Sperm modifiers of female drive.

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Abstract:

Introduction

Despite the apparent unity of the organism, occasionally alleles can gain an evolutionary advantage at a cost to individual fitness [**?**], often by exploiting meiosis and gametogensis. Female meiosis, an asymmetric event in which only one of two alternate alleles enters the egg, with the others consigned to the polar body, is one such occasion [**?** **?**]. An allele that biases female meiosis in its favor (i.e. a meiotic driver), may increase in frequency even if this driver entails a pleiotropic fitness cost [**?**], generating a genetic conflict between the success of the driver and organismal fitness. Meiotic drivers observed in nature (in both plants [**?** **?** **?**], and animals [**?** **?** **?**]) highlight this conflict – the selfish benefits of drive and the associated pleiotropic fitness costs sustain a balanced polymorphism [**?**], and often generate on ongoing evolutionary escalation of drive suppressors and enhancers [**?** **?**]. The threat of meiotic drive to organismal fitness is potentially so severe that it has been hypothesized that many basic properties of meiosis and oögenesis, including the initial genome doubling in meiosis I [**?**], the commonness of arrested female meiosis [**?**], and sex differences in the recombination rate [**?** **?**] have evolved to disrupt meiotic drive and enforce fairness.

It is therefore somewhat surprising that despite the intense evolutionary pressure on female meiosis to prevent meiotic drive, it is potentially open to sabotage by a virtual stranger – a haploid sperm genome. That is, in many animal species, the completion of female meiosis requires fertilization of the egg, and there is ample opportunity for interaction between the sperm and female meiotic machinery. If, for example, an allele in sperm could facilitate meiotic drive by a genetically equivalent allele in a heteromorphic dyad, such an allele could presumably bias meiosis in its favor and rapidly spread through the population. At first sight, it seems as although female meiosis is primed to be exploited by selfish sperm systems.

Why then is the requirement of fertilization to complete female meiosis so ubiquitous? It is certainly not the case that animals are mechanistically incapable of evolving past this requirement. There is considerable variation in which stage of meiosis requires fertilization,

and a number of animal clades (should we try and lower bound how many transitions?) have evolved to allow the completion of female meiosis upon ovulation.

It is also not the case that sperm is mechanistically incapable of influencing the outcome of female meiosis. Mechanistic evidence for this possibility comes from *C. elegans*, where experimentally suppressing XXX leads to premature deployment of the aster (a vital component of mitotic machinery) provided by the sperm, disrupting MII meiotic segregation in the egg, leading to a triploid zygote. Additionally, genetic evidence suggests that the transmission patterns in heterozygous females can depend on sperm haplotype. Specifically, the two best characterized female meiotic drive systems in mouse (In and Om), both operate by distorting the second meiotic division, and in both systems the outcome of female meiosis depends the genotype of the fertilizing sperm [**?** **?**].

In this article we explore through simple population genetic models the consequences of alleles that influence the outcome of female meiosis. We use these models to argue that it is actually surprisingly hard for the influence of sperm on the outcome of meiosis to drive sustained conflict. In fact we find that sperm and egg genomes' interests are often aligned as they are both invested in the fate of the zygote they will form (as was suggested for the In locus [**?**]). This suggests that females are unlikely to evolve to prevent the influence of sperm on meiosis, and indeed features of meiosis may evolve that facilitate the interaction of sperm with female meiosis.

Results

YB: I think we should do our best to be very short and sweet here. There are many opportunities to move off to cool math and cool biological scenarios. We should fight all of them and focus on mission critical results. All others can go in supp or appease reviewers. Lets talk about why the critical results are. To me its (1) male enhancement of female drive cannot maintain a stable polymorphisms, and (2) An allele in sperm can evolve to suppress

its drive in females.

