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Population genetics of complex life-cycle parasites: an illustration with trematodes

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Abstract

Accurate inferences on population genetics data require a sound underlying theoretical null model. Organisms alternating sexual and asexual reproduction during their life-cycle have been largely neglected in theoretical population genetic models, thus limiting the biological interpretation of population genetics parameters measured in natural populations. In this article, we derive the expectations of those parameters for the life-cycle of monoecious trematodes, a group comprising several important human and livestock parasites that obligatorily alternate sexual and asexual reproduction during their life-cycle. We model how migration rates between hosts, sexual and asexual mutation rates, adult selfing rate and the variance in reproductive success of parasites during the clonal phase affect the amount of neutral genetic diversity of the parasite (effective population size) and its apportionment within and between definitive hosts (using F-statistics). We demonstrate, in particular, that variance in reproductive success of clones, a parameter that has been completely overlooked in previous population genetics models, is very important in shaping the distribution of the genetic variability both within and among definitive hosts. Within definitive hosts, the parameter F_{IS} (a measure of the deviation from random mating) is decreased by high variance in clonal reproductive success of larvae but increased by high adult self-fertilisation rates. Both clonal multiplication and selfing have similar effects on between-host genetic differentiation (F_{ST}). Migration occurring before and after asexual reproduction can have different effects on the patterns of F_{IS}, depending on values of the other parameters such as the mutation rate. While the model applies to any hermaphroditic organism alternating sexual and clonal reproduction (e.g. many plants), the results are specifically discussed in the light of the limited population genetic data on monoecious trematodes available to date and their previous interpretation. We hope that our model will encourage more empirical population genetics studies on monoecious trematodes and other organisms with similar life-cycles.

Keywords: F-statistics; Complex life-cycle; Asexual reproduction; Self-fertilisation; Effective population size; Trematodes

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1. Introduction

The study of population genetic structure of living organisms is central to the understanding of micro-evolutionary processes (Nevo et al., 1984; Nadler, 1995). For small organisms and in particular parasites, the analysis of genetic variation at different hierarchical levels is often the only way to investigate natural population parameters such as gene flow, size of reproductive units and breeding strategies (Nadler, 1995). Population genetic structure can also constitute a powerful tool to investigate epidemiological patterns (Paterson and Viney, 2000).

However, interpreting measurements of genetic variation and its distribution in terms of biological parameters such as dispersal/transmission rates, breeding systems or effective population size is often very difficult. Two main reasons can be invoked to explain this difficulty: (i) a multiplicity of causes can explain specific patterns of genetic variation (e.g. heterozygote deficits can be explained by self-fertilisation, preferential mating between kin, Walhund effects, selection) (Hartl and Clark, 1997), (ii) the lack of clear expectations when the organisms under scrutiny display life-cycles that greatly depart from those used in theoretical population genetic models. Parasites with

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complex life-cycles such as digenean trematodes clearly belong to this category of organisms.

All trematodes (about 8000 species; e.g. De Meeûs and Renaud, 2002) are parasitic, many of them being medically and/or economically relevant (e.g. *Schistosoma* spp.; *Fasciola* spp.; *Paragonimus* spp. and *Clonorchis* spp.) (Combes, 2001). They are characterised by complex life-cycles with an obligate alternation of asexual and sexual reproduction during their lifespan. The asexual phase occurs within an invertebrate intermediate host (generally a mollusk) in which genetically identical larvae (clones) are produced whereas the sexual phase occurs in the vertebrate definitive host (aquatic or not). To date, no study has investigated the impact of this clonal phase on the genetic structure of parasites within definitive hosts or the importance of the obligate alternation of sexual and asexual reproduction. It has however been suggested that the severe deficits of heterozygotes observed in monoecious trematode populations might be produced by the aggregation of clones among hosts, the possibility of selfing as well as mating within clones (Lydeard et al., 1989; Mulvey et al., 1991; Vilas et al., 2003). Clonal reproduction could also contribute to the strong genetic differentiation observed between hosts and geographic locations (Mulvey et al., 1991; Theron et al., 2004). These arguments are strictly verbal and it remains largely unclear how and how much each of these factors shapes the distribution of genetic variation both within and between hosts thus precluding biological interpretation of population genetic parameters estimated from real data.

