Why does female meiosis allow the opportunity for exploitation by selfish sperm? BETTER TITLE?

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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 [5], 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 [16, 12]. 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 [15], generating a genetic conflict between the success of the driver and organismal fitness. Meiotic drivers observed in nature (in both plants [4, 8, 7], and animals [1, 17, 13]) highlight this conflict – the selfish benefits of drive and the associated pleiotropic fitness costs sustain a balanced polymorphism [15], and often generate on ongoing evolutionary escalation of drive suppressors and enhancers [6, 7]. 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 [10], arrested female meiosis [11], centromere mechinery [**?**], and sex differences in the recombination rate [9, 3] 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 many potentially 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 [2, 17].

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 [14]). 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

A) Invasion of the population by a driving allele that promotes itself.

The standard model of female meiotic drive is two allele model, where the allele 1 is transmitted d fraction of the time through female meiosis ($d > \frac{1}{2}$), regardless of the genotype of

the sperm. 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 < 0.75?. 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.

We can model a simple sperm dependent meiotic drive system, by modifying this model so that the allele only drives during female meiosis if it fertilized by a sperm carrying that allele (see Figure 1). Under what conditions can this self propograting driver allele spread, and could it drive the evolution of supressors?

We first consider the situation where the driving allele has no fitness consequences in heterozygotes, only in homozygotes (whose relative fitness is $1-s$). A standard meiotic drive allele can always invade the population in this situation, as it is initially only present mostly in heterozygotes and rarely suffers the consequences of the problems in homozygotes. However, if the cost in homozygotes is strong enough ($s > XXd$), then the allele is prevented from reaching fixation and instead is maintained as a balanced polymorphism in the population [15]. Such balanced polymorphisms can then drive the evolution of supressors of drive [**?**], and most of our examples of drive systems are of this form.

Under a recessive fitness cost model our sperm dependent driver actually has far more restrictive conditions to invade the population, than a standard meiotic driver (see Figure 2). That is because our allele which drives only when it is present in the fertilizing sperm is guarenteed to form a homzygote. Thus, to even spread in the population when it is rare, our sperm-dependent driver has to overcome the cost it suffers in the homozygote state.

When conditions are suitable for such alleles to spread into the population, they spread slowly through low frequencies as they rarely drive as they are unlikely to be fertilized by a sperm with the right allele. Once they become established they spread rapidly to fixation due to their positive frequency dependent behavior (Inset in Figure 2). Unlike standard meiotic

drive systems these alleles can not become balanced in the population by homozygote cost, as they have already over come this cost just to enter the population.

Things are even worse for the sperm-dependent driver if it suffers any fitness cost in the heterozygote. Our standard driver can invade the population from low frequency if its drive in heterozygotes out weighs the fitness cost they suffer (XXX). However, when at low frequency our sperm dependent driver is often in heterozygotes but will only drive if fertilized by the same allele. If our allele incurs even very weak costs in heterozygotes it can be prevented from spreading from very low frequencies, unless its drive is very strong. The dynamics of our sperm-dependent drivers with an additive cost resemble an underdominant polymorphism (in that the system is bistable). Below a cutoff frequency the allele is unable to enter the population (in a deterministic model) as it is paying the cost of the drive but drive is ineffective (see Figure S**??**). Above this frequency the allele increases deterministically as its drive is sufficiently effective becayse heterozygote eggs are fertilized by sperm with our allele sufficiently often to beat the costs. This bistability suggests that sperm-dependent drivers will often be unable to enter into reasonably sized populations, and if they do they should rapidly be spread fixation.

A model where the sperm allele affects outcome of female meiosis 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 qualitatively to those based on the allele of the fertilizing sperm (see Supplementary Figures XXX and XXX).

Given the difficulty that meotic drive alleles that promote themselves through sperm have even entering the population, and the speed at which they fix if they do, it seems very unlikely that such alleles could drive the evolution of female

