc.) encompass and underly a great diversity of life histories. In spite of the occurrence of highly conserved pathways, as studied under evolutionary developmental biology and comparative genomics (Carroll et al. 2005 ; Hall 2012), the heterogeneity and divergence of invertebrates is reflected notably in their molecular equipment and in the way their biological functions are regulated (development, metabolism, homeostasis, reproduction…). In the context of ecotoxicology, such discrepancies translate into heterogeneous sensitivity to chemical components such as PPPs, whose toxic modes of action can be highly specific (e.g., inhibition of enzymes or receptors through the binding to specific sites in a particular taxonomic group). This heterogeneity in physiological functioning across large metazoan lineages (non vertebrates) is puzzling and contributes to the difficulty to assess biological disturbance by xenobiotics such as PPPs when they are released into the environment.

Aquatic life is represented by all these phyla, sometimes exclusively (e.g., non-bilaterian metazoans). Therefore, understanding the impact of PPPs on aquatic invertebrates implies that diversity and heterogeneitiy is to be considered as pervasive and ubiquitous, notably in terms of taxonomic biodiversity (the majority of animal species), complexity (e.g., body plan of a placozoan vs a cephalopod mollusc), life style (sessile, mobile, parasitic forms…), life cycle (fully aquatic or not, including dormancy stages), lifespan, voltinism, semel- vs iteroparity, reproductive mode (scissiparity, parthenogenesis, which can be partial, cyclic, or obligatory, hermaphroditism, separate sexes), dispersal (internal vs external fertilization, phoresis, parasitic cycle..), as well as functional ecology and position in foodwebs. With respect to aquatic environments inhabited by invertebrates, diversity is also pervasive, in terms of salinity (freshwater, brackish, and marine waters), typology (lentic vs lotic systems), connectivity (dendritic hydrographic networks, interconnected marshes, estuaries…), anthropization (from ponds and other artificial water bodies to deep ocean waters), and vulnerability against chemical contamination including PPPs (proximity to treated agricultural zones, multiple modes of transfer).

Invertebrates exhibit some propensity in terms of sensitivity to toxicants, which results from (1) phylogenetic proximity between some groups and the organisms targeted by PPPs (e.g., aquatic arthropods and crop insect pests), (2) a central position within biotic interactions, especially foodwebs, which increases their ecological vulnerability to the disturbance of lower trophic levels sensitive to pesticides such as herbicides and fungicides, as well as their role in propagating indirect effects to higher levels such as predators, (3) sensitivity of species which phenology is in line with PPP applications (e.g.,seasonal reproduction of univoltine organisms and reprotoxic substances), (4)

relatively short lifespan and increased risk of micro-evolutionary effects induced by PPPs (multi- and transgenerational effects, evolution of resistance, etc.), and (5) high fluctuation in population size and isolation degree, which exacerbates demographic stochasticity and its consequences (Allee effect, random genetic drift), especially in species with low mobility and dispersal, as well as those with a complete aquatic lifecycle in discontinuous and semi-permanent habitats (marshes and ditches in agricultural landscapes).

Eco-evolutionary processes altered or induced by PPPs

With respect to evolutionary impacts of environmental change and degradation, a brief recall of basics may be useful here before focusing on the particular case of PPPs. The ability of natural species to respond adaptively to environmental change relies on a combination of characteristics inherited through macroevolution (since their ancestral lineage) and of on-going microevolutionary (population-level) processes that continuously shape their genetic diversity and adaptive potential (Brady et al. 2017b). Such responses may thus either reflect ancestral exposure to stressful conditions, be they abiotic (e.g. oxidative stress and aerobic mode of life) or biotic (e.g. host-parasite and host-pathogen coevolution), or more recent and novel stressors, to which species ancestors were naive (various xenobiotic substances). Adaptation is by itself an ambiguous term, which can be understood either as the phenotypic expression of an already adapted state (the result of past evolution induced by ancient selective pressures, for example, lungs as a breathing system adapted to terrestrial life) or as the evolutionary process « in action » leading to this state, i.e., the on-going selection of advantageous genetic variants (Bateson and Gluckman, 2011). The latter implies that variation at the adaptive trait occurs in the population and has a heritable genetic component upon which natural selection can operate. By contrast, the former (the achieved adapted phenotype) is expected to present limited genetic variation and thereby low ability to respond to new selective factors, due to longstanding evolutionary constraints (see Arnold 1992).

