PHILOSOPHICAL TRANSACTIONS B

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Opinion piece

Cite this article: Dapper AL, Payseur BA. 2017 Connecting theory and data to understand recombination rate evolution. *Phil. Trans. R. Soc. B* **372**: 20160469. http://dx.doi.org/10.1098/rstb.2016.0469

Accepted: 7 July 2017

One contribution of 13 to a theme issue 'Evolutionary causes and consequences of recombination rate variation in sexual organisms'.

Subject Areas:
evolution, genetics

Keywords:
recombination rate, theory, meiotic recombination, evolution, genetic variation

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Connecting theory and data to understand recombination rate evolution

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Meiotic recombination is necessary for successful gametogenesis in most sexually reproducing organisms and is a fundamental genomic parameter, influencing the efficacy of selection and the fate of new mutations. The molecular and evolutionary functions of recombination should impose strong selective constraints on the range of recombination rates. Yet, variation in recombination rate is observed on a variety of genomic and evolutionary scales. In the past decade, empirical studies have described variation in recombination rate within genomes, between individuals, between sexes, between populations and between species. At the same time, theoretical work has provided an increasingly detailed picture of the evolutionary advantages to recombination. Perhaps surprisingly, the causes of natural variation in recombination rate remain poorly understood. We argue that empirical and theoretical approaches to understand the evolution of recombination have proceeded largely independently of each other. Most models that address the evolution of recombination rate were created to explain the evolutionary advantage of recombination rather than quantitative differences in rate among individuals. Conversely, most empirical studies aim to describe variation in recombination rate, rather than to test evolutionary hypotheses. In this Perspective, we argue that efforts to integrate the rich bodies of empirical and theoretical work on recombination rate are crucial to moving this field forward. We provide new directions for the development of theory and the production of data that will jointly close this gap.

This article is part of the themed issue 'Evolutionary causes and consequences of recombination rate variation in sexual organisms'.

1. Introduction

During meiosis, germ cells generate DNA double-strand breaks. A minority of these breaks are repaired as crossovers between homologous chromosomes. This process of recombination diversifies offspring genomes, interacting with other evolutionary forces to shape major features of the genome landscape, including nucleotide diversity [1–4], codon bias [5], base composition [6] and repetitive element density [7,8]. The number and placement of crossovers along chromosomes are tightly controlled, with aberrations reducing fertility and offspring viability [9]. Owing to the significance of recombination for evolution and reproduction, the rate at which this process occurs has long been of interest to biologists.

The observation that the recombination rate varies among individuals, among populations and among species (reviewed by [10–12]) raises the questions of how and why this fundamental genomic characteristic evolves. In this Perspective, we suggest that despite decades of research relevant to these questions, evolutionary biologists remain surprisingly far away from answering them. We argue that an important barrier to progress has been a lack of coordination between theoretical and empirical studies. Successes at documenting variation in recombination rate often proceed without an underlying theoretical framework, challenging the ability to test hypotheses and convert observed patterns into inferences about evolutionary process. Theoretical advances that reveal the population genetic conditions under which recombination is predicted to evolve ignore key

biological aspects of recombination rate variation, including genetic complexity and genomic scale.

Our goal is to catalyse alignment and integration of theoretical and empirical efforts to understand recombination rate evolution. We begin with a short overview of existing theory on the evolution of recombination rate, highlighting the key predictions and ingredients of existing models. Next, we describe how empirical work can better evaluate theoretical predictions and we motivate the data-based examination of the role of natural selection in recombination rate evolution. Finally, we suggest new directions for theory that capture observed patterns of recombination rate variation.

2. General features of theoretical models of recombination rate evolution

Like other phenotypes, recombination rate has the potential to affect individual fitness and experience direct selection, in this case by impacting gamete viability (direct selection—table 1). In contrast with most other traits, recombination rate itself shapes offspring genotype frequencies, raising the possibility of indirect selection. This type of indirect selection on recombination rate can be mediated by short-term or long-term advantages [13]. Short-term benefits occur when recombination breaks apart deleterious gene combinations and immediately increases the mean fitness in the next generation. Long-term benefits accrue when recombination increases the additive genetic variance in a population, enabling selection (on other traits) to act more efficiently [13]. Understanding how recombination rate evolves requires knowledge of the magnitude and direction of direct selection, short-term indirect selection and long-term indirect selection. The sum of these effects determines whether alleles that modify recombination rate spread through a population [13,14].

