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Are all sex chromosomes created equal?

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Three principal types of chromosomal sex determination are found in nature: male heterogamety (XY systems, as in mammals), female heterogamety (ZW systems, as in birds), and haploid phase determination (UV systems, as in some algae and bryophytes). Although these systems share many common features, there are important biological differences between them that have broad evolutionary and genomic implications. Here we combine theoretical predictions with empirical observations to discuss how differences in selection, genetic properties and transmission uniquely shape each system. We elucidate how the differences among these systems can be exploited to gain insights about general evolutionary processes, genome structure, and gene expression. We suggest directions for research that will greatly increase our general understanding of the forces driving sex-chromosome evolution in diverse organisms.

Sex chromosomes inhabit unique evolutionary environments

Sex chromosomes are interesting to evolutionary geneticists for two very different reasons. The first is because of their role in sex determination. A second and more general reason is that sex chromosomes provide unique opportunities to study the fundamental evolutionary forces that act on all of the genome. Because of their unusual pattern of transmission (Figure 1), any biological difference between the sexes can cause sex chromosomes to experience distinct evolutionary environments. Important sex differences that influence sex-chromosome evolution include mutation rates, sexual selection, sexually antagonistic selection (Glossary), recombination rates, effective population sizes, and diverse forms of genetic conflict [1–12]. Traditionally, most of our knowledge on the biology of sex chromosomes stems from a few well-studied model organisms, notably mammals and *Drosophila melanogaster*. With the advent of genomic approaches, our understanding of the diversity of sex-chromosome systems in nature and their genetic properties has increased

Glossary

Androdioecy: a breeding system with both males and hermaphrodites.
Dioecy: a breeding system with separate sexes (males and females).
Dosage compensation: hyper-transcription of the single Z or X chromosome in the heterogametic sex to balance the ratio of sex-linked to autosomal gene products.
Environmental sex determination (ESD): sex determination caused by an environmental cue such as temperature. This contrasts with genetic sex determination (GSD) where sex determination is caused by the genotype of the individual.
Gynodioecy: a breeding system with both hermaphrodites and females.
Hemizygous: a sex chromosome present in only one copy in the heterogametic sex: the Y chromosome in XY systems and the W chromosome in ZW systems.
Heterogametic: the sex with two types of sex chromosomes: males in XY systems and female in ZW systems. All diploid individuals in UV systems are heterogametic.
Hill–Robertson effect: the reduction in the overall effectiveness of selection between linked sites in finite populations. This effect is extreme in the non-recombining segment of Y and W chromosomes because of their reduced population sizes and lack of recombination.
Homogametic: the sex with one type of sex chromosome in the diploid phase. In XY systems, females (which have an XX genotype) are the homogametic sex, whereas in ZW systems it is the males (which have a ZZ genotype).
Male-biased mutation: increased mutation rates in the male germline, possibly resulting from the higher number of male meioses.
Meiotic drive: any phenotype occurring during meiosis or gametogenesis that lowers the production of the non-carrier gamete type.
Meiotic sex-chromosome inactivation (MSCI): inactivation of the X or Z chromosome in the latter stages of meiosis in the heterogametic sex. Sometimes called male germline X inactivation, although it also takes place in females in ZW systems.
Muller's ratchet: the increased accumulation of deleterious mutations caused by drift in non-recombining parts of the genome.
Pseudoautosomal region (PAR): segments of sex chromosomes that recombine in the heterogametic sex.
Selective sweep: the fixation of an allele by positive selection. This results in decreased genetic variation at linked sites (nearby regions of the chromosome).
Sexually antagonistic selection: selection in which alleles have different relative fitnesses in males and females.
Sexually-antagonistic zygotic drive (SAZD): selection on sex chromosomes to harm individuals of the non-carrier sex.
Sex-determining region (SDR): the region of a sex chromosome that carries the sex-determination factor(s) and that does not recombine in the heterogametic sex.
UV sex-chromosome system: a system in which sex is determined genetically during the haploid phase of the life cycle. Females carry the U chromosome and males the V chromosome.
XY sex-chromosome system: a genetic sex-determining system in which females are homogametic (with an XX genotype) and males are heterogametic (with a XY genotype).
ZW sex-chromosome system: a genetic sex-determining system in which females are heterogametic (with an ZW genotype) and males are homogametic (with a ZZ genotype).

