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Review

# Can environmental change affect host/parasite-mediated speciation?☆

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ABSTRACT

Parasitism can be a driver of species divergence and thereby significantly alter species formation processes. While we still need to better understand how parasite-mediated speciation functions, it is even less clear how this process is affected by environmental change. Both rapid and gradual changes of the environment can modify host immune responses, parasite virulence and the specificity of their interactions. They will thereby change host–parasite evolutionary trajectories and the potential for speciation in both hosts and parasites. Here, we summarise mechanisms of host–parasite interactions affecting speciation and subsequently consider their susceptibility to environmental changes. We mainly focus on the effects of temperature change and nutrient input to ecosystems as they are major environmental stressors. There is evidence for both disruptive and accelerating effects of those pressures on speciation that seem to be context-dependent. A prerequisite for parasite-driven host speciation is that parasites significantly alter the host's Darwinian fitness. This can rapidly lead to divergent selection and genetic adaptation; however, it is likely preceded by more short-term plastic and transgenerational effects. Here, we also consider how these first responses and their susceptibility to environmental changes could lead to alterations of the species formation process and may provide alternative pathways to speciation.



**Contents**



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## 1. Introduction

Current biodiversity studies focus on species extinction rates and how they are amplified by human-mediated environmental change (Thomas et al., 2004; Barnosky et al., 2011). Whether changing environments affect the processes that give rise to new species is, however, rarely considered (but see Vonlanthen et al., 2012; Smith et al., 2014; Condamine et al., 2013). Host–parasite interactions represent one such evolutionary process. They are major parts of ecosystems and as such vary with ecological settings and environmental change (Lafferty and Kuris, 1999; Lazzaro and Little, 2009; Wolinska and King, 2009). Ecological settings can entail, but are not restricted to, the presence and abundance of intermediate and final hosts for the different parasite species, but also further ecological interactions such as predation or competition. Global change affects individuals, e.g. by affecting the trade-offs for the host involving immunity and defence strategies or transmission pathways for the parasite (Schmid-Hempel, 2003; Lafferty and Kuris, 2005; Kutzer and Armitage, 2016); the interaction between hosts and parasites (Mostowy and Engelstädter, 2011; Budria and Candolin, 2014); and the ecological settings when host or parasite community composition or population structure change (Lafferty and Kuris, 2005; Buser et al., 2012; Scharsack et al., 2012; IPCC, 2014) (Fig. 1). The consequences of all these alterations depend on the specific characteristics of the "disease triangle" (Stevens, 1960; Budria and Candolin, 2014): (i) the host corner includes the variation of its life history traits, its immunity (innate and/or acquired) and its abundance; (ii) the parasite corner comprises its transmission rates, its ability to accomplish its life cycle and its virulence. Lastly, (iii) the environment corner represents the ecosystem in which the host and the parasite live – and the initial source of change we consider in this review (Fig. 1).

Reciprocal feedbacks between ecological settings and evolutionary dynamics are the topic of eco-evolutionary research (Schoener, 2011), and such dynamics may well play an important role in shaping host and parasite evolution through time. However, as these mechanisms are not yet well understood it would be too speculative to describe how they may shape speciation at this point. We have therefore excluded eco-evolutionary dynamics from further discussion in this review.

For a glossary of key terms see Table 1.

### 1.1. The genetic basis of host–parasite interactions

Classic host–parasite theory describes coevolutionary dynamics via mirrored changes in allele frequencies in host and parasite populations. Two main scenarios are usually considered (Woolhouse et al., 2002; Gandon et al., 2008): (i) Arms races are characterised by recurrent selective sweeps of alleles. Theoretically, those alleles can be present in the population at a polymorphic locus or could arise from de novo mutations. (ii) Cycling allele frequencies describe the maintenance of the same genetic variants by constant negative frequency-dependent selection. Cycling allele frequencies have also been dubbed "Red Queen dynamics" (van Valen, 1973). In both scenarios, host–parasite interactions promote the maintenance of genetic diversity (either between or within populations) and create variation on which natural selection can act (Summers et al., 2003).

### 1.2. Speciation patterns on fitness landscapes for hosts and parasites

Speciation depends on the reduction of gene flow between populations or incipient species (Coyne and Orr, 2004); if we think of different host populations (and reciprocally of different parasite populations) as occupying specific peaks of an adaptive landscape, the speciation potential is defined by the distinctiveness of these peaks and by the potential for gene flow among them. If gene flow is low enough or at least restricted for key genomic regions due to divergent selection, local adaptation occurs as selection can promote traits which increase fitness at one particular peak. Ultimately, local adaptation can lead to speciation as reproductive isolation builds up via behavioural barriers and/or via genetic incompatibilities (Coyne and Orr, 2004). Under which conditions local adaptation leads to speciation remains an open question, but strong selective forces like host–parasite interactions are likely to support this outcome (Summers et al., 2003; Eizaguirre et al., 2009; Karvonen and Seehausen, 2012). Host–parasite interactions can alter speciation mechanisms only if they affect Darwinian fitness, i.e. the reproductive output of the speciating partner, and thereby change overall selection. Fitness effects are central to both arms race and Red Queen dynamics; however, arms races should lead to faster local adaptation and population divergence.

The fourfold effect of environmental change on hosts, parasites, their interactions and the ecological community affect local adaptation mechanisms in different ways. We consider two categories of change: firstly, environmental change can affect the host or the parasite individually and change their capacity to track adaptive peaks in the fitness landscape (or even mediate a switch to a different adaptive peak). Secondly, it can affect host–parasite interactions and the ecological settings, resulting in a change of the adaptive landscape itself. In the present article, we did not aim to review the entire literature on how global change affects host–parasite interactions as excellent reviews (e.g., Harvell et al., 2002; Lips et al., 2008; Tylianakis et al., 2008; Wolinska and King, 2009) and models (Mostowy and Engelstädter, 2011; Molnár et al., 2013) exist. Instead, after a general overview, we focus on host–parasite interactions and coevolution as fuel for speciation and how these dynamics are modified by environmental changes.

The focus of the present review is mainly on animal hosts, with the exception of some experimental coevolution studies, which have almost exclusively been carried out with bacteria hosts and phage parasites. We concentrate on the direct effects of temperature (global warming) and nutrient input to ecosystems (eutrophication). These two abiotic factors are most widely studied and known to have strong effects on host–parasite interactions (e.g., Harvell et al., 2002; Johnson et al., 2007).

## 2. Environmental change affects disease ecology

### 2.1. Rising temperatures

Current climate models predict a global average increase of air temperatures in the range of 1–4 °C by 2100 (IPCC, 2014) – a pace exceeding that of past climatic modifications. Change in temperature is expected to influence species occurrence and distribution with up to 37% of all extant species "committed to extinction" due

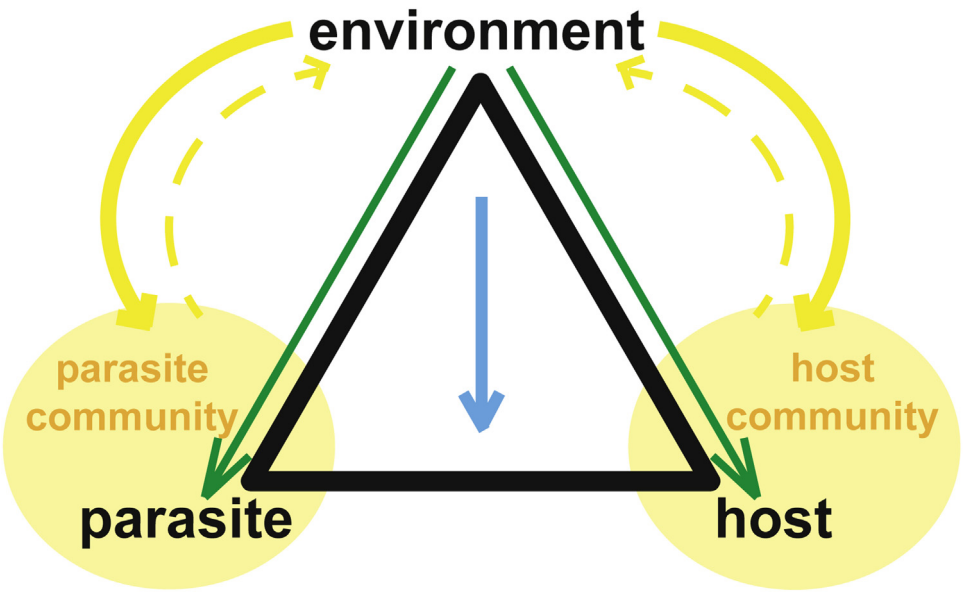


**Fig. 1.** Multiple effects of environmental changes on host–parasite interactions. Environmental change can affect parasite and host individuals directly (e.g., through changing physiological requirements – green arrows). It can alter dynamics in the interaction between the two species (e.g., by changing specificity of responses – light blue arrow). Furthermore, it can change the ecological settings in which the interaction takes place, thereby modifying evolutionary trajectories (e.g., through changes in host or parasite communities – solid yellow arrows). Some, if not all changes in hosts, parasites and their interactions are likely to have repercussions on the surrounding ecosystem (dashed yellow arrows). As little is known about such host/parasite-related eco-evolutionary processes and their importance, we do not discuss them at length in the present review.

