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Driven Apart: The Evolution of Ploidy Differences between the Sexes under Antagonistic Selection

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ABSTRACT: Sexual reproduction in eukaryotes implies a biphasic life cycle with alternating haploid and diploid phases. The nature of the biphasic life cycle varies markedly across taxa, and often either the diploid or the haploid phase is predominant. Why some taxa spend a major part of their life cycle as diploids and others as haploids remains a conundrum. Furthermore, ploidy levels may not only vary across life cycle phases but may also differ between males and females. The existence of two life cycle phases and two sexes bears a high potential for antagonistic selection, which in turn may influence the evolution of ploidy levels. We explored the evolution of ploidy levels when selection depends on both ploidy and sex. Our analyses show that antagonistic selection may drive the ploidy levels between males and females apart. In a subsequent step, we explicitly explored the evolution of arrhenotoky (i.e., haploid males and diploid females) in the context of antagonistic selection. Our model shows that selection on arrhenotoky depends on male fitness but evolves regardless of the fitness consequences to females. Overall we provide a plausible explanation for the evolution of sex differences in ploidy levels, a principle that can be extended to any system with asymmetric inheritance.

Keywords: sexually antagonistic selection, sexual conflict, ploidy levels, arrhenotoky, biphasic life cycle, sex chromosomes, haploid males, haplodiploidy.

Introduction

A necessary consequence of sexual reproduction in eukaryotes is the evolution of a biphasic life cycle with alternating haploid (gametophytic or gametic) and diploid (sporophytic) phases (Raper and Flexer 1970; Mable and Otto 1998). Nevertheless, the proportion of the life cycle spent in each phase varies dramatically among species. Higher animals and some brown algae grow mitotically only in the diploid phase (diplontic life cycles), whereas

other eukaryotes, such as many protozoa, algae, and fungi, undergo mitosis only as haploids (haplontic life cycles), and yet other taxa, particularly plants, divide mitotically in both phases (haplodiplontic life cycle; Bell 1994; Mable and Otto 1998). The evolutionary advantages of life cycles dominated by the haploid phase, the diploid phase, or balanced between both has been subject to extensive theoretical (Muller 1932; Perrot et al. 1991; Otto and Goldstein 1992; Jenkins 1993; Hughes and Otto 1999) and empirical work (e.g., Adams and Hansche 1974; Weiss et al. 1975; Gerstein et al. 2011). Understanding the evolution of ploidy levels informs many other aspects of evolution that are ploidy dependent, including the rate of adaptation (Orr and Otto 1994), the extent of inbreeding depression (Charlesworth and Charlesworth 1987), and the load of deleterious mutations (Charlesworth and Charlesworth 1992), among other features.

Previous work on the advantages of haploidy and diploidy and the evolutionary transitions between them has focused on selection that is the same in all individuals: alleles are either always advantageous or always deleterious. Yet, standing genetic variation is enriched for cases where selection acts in opposite directions in different individuals, either different sexes ("sexually antagonistic selection") or different ploidy levels ("ploidally antagonistic selection") or both, because such opposing selective forces can balance and maintain a polymorphism (Ewing 1977; Curtsinger 1980; Rice 1984; Bond(uriansky and Chenoweth 2009; Immler et al. 2012). In this article, we explore how antagonistic selection influences life cycle evolution. In particular, we identify those cases that tend to favor the predominance of haploidy or of diploidy. Interestingly, there are some cases where antagonistic selection among both sexes and ploidy levels drives the evolution of extended haploid phases in one sex and diploid phases in the other sex. We thus discuss these results in light of the evolution of arrhenotoky (i.e., haploid males and diploid females); we use the term "arrhenotoky" rather than the

less technical term "haplodiploidy," because the latter is easily misread and confused with the alternation of haploid and diploid generations, which are also sometimes referred to as haplodiploid life cycles. We briefly review previous work on related models before introducing a model of antagonistic selection, allowing for a modifier that alters the relative proportions of individuals in the haploid and diploid phase.

By having two copies of each gene, diploidy protects individuals from the deleterious effects of mutations, which are largely masked by wild type alleles (Perrot et al. 1991); additionally, diploidy increases the chance that an individual bears a beneficial mutation (Paquin and Adams 1983). On the other hand, because selection is more efficient in the haploid state, deleterious mutations are more likely to be purged and advantageous mutations more likely to fix in species with extensive haploid phases. Evolutionary transitions among ploidy levels are thus influenced by the relative importance of short-term individual-level benefits and longer-term advantages of more efficient selection, the strength of which depends on the frequency of recombination, the mating system, and population structure of the species (Otto and Goldstein 1992; Orr and Otto 1994; Otto and Marks 1996). Explaining the maintenance of both phases has, however, been more difficult, and many explanations rely on ecological advantages of ploidy diversity. For example, having extensive haploid and diploid phases might be evolutionarily favored because competition is reduced between individuals of different ploidy levels (Hughes and Otto 1999), or because the life cycle better matches seasonal fluctuations (Bessho and Iwasa 2010), or because dispersal and growth are more efficient in different phases (Bell 1997).

In addition to the alternation of haploid and diploid phases, several systems are characterized by the coexistence of haploid and diploid individuals within the same stage in the life cycle. In arrhenotokous animals, for example, diploid females result from syngamy, whereas haploid males are parthenogenetically produced by females. Arrhenotoky has evolved independently at least 17 times and is found among monogonont rotifers, mites, thrips, and hymenoptera (White 1973; Crespi 1993; Norton et al. 1993). Similarly, pseudo-arrhenotoky where the male genome is eliminated or silenced after fertilization is relatively common, particularly in mites (Helle and Bolland 1967; Helle et al. 1978; Cruickshank and Thomas 1999) and scale insects (Hughes-Schrader 1930; Nur 1980; Ross et al. 2010). Interestingly, it is generally the males that are haploid whereas haploid females are very rare in the animal kingdom (haploid females are known solely from the false spider mite *Brevipalpus phoenicis*; Weeks et al. 2001). Hypotheses about how and why arrhenotoky has evolved have been extensively reviewed (Beukeboom 1995; Normark

2003; Heimpel and de Boer 2008). The most commonly considered explanations for the evolution of haploid males include the enhanced ability of mothers to control sex ratios (Hamilton 1967), the purging of deleterious mutations through haploid males (Goldstein 1994; Richerd et al. 1994; Smith 2000), the increased reproductive assurance afforded by parthenogenetic reproduction in the absence of males (Stebbins 1950), and a transmission advantage to arrhenotoky because maternal genes are transmitted to grandchildren via sons 100% of the time (as suggested by Whiting 1945; see models by Bull 1979, 1981).

