

1 **Migration highways and migration barriers created by host-parasite interactions**

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3 Quan-Guo Zhang<sup>1</sup> and Angus Buckling<sup>2</sup>

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5 **Authors' affiliations:**

6 <sup>1</sup> State Key Laboratory of Earth Surface Processes and Resource Ecology and MOE Key

7 Laboratory for Biodiversity Science and Ecological Engineering, Beijing Normal

8 University, Beijing 100875, China

9 <sup>2</sup> ESI & CEC, Biosciences, University of Exeter, Penryn, Cornwall, TR10 9EZ, UK

10

11 **Emails:** zhangqg@bnu.edu.cn (QGZ), and A.J.Buckling@exeter.ac.uk (AB)

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23 **Correspondence:** Quan-Guo Zhang, College of Life Sciences, Beijing Normal  
24 University, Beijing 100875, P. R. China; Phone: +86 10 58802308; Fax: +86 10  
25 58802308; Email: zhangqg@bnu.edu.cn.

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34

35 **Abstract**

36 Coevolving parasites may play a key role in host migration and population structure.  
37 Using coevolving bacteria and viruses, we test general hypotheses as to how coevolving  
38 parasites affect the success of passive host migration between habitats that can support  
39 different intensities of host-parasite interactions. First, we show that parasites aid  
40 migration from areas of intense to weak coevolutionary interactions and impede  
41 migration in the opposite direction, as a result of intraspecific apparent competition  
42 mediated via parasites. Second, when habitats show qualitative difference such that some  
43 environments support parasite persistence while others do not, different population  
44 regulation forces (either parasitism or competitive exclusion) will reduce the success of  
45 migration in both directions. Our study shows that coevolution with parasites can  
46 predictably homogenizes or isolates host populations, depending on heterogeneity of  
47 abiotic conditions, with the second scenario constituting a novel type of “isolation by  
48 adaptation”.

49

50 **Keywords:** adaptation, coevolution, consumer-resource interactions, experimental  
51 evolution, geographic mosaic of coevolution, local adaptation, isolation by adaptation

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54

55 **INTRODUCTION**

56 Migration is one of the principal forces to drive population dynamics and evolution  
57 (Wright 1943; Holt & Gomulkiewicz 1997; Lenormand 2002; Morjan & Rieseberg 2004;  
58 Morgan *et al.* 2005; Forde *et al.* 2007; Savolainen *et al.* 2007), hence understanding the  
59 likelihood of successful migration is crucial. Coevolution with parasites has long been  
60 recognized as an important factor determining the success of migration of host  
61 populations. This, for example, has been a generally accepted explanation for the  
62 successful colonization of the New World by Eurasian civilizations, where the resident  
63 human hosts were less well-defended against parasites co-dispersing with the immigrant  
64 hosts (Diamond 1999). However, a general understanding is still lacking about the  
65 ecological contexts in which coevolving parasites help or hinder host migration. Here we  
66 focus on how environmental heterogeneity in abiotic conditions can influence parasite-  
67 mediated host migration success.

68         In the absence of parasites, adaptation to heterogeneous environments may lead to  
69 local adaptation; and this can limit the colonization of subsequent immigrants and thus  
70 reduce gene flow, namely “isolation by adaptation” (Thompson 2005; Orsini *et al.* 2013).  
71 In principle, coevolution with parasites can also result in host or parasite local adaptation  
72 (i.e., higher fitness on local versus foreign populations of the interacting species) which  
73 itself can predictably affect immigration success. While abiotic environmental  
74 heterogeneity can sometimes enhance such host-parasite specialization (Lopez-Pascua *et*  
75 *al.* 2012; Gorter *et al.* 2016), it may also create spatial variation in the strength of  
76 coevolutionary interactions, with some habitats containing universally more resistant  
77 hosts and more infectious parasites than others (Thompson 1994; Hochberg & van Baalen

78 1998; Thompson 1999; Gomulkiewicz *et al.* 2000; Thrall & Burdon 2003; Thompson  
79 2005; Laine 2008; Wolinska & King 2009). Nonetheless, rather than the resultant  
80 between-habitat variation in local adaptation making it harder to predict the average  
81 effect of parasites on immigration success, we suggest that environmental heterogeneity  
82 will actually have highly predictable effects on immigration success.

83         First, a host-parasite system may show quantitative variation in the intensity of  
84 coevolutionary interactions among habitats. For example, hosts and parasites often  
85 evolve strong defences and counter-defences, respectively, in high-productivity habitats  
86 due to large population sizes and thus intense selection for defences as well as rapid  
87 supply of genetic variation (Hochberg & van Baalen 1998; Forde *et al.* 2004; Lopez-  
88 Pascua & Buckling 2008; Best *et al.* 2010). It is suggested that immigrants from such  
89 “coevolutionary hot spots” are then more likely to invade “cold spots” where coevolution  
90 is weaker, but migration in the opposite direction may be impeded (Thompson 1999;  
91 Thompson 2005; Forde *et al.* 2007; Lopez-Pascua *et al.* 2010). Under this scenario,  
92 parasitism is the predominate population regulation force for the hosts and is likely to  
93 augment the effect of dispersal in homogenizing dynamics of multiple local populations,  
94 via parasite-mediated intraspecific competition (Holt & Barfield 2009; Ricklefs 2010).  
95 Previous studies have provided indirect support by tracking the spread of host resistance  
96 and parasite infectivity traits, but the fate of immigrants was not directly examined (Forde  
97 *et al.* 2007; Lopez-Pascua *et al.* 2010). Second, environmental heterogeneity may also  
98 cause qualitative differences in host-parasite interactions, e.g., when there is a mismatch  
99 between hosts and parasites in requirements for abiotic environmental conditions and  
100 thus parasites survive only in a portion of habitats occupied by their hosts (Fels & Kaltz