**Table 1**
Glossary of important terms.

| | |
|---|---|
| Antagonistic pleiotropic effects | Multiple functions of the same gene(s) with opposing fitness effects. |
| Co-locally adapted gene complexes | Groups of genes within the parasite and within the host that are locally adapted, including adaptation to the genes of their antagonist. |
| Divergent selection | Divergent selection occurs when two populations experience different selective pressures, which promote increasing population differentiation. |
| Ecological settings | All biotic factors outside of the direct host-parasite interaction, i.e. the community ecology of the ecosystem. |
| Environmental change | For the present review, environmental change is defined as changes in abiotic parameters of an ecosystem, such as temperature or nutrient influx. |
| Fitness landscape | Also called adaptive landscape, a three-dimensional visualisation of the fitness distribution (z axis) across different trait combinations (x and y axes), first introduced by Wright (1932). |
| Genetic assimilation | The incorporation of a characteristic, initially occurring due to plasticity, into the genetic makeup of a population such that it becomes fixed independently of the environmental conditions eliciting the plasticity. |
| Host–parasite interaction | This umbrella term encompasses influences of hosts on parasites, influences of parasites on hosts and mechanisms that arise from the combination of these mutual influences. |
| Innate and adaptive immunity | The innate immune system includes all immune defence components which are part of the primary response to an infection, irrespective of prior encounter of the infective agent. The adaptive immune system, alternatively called acquired immune system, is formally described only in vertebrates and includes all mechanisms which involve immune memory. |
| Local adaptation | Process whereby selection mediated by local conditions for a population leads to its evolutionary acquisition of traits that confer higher fitness under these specific conditions than elsewhere. |
| Phenotypic plasticity | The capacity of one genotype to produce different phenotypes under different environmental conditions. |
| Transgenerational immune priming (TGIP) | Process whereby an immune challenge of the parent leads to changes in the immunological makeup of the offspring such that it reacts differently when in turn presented with the immune challenge. |

to climate change (Thomas et al., 2004). Those predictions, however, do not include species interactions and evolutionary change which will significantly alter the fate of species (Dawson et al., 2011; Moritz and Agudo, 2013). It is therefore important to improve our understanding of host–parasite interactions and subsequent evolution in response to environmental changes in general and temperature changes in particular (Harvell et al., 2002; Altizer et al., 2013).

Increases in parasite virulence and transmission rates are the most commonly described responses to rising temperatures (e.g., Kutz et al., 2005; Larsen and Mouritsen, 2014). For instance, the bacterial parasite *Pasteuria ramosa* castrates a much larger proportion of its host *Daphnia magna* at higher temperatures (Mitchell et al., 2005). Similarly, the tapeworm *Schistocephalus solidus* shows higher growth rates in three-spined sticklebacks at higher temperatures (MacNab and Barber, 2012). This physiological response is accompanied by heat-seeking behaviour in infected sticklebacks which could have damaging effects on host populations and aquatic ecosystems (MacNab and Barber, 2012).

So far it has not been directly tested how evolutionary trajectories of host resistance change under elevated temperatures. However, it has been observed that perch (*Perca fluviatilis*) living in an experimental lake have evolved towards increased resistance to the trematode *Diplostomum baeri* over several years of warming due to the effluents of a nuclear power plant (Mateos-Gonzalez et al., 2015). Even though performed *in natura* and hence associated with several confounding factors, this study shows that adaptation to increased water temperature may also lead to increased resistance. Several mechanisms can contribute to such rapid changes: (i) Increased variation in host life history traits upon parasite exposure at a higher temperature may reveal genetic variation in the population and make it available for selection (Schade

et al., 2014). (ii) Temperature increases can reinforce selection on immune genes, thereby accelerating host adaptation (Wegner et al., 2008; Björklund et al., 2015). (iii) Hosts further experience changes in immune parameters (e.g., immune cell counts, immune gene expression) as a response to temperature variation (Lazzaro and Little, 2009; Wolinska and King, 2009; Dittmar et al., 2014). As of yet, it is unclear what these changes translate into, as most observed changes are redistributions of investment in different immune parameters rather than clear reductions or increases in immune response. Even when a clear directional effect is visible, such as a reduction in immune cell counts, this does not necessarily lead to changes in host–parasite interactions (Landis et al., 2012). Furthermore, host resistance can be improved through plastic effects such as (iv) maternal effects, when mothers stressed by warmer environments produce more resistant offspring (Garbutt et al., 2014). And finally, (v) host behaviours such as foraging strategies or habitat choice can shift under climate change (e.g. in fish, Graham and Harrod, 2009), interacting with simultaneous effects of climate change on parasites (Lohmus and Björklund, 2015).

In addition to direct effects on hosts and/or parasites, global warming can also affect their interactions (Scharsack et al., 2016). This will be particularly prominent if change in parasite virulence and change in host resistance are asynchronous or mismatched. We predict such effects for systems where both parasite and host fitness are affected. A case in point is the bacterial parasite *Pasteuria ramosa* which increases spore production at high temperatures in a genotype-dependent manner and its invertebrate *Daphnia magna* host whose genotypes show variable responses to temperature in infection susceptibility and Darwinian fitness (Mitchell et al., 2005; Vale et al., 2008).

Thus, it is clear that integrated studies of temperature stress effects on host genotypes and parasite genotypes ($G \times G \times E$) are needed to understand the net effects of temperature changes on host–parasite interactions and predict their evolutionary outcomes. The development of models that integrate environmental effects on physiological factors into epidemiology will allow the broad use of future experimental data for more predictive power (Morley and Lewis, 2014; Dobson et al., 2015).

In general, temperature increases tend to reinforce parasite virulence and selection for host resistance (Scharsack et al., 2016), thereby likely accelerating host–parasite coevolution, either through (recurrent) allele sweeps or Red Queen dynamics. On the adaptive landscape, accelerated rates of coevolution would lead to more pronounced adaptive peaks and thereby to reduced gene flow between them. It is important to note, though, that directional selection imposed by global warming is also predicted to be accompanied by extreme climatic events and temperature fluctuations (IPCC, 2014). Extreme events may further support recurrent selective sweeps. Possible resulting antagonistic pleiotropic effects of affected genes are likely to be revealed after the climatic event. Furthermore, fluctuating conditions can favour phenotypic plasticity as discussed in Section 6 of the present review.

### 2.2. Eutrophication

Anthropogenic eutrophication is a major threat to aquatic ecosystems (Elser et al., 2009; Smith and Schindler, 2009). Eutrophication from urbanisation or agriculture can force a switch between alternative stable states (Scheffer et al., 2001), modify trophic cascades (Kratina et al., 2012) and reduce biodiversity by, for instance, enhancing speciation reversal (Vonlanthen et al., 2012).

Under eutrophic conditions, there is an overall tendency for increased parasite virulence and densities, especially for generalist parasites (Johnson et al., 2010). These effects are often driven by increased densities of intermediate hosts, effectively changing parasite life history (McKenzie and Townsend, 2007).

On the host side, variation in nutrient levels can force physiological modification as defence mechanisms are traded off against homeostasis and metabolism. This could either impair or promote local adaptation of the host: on the one hand, increased nutrient load may be associated with relaxed parasite-mediated selection on the host if susceptible individuals can compensate costs of immunity and survive long enough to reproduce. Furthermore, eutrophication can affect host behaviour, including interference with mate choice due to breakdown of cues, whether visual or olfactory (Budria and Candolin, 2015). One the other hand, insufficient nutrient supply can impair the specificity of host defences if investments into defence mechanisms are reduced (Brunner et al., 2014). Therefore, it seems that species are mostly adapted to an intermediate level of nutrients and those conditions are optimal for the evolution of local adaptation to parasites. Overall, any environmental change that will allow the host to reduce trade-offs involving immunity will be associated with relaxed selection as greater resistance is achieved without evolution. The predictable consequence of such relaxed selection is the breakdown of local adaptation by increased gene flow. Mathematical models show that the net effect of eutrophication on a host–parasite system will depend largely on the ability of the host to utilise the additional nutrients for its immune defence (Becker and Hall, 2014; Becker et al., 2015).

An increase in nutrient availability can also affect the specificity or type of host–parasite interactions (e.g., bumblebees/*Crithida*: Sadd, 2011; bacteria/phages: Lopez Pascua et al., 2014) and increase heterogeneity of infection outcomes between individuals and locations (Johnson et al., 2010; Becker et al., 2015). Productivity of natural systems often varies throughout the year and the seasons, which alters the effective strength of selection (Smith and Schindler, 2009). Fluctuating productivity can constrain coevolution when fluctuation frequency is faster than selective sweeps as shown in experimental coevolution of bacteria and phages (Harrison et al., 2013). This suggests that seasonal variation or recurring spikes of nutrients may disrupt the potential for local adaptation inherent to host–parasite interactions.

## 3. Influences of host–parasite interactions on parasite speciation

Mechanisms of parasite speciation still remain poorly understood as most studies concentrate on the ecological effects and macroevolutionary patterns while focusing relatively less on microevolutionary mechanisms (Huyse et al., 2005; Poulin and Morand, 2000). This is surprising given that parasites are likely the most abundant life form on Earth and major ecosystem components (Windsor, 1998; Kuris et al., 2008). They are even thought to represent the lifestyle most likely to involve population subdivision and subsequent speciation (Price, 1980). There are two major hypotheses for parasite speciation: speciation by cospeciation with their host and speciation by host switching (e.g., Littlewood et al., 1997; Huyse et al., 2005).

### 3.1. Parasite speciation by cospeciation

As parasites depend on the survival of hosts and their evolution, they are considered likely to cospeciate with their host (Fahrenholz's rule; Eichler, 1948). Cospeciation is even assumed to be the default evolutionary outcome of parasitism (Johnson et al., 2003). Cospeciation rates seem to be linked to the degree of specialisation (Thompson, 1994): a strong association between host and parasite combined with the inability of the parasite to survive on different hosts due to specialisation will prevent gene flow among parasite populations. Clear examples for recurrent cospeciation, reflected in matching parasite and host phylogenies, come

from systems with a very strict host–parasite association. Examples include pocket gophers (Geomyidae) and their chewing lice parasites (Trichodectidae) or marine teleost fishes and copepod parasites of the genus *Chondracanthus* (Hafner and Page, 1995; Paterson and Poulin, 1999).

