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The evolution of sex ratios and sex-determining systems

Tobias Uller[1], Ido Pen[2], Erik Wapstra[3], Leo W. Beukeboom[4] and Jan Komdeur[5]

[1] School of Biological Sciences, University of Wollongong, Wollongong, NSW 2522, Australia
[2] Theoretical Biology, Centre for Ecological and Evolutionary Studies, University of Groningen, PO Box 14, 9750 AA Haren, the Netherlands
[3] School of Zoology, Locked Bag 5, University of Tasmania, Hobart 7001, Tasmania, Australia
[4] Evolutionary Genetics, Centre for Ecological and Evolutionary Studies, University of Groningen, PO Box 14, 9750 AA Haren, the Netherlands
[5] Animal Ecology, Centre for Ecological and Evolutionary Studies, University of Groningen, PO Box 14, 9750 AA Haren, the Netherlands

Sex determination is a fundamental process governed by diverse mechanisms. Sex ratio selection is commonly implicated in the evolution of sex-determining systems, although formal models are rare. Here, we argue that, although sex ratio selection can induce shifts in sex determination, genomic conflicts between parents and offspring can explain why single-factor systems (e.g. XY/XX or ZW/ZZ) are common even in species that experience selection for biased sex ratios. Importantly, evolutionary shifts in sex determination do not always result in the biased production of sons and daughters *sensu* sex ratio theory. Thus, equal sex ratios might be an emergent character of sex-determining systems even when biased sex ratios are favored by selection.

Introduction

Sex determination (see Glossary) is a fundamental process in all sexual organisms. However, the mechanisms behind it are diverse, ranging from homo- or heterogametic genotypic sex determination (GSD) to environmental sex determination (ESD) [1–3]. Furthermore, the underlying molecular mechanisms of superficially similar sex-determining systems (such as male heterogamety, XY/XX) can also show large interspecific variation [4]. This evolutionary lability of sex-determining mechanisms is surprising given that fundamental developmental processes should be subject to strong selection, thereby reducing genetic variation and, consequently, limiting the potential for evolutionary shifts. Thus, the intuitive rigidity of sex-determining systems does not correspond to factual patterns observed in natural populations and warrants further explanation.

Sex determination can have consequences for the primary sex ratio and, therefore, selection for biased sex ratios might induce evolutionary shifts in sex-determining mechanisms [1]. Here, we review recent models of sex determination and argue that a better understanding of its evolution requires a more extensive use of mechanistic models that reflect the levels at which a response to selection can occur. Furthermore, we emphasize that even when sex ratio selection induces a shift in sex determination, the proportion of sons at equilibrium often does not deviate substantially from 50%, suggesting that there are fundamental constraints on the production of biased sex ratios.

Sex ratio selection and the evolution of genotypic sex determination

Early work by Darwin, Düsing and Fisher (see Refs [5,6] for an historical overview) showed that an even primary sex ratio is usually evolutionarily stable because of frequency-dependent selection against the most common sex. Consequently, selection should favor sex-determining mechanisms that ensure equal proportions of sons and

Glossary

Antagonistic pleiotropy: one gene has positive effects on overall fitness through its impact on one trait but negative effects on overall fitness through its impact on another trait.
Environmental sex determination (ESD): the process by which sex differentiation is determined by external environmental factors (e.g. temperature or pH) during offspring development.
Frequency dependence: selection in which the fitness of a genotype or phenotype is not constant but varies according to the frequency of that genotype or phenotype relative to others. Typically, when rare, the particular genotype is at an advantage compared with the other possible genotypes (or phenotypes), but, when common, is at a disadvantage.
Genotypic sex determination (GSD): the process by which sex differentiation is determined primarily by genetic factors, most commonly on the sex chromosomes.
Haplodiploidy: a sex-determinating system where sex is determined by ploidy level. Males are haploid and develop from unfertilized eggs, whereas females are diploid and develop from fertilized eggs. Females typically have control over fertilization.
Heterogamety: the sex with a pair of non-homologous sex chromosomes (e.g. male XY in mammals; female ZW in birds). The heterogametic sex produces two different types of gamete, one with one type of sex chromosome and one with the other.
Homogamety: the sex with a pair of homologous sex chromosomes (e.g. female XX in mammals; male ZZ in birds) and, therefore, producing gametes with one type of sex chromosome.
Genomic conflict: conflict that occurs when genes affecting the same trait experience different selection pressures because they follow different transmission rules or experience opposing selection at different levels, such as in parents versus offspring.
Sex determination: any of various mechanisms in which the sex of the individual animal (or plant) is determined.
Sex differentiation: differentiation of undifferentiated gonads into male and female.
Temperature-dependent sex determination (TSD): the process by which sex differentiation is determined by temperature during offspring development.

Corresponding author: Komdeur, J. (j.komdeur@rug.nl).
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daughters. This result readily explains the commonly observed single-factor genotypic sex determination system where offspring sex is determined by the presence or absence of an allele on a single gene locus and, thus, by random segregation of genes in meiosis. Heteromorphic sex chromosomes (e.g. XX/XY) can subsequently evolve via chromosome degeneration [7,8], under which one of the chromosomes loses most of its functional genomic material.