Identifying the conditions under which indirect selection favours increases in recombination has been a particular emphasis of theory treating the evolution of recombination rate. A first class of models, called optimality [15] or intrinsic models [16], examines how recombination rate optimizes group-level traits, such as equilibrium mean fitness [17–25] or mutational load [23,26–30]. This set of models compares populations that vary in recombination rate [15], but does not explicitly consider genetic modifiers of the trait. The second class of models, termed modifier [15] or extrinsic models [16], examines how various forms of individual-level selection change recombination rate [31,32]. In this group of models, a genetic modifier of recombination rate is treated as a single, Mendelian locus at which different alleles confer different recombination rates to individuals. The frequency of crossing-over in a specific genomic interval between two additional loci is considered. By varying selection pressures and tracking the change in frequency of modifier alleles, these models explicitly analyse the expected change in recombination rate within a single population. Modifier models have been favoured over optimality arguments because they invoke individual-level, rather than group-level, selection and they tend to reveal complex, short-term dynamics [15].

The opportunity for indirect selection on recombination rate depends on the degree and form of non-random associations between alleles at different loci, or linkage disequilibrium (LD). LD between two loci harbouring alleles A, a and B, b (respectively) can be measured as the deviation (D_{AB}) of the haplotype's frequency (p_{AB}) from its expected frequency, given individual allele frequencies (p_A and p_B) and free recombination:

$$D_{AB} = p_{AB} - p_A p_B. \tag{2.1}$$

When the population is at linkage equilibrium ($D_{AB} = 0$), recombination does not affect offspring genotype frequencies because the association between alleles cannot be further randomized and indirect selection on recombination rate cannot be generated. As a result, most population genetic theory on the evolution of recombination focuses on understanding how evolutionary processes generate and/or maintain LD.

Two potentially important determinants of LD that have received considerable attention from theoreticians are epistasis and genetic drift [14]. In this context, epistasis is usually defined as non-additive allelic effects across loci, such that the mean phenotype for a given multi-locus genotype does not match its expected value, given the mean phenotypes of the individual alleles [33–35]. Epistasis for fitness results in selection for beneficial combinations of alleles, increasing their frequency within a population and generating LD [36]. Epistatic scenarios range from pairwise interactions between alleles to nonlinear cumulative effects of new mutations; both are featured in the theory of recombination rate evolution [37,38]. In finite populations, genetic drift leads to non-random associations between beneficial and deleterious alleles, thereby delaying the response to selection [39].

Even when epistasis and/or genetic drift generate LD, it remains unclear whether more recombination should be generally beneficial. Reducing LD can increase 'recombination load' by breaking apart beneficial combinations of alleles that have accumulated due to selection [13,40,41]. Thus, recombination may impede adaptation and eventually be eliminated, as recombination-reducing modifiers become associated with beneficial allelic combinations and spread through the population [13,40]. This concept is formalized in the 'Reduction Principle', which states that only modifiers that reduce recombination rate can invade a population under equilibrium conditions (reduction principle—table 1) [15,41–43]. The widespread persistence of crossing-over despite these theoretical constraints is referred to as the paradox of recombination [41]. However, equilibrium conditions require idealized large populations with no mutation, no migration, random mating and constant viability selection [15]. Such populations are likely rare in nature. By identifying conditions under which sets of these assumptions are routinely violated, theoreticians have generated a rich body of work that describes sources of indirect selection on recombination rate. Eight of these theoretical models are outlined in table 1. Here, we briefly describe three main categories of hypotheses that predict indirect selection for increased recombination rate.

