The role of the environment in the evolutionary ecology of host parasite interactions
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Pedro F. Vale [a], Lucie Salvaudon [b,*], Oliver Kaltz [c], Simon Fellous [c,d]

[a] Institute of Evolutionary Biology, School of Biological Sciences, University of Edinburgh, Ashworth Labs, West Mains Road, EH9 3JT Edinburgh, UK
[b] Laboratoire Ecologie, Systématique et Evolution, UMR 8079, Univ Paris-Sud 11, Orsay Cedex, F-91405, CNRS, Orsay Cedex,
F-91405, AgroParisTech, Orsay Cedex, F-91405, France
[c] UPMC Univ Paris 06, Laboratoire de Parasitologie Evolutive - UMR 7103, 7 quai St. Bernard, 75252 Paris, France
[d] Imperial College London at Silwood Park, SL5 7PY, Ascot, UK

1. Introduction

It has long been recognised that the expression of quantitative traits will be different depending on the environment (Falconer, 1952). If traits affecting fitness are expressed differently in different environments, this could lead to changes in the direction and strength of selection on these traits. If the sign and magnitude of fitness differences between genotypes changes across environments (termed genotype-by-genotype $(G \times E)$ interactions), this could promote the co-occurrence of different genotypes through heterogeneous selection (Gillespie and Turelli, 1989; Byers, 2005).

Over the past few years, the application of this idea to host–parasite systems has generated work addressing the role of environmental variation on the expression of traits involved in infection (Ferguson and Read, 2002; Mitchell et al., 2005; Lambrechts et al., 2006a; Salvaudon et al., 2007), and on the general impact that context-dependent selection may have on the coevolutionary process (Thompson, 1994, 1999). The environment of parasites is made up of many factors. First, the genotype of the host can be considered an "environment" in which the parasite must survive, and interactions between host and parasite genotypes $(G \times G$ interactions) can result in

shared control of epidemiological traits by both host and parasite, with implications for evolutionary trajectories of virulence and resistance (Restif and Koella, 2003; Lambrechts et al., 2006b; Salvaudon et al., 2007). Moreover, various biotic or abiotic factors may affect the expression of host and parasite traits, thereby adding another level of complexity $(G \times G \times E$ interactions).

What are the consequences of this complexity? From a standard quantitative genetics point of view, the efficiency of selection on host and parasite genotypes will depend on the expressed genetic variance, and such expression of variance is known to be environment-dependent (Falconer, 1981). Consequently, environmental variation may influence the intensity of coevolution, potentially creating coevolutionary cold and hot spots in different environments (Thompson, 1994, 1999). Further, selection may favour different (combinations of) host and parasite genotypes in different environments, thus shaping the geographic distribution of genetic diversity and patterns of local adaptation in host and parasite. A strong impact of the environment may even alter coevolutionary trajectories, thereby generating different evolutionary optima for attack and defence (Hochberg and van Baalen, 1998) or changing the nature of the interaction (e.g., from mutualistic to antagonistic). In this context, it is important to remember that evolution is a population-level process and that the effect of selection will depend on several aspects of population genetics, such as population size, spatial structure or migration, all of which are themselves potentially influenced by environmental conditions.

Despite the increasing number of examples from laboratory host–parasite systems indicating the occurrence of environment-dependent interactions, their importance in changing the strength and direction of selection in the field remains obscure. Thus, perhaps the most challenging question is then to ask how robust genotype interactions are against environmental variation in the wild: does the "E" in G × G × E really matter? Answers to this question will not only provide important insights in the coevolutionary process and the causes of the maintenance of genetic diversity, but also matter from an applied perspective. Indeed, being able to predict the fate of particular genes or genotypes (e.g., introduced resistance genes) in variable environments is of extreme importance for disease control programs. A 1-day meeting (5th December 2007), organized by the *Laboratoire de Parasitologie évolutive* (Université Pierre & Marie Curie, Paris, France) and *Laboratoire Ecologie, Systématique et Evolution* (Université Paris-Sud 11–CNRS, France), brought together researchers from Europe and the USA, working on a variety of microbial, animal and plant systems, to discuss the role of the environment on the evolutionary ecology of host–parasite interactions. Here follows a report on the proceedings of this meeting.

2. Summary of presentations

The meeting was divided into two sessions, each concluding with a general discussion. The morning session focused on the coevolutionary process and how experimental studies can contribute to the understanding of evolution in variable environments. Michael Hochberg (University of Montpellier) highlighted the importance of considering variation in ecological processes. Describing an experimental coevolution approach using the *Pseudomonas fluorescens*-phage Phi2 host–parasite system (Buckling and Rainey, 2002), he explored how varying levels of disturbance could affect the evolution of resistance to parasites. His findings indicated that the highest levels of resistance occur at intermediate levels of disturbance, presumably because the force of infection is highest at intermediate levels.