101 2006; Laine 2007; King *et al.* 2009; Zhang & Buckling 2011). In this situation, parasites  
102 may impede host migration in both directions. Hosts from parasite-present habitats will  
103 be competitively inferior when introduced into parasite-free environments as they carry  
104 costly, unnecessary, defence traits (Bergelson & Purrington 1996; Bohannan & Lenski  
105 2000; Buckling *et al.* 2006); whereas hosts from parasite-free environments will suffer  
106 high mortality due to parasitism when invading a parasite-present habitat. Here the  
107 presence of parasite species increase the niche dimensionality for the host species, and  
108 their response to the abiotic environment results in distinct population regulation forces  
109 (parasitism versus competition) for the hosts in different habitats. No previous work has  
110 tested this hypothesis.

111         We tested these ideas using experimental populations of the bacterium  
112 *Pseudomonas fluorescens* SBW25 and its lytic bacteriophage virus SBW25Φ2. This  
113 host-parasite system can undergo intensive antagonistic coevolution between resistance  
114 and infectivity traits under certain, benign, laboratory environments (Buckling & Rainey  
115 2002), with increased resistance and infectivity associated with growth rate costs  
116 (Buckling *et al.* 2006; Poullain *et al.* 2008). Low temperature can limit the rate of  
117 bacterial (and thus phage) growth and constitutes a low-productivity environment (Gorter  
118 *et al.* 2016). High temperature, within a certain range, can prevent phage growth while  
119 having little impact on bacterial growth, and therefore creates a parasite-free environment  
120 (Zhang & Buckling 2011). In the present study we first allowed just bacteria or bacteria  
121 and phages to (co)evolve in different temperature environments for a period of time  
122 without migration, and then imposed experimental dispersal on those populations and  
123 examined the success of host immigrants. With this experimental approach we were able

124 to unambiguously study how coevolution with parasites affects host immigration success  
125 in heterogeneous environments.

126

## 127 **METHODS**

### 128 **Strains and culture conditions**

129 This study used two bacterial strains, *Pseudomonas fluorescens* SBW25 (Rainey &  
130 Bailey 1996), and a modified variant SBW25EeZY6KX (Bailey *et al.* 1995), and one  
131 bacteriophage strain, SBW25Φ2 (Buckling & Rainey 2002). SBW25EeZY6KX contains  
132 two constitutively expressed marker gene cassettes, one consisting of genes encoding  
133 kanamycin resistance and catechol 2,3-dioxygenase and the other consisting of lacZY  
134 genes enabling the utilization of lactose. SBW25EeZY6KX shows no detectable  
135 difference in fitness from the wild-type SBW25 strain in the nutrient medium (M9KB)  
136 used in the present study (Fig. S1), but is resistant to the antibiotic kanamycin and has a  
137 blue color when grown as colonies on agar plates supplemented with X-gal (SBW25  
138 colonies being yellow).

139 Bacteria and phages were grown in static microcosms of 6 mL of M9KB medium  
140 (M9 salt solution supplemented with 10 g L<sup>-1</sup> glycerol and 20 g L<sup>-1</sup> proteose peptone no.  
141 3) in 30 mL glass tubes with loose lids. We considered the 25 °C habitat as a benign  
142 environment that supports strong coevolution between bacterial resistance and phage  
143 infectivity; the 15 °C habitat is a low-productivity habitat where coevolution is weak; and  
144 the 31 °C habitat soon becomes a parasite-free environment, hence there is greatly  
145 reduced selection for resistance. The assumptions were shown to be true by comparing  
146 bacterial resistance/phage infectivity between these environments (see Results).

147

148 **Evolution/coevolution experiment and measurement of resistance and infectivity**

149 The aim of the study was to examine how coevolution with phages affects the success of  
150 bacterial migration between the 25 and 15 °C habitats (migration of either 25-to-15 or 15-  
151 to-25 direction), and between the 25 and 31 °C habitats (migration of 25-to-31 or 31-to-  
152 25 direction). Forty-eight “metapopulations” were assembled, 24 of which were grown  
153 with bacteria only (evolution lines) and the other 24 with both bacteria and phages  
154 (coevolution lines). Each metapopulation consisted of one “source” and one “recipient”  
155 microcosm. For example, 12 metapopulations were assigned to 25-to-15 migration  
156 treatment, six of which were grown with bacteria only and the other six with both  
157 bacteria and phages; and source microcosms of these metapopulations were incubated at  
158 25 °C, and recipient ones, 15 °C.

159 Every microcosm was initially inoculated with  $\sim 10^8$  bacterial cells, with or  
160 without  $\sim 10^5$  phage particles. All source microcosms were inoculated with bacterial  
161 strain SBW25EeZY6KX, and recipient, SBW25. Then cultures were propagated for 6  
162 serial transfers, one transfer every 48 h. At each transfer, 60  $\mu$ L (1%) of culture from  
163 each microcosm was transferred to fresh media. During the 6 transfers of the  
164 evolution/coevolution experiment, all microcosms evolved independently and there was  
165 no dispersal between the source and recipient microcosms.

