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Co-existence of hosts and sex ratio distorters in structured populations

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ABSTRACT

Vertically transmitted parasites occur in several invertebrate species, and alter host reproduction by a variety of mechanisms, including sex ratio distortion via feminization. Efficient feminizers are predicted to drive homogenous host populations extinct due to the absence of males. However, group (interdemic) selection may enable host–parasite co-existence through extinction–colonization turnover of local subpopulations. Here we analyse the effects of feminizers on host metapopulations, in relation to the underlying mechanism of host sex determination. We examine host metapopulations with (a) fixed probabilistic sex ratio control, (b) female heterogamety (WZ/ZZ) and (c) male heterogamety (XX/XY) with and without YY viability. Under some circumstances, host and parasite can co-exist in metapopulations despite deterministic instability of local populations, in which case the parasite persists at lower frequency than predicted for homogenous populations. However, co-existence is sensitive to host sex determining mechanism. Long-term co-existence is unlikely in chromosomal systems, where sex ratio selection and novel mating type combinations result in the loss of female-determining alleles from infected host subpopulations. The consequent loss of uninfected females precludes stochastic parasite exclusion and thus prevents local population recovery. Hence, host–feminizer co-existence via interdemic selection requires intrinsic patch recovery in addition to recolonization from neighbouring subpopulations. We conclude that metapopulation structure can only buffer host populations against parasite-mediated extinction if female-determining alleles are retained in the host population.

Keywords: cytoplasmic inheritance, *Gammarus duebeni*, levels of selection, metapopulation, sex determination, sex ratio distorter.

INTRODUCTION

Parasitic sex ratio distortion and related phenomena are of interest to evolutionary biologists because these systems may provide insight into genomic conflict (Hurst *et al.*, 1996; Werren and Beukeboom, 1998) and the levels-of-selection debate (Werren and Beukeboom, 1993; Frank, 1997a). Cytoplasmically inherited organisms or non-Mendelian genetic elements are selected to bias the host sex ratio towards the transmitting sex, and are therefore in conflict with the host (autosomal) genome, which is in general selected to produce

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a 1:1 sex ratio (Fisher, 1930). However, if sex ratio distorters increase in frequency towards fixation, the host population may be driven extinct due to rarity of one sex (Hamilton, 1967; Hatcher *et al.*, 1999). This latter possibility has led to the suggestion that interdemic (population-level) selection might regulate the frequency of sex ratio factors (Wallace, 1948; Heuch, 1978; Bull, 1983; Werren *et al.*, 1988; Werren and Beukeboom, 1993; McCauley and Taylor, 1997).

A number of strategies have been identified for parasitic sex ratio bias (reviewed in Dunn *et al.*, 1995; Werren, 1997), including meiotic drive (Jaenike, 1996), direct sex ratio distortion (Werren, 1987) and distortion of sex determination via feminization (Dunn *et al.*, 1995). Feminizers are predicted to spread through homogenous host populations if they bias the host sex ratio sufficiently towards females (Bull, 1983). In the absence of host sex ratio evolution, infected females are predicted to increase to an equilibrium prevalence (the population of females infected), dependent on transmission and feminization efficiency, viability effects, the uninfected host sex ratio and the sex determining mechanism (Bull, 1983; Taylor, 1990; Hatcher and Dunn, 1995). However, maintenance of sex ratio distorters at a stable prevalence has been regarded as theoretically unlikely. If the parasite has 100% transmission (and feminization) efficiency, it will reach fixation and drive the host population extinct due to the absence of males (Bull, 1983; Werren, 1987). Even feminizers with inefficient transmission may cause deterministic decline of finite host populations if host males have limited mating capacity (Hatcher *et al.*, 1999). The parasite may also be driven to fixation by compensatory sex ratio selection on the host (Werren, 1987; Hatcher and Dunn, 1995). Finally, if the host has female heterogamety (WZ/ZZ sex determination), novel mating combinations involving ZZ infected females lead to elimination of the W chromosome and fixation of the parasite (Taylor, 1990).

In contrast to the theory, sex ratio distorters appear to be relatively stable in natural populations. In the case of feminizers, two systems have been studied extensively. Bacteria of the genus *Wolbachia* feminize terrestrial isopods with female heterogamety (*Armadillidium vulgare*: Rigaud and Juchault, 1993) and with male heterogamety (*A. nasatum*: Rigaud *et al.*, 1997). Infection frequency differs between populations and is generally lower than that predicted for infinite populations (Juchault *et al.*, 1992, 1993). At least three microsporidian species feminize the amphipod *Gammarus duebeni* (*Octosporea effeminans*: Bulnheim and Vavra, 1968; *Thelohania herediteria*: Bulnheim, 1971; *Nosema granulosis*: Terry *et al.*, 1998, 1999). *G. duebeni* has environmental sex determination which may involve polyfactorial genetic (but not heterogametic) control (Watt, 1994). It is found in a variety of brackish water habitats and structure parameters are expected to vary between populations (Naylor *et al.*, 1988). Parasite prevalence differs between populations and is consistently lower than that predicted for infinite populations (Dunn and Hatcher, 1997).

For other sex ratio distorters, it has been argued that interdemic selection may enable co-existence via differential rates of productivity and extinction of infected and uninfected populations (Heuch, 1978; Werren, 1987; Werren *et al.*, 1988). Models by Heuch (1978), Heuch and Chanter (1982) and Stenseth (1985) support this hypothesis for suspected Y-linked meiotic drive in the butterfly *Acraea encedon*. Models of other systems present conflicting results. Werren and Beukeboom (1993) found that population subdivision with temporary mating demes in the haplodiploid wasp *Nasonia vitripennis* reduced the equilibrium frequency of the paternally transmitted parasitic B chromosome PSR. Wade and Stevens (1994) showed that population subdivision limited the spread of cytoplasmic incompatibility agents in *Tribolium castaneum*, but did not affect the eventual equilibrium

frequency. In contrast, Frank (1997a) concluded that population structure is required for the evolution of cytoplasmic incompatibility. It is unclear how these results relate to crustacean feminizer systems, as stepping stone metapopulation models are more appropriate than temporary mating demes (Naylor *et al.*, 1988) and hosts utilize different sex determining mechanisms (Watt, 1994; Hatcher and Tofts, 1995).

In this paper, we use individual-based models (IBMs) to examine whether Heuch (1978) and related arguments apply to feminizers, and whether host sex determining mechanism influences the outcome. We investigate whether population structure enables co-existence or can account for lower observed prevalences than previously predicted. We also develop an analytical, spatially abstract model to act as an independent control for the simulation approach and to investigate the effects of local population recovery rates on global dynamics.

INDIVIDUAL-BASED MODELS

Our approach is an extension of stochastic cellular automata methods (individual-based model: IBM); we fully include the interactions between individuals within local populations (which can be regarded as automata) so as not to circumscribe the state-space of the system. Simulations were written in the C programming language and conducted on Sun Sparc 5 and 10 workstations and Apple Power PC. We developed IBMs to investigate parasite–host interactions in (1) a stepping-stone metapopulation and (2) within single, finite populations.

Analytical results for the general system in which uninfected host sex ratio is fixed at 1/2 are presented in Hatcher *et al.* (1999). This work demonstrated that populations infected with maternally inherited feminizers would undergo deterministic extinction if

$$B\Lambda(1 - t) \leq 1 \tag{1}$$

where t = transmission efficiency of the parasite (proportion of offspring that inherit the infection from infected mothers); Λ = average number of surviving offspring produced by each mating (we assume no fitness effect of parasitism on fecundity or survival); B = the male mating limit: the minimum of either the ratio of females to males (assuming every female mates, no matter how few males are left) or a constraint $B_{\max}$ imposed by temporal, behavioural or physiological factors.

We used stochastic (branching process) models to examine the eventual fate of populations (Hatcher *et al.*, 1999). As the population nears extinction, one of two outcomes is possible. Either the last male (or males) mates with an infected female, and both parasite and host are extinguished due to absence of males in the subsequent generation; or only uninfected females are mated, so the parasite is eliminated, allowing the host population to recover. In the current study, we compare outcomes for populations with different sex determining mechanisms after a feminizer-induced population crash. We use condition (1) to set parameters so as to induce a crash in finite populations. We use IBMs as the inclusion of explicit genotypes for gender increases the number of types such that analysis of branching processes becomes intractable. We first describe the procedures used to model various mechanisms of sex determination for both types of IBM, and then describe the models and their analysis.

Sex determining mechanisms

Fixed sex ratio control

Sex is determined probabilistically for each individual, according to the infection status of mothers. Each offspring of an uninfected female becomes female with probability $x = 1/2$ (as assumed in Hatcher *et al.*, 1999). Infected females produce infected offspring with probability t; all infected offspring develop as females (i.e. we assume complete feminization by the parasite). The uninfected offspring of infected females become female with probability $x = 1/2$.

