Evolutionary Ecology Research, 2005, **7**: 1183–1190

Competitive co-existence of vertically and horizontally transmitted parasites

Curtis M. Lively,* Keith Clay, Michael J. Wade and Clay Fuqua

Department of Biology, Indiana University, Bloomington, IN 47405-3700, USA

ABSTRACT

Questions: Can vertically transmitted parasites (VTPs) serve as indirect mutualists by excluding more virulent, horizontally transmitted parasites (HTPs)? How does the efficiency of vertical transmission affect: (1) the equilibrium number of hosts infected by each type of parasite; (2) the total number of hosts in the population; and (3) virulence of the horizontally transmitted parasite? How does reproductive output by the horizontally transmitted parasite affect the frequency of infection by both parasite types?

Methods and assumptions: We used a deterministic computer simulation to determine host-population dynamics following introduction of a vertically transmitted parasite. We assumed that the vertically transmitted parasite precludes infection by the horizontally transmitted parasite. We allowed for the possibility that virulence of the horizontally transmitted parasite depends on host density.

Conclusions: Vertically transmitted parasites can serve as indirect mutualists by excluding more virulent horizontally transmitted parasites. As such, selection would be expected to favour VTP strains that most efficiently exclude horizontally transmitted parasites. In addition, the total number of hosts at equilibrium increases (and HTP frequency decreases) with the efficiency of vertical transmission. Increasing the reproductive output of the horizontally transmitted parasite has little effect on the frequency of that parasite at equilibrium, but greatly increases the frequency of hosts infected with the vertically transmitted parasite. When virulence of the horizontally transmitted parasite is density dependent, the vertically transmitted parasite indirectly increases virulence by increasing host density at equilibrium.

Keywords: horizontal transmission, pathogen, symbiont, vertical transmission, virulence.

INTRODUCTION

Virtually all organisms serve as hosts for a diversity of microbial parasites and pathogens that spread horizontally among individuals. However, many organisms are also hosts for parasites that are transmitted vertically (trans-ovarially) through eggs. For example, Buchner describes the regular occurrence of vertically transmitted bacteria within the female reproductive organs of many arthropods, especially blood-sucking and sap-sucking

* Author to whom all correspondence should be addressed. e-mail: clively@indiana.edu

species (Buchner, 1965). *Wolbachia* is an especially well-known example of a vertically transmitted parasite that occurs in a diversity of arthropods (Werren, 1997). Similarly, the Rocky Mountain wood tick (*Dermacentor andersonii*) is frequently infected by the avirulent vertically transmitted parasites *Rickettsia peacockii* and *Francisella* spp. (Niebylski *et al.*, 1997). Vertically transmitted parasites are also found in plants where a variety of viruses and fungi are regularly transmitted through the seeds of their hosts (Mink, 1993; Johansen *et al.*, 1994; Clay and Schardl, 2002). For example, many cool-season grasses are infected by systemic fungal endophytes that are vertically transmitted through seeds (Schardl, 1996).

Theory suggests that a vertically transmitted parasite must enhance host fitness or be lost from the host population (Fine, 1975; Ewald, 1987; Lipsitch *et al.*, 1995, 1996). In some cases, the vertically transmitted parasite produces biochemical compounds critical for proper metabolism of the host (Buchner, 1965; Moran and Baumann, 1994) for defence against predators (Clay and Schardl, 2002), but in other systems there is no clear benefit. Here we present results suggesting that one benefit of infection by vertically transmitted parasites is the prevention of infection by more virulent, horizontally transmitted parasites.

MODEL

We used a discrete-time model to consider the dynamics of three different kinds of hosts: uninfected, infected with the horizontally transmitted parasite and infected with the vertically transmitted parasite. The parasites are restricted to a single mode of transmission. One parasite is strictly horizontally transmitted and the other is strictly vertically transmitted. Hence, there is no possibility for mixed transmission as in the models by Lipsitch *et al.* (1995, 1996). Thus the parasites are either different species, or reproductively isolated strains of the same species.

