ANNUAL REVIEWS

Annual Review of Genetics

Recombination Rate Variation in Social Insects: An Adaptive Perspective

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Annu. Rev. Genet. 2024. 58:159–81

First published as a Review in Advance on July 10, 2024

The *Annual Review of Genetics* is online at genet.annualreviews.org

https://doi.org/10.1146/annurev-genet-111523-102550

Keywords

Red Queen hypothesis, Hill–Robertson interference, longevity, Hymenoptera, selective interference

Abstract

Social insects have the highest rates of meiotic recombination among Metazoa, but there is considerable variation within the Hymenoptera. We synthesize the literature to investigate several hypotheses for these elevated recombination rates. We reexamine the long-standing Red Queen hypothesis, considering how social aspects of immunity could lead to increases in recombination. We examine the possibility of positive feedback between gene duplication and recombination rate in the context of caste specialization. We introduce a novel hypothesis that recombination rate may be driven up by direct selection on recombination activity in response to increases in lifespan. Finally, we find that the role of population size in recombination rate evolution remains opaque, despite the long-standing popularity of this hypothesis. Moreover, our review emphasizes how the varied life histories of social insect species provide an effective framework for advancing a broader understanding of adaptively driven variation in recombination rates.

1. INTRODUCTION

Variation in rates of meiotic recombination may affect the composition and architecture of genomes, population-level responses to selection, and speciation across all eukaryotes (45, 119). Through the exchange of DNA between homologous chromosomes during gamete formation, meiotic recombination can create novel genotypes with preexisting alleles, making it one of the preeminent drivers of genetic novelty in sexually reproducing organisms (7). However, our understanding of why rates of recombination vary across genomes, taxa, populations, and species remains unresolved, despite a century of protracted effort (95, 119).

While recombination appears to be essential to gamete formation by virtue of stabilizing chromosomes during meiosis, the rate of recombination often exceeds what is mechanistically necessary for proper chromosome segregation, invoking adaptive explanations for the excess (95). These potential explanations are generally related to uniting fitness-increasing alleles on the same chromosome. However, recombination also has the capacity to disassociate fitness-increasing alleles (7, 95), suggesting a selective balance between the benefits and potential costs of allele shuffling via recombination. How this balance is optimized by (sometimes opposing) selective pressures has proven to be difficult to resolve because we poorly understand how demographic and ecological variables, such as population size or immune challenges, affect rates of recombination. Theoretical and empirical tests of the same adaptive hypothesis have sometimes yielded conflicting results when tested across different environments and taxa (119).

One particularly useful group to understand the selection of genome-wide recombination rates is the aculeate Hymenoptera, which includes the ants, bees, and wasps. Within the Hymenoptera, there is substantial variation in life history strategy, demography, and genome-wide rates of meiotic recombination (78, 133) (**Figure 1**). There has been considerable interest as to why recombination is especially variable in the aculeates, particularly why extraordinarily high genome-wide

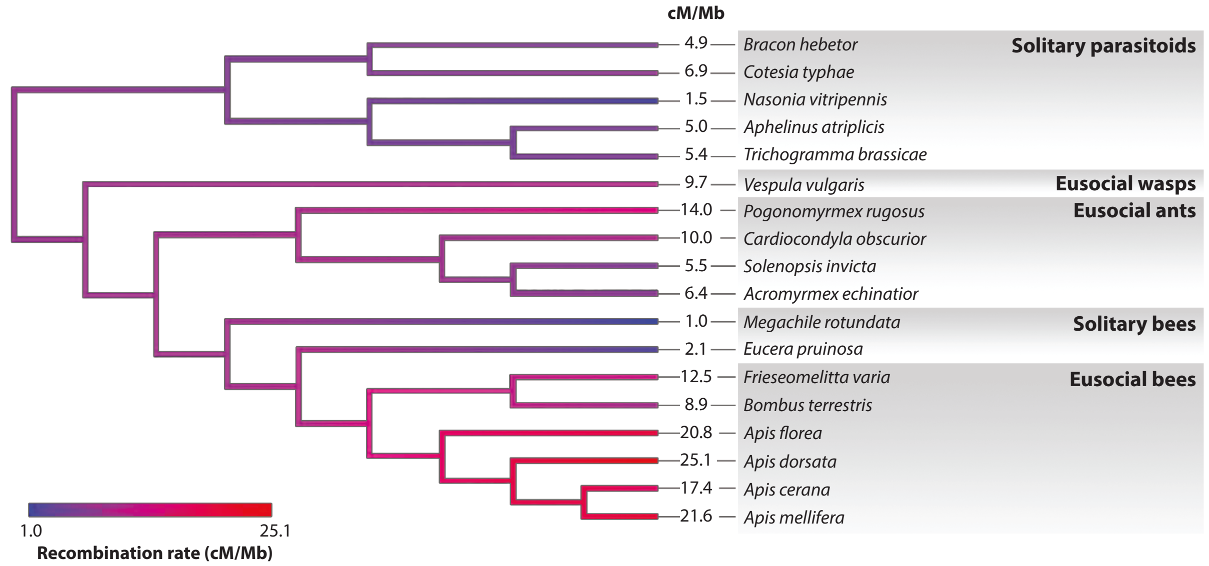

Figure 1

Recombination rates (cM/Mb) available for hymenopteran species. The two solitary bee species *Eucera pruinosa* and *Megachile rotundata* along with the solitary parasitoids have the lowest rates of recombination within aculeates. contMap of the phytools R package was used for the reconstruction of ancestral rates (94). Figure adapted from an illustration created by Erica Brus.

HILL–ROBERTSON INTERFERENCE AND RECOMBINATION

Novel alleles arising at different positions on the same chromosome at roughly the same time are unlikely to all arise in one individual. When these alleles affect fitness, selection at one position of a chromosome interferes with selection at another position on the same chromosome (39, 86). This is because the advantage provided by a fitness-increasing allele in an individual is neutralized by the absence of a fitness-increasing allele at another position. Over time, individuals with no novel fitness-increasing alleles are removed from the population, resulting in a mix of individuals with fitness-increasing alleles at one position or another.

Known as Hill–Robertson interference, this buildup of negative linkage disequilibrium (LD) among fitness-increasing alleles favors the evolution of recombination (20, 47, 86). An individual that recombines gametes that have fitness-increasing alleles at different positions onto the same gamete will produce offspring more fit than the rest of the population, enabling the spread and fixation of a haplotype with co-occurring fitness-increasing alleles as well as the spread and fixation of recombination as a phenomena (20, 47, 86).

recombination rates relate to eusociality (50, 101, 116, 130). The repeated origins and elaborations of eusociality in aculeates have resulted in a range of mating systems and social lifestyles that influence effective population size (N_e) and selection pressures thought to be related to recombination. Additionally, the aculeates have one of the most dynamic ranges of recombination rates known for any animal group, from a low genome-wide recombination rate in the leafcutter bee (50) to the highest rates of recombination observed among all animals in closely related honey bees (101). This makes the aculeates a potentially informative group for studying the ultimate causes of recombination rate variation (54).

Here, we evaluate classic and novel hypotheses for variation in recombination rate in light of new data from the Hymenoptera and other taxa. We compare data among eusocial hymenopteran species and between the Hymenoptera and other taxa to explore how different traits shape the balance between the costs and benefits of recombination. We approach classic adaptive hypotheses for recombination variation, such as Hill–Robertson interference (HRI; see the sidebar titled Hill–Robertson Interference and Recombination) and the Red Queen hypothesis, while proposing novel addendums, such as how drastic increases in longevity may affect HRI or how socially mediated immune responses could affect parasite–host dynamics. This review is far from comprehensive or conclusive, but we summarize how recent recombination studies can update our perspective on adaptive hypotheses for variation in recombination rate, especially as it relates to the elevated rates observed among social species.

Eusociality: the overlap of generations, reproductive division of labor, and cooperative care of offspring in an organism

Hill–Robertson interference: selection acting at more than one physically linked loci, resulting in impeded efficacy of selection at each loci in question

2. IMMUNITY: RED QUEENS RUNNING THE COLONY?

Coevolutionary relationships between hosts and their parasites or pathogens have long been thought to be a potential driver of selection for meiotic recombination (7, 83, 103). (We will use parasite hereafter to encompass all viruses, parasites, and other pathogens that cause disease in insects.) Both the host and parasite evolve rapidly in response to each other's latest adaptations. What constitutes an optimal combination of host alleles could change rapidly in such co-antagonistic relationships (20, 32, 103), which could favor the reshuffling of alleles via recombination (83, 103). This dynamic forms the basis of the Red Queen hypothesis (RQH), in reference to the Red Queen's advice that Alice must run to keep in place in Lewis Carroll's *Through the Looking-Glass* (9). Despite being essential to advancing our understanding of the origins and maintenance of eukaryotic sex and recombination, exact definitions of the RQH vary considerably (19, 64, 121).

For this article, we are defining the RQH as the assertion that selection for recombination can be driven by a coevolutionary relationship between parasites and hosts.

In support of the RQH, selection for increased host recombination in response to the presence of parasites has been demonstrated across a range of theoretical conditions (20, 32, 40, 57). Empirically, increases in genome-wide recombination rates of individuals or populations experimentally exposed to parasites have been documented in mosquitoes, flies, and beetles (56, 114, 115, 137). Furthermore, there are several natural experiments that show evidence of increased recombination as a response to antagonistic coevolution. For example, the genes required for host exploitation were found in regions of locally elevated recombination within the genome of a wheat parasite (81). Likewise, venom genes in two species of rattlesnake are found in regions of high recombination, which could be favored in response to toxin-resistant prey (105). These findings support the hypothesis that increased rates of meiotic recombination can provide a fitness advantage in the face of antagonistic parasite pressure. However, the degree to which parasite–host interactions drive recombination rate variation across taxa remains unclear.

The RQH has been a long-standing explanation for the high rate of recombination found among the eusocial Hymenoptera (57, 116). In a eusocial colony, there is increased potential for horizontal parasite transfer because hundreds to thousands of adults share the same (often warm) space. The potential for vertical transfer is increased through extended maternal care and adult–offspring interactions. Moreover, most of this large network of vertical and horizontal interactions consists of siblings and half-siblings, further deepening immune problems, as an individual who is genetically susceptible to a parasite is likely to be interacting primarily with other individuals who share the same genotype and are thus also susceptible (37, 106). Additionally, immunity against viruses in honey bees seems to be mediated by numerous noncanonical genes that are only partially overlapping among different viruses (72). This could mean infections from more than one virus could result in an increase in the number of immune loci under selection, which would correspond to increased HRI in eusocial species with increased viral exposure (17, 47). This suite of added risk of exposure and infection could have a dramatic effect on the strength of selection for improved immunity across physiological and behavioral dimensions in the eusocial Hymenoptera, resulting in the increased rates of recombination observed relative to solitary hymenopterans (57, 69).