Female heterogamety

For the initial generation, each individual was assigned one Z chromosome, and the identity of the other sex chromosome was decided on the basis of an unbiased binomial trial. Males (ZZ) and females (WZ) were chosen at random to form pairs. Each offspring inherited one paternal and one maternal chromosome chosen without bias. The infection status was then determined as above if the mother was parasitized. Infected offspring were designated as infected females, but retained their genotype (hence infected ZZ counts as a female under the mating rules).

Male heterogamety

As above, with X replacing Z and Y replacing W (XX = female; XY = male). In subsequent generations, YY genotypes appear, the sex of which depends on infection status (uninfected = male; infected = female). Three models of YY fate were investigated:

- *YY viable*: YY are treated as other genotypes with respect to subsequent survival.
- *YY lethal*, *no replacement*: Individuals with YY genotype die and are not replaced, thereby reducing the effective fecundity of $*Y \times *Y$ matings (appropriate for systems in which lethality is delayed or fertilization is external with no re-utilization of resources).
- *YY lethal*, *with replacement*: Individuals with YY genotype die, but are replaced by a new offspring formed as above. Hence $*Y \times *Y$ pairs produce as many potentially viable offspring as other pairings, but gene frequencies are still affected.

Metapopulation IBMs

The IBM for a metapopulation consisted of 30×30 discrete patches (subpopulations) arranged as a two-dimensional torus. Each patch was initialized with N_0 individuals that interacted in the manner described below for single populations. Dispersal between patches occurred at the adult stage after offspring production and density-independent mortality. Dispersers were drawn from a binomial distribution with parameters N_0 and μ, and each moved to one of the eight neighbouring patches with unbiased probability. Subpopulations exceeding N_0 were then truncated to N_0 adults. This form of strict cut-off can be regarded as a contest form of density-dependent regulation. The range of parameters that lead to extinction is increased slightly under various forms of density-dependent host population regulation (Hatcher *et al.*, 1999). Random mating and sex allocation then proceeded as below for within-population IBMs.

Metapopulation IBMs were run for 1000 generations, recording genotype and infection frequencies per patch per generation, and the number of generations to extinction of parasite or host. Summary statistics were collected over generations 600–1000 to minimize the effects of initialization. We measured parasite prevalence (the proportion of females infected) and the relative mating success of infected females as a moving average (and ranges) over this interval, also averaging over the entire metapopulation.

For single populations (and for patches within metapopulations), the sex of each initial occupant was allocated according to the sex determining mechanism. One female was replaced by an infected female in the initial population. Mating proceeded via drawing females without replacement, up to B times the number of males. Offspring were produced from a binomial distribution with parameters λ and α (representing fecundity and density-independent survival, respectively). On the basis of parameter estimates for *G. duebeni* (Hatcher *et al.*, 1999), we used $\lambda = 16$ and $\alpha = 0.2$, producing a mean of 3.2 offspring per female. Gender and genotype were then allocated, with each offspring of an infected female having probability t of becoming a parasitized female. Each population was kept at or below its initial density by drawing without replacement from the offspring up to N_0 survivors.

Host–parasite persistence in metapopulations

Figure 1 shows the persistence time for the metapopulation containing both hosts and their feminizing parasites in relation to host patch fidelity (the proportion of hosts that remain in their natal patch at each generation), for parameters satisfying condition (1). Host–parasite persistence was very sensitive to the model of host sex determination. Under fixed sex ratio control, intermediate host dispersal rates permitted co-existence for at least 1000 generations despite deterministic extinction of local populations (Fig. 1a). However, in WZ/ZZ or XX/XY (YY viable) systems, parasite and host co-existed only for a very limited range of host dispersal hosts (Fig. 1b,c). In contrast, XX/XY hosts with YY inviability persisted with the parasite over a range of conditions similar to that for fixed sex ratio control (Fig. 1d).

For persistent systems, host and parasite co-exist through a turnover between infected, empty and uninfected patch states: infected populations are driven extinct as males become rare, but the patches recover or are recolonized by uninfected hosts (Heuch, 1978). However, if patch fidelity is low (dispersal high), the metapopulation behaves as a single (large) population and male rarity-induced population crash leads to rapid extinction of the host and parasite, conforming to our predictions for single populations (Hatcher *et al.*, 1999). If dispersal is very low, each patch behaves as a small autonomous population and overall extinction occurs because local populations go extinct and are not recolonized at a sufficient rate.

Parasite prevalence over metapopulations

Averaged over the metapopulation as a whole, the prevalence observed in these simulations (Figs 1, 2) was considerably lower than that predicted for unstructured populations (for these parameters, prevalence in a homogenous population ≈ 0.57; Hatcher and Dunn, 1995). With a local population size $N_0 = 40$, running mean prevalence remained below 0.4 for fixed sex ratio control (Fig. 2a). For the limited dispersal range that permitted co-existence in the WZ/ZZ model, average prevalence remained very low (≈ 0.05; Fig. 2b). Parasite prevalence

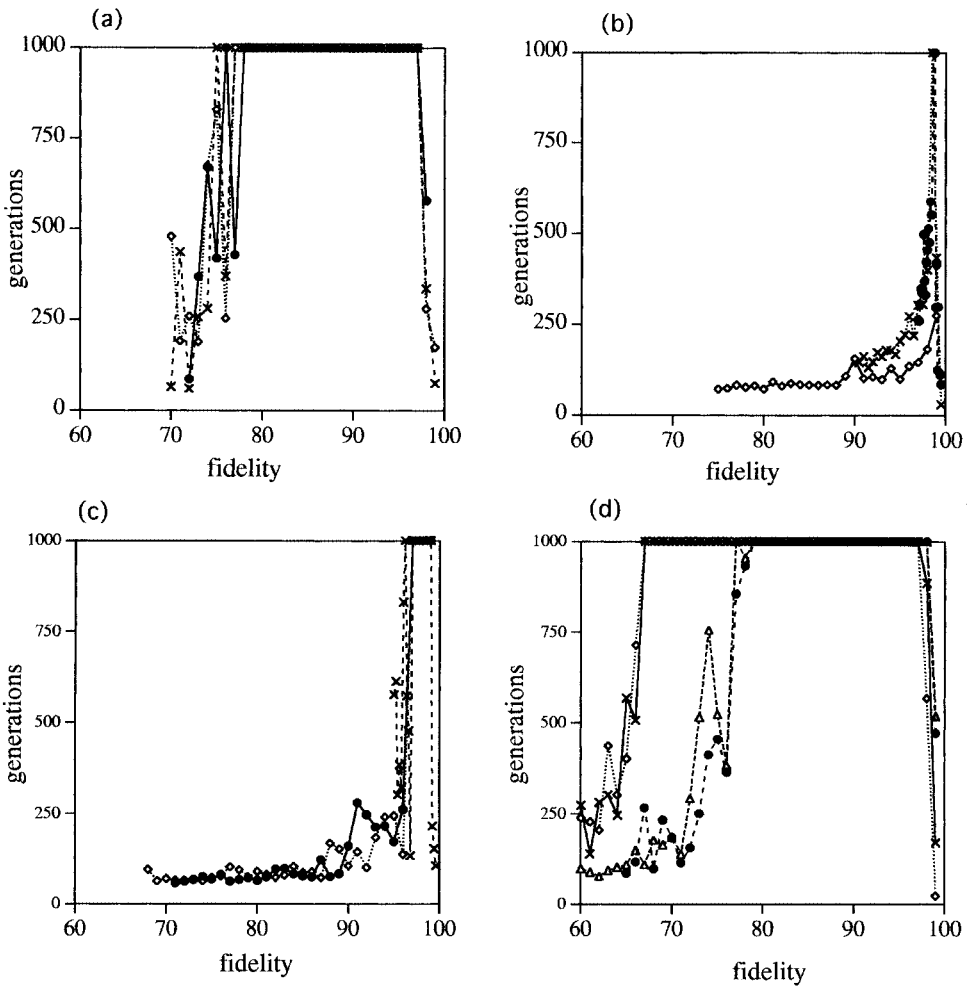


Fig. 1. Parasite persistence in relation to dispersal frequency. Graphs show the number of generations that the feminizer persists in the metapopulation against patch fidelity. (a) Fixed sex ratio control; (b) WZ/ZZ; (c) XX/XY, YY viable; (d) XX/XY, YY inviable (diamond and cross: YY inviable, no replacement; circle and triangle: YY inviable, with replacement). Different labels within each graph indicate data for replicate runs. Parameters: $N_0 = 40$, $t = 0.7$, $\lambda = 16$, $s = 0.2$, $B = 1$. For models in (d), an adjusted transmission efficiency of $t = 0.75$ was used to offset loss of transmission due to YY inviability (resulting in an equivalent equilibrium prevalence to $t = 0.7$ for fixed models under infinite population assumptions).

remained below the infinite population prediction in XY systems (Fig. 2c,d) and also depended on the model of YY inviability (Figs 1d, 2d).