The birth and death rates for all three kinds of hosts depend on total host population size. For example, the number of uninfected hosts at time $t + 1$ is:

$$U_{t+1} = U_t - (d_U + c_U N_t)U_t + [(b_U - a_U N_t)U_t + (b_H - a_H N_t)H_t + (b_V - a_V N_t)(1 - p)V_t]\exp(-\beta H_t/N_t) \quad (1)$$

where U_t is the number of uninfected hosts at time t, and H_t and V_t are the number of individuals infected by horizontally and vertically transmitted parasites, respectively. The second term gives the number of deaths by individuals in the infected class, where d_U is the intrinsic probability of death and c_U is a constant that scales the effect of total population size, N_t, on the death rate. The third term gives the gains to the uninfected class through offspring that are born to uninfected individuals, as well offspring born to individuals that are infected with the horizontally transmitted parasite (H_t), and individuals infected with the vertically transmitted parasite (V_t). Here b_U, b_H and b_V are, respectively, the intrinsic birth rates of uninfected individuals, individuals infected with the horizontally transmitted parasite, and individuals infected with the vertically transmitted parasite. Similarly, a_U, a_H and a_V are, respectively, the constants that scale the effect of population density on the birth rates of uninfected individuals, individuals infected by the horizontally transmitted parasite and individuals infected by the vertically transmitted parasite. The variable p is the probability that the vertically transmitted parasite is successfully transmitted to the next generation. Finally, the probability of transmission by the horizontally transmitted parasite is given as $1 - \exp(-\beta H_t/N_t)$, where β is the number of propagules produced by an infection that become available for transmission; it is also convergent on R_0 as host population

size increases. Thus the probability that offspring remain uninfected by the horizontally transmitted parasite is $\exp(-\beta H_t/N_t)$. We assume that only juveniles can become infected. Similarly, the number of hosts infected with the horizontally transmitted parasite at time $t+1$ is:

$$H_{t+1} = H_t - (d_H + c_H N_t)H_t + [(b_U - a_U N_t)U_t + (b_H - a_H N_t)H_t + (b_V - a_V N_t)(1-p)V_t][1 - \exp(-\beta H_t/N_t)] \quad (2)$$

Finally, the number of hosts infected with the vertically transmitted parasite at time $t+1$ is:

$$V_{t+1} = V_t - (d_V + c_V N_t)V_t + (b_V - a_V N_t)pV_t \quad (3)$$

Several assumptions go into these recursions. One is that individuals born with the vertically transmitted parasite cannot be infected by the horizontally transmitted parasite. This assumption makes sense if the vertically transmitted parasite is capable of excluding the horizontally transmitted parasite by prior occupation of the host. Another assumption, stated above, is that transmission is strictly horizontal in the horizontally transmitted parasite and strictly vertical in the vertically transmitted parasite. Finally, infected individuals ($H_t + V_t$) are assumed to have the same effect as uninfected individuals (U_t) on the birth and death rates of all three classes. In other words, each kind of individual is the same in determining the effective total population size.

The simulations began by introducing a single uninfected host into the population. The simulation was then run for 200 generations, during which time the host population came into a stable equilibrium. At generation 200, a single host infected with the horizontally transmitted parasite was introduced into the population, and the simulation was run for an additional 200 generations. During this period, the frequency of hosts infected with the horizontally transmitted parasite came into a stable equilibrium. Finally, at generation 400, a single host infected with the vertically transmitted parasite was introduced into the population, and the dynamics were followed for an additional 200 generations. For the entire simulation, if/then statements were used to constrain death rates to be less than or equal to one (i.e. $d_i + c_i N_t \leq 1$), and to constrain birth rates to be greater than or equal to zero (i.e. $b_i - a_i N_t > 0$).

We also calculated parasite virulence in two ways. First, we calculated the density-independent virulence, VIR_{DI}, as:

$$VIR_{DI} = 1 - \frac{1 + b_H - d_H}{1 + b_U - d_U} = 1 - \frac{1 + r_H}{1 + r_U} \quad (4)$$

This calculation of virulence is different from the standard calculation in the epidemiological literature, which is focused strictly on the parasite-induced host mortality. The present definition includes the effects of the parasite on both the death rate and the birth rate of an infected host relative to these same parameters in an uninfected host. In general, the measure is more similar to measures of inbreeding depression in population biology (e.g. Johnston and Schoen, 1994; Whitlock, 2002) than it is to the standard epidemiological measures of virulence (e.g. Anderson and May, 1981; Bremermann and Pickering, 1983; Frank, 1996).

