Quantifying the effects of parasites on the maintenance of sex

Sang Woo Park, Benjamin M Bolker

November 16, 2017

1 Introduction

Sexually reproduction is followed by numerous costs (Lehtonen et al., 2012), and these costs are often attributed to cost of producing males (Smith, 1978). As males cannot produce offspring, a sexually reproducing population should be outgrown by an asexually reproducing population growing twice as fast (given that the sexual population produces 50% males and 50% females) – hence the infamous *two-fold cost of sex* (Smith, 1978). However, the two-fold cost of sex relies on the assumption that all else is equal, and this is not necessarily true in nature. In fact, sexual reproduction is much more common in nature (Vrijenhoek, 1998). So what drives sex to persist?

One explanation for sex is the Red Queen Hypothesis (Bell, 1982). The Red Queen Hypothesis predicts sexually reproducing organisms to overcome the two-fold cost of sex under strong parasite selection by producing genetically diverse offspring that are resistant to infection (Haldane, 1949; Jaenike, 1978; Hamilton, 1980). Hosts with rare genotypes are expected to result in higher fitness and become common eventually. Furthermore, parasites coevolves with the host population to infect the common "rare" genotype [CITE], and negative frequeny dependnece drives an oscillation in genotypic frequencies in host and parasite populations (Clarke, 1976; Hamilton, 1980).

Since the Red Queen Hypothesis has been postulated, much of theoretical work has focused on figuring out conditions under which parasites can maintain sexual reproduction.

On the other hand, empiricists have tried to quantify the Red Queen.

While the Red Queen Hypothesis is well supported both empirically and theoretically, there still remains a gap between theory and data. Many models for Red Queen Hypothesis rely on simplifying assumption that are not applicable to natural populations (Ashby and King, 2015). For example,

Recent studies have shown that ecological feedbacks can allow sex to be maintained more easily [CITE]. We find that a simple model can capture the dynamics Here, we try to bridge this gap further.

In this study, we extend the model suggested by Lively (2010b) to include stochasticity and population structure and fit the to data from Dagan et al.

(2013); McKone et al. (2016); Vergara et al. (2014) using approximate bayesian computation (ABC). [Something about what we found out from the model fitting] Using posterior distributions obtained from the fit, we perform power analysis to test the idea that infection prevalence is positively correlated with frequency of sexual reproduction Lively (2001). We find that cycling of parasites and hosts can lead to negative correlation between prevalence of infection and sex. Instead, positive correlated predicted by Lively (2001) is driven by populations that do not go through Red Queen dynamics (i.e., having low level of sexual and infection).

2 Methods

2.1 Model

We model obligate sexual hosts competing with obligate asexual hosts in multiple population by extending the model introduced by Lively (2010b). A model that Lively (2010b) used is essentially an SI model on a discrete time scale with natural mortality and virulence (reduction in offspring production by infected hosts). It is a suitable canditate for this study as it captures essential structures that are present in basic epidemiological and population population dynamics models and is general enough to be applied to broad systems in nature. We do not consider mechanistic details of the snail-trematode system such as life history of trematodes (Vergara et al., 2014) as it would require us to estimate or make assumptions on parameters on mechanisms, both of which are unrealistic.

All hosts are assumed to be diploids with two biallelic loci, and parasites are assumed to be haploids. Let $S_{ij}^k(t)$ and $A_{ij}^k(t)$ be the number of sexual and asexual hosts with genotype ij from population k at generation t. For simplicity, we drop the superscript representing population and write $S_{ij}(t)$ and $A_{ij}(t)$ unless necessary. Following Lively (2010b), the expected number of offsprings (without recombination or outcrossing) produced by a sexual population is given by

$$S'_{ij} = c_b(1-s)\left(W_U S_{ij,U}(t) + W_I S_{ij,I}(t)\right), \tag{1}$$

where s is the proportion of males produced, $S_{ij,U}$ and $S_{ij,I}$ are the number of uninfected and infected sexual hosts in a population, and W_U and W_I are their corresponding fitnesses. We allow for cost of sex to vary by multiplying c_b to the growth term ($2/c_b$ corresponds to two fold cost of sex) (Ashby and King, 2015). Equivalently, S'_{ij} is the amount of genotypic contribution by sexual hosts to the next generation.

