Biol. Rev. (2003), **78**, pp. 639–675. © *Cambridge Philosophical Society*
DOI: 10.1017/S146479310300616X *Printed in the United Kingdom*

Parasitic exploitation as an engine of diversity

KYLE SUMMERS*, SEA McKEON, JON SELLARS, MARK KEUSENKOTHEN, JAMES MORRIS, DAVID GLOECKNER, COREY PRESSLEY, BLAKE PRICE and HOLLY SNOW

Department of Biology, *East Carolina University*, *Greenville*, *NC* 27858, *USA* (e-mail: summersk@mail.ecu.edu)

(*Received* 24 *January* 2002; *revised* 2 *January* 2003; *accepted* 6 *January* 2003)

ABSTRACT

Parasitic exploitation occurs within and between a wide variety of taxa in a plethora of diverse contexts. Theoretical and empirical analyses indicate that parasitic exploitation can generate substantial genetic and phenotypic polymorphism within species. Under some circumstances, parasitic exploitation may also be an important factor causing reproductive isolation and promoting speciation. Here we review research relevant to the relationship between parasitic exploitation, within species-polymorphism, and speciation in some of the major arenas in which such exploitation has been studied. This includes research on the vertebrate major histocompatibility loci, plant–pathogen interactions, the evolution of sexual reproduction, intragenomic conflict, sexual conflict, kin mimicry and social parasitism, tropical forest diversity and the evolution of language. We conclude by discussing some of the issues raised by comparing the effect of parasitic exploitation on polymorphism and speciation in different contexts.

Key words: parasitism, exploitation, polymorphism, speciation, MHC, plant–pathogen, kin recognition, sexual conflict, intragenomic conflict, tropical diversity, language evolution.

CONTENTS

I. Introduction 640
II. Arms races and coevolution 640
III. Parasite–host coevolution and polymorphism 644
IV. Parasites and the evolution of sexual reproduction 649
V. Parasite–host coevolution and speciation 650
VI. Intragenomic conflict and polymorphism 651
VII. Intragenomic conflict and speciation 653
VIII. Sexual conflict and polymorphism 655
IX. Sexual conflict and speciation 656
X. Kin mimicry and polymorphism 657
XI. Kin mimicry and speciation 661
XII. Parasitism and tropical community diversity 662
XIII. Inter-group conflict, espionage and language diversity 664
XIV. Discussion 665
XV. Conclusions 667
XVI. Acknowledgements 668
XVII. References 668

* Author for correspondence.

I. INTRODUCTION

When one organism attempts to exploit resources that are part of another organism, this can produce selection for change in the organism that is being exploited. In turn, effective defence selects for change in the exploiter (Van Valen, 1973). Exploiter–victim dynamics characterize many different interactions between and within organisms (Seger, 1992; Hurst, Atlan & Bengtsson, 1996). Haldane (1949) pointed out that these kinds of conflicts generate diversity both within and between species. He identified infectious disease as a critical factor generating rapid evolutionary change and genetic polymorphism in both hosts and parasites. He also proposed that 'the selection of rare biochemical genotypes has been an important agent not only in keeping species variable, but also in speciation'. Classic parasite–host interactions are one of many mutually antagonistic kinds of relationships having an exploiter–victim dynamic. Here we review various arenas in which such evolutionary conflicts can occur, and the theoretical and empirical support for the claim that these conflicts lead to polymorphism within species and divergence and reproductive isolation between lineages (speciation). We focus on parasitic exploitation, because such exploitation comes in a wide variety of forms and because it can produce strong selection pressures.

The arenas in which parasitic exploitation occur are diverse, and include parasite–host coevolution, intragenomic conflict, the evolution of sexual reproduction, self and non-self recognition, recognition of kinship, social parasitism, brood parasitism, sexual conflict, mimicry (particularly Batesian mimicry), parasitic mutualism, ecological community diversity, and language evolution, among others.

In classical host–parasite interactions, strong selection acts on the host because of the disparity in generation times of the host and parasite (Hamilton, 1980; but see Frank, 1996*b* and Lively, 1999). In other 'parasitic' systems, such as sexual conflict or kin mimicry, selection to avoid parasitism is strong simply because the costs of being parasitized can be quite high (e.g. Rice, 1996).

Diversity is a broad term, and can be used to refer to variation at many different levels. In studies of classic parasite–host interactions, the focus of interest is typically on genetic polymorphism associated with parasite virulence and host resistance (May & Anderson, 1983). However, interactions in other contexts that may involve parasitic exploitation (e.g. sexual conflict) often focus on phenotypic variation in response to parasitic exploitation (e.g. courtship displays, genital morphology). Here we consider theoretical and empirical research that addresses either genetic or phenotypic diversity, with the implicit assumption that genetic diversity will frequently underlie phenotypic diversity. Parasitic exploitation may also drive phenotypic diversity (via phenotypic plasticity) even in the absence of underlying genetic variation. The nature of genetic diversity is also potentially diverse, including numbers of alleles at particular loci, evenness of allelic distributions, proportions of heterozygous loci, and variation in locus copy number, among other measures. Each of these measures of genetic diversity can be influenced by parasitic exploitation.

Parasitic exploitation has the potential to promote reproductive isolation (Haldane, 1949; Turelli, Barton & Coyne, 2001). The most obvious mechanism is one in which hybrids have low fitness relative to specifically coevolved local genotypes (Haldane, 1949). Here we focus on the potential for allopatric speciation. We will not discuss parapatric or sympatric speciation in the interest of brevity. However, the mechanisms whereby parasitic exploitation may contribute to reproductive isolation between allopatric populations may have similar effects in parapatry and sympatry.

Parasitic exploitation occurs in arenas spanning a variety of different levels of biological organization. The complexity and specific circumstances characteristic of these different arenas has led to field-specific jargon and a lack of communication between workers in different fields. Nevertheless, many of the issues discussed in this review are inter-related, and the conclusions and generalizations that emerge from one field are frequently relevant to exploiter–victim dynamics in other fields. For example, major histocompatibility complex (MHC) diversity may be influenced both by classical parasite–host interactions, and by sexual conflict over mating (Potts & Wakeland, 1990). In the discussion, we review several cases where different fields converge in particular examples of parasitism and diversity. One purpose of this review is to stimulate interest in the idea that factors identified as crucial in one field of study may provide novel insights into other fields of study. In the interest of brevity, we have excluded some areas from this review. However, we hope to stimulate interest in parallels with areas not reviewed in detail.

II. ARMS RACES AND COEVOLUTION

We first present a descriptive and organizational framework for coevolutionary interactions including the most common types discussed in the literature. Table 1

Table 1. *Categories of coevolutionary interactions and associated aspects of polymorphism and diversity*

	Type of variation	Genetic basis	Cost of phenotype	Specificity	Frequency dependence	Age of allelic diversity	Within-population polymorphism	Between-population divergence
Escalating arms race	Quantitative	Polygenic	High	Low	Low	Recent	Low to intermediate	High
Specific coevolution	Quantitative	Polygenic	Intermediate	High	High	Ancient	Intermediate	High
Overdominance	Qualitative	Variable loci, limited alleles	Variable	High	Intermediate	Ancient	Intermediate	Intermediate
Gene-for-gene	Qualitative	Variable loci, limited alleles	High	Low	Low	Variable	Intermediate	Intermediate
Matching alleles (limited cycling)	Qualitative	Variable loci, intermediate alleles	Low	High	High	Ancient	High	High
Matching alleles (infinite alleles)	Qualitative	Variable loci, multiple alleles	Absent	High	High	Variable	Variable	High

lists various types of coevolutionary interactions and the properties typically associated with them on the basis of previous theoretical or empirical analyses.

There are two main expectations with regard to the pattern of coadaptation between exploiters and victims (Berenbaum & Zangerl, 1998): directional selection leading to an arms race in antagonistic interactions, and stable or fluctuating polymorphism of defences and counter-defences maintained by heterozygote advantage, or negative frequency-dependent selection. A related distinction has also been made between coevolution that results in universally effective attack and defence phenotypes, *versus* phenotypes that are only effective in countering specific modes of attack or defence (Foitzik *et al.*, 2001). In general, arms races are associated with lower levels of polymorphism (because a single type dominates within populations) whereas negative frequency-dependent selection tends to maintain higher levels of polymorphism within populations. However, if more effective attack or defence phenotypes (and underlying genotypes) are associated with substantial costs, this can maintain diversity within populations (Frank, 1994). If such costs differ between populations (due to ecological differences), then this will drive divergence between populations.

A distinction also is sometimes made between organismal and molecular coevolution. This distinction is not fundamental, but rather provides a useful separation for the purpose of analysis. Ultimately, changes at the molecular level underlie the changing interactions at the phenotypic level in organismal coevolution, and of course molecular interactions are a form of phenotypic interaction. To date, most studies of coevolution at the morphological, physiological or behavioural level do not consider changes at the molecular level in detail, but that is likely to change in the future (e.g. Geffeney *et al.*, 2002).

Organismal coevolution typically involves an 'escalating' arms race, in which quantitatively expressed phenotypic traits [morphological, physiological or behavioural features such as shell thickness and claw strength (Vermeij, 1994)] under polygenic control (Thompson, 1994) undergo reciprocal increases over evolutionary time (Brodie & Brodie, 1999). This type of coevolution typically involves some type of cost of production (Seger, 1992). It is often not frequency-dependent, involving universally effective phenotypes, which may be held at different equilibrium points in different populations due to the effect of ecologically imposed variation in costs (Foitzik *et al.*, 2001; Geffeney *et al.*, 2002) or to random founder events (Berenbaum & Zangerl, 1998). Escalating arms races may be characterized by intermediate or low levels of polymorphism

within populations, but high divergence between populations (depending on the scale of variation of ecological factors controlling costs for different populations or species). Escalating arms races typically involve direct interactions, rather than recognition and evasion of recognition. Across the geographic range of the interaction, the selective environment may vary, and with it the degree of elaboration of exploitative and defensive traits (Thompson, 1999). Nevertheless, the defensive ability of the victim and exploitative ability of the parasite should remain matched in sympatry (Berenbaum & Zangerl, 1998). Escalating arms races can also occur at the molecular level (e.g. quantitative increases in the production of a toxin and a detoxifying enzyme).

Organismal coevolution may involve specific matching changes in form or function, rather than escalation. An example would be changes in the shape of mating-related structures in the morphology of males and females (Eberhard, 1985). This type of coevolution shares some of the properties of an escalating arms race, including polygenic control, but differs in other respects. The costs of the features involved in the interaction between the parasite and the host are likely to be lower (because the features may be changed rather than added on). Whereas the success of structures or tactics is usually not frequency dependent in an escalating arms race, it often is in specific coevolution (e.g. Hori, 1993). Negative frequency dependence in specific organismal coevolution promotes polymorphism within populations.

Coevolution between parasites and hosts is often mediated at the molecular level, typically via host recognition of parasite elicitors (Bergelson *et al.*, 2001). Molecular coevolution typically involves rapid evolution of recognition ability by hosts and evasion by parasites (as opposed to features that directly determine success or failure, such as shell thickness and claw strength in interactions between clams and crabs). Molecular coevolution also differs from organismal coevolution in that the phenotypes are typically less costly (Seger, 1992). There are, however, exceptions to these distinctions. For example, molecular interactions may involve the production of destructive enzymes and enzyme inhibitors, and such interactions are likely to be direct and costly (Bishop, Dean & Mitchell-Olds, 2000). Furthermore, organismal coevolution can involve visual, olfactory, tactile or auditory recognition and mimicry (e.g. Davies, Bourke & De Brooke, 1989).

The interactions involved in molecular coevolution are the subject of an exploding scientific literature (see below). Such interactions typically involve a limited number of loci, although this is not a requirement from a theoretical perspective (Frank, 1993*b*). We have divided molecular coevolution into several categories.

Table 2. *Resistance of host genotypes to parasite genotypes under the gene-for-gene and the matching alleles models of the specificity of parasite–host interaction*

Host	Parasite	
Gene-for-gene	Avirulent	Virulent
Resistant	Resistant	Susceptible
Susceptible	Susceptible	Susceptible
Matching alleles	Type A	Type B
Type 1	Resistant	Susceptible
Type 2	Susceptible	Resistant

The first two categories are gene-for-gene coevolution and matching-alleles coevolution (Table 2). The gene-for-gene model of parasite–host interactions was developed by Flor (1956, 1971) on the basis of his investigations of the genetics of resistance and virulence in flax (*Linum usitatissimum*) and its fungal pathogen, flax rust (*Melamspora lini*). In the simplest form of the standard gene-for-gene model, the host has two phenotypes, resistant (R) and susceptible (S), and the pathogen has two phenotypes, avirulent (A), and virulent (V). A key feature of the gene-for-gene model is that parasites with the virulent genotype are universally virulent; they can exploit all hosts. Hence, resistant hosts are only resistant to avirulent parasites (Frank, 1994). The gene-for-gene model of specificity underlies a variety of theoretical models that have been constructed to explain observed levels of genetic polymorphism (Burdon, 1987). These models assume that virulence alleles are associated with a cost, otherwise they would go to fixation (Frank, 1994). For the same reason, host resistance alleles are also assumed to have an associated cost.

The gene-for-gene model stands in contrast to matching-alleles models (Table 2). In these models, matching of parasite and host alleles produces a specific outcome. For example, each host allele may cause recognition of and resistance to a matching parasite allele (Frank, 1994). Alternatively, each parasite allele might be able to attack only a single host resistance allele. In either case, each parasite genotype functions as either a resistance or a susceptibility allele, depending on the host genotype, and *vice versa*. Matching-alleles models do not require costs of resistance and virulence to explain the maintenance of high levels of polymorphism, because of the negative frequency-dependence inherent in these models (Kniskern & Rausher, 2001).

These two models are really two ends of a continuum going from parasites with a wide host range

Table 3. *Theoretical results pertaining to levels of polymorphism driven by parasite host dynamics* (*after Frank,* 1991 *a,* 1993 *a, b,* 1994, 1996, 2000 *a, b*)

Factor	Effect on polymorphism
Quantitative *versus* qualitative interactions	Qualitative interactions promote higher diversity
Specificity of attack and defence	Specific interactions promote diversity
Parasite virulence	Increased virulence promotes diversity
Population subdivision	Reduces within population variation, but increases divergence between populations
Number of alleles/phenotypes	Polymorphism increases with increasing numbers of alleles/phenotypes
Potential rate of population increase in the parasite (epidemic index)	High epidemic index reduces variation within populations, but increases divergence between populations

(gene-for-gene models) to parasites with a narrow host range (matching-alleles models) (Agrawal & Lively, 2002). Both matching-alleles and gene-for-gene interactions can produce substantial polymorphism within populations, although gene-for-gene systems are generally somewhat less polymorphic, depending on the cost of host resistance and parasite virulence (Agrawal & Lively, 2002).

The number of alleles involved in matching-alleles systems is a matter of debate: some researchers have advocated the position that there are a limited number of 'good answers' (e.g. Hamilton, Axelrod & Tanese, 1990), whereas others have argued that there is an unlimited set of alleles that are continuously replaced (e.g. Kniskern & Rausher, 2001). It is possible that the number of available alleles in the set evolves. In hosts under strong selection by parasites, selection will favour host immunotypes that recognize parasite ellicitors that are constrained in their ability to vary for functional reasons (just as scientists search for invariant targets when designing drugs). Hence, the process of coevolution itself may reduce the number of 'good answers' available to parasites and hosts, consistent with Hamilton's prediction. In either case, matching-alleles systems involve highly specific host recognition of parasite elicitors, and there is strong negative frequency dependence. Typically these systems are assumed to have limited or no costs of production. Theoretical and empirical studies of these types of interactions show that they can produce rapid divergence between populations (Frank, 1994). The degree of variation within populations under matching-alleles systems (especially those with infinite alleles) depends in part on the importance of selective sweeps, in which a single allele sweeps through the population, eliminating all other variants. If this form of episodic selection is frequent, then levels of polymorphism within populations should tend to be low, and allelic variation will be relatively recent (Bergelson *et al.*, 2001; Frank, 2002).

Overdominance is a classic form of coevolutionary interaction in which heterozyotes have an advantage over either homozygote. This is driven by the ability of heterozygous hosts to recognize a wider range of parasite elicitors (Hughes, 1999). Overdominance may involve heterozygosity at multiple loci, but in the absence of negative frequency dependence it generates relatively low allelic diversity at each locus.

Generally speaking, theoretical models of many different kinds of antagonistic coevolution (particularly those involving qualitative interactions) produce cyclical or erratic patterns of persistent and rapid evolutionary change in the phenotypic attributes that modulate the antagonistic interaction, and predict substantial genetic polymorphism associated with these traits (Seger, 1992). Models of antagonistic coevolution incorporating quantitative interactions can also produce dynamic cycling behaviour, and evidence for frequency-dependent cycling in quantitative interactions under polygenic control has been found in plant-herbivore systems (Berenbaum & Zangerl, 1998). However, theoretical considerations suggest that frequency-dependent cycling becomes less likely as the gradations of attack and defence phenotypes (and the number of underlying polygenes) increase, because the population is more likely to be trapped on an 'adaptive peak' with higher peaks separated by troughs that cannot by crossed by the hybrids of intermediate fitness (Seger, 1992). This may reduce polymorphism within species, but may promote speciation (Seger, 1992).

S. A. Frank (Frank, 1991 *b*, 1993 *a, b*, 1994, 1996 *a, b*, 2000 *a, b*) has carried out extensive theoretical investigations of the relationship between parasite–host

coevolution and associated genetic polymorphism, taking a variety of factors into account. His work has led to a number of important generalizations (Table 3). Many of these factors have not yet been adequately quantified in natural or even experimental systems. For example, there is still considerable debate concerning the degree of genotype specificity in parasite–host interactions (Little, 2002). Some studies indicate substantial specificity (e.g. Carius, Little & Ebert, 2001), but more research is needed.

III. PARASITE–HOST COEVOLUTION AND POLYMORPHISM

A variety of evidence suggests that parasite–host coevolution drives polymorphism in virulence and resistance genes (Frank, 2002). The number of genes involved in host resistance is not known with certainty, but is likely to be large (Hamilton *et al.*, 1990). For example, approximately 14% of the 21 000 genes in the genome of *Arabidopsis thaliana* are related to defence against pathogens (Bishop *et al.*, 2000). In mice, 50 loci distributed over 17 chromosomes are known to affect resistance to retroviruses alone (O'Brien & Evermann, 1988). Somatic mechanisms that generate immunotype variation within hosts may buffer selection in favour of genetic variation (Frank, 2002). Nevertheless, levels of genetic heterozygosity in genes involved in immune recognition are typically very high, with deficiencies of homozygotes, uniform allelic frequency distributions and high allelic diversity (Hedrick, 1994). For example, the three Class I major histocompatibility complex loci in humans (A, B and C) have 175, 349 and 90 known alleles, respectively (Frank, 2002).

Most of the research done on parasite–host interactions and diversity in vertebrates has focused on genes of the major histocompatibility complex (MHC), which are known to be involved in immune function (Klein, 1986). The MHC codes for receptor molecules that bind protein fragments from parasites (epitopes) and present them for recognition by specific cells that can destroy invading or infected cells, eliminating the parasites (Figs 1 and 2).

Doherty & Zinkernagel (1975) argued that heterozygosity allows presentation of a broad array of antigens. This is known as the overdominance hypothesis, in which two different alleles provide better protection against parasitic attack than a single allele. Negative frequency-dependent selection (in which rare alleles are more likely to be resistant to common parasite genotypes) has also been proposed as an important factor in the maintenance of genetic diversity of vertebrate populations (Bodmer & Bodmer, 1978). Both overdominance and negative frequency dependence assume trade-offs between MHC genotypes, so that a genotype resistant to one type of pathogen is susceptible to others (Apanius *et al.*, 1997). Evidence for this type of trade-off has been found in humans and mice (Apanius *et al.*, 1997). Trade-offs may also exist between MHC genotypes and tissue damage, such that certain genotypes produce a more effective immune response, but also cause collateral tissue damage to the host (Frank, 2002).

In humans, associations between MHC genotypes and susceptibility have been found for a variety of diseases, including leprosy, tuberculosis, and malaria (Hill, 1998). Polymorphism of the MHC is associated with variation in the ability of the human host to bind particular antigenic variants (Yewdell & Bennink, 1999). For example, MHC Class I receptors bind with high affinity to peptides from strains of the malaria parasite to which those MHC genotypes display resistance (Hill *et al.*, 1992). There is also evidence for geographic variation in MHC genotype frequencies and associated susceptibility to disease in humans, which is consistent with the possibility of coevolution between parasite and host (Apanius *et al.*, 1997). For example, the Class I MHC type allele B35 binds to the common epitopes from the malaria parasite *Plasmodium falciparum* (Gilbert *et al.*, 1998). The B35 allele occurs at high frequencies in regions with endemic malaria.

Experimental studies of mice, rats, chickens and cows also provide evidence of associations between disease resistance and MHC genotype (Fu, Villas & Blankenhorn, 1991; Hlozanek, Corbel & Dieterlen-Lievre, 1994). Transgenic mice lacking Class I MHC and associated T-cell function have reduced ability to resist disease (e.g. Bender *et al.*, 1992; Flynn *et al.*, 1992). Recent research on mice provides direct evidence in favour of heterozygote advantage at the MHC for resistance to multiple parasite infections (Penn, Damjanovich & Potts, 2002).