### 3.2. Parasite speciation by host switching

Speciation by host switching is akin to the colonisation of a new habitat (in this case a new host species) and is likely promoted by environmental changes (Hoberg and Brooks, 2008). Monogenean parasites are probably the best example for speciation with a high rate of host switching (Bakke et al., 2002). Molecular data show that sister species of the *Gyrodactylus* genus often live on very distantly related fish hosts, a pattern typical for speciation by host switching (Cable et al., 1999). Similarly, morphology-based phylogenies found discrepancies between host and parasite phylogenies, pointing towards host switching as the origin of some major gyrodactylid lineages (Malmberg, 1998). Speciation of gyrodactylids is often referred to as "adaptive radiation" with host switches as key innovations, broadening the niche spectrum and increasing evolutionary potential (Zietara and Lumme, 2002). Similar to cospeciation, tight association between hosts and parasites is a decisive factor for speciation upon host switching (Zietara and Lumme, 2002).

### 3.3. Within-host speciation and hybridisation

In addition to the classic routes of co-speciation and host switching, parasite speciation may be explained by further mechanisms like within-host speciation (De Meeûs et al., 1998; Poulin and Morand, 2000). One example is the recently uncovered radiation of the monogenean genus *Cichlidogyrus*. Those ectoparasites show strong specificity for their cichlid hosts and have little opportunity for ecological transfer due to their hosts' low dispersal rates (Grégoir et al., 2015). Furthermore, the topology-based phylogeny and the monophyly of associated hosts suggest an important role for within-host speciation (Vanhove et al., 2015).

The presence of several parasite species on a host may also promote hybridisation amongst parasite species (Johnson et al., 2003; King et al., 2015). In a study on *Schistocephalus solidus*, a cestode parasite of the three-spined stickleback (*Gasterosteus aculeatus*), and *Schistocephalus pongitii,* a related parasite of the nine-spined stickleback (*Pungitius pungitius*), Henrich et al. (2013) showed that hybrid worms can infect both fish types while pure lines are host-specific. Different long-term evolutionary scenarios could arise from this: hybridisation could provide a mechanism to expand host range when host abundance declines and thereby promote parasite speciation if subsequent gene flow is reduced. If hybridisation does not increase the parasite's host range beyond the two initial hosts, however, the two parasite species could even merge into one and the evolutionary outcome would be reverse speciation.

So the question is, when should parasite speciation be expected? As the best overall predictor, increased host specialisation will narrow the adaptive peaks for each parasite population and therefore promote local adaptation and decrease gene flow, favouring the emergence of co-locally adapted gene complexes and species (Summers et al., 2003; Greischar and Koskella, 2007). Specialising parasites should therefore be more likely to speciate than generalist parasites (Johnson et al., 2003), and shifts of parasites along the generalist–specialist continuum may be the key to changes in speciation potential.

## 4. Influences of host–parasite interactions on host speciation

Parasites were recognised as a major evolutionary force more than 60 years ago and research efforts to understand their contribution to host evolution have increased ever since (Haldane, 1949; Schmid-Hempel, 2011). Nowadays, they are seen as "agents promoting diversity" (Summers et al., 2003), supporting the maintenance of genetic variation via mechanisms such as coevolutionary arms races, cycling allele frequencies and by selecting for the maintenance of sexual reproduction (Hamilton and Zuk, 1982; Hamilton et al., 1990; Milinski, 2006) (see Table 2 for a historic overview of host speciation research).

Even though parasites have long been associated with population divergence and the maintenance of genetic diversity in their host (Buckling and Rainey, 2002; Summers et al., 2003), their potential to contribute to speciation processes has only recently been conceptualised (Eizaguirre et al., 2009; Eizaguirre and Lenz, 2010; Karvonen and Seehausen, 2012; Thornhill and Fincher, 2013). These conceptual studies propose multiple, not mutually exclusive selective mechanisms – all relying on local differences in parasite communities. Notably, the concepts available to date were mostly developed for vertebrate hosts, and corresponding mechanisms remain to be studied for invertebrate hosts.

### 4.1. Speciation via "magic traits"

Magic traits have been defined as "a trait subject to divergent selection and a trait contributing to non-random mating that are pleiotropic expressions of the same gene(s)" (Gavrilets, 2004; Servedio et al., 2011). Pleiotropy in the context of a magic trait refers to linked phenotypic effects under both natural and sexual selection, rather than necessarily to two distinguishable phenotypic traits (Servedio et al., 2011).

The genes of the major histocompatibility complex (MHC) have been proposed to encode for an automatic magic trait in jawed vertebrates (Eizaguirre et al., 2009) as they are under direct parasite-mediated selection (Eizaguirre et al., 2012a) and are strongly involved in mate choice (Reusch et al., 2001; Milinski et al., 2005; Eizaguirre et al., 2011). Here, parasite resistance will vary due to (i) contrasting parasite communities between host habitats/niches; (ii) large genetic diversity existing at the MHC in the host population (reviewed in Piertney and Oliver, 2006; Spurgin and Richardson, 2010) and (iii) local adaptation of the MHC (Eizaguirre et al., 2012b). When MHC alleles are critical for parasite resistance, hybrids have suboptimal fitness (Milinski et al., 2005), and if mate choice is at least partly based on MHC genotypes, this magic trait can channel speciation (Eizaguirre and Lenz, 2010).

Even though evidence, mainly from fish systems (e.g., stickleback, whitefish), has accumulated, it remains an open question at which point selection that favours the maintenance of MHC diversity will select for assortative mating (Nuismer et al., 2008) and hence significantly contribute to speciation. Several studies have shown that populations of vertebrate species can differ in their MHC allele pools even when no one would consider them distinct species (birds: Bonneaud et al., 2006; newts: Babik et al., 2008; fish: Tobler et al., 2014). Future studies will have to focus on understanding exactly when an MHC-related adaptive peak switch promotes speciation.

### 4.2. Speciation via behavioural differentiation ("parasite-driven-wedge model")

Behaviours can significantly contribute to speciation as exemplified by mate choice (e.g., Boughman, 2001). Interestingly, there also exist numerous behaviours that are part of host defence.

**Table 2**
Major theoretical proposals and experimental evidence of parasite-mediated host speciation.

| Study type | Main conclusion | Proposed speciation mechanism | Reference |
|---|---|---|---|
| Theory<br>Mathematical model | Parasite pressure should accelerate host evolution and promote population divergence by selecting for resistant genotypes.<br>Close association of host and parasite species should lead to antagonistic cycling of population densities. | Parasite-mediated host population divergence.<br>Change in population density opens up niches for speciation. | Haldane, 1949 |
| Experiment | Parasite pressure promotes host diversification in allopatry and limits it in sympatry. | Parasite-mediated host population divergence | Buckling and Rainey, 2002 |
| Review | Lack of empirical evidence for host speciation.<br>Host speciation should be favoured when host is ahead in coevolutionary arms race. | Local adaptation of host can promote population divergence. | Summers et al., 2003 |
| Mathematical model | Assortative mating can evolve from host–parasite interaction in a matching allele mode of resistance. | Assortative mating can promote population divergence in host parasite coevolution. | Nuismer et al., 2008 |
| Meta-analysis<br>Theoretical approach | Language diversity (behavioural barrier) is correlated with parasite diversity.<br>Parasites can promote host speciation through selection for assortative sociality and philopatry (behavioural barriers). | Parasite-driven-wedge model. | Fincher and Thornhill, 2008 |
| Mathematical model | MHC genes underlie a magic trait involved in both natural and sexual modes of selection. | MHC as magic trait.<br>Reduced hybrid/migrant fitness. | Eizaguirre et al., 2009 |
| Review | Parasites may counteract biodiversity increase by preventing secondary contact of sister taxa. | Parasites depress diversification by preventing secondary contact. | Ricklefs, 2010 |
| Review | Multiple parasite-mediated selection mechanisms can support ecological speciation. | Host local adaptation as basis of population divergence.<br>MHC encodes a magic trait. | Eizaguirre and Lenz, 2010 |
| Mathematical model | Antagonistic coevolution of hosts and parasites can promote phenotypic diversification. | Host–parasite coevolution can support diversification across a metapopulation. | Yoder and Nuismer, 2010 |
| Review | Many case studies show parasites' contribution to divergence via three mechanisms but integration with general theory of ecological speciation still missing. | Magic trait (assortative mating by pleiotropy).<br>Ecology-based sexual selection (parasite-driven-wedge).<br>Reduced hybrid/immigrant fitness. | Karvonen and Seehausen, 2012 |
| Review | The broad spectrum of host defence mechanisms represents a major part of animal diversity and immunological divergence helps explain macroevolutionary divides. | Multiple, including MHC encoding a magic trait and parasite-driven-wedge. | Loker, 2012 |
| Experiment | MHC genotypes are locally adapted both in allelic diversity and specificity. | Local adaptation of adaptive immunity. | Eizaguirre et al., 2012b |
| Experiment | Reproductive isolation is greater after coevolution with parasite compared to evolution without parasite. | Coevolution accelerates population divergence. | Bérénos et al., 2012 |

They can be divided into pre-infection defences, such as avoidance of locations with high parasite prevalence, and post-infection defences, such as grooming behaviour (Schmid-Hempel, 2011). These defences will differ between host populations according to their parasite communities and should therefore be locally adapted. Besides localised behavioural defence syndromes, differences in parasite communities should promote local assortative sociality as an anti-contagion behaviour (Fincher and Thornhill, 2008). After these behaviours become correlated through linkage of their genetic basis, they can reinforce each other, which is described as a behavioural "wedge" (Thornhill and Fincher, 2013). Wedges promote population segregation and ultimately divergence (parasite-driven-wedge model by Thornhill and Fincher, 2013). While the focus of this model is on host behaviour rather than host genetics, the basis of both the magic trait and the parasite-driven-wedge models is the combination of natural and sexual selection. They do not appear to be mutually exclusive and may even be acting synergistically.