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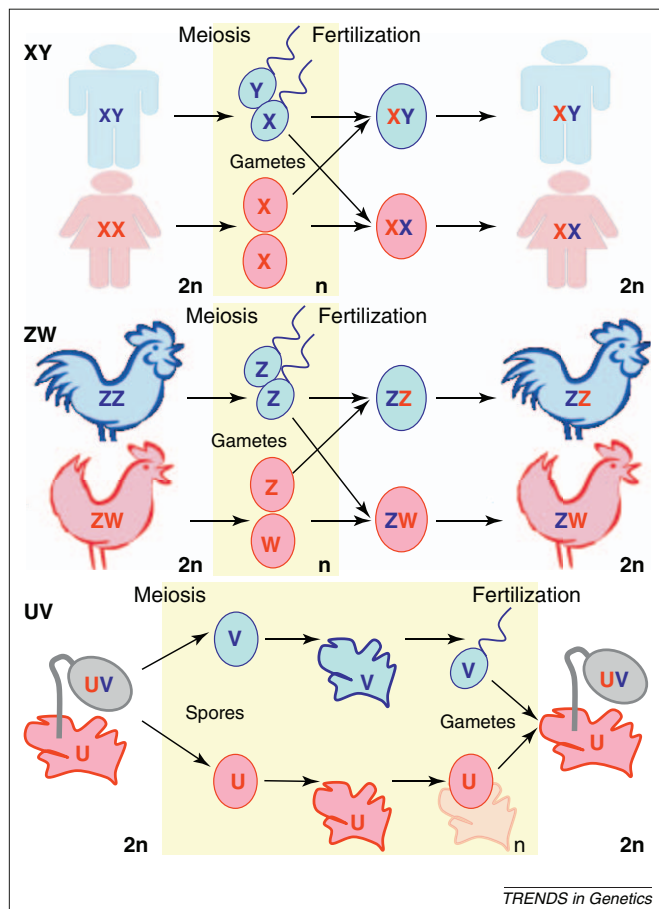* Authors are listed alphabetically.

Figure 1. The differences in inheritance and sex specification between XY, ZW and UV sex-chromosome systems. Females are shaded in red, males are in blue. In XY systems, the Y chromosome is confined to males, and males inherit their X chromosome from their mother. For females, each parent contributes one X chromosome. In ZW systems, the W chromosome is female-specific, and females always inherit their single Z chromosome from their father. Males inherit one Z chromosome from each parent. In UV systems, sex is expressed in the haploid phase, with U chromosomes confined to females and V chromosomes limited to males. Males and females produce sperm and eggs, respectively, by mitosis, and fertilization results in the UV diploid phase. Because the diploid UV is non-sexed, we have illustrated it in grey. Meiotic segregation in the UV diploid results in the production of female (U) and male (V) spores, which ultimately develop into sexually mature haploid individuals.

dramatically, and will continue to do so. In this review we seek to synthesize these new data with evolutionary theory to illuminate topics as diverse as breeding-system evolution and genomic conflict. By pointing out theoretical predictions lacking empirical support, we also hope to stimulate research into aspects of sex chromosomes that are less well understood.

Sex chromosomes have evolved independently many times in animals and plants [13–16]. In organisms that mate as diploids (e.g. animals and flowering plants), sex-chromosome systems take two forms [14]. In XY systems, males are heterogametic (XY) and females homogametic (XX), whereas in ZW systems females are heterogametic (ZW) and males homogametic (ZZ). Less well known is a third type of sex-chromosome system. In some algae and bryophytes there are male and female sexes that are genetically determined during the haploid phase of the life cycle [14]. We will include this system in our discussions here because it has unique evolutionary and genetic properties with no parallel in diploid systems. To facilitate comparison with XY and ZW systems, we use U and V to refer to their female and male sex chromosomes, respectively (Box 1).

Sex chromosomes are linkage groups whose inheritance is correlated with sex: U and W chromosomes are limited to females, V and Y chromosomes are limited to males, and the X and Z chromosomes are carried 2/3 of the time in females and males, respectively (Figure 1). A key feature of these chromosomes is the sex-determining region (SDR) that carries the sex-determining factor(s) and that does not recombine in the heterogametic sex. The SDR can be as small as a single locus or as large as an entire chromosome [14,17]. The evolution of reduced recombination between the sex-determining locus and adjacent parts of the sex chromosome is thought to result from sexually antagonistic selection, in which alleles at a locus have different relative fitnesses in males and females. Decreased recombination between a locus under sexually antagonistic selection and the SDR links together the genes that determine one sex with the alleles that increase the fitness of that sex [14,17]. Consequently, selection can favor ex-

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The life cycle of all sexual eukaryotes alternates between diploid and haploid stages. Although sex determination in many systems occurs in the diploid stage, strongly dimorphic sexes can also be determined by genetic factors in the haploid stage. This sexual system is best developed in the bryophytes [31,32] and macroalgae [14,72,73]. To emphasize differences between haploid and diploid sex determination, we refer to the haploid sex chromosomes as U and V. Females (so-defined because they make large gametes) carry a U chromosome, whereas haploid males (defined because they make small gametes) carry a V chromosome. The UV system is thus distinct from the mating types found in yeast and some algae, and it provides a fascinating contrast that has no exact parallel in XY and ZW systems.