Pathogens can evolve in a variety of ways that impose diversifying selection on hosts. Six detailed mechanisms of pathogen-driven selection on the MHC have been proposed, each consistent with either heterozygote advantage or frequency-dependent selection or (in most cases) both (Potts & Slev, 1995). (1) Elimination of binding by specific host T-cell receptors to the parasite proteins (epitopes). (2) Incomplete T-cell receptor binding leading to T-cell anergy (lack of response). (3) Mimicry of host peptides by the parasite. (4) Elimination of epitope binding by the host MHC. (5) Differences in the peptide binding range of the host

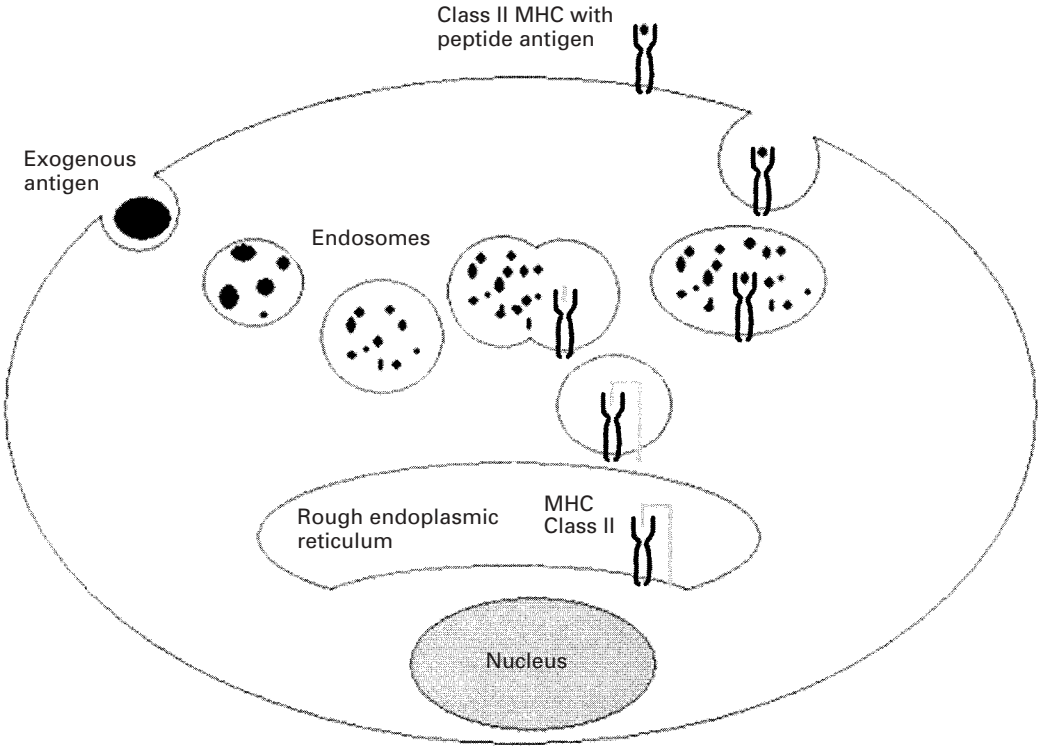

Fig. 1. Processing pathways in the major histocompatibility complex (MHC). This figure illustrates peptide fragment (epitope) acquisition by MHC Class II molecules followed by cell-surface expression of a peptide–MHC complex. Peptide acquisition by MHC Class I molecules occurs in a similar manner, but through a separate cytosolic pathway. Reproduced with permission from J. Capraro and T. McConnell.

MHC. (6) Response to allo-MHC antigens carried by parasites. Each of these mechanisms involves pathogen escape from host recognition. They provide a mechanistic framework for empirical tests of the interaction between hosts and parasites, and their effect on diversifying selection (Potts & Slev, 1995). Fig. 2 illustrates three common mechanisms. These mechanisms entail the evolution of escape variants in the pathogens. Hence, diversifying selection between hosts and parasites is reciprocal, and host immune responses select for parasite polymorphism.

Laboratory studies demonstrate directly that host immune response can select for variation in parasites. Transgenic mice that express specific T-cell receptor types generate escape variants when infected by lymphocytic choriomeningitis virus (Pircher *et al.*, 1990). Studies of the specific amino acid substitutions generated in response to the specific immunotype (Puglielli *et al.*, 2001), combined with structural analysis of the binding of specific parasite epitopes to the transgenic mouse immunotype (MHC D^b) (Tissot *et al.*, 2000) demonstrated that the particular escape variant disrupts binding of the epitopes to the MHC (Puglielli *et al.*, 2001). This combination of experimental evolution and structural analysis can reveal the precise molecular mechanisms mediating the interaction between parasite and host genotypes. Similar studies have been carried out in other parasite–host systems (reviewed in Frank, 2002).

Epitopes recognized by T-cells are particularly variable in natural populations (Zevering, Khamboonruang & Good, 1994), which suggests that selection by host MHC genotypes has favoured variation in parasite genotypes (and hence epitopes) to escape T-cell recognition. Strong evidence for the role of parasite–host interactions as a selective agent favouring MHC gene polymorphism within species and diversification between populations and species comes from comparative DNA sequence analyses performed by Austin Hughes and colleagues (Hughes & Nei, 1988; Hughes, 1999). Hughes has utilized differences in patterns of synonymous and non-synonymous substitution rates expected under neutral evolution and natural selection to demonstrate strong diversifying selection on the MHC in a variety of different contexts. Rates of non-synonymous substitution (per non-synonymous site) in regions of the MHC loci that interact directly with foreign peptides (peptide binding regions) are

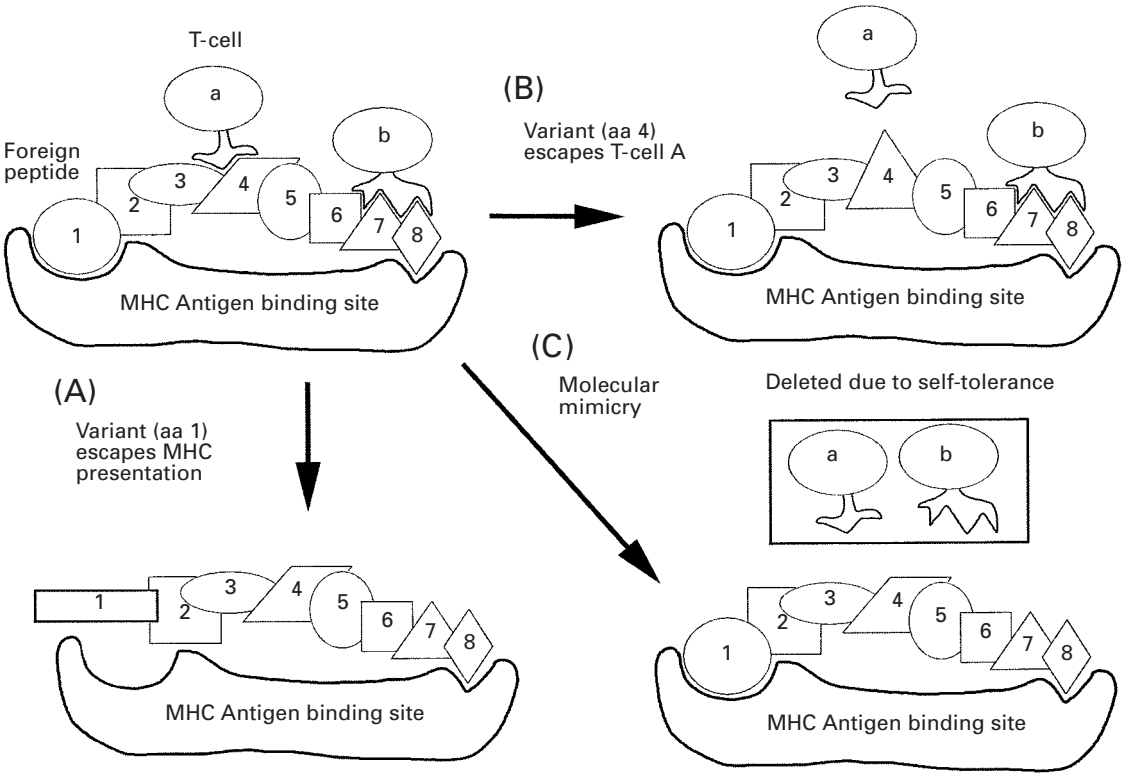

Fig. 2. Three common models of pathogen escape from major histocompatibility complex (MHC)-dependent immune system recognition. Numbered shapes represent amino acids (aa) of a foreign peptide. Lettered structures represent T-cell receptors. (A) A change in the peptide prevents binding to the MHC. (B) A change in the peptide prevents binding to the T-cell receptor. (C) Molecular mimicry of host proteins prevents T-cell receptor binding (T-cells that recognize host proteins are destroyed). Because multiple T-cell receptors can bind to foreign peptides, mechanism B may not lead to escape from recognition. Redrawn from Potts & Slev (1995), with permission from the authors, Immunological Reviews, and Blackwell Publishing.

significantly higher than rates of synonymous substitution (per synonymous site), as expected under diversifying selection (Hughes & Nei, 1988; Hughes & Yeager, 1998). Recent studies of other loci involved with resistance to parasitic attack show similar results (e.g. Zhang, Dyer & Rosenberg, 2000).

Takahata & Nei (1990) showed that polymorphism can persist for longer than expected (under neutral evolution) with overdominant selection or negative frequency-dependent selection. The presence of trans-species polymorphism (Klein & Arden, 1982) suggests that one of these two modes of selection has been in operation. Hughes (1999) argues that overdominant selection has been the most potent force, but this requires further investigation.

These analyses complement comparative DNA sequence analysis of genes in the malaria parasite (*Plasmodium falciparum*), which demonstrate that regions likely to be part of epitopes have high ratios of non-synonymous to synonymous substitutions relative to other regions. In the C-terminal non-repeat region (CTNR) of *P. falciparum* circumsporozite proteins, the rate of non-synonymous substitution significantly exceeds that of synonymous substitution, and most non-synonymous substitutions change the nature of the protein, specifically the residue charge (Hughes & Hughes, 1995). Most MHC-bound peptides are derived from this region (Good *et al.*, 1988). Hence, it is likely that selection imposed by immune surveillance is acting to diversify this region (Hughes, 1999). Recent research has revealed that parasite interactions with host immune systems impose selection in favour of polymorphism in a variety of parasites, such as foot-and-mouth disease virus (FMDV) (Haydon *et al.*, 2001) and human immunodeficiency virus (HIV) (Yamaguchi-Kabata & Gojobori, 2000). These studies have employed sophisticated maximum likelihood models to identify the exact nucleotide sites that are under strong

positive selection (Nielsen & Yang, 1998). This is important because escape from immune system recognition may involve changes in only a few amino acids (Frank, 2002).

Comparisons between different species indicate that rates of diversification are particularly high for genes involved in parasite–host interactions (immune system genes). Murphy (1993) compared 615 orthologous pairs of human and murine rodent proteins and found a significantly higher mean amino acid difference in host defence receptors and ligands relative to other categories of proteins (i.e. proteins not involved in immune functions). Hughes (1997) analysed immunoglobin superfamily C2 domains from molecules expressed in immune system cells and compared them with C2 domains from the same superfamily expressed in other tissues. Rates of non-synonymous substitution were significantly higher for genes expressed in the immune system only, or in both the immune system and other systems, relative to genes not expressed in the immune system. This result strongly supports the claim that genes associated with immune function diverge more rapidly between species than other genes.

Several factors have been proposed to influence the extreme polymorphism of the MHC, including gene conversion under weak selection (Parham & Ohta, 1996), non-random mate choice with respect to MHC genotype (Thomas, 1974; Potts, Manning & Wakeland, 1991), and kin discrimination (Potts & Wakeland, 1990). However, the preponderance of current evidence is consistent with interspecific parasite–host coevolution as the major selective force maintaining MHC diversity (Hughes, 1999).

Variation in defence against parasites in bacteria can also be seen as a frequency-dependent coevolutionary race with parasites (Lenski, 1984; Levin, 1986). Bacterial restriction–modification (R–M) enzymes are used to defend against viral attack. Restriction enzymes cut DNA molecules that carry a specific sequence of nucleotides, while modification enzymes recognize the same sequence, but modify the recognition site in a way that protects it from restriction. The bacteria's own DNA is modified, but viral DNA that is not recognized is cut and thus destroyed. Surveys of viral isolates by Korona, Korona & Levin (1993) have revealed a diverse array of defences against restriction in natural populations of viruses. Evidence suggests that defence against bacteriophage infection has been a driving factor in bacterial and viral genetic diversity (Korona *et al.*, 1993; Frank, 1994). Recent research has demonstrated long-term coevolution between bacteria and bacteriophage (Buckling & Rainey, 2002). In this case, coevolution involved directional selection, with increasing bacterial resistance and phage infectivity within populations. Replicate experiments demonstrated that coevolution produced rapid genetic diversification between populations (Buckling & Rainey, 2002).

Genetic polymorphism associated with host resistance and pathogen virulence is common in plants (Burdon, 1987). Studies of plant–pathogen interactions (particularly in agriculturally important crop plants) have demonstrated repeatedly that the presence of a pathogen produces negative frequency-dependent selection (Thompson & Burdon, 1992; Bergelson *et al.*, 2001).

The mechanisms underlying plant resistance and pathogen virulence probably involve specific recognition of a pathogen-generated ligand (produced by an avirulence gene) by a plant receptor encoded by a resistance gene (Staskawicz *et al.*, 1995). This conforms to an elicitor–receptor model of agonistic interaction mediated by recognition and evasion (De Wit, 1997). Elicitor–receptor interactions have been demonstrated in many agricultural systems, and the number continues to grow rapidly (Thompson, 1994).

A variety of studies have now confirmed the elicitor–receptor model, and provide detailed information on the nature of elicitors and receptors at the molecular level (Ji, Smith-Backer & Keen, 1998). For example, small peptides produced by the tomato leaf mould pathogen *Cladosporium fulvum* show the characteristics of an avirulence gene-encoded elicitor: the purified peptides elicited a hypersensitive response on tomato cultivars that were resistant to the *C. fulvum* race used to obtain the peptide (Van den Ackerveken, Van Kan & De Wit, 1992). A variety of resistance genes have been cloned and sequenced in the past decade. For example, the *Pto* gene in tomato confers resistance to strains of *Pseudomonas syringae* pv. *tomato* carrying the avirulence gene *avrPto*. The *Pto* gene was cloned into a yeast artificial chromosome vector, and genetic markers linked to *Pto* were used to identify the gene. The *Pto* product is a serine/threonine protein kinase (Martin *et al.*, 1993). Experimental evidence indicates that *Pto* interacts directly with a cognate avirulence gene, *AvrPto* (Scofield *et al.*, 1996; Tang *et al.*, 1996).

A number of other resistance genes have also been cloned, sequenced and analysed recently (De Wit, 1997), such as the tomato *Cf-9* gene (Jones *et al.*, 1994), several flax *L* genes (Ellis *et al.*, 1997), the *Xa21D* gene in rice (Wang *et al.*, 1998) the *RPP8* locus in *Arabidopsis thaliana* (McDowell *et al.*, 1998), and several receptor genes in lettuce (Meyers *et al.*, 1998). Most of these genes have leucine-rich repeat (LRR) and nucleotide-binding site regions in the proteins they encode (Bent,

1996). The LRRs in plant proteins probably bind elicitor molecules from pathogens and mediate recognition (Dixon *et al.*, 1996). A number of researchers have suggested that these LRR proteins are involved in recognition and defence-initiation systems that resemble the immune systems of both vertebrates and invertebrates (e.g. Staskawicz *et al.*, 1995; Ji *et al.*, 1998).

Recent research on the molecular evolution of plants and their pathogens has revealed strong evidence for arms races or negative frequency-dependent selection on host resistance genes and pathogen elicitor and counter-defence genes (Stahl & Bishop, 2000). Comparisons among DNA sequences of R (resistance) gene family members have revealed positive selection acting on LRR regions (as demonstrated by ratios of nonsynonymous to synonymous substitution) in *Arabidopsis* (McDowell *et al.*, 1998), tomato and lettuce (Meyers *et al.*, 1998), rice (Wang *et al.*, 1998) and flax (Ellis *et al.*, 1997), among others (e.g. Baker *et al.*, 1997). In lettuce, there was an alternating pattern of conserved and hypervariable regions in the LRR-encoding region. The conserved regions corresponded to amino acids that form the structural backbone of the LRR, whereas the hypervariable regions are likely to form β-sheets that are involved in ligand binding (Meyers *et al.*, 1998). The putative ligand-binding surfaces had nonsynonymous to synonymous substitution rates significantly higher than 1, demonstrating diversifying selection in the maintenance of hypervariability (Meyers *et al.*, 1998). Similar evidence that diversifying selection is acting on predicted β-sheet ligand-binding portion of the LRR has been found in a variety of other plants involved in interactions with a variety of pathogens (e.g. McDowell *et al.*, 1998; Meyers *et al.*, 1998; Wang *et al.*, 1998; Ellis *et al.*, 1999). Overall, research on resistance genes in plants has provided strong evidence that plant–pathogen coevolution mediated through recognition of specific parasite-produced elicitors drives the evolution of host resistance genes via negatively frequency-dependent fitness effects (Bergelson *et al.*, 2001).

The studies cited above focused on classic plant–pathogen interactions mediated via elicitor recognition and response by the host plant. Antagonistic coevolution can also occur through direct interactions between generalized defensive substances (e.g. enzymes and inhibitors, or toxins and detoxifying enzymes) that mediate interactions between plants and pathogens (Stahl & Bishop, 2000). Accelerated amino acid substitution rates indicate positive selection acting on Class I chitinases (which break down pathogen cell walls) in the genus *Arabis* (Bishop, Dean & Mitchell-Olds, 2000). Maximum likelihood models of codon substitution (Nielsen & Yang, 1998) were used to identify 15 specific amino acid sites under positive selection. Using X-ray crystallographic data on protein structure, the authors were able to identify which residues formed the active-site cleft that acts in substrate binding. They were then able to confirm that the sites identified by molecular evolutionary analysis were in the cleft predicted as the active site via structural analysis (Bishop *et al.*, 2000). This study provides strong evidence that plant chitinases are coevolving with pathogen-produced chitinase inhibitors, with selection driving the continuous evolution of chitinase diversity.

Studies of plant–pathogen interactions at the population level in the field have provided only mixed support for the hypothesis that plant–pathogen coevolution drives genetic diversity. Some studies have provided evidence for this hypothesis (e.g. Schmid, 1994; Chaboudez & Burdon, 1995), but others have not. For example, in wheat frequency-dependent selection is caused by stripe rust, as rare genotypes have a higher resistance to the pathogen (Brunet & Mundt, 2000). Selection was negatively frequency-dependent, as host fitness increased with decreasing genotype frequencies. However, at times negative frequency dependence was found in the absence of disease. This indicates that factors other than disease contribute to the maintenance of genetic polymorphism in wheat, and may be more important than pathogen pressure in this system (Brunet & Mundt, 2000). A variety of other studies have produced results that do not match expectations of frequency-dependent dynamics driven by parasite–host coevolution (Little, 2002).

Comparative studies of the relationship between parasitism and host genetic diversity are rare, although Poulin, Marshall & Spencer (2000) carried out a phylogenetically controlled comparative analysis of the relationship between parasite species richness and genetic diversity across 40 species of North American freshwater fishes. They found no significant relationship between parasite species richness and host genetic diversity, which contradicts a prediction of the parasite–host coevolution hypothesis.

The lack of concordance between the results of studies of coevolutionary interactions between specific hosts and parasites at the molecular level (providing strong evidence of diversifying selection) on the one hand, and the results of some ecological and comparative studies of parasitism and polymorphism (which have not always indicated a significant relationship) on the other hand, can be explained by incorporating a geographic perspective on coevolutionary interactions (Thompson, 1994).

Mathematical models incorporating both genetics and ecology (May & Anderson, 1990; Frank, 1991*a*) suggest that the trajectory of parasite–host coevolution in natural populations may depend to a large degree on the demographic structure and ecological setting of the interacting populations, which may differ dramatically among geographic areas (Thompson, 1994). Population bottlenecks, periodic extinctions, asexual reproduction, genetic drift and migration may strongly influence polymorphism (Burdon & Thrall, 1999). Evolutionary loss of defences in the absence of enemies, correlations between defence characters and life-history characters, geographic variation in expression of defences caused by environmental variation, differences in selection pressure due to different suites of enemy species and competing intraspecific genotypes, and genetic drift can all create a genetic mosaic in the intensities and specificities of antagonistic coevolution between populations or species in different geographic regions (Thompson, 1999). Hence, while parasite–host coevolution does promote polymorphism in many cases, it does not do so at all times or at all places.

IV. PARASITES AND THE EVOLUTION OF SEXUAL REPRODUCTION

Closely related to the general question of parasite–host interactions and within-species polymorphism is the relationship between parasitism and the evolution of sexual reproduction as a mechanism to increase genetic diversity via recombination. Williams (1975) and Maynard Smith (1978) argued that, all else being equal, asexually reproducing organisms should have a substantial reproductive advantage, but that changing environmental conditions might favour sexual reproduction. Hamilton (1975) suggested that biological interactions might be critical in producing rapidly changing environmental conditions. Jaenike (1978) and Glesener & Tilman (1978) independently developed the hypothesis that biotic interactions provide the key selection pressures favouring sexual reproduction, using verbal models and comparative analysis, respectively. Since then, the hypothesis that parasitism drives sexual recombination has come to be known as the Red Queen Hypothesis [following Van Valen's (1973) hypothesis concerning interspecific interactions].

This hypothesis has been extensively explored by W. D. Hamilton (e.g. Hamilton, 1980; Hamilton *et al.*, 1990) and others (e.g. West, Lively & Read, 1999). If sex is to be stable throughout a population, it must have at least a twofold advantage (Hamilton *et al.*, 1990). Simulations of parasite exploitation of sexual and asexual hosts provide support for the proposition that parasitism can cause selection to favour sexual reproduction in hosts under a variety of assumptions concerning the nature of selection (hard *versus* soft), the number of parasite species, the number of loci involved in parasite resistance and parasitic exploitation, the sexuality of parasites, and the levels of recombination produced by host sexuality (Hamilton *et al.*, 1990).

A considerable amount of theoretical work has been undertaken on the evolution of sexual recombination since Hamilton's pioneering simulations. For example, utilizing a population genetic model, Peters & Lively (1999) show that (given sufficiently high parasite virulence) antagonistic coevolution leads to a multi-step feedback loop involving fluctuating linkage disequilibrium and positive and negative epistasis in both the parasite and host. Because of the time lag required for a response to selection, there are periods during which epistasis and linkage disequilibrium are of opposite sign, such that fit genotypes are rare and common genotypes are unfit. Given a reasonably rapid rate of cycling, sexual recombination is favoured because it breaks up disadvantageous linkage disequilibria (Peters & Lively, 1999). Under a wide range of parameter values, the sign of epistasis changes every 2–5 generations, which is consistent with the rate required for selection to favour sexual recombination in previous models (Barton, 1995).

Testing the Red Queen Hypothesis has proven to be difficult, but evidence relevant to the hypothesis has been accumulating in recent years. The hypothesis predicts cycling of host and parasite genotype frequencies, and it predicts that rare clones will have an advantage because they are more likely to resist parasitic attack. Curtis Lively has generated a large body of empirical evidence concerning the effect of parasitism on the evolution of sex. His research has primarily focused on trematode parasites in snails from New Zealand streams and lakes. *Potamopyrgus antipodarum* offers an excellent model for this work as parthenogenetic and sexual snails coexist within the natural range of this species (Lively, 1992). Early observations led to the conclusion that the advantage of sex for the host is to produce genetically diverse offspring, while the advantage of sex to the parasite is to track these common genotypes (Lively, 1987). Male frequency was directly correlated with the frequency of infected individuals (Lively, 1987). Lively (1992) demonstrated that this correlation was independent of population size, further supporting the Red Queen Hypothesis.