### 4.3. Theory gaps for parasite-mediated host speciation

Many as yet unexplored aspects of selection through parasite pressure could contribute to host speciation (Summers et al., 2003). Especially the onset of population divergence by parasite influence remains to be explained (Eizaguirre and Lenz, 2010; Karvonen and Seehausen, 2012). While it is clear that speciation potential depends to a large extent on the interaction mechanisms between host and parasite (Summers et al., 2003), which specific parameters define the speciation potential remains to be investigated. In fact, an important next step in research on parasite-driven speciation will be to characterise combinations of the different variables which are important for local adaptation of hosts to their parasites

(gene flow, generation time, population size etc.) and the rise of reproductive isolation from that local adaptation.

This next step in research also relates to the remaining conundrum that parasites have a double potential of promoting both the maintenance of polymorphism within a host population and the divergence between host populations (Haldane, 1949). Ample evidence for both mechanisms has been collected since Haldane's times (Schmid-Hempel, 2011) but how they are balanced and how environmental conditions may favour one over the other remains an open question.

Lastly, plasticity effects and epigenetic inheritance are just now in the process of being integrated into evolutionary theory in general and into host–parasite theory in particular (Mason, 2015; Nonaka et al., 2015; Vilcinskas, 2016). We present some potential constraints and contributions of plasticity to host/parasite-related speciation mechanisms in Section 6.

## 5. How can environmental change interact with host–parasite interactions in their effect on speciation dynamics?

### 5.1. Individual-based effects

Several studies have shown that, following environmental change, parasites tend to be ahead in the arms race with their hosts, at least immediately after a temperature increase or eutrophication event (Mitchell et al., 2005; Johnson et al., 2010; MacNab and Barber, 2012; Scharsack et al., 2016). However, increased resistance as a by-product of adaptation to a warming environment illustrates that hosts may also benefit from increased temperatures (Mateos-Gonzalez et al., 2015). Such effects, whether increased virulence of the parasite or increased resistance of the host, are typical for arms race dynamics and should accelerate progress towards speciation if slight differences between populations lead to different evolutionary trajectories. These individual effects represent the capacity of hosts and parasites to track adaptive peaks of their respective fitness landscape.

In relation to behavioural mechanisms, environmental change can result in relaxed selection on mate choice: for instance, eutrophication decreases visibility in aquatic habitats and investment of male three-spined sticklebacks in nuptial colouration becomes maladaptive as it is costly but does not lead to increased mating success anymore (Candolin et al., 2007). Relaxed selection may allow more infected individuals to reproduce as females cannot detect parasitised males based on nuptial colour (Candolin et al., 2014). Many systems also rely on olfactory cues (Milinski, 2014), which may be damaged under eutrophication and increased pH (Candolin et al., 2014). Altogether, this may result in the maintenance of susceptibility alleles in the population and may break down the process of local adaptation. Since mate choice is central to both major theories of parasite-mediated host speciation, relaxed sexual selection has the potential to strongly disrupt the progress towards speciation.

### 5.2. Change in host–parasite interactions and ecological settings

The potential of environmental change to interfere with fine-tuned host–parasite specificity could be particularly problematic for speciation. If coevolutionary dynamics, which promote local adaptation, are part of the basis of ongoing speciation, disruption of these mechanisms would hinder the progress towards divergence. To date, evidence for such disruption (i.e. $G \times G \times E$ effects) comes exclusively from studies focusing on one host generation (e.g., Sadd, 2011; Tack et al., 2015). It remains therefore unclear whether specificity in those interactions can be rebuilt over evolutionary time under the new environmental conditions. If parasite virulence or host resistance increase as a response to environmental changes, this should promote the evolution of renewed local adaptation and therefore specificity of host–parasite interactions. Using mathematical models, Mostowy and Engelstädter (2011) found potential for environmental change to either disrupt or promote classic Red Queen dynamics depending on the genetic basis of host–parasite specificity affected by the environmental change.

Modifications of species distributions and assemblages are one of the major consequences of climate change (IPCC, 2014) that will affect host–parasite interactions. Environmental stress can increase parasite numbers if it promotes host susceptibility or increases host density and thereby also transmission potential (Lafferty and Kuris, 2005). Reversely, parasite numbers can decrease if the parasite is more affected by the environmental change than the host and has a reduced infection potential (Lafferty and Kuris, 2005). This leads to changes in parasite communities and dynamics, altering the selection pressures they exert on their host populations. If these effects differ locally and lead to increasingly distinct parasite communities of different host populations, this could support parasite-driven host speciation either via magic traits or by the parasite-driven-wedge model. Such divergence of parasite communities would correspond to a divergence of adaptive peaks in the fitness landscape, thereby promoting divergence of the host populations and reducing gene flow between them as they track these adaptive peaks.

Reciprocally, modifications of host communities could increase opportunities for parasite speciation via host switches. This is based on increased niche opportunities when the original host's distribution range expands or shifts and contact with potential new hosts is increased. Host switches and subsequent parasite speciation are further promoted by ecological fitting, the principle by which a species persists in whichever habitat (in this case on whichever host) is suitable for its survival (Janzen, 1985). The most recent evidence from parasite phylogenies suggests that ecological fitting opportunities are very frequent, supporting the view that host switches are a major part of parasite diversification, especially in changing environments (Hoberg and Brooks, 2008, 2015).

From the perspective of a parasite's fitness landscape, environmental change may (i) bring adaptive peaks (representing different host species) closer together, thereby facilitating switches to a new peak by part of the population, followed by local adaptation of each resulting subpopulation, but also (ii) create new peaks with more species becoming potential hosts suitable for ecological fitting of the parasite. In the latter case, previously maladaptive alleles may become beneficial under global change.

### 5.3. When does environmental change promote host or parasite speciation?

While most research on parasites and global change is concerned with epidemics and their link to extinction risks, there may also be potential for speciation. Parasites' diversification potential may be aided by ecological fitting in response to environmental change. This could further drive diversification in their hosts as parasite communities diverge between populations and thereby increase divergent selection. However, this potential is contingent on host species surviving the environmental change and retaining some evolutionary potential (i.e., genetic diversity). Rapid evolutionary dynamics of host–parasite systems in changing environments are therefore a double-edged sword for biodiversity conservation: they can support host genetic diversity (existing and arising) and thereby buffer the effects of environmental change and even support, in some cases, the formation of new species.

At the same time, environmental change can favour disease outbreaks which will threaten host populations and species, especially if stress is exacerbated by the need for physiological adaptation to the new environment (Altizer et al., 2003, 2013). Ultimately, this could increase extinction rates.

Global change is predicted to increase frequencies of extreme events (IPCC, 2014), which could have different effects on evolutionary trajectories of host–parasite interactions: one rapid shift or gradual change in the environment should lead to continuous selection in a predictable direction likely reinforcing selection in the host–parasite interaction (Fig. 2b), whereas multiple changes in the environment would repeatedly alter the defence–exploitation balance of host–parasite interactions. We propose two possible evolutionary outcomes for recurrent changes based on fitness landscape modifications. Firstly, the need for hosts and parasites to readapt to moving adaptive peaks over and over could promote population divergence as these recurrent events of strong selection would promote local adaptation, through recurrent sweeps, with varying evolutionary trajectories in varying habitats/niches (Fig. 2c). This outcome is likely if the events of environmental change are separated by enough evolutionary time (i.e., at least one generation turnover of host and parasite each) to allow the fitness landscape to change. Importantly, this reinforcement scenario relies on the assumption that coevolution and adaptation to a changing environment are synchronous or overlapping. The second scenario would see an increase in phenotypic plasticity as adaptive peaks keep moving and the ability of individuals to deal with different environmental conditions in one lifetime is promoted by selection (Fig. 2d). This is likely to happen if multiple changes happen within one generation of the host or parasite. In particular, such a rapidly changing environment may create variable costs of parasitism that prevent a continuous selection for specific defence mechanisms (Sandland and Minchella, 2003) and thereby disrupt host speciation. However, other speciation mechanisms may come into play through the rise of plasticity related to parasitism.

## 6. Future challenges of host–parasite research: plasticity, transgenerational immune priming and adaptive evolution in changing environments

In this section, we concentrate on the role of plasticity (in all its guises) on host speciation, as the parasite literature provides fewer examples – even though phenotypic plasticity is certainly an important characteristic of generalist parasites (Leggett et al., 2013). Many plastic responses of hosts to parasites are known for which the underlying genetic basis remains unclear. Phenotypic plasticity is increasingly recognised as an important mechanism with multiple, sometimes antagonistic, roles in ecological speciation (Pfennig et al., 2010; Thibert-Plante and Hendry, 2011; Fitzpatrick, 2012). The extent of phenotypic plasticity in a given trait can be described by the "reaction norm", which is the relationship between the phenotypic trait and an environmental variable for a given genotype.