(a) Negative epistasis

Negative epistasis describes genetic interactions in which two beneficial alleles, when present in the same individual, increase fitness less than expected based upon their separate effects or conversely, when two deleterious alleles decrease fitness more than expected based upon their separate effects. As a result, negative epistasis maintains LD, characterized by a paucity of genotypes with the most extreme fitness values and an excess of individuals near the mean fitness value [44]. By reducing LD, recombination generates more extreme phenotypes, increasing the genetic variance in the population. Greater genetic

Table 1. An overview of nine hypotheses proposed to explain the evolution of recombination rate (direct selection, plus eight models of indirect selection). Each theoretical model differs in the key requirements that must be met for indirect selection on recombination rate to occur. There are no formal theoretical models underlying the direct selection hypothesis. We highlight the role of epistasis, linkage disequilibrium (LD) and drift in each model. Among models of indirect selection on recombination rate, there is also variation on whether the genetic modifier of recombination rate must be linked to other loci under direct selection. We describe a set of simple, testable predictions that arise from each model and describe the expected direction of selection on recombination rate. LD, linkage disequilibrium.

hypothesis	key requirements	epistasis	linkage disequilibrium	drift	linked modifier	predictions	direction of effect
direct selection	an optimal number of crossovers per chromosome is required for successful meiosis	none	none	no	no prediction	upper and lower bounds on recombination rate	stabilizing (increases or decreases) around an optimal recombination rate
reduction principle	large, equilibrium populations with no mutation, no migration, random mating and constant viability selection	not required	initial LD is required	no	no requirement	no recombination; genetic modifiers that decrease recombination rate spread	decrease
negative epistasis	pervasive, weak, negative epistasis and recurrent deleterious mutations or selective sweeps (directional selection)	weak, negative epistasis	negative, arises due to epistatic selection; disadvantageous	no	linked modifier relaxes the requirement for weak epistasis	increase in recombination rate following episodes of strong directional selection	increase if requirements met, otherwise decrease
temporal heterogeneity	rapid, temporal fluctuations in the environment favour different combinations of alleles	the sign of epistasis changes every two to five generations	the sign of LD tracks changes in the sign of epistasis	no	linked modifiers	increase in recombination rate in environments with rapid and consistent temporal variation	increase if requirements met, otherwise decrease
host–parasite interactions	rare combinations of alleles have an advantage via resistance to parasites	the sign of epistasis changes every two to five generations	the sign of LD tracks changes in the sign of epistasis	no	linked modifiers	increased recombination in populations exposed to virulent parasites	increase if requirements met, otherwise decrease
inter-locus sexual conflict	inter-locus sexual antagonism is common and rare combinations of alleles are advantageous	the sign fluctuates at a frequency dependent on the strength of sexual selection	the sign of LD tracks changes in the sign of epistasis	no	unlinked modifiers	positive correlation between recombination rate and strength of sexual conflict	increase if requirements met, otherwise decrease
spatial heterogeneity	environmental selection pressures vary between populations with frequent migration	variable: none, positive, or negative	variable: positive or negative; generated by epistasis and/or spatial heterogeneity	no	variable: linked, loosely linked, or unlinked	more variation in recombination rate among populations in highly spatially variable environments	increase if requirements met, otherwise decrease
Hill–Robertson effect	population is finite and subject to selection	not required	negative, generated by drift	yes	linked modifiers	higher recombination rate with lower effective population size	increase if requirements met, otherwise decrease
fitness-associated recombination (FAR)	recurrent deleterious mutations, modifier sensitive to haplotype fitness	not required	positive, generated between fitness-determining loci	no	linked modifiers	negative correlation between fitness and recombination rate	stabilizing (increases or decreases) around an optimal recombination rate

variance allows populations to purge recurrent deleterious mutations more efficiently and respond to directional selection more rapidly (negative epistasis—table 1) [40,44,45]. As a result of these long-term benefits, genetic modifiers that increase the recombination rate may become associated with beneficial allele combinations and spread through the population [13,29,42,44,46].

