

Polymorphism in Multilocus Host–Parasite Coevolutionary Interactions

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ABSTRACT

Numerous loci in host organisms are involved in parasite recognition, such as major histocompatibility complex (MHC) genes in vertebrates or genes involved in gene-for-gene (GFG) relationships in plants. Diversity is commonly observed at such loci and at corresponding loci encoding antigenic molecules in parasites. Multilocus theoretical models of host–parasite coevolution predict that polymorphism is more likely than in single-locus interactions because recurrent coevolutionary cycles are sustained by indirect frequency-dependent selection as rare genotypes have a selective advantage. These cycles are stabilized by direct frequency-dependent selection, resulting from repeated reinfection of the same host by a parasite, a feature of most diseases. Here, it is shown that for realistically small costs of resistance and virulence, polycyclic disease and high autoinfection rates, stable polymorphism of all possible genotypes is obtained in parasite populations. Two types of epistatic interactions between loci tend to increase the parameter space in which stable polymorphism can occur with all possible host and parasite genotypes. In the parasite, the marginal cost of each additional virulence allele should increase, while in the host, the marginal cost of each additional resistance allele should decrease. It is therefore predicted that GFG polymorphism will be stable (and hence detectable) when there is partial complementation of avirulence genes in the parasite and of resistance genes in the host.

HOST–PARASITE interactions are recognized as a major evolutionary force producing biological diversity. Genetic variation for resistance reduces the probability that an individual parasite can infect an individual host (MAY and ANDERSON 1990) and conversely, genetic diversity at parasite recognition loci increases the range of potentially susceptible hosts. Spatial and temporal genetic polymorphism is commonly found in nature at loci involved in host–parasite recognition such as the major histocompatibility complex (MHC) in vertebrates (APANUS *et al.* 1997; HILL 2001) or genes involved in gene-for-gene (GFG) relationships, a common feature of plant–parasite interactions (THRALL *et al.* 2001; LAINE 2004). In both the MHC and the GFG systems, hosts and parasites may have multiple interacting loci (APANUS *et al.* 1997; HILL 2001; PALOMINO *et al.* 2002). Interactions among several plant resistance (*RES*) genes and parasite avirulence (*AVR*) genes have been documented for numerous diseases, of which the best studied include barley powdery mildew (JORGENSEN 1994), flax rust (THRALL *et al.* 2001), and rice blast (DEWIT 1992), as well as several diseases of the model plant *Arabidopsis thaliana* (HOLUB 2001).

In multilocus systems of host–parasite interactions, negative indirect frequency-dependent selection (FDS)

is thought to account for the great polymorphism found in MHC genes (APANUS *et al.* 1997; HILL 2001; BORGHANS *et al.* 2004) and GFG genes (FRANK 1993a; SASAKI 2000; SALATHE *et al.* 2005; SEGARRA 2005). In this hypothesis, host and parasite genotypes have a selective advantage when they are rare in coevolving populations. This leads to sustained coevolutionary cycles because when a parasite rare allele is selected, its frequency increases, selecting in turn for the corresponding resistant host genotype. It is hypothesized that these regular cycles of genotype frequencies prevent invasion by a single genotype, especially when mutations introduce new alleles in populations (SASAKI 2000; BORGHANS *et al.* 2004). An important question about coevolution is therefore whether or not multilocus interactions are sufficient to maintain polymorphism by themselves or if other ecological and biological factors are required.

In GFG relationships in plants, resistance is induced if the plant has a resistance (*RES*) gene enabling recognition of a specific parasite avirulence (*AVR*) protein (DANGL and JONES 2001). The parasite is not detected by the host and resistance is not induced if the host has a susceptibility allele (*res*) or the parasite has a virulence allele (*avr*). The asymmetry of the GFG interaction implies that in the absence of other factors, there will be an “arms race,” as successive pairs of *RES* and *AVR* alleles are driven to fixation in host and parasite populations, respectively (BERGELSON *et al.* 2001; HOLUB 2001). Accounting for the diversity observed at host and parasite

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