In haploid sex-determination systems, the diploid stage is always heterogametic (UV). The multicellular haploid males and females make genetically-based, asymmetric contributions to fertilization. Sex is not determined at fertilization, as in animals or angiosperms. Instead, the U and V chromosomes pair in diploids at meiosis, and the sex of the haploid offspring is determined by whether it carries a female (U) or male (V) chromosome. Importantly, there is no distinction between heterogametic and homogametic sexes, and both the U and V are always hemizygous in the diploid phase. Although recombination is suppressed on both the U and V – to prevent male-specific alleles from recombining onto a female-determining chromosome, and vice versa – neither chromosome is expected to experience extensive degeneration because both are exposed to purifying selection as haploids. This symmetrical pattern of inheritance means that loci on the U and the V chromosomes have half the effective population size of loci on an autosome (all else equal) (Figure 2). The UV system does allow for the accumulation of sexually antagonistic alleles, making this system fundamentally different from self-incompatibility loci in angiosperms or fungal mating-type loci, which are not correlated with major mating asymmetries.

U and V chromosomes in many bryophytes are often heteromorphic – the female U is generally larger – and can be either smaller or larger than the autosomes [74]. The limited available data suggest that gene density on U and V chromosomes is lower than that of autosomes [31]. The life history of haploid mating species suggests that structural differences between the U and V chromosomes are likely to proceed by the accumulation of genetic material (transposable elements or genes related to sex-specific functions) rather than gene loss [75], but this hypothesis remains untested.

pansion of the non-recombining SDR to include many more genes than those essential for sex determination. The remaining segments of sex chromosomes that continue to recombine in the heterogametic sex are termed the pseudoautosomal regions (PAR) (see Otto *et al.*, this issue).

The homogametic sex chromosomes (X and Z) superficially resemble autosomes and are generally gene-rich [14]. By contrast, several processes cause the SDR of Y and W chromosomes to degenerate rapidly (Box 2). Indeed, many ancient Y and W chromosomes carry few functional genes. For example, there are only about 20 genes (single- and multi-copy) on the primate Y chromosome [18], which is some 160 Ma old. With haploid sex determination, recombination is suppressed on both the U and V chromosomes. Consequently they experience similar degenerative forces as Y and W chromosomes, and one might expect a higher frequency of slightly deleterious mutations on both sex chromosomes. However, because both U and V chromosomes are expressed as haploids they are protected from complete genetic deterioration. A similar logic applies to sex chromosomes in plants, which are expressed in the haploid genome in gametophytes. The following sections are organized around three questions: do some sex-chromosome systems evolve more frequently than others? How do sex-limited chromosomes (W, Y, U, and V) evolve? How do homogametic sex chromosomes (Z and X) evolve? We use these to explore a diverse range of evolutionary issues including the relative importance of adaptation and degenerative processes, the implications of genomic conflict, and the consequences of sexual selection.

Box 2. Degeneration of non-recombining sex chromosomes

Non-recombining segments of the genome deteriorate as the result of mutation, selection, and genetic drift. Mutation generates both beneficial and deleterious alleles. Recombination increases the efficacy of natural selection acting on this genetic variation by allowing it to act on the mutations independently. Consequently, the suppression of recombination in the SDR of sex-limited chromosomes (W, Y, U, and V) causes them to degenerate. Studies of this process allow us to understand better the evolutionary consequences of recombination throughout the genome.

Degeneration of the non-recombining SDR can be understood in terms of the 'Hill–Robertson effect', which tells us that directional selection at one locus interferes with the action of selection at a linked locus. The results are decreased rates of adaptive evolution and increased rates of fixation of deleterious mutations. Those effects are particularly acute in the SDR because all the loci that it carries are completely linked (that is, there is no recombination).

Three forms of the Hill–Robertson effect are thought to be involved in the degeneration of the SDR. (i) As the result of Muller's ratchet, a deleterious mutation segregating at one locus in the SDR makes it more likely that deleterious mutations elsewhere in the SDR will become fixed. This is because segregating deleterious mutations decrease the effective population size of the SDR and so increase the power of genetic drift relative to selection. This process is particularly effective with the elimination of strongly deleterious mutations, leading to the accumulation of slightly deleterious mutations. (ii) Genetic hitchhiking can fix a deleterious mutation on the SDR when a beneficial mutation with a larger effect at another locus spreads by positive selection. Here, adaptation at some loci will result in degeneration of others. (iii) By contrast, the ruby in the rubbish mechanism considers how beneficial mutations on the SDR can be prevented from spreading. When a beneficial mutation appears on an SDR that already carries deleterious alleles with stronger effects, the beneficial mutation will be eliminated by selection, reducing the rate of adaptive evolution in the SDR.