In the sections below, we review the unique features of social insect life histories that could favor increases in recombination via the RQH. In doing so, we also provide insights into the limitations of increased recombination as a response to coevolving immune pressures. Specifically, we explore how gaining a social immune system could select for increased recombination and how variation in rates of polyandry among eusocial species can inform our understanding of why recombination rates vary in host–parasite dynamics.

2.1. Social Immunity and Recombination: Smells like Trouble

One of the implicit assumptions of the RQH as an explanation for elevated recombination in social insect species is that they face more persistent and rapidly changing pathogen pressure than solitary species. However, there have been few direct comparisons between solitary and social insect disease dynamics, leaving this assumption untested. Viruses and parasites are widespread in solitary bees and have the capacity to greatly impact their fitness as well (26, 34, 108, 126). There are also a number of shared viruses between social and solitary species (31). Moreover, some solitary bee species nest in aggregations, putting many individuals in contact with one another (21). Lastly, in a study of locally elevated rates of recombination in the honey bee *Apis mellifera* and the ant *Cardiocondyla obscurior*, local rates of recombination were not elevated near genes related to canonical immune function in arthropods (58, 69). From the perspective of the RQH, these findings invite the consideration of immune functions that are unrelated to innate immunity and specific to the eusocial Hymenoptera.

One such immune function could be chemical detection, which is the first step in parasite defense (17, 61). Eusocial insects have many opportunities to chemically detect parasitized individuals relative to solitary relatives (61). Extended maternal care, progressive provisioning, and overlap of generations ensure that a parasitized individual will spend more time exposed to other adults as both a larva and adult, thus increasing the opportunity to detect and remove a parasite or isolate the afflicted individual. Many solitary bees, however, are not present when their adult offspring emerge and encase their developing brood in cells, often blocking access to previously capped cells (21). This drastically limits solitary bees' opportunities to detect parasites and pathogens.

Furthermore, once detected, eusocial hymenopterans have more ways to mitigate the impact of parasites. Sustained access to offspring and siblings allows for grooming behavior, where related individuals can be checked for parasites before they spread (11, 120). Infected individuals are often killed, removed, or self-removed from the colony to prevent further spread of parasites (17, 38). The queen and workers can abscond and rebuild a colony, abandoning parasitized brood as a form of defense (61). By contrast, solitary insects are unable to engage in allogrooming behavior, and it is costly for them to abandon a nest during construction or kill developing brood because each offspring represents a much larger reproductive investment compared to a queen (21, 78). The social immune system of eusocial hymenopterans represents a suite of effective responses to detection and response to disease lacking in their solitary counterparts (61). However, whether such response behaviors occur depends on the efficacy of parasite detection through chemical sensing (35, 92). From a perspective of host–parasite coevolution, the eusocial Hymenoptera should experience greater selection on chemosensory genes that improve the ability to detect parasites relative to their solitary counterparts, as they are requisite for a suite of immune responses unavailable to solitary hymenopterans.

Coevolution theory predicts that the genotype for optimized parasite detection shifts or oscillates over time as parasites are selected to evade host detection (19, 103). Gene families involved in arthropod chemical signaling and detection are diverse, dynamic in their lineage-specific expansions, and often rapidly evolving across the Hymenoptera (10, 65). The polygenic nature of parasite detection, combined with strong selection for parasites to evade detection, could create the conditions for sustained HRI, as the ideal genotype for parasite detection is in constant flux (24, 124). Simulations have demonstrated that sustained selective interference as a consequence of host–parasite interactions can reliably select for the presence of recombination in populations of sexually reproducing organisms (20, 40). An immune gene involved in ongoing host–parasite interactions need not be linked with other immune genes, as selective interference can also be generated by a beneficial immune allele arising in poor genetic backgrounds (40). These theoretical findings support the hypothesis that parasites may drive increased recombination in the eusocial Hymenoptera by creating ongoing selective interference among chemosensory genes that mediate detection of parasites.

There is also empirical evidence to support this hypothesis. Chemical detection of parasites by the eusocial Hymenoptera appears to be underpinned by multiple loci, potentially increasing HRI in a host–parasite evasion–detection dynamic. Evidence for this comes from the redundancy among genes capable of distinguishing chemical phenotypes in the eusocial Hymenoptera. For example, in the jumping ant *Harpegnathos saltator*, only a small subset of odorant receptors (ORs) were needed to distinctly characterize the hydrocarbon profiles on male, worker, and reproductive female cuticles (118). In a study on chalkbrood fungus, only one out of three different hydrocarbons present on the cuticle of infected honey bee larvae was needed to elicit a larva removal

Haplotype: a physically linked set of alleles that are coinherited

response from workers (122). Taken together, these findings suggest that multiple ORs have the capacity to detect parasites through exposure to several independent chemicals. Honey bee research has further suggested that parasite detection is polygenic in nature and relies on genetic variation at multiple loci. In both *Apis cerana* and *A. mellifera*, multiple chemosensory genes are differentially expressed between bees engaging in Varroa sensitive hygiene and those that are not (49, 79). In honey bees, a hygienic response to pupae infected with Varroa mites is underpinned by multiple loci, with different studies detecting different quantitative trait loci (QTLs) (88, 129), and significant QTLs only explaining a small percentage of the variance in hygienic behavior response (129). Thus, HRI among a variety of chemosensory genes could be either an alternative or complement to selective interference occurring among canonical immune genes due to host–parasite interaction.

In summary, the evolution of social immunity presents an intriguing possible explanation for the high rates of recombination observed in eusocial hymenopterans. Social species have more opportunities to detect parasites and a broader repertoire of behaviors to respond to these parasites. The biology of chemosensation in the Hymenoptera supports the hypothesis that ongoing selection for parasite detection could cause sustained HRI. This presents a compelling avenue for testing the impact of social immune function as a driver for variation in hymenopteran recombination rates. We encourage future analyses integrating transcriptomic data tied to variation in the ability to detect parasites and local rates of recombination across hymenopteran species. If social immune behavior is selecting for increases in recombination, we predict a positive correlation between the number of genes tied to variation in parasite detection on a chromosome and the recombination rate of that chromosome in eusocial hymenopterans. By contrast, we predict no such correlation in the solitary hymenopterans. Broadly, this research can help to illuminate the ubiquity of the RQH as an explanation for recombination by assessing how the gain of novel immune systems can alter host–parasite dynamics and how that may affect the strength of selection for increased recombination.

2.2. Polyandry and Recombination: Complementary Strategies

We have so far been focused on the reshuffling of beneficial alleles as they are selected to create optimal haplotypes in the face of constant parasite pressure. However, this response to parasitism requires sufficient standing or novel genetic diversity, which poses a special challenge for eusocial insects, as ants, bees, and termites are known to harbor extremely low genetic diversity levels compared to other animals (97). Increased genotypic variation within a colony buffers it from the fatal potential of a single genotype being highly susceptible to a strain of disease (4). There is not strong evidence to suggest that increased recombination is an effective source of genetic diversity for immune responses in social insects. First, increasing recombination as a means to increase genetic diversity comes with the potential for the dissociation of important linked alleles that are unrelated to host–parasite dynamics, as well as deleterious genomic instabilities during cell division (71, 95). Additionally, a simulation of honey bee colony dynamics suggests that recombination has a nominal effect on quantitative genetic diversity within a colony (102). However, this same simulation revealed another potential mechanism for generating diversity within a colony: polyandry (102). Indeed, studies of both ants and honey bees find that increased numbers of patrilines reduce the variance of host response to disease, suggesting that standing genotypic variation can have a moderating effect on disease and can be achieved through multiple mating (41, 123).

Given the questionable effect of recombination on colony-level genetic variation relative to polyandry (71, 102), it seems unlikely that selection for increased standing genetic variation resulted in increased recombination rates in the eusocial Hymenoptera. This suggests that increased recombination rates and polyandry provide complementary effects on genetic and allelic diversity with regard to host–parasite evolution in social insects. In an environment of constant disease pressure, increases in multiple mating can buffer the effect of parasites and disease through genotypic diversity, but only recombination can create novel haplotypes, which are essential for a rapid response to selective interference (39, 47). Furthermore, as multiple mating becomes fixed as a population-wide trait, the variation in genotypic diversity between colonies decreases (102), presumably reducing variation in fitness among polyandrous colonies in a population (100). Recombination then becomes especially valuable as it provides the potential to increase the fitness of its reproductive offspring by uniting fitness-increasing alleles onto the same haplotype. This would provide increased fitness related to disease in a population with homogeneous fitness values (47). Lastly, highly eusocial queens can produce many reproductive offspring, lowering the cost of making a bad haplotype given that the benefit of making a good haplotype will increase fitness in such species (28).

In effect, multiple mating can be viewed as a short-term strategy, and elevated recombination as a long-term response to disease pressure. Multiple mating can immediately increase colony genetic diversity and directly improve disease resistance or colony productivity (76, 123). This is crucial to the reproductive success of queens, as the fitness of social insects largely relies on colony success. By contrast, recombination can act as a long-term complement by improving the germline with respect to immune challenges. A queen can produce males and gynes with improved immune haplotypes, making their respective colonies more fit than the previous generation (69, 116).

The RQH has already been proposed as a potential explanation for why eusocial aculeates have elevated rates of recombination when compared to solitary counterparts (69). However, viewing the relationship between the degree of multiple mating and rates of recombination as a complementary response to parasite pressures extends the RQH to be a potential explanation for why there is such considerable variation in rates of recombination among the eusocial Hymenoptera, with the added possibility of some species having greater parasitism than others. Under this extended version of the RQH, we would expect a positive correlation between the number of times the queen mates and genome-wide recombination rate in the Hymenoptera. Indeed, this is observed among the species for which these data are available (**Figure 2**). However, it is worth noting that the strong relationship between multiple mating and rate of recombination may be caused by factors unrelated to immunity (see the sidebar titled The Selfish Supergene: Polyandry and Recombination in the Eusocial Hymenoptera). Further exploring the relationship between polyandry, recombination, and degree of parasitism in the eusocial aculeates can advance our understanding of the validity of the RQH, while also allowing for the exploration of scenarios where increased recombination acts as an adaptive response in tandem with other phenomena.