Compared to purely ecological studies, approaches designed to tackle evolutionary effects of PPPs are recent, and therefore much less numerous. This is in line with the recent awareness that ecological and evolutionary processes may operate at a similar pace, due to intensified human-induced environmental disturbances and invertebrate biodiversity crisis. Appropriately, the ever increasing number of cases of genetic resistances observed in pests, as adaptation to PPPs (see Sparks et al. 2021),illustrates quite well how rapid such evolutionary effects can be in agrosystems. This and the current knowledge on resistance modes of propagation and molecular basis (Paris and Després 2012 ; Ffrench-Constant 2013) provide strong arguments to consider evolutionary effects when it comes to address biodiversity impacts of PPPs. However, the demonstration of an evolutionary impact is not an easy task, due to

many confusing factors and unknown parameters (population history and level of genetic variation) and studies appropriately designed to this end are not plethora.

Traditional ecotoxicological approaches mainly focus on direct effects measured or estimated during exposure, which prevents from detecting any post-exposure consequences (see Beketov and Liess, 2008), including evolutionary changes. Delayed effects may be lethal or sublethal, affecting organisms later in their life or in their progeny (parental effects, inter- and transgenerational effects, of epigenetic or genetic nature). In turn, such effects have consequences at the population level, in terms of growth rate and fitness, as well as phenotypic and genetic diversity, and trait heritability (see Medina et al. 2007 ; Hoffmann and Willi 2008 ; Bickham 2011 ; Coutellec and Barata 2011 ; Oziolor et al. 2016, Brady et al. 2017a). Such delayed effects have been shown in the laboratory after several days following pulse exposure of various invertebrates exposed to thiacloprid at concentrations with moderate toxicity. For example, in the case of the crustacean *Gammarus pulex* exposed to thiacloprid, the LC50 (concentration that kills 50% of test individuals) was found 50 times lower 17 days after a 24h long exposure than that estimated one day post-exposure (Beketov and Liess 2008). Likewise, in the damselfly *Coenagrion scitulum* exposed as larvae to the pyrethrinoid insecticide esfenvalerate at environmental concentrations, a reduction of locomotory capacity in adults was observed, leading to a lowered ability to expand to the north as a response to climate change (Dinh et al. 2016). In the trichopteran insect *Brachycentrus americanus*, females decreased their investment in reproduction when exposed at pupal stage to the same insecticide (Palmquist et al. 2008).

Phenotypic plasticity as a response to PPPs

Facing new stressors, natural populations can respond plastically or genetically. The former process is known as *phenotypic plasticity*, the ability of a genotype to produce distinct phenotypes when exposed to different environments throughout its ontogeny (Pigliucci 2005). Phenotypic plasticity can be supported by an epigenetic basis (see Hallgrimsson and Hall, 2011; Ashe et al. 2021). Despite the confusion around the concept of plasticity and how it differs from immediate and transient homeostatic response to stress, an inclusive definition seems to have become consensual, which considers both an irreversible component, determined during parental or early exposure (*developmental plasticity*)– see Plautz and Salice (2013) for an example of contaminant exposure during embryonic development in a gastropod - and a later, reversible component induced by the environment experimented during the post-embryonic life course of the organism (*phenotypic flexibility*, which can affect behavior, physiology, and morphology) (Piersma and Drent, 2003 ; Beaman et al. 2016 ; Lande 2019). One classical example in ecotoxicology for phenotypic flexibility is the acclimation during pre-exposure to chronic concentrations of a toxicant that increases the acute tolerance in case of subsequent exposure to the same chemical. Although studies addressing the