Are some sex-chromosomes systems more common than others?
Although XY systems are most familiar, the available data do not allow us to determine yet whether they are in fact more common than ZW systems in nature. The prevalence of different types of sex chromosomes depends on the rates of origin, the rates of transitions between the systems, and the rates of phyletic diversification. We now look at each of these factors.

Origins of sex chromosomes
New sex chromosomes can originate in a hermaphroditic lineage during a transition to dioecy (separate sexes). This transition is facilitated by factors that are predicted to make XY systems arise more frequently than ZW systems [19]. The evolutionary sequence that is most favorable occurs when a recessive male-sterility mutation first spreads, generating a population with both females and hermaphrodites (gynodioecy). Second, a dominant female-sterility mutation spreads in the hermaphrodites, creating males and so completing the transition to separate sexes. This evolutionary pathway is facilitated when the two sterility loci are tightly linked, forming a neo-Y chromosome. Although relatively few independent origins of sex chromosomes have been studied, empirical data from plants thus far support these predictions. In angiosperms, where sex chromosomes have originated in hermaphrodites multiple times, XY systems are predominant [20]. In animals, counter-examples can be found in crustaceans, which have androdioecy (a mixture of hermaphrodites and males) [21] and both XY and ZW systems [14]. The evolution of the UV sex-chromosome system presumably proceeds through the same stages as in diploids.

Alternatively, sex chromosomes can originate in a dioecious lineage with environmental sex determination (ESD) [14,22,23]. The evolution of sex chromosomes occurs with the spread a dominant masculinizing mutation, which leads to an XY system, or of a dominant feminizing mutation, which leads to a ZW system. These events can be driven by environmentally-dependent fitness advantages to one sex over the other and by selection on the sex ratio [14,22]. Some taxa are prone to female-biased sex ratios (because of ESD and endosymbionts like *Wolbachia*) which favor male-determining mutations and hence XY systems.

A new sex-chromosome system can also arise in a dioecious lineage with polygenic sex determination when a major sex-determining factor sweeps to fixation (selective sweep) because that gene (or one linked to it) is beneficial to the heterogametic sex [24]. Sexual selection is generally stronger in males, and this could favor the origin of XY over ZW sex determination.

In summary, several lines of theory suggest that XY systems are easier to evolve *de novo* than ZW systems. A major goal for future research will be to test this prediction empirically.

Transitions between XY and ZW systems
New sex chromosomes can arise when a new sex-determining locus hijacks a preexisting sex-chromosome system. Transitions between XY and ZW have been documented in diverse groups including anurans [25], fishes [26], and

insects [27]. These transitions are possible if the ancestral Y or W chromosome has not greatly degenerated, and four hypotheses have been proposed to drive them [14,28]. Small population size could cause a new sex chromosome to drift to fixation. Second, if a new sex-determining gene increases the fitness of the carrier, this pleiotropic effect can drive it to fixation. Third, in populations with sex-biased sex ratios, selection will favor an alternative sex-chromosome mechanism if it overproduces the minority sex. Fourth, a sex-change mutation that appears on an autosome near a locus under sexually antagonistic selection can create a neo-sex chromosome and cause it to replace the ancestral sex chromosomes. There have been no quantitative tests of any of these hypotheses.

A phylogenetic analysis in anurans suggests that shifts from ZW to XY are more frequent than the reverse [25]. Why should there be such a bias? First, there could be differences in the frequencies of masculinizing and feminizing mutations. For example, loss-of-function mutations that cause development to a default sex might be more frequent than gain-of-function mutations, leading to differences in the rates of origin of new sex-determining systems (i.e. if males are the default sex, XY systems would be created more easily). A possible example of this effect is found in a marine isopod [29]. Second, new ZW and XY systems could differ in how easily they can be established once they appear by mutation. Three species are known in which X, Y, and W chromosomes coexist in the same population [14]. In all three, the W is dominant to the Y, and the Y dominant to the X. Theory shows that dominant sex-determination systems can spread more easily than recessive ones, and this favors transitions from XY to ZW (counter to observations in frogs) [28]. The relative contributions of these two factors to biasing transitions between XY and ZW systems remains an open question.