A study of genotypically identifiable parthenogenetic clones of *P. antipodarum*, in Lake Poerua, New

Zealand (Dybdahl & Lively, 1998) also supported the hypothesis. The frequencies of four clonal genotypes of the snail were tracked over a 5-year period to investigate whether selection by parasites was operating in a time-lagged manner, and to determine if common genotypes could be tracked by a highly virulent trematode parasite, *Microphallus* sp. Infection rates for clones were positively correlated with the frequency of the clone the previous year, but not with the contemporary frequency of the clone, indicating a time-lagged response by the parasite to host genotype frequency. In the laboratory, experimental exposures to parasites showed that recently common clones were more susceptible to attack than rare clones, indicating that rare genotypes have an advantage (Dybdahl & Lively, 1998).

In more recent experiments (Lively & Dybdhal, 2000), infection rates in rare and common clones of snails from Lake Poerua were compared with those in snails from Lake Ianthe in reciprocal parasite cross-inoculation experiments. These experiments demonstrated local adaptation: snails from both lakes were more susceptible to local parasites than to parasites from the other lake. Furthermore, rare clones from Lake Poerua were less susceptible than common clones to locally derived parasites, but not to parasites from Lake Ianthe. These results demonstrate that local adaptation is caused by parasite tracking of locally common host genotypes, consistent with a central prediction of the Red Queen Hypothesis.

Ecological models using parameters derived from Lively's previous research predict oscillating changes in host and parasite fitness over time, corroborating the results of the field research (Dybdahl & Lively, 1998; Lively, 1999; Peters & Lively, 1999). Research on parasitism in other animals also provides support for the Red Queen Hypothesis (e.g. Lively, Craddock & Vrijenhoek, 1990). Some research on plants also supports the hypothesis (e.g. Schmid, 1994). However, not all empirical studies have found evidence in favour of the Red Queen Hypothesis. For example, susceptibility to *Phomopsis subordinaria* stalk disease of *Plantago lanceolata* genotypes was observed in three populations with varying degrees of infection (de Nooij & van Damme, 1988). There was no relationship between the frequency of the disease and host susceptibility, contrary to a prediction of the Red Queen Hypothesis.

Models of parasite–host interactions that favour sexual reproduction typically assume that parasite adaptation to one genotype entails lower fitness on other host genotypes, consistent with matching-alleles models (e.g. Peters & Lively, 1999). Parker (1994) has argued that in many cases the genetic details of plant–pathogen interactions fit a gene-for-gene rather than a matching-allele model of parasite–host specificity (see above). Parker (1994) developed single-locus models incorporating the gene-for-gene mechanisms of parasite–host interaction specificity. These models suggested that parasitism is less likely to drive selection for sexual reproduction than it is under the matching-alleles assumption (Parker, 1994). However, more recent models (e.g. Sasaki, 2000) indicate that parasite–host coevolution under a multi-locus gene-for-gene system can produce strong selection for polymorphism, supporting the Red Queen Hypothesis. Furthermore, Agrawal & Lively (2002) have demonstrated that gene-for-gene and matching-allele models represent two ends of a continuum (see above), and that selection in favour of sexual recombination occurs across a large part of the continuum. Hence, recent theoretical results support the contention that the Red Queen Hypothesis is widely relevant.

V. PARASITE–HOST COEVOLUTION AND SPECIATION

Hutchinson (1959) suggested that specialization of parasites on hosts could lead to the divergence of parasite species. Parasites tend to be extremely specialized, and extreme specialization is most common in parasitic species (Thompson, 1994). Extreme specialization has evolved so commonly in species that feed parasitically because the parasite lifestyle produces a sequence of hurdles to interacting with multiple species not found in free-living species. Price (1980) found a relationship between continuous contact and specialization. Other studies have also found this link (reviewed in Thompson, 1994). Parasitic populations are often geographically differentiated, with specialization on different hosts in different geographic regions (Thompson, 1994). In some cases, this has led to genetic differentiation and speciation among populations. Price (1980) argued that the parasitic lifestyle is more likely than other kinds of life histories to lead to population subdivision, geographic differentiation, and the formation of sibling species.

A variety of theoretical models of this process have provided support for idea that parasite specialization can lead to speciation (e.g. Maynard Smith, 1966; Rice, 1987). These models generally assume genetic trade-offs (antagonistic pleiotropy) in the ability of parasite genotypes to exploit different hosts or exist in different habitats, in order to produce selection for specialization. Some evidence for this type of trade-off has been found (Mackenzie, 1996), although such evidence seems to be rare (Jaenike, 1990).

Kawecki (1998) has developed a model that does not rely on the existence of such trade-offs to explain host specialization. If parasites and hosts are constantly engaged in never-ending coevolution, then parasite lineages that specialize on a specific host type will have an advantage over generalist parasites. This advantage accrues because the specialized lineage is more consistently exposed to the selective environment provided by its particular host, and evolves more quickly in response to that environment (relative to a generalist parasite). Assuming such non-equilibrium dynamics leads to the evolution of parasite lineage diversification under a variety of assumptions about the genetic determination of virulence and resistance in parasite and host, respectively (Kawecki, 1998). Kawecki's (1998) hypothesis predicts that parasites that specialize on rapidly coevolving hosts will be particularly speciose, but comparative tests of this prediction have not yet been carried out. The flip side of this hypothesis is that parasite–host coevolution should promote host speciation as well, consistent with Haldane's (1949) hypothesis.

The propensity for speciation in hosts and parasites may also be influenced by the nature of parasite virulence and host resistance. Under local adaptation, local parasites are more effective than foreign parasites at exploiting local hosts, whereas under local maladaptation the reverse is true (i.e. transplantation experiments should demonstrate higher virulence of transplanted pathogens) (Kniskern & Rausher, 2001).

Under local adaptation (when host resistance is rare), foreign host genotypes should generally have an advantage, whereas foreign parasite genotypes will not. In this situation, hybrids between local and foreign hosts have an advantage (because they can effectively resist local parasites), whereas hybrids between local and foreign parasites should not have an advantage in exploiting local hosts. This situation should favour reproductive isolation between parasite populations, but not between host populations. Under local maladaptation, in which hosts more effectively resist local parasites, hybrids between foreign and local hosts do not resist parasites more effectively (whereas foreign and local parasite hybrids should be at least as fit as local parasites). This should promote reproductive isolation among host populations, but not among parasite populations. In sum, reproductive isolation among host populations should be more likely (*ceteris paribus*) under local maladaptation than under local adaptation. Conversely, reproductive isolation among parasite populations should be more likely under local adaptation. At present, the data are too sparse to test this prediction.

VI. INTRAGENOMIC CONFLICT AND POLYMORPHISM

There has been an explosion of empirical and theoretical research on selfish genetic elements and intragenomic conflict (reviewed by Hurst, Atlan & Bengtsson, 1996). Initially thought to be of relatively minor importance, some authors have suggested that selfish genetic elements have a more substantial influence on population genetics, molecular evolution and genomic anatomy than previously believed. For example, genetic conflicts probably played crucial roles in some of the major transitions of life (Maynard Smith & Szathamary, 1995), and in the evolution of genome size and structure, meiosis, multicellularity, diploidy, anisogamy and sex determination, among other things (Hurst *et al.*, 1996). This provides some indication of the potential for diversification inherent in intragenomic conflict. The more varied and complex the features moulded by intragenomic conflict are, the more potential there is for intragenomic conflict to generate diversity both within and between species.

The proportion of the genome involved in intragenomic conflict is likely to be large. Major portions of the genome consist of non-coding sequences, such as transposable elements (Doolittle & Sapienza, 1980). Considerable attention has focused on the hypothesis that these components of the genome may consist of parasitic selfish DNA (Doolittle & Sapienza, 1980; Orgel & Crick, 1980). Population genetic studies of *Drosophila melanogaster* have provided support for this hypothesis (Charlesworth, Sniegowski & Stephan, 1994), as have comparative studies of genome size and developmental rates (Pagel & Johnstone, 1992). Transposable elements are dominant components of many genomes (Kumar & Bennetzen, 1999), and may have led to enhanced genetic diversity in a variety of different taxa, including animals (Emery *et al.*, 1999), plants (Lonnig & Saedler, 1997), and fungi (Daboussi, 1996).

Genetic conflicts can have several different outcomes (Table 4; Hurst *et al.*, 1996). Theoretical analysis indicates that coevolution between selfish genetic elements and repressors can generate substantial polymorphism, particularly if repression is costly (Randerson, Smith & Hurst, 2000). It is probably premature to attempt an estimate of the prevalence of coevolution due to intragenomic conflict, but a large and growing number of examples have appeared in the literature. The available evidence suggests that selfish genetic elements and their suppressors tend to be highly polymorphic (Hatcher, 2000).

Table 4. *Possible outcomes of genetic conflicts and effects on polymorphism and divergence* (*after Hurst et al.*, 1996)

Outcome	Effect on polymorphism	Effect on divergence
Conflict extinguished	Reduced	Reduced
Host extinction	Eliminated	Eliminated
Fixation of selfish element	Reduced	Increased (with fixation of different elements in different populations)
Stalemate between selfish elements and suppressors	Increased	Increased (if equilibrium points differ between populations)
Escalating arms race	Increased or reduced (depending on cost of drive and suppression)	Increased
Negative frequency-dependent coevolution	Increased	Increased

Hurst (1994) shows that there has been a substantial amount of turnover in Y-linked genes and putative X-linked suppressors. This is consistent with coevolution between Y-linked selfish genetic elements and X-linked suppressors. For example, there is substantial variation among clades of rodents in *Zfy* copy number (Bianchi *et al.*, 1992). There has also been rapid sequence divergence of *Sry* [which Hurst (1994) argues is likely to act as a selfish genetic element] in several mammalian lineages (Whitfield, Lovell-Badge & Goodfellow, 1993). Evidence also indicates that the divergence is the result of positive selection, a key sign of parasite–host coevolution. For example, the ratio of non-synonymous to synonymous substitutions in *Sry* between humans and other primates reaches 1.88, as compared to a range of 0.05–0.2 for a large sample of intragenic comparisons across these taxa (Wolfe & Sharp, 1993). In a comparison of *Sry* sequences among seven species of rodents, the ratio of non-synonymous to synonymous changes ranged from 0.33 to 0.45 (Tucker & Lundrigan, 1993).

Haig (1993) has suggested that interactions between a mother and her foetus have strong elements of parasitic exploitation on the part of genes in the foetus, which has led to the evolution of complex morphological structures at the interface of the foetal and maternal circulation (e.g. the trophoblast) and to hormonal manipulation via specialized hormones. Haig (1993) notes that the structure of the trophoblast is remarkably variable between different species of mammals, and suggests that this diversity may have been driven by the historically contingent coevolution engaged in by mothers and foetuses in different mammalian lineages. He argues that human chorionic gonadotropin (hCG) mediates foetal-maternal conflict over resource acquisition, and that this led to rapid divergence between this gene and the ancestral protein human luteinizing hormone (hLH). The proteins show only 80% amino acid identity, and their nucleotide sequences show a high rate of non-synonymous relative to synonymous substitution (Talmadge, Vamvakopoulos & Fiddes, 1984). Haig (1993) also argues that the human foetus and mother are involved in an evolutionary tug of war over glucose levels in the maternal circulation. He proposed that this conflict is mediated by placental growth hormone (PGH) and placental lactogen (PL). Hurst (1994) points out that placental lactogens show very high rates of substitution among ruminants and between rats and mice, with high rates of non-synonymous to synonymous substitution (Wallis, 1993; Wolfe & Sharp, 1993).

The biochemical specificity of interactions is critical with respect to the evolution of diversity (Frank, 2000*a*): higher specificity allows for more diversity. High biochemical specificity means that an increase in the effectiveness of defence against one particular attack allele leads to a decline in the effectiveness of defence against other attack alleles. The specific nature of the biochemical moves and countermoves that characterize genetic conflicts can differ among lineages, contributing to differentiation and diversification. The potential range of alleles involved is also critical to expected levels of diversity. If there are many specific biochemical changes that can cause meiotic drive (for example), and each change requires a biochemically specific form of suppression, then the evolutionary trajectory of the system will be highly contingent. Conversely, a limited number of potential biochemical mechanisms for drive will curtail the number of different evolutionary trajectories, reducing the potential extent of diversification (Frank, 1998).

Frank (2000*a*) discusses several cases of intragenomic conflict in which the biochemical specificity of the interaction of the selfish elements and the suppressor plays a crucial role in the generation of diversity. For example, cytoplasmic genes are generally not mixed by sexual reproduction, and hence are predominantly transmitted through one sex (typically the female sex in animals and angiosperms). This causes genetic conflict in which cytoplasmic elements (e.g. mitochondria) manipulate the 'host' to bias transmission in their own favour.

In plants, mitochondria that abort pollen cause a reallocation of resources, and an increase in the number or size of seeds. In petunias (*Petunia hybrida*), the mitochondria may deteriorate during pollen development, preventing pollen production (Folkerts & Hanson, 1991). In the wild, there are multiple cytotypes (each of which can cause male sterility). In response to this type of manipulation, nuclear genes have evolved that can restore pollen fertility (Schnable & Wise, 1998). However, nuclear restorers are polymorphic at several loci, and are apparently specific for particular mitochondrial mutants, because each allele is only effective at restoring fertility when associated with a particular cytotype (Frank, 2000*a*).

Suppression of the action of selfish genetic elements also plays a key role in the generation of polymorphism (Frank, 2000). For example, B chromosomes (large pieces of nuclear DNA other than the standard chromosomes) frequently show the properties of selfish genetic elements, such as a tendency to increase in number during transmission, while imposing a cost on their host (Jones, 1991). Recent evidence from research on grasshoppers in Spain (Camacho *et al.*, 1997; Zurita *et al.*, 1998) indicates that there are high levels of polymorphism among populations in B chromosome variants, with 40 different types identified. Crossing studies (Herrera *et al.*, 1996) demonstrate that these B chromosome variants can cause drive in new populations, but are suppressed against the genetic background of their local population, suggesting the frequent evolution of suppressors. Camacho *et al.* (1997) suggested that polymorphism is driven by a process of drive, suppression, and then the evolution of new driving variants that replace locally repressed variants. This process has recently been observed (Zurita *et al.*, 1998) in Torox, Spain, where a new driving B chromosome variant invaded a population and replaced the previously dominant but effectively suppressed variant.

The diversity of cytonuclear interactions in systems with high specificity (e.g. cytoplasmic male sterility) can combine with population structure to affect polymorphism (Frank, 2000*a*). If there are only a few matching types, then each population will contain most of the potential genetic diversity, and local interaction will drive the evolutionary dynamics. Conversely, if there are many matching types, then some populations are likely to lose alleles, and extinctions and colonizations among populations will become important. These population-level dynamics can provide a new level of selection in favour of diversity. As a new cytotype spreads in a local population without resistance alleles, it will drive down the frequency of other cytotypes that are controlled by resistant alleles. This causes their nuclear restorers to go extinct (because they are no longer needed), and local extinction leads to another round of colonization. This process maintains spatial variation among populations. Hence diversity can drive further diversity through population-level processes.

VII. INTRAGENOMIC CONFLICT AND SPECIATION

A number of authors have suggested that intragenomic conflict can drive reproductive isolation and hence speciation (e.g. Frank, 1991*b*; Hurst & Pomiankowski, 1991). For example, in cytoplasmic incompatibility, maternally inherited cytoplasmic bacteria cause the death of progeny of infected females when they mate with an infected male. This provides an advantage by eliminating offspring which do not contain clonal relatives of the bacteria in the infected male (Turelli, 1994). Cytoplasmic incompatibility factors usually reach high frequencies within populations, and once high frequency is achieved incompatibility will become very rare within the population. However, in crosses between populations, incompatibility is much more likely, because the two populations may have disparate cytoplasmic incompatibility factors (Turelli, 1994).

Hurst & Schilthuizen (1998) reviewed the importance of selfish genetic elements in speciation, focusing on *Medea* genes, meiotic drive genes, transposable elements and cytoplasmic incompatibility inducing *Wolbachia* spp. infections. *Medea* genes combine a maternal effect toxin and antidote in the embryos of mothers that carry the gene. The genes increase in frequency in populations that carry them by killing individuals that do not bear them. These genes will cause high embryonic mortality in F_1 hybrid backcrosses, hence reducing the fitness of hybrids. However, these genes are likely to increase deterministically once they have invaded the population. Once the *Medea* gene spreads in the population that originally did not have it, it will no longer contribute to the

evolution of reproductive isolation between the populations.

Hurst & Pomiankowski (1991) proposed that heterogametic (male) hybrids of two populations, one of which has X chromosome meiotic drive and suppression, and one of which has Y chromosome drive and suppression, might combine two driving sex chromosomes in a single individual, and be infertile as a result. Hurst & Schilthuizen (1998) noted that there is no empirical evidence for this phenomenon, and the rarity of Y chromosome drive makes it unlikely to be common. Both Frank (1991*b*) and Hurst & Pomiankowski (1991) argued that the loss of suppression of a meiotic drive gene in a novel population could cause sterility in heterogametic hybrids. This argument relies on drive causing sterility in hybrids. Some evidence for this has come from the t complex in mice, which contains a meiotic driver (Pomiankowski & Hurst, 1993). Hybrid males from crosses between *Mus spretus* and *M. musculus* are sterile, and the genes causing sterility map to the same region of the genome as the meiotic driver, on chromosome 17. Both drive and sterility appear to be associated with the *Tcte*2 gene (Braidotti & Barlow, 1997). Hybrid sterility is also associated with the *Stellate* gene in *D. melanogaster*, which is believed to be a meiotic driver (Hurst, 1996).

Transposable elements can increase in frequency by spreading through the genome, while imposing some cost on the host through disruption of functional genes. Typically, transposable element activity is relatively benign within the population in which they have spread, but more disruptive in hybridizations (Hurst & Schilthuizen, 1998). This has led to the proposal that transposable elements may cause reproductive isolation (Bingham, Kidwell & Rubin, 1982). Theoretically, this is a possibility, but there is no empirical evidence for a relationship between the frequency of transposable elements and hybrid inviability and sterility in drosophilids, where these factors are relatively well studied (Coyne, 1992). Furthermore, just as for *Medea* genes, if the transposable elements were transferred to the new population, they would quickly spread and adapt to that population, so that hybrids would no longer be negatively affected (Hurst & Schilthuizen, 1998).

Cytoplasmic incompatibility can be caused by the bacterial symbiont, *Wolbachia* spp. When males infected with this bacteria mate with an uninfected female, the eggs of that female die. This causes a decrease in the reproductive output of uninfected females relative to infected females, ultimately causing the infected cytotype to become fixed in the population. When individuals from different populations are infected by different strains of *Wolbachia* spp., this can lead to inviability of the offspring from crosses of males or females from either population, and hence to effective isolation of the populations (Coyne, 1992).

Research on parasitoid wasps of the genus *Nasonia* suggests that *Wolbachia* spp. infection can produce strong reciprocal reproductive isolation before strong postzygotic isolation arises due to other causes. Research on two distantly related species, *N. vitripennis* and *N. giraulti* (Breeuwer & Werren, 1990), and two closely related species (*N. giraulti* and *N. longicornis*) (Bordenstein, O'Hara & Werren, 2001), has demonstrated bidirectional cytoplasmic incompatibility due to the presence of different *Wolbachia* spp. strains. Experimental removal of the *Wolbachia* spp. infections, via antibiotic treatment, demonstrated that the effects were due solely to the presence of *Wolbachia* spp. Bordenstein *et al.* (2001) further demonstrated that the reproductive isolation between *N. giraulti* and *N. longicornis* was not accompanied by significant reproductive isolation due to other post-zygotic isolating mechanisms, such as interspecific sperm-egg incompatibility, inviability or sterility of F_2 hybrid males, or inviability or sterility of F_1 females. These results suggest that cytoplasmic incompatibility is an important factor promoting speciation in these wasps.

Recent research suggests that genomic imprinting plays a role in speciation. Haig & Graham (1991) have argued that sexual conflicts are mediated through parental imprinting, in that the paternal half of the genome in an embryo expresses the interests of the father in acquiring more resources from the mother than the mother (and the maternal half of the embryo's genome) is selected to provide. In some cases, this has apparently led to biochemical conflicts mediated via growth-promoting factors expressed only by the paternal half of the genome (because they are maternally imprinted) and 'decoy' receptors expressed only by the maternal half of the genome (they are paternally imprinted). For example, in mice, growth effects can be mediated by insulin-like growth factor 2 (IGF2), and a decoy receptor that is a derivative of mannose 6-phosphate receptor called the IGF type 2 receptor. The decoy receptor transports the growth factor to lysosomes, where they are destroyed (Moore & Haig, 1991). This conflict might also be expected to lead to rapid evolutionary change in the sequences of these two genes, although comparative analysis does not support this expectation (McVean & Hurst, 1997). However, recent evidence demonstrates that imprinted loci affecting growth can evolve rapidly in separate species, causing reproductive isolation (Vrana *et al.*, 2000).

Vrana *et al.* (2000) used two species of mice with different mating systems, which are expected to have different patterns of imprinting: *Peromyscus polionotus* has a monogamous mating system, and *Peromyscus maniculatus* has a promiscuous mating system. Vrana *et al.* (2000) showed that crosses between these two species produce inviable hybrids. Inviability is caused by syndromes of over-growth or under-growth, as expected if imprinted genes influencing growth are involved. Using genetic crossing experiments, these researchers determined that paternally imprinted genes are critical in causing hybrid inviability. This suggests that intragenomic conflict between paternally and maternally imprinted genes can drive the evolution of reproductive isolation and hence provide a key impetus for speciation and diversity.

The diversity of intragenomic conflicts provides a variety of potential mechanisms for the generation of polymorphism both within and between populations, and in some cases these processes can promote the evolution of reproductive isolation and speciation. It is likely that many forms of intragenomic conflict await discovery, and so the contribution of genetic conflicts to genetic diversity may currently be underestimated. For example, Kusano *et al.* (1995) argue that restriction modification (RM) systems, which have traditionally been thought to have evolved solely to protect organisms from invasion by foreign DNA or RNA, are instead 'protection rackets' consisting of selfish genetic elements that monopolize specific sequences. Kusano *et al.* (1995) suggest that competition among different RM systems has led to enhanced genetic diversity of recognition sites.