Asexual hosts are assumed to be strictly clonal. Then, the expected number of offsprings produced by an asexual population is given by

$$A'_{ij} = W_U A_{ij,U}(t) + W_I A_{ij,I}(t), \tag{2}$$

where $A_{ij,U}$ and $A_{ij,I}$ are the number of uninfected and infected asexual hosts in a population.

We assume that there is mixing between population, determined by rate ϵ_{mix}. Then, the expected number of offspring in the next generation (accounting for contributions from all populations) is given by

$$\begin{aligned}
\mathrm{E}\left(S_{ij}^{k}(t+1)\right) &= \mathrm{Sex}\left(\left(1-\epsilon_{\text{mix}}\right)\left(S_{ij}^{k}\right)' + \frac{\epsilon_{\text{mix}}}{n_{\text{population}}-1}\sum_{l\neq k}\left(S_{ij}^{l}\right)'\right), \\
\mathrm{E}\left(A_{ij}^{k}(t+1)\right) &= \left(1-\epsilon_{\text{mix}}\right)\left(A_{ij}^{k}\right)' + \frac{\epsilon_{\text{mix}}}{n_{\text{population}}-1}\sum_{l\neq k}\left(A_{ij}^{l}\right)',
\end{aligned} \tag{3}$$

where Sex is a function defined by recombination at a rate r_{host} and outcrossing, and $n_{\text{population}}$ is the number of populations present in the system. We then take a poisson random variable to simulate process error and allow for stochastic migration to avoid fixation:

$$\begin{aligned}
S_{ij}^{k}(t+1) &\sim \mathrm{Poisson}\left(\lambda = \mathrm{E}\left(S_{ij}^{k}(t+1)\right)\right) + \mathrm{Bernoulli}\left(p = p_{ij,\text{sex}}\right), \\
A_{ij}^{k}(t+1) &\sim \mathrm{Poisson}\left(\lambda = \mathrm{E}\left(A_{ij}^{k}(t+1)\right)\right) + \mathrm{Bernoulli}\left(p = p_{ij,\text{asex}}\right),
\end{aligned} \tag{4}$$

where $p_{ij,\text{sex}}$ and $p_{ij,\text{asex}}$ are the probability of a sexual and an asexual host with genotype ij entering the popualation.

Infection is modeled using the matching alleles model (Otto and Michalakis, 1998). We assume that heterozygous individuals are equally susceptible to parasites that match either genotypes

The expected number of infected hosts that carry parasite with genotype i at generation t is given by:

$$I_i(t) = \sum_{p} 2^{\delta_{ij}}\left(S_{ip,i,I}(t) + A_{ip,i,I}(t)\right), \tag{5}$$

where $S_{ip,i,I}$ and $A_{ip,i,I}$ are the expected number of sexual and asexual hosts infected with genotype i parasite. Following Ashby and King (2015), we assume that mutation can occur in one locus with probability r_{parasite}. We also allow for external migration of an infected host carrying parasite i with probability $p_{i,\text{parasite}}$ to avoid fixation.

The amount of infectious contacts made by infected hosts from a population is given by $\lambda_i^k = \beta^k I_i'^k(t)$, where β^K is the transmission rate at each population, and $I_i'(t)$ is the number of infected hosts accounting for mutation. Since we allow for mixing between population, infected hosts in a population can make contact to susceptible hosts in other populations as well. Then, all infectious contacts made by infected hosts that applies to a host in a single population is

$$\lambda_{i,\text{total}} = (1-\epsilon_{\text{site}})\lambda_i + \frac{\epsilon_{\text{site}}}{n_{\text{site}}-1}\sum_{l\neq k}\lambda_i^l \tag{6}$$

Then, the force of infection that a susceptible host experiences is

$$\mathrm{FOI}_{ij}^{k} = \frac{\lambda_{i,\text{total}} + \lambda_{j,\text{total}}}{2N(t+1)} \tag{7}$$

The probability of infection for a host with genotype ij at site k in the next generation is

$$P_{ij}^{k}(t+1) = 1 - \exp\left(\mathrm{FOI}_{ij}^{k}\right). \tag{8}$$

Finally, number of infected hosts in the next generation is determined by a binomial process:

$$\begin{aligned} S_{ij,I}(t+1) &\sim \mathrm{Binom}(S_{ij}(t+1), P_{ij}), \\ A_{ij,I}(t+1) &\sim \mathrm{Binom}(A_{ij}(t+1), P_{ij}). \end{aligned} \tag{9}$$