Our second measure of virulence was similar in form, but depended on host density at time t. This density-dependent measure of virulence, VIR_{DD}, was calculated as

$$VIR_{DD} = 1 - \frac{1 - (d_H - c_H N_t) + (b_H + a_H N_t)}{1 - (d_U - c_U N_t) + (b_U + a_U N_t)} \quad (5)$$

As above, if/then statements were used to constrain death rates to be less than or equal to one (i.e. $d_i + c_i N_t \leq 1$), and birth rates to be greater than or equal to zero (i.e. $b_i - a_i N_t \geq 0$). This measure is similar to the density-independent measure of virulence (described above) by including the effect of the parasite on both death rates and birth rates, but also includes the effects of total host density on virulence. We calculated this density-dependent measure of virulence every generation in the simulation.

The simulation was successfully checked against several analytically derived benchmarks. First, in the absence of infection by either the vertically or horizontally transmitted parasite, the equilibrium number of hosts is expected to be the solution for $N_t = U_t = U_{t+1}$. For the case in which $D_U = d_U + c_U N_t \leq 1$, the equilibrium solution, $\hat{U}$, can be shown to be $(b_U - d_U)/(a_U + c_U)$ (Gotelli, 1995; Wilson, 2000). Otherwise, the solution is $\hat{U} = (b_U - 1)/a_U$.

The condition for spread of the horizontally transmitted parasite in an uninfected host population at equilibrium is $R_0 > 1$ (Anderson and May, 1979). Here R_0 is equal to H_{t+1} for the special case of $H_t = 1$, giving:

$$R_0 = 1 - DH + e^{-\beta N_t}(B_H + B_U(N_t - 1)) \quad (6)$$

In the limit, as N_t goes to infinity, D_H and B_U both go to 1; and R_0 goes to $R_0 = \beta$. Thus for large uninfected populations at equilibrium, invasion by the horizontally transmitted parasite requires that the number of surviving spores is greater than one.

The condition for invasion by the vertically transmitted parasite is $V_{t+1} > 1$ for $V_t = 1$, which requires that $p > (d_V + c_V \hat{N})/(b_V - a_V \hat{N})$ for $D_V < 1$, and $p > 1/(b_V - a_V \hat{N})$ for $D_V \geq 1$. For both cases, if the vertically transmitted parasite is completely avirulent ($a_V = a_U$, $b_V = b_U$, $c_V = c_U$, $d_V = d_U$), the condition becomes $p > 1$ for invasion into an uninfected population at equilibrium, $\hat{U}$. The result is analogous to previous results showing that vertically transmitted parasites would be eliminated if they reduce host fitness in any way (Fine, 1975). The vertically transmitted parasite might, however, invade a population that is at least partly infected by the horizontally transmitted parasite if the number of hosts at equilibrium is less than that in an uninfected population.

RESULTS

For values of R_0 greater than one, the results were typified by a rapid spread of the horizontally transmitted parasite following its introduction at generation 200 (Fig. 1). In addition, the total number of hosts declined, and the total number of uninfected individuals decreased dramatically, as the horizontally transmitted parasite increased in frequency. Then, following the introduction of the vertically transmitted parasite, the number of hosts infected by the horizontally transmitted parasite decreased rapidly as the vertically transmitted parasite spread in the population. The number of uninfected hosts also increased slightly as the vertically transmitted parasite increased in frequency.

While these results were typical in a qualitative sense, we also found that the results were sensitive to the transmission probability for the vertically transmitted parasite. Specifically, as the transmission probability increased, we found that the frequency of hosts infected with the vertically transmitted parasite increased; the frequency of uninfected hosts also increased slightly, and hosts infected by the horizontally transmitted parasite decreased (Fig. 2a). In addition, we found that the total number of hosts in the population increased almost two-fold as the vertical transmission probability increased (Fig. 2b). Hence the presence of a vertically transmitted parasite can decrease the frequency of infection by the