(b) Heterogeneity in selection

Heterogeneity in selection pressure over time, across space, or between the sexes can generate LD (table 1). Fluctuating environments can favour increased recombination rate when allelic combinations that are advantageous at one time point become disadvantageous at another time point, resulting in an overabundance of deleterious allelic combinations when environmental conditions change (temporal heterogeneity—table 1) [13,37,40,47–49]. In this scenario, recombination produces short-term benefits by breaking up maladaptive allelic combinations and immediately increasing mean fitness among offspring [13]. However, the degree to which recombination is favoured is highly sensitive to the frequency of environmental fluctuation. To account for the high levels of recombination that are observed, fluctuations must occur every 2–5 generations and cycle with a period of 4–10 generations [13,47].

Whereas abiotic factors are unlikely to produce such rapid, consistent changes in the sign of epistasis, biotic factors offer clear potential [13,50]. In particular, coevolution between hosts and parasites can generate epistatic fluctuations of the form needed to favour recombination (host–parasite interactions—table 1) [48,51]. This occurs when under-represented combinations of alleles offer increased resistance to sufficiently virulent parasites, which adapt to the most abundant genotypes within a population [37,48]. In this scenario, recombination produces rare combinations of alleles that are less susceptible to parasites [37,48]. Inter-locus sexual conflict can also generate disadvantageous allelic combinations due to antagonistic coevolution between the sexes (inter-locus sexual conflict—table 1) [52]. In addition to varying over time, selection can also vary over space. Spatial variation in the strength or direction of selection among populations can generate differences in local allele frequencies. With migration, these differences produce LD among offspring (spatial heterogeneity—table 1) [14]. The direction and magnitude of the indirect selection on recombination rate produced by migration are determined by the similarity in selection pressures between the two populations [14,53,54]. For example, recombination modifiers that reduce the recombination rate are expected to frequently, but not always, spread in the face of maladaptive gene flow, potentially playing an important role in the process of speciation [53,54].

(c) Genetic drift

Within finite populations, the interaction between genetic drift and selection results in the build-up of LD [39,55,56]. Genetic drift generates positive LD, when a beneficial mutation arises on the background of another beneficial allele, and negative LD, when a beneficial mutation arises on the background of a deleterious allele. Haplotypes with double beneficial alleles can quickly fix, thereby eliminating positive LD. In contrast, the association between beneficial and deleterious alleles may persist and slow the response to selection [39,57]. The net effect is an accumulation of negative LD, referred to as the Hill–Robertson effect [55,58]. By breaking down LD, recombination modifiers can free beneficial mutations from their backgrounds and increase in frequency within populations due to their association with advantageous haplotypes (Hill–Robertson effect—table 1) [39,55–57].

3. Generating data that address existing theory

Theoretical work has provided an increasingly detailed picture of the evolutionary advantages to recombination, but the causes of natural variation in recombination rate remain poorly understood. Here, we highlight some empirical findings on the evolution of recombination rate, describe their current disconnect with existing theory and recommend empirical approaches to bridge this divide.

(a) Measuring recombination rate

Multiple methods can be used to measure recombination rate, depending on the genomic scale of interest (figure 1). The total number of crossovers in a genome can be estimated by counting chiasmata (the physical bridges formed between homologous chromosomes) or in some species, by counting foci of the MLH1 mismatch repair protein (which localize to crossover sites and can be visualized with immunofluorescence) in meiotic cells [59]. These approaches characterize recombination in single cells; the recombination rate of an individual is estimated as the average number of crossovers among cells. A second method for estimating recombination rate is to examine the transmission of polymorphic DNA markers on the same chromosome in crosses or pedigrees. By comparing parent and offspring genotypes, the frequency of recombination between a pair of markers can be calculated and converted to a genetic distance. One centiMorgan (cM) is defined as the expected number of crossovers between markers in 100 meioses [60]. This linkage mapping approach enables the profiling of recombination rate variation along chromosomes. The genomic level of resolution depends on the number of meioses surveyed and is typically on the scale of megabases (Mb). Two methods enable estimation of recombination rate on finer (kilobase; kb) scales. The frequencies of marker haplotypes in very large numbers of sperm reveal recombination rates for individual males in targeted genomic regions [61]. Alternatively, patterns of LD among single nucleotide polymorphisms (SNPs) in samples of unrelated individuals can be converted to recombination rates using population genetic models [62]. This approach, which yields time- and sex-averaged recombination rate estimates for populations, can be applied to the entire genome. In all methods, the recombination rate between markers is typically standardized across interval sizes by dividing by the number of base pairs separating markers.