Expected number of individuals infected with haplotype i in the next generation is given by a ratio of λ:

$$\begin{aligned} S_{ij,i,I}(t+1) &= \frac{\lambda_{i,\mathrm{total}}}{\lambda_{i,\mathrm{total}} + \lambda_{j,\mathrm{total}}} S_{ij,I}(t+1) \\ A_{ij,i,I}(t+1) &= \frac{\lambda_{i,\mathrm{total}}}{\lambda_{i,\mathrm{total}} + \lambda_{j,\mathrm{total}}} A_{ij,I}(t+1) \end{aligned} \tag{10}$$

2.2 Simulation design and parameterization

Most Red Queen models have studied a competition between a single asexual genotype and sexual genotypes or have assumed equal genetic diversity of asexual and sexual hosts (see (Ashby and King, 2015)) but neither of these assumptions are realistic. Instead, Ashby and King (2015) adopted a more realistic approach by allowing for stochastic migration of an asexual genotype to a population. Here, we combine these methods. We allow for stochastic migration of migration of asexual hosts with genotypes genotypes but fix number of asexual genotypes (denoted by G_{asex}) that can be present in the population, while the number of sexual genotypes (G_{sex}) that can be present in the population is equal to size of the genotypic space (= 10 in diploid hosts with two biallelic loci).

In the beginning of every simlation, G_{asex} is randomly chosen between 1 and 10 and asexual genotypes that can be introduced to the population are uniformly sampled from the entire genotypic space. To account for differing number of sexual and asexual genotypes, we let

$$\begin{aligned} p_{ij,\mathrm{sex}} &= 1 - (1 - p_{\mathrm{host}})^{1/G_{\mathrm{sex}}}, \\ p_{ij,\mathrm{asex}} &= \begin{cases} 1 - (1 - p_{\mathrm{host}})^{1/G_{\mathrm{asex}}} & \text{if } ij \in \{\text{asexual genotypes}\} \\ 0 & \text{otherwise} \end{cases}, \end{aligned} \tag{11}$$

where p_{host} is the probability that at least one sexual and asexual host enters the population in a generation. We scale the probability of infected host carrying parsite genotype i in a similar way for interpretability:

$$p_{i,\mathrm{parasite}} = 1 - (1 - p_{\mathrm{infected}})^{1/4}, \tag{12}$$

where p_{infected} is the probability that at least one infected host enters the population in a generation.

Something about prior distribution...

Each simulation consists of 40 populations. Every population consists of 2000 sexual hosts where 80 of them are infected. They are assumed to be in Hardy-Weinberg equilibrium with ratio between alleles being exactly half. Simulation runs for 500 generations without introduction of asexuals. At generation 501, 10 asexual hosts of a single genotype are introduced to each population (note that asexual genotype introduced can vary across population) and simulation runs for 600 generations while allowing for stochastic migration of asexuals.

2.3 Approximate Bayesian Computation

We use Approximate Bayesian Computation (ABC) to fit the model.

2.4 Data

We consider two snail-trematode population in New Zealand (McKone et al., 2016; Vergara et al., 2014) and a similar snail-trematode population in Isral (Dagan et al., 2013). First, the snail-trematode system in New Zealand has been extensively studied under the Red Queen Hypothesis [CITE] so we expect a Red Queen model to fit well. Second, [Something about Israel snails being different]. Finally, by considering both spatial (Dagan et al., 2013; McKone et al., 2016) and spatiotemporal data (Vergara et al., 2014), we can compare how structure of the data may affect model fits. Data for Vergara et al. (2014) and Dagan et al. (2013) were obtained from their Dryad repository [CITE] and data for McKone et al. (2016) was extracted from their figure.

3 Results

3.1 Parameter estimation

Our model estimates wide ranges of parameters across data sets (Fig. 1). The most surprising result is the wide posterior of the scale parameter, c_b, for cost of sex (Fig. 1). Ashby and King (2015) defined c_b as additional costs and benefits of sex, where $c_b = 1$ corresponds the two fold cost. Under their interpretation, our estimate corresponds to the following 95% credible intervals for cost of sex: [???]. However, the meaning of the parameter changes from an inferential point of view.