3. QUEEN AND WORKER ELABORATION

Selection for the elaboration of eusociality may have resulted in selection for elevated rates of recombination in the Hymenoptera. Under this hypothesis, recombination rate is indirectly selected for if it improves colony fitness by promoting caste specialization (54, 130). The base assumptions of this hypothesis are that loci underlying caste-biased phenotypes will often be in tight physical linkage, and that selection for caste specialization will result in selection at multiple loci, resulting in HRI. This could select for increased recombination in turn, favoring individuals that can unite high-fitness queen and worker alleles onto the same haplotype. Below, we explore emerging evidence revealing whether caste-divergent loci are physically linked and whether such regions are linked to high recombination rates.

Gyne: an unmated female reproductive individual of eusocial bees, ants, or wasps

Caste: A labor role (most often referring to a queen or worker) of individuals within eusocial colonies that is characterized by a distinct set of behaviors and morphologies

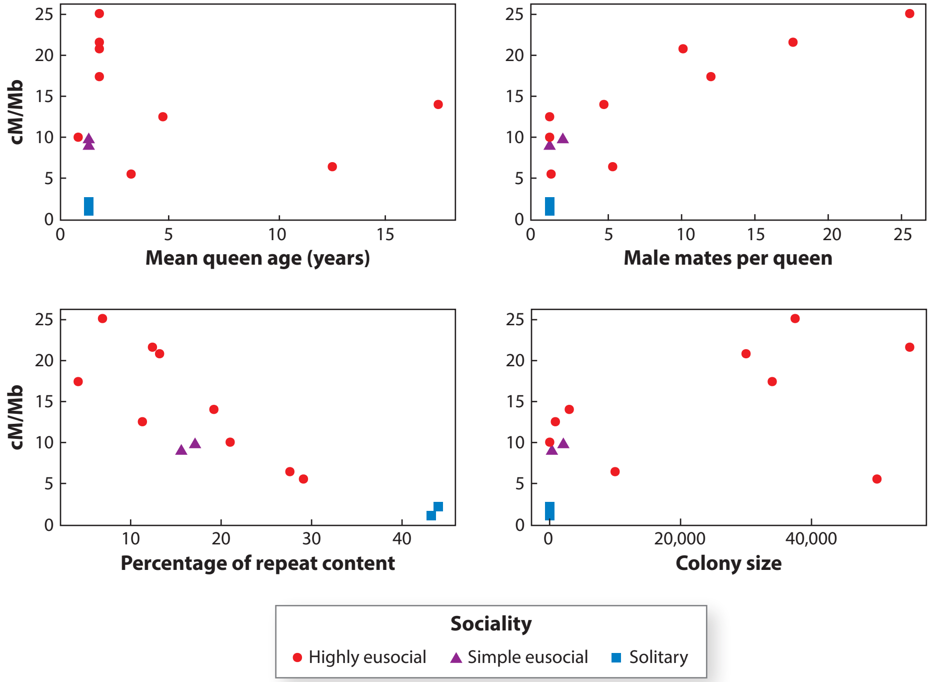

Figure 2

Genome-wide recombination rates (cM/Mb) of the aculeates plotted against the mean queen age in years, the average number of males that a queen mates with, the percent of genome assembly composed of repeat content, and the average number of adult individuals in a colony for each aculeate species that has genome-wide rates of recombination available.

The duplication of a gene with pleiotropic effects can allow for the caste specialization of the gene duplicates (29). The gene duplicates of a formerly multifunctional gene experience genetic release and are able to become optimized for caste-specific functions, allowing for fitness benefits associated with elaborated castes (29, 93). This could be duplication with a divergent outcome, where one duplicate is biased toward worker functions and the other toward queens, or duplication allowing further specialization of genes expressed in the same caste. Given that genes are often duplicated in close proximity on a chromosome (14, 110), selection on the duplicates for a caste-specialized function could cause selective interference, favoring individuals with increased rates of recombination among gene duplicates in close physical linkage.

Support for caste-divergent specialization of gene duplicates in linkage across eusocial insects is inconsistent. For example, in studies of the duplication and expression of vitellogenin paralogs in *Pogonomyrmex barbatus* and the *Formica* genus, there is support for caste-divergent specialization of gene duplicates, with paralogs having caste-divergent expression patterns between queens and workers (16, 80). Conversely, paralogous OR genes, which are thought to be critical to social interaction, were not found to have caste-specific expression in the leafcutter ant *Atta vollenweideri*, with each caste expressing all of the OR genes identified (59). Lastly, in *A. mellifera*, Chau & Goodisman (12) found no strong evidence of caste-divergent expression patterns among gene duplicates, with biased expression of gene duplicate pairs being largely caste concordant. Given the high rates of recombination in *A. mellifera*, these findings are not congruent with increased recombination as a

THE SELFISH SUPERGENE: POLYANDRY AND RECOMBINATION IN THE EUSOCIAL HYMENOPTERA

The formation and persistence of supergenes, or multigene regions with restricted recombination, can negatively impact colony fitness. Regions with a sustained lack of recombination can lead to the genetic determination of colony traits that were previously sensitive to environmental inputs, such as nutrition and other social cues. Ultimately, this environmental inflexibility may diminish a colony's fitness. For example, supergenes biasing larval development toward queens may selfishly spread in a population at the expense of colonial worker production (2, 4, 42, 62). Together with insufficient worker numbers, such supergenes can also generate sex ratio imbalances (2, 3, 30). This is in addition to the deleterious buildup that accompanies nonrecombining regions (36).

This may explain the strikingly positive relationship between polyandry among queens and the rate of recombination in eusocial hymenopterans (**Figure 2**). One possible explanation for this strong relationship is that recombination and polyandry could act as countervailing forces to supergenes in complementary ways. Recombination can counteract emerging genetic determination that is reliant on multiple alleles. Queens with higher rates of recombination can increase the chance of disbanding an allele combination that would cause genetic determination of a reproductive or behavioral trait detrimental to the colony's reproductive success, thereby improving their fitness relative to queens with lower rates of recombination. Polyandry, on the other hand, can mitigate the effects of caste-biasing supergenes that have already emerged. A queen can mate with males that carry non-caste-biasing genotypes, allowing for the necessary amount of workers to rear gynes in spite of the presence of queen-biased selfish supergenes. Improving our understanding of what makes some species more predisposed to the emergence of supergenes could help to determine whether elevated polyandry and recombination rate are related to selfish supergenes in the eusocial Hymenoptera.

result of widespread selective interference being driven by caste-divergent loci that are physically linked. However, more gene expression studies with a focus on how gene duplicates are expressed in different castes are needed in conjunction with genome-wide recombination rates to further test the validity of this hypothesis.

While there is little evidence for caste-divergent genes driving selection for increased recombination, duplicated genes that specialize in the same caste could select for increases in recombination. For example, gene duplicates in honey bees were found to be caste concordant in their patterns of expression bias across castes (12). Caste-biased expression in honey bees was more likely to be found in genes that were duplicates rather than singletons (12). If the respective caste is selected to further specialize, this can cause the selective interference necessary to favor recombination. In keeping with this, gene duplication counts have been positively associated with social complexity in the Hymenoptera (12). Also, worker-biased genes are enriched in regions of locally elevated recombination in *A. mellifera*, as are ergatoid male-biased (a distinct male caste in some ants) genes in *C. obscurior* (53, 58). These findings point to the possibility that selection for the specialization of genes that are biased toward the same caste could indirectly select for increased recombination.

Additionally, elevated rates of recombination may coincide with gene duplication events, provided that the mechanistic changes responsible for increases in homologous recombination also lead to an increase in unequal crossover and gene duplication. In a genome-wide analysis of hundreds of gene duplicates from the effector family in a wheat powdery mildew, effector genes were found to vary extensively among individuals in copy numbers and were enriched around recombination breakpoints (81). Likewise, there are significant positive associations between the regions with duplicated genes and elevated local rates of recombination in *Caenorhabditis elegans* and across

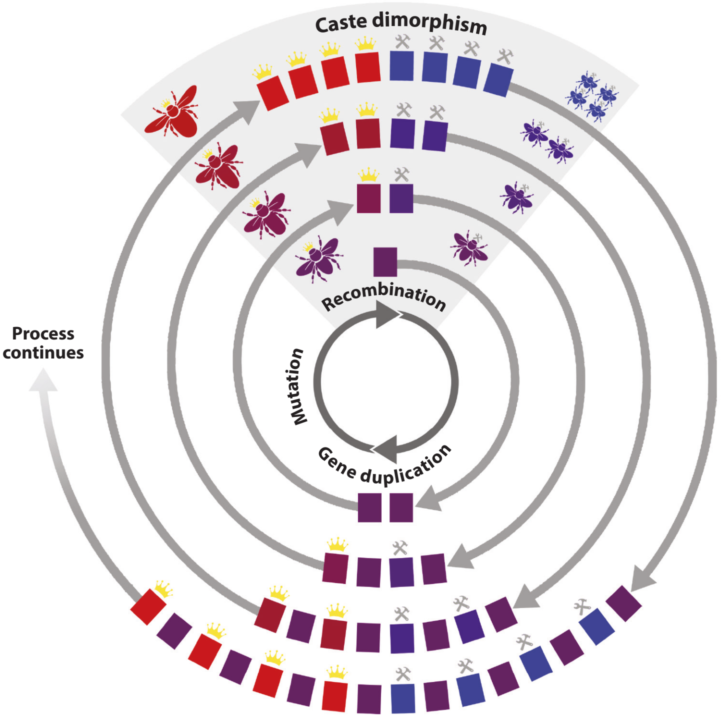

Figure 3

Selection for caste dimorphism creating positive feedback between the rate of recombination and the frequency of gene duplication. Gene duplication enables the pleiotropic release of genes. Mutation in novel and previous duplicates creates genes further specialized to a caste. This causes negative linkage disequilibrium among specialized genes, favoring increased recombination to unite them on the same haplotype. This results in an increased chance of further gene duplication, mutations toward caste specialization of novel duplicates, and selection for higher rates of recombination, and the process repeats itself. Genes are represented by colored squares, the queen-specialized genes are represented by a crown, and worker-specialized genes are represented by tools. Colors indicate the degree of caste specialization for genes and caste phenotype. The queen phenotype is represented in the left diagonal region and the worker phenotype in the right diagonal region. Figure adapted from an illustration created by Erica Brus.

angiosperms, suggesting increased recombination could be accompanied by increases in unequal crossovers (73, 127).