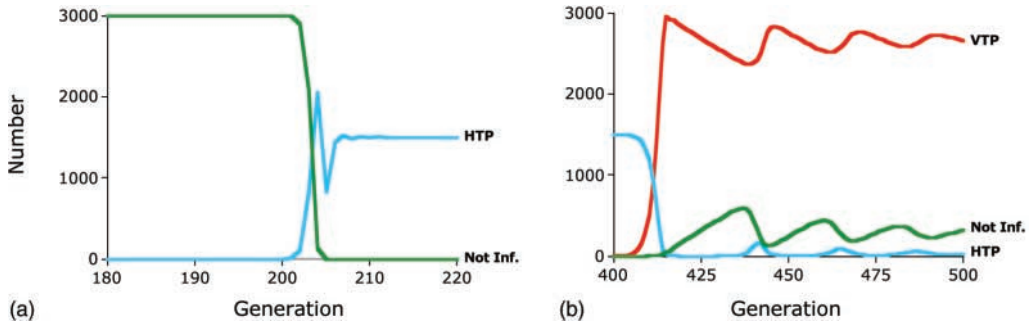

Fig. 1. Representative run from the simulation showing the number of individuals that were uninfected (Not Inf.), infected with the horizontally transmitted parasite (HTP), and infected with the vertically transmitted parasite (VTP). The horizontally transmitted parasite was introduced into the population at generation 200, and the vertically transmitted parasite was introduced at generation 400. (a) Generations 180–220, showing the invasion and replacement of the uninfected population by a population at a lower density infected by the horizontally transmitted parasite. (b) Generations 400–500, showing the invasion of the vertically transmitted parasite, and the dramatic reduction in the number of hosts infected by the horizontally transmitted parasite; uninfected hosts also show a slight increase in frequency. Parameters for this run were: $d_U = d_H = d_V = 0.1$; $b_U = b_H = b_V = 2.5$; $c_U = c_V = 0.0005$ and $c_H = 0.001$; $a_U = a_V = 0.0005$ and $a_H = 0.001$; $\beta = 10$; and $t = 0.99$.

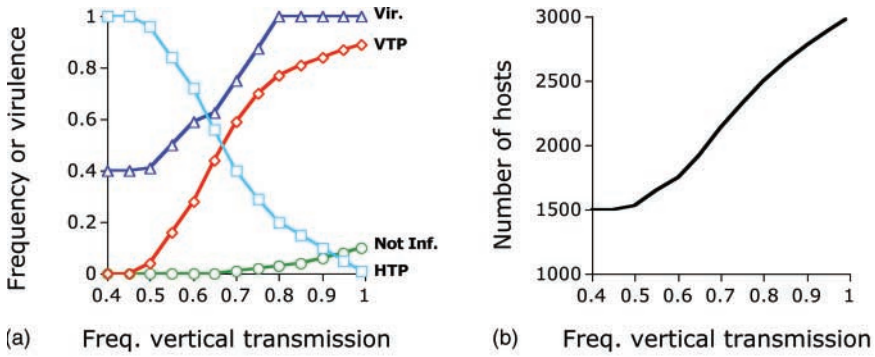

Fig. 2. Effect of vertical transmission efficiency on (a) the mean frequency of individuals that were uninfected (Not Inf.), infected with the horizontally transmitted parasite (HTP), infected with the vertically transmitted parasite (VTP), and on the virulence (Vir.) of the horizontally transmitted parasite. (b) Effect of vertical transmission efficiency on the number of hosts in the population. Parameters for this run were: $d_U = d_H = d_V = 0.1$; $b_U = b_H = b_V = 2.5$; $c_U = c_V = 0.0005$ and $c_H = 0.001$; $a_U = a_V = 0.0005$ and $a_H = 0.001$; and $\beta = 10$. Means were calculated for generations 550–600. The density-independent virulence calculated from this set of parameters was zero.

horizontally transmitted parasite and increase host population size, and the effect appears to increase in line with the transmission success of the vertically transmitted parasite.

We also found that the density-dependent virulence increased as the transmission of the vertically transmitted parasite increased (Fig. 2a). This result, although surprising at first, makes sense because the total host density increases with transmission success, and our measure of virulence depends directly on host density. Hence the spread of the vertically transmitted parasite has three major effects: it increases total host density, it increases the