(b) Towards hypothesis-based empirical studies

Empirical studies using methods described above have begun to describe how recombination rate varies along multiple evolutionary timescales. Individuals from the same species differ in the number and/or placement of crossovers [11,63–78]. Species pairs display divergent recombination rates in specific genomic intervals or across the genome [79–85]. Across the phylogeny of eutherian mammals, more closely related species tend to show more similar genome-wide recombination rates [10,86–88]. Nevertheless, these patterns remain disconnected from the theoretical hypotheses reviewed above, and few

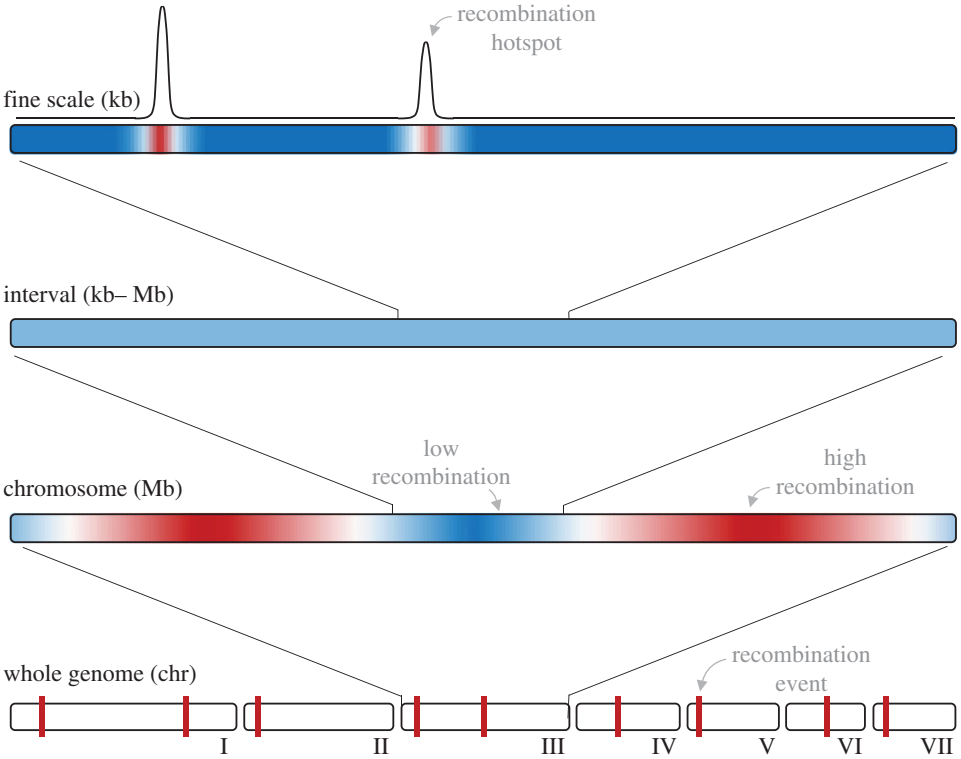

Figure 1. Genomic scales on which recombination rate can be measured. (Online version in colour.)

inferences about the underlying evolutionary processes have been reported.

Among existing theoretical hypotheses for the evolution of recombination rate, long-term indirect selection has received the most empirical attention (negative epistasis—table 1). The results of these studies have been largely inconclusive. Recombination rate increases in response to artificial selection targeting unrelated phenotypes in some experiments (reviewed by [41,57]). Although similar patterns might be expected to be associated with domestication [89], domesticated plants and animals show little to no evidence for expanded genetic maps compared to their wild relatives [90–92]. Another empirical approach that has been employed is to determine whether the conditions required for different theoretical hypotheses about the evolution of recombination rate exist. For example, theoretical models have clearly demonstrated that if indirect selection drives recombination rate evolution, the magnitude and sign of LD and epistasis must play key roles [14]. Although some empirical studies have attempted to quantify these variables (at least in experimental populations; reviewed in [93]), a connection to variation in recombination rate itself is still missing. We encourage empirical work that goes beyond evaluating the assumptions of existing models to directly testing their predictions.