It is possible that selection for caste specialization on recently duplicated genes could favor elevated rates of recombination. This, in turn, could result in more gene duplication events, further increasing the number of loci under selection for caste specialization and for increased rates of recombination (**Figure 3**). In support of this, a study conducted across arthropods showed that highly eusocial hymenopterans had elevated rates of gene gains relative to other arthropods (125), suggesting that elevated rates of recombination may coincide with an increased rate of gene duplication in species with highly specialized castes. However, the recombination rate and the chance of unequal crossover do not appear to be consistently correlated. Evidence to the contrary can be found in butterflies, with local recombination rates having no significant relationship with gene duplicates (113), and in a significant negative relationship between recombination rate and unequal crossovers in the fungal plant pathogen *Claviceps purpurea* (136). Further testing of the relationship between local rates of recombination, the rate of gene family expansion, and caste-biased expression of gene duplicates will be needed to examine the possibility of a positive feedback loop driving increased recombination rates through selection for specialized castes in the eusocial Hymenoptera.

4. LONGEVITY

The deleterious effects of aging could provide an adaptive explanation for the variable rates of recombination observed in the eusocial Hymenoptera. Specifically, elevated recombination rates could be an adaptive response to age-related oxidative stress and the proliferation of transposable elements (TEs). The negative fitness effects of these phenomena can be profound across an organism's lifetime and can ultimately lead to organism dysfunction and even mortality (23, 77). If we assume that the accumulation of these effects occurred at a rate that was detrimental to reproduction only after several years, individuals with annual life cycles would not have strong selection against TE accumulation or stress-related damage relative to perennial individuals that reproduce throughout their lifetimes, such as social insect queens. Among the species for which we have genome-wide recombination rates, many of those with high rates of recombination are eusocial with queens that live for years and reproduce throughout their lives (48). Particularly, the species with very high recombination rates have long-lived queens that produce exceptionally high numbers of eggs for an insect. By contrast, the solitary short-lived species have the lowest recombination rates (**Figure 1**). Undoubtedly, evidence for a correlation between genome-wide recombination and age is mixed across taxa (119). However, the increase in adult lifespan across reproductive castes in eusocial species loosely corresponds with increased rates of recombination relative to the solitary Hymenoptera (**Figure 2**), supporting the possibility that age-mediated selection against deleterious genomic effects could in part account for the elevated rates of recombination observed in the eusocial Hymenoptera.

Interestingly, recombination may be able to mitigate the effects of these two aging-related phenomena either indirectly or directly. Increased selection for reduced TEs or improved response to oxidative stress could generate sufficient HRI to indirectly select for the increased recombination observed in the eusocial Hymenoptera. Additionally, shifts in rates of meiotic recombination could also be a result of selection for mechanisms that directly address the damaging effects of oxidative stress and TE accumulation: ectopic recombination and DNA repair via homologous recombination (55, 66) (**Figure 4**). Here, we explore extended queen lifespan as a source of increased recombination rates in the Hymenoptera, specifically as a response to the accumulation of TEs and DNA damage. In doing so, we consider whether this relationship is a consequence of indirect selection in response to negative linkage disequilibrium (LD) between alleles at longevity-related loci or rather a byproduct of direct selection on processes with mechanistic overlap that can repair DNA or dissolve TEs.

Ectopic recombination: recombination between chromosomes at nonhomologous positions (this could be recombination between homologous or nonhomologous chromosomes)

Linkage disequilibrium (LD): nonrandom co-occurrence of alleles in a population (alleles in negative LD co-occur less often than expected by chance)

4.1. Oxidative Stress

The oxidative stress theory of aging asserts that aging is a consequence of cumulative oxidative damage throughout an organism's lifetime (5). Reactive oxygen species can cause double-strand breaks, impede the efficacy of DNA replication forks, and cause single-stranded DNA gaps, which can result in cancer and other fatal diseases if not properly repaired (1, 66). Slowing the accumulation of oxidative damage in long-lived organisms can be achieved in part through the repair of damaged DNA. DNA repair involves proteins that are also critical to meiotic recombination and is often mediated through the recombination of DNA in cells throughout the body (66). As with meiotic recombination, repair via homologous recombination in somatic cells is mediated by targeting double-strand breaks, homology searches, and strand invasion (1). Given the mechanistic

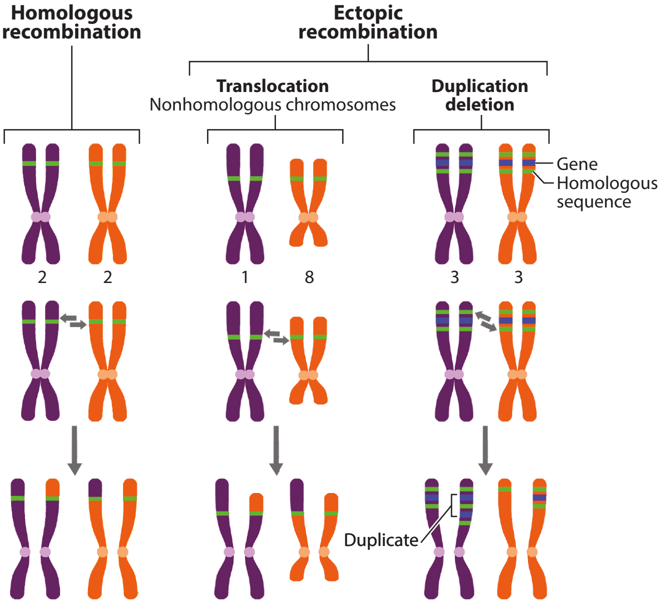

Figure 4

(*Left*) Homologous recombination as a result of DNA exchange between a pair of homologous chromosomes (chromosomes 2 and 2) during gamete formation. (*Center*) Translocation as a result of recombination initiated between homologous sequences on nonhomologous chromosomes (chromosomes 1 and 8). (*Right*) Gene duplication and deletion as a result of recombination between homologous sequences at different positions on homologous chromosomes (chromosomes 3 and 3). Figure adapted from an illustration created by Erica Brus.

overlap of meiotic recombination and DNA repair via recombination, if oxidative stress is not limited to just somatic cells, it is conceivable that increases in crossover events in the progenitors of gametes are actually a response to increased DNA damage.

A wide range of oxidative stressors induce DNA repair by homologous recombination, and the effect of oxidative stress has also been linked to variation in rates of meiotic recombination. For example, pharmacologically induced production of a variety of reactive oxygen species has been shown to induce homologous recombination in a Chinese hamster ovarian cell line (22, 134, 135). A similar set of results is found when oxidative damage is increased with paraquat treatments in insects. In *Drosophila melanogaster* females, there is a negative relationship between rates of meiotic recombination and resistance to paraquat (43). And while there was not a significant increase in meiotic recombination rate following paraquat treatment in *A. mellifera* queens, there was an upward trend, with two queens having a significant increase in the ratio of recombinant to nonrecombinant offspring (63). These findings are consistent with a potential link between elevated DNA repair as a consequence of oxidative stress and increases in rates of meiotic recombination.

If the elevated recombination rates of the eusocial Hymenoptera are a result of a marked increase in lifespan, then we would expect recombination rates to increase with age, as the oxidative stress theory of aging predicts an ongoing accumulation of DNA damage. Consistent with this prediction, *D. melanogaster* has a significant increase in recombination rate with age (44). In a study of cattle, while recombination rate declined slightly from early to middle age, recombination rate then increased from middle to old age and was highest in the oldest age group of the cattle studied (112). Likewise, studies of *Drosophila pseudoobscura* indicate a similar pattern of a decrease in recombination rate at middle age and the highest rates of recombination at old age (74, 90). Several studies of XX humans have found a significant increase in recombination with age (15, 60, 75). However, another study found the opposite: a significant decrease in the recombination rate of women with age (46). Generally, there appears to be a trend between organismal age and the rate of meiotic recombination. Whether that is primarily a consequence of DNA repair of oxidative damage during gametogenesis remains to be seen.

Critical to this novel age-mediated stress hypothesis for recombination, homologous recombination associated with DNA repair and meiotic recombination events may be resolved as crossovers or noncrossovers at different rates. While a crossover involves the exchange of entire chromosome arms during the recombination process, a noncrossover is the replacement of a segment of DNA from a sister chromosome, with the flanking DNA of the chromosome remaining intact (45). Somatic recombination events are rarely resolved as crossovers (22). In a study that induced homologous recombination through oxidative stress in the Chinese hamster, gene conversion without an accompanying crossover was the principal pathway for homologous recombination repair (22). This is in contrast to the finding that the elevated rates of recombination in long-lived honey bee queens compared to the rates in the relatively short-lived bumblebee queens are primarily driven by a marked increase in the number of crossover events (52). Together, these findings suggest that increased DNA repair during gametogenesis of old queens is not likely to be the principal driver of elevated recombination rates in the eusocial Hymenoptera. However, increased HRI related to selection on genes improving oxidative stress resistance or response could be driving the increases in recombination rates observed in the eusocial Hymenoptera.

4.2. Transposable Elements

TEs continue to spread through the genome throughout an organism's lifetime (25), which may result in fitness costs for long-lived species (13, 23, 77). Selection should then favor an increase in TE-silencing mechanisms among the eusocial Hymenoptera, whose reproductives have a longer adult lifespan than their solitary counterparts. One such mechanism is ectopic recombination among TEs, which can cause the deletion of DNA segments important for transposition (70), rendering TEs nontransposable (55, 68). Interestingly, there is evidence that rates of meiotic recombination are correlated with rates of ectopic recombination (55, 67). This could suggest that elevated levels of meiotic recombination may lead to more effective TE suppression through an associated increase in ectopic recombination rates. Additionally, high levels of meiotic recombination may also mitigate the fitness consequences of TE proliferation by dissociating a TE from an ideal genetic background during offspring gamete formation (67, 81).

While there are exceptions, there is generally a negative relationship between local rates of recombination and the TE density in that region (55). Additionally, multiple comparative studies have shown that the evolutionary age of a TE correlates negatively with local recombination rates, suggesting that TEs do not persist in regions of high recombination (55). In general, these findings provide support for the novel hypothesis that recombination is elevated in the long-lived eusocial Hymenoptera to mitigate the effects of TE accumulation.