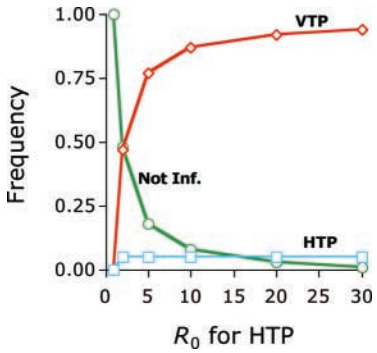

Fig. 3. Effect of R_0 for the horizontally transmitted parasite on the mean frequency of individuals that were uninfected (Not Inf.), infected with the horizontally transmitted parasite (HTP), and infected with the vertically transmitted parasite (VTP). Parameters for this run were: $d_U = d_H = d_V = 0.1$; $b_U = b_H = b_V = 2.5$; $c_U = c_V = 0.0005$ and $c_H = 0.001$; $a_U = a_V = 0.0005$ and $a_H = 0.001$; and $p = 95$. Means were calculated for generations 550–600.

virulence of the horizontally transmitted parasite, and it dramatically reduces the frequency of hosts infected with the horizontally transmitted parasite (HTP).

Finally, we found that increasing the number of successful propagules released by each HTP-infected host (closely related to R_0) increased the frequency of hosts infected by the vertically transmitted parasite at equilibrium (Fig. 3).

DISCUSSION

The results suggest that a vertically transmitted parasite can have several rather dramatic effects on host populations. First, the vertically transmitted parasite can greatly reduce the frequency and number of hosts infected by a horizontally transmitted parasite at equilibrium (Fig. 1). Second, it can increase the number of hosts in the population at equilibrium relative to a population infected only by the horizontally transmitted parasite (Fig. 2b). And third, it can increase the impact of disease on infected hosts when virulence is density dependent (Fig. 2a). In addition, we found that increasing the number of propagules (and hence increasing R_0) released by HTP infections had little effect on the frequency of hosts infected by the horizontally transmitted parasite; but it dramatically increased the frequency of hosts infected with the vertically transmitted parasite (Fig. 3).

We also found that the vertically transmitted parasite cannot increase in an uninfected population of hosts, but that it could increase in a host population infected with the horizontally transmitted parasite. The result is similar to that achieved in the model of Lipsitch *et al.* (1996). Their model focuses primarily on competition between two parasite strains that have both vertical and horizontal transmission. However, they did allow the case where one strain was strictly vertically transmitted (see Lipsitch *et al.*, 1996, p. 1731). They found that such a strain could only increase in a population infected by a horizontally transmitted strain of parasite, but that it would not cause the elimination of the horizontally transmitted parasite. Although the details of our model differ, we obtained the same basic result. In our model, the vertically transmitted parasite can increase in a host population having a high prevalence of infection by the horizontally transmitted parasite, because the latter depresses the number of hosts at equilibrium. So, for example, in Fig. 1, the

number of hosts before invasion by the horizontally transmitted parasite is 3000. The transmission probability, p, for the vertically transmitted parasite must exceed one for it to increase, which is biologically impossible. But following the spread of the horizontally transmitted parasite in the population, the number of hosts in the population is reduced to 1500. The effect of host density on the birth and death rates of individuals is reduced, and the condition for invasion of the vertically transmitted parasite becomes $p > 0.5$. Thus, in our model, the spread of the vertically transmitted parasite depends on the negative effect that the horizontally transmitted parasite has on host density.

Finally, the results suggest a possible interesting side-effect of invasion by the vertically transmitted parasite. The rapid spread of the vertically transmitted parasite into a HTP-infected population resulted in an equally rapid increase in the total number of hosts (Fig. 2b). The result likely follows from the fact that the carrying capacity of a population heavily infected with the vertically transmitted parasite is higher than the carrying capacity of the same host population infected only by the horizontally transmitted parasite. And as a consequence, the virulence of the horizontally transmitted parasite increased dramatically (Fig. 2a) due to the negative effects of host density on the birth and death rates of HTP-infected hosts. Thus our results suggest that, in nature, the horizontally transmitted parasite may be less prevalent following the spread of a vertically transmitted parasite; however, it may also be more virulent. More generally, genetic, physiological and ecological factors that lead to resistance in some fraction of the host population may indirectly increase the impact of disease in infected individuals by increasing the equilibrium density of hosts.

Taken together, the results suggest that, if there is variation among vertically transmitted parasite strains, selection would favour those strains that are most successful at suppressing infection by horizontally transmitted parasites, especially if the latter are highly virulent. One example of suppression is seen in fungal endophytes infecting grasses. These systemic fungi (family Clavicipitaceae, Ascomycota) occur inter-cellularly in above-ground host tissues. Some species produce a fruiting body (stroma) that produces ascospores that can contagiously infect new hosts (Chung and Schardl, 1997). However, other endophytes colonize ovules and become vertically transmitted through seeds (Clay and Schardl, 2002). Empirical research on one species, *Brachypodium sylvaticum*, in Europe suggests that infection of host plants by vertically transmitted endophytes reduces the likelihood of superinfection by stroma-forming, contagiously spreading endophytes (Meijer and Leuchtmann, 2000).