As we have pointed out, fluctuating environmental conditions could be a major risk for host speciation. But what if the trajectories to speciation were to start with plastic differentiation, with genetic assimilation and differentiation to occur later in the speciation process? Phenotypic plasticity can be predictive of adaptive change, especially under fluctuating conditions (Schaum and Collins, 2014). A study by Draghi and Whitlock (2012) using a gene network model suggests that plastic populations tend to have higher mutational and standing genetic variance. This shows that at least under some conditions, plastic responses to new combinations of parasites and environmental conditions could promote adaptive evolution, provided the plastic effects are heritable to some extent.

Transgenerational immune priming (TGIP) is an example of plastic effects spanning generations (Poulin and Thomas, 2008). TGIP can provide advantages through immune memory and/or increased tolerance of parasitism (e.g., Roth et al., 2012; Kaufmann et al., 2014) but it can also impose costs such as delayed sexual maturity (Beemelmanns and Roth, 2016). Such effects are likely mediated by shifts in epigenetic markers which lead to reprogrammed transcription in the next host generation (Beemelmanns and Roth, 2016; Vilcinskas, 2016). Overall, it is clear that TGIP could play a major role in parasite-driven speciation, especially in changing environments, as it provides a heritability mechanism for plastic responses to new selection regimes.

A related mechanism of plasticity is gene regulation. Gene expression shows evolutionary signatures of rapid and local adaptation to parasite communities (Lenz et al., 2013; Lenz, 2015) and can mediate specificity in responses to different parasite genotypes (Haase et al., 2016). Stutz et al. (2015) recently showed that within four months, target gene expression profiles of three-spined sticklebacks transplanted between different lakes became more similar to resident fish than fish from their population of origin. This is likely due to the differences in parasite communities between lakes and illustrates the importance of gene expression as a fast acclimation mechanism to local parasite communities. However, expression profiles are also part of the adaptive process as their genetic basis evolves towards expression profiles fine-tuned to local parasite strains (Haase et al., 2016). These antagonistic drivers of gene expression profiles steer the evolution of expression plasticity, i.e. the change of reaction norms over time. It is also important to note that, unlike other pressures, the molecular response to parasitism is often mediated, at least for the adaptive immune system, by key/lock-like systems (Janeway et al., 2001). Even when gene expression levels of individuals from different populations are similar when experiencing the same parasite community, the resulting effects may be different if parasite-derived antigens are poorly recognised, for instance, by MHC molecules. Hence an adaptive immune response will be characterised by the alleles (which have a genetic basis only) and the expression level of the genes (which can have a genetic and/or a plastic basis) together.

Global change will elicit both adaptive and maladaptive plasticity. Adaptive plasticity may support parasite-driven population divergence but take longer to be fixed in the genome as it decreases selective pressure on the genetic basis of the plastic traits (Ghalambor et al., 2007). The more accommodation of environmental change depends on plasticity, the more genetic fixation of traits will depend on genetic assimilation. The rise of genetic incompatibilities may then provide the basis for reproductive isolation (Kaufmann et al., 2015). Counterintuitively, maladaptive plasticity can facilitate adaptive evolution at the genetic basis as it increases the strength of natural selection by moving phenotypes further away from the local optimum (Ghalambor et al., 2015). While the study by Ghalambor and coworkers investigated responses to predation, similar effects can be predicted when environmental change and parasitism cause the maladaptive plasticity. Adaptive plasticity therefore facilitates fast acclimation to a new environment whereas maladaptive plasticity will promote the speed of adaptive evolution of the genetic basis. Altogether, this array of plasticity effects is likely to facilitate parasite-mediated speciation in changing environments, particularly when it acts in concert with adaptation at the sequence level.

## 7. Concluding remarks

Overall, environmental change can clearly affect host/parasite-mediated speciation. It seems that besides the widely acknowledged increase in species extinction rates, environmental change

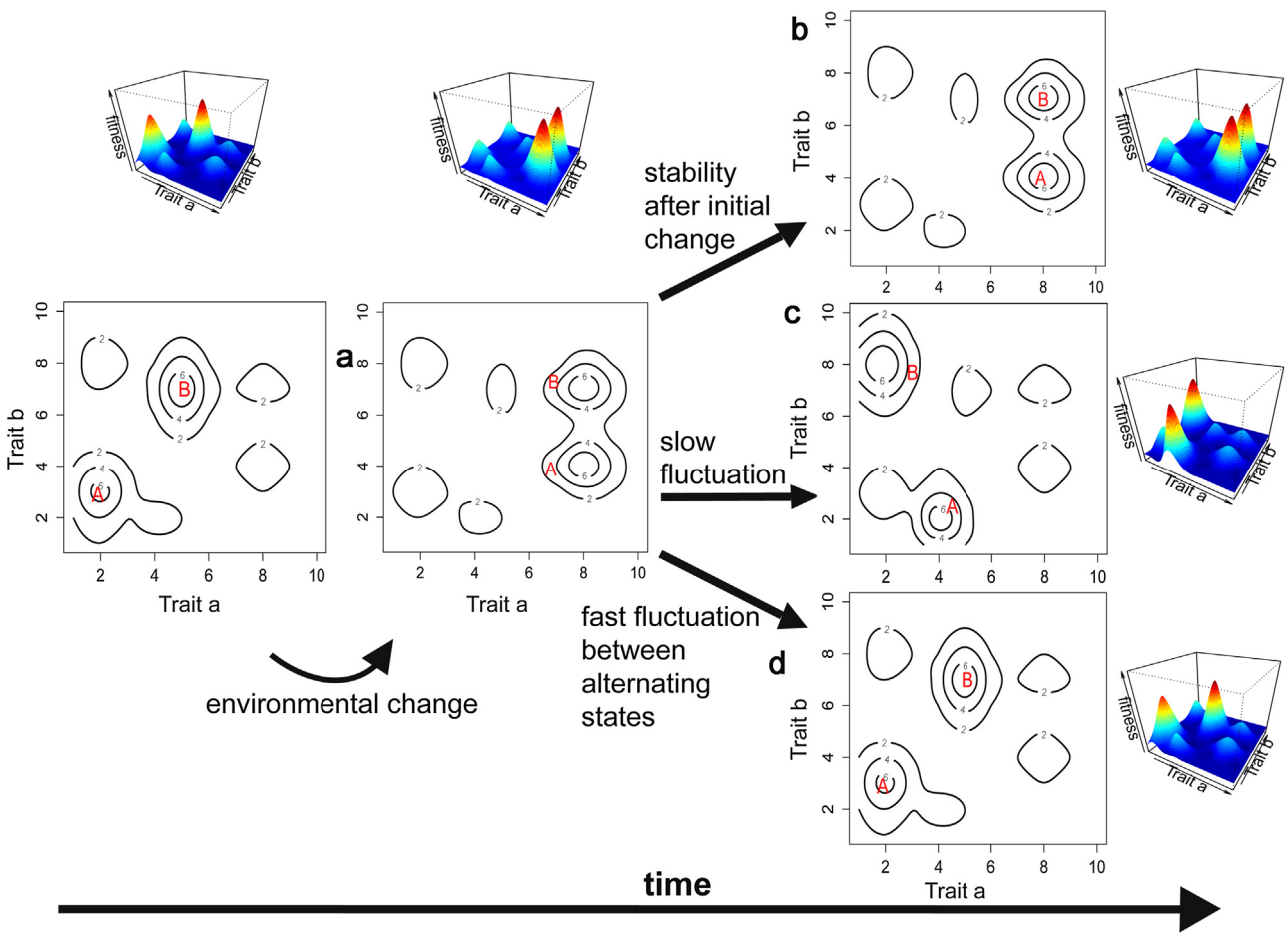


**Fig. 2.** Fitness landscapes and local adaptation under different dynamics of environmental change. Fitness landscapes are shown both as contour plots with mean phenotypes of two populations (A and B) and as perspective plots to illustrate fitness peaks. (a) Upon a change in the environment, average phenotypes will differ due to phenotypic plasticity. In this example, adaptive plasticity brings the population means closer to the new fitness peaks, thereby increasing average fitness in the populations. (b) If the environment remains stable after the initial change, adaptive evolution will drive the phenotypic population means (A and B) towards the optimal fitness peaks over time. (c) If environmental conditions fluctuate, but at a frequency allowing evolutionary change in the populations before conditions are reversed, the fitness landscape has changed due to evolution when conditions revert and phenotypic population means will appear close to the new, alternative fitness peaks. (d) If environmental conditions fluctuate at a higher frequency, the fitness landscapes (a) and (d) will recur with every environmental fluctuation as selection will not eliminate genotypes with lower fitness before conditions revert again. In this scenario, the net evolutionary effect will be selection for increased phenotypic plasticity as individuals coping well with both environmental states have a selective advantage. These fitness landscapes are a thought experiment and were generated with the "fields" package in R (Nychka et al., 2015).

may also lead to increased speciation rates under given circumstances. One reinforced speciation driver may be host–parasite interactions. Much further research is required to determine whether this will result in a generally increased turnover of species or if one of these mechanisms strongly outweighs the other. Two of the most pressing questions regarding host/parasite-mediated speciation are: what are the conditions promoting speciation over the maintenance of polymorphism and what is the role of plasticity in speciation, particularly under rapidly changing environmental conditions? From the literature to date, it appears that the responses to those questions will be system-specific, i.e. context- dependent, and the more studies will be conducted on this topic, the more predictive power will be gained.