From a theoretical perspective, the best models are those that make realistic assumptions and generate recombination rate evolution across the broadest parameter space. Based on these criteria, models that consider the combined action of genetic drift and selection suggest that Hill–Robertson effects may constitute a pervasive form of indirect selection on recombination rate. The major assumptions of these models—that populations are finite, are subject to recurrent mutation, and experience pervasive selection—likely apply to most natural populations [39]. But direct tests of predictions from this model are needed. Comparing recombination rates in conspecific pairs of populations with different effective population sizes (Hill–Robertson effect—table 1) and little to no evidence for gene flow would be one way to evaluate the importance of Hill–Robertson effects for recombination rate evolution [39].

(c) The role of selection

Although theoretical work is strongly biased towards selective explanations, there is limited empirical evidence for a role of selection in the evolution of recombination rate [12]. Three components must be present for the process of natural selection to occur: variation, inheritance and fitness differences. As mentioned above, empirical studies have documented extensive variation in recombination rate between individuals. Ample evidence indicates that phenotypic variation in recombination rate has a heritable component. Recombination rate shows resemblance among relatives in human pedigrees [69,94,95], differs among lines raised in a common environment [66,74,76,87,96,97] and responds to artificial selection in *Drosophila melanogaster* and other insects [63,65,98–113]. Broad-sense or narrow-sense heritability estimates from humans, mice, insects and maize range from 0.08 to 0.69 [94,95,99,100, 102,112,114–116]. A few observations raise the prospect that recombination rate could affect fitness. Fecundity and recombination rate may be positively correlated in human mothers [69,117,118]. Phylogenetic comparative methods suggest that the genome-wide recombination rate has increased during mammalian evolution [88]. PRDM9, a protein that helps determine the position of crossovers in mice and humans, possesses one of the most rapidly evolving (zinc-finger) domains in mammals [119,120]. Finally, cellular needs to avoid non-disjunction (by generating at least one crossover per chromosome or chromosome arm) [117,121–124] and to minimize costs of double-strand break repair should impose selective bounds on the genome-wide recombination rate in nature [9,10,121,122].

A host of experiments using insects attempted to increase and/or decrease the recombination rate by direct artificial selection [63,65,98–113]. All but one study focused on crossover rates in individual genomic intervals monitored by visible markers. Ten of 15 studies that tried to increase the recombination rate were successful in at least one line; six of 15 studies were able to decrease crossing-over. Among the subset of experiments that applied both selection for higher and lower recombination rate, there was no obvious asymmetry in results. Although these reports are restricted to a few species of insects (mostly *D. melanogaster*) and results were highly variable both between and within experiments, this series at least demonstrates the potential for recombination rate to respond to directional selection in nature.

This summary underscores a few notable barriers to understanding the role of selection in recombination rate evolution. Whereas most models focus on indirect selection, patterns of variation in recombination rate and the functional role of recombination in meiosis suggest that direct selection may contribute to the evolution of this trait. In addition, empirical evidence for a relationship between recombination rate and fitness in natural populations is lacking [12]. Measuring both direct and indirect selection pressures on recombination rate in nature is a necessary next step to connecting data with existing theoretical predictions.