Rough order of rest of text

Lay out Model

We imagine that drive acts in such a way that an allele promote itself into a fraction of d eggs ($d > 1/2$, when it is present in a heterozygote, forcing the other allele to be present in $1 - d$ eggs. In mammals, fertilization takes place at MII, so we imagine this drive must be taking place at MII in order for a sperm to have any influence. For drive to take place at MII there has to be an uneven number of crossovers between the centromere and the drive locus, such that realistically d is bounded to be $< XX$. In other systems where fertilization occurs during MI, sperm could influence either drive at MI or MII, and drivers at MI can have a $d = 1$ if they occur in tight linkage with the centromere.

Cartoon figure of sperms meeting eggs with different genotypes?

Cost of alleles

We'll setup a model where the sperm allele affects outcome of female meiosis. This may not be biologically realistic as there is very little sperm expression. More realistically the male genotype that produced the sperm may be more relevant, as males could place products in their sperm that influenced the outcome of female meoisis. However, in practice models that allow the influence of fertilizing male genotype on female meiosis seem to behave very similiarly to those based on the allele of the fertilizing sperm. For simplicity we'll focus on models based on the allele of the sperm, as it's bloodly complicated enough already.

A) Invasion by single self promoting allele

show that such alleles:

1. can't be balanced,

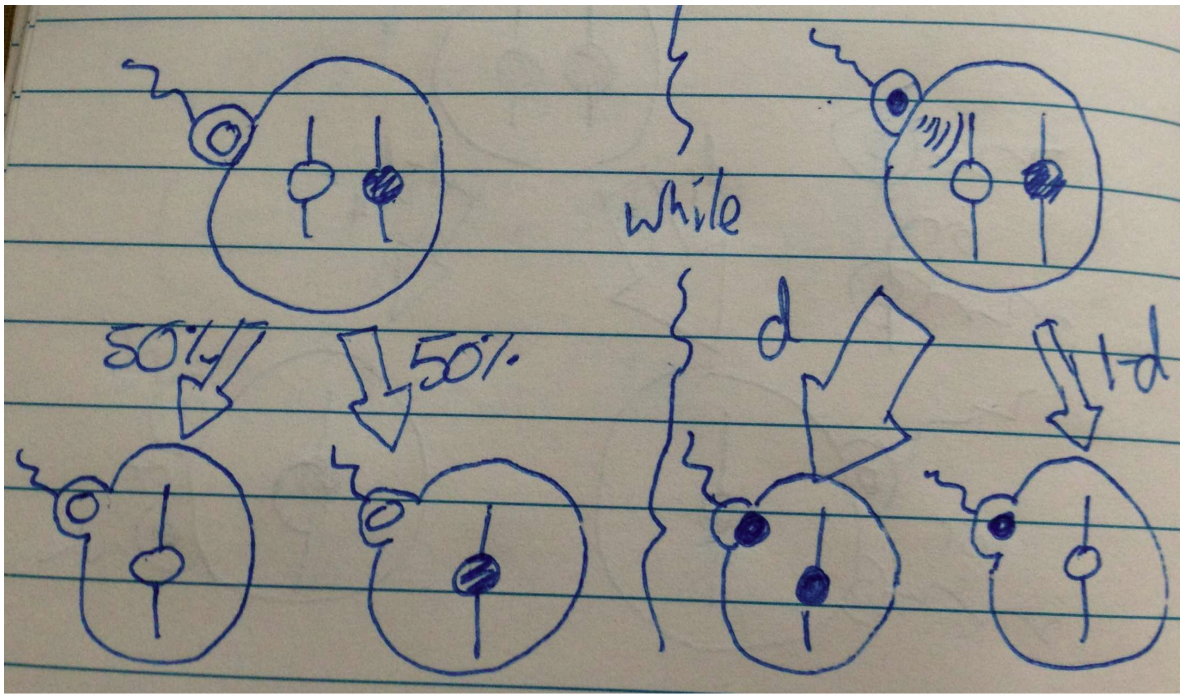

Figure 1: transmission probabilities for alleles through female meiosis depend on sperm genotype. 2 allele models