For both fixed sex ratio control and chromosomal sex determination, high dispersal rates resulted in strong fluctuations in prevalence (Fig. 3a,b), and at too high a dispersal rate the parasite (and/or host) was eliminated. The strength of fluctuation was linked to the parasite's effect on host population size (Fig. 3c): at high dispersal rates, the parasite becomes

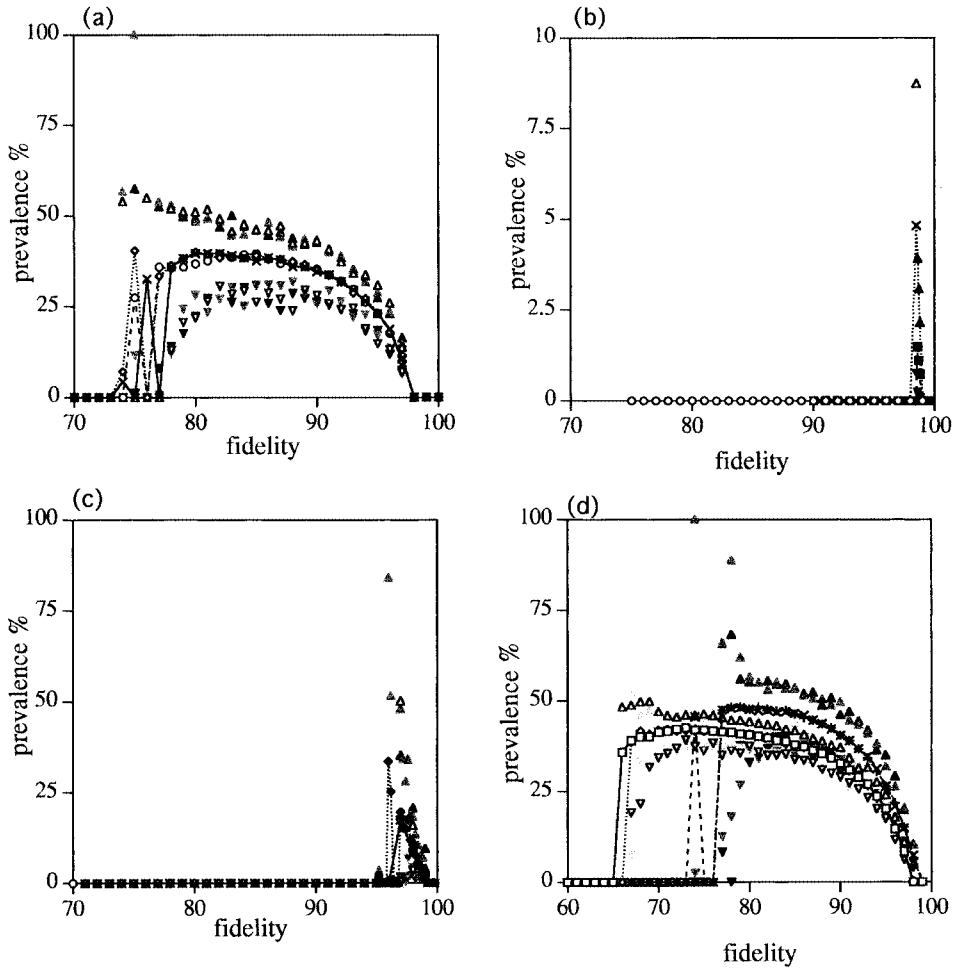
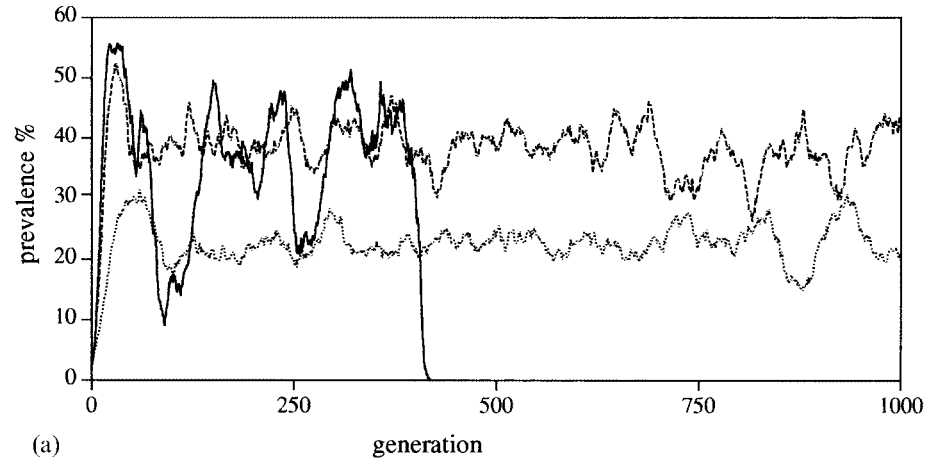


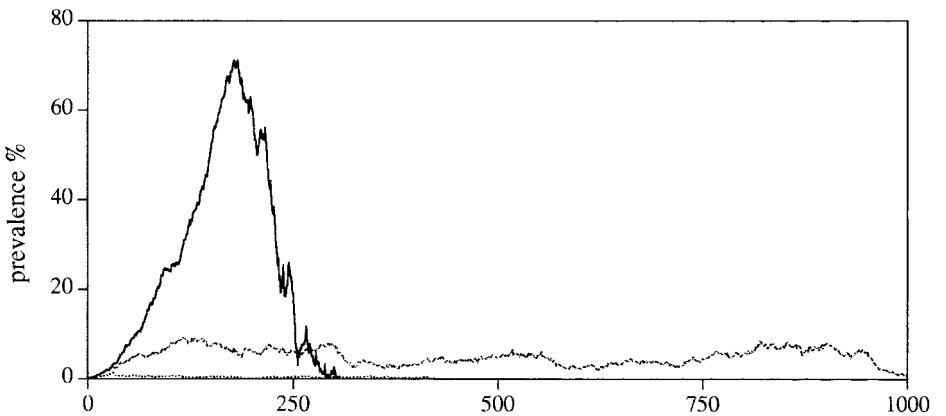
Fig. 2. Relationship between parasite prevalence and dispersal frequency. Graphs show mean prevalence against patch fidelity. Triangles indicate range measured over generations 600–1000 (apex up: maximum; apex down: minimum). (a) Fixed sex ratio control; (b) WZ/ZZ; (c) XX/XY, YY viable; (d) XX/XY, YY inviable (diamond, square: YY lethal, no replacement; crosses: YY lethal, with replacement). Different labels and shading indicate replicate runs. Parameters as Fig. 1.

distributed throughout the metapopulation and can have a considerable impact on total population size. Fluctuations are damped at lower dispersal rates, as the parasite is restricted to fewer patches (prevalence is low: Fig. 3a,b); hence host population size is less affected (Fig. 3c).

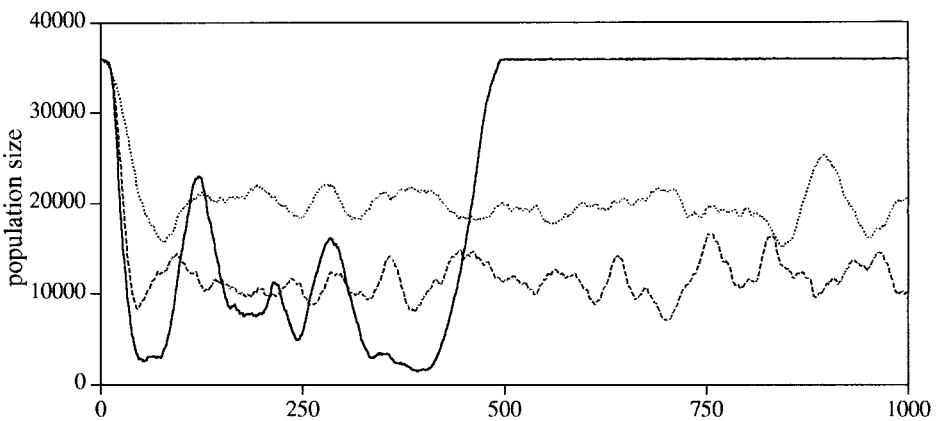
Figure 3d shows the effect of parasite transmission efficiency on prevalence for hosts with fixed sex ratio control. Host–parasite co-existence was unlikely if the parasite had high transmission efficiency ($t = 0.85$ and above): for large t, persistence occurred only at low dispersal rates and average prevalence was much reduced. The results imply that efficient parasites will lead to rapid local population crashes and can only be maintained if host dispersal is low enough to limit spread of infection. If sex ratio distortion is insufficient to


60
50
40
30
20
10
0
prevalence %
0
250
500
750
1000
generation

(a)


80
60
40
20
0
prevalence %
0
250
500
750
1000
generation

(b)


40000
30000
20000
10000
0
population size
0
250
500
750
1000
generations

(c)