One prediction of this hypothesis is that TE suppression has larger fitness benefits among long-lived organisms than in their short-lived relatives. In support of this prediction, an evolutionary reduction in lifespan in two separate lineages of killifish was accompanied by an expansion of TE content in their genomes (18). This suggests that selection on TE suppression was relaxed in short-lived fish. Additionally, there is evidence to suggest that the relationship between TE abundance and the rate of recombination may be altered by age. On the scale of the megabase, eukaryotes with relatively short lives, such as *C. elegans*, *D. melanogaster*, and *Arabidopsis thaliana*,

Inversion: a recombination event resulting in the reversed positioning of a segment of DNA within a chromosome

Translocation: recombination among nonhomologous chromosomes resulting in the transference of a DNA segment to a nonhomologous chromosome

were found to have weakly negative, insignificant, or even positive relationships between recombination rates and TE abundance, in contrast to the strong negative relationships observed among longer-lived species, such as *Homo sapiens* and *Eucalyptus grandis* (55). Indeed, the negative relationship between repeat content and the rate of recombination in the eusocial Hymenoptera appears striking (**Figure 2**). This could suggest that selection for increased recombination rates may be linked to TE suppression in long-lived species but not in short-lived ones.

A second line of support for the prediction that TE suppression has larger fitness benefits among long-lived organisms than their short-lived relatives comes from patterns of TE suppression in social insect queens. In a species of eusocial termite, microRNAs that interfere with TE expansion throughout the genome were found expressed in long-lived reproductive individuals but not in shorter-lived workers (25). Additionally, in a comparison of PIWI-interacting RNAs (piRNAs) that target TEs in the tissues of *Temnothorax rugatulus* queens and foragers, there were many more significantly upregulated piRNAs in queens than in foragers (111). Lastly, in a study profiling piRNAs in age-matched honey bee larvae, the proportion of piRNAs targeting TEs is greater in queen-destined larvae than worker-destined ones (131). Together, these studies suggest that TE suppression is particularly beneficial in long-lived queens of the eusocial Hymenoptera.

There are some limits to the benefits of recombination that should be evaluated with regard to this TE suppression hypothesis. First, the rates of recombination are correlated with rates of ectopic recombination (55, 70, 99), which can result in fatal inversions and translocations (**Figure 4**). Given that TE-rich regions are implicitly rich with repeat sequences, the probability of ectopic recombination in conjunction with high recombination rates can increase considerably (55, 70, 99). There is evidence of the detrimental effect that ectopic recombination among TEs has had in humans (104). It is conceivable that the benefit of creating haplotypes free of TEs via recombination may not outweigh the associated risks in all contexts. Indeed, a recent theoretical study of the evolutionary relationship between TEs and recombination that accounted for HRI and ectopic recombination found that while HRI is a viable source of indirect selection for recombination, the direct effects on fitness from deleterious ectopic recombination largely drive recombination rates down in populations (99). Perhaps that is not the case in social insects, where the number of offspring produced is high and resources invested in unfit offspring can readily be recycled through brood cannibalism (109).

Ironically, direct selection for increases in ectopic recombination could present an alternative explanation to HRI for high rates of recombination and low TE content in hymenopterans. While ectopic recombination events are potentially detrimental to gametes (104), ectopic recombination among TEs can also result in rendering TEs nonfunctional while still producing viable offspring (55). Ectopic recombination of TEs has been proposed as a driver of genome reduction in plants (70) and even as a precision-based mechanism for the removal of Alu elements in primates (68, 70). Also, increased ectopic recombination is associated with increases in rates of meiotic recombination in yeast and wheat fungus (67, 81). Similar patterns have been found in the Hymenoptera. For example, all ants documented so far have high rates of recombination (58, 116, 117) and also appear to have high rates of chromosome evolution via ectopic recombination. In a study of the pharaoh and clonal raider ants, there was an average of less than four orthologs shared per syntenic block of DNA between the two species (33). This suggests that high rates of homologous meiotic recombination could be accompanied by high rates of ectopic recombination in the eusocial aculeates as well.

There is also circumstantial evidence that selection for ectopic recombination to render TEs inert in the Hymenoptera could be related to lifespan in particular. Long terminal repeat (LTR) retrotransposons appear to have a consistent significant negative relationship with rates of recombination across taxa on the scale of the megabase (55). Interestingly, a comparative genomic study

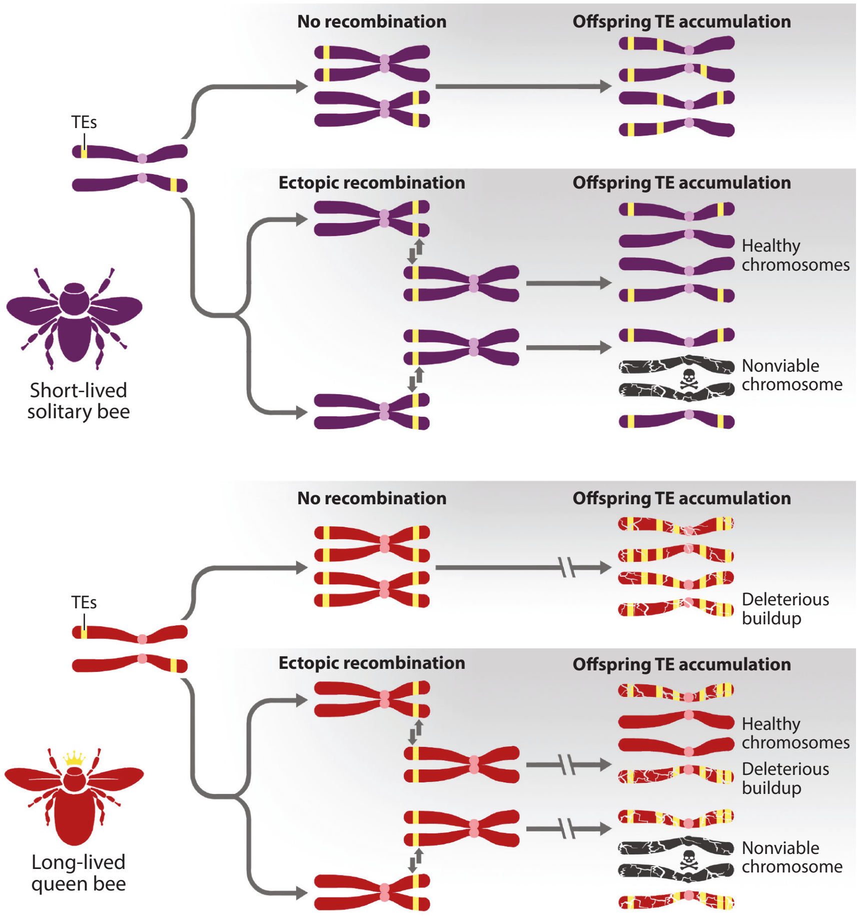

Figure 5

Fitness effects of recombination in short- and long-lived queens in relation to transposable elements (TEs). In the absence of recombination, ectopic recombination events will not occur and TEs will be vertically transmitted. TEs then proliferate in the female's subsequent generation. For long-lived queens, the additional time results in more TE accumulation in one generation and a stronger effect on fitness (indicated by chromosomes labeled deleterious buildup). In the presence of recombination, ectopic recombination events among TEs can occur, rendering TEs incapable of spreading and increasing fitness (healthy chromosomes), and sometimes create nonviable chromosomes at the expense of fitness. The trade-offs associated with ectopic recombination favor recombination in long-lived queens of social insects but not in solitary species. Figure adapted from an illustration created by Erica Brus.

of solitary and eusocial bees found that only the long-lived eusocial bees had lower LTR content than solitary bees, while the short-lived eusocial bumblebees did not (51). Among these species, *Bombus terrestris* has been found to have roughly one-third of the rate of recombination of the two *Apis* species (52, 101). Ectopic recombination could prevent retrotransposons such as LTRs from being able to transpose and affect queen fitness throughout their long lives, potentially favoring individuals with increased ectopic recombination (**Figure 5**).

The relationship between TEs, ectopic recombination, age, and genome-wide recombination rates is far from resolved and will require future research to elucidate. Generally, more TE and recombination rate research will be needed to determine if a relationship between TE content and recombination rate is significant in the Hymenoptera and whether the gain of sociality has a significant effect on that relationship.

5. DEMOGRAPHIC CONSEQUENCES OF EUSOCIALITY

Decreases in population size are thought to select for increased recombination. In theory, selection acts less efficiently in smaller populations, where genetic drift has a larger effect on allele frequency changes (8, 87). Drift increases negative LD among fitness-increasing alleles by chance fluctuations in allele frequencies, favoring individuals that can unite such fitness-increasing alleles in the haplotypes of their offspring through increased recombination rates (8, 87). Because drift is a stronger evolutionary force in small populations, the selection for increased recombination as a response to drift is predicted to be stronger in populations with smaller breeding population sizes (8, 87). Indeed, there is theoretical evidence that selection for increased recombination is highest in small populations (8, 87).

In contrast to theoretical findings, empirical relationships between N_e and recombination rate are often inconsistent across taxa (82, 91, 96, 98, 119). Nevertheless, a reduction of population size in the eusocial Hymenoptera has long been invoked as a potential explanation for their increased rates of recombination, which is thought to be due to extreme reproductive skew (116). Holding census population constant, eusocial species with reproductive division of labor have fewer reproducing individuals than solitary species without it. This reproductive skew can be increased by two principal means: an increase in the ratio of workers to queens (116) and the severity of the loss of totipotency in workers (some species have workers that can lay viable male eggs, while others have completely sterile workers) (130). Indeed, among the social Hymenoptera, there appears to be a generally positive relationship between the number of workers per colony and the genome-wide rate of recombination (**Figure 2**). Additionally, a recent comparative study found that complete loss of totipotency in workers was tied to increased relaxed selection among ants (6), which is what would be expected if the evolution of sterile workers leads to reduced N_e. Lastly, the origins of eusociality are associated with an increased ratio of nonsynonymous to synonymous substitutions (dN/dS) among Hymenoptera lineages (132), which is indicative of reduced purifying selection stemming from reduced N_e (132). Widespread relaxed selection was also found in eusocial termites compared to solitary cockroaches, suggesting that a relationship between the gain of eusociality and the reduction of N_e size may be widespread (27). Taken together, these findings support the possibility that increased reproductive skew through loss of worker totipotency and increases in worker number could reduce N_e sufficiently to favor increases in recombination rate.

Yet whether reductions in population size have selected for increased rates of recombination among the eusocial Hymenoptera remains unclear. Weyna & Romiguier (132) found that the gain of eusociality had a marginal effect on inflated dN/dS relative to the effect of being a pollinator, suggesting that pollinators may have smaller N_e than nonpollinators, regardless of social phenotype. Despite this, the solitary bees *Megachile rotundata* and *Eucera pruinosa* have lower rates of recombination than all eusocial aculeates (50, 89, 119) (**Figure 1**), not just the eusocial bees. Moreover, the population sizes of solitary bees appear to be similar to those of ants and vespids, yet recombination rates are substantially lower (50, 89, 132).