It remains, however, an open question about how ploidy levels might evolve when selection is antagonistic, acting in opposite directions in different types of individuals. It is now well established that many genes are under antagonistic selection across the two sexes leading to inter- and intralocus sexual conflict (Rice 1998; Arnqvist and Rowe 2005; Bonduriansky and Chenoweth 2009). While theoretical and empirical studies on sexually antagonistic selection are becoming more abundant (Delph et al. 2010; Innocenti and Morrow 2010; reviewed in Arnqvist and Rowe 2005), relatively little has been done to investigate the extent of antagonistic selection between ploidy levels, including the possibility of sex-by-ploidy interactions (Ewing 1977; Immler et al. 2012). Ploidally antagonistic selection may in turn drive the evolution of life cycles and alter the relative frequencies of haploids and diploids. Previous work on this question has considered special cases, focusing either on additive selection in diploids or on selection during the short haploid phase of predominantly diploid organisms. In particular, Jenkins (1993) considered additive selection in diploids, without selective differences between the sexes, in which case a polymorphism is not expected; she found that the ploidy level that maximizes fitness would evolve. Others have explored meiotic drive and sex ratio distortion as examples where alleles can be favored during the short gametic phase that are detrimental to fitness in the diploid phase (Reiss 1987; see Burt and Trivers 2006 for review). Such conflicts may explain why gene expression in male gametes is often strongly reduced in animals (Haig and Bergstrom 1995; Joseph and Kirkpatrick 2004). In addition, the effects of arrhenotoky on the dynamics of sexual conflict are still poorly understood, and it has been suggested that sexual conflict is more likely to be resolved in favor of the diploid female, compared to the case where both sexes are diploid (Kraaijeveld 2009). However, there has been no formal theoretical exploration of how ploidy levels may evolve in the face of sex-specific selection. In the following sections, we examine the evolution of ploidy when selection differs between the ploidy levels and the sexes.

The Evolution of Ploidy under Antagonistic Selection

In the first model, we determine the selective forces shaping the extent of haploid and diploid phases within a life cycle in the context of antagonistic selection, allowing for the possibility of ploidally antagonistic selection or sexually antagonistic selection or both. More specifically, we start with a general scenario where both diploids and haploids are dioecious (fig. 1A), but we can consider situations where both diploids and haploids are monoecious or diploids are monoecious and haploids are dioecious by adjusting selection in males and females accordingly. To explore the evolution of ploidy levels, we develop and analyze a model that tracks evolutionary change at both a selected locus and a modifier locus that governs ploidy levels. The model is structurally similar to that in Otto and Goldstein (1992) but allowing ploidy- and sex-dependent selection for all genotypes.

Table 1 specifies the fitness of each sex at each ploidy level, according to the genotype at the viability locus with alleles A and a. Fitness is given by $\tilde{w}_l^i = 1 - z_l^i$ in haploid adults and $w_l^i = 1 - s_l^i$ in diploid adults; these are allowed to differ between males and females (superscript $i = $ m for male and f for female, respectively), as well as among the genotypes (subscript $l = AA$, Aa, aa, A, or a). In addition, the gametes of all individuals may experience selection as haploids, with gametic fitness $v_l^i = 1 - t_l^i$. The selection coefficients may be positive or negative, with the constraint that fitness must be positive ($0 \leq 1 - t_l^i$, $0 \leq 1 - z_l^i$, and $0 \leq 1 - s_l^i$). Ploidally antagonistic selection occurs, for example, when a is favored during the gametophytic stage ($\tilde{w}_A^i < \tilde{w}_a^i$) while A is favored during the sporophytic stage ($w_{AA}^i > w_{Aa}^i > w_{aa}^i$). Sexually antagonistic selection occurs when the direction of selection is opposite in males and females. When ($\tilde{w}_A^m - \tilde{w}_a^m$) and ($\tilde{w}_A^f - \tilde{w}_a^f$) have opposite sign, there is sexually antagonistic selection in the haploid phase, whereas when ($w_{AA}^m - w_{aa}^m$) and ($w_{AA}^f - w_{aa}^f$) have opposite sign (assuming heterozygotes are intermediate), there is sexually antagonistic selection in the diploid phase (see appendix, available online, for more detail).

The model assumes a regular alternation between a haploid and a diploid phase, but the timing of meiosis with respect to syngamy varies among genotypes. A modifier locus (with alleles C_1 and C_2) determines the timing of meiosis and hence the proportion of individuals whose life cycle is dominated by the diploid phase. After syngamy (assumed to involve random union of a male and female gamete), the modifier gene affects the chance that meiosis happens early or late, generating a haploid or diploid individual. Unless selection is very strong, this model behaves qualitatively similarly to one where the modifier alters the proportion of the life cycle spent in

the diploid and haploid phases, both of which experience selection (Otto 1994), but the analysis is simplified. When there are separate male and female individuals in the diploid phase ("sporophytic dioecy"), the modifier is allowed to control the proportion of diploidy/haploidy differently in males and females. Specifically, the probability that a diploid carrying alleles j and k at the ploidy locus undergoes meiosis late (and remains diploid during selection) is d_{jk}^m and d_{jk}^f (with $0 \leq d_{jk}^i \leq 1$) for males and females, respectively (table 2). Regardless of the timing of meiosis, recombination occurs during meiosis between the viability and ploidy loci at the same rate r. We census allele frequencies at the gamete stage after selection and after all individuals have undergone meiosis (see recursions in the appendix).

Given that the system has reached a stable polymorphic equilibrium at the viability locus, we investigate whether allele C_2 can invade if it alters the proportion of diploids in the population. For tractability, we assume weak selection on males and females, such that the terms t_l^m, t_l^f, z_l^m, z_l^f, s_l^m, and s_l^f are proportional to a small term, ξ. Here we summarize the analytical results, but the full derivation can be found in the supplementary Mathematica 8.0 file, available online.