166 At transfer 6, samples of bacteria and phages were drawn from the coevolution  
167 lines (where both bacteria and phage were inoculated). Dilutions of the 6-transfer-old  
168 cultures were spread onto agar plates, and incubated for 48 h at 25 °C, to obtain  
169 independent bacterial colonies. Phage samples were isolated from cultures by mixing



170 100  $\mu$ L of chloroform and 900  $\mu$ L of each culture, which was then vortexed to lyse the  
171 bacterial cells, and centrifuged at 15 800 g for 2 min to pellet the bacterial debris, leaving  
172 a suspension of phages in the supernatant. Phage density measurement (spotting phage  
173 dilutions onto soft agar plates containing the ancestral bacterial cells and counting plaque  
174 forming units after 24 h incubation at 25 °C) suggested that all phage lines at 25 and  
175 15 °C survived until transfer 6, and all phage lines at 31 °C went extinct. Bacterial  
176 resistance/phage infectivity was compared between the source and recipient microcosms  
177 within each metapopulations. This was achieved by a reciprocal challenge test:  
178 resistance of bacteria from the source and recipient microcosms was estimated against  
179 phages from both source and recipient microcosms. To measure the resistance a bacterial  
180 population against a given phage population, we streaked suspensions of 20 independent  
181 bacterial colonies across a line of phage (20  $\mu$ L) that had previously been streaked and  
182 dried on a M9KB agar plate. A colony was scored as resistant if there was no sign of  
183 growth inhibition by the phage after 24 h incubation (at 25 °C), otherwise it was  
184 susceptible. Resistance of the bacterial population was defined as the proportion of  
185 resistant colonies. Assays of bacterial resistance to phages from microcosms maintained  
186 at 31 °C were not performed due to phage extinction. Note that bacterial resistance in the  
187 evolution lines (metapopulations inoculated with bacteria only), measured in the same  
188 way against the ancestral phage, was non-detectable.

189

### 190 **Dispersal experiment**

191 Immediately after transferring the 6-transfer-old cultures to fresh microcosms, we moved  
192 5% of culture from each source microcosm to its corresponding recipient microcosm

193 (phages and bacteria dispersed simultaneously in the coevolution metapopulations). The  
194 success of immigrant bacteria in recipient microcosms during transfer 7 was estimated as  
195 follows. Initial and final densities of immigrant (SBW25EeZY6KX) and resident  
196 (SBW25) bacteria were measured by plating diluted cultures onto M9KB agar plates  
197 ( $10^6$ -fold dilutions plated onto agar plates with X-gal, on which both SBW25 that showed  
198 a yellow color and SBW25EeZY6KX that was blue could grow; and  $10^4$ -fold dilutions  
199 plated onto agar plates with both X-gal and kanamycin, where only SBW25EeZY6KX  
200 could grow), and counting the number of colony forming units (CFUs) after 48 h  
201 incubation at 25 °C. For each metapopulation, we estimated the success of migration in  
202 terms of per capita growth rate of immigrant bacteria relative to residents in the recipient  
203 microcosm, as a “selection-rate constant” (Lenski *et al.* 1991). A Malthusian parameter  
204 was calculated for both immigrant and resident populations,  $m = \log_{10}(N_f/N_0)/(1 \text{ transfer})$ ,  
205 where  $N_0$  and  $N_f$  were the initial and final densities. The selection-rate constant was  $r =$   
206  $m_{\text{immigrant}} - m_{\text{resident}}$ . An  $r$  value of zero suggests no difference in growth rate between  
207 immigrants and residents; and  $r > 0$  indicates an advantage of immigrants in population  
208 growth (more specifically, an  $r$  value of 1 indicates a 10-fold increase in the ratio of  
209 immigrant versus resident abundances), while  $r < 0$  suggests a failure of immigrants to  
210 invade the resident population. Note that in this study, as in many microbial systems,  
211 dispersal was passive, and random in terms of the composition of dispersing individuals  
212 (which were randomly drawn from a source population), while the estimate of migration  
213 success was an average measure on the population level. We cannot rule out a possibility  
214 that a positive value of migration success was contributed to by only a portion of  
215 immigrant genotypes, with other genotypes failing to invade the recipient habitats; in this

216 case, our “selection-rate constant” measure may become an underestimate for the  
217 invasion ability of the specific genotypes that did colonize the recipient habitats.

218

### 219 **Data analyses**

220 Data were analyzed in the R environment. Bacterial resistance data were arcsine  
221 transformed before analysis. Resistance data from metapopulations of 25-to15 or 15-to-  
222 25 migration direction were analyzed using mixed-effect linear models, with the type of  
223 origin microcosm (source versus recipient) of the tested bacteria and that of the tested  
224 phages as two categorical explanatory variables and metapopulation ID as a random  
225 factor. Resistance data from metapopulations of 25-to-31 or 31-to-25 migration direction,  
226 which involved measurement of resistance of bacteria against phages from the 25, but not  
227 the 31 °C, microcosms (as phages went extinct at 31 °C) were analyzed using paired  
228 Wilcoxon signed-rank test (parametric analyses were not appropriate due to violation of  
229 the assumptions of equal variances and normal error distributions). Selection-rate  
230 constant data were square-root transformed while preserving the original positive or  
231 negative signs, and analyzed using ANOVA, with migration direction and the presence of  
232 phages as two categorical explanatory variables. For coevolution metapopulations under  
233 migration between the 25 and 15 °C habitats, we also calculated the difference in  
234 bacterial resistance between source and recipient microcosms (averaged across two types  
235 of tested phages, i.e., that from source or recipient microcosms) at transfer 6, and tested  
236 for its correlation with the success of bacterial migration in the dispersal experiment  
237 (transfer 7).