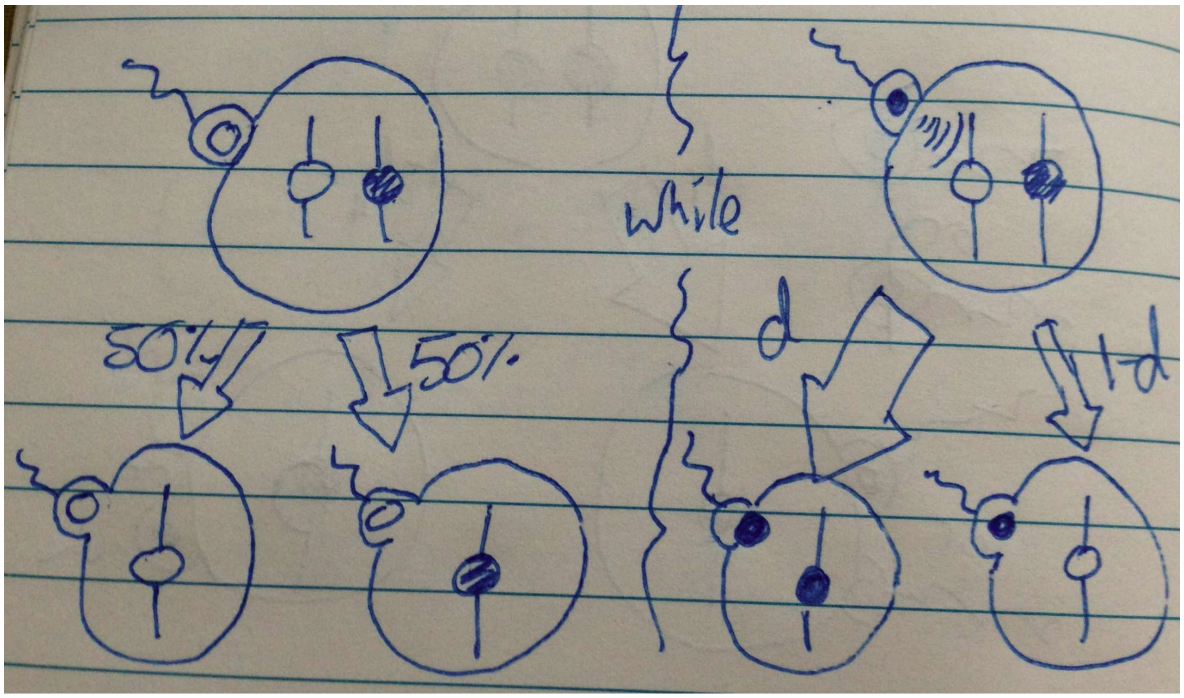

Figure 1: transmission probabilities for alleles through female meiosis depend on sperm genotype. 2 allele model

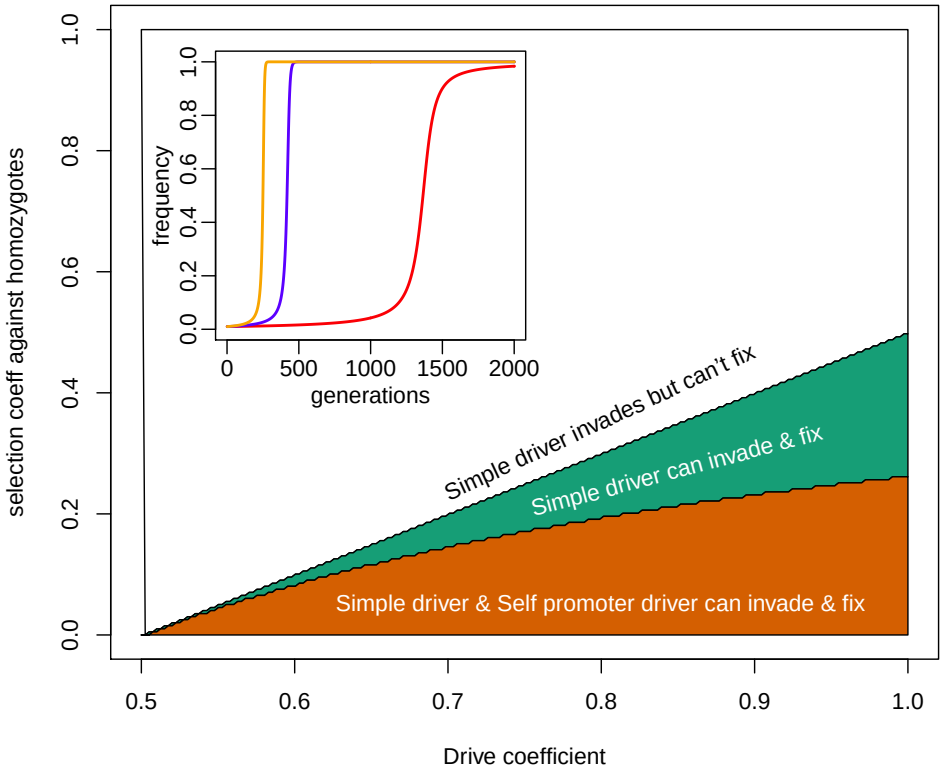

Figure 2: Invasion analysis. Likely merge with Figure 1.