contribution of phenotypic plasticity to PPP tolerance remain extremely rare in comparison for instance with a growing number of studies documenting this mechanism for metallic contaminants, a recent illustration was reported for the tolerance of the freshwater crustacean *Gammarus pulex* pre-exposed in the laboratory to the neonicotinoid insecticide clothianidin (Siddique et al 2021). The response is moreover considered « adaptive » if the phenotype produced in a given environment effectively increases the genotypic fitness in that environment. This adaptive value implies some level of environmental predictability (e.g., seasonal variation of temperature, light, presence of a predator, etc.). At the population level, plasticity can thus itself be subject to natural selection, although empirical evidences are not overwhelming (Van Buskirk and Steiner 2009 ; Arnold et al. 2019). Phenotypic plasticity can offer a way to adapt in stressful environments when population genetic diversity is already depreciated (Baldanzi et al. 2017). It is often viewed as a way to respond to rapid environmental change (Fox et al. 2019), as already suggested as plausible mechanism for population maintain in field contamination context (see an example in the annelid by Kille et al 2013). A spectacular example of such a response is found in daphnids, who develop defense structures (helmets, spines) in the presence of predator cues (Weiss et al. 2004). It is interesting to note that such morphological modifications can also be induced by chemicals such as insecticides carbaryl and endosulfan (Barry 2000), and that more generally, epigenetic alterations can be induced by various xenobiotics (see Vandegehuchte and Janssen 2014) including PPPs (e.g., vinclozolin, Skinner and Anway, 2007). Because some epigenetic changes may be transmitted to next generations along with genetic information (Schmid et al. 2018 ; Nilsson et al. 2022), it is now admitted that epigenetics plays a role in adaptation, through interactions with genetic variation and evolutionary forces (Bonduriansky et al. 2012).

Selective effects of PPPs

Besides rapid plasticity, population adaptive responses may also rely on the selection of natural genetic variants. This type of response implies that genetic variation pre-exists in the population at genes involved in the responsive traits, and that a positive relationship occurs between the trait value and fitness. In an ecotoxicological context, stress response may be generated by various molecular and cellular mechanisms. The evolution of multiple resistances to pesticides in target species provides a corpus of knowledge about some of these mechanisms. Genetic resistance, as a case of evolutionary adaptation due to selective effects of PPPs, can result from different evolutionary processes : selection of advantageous variants from extant genetic variation in the population, point *de novo* mutation, horizontal transfer, and adaptive introgression by hybridization (Hawkins et al. 2019). Metabolic resistance, which results from a higher capacity to metabolize the pesticide, is supposed to be multigenic and to spread through selection on extant variation. On the contrary, target site resistance is

monogenic and may imply spontaneous *de novo* mutations. In target species, selection is strong and may favor a new advantageous mutation more rapidly than in non-target species.

The evolution of tolerance to various insecticides in non-target aquatic invertebrates reveals a process of genetic selection induced by chronic or repeated exposure. Such an evolution was observed in the crustacean *Hyalella azteca* species complex as a response to persistent pyrethroids in sediments of californian hydrosystems (Weston et al. 2013; Major et al. 2018). Authors of this extensive study combined laboratory toxicity assessment and genotyping of natural populations sampled in sites with different loads of contamination by pyrethroids. Resistances prove to be multiple, implying parallel evolution of distinct alternative mutations already described in pest insects at the pyrethrinoid target gene, which encodes for the sodium channel protein (*vgsc*). Similarly, another point mutation was discovered that confers resistance to organophosphates and carbamates, especially in agricultural landscapes, by leading to a substitution in the amino acid sequence (glycine to serin at position 119) of acetylcholine esterase (AchE) (Major et al. 2020). The study moreover suggests a duplication of the gene *ace-1* (encoding AchE), which confers resistance to chlorpyrifos. Following the description of the major role played by genetic determinism in the observed tolerance to pyrethroids, a study has complemented this vision of genetic mutants resistant to PPPs, demonstrating that plasticity processes linked to the activation of detoxification enzymatic systems also underpin tolerance in the same *Hyalella* populations chronically exposed to PPPs (Fung et al 2021). Beyond intraspecific (population-level) evolutionary impacts associated with the loss of genetic diversity induced by directional selection as well as potential cost of resistance (Coustau et al. 2000 ; see below), the accumulation of pyrethroids in resistant populations of *H. azteca* raises the question of functional consequences at the level of ecosystems, astheir (secondary) consumers are expected to concentrate bioccumulable pesticides in higher amounts than when predating on non tolerant preys (Hartz et al. 2021).