VIII. SEXUAL CONFLICT AND POLYMORPHISM

Sexual conflict occurs when the reproductive strategies of males and females are in conflict. In species without strict monogamy, strategies that increase the reproductive success of one sex may do so at the expense of the other (Trivers, 1972). Analogous to host–parasite interactions, sexual conflict may fuel antagonistic coevolution between the sexes, as members of each sex attempt to exploit members of the opposite sex to maximize their own reproductive gain (Holland & Rice, 1999). Male exploitation, in particular, has a parasitic component, in that males usually make little or no contribution to offspring growth or survival, but instead parasitize female reproductive effort (Trivers, 1972). Sexually antagonistic coevolution may fuel both within-species diversity and speciation (Rice, 1996, 1998).

In species with minimal male parental investment, such as *D. melanogaster*, antagonistic coevolution caused by sexual conflict involves interactions both between males and females, and between different males. Males are selected to produce seminal fluids that reduce a mate's propensity to re-mate, and to prevent his sperm from being displaced. Males are also selected to produce seminal fluid with offensive capabilities, such as the ability to persuade females to re-mate, and to displace the sperm of previous males (Rice & Holland, 1997).

Males use a variety of offensive and defensive strategies, and these often reduce female fitness (Stockley, 1997). For example, seminal toxins in *D. melanogaster* serve to increase female ovulation rates (Chen, 1984) and reduce female desire to re-mate (Aigaki *et al.*, 1991). These seminal toxins also reduce female life span (Fowler & Partridge, 1989). Furthermore, the effects of the toxins are cumulative so that the more a female receives the more deleterious the effects (Chapman *et al.*, 1995).

Johnstone & Keller (2000) develop a game theoretical model that indicates that male *D. melanogaster* are selected to transfer large doses of toxin to females. The large doses of toxin inhibit females from re-mating and increase the males' share of paternity, despite the fact that this reduces female fitness.

In *D. melanogaster* (and many other species) internal fertilization produces direct chemical interaction between individuals. This promotes antagonistic coevolution, in which gene products change via mutations and counter-mutations. Rice (1996) demonstrated experimentally that male and female *D. melanogaster* are engaged in antagonistic coevolution involving seminal toxins and female resistance to those toxins. In his experiment, he kept a separate stock of females from which target females were drawn and allowed to mate with each generation of experimental males. Experimental male lines were allowed to evolve in response to the phenotype of non-evolving target females, but females could not evolve in response to male phenotypes. He found that the males rapidly adapted to the fixed female phenotype. Male fitness increased while female fitness declined. Experimental males had more success re-mating females previously mated by control males, had an increased ability to prevent control males from re-mating with females previously mated by experimental males, and were better able to displace sperm present in female reproductive tracts. Female life spans were substantially decreased. This decrease in life span was associated with seminal toxins. There

was no increase in female fecundity. Rice (1996) concludes that sexual conflict is a strong force generating continuous antagonistic coevolution between the sexes.

Sexual conflict is a form of intergenomic conflict, which exists between non-allelic genes residing in different individuals (Rice & Holland, 1997). This conflict may be present between alleles residing at the same locus (intralocus conflict) or at different loci (interlocus conflict). In a process dubbed interlocus contest evolution (ICE), intergenomic conflict drives antagonistic coevolution between loci within the genome of a single species. ICE drives genetic and phenotypic divergence among isolated populations through recurrent gene substitution of divergent alleles at antagonistically interacting loci. Rapid evolution at a particular locus is a sign that ICE may be occurring, because ICE speeds the rate of evolution when an allelic substitution at one locus selects for a new allele at an interacting locus (Rice & Holland, 1997).

Just as evidence for positive selection has been found in a variety of genes associated with host–parasite interactions (see above), a number of studies have identified positive selection acting on genes associated with sexual reproduction or recombination, as predicted by the ICE hypothesis. For example, research on the male ejaculatory protein, Acp26Aa, has revealed strong evidence that positive selection is acting on this locus. Comparisons between species within the *D. melanogaster* subgroup, and among populations of *D. melanogaster*, revealed high ratios of non-synonymous to synonymous substitutions (Tsaur & Wu, 1997; Tsaur, Chau-Ti & Wu, 1998). Furthermore, these comparisons revealed substantial within-species non-synonymous polymorphism. Analysis of Acp26Aa sequence polymorphism in *D. mauritania* demonstrated high levels of non-synonymous polymorphism and elevated sequence divergence between *D. mauritania* and *D. melanogaster* (Tsaur, Chau-Ti & Wu, 2001). This is consistent with the predicted effects of sexually antagonistic coevolution during divergence between species (Rice, 1998), and also suggests that negative frequency-dependent selection or overdominant selection must be acting to promote polymorphism within a species at this locus (Tsaur *et al.*, 1998).

Similar results have been found in studies of marine invertebrate gamete-recognition proteins (Metz & Palumbi, 1996). Surveys of sequenced genes involved in male–female reproductive interactions in model organisms (e.g. *D. melanogaster* and its close relatives) have found significantly higher ratios of non-synonymous to synonymous substitution rates (Civetta & Singh, 1998). These results are consistent with the predictions of the ICE hypothesis. Rice & Holland (1997) further suggest that ICE plays an important role in morphological, physiological and behavioural interactions between males and females, such as courtship displays.

An important component of the sexually antagonistic coevolution hypothesis is that males and females coevolve (Rice, 1998). This could involve tradeoffs or high levels of specificity, such that the success of particular male genotypes will be context-dependent, depending on the female genotype with which it interacts. Evidence in favour of this kind of specificity has been found in several recent studies (e.g. Palumbi, 1999). The hypothesis also predicts that females will evolve to resist signals or stimulation by common male genotypes. Recent research has demonstrated this effect in *D. melanogaster* (Clark, Begun & Prout, 1999; Andres & Arnqvist, 2000). The sexual conflict hypothesis also predicts that female reproductive proteins, which interact with male reproductive proteins, will show evidence of positive selection, since they should evolve in response to evolutionary changes in male proteins (Rice, 1996). Research on the evolution of female reproductive proteins in a variety of species of mammals supports this prediction: an analysis of non-synonymous and synonymous rates of substitution in three fertilization proteins involved in sperm reception and recognition demonstrates high levels of positive selection driving the divergence of these loci (Swanson *et al.*, 2001). Finally, recent research has demonstrated associations between the defence phenotypes of male *D. melanogaster* and the amount of harm caused to females; those male genotypes that reduce female fitness the most have the largest fitness advantage (most effective defence) (Civetta & Clark, 2000). This is the first evidence for a genetic polymorphism in males that is associated with variation in both male fitness and harm to females (Rice, 2000).

Other hypotheses attributing genetic and phenotypic diversity to sexual conflict have been proposed. For example, Hill (1994) proposed that sexual conflict may lead to an evolutionary arms race fueled by female demand for reliable signals of male quality and selection on males to express these signals independently of quality (i.e. males will evolve 'shortcuts' to trait production). This conflict provides an evolutionary mechanism for trait elaboration via adaptive female choice.

IX. SEXUAL CONFLICT AND SPECIATION

Rice (1998) argued that sexually antagonistic coevolution is likely to be a major factor promoting genetic divergence leading to both pre-zygotic and post-zygotic reproductive isolation and speciation. Gavrilets

(2000*a*) suggested that sexual conflict drives the rapid evolution of reproductive barriers. He developed a mathematical model demonstrating that a continual change in male and female reproductive traits at a constant speed is expected whenever females experience fitness loss from having too many compatible males. Females continuously evolve to lower the mating rate, while males continuously evolve to increase it. Gavrilets (2000*a*) and others argue that females have an optimum mating rate that reflects the trade-offs between the positive and negative effects of multiple mating on female fitness. Males are often selected to coerce or seduce females to mate above these optima (Arnqvist & Nilsson, 2000). This is the essence of sexual conflict, and it leads to perpetual changes in traits responsible for reproductive isolation and thus speciation (Gavrilets, 2000*a*, *b*).

Arnqvist *et al.* (2000) argue that intersexual conflict spurs the perpetual coevolution of reproductive anatomy, physiology and behaviour. In allopatric populations, these traits will diverge and contribute to both pre- and post-zygotic reproductive isolation, so that the speciation process will be accelerated. This hypothesis predicts that speciation rates will be low in clades that are monandrous (females are monogamous and intersexual conflict is low), relative to speciation rates in clades that are polyandrous (females mate multiply and intersexual conflict is high). Arnqvist *et al.* (2000) compared speciation rates among monandrous and polyandrous clades of insects. On average, polyandrous clades speciate four times faster than monandrous clades. It was concluded that sexual conflict is an important 'engine of speciation'.

Parker & Partridge (1998) reviewed both between- and within-locus sexual conflict to determine their role in the genetic differentiation of populations and the evolution of reproductive isolation, and thus speciation. They conclude that both between- and within-locus conflict may contribute to the evolution of pre- and post-zygotic reproductive isolation. They generally agree with the Rice & Holland (1997) contention that sexual conflict over mate quality within populations promotes genetic divergence between populations with restricted gene flow. However, whether sexual conflict restricts or facilitates the evolution of reproductive isolation between populations probably depends upon how resolutions for the conflict are reached. In populations where 'male-win' scenarios (males are likely to defeat female resistance to mating) are probable, then isolation may be impeded. In populations where 'female-win' scenarios (females are more able to resist male mating attempts) are likely, then isolation may be promoted, with male persistence acting as a major catalyst to speciation by increasing selection on female resistance.

A variety of evidence supports the argument that sexually antagonistic coevolution can lead to rapid reproductive isolation and speciation (Rice, 1998). A number of studies have demonstrated that genes involved in sexual interactions diverge at extraordinarily high rates (see above). Incompatibility of reproductive tract interactions characterizes even the early stages of the evolution of reproductive isolation (Gregory & Howard, 1994). Even different strains of *D. melanogaster* maintained in the laboratory can rapidly develop reproductive tract incompatibility (DeVries, 1964). There is also evidence that hybrid infertility evolves more quickly than hybrid inviability, as predicted by the sexual conflict hypothesis (Wu & Davis, 1993; True, Weir & Laurie, 1996).

The study of sexual conflict is an active area of investigation, and there is convincing evidence that these conflicts can generate substantial polymorphism at both the genetic and phenotypic level, and that they contribute to reproductive isolation and speciation.

X. KIN MIMICRY AND POLYMORPHISM

The current high level of interest in kin recognition and the potential for exploitation of kin recognition systems began with W. D. Hamilton's classic work on inclusive fitness and the evolution of interactions among kin (Hamilton, 1964). Hamilton (1964) noted that discrimination on the basis of kinship would facilitate the evolution of a number of different altruistic behaviours.

Kin recognition must involve cues produced by one individual that are matched to a template produced by another individual (Sherman, Reeve & Pfennig, 1997). A variety of different mechanisms of kin recognition have been proposed, with a variety of different kinds of templates and cues (Sherman *et al.*, 1997). Common kin recognition mechanisms are listed in Table 5. The literature on the mechanisms of kin recognition is vast and contains a variety of controversies. For example, some researchers have argued that kin recognition may be mediated by recognition alleles (Hamilton, 1964), green-beard alleles (alleles that produce a trait, recognition of the trait in others, and a propensity to behave altruistically toward those with the trait) (Ridley & Grafen, 1981), or self-referent phenotype matching (Sherman, 1991), whereas others have argued that these mechanisms are unlikely to evolve (Alexander & Borgia, 1978; Alexander, 1991). These controversies are beyond the scope of this review.

Table 5. *Mechanisms of kin recognition/discrimination, including the nature of the recognition template and cues*

Mechanism	Properties	Template	Cue
Spatial proximity	Discriminate based on location of interaction	Learned or innate	Environmental
Recognition alleles	Specific gene or linkage group determines phenotype, recognition and discrimination	Innate	Innate
Self-referent phenotype matching	Inherited or acquired phenotype of the individual is used to learn a template	Learned (from self)	Acquired or innate
Associative learning	Based on prior interactions with specific individuals (typically nestmates)	Learned (from other individuals)	Acquired or innate
(a) Special events	Imprinting or instruction during a specific period	Learned	Acquired or innate
(b) Cumulative association	Long-term associations determine template	Learned	Acquired or innate

The mechanisms of kin recognition are relevant to the subject of this review, in that the nature of the cues utilized for recognition impacts the nature of selection caused by kin mimicry. For example, if cues used for recognition are genetically determined, then selection for cue diversity can favour genetic diversity in the genes encoding the cues (via negative frequency dependence or overdominance). Alternatively, if cues are acquired from the environment, then selection for cue diversity may not produce increased genetic diversity, but rather be mediated by selection on habitat choice relative to environmentally acquired cues. Environmentally mediated cues could be more susceptible to parasitism in the long run, because they do not coevolve with parasite pressure (although habitat selection preferences could coevolve).

Crozier & Dix (1979) proposed a genetic model that addressed the relationship between kin recognition mechanisms and cue or label diversity, assuming genetically encoded cues. The model was designed to address the problem of recognition in haplo-diploid insects, and focused on mechanisms that would allow discrimination between nest mates and non-nest mates. The model focused on the evolution of genetically based pheromonal cues used for recognition and discrimination. Individuals are accepted as nest mates if they share one or both alleles at the recognition locus (or loci) with a guard insect. Crozier & Dix (1979) focused on the effects of genetic variation and of different types of reference-matching templates on recognition errors. Two different template types were considered. The first type was an 'individualistic' model, in which individuals have a recognition template that reflects their own genotype, and other individuals are accepted as nest mates if they match 'self' at one or both alleles at each locus. The second kind of template was a 'gestalt' model in which all pheromonal products in the nest are pooled into one composite label, and the pheromonal profiles of individuals have to match to trigger acceptance. Crozier & Dix (1979) demonstrated that the gestalt model allows for much greater precision in distinguishing members of one variable population from members of another.

A variety of extensions of the Crozier & Dix (1979) approach have been published. Getz (1981) developed the concept of a 'kingram', which specifies the frequency distribution of the degree to which a given class of relatives share labels, and the overlap of that distribution with the frequency distributions for other classes of relatives and non-relatives. Beecher (1982) devised a method to compare the information content in recognition cues using information theory. Lacy & Sherman (1983) used a quantitative genetic model to address the effect of genetic variation, the type of kinship distinction to be made, and the choice of referent (e.g. self, sib-group, etc.) on the recognition error rate in more detail. Reeve (1989) developed a general model of recognition acceptance thresholds, taking into account the relative costs and benefits of both acceptance and rejection.

Crozier (1986) presented the first model to examine the evolutionary dynamics of recognition cues. He considered the case of clonal recognition in marine invertebrates, which mediates clonal aggression. He argued that individuals carrying a rare recognition allele would be at a disadvantage, because they would be subject to more aggression than individuals carrying common alleles. Using a single-locus population genetic model, with two alleles, he sought conditions for a stable polymorphism. He found that there was no stable equilibrium, and that population allele frequencies tended to go to either 0 or 1, eliminating polymorphism.

Crozier (1986) considered the case in which aggression had only costs, and no benefits. He did not consider the case where different individuals fuse, which is a common event in many marine invertebrates (Buss, 1987). Buss (1987) proposed that fusion could be beneficial (via inclusive fitness effects) if fusion is limited to close relatives. He also proposed that the highly polymorphic allorecognition systems of clonal invertebrates evolved to limit fusion partners to close relatives, and thus prevent parasitism by non-relatives.

Grosberg & Quinn (1987) developed a game theoretical approach to address the evolution of genetically encoded label diversity under a model of aggression with both costs and benefits, a model of fusion with both costs and benefits, and a model combining aggression and fusion. They found that models of aggression would not produce negative frequency dependence and stable polymorphism, even when both the costs and benefits of aggression were considered. However, they found that models of fusion that considered both costs and benefits did produce stable polymorphism when the costs of fusion outweigh the benefits. As Grosberg & Quinn (1987) point out, these costs are likely to be associated with the costs of fusing with non-kin, and consequently being parasitized by an unrelated genotype. Grafen (1990) used a verbal model to confirm that label diversity in kin recognition systems will be favoured when there is a substantial risk of parasitic exploitation of nepotistic benefits by non-kin.

Research on the colonial protochordate, *Botryllus schlosseri*, supports the hypothesis that parasitic exploitation can drive the extreme polymorphism in loci involved in clonal recognition in marine invertebrates. Many marine invertebrates undergo transplantation interactions in nature, which can result in chimeras with fused vascular systems (Buss, 1987). In *B. schlosseri*, the probability of fusion is regulated by a highly polymorphic fusibility/histocompatibility locus (Scofield *et al.*, 1982). Grosberg & Quinn (1986) demonstrated that this locus regulates kin recognition and the spatial distribution of genotypes in the field. The highly polymorphic nature of this locus ensures that allele matching matching occurs only with relatives under natural conditions (Grosberg & Quinn, 1986).

Sabadin & Zaniolo (1979) demonstrated that within chimeras of *B. schlosseri*, germ-line cells of one member of a chimera can migrate and establish themselves within the gonads of its chimeric partner(s), and gain access to the germ-line cell lineage of the partner, resulting in germ-line parasitism. Stoner & Weissman (1996) demonstrated experimentally that germ-line parasitism is common in *B. schlosseri* in the field, but can be prevented by rejection of fusion. Stoner, Rinkevich & Weissman (1999) used microsatellite analysis to demonstrate that germ-line parasitism is a heritable trait, with some lineages being particularly successful at exploitation. Their results suggest that antagonistic coevolution between parasitic and host genotypes within the same species is driving the evolution of the polymorphism seen at the fusibility/histocompatibility locus. An alternative explanation for diversity at histocompatibility loci is that these loci may be involved in mate recognition (to avoid inbreeding). Recent research on several species of marine invertebrates indicates that mate choice does not maintain polymorphism at the histocompatibility loci in these animals (Grosberg & Hart, 2001).

Here we focus on kinship/nest mate recognition and parasitism in the social insects [termites (Isoptera), wasps, bees and ants (Hymenoptera)]. These insects generally live in a colony or nest, and recognition of nest mates (who should be closely related kin) is critical to survival (Michener & Smith, 1987). Social insects, including termites, ants and some species of bees and wasps, are distinguished by cooperative brood care, overlapping generations and caste dimorphism (Wilson, 1971). The success of the social insects, in terms of extraordinary species diversity and abundance, and the concentration of resources in their nests, have given rise to a wide variety of parasitic strategies, by both hymenopterans and other species (Wilson, 1971). Parasitism in social insects culminates in social parasitism, in which members of one species or colony use members of another to rear their own progeny. There are many interspecific and intraspecific social parasites in social insects (Wilson, 1971). Interspecific parasites can be distantly related species or other social insects. For example, some beetles (Vander Meer & Wojcik, 1982) and some syrphid flies (Howard, McDaniel & Blomquist, 1980) have evolved to be social parasites of hymenopterans. Interspecific socially parasitic hymenopterans include wasps (Bagneres *et al.*, 1996),

bees (Michener, 1970), and especially ants (Holldobler & Wilson, 1990). Approximately 220 of the 10 000 known species of ants are social parasites (Holldobler & Wilson, 1990). Social parasitism in ants involves several different specialized forms, including temporary parasitism (colony foundation with the aid of a foreign species), dulosis (slave-making) and inquilism (permanent parasitism, with the parasite species often being workerless).

A variety of kin recognition mechanisms occur in social insects, but cuticular hydrocarbon profiles are considered to be the main chemical cues responsible for nest mate recognition in social insects (Lenoir *et al.*, 2001). Cuticular hydrocarbons have been shown to play a significant role in both species and kin recognition in many species of social insects (Singer, 1998). For example, experiments have demonstrated the importance of cuticular hydrocarbons for nest mate recognition in the ants *Camponotus vagus* (Bonavita-Cougourdan, Clement & Lange, 1987), *Cataglyphis cursor* (Nowbahari *et al.*, 1990), and *Cataglyphis niger* (Lahav *et al.*, 1999). In the wasp *Polistes metricus*, experiments have demonstrated that wasps learn the odours of cuticular hydrocarbons in the nest and use this odour to form a template used to discriminate kin from non-kin (Gamboa *et al.*, 1996; Singer & Espelie, 1996). In termites, kin discrimination between colonies of *Reticulitermes* spp. is at least partially mediated by cuticular hydrocarbon phenotypes (Haverty *et al.*, 1999). The cuticular hydrocarbon profiles of insects vary between species, populations, sexes and life stages (Singer, 1998). This suggests that these profiles are at least partially under genetic control. Recent experiments on kin recognition in ants also support the hypothesis that cues used in kin recognition are under genetic control (Beye *et al.*, 1998).

In some species of ants, research suggests that individuals share hydrocarbon cues in order to produce a common 'gestalt' hydrocarbon profile, corresponding to the 'gestalt model' of Crozier & Dix (1979) discussed above. This model has been supported by research on a variety of species (Vander Meer & Morel, 1998). Research on *C. niger* demonstrates that individual ants acquire a common, uniform colony odour (Soroker *et al.*, 1994) and recent research confirms this finding in two other species of ants (Lenoir *et al.*, 2001). However, some species of ants with small colony sizes may conform more to the individualistic model (Soroker, Fresneau & Hefetz, 1998).

A number of social parasites have been shown to mimic the cuticular hydrocarbon profiles of their hosts, either by producing the hydrocarbons or by acquiring them from the hosts or their nest. In ants, the cuckoo ant (*Leptothorax kutteri*) acquires the hydrocarbon profile of its host through intensive grooming of the host queen (Franks *et al.*, 1990). In wasps, invading female *Polistes atrimandibularis* (which are obligate social parasites) change their hydrocarbon profiles over the colony season to match that of the host (*Polistes biglumis bimaculata*) (Bagneres *et al.*, 1996). Whether this involves biosynthesis or simply acquisition is not yet clear. Many species of socially parasitic hymenoptera are closely related to their hosts (see below), and so chemical mimicry of host hydrocarbon profiles may require relatively small amounts of profile modification in these species. However, even extremely distantly related social parasites have evolved the ability to synthesize hydrocarbon profiles that closely mimic those of their hosts. For example, socially parasitic staphylinid beetles (*Trichopsenius frosti*) synthesize hydrocarbon profiles that mimic those of their host termite (*Reticulitermes flavipes*) (Howard *et al.*, 1980). There are a number of other examples in which social parasites have evolved an innate ability to mimic the chemical profile of their hosts (e.g. Akino *et al.*, 1999; Elmes *et al.*, 1999).