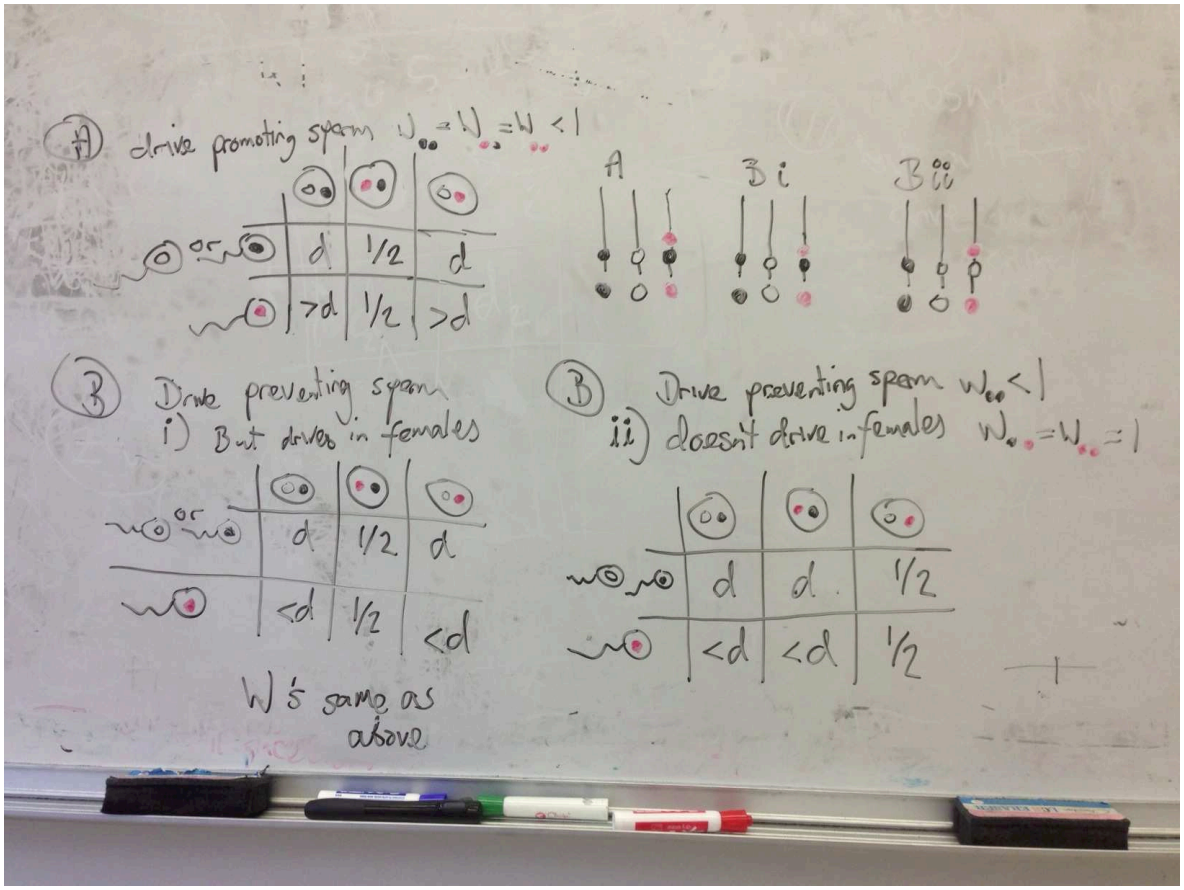

Figure 3: transmission probabilities righthand allele through female meiosis

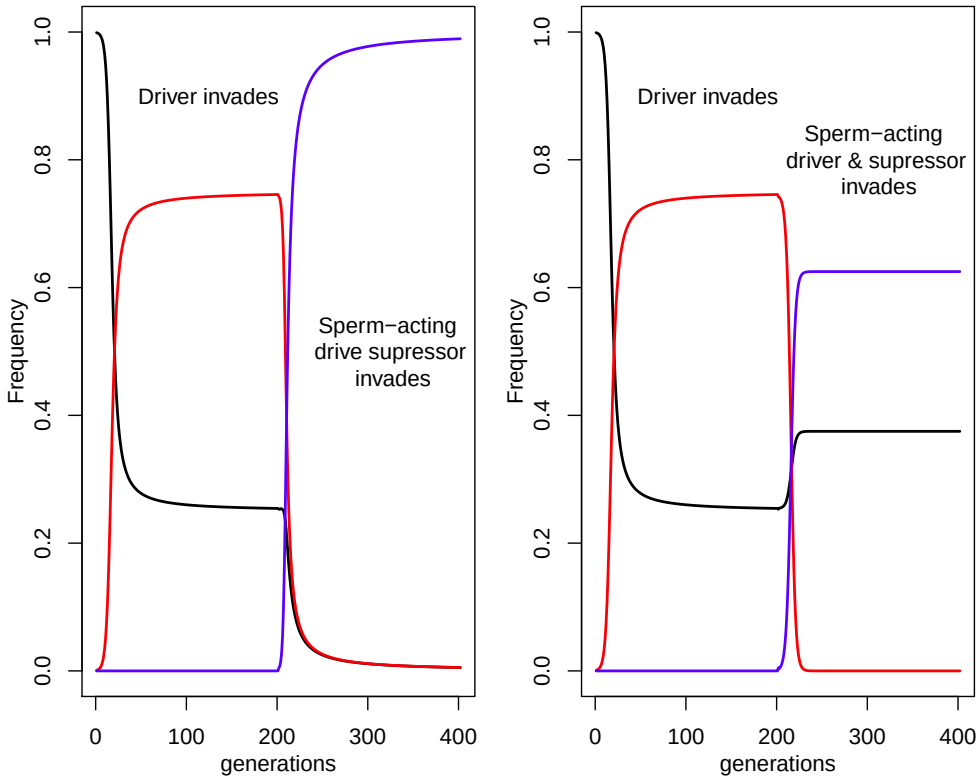

Figure 4: Trajectories of two sperm-based supressors of drive. Possibly merge this figure the 3 allele cartoon

B) A more biologically realistic selfish sperm-egg haplotype system

These self promoting alleles are somewhat biologically unrealistic as we are hypothesizing a newly evolved allele that both drives in female meiosis and has the ability to influence that drive in sperm. Perhaps it is more realistic to think that a female drive system first evolves and is maintained as a polymorphism in the population. This can then allow another allele to appears that further facilitates female meiotic drive through its action in the sperm.

Our sperm-acting allele will be best able to spread if it arises in very close linkage with the initial meiotic drive system as then it could potentially hitchhiking due to the additional drive it causes. Polymorphic transmission distortion systems have often evolved complex sets of inversions to prevent their breakup [**?**], so it is reasonable to assume that for some female drive systems there may be a reasonably large mutational target allowing our allele to arise in tight linkage. Assuming very tight linkage we can model this system using a model with three alleles at the same locus. The first two alleles (A and B) consist of our ancestral non-driver and our original driver allele. The third allele (C) is the combined haplotype of our driver allele and the fully linked sperm-acting promotor of drive. See Figure 3 for a simple schematic of this drive model.

The problem for our sperm-acting promoter of drive (the novel C allele), is that in order to have had time to evolve our original drive system (B) has to be trapped at drive-homozygote disadvantage selection balance. Our new allele has arisen on the drive background so it suffers from the same disadvantage. Worse yet, when our new allele it is rare it is often not helping itself drive in females but instead B (C sperm meeting AB eggs). As C facilitiates B these interactions will frequently form BC heterozygote which suffers from the full effect fitness costs as BB.