Speciation and extinction

The prevalence of sex-chromosome systems is also affected by rates of diversification. In contrast to animals, all known sex chromosomes in angiosperms are young (<10 Ma) [20]. Dioecious angiosperms (all of which have sex chromosomes) have lower diversification rates than hermaphroditic lineages [30]. That might suggest sex chromosomes decrease diversification rates, but the cause might be dioecy itself. In dioecious bryophytes, both old [31] and young [32] UV sex chromosomes are present, but the relationship between sex chromosomes and diversification rates remains to be established. There are clearly abundant opportunities for phylogenetic analyses to establish the frequencies of different sex-chromosome systems and to untangle how their phylogenetic distribution is determined by rates of origin, transition, and diversification.

How do sex-limited chromosomes (U, V, W and Y) evolve?

U, V, W and Y chromosomes experience different mutation rates, recombination rates, effective population sizes, migration rates, and sexual selection. Those differences impact upon how suppression of recombination evolves, the degeneration of the SDR, and the outcome of sexually antagonistic selection.

Reduced recombination and degeneration

Recombination can accelerate adaptive evolution and ameliorate maladaptive evolutionary forces. We have seen that sex-chromosome evolution generates a non-recombining region, the SDR. A classic pattern seen in many taxa is that suppression of recombination causes this region to degenerate (Box 2). The boundary between the non-recombining SDR and the recombining PAR is evolutionarily dynamic. Changes in the boundary cause parts of sex chromosome to experience newly suppressed recombination (when the SDR expands) or to experience recombination once again (when it contracts).

Theory suggests that the non-recombining SDR of Y and V chromosomes could expand more rapidly than those on W and U chromosomes [14,33]. Sexual selection is typically stronger in males than females. This could result in more frequent sex-antagonistic selection with alleles beneficial to males and detrimental to females, which favors expansion of the SDR on Y and V chromosomes. The UV system provides a fascinating contrast. The male-limited V and female-limited U chromosomes are always paired in diploids, and evolution of a sexually antagonistic allele in either sex thus selects for suppressed recombination. That situation could favor more rapid expansion of the SDR in UV systems than in diploid systems where suppressed recombination is driven by sexually antagonistic alleles that favor only the heterogametic sex. To date there have been no empirical tests of these predictions. The best opportunities would be in comparisons from systems with large PARs. The orthologous and largely undifferentiated Z and W sex chromosomes of ratite birds and boid snakes are two promising possibilities [34,35]. The general question of why the SDR is still small and the PAR large in some ancient sex chromosomes remains an unsolved mystery (see Otto *et al.*, this issue).

Theory also predicts that the non-recombining SDR of Y chromosomes should degenerate more rapidly than their W chromosome counterparts. Males typically have higher mutation rates [6,36] and lower effective population sizes (Figure 2) than females. Consequently, a Y chromosome (which is always carried in a male) is expected to accumulate deleterious mutations more quickly, both by drift and by hitchhiking with advantageous mutations, and to accumulate advantageous mutations more slowly [37]. Rapid degeneration of recently formed Y chromosomes has been demonstrated in *Drosophila* [38] and sticklebacks [39]. However, there are few empirical data for young W chromosomes, and comparing rates of degeneration of recently evolved W and Y chromosomes will be of great interest. In plants, both sex chromosomes are expressed during the haploid pollen phase of the life cycle, and this might constrain their degeneration compared to animals – in which all chromosomes are inactive in mature sperm. In UV systems, both chromosomes are expressed in the haploid phase, and this also constrains the degree to which they can degenerate. Nevertheless, male bryophytes (which produce many small, dispersing gametes) could have a greater variance in reproductive success than females (which produce few large, retained gametes). The processes describe above could therefore cause the evolution of differences between the female-limited U and the male-limited V.
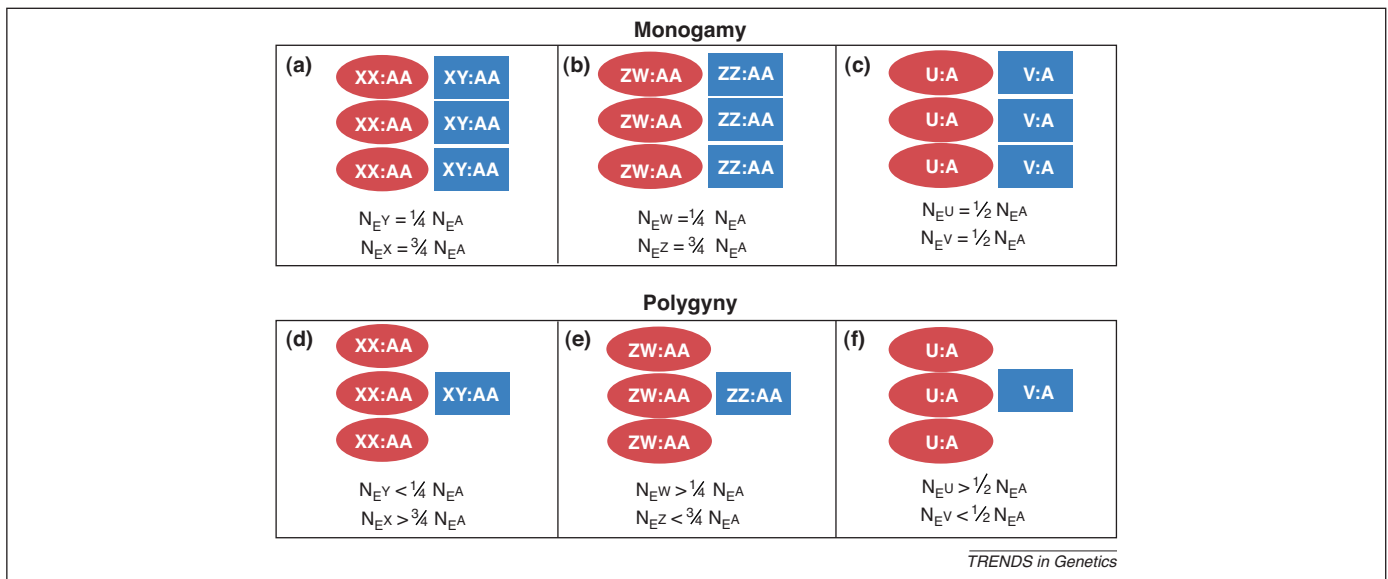
Figure 2. Mating system and sexual selection influence the effective population sizes (N_E) of different sex chromosomes in different ways. Female individuals are shown as red ovals, males as blue rectangles. In monogamous systems, the effective population size of the Y **(a)** and W **(b)** chromosomes (N_{EY} and N_{EW}, respectively) are both 1/4 that of the autosomes, and N_{EX} and N_{EZ} are both 3/4 that of the autosomes. N_{EY} and N_{EZ} decrease when sexual selection affects males, whereas N_{EX} and N_{EW} increase **(d,e)**. In UV systems, N_{EU} and N_{EV} are equal under monogamy **(a)** but unequal with sexual selection **(f)**.