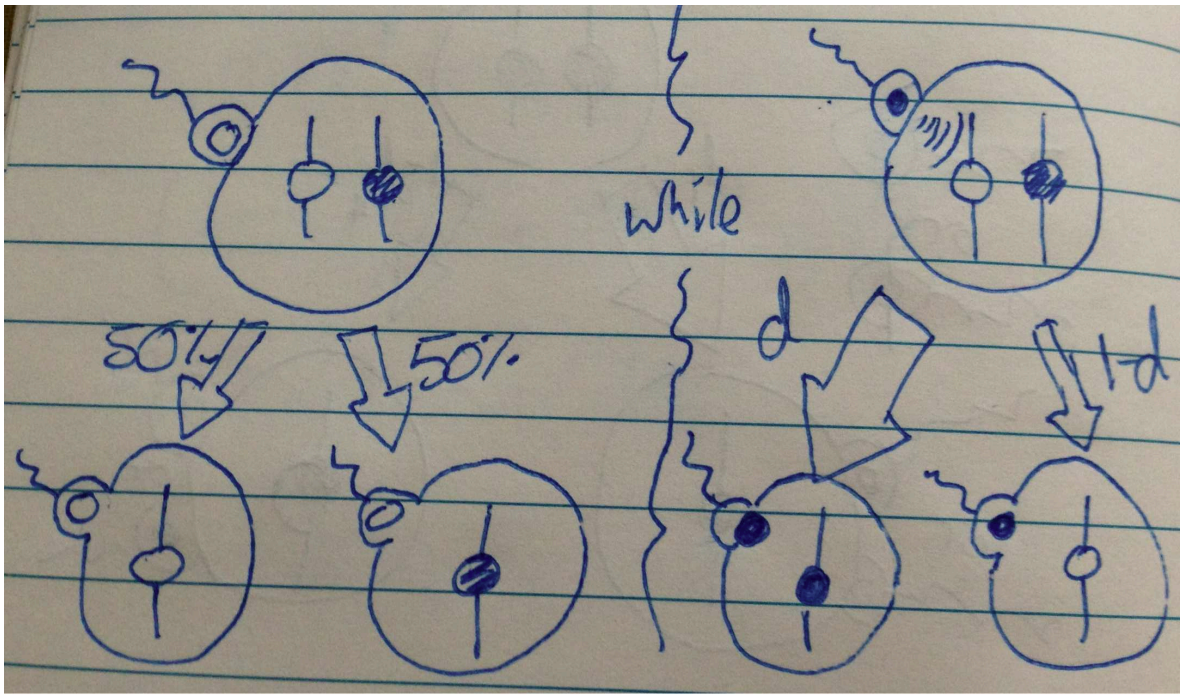

Figure 2: transmission probabilities for alleles through female meiosis depend on sperm genotype. 2 allele models

2. and homozygous problems are tested out at low freq.

3. Any heterozygous problems, leads to a bistable allele

4. If these alleles take off they speed through to fixation

5. If allele has any drive ability in absence of sperm effect that is what allows it to enter the population and sperm effect isn't a further cause of conflict. What if anything do we mean by this?

6. PERHAPS HERE WE INTRODUCE A SELF-RESTRAINING ALLELE

Conclusion, such alleles are unlikely to cause evolution of female supressors, they test hemselves in a homozygous state when they enter the population, and sweep quickly (all the way to fixation) if they enter the pop at all.

B) A more biologically realistic selfish sperm system

Three allele systems. See Figure 3

Perhaps these self promoting alleles are biologically unrealistic as new alleles needs both ability to drive in female meiosis and to influence that drive in sperm. Perhaps more realistic to think that a female drive system evolves, and then a sperm modifier appears. This will only occur if original system is trapped at drive-selection balance. So driver must have homozygous cost.