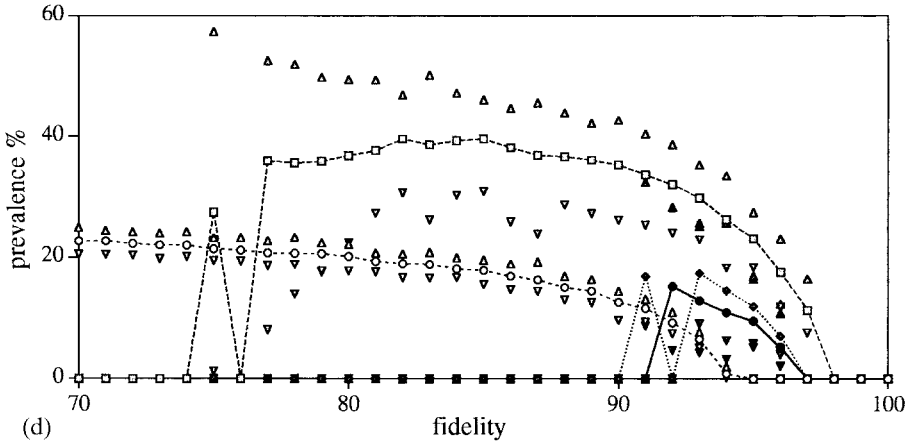


Fig. 3. Parasite population dynamics and relationship between prevalence and transmission. (a) Parasite prevalence across metapopulation; fixed sex ratio control. Example time-series for three different host dispersal rates are shown (solid line: probability of dispersal per host per generation $\mu = 0.25$; dashed: $\mu = 0.15$; dotted: $\mu = 0.05$). (b) Parasite prevalence in WZ/ZZ metapopulation (solid line: $\mu = 0.03$; dashed: $\mu = 0.015$; dotted: $\mu = 0.01$). (c) The effect of parasitism on total metapopulation size; fixed sex ratio control. The time-series and labels are for the simulation runs depicted in Fig. 3a. (d) Mean parasite prevalence in relation to fidelity for differing transmission efficiency t (fixed sex ratio control). Open circles: $t = 0.55$; squares: $t = 0.7$; diamonds: $t = 0.85$; solid circles: $t = 0.95$. Triangles show maxima and minima (generations 600–1000) for each run (shaded to match label for that run). Other parameters as Fig. 1.

drive deterministic extinction by condition (1) (for example, $t = 0.55$ in Fig. 3d), the parasite is maintained for a broad range of dispersal rates and average prevalence conforms to the predictions of infinite population models (Hatcher and Dunn, 1995).

In metapopulations comprising larger local populations, parasite prevalence tended to be more stable (Fig. 4a). The range of dispersal rates that permit co-existence and the mean prevalence attained also increased slightly with population size (Fig. 4b). However, prevalence across the metapopulation remained lower than that predicted for unstructured populations.

Relative mating success of infected females

Infected females had lower mean mating success than uninfected females across the metapopulation (Fig. 5a,b; for parameter ranges satisfying condition (1), fixed sex ratio control). Infected females exist only in patches where males are becoming rare, and hence suffer reduced mate encounter rates relative to uninfected females. If male mating capacity is limiting, this results in reduced relative fitness of infected females. Such a fitness effect would not be observed at the organism scale (we assume encounter rates and mate choice are independent of infection status) and represents an 'emergent' effect at the level of the metapopulation. Relative mating success tracked parasite prevalence (Fig. 5b) and in part accounts for the disparity between the prevalence predictions of structured and homogenous models. This was assessed by taking the running mean relative mating success

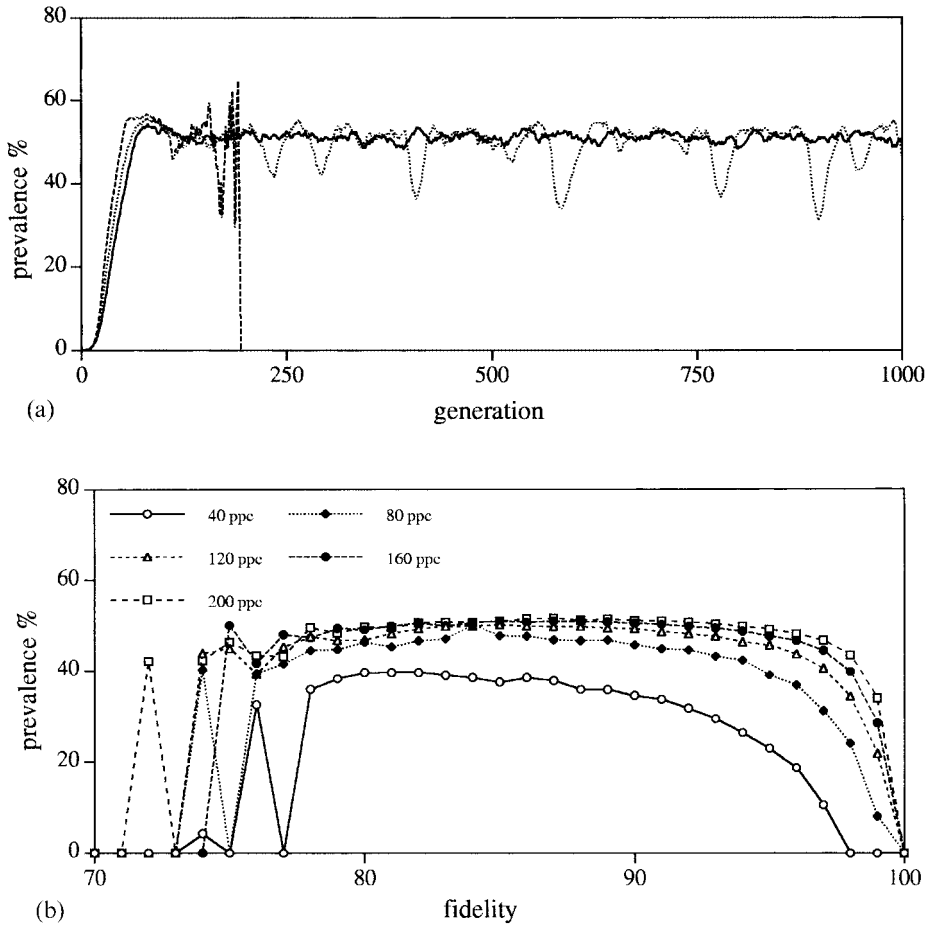


Fig. 4. The influence of local population size on parasite prevalence across a metapopulation. (a) Example time-series for metapopulation with local population size $N_0 = 200$, for different host dispersal rates (dashed line: $\mu = 0.3$; dotted: $\mu = 0.2$; solid: $\mu = 0.1$). (b) Mean prevalence and patch fidelity for different local population sizes (as indicated in key). Other parameters as Fig. 1.

(averaged across the metapopulation for each run) as an estimate of relative fitness (W), and substituting into an infinite population model to predict parasite prevalence P_{exp}:

$$P_{exp} = \frac{Wt - x}{W(t + x - tx)} \tag{2}$$

The parameters t and x are transmission efficiency and underlying host sex ratio respectively, as defined previously. Equation (5) follows the derivation of Hatcher and Dunn (1995), but differs in that here W represents relative mating success, whereas Hatcher and Dunn took W as a viability effect.

P_{exp} was compared to the running mean prevalence P_{obs} measured across the metapopulation for that run (Fig. 5c). The results show that relative mating success is quite an accurate