238

239 **RESULTS**

240 **Migration between the 25 and 15 °C habitats**

241 Measurement of bacterial resistance and phage infectivity for the coevolution lines at  
242 transfer 6 (prior to the dispersal experiment) confirmed that the 25 °C environment was a  
243 coevolutionary hot spot relative to the 15 °C environment. For metapopulations assigned  
244 to the 25-to-15 dispersal treatment, the source (25 °C) microcosms had higher bacterial  
245 resistance and higher phage infectivity relative to the recipient (15 °C) microcosms:  
246 bacterial resistance against phages was higher when the tested bacteria were from the  
247 source (25 °C) microcosms, but lower when the tested phages were from the source  
248 (25 °C) microcosms (mixed-effect linear model, bacteria,  $F_{1,15} = 7.24$ ,  $P = 0.017$ ; phages,  
249  $F_{1,15} = 6.51$ ,  $P = 0.022$ ; bacteria  $\times$  phages interaction,  $F_{1,15} = 0.697$ ,  $P = 0.420$ ; Fig. 1a).  
250 For metapopulations assigned to the 15-to-25 dispersal treatment, the source (15 °C)  
251 microcosms had lower bacterial resistance relative to the recipient (25 °C) microcosms,  
252 and phage infectivity did not show a significant difference between the two environments  
253 (bacteria,  $F_{1,15} = 16.01$ ,  $P = 0.001$ ; phage,  $F_{1,15} = 1.91$ ,  $P = 0.187$ ; bacteria  $\times$  phages  
254 interaction,  $F_{1,15} = 0.363$ ,  $P = 0.556$ ; Fig. 1b).

255         During the dispersal experiment, the presence of coevolving phages increased the  
256 success of bacterial migration from the 25 to 15 °C habitats, but decreased migration  
257 success in the opposite direction (ANOVA analysis of selection-rate constant, dispersal  
258 direction,  $F_{1,20} = 13.0$ ,  $P = 0.002$ ; phage,  $F_{1,20} = 0.004$ ,  $P = 0.951$ ; direction  $\times$  phage  
259 interaction,  $F_{1,20} = 8.83$ ,  $P = 0.008$ ; Fig. 2). Specifically, in metapopulations without  
260 phages, immigrant bacteria did not show a significant difference in growth rate from  
261 resident bacteria in either dispersal direction (selection-rate constant not different from

262 zero, one-sample t test, 25-to-15 dispersal,  $t = 1.46$ ,  $df = 5$ ,  $P = 0.205$ ; 15-to-25 dispersal,  
263  $t = 0.526$ ,  $df = 5$ ,  $P = 0.622$ ). However, in the presence of coevolving phages, immigrant  
264 bacteria from the 25 °C microcosms had a population growth advantage when introduced  
265 into the 15 °C microcosms (selection-rate constant larger than zero,  $t = 3.07$ ,  $df = 5$ ,  $P =$   
266  $0.028$ ), while 15 °C migrants failed to invade 25 °C populations (selection-rate constant  
267 almost significantly smaller than zero,  $t = -2.27$ ,  $df = 5$ ,  $P = 0.073$ ). Across all the  
268 coevolution metapopulations, the relative growth rate of immigrant bacteria in the  
269 recipient microcosms was positively correlated with the difference between source and  
270 recipient microcosms in bacterial resistance (Pearson's correlation test,  $r = 0.833$ ,  $df = 10$ ,  
271  $P < 0.001$ ; Fig. S2).

272

### 273 **Migration between the 31 and 25°C habitats**

274 As hypothesized, bacterial resistance evolved to a much lower level in the 31 °C  
275 compared with the 25 °C environment. As phages went extinct in all 31 °C microcosms,  
276 measurement of resistance involved challenging bacteria from both the 25 and 31 °C  
277 microcosms against phages from the 25 °C microcosms only. For metapopulations  
278 assigned to either 25-to-31 or 31-to-25 dispersal treatment, bacteria from the 31 °C  
279 microcosms showed non-detectable resistance, which was much lower than the resistance  
280 of bacteria from the 25 °C microcosms (paired Wilcoxon test, 25-to-31 dispersal  
281 metapopulations,  $P = 0.036$ ; 31-to-25 dispersal metapopulations,  $P = 0.031$ ; Fig. 3).

282 The success of bacterial migration in either direction was significantly reduced in  
283 metapopulations with phages, and the impact of phages was strongest for the 31-to-25  
284 dispersal (ANOVA, dispersal direction,  $F_{1,20} = 37.4$ ,  $P < 0.001$ ; phage,  $F_{1,20} = 49.8$ ,  $P <$

285 0.001; direction  $\times$  phage interaction,  $F_{1,20} = 7.12$ ,  $P = 0.015$ ; Fig. 4). In the absence of  
286 phages, immigrant bacteria from the 25 °C microcosms showed no difference in growth  
287 rate from the residents when introduced into the 31 °C microcosms (selection-rate  
288 constant not different from zero,  $t = -1.19$ ,  $df = 5$ ,  $P = 0.289$ ), while immigrant bacteria  
289 from the 31 °C microcosms showed lower growth rates relative to residents when  
290 introduced into the 25 °C microcosms (selection-rate constant smaller than zero,  $t = -$   
291  $10.41$ ,  $df = 5$ ,  $P < 0.001$ ). In metapopulations with phages, immigrant bacteria had lower  
292 growth rates than residents in both dispersal directions (selection-rate constant smaller  
293 than zero, 25-to-31 dispersal,  $t = -8.52$ ,  $df = 5$ ,  $P < 0.001$ ; 31-to-25 dispersal,  $t = -16.85$ ,  
294  $df = 5$ ,  $P < 0.001$ ).