Equilibrium under Antagonistic Selection

Immler et al. (2012) investigated the conditions under which a polymorphism would be maintained with ploidally and/or sexually antagonistic selection. In this previous work, all individuals experienced selection in both the haploid and diploid phases, with an alternation of generations. Here, individuals experience adult selection either as haploids or as diploids but all experience gametic selection (fig. 1A). Nevertheless, the conditions maintaining a polymorphism are similar when haploidy and diploidy are equally prevalent, as detailed in the supplementary Mathematica 8.0 file. With weak selection in a population fixed for the C_1 allele, there are three equilibria for the frequency of allele A at the gamete stage: 0, 1, and the polymorphic equilibrium

$$\hat{p} = \frac{\Delta \mathrm{sel}^f + \Delta \mathrm{sel}^m}{d_{11}^f(w_{Aa}^f - w_{aa}^f - w_{AA}^f) + d_{11}^m(w_{Aa}^m - w_{aa}^m - w_{AA}^m)} + O(\xi),$$

(1)

where $O(\xi)$ represents smaller terms of order ξ and where $\Delta \mathrm{sel}$ is the net fitness difference between A and a in individuals of sex i,

$$\Delta \mathrm{sel}^i = (v_A^i - v_a^i) + d_{11}^i(w_{Aa}^i - w_{aa}^i) + (1 - d_{11}^i)(\tilde{w}_A^i - \tilde{w}_a^i).$$

When all individuals experience selection as diploids ($d_{11}^f = d_{11}^m = 1$), equation (1) has the same form as the
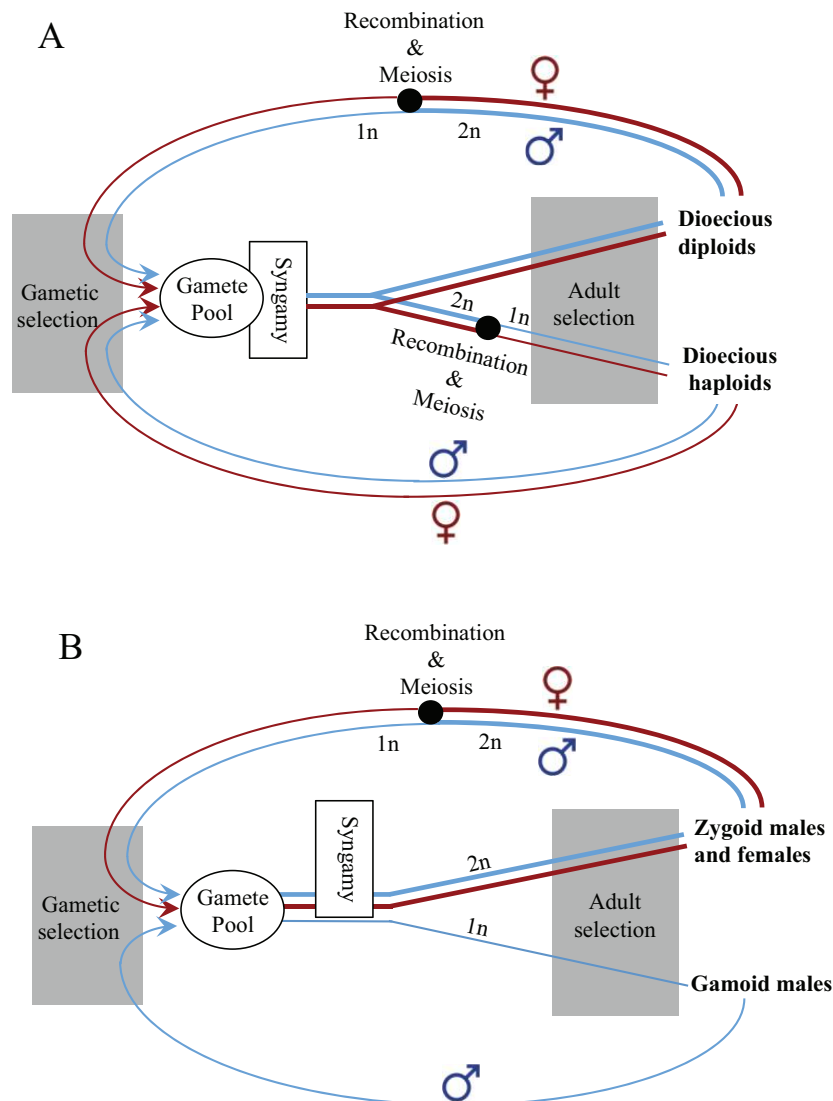
Figure 1: We model modifier genes that alter the likelihood that meiosis happens early in the life cycle (*lower half*) or late (*upper half*), thereby impacting the ploidy phase experiencing selection (gray boxes). Two types of species are considered, depending on whether they exhibit separate sexes. *A,* Both phases are dioecious, so that antagonistic selection exists between the sexes and the ploidy levels. Here the parameter d_{jk}^i determines the probability that a diploid individual of sex i will follow the upper half of the life cycle (late meiosis and recombination), whereas $(1 - d_{jk}^i)$ determines the probability of following the lower half of the life cycle (early meiosis and recombination). *B,* The diploid phase is dioecious and the haploid phase consists entirely of haploid males coming from unfertilized eggs. In this case, parameter d_j determines the probability that a male is produced from a fertilized egg and is diploid (upper half of the life cycle), and $1 - d_j$ determines the probability that a male is produced from an unfertilized egg and is haploid (lower half of the life cycle). For additional details see appendix, available online. Fitness parameters w and $\tilde{w}$ in table 1 refer to "adult selection," and v refers to "gametic selection."

classic diploid model of selection, allowing for separate sexes. Selection in gametes and in haploid adults then raises or lowers the frequency of allele A, depending on the relationships $v_A^i - v_a^i$ in gametes and $\tilde{w}_A^i - \tilde{w}_a^i$ in adult (gametophytic) haploids.