Fabrice Vavre (University of Lyon) continued the session by discussing work from several insect systems where vertically transmitted bacterial symbionts (among which *Wolbachia*) are present. He described work showing that cost of *Wolbachia* infections and bacterial load is not only temperature dependent (Mouton et al., 2006) but sometimes depends on the specific combinations of genotypes of *Wolbachia* that are present and on the host genotype (Mouton et al., 2004; Mouton et al., 2007). More generally, it was shown that the co-occurrence of different genotypes or species of symbionts within the same host species was different from random. This suggests that the presence of a particular symbiont can create an extended host phenotype protecting the host against infection by other symbionts, against attack by other enemies (Oliver et al., 2003) or allowing the extension of the host niche (Tsuchida et al., 2004).

This was followed by an example of how environmental variation can be an important factor when applied to agricultural systems. Mamadou Mboup (INRA-AGROPAR-ITECH, Grignon) spoke about his work on the plant pathogen Wheat Yellow Rust (*Puccinia striiformis*). In France, this pathogen exhibits a geographical structure, with some isolates only existing in the North or only in the South. Controlled greenhouse and field experiments revealed temperature-dependent variation in germination and infection rates among pathotypes, likely to confer a selective advantage to Southern pathotypes to the higher temperatures in the South. Conversely, Southern pathotypes are not found in the North because they cannot infect Northern wheat cultivars.

The morning session finished with Pedro Vale (University of Edinburgh) describing work on the freshwater crustacean *Daphnia magna* and its naturally occurring bacterial parasite *Pasteuria ramosa*. In experiments that included both host and parasite genetic variation and thermal variation, he showed evidence for temperature-dependent costs of parasitism, and for the presence of G × G interactions for infectivity and G × E interactions for parasite transmission stage production and time to host death. Although there was no evidence in these experiments that G × G × E interactions occurred (i.e. patterns of infectivity were generally robust to environmental variation), variation in the number of transmission stage spores produced could alter infectivity levels in subsequent infection cycles, as spore dose has been shown to affect infectivity in this system.

The afternoon session was aimed at discussing how to integrate environmental fluctuations into theoretical models of host and parasite evolution. Curiously, only two out of the five speakers described work using a mathematical modelling approach. This is possibly a reflection of how the theoretical tools to study these effects still lag behind the experimental evidence for their occurrence. Olivier Restif (Cambridge University) alluded to this problem, saying that traditionally, ecological interactions such as competition, predation, and parasitism have all been studied separately and as such have their own theoretical frameworks. He attempted to integrate at least two of these interactions (competition and parasitism) by developing a model where hosts vary in their resistance (reduced likelihood of becoming infected) and tolerance (reduction in the detrimental effects of infection) under varying levels of migration and fragmentation. He showed how this approach could be useful to understand under what conditions we can expect variation in resistance and tolerance to coexist. Building upon existing parasite-mediated competition models (Miller et al., 2005), he suggested that coexistence depended strongly on the degree of fragmentation of the host population. Nevertheless, when the same questions were investigated with stochastic simulations, transient dynamics associated with small population sizes modified the outcome of competition in the presence of a shared parasite. This illustrates the great importance of the modelling methodology.

Benjamin Roche (Institut de Recherche pour le Développement, Montpellier) also presented a mathematical modelling approach to elucidate the most likely transmission routes of avian influenza. He hypothesised that water-borne transmission was a likely transmission route and supported this by fitting data collected from bird populations in Southern France to a Susceptible-Infected-Removed epidemiological model, to

which he incorporated an additional class of water-borne transmission.

The remainder of speakers described results from experimental systems. Peter Tiffin (University of Minnesota) added an interesting twist by describing G × G × E interaction not in a host–parasite system but in a Legume-*Rhizobium* mutualism. From the plant perspective, the rhizobia are beneficial because they provide nitrogen to the plant but the mutualism involves a cost of carbon needed to maintain the rhizobia. He argued that the unstable dynamics observed in antagonist coevolution between hosts and parasites could also be expected in mutualisms if sub-optimal rhizobia genotypes (or ''cheaters'') are common and plant hosts evolve to preferentially associate with or reward rhizobia genotypes that are more beneficial. The experiments he described with a genetically variable *Medicago truncatula–Sinorhizobium medicae* system showed evidence for G × G interactions. Moreover, mixed inoculations by two *Sinorhizobium* genotypes were more costly to the host than single inoculations, but only when nitrogen was added to the soil—suggesting that the selection acting on species involved in mutualisms will depend on both the abiotic and biotic environment (Heath and Tiffin, 2007).

Richard Preziosi (University of Manchester) followed, using a community genetics approach to study the interaction of barley and aphids in the absence and presence of rhizosphere bacteria. Community genetics aims to ascertain how much genetic variation in one species affects other species in the community. Within this framework he provided a further example of G × G × E interactions, and in one example these explained almost 40% of the variation in host fitness (Tetard-Jones et al., 2007). R. Preziosi emphasised the need to quantify the effect sizes of these interaction effects if we are to gain insight into their relevance in the wild.