Social parasites can impose a heavy cost on their hosts (Holldobler & Wilson, 1990), and hence can produce strong selection in favour of kin recognition systems. Social parasites, in turn, should evolve in response to their hosts, in order to maintain kin mimicry and other forms of exploitation (Davies *et al.*, 1989). Hence, this system provides all the ingredients for antagonistic coevolution.

To date, there has been little research conducted to determine whether social parasites do, in fact, coevolve with their hosts. Recently, Foitzik *et al.* (2001) carried out the first study of parasite–host coevolution in slave-making ants. Slave-makers impose a particularly strong selection pressure on their hosts, and hence are excellent candidates for studies of coevolution. Foitzik *et al.* (2001) used field studies to demonstrate that the selection pressure (as measured by colony size, abundance and raiding frequency) exerted by slave-makers (*Protomognathus americanus*) on hosts (*Leptothorax longispinosus*) was highest in New York populations, relative to populations from West Virginia and Vermont. Slave-makers from New York were more effective at exploiting all host populations, and hosts from New York were more effective at defending against all slave-maker populations. These results are consistent with the presence of an escalating arms race between parasites and hosts, mediated by behavioural strategies of attack and defence (Foitzik *et al.*, 2001). Recognition mechanisms may be less important in interactions between slave-makers and their hosts, because success or failure

is determined by direct interactions during raids. However, this study does illustrate the potential for socially antagonistic coevolution between social parasites and their hosts.

Recent research has demonstrated overdominant selection mediated by a 'green-beard' gene in fire ants (Keller & Ross, 1998). Queens in polygynous colonies that have the BB genotype at the Gp-9 locus are recognized on the basis of an odour cue and killed by heterozygous (Bb) workers. Queens with the bb genotype die prematurely due to intrinsic factors. This behaviour may indicate selection acting on the workers to maintain polygyny in some colonies (Grafen, 1998). This bizarre form of overdominance demonstrates that genetically mediated kin recognition and discrimination can promote genetic polymorphism within species.

Research on wasps and ants suggests that heritable or partially heritable cues are commonly used as labels of kinship status (Beye *et al.*, 1998). Unlike research on selection acting at the molecular level in host–parasite systems such as the MHC or reproductive molecules such as gamete recognition proteins, there is almost no information on the genes underlying the expression of the cues or receptors mediating kin recognition. However, this is a very promising area for future research. Recent research has identified candidate loci associated with cuticular hydrocarbon profiles in *D. melanogas*ter (Takahashi *et al.*, 2001). The identification of these loci may provide the opportunity to identify similar loci in social insects, and to investigate the occurrence of positive selection. The socially antagonistic coevolution hypothesis predicts that intraspecific and interspecific non-synonymous divergence will be particularly high at such loci in species or populations experiencing high levels of social parasitism.

Recently, the Gp-9 gene in fire ants and closely related species has been cloned and sequenced (Krieger & Ross, 2002). This gene is involved in recognition and the social regulation of queen monogyny and polygyny (see above). Sequence comparisons of non-synonymous and synonymous changes between populations and species revealed significant diversifying selection at this locus (Krieger & Ross, 2002). This is the first example of a molecular evolutionary analysis of a gene involved in the recognition of conspecifics (and hence potentially involved in socially parasitic interactions).

However, the prediction of rapid evolution of genes involved in kin mimicry is only relevant to species in which chemical mimicry is mediated by parasite biosynthesis of host cuticular hydrocarbon profiles. In cases where parasites acquire their hydrocarbon profiles from their hosts, rapid evolution at loci controlling cuticular hydrocarbon profiles is not predicted to occur.

The frequency with which kin mimicry is mediated by parasite biosynthesis (as opposed to acquisition of host recognition cues from the host nest or colony) is not yet clear. Lenoir *et al.* (2001) argue that most kin mimicry by hymenopteran social parasites is accomplished by camouflage, in which the parasite acquires the hosts' hydrocarbon profile through contact with the hosts or their nest material. However, this conclusion was based on a small number of studies relative to the total number of social parasites, so further research is needed.

Even social parasites that rely on acquiring labels of kinship from the hosts or the nest must first penetrate the nest in order to acquire host labels (Schmid-Hempel, 1998). In the temporary social parasite *Bothriomyrmex syrius*, queens release a ketone that is similar to an alarm pheromone produced by the host (*Tapinoma simrothi*). This substance appears to aid the queen in invading the nest, possibly by causing confusion (Lloyd, Schmuff & Hefetz, 1986). Some slave-maker ants produce chemicals that appear to confuse their hosts during nest invasion (Regnier & Wilson, 1971). Regnier & Wilson (1971) called these chemicals 'propaganda' pheromones. Propaganda pheromones have been identified and characterized in several socially parasitic ant species (e.g. *Harpagoxenus sublaevis*; Ollett *et al.*, 1987). Other authors have argued that some of the chemicals produced by slave makers may act to pacify host ants during raids (Topoff *et al.*, 1988). These have come to be known as appeasement substances. Recently, appeasement substances have been found to play an important role in nest usurpation by European slave-maker ants (*Polyergus breviceps*; Mori *et al.*, 2000; Visicchio *et al.*, 2000). The substances are mixtures of esters, containing a high proportion of decyl butanoate (D'Ettore *et al.*, 1998). Propaganda and appeasement substances are typically synthesized by the social parasites, rather than being acquired from the host. Hence, with respect to antagonistic coevolution, genes coding for propaganda and appeasement substances and their host receptor loci are predicted to evolve rapidly within and between species.

XI. KIN MIMICRY AND SPECIATION

Social parasitism has been suggested to lead to speciation in social parasites by several researchers (Buschinger, 1990; Bourke & Franks, 1991). Emery (1909) hypothesized that social parasites are always closely related to their hosts. This hypothesis led to a

stronger claim, known as Emery's Rule, that social parasites are more closely related to their hosts than to any other free-living taxa (Le Masne, 1956). This hypothesis, in turn, is associated with the hypothesis that social parasites arise through sympatric speciation, although allopatric speciation is also consistent with Emery's hypothesis (Buschinger, 1990; Bourke & Franks, 1991). Alternatively, allopatric speciation could have originally divided host and parasite as sister taxa, with parasitism occurring after the re-establishment of sympatry (social deception hypothesis: Carpenter *et al.*, 1993), or certain lineages could have evolved into parasitic specialist clades, members of which tend to parasitize congeners (Ward, 1996).

Evidence in favour of the sympatric speciation hypothesis has recently been found in fungus-growing ants (Schultz, Bekkevold & Boomsma, 1998). *Acromyrmex insinuator* is extremely similar to and closely related to its host, *A. octospinosus*, and yet is reproductively isolated from the host. It is apparently an incipient social parasite. The fact that it is only found in the nests of its hosts suggests that it may have originated via sympatric speciation. However, recent research on a variety of social insects indicates that social parasites and their hosts are not always sister taxa, and in some cases are more closely related to other free-living species than to their hosts (e.g. Choudhary *et al.*, 1994; Ward, 1996; Sanetra & Buschinger, 2000). These results do not rule out the possibility that parasites and their hosts originally diverged into sister taxa via sympatric speciation in some cases, but they do not support that hypothesis. The results are consistent with the hypothesis that social parasites are typically closely related to their hosts. Exceptions to this trend have been found, in which socially parasitic ants exploit extremely distant taxa as hosts (e.g. Maschwitz *et al.*, 2000), but these are rare.

The socially antagonistic coevolution hypothesis does not require that parasitic species and their hosts are closely related, but does predict that socially parasitic species and their hosts will show rapid evolution at the loci that encode labels used by the hosts for kinship and nest mate recognition (see above). The hypothesis also predicts that interspecific socially parasitic species and their hosts will show high rates of speciation, as parasitic exploitation of hosts can drive rapid evolution of cues relevant to species recognition, and hence contribute to rapid reproductive isolation between separate host and parasite populations. Again, this prediction is only relevant to interspecific parasitism that is mediated by cues that are synthesized by the parasite, rather than cues that are acquired from the host by the parasite. This emphasizes the importance of understanding underlying mechanisms when making predictions regarding evolutionary outcomes.

By contrast, intraspecific social parasites and their hosts may be less prone to speciation if the cues used for kin recognition are different from those used for species recognition. Aggression toward non-kin is often favoured in the context of sharing resources, but non-kin are likely to be preferred in the context of mating. Hence, the socially antagonistic coevolution hypothesis predicts (subject to the caveat mentioned previously regarding mechanisms) that rates of speciation will be particularly high in clades that are characterized by high levels of interspecific social parasitism. The ants are a particularly promising place to investigate this prediction. The large number of ant species, and the large numbers of socially parasitic species within the ants, makes the kind of comparative analysis carried out by Arnqvist *et al.* (2000) on polyandrous and monandrous insects (to test the effect of sexual conflict on speciation rates) feasible for investigating the effect of social parasitism on speciation rates.

As mentioned above, social parasites (such as slave-making ants) do not necessarily mimic kinship with their hosts. However, even in these cases, other aspects of the parasites and their hosts can coevolve, such as propaganda and appeasement substances (and host responses to them), fighting tactics, and escape and pursuit tactics (Davies *et al.*, 1989). These features may evolve along different trajectories in different populations of social parasites and hosts. This can drive divergence in these features between populations of both hosts and parasites, resulting in reduced hybrid fitness for hybrids between populations. Hence, social parasite–host coevolution can drive reproductive isolation in a manner similar to that caused by other forms of parasite–host coevolution (see above). This area is ripe for empirical research.

XII. PARASITISM AND TROPICAL COMMUNITY DIVERSITY

The bastion of extant organismal diversity lies within tropical moist forests (Erwin, 1982). While numerous hypotheses have tried to address the idea of tropical diversity (Connell, 1979; Chesson & Warner, 1981; Tilman, 1982; Hubbell, 2001), the idea of exploitative relationships as an engine of species diversity in the rainforests has been persistent from the early 1970s. Diversity of forests is directly tied to the diversity of woody plants, which provide primary structure to the ecosystem, and support the numerous producers and consumers (Gentry, 1988). For this reason, explorations

of tropical diversity have centered on the diversity of trees. The works of Janzen (1970), and Connell (1971) form the basis of a theory (known as the 'Escape Hypothesis'; Howe & Smallwood, 1982) that suggests that parasitism of seeds and young trees would be greatest in proximity to the parent trees and conspecific adults, favouring increased distances between individuals of a species. This frequency-dependent spacing mechanism would create ecological and spatial areas that could be filled by other species, promoting the alpha diversity of the forest.

The role of insect herbivores in the diversification of tropical communities hinges on the matter of host specificity. One explanation of tropical diversity has been that tropical species tend to have narrower ecological niches than their temperate counterparts (MacArthur, 1969). With insect herbivores forming the base of numeric diversity in tropical moist forests (Erwin, 1995), the host plant specificity of each of these species is important not only for speciation in insects, but for the maintenance of forest diversity that will allow these groups to persist as taxa through the Escape Hypothesis. If generalist taxa are dominant, we can expect more uniform depredation of young trees and a reduction in the effects of the Escape Hypothesis on community structure.

The work of J. A. Barone (1998) on the insect herbivores of Barro Colorado Island (BCI), Panama has provided strong support for the Escape Hypothesis. Barone (1998) studied 10 common host tree species, and found that most of the insect species in his study were specialists, limited to a narrow range of hosts (26 % were limited to a single host species). Barone's study was explicit in examining herbivorous specificity from the perspective of the tree, not the herbivore. Barone (1998) also showed that the amount of damage done to young leaves was primarily caused by specialized insect pests.

Harms *et al.* (2000) carried out a community study of 53 tree species to test the influence of density-dependent recruitment on diversity on BCI. The density of seeds and seedlings was calculated for each species in the study, with all 53 species showing negatively density-dependent recruitment. Diversity of seeds was compared to (a) expected diversity of seedlings after taking recruitment success of individual species into consideration, but without density-dependent effects, (b) expected diversity of seedlings using a species-specific estimate of density dependence and (c) diversity of seedlings within the plots. The analysis showed considerably lower diversity for seeds than recruiting seedlings did. The two groups were not correlated, showing that diversity increased during the transition from seed to seedling. Although differing recruitment success and species-specific life history strategies may explain part of the diversity observed, density-dependent mechanisms consistent with the Escape Hypothesis were supported as a significant contributor to diversity in the community (Harms *et al.*, 2000).

Wills & Condit (1999) examined the role of the Escape Hypothesis on a community level. Their quadrat-based analysis compared the tree diversity and frequency-dependent mortality in two matched rainforest plots in Panama and Malaysia. In support of the Escape Hypothesis, negative correlations between crowding or within-species biomass were seen with recruitment. Measures of diversity (evenness, Simpson's index, Macintosh's Index) were positively correlated with numbers and biomass for tree species over time, implying that frequency-dependent effects on tree populations maintain diversity in both an Old World and New World rainforest.

Webb & Peart (1999) attempted to measure the density-dependent effects predicted by the Escape Hypothesis within a tropical forest community in Borneo. Their system contained 350 morphospecies in 50 families. Within a 150 ha area, 28 stratified random sampling locations were allocated. Each location contained a central 36 m^2 seedling plot in which the densities of all seedlings were measured as well as the basal areas and densities of each tree species. Seedling survival was measured in a subset of 12 sampling locations. Consistent with the Escape Hypothesis, seedling survival was inversely related to tree species abundance, measured as basal area. Seedling survival was also negatively associated with adult tree density. Conspecific seedling density was found to have a negative association with seedling survival.

Fungal pathogens present a major threat to the survival of young tropical trees (Augspurger, 1983). A study by Gilbert, Hubbell & Foster (1994) conducted on BCI examined the density and distance-dependent factors of a fungal pathogen (canker disease) exploiting both juvenile and adult trees (*Ocotea whitei*). In support of the Escape Hypothesis, incidence of the expression of the canker disease was clearly dependent on the density of individuals. Juvenile trees expressing the disease were closer to their nearest conspecific juvenile than healthy trees. Distance to the nearest conspecific adult tree also correlated positively with freedom from infection.

In another study by Gilbert *et al.* (2001), two cohorts of *O. whitei* were followed over six years, with annual censuses of mortality, size, density, and distance to conspecific adults. In early stages, the pattern of

seedling mortality was consistent with the Escape Hypothesis, with juvenile distribution shifting away from parent trees. After six years however, the majority of seedlings were found within 13 m of an adult, within the crown diameters of the adults that produced them. The authors conclude that further long-term demographic data are necessary to determine the role of the Escape Hypothesis in natural tree communities.

Investigations of diversity in temperate systems have also supported the Escape Hypothesis. Packer & Clay (2000) provide experimental evidence linking seedling mortality in *Prunus serotina* to pathogens occupying soil beneath conspecific trees. Moreover, the resulting patterns of seedling density and distance-to-adult are consistent with the hypothesis: while most seedlings of *P. serotina* germinate within 10 m of the parent tree, this group also has the lowest probability of survival. As the cohorts of young trees aged, the average distance between surviving offspring and parent trees continued to increase over two years.

Not all studies have supported the Escape Hypothesis. Basset (1999) sampled insects on five host tree species in Guyana, and sorted them into generalist *versus* specialist species. He concluded that most of the species identified were generalists. However, unlike Barone (1998), he did not quantify the damage done to the plants by the different species. Hence the relevance of this study to predictions of the Escape Hypothesis is questionable. Burkey (1994), in an experimental study of seed predation on *Brosimum alicastrum* (Moraceae), found evidence that seeds occurring at high densities were less susceptible to predation by rodents and ants than seeds occurring at low densities (which are typically further from the parent). These results were consistent with the 'Predator-Satiation Model' (Janzen, 1976).

Other alternatives to the Escape Hypothesis have been proposed (e.g. Langenheim & Stubblebine, 1983), but the weight of the evidence indicates that density and frequency-dependent herbivory and parasitism do play a crucial role in promoting diversity in those tropical ecosystems where the question has been investigated intensively.

XIII. INTER-GROUP CONFLICT, ESPIONAGE AND LANGUAGE DIVERSITY

The evolution of language is a complex process in which natural selection plays a pivotal role (Pinker, 1994). The precise ways in which selection moulded language are still the subject of considerable debate. Recently, Martin Nowak and his colleagues have attempted to reconstruct the evolution of language using a game theoretical approach (e.g. Nowak, Plotkin & Jansen, 2000). This approach has resulted in great strides in our understanding of language evolution. However, to date, most studies of the evolution of language have investigated how important properties of language can arise and be maintained when the individuals using language have coincident interests (Lachmann, Szamado & Bergstrom, 2001).

Human evolution has been characterized by persistent conflicts of interest at both large and small scales (Alexander, 1979). Inter-group conflicts among small groups, bands, tribes, city-states and lately nation-states have been a major selective force moulding human cognitive capacities (Alexander, 1979, 1987). Within-group conflicts likely played a key role in selecting for enhanced cognitive capacities (Alexander, 1987; Whiten & Byrne, 1988). It is likely that these conflicts of interest profoundly influenced the evolution of language (Lachmann *et al.*, 2001).

Recently, Nettle (1999) and Dunbar (1999) have argued that conflicts of interest within and between human social groups have been a key driving force in the evolution of language diversity. Large social groups can provide certain advantages to group members, but some of these advantages are vulnerable to exploitation by individuals ('freeloaders') who reap the benefits but do not pay the costs of group membership (Dunbar, 1999). This problem is closely related to the 'Tragedy of the Commons' or Common Pool Resources problem, in which group members take more than their sustainable fair share of group-controlled resources (Orstrom, Gardiner & Walker, 1994). Models of cooperation within groups suggest that freeloading is likely to be a more severe problem when groups are large, when they are fragmented in space, and when they are ephemeral (Enquist & Leimar, 1993).

One solution to the freeloader problem involves restricting cooperation to kin. This reduces or neutralizes the inclusive fitness costs of freeriding because the benefits are received by individuals likely to share genes with those suffering the costs (Dunbar, 1999). Evidence for kin-biased sharing of information concerning communal resources is abundant (e.g. Palmer, 1981). Restricting cooperation to kin entails some form of kin recognition, as noted above. Language dialects should be useful in this regard, because they change rapidly and they can be learned fluently only during a specific time window (Nettle & Dunbar, 1997). Pronunciation in particular is highly variable across time and space. Sharing a dialect implies a common geographic origin and possibly even a temporal cohort (Dunbar, 1999). Nettle & Dunbar (1997) developed simulation models

of dialects as markers of kinship in a reciprocal exchange game in which some individuals pursued a freeloading strategy involving mimicry of dialects. The results suggested that dialects could effectively prevent freeriding by non-relatives given reasonably long memory spans and rapid rates of dialect change. Dunbar (1999) argues that the critical period of language acquisition itself may have evolved as a means of ensuring the accuracy of language dialects as badges of group membership or kinship.

Recognition of group membership should also be critical with respect to reciprocal exchange interactions among non-kin, especially those involving indirect reciprocity (the donation of goods or services in order to enhance one's reputation as a generous or effective partner in social interactions; Alexander, 1987). The return does not come from the person receiving the goods or services directly, but rather flows from the enhanced reputation of the donor as a result of the dissemination of information about the act of donation through the group via observation and gossip. It is likely to be important in this case that the act of donation benefits a group member, both to ensure that the benificiary will spread news of the interaction within the group, and to ensure that the act benefits someone who is likely to have friends and relatives within the group.

Inter-group conflict may be the driving force behind much of the extreme cooperation that characterizes human social groups (e.g. Alexander, 1979, 1987). As human population densities increased over the past 40 000 years, and humans became capable of displacing or killing all other competing species, the major problem facing humans became access to resources controlled by other groups of humans. Inter-group competition and warfare have played critical roles in the fates of human societies (Diamond, 1997). Espionage, sabotage and other forms of invasive tactics that depend on effective mimicry or camouflage have played crucial roles in warfare since its origin (Keegan, 1994). Under these circumstances, language dialects could be particularly useful as markers of group membership, allowing the detection of foreign spies and other infiltrators.

Finally, Nettle (1999) has argued that an important correlate of the idea that language variation will exclude outsiders is that insiders will be further constrained to remain within a group. Enquist and Leimar's (1993) simulation models suggest that one of the major difficulties in establishing stable reciprocal relationships within groups occurs when defectors can easily leave the group without paying their debts. If language dialects make between-group discrimination more likely and effective, then defection becomes more difficult.

Many accounts of language divergence assume a process akin to genetic drift (e.g. Cavalli-Sforza & Feldman, 1981). However, ethnographic research on language indicates that dialects can and do evolve and persist in the face of a substantial flow of goods and personnel, and continued communication between social groups (Barth, 1969). There is evidence to suggest that when dialects are threatened by an influx of outsiders, those who speak the dialect increase the use of those linguistic features that make their dialect distinctive, leading to enhanced linguistic divergence (Labov, 1972). Research also indicates that people are extremely sensitive to dialect differences, and that they use such differences as a basis for character judgments (Chambers, 1995). There is considerable evidence that people do discriminate on the basis of language dialects (Nettle, 1999). People express greater feelings of solidarity towards unknown individuals using their own dialect relative to strangers that use other dialects (Giles & Powesland, 1975), and are more likely to help strangers with similar dialects in simulated situations requiring aid (Feldman, 1968; Harris & Bardin, 1972).

The process of coevolution leading to language diversity (as discussed above) is a cultural one, and is not likely to have any corresponding effect on genetic polymorphism. Nevertheless, the example illustrates that parasitic exploitation can generate cultural as well as genetic diversity.

XIV. DISCUSSION

Theory and evidence indicate that parasitic exploitation has a pervasive effect on polymorphism within populations and divergence between populations and species. Conflicts involving parasitic exploitation occur between different elements in the genome (intragenomic conflict), males and females (sexual conflict), relatives (parent–offspring conflict, sibling conflict), conspecifics (brood parasitsm, kin mimicry), and different species (classical parasite–host interactions, brood parasitism, social parasitism). Despite substantial differences between these kinds of interactions, they can all generate polymorphism and divergence. Any particular conflict may involve a limited number of loci, but evidence is accumulating that there are multiple conflicts at many levels of biological organization (Maynard Smith & Szathamary, 1995; Keller, 1999). These conflicts are likely to account for a significant amount of polymorphism in total. Their effects

have left signatures on the genomes of both hosts and parasites, as revealed by a growing number of studies of the molecular evolution of sequence diversity.