295

## 296 **DISCUSSION**

297 While the effects of migration on host-parasite coevolution have been extensively studied  
298 (Lively 1999; Nuismer 1999; Gandon & Michalakis 2002; Forde *et al.* 2004; Morgan *et*  
299 *al.* 2005; Kerr *et al.* 2006; Forde *et al.* 2007; Morgan *et al.* 2007; Vigneux *et al.* 2008;  
300 Gandon & Nuismer 2009; Lopez-Pascua *et al.* 2010), the question of how the success of  
301 migration is driven by host-parasite coevolution has received less attention. Here our  
302 experiments with a bacterium-phage system suggest that parasites may predictably  
303 increase or decrease the success of host migration, depending on how host-parasite  
304 interactions vary across abiotic environments. The present study examined how host-  
305 parasite interactions affect the success of passive migration, and not the evolution of  
306 dispersal rates. However, our findings do provide insights into how parasite-imposed

307 selection might act on the evolution of migration rates, by identifying the conditions  
308 under which migration is helped or hindered.

309         While adaptation to the abiotic environment affected migration in some contexts  
310 (adaptation to 31 °C led to a reduction in fitness at 25 °C, but not vice versa, for unknown  
311 reasons), environment-dependent host-parasite coevolution showed much more  
312 pronounced effects. Our results confirmed that in environments where parasites are a  
313 ubiquitous selection pressure (the linked 25 °C and 15 °C microcosms), intraspecific  
314 apparent competition could lead to highly asymmetrical migration between habitats that  
315 show quantitative variation in the extent of evolved resistance and infectivity.  
316 Specifically, the presence of coevolving phage parasites increased the success of bacterial  
317 migration from the 25 to 15 °C habitats, and decreased the success of migration in the  
318 opposite direction, while environmental conditions had no significant impact on  
319 immigration success in the absence of parasites (Fig. 2); this effect can well be explained  
320 by the difference in resistance between immigrant and resident bacteria (Fig. 1; Fig. S2).  
321 Possible explanations for the differences in evolved resistance and infectivity include  
322 greater population sizes (Fig. S1) or mutation rates (Gillooly *et al.* 2005) at high  
323 temperatures resulting in an increased supply of genetic variation and thus faster  
324 coevolution (Gorter *et al.* 2016), or elevated costs of resistance in low-productivity (here,  
325 low-temperature) environments limiting arms-race-like coevolution and favoring  
326 fluctuating selection dynamics (Hall *et al.* 2011; Lopez-Pascua *et al.* 2014).

327         The scenario discussed above (intraspecific apparent competition leading to  
328 highly asymmetrical migration between habitats) has important implications for our  
329 understanding of synchronization of population dynamics in changing environments.

330 Populations of consumer-resource species interactions are more prone to the  
331 synchronizing effects of dispersal than those of single species, as predicted by ecological  
332 models of spatial coupling of predation effects (Vasseur & Fox 2009; Vogwill *et al.* 2009;  
333 Duncan *et al.* 2015). Our results here imply that genetic homogenization of populations  
334 may also be involved in population synchronization if coevolution takes place between  
335 the interacting species. It is unclear whether this will lead to distinct predictions for the  
336 long-term population dynamics.

337         Our second key finding is that, when habitats show qualitative variation in host-  
338 parasite interactions such that some environments support parasite persistence while  
339 others do not, migration in either direction can be reduced by coevolutionary interactions  
340 with parasites. This was shown by our treatments involving bacterial migration between  
341 the 25 and 31 °C environments. The 31°C treatment prevented phage growth but had  
342 little impact on bacterial growth, creating a parasite-free environment where selection for  
343 host resistance was lacking. Immigrants moving from this parasite-free environment to  
344 the habitat with parasites were selected against because of the lack of resistance.  
345 Meanwhile, resistant bacteria that migrated into parasite-free habitats were also selected  
346 against because of fitness costs of resistance, which has been well-documented in this  
347 system (Buckling *et al.* 2006; Lopez-Pascua & Buckling 2008).

348         When populations evolve under divergent selection in different habitats, local  
349 adaptation may lead to population diversification, with reduced gene flow (Thompson  
350 2005; Orsini *et al.* 2013). Such “isolation by adaptation” occurred between parasite-  
351 present and parasite-free environments in our experiment. This is because the hosts were  
352 under distinct selection forces across the two types of environments (parasitism versus



353 competition), which resulted from the response of the parasites to heterogeneous abiotic  
354 environments. Therefore, geographic structure of parasites set by physical factors may  
355 result in population isolation in hosts, with a potential for promoting population  
356 diversification and speciation.

357         Our experimental design involved simultaneous migration of hosts and parasites,  
358 a situation that is likely to be the norm in nature. However, if hosts migrated alone, it is  
359 likely that immigrants would be disfavored in all contexts. First, where habitats differ  
360 quantitatively in the strength of coevolutionary interactions, the success of the intensely  
361 coevolving host immigrants is a direct consequence of the presence of their intensely  
362 coevolved parasites. In the absence of these parasites, it is likely that levels of evolved  
363 defences would be too costly in the evolutionary cold spots. Second, in the context  
364 where environments showed qualitative variation in parasite persistence, simultaneous  
365 host/parasite migration is effectively the same as host-only migration.