A new modifier allele, C_2, was then introduced into a population at this polymorphic equilibrium and tracked

to determine whether selection favored an expansion of the haploid $(d_{12}^i < d_{11}^i)$ or diploid $(d_{12}^i > d_{11}^i)$ phase. Specifically, we used the leading eigenvalue (λ) of the local stability matrix to determine whether C_2 would invade ($\lambda > 1$) or not ($\lambda < 1$) and how this depended on the effect of the modifier on ploidy. Writing the eigenvalue as a power series in ξ, $\lambda = \lambda_0 + \lambda_1 \xi + \lambda_2 \xi^2 + ...$, we find that

Table 1: Fitnesses of diploid and haploid viability genotypes in male and female gametes and adults

Genotype	Sex	Viability
Gametic selection:		
A	M	$v_A^m = 1 - t_A^m$
A	F	$v_A^f = 1 - t_A^f$
a	M	$v_a^m = 1 - t_a^m$
a	F	$v_a^f = 1 - t_a^f$
Adult selection:		
Diploid males and females:		
AA	M	$w_{AA}^m = 1 - s_{AA}^m$
AA	F	$w_{AA}^f = 1 - s_{AA}^f$
Aa	M	$w_{Aa}^m = 1 - s_{Aa}^m$
Aa	F	$w_{Aa}^f = 1 - s_{Aa}^f$
aa	M	$w_{aa}^m = 1 - s_{aa}^m$
aa	F	$w_{aa}^f = 1 - s_{aa}^f$
Haploid males and females:		
A	M	$\tilde{w}_A^m = 1 - z_A^m$
A	F	$\tilde{w}_A^f = 1 - z_A^f$
a	M	$\tilde{w}_a^m = 1 - z_a^m$
a	F	$\tilde{w}_a^f = 1 - z_a^f$
Gamoid males:		
A	M	$\tilde{w}_A^m = 1 - z_A$
a	M	$\tilde{w}_a^m = 1 - z_a$

$$\lambda = 1 + (d_{12}^f - d_{11}^f)\frac{\bar{w}^f - \bar{\tilde{w}}^f}{2}$$
$$+ (d_{12}^m - d_{11}^m)\frac{\bar{w}^m - \bar{\tilde{w}}^m}{2} + O(\xi^2, \mu), \quad (2)$$

where $\bar{w}^i$ is the mean fitness in sex i within the adult diploid stage

$$\bar{w}^i = \hat{p}^2 w_{AA}^i + 2\hat{p}(1-\hat{p})w_{Aa}^i + (1-\hat{p})^2 w_{aa}^i,$$

$\bar{\tilde{w}}^i$ is the mean fitness in sex i within the adult haploid stage

$$\bar{\tilde{w}}^i = \hat{p}\tilde{w}_A^i + (1-\hat{p})\tilde{w}_a^i,$$

and μ is the mutation rate between alleles A and a (assumed small relative to the selection coefficients). In other words, a modifier that increases diploidy in a particular sex, i, is favored if the mean fitness in diploids ($\bar{w}^i$) is greater than the mean fitness in haploids ($\bar{\tilde{w}}^i$) in that sex. Thus, ploidy in males and females should evolve such that the ploidy/sex combination with the lowest antagonistic load (highest fitness) becomes more prevalent. It is important to note that the modifier allele can evolve even if a polymorphism is absent (indicated by light regions in fig. 2). In other words, the average difference in fitness between haploids and diploids drives the modifier to be selected, even when A (or a) is fixed. A similar result was obtained by Jenkins (1993), who focused on the proportion of time spent in the haploid versus diploid phases,

assuming additive and sex-independent selection. While such selection does not allow a polymorphism to be maintained, Jenkins also found that ploidy levels would evolve toward the ploidy of highest fitness, given the genetic background. Furthermore, mutations have negligible impact on whether or not C_2 could invade because the leading order terms in equation (2) determine whether λ is greater than 1, and these do not depend on the mutation rate (as expected from the small parameter theorem of Karlin and McGregor 1972a, 1972b). Hence, ploidy should evolve in a similar fashion whether the loci are fixed or at a mutation-selection balance, unless the fitness terms in equation (2) disappear because haploids and diploids are equally fit at fixation ($\bar{w}^i = \bar{\tilde{w}}^i$). Previous models (e.g., by Otto and Goldstein 1992) assume that haploids and diploids are equally fit when fixed for the same allele (A or a), so that smaller-order terms drive the evolution of the modifier, but recent empirical data suggest that haploids and isogenic diploids bearing the same alleles can differ in fitness (Gerstein et al. 2011).

In the above, the rate of recombination r is assumed large relative to the weak selection coefficients, and as a consequence, genetic associations and recombination rates do not influence the evolutionary outcome. To explore the potential effect of genetic associations, we rederived the eigenvalues for the case of complete linkage ($r = 0$), in which case two eigenvalues describe the dynamics of the rare C_2 allele (one for the AC_2 haplotype and one for aC_2). Qualitatively, we find that whatever ploidy level is favored at high rates of recombination is also favored with tight linkage. In addition, however, modifiers reducing the extent of that ploidy level can also be favored when linkage is tight. This occurs whenever the relative fitness of the two ploidy levels differs between carriers of the A and a alleles (see Zörgö et al. 2013 for an empirical example), such that modifiers promoting haploidy can spread in association with one allele and modifiers promoting diploidy can spread with the other allele, allowing ploidy levels to evolve quixotically, depending on the nature and location of selected alleles. Detailed results are presented in the Supplementary Materials.

Figure 2 explores the outcome of ploidy evolution under different selective scenarios. Parameters were set so that differential selection between the sexes was restricted to either the diploid phase (fig. 2A, 2C) or the haploid phase (fig. 2B, 2D), with varying degrees of dominance in heterozygous diploids (*top* vs. *bottom* panels). Depending on the nature of selection, increased diploidy may be favored in both sexes (gray), increased haploidy in both sexes (green), or the sexes may be driven apart in ploidy (red: more haploid males/diploid females; blue: more diploid males/haploid females). Interestingly, diploidy can spread in both sexes (gray areas in fig. 2A, 2C) when selection

Table 2: Effect of the modifier on the proportion of diploid and haploid individuals of a given sex; the last two rows are specific to the arrhenotoky model

Genotype	Sex	Proportion diploid	Proportion haploid
C_1C_1	M	d_{11}^{m}	$1 - d_{11}^{m}$
C_1C_1	F	d_{11}^{f}	$1 - d_{11}^{f}$
C_1C_2	M	d_{12}^{m}	$1 - d_{12}^{m}$
C_1C_2	F	d_{12}^{f}	$1 - d_{12}^{f}$
C_2C_2	M	d_{22}^{m}	$1 - d_{22}^{m}$
C_2C_2	F	d_{22}^{f}	$1 - d_{22}^{f}$
Arrhenotoky model:			
C_1	F	d_{1}^{f}	$1 - d_{1}^{f}$
C_2	F	d_{2}^{f}	$1 - d_{2}^{f}$

strongly favors *aa* diploids (bottom left corner) or *AA* diploids (top right corner) because allele frequencies change accordingly (similarly, haploidy may be favored with selection for or against allele *A* in fig. 2*B*, 2*D*). Essentially, in these cases, selection in one phase is stronger than selection in the other phase, driving the allele frequencies to change in a manner that favors that phase.