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## References

Altizer, S., Harvell, D., Friedle, E., 2003. Rapid evolutionary dynamics and disease threats to biodiversity. Trends Ecol. Evol. 18, 589–596.
Altizer, S., Ostfeld, R.S., Johnson, P.T.J., Kutz, S., Harvell, C.D., 2013. Climate change and infectious diseases: from evidence to a predictive framework. Science 341, 514–519.
Babik, W., Pabijan, M., Radwan, J., 2008. Contrasting patterns of variation in MHC loci in the Alpine newt. Mol. Ecol. 17, 2339–2355.
Bakke, T.A., Harris, P.D., Cable, J., 2002. Host specificity dynamics: observations on gyrodactylid monogeneans. Int. J. Parasitol. 32, 281–308.
Barnosky, A.D., Matzke, N., Tomiya, S., Wogan, G.O.U., Swartz, B., Quental, T.B., Marshall, C., McGuire, J.L., Lindsey, E.L., Maguire, K.C., Mersey, B., Ferrer, E.A., 2011. Has the Earth's sixth mass extinction already arrived? Nature 471, 51–57.
Becker, D.J., Hall, R.J., 2014. Too much of a good thing: resource provisioning alters infectious disease dynamics in wildlife. Biol. Lett. 10, 20140309.
Becker, D.J., Streicker, D.G., Altizer, S., 2015. Linking anthropogenic resources to wildlife-pathogen dynamics: a review and meta-analysis. Ecol. Lett. 18, 483–495.
Beemelmanns, A., Roth, O., 2016. Biparental immune priming in the pipefish *Syngnathus typhle*. Zoology 119, 262–272.
Bérénos, C., Schmid-Hempel, P., Wegner, K.M., 2012. Antagonistic coevolution accelerates the evolution of reproductive isolation in *Tribolium castaneum*. Am. Nat. 180, 520–528.
Björklund, M., Aho, T., Behrmann-Godel, J., 2015. Isolation over 35 years in a heated biotest basin causes selection on MHC class IIß genes in the European perch (*Perca fluviatilis* L.). Ecol. Evol. 5, 1440–1455.
Bonneaud, C., Chastel, O., Federici, P., Westerdahl, H., Sorci, G., 2006. Complex Mhc-based mate choice in a wild passerine. Proc. R. Soc. B 273, 1111–1116.

Boughman, J.W., 2001. Divergent sexual selection enhances reproductive isolation in sticklebacks. Nature 411, 944–948.
Brunner, F.S., Schmid-Hempel, P., Barribeau, S.M., 2014. Protein-poor diet reduces host-specific immune gene expression in *Bombus terrestris*. Proc. R. Soc. Biol. Sci. 281, 20140128.
Buckling, A., Rainey, P.B., 2002. The role of parasites in sympatric and allopatric host diversification. Nature 420, 496–499.
Budria, A., Candolin, U., 2014. How does human-induced environmental change influence host–parasite interactions? Parasitology 141, 462–474.
Budria, A., Candolin, U., 2015. Human-induced eutrophication maintains high parasite prevalence in breeding threespine stickleback populations. Parasitology 142, 719–727.
Buser, C.C., Spaak, P., Wolinska, J., 2012. Disease and pollution alter *Daphnia* taxonomic and clonal structure in experimental assemblages. Freshw. Biol. 57, 1865–1874.
Cable, J., Harris, P.D., Tinsley, R.C., Lazarus, C.M., 1999. Phylogenetic analysis of *Gyrodactylus* spp. (Platyhelminthes: Monogenea) using ribosomal DNA sequences. Can. J. Zool. 77, 1439–1449.
Candolin, U., Salesto, T., Evers, M., 2007. Changed environmental conditions weaken sexual selection in sticklebacks. J. Evol. Biol. 20, 233–239.
Candolin, U., Nieminen, A., Nyman, J., 2014. Indirect effects of human-induced environmental change on offspring production mediated by behavioural responses. Oecologia 174, 87–97.
Condamine, F.L., Rolland, J., Morlon, H., 2013. Macroevolutionary perspectives to environmental change. Ecol. Lett. 16, 72–85.
Coyne, J.A., Orr, H.A., 2004. Speciation. Sinauer Associates, Sunderland, MA.
Dawson, T.P., Jackson, S.T., House, J.I., Prentice, I.C., Mace, G.M., 2011. Beyond predictions: biodiversity conservation in a changing climate. Science 332, 53–58.
De Meeûs, T., Michalakis, Y., Renaud, F., 1998. Santa Rosalia revisited: or why are there so many kinds of parasites in the garden of earthly delights? Parasitol. Today 14, 10–13.
Dittmar, J., Janssen, H., Kuske, A., Kurtz, J., Scharsack, J.P., 2014. Heat and immunity: an experimental heat wave alters immune functions in three-spined sticklebacks (*Gasterosteus aculeatus*). J. Anim. Ecol. 83, 744–757.
Dobson, A., Molnár, P.K., Kutz, S., 2015. Climate change and Arctic parasites. Trends Parasitol. 31, 181–188.
Draghi, J.A., Whitlock, M.C., 2012. Phenotypic plasticity facilitates mutational variance, genetic variance, and evolvability along the major axis of environmental variation. Evolution 66, 2891–2902.
Eichler, W., 1948. Some rules in ectoparasitism. Ann. Mag. Nat. Hist. Ser. 12, 588–598.
Eizaguirre, C., Lenz, T.L., 2010. Major histocompatibility complex polymorphism: dynamics and consequences of parasite-mediated local adaptation in fishes. J. Fish Biol. 77, 2023–2047.
Eizaguirre, C., Lenz, T.L., Traulsen, A., Milinski, M., 2009. Speciation accelerated and stabilized by pleiotropic major histocompatibility complex immunogenes. Ecol. Lett. 12, 5–12.
Eizaguirre, C., Lenz, T.L., Sommerfeld, R.D., Harrod, C., Kalbe, M., Milinski, M., 2011. Parasite diversity, patterns of MHC II variation and olfactory based mate choice in diverging three-spined stickleback ecotypes. Evol. Ecol. 25, 605–622.
Eizaguirre, C., Lenz, T.L., Kalbe, M., Milinski, M., 2012a. Rapid and adaptive evolution of MHC genes under parasite selection in experimental vertebrate populations. Nat. Commun. 3, 621–626.
Eizaguirre, C., Lenz, T.L., Kalbe, M., Milinski, M., 2012b. Divergent selection on locally adapted major histocompatibility complex immune genes experimentally proven in the field. Ecol. Lett. 15, 723–731.
Elser, J.J., Andersen, T., Baron, J.S., Bergström, A.-K., Jansson, M., Kyle, M., Nydick, K.R., Steger, L., Hessen, D.O., 2009. Shifts in lake N:P stoichiometry and nutrient limitation driven by atmospheric nitrogen deposition. Science 326, 835–837.
Fincher, C.L., Thornhill, R., 2008. A parasite-driven-wedge: infectious diseases may explain language and other biodiversity. Oikos 117, 1289–1297.
Fitzpatrick, B.M., 2012. Underappreciated consequences of phenotypic plasticity for ecological speciation. Int. J. Ecol. 2012, 1–12.
Gandon, S., Buckling, A., Decaestecker, E., Day, T., 2008. Host–parasite coevolution and patterns of adaptation across time and space. J. Evol. Biol. 21, 1861–1866.
Garbutt, J.S., Scholefield, J.A., Vale, P.F., Little, T.J., 2014. Elevated maternal temperature enhances offspring disease resistance in *Daphnia magna*. Funct. Ecol. 28, 424–431.
Gavrilets, S., 2004. Fitness Landscapes and the Origin of Species. Princeton University Press, Princeton.
Ghalambor, C.K., McKay, J.K., Carroll, S.P., Reznick, D.N., 2007. Adaptive versus non-adaptive phenotypic plasticity and the potential for contemporary adaptation in new environments. Funct. Ecol. 21, 394–407.