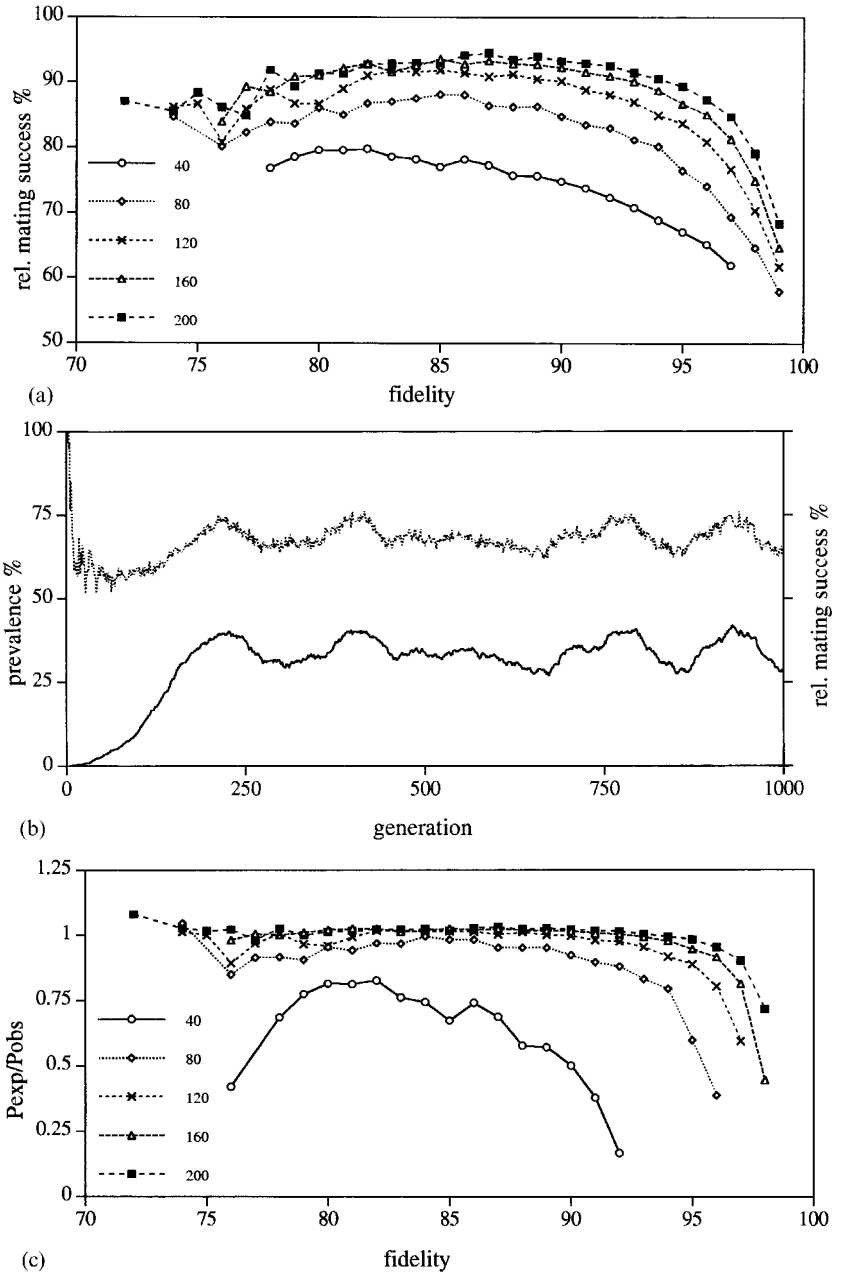


Fig. 5. The influence of relative mating success on parasite prevalence. (a) Relative mating success of infected females versus patch fidelity for different local population sizes (as indicated in key). (b) Relative mating success (dashed line) of infected females and prevalence (solid line) across metapopulation with local population size 200. (c) Relative mating success as a predictor of average prevalence across the metapopulation, plotting the ratio P_{exp}/P_{obs} against patch fidelity for five local population sizes (as indicated in key). P_{exp} = prevalence predicted from Model (2) with W = simulation measure of infected female relative mating success. P_{obs} = prevalence as measured from the simulation.

predictor of prevalence when local population size is large (the ratio $P_{exp}/P_{obs} \approx 1$ for above about 100 hosts per patch). At smaller local population sizes, the prevalence observed was somewhat higher than that predicted from equation (2).

Single population IBMs

The rules described above for within-population interactions were used to simulate outcomes for single (isolated) populations. Initial population densities N_0 in the range 10–1500 were investigated. The outcome of each simulation was classified as (a) failure of parasite to invade initially; (b) successful invasion and subsequent crash, host and parasite extinguished; or (c) successful invasion and subsequent crash, parasite only extinguished. We calculated the mean and variance for time to population extinction (after successful invasion) across replicates for each parameter set. For genotypic models, the mean and variance for duration of the X or W chromosomes were also recorded.

Under conditions satisfying inequality (1), simulated populations invariably fell into one of the three categories (a)–(c) above (Table 1). Parasite exclusion and potential host population recovery differed between sex determination models: at population sizes above 100, 20–30% of populations recovered in the cases of fixed sex ratio control or XX/XY with YY inviability, whereas less than 1% recovered under WZ/ZZ and XX/XY with all genotypes viable.

Loss of female-determining chromosomes

Probability of recovery was linked to the fate of female-determining chromosomes in the population. In WZ and XY systems with YY viable, female-determining chromosomes were eliminated from the population before the population went extinct (the persistence time of X and W chromosomes was significantly shorter than that for the population; $P < 0.05$ for each population size; corrected *t*-tests) (Fig. 6a). This concurs with the numerical study of Taylor (1990). X and W chromosomes are eliminated as feminization induces novel mating combinations (for example, XY infected female × XY male) and genotypes yielding males (the rarer sex) are favoured by frequency-dependent Fisherian selection. The mean time for X elimination (population size 1000) was longer than for W, a result of the three-fold higher initial frequency of X. Elimination of sex determining chromosomes/alleles is not possible under fixed sex ratio control or if YY offspring are inviable (Fig. 6b; no significant difference between persistence time of X and whole population for either YY inviability models).

Parasite persistence and population recovery

Population persistence time differed between sex determination models: persistence time for systems in which the female chromosome is eliminated (Fig. 6a) exceeded that for systems with no chromosome elimination (Fig. 6b). The rate of population crash is determined by sex ratio (males, being the limiting sex, determine the number of matings at successive generations), which is expected to differ between systems during the transient phase.

Parasite exclusion occurs when the host population declines to very small size because the last males chance to mate only with uninfected females, or because of chance failure of parasite transmission. If female-determining chromosomes are eliminated, the resulting population is monogenous for sex determination and all females are infected (Werren, 1987;

Table 1. Outcomes in single populations*

Population size	Fixed s.r.		WZ		XY		YY no r.		YY rep.	
	h. ext.	p. elim.	h. ext.	p. elim.	h. ext.	p. elim.	h. ext.	p. elim.	h. ext.	p. elim.
10	0.4786	0.1431	0.3612	0.1879	0.3374	0.1977	0.3039	0.2295	0.3453	0.2175
20	0.3751	0.1586	0.3455	0.1195	0.3022	0.1494	0.2161	0.2147	0.2816	0.2054
30	0.3620	0.1456	0.3762	0.0564	0.3397	0.0868	0.2046	0.1779	0.2959	0.1690
40	0.3792	0.1221	0.3904	0.0273	0.3643	0.0469	0.2130	0.1485	0.3253	0.1389
50	0.3881	0.1119	0.4074	0.0125	0.3832	0.0273	0.2247	0.1403	0.3382	0.1186
60	0.3914	0.1090	0.4091	0.0045	0.3928	0.0173	0.2392	0.1195	0.3564	0.1054
70	0.3932	0.0995	0.4222	0.0026	0.4004	0.0146	0.2451	0.1130	0.3615	0.1084
80	0.3969	0.1082	0.4231	0.0009	0.4086	0.0117	0.0620	0.1079	0.3644	0.1004
90	0.4069	0.1011	0.4221	0.0007	0.4007	0.0080	0.2617	0.1018	0.3637	0.1088
100	0.4053	0.0975	0.4214	0.0010	0.4080	0.0079	0.2795	0.0995	0.3773	0.1050
200	0.4065	0.1038	0.4317	0.0000	0.4313	0.0039	0.2962	0.0940	0.3954	0.1046
300	0.4137	0.1061	0.4290	0.0000	0.4310	0.0030	0.2954	0.1038	0.3937	0.1074
400	0.4197	0.1056	0.4309	0.0000	0.4337	0.0033	0.2938	0.1001	0.3851	0.1103
500	0.4076	0.1056	0.4423	0.0000	0.4451	0.0021	0.2910	0.1013	0.4001	0.1113
1000	0.4196	0.1077	0.4422	0.0000	0.4568	0.0019	0.2996	0.0969	0.4012	0.1039

* The probabilities (mean over 10,000 replicates) of host and parasite extinction for populations of different size for fixed sex ratio control (Fixed s.r.), and heterogamety models WZ, XY (all genotypes viable) (YY no r. = YY lethal, no replacement; YY rep. = YY lethal, with replacement). Probability of host (and consequently parasite) extinction = h. ext; parasite elimination only (and potential subsequent recovery of host) = p. elim. Initial failure of parasite to invade (not shown) accounts for the remainder of the probability space. Parameters as Fig. 1.

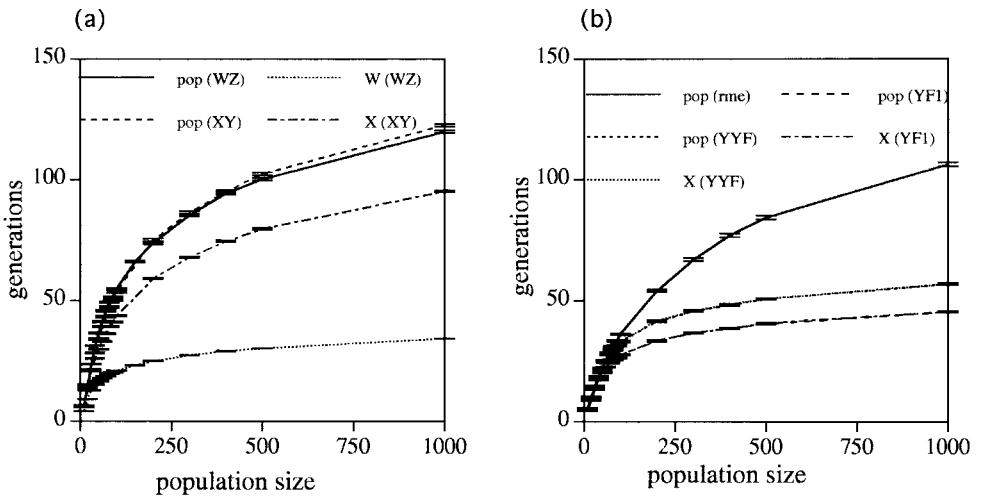


Fig. 6. Host–parasite co-existence in single populations. Graphs show the number of generations that parasite and host co-exist versus population size (mean of 10,000 replicates; error bars show 95% confidence intervals). (a) XX/XY and WZ/ZZ sex determination (as labelled: pop = host–parasite population duration; X, W = chromosome duration). (b) Fixed sex ratio control (pop. rme) and XX/XY with YY inviable (no replacement: YYF; with replacement: YF1).