As illustrated in figure 2, antagonistic selection between the sexes and the phases of a life cycle can drive the ploidy levels in males and females apart. For example, if one allele (say *a*) generally increases fitness except in the male diploid phase, then evolution can favor females that remain in the diploid phase while males undergo meiosis early (red regions in fig. 2). Conversely, the evolution of a short diploid phase can be favored in females but not males when allele *a* increases fitness except in the female diploid phase (blue regions in fig. 2). Conditions for the evolution of different ploidy levels between the sexes were broadest when selection was sex-specific during the diploid phase and when the fittest allele tended to be dominant, that is, relatively strong masking (fig. 2*A*). It is worth emphasizing that the ploidy levels of males and females can be driven apart even when allele *A* or *a* is fixed (light red and blue regions). In such cases (without a polymorphism), there technically is no selection at the A locus, let alone antagonistic selection. Nevertheless, the fitness of the fixed allele may vary across the sexes and ploidy levels, driving the evolution of the modifier toward the ploidy level of higher fitness for each sex.

Antagonistic Selection and the Evolution of Arrhenotoky

The above result suggests that ploidy levels may diverge between the sexes when selection is sex specific. Such divergence in ploidy levels is characteristic of arrhenotokous and pseudo-arrhenotokous species where males are haploid and females are diploid (fig. 1*B*). Nevertheless, such systems differ from the model developed above in that male haploids inherit the haploid genome of the egg from which they develop, rather than from meiosis of a diploid male. We thus developed an explicit model of arrhenotoky to clarify the conditions under which haploidy in males and diploidy in females may evolve. This model may also provide insight into the evolution of other asymmetric genetic systems such as for genes located on sex chromosomes (X/Y, Z/W) or under certain conditions of genetic imprinting.

We alter the previous model such that adult males can be produced from either fertilized eggs (diploid males) or unfertilized eggs (haploid males). To distinguish these males from each other (and also from haploid eggs and sperm), we follow Kondrashov (1997) and use the terms "zygoid" in reference to diploid males and "gamoid" in reference to haploid males. These terms are needed to distinguish clearly between haploid and diploid phases within the life cycle and different ploidy levels among males. In a first approach, we assume that the haploid maternal genotype (i.e., the allele carried by the egg at the modifier locus, C_j) determines the probability that the son is zygoid (d_j^{f}) versus gamoid ($1 - d_j^{f}$; table 2). Sex of the zygotes is assumed to be under maternal control (nongenetic), and we do not explicitly track genes affecting the primary sex ratio. Fitnesses for the gamoid males are set to $\tilde{w}_A^m = 1 - z_A$ and $\tilde{w}_a^m = 1 - z_a$ for *A*-and *a*-bearing males, respectively (table 1). We assume here that females receive enough sperm to fertilize each egg, but we account for the additional advantage to arrhenotoky from reproductive assurance in the supplementary Mathematica 8.0 file.

Assuming maternal gametic control of arrhenotoky and weak selection, the frequency of allele *A* at equilibrium becomes either 0, 1, or

$$\hat{p} = \frac{(2 - d_1^{f})[(w_{Aa}^{f} - w_{aa}^{f}) + (v_A^{f} - v_a^{f})] + \Delta \text{sel}^{m}}{(2 - d_1^{f})(2w_{Aa}^{f} - w_{AA}^{f} - w_{aa}^{f}) + d_1^{f}(2w_{Aa}^{m} - w_{AA}^{m} - w_{aa}^{m})},$$
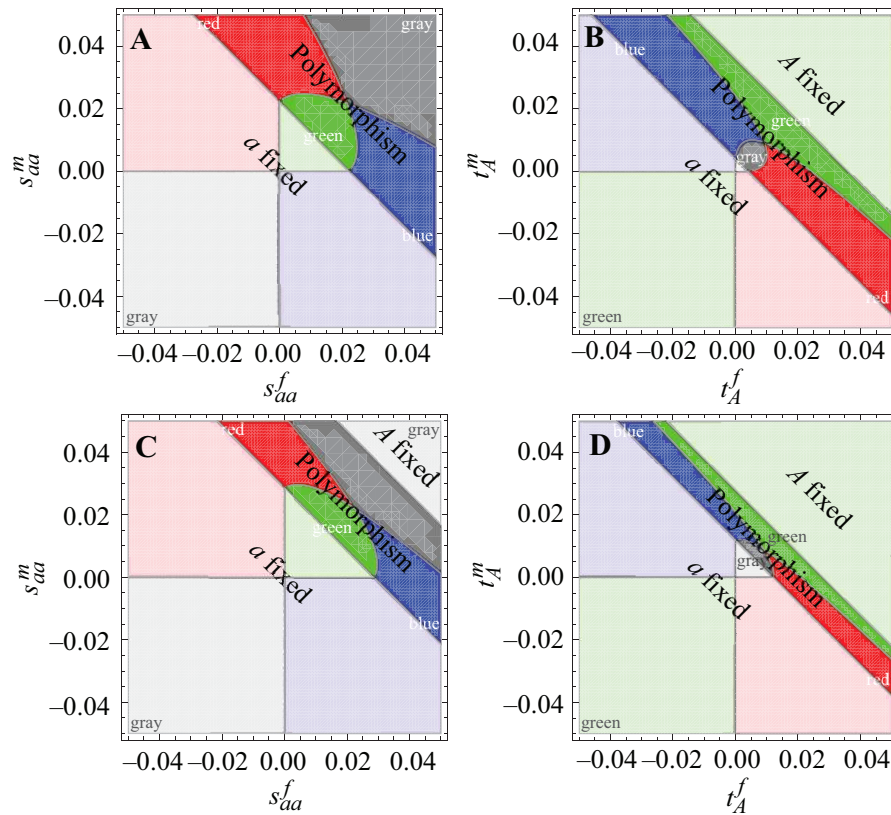
(3)