The effects of parasitic exploitation on population divergence, reproductive isolation and speciation require further investigation, but are likely to be substantial. Recently, considerable attention has focused on the effect of adaptation to distinct ecological niches on speciation (reviewed in Schluter, 2001). Speciation generated by coevolution is a form of ecological speciation in that it involves adaptation to distinct 'niches' by different populations. However, it is distinct in that the niches are continuously changed by coevolution. Because of the contingent nature of coevolutionary interactions, the selection pressures on different populations tend to diverge rapidly over time. Divergence tends to proceed even in the absence of distinct environments, providing a continuous engine of speciation (West-Eberhard, 1983).

Research on coevolutionary interactions involving parasitic exploitation is being carried out in diverse contexts, which should provide opportunities for constructive cross-fertilization of concepts and theories between fields of inquiry. Unfortunately, the lack of concordance in the use of the same words and expressions by different researchers and research groups has the potential to lead to considerable confusion. For example, many researchers (particularly those investigating the molecular mechanisms of plant–pathogen interactions) have used the term 'gene-for-gene' to characterize any interaction that involves recognition of a pathogen elicitor by a host receptor (e.g. De Wit, 1997). On the other hand, theoretical evolutionary biologists typically use the term 'gene-for-gene' to refer to a specific kind of host–pathogen interaction (one which involves universal virulence alleles), which contrasts with other models of interaction specificity such as the matching-alleles model (Frank, 1994).

In spite of differences in terminology, some of the categories of research discussed separately in this review are already being treated in a synthetic framework. For example, recent research on interactions between mitochondrial genotypes and sex chromosomes in *Drosophila* synthesize theoretical and empirical research on intragenomic conflict with sexually antagonistic coevolution (Rand, Clark & Kann, 2001). Both theoretical and empirical studies have demonstrated that selection will not maintain joint nuclear–cytoplasmic polymorphism unless there is some form of frequency-dependent or sex-specific selection (Clark, 1984). Empirical research on *D. melanogaster* has demonstrated a lack of nuclear–cytoplasmic fitness interactions within populations (Clark, 1985), although such interactions have been found between populations (Clark & Lyckegaard, 1988).

However, theoretical models of nuclear–cytoplasmic interactions involving X chromosomes (with a haplodiploid pattern of inheritance) suggest much more permissive conditions for maintaining nuclear and cytoplasmic polymorphism under antagonistic nuclear–cytoplasmic fitness interactions (Rand *et al.*, 2001). These types of fitness interactions between X chromosome and mitochondrial genotypes have been demonstrated by experimental crosses in *D. melanogaster* (Rand *et al.*, 2001). Significant negative correlations were found between the relative fitness of male and female genotypes when tested against alternative cytoplasmic genotypes. This demonstrates that cytoplasmic genotypes that increase fitness in males decrease fitness in females, and *vice versa*. This is a signature of sexual antagonism at the genetic level (Rice & Holland, 1997), which in this case is expressed as a form of intragenomic conflict between mitochondrial genes and genes on the X chromosomes within males and females (Rand *et al.*, 2001). Recent research on *D. melanogaster* suggests that this type of sexually antagonistic intragenomic conflict may be pervasive (Chippindale, Gibson & Rice, 2001).

In another example of cross-fertilization, recent research has connected the study of intragenomic conflict to research on the Red Queen Hypothesis and the evolution of recombination. As discussed above, research on B chromosomes indicates that they undergo dynamic evolution, with the invasion of new harmful drivers, their spread in the population, followed by the spread of effective suppressors and the suppression of meiotic drive, followed by the spread of new harmful B chromosome mutants. Camacho *et al.* (2002) have recently demonstrated that there is a correlation between levels of parasitism by B chromosomes in a population and the frequency of crossing over (as measured by chiasmata frequency) in the population. Furthermore, the effect of B chromosomes depended on their stage in the evolutionary process. B chromosomes that were 'virulent' (not effectively suppressed yet) were associated with significantly higher levels of recombination than B chromosomes that had been neutralized by suppressors. This provides dramatic support for the Red Queen Hypothesis, but in the context of selfish genetic elements and intragenomic conflict.

This review suggests that parasitic exploitation is pervasive, and plays a role in the generation of diversity in many different contexts. Hence, it is possible that parasitic exploitation has played a role in the evolution of diversity in some systems where other

hypotheses have generally been accepted as the sole explanation of diversity. For example, considerable attention has focused the evolution of genetic diversity at loci (particularly the S locus) controlling self-incompatibility in plants. Wright (1939) developed models of S-allele diversity under the assumption that rare S-alleles have an advantage because pollen carrying such alleles is less likely to land on a stigma with the same allele, and hence more likely to result in a compatible fertilization. Cope (1962) developed the theory that self-incompatibility systems will evolve towards an equilibrium condition at which allele frequencies are equal, resulting in maximal allelic diversity. Since then, a variety of theoretical analyses have confirmed the hypothesis that self-incompatibility systems designed to reduce inbreeding can maintain high levels of genetic diversity (Uyenoyama, 2000).

While self-incompatibility is certainly involved in generating and maintaining S-allele diversity, other factors may also be important, such as sexual conflict. Sexual selection is probably a common phenomenon in plants (Snow & Spira, 1991). Pollen competition occurs, paralleling sperm competition in animals (Snow & Spira, 1996). Multiple fertilization may lead to sexual conflict in plants, just as it does in *D. melanogaster* and other animals. If pollen has evolved to have negative effects on plants as a by-product of effects designed to enhance pollen reproductive success (analogous to the effects of sperm seminal fluid discussed above) then this could also generate sexually antagonistic coevolution and associated polymorphism.

In sporophytic self-incompatibility systems, there is a family of related genes which appear to be involved in recognition at the cellular level, called S locus glycoproteins (Nasrallah & Nasrallah, 1993). Other genes that are structurally similar to S locus genes but not linked to the S locus (S locus-related genes) have also been sequenced. The exact functions of these genes have not been identified, but they appear to be involved in some form of pollination response (Nasrallah & Nasrallah, 1993). Hence, there are a number of loci involved in reproduction that may function not just in self-incompatibility but also in deactivating negative effects of pollen on ovules.

Studies of DNA sequence variability in both sporophytic and gametophytic self-incompatibility systems reveal the presence of high variability and ancient allelic diversity (Nasrallah & Nasrallah, 1993; Ishimizu *et al.*, 1998). Comparisons of synonymous and non-synonymous substitution rates in S-allele-specific recognition sites in Japanese pear (*Pyrus pyrifolia*) and apple (*Malus* spp.) have revealed strong evidence for diversifying selection (Ishimizu *et al.*, 1998). The sexual conflict hypothesis predicts that levels of polymorphism and rates of divergence will be particularly high in species subject to high levels of pollen competition.

XV. CONCLUSIONS

(1) There is a large body of evidence that is consistent with an important role for parasites in the maintenance of MHC polymorphism, and *vice versa*.

(2) Research on the molecular genetics of plant defence and pathogen attack systems, and molecular evolutionary analysis of adaptive evolution in those systems, has provided strong evidence in favour of the hypothesis that plants are involved in continuous arms races or coevolutionary cycling with pathogens, which drives diversity in both plant resistance and pathogen virulence loci.

(3) The Red Queen Hypothesis predicts that parasites impose selection in favour of sexual reproduction on their hosts. Observational and experimental research on snails with facultative sexuality and their trematode parasites provide strong support for the predictions of this hypothesis.

(4) Theory suggests that parasite–host coevolution should enhance speciation rates in both parasites and hosts, but empirical evidence for this phenomenon is lacking.

(5) Intragenomic conflict is a recent field of inquiry, yet there is already a wealth of examples supporting the hypothesis that these conflicts generate substantial genetic diversity within populations.

(6) The hypothesis that intragenomic conflict can drive reproductive isolation and speciation remains speculative, but recent research on *Wolbachia* spp. and on genomic imprinting provides important support for the hypothesis.

(7) The study of sexual conflict has blossomed in recent years, and has provided a wealth of theoretical and empirical research supporting the hypothesis that sexual conflict can generate intraspecific polymorphism.

(8) Recent theory and comparative analysis support the hypothesis that sexual conflict drives reproductive isolation and speciation.

(9) Theory suggests that kin mimicry can drive the evolution of polymorphism in the genes underlying recognition cues, and research on marine invertebrates supports this hypothesis. The social insects provide a fertile arena for further investigation in this area.

(10) The hypothesis that socially antagonistic coevolution can drive the evolution of reproductive isolation remains speculative, but is ripe for comparative analysis.

(11) The hypothesis that specialization by pathogens and herbivores drives community diversity in tropical rainforests has been supported by several recent studies, but further research is warranted.

(12) Recent theory and evidence support the hypothesis that a history of inter-group conflict and the use of certain language features as labels of group membership contributed to dialect diversification among human groups.

XVI. ACKNOWLEDGEMENTS

We thank Steven Frank, Richard Alexander, Richard Grosberg, James Mallett, David Haig, Allen Herre, Dale Clayton and one anonymous referee for discussion and comments on the manuscript. We thank Wayne Potts, Jerry Capraro and Tom McConnell for permission to reproduce figures. This paper is dedicated to the memory of William D. Hamilton, who made extensive contributions to the hypothesis that parasitic exploitation drives the evolution of polymorphism and divergence in many different contexts. His broad vision of the effect of parasitism on diversity was the inspiration for this paper.

XVII. REFERENCES

Agrawal, A. & Lively, C. M. (2002). Infection genetics: gene-for-gene versus matching-alleles models and all points in between. *Evolutionary Ecology Research* **4**, 79–90.

Aigaki, T., Fleischmann, I., Chen, P. & Kubli, E. (1991). Ectopic expression of sex peptide alters reproductive-behavior of female *Drosophila melanogaster*. *Neuron* **7**, 557–563.

Akino, T., Knapp, J., Thomas, J. & Elmes, G. (1999). Chemical mimicry and host specificity in the butterfly Maculinea rebeldi, a social parasite of Myrmica ant colonies. *Proceedings of the Royal Society of London Series B* **266**, 1419–1426.

Alexander, R. D. (1979). *Darwinism and Human Affairs*. University of Washington Press, Seattle, Washington, DC.

Alexander, R. (1987). *The Biology of Moral Systems*. Aldine de Gruyter, New York.

Alexander, R. (1991). Social learning and kin recognition: an addendum and reply to Sherman. *Ethology and Sociobiology* **12**, 387–399.

Alexander, R. & Borgia, G. (1978). Group selection, altruism, and the levels of organization of life. *Annual Review of Ecology and Systematics* **9**, 449–474.

Andres, J. & Arnqvist, G. (2000). Genetic divergence of the seminal signal-receptor system in houseflies: the footprints of sexually antagonistic coevolution? *Proceedings of the Royal Society of London Series B* **267**, 399–405.

Apanius, V., Penn, D., Slev, P. R., Ruff, L. R. & Potts, W. K. (1997). The nature of selection on the major histocompatibility complex. *Critical Reviews in Immunology* **17**, 179–224.

Arnqvist, G., Edvardsson, M., Friberg, U. & Nilsson, T. (2000). Sexual conflict promotes speciation in insects. *Proceedings of the National Academy of Sciences U.S.A.* **97**, 10460–10464.

Arnqvist, G. & Nilsson, T. (2000). The evolution of polyandry: multiple mating and female fitness in insects. *Animal Behaviour* **60**, 145–164.

Augspurger, C. K. (1983). Seed dispersal of the tropical tree, *Platypodium elegans*, and the escape of its seedlings from fungal pathogens. *Journal of Ecology* **71**, 759–771.

Bagneres, A., Lorenzi, M., Dusticier, G., Turillazzi, S. & Clement, J. (1996). Chemical usurpation of a nest by paper wasp parasites. *Science* **272**, 889–892.

Baker, B., Zambryski, P., Staskawicz, B. & Dinesh-Kumar, S. (1997). Signaling in plant–microbe interactions. *Science* **276**, 726–733.

Barone, J. A. (1998). Host-specificity of folivorous insects in a moist tropical forest. *Journal of Animal Ecology* **67**, 400–409.

Barth, F. (1969). *Ethnic Groups and Boundaries*. Allen & Unwin, London.

Barton, N. (1995). A general model for the evolution of recombination. *Genetical Research* **65**, 123–144.

Basset, Y. (1999). Diversity and abundance of insect herbivores foraging on seedlings in a rainforest in Guyana. *Ecological Entomology* **24**, 245–259.

Beecher, M. (1982). Signature systems and kin recognition. *American Zoologist* **22**, 477–490.

Bender, B., Croghan, T., Zhang, L. & Small, P. J. (1992). Transgenic mice lacking class I major histocompatibility complex-restricted T cells have delayed viral clearance and increased mortality after influenza virus challenge. *Journal of Experimental Medicine* **175**, 1143–1145.

Bent, A. (1996). Plant disease resistance genes: function meets structure. *Plant Cell* **8**, 1757–1771.

Berenbaum, M. & Zangerl, A. (1998). Chemical phenotype matching between a plant and its insect herbivore. *Proceedings of the National Academy of Sciences U.S.A.* **95**, 13743–13748.

Bergelson, J., Kreitman, M., Stahl, E. & Tian, D. (2001). Evolutionary dynamics of plant R-genes. *Science* **292**, 2281–2285.

Beye, M., Neumann, P., Chapuisat, M., Pamilo, P. & Moritz, R. (1998). Nestmate recognition and the genetic relatedness of nests in the ant *Formica pratensis*. *Behavioral Ecology and Sociobiology* **43**, 67–72.

Bianchi, N., Bianchi, M., Pamilo, P., Vidal-Rioja, L. & De La Chapelle, A. (1992). Evolution of zinc finger-Y and zinc finger-X genes in Oryzomyne-Akodontine rodents (Cricetidae). *Journal of Molecular Evolution* **34**, 54–61.

Bingham, P., Kidwell, M. & Rubin, G. (1982). The molecular basis of *P–M* hybrid disgenesis: the role of the *P* element, a *P*-strain-specific transposon family. *Cell* **29**, 995–1004.

Bishop, J., Dean, A. & Mitchell-Olds, T. (2000). Rapid evolution in plant chitinases: molecular targets of selection in plant–pathogen coevolution. *Proceedings of the National Academy of Sciences U.S.A.* **97**, 5322–5327.

Bodmer, W. & Bodmer, J. (1978). Evolution and function of the HLA system. *British Medical Bulletin* **34**, 309–316.

Bonavita-Cougourdan, A., Clement, J. & Lange, C. (1987). Nestmate recognition: the role of cuticular hydrocarbons in the ant *Camponotus vagus*. *Scope of Entomological Science* **22**, 1–10.

Bordenstein, S., O'Hara, F. & Werren, J. (2001). *Wolbachia*-induced incompatibility precedes other hybrid incompatibilities in *Nasonia*. *Nature* **409**, 707–710.

Bourke, A. & Franks, N. (1991). Alternative adaptations, sympatric speciation and the evolution of parasitic, inquiline ants. *Biological Journal of the Linnaen Society* **43**, 157–178.

Braidotti, G. & Barlow, D. (1997). Identification of a male meiosis-specific gene, *Tcte2*, which is differentially spliced in species that form sterile hybrids with laboratory mice and deleted t chromosomes showing meiotic drive. *Developmental Biology* **186**, 85–99.

Breeuwer, J. & Werren, J. (1990). Microorganisms associated with chromosome destruction and reproductive isolation between two insect species. *Nature* **346**, 558–560.

Brodie, E. I. & Brodie, E. J. (1999). Predator–prey arms races. *Bioscience* **49**, 557–568.

Brunet, J. & Mundt, C. (2000). Disease, frequency-dependent selection, and genetic polymorphism: experiments with stripe rust and wheat. *Evolution* **54**, 406–415.

Buckling, A. & Rainey, P. B. (2002). Antagonistic coevolution between a bacterium and a bacteriophage. *Proceedings of the Royal Society of London Series B* **269**, 931–936.

Burdon, J. (1987). *Diseases and Plant Population Biology*. Cambridge University Press, Cambridge.

Burdon, J. & Thrall, P. (1999). Spatial and temporal patterns in coevolving plant and pathogen associations. *American Naturalist* **153**, S15–S33.

Burkey, T. V. (1994). Tropical tree species diversity: a test of the Janzen–Connell model. *Oecologia* **97**, 533–540.

Buschinger, A. (1990). Sympatric speciation and radiative evolution of socially parasitic ants – heretic hypotheses and their factual background. *Zeitschrift fur Zoolgische Systematik und Evolutionforschung* **28**, 241–260.

Buss, L. (1987). *The Evolution of Individuality*. Princeton University Press, Princeton.

Camacho, J., Shaw, M., Lopez-Leon, M., Pardo, M. & Cabrero, J. (1997). Population dynamics of a selfish B chromosome neutralized by the standard genome in the grasshopper *Eyprepocnemis plorans*. *American Naturalist* **149**, 1030–1050.

Camacho, J. P. M., Bakkali, M., Corral, J. M., Cabrero, J., Lopez-Leon, M. D., Aranda, I., Martin-Alganza, A. & Perfectti, F. (2002). Host recombination is dependent on the degree of parasitism. *Proceedings of the Royal Scoiety of London Series B* **269**, 2173–2177.

Carius, J.-J., Little, T. J. & Ebert, D. (2001). Genetic variation in a host–parasite association: potential for coevolution and frequency dependent selection. *Evolution* **55**, 1136–1145.

Carpenter, J., Strassmann, J., Turillazzi, S., Hughes, C., Solis, C. & Cervo, R. (1993). Phylogenetic relationships among paper wasp social parasites and their hosts (Hymenoptera: Vespidae: Polistinae). *Cladistics* **9**, 129–146.

Cavalli-Sforza, L. & Feldman, M. (1981). *Cultural Transmission and Evolution: A Quantitative Approach*. Princeton University Press, Princeton.

Chaboudez, P. & Burdon, J. J. (1995). Frequency-dependent selection in a wild plant–pathogen system. *Oecologia* **102**, 490–493.

Chambers, J. (1995). *Sociolinguistic Theory*. Basil Blackwell, Oxford.

Chapman, T., Liddle, L. F., Kalb, J. M., Wolfner, M. F. & Partridge, L. (1995). Cost of mating in *Drosophila melanogaster* females is mediated by male accessory gland products. *Nature* **373**, 241–244.

Charlesworth, B., Sniegowski, P. & Stephan, W. (1994). The evolutionary dynamics of repetitive DNA in eukaryotes. *Nature* **371**, 215–220.

Chen, P. S. (1984). The functional morphology and biochemistry of insect male accessory glands and their secretions. *Annual Review of Biochemistry* **29**, 233–255.

Chesson, P. L. & Warner, R. R. (1981). Environmental variability promotes coexistence in lottery competitive systems. *American Naturalist* **117**, 923–943.

Chippindale, A. K., Gibson, J. R. & Rice, W. R. (2001). Negative genetic correlation for adult fitness between sexes reveals ontogenetic conflict in *Drosophila*. *Proceedings of the National Academy of Sciences U.S.A.* **98**, 1671–1675.

Choudhary, M., Strassmann, J., Queller, D., Turillazzi, S. & Cervo, R. (1994). Social parasites in polistine wasps are monophyletic-implications for sympatric speciation. *Proceedings of the Royal Society of London Series B* **257**, 31–35.

Civetta, A. & Clark, A. (2000). Correlated effects of sperm competition and postmating female mortality. *Proceedings of the National Academy of Sciences U.S.A.* **97**, 13162–13165.

Civetta, A. & Singh, R. (1998). Sex-related genes, directional sexual selection, and speciation. *Molecular Biology and Evolution* **15**, 901–909.

Clark, A. G. (1984). Natural selection with nuclear and cytoplasmic transmission. I. A deterministic model. *Genetics* **107**, 679–701.

Clark, A. G. (1985). Natural selection with nuclear and cytoplasmic transmission. II. Test with *Drosophila* from diverse populations. *Genetics* **111**, 97–112.

Clark, A. G. & Lyckegaard, E. M. S. (1988). Natural selection with nuclear and cytoplasmic transmission. III. Joint analysis of segregation and mitochondrial DNA in *Drosophila melanogaster*. *Genetics* **118**, 471–481.

Clark, A., Begun, D. & Prout, T. (1999). Female × male interactions in *Drosophila* sperm competition. *Science* **283**, 217–220.

Connell, J. H. (1971). On the role of natural enemies in preventing competitive exclusion in some marine animals and in rain forest trees. In *Dynamics of Populations* (eds. P. J. den Boer and G. R. Gradwell), pp. 298–313. Centre for Agricultural Publishing and Documentation, Wageningen, The Netherlands.

Connell, J. H. (1979). Tropical rain forests and coral reefs as open nonequilibrium systems. In *Population Dynamics* (eds. R. M. Anderson, B. D. Turner and L. R. Turner), pp. 141–163. Blackwell Scientific, Oxford.

Cope, F. W. (1962). The effects of incompatibility and compatibility on genotype proportions in populations of *Theobroma cacao* L. *Heredity* **17**, 183–195.

Coyne, J. (1992). Genetics and speciation. *Nature* **355**, 511–515.

Crozier, R. (1986). Genetic clonal recognition abilities in marine invertebrates must be maintained by selection for something else. *Evolution* **40**, 1100–1101.

Crozier, R. & Dix, M. (1979). Analysis of two genetic models for the innate components of colony odor in social Hymenoptera. *Behavioral Ecology and Sociobiology* **4**, 217–224.

D'Ettore, P., Errard, C., Ibarra, F., Francke, W. & Hefetz, A. (1998). Sneak or repel your enemy: Dufour's gland repellent as a strategy for successful usurpation in the slave-maker *Polyergus rufescens*. *Chemoecology* **10**, 135–162.

Daboussi, M. (1996). Fungal transposable elements: generators of diversity and genetic tools. *Journal of Genetics* **75**, 325–339.

Davies, N., Bourke, A. & De Brooke, M. (1989). Cuckoos and parasitic ants: interspecific brood parasitism as an evolutionary arms race. *Trends in Ecology and Evolution* **4**, 274–278.

de Nooij, M. & van Damme, J. (1988). Variation in host susceptibility among and within populations of *Plantago lanceolata* L. infected by the fungus *Phomopsis subordinaria* (Desm.) Trav. *Oecologia* **75**, 535–538.

DeVries, J. (1964). Insemination and sperm storage in *Drosophila melanogaster*. *Evolution* **18**, 271–272.

De Wit, P. (1997). Pathogen avirulence and plant resistance: a key role for recognition. *Trends in Plant Sciences* **2**, 452–458.

Diamond, J. (1997). *Guns, Germs and Steel*. Norton, New York.