Genomic conflict in the form of meiotic drive can also contribute to degeneration of the SDR of sex chromosomes (Box 3). The reduced recombination makes Y and W chromosomes hotspots for meiotic drive, and this causes biased sex ratios. Selection to restore a balanced sex ratio can then favor silencing of genes on the Y and W chromosomes and hence their degeneration [40]. Meiotic drive is often associated with lower fertility in males but not in females. Selection against drive will therefore be stronger in XY males than ZW females, and this then leads Y chromosomes to decay faster than W chromosomes. Biased sex ratios are also found in mosses with the UV system, consistent with sex-chromosome drive in these species [32]. As in the XY system, UV sex-ratio distortion reduces fertility [41].

The asymmetric transmission of sex chromosomes can also contribute to their degeneration via sexually-antagonistic zygotic drive (SAZD) [10]. Here the heterogametic sex chromosome is selected to harm sibs and offspring of the sex that does not carry that chromosome, thereby gaining more resources (Box 3). Because of differences between the sexes in parental care and in the transmission of epigenetic effects, SAZD should evolve more easily in ZW compared to XY species. For example, maternal care and products packaged in eggs (such as steroid hormones or RNAs) offer W chromosomes mechanisms to enhance their own transmission by harming sons. This generates stronger selection to inactivate the female-limited W chromosomes, and will cause a W to decay faster than a Y. Genetic conflict in the UV sex-determining system over the allocation of resources to the diploid is also likely to be frequent, because only the female parent (U) is attached to and provides for the heterogametic (UV) diploid offspring. Thus, alleles promoting the growth of large diploids should be favored on the V chromosome, whereas alleles moderating the transfer of nutrients from the female haploid to the dependent diploid offspring should be favored on the U. Again, all of these predictions await empirical testing.

The evolution of gene content

A male-beneficial (or female-beneficial) allele appearing near the SDR of the Y (or W) chromosome is nearly or completely free of potential sexually antagonistic selection, and therefore can become established more easily than on

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Box 3. Genomic conflict and sex chromosomes

Genetic conflict arises when the fitness of one component of the genome is increased at the expense of another, non-homologous component. Conflict can occur between genomes (e.g. maternal–fetal conflict during pregnancy) and within genomes (e.g. cyto–nuclear conflict as a result of differing lines of descent).