Figure 2: The evolution of ploidy levels in males and females with sex- and ploidy-dependent selection. *A, C,* Selection varies in diploid females and males along the axes (*X:* s_{aa}^f; *Y:* s_{aa}^m) with remaining parameters set to $s_{AA}^i = 0$, $z_A^i = 0.01$, $z_a^i = 0$. *B, D,* Selection varies in haploid females and males (*X:* z_A^f; *Y:* z_A^m), setting $s_{aa}^i = 0.02$ and $s_{AA}^i = 0$. Dominance in diploids, h^i (defined as $s_{Aa}^i = h^i s_{aa}^i$ in individuals of sex *i*) was set to $h^i = 0.1$ (*A, B*) or $h^i = 0.3$ (*C, D*). Dark colors indicate that a polymorphism is maintained, while light colors indicate that either allele *A* or *a* is fixed. Color indicates selection on ploidy (gray = increased diploidy favored in both sexes, red = increased diploidy favored in females only, blue = increased diploidy favored in males only, and green = increased haploidy favored in both sexes). Unless otherwise specified, the initial modifier frequency was set to $d_{11}^i = 0.5$, introducing modifier alleles that increase or decrease the extent of diploidy by 0.01. Panels are based on the weak selection approximations in equations (1) and (2) but are nearly identical to exact numerical calculations. Selection is sexually antagonistic in the top left and bottom right quadrant in all panels. Selection is ploidally antagonistic in at least one sex in all but the bottom left quadrant.

where Δsel^m is as used in equation (1), except now with d_1^f in place of d_{11}^m. We again introduce the C_2 allele and examine whether it is able to invade as a function of its effect on the proportion of gamoid versus zygoid males. Even if selection is absent, however, the leading eigenvalue does not equal 1, because of the transmission advantage favoring arrhenotoky. The modifier gains a transmission advantage and is able to spread if it increases the production of gamoid rather than zygoid sons from eggs, because gamoid sons transmit the maternal copy of the modifier allele to all of the son's gametes, rather than to only half of them (Whiting 1945; Brown 1964; Hartl and Brown 1970; Bull 1979, 1981). This transmission advantage, also known as an "automatic frequency response," leads to the invasion of gamoid males even if all individuals are equally fit.

Despite this transmission advantage, arrhenotoky need not evolve if gamoid sons are sufficiently less fit than zygoid sons across the genome (by a factor W_g). Assuming selection due to the *A* locus is weak, but fitness differences across the genome need not be (i.e., setting $s_{jk} = t_j = z_j = 0$ but allowing arbitrary values of W_g), the rate of spread of a new C_2 allele altering the degree of arrhenotoky is governed by the leading eigenvalue:

$$\lambda_{transmission} = A + \sqrt{(1 - A)^2 + \frac{(d_1^f - d_2^f)(W_g - 1/2)}{2[d_1^f + W_g(1 - d_1^f)]}},$$

(4)

where

$$A = \frac{1}{4} + \frac{d_1^f}{4[d_1^f + W_g(1 - d_1^f)]}.$$

As long as gamoid males are at least half as fit as zygoid males ($W_g > 1/2$), the C_2 allele spreads whenever it increases the extent of arrhenotoky (i.e., $\lambda_{\text{transmission}} > 1$ whenever $d_2^f < d_1^f$). Conversely, we do not expect arrhenotoky to evolve if haploidy substantially reduces the fitness of males ($W_g < 1/2$). Assuming different forms of sex determination, this result was obtained previously by Bull (1979, 1981) in modifier models tracking the rate at which females produce unreduced gametes, which always develop as males.

In the supplementary Mathematica 8.0 file, we explore the additional benefit of reproductive assurance that arrhenotoky can provide, assuming that a female mates with probability m. With probability $1 - m$, she remains unmated and produces gamoid sons only in proportion to her propensity toward arrhenotoky, $1 - d_i^f$. If she has a low propensity (d_i^f high), then most of her unfertilized eggs are wasted. In this case, arrhenotoky evolves as long as $W_g > m/2$. If mating opportunities are rare (m low), arrhenotoky can evolve despite an even stronger fitness cost to haploid males (i.e., even with $W_g < 1/2$).

The transmission advantage and the genome-wide effects of male haploidization (W_g) are thus the primary drivers of transitions to arrhenotoky. Nevertheless, we can assess the impact that fitness differences at a particular locus might have by determining the change to the leading eigenvalue that arises from selection at the A locus. Here, we assume that the effects of the modifier are weak, with $d_2^f = d_1^f + O(\xi)$, and that selection is weak (except W_g). Performing a Taylor series, we find

$$\lambda_{\text{total}} = \lambda_{\text{transmission}} + \Delta w_m \frac{(3 + d_1^f) W_g}{2[2d_1^f + 3W_g(1 - d_1^f)]^2}, \quad (5)$$

where

$$\Delta w_m = \bar{w}_2^m - \bar{w}_1^m$$

and

$$\bar{w}_j^m = (1 - d_j^f)[\hat{p}(1 - z_a) + (1 - \hat{p})(1 - z_a)]$$
$$+ d_j^f[\hat{p}^2(1 - s_{aa}^m) + 2\hat{p}(1 - \hat{p})(1 - s_{aa}^m) + (1 - \hat{p})^2(1 - s_{aa}^m)].$$

Thus, each selected locus tends to drive the system toward the adult male ploidy level that increases male fitness (fig. 3A). Selection on a particular locus only makes a difference, however, if the genome-wide difference in gamoid and zygoid males is close to the point of canceling the transmission advantage of arrhenotoky (fig. 3B).

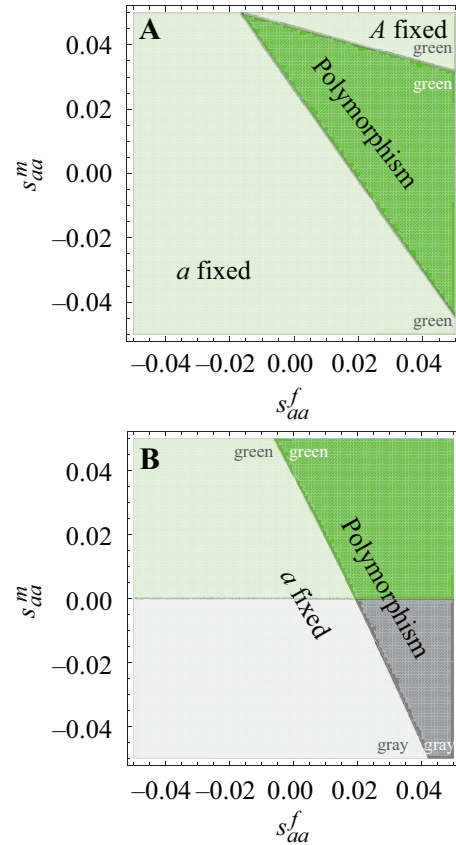We next explored diploid maternal control of male ploidy level. Specifically, the probability that a son is zygoid