In the absence of the parameter c_b (i.e, when $c_b = 1$), our model assumes two fold cost of sex in growth rate. Then, an estimate of $c_b > 1$ can be interpreted as the amount of additional compensation required in order to overcome the two fold cost of sex. Additional compensation may imply other mechanisms that maintains, reduced cost of sex, or higher genetic diversity, a point to which we

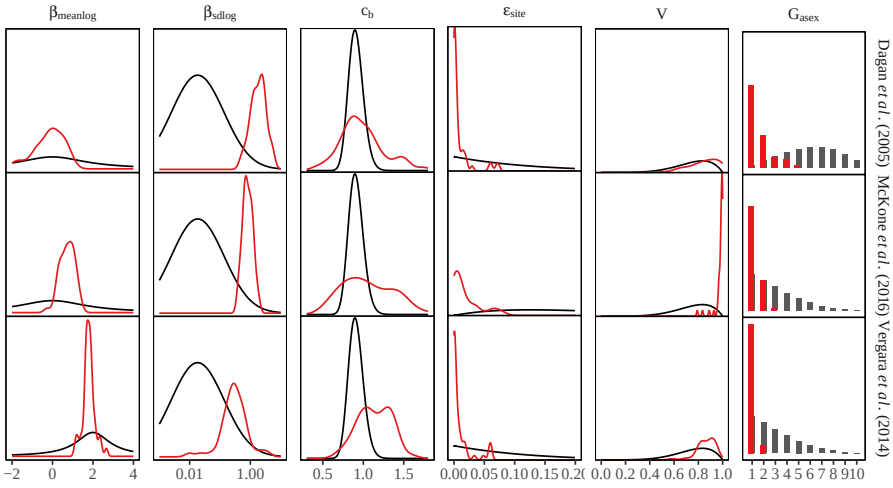


Figure 1: **Need caption.** Need caption

will come back later. Likewise, an estimate of $c_b < 1$ implies that the model can sufficiently produce observed data.

We also find that the model estimates high virulence overall and almost 100% virulence for the system observed by McKone et al. (2016).

3.2 Model fit

We find that a simple Red Queen model with spatial structure can match observed mean and variation in proportion infected and sexually reproducting well (Fig. 2). The one discrepancy is that the model overestimates prevalence of infection, given similar level of sexual reproduction. The difference between model prediction and observed data can tell us about our model as well as the snail-trematode system. This discrepancy is likely to be caused by the most obvious limitation of the model: two biallelic loci is not sufficient to capture the genetic diversity of the snail-trematode system. Other theoretical studies have shown that higher genetic diversity can reduce prevalence of infection and lead to better maintenance of sexual reproduction (Lively, 2010a; King and Lively, 2012; Ashby and King, 2015).

We also compared mean infection prevalence and mean proportion of sexually reproducing hosts of each simulated population against observed data (Fig. 3). Although simulated data could match the chosen summary statistics of the snail population in Israel (Dagan et al. (2013) in Fig. 2), we find that our model does not capture the observed trend (Dagan et al. (2013) in Fig. 3).