While shifts in reproductive skew through an increase in worker number and loss of worker totipotency have been the primary considerations for reduced N_e in the eusocial aculeates, several other factors could also affect N_e, confounding the relationship between the degree of reproductive skew and population size in the eusocial aculeates. For example, theoretical work has found that the production of males by workers can actually drive down N_e rather than increase it, assuming there is not a strong male bias in the breeding population (84). A lack of data across species prevents a formal test of the role of worker sterility on N_e. Additionally, unique aspects of mating systems among species can complicate our understanding of how reproductive skew affects N_e. For example, *C. obscurior* has high rates of recombination and sterile workers (58). However, they also have wingless males that do not leave the colonies and inbreed with sibling queens, presumably reducing N_e (107). Increased age of reproductives is also tied to a decrease in N_e, and the lifespans of eusocial aculeates vary extremely. The *Pogonomyrmex* genus of ants has species living over 15 years (128), while *C. obscurior* queens live less than a year (85). Even with the assumption that low N_e is driving up recombination rate, it remains unclear whether *Pogonomyrmex rugosus* rates of recombination are elevated relative to *C. obscurior* due to a longer lifespan, greater reproductive skew, or other factors not considered. Ultimately, the assessment of the role of reproductive skew in recombination rate variation will require an increase in the number of hymenopteran linkage maps of species with well-characterized life histories.

6. CONCLUSION

The social Hymenoptera, with several species that have exceptionally high recombination rates, present an exciting opportunity to explore adaptive hypotheses for variation in recombination rate. For example, their unique life history enables the exploration of long-standing hypotheses, such as those underpinned by HRI, in novel ways. In the case of the RQH, we can test whether recombination rates evolve as a consequence of not only increased immune pressure, but also novel immune systems (e.g., a social immune system). Additionally, we can better understand how breeding population size affects the strength of selection for recombination by taking advantage of the extreme variation in reproductive skew across species. Furthermore, the aspects of social Hymenoptera biology invoke novel adaptive hypotheses. For example, rigorous testing of the queen and worker divergence hypothesis may expose ways in which the evolution of dimorphism may actually promote an increase in recombination rather than its suppression. Lastly, the marked variation in queen lifespan among eusocial aculeates also invites the exploration of novel hypotheses surrounding TE accumulation and oxidative stress, which could result in elevated rates of recombination through direct selection for recombination activity.

Considerable progress toward understanding why eusocial aculeates have the highest rates of recombination among animals has been made in recent years (50, 52, 58, 130). Notably, rates of recombination have been found to be elevated in eusocial species relative to those of solitary ones across three lineages with independent origins of sociality (50, 116, 117). Additionally, relationships have emerged between recombination rates and genomic features related to eusociality, such as caste-biased genes (54). We present the novel insight that recombination rate may also be related to polyandrous mating and repeat content of genomes, which are traits germane to several adaptive hypotheses for elevated recombination. Addressing the challenges to understanding recombination rate variation in social insects will take considerable time, resources, and coordination across research communities. Nevertheless, such efforts would constitute a worthwhile endeavor, as the study of natural variation among the social Hymenoptera represents a tractable and promising observational complement to experimental and theoretical approaches. As such, continuing recombination rate research in eusocial aculeates could result in a meaningful advancement of our understanding of why recombination, a process with profound effects on heredity and evolution, varies so substantially across eukaryotes.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

ACKNOWLEDGMENTS

We would like to thank Erica Brus for leading the figure design process and Priscila Santos and Ren Weinstock for helpful discussion. We also recognize critical support from the Natural Sciences and Engineering Research Council of Canada (RGPIN-2022-03629), the European Research Council (ERC-2020-StG-948688 RoyalMess project), and the National Science Foundation (IOS grant 2142778).

LITERATURE CITED

1. Ait Saada A, Lambert SAE, Carr AM. 2018. Preserving replication fork integrity and competence via the homologous recombination pathway. *DNA Repair* 71:135–47
2. Anderson KE, Linksvayer TA, Smith CR. 2008. The causes and consequences of genetic caste determination in ants (Hymenoptera: Formicidae). *Myrmecol. News* 11:119–32
3. Avril A, Purcell J, Béniguel S, Chapuisat M. 2020. Maternal effect killing by a supergene controlling ant social organization. *PNAS* 117(29):17130–34
4. Baer B, Schmid-Hempel P. 2001. Unexpected consequences of polyandry for parasitism and fitness in the bumblebee, *Bombus terrestris*. *Evolution* 55(8):1639–43
5. Barja G. 2019. Towards a unified mechanistic theory of aging. *Exp. Gerontol.* 124:110627
6. Barkdull M, Moreau CS. 2023. Worker reproduction and caste polymorphism impact genome evolution and social genes across the ants. *Genome Biol. Evol.* 15(6):evad095
7. Barton NH, Charlesworth B. 1998. Why sex and recombination? *Science* 281(5385):1986–90
8. Barton NH, Otto SP. 2005. Evolution of recombination due to random drift. *Genetics* 169(4):2353–70
9. Bell G. 2019. *The Masterpiece of Nature: The Evolution and Genetics of Sexuality*. Abingdon, UK: Routledge
10. Brand P, Ramírez SR. 2017. The evolutionary dynamics of the odorant receptor gene family in corbiculate bees. *Genome Biol. Evol.* 9(8):2023–36
11. Casillas-Pérez B, Bod'ová K, Grasse AV, Tkačik G, Cremer S. 2023. Dynamic pathogen detection and social feedback shape collective hygiene in ants. *Nat. Commun.* 14(1):3232
12. Chau LM, Goodisman MAD. 2017. Gene duplication and the evolution of phenotypic diversity in insect societies. *Evolution* 71(12):2871–84
13. Chen H, Zheng X, Xiao D, Zheng Y. 2016. Age-associated de-repression of retrotransposons in the *Drosophila* fat body, its potential cause and consequence. *Aging Cell* 15(3):542–52
14. Christiaens JF, Van Mulders SE, Duitama J, Brown BA, Ghequire MG, De Meester L. 2012. Functional divergence of gene duplicates through ectopic recombination. *EMBO Rep.* 13(12):1145–51
15. Coop G, Wen X, Ober C, Pritchard JK, Przeworski M. 2008. High-resolution mapping of crossovers reveals extensive variation in fine-scale recombination patterns among humans. *Science* 319(5868):1395–98
16. Corona M, Libbrecht R, Wurm Y, Riba-Grognuz O, Studer RA, Keller L. 2013. Vitellogenin underwent subfunctionalization to acquire caste and behavioral specific expression in the harvester ant *Pogonomyrmex barbatus*. *PLOS Genet.* 9(8):e1003730
17. Cremer S, Armitage SA, Schmid-Hempel P. 2007. Social immunity. *Curr. Biol.* 17(16):R693–702
18. Cui R, Medeiros T, Willemsen D, Iasi LNM, Collier GE, et al. 2019. Relaxed selection limits lifespan by increasing mutation load. *Cell* 178(2):385–99.e20
19. Da Silva J. 2018. Red Queen theory. In *Encyclopedia of Life Sciences*, ed. John Wiley & Sons, Ltd., pp. 1–7. Hoboken, NJ: Wiley. **https://doi.org/10.1002/9780470015902.a0028127**
20. Da Silva J, Galbraith JD. 2017. Hill–Robertson interference maintained by Red Queen dynamics favours the evolution of sex. *J. Evol. Biol.* 30(5):994–1010
21. Danforth BN, Minckley RL, Neff JL. 2019. *The Solitary Bees: Biology, Evolution, Conservation*. Princeton, NJ: Princeton Univ. Press
22. Defoort EN, Kim PM, Winn LM. 2006. Valproic acid increases conservative homologous recombination frequency and reactive oxygen species formation: a potential mechanism for valproic acid-induced neural tube defects. *Mol. Pharmacol.* 69(4):1304–10