Lastly, Oliver Kaltz (University Pierre & Marie Curie, Paris) also described experimental work carried out by his research group. He asked the question ''What if hosts and parasites have different thermal optima?'' He provided an answer using a model system consisting of the protozoan *Paramecium caudatum* and its bacterial parasite *Holospora undulata*. By conducting experimental infections at 23 and 35 °C, he found that infection increased host survival at high temperature, possibly due to parasite-induced over-expression of heat-shock proteins. However, in experimental populations, prevalence rapidly declined at 35 °C, indicating that the parasite cannot survive at this temperature. Despite these general effects, the amount of genetic variation in tolerance expressed in the host varied between temperatures, suggesting that strength of selection could be environment-dependent.

3. Discussions and perspectives

This meeting provided a forum for stimulating discussion regarding the relevance of interactions between genotypes and environment in natural host–parasite systems. A positive aspect was the presence of researchers working on a broad spectrum of interactions – from mutualists to obligate killing parasites – in both animal and plant systems. Bringing together this diverse expertise served to highlight that G × G and G × E interactions are ubiquitous in host–parasite systems, at least when assessed in experimental settings. Below we highlight some of the questions addressed during the open discussion sessions.

3.1. Does environmental variation affect coevolutionary outcomes?

It is still unknown whether the interactions between genotypes and with the environment are important factors driving the evolution of host–parasite relationships, or if they are mainly noise, introducing some variation in the expression of traits, but not enough to override the main genotypic effects. Indeed, if the contrast in fitness effects due to environmental variation were not large, this would reduce the relevance of such interactions in affecting the coevolutionary process, and question their importance in the maintenance of genetic variation (Maynard Smith and Hoekstra, 1980; Gillespie and Turelli, 1989; Byers, 2005). The general opinion was that any attempt to answer this question would require more sampling of natural populations in order to gain information on levels of genetic variation in traits involved in the infection process. This can be complemented by experimental evolution approaches that test specific hypotheses about how coevolution could be affected by environmental variation, and using modelling approaches are instrumental in generating testable hypotheses.

3.2. Testing the effect of environmental variation on coevolution

Apart from identifying genotypes, the challenge in natural populations is equally to identify the relevant environmental factors at play and design the appropriate experiments to validate their effects. Experimental evolution provides an approach to address the role of the environment. By manipulating the relevant factors in experimental microcosms, we can explore the impact of environmental conditions on real-time coevolutionary change. However, it was generally agreed that this potentially very powerful approach has nonetheless important limits. While it can help us to generate hypotheses or to validate specific predictions of theoretical models, it remains restricted to particular model systems and simple experimental communities. Simply identifying that traits are expressed differently in different environments only tells us that G × E interactions can occur, but without quantifying the effect sizes of these interactions in natural populations we can say little about how or if they will change evolutionary outcomes. Thus, clearly, experimental evolution cannot replace studies on G × G × E in natural populations. To this end, P. Tiffin raised the potential for testing whether local adaptation has altered the relative costs and benefits in the *Medicago-Sinorhizobium* mutualism by examining populations growing in environments with differing levels of abiotic N availability—such as those near and far from agricultural fields. Studying environmental variation and measuring selection coefficients in natural populations still presents a formidable challenge.

3.3. How does environmental spatiotemporal variation affect coevolutionary processes?

Many factors could modify the effects of G × G × E interactions host–parasite coevolution and several speakers underlined the important role of explicit spatial structure and temporal variation. In particular, gene flow due to migration could disturb adaptation to local environments, or make it difficult to identify adaptations to particular environments, thereby increasing the spatial scale of field studies needed to identify G × E interactions. This relates directly to the issue of discerning the spatial scale at which environmental variation occurs (e.g. microclimate in the immediate neighbourhood of a plant vs. regional average temperature). The relevance of considering the temporal scale of fluctuations was also discussed. Generally, if the environment varies very quickly (daily variation in temperature, for example) then there might not be enough time for selection to produce specific adaptations to any one environmental condition. In such cases, instead of maintaining genetic variation through heterogeneous selection, this could select for phenotypic plasticity and generalist strategies. What this means in terms of host–parasite interactions remains unclear. To our knowledge, no one has explicitly integrated environmental fluctuations in the theoretical framework of host–parasite coevolution.

3.4. Implications for health and disease

The importance of interactions between host and parasite genotypes and with their environment is not only important for our understanding of evolution, but could also have applied consequences for health policies. If nothing else, it emphasizes the need to consider the role of heterogeneity – genetic and environmental – in host–parasite systems. Indeed, if infection outcomes are context-dependent, anti-parasitic intervention strategies could be thwarted when the environmental variation encountered in the wild is not taken into account.

Acknowledgements

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