Taylor, 1990). Intrinsic population recovery via chance exclusion of the parasite cannot occur in such populations due to the absence of uninfected females. Hence, if the sex ratio distorting effects of parasitism are severe enough to cause deterministic population decline (equation 1), systems with chromosomal sex determination and all genotypes viable will inevitably decline locally to extinction. Paradoxically, although elimination of female chromosomes may lengthen the decline phase, it precludes eventual population recovery.

LEVINS-TYPE DETERMINISTIC MODEL

The IBMs are somewhat limited as they can only be explored by execution and are extremely computationally intense. However, we can abstract aspects of the problem to a model in the style of Levins (1969). During the initial stages of infection within a patch, we assume that most dispersers are uninfected. Once parasite spread within a patch is complete, then most (or all; Taylor, 1990) of the dispersing females will be infected. Hence we can consider the metapopulation to be composed of three patch types:

- E = extinct, no animals present;
- C = clear, occupied by uninfected hosts;
- I = infectious, high prevalence of infected females.

We assume that a patch becomes infected with some probability s after the arrival of an infected host. Having been invaded, a patch will go extinct at rate e in units of the time to become infectious. During the infectious phase, the relative frequency of infected hosts is p. The probability of parasite extinction and intrinsic population recovery as the population crashes is denoted by r. Males and females are assumed to have an equal probability

m of dispersing to any patch in the metapopulation. Assuming that dispersal occurs in the adult phase before mating, recolonization of an extinct patch requires the simultaneous arrival (relative to our adjusted time scale) of both an uninfected female and a male.

Based on the above assumptions, we derive the following difference equations for the proportions of the three patch types:

$$\Delta E = e(1-r)I - \frac{m^2C^2E^2}{2} \tag{3}$$

$$\Delta C = \frac{m^2C^2E^2}{2} - spmCI + erI \tag{4}$$

$$\Delta I = spmCI - eI \tag{5}$$

This model differs from the standard Levins approach in that patch recolonization is a non-linear function of the population proportions, as a result of sexual reproduction and migration at the adult phase prior to mating (analogous to the timing of migration in the simulation model). An alternative model in which dispersal occurs at the adult stage after mating was also examined. This model does not require simultaneous arrival of both a male and a female to colonize a patch:

$$\Delta E = e(1-r)I - mCE \tag{6}$$

$$\Delta C = mCE - spmCI + erI \tag{7}$$

$$\Delta I = spmCI - eI \tag{8}$$

When local population recovery (r) is set to zero, equations (3)–(5) have the following solutions for $\mathrm{d}C = \mathrm{d}E = 0$ (setting $I = 1 - C - E$):

$$(E = 0,\ C = 1) \tag{9}$$

$$\left(E = \frac{-2ms^2p^2 + 2\sqrt{m^2s^4p^4 - 2e^2msp + 2em^2s^2p^2}}{2em},\ C = \frac{e}{spm}\right) \tag{10}$$

$$(C = 0,\ E = 1) \tag{11}$$

The phase plane (Fig. 7a) is characterized by the invasion line dictated by $e/spm \leq 1$, above which the only singularity is ($C = 1$, $E = 0$), which is stable. There is a Höpf bifurcation where the stable solution becomes a stable cycle; the value of this phase change was determined numerically, as it is the result of an eighth-order equation.

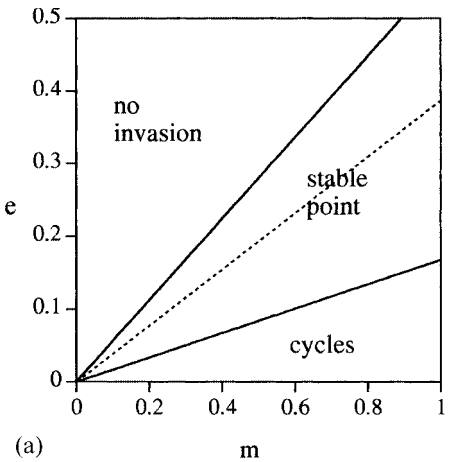
When dispersal is assumed to occur after mating (equations 6–8), we obtain the following solutions (with $r = 0$):

$$(E = 0,\ C = 1) \tag{12}$$

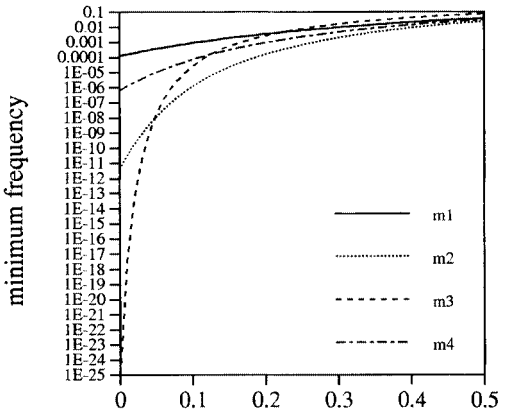
$$\left(E = \frac{spm - e}{m(sp+1)},\ C = \frac{e}{spm}\right) \tag{13}$$

$$(C = 0,\ E = 1) \tag{14}$$

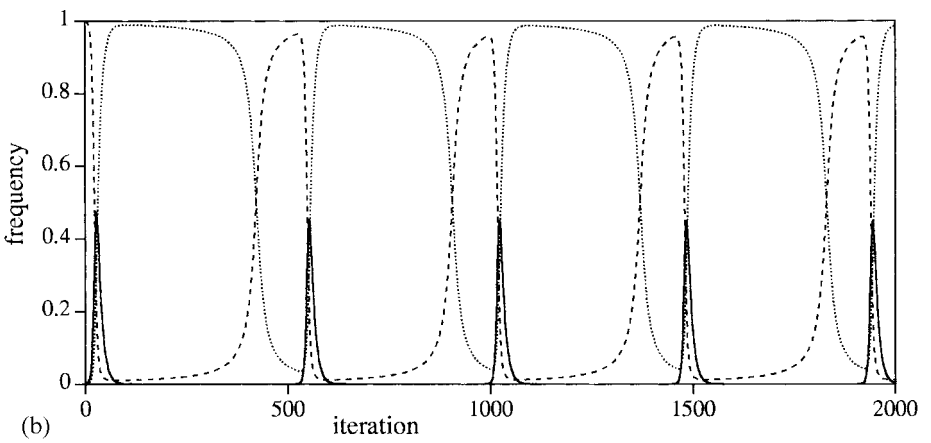
The phase plane is characterized by the same criterion for parasite invasion (Fig. 7a). There is a change of behaviour from a monotonic approach to a stable point, to a stable


no
invasion
stable
point
cycles
e
m
0.5
0.4
0.3
0.2
0.1
0
0
0.2
0.4
0.6
0.8
1

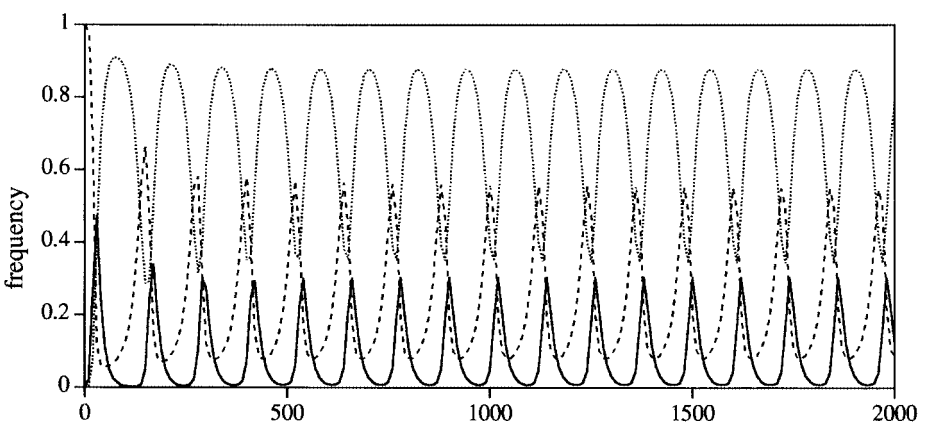
(a)


minimum frequency
prob. recovery (r)
m1
m2
m3
m4
0.1
0.01
0.001
0.0001
1E-05
1E-06
1E-07
1E-08
1E-09
1E-10
1E-11
1E-12
1E-13
1E-14
1E-15
1E-16
1E-17
1E-18
1E-19
1E-20
1E-21
1E-22
1E-23
1E-24
1E-25
0
0.1
0.2
0.3
0.4
0.5

(d)


frequency
iteration
1
0.8
0.6
0.4
0.2
0
0
500
1000
1500
2000

(b)


frequency
iteration
1
0.8
0.6
0.4
0.2
0
0
500
1000
1500
2000

(c)

point after damped oscillations, given by $e = (4s^2p^2m)/(1 + 4sp)$. No stable cycles are possible for this model.