23. Dennis S, Sheth U, Feldman JL, English KA, Priess JR. 2012. *C. elegans* germ cells show temperature and age-dependent expression of *Cer1*, a Gypsy/Ty3-related retrotransposon. *PLOS Pathog*. 8(3):e1002591
24. Ebert D, Fields PD. 2020. Host-parasite co-evolution and its genomic signature. *Nat. Rev. Genet.* 21(12):754–68
25. Elsner D, Meusemann K, Korb J. 2018. Longevity and transposon defense, the case of termite reproductives. *PNAS* 115(21):5504–9
26. Eves JD, Mayer DF, Johansen CA. 1980. *Parasites, Predators, and Nest Destroyers of the Alfalfa Leafcutting Bee*, Megachile rotundata. Pullman, WA: West. Reg. Ext. Publ.
27. Ewart KM, Ho SYW, Chowdhury A-A, Jaya FR, Kinjo Y, et al. 2023. Pervasive relaxed selection in termite genomes. bioRxiv 2023.11.01.565207. **https://doi.org/10.1101/2023.11.01.565207**
28. Fuchs S, Moritz RFA. 1999. Evolution of extreme polyandry in the honeybee *Apis mellifera* L. *Behav. Ecol. Sociobiol.* 45(3):269–75
29. Gadagkar R. 1997. The evolution of caste polymorphism in social insects: genetic release followed by diversifying evolution. *J. Genet.* 76(3):167–79
30. Gadau J, Fewell JH. 2022. Supergenes, supergenomes, and complex social traits. *PNAS* 119(2):e2118971118
31. Galbraith DA, Fuller ZL, Ray AM, Brockmann A, Frazier M, et al. 2018. Investigating the viral ecology of global bee communities with high-throughput metagenomics. *Sci. Rep.* 8(1):8879
32. Gandon S, Otto SP. 2007. The evolution of sex and recombination in response to abiotic or coevolutionary fluctuations in epistasis. *Genetics* 175(4):1835–53
33. Gao Q, Xiong Z, Larsen RS, Zhou L, Zhao J, et al. 2020. High-quality chromosome-level genome assembly and full-length transcriptome analysis of the pharaoh ant *Monomorium pharaonis*. *GigaScience* 9(12):giaa143
34. Goodell K. 2003. Food availability affects *Osmia pumila* (Hymenoptera: Megachilidae) foraging, reproduction, and brood parasitism. *Oecologia* 134:518–27
35. Guarna MM, Melathopoulos AP, Huxter E, Iovinella I, Parker R, et al. 2015. A search for protein biomarkers links olfactory signal transduction to social immunity. *BMC Genom*. 16(1):63
36. Haigh J. 1978. The accumulation of deleterious genes in a population—Muller's ratchet. *Theor. Popul. Biol.* 14(2):251–67
37. Hamilton WD. 2001. Land of the rising sun: kinship, recognition, disease, and intelligence: constraints of social evolution. In *Narrow Roads of Gene Land*, Vol. 2, pp. 367–412. Oxford, UK: Oxford Univ. Press
38. Heinze J, Walter B. 2010. Moribund ants leave their nests to die in social isolation. *Curr. Biol.* 20(3):249–52
39. Hill WG, Robertson A. 1968. Linkage disequilibrium in finite populations. *Theor. Appl. Genet.* 38(6):226–31
40. Hodgson EE, Otto SP. 2012. The red queen coupled with directional selection favours the evolution of sex. *J. Evol. Biol.* 25(4):797–802
41. Hughes WOH, Boomsma JJ. 2004. Genetic diversity and disease resistance in leaf-cutting ant societies. *Evolution* 58(6):1251–60
42. Hughes WOH, Boomsma JJ. 2008. Genetic royal cheats in leaf-cutting ant societies. *PNAS* 105(13):5150–53
43. Hunter CM, Huang W, Mackay TFC, Singh ND. 2016. The genetic architecture of natural variation in recombination rate in *Drosophila melanogaster*. *PLOS Genet*. 12(4):e1005951
44. Hunter CM, Robinson MC, Aylor DL, Singh ND. 2016. Genetic background, maternal age, and interaction effects mediate rates of crossing over in *Drosophila melanogaster* females. *G3* 6(5):1409–16
45. Hunter N. 2015. Meiotic recombination: the essence of heredity. *Cold Spring Harb. Perspect. Biol.* 7(12):a016618
46. Hussin J, Roy-Gagnon M-H, Gendron R, Andelfinger G, Awadalla P. 2011. Age-dependent recombination rates in human pedigrees. *PLOS Genet*. 7(9):e1002251
47. Iles MM, Walters K, Cannings C. 2003. Recombination can evolve in large finite populations given selection on sufficient loci. *Genetics* 165(4):2249–58
48. Jaimes-Nino LM, Heinze J, Oettler J. 2022. Late-life fitness gains and reproductive death in *Cardiocondyla obscurior* ants. *eLife* 11:e74695

49. Ji T, Yin L, Liu Z, Liang Q, Luo Y, et al. 2014. Transcriptional responses in eastern honeybees (*Apis cerana*) infected with mites, *Varroa destructor*. *Genet. Mol. Res.* 13(4):8888–900
50. Jones JC, Wallberg A, Christmas MJ, Kapheim KM, Webster MT. 2019. Extreme differences in recombination rate between the genomes of a solitary and a social bee. *Mol. Biol. Evol.* 36(10):2277–91
51. Kapheim KM, Pan H, Li C, Salzberg SL, Puiu D, et al. 2015. Genomic signatures of evolutionary transitions from solitary to group living. *Science* 348(6239):1139–43
52. Kawakami T, Wallberg A, Olsson A, Wintermantel D, De Miranda JR, et al. 2019. Substantial heritable variation in recombination rate on multiple scales in honeybees and bumblebees. *Genetics* 212(4):1101–19
53. Kent CF, Shermineh M, Harpur BA, Zayed A. 2012. Recombination is associated with the evolution of genome structure and worker behavior in honey bees. *PNAS* 109(44):18012–17
54. Kent CF, Zayed A. 2013. Evolution of recombination and genome structure in eusocial insects. *Commun. Integr. Biol.* 6(2):e22919
55. Kent TV, Uzunović J, Wright SI. 2017. Coevolution between transposable elements and recombination. *Philos. Trans. R. Soc. B* 372(1736):20160458
56. Kerstes NA, Bérénos C, Schmid-Hempel P, Wegner KM. 2012. Antagonistic experimental coevolution with a parasite increases host recombination frequency. *BMC Evol. Biol.* 12(1):18
57. Kidner J, Moritz RFA. 2015. Host-parasite evolution in male-haploid hosts: an individual based network model. *Evol. Ecol.* 29:93–105
58. Klein A. 2015. *Endosymbiosis, co-option and recombination: mechanisms to generate evolutionary novelty in the ant* Cardiocondyla obscurior. PhD Thesis, Univ. Regensburg
59. Koch SI, Groh K, Vogel H, Hannson BS, Kleineidam CJ, Grosse-Wilde E. 2013. Caste-specific expression patterns of immune response and chemosensory related genes in the leaf-cutting ant, *Atta vollenweideri*. *PLOS ONE* 8(11):e81518
60. Kong A, Barnard J, Gudbjartsson DF, Thorleifsson G, Jonsdottir G, et al. 2004. Recombination rate and reproductive success in humans. *Nat. Genet.* 36(11):1203–6
61. Kurze C, Routtu J, Moritz RF. 2016. Parasite resistance and tolerance in honeybees at the individual and social level. *Zoology* 119(4):290–97
62. Lacy KD, Shoemaker D, Ross KG. 2019. Joint evolution of asexuality and queen number in an ant. *Curr. Biol.* 29(8):1394–400.e4
63. Langberg K, Phillips M, Rueppell O. 2018. Testing the effect of paraquat exposure on genomic recombination rates in queens of the western honey bee, *Apis mellifera*. *Genetica* 146(2):171–78
64. Latrille T, Duret L, Lartillot N. 2017. The Red Queen model of recombination hot-spot evolution: a theoretical investigation. *Philos. Trans. R. Soc. B* 372(1736):20160463
65. Legan AW, Jernigan CM, Miller SE, Fuchs MF, Sheehan MJ. 2021. Expansion and accelerated evolution of 9-exon odorant receptors in *Polistes* paper wasps. *Mol. Biol. Evol.* 38(9):3832–46
66. Li X, Heyer W-D. 2008. Homologous recombination in DNA repair and DNA damage tolerance. *Cell Res.* 18(1):99–113
67. Lichten M, Borts RH, Haber JE. 1987. Meiotic gene conversion and crossing over between dispersed homologous sequences occurs frequently in *Saccharomyces cerevisiae*. *Genetics* 115(2):233–46
68. Liu GE, Alkan C, Jiang L, Zhao S, Eichler EE. 2009. Comparative analysis of *Alu* repeats in primate genomes. *Genome Res.* 19(5):876–85
69. Liu H, Zhang X, Huang J, Chen J-Q, Tian D, et al. 2015. Causes and consequences of crossing-over evidenced via a high-resolution recombinational landscape of the honey bee. *Genome Biol.* 16(1):15
70. Liu P, Cuerda-Gil D, Shahid S, Slotkin RK. 2022. The epigenetic control of the transposable element life cycle in plant genomes and beyond. *Annu. Rev. Genet.* 56:63–87
71. Lobkovsky AE, Wolf YI, Koonin EV. 2016. Evolvability of an optimal recombination rate. *Genome Biol. Evol.* 8(1):70–77
72. Lu RX, Bhatia S, Simone-Finstrom M, Rueppell O. 2023. Quantitative trait loci mapping for survival of virus infection and virus levels in honey bees. *Infect. Genet. Evol.* 116:105534
73. Ma F, Lau CY, Zheng C. 2022. Dynamic evolution of recently duplicated genes in *Caenorhabditis elegans*. bioRxiv 2022.03.10.483751. **https://www.biorxiv.org/content/10.1101/2022.03.10.483751v1**

74. Manzano-Winkler B, McGaugh SE, Noor MAF. 2013. How hot are drosophila hotspots? Examining recombination rate variation and associations with nucleotide diversity, divergence, and maternal age in *Drosophila pseudoobscura*. *PLOS ONE* 8(8):e71582

75. Martin HC, Christ R, Hussin JG, O'Connell J, Gordon S, et al. 2015. Multicohort analysis of the maternal age effect on recombination. *Nat. Commun.* 6(1):7846

76. Mattila HR, Reeve HK, Smith ML. 2012. Promiscuous honey bee queens increase colony productivity by suppressing worker selfishness. *Curr. Biol.* 22(21):2027–31

77. Maxwell PH, Burhans WC, Curcio MJ. 2011. Retrotransposition is associated with genome instability during chronological aging. *PNAS* 108(51):20376–81

78. Michener CD. 2000. *The Bees of the World*, Vol. 1. Baltimore, MD: Johns Hopkins Univ. Press

79. Mondet F, Alaux C, Severac D, Rohmer M, Mercer AR, Le Conte Y. 2015. Antennae hold a key to *Varroa*-sensitive hygiene behaviour in honey bees. *Sci. Rep.* 5(1):10454

80. Morandin C, Havukainen H, Kulmuni J, Dhaygude K, Trontti K, Helanterä H. 2012. Not only for egg yolk—functional and evolutionary insights from expression, selection, and structural analyses of *Formica* ant vitellogenins. *Mol. Biol. Evol.* 31(8):2181–93

81. Müller MC, Praz CR, Sotiropoulos AG, Menardo F, Kunz L, et al. 2019. A chromosome-scale genome assembly reveals a highly dynamic effector repertoire of wheat powdery mildew. *New Phytol.* 221(4):2176–89

82. Muñoz-Fuentes V, Marcet-Ortega M, Alkorta-Aranburu G, Linde Forsberg C, Morrell JM, et al. 2015. Strong artificial selection in domestic mammals did not result in an increased recombination rate. *Mol. Biol. Evol.* 32(2):510–23

83. Neiman M, Lively CM, Meirmans S. 2017. Why sex? A pluralist approach revisited. *Trends Ecol. Evol.* 32(8):589–600

84. Nomura T, Takahashi J. 2012. Effective population size in eusocial Hymenoptera with worker-produced males. *Heredity* 109(5):261–68

85. Oettler J, Schrempf A. 2016. Fitness and aging in *Cardiocondyla obscurior* ant queens. *Curr. Opin. Insect Sci.* 16:58–63

86. Otto SP. 2021. Selective interference and the evolution of sex. *J. Hered.* 112(1):9–18

87. Otto SP, Barton NH. 2001. Selection for recombination in small populations. *Evolution* 55(10):1921–31

88. Oxley PR, Spivak M, Oldroyd BP. 2010. Six quantitative trait loci influence task thresholds for hygienic behaviour in honeybees (*Apis mellifera*). *Mol. Ecol.* 19(7):1452–61