In the same line, recent works suggest the development of resistance to insecticides in another freshwater crustacean, *Gammarus pulex*, through the observation of differential sensitivity to the neonicotinoid clothianidin between individuals sampled in populations exposed to different concentrations of PPPs (Becker and Liess 2017 ; Shahid et al. 2018 ; Becker et al. 2020). However, the resistance factors in this case are much weaker (of the order of 2 or 3) compared with studies on *Hyalella* (*e.g.* tolerance factors of up to 550, Weston et al 2013). Authors of these studies invoke factors susceptible to modulate the evolution of genetic resistance in gammarids, such as the proximity of non-tolerant populations (decreasing the efficiency of selection by gene flow from non-adapted populations), as well as low taxonomic biodiversity of the community, which would relax interspecific competition and thereby reinforce intraspecific competition (and selection) in gammarids. Temporal fluctuations in tolerance levels were recorded in the field, with an unexpected pattern of negative correlation with exposure levels along the seasons, explained as a reduction in potential variability of sensitivities within populations at the maximum of the cultural treatments, which may induce high

lethal stress in streams (Becker et al. 2020). The genetic or plastic nature of tolerance seems here again not totally exclusive depending on the exposure history of populations (Siddique et al 2021). Furthermore, evolution of resistance to these insecticides is not systematic, especially in environments with more diversified contamination profiles or affected by multiple stressors. This is the conclusion reached by studies of amphipod tolerance, which reported increased susceptibilities to PPPs in agricultural environments (Schneeweiss et al 2023), for example, or in aquatic environments under urban influence, which are also impregnated with insecticides (Švara et al 2021, Grethlein et al 2022). In another vein, a population genomics approach, without *a priori*, designed to identify genomic regions involved in the response to selection (local adaptation) suggests that PPPs affect the distribution of genetic diversity in populations of the ephemeropteran insect *Andesiops torrens* in Chile, through the detection of two genes under selection which are involved in cuticular resistance to insecticides (*LDL receptor-related protein 2* and *Dump*) (Gouin et al. 2019).

Under conditions of severe stress, population ability to react through genetic adaptation following a phase of demographic decline is at the base of the evolutionary rescue concept (Bell 2017). Interestingly, the above-mentioned study on daphnid exposure to copper also shows that if the majority of exposed populations finally decline or go to extinction, some of them exhibit a U-shaped dynamics consistent with this phenomenon (Loria et al. 2022).

Cost of genetic adaptation

Resistance to PPPs may imply a cost, revealed by a decrease in fitness (defined as the ability of an organism to leave offspring in the next generation of the population) when the selective pressure is alleviated, or when an additional factor is surimposed. The concept of fitness cost reflects this decrease and relies on the observation that in absence of PPP, resistant genes are generally rare in populations (an indication that they would be selected against), and that resistance is often unstable in experimental lines or populations (Coustau et al. 2000). A recent review encompassing 170 studies published on the cost of resistance to insecticides in target insects showed that in 60% of the cases, resistance effectively implies a fitness cost (Freeman et al. 2021). This cost is particularly expressed as a return of the strain to the sensitive state in absence of treatment (reversion), and by a decreased reproduction. However, the generality of this result masks differences among insecticide classes, with a cost less frequently reported for organochlorids, pyrethrinoids, neonicotinoids and Bt. In aquatic invertebrates (not directly targeted by PPPs), although this type of effect is still largely understudied, one can mention the seminal works of Jansen & coll. on the effects of the carbamate carbaryl to *Daphnia magna*. These studies showed that the level of tolerance expressed in exposed natural populations lowers under laboratory conditions in absence of the insecticide (Jansen et al. 2015), and that clonal strains resistant to carbaryl (following experimental exposure) prove to be more sensitive to parasites than their non-resistant counterparts (Jansen et al. 2011). Another example is provided in

aquatic arthropods by a study showing a cost of resistance to chlorpyrifos in the- mosquito *Culex pipiens*, that is expressed in presence of Bti, and translates both by a reduced larval survival and a higher vulnerability to its predator *Plea minutissima* (Delnat et al. 2019). Tolerance to neurotoxic insecticides observed in field populations of freshwater amphipods also documented the potential fitness costs induced by multi-generational exposure to PPPs. Pyrethroid resistance in *Hyalella* has hence been associated to fitness costs for tolerant organisms with increased susceptibility to thermal stress and lower reproductive capacities (Heim et al 2018). Neonicotinoid tolerance in *Gammarus pulex* population from agricultural areas goes with reduced demographic growth when populations are cultured under PPP-free conditions in the laboratory (Siddique et al 2020), and increased susceptibility to elevated temperature (Siddique et al 2021). These observations highlight a major challenge in the context of ongoing global change, characterized by multiple stress situations in the future aquatic environment.