Figure 3: The evolution of arrhenotoky with sex- and ploidy-dependent selection. Selection in diploid females and in diploid (zygoid) males is varied along the axes (X: s_{aa}^f; Y: s_{aa}^m). *A,* Gamoid males are favored largely because of a transmission advantage (green), but if gamoid males are much less fit (*B*), then zygoid males may be favored (gray). The genome-wide relative fitness of gamoid to zygoid males, W_g, was set to 0 in *A* and to 1/2 in *B*. The latter allows the additional effects of the *A* locus to be visualized: when s_{aa}^m is negative, zygoid males become more than twice as fit as gamoid males, preventing the evolution of arrhenotoky (bottom half of graph). Dark colors indicate that a polymorphism is maintained, while light colors indicate the fixation of *A* or *a*. Sexually antagonistic selection is present in the top left and bottom right quadrant in both panels, but only the fitness of males (*Y*-axis) impacts whether gamoid or zygoid males are favored. The selection parameters were set to zero except for s_{aa}^m (*Y*-axis), s_{aa}^f (*X*-axis), $t_A^i = 0.01$ (*A*), with $h = 0.1$ and $d_1^f = 0.5$, introducing modifier alleles that increase or decrease the extent of diploidy by 0.001.

(d_{ij}^f) or gamoid ($1 - d_{ij}^f$) is determined by the two alleles carried by a female at the modifier locus ($C_i C_j$). The equilibrium and the leading eigenvalues continue to be described by equations (3), (4) and (5), with d_{11}^f replacing d_1^f (see supplementary Mathematica 8.0 file for details). Thus, to the order of these analyses, the evolution of arrhenotoky is unaffected by whether the type of sons is determined by the genotype of the mother or the egg.

The evolution of arrhenotoky has interesting fitness consequences for females. Because female fitnesses do not enter equations (4) or (5), the mean fitness of females may rise or fall with a change in the fraction of gamoid and zygoid males, depending on the nature of sexually and ploidally antagonistic selection. Consider, for example, a case where selection acts in opposite directions upon females and male zygoids, with $\tilde{w}_{AA}^{\mathrm{f}} = 1$, $\tilde{w}_{Aa}^{\mathrm{f}} = 0.9$, $\tilde{w}_{aa}^{\mathrm{f}} = 0.8$ and $\tilde{w}_{AA}^{\mathrm{m}} = 0.8$, $\tilde{w}_{Aa}^{\mathrm{m}} = 0.9$, and $\tilde{w}_{aa}^{\mathrm{m}} = 1$ and where gamoid males have relatively high fitness with $\tilde{w}_{A}^{\mathrm{m}} = 1.5$ and $\tilde{w}_{a}^{\mathrm{m}} = 1.1$. If all males in the population were initially zygoid, an allele increasing gamoid male production would spread (both because of the transmission advantage and because gamoid males are fitter than zygoid males); this evolutionary shift toward haploid males causes the A allele to rise in frequency (because $\tilde{w}_{A}^{\mathrm{m}} > \tilde{w}_{a}^{\mathrm{m}}$), which increases the mean fitness of females in this example. Conversely, if $\tilde{w}_{A}^{\mathrm{m}} = 1.1$ and $\tilde{w}_{a}^{\mathrm{m}} = 1.5$, the evolution of gamoid males would still be favored, but now A would decline in frequency, reducing female fitness.

Another question of interest is why arrhenotoky involves male haploidy rather than female haploidy in all examples known to date. We performed an analysis similar to that above (supplementary Mathematica 8.0 file), where a fraction of eggs, d_1^{f}, now become unfertilized haploid females (gamoids), with d_1^{f} under maternal gametic control. The transmission advantage is again described by equation (4) but with

$$A = \frac{1}{4} + \frac{d_2^{\mathrm{f}} + 2W_g(1 - d_2^{\mathrm{f}})}{4[d_1^{\mathrm{f}} + W_g(1 - d_1^{\mathrm{f}})]}.$$

Thus, arrhenotoky with female gamoids gains the same transmission advantage and would be favored as long as gamoid females are at least half as fit as zygoid females ($W_g > 1/2$ or $W_g > m/2$ if we include reproductive assurance to unmated females that produce haploid daughters). In this context, one could account for the higher prevalence of male arrhenotoky than female arrhenotoky if females were more susceptible to a fitness reduction as haploids than males (i.e., W_g is lower in females than males). This is plausible if problems with gamete production via mitosis rather than meiosis directly reduce female fertility through a reduction in egg number, but male fertility depends more on access to mates than on sperm number. In addition, female arrhenotoky would be at a colonization disadvantage, because a single unmated female could not produce and then mate with sons, producing instead an asexual parthenogenetic line of haploid females. More generally, if mating opportunities are rare and unmated females produce daughters, the resulting female-biased skew in the sex ratio could reduce mating opportunities even further (lowering m), leading to an increasing advantage

to haploid female production. Eventually this process is expected to lead to a line of asexually reproducing haploid females (Bull 1979), with the attendant long-term disadvantages attributed to asexuality (Maynard Smith 1978; Otto 2009).

Discussion

Fitness differences associated with ploidally and/or sexually antagonistic selection can drive ploidy levels to evolve in such a way as to increase the frequency of the ploidy level of higher average fitness (see also Jenkins 1993). Interestingly, our general model suggests that ploidy levels in the two sexes may be driven apart whenever haploidy improves the fitness of one sex but diploidy improves the fitness of the other sex. Such a scenario could lead to the evolution of differential ploidy levels between males and females, as observed in arrhenotokous species. It has been suggested that diploidy in females and haploidy in males is one way to resolve intralocus sexual conflict in favor of the females (Kraaijeveld 2009). We explored this possibility by explicitly modeling the evolution of arrhenotoky (i.e., haploid males and diploid females) under ploidally antagonistic selection. We found, however, that the effects on female fitness have negligible influence on how the ploidy of males evolves. Instead, whether arrhenotoky evolves is determined primarily by the inherent transmission advantage for females producing gamoid sons and secondarily by the relative fitness of gamoid (haploid) and zygoid (diploid) males. The fitness of females is irrelevant to the order of these effects (see examples in fig. 3). Below we discuss the implications of our findings both for the evolution of ploidy in general and for arrhenotoky in particular.