Dixon, M., Jones, D., Keddie, J., Thomas, C., Harrison, K. & Jones, J. (1996). The tomato *Cf-2* disease resistance locus comprises two functional genes encoding leucine-rich repeat proteins. *Cell* **84**, 451–459.

Doherty, P. & Zinkernagel, R. (1975). Enhanced immunological surveillance in mice heterozygous at the H-2 gene complex. *Nature* **256**, 50–52.

Doolittle, W. & Sapienza, C. (1980). Selfish genes, the phenotype paradigm and genome evolution. *Nature* **284**, 601–603.

Dunbar, R. (1999). Culture, honesty and the freerider problem. In *The Evolution of Culture* (ed. R. Dunbar). Rutgers University Press, New Brunswick, NJ.

Dybdahl, M. & Lively, C. (1998). Host–parasite coevolution: evidence for rare advantage and time-lagged selection in a natural population. *Evolution* **52**, 1057–1066.

Eberhard, W. G. (1985). *Sexual Selection and Animal Genitalia*. Harvard University Press, Cambridge, MA.

Ellis, J., Lawrence, G., Ayliffe, M., Anderson, P., Collins, N., Finnegan, J., Frost, D., Luck, J. & Pryor, T. (1997). Advances in the molecular genetic analysis of the flax–flax rust interaction. *Annual Review of Phytopathology* **35**, 271–291.

Ellis, J., Lawrence, G., Luck, J. & Dodds, P. (1999). Identifications of regions in alleles of the flax rust resistance gene L that determine differences in gene-for-gene specificity. *Plant Cell* **11**, 495–506.

Elmes, G., Barr, B., Thomas, J. & Clarke, R. (1999). Extreme host specificity by *Microdon mutabilis* (Diptera: Syrphidae), a social parasite of ants. *Proceedings of the Royal Society of London Series B* **266**, 447–453.

Emery, C. (1909). Uber den ursprung der dulotischen, parasitischen und myrmekophilen Ameisen. *Biologisches Centralblatt* **29**, 352–362.

Emery, P., Robinson, T., Duddington, R. & Brookfield, J. F. Y. (1999). What is the impact of transposable elements an host genome variability? *Proceedings of the Royal Society of London Series B* **266**, 1677–1683.

Enquist, M. & Leimar, O. (1993). The evolution of cooperation in mobile organisms. *Animal Behaviour* **45**, 747–757.

Erwin, T. L. (1982). Tropical forests: their richness in Coleoptera and other arthropod species. *The Coleopterists Bulletin* **36**, 74–75.

Erwin, T. L. (1995). Measuring arthropod biodiversity in the tropical forest canopy. In *Forest Canopies* (eds. M. D. Lowman and N. M. Nadkarni), pp. 109–127. Academic Press, San Diego.

Feldman, R. (1968). Responses to compatriots and foreigners who seek assistance. *Journal of Personality and Social Psychology* **10**, 202–214.

Flor, H. (1956). The complementary genic systems in flax and flax rust. *Advances in Genetics* **8**, 29–54.

Flor, H. (1971). Current status of the gene-for-gene concept. *Annual Review of Phytopathology* **9**, 275–296.

Flynn, J., Goldstein, M., Triebold, K., Koller, B. & Bloom, B. (1992). Major histocompatibility complex class I-restricted T cells are required for resistance to *Mycobacterium tuberculosis* infection. *Proceedings of the National Academy of Sciences U.S.A.* **89**, 12013–12017.

Folkerts, O. & Hanson, M. R. (1991). The male sterility-associated PCF gene and the normal ATP9-1 gene in petunia are located on different mitochondrial-DNA molecules. *Genetics* **129**, 885–895.

Foitzik, S., DeHeer, C., Hunjan, D. & Herbers, J. (2001). Coevolution in host–parasite systems: behavioural strategies of slave-making ants and their hosts. *Proceedings of the Royal Society of London Series B* **268**, 1139–1146.

Fowler, K. & Partridge, L. (1989). A cost of mating in female fruit flies. *Nature* **338**, 760–761.

Frank, S. (1991*a*). Divergence of meiotic-drive suppression systems as an explanation for sex-biased hybrid sterility and inviability. *Evolution* **45**, 262–267.

Frank, S. A. (1991*b*). Ecological and genetic models of host–pathogen coevolution. *Heredity* **67**, 73–82.

Frank, S. (1993*a*). Coevolutionary genetics of plants and pathogens. *Evolutionary Ecology* **7**, 45.

Frank, S. A. (1993*b*). Specificity versus detectable polymorphism in host–parasite genetics. *Proceedings of the Royal Society of London Series B* **254**, 191–197.

Frank, S. A. (1994). Recognition and polymorphism in host–parasite genetics. *Proceedings of the Royal Society of London Series B* **346**, 283–293.

Frank, S. (1996*a*). Problems inferring the specificity of plant–pathogen genetics. *Evolutionary Ecology* **10**, 323–325.

Frank, S. (1996*b*). Statistical properties of polymorphism in host–parasite genetics. *Evolutionary Ecology* **10**, 307–317.

Frank, S. A. (1998). *Foundations of Social Evolution*. Princeton University Press, Princeton.

Frank, S. A. (2000*a*). Polymorphism of attack and defense. *Trends in Ecology and Evolution* **15**, 167–171.

Frank, S. A. (2000*b*). Specific and non-specific defense against parasitic attack. *Journal of Theoretical Biology* **202**, 283–304.

Frank, S. A. (2002). *Immunology and the Evolution of Infectious Disease*. Princeton University Press, Princeton.

Franks, N., Blum, M., Smith, R. & Allies, A. (1990). Behavior and chemical disguise of cuckoo ant *Leptothorax kutteri* in relation to its host *Leptothorax acervorum*. *Journal of Chemical Ecology* **16**, 1431–1444.

Fu, U., Villas, P. & Blankenhorn, E. (1991). Genetic control of rat T-cell response to *Staphylococcus aureus* enterotoxins (SE). *Immunology* **74**, 484.

Gamboa, G., Grudzien, T., Espelie, K. & Bura, E. (1996). Identification of recognition pheromones in social wasps: combining chemical and behavioural evidence. *Animal Behaviour* **51**, 625–629.

Gavrilets, S. (2000*a*). Rapid evolution of reproductive barriers driven by sexual conflict. *Nature* **403**, 886–889.

Gavrilets, S. (2000*b*). Sexual conflict and speciation. *Nature* **407**, 150.

Geffeney, S., Brodie, E. D. Jr., Ruben, P. C. & Brodie, E. D. III. (2002). Mechanisms of adaptation in a predator–prey arms race: TTX-resistant sodium channels. *Science* **297**, 1336–1339.

Gentry, A. H. (1988). Changes in plant community diversity and floristic composition on environmental and geographical gradients. *Annals of the Misourri Botanical Garden* **75**, 1–34.

Getz, W. (1981). Genetically bases kin recognition systems. *Journal of Theoretical Biology* **92**, 209–226.

Gilbert, G. S., Harms, K. E., Hamill, D. N. & Hubbell, S. P. (2001). Effects of seedling size, El Nino drought, seedling density, and distance to nearest conspecific adult on 6-year survival of *Ocotea whitei* seedlings in Panama. *Oecologia* **127**, 509–516.

Gilbert, G. S., Hubbell, S. P. & Foster, R. B. (1994). Density and distance-to-adult effects of a canker disease of trees in a moist tropical forest. *Oecologia* **98**, 100–108.

Gilbert, S. C., Plebanski, M., Gupta, S., Morris, J., Cox, M., Aidoo, M., Kwiatkowski, D., Greenwood, B. M., Whittle, H. C. & Hill, A. V. S. (1998). Association of malaria parasite population structure, HLA, and immunological antagonism. *Science* **279**, 1173–1177.

Giles, H. & Powesland, P. (1975). *Speech Style and Social Evaluation*. Academic Press, London.

Glesener, R. & Tilman, D. (1978). Sexuality and the components of environmental uncertainty: clues from geographic parthenogenesis in terrestrial animals. *American Naturalist* **112**, 659–673.

Good, M. F., Miller, L., Kumar, S., Quakyi, I., Keister, D., Adams, J., Moss, B., Berzofsky, J. A. & Carter, R. (1988). Limited immunological recognition of critical malaria vaccine candidate antigens. *Science* **242**, 574–582.

Grafen, A. (1990). Do animals really recognize kin? *Animal Behaviour* **39**, 42–54.

Grafen, A. (1998). Green beard as death warrant. *Nature* **394**, 521–523.

Gregory, P. & Howard, D. (1994). A post insemination barrier to fertilization isolates two closely related groups of crickets. *Evolution* **48**, 705–710.

Grosberg, R. & Hart, M. (2001). Mate selection and the evolution of highly polymorphic self/nonself recognition genes. *Science* **289**, 2111–2114.

Grosberg, R. & Quinn, J. (1986). The genetic control and consequences of kin recognition by the larvae of a colonial marine invertebrate. *Nature* **322**, 456–459.

Grosberg, R. & Quinn, J. (1987). The evolution of allorecognition specificity. In *Invertebrate Historecognition* (eds. R. Grosberg, D. Hedgecock and K. Nelson). Plenum Press, New York.

Haig, D. (1993). Genetic conflicts in human pregnancy. *Quarterly Review of Biology* **68**, 495–532.

Haig, D. & Graham, C. (1991). Genomic imprinting and the strange case of the insulin-like growth factor-II receptor. *Cell* **64**, 1045–1046.

Haldane, J. (1949). Disease and evolution. *La Ricerca Scientifica* **19**, 68.

Hamilton, W. (1975). Gamblers since life began: barnacles, aphids, and elms. *The Quarterly Review of Biology* **50**, 175–180.

Hamilton, W. (1980). Sex *versus* non-sex *versus* parasite. *Oikos* **35**, 282–290.

Hamilton, W., Axelrod, R. & Tanese, R. (1990). Sexual reproduction as an adaptation to resist parasites (a review). *Proceedings of the National Academy of Sciences U.S.A.* **87**, 3566–3573.

Hamilton, W. D. (1964). The genetical evolution of social behaviour. I, II. *Journal of Theoretical Biology* **7**, 1–52.

Harms, K. E., Wright, S. J., Calderon, O., Hernandez, A. & Herre, E. A. (2000). Pervasive density dependent recruitment enhances sealing diversity in a tropical forest. *Nature* **404**, 493–495.

Harris, M. & Bardin, H. (1972). The language of altruism: the effects of language, dress and ethnic group. *Journal of Social Psychology* **97**, 37–41.

Hatcher, M. (2000). Persistence of selfish genetic elements: population structure and conflict. *Trends in Ecology and Evolution* **15**, 271–277.

Haverty, M., Copren, K., Getty, G. & Vernard, R. (1999). Agonistic behavior and cuticular hydrocarbon phenotypes of colonies of *Reticulitermes* (Isoptera: Rhinotermitidae) from Northern California. *Annals of the Entomological Society of America* **92**, 269–277.

Haydon, D. T., Bastos, A. D., Knowles, N. J. & Samuel, A. R. (2001). Evidence for positive selection in foot-and-mouth disease virus capsid genes from field isolates. *Genetics* **157**, 7–15.

Hedrick, P. (1994). Evolutionary genetics of the major histocompatibility complex. *American Naturalist* **143**, 945–964.

Herrera, J., Lopez-Leon, M., Cabrero, J., Shaw, M. W. & Camacho, J. P. M. (1996). Evidence for B chromosome driven suppression in the grasshopper *Eyprepocnemis plorans*. *Heredity* **76**, 633–639.

Hill, A. V. S. (1998). The immunogenetics of human infectious diseases. *Annual Review of Immunology* **16**, 593–617.

Hill, A. V. S., Elvin, J., Willis, A., Aidoo, M., Allsopp, C., Gotch, F., Gao, X., Takiguchi, M., Greenwood, B., Townsend, A., McMichael, A. & Whittle, H. (1992). Molecular analysis of the association of HLA-B53 and resistance to severe malaria. *Nature* **360**, 434.

Hill, G. (1994). Trait elaboration via adaptive mate choice: sexual conflict in the evolution of signals of male quality. *Ethology Ecology & Evolution* **6**, 351–370.

Hlozanek, I., Corbel, C. & Dieterlen-Lievre, F. (1994). The major histocompatibility complex of chickens controls the infection of early chicken embryos by MC29 virus. *Virology* **203**, 29.

Holland, B. & Rice, W. (1999). Experimental removal of sexual selection reverses intersexual antagonistic coevolution and removes a reproductive load. *Proceedings of the National Academy of Sciences U.S.A.* **96**, 5083–5088.

Holldobler, B. & Wilson, E. (1990). *The Ants*. Harvard University Press, Cambridge, MA.

Hori, M. (1993). Frequency-dependent natural selection in the handedness of scale-eating cichlid fish. *Science* **260**, 216–219.

Howard, R., McDaniel, C. & Blomquist, G. (1980). Chemical mimicry as an integrating mechanism: cuticular hydrocarbons of a termitophile and its host. *Science* **210**, 431–433.

Howe, H. F. & Smallwood, J. (1982). Ecology of seed dispersal. *Annual Review of Ecology and Systematics* **13**, 201–228.

Hubbell, S. P. (2001). *The Unified Neutral Theory of Biodiversity and Biogeography*. Princeton University Press, Princeton, NJ.

Hughes, A. (1997). Rapid evolution of immunoglobulin superfamily C2 domains expressed in immune system cells. *Molecular Biology and Evolution* **14**, 1–5.

Hughes, A. (1999). *The Adaptive Evolution of Genes and Genomes*. Oxford University Press, Oxford.

Hughes, A. & Hughes, M. (1995). Self peptides bound by HLA class I molecules are derived from highly conserved regions of a set of evolutionarily conserved proteins. *Immunogenetics* **41**, 257–262.

Hughes, A. & Nei, M. (1988). Pattern of nucleotide substitution at major histocompatibility complex class I loci reveals overdominant selection. *Nature* **335**, 167.

Hughes, A. & Yeager, M. (1998). Natural selection at major histocompatibility complex loci of vertebrates. *Annual Review of Genetics* **32**, 415–435.

Hurst, G. & Schilthuizen, M. (1998). Selfish genetic elements and speciation. *Heredity* **80**, 2–8.

Hurst, L. (1994). Embryonic growth and the evolution of the mammalian Y Chromosome. II. Suppression of selfish Y-linked growth factors may explain escape from X-inactivation and rapid evolution of Sry. *Heredity* **73**, 233–243.

Hurst, L. (1996). Further evidence consistent with *Stellate's* involvement in meiotic drive. *Genetics* **142**, 641–643.

Hurst, L., Atlan, A. & Bengtsson, B. (1996). Genetic conflicts. *Quarterly Review of Biology* **71**, 317–364.

Hurst, L. & Pomiankowski, A. (1991). Causes of sex ratio bias may account for unisexual sterility in hybrids: a new explanation for Haldane's rule and related phenomena. *Genetics* **128**, 841–858.

Hutchinson, G. (1959). Homage to Santa Rosalia or why are there so many kinds of animals? *American Naturalist* **93**, 145–159.

Ishimizu, T., Endo, T., Yamaguchi-Kabata, Y., Nakamura, K. T., Sakiyama, F. & Norioka, S. (1998). Identification of regions in which positive selection may operate in S-RNase of Rosaceae: implication for S-allele-specific recognition sites in S-RNase. *FEBS Letters* **440**, 337–342.

Jaenike, J. (1978). A hypothesis to account for the maintenance of sex within populations. *Evolutionary Theory* **3**, 191–194.

Jaenike, J. (1990). Host specialization in phytophagous insects. *Annual Review of Ecology and Systematics* **21**, 243–273.

Jaenike, J. (1999). Suppression of sex-ratio meiotic drive and the maintenance of Y-chromosome polymorphism in *Drosophila*. *Evolution* **53**, 164–174.

Janzen, D. H. (1970). Herbivores and the number of tree species in tropical forests. *American Naturalist* **104**, 501–528.

Janzen, D. H. (1976). Why bamboos wait so long to flower. *Annual Review of Ecology and Systematics* **2**, 465–492.

Ji, C., Smith-Backer, J. & Keen, N. (1998). Genetics of plant–pathogen interactions. *Current Opinion in Biotechnology* **9**, 202–207.

Johnstone, R. & Keller, L. (2000). How males can gain by harming their mates: sexual conflict, seminal toxins, and the cost of mating. *American Naturalist* **156**, 368–377.

Jones, D., Thomas, C., HammondKosack, K., Balintkurti, P. & Jones, J. (1994). Isolation of the tomato Cf-9 gene for resistance to cladosporium-Fulvum by transposon. *Science* **266**, 789–793.

Jones, R. (1991). B chromosome drive. *American Naturalist* **137**, 430–442.

Kawecki, T. J. (1998). Red Queen meets Santa Rosalia: arms races and the evolution of host specialization in organisms with parasitic lifestyles. *American Naturalist* **152**, 635–651.

Keegan, J. (1994). *A History of Warfare*. Alfred A. Knopf, New York.

Keller, L. (1999). *Levels of Selection in Evolution*. Princeton University Press, Princeton.

Keller, L. & Ross, K. (1998). Selfish genes: a green beard in a red fire ant. *Nature* **394**, 573–575.

Klein, J. (1986). *Natural History of the Major Histocompatibility Complex*. Wiley, New York.

Klein, J. & Arden, B. (1982). Biochemical comparison of major histocompatibility complex molecules from different subspecies of *Mus musculus*: evidence for trans-specific evolution of alleles. *Proceedings of the National Academy of Sciences U.S.A.* **79**, 2342–2346.

Kniskern, J. & Rausher, M. (2001). Two modes of host–enemy coevolution. *Population Ecology* **43**, 3–14.

Korona, R., Korona, B. & Levin, B. (1993). Sensitivity of naturally occurring coliphages to Type I and Type II restriction and modification. *Journal of General Microbiology* **139**, 1283–1290.

Krieger, M. J. B. & Ross, K. G. (2002). Identification of a major gene regulating complex social behavior. *Science* **295**, 328–332.

Kumar, A. & Bennetzen, J. (1999). Plant retrotransposons. *Annual Review of Genetics* **33**, 479–532.

Kusano, K., Naito, T., Handa, N. & Kobayashi, I. (1995). Restriction modification systems as genomic parasites in competition for specific sequences. *Proceedings of the National Academy of Sciences U.S.A.* **92**, 11095–11099.

Labov, W. (1972). *Sociolinguistic Patterns*. University of Pennsylvania Press, Philadelphia.

Lachmann, M., Szamado, S. & Bergstrom, C. (2001). Cost and conflict in the evolution of human language. *Proceedings of the National Academy of Sciences U.S.A.* **98**, 13189–13194.

Lacy, R. & Sherman, P. (1983). Kin recognition by phenotype matching. *American Naturalist* **121**, 489–512.

Lahav, S., Soroker, V., Hefetz, A. & Vander Meer, R. (1999). Direct behavioral evidence for hydrocarbons as ant recognition discriminators. *Naturwissenschatfen* **86**, 246–249.

Langenheim, J. & Stubblebine, W. (1983). Variation in leaf resin composition between parent tree and progeny in *Hymenaea*: implications for herbivory in the humid tropics. *Biochemical Systematics and Ecology* **11**, 97–106.

Le Masne, G. (1956). Recherches sur les fourmis parasites *Plagiolepis grassi* et l'evolution de *Plagiolepis* parasites. *Comptes Rendus des Seances de l'Academie des Sciences* **243**, 673–675.

Lenoir, A., D'Ettore, P., Errard, C. & Hefetz, A. (2001). Chemical ecology and social parasitism in ants. *Annual Review of Entomology* **46**, 573–599.

Lenski, R. E. (1984). Coevolution of bacteria and phages: are there endless cycles of bacteria defenses and phage counterdefenses? *Journal of Theoretical Biology* **108**, 319–325.

Levin, B. R. (1986). Restriction modification immunity and the maintenance of genetic diversity in Bacterial populations. In *Evolutionary Processes and Evolutionary Theory* (eds. S. Karlin and T. Nero), pp. 669–688. Academic Press, New York.

Little, T. J. (2002). The evolutionary significance of parasitism: do parasite-driven genetic dynamics occur ex-silico? *Journal of Evolutionary Biology* **15**, 1–9.

Lively, C. (1987). Evidence from a New Zealand snail for the maintenance of sex by parasitism. *Nature* **328**, 519–521.

Lively, C. (1992). Parthenogenesis in a freshwater snail: reproductive assurance *versus* parasitic release. *Evolution* **46**, 907–913.

Lively, C. (1999). Migration, virulence and the geographic mosaic of adaptation by parasites. *American Naturalist* **153**, S34–S47.

Lively, C., Craddock, C. & Vrijenhoek, R. (1990). Red queen hypothesis supported by parasitism in sexual and clonal fish. *Nature* **344**, 864–866.

Lively, C. & Dybdhal, M. (2000). Parasite adaptation to locally common host genotypes. *Nature* **405**, 679–681.

Lloyd, H., Schmuff, N. & Hefetz, A. (1986). Chemistry of the anal glands of *Bothriomyrmex syrius* Forel: olfactory mimetism and temporary social parasitism. *Comparative Biochemistry and Physiology* **83B**, 71–73.

Lonnig, W. & Saedler, H. (1997). Plant transposons: contributors to evolution? *Gene* **205**, 245–253.

MacArthur, R. H. (1969). Patterns of communities in the tropics. *Biological Journal of the Linnean Society* **1**, 19–30.

Mackenzie, A. (1996). A trade-off for host plant utilization in the black bean aphid, *Aphis fabae*. *Evolution* **50**, 155–162.

Martin, G. B., Brommonschenkel, S. H., Chunwongse, J., Frary, A., Ganal, M. W., Spivey, R., Wu, T. Y., Earle, E. D. & Tankley, S. D. (1993). Map-based cloning of a protein-kinase gene conferring disease resistance in tomato. *Science* **262**, 1432–1436.

Martin, G., Brommonschenkel, S., Chunwongse, J., Frary, A., Ganal, M., Spivey, R., Wu, T., Earle, E., Maschwitz, U., Dorow, W., Buschinger, A. & Kalytta, G. (2000). Social parasitism involving ants of different subfamilies: *Polyrhacis lama* (Formicinae) an obligatory inquiline of *Diacamma* sp. (ponerinae) in Java. *Insectes Sociaux* **47**, 27–35.

May, R. & Anderson, R. (1983). Parasite–host coevolution. In *Coevolution* (eds. D. Futuyma and M. Slatkin). Sinauer, Sunderland, MA.