Sample population dynamics for the first model (equations 3–5) are shown in Fig. 7b (for $r = 0$). This example shows asymmetric cycles in C, E and I wherein the frequency of infected patches remains at very low levels for extended periods of time. Such a rare parasite is unlikely to be sustained in real systems where stochastic events may dominate. For instance, if we consider the initial value of I to represent one infected individual, then the first minimum value of I (many orders of magnitude below that initial value) should be considered to represent no infected individuals.

When the recovery parameter r is left free, the stable solution for C remains unchanged, but the relationship between E and I is altered in both models. The solutions for the first model can be obtained by standard methods (not presented here for reasons of space). For the second model (equations 6–8):

$$(E = 0,\ C = 1) \tag{15}$$

$$\left(E = \frac{spm - e - r(spm + e)}{m(sp + 1 - rsp)},\ C = \frac{e}{spm}\right) \tag{16}$$

$$(C = 0,\ E = 1) \tag{17}$$

It can be shown for this model that the stable value of E decreases with increasing r; hence the equilibrium parasite prevalence ($I = 1 - C - E$) increases with patch recovery rate. Increasing r also has a damping effect on the population dynamics (Fig. 7c). This was investigated for the first model by calculating the minimum frequency of I for various values of r using numerical iteration. As r is increased from zero initially, the minimum frequency increases rapidly at first but is relatively insensitive to changes in r above about 0.2 (Fig. 7d). The effect of recovery is thus to stabilize the interaction: increasing recovery brings the parasite to a minimum frequency that may escape stochastic elimination.

The shape of the phase plane for these models is a good qualitative match to the behaviour observed in our simulations. At high patch fidelity (low dispersal), the parasite is unlikely to invade. At medium patch fidelity, parasite–host co-existence becomes possible; at low patch fidelity, we observe cycles that may overshoot leading to parasite, and possibly population, extinction. The effect of the sex determining mechanism is to alter r (the intrinsic rate of patch recovery). From the single population simulations we estimate

Fig. 7. Levins-type model of parasite–host dynamics. (a) Phase plane for solutions to the models. For example parameters $p = 0.7$ and $s = 0.8$, solid lines differentiate between the zones of no solution, single stable non-zero equilibrium and cycles for equations (3)–(5). For this model, single stable points are reached via damped oscillations for all parameter values in the stable zone. For equations (6)–(8), the zones of no invasion and stable points are split along the same solid line. The dotted line differentiates between stable points reached via damped oscillations (below) or critical damping (above line). (b) Example time-series showing cycles with long periods of cryptic parasitism (equations 3–5). Dashed line: frequency of uninfected patches; dotted line: empty patches; solid line: infected patches. Parameters: $p = 0.7$, $s = 0.8$, $m = 0.8$, $e = 0.1$, $r = 0$. (c) Example time-series when local populations have intrinsic recovery ($r = 0.2$; equations 3–5). Other parameters and key as in Fig. 7b. (d) Influence of recovery (r) on parasite prevalence. Graph shows minimum frequency of infected patches against r for four parameter sets (m1: $p = 0.7$, $s = 0.8$, $e = 0.1$, $m = 0.5$; m2: $p = 0.9$, $s = 0.8$, $e = 0.1$, $m = 0.5$; m3: $p = 0.7$, $s = 0.8$, $e = 0.1$, $m = 0.9$; m4: $p = 0.7$, $s = 0.9$, $e = 0.1$, $m = 0.5$).

$r \approx 0.11$ for fixed sex ratio control (at population size 1000; Table 1); but for the genotypic models (YY viable) r approaches zero. The relationship between co-existence and sex determination from the simulations (Fig. 1) is matched by the effect of r on the likelihood of the parasite becoming cryptic in the Levins model (Fig. 7d). Hence, both forms of model produce similar qualitative predictions, despite the different population structures assumed.

DISCUSSION

The following observations arise from this study:

- Metapopulation structure may enable parasite–host co-existence despite transience of local populations, through turnover of infected, uninfected and extinct patches. The dynamics are driven by feminizer-induced male rarity, with consequent deterministic decline within infected patches.
- Persistence and parasite prevalence depend on the host's sex determining mechanism: co-existence is unlikely for WZ or XY systems with homogametic viability, but is possible for fixed sex determination or XY with YY inviability.
- In persistent systems, parasite prevalence is maintained at a lower level than that predicted for unstructured populations (for conditions where deterministic local decline is predicted). The average mating success of infected females is below that of uninfected females (despite no difference in organism-level parameters) and provides a good predictor of metapopulation-level prevalence.
- Persistence and prevalence across the metapopulation are sensitive to host dispersal and parasite transmission; highly efficient parasites can be maintained only at low dispersal rates, resulting in a lower average prevalence.

The IBMs and analytical results indicate that metapopulation structure can stabilize an otherwise transient relationship for some models of sex determination, in agreement with Heuch (1978). Maintenance of host and sex ratio distorter results from extinction of infected patches and recolonization from uninfected patches, and can be considered a form of group selection (Heuch, 1978). However, we find that this process can only occur for limited transmission and dispersal rates and for a subset of sex determining mechanisms. With high host dispersal, the metapopulation approximates a single finite population; under low dispersal, local populations behave independently. High transmission efficiency reduces the range of dispersal rates that permit co-existence. Under male and female heterogamety, parasite–host co-existence is unlikely if all genotypes are viable and local populations are predicted deterministically to decline.

The models of Heuch (1978), Heuch and Chanter (1982) and Stenseth (1985) assumed 100% transmission of meiotic drive elements and a fixed 50 : 50 mechanism of sex determination. By including explicit models of host sex determination, we find that host–sex ratio distorter co-existence is not necessarily enhanced in metapopulations; under heterogametic sex determination, the association remains unstable if all genotypes are viable. Such systems eliminate female-determining alleles, as predicted by homogenous population models of heterogamety (Taylor, 1990) and implied more generally as a result of compensatory sex ratio evolution (Werren, 1987; Hatcher and Dunn, 1995). This reduces the probability of intrinsic population recovery, as males can only mate with infected females. The analytical models demonstrate that low rates of intrinsic recovery reduce the

probability of long-term parasite persistence: the parasite undergoes asymmetric cycles with long periods of very low frequency during which it would be vulnerable to stochastic elimination (Frank, 1997b). These results are consistent with the simulations showing only a very narrow range of parameters for parasite persistence. The similar behaviours of the IBMs and Levins equations suggest that this phenomenon is robust to alternative types of population structure and dispersal regime.

For stable associations, average parasite prevalence appears consistently lower than that predicted for infinite populations (for conditions satisfying the deterministic extinction criterion). Empirical measures for sex ratio distorters in *Gammarus duebeni* show prevalence in the range 10–40%, consistent with our fixed sex ratio control simulations (Dunn and Hatcher, 1997). Parasite prevalence in *Armadillidium vulgare* is intermediate between that predicted here for stepping stone metapopulations and elsewhere for infinite populations (Juchault *et al.*, 1992, 1993). The W chromosome appears to have been eliminated from at least three European populations of *Armadillidium vulgare* as a result of two feminizing factors (Rigaud *et al.*, 1997). The long-term persistence of feminizers in these populations (Juchault *et al.*, 1992, 1993) may indicate partial paternal transmission or interaction between the feminizers (Juchault *et al.*, 1992), or that male mate limitation in relation to transmission rate is not low enough to induce local population crashes (although there is laboratory evidence for some degree of mate limitation: T. Rigaud, personal communication).

The disparity between prevalence in metapopulation and unstructured population models is largely due to an emergent effect on the mating success of infected females. As males become rare in infected local populations, with constraints on male mating, females in these patches suffer reduced mating success. This affects infected females disproportionately as they only occur in infected patches. It is unlike classical fitness differences (e.g. emergence time effects on mating success: Chanter and Owen, 1972; sperm depletion of males carrying X-linked meiotic drive elements in *Drosophila*: Jaenike, 1996), as the disparity is only apparent when mating success is averaged across the metapopulation. A similar result has been demonstrated analytically for cytoplasmic male sterility factors in plants (McCauley and Taylor, 1997). Our simulations suggest that this mating disadvantage can account for more than 95% of the disparity between structured and homogenous prevalence predictions for moderate or large local population size (Fig. 5c).

Our results also suggest that, in contrast to the predictions of unstructured population models, high transmission efficiency may result in *lower* average long-term prevalence. For the fixed sex ratio system, parasites with high transmission efficiency are only maintained at low host dispersal rates, and average prevalence is reduced. This pattern can be explained in terms of selection processes acting at different levels; under strong male mating constraints, the dynamics are driven by feminizer-induced male rarity. Within patches, high transmission and feminization efficiency are favoured under individual (genic) selection on the parasite (Bull, 1983), but at the metapopulation scale, parasites with lower transmission efficiency drive local population extinction at a slower rate, attaining higher frequencies and more probable persistence overall. The evolutionary outcome would depend on the relative rates of individual and interdemic selection processes (McCauley and Taylor, 1997).