ACKNOWLEDGEMENTS

This study was supported by the NSF Ecology of Infectious Diseases Program (DEB-0223813 and DEB-03268742).

REFERENCES

Anderson, R.M. and May, R.M. 1979. Population biology of infectious diseases: part 1. *Nature*, **280**: 361–367.

Anderson, R.M. and May, R.M. 1981. The population dynamics of microparasites and their invertebrate hosts. *Proc. R. Soc. Lond. B*, **291**: 451–524.

Bremermann, H.J. and Pickering, J. 1983. A game-theoretical model of parasite virulence. *J. Theor. Biol.*, **100**: 411–426.

Buchner, P. 1965. *Endosymbiosis of Animals with Plant Microorganisms*. New York: Wiley Interscience.

Chung, K.R. and Schardl, C.L. 1997. Sexual cycle and horizontal transmission of the grass symbiont, *Epichloe typhina*. *Mycol. Res.*, **101**: 295–301.

Clay, K. and Schardl, C.L. 2002. Evolutionary origins and ecological consequences of endophyte symbiosis with grasses. *Am. Nat.*, **160**: S99–S127.

Ewald, P.W. 1987. Transmission modes and the evolution of the parasitism–mutualism continuum. *Ann. NY Acad. Sci.*, **503**: 295–306.

Fine, P.E.M. 1975. Vectors and vertical transmission: an epidemiological perspective. *Ann. NY Acad. Sci.*, **266**: 173–194.

Frank, S.A. 1996. Models of parasite virulence. *Quart. Rev. Biol.*, **71**: 37–78.

Gotelli, N.J. 1995. *A Primer of Ecology*. Sunderland, MA: Sinauer Associates.

Johansen, E., Edward, M.C. and Hampton, R.O. 1994. Seed transmission of viruses: current perspectives. *Annu. Rev. Phytopathol.*, **32**: 363–386.

Johnston, M.O. and Schoen, D.J. 1994. On the measurement of inbreeding depression. *Evolution*, **48**: 1735–1741.

Lipsitch, M., Nowak, M.A., Ebert, D. and May, R.M. 1995. The population dynamics of vertically and horizontal transmitted parasites. *Proc. R. Soc. Lond. B*, **260**: 321–327.

Lipsitch, M., Siller, S. and Nowak, M.A. 1996. The evolution of virulence in pathogens with vertical and horizontal transmission. *Evolution*, **50**: 1729–1741.

Meijer, G. and Leuchtmann, A. 2000. The effects of genetic and environmental factors on disease expression (stroma formation) and plant growth in *Brachypodium sylvaticum* infected by *Epichloe sylvatica*. *Oikos*, **91**: 446–458.

Mink, G.I. 1993. Pollen- and seed-transmitted viruses and viroids. *Annu. Rev. Phytopathol.*, **31**: 375–402.

Moran, N. and Baumann, P. 1994. Phylogenetics of cytoplasmically inherited microorganisms of arthropods. *Trends Ecol. Evol.*, **9**: 15–20.

Niebylski, M.L., Schrumpf, M.E., Burgdorfer, W., Fischer, E.R., Gage, K.L. and Schwan, T.G. 1997. *Rickettsia peacockii* sp. nov., a new species infecting wood ticks, *Demacentor andersoni*, in western Montana. *Int. J. Syst. Bacteriol.*, **47**: 446–452.

Schardl, C.L. 1996. *Epichloe* species: fungal symbionts of grasses. *Annu. Rev. Phytopathol.*, **34**: 109–130.

Werren, J.H. 1997. Biology of *Wolbachia*. *Annu. Rev. Entomol.*, **42**: 587–609.

Whitlock, M.C. 2002. Selection, load and inbreeding depression in a large metapopulation. *Genetics*, **160**: 1191–1202.

Wilson, W. 2000. *Simulating Ecological and Evolutionary Systems in C*. Cambridge: Cambridge University Press.