The Evolution of Ploidy

Our finding that selective differences across ploidy levels and/or sexes facilitates the invasion of the ploidy level associated with the higher fitness may help explain some fundamental patterns in the taxonomic distribution of haploidy and diploidy. Sexually reproducing eukaryotes generally exhibit a biphasic life cycle but the relative duration of each phase varies enormously. It is striking that the proportion of haploids versus diploids exhibits marked differences between major taxonomic groups, and such a pattern is difficult to explain either purely in terms of transmission genetics or the immediate benefits of alternating ploidy levels per se (Kondrashov 1997). With antagonistic selection, suppressing the expression of genes is a possible means of resolving intralocus conflict (Rice 1984). In the context of ploidally antagonistic selection, suppression can be achieved either by evolving ploidy-

limited expression or by reducing the extent of the ploidy level of lowest fitness, which may help explain the dominance of one ploidy level over the other in many taxa.

When fitness differs between haploids and diploids, selection drives ploidy evolution to increase the phase of highest fitness. Interestingly, with ploidally antagonistic selection, this creates an evolutionary ratchet. As evolution favors the expansion of the currently most fit ploidy level, allele frequencies shift toward the alleles that are most fit in the expanding ploidy phase (equation [1]), which will cause that ploidy phase to become even fitter relative to the other ploidy phase, driving further expansion of this phase. Thus, ploidally antagonistic selection can destabilize haplodiplontic life cycles, ultimately favoring either haplonty or diplonty.

The Evolution of Haploid Males and Diploid Females

The phenomenon of different ploidy levels between the sexes is relatively widespread and can be found in organisms with arrhenotokous and pseudo-arrhenotokous sex determination (haploid males and diploid females), but the principle can be extended to any system with asymmetric inheritance (e.g., sex chromosomes, certain conditions of genetic imprinting; Rice 1984; Hedrick and Parker 1997; Normark 2006). As found in earlier models, arrhenotoky can spread independently of the relative fitness of the haploid and diploid males simply because of a transmission advantage favoring females producing haploid sons (Brown 1964; Hartl and Brown 1970; Bull 1979, 1981). The lack of transmission of genes from fathers to sons generates counter-selection in fathers, however, to override maternal or egg control over the production of haploid males and ensure that the male transmits his genes to sons, if possible (Bull 1979).

The model developed here clarifies that the main factors influencing the evolution of arrhenotoky, besides its transmission advantage, are the relative fitness of haploid versus diploid males (W_g) and the reproductive assurance that unmated females gain (assumed here to be proportional to the propensity towards arrhenotoky). If mating opportunities are limited (m), arrhenotoky evolves as long as haploid males if they are sufficiently fit $W_g > m/2$. We further show that male ploidy evolves irrespective of the costs or benefits to females, and we provide examples where the evolution of arrhenotoky leads either to an increase or a decrease in female fitness. This fact undermines the idea that arrhenotoky may have evolved as a possible resolution of sexual conflict.

Conclusions

We find that ploidally antagonistic selection may drive a ratcheting evolutionary process. First, the ploidy level of highest fitness expands, shifting allele frequencies in its favor. This shift in allele frequency subsequently favors further expansion of that ploidy level. Our model also suggests, however, that ploidy evolution may not proceed equally in the two sexes. With both ploidally and sexually antagonistic selection, the ploidy levels may be driven apart between the two sexes. When explicitly investigating the evolution of arrhenotoky under antagonistic selection, we find that the ploidy level in males evolves in a manner that is insensitive to the fitness consequences to females. Our findings therefore imply that the evolution of arrhenotoky does not necessarily represent a resolution of sexual conflict in favor of females but depends more directly on the relative fitness of haploid versus diploid males.

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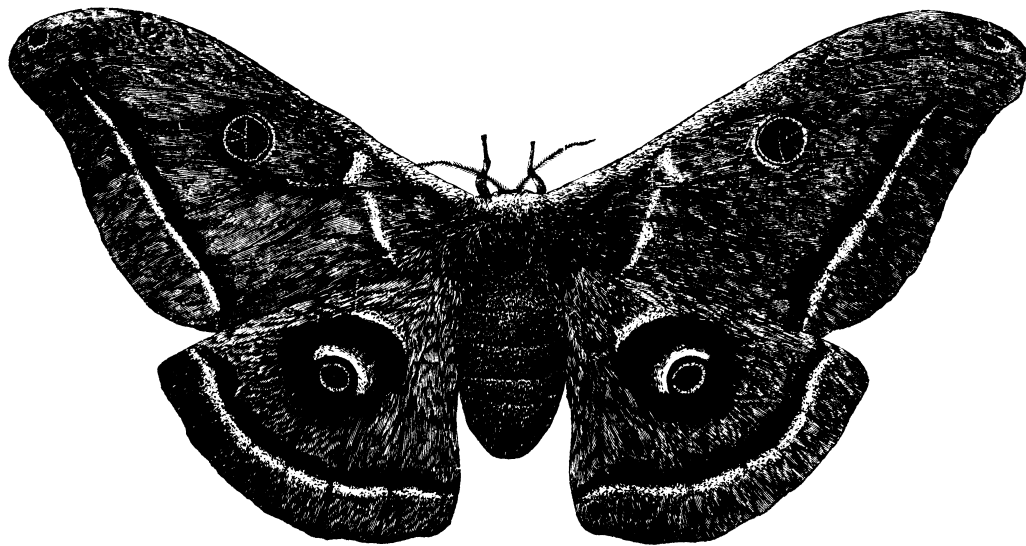
"Cocoons can be retarded in hatching out by being put in a very cold room—an ice-house, for instance; in this way they can be made to hatch another year, or nearly twenty-one months after they have been in the cocoon. In fact, the time of their appearance can be put back for an indefinite period, as life is nearly suspended. Reaumur states, that, at the time he was writing, he had in his cellar pupæ which had been there for five years, which were still living. I have myself kept pupæ of sphingidæ, or hawkmoths, for three years in my cellar. At the time I went to Europe, they were still living, but on my return I found that the rats had eaten them." From "The American Silk Worm (Concluded)" by L. Trouvelot (*American Naturalist*, 1867, 1:145–149).