Non adaptive evolutionary impacts of PPPs

Besides selective effects that may be exerted by the chronic presence of a given family of PPPs, the chemical pressure related to the recurrent use of complex cocktails of molecules in agricultural systems may also affect the genetic diversity of exposed populations, through demographic impairment, as already evocated above for field daphnids populations (Coors et al 2009). This type of effects was also illustrated in the gastropod *Lymnaea stagnalis*, in outdoor mesocosm experiments where mixtures of PPPs were applied, as a result of treatment programs and following various ways of transfer from the treated parcels to the surrounding aquatic systems (aerial drift, run-off, and drainage ; Auber et al. 2011). The experiment showed that in a few generations, treatments decreased population neutral genetic diversity (microsatellite markers) and increased population genetic differentiation, as theoretically expected due to random genetic drift (Coutellec et al. 2013). Similarly, by experimentally manipulating effective population size in order to calibrate demographic reductions potentially induced by toxicants, we also detected a rapid effect of random drift load in this species, by observing significant heterosis among small populations (Coutellec and Caquet 2011). This effect is indicative of impaired adaptive potential associated with reduced population genetic diversity, and of increased extirpation risk due to the random accumulation of spontaneous slightly deleterious mutations (Whitlock et al. 2000). Although not directly triggered by PPPs in the cited study, this finding points to the genetic risk incurred by populations when their demography is recurrently impaired by PPPs. Last, among other evolutionary forces able to interact with the selective potential of PPPs, inbreeding needs to be mentioned. Using experimental evolution in *L. stagnalis*, a synergistic interaction could be highlighted between the pro-oxidant herbicide diquat and inbreeding induced by self-fertilization as compared to cross-fertilization (Duval et al. 2016).

Research needs and perspectives

While evolutionary processes become better incorporated into ecology, their study remains limited in ecotoxicology, despite early awareness of the scientific community (Van Straalen and Timmermans 2002). However, the level of knowledge of such effects is continuously improved. Regarding PPPs, aquatic invertebrates, as a group of unintentional targets particularly vulnerable, deserves specific attention in this respect. However, face to the challenge that represents the demonstration of evolutionary impacts on natural populations (the response of which depends upon population genetic diversity, isolation, and exposure history) and of their consequences at the ecosystem level (which may be masked by a number of others factors or missed because unanticipated), it seems unrealistic to directly incorporate evolutionary principles into ecological risk assessment procedures. Nonetheless, from the information compiled in the present study, it appears that ecological risk assessment of PPPs would gain a significant step in scientific soundness if it could more explicitly consider evolutionary components of population responses. We hereby propose a few avenues that might help progress in this way. First, the consideration of genetic variation in standardized toxicity testing could represent a relevant issue for reflection towards this endeavor (see e.g., Côte et al. 2015). Next, the coupling of laboratory approaches and field population monitoring in ecologically relevant species might provide a way to complement *a priori* ERA, once a substance has been authorized. Last, the current corpus of results acquired on evolutionary impacts of PPPs could be implemented in a rational approach of knowledge sharing allowing the development of extrapolation strategies, for example, through the use of phylogenetic components of species sensitivity (Brady et al. 2017b ; Lalone et al. 2018), and through the search of mechanistic links between organism responses and evolutionary « modes of action » of PPPs. This type of approach could fit in with an evolutionary extension of the currently expanding concept of adverse outcome pathway (Ankley et al. 2010). Moreover, by using in particular tools offered today by environmental omics, we can quickly hope for new gains in mechanistic knowledge on the eco-evolutionary effects of contaminants based on the coupling of multigenerational experiments in the laboratory and field studies in historically exposed populations (in gammarids, see e.g., Gouveia et al. 2018). This knowledge on the genetic, epigenetic, or plastic nature of tolerance, on the physiological costs potentially induced by these adaptive or maladaptive phenomena should thus advance our understanding of the spatial and temporal dynamics of evolutionary impacts of environmental contamination. From this, we could be able to better decide on the relevance and way of inclusion of the examination of evolutionary processes in the predictive risk assessment schemes for

PPPs, but also in our analysis of the causes of the ongoing decline of aquatic biodiversity in agricultural landscapes.

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