366         In summary, our study shows that coevolving parasites may have diverse  
367 predictable effects on host migration in heterogeneous environments, and thus may  
368 promote population homogenization in some environmental contexts, but population  
369 isolation under other conditions. This is because the responses to abiotic environments  
370 determine how the presence of parasites can alter the heterogeneity among habitats for  
371 hosts in terms of selection agents. Therefore the consequences of the environmental  
372 dependence in host-parasite coevolutionary interactions for metapopulation dynamics and  
373 between-population diversity deserve more research, particularly in the context that  
374 migration and adaptation are needed for species persistence under climate change.

375

376

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382

383

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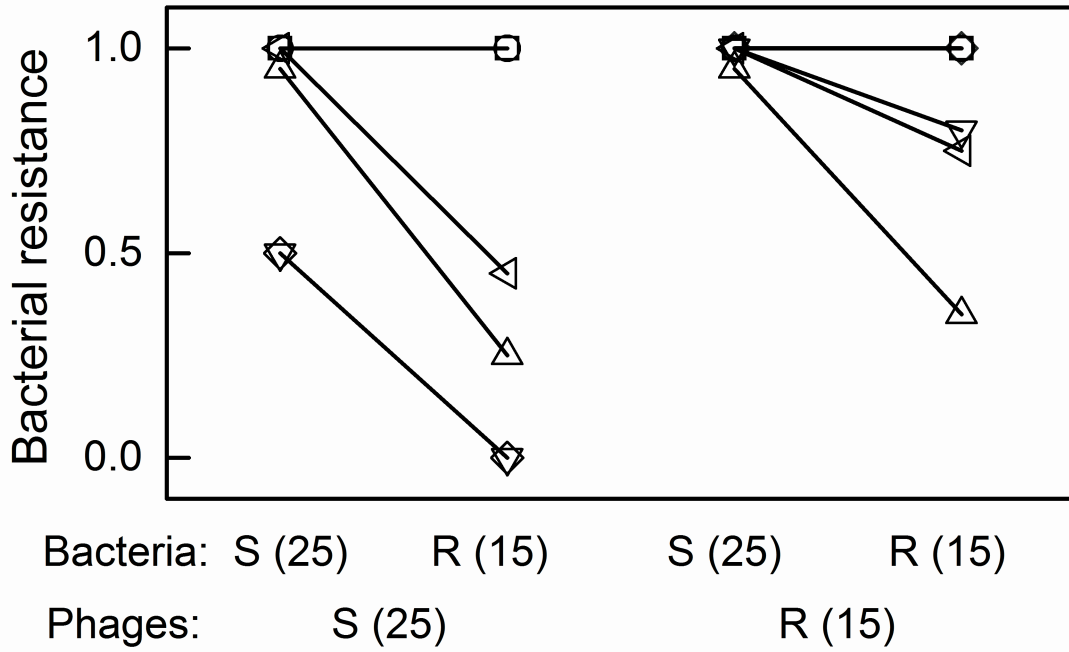
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561 **SUPPORTING INFORMATION**

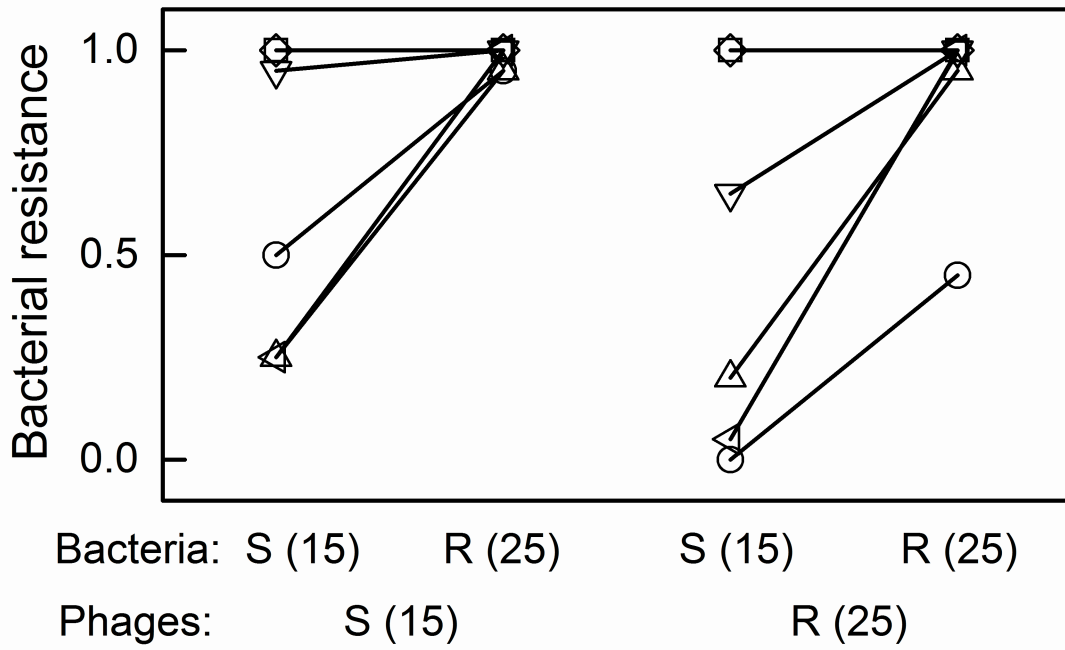
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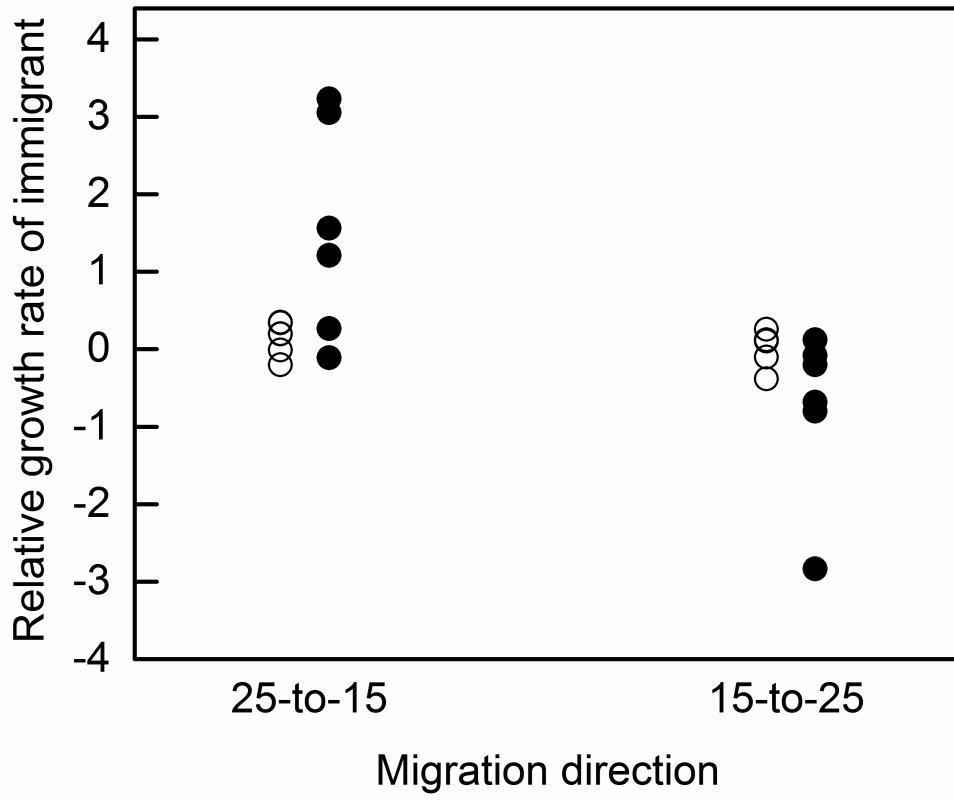
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**(a) 25-to-15 migration**