We offer several suggestions to elucidate the contributions of selection to recombination rate evolution. First, we encourage empirical work that better defines the lower and (especially) the upper bounds on recombination rate that reflect meiotic constraints. Widely cited lower bounds—one crossover per chromosome or one crossover per chromosome arm—are still based on data from a small number of species, and it is possible that this limit itself evolves [122]. Potential ceilings on the recombination rate remain poorly defined. Better characterization of the bounds on recombination rate and their meiotic causes would identify potential sources of purifying and stabilizing selection. Second, researchers should strive to connect variation in recombination rate with the natural environment. The question of whether recombination rate shows clines across gradients of geography and other environmental variables remains to be addressed. Third, quantitative genetic methods can be used to determine whether other patterns of recombination rate variation are consistent with neutral expectations. Genetic variance in recombination rate can be partitioned between and within populations using laboratory crosses. If recombination rate evolves neutrally, this partitioning should match levels of population structure at neutral molecular markers [125,126]; departures from this prediction could indicate directional or stabilizing selection on recombination rate. Finally, quantifying the distribution of mutational effects on recombination rate (using mutation-accumulation experiments and other approaches) ultimately will be necessary in order to draw firm conclusions about the role of selection in recombination rate evolution.

4. Developing models that address empirical patterns

Just as empirical approaches have largely failed to address theory in the context of recombination rate evolution, existing models have struggled to produce empirically testable hypotheses. Here, we describe how to advance theoretical studies of recombination rate evolution by grounding them with established empirical knowledge.

(a) Recombination rate as a quantitative trait

Empirical evidence demonstrates that recombination rate is a quantitative trait [12,113], with variance among individuals reflecting the cumulative effects of many underlying mutations and environmental influences. Sequence variants in or near 21 known genes are associated with recombination rate variation within populations of humans [127–129], domesticated cattle [130,131], or wild Soay sheep [116] . Variants in five of these genes correlate with recombination rate in multiple species: *Rnf212* [116,127,128,130], *Cplx1* [116,128,131], *Rec8* [116,130, 131], *Msh4* [128,131] and *Prdm9* [128,131]. Repeated association with a common set of genes raises the prospect that recombination rate variation harbours moderate genetic complexity [116]: a handful of variants have large enough effects to be detected on top of a polygenic background. Furthermore, suites of quantitative trait loci (QTL) confer differences in the genome-wide recombination rate between inbred strains of house mice belonging to different subspecies [132–134]. Although some alleles have appreciable phenotypic effects [128,132], most variance in recombination rate remains unexplained in the examined populations and crosses, suggesting an important role for environmental factors [116]. Taken together, this empirical evidence strongly supports the conclusion that recombination rate is a complex trait.

By contrast, existing theory focuses on population genetic models, which either ignore the genetic architecture of recombination rate (optimality arguments) or assume that recombination rate is a simple Mendelian trait (modifier models) [15,16]. While quantitative genetic theory has been applied to understand how indirect selection on a recombination modifier can be generated by direct selection on a complex trait [46], models that assume recombination rate itself is a complex trait are missing. The disconnect between the complex genetic underpinnings of recombination rate and the simplicity of the genetic architecture assumed in theoretical models is striking. Modelling recombination rate as a quantitative trait is likely to uncover novel evolutionary dynamics and to produce predictions that are straightforward to test.

(b) Genomic scale of recombination rate evolution

Another empirical observation is that distinct patterns of variation in recombination rate are sometimes observed on different genomic scales. Thus, the tempo and mode of recombination rate evolution may depend on the genomic scale on which it is measured [11,135,136] (figure 1). Patterns of LD indicate that both humans [80,82,137] and bonobos [83] share few recombination hotspots with chimpanzees, implying rapid evolution of recombination rate on the fine (kb) scale. By contrast, recombination rates calculated across larger chromosomal regions (from linkage maps or patterns of LD) usually show higher correlations among closely related species or conspecific populations [11,81,83,135,136,138–140], with statistically divergent intervals comprising a minority of the genome [85]. Intriguingly, recombination hotspots and double-strand break hotspots appear to be evolutionarily stable in finches [141] and budding yeast (respectively) [142], suggesting that the rapid divergence of recombination rate on the fine scale observed in mammals could be the

exception [143]. Importantly, it is unclear how the evolution of recombination rate—including the form and intensity of selection—translates across genomic scales.

Models that address the evolution of recombination rate were generated to explain the evolutionary advantage of recombination, rather than quantitative differences in rate among individuals. One consequence of this motivation is that existing theory does not directly address genomic scale, focusing instead on single intervals of undefined physical size. It is difficult to use theoretical results for selection on a single interval to understand genome-wide patterns of variation in recombination rate, which can be measured empirically. We encourage the development of theory that parses and synthesizes the evolution of recombination rate across genomic scales [144].