Ghalambor, C.K., Hoke, K.L., Ruell, E.W., Fischer, E.K., Reznick, D.N., Hughes, K.A., 2015. Non-adaptive plasticity potentiates rapid adaptive evolution of gene expression in nature. Nature 525, 372–375.
Graham, C.T., Harrod, C., 2009. Implications of climate change for the fishes of the British Isles. J. Fish Biol. 74, 1143–1205.
Grégoir, A.F., Hablützel, P.I., Vanhove, M.P.M., Pariselle, A., Bamps, J., Volckaert, F.A.M., Raeymaekers, J.A.M., 2015. A link between host dispersal and parasite diversity in two sympatric cichlids of Lake Tanganyika. Freshw. Biol. 60, 323–335.
Greischar, M.A., Koskella, B., 2007. A synthesis of experimental work on parasite local adaptation. Ecol. Lett. 10, 418–434.
Haase, D., Rieger, J.K., Witten, A., Stoll, M., Bornberg-Bauer, E., Kalbe, M., Schmidt-Drewello, A., Scharsack, J.P., Reusch, T.B.H., 2016. Comparative transcriptomics of stickleback immune gene responses upon infections by two helminth parasites, *Diplostomum pseudospathaceum* and *Schistocephalus solidus*. Zoology 119, 307–313.
Hafner, M.S., Page, R.D.M., 1995. Molecular phylogenies and host–parasite cospeciation: gophers and lice as a model system. Phil. Trans. R. Soc. Lond. B. 349, 77–83.
Haldane, J.B.S., 1949. Disease and evolution. Ric. Sci. 19, 68–76.
Hamilton, W.D., Zuk, M., 1982. Heritable true fitness and bright birds: a role for parasites? Science 218, 384–387.
Hamilton, W.D., Axelrod, R., Tanese, R., 1990. Sexual reproduction as an adaptation to resist parasites (a review). Proc. Natl. Acad. Sci. U. S. A. 87, 3566–3573.
Harrison, E., Laine, A.-L., Hietala, M., Brockhurst, M.A., 2013. Rapidly fluctuating environments constrain coevolutionary arms races by impeding selective sweeps. Proc. R. Soc. Biol. Sci. 280, 20130937.
Harvell, C.D., Mitchell, C.E., Ward, J.R., Altizer, S., Dobson, A.P., Ostfeld, R.S., Samuel, M.D., 2002. Climate warming and disease risks for terrestrial and marine biota. Science 296, 2158–2163.
Henrich, T., Benesh, D.P., Kalbe, M., 2013. Hybridization between two cestode species and its consequences for intermediate host range. Parasit. Vectors 6, 33.
Hoberg, E.P., Brooks, D.R., 2008. A macroevolutionary mosaic: episodic host-switching, geographical colonization and diversification in complex host–parasite systems. J. Biogeogr. 35, 1533–1550.
Hoberg, E.P., Brooks, D.R., 2015. Evolution in action: climate change, biodiversity dynamics and emerging infectious disease. Phil. Trans. R. Soc. Lond. B 370, 1–7.
Huyse, T., Poulin, R., Théron, A., 2005. Speciation in parasites: a population genetics approach. Trends Parasitol. 21, 469–475.
IPCC, 2014. Climate Change 2014: Synthesis Report Contributions of Working Groups I, II and III to the Fifth Assessment Report of the IPCC. Edited by Core Writing Team, Pachauri R.K., Meyer L.A. Intergovernmental Panel on Climate Change, Geneva.
Janeway, C.A., Travers, P., Walport, M., Shlomchik, M.J., 2001. Immunobiology: The Immune System in Health and Disease, 5th ed. Garland Science, New York.
Janzen, D.H., 1985. On ecological fitting. Oikos 45, 308–310.
Johnson, K.P., Adams, R.J., Page, R.D.M., Clayton, D.H., 2003. When do parasites fail to speciate in response to host speciation? Syst. Biol. 52, 37–47.
Johnson, P.T.J., Chase, J.M., Dosch, K.L., Hartson, R.B., Gross, J.A., Larson, D.J., Sutherland, D.R., Carpenter, S.R., 2007. Aquatic eutrophication promotes pathogenic infection in amphibians. Proc. Natl. Acad. Sci. U. S. A. 104, 15781–15786.
Johnson, P.T.J., Townsend, A.R., Cleveland, C.C., Glibert, P.M., Howarth, R.W., McKenzie, V.J., Rejmankova, E., Ward, M.H., 2010. Linking environmental nutrient enrichment and disease emergence in humans and wildlife. Ecol. Appl. 20, 16–29.
Karvonen, A., Seehausen, O., 2012. The role of parasitism in adaptive radiations – when might parasites promote and when might they constrain ecological speciation? Int. J. Ecol. 2012, 1–20.
Kaufmann, J., Lenz, T.L., Milinski, M., Eizaguirre, C., 2014. Experimental parasite infection reveals costs and benefits of paternal effects. Ecol. Lett. 17, 1409–1417.
Kaufmann, J., Eizaguirre, C., Milinski, M., Lenz, T.L., 2015. The contribution of post-copulatory mechanisms to incipient ecological speciation in sticklebacks. Biol. Lett. 11, 20140933.
King, K.C., Stelkens, R.B., Webster, J.P., Smith, D.F., Brockhurst, M.A., 2015. Hybridization in parasites: consequences for adaptive evolution, pathogenesis, and public health in a changing world. PLoS Pathog. 11, e1005098.
Kratina, P., Greig, H.S., Thompson, P.L., Carvalho-Pereira, T.S.A., Shurin, J.B., 2012. Warming modifies trophic cascades and eutrophication in experimental freshwater communities. Ecology 93, 1421–1430.
Kuris, A.M., Hechinger, R.F., Shaw, J.C., Whitney, K.L., Aguirre-Macedo, L., Boch, C.A., Dobson, A.P., Dunham, E.J., Fredensborg, B.L., Huspeni, T.C., Lorda, J., Mababa, L., Mancini, F.T., Mora, A.B., Pickering, M., Talhouk, N.L., Torchin, M.E., Lafferty, K.D., 2008. Ecosystem energetic implications of parasite and free-living biomass in three estuaries. Nature 454, 515–518.
Kutz, S.J., Hoberg, E.P., Polley, L., Jenkins, E.J., 2005. Global warming is changing the dynamics of Arctic host–parasite systems. Proc. R. Soc. B 272, 2571–2576.
Kutzer, M.A.M., Armitage, S.A.O., 2016. Maximising fitness in the face of parasites: a review of host tolerance. Zoology 119, 281–289.
Lafferty, K.D., Kuris, A.M., 1999. How environmental stress affects the impacts of parasites. Limnol. Oceanogr. 44, 925–931.
Lafferty, K.D., Kuris, A.M., 2005. Parasitism and environmental disturbances. In: Thomas, F., Renaud, F., Guegan, J.-F. (Eds.), Parasitism and Ecosystems. Oxford University Press, Oxford, pp. 113–123.
Landis, S.H., Kalbe, M., Reusch, T.B.H., Roth, O., 2012. Consistent pattern of local adaptation during an experimental heat wave in a pipefish –trematode host–parasite system. PLoS One 7, e30658.
Larsen, M.H., Mouritsen, K.N., 2014. Temperature–parasitism synergy alters intertidal soft-bottom community structure. J. Exp. Mar. Bio. Ecol. 460, 109–119.
Lazzaro, B.P., Little, T.J., 2009. Immunity in a variable world. Phil. Trans. R. Soc. Lond. B 364, 15–26.
Leggett, H.C., Buckling, A., Long, G.H., Boots, M., 2013. Generalism and the evolution of parasite virulence. Trends Ecol. Evol. 28, 592–596.
Lenz, T.L., 2015. Transcription in space – environmental vs. genetic effects on differential immune gene expression. Mol. Ecol 24, 4583–4585.
Lenz, T.L., Eizaguirre, C., Rotter, B., Kalbe, M., Milinski, M., 2013. Exploring local immunological adaptation of two stickleback ecotypes by experimental infection and transcriptome-wide digital gene expression analysis. Mol. Ecol. 22, 774–786.