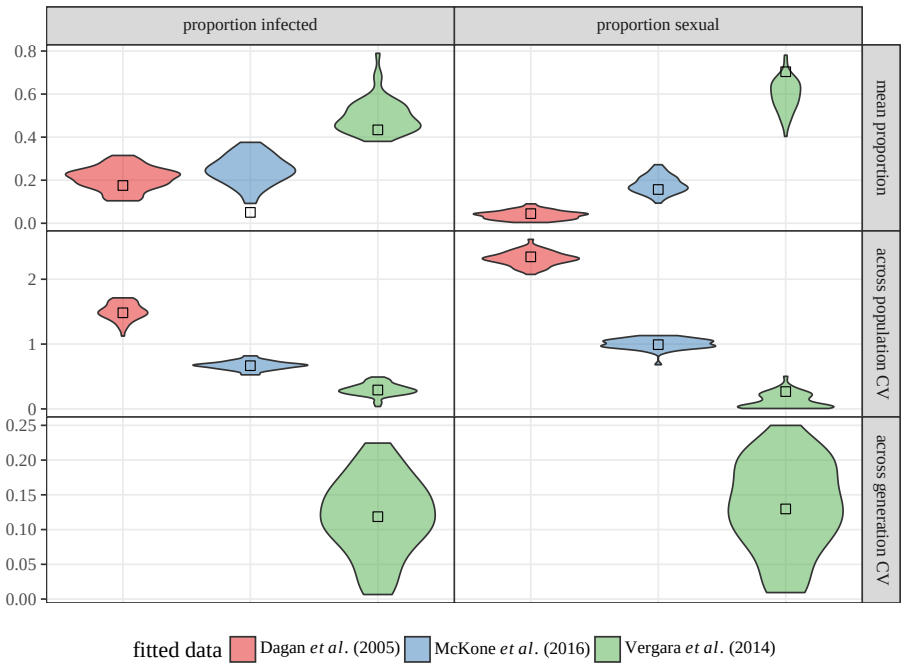
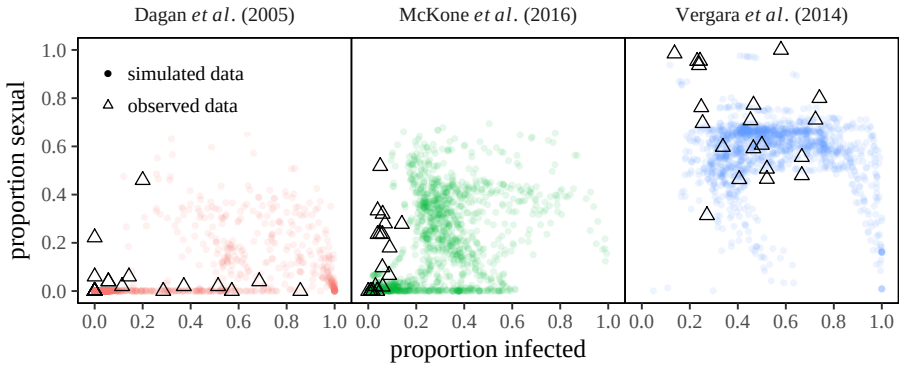


Figure 2: **Need caption.** Need caption



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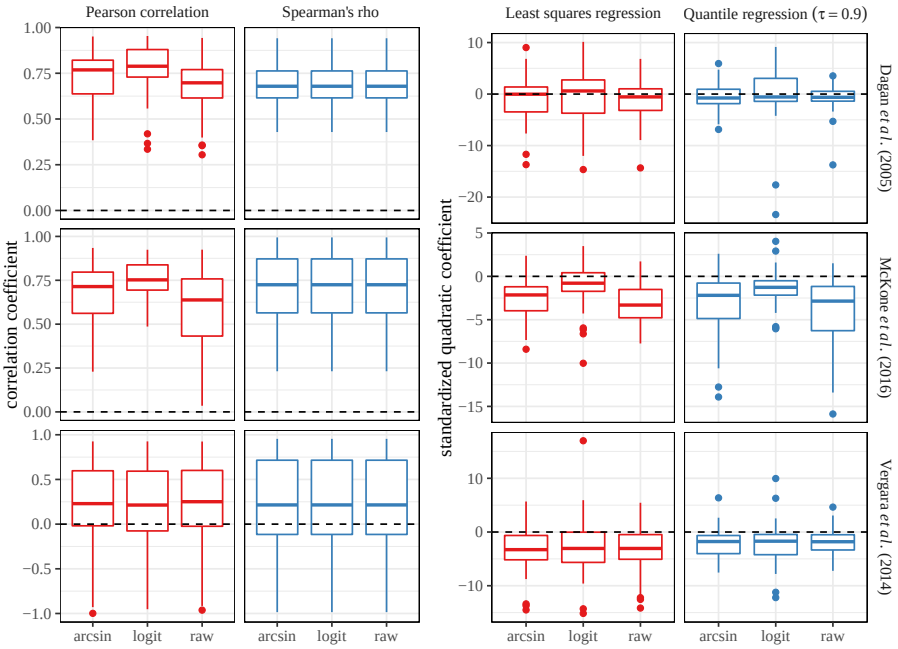

Figure 4: **Need caption.** Need caption

3.3 Power analysis

4 Discussion

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