In this article, we use a finite island model to explore the effects of the alternation of sexual and asexual reproduction in monoecious trematodes on the partitioning of variance among and within definitive hosts. Apportionment of genetic variation at different hierarchical levels is described using the commonly used fixation indices (also called F-statistics: F_{IS} and F_{ST}; Wright, 1965). The model allows investigating how gene variation is affected by (i) the degree of mixing among parasites originating from different hosts at each new infection (represented in the model by the migration rates before and after clonal reproduction), (ii) sexual and asexual mutation rates, (iii) different self-fertilisation rates in adult parasites within definitive hosts and (iv) the variance in the reproductive success of parasites during the larval clonal phase (which may be seen as a measure of 'reproductive skew'). Finally, this model allows investigation of the effect of different population parameters on the effective population size of trematodes.

2. Materials and methods

2.1. Assumptions and parameter definitions

As trematodes exploit different hosts over their life-cycle, we have to define separately the genetic structure of parasite populations in intermediate and definitive hosts. An Adult Parasite Subpopulation (thereafter abbreviated APS) is composed of all adult parasites within the same definitive host individual (sometimes referred as 'infrapopulation'). A Larval Parasite Subpopulation (LPS thereafter) is composed of parasite larvae reproducing asexually. As there is no genetic recombination at this stage, LPSs can be defined more loosely than APSs. One could for example consider a LPS as the parasites within the same intermediate host only, or more generally as all larvae found in a subpopulation of intermediate hosts (e.g. within a puddle). Due to the absence of genetic recombination at the larval stage, the exact definition of LPS does not affect the outcome of the model. The term 'population' corresponds to the hierarchical level encompassing all APSs or LPSs. To avoid any confusion, we will specify throughout the text whether we are referring to larval parasites or adult parasites.

We consider a monoecious population of trematodes subdivided into n APSs (finite island model), each consisting of N parasite individuals. The detailed life-cycle is represented in Fig. 1. As trematodes may reproduce by self-fertilisation (see e.g. Trouvé et al., 1996), we incorporate partial selfing in our model. Thus, for adults, reproduction within definitive host comprises selfing with probability s and random outbreeding with the corresponding probability $1-s$. For simplicity, we assume non-overlapping generations (the individuals reproduce and die). According to the island model, we assume that a proportion $1-m_1$ of the offspring produced in the same definitive host remains clustered and subsequently infects the same intermediate host (or subpopulation of intermediate hosts), while the remaining offspring m_1 infect other intermediate host (or subpopulation of intermediate hosts) at random. We further assume that, just after infection, each LPS contains exactly N parasite individuals. These N individuals produce a large number of asexual offspring within the intermediate host and die. The parameter c represents the amount of

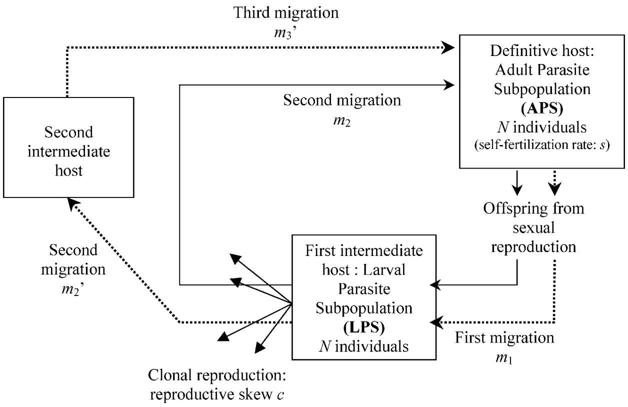

Fig. 1. Schematic representation of the life-cycle of monoecious trematodes with one (full line) or two intermediate hosts (dashed line). In our model, we followed the life-cycle with only one intermediate host. However, the second life-cycle can reduce to the first one by considering that m_2 is just $m_2' + m_3'$.