Genetic conflicts can act on sex chromosomes at multiple levels. Hamilton [40] suggested that the inactivation of the Y (or W) chromosome might reflect the recurrent emergence of meiotic-drive genes on these chromosomes. All meiotic-drive elements that have been examined in detail entail linkage between a driving allele and an insensitive allele at the responder locus; linkage between these alleles prevents the formation of a 'suicide combination' that can drive against itself and would therefore be quickly eliminated from the population. A lack of recombination implies that sex chromosomes are particularly prone to evolve meiotic-drive elements because any gene on the X/Z (or Y/W) can drive against any responder site on the Y/W (or X/Z). Driving X/W or Z/Y chromosomes cause female- or male-biased sex ratios, triggering an evolutionary response in the genome to suppress X/W or Z/Y chromosome drive. Selection to silence drivers on the permanently heterozygous Y or W chromosome could have directly contributed to their degeneration. One mechanism by which many potential drivers on the X or Z could be inactivated is through transcriptional silencing of most genes on the X or Z chromosome during the heterogametic meiosis (MSCI).

The logic of sex-chromosome meiotic drive can be extended into the next generation because sons and daughters of the heterogametic parent carry different sex chromosomes [10]. Just as sperm competition selects the X and Y (Z and W) to disrupt the production of the gamete type that does not carry them, competition between siblings selects the X and Y (Z and W) to harm the sex of offspring that does not carry them. This sexually antagonistic 'zygotic drive' is predicted to take place via phenotypes that harm the non-carrier sex of offspring via trans-generational epigenetic effects, asymmetric parent–offspring interactions, and/or increased aggression/less altruism between opposite-sex offspring.

an autosome. It is thus expected that sex-limited chromosomes will be enriched in genes beneficial to the sex where they are found. Males are typically subject to sexual selection pressures that are stronger and more rapidly shifting, and Y chromosomes are therefore likely to carry a higher number of male-beneficial alleles than W chromosomes. In fact, groups such as poeciliid fishes do have genes for size and color that increase male mating success and which are located on the Y chromosome [42]. Accumulation of sex-beneficial mutations is expected to be even more extreme in UV systems where haploid selection maintains the gene content of both sex chromosomes. However, as discussed earlier, sexually antagonistic selection can trigger the invasion of a new sex chromosome, such that sexually antagonistic genes can reside on a chromosome from its very origin. An interesting problem for future empirical study therefore is – which came first, the sex chromosomes or the sexually antagonistic genes that they carry?

How do homogametic sex chromosomes (X and Z) evolve?
Homogametic sex chromosomes have a unique pattern of transmission and ploidy. As a result they have unusual properties with consequences for genetic variation and evolutionary rates, gene content, sexual selection, and patterns of gene expression.

Consequences of selection and drift
X and Z chromosomes have several features that alter how selection acts on the genes they carry. First, they spend different fractions of their evolutionary lives in each sex (Figure 1). This favors the maintenance of polymorphisms with sexually antagonistic effects compared to autosomes [43]. Second, homogametic sex chromosomes are hemizygous 1/3 of the time. Deleterious recessive alleles therefore experience stronger purifying selection, and recessive advantageous mutations are more likely to avoid loss when rare. These effects can affect the evolution of X- and Z-linked loci relative to autosomes [44].

Genes on homogametic sex chromosomes have 3/4 as many copies as their autosomal counterparts in a population (Figure 2). The ratio of the effective population sizes of sex chromosomes to autosomes is also affected by sexual selection: when there is greater fitness variation in males the ratio is decreased below 3/4 for Z chromosomes and is increased above 3/4 for X chromosomes. Because a smaller effective population size decreases the strength of selection relative to drift, those changes in turn will affect the corresponding ratios of neutral polymorphism and rates of neutral or weakly selected substitutions [2,3,45]. These facts can be used to estimate the relative variances in male and female lifetime fitness from molecular data [46].

Accelerated evolutionary rates of X- and Z-linked genes – referred to as the faster-X effect and the faster-Z effect – have been observed in birds, mammals and *Drosophila*. These result from different processes and the different way that sexual selection in males affects the effective population sizes of the X and Z chromosomes (Figure 2). Faster-X in *Drosophila* is modest [47] and largely due to the effects of selection on hemizygous males rather than differences in X and autosome effective population sizes [48]. Mammals

show a strong faster-X effect [49], whereas birds show clear signs of accelerated Z evolution [34], which results largely from increased genetic drift rather than adaptive mutations [49]. Thus, empirical patterns are complicated and influence by multiple factors, and no simple generalizations for the prevalence of faster-X and faster-Z have yet been established.

Sex differences in selection can also affect the types of genes carried on the X and Z, causing them to be 'masculinized' or 'feminized'. The X chromosome is present 2/3 of the time in females, and is always hemizygous in males; therefore dominant mutations favoring females and recessive mutations favoring males are initially more likely to spread when X-linked than when autosomal [1], and the reverse pattern is expected for Z chromosomes. These processes are expected to both feminize and de-masculinize the genetic content of the X. Conversely, the Z should become both masculinized and de-feminized. Sex differences in gene expression patterns in flies, mammals, and birds are consistent with these predictions [50–53], but those differences can also be explained by other hypotheses, as we will now discuss.