1. Setup a drive-selection balanced polymorphism in std. drive model. Do this by imagining the sperm-influence allele arising on the background of the driver, so the allele

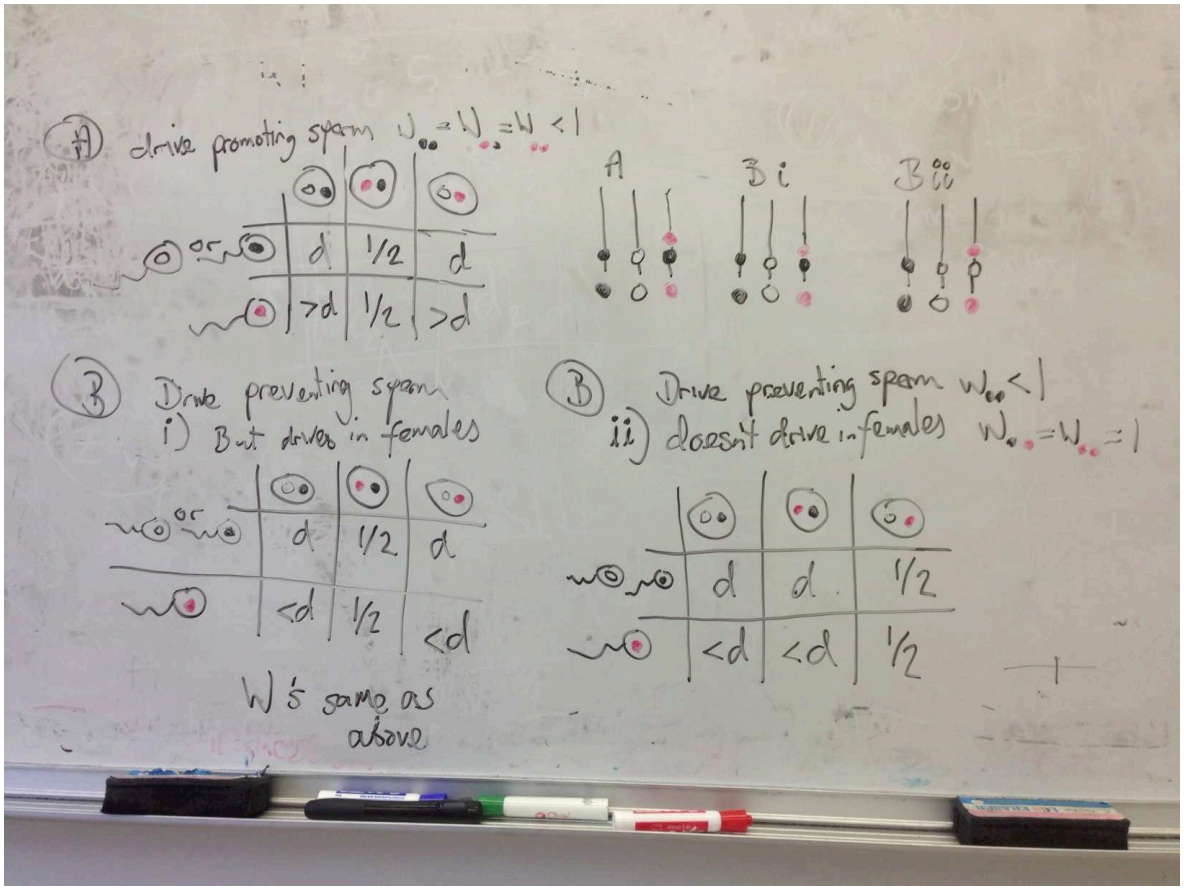

Figure 3: transmission probabilities righthand allele through female meiosis

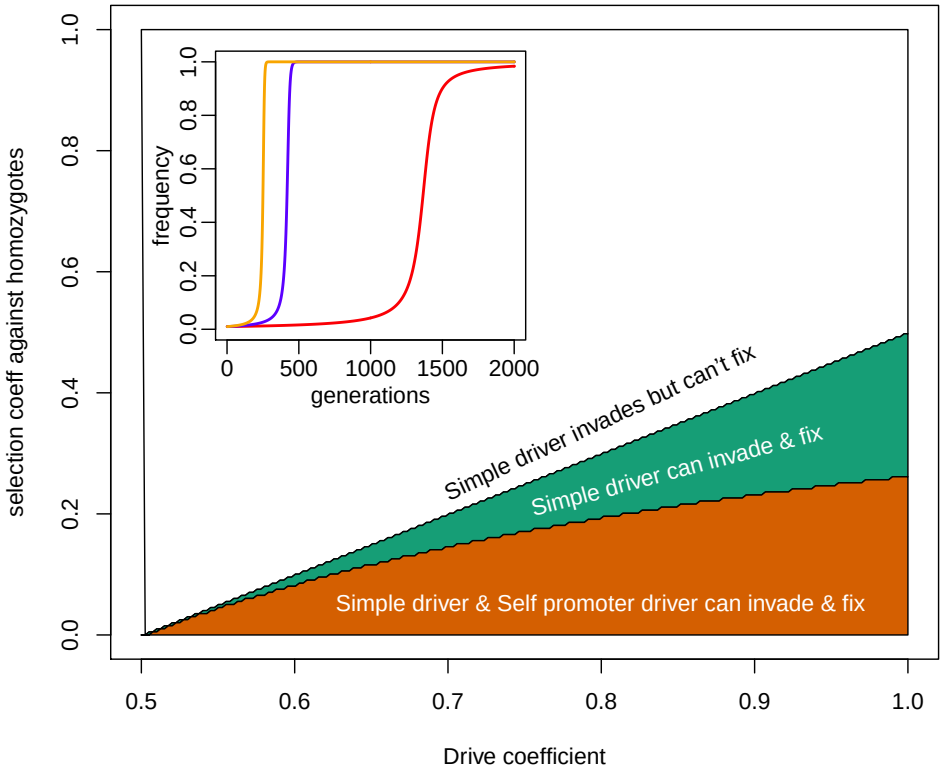

Figure 4: Invasion analysis. Likely merge with Figure 1.

has drive capabilities, and can have had time to evolve new biology. Evolving on the new background means that the allele suffers the fitness consequences of the driver. See A in Figure 3

2. Sperm-based enhancers of drive can't invade (can they in some situations?).

3. Intuition is that the driver has already driven to a frequency where it is held in check by its cost in homozygotes. The sperm allele thus can't really help as it creates zygotes which suffer the homozygous fitness consequences.

0.1 So what can evolve?

So what can happen?

1. Alleles that arise in linkage with drive systems, which when in sperm switch off drive, can spread. They benefit from drive, but avoid some of the consequences ((Bi) in Figure 3). Overall as a side product they are benefiting all in pop.

2. Presumably alleles that actually switch the allele that drives may do even better? As they'd end up in hets. Although they'd not drive, so hard to say. YB: There is evidence that In distorts meiosis in the other direction (they still drive when rare i.e. when not fused with drive supp sperm)

3. Alleles that cause sperm to switch off drive that arise on other background or unlinked to the drive system are selected, and spread as fast as female supressors of drive ((Bii) in Figure 3)..

4. Alleles that in females facilitate the action of sperm supressors of drive (or vis versa) can spread. Haven't actually checked this.

Conclusions.

Discussion of general conclusion that females have little reason to evolve supression mechanisms to prevent sperm influence on meiosis. General logic that sperm genome has to live in a zygote with consequences of its effect on female meiosis, so it can not generate too dire a consequence. I THINK THERE IS A MORE SUBTLE POINT . The sperm has special knowledge that if it allows drive it will end up in the low fitness homozygote.

This logic may not hold for sex chromosomes. In ZW systems Male modification of recombination rates POssibility that this could happen in plants if pollen emit signals to "egg" Discussion of OM and IN.