However, selection for equal sex ratios is not universal. For example, if one of the sexes is more costly to produce in terms of parental energetic expenditure, selection favors a sex ratio that is biased towards the cheaper sex [9,10]. Consequently, it would appear that a sex-determining system with equal probability of inheritance of the male or female factor will no longer be favored by selection. To address the evolutionary dynamics of sex determination under such circumstances, it is necessary to understand the levels at which a genetic response to selection can occur [11].

There are four main categories of genes that can be the focus of selection on sex determination (Figure 1): (i) sex-determining genes expressed within the offspring, affecting the probability of developing into male or female, such as the sex-determining region Y (SRY) present on the mammalian Y chromosome [12]; (ii) genes acting in the parents and biasing the distribution of genetic sex-determining factors among the offspring; for example, genes controlling sex chromosome segregation [13]; (iii) parental effects genes, that is, genes expressed in the parents but where the gene product (e.g. mRNA or yolk hormones) acts as a sex-determining factor in the offspring, [11,14]; and (iv) genes acting in the parents and biasing the distribution of external environmental sex-determining factors among the offspring; for example, via choice of oviposition sites in species with ESD [15,16]. In theory, all these gene categories could respond to selection, and the evolution of sex determination will depend, to some extent, on the level of genetic variation for each category and on potential constraints on an evolutionary response owing to, for example, antagonistic pleiotropy or genomic conflict.

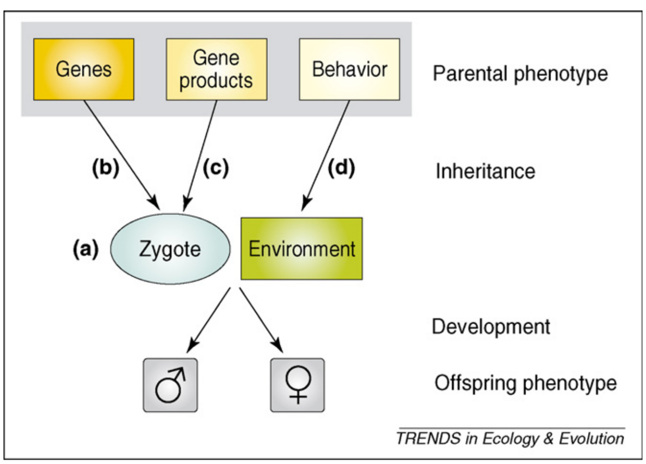

Figure 1. Interacting components of the sex-determining system. Sex determination can be viewed as the outcome of interactions among genetic factors in the offspring genome, parentally transmitted gene products and environmental conditions experienced during development. These factors, and their relative contribution to sex determination, can respond to direct or indirect selection via changes in: **(a)** genes expressed within the offspring that affect the probability of developing into a male or female; **(b)** segregation of genetic sex-determining factors (either under parental control or as intra- and extranuclear sex ratio distorters); **(c)** parentally produced sex-determining factors (e.g. transfer of mRNA); and **(d)** parental transmission of environmental sex-determining factors (e.g. via behavioral choice of oviposition site). The evolutionary response to selection depends upon the level of variation in genetic components of offspring or parental control and upon the intra- and intergenomic conflicts that arise from conflicting selection pressures within and between generations.

GSD under zygotic influence

Perhaps the simplest scenario of sex ratio selection driving the evolution of sex determination is when all sex-determining genes are expressed in the offspring and there is no environmental sensitivity or fitness difference among genotypes other than that arising from sex ratio variation. Building on early insights by Bull [1], Kozielska and co-workers [17] addressed the evolution of multi-factor sex determination by modeling a three-locus system with each locus having two alleles, similar to the system found in the housefly *Musca domestica* (Box 1). Selection for biased sex ratios was assumed to act via differential costs of producing sons and daughters. The model generated several outcomes that are important for the evolution of sex determination. First, multi-factor sex-determining systems can be stable both with and without selection for biased sex ratios. Second, even under sex ratio selection, one of the sex-determining factors can go to fixation, ultimately reducing sex determination to a two-locus system. Third, selection for biased sex ratios alone is insufficient to induce a complete shift in heterogamety, but the strength of selection influences the final genotype frequencies. Thus, sex ratio selection alone seems incapable of explaining the observed multi-factor sex determination system in houseflies.

GSD under both parental and zygotic influence

The emergence of new sex-determining factors acting in the offspring might interfere with normal sexual development (e.g. via antagonistic pleiotropy) and, therefore, might be initially selected against [4]. An alternative evolutionary response to selection for biased sex ratios would therefore be maternal control over offspring sex, for example, by female control over sex chromosome segregation [13,18]. However, as first identified by Trivers [19], parents and offspring can have different 'optima' for sex ratios, with the parental genome usually favoring a more biased sex ratio than does the offspring genome ([19] but see Ref. [20]). Thus, when expression of sex-determining genes occurs in both generations, intergenomic conflicts might affect the evolutionary outcome of sex determination (Box 2).

Building on these insights, Werren and co-workers [21,22] showed that, when the brood sex ratio affects offspring or parental fitness, conflict between genes expressed in the parent and those expressed in the offspring can result in the evolution of a dominant single sex-determining locus expressed in the offspring. If male offspring reduce the fitness of the overall brood or the fitness of its parents (the 'family' fitness), a dominant *Mm* male–*mm* female system evolves. However, if female offspring reduce family fitness, a dominant *Ff* female–*ff* male system evolves [22]. Eventually, the presence of dominant sex determination is likely to result in heteromorphic sex chromosomes, with