Lips, K.R., Diffendorfer, J., Mendelson, J.R.I., Sears, M.W., 2008. Riding the wave: reconciling the roles of disease and climate change in amphibian declines. PLoS Biol. 6, e72.
Littlewood, D.T.J., Rohde, K., Clough, K.A., 1997. Parasite speciation within or between host species? Phylogenetic evidence from site-specific polystome monogeneans. Int. J. Parasitol. 27, 1289–1297.
Lohmus, M., Björklund, M., 2015. Climate change: what will it do to fish–parasite interactions? Biol. J. Linn. Soc. 116, 397–411.
Loker, E.S., 2012. Macroevolutionary immunology: a role for immunity in the diversification of animal life. Front. Immunol. 3, 25.
Lopez Pascua, L., Hall, A.R., Best, A., Morgan, A.D., Boots, M., Buckling, A., 2014. Higher resources decrease fluctuating selection during host–parasite coevolution. Ecol. Lett. 17, 1380–1388.
MacNab, V., Barber, I., 2012. Some (worms) like it hot: fish parasites grow faster in warmer water, and alter host thermal preferences. Glob. Chang. Biol. 18, 1540–1548.
Malmberg, G., 1998. On the evolution within the family Gyrodactylidae (Monogenea). Int. J. Parasitol. 28, 1625–1635.
Mason, P.A., 2015. On the role of host phenotypic plasticity in host shifting by parasites. Ecol. Lett., http://dx.doi.org/10.1111/ele.12555.
Mateos-Gonzalez, F., Sundström, L.F., Schmid, M., Björklund, M., 2015. Rapid evolution of parasite resistance in a warmer environment: insights from a large scale field experiment. PLoS One 10, e0128860.
McKenzie, V.J., Townsend, A.R., 2007. Parasitic and infectious disease responses to changing global nutrient cycles. Ecohealth 4, 384–396.
Milinski, M., 2006. The major histocompatibility complex, sexual selection and mate choice. Annu. Rev. Ecol. Evol. Syst. 37, 159–186.
Milinski, M., 2014. Arms races, ornaments and fragrant genes: the dilemma of mate choice in fishes. Neurosci. Biobehav. Rev. 46, 567–572.
Milinski, M., Griffiths, S., Wegner, K.M., Reusch, T.B.H., Haas-Assenbaum, A., Boehm, T., 2005. Mate choice decisions of stickleback females predictably modified by MHC peptide ligands. Proc. Natl. Acad. Sci. U. S. A. 102, 4414–4418.
Mitchell, S.E., Rogers, E.S., Little, T.J., Read, A.F., 2005. Host–parasite and genotype-by-environment interactions: temperature modifies potential for selection by a sterilizing pathogen. Evolution 59, 70–80.
Molnár, P.K., Kutz, S.J., Hoar, B.M., Dobson, A.P., 2013. Metabolic approaches to understanding climate change impacts on seasonal host–macroparasite dynamics. Ecol. Lett. 16, 9–21.
Moritz, C., Agudo, R., 2013. The future of species under climate change: resilience or decline? Science 341, 504–508.
Morley, N.J., Lewis, J.W., 2014. Temperature stress and parasitism of endothermic hosts under climate change. Trends Parasitol. 30, 221–227.
Mostowy, R., Engelstädter, J., 2011. The impact of environmental change on host–parasite coevolutionary dynamics. Proc. R. Soc. B 278, 2283–2292.
Nonaka, E., Svanbäck, R., Thibert-Plante, X., Englund, G., Brännström, Å., 2015. Mechanisms by which phenotypic plasticity affects adaptive divergence and ecological speciation. Am. Nat. 186, E126–143.
Nuismer, S.L., Otto, S.P., Blanquart, F., 2008. When do host–parasite interactions drive the evolution of non-random mating? Ecol. Lett. 11, 937–946.
Nychka, D., Furrer, R., Sain, S., 2015. Fields: Tools for Spatial Data. R Package Version 8. 2-1 http://CRAN.R- project.org/package=fields.
Paterson, A.M., Poulin, R., 1999. Have chondracanthid copepods co-speciated with their teleost hosts? Syst. Parasitol. 44, 79–85.
Pfennig, D.W., Wund, M.A., Snell-Rood, E.C., Cruickshank, T., Schlichting, C.D., Moczek, A.P., 2010. Phenotypic plasticity's impacts on diversification and speciation. Trends Ecol. Evol. 25, 459–467.
Piertney, S.B., Oliver, M.K., 2006. The evolutionary ecology of the major histocompatibility complex. Heredity (Edinb.) 96, 7–21.
Poulin, R., Morand, S., 2000. The diversity of parasites. Q. Rev. Biol. 75, 277–293.
Poulin, R., Thomas, F., 2008. Epigenetic effects of infection on the phenotype of host offspring: parasites reaching across host generations. Oikos 117, 331–335.
Price, P., 1980. Evolutionary Biology of Parasites. Princeton University Press, Princeton.
Reusch, T.B.H., Häberli, M.A., Aeschlimann, P.B., Milinski, M., 2001. Female sticklebacks count alleles in a strategy of sexual selection explaining MHC polymorphism. Nature 414, 300–302.
Ricklefs, R.E., 2010. Host–pathogen coevolution, secondary sympatry and species diversification. Phil. Trans. R. Soc. Lond. B 365, 1139–1147.
Roth, O., Klein, V., Beemelmanns, A., Scharsack, J.P., Reusch, T.B.H., 2012. Male pregnancy and biparental immune priming. Am. Nat. 180, 802–814.
Sadd, B.M., 2011. Food-environment mediates the outcome of specific interactions between a bumblebee and its trypanosome parasite. Evolution 65, 2995–3001.
Sandland, G.J., Minchella, D.J., 2003. Costs of immune defense: an enigma wrapped in an environmental cloak? Trends Parasitol. 19, 571–574.
Schade, F.M., Shama, L.N.S., Wegner, K.M., 2014. Impact of thermal stress on evolutionary trajectories of pathogen resistance in three-spined stickleback (*Gasterosteus aculeatus*). BMC Evol. Biol. 14, 164.
Scharsack, J.P., Schweyen, H., Schmidt, A.M., Dittmar, J., Reusch, T.B.H., Kurtz, J., 2012. Population genetic dynamics of three-spined sticklebacks (*Gasterosteus aculeatus*) in anthropogenic altered habitats. Ecol. Evol. 2, 1122–1143.
Scharsack, J.P., Franke, F., Erin, N.I., Kuske, A., Büscher, J., Stolz, H., Samonte, I.E., Kurtz, J., Kalbe, M., 2016. Effects of environmental variation on host–parasite interaction in three-spined sticklebacks (*Gasterosteus aculeatus*). Zoology 119, 375–383.
Schaum, C.E., Collins, S., 2014. Plasticity predicts evolution in a marine alga. Proc. R. Soc. Biol. Sci. 281, 20141486.
Scheffer, M., Carpenter, S., Foley, J.A., Folke, C., Walker, B., 2001. Catastrophic shifts in ecosystems. Nature 413, 591–596.
Schmid-Hempel, P., 2003. Variation in immune defence as a question of evolutionary ecology. Proc. R. Soc. B 270, 357–366.
Schmid-Hempel, P., 2011. Evolutionary Parasitology: The Integrated Study of Infections, Immunology. In: Ecology and Genetics. Oxford University Press, Oxford.
Schoener, T.W., 2011. The newest synthesis: understanding the interplay of evolutionary and ecological dynamics. Science 331, 426–429.
Servedio, M.R., Van Doorn, G.S., Kopp, M., Frame, A.M., Nosil, P., 2011. Magic traits in speciation: magic but not rare? Trends Ecol. Evol 26, 389–397.
Smith, T.B., Kinnison, M.T., Strauss, S.Y., Fuller, T.L., Carroll, S.P., 2014. Prescriptive evolution to conserve and manage biodiversity. Annu. Rev. Ecol. Evol. Syst. 45, 1–22.
Smith, V.H., Schindler, D.W., 2009. Eutrophication science: where do we go from here? Trends Ecol. Evol. 24, 201–207.
Spurgin, L.G., Richardson, D.S., 2010. How pathogens drive genetic diversity: MHC, mechanisms and misunderstandings. Proc. R. Soc. B 277, 979–988.
Stevens, R.B., 1960. Cultural practices in disease control. In: Horsfall, J.G., Dimond, A.E. (Eds.), Plant Pathology – An Advanced Treatise. Academic Press, New York, pp. 357–429.
Stutz, W.E., Schmerer, M., Coates, J.L., Bolnick, D.I., 2015. Among-lake reciprocal transplants induce convergent expression of immune genes in threespine stickleback. Mol. Ecol. 24, 4629–4646.
Summers, K., McKeon, S., Sellars, J., Keusenkothen, M., Morris, J., Gloeckner, D., Pressley, C., Price, B., Snow, H., 2003. Parasitic exploitation as an engine of diversity. Biol. Rev. 78, 639–675.
Tack, A.J.M., Laine, A.-L., Burdon, J.J., Bissett, A., Thrall, P.H., 2015. Below-ground abiotic and biotic heterogeneity shapes above-ground infection outcomes and spatial divergence in a host–parasite interaction. New Phytol. 207, 1159–1169.
Thibert-Plante, X., Hendry, A.P., 2011. The consequences of phenotypic plasticity for ecological speciation. J. Evol. Biol. 24, 326–342.
Thomas, C.D., Cameron, A., Green, R.E., Bakkenes, M., Beaumont, L.J., Collingham, Y.C., Erasmus, B.F.N., De Siqueira, M.F., Grainger, A., Hannah, L., Hughes, L., Huntley, B., Van Jaarsveld, A.S., Midgley, G.F., Miles, L., Ortega-Huerta, M.A., Peterson, A.T., Townsend Peterson, A., Phillips, O.L., Williams, S.E., 2004. Extinction risk from climate change. Nature 427, 145–148.
Thompson, J., 1994. The Coevolutionary Process. University of Chicago Press, Chicago.
Thornhill, R., Fincher, C.L., 2013. The parasite-driven-wedge model of parapatric speciation. J. Zool. 291, 23–33.
Tobler, M., Plath, M., Riesch, R., Schlupp, I., Grasse, A., Munimanda, G.K., Setzer, C., Penn, D.J., Moodley, Y., 2014. Selection from parasites favours immunogenetic diversity but not divergence among locally adapted host populations. J. Evol. Biol. 27, 960–974.
Tylianakis, J.M., Didham, R.K., Bascompte, J., Wardle, D.A., 2008. Global change and species interactions in terrestrial ecosystems. Ecol. Lett. 11, 1351–1363.
Vale, P.F., Stjernman, M., Little, T.J., 2008. Temperature-dependent costs of parasitism and maintenance of polymorphism under genotype-by-environment interactions. J. Evol. Biol. 21, 1418–1427.
van Valen, L., 1973. A new evolutionary law. Evol. Theory 1, 1–30.
Vanhove, M.P.M., Pariselle, A., Van Steenberge, M., Raeymaekers, J.A.M., Hablützel, P.I., Gillardin, C., Hellemans, B., Breman, F.C., Koblmüller, S., Sturmbauer, C., Snoeks, J., Volckaert, F.A.M., Huyse, T., 2015. Hidden biodiversity in an ancient lake: phylogenetic congruence between Lake Tanganyika tropheine cichlids and their monogenean flatworm parasites. Sci. Rep. 5, 13669.
Vilcinskas, A., 2016. The role of epigenetics in host–parasite coevolution: lessons from the model host insects *Galleria mellonella* and *Tribolium castaneum*. Zoology 119, 273–280.
Vonlanthen, P., Bittner, D., Hudson, A.G., Young, K.A., Müller, R., Lundsgaard-Hansen, B., Roy, D., Di Piazza, S., Largiader, C.R., Seehausen, O., 2012. Eutrophication causes speciation reversal in whitefish adaptive radiations. Nature 482, 357–363.
Wegner, K.M., Kalbe, M., Milinski, M., Reusch, T.B.H., 2008. Mortality selection during the 2003 European heat wave in three-spined sticklebacks: effects of parasites and MHC genotype. BMC Evol. Biol. 8, 124.
Windsor, D.A., 1998. Most of the species on Earth are parasites. Int. J. Parasitol. 28, 1939–1941.
Wolinska, J., King, K.C., 2009. Environment can alter selection in host–parasite interactions. Trends Parasitol. 25, 236–244.
Woolhouse, M.E.J., Webster, J.P., Domingo, E., Charlesworth, B., Levin, B.R., 2002. Biological and biomedical implications of the co-evolution of pathogens and their hosts. Nat. Genet. 32, 569–577.
Wright, S., 1932. The roles of mutation, inbreeding, crossbreeding and selection in evolution. In: Jones, D.F. (Ed.), Proceedings of the Sixth International Congress on Genetics, vol. 1. Ithaka, NY, pp. 356–366.
Yoder, J.B., Nuismer, S.L., 2010. When does coevolution promote diversification? Am. Nat. 176, 802–817.
Zietara, M.S., Lumme, J., 2002. Speciation by host switch and adaptive radiation in a fish parasite genus *Gyrodactylus* (Monogenea, Gyrodactylidae). Evolution 56, 2445–2458.