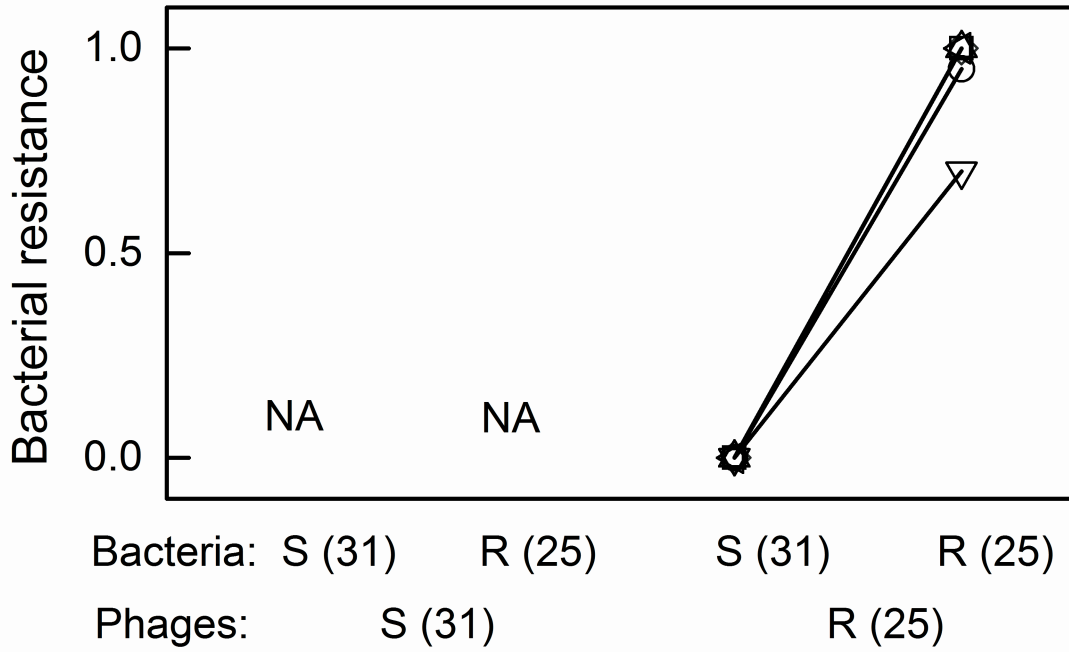
**(b) 15-to-25 migration**



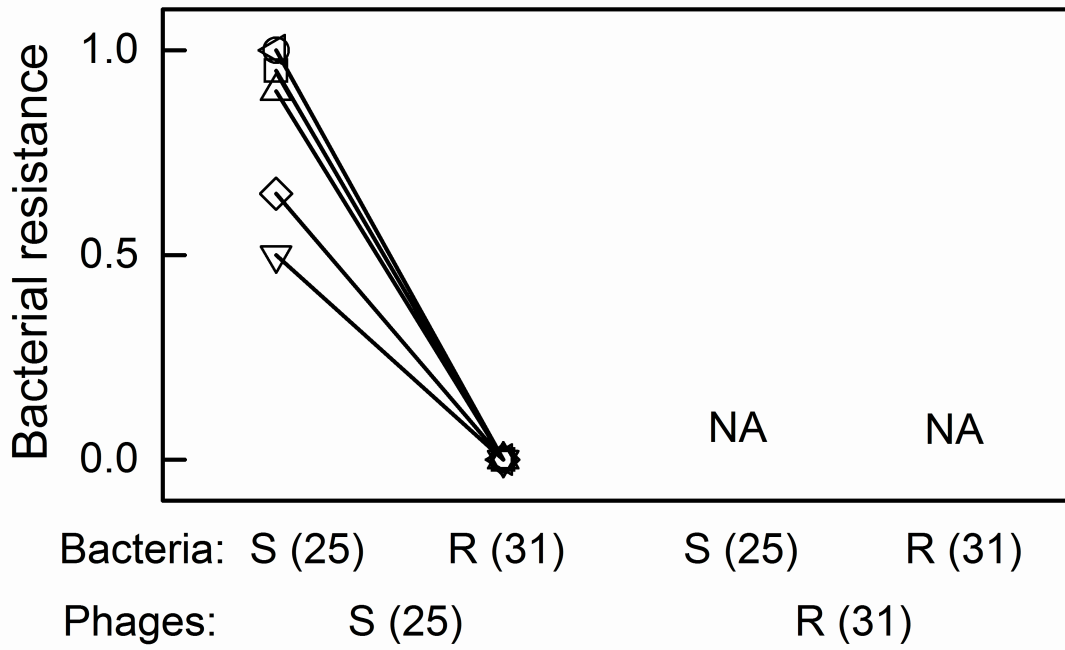


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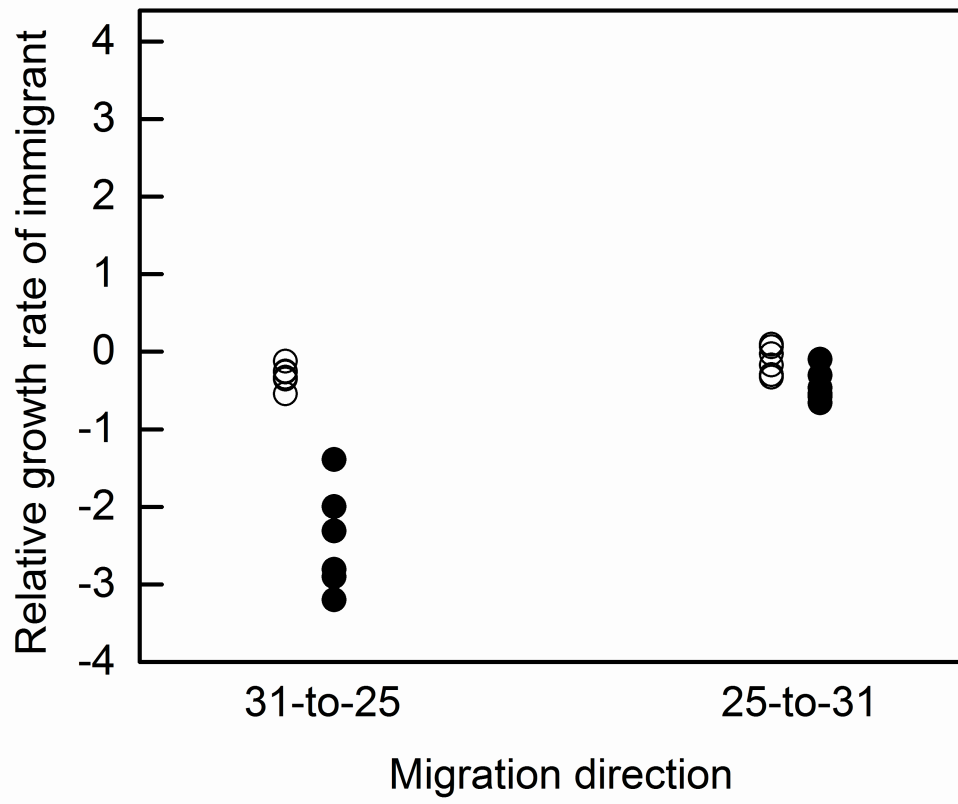
**(a) 31-to-25 migration**



**(b) 25-to-31 migration**



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570 **Figure legend**

571

572 Fig. 1 Resistance of bacteria to phages in metapopulations assigned to 25-to-15 (a) and  
573 15-to-25 (b) coevolution treatments. Numbers in x-axis titles indicate culture  
574 environment (25 or 15 °C) where the tested bacteria and tested phages were sampled  
575 from; “S” represents source microcosms, and “R” recipient microcosms. Within every  
576 panel each symbol indicates tests from one individual metapopulation (six replicate  
577 metapopulations per treatment).

578

579 Fig. 2 Growth rate of immigrant bacteria relative to residents in metapopulations of the  
580 25 and 15 °C habitats, in the absence (open circles) or presence (filled circles) of  
581 coevolving phages.

582

583 Fig. 3 Resistance of bacteria to phages in metapopulations assigned to 31-to-25 (a) and  
584 25-to-31 (b) coevolution treatments. Numbers in x-axis titles indicate culture  
585 environment (31 or 25 °C) where the tested bacteria and tested phages were sampled  
586 from; “S” represents source microcosms, and “R”, recipient microcosms. Note that data  
587 for resistance against phages from the 31 °C habitat are missing due to phage extinction.

588

589 Fig. 4 Growth rate of immigrant bacteria relative to residents in metapopulations of the  
590 31 and 25 °C habitats, in the absence (open circles) or presence (filled circles) of  
591 coevolving phages.

592