May, R. & Anderson, R. (1990). Parasite–host coevolution. *Parasitology* **100**, S89–S101.

Maynard Smith, J. (1966). Sympatric speciation. *American Naturalist* **100**, 637–650.

Maynard Smith, J. (1978). *The Evolution of Sex*. Cambridge University Press, Cambridge.

Maynard Smith, J. & Szathamary, E. (1995). *The Major Transitions in Evolution*. W. H. Freeman, Oxford.

McDowell, J., Dhandaydham, M., Long, T., Aarts, M., Goff, S., Holub, E. & Dangl, J. (1998). Intragenic recombination and diversifying selection contribute to the evolution of the downy mildew resistance at the RPP8 locus of *Arabidopsis*. *Plant Cell* **10**, 1861–1874.

McVean, G. & Hurst, L. (1997). Molecular evolution of imprinted genes: no evidence for antagonistic coevolution. *Proceedings of the Royal Society of London Series B* **264**, 739–746.

Metz, E. & Palumbi, S. (1996). Positive selection and sequence rearrangements generate extensive polymorphism in the gamete recognition protein bindin. *Molecular Biology and Evolution* **13**, 397–406.

Meyers, B., Shen, K., Rohani, P., Gaut, B. & Michelmore, R. (1998). Receptor-like genes in the major resistance locus of lettuce are subject to divergent selection. *Plant Cell* **11**, 1833–1846.

Michener, C. (1970). Social parasites among African allodapine bees (Hymenoptera, Anthophoridae, Ceratinini). *Zoological Journal of the Linnaen Society* **49**, 199–215.

Michener, C. & Smith, B. (1987). Kin recognition in primitively eusocial insects. In *Kin Recognition in Animals* (eds. D. Fletcher and C. Michener). John Wiley and Sons, New York.

Moore, T. & Haig, D. (1991). Genomic imprinting in mammalian development: a parental tug-of-war. *Trends in Genetics* **7**, 45–49.

Mori, A., Grasso, D., Visicchio, R. & Le Moli, F. (2000). Colony founding in *Polyergus rufescens*: the role of the Dufour's gland. *Insectes Sociaux* **47**, 7–10.

Murphy, P. M. (1993). Molecular mimicry and the generation of host defense protein diversity. *Cell* **72**, 823–826.

Nasrallah, J. B. & Nasrallah, M. E. (1993). Pollen-stigma signaling in the sporophytic self-incompatibility response. *Plant Cell* **5**, 1325–1335.

Nettle, D. (1999). Language variation and the evolution of societies. In *The Evolution of Culture* (eds. R. Dunbar, C. Knight and C. Power). Rutgers University Press, New Brunswick, NJ.

Nettle, D. & Dunbar, R. (1997). Social markers and the evolution of reciprocal exchange. *Current Anthropology* **38**, 93–99.

Nielsen, R. & Yang, Z. (1998). Likelihood models for detecting positively selected amino acid sites and applications to the HIV-1 envelope gene. *Genetics* **148**, 929–936.

Nowak, M., Plotkin, J. & Jansen, V. (2000). The evolution of syntactic communication. *Nature* **404**, 495–498.

Nowbahari, E., Lenoir, J., Clement, J., Lange, C., Bagneres, A. & Joulie, C. (1990). Individual, geographical and experimental variation of cuticular hydrocarbons of the ant *Cataglyphis cursor* (Hymenoptera: Formicidae): their use in nest and subspecies recognition. *Biochemical Systematics and Ecology* **18**, 63–73.

O'Brien, S. & Evermann, J. (1988). Interactive influence of infectious disease and genetic diversity in natural populations. *Trends in Ecology and Evolution* **3**, 254–259.

Ollett, D., Morgan, E., Attygalle, A. & Billen, J. (1987). The contents of the Dufour gland of the ant *Harpagoxenus sublaevis* (Hymenoptera: Formicidae). *Zeitschrift fur Naturforsch. Teil A* **42c**, 141–146.

Orgel, L. & Crick, F. (1980). Selfish DNA: the ultimate parasite. *Nature* **284**, 604–607.

Orstrom, E., Gardiner, R. & Walker, J. (1994). *Rules, Games and Common Pool Resources*. University of Michigan Press, Ann Arbor.

Packer, A. & Clay, K. (2000). Soil pathogens and spatial patterns of seedling mortality in a temperate tree. *Nature* **404**, 278–281.

Pagel, M. & Johnstone, R. (1992). Variation across species in the size of the nuclear genome supports the junk-DNA explanation for the C-value paradox. *Proceedings of the Royal Society of London Series B* **249**, 119–124.

Palmer, C. (1981). Kin-selection, reciprocal altruism and information sharing among Maine lobstermen. *Ethology and Sociobiology* **12**, 221–235.

Palumbi, S. (1999). All males are not created equal: fertility differences depend on gamete recognition polymorphisms in sea urchins. *Proceedings of the National Academy of Sciences U.S.A.* **96**, 12632–12637.

Parham, P. & Ohta, T. (1996). Population biology of antigen presentation by MHC class I molecules. *Science* **272**, 67–74.

Parker, G. & Partridge, L. (1998). Sexual conflict and speciation. *Philosophical Transactions of the Royal Society of London* **353**, 261–274.

Parker, M. (1994). Pathogens and sex in plants. *Evolutionary Ecology* **8**, 560–584.

Penn, D. J., Damjanovich, K. & Potts, W. K. (2002). MHC heterozygosity confers a selective advantage against multiple-strain infections. *Proceedings of the National Academy of Sciences U.S.A.* **99**, 11260–11264.

Peters, A. & Lively, C. (1999). The Red Queen and fluctuating epistasis: a population genetic analysis of antagonistic coevolution. *American Naturalist* **154**, 398–405.

Pinker, S. (1994). *The Language Instinct*. William Morrow, New York.

Pircher, H., Moskophidis, D., Rohrer, U., Burki, K., Hengartner, H. & Zinkernagl, R. M. (1990). Vrial escape by selection of cytotoxic T cell-resistant virus variants *in vivo*. *Nature* **346**, 629–633.

Pomiankowski, A. & Hurst, L. (1993). Genomic conflicts underlying Haldane's rule. *Genetics* **133**, 425–432.

Potts, W., Manning, C. & Wakeland, E. (1991). Mating patterns in seminatural populations of mice influenced by MHC genotype. *Nature* **352**, 619.

Potts, W. & Slev, P. (1995). Pathogen-based models favoring MHC genetic diversity. *Immunological Reviews* **143**, 181–198.

Potts, W. & Wakeland, E. (1990). Evolution of diversity at the major histocompatibility complex. *Trends in Ecology and Evolution* **5**, 181.

Poulin, R., Marshall, L. & Spencer, H. (2000). Metazoan parasite species richness and genetic variation among freshwater fish species: cause or consequence? *International Journal for Parasitology* **30**, 697–703.

Price, P. (1980). *Evolutionary Biology of Parasites*. Princeton University Press, Princeton.

Puglielli, M. T., Zajac, A. J., van der Most, R. G., Dzuris, J. L., Sette, A., Altman, J. D. & Ahmed, R. (2001). *In vivo* selection of a lymphocytic choriomeningitis virus variant that affects recognition of the GP330043 epitope by H-2D^b but not H-2K^b. *Journal of Virology* **75**, 5099–5107.

Rand, D. M., Clark, A. G. & Kann, L. M. (2001). Sexually antagonistic cytonuclear fitness interactions in *Drosophila melanogaster*. *Genetics* **159**, 173–187.

Randerson, J., Smith, N. & Hurst, L. (2000). The evolutionary dynamics of male killers and their hosts. *Heredity* **84**, 152–160.
Reeve, H. K. (1989). The evolution of conspecific acceptance thresholds. *American Naturalist* **133**, 407–435.
Regnier, F. & Wilson, E. (1971). Chemical communication and 'propaganda' in slave-maker ants. *Science* **172**, 267–269.
Rice, W. (1987). Speciation via habitat specialization: the evolution of reproductive isolation as a correlated character. *Evolutionary Ecology* **1**, 301–315.
Rice, W. (1996). Sexually antagonistic male adaptation triggered by experimental arrest of female evolution. *Nature* **381**, 232–234.
Rice, W. (1998). Intergenomic conflict, interlocus antagonistic coevolution, and the evolution of reproductive isolation. In *Endless forms: Species and Speciation* (eds. D. Howard and S. Berlocher). Oxford University Press, Oxford.
Rice, W. (2000). Dangerous liaisons. *Proceedings of the National Academy of Sciences U.S.A.* **97**, 12953–12955.
Rice, W. & Holland, B. (1997). The enemies within: intergenomic conflict, interlocus contest evolution (ICE), and the intraspecific Red Queen. *Behavioral Ecology and Sociobiology* **41**, 1–10.
Ridley, M. & Grafen, A. (1981). Are green beard genes outlaws? *Animal Behaviour* **29**, 1192–1194.
Sabadin, A. & Zaniolo, G. (1979). Sexual differentiation and germ cell transfer in the colonial ascidian *Botryllus schlosseri*. *Journal of Experimental Zoology* **207**, 289–304.
Sanetra, M. & Buschinger, A. (2000). Phylogenetic relationships among social parasites and their hosts in the ant tribe Tetramoriini (Hymenoptera: Formicidae). *European Journal of Entomology* **97**, 95–117.
Sasaki, A. (2000). Host–parasite coevolution in a multilocus gene-for-gene system. *Proceedings of the Royal Society of London Series B* **267**, 2183–2188.
Schluter, D. (2001). *The Ecology of Adaptive Radiation*. Oxford University Press, Oxford.
Schmid, B. (1994). Effects of genetic diversity in experimental stands of *Solidago altissima* – evidence for the potential role of pathogens as selective agents in plant populations. *Journal of Ecology* **82**, 165–175.
Schmid-Hempel, P. (1998). *Parasites in Social Insects*. Princeton University Press, Princeton, NJ.
Schnable, P. S. & Wise, R. P. (1998). The molecular basis of cytoplasmic male sterility and fertility restoration. *Trends in the Plant Sciences* **3**, 175–180.
Schultz, T., Bekkevold, D. & Boomsma, J. (1998). *Acromyrmex insinuator* new species: an incipient social parasite of fungus-growing ants. *Insecetes Sociaux* **45**, 457–471.
Scofield, S., Tobia, C., Rathjen, J., Chang, J., Lavelle, D., Michelmore, R. & Staskawicz, B. (1996). Molecular basis of gene-for-gene specificity in bacterial speck disease of tomato. *Science* **274**, 2063–2065.
Scofield, V., Schlumpberger, J., West, L. & Weissman, I. (1982). Protochordate allorecognition is controlled by a MHC-like gene system. *Nature* **295**, 499–502.
Seger, J. (1992). Evolution of exploiter–victim relationships. In *Natural Enemies: The Population Biology of Predators, Parasites and Diseases* (ed. M. Crawley). Blackwell, Oxford.
Sherman, P. (1991). Multiple mating and kin recognition by self-inspection. *Ethology and Sociobiology* **12**, 377–386.
Sherman, P. W., Reeve, H. K. & Pfennig, D. W. (1997). Recognition systems. In *Behavioral Ecology: An Evolutionary Approach* (eds. J. R. Krebs and N. B. Davies), pp. 69–96. Blackwell, Oxford.
Singer, T. (1998). Roles of hydrocarbons in the recognition systems of insects. *American Zoologist* **38**, 394–405.
Singer, T. & Espelie, K. (1996). Nest surface hydrocarbons facilitate nestmate recognition for the social wasps, *Polistes metricus* Say (Hymenoptera: Vespidae). *Journal of Insect behavior* **9**, 857–870.
Snow, A. A. & Spira, T. P. (1991). Pollen vigor and the potential for sexual selection in plants. *Nature* **352**, 796–797.
Snow, A. A. & Spira, T. P. (1996) Pollen-tube competition and male fitness in *Hibiscus moscheutos*. *Evolution* **50**, 1866–1870.
Soroker, V., Fresneau, D. & Hefetz, A. (1998). Formation of colony odor in ponerine ant *Pachycondyla apicalis*. *Journal of Chemical Ecology* **24**, 1077–1090.
Soroker, V., Vienne, C., Hefetz, A. & Nowbahari, E. (1994). The postpharyngeal gland as a 'gestalt' organ for nestmate recognition in the ant *Cataglyphis niger*. *Naturwissenschaften* **81**, 510–513.
Stahl, E. & Bishop, J. (2000). Plant–pathogen arms races at the molecular level. *Current Opinion in Plant Biology* **3**, 299–304.
Staskawicz, B., Ausubel, F., Baker, B., Ellis, J. & Jones, J. (1995). Molecular genetics of plant disease resistance. *Science* **268**, 661–667.
Stockley, P. (1997). Sexual conflict resulting from adaptations to sperm competition. *Trends in Ecology and Evolution* **12**, 154–159.
Stoner, D., Rinkevich, B. & Weissman, I. (1999). Heritable germ and somatic cell lineage competitions in chimeric colonial protochordates. *Proceedings of the National Academy of Sciences U.S.A.* **96**, 9148–9153.
Stoner, D. & Weissman, I. (1996). Somatic and germ cell parasitism in a colonial ascidian: possible role for a highly polymorphic allorecognition system. *Proceedings of the National Academy of Sciences U.S.A.* **93**, 15254–15259.
Swanson, W., Yang, Z., Wolfner, M. & Aquadro, C. (2001). Positive Darwinian selection drives the evolution of several female reproductive proteins in mammals. *Proceedings of the National Academy of Sciences U.S.A.* **98**, 2509–2514.
Takahashi, A., Tsaur, S., Coyne, J. & Wu, C. (2001). The nucleotide changes governing cuticular hydrocarbon variation and their evolution in *Drosophila melanogaster*. *Proceedings of the National Academy of Sciences U.S.A.* **98**, 3920–3925.
Takahata, N. & Nei, M. (1990). Allelic genealogy under overdominant and frequency dependent selection and polymorphism of major histocompatability complex loci. *Genetics* **124**, 967–975.
Talmadge, K., Vamvakopoulos, N. & Fiddes, J. (1984). Evolution of the genes for the B subunits of human chorionic gonadotropin and luteiniziing hormone. *Nature* **307**, 37–40.
Tang, X., Frederick, R., Zhou, J., Halterman, D., Jia, Y. & Martin, G. (1996). Initiation of plant disease resistance by physical interaction of *AvrPto* and *Pto* kinase. *Science* **274**, 2060–2063.
Thomas, L. (1974). Biological signals for self-identification. In *Progress in Immunology II* (eds. L. Brent. and J. Holborrow). North-Holland, Amsterdam.
Thompson, J. (1994). *The Coevolutionary Process*. University of Chicago Press, Chicago.
Thompson, J. (1999). Specific hypotheses on the geographic mosaic of coevolution. *American Naturalist* **153**, S1–S14.
Thompson, J. N. & Burdon, J. (1992). Gene-for-gene coevolution between plants and parasites. *Nature* **360**, 121–125.
Tilman, D. (1982). *Resource Competition and Community Structure*. Princeton University Press, Princeton.
Tissot, A. C., Ciatto, C., Mitti, P. R. E., Grutter, M. G. & Pluckthun, A. (2000). Viral escape at the molecular level

explained by quantitative T-cell receptor/peptide/MHC interactions and the crystal structure of a peptide/MHC complex. *Journal of Molecular Biology* **202**, 873–885.

Topoff, H., Cover, S., Greenberg, L., Goodloe, S. & Sherman, P. (1988). Colony founding by queens of the obligatory slave-making ant, *Polyergus breviceps*: the role of the Dufour's gland. *Ethology* **78**, 209–218.

Trivers, R. L. (1972). Parental investment and sexual selection. In *Sexual Selection and the Descent of Man* (ed. B. Campbell), pp. 136–179. Aldine-Atherton Press, Chicago.

True, J., Weir, B. & Laurie, C. (1996). A genome-wide survey of hybrid incompatibility factors by the introgression of marked segments of *Drosophila mauritania* chromosomes into *Drosophila simulans*. *Genetics* **142**, 819–837.

Tsaur, S., Chau-Ti, T. & Wu, C. (1998). Positive selection driving the evolution of a gene of male reproduction, Acp26Aa, of *Drosophila*: II. Divergence versus polymorphism. *Molecular Biology and Evolution* **15**, 1040–1046.

Tsaur, S., Chau-Ti, T. & Wu, C. (2001). Sex in *Drosophila mauritiana*: a very high level of amino acid polymorphism in a male reproductive protein gene, Acp26Aa. *Molecular Biology and Evolution* **18**, 22–26.

Tsaur, S. & Wu, C. (1997). Positive selection and the molecular evolution of a gene of male reproduction, Acp26Aa of *Drosophila*. *Molecular Biology and Evolution* **14**, 544–549.

Tucker, P. & Lundrigan, B. (1993). Rapid evolution of the sex determining locus in Old World mice and rats. *Nature* **364**, 715–717.

Turelli, M. (1994). Evolution of incompatibility-inducing microbes and their hosts. *Evolution* **48**, 1500–1513.

Turelli, M., Barton, N. & Coyne, J. (2001). Theory and speciation. *Trends in Ecology and Evolution* **16**, 330–343.

Uyenoyama, M. K. (2000). A prospectus for new developments in the evolutionary theory of self-incompatibility. *Annals of Botany* **85**, 247–257.

Van den Ackerveken, G., Van Kan, J. & De Wit, P. (1992). Molecular analysis of the avirulence gene avr9 of the fungal tomato pathogen *Cladosporium fulvum* fully supports the gene-for-gene hypothesis. *Plant Journal* **2**, 359–366.

Van Valen, L. (1973). A new evolutionary law. *Evolutionary Theory* **1**, 1–30.

Vander Meer, R. & Morel, L. (1998). Nestmate recognition in ants. In *Communication in Social Insects: Ants, Wasps, Bees, and Termites* (eds. R. Vander Meer, M. Breed, K. Espelie and M. Winston). Westview, Boulder, CO.

Vander Meer, R. K. & Wojcik, D. P. (1982). Chemical mimicry in the myrmecophilous beetle *Myrmecaphodius excavaticollis*. *Science* **218**, 806–808.

Vermeij, G. J. (1994). The evolutionary interaction among species: selection, escalation, and coevolution. *Annual Review of Ecology and Systematics* **25**, 219–236.

Visicchio, R., Sledge, M., Mori, A., Grasso, D., Le Moli, F., Turillazzi, S., Moneti, G., Spencer, S. & Jones, G. R. (2000). Dufour's gland contents of the queens of the slave-making ant *Polyergus rufescens* and its host species *Formica cunicularia*. *Ethology Ecology and Evolution* **12**, 67–73.

Vrana, P., Fossella, J., Matteson, P., del Rio, T., O'Neill, M. J. & Tilghman, S. M. (2000). Genetic and epigenetic incompatibilities underlie hybrid dysgenesis in Peromyscus. *Nature Genetics* **25**, 120–124.

Wallis, M. (1993). Remarkably high rate of molecular evolution of ruminant placental lactogens. *Journal of Molecular Evolution* **37**, 86–88.

Wang, G. L., Ruan, D. L., Song, W. Y., Sideris, S., Chen, L. L., Pi, L. Y., Zhang, S. P., Zhang, Z., Fauquet, C., Gaut, B. S., Whalen, M. C. & Ronald, P. C. (1998). Xa21D encodes a receptor-like molecule with a leucine-rich repeat domain that determines race-specific recognition and is subject to adaptive evolution. *Plant Cell* **10**, 765–779.

Ward, P. (1996). A new workerless social parasite in the ant genus *Pseudomyrmex* (Hymenoptera: Formicidae), with a discussion of the origin of social parasitism in ants. *Systematic Entomology* **21**, 253–263.

Webb, C. O. & Peart, D. R. (1999). Seedling density dependence promotes coexistence of Bornean rain forest trees. *Ecology* **80**, 2006–2017.

West, S. A., Lively, C. M. & Read, A. F. (1999). A pluralist approach to sex and recombination. *Journal of Evolutionary Biology* **12**, 1003–1012.

West-Eberhard, M. J. (1983). Sexual selection, social competition, and speciation. *Quarterly Review of Biology* **58**, 155–183.

Whiten, A. & Byrne, R. (1988). The Machiavellian Intelligence hypothesis: editorial. In *Machiavellian Intelligence* (eds. R. Byrne and A. Whiten), pp. 1–10. Oxford University Press, Oxford.

Whitfield, S., Lovell-Badge, R. & Goodfellow, P. (1993). Rapid sequence evolution of the mammalian sex-determining gene SRY. *Nature* **364**, 713–715.

Williams, G. (1975). *Sex and evolution*. Princeton University Press, Princeton.

Wills, C. & Condit, R. (1999). Similar non-random processes maintain diversity in two tropical rainforests. *Proceedings of the Royal Society of London* **266**, 1445–1452.

Wilson, E. (1971). *The Insect Societies*. Harvard University Press, Cambridge, MA.

Wolfe, K. & Sharp, P. (1993). Mammalian gene evolution: nucleotide sequence divergence between mouse and rat. *Journal of Molecular Evolution* **37**, 441–456.

Wright, S. (1939). The distribution of self-sterility alleles in populations. *Genetics* **24**, 538–552.

Wu, C. & Davis, A. (1993). Evolution of post-mating reproductive isolation: the composite nature of Haldane's rule and its genetic basis. *American Naturalist* **142**, 187–212.

Yamaguchi-Kabata, Y. & Gojobori, T. (2000). Reevaluation of amino acid variability of the human immunodeficiency virus type 1 gp120 envelope glycoprotein and prediction of new discontinuous epitopes. *Journal of Virology* **74**, 4335–4350.

Yewdell, J. W. & Bennink, J. R. (1999). Immunodominance in major histocompatibility complex class I-restricted T lymphocyte responses. *Annual Review of Immunology* **17**, 51–88.

Zevering, Y., Khamboonruang, C. & Good, M. (1994). Natural amino acid polymorphisms of the circumsporozite protein of *Plasmodium falciparum* abrogate specific human CD4+T cell responsiveness. *European Journal of Immunology* **24**, 1418.

Zhang, J., Dyer, K. & Rosenberg, H. (2000). Evolution of the rodent eosinophil-associated RNase gene family by rapid gene sorting and positive selection. *Proceedings of the National Academy of Sciences U.S.A.* **9**, 4701–4706.

Zurita, S., Cabrero, J., Lopez-Leon, M. & Camacho, J. (1998). Polymorphism and regeneration for a neutralized selfish B chromosome. *Evolution* **52**, 274–277.