Gene expression
Homogametic sex chromosomes show several fascinating patterns related to gene expression. First, genes with sex-biased gene expression are non-randomly distributed on X and Z chromosomes and autosomes. Genes that are upregulated in the testis tend to be under-represented on the *Drosophila* X, and genes on the X in *Drosophila* and mammals are more likely than genes on autosomes to produce duplicates or retrogenes that have testis-specific expression [54–56]. Similarly, genes expressed during oogenesis in birds are less common on the Z chromosome [57], although this is largely confounded by incomplete dosage compensation which causes male-biased expression as a result of higher copy-number [58,59]. Meiotic sex-chromosome inactivation (the transcriptional inactivation of sex chromosomes during the heterogametic meiosis; see below) can also influence the distribution of sex-biased genes [59–61] by favoring the translocation of genes important in gametogenesis from the sex chromosomes to the autosomes.

Second, genes on X or Z chromosomes are hemizygous in the heterogametic sex. Dosage-compensation mechanisms have evolved to balance the X:A ratios of gene products in males (or Z:A in females) because differences in the copy-numbers of X- and Z-linked genes between the sexes can upset genetic networks that include both sex-linked and autosomal genes. Dosage-compensation mechanisms are documented in varied taxa with XY sex determination including *Drosophila*, *Anopheles gambiae*, *Caenorhabditis elegans*, and therian mammals [62–64], although recent evidence suggests that true dosage-compensation is limited to *Drosophila* and possibly *Anopheles* [65]. By contrast, several taxa with ZW sex determination, including birds, lepidopterans, and *Schistosoma mansoni*, have largely incomplete Z chromosome dosage-compensation [51,58,66]. This suggests that dosage compensation could be more prevalent in XY versus ZW systems [67]. However, several counter-examples to this tantalizing initial pattern exist,

including sticklebacks [68], monotremes [69], and also the imperfect dosage-compensation in *Tribolium castaneum* [70]. Whether these are exceptions to a general pattern, or whether there is no consistent relation between dosage compensation and sex-determination system, remains unclear.

Finally, the X and Z chromosomes of *Drosophila*, mammals, and birds are transcriptionally repressed in the germline of the heterogametic sex during meiosis, a process known as meiotic sex-chromosome inactivation (MSCI) [59,61]. MSCI could be related to a general meiotic silencing of unpaired chromatin, and this in turn might be a defense against transposon invasion [61], but the fact that a substantial fraction of X-linked genes escape MSCI argues against this simple explanation. Another hypothesis is that accumulation of female-beneficial sexually antagonistic alleles on the X selects against transcription of this chromosome during male meiosis; likewise, there is selection to repress transcription from the Z in females if male-beneficial alleles have accumulated on the Z [71]. A third hypothesis to explain MSCI involves the silencing of meiotic-drive genes during heterogametic meiosis (Box 3). Although MSCI has not been examined in the diploid phase of any species with a UV system, the composition of UV chromosomes is likely to be shaped by transposable elements, sexual antagonism, and sex-ratio distorters. Evaluating these hypotheses in a plurality of systems offers the greatest promise for gaining deeper insights into the forces that govern sexual dimorphism and the architecture of transcription.

Concluding remarks

Contrasting the properties of XY, ZW, and UV chromosomes helps us to understand the evolution of each of these systems. Further, their differences, as well as contrasts with species that lack sex chromosomes entirely, provide opportunities to assess the relative importance of basic evolutionary forces, such as sex-specific selection pressures. Our review identifies several key areas of empirical research where tests of alternative hypotheses are needed. Much of our understanding of how ZW versus XY systems evolve is based on a few well-studied model taxa (in particular, mammals, *Drosophila*, and chicken). Recent advances in genomics now allow us to address these questions in a diversity of taxa that traditionally were out of reach for genetic or genomic analysis; this will greatly broaden our understanding of the general forces driving sex-chromosome evolution and permit asking many outstanding questions (Box 4).

Box 4. Outstanding questions

- Do their rates of origin, and rates of transitions between them, differ for the XY and ZW systems?
- Do Y chromosomes degenerate more rapidly than W chromosomes?
- Do the non-recombining regions of Y and W chromosomes expand at different rates?
- Is dosage compensation more prevalent on X than Z chromosomes?
- Are sexual conflict, sexual selection, and the evolution of sexual dimorphism weaker in the absence of sex chromosomes?

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