(c) Plasticity and recombination rate evolution

Temperature, nutrient availability, pheromones and other environmental variables are known to modulate crossover number [145–152]. Furthermore, *D. melanogaster* females produce a higher proportion of recombinant offspring after they are infected by parasites [153]. Although the evolution of recombination rate has not been directly tied to these factors, natural variation in this phenotype is likely to be shaped by the external environment.

Theoretical models have explored the evolutionary dynamics of plastic genetic modifiers that only increase the rate of recombination in low-fitness individuals (fitness-associated recombination (FAR)—table 1) [154,155]. Among haploid species, FAR generates selection for increased recombination over an expansive parameter space and does not require epistasis, initial LD, or finite population size, suggesting that it may be a powerful mechanism for the evolution of recombination rate [154]. By contrast, the evolution of FAR appears to be extremely restricted in diploid organisms because it requires that the modifier assess haplotype, rather than organismal, fitness [155]. Thus, these models are unable to provide a general adaptive explanation for the empirical observations described above.

(d) Sex differences in recombination rate

Recombination rates can also experience discordant evolutionary trajectories in the two sexes. In some species, only one sex recombines; the other (achiasmate) sex is the heterogametic one [156–159]. In most species that recombine, crossing-over happens in both sexes, but the degree of sexual dimorphism in the total number of crossovers (heterochiasmy) varies substantially among species [160–162]. There is limited evidence of higher genetic variance for recombination rate among females than among males within species [116,128]. Both genetic variants with sex-specific effects and variants with sex-shared effects on recombination rate have been identified [116,128,131]. Sexually dimorphic genomic patterns in crossover positioning—including higher recombination near centromeres in female vertebrates [67,72,116,131,161,163–167]—raise the prospect that the decoupling of recombination rate evolution in the two sexes could extend to finer genomic scales.

Theoretical models have also investigated the evolution of sex differences in recombination rate [168,169]. While selection for the suppression of recombination on sex chromosomes can be generated rapidly, the evolution of sex differences in recombination rate on autosomes has been more difficult to explain [32]. Similar to FAR, it is unlikely that sex differences in the strength of selection in diploid adults can generate selection for sex differences in recombination rate [32,168]. Selection for heterochiasmy is more likely to be caused by sex differences in the strength of haploid-level selection or in the strength of selection on imprinted genes, which are effectively haploid [160,168]. In such cases, it is expected that the sex experiencing strong haploid selection will exhibit less recombination [168]. Nevertheless, theory that explains the major empirical characteristics of heterochiasmy evolution is not yet available.

5. Conclusion

Forging stronger connections between theory and data in recombination rate evolution holds considerable potential to advance the field. The rich body of theory on the evolution of recombination rate provides a strong framework for generating hypothesis-driven empirical studies. We encourage biologists to collect data that can be used to directly test these hypotheses. Furthermore, established approaches from evolutionary biology should be applied to answer the basic question of whether recombination rate experiences selection in natural populations. Likewise, empirical investigations uncovering patterns of variation in recombination rate, as well as its genetic underpinnings, are generating exciting new avenues for theoretical development. Models that treat recombination rate as a quantitative trait and explicitly incorporate genomic scale are likely to provide novel and increasingly realistic predictions that will lend themselves to empirical examination. A meaningful integration between theoretical and empirical studies should be the next step towards understanding how recombination rate evolves.

Data accessibility. This article has no additional data.

Competing interests. We declare we have no competing interests.

Funding. A.L.D. was supported by NHGRI Training Grant to the Genomic Sciences Training Program 5T32HG002760. B.A.P. was supported by NIH grants R01GM120051 and R01GM100426, and NSF grant DEB 1353737.

Acknowledgements. We thank April Peterson, Michael Wade, Jessica Stapley, Daniel Ortiz-Barrientos and multiple anonymous reviewers for useful comments on drafts of this article. We thank the editors of this special issue for inviting us to contribute.

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