Other theoretical treatments have shown that, under certain conditions, metapopulation structure can stabilize otherwise transient associations, including meiotic drive (Ardlie, 1998), host–parasitoid (Comins *et al.*, 1992; Taylor, 1998), predator–prey (Sabelis *et al.*, 1991) and competitive (Hassell *et al.*, 1994; Dytham and Shorrocks, 1995) interactions. Our analysis suggests that the inclusion of evolutionary dynamics may affect the robust-

ness of these conclusions. In the host–feminizer system, selection against female-determining alleles in the host reduces the chances of intrinsic subpopulation recovery, which diminishes the rescuing effect induced by population structure. More generally, selection may operate on a time scale similar to that of ecological dynamics (Dieckmann, 1997), thus proscribing the state-space and affecting the types of interaction that are possible.

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REFERENCES

Ardlie, K.G. 1998. Putting the brake on drive: Meiotic drive of *t* haplotypes in natural populations of mice. *Trends Genet.*, **14**: 189–193.

Bull, J.J. 1983. *Evolution of Sex Determining Mechanisms*. Menlo Park, CA: Benjamin Cummings.

Bulnheim, H.-P. 1971. Entwicklung, Obertraging und parasitwirtbeziehungen vo *Thelohania hereditteria* sp. n. (Protozoa, microsporidia). *Z. Parasitkde*, **35**: 244–260.

Bulnheim, H.-P. and Vavra, J. 1968. Infection by the microsporidian *Octosporea effeminans* sp. n. and its sex determining influence in the amphipod *Gammarus duebeni. J. Parasitol.*, **54**: 241–248.

Chanter, D.O. and Owen, D.F. 1972. The inheritance and population genetics of sex ratio in the butterfly *Acraea encedon. J. Zool. Lond.*, **166**: 363–383.

Comins, H.N., Hassell, M.P. and May, R.M. 1992. The spatial dynamics of host–parasitoid systems. *J. Anim. Ecol.*, **61**: 735–748.

Dieckmann, U. 1997. Can adaptive dynamics invade? *Trends Ecol. Evol.*, **12**: 128–131.

Dytham, C. and Shorrocks, B. 1995. Aggregation and the maintenance of genetic diversity: An individual-based cellular model. *Evol. Ecol.*, **9**: 508–519.

Dunn, A.M. and Hatcher, M.J. 1997. Prevalence, transmission and intensity of infection by a microsporidian sex ratio distorter in natural *Gammarus duebeni* populations. *Parasitology*, **114**: 231–236.

Dunn, A.M., Hatcher, M.J., Terry, R.S. and Tofts, C. 1995. Evolutionary ecology of vertically transmitted parasites: Transovarial transmission of a sex ratio distorter in *Gammarus duebeni. Parasitology*, **111**: S91–S110.

Fisher, R.A. 1930. *The Genetical Theory of Natural Selection*. Oxford: Clarendon Press.

Frank, S.A. 1997a. Cytoplasmic incompatibility and population structure. *J. Theor. Biol.*, **184**: 327–330.

Frank, S.A. 1997b. Spatial processes in host–parasite genetics. In *Metapopulation Biology* (I. Hanski and M.E. Gilpin, eds), pp. 325–352. San Diego, CA: Academic Press.

Hamilton, W.D. 1967. Extraordinary sex ratios. *Science*, **156**: 477–488.

Hassell, M.P., Comins, H.N. and May, R.M. 1994. Species coexistence and self-organizing spatial dynamics. *Nature*, **370**: 290–292.

Hatcher, M.J. and Dunn, A.M. 1995. Evolutionary consequences of sex ratio distortion by cytoplasmically inherited feminizing factors. *Phil. Trans. R. Soc. Lond. B*, **348**: 445–456.

Hatcher, M.J. and Tofts, C. 1995. The effect of point of expression on ESS sex ratios. *J. Theor. Biol.*, **175**: 263–266.

Hatcher, M.J., Taneyhill, D.E., Dunn, A.M. and Tofts, C. 1999. Population dynamics under parasitic sex ratio distortion. *Theor. Pop. Biol.*, **56**: 11–28.

Heuch, I. 1978. Maintenance of butterfly populations with all-female broods under recurrent extinction and recolonization. *J. Theor. Biol.*, **75**: 115–122.

Heuch, I. and Chanter, D.O. 1982. The persistence of abnormal sex ratios in the African butterfly, *Acraea encedon. Oikos*, **38**: 228–233.

Hurst, L.D., Atlan, A. and Bengtsson, B.O. 1996. Genetic conflicts. *Q. Rev. Biol.*, **71**: 317–364.

Jaenike, J. 1996. Sex-ratio meiotic drive in the *Drosophila quinaria* group. *Am. Nat.*, **148**: 237–254.

Juchault, P., Rigaud, T. and Mocquard, J.P. 1992. Evolution of sex-determining mechanisms in a wild population of *Armadillidium vulgare* Latr. (Crustacea, Isopoda): Competition between two feminizing parasitic sex factors. *Heredity*, **69**: 382–390.

Juchault, P., Rigaud, T. and Mocquard, J.P. 1993. Evolution of sex determination and sex ratio variability in wild populations of *Armadillidium vulgare* (Latr.) (Crustacea, Isopoda): A case study in conflict resolution. *Acta Oecologica*, **14**: 547–562.

Levins, R. 1969. Some demographic and genetic consequences of environmental heterogeneity for biological control. *Bull. Entomol. Soc. Am.*, **15**: 237–240.

McCauley, D.E. and Taylor, D.R. 1997. Local population structure and sex ratio: Evolution in gynodioecious plants. *Am. Nat*., **150**: 406–419.

Naylor, C., Adams, J. and Greenwood, P. 1988. Population dynamics and adaptive sexual strategies in a brackish water crustacean, *Gammarus duebeni. J. Anim. Ecol.*, **57**: 493–507.

Rigaud, T. and Juchault, P. 1993. Conflict between feminizing sex ratio distorters and an autosomal masculinizing gene in the terrestrial isopod. *Armadillidium vulgare* Latr. *Genetics*, **133**: 247–252.

Rigaud, T., Juchault, P. and Mocquard, J.P. 1997. The evolution of sex determination in isopod crustaceans. *Bioessays*, **19**: 409–416.

Sabelis, M.W., Diekmann, O. and Jansen, V.A.A. 1991. Metapopulation persistence despite local extinction: Predator–prey models of the Lotka-Volterra type. *Biol. J. Linn. Soc.*, **42**: 267–283.

Stenseth, N.C. 1985. A new hypothesis for explaining the maintenance of the all-female broods in the African butterfly *Acraea encedon. Hereditas*, **103**: 205–209.

Taylor, A.D. 1998. Environmental variability and the persistence of parasitoid–host metapopulation models. *Theor. Pop. Biol.*, **53**: 98–107.

Taylor, D.R. 1990. Evolutionary consequences of cytoplasmic sex ratio distorters. *Evol. Ecol.*, **4**: 235–248.

Terry, R.S., Smith, J.E. and Dunn, A.M. 1998. Impact of a novel feminizing microsporidian parasite on its crustacean host. *J. Eukaryotic Microbiol.*, **45**: 497–501.

Terry, R.S., Smith, J.E., Bouchon, D., Rigaud, T., Duncanson, P., Sharpe, R.G. and Dunn, A.M. 1999. Ultrastructural characterisation and molecular taxonomic identification of *Nosema granulosis* n. sp., a transovarially transmitted feminizing (TTF) microsporidium. *J. Eukaryotic Microbiol.*, **46**: 492–499.

Wade, M.J. and Stevens, L. 1994. The effect of population subdivision on the rate of spread of parasite-mediated cytoplasmic incompatibility. *J. Theor. Biol.*, **167**: 81–87.

Wallace, B. 1948. Studies on 'sex ratio' in *Drosophila pseudoobscura*. I. Selection and 'sex ratio'. *Evolution*, **2**: 189–217.

Watt, P.J. 1994. Parental control of sex ratio in *Gammarus duebeni*, an organism with environmental sex determination. *J. Evol. Biol.*, **7**: 177–187.

Werren, J.H. 1987. The coevolution of autosomal and cytoplasmic sex ratio factors. *J. Theor. Biol.*, **124**: 313–334.

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

Werren, J.H. and Beukeboom, L.W. 1993. Population genetics of a parasitic chromosome: Theoretical analysis of psr in subdivided populations. *Am. Nat.*, **142**: 224–241.

Werren, J.H. and Beukeboom, L.W. 1998. Sex determination, sex ratios, and genetic conflict. *Ann. Rev. Ecol. Syst.*, **29**: 233–261.

Werren, J.H., Nur, U. and Wu, C.-I. 1988. Selfish genetic elements. *Trends Ecol. Evol.*, **3**: 297–302.