89. Pope NS, Singh A, Childers AK, Kapheim KM, Evans JD, López-Uribe MM. 2023. The expansion of agriculture has shaped the recent evolutionary history of a specialized squash pollinator. *PNAS* 120(15):e2208116120

90. Pownall KA, Taylor HN, Altindag UH, Stevison LS. 2020. Maternal age alters recombination rate in *Drosophila pseudoobscura*. bioRxiv 2020.07.20.212548. **https://www.biorxiv.org/content/10.1101/2020.07.20.212548v2**

91. Price DJ, Bantock CR. 1975. Marginal populations of *Cepaea nemoralis* (L.) on the Brendon Hills, England. II. Variation in chiasma frequency. *Evolution* 29(2):278–86

92. Qiu H-L, Cheng D-F. 2017. A chemosensory protein gene *Si-CSP1* associated with necrophoric behavior in red imported fire ants (Hymenoptera: Formicidae). *J. Econ. Entomol.* 110(3):1284–90

93. Rehan SM, Toth AL. 2015. Climbing the social ladder: the molecular evolution of sociality. *Trends Ecol. Evol.* 30(7):426–33

94. Revell LJ. 2013. Two new graphical methods for mapping trait evolution on phylogenies. *Methods Ecol. Evol.* 4(8):754–59

95. Ritz KR, Noor MA, Singh ND. 2017. Variation in recombination rate: adaptive or not? *Trends Genet.* 33(5):364–74

96. Robledo-Ruiz DA, Gan HM, Kaur P, Dudchenko O, Weisz D, et al. 2022. Chromosome-length genome assembly and linkage map of a critically endangered Australian bird: the helmeted honeyeater. *GigaScience* 11:giac025

97. Romiguier J, Gayral P, Ballenghien M, Bernard A, Cahais V, et al. 2014. Comparative population genomics in animals uncovers the determinants of genetic diversity. *Nature* 515(7526):261–63

98. Ross-Ibarra J. 2004. The evolution of recombination under domestication: a test of two hypotheses. *Am. Nat.* 163(1):105–12
99. Roze D. 2023. Causes and consequences of linkage disequilibrium among transposable elements within eukaryotic genomes. *Genetics* 224(2):iyad058
100. Rueppell O, Johnson N, Rychtář J. 2008. Variance-based selection may explain general mating patterns in social insects. *Biol. Lett.* 4(3):270–73
101. Rueppell O, Kuster R, Miller K, Fouks B, Rubio Correa S, et al. 2016. A new metazoan recombination rate record and consistently high recombination rates in the honey bee genus *Apis* accompanied by frequent inversions but not translocations. *Genome Biol. Evol.* 8(12):3653–60
102. Rueppell O, Meier S, Deutsch R. 2012. Multiple mating but not recombination causes quantitative increase in offspring genetic diversity for varying genetic architectures. *PLOS ONE* 7(10):e47220
103. Salathé M, Kouyos RD, Bonhoeffer S. 2009. On the causes of selection for recombination underlying the Red Queen Hypothesis. *Am. Nat.* 174(S1):S31–42
104. Sasaki M, Lange J, Keeney S. 2010. Genome destabilization by homologous recombination in the germ line. *Nat. Rev. Mol. Cell Biol.* 11(3):182–95
105. Schield DR, Perry BW, Adams RH, Holding ML, Nikolakis ZL, et al. 2022. The roles of balancing selection and recombination in the evolution of rattlesnake venom. *Nat. Ecol. Evol.* 6(9):1367–80
106. Schmid-Hempel P. 1998. *Parasites in Social Insects*, Vol. 60. Princeton, NJ: Princeton Univ. Press
107. Schmidt CV, Schrempf A, Trindl A, Heinze J. 2016. Microsatellite markers for the tramp ant, *Cardiocondyla obscurior* (Formicidae: Myrmicinae). *J. Genet.* 95(Suppl. 1):1–4
108. Schoonvaere K, Smagghe G, Francis F, de Graaf DC. 2018. Study of the metatranscriptome of eight social and solitary wild bee species reveals novel viruses and bee parasites. *Front. Microbiol.* 9:177
109. Schultner E, Oettler J, Helanterä H. 2017. The role of brood in eusocial Hymenoptera. *Q. Rev. Biol.* 92(1):39–78
110. Schwartz M, Zlotorynski E, Goldberg M, Ozeri E, Rahat A, et al. 2005. Homologous recombination and nonhomologous end-joining repair pathways regulate fragile site stability. *Genes Dev.* 19(22):2715–26
111. Seistrup A-S, Choppin M, Govind S, Feldmeyer B, Kever M, et al. 2023. Age- and caste-independent piRNAs in the germline and miRNA profiles linked to caste and fecundity in the ant *Temnothorax rugatulus*. *Mol. Ecol.* 32:6027–43
112. Shen B, Freebern E, Jiang J, Maltecca C, Cole JB, et al. 2021. Effect of temperature and maternal age on recombination rate in cattle. *Front. Genet.* 12:682718
113. Shipilina D, Näsvall K, Höök L, Vila R, Talavera G, Backström N. 2022. Linkage mapping and genome annotation give novel insights into gene family expansions and regional recombination rate variation in the painted lady (*Vanessa cardui*) butterfly. *Genomics* 114(6):110481
114. Singh ND. 2019. Wolbachia infection associated with increased recombination in *Drosophila*. *G3* 9(1):229–37
115. Singh ND, Criscoe DR, Skolfield S, Kohl KP, Keebaugh ES, Schlenke TA. 2015. Fruit flies diversify their offspring in response to parasite infection. *Science* 349(6249):747–50
116. Sirviö A, Gadau J, Rueppell O, Lamatsch D, Boomsma JJ, et al. 2006. High recombination frequency creates genotypic diversity in colonies of the leaf-cutting ant *Acromyrmex echinatior*. *J. Evol. Biol.* 19(5):1475–85
117. Sirviö A, Johnston JS, Wenseleers T, Pamilo P. 2011. A high recombination rate in eusocial Hymenoptera: evidence from the common wasp *Vespula vulgaris*. *BMC Genet*. 12(1):95
118. Slone JD, Pask GM, Ferguson ST, Millar JG, Berger SL, et al. 2017. Functional characterization of odorant receptors in the ponerine ant, *Harpegnathos saltator*. *PNAS* 114(32):8586–91
119. Stapley J, Feulner PGD, Johnston SE, Santure AW, Smadja CM. 2017. Variation in recombination frequency and distribution across eukaryotes: patterns and processes. *Philos. Trans. R. Soc. B* 372(1736):20160455
120. Stroeymeyt N, Grasse AV, Crespi A, Mersch DP, Cremer S, Keller L. 2018. Social network plasticity decreases disease transmission in a eusocial insect. *Science* 362(6417):941–45
121. Strotz LC, Simões M, Girard MG, Breitkreuz L, Kimmig J, Lieberman BS. 2018. Getting somewhere with the Red Queen: chasing a biologically modern definition of the hypothesis. *Biol. Lett.* 14(5):20170734

122. Swanson JA, Torto B, Kells SA, Mesce KA, Tumlinson JH, Spivak M. 2009. Odorants that induce hygienic behavior in honeybees: identification of volatile compounds in chalkbrood-infected honeybee larvae. *J. Chem. Ecol.* 35:1108–16
123. Tarpy DR. 2003. Genetic diversity within honeybee colonies prevents severe infections and promotes colony growth. *Proc. R. Soc. Lond. B* 270(1510):99–103
124. Tellier A, Moreno-Gámez S, Stephan W. 2014. Speed of adaptation and genomic footprints of host–parasite coevolution under arms race and trench warfare dynamics. *Evolution* 68(8):2211–24
125. Thomas GWC, Dohmen E, Hughes DST, Murali SC, Poelchau M, et al. 2020. Gene content evolution in the arthropods. *Genome Biol.* 21(1):15
126. Tian T, Piot N, Meeus I, Smagghe G. 2018. Infection with the multi-host micro-parasite *Apicystis bombi* (Apicomplexa: Neogregarinorida) decreases survival of the solitary bee *Osmia bicornis*. *J. Invertebr. Pathol.* 158:43–45
127. Tiley GP, Burleigh JG. 2015. The relationship of recombination rate, genome structure, and patterns of molecular evolution across angiosperms. *BMC Evol. Biol.* 15(1):194
128. Tschinkel WR, King JR. 2017. Ant community and habitat limit colony establishment by the fire ant, *Solenopsis invicta*. *Funct. Ecol.* 31(4):955–64
129. Tsuruda JM, Harris JW, Bourgeois L, Danka RG, Hunt GJ. 2012. High-resolution linkage analyses to identify genes that influence *Varroa* sensitive hygiene behavior in honey bees. *PLOS ONE* 7(11):e48276
130. Waiker P, De Abreu FCP, Luna-Lucena D, Freitas FCP, Simões ZLP, Rueppell O. 2021. Recombination mapping of the Brazilian stingless bee *Frieseomelitta varia* confirms high recombination rates in social hymenoptera. *BMC Genom.* 22(1):673
131. Wang W, Ashby R, Ying H, Maleszka R, Forêt S. 2017. Contrasting sex-and caste-dependent piRNA profiles in the transposon depleted haplodiploid honeybee *Apis mellifera*. *Genome Biol. Evol.* 9(5):1341–56
132. Weyna A, Romiguier J. 2021. Relaxation of purifying selection suggests low effective population size in eusocial Hymenoptera and solitary pollinating bees. *Peer Community J.* 1:e2
133. Wilson EO. 1963. The social biology of ants. *Annu. Rev. Entomol.* 8:345–68
134. Winn LM. 2003. Homologous recombination initiated by benzene metabolites: a potential role of oxidative stress. *Toxicol. Sci.* 72(1):143–49
135. Winn LM, Kim PM, Nickoloff JA. 2003. Oxidative stress-induced homologous recombination as a novel mechanism for phenytoin-initiated toxicity. *J. Pharmacol. Exp. Ther.* 306(2):523–27
136. Wyka S, Mondo S, Liu M, Nalam V, Broders K. 2022. A large accessory genome and high recombination rates may influence global distribution and broad host range of the fungal plant pathogen *Claviceps purpurea*. *PLOS ONE* 17(2):e0263496
137. Zilio G, Moesch L, Bovet N, Sarr A, Koella JC. 2018. The effect of parasite infection on the recombination rate of the mosquito *Aedes aegypti*. *PLOS ONE* 13(10):e0203481