Sperm-acting selfing alleles are therefore at a profound disadvantage in this scenerio, even more so than under the previous two allele model. We have found no parameter range of this three allele system that allows the selfish sperm-acting allele C to invade the population.

There are other types of sperm acting alleles that influence female meiosis that can invade the population. In particular sperm-acting alleles that act to restore the fairness of meiosis in females can spread. We could imagine that these act by disrupting whatever mechanistic asymmetry in female meiotic segregation the drive initially evolved to exploit [12].

If these sperm-acting disrupting alleles arise at unlinked loci or on the A background they can readily invade a population segregating for the drive system (AB, see Figure). The invasion of such allele will lower the frequency of the original drive system (perhaps to zero) and will spread to fixation if they do not carry strong fitness costs (Figure 3 and 4A).

Intriguingly these sperm-acting distrupting alleles can also spread when they arise tightly linked to the original drive system (B), forming an novel third allele/haplotype C (Figures 3 and 4B). This new allele spreads to displace the original drive system (B) as it benefits from drive but by disrupting drive when it is in the sperm it forms the deleterious BC and CC combinations less often (than the analogous combinations for the B allele). Do we mention the In and Om locus here or in the discussion as a potential e.g. Do we mention the fact that the frequency of these newly invade sperm dodging alleles can be lower than the original system?

Finally given a system of a balanced meiotic drive system which avoid its own ill effects through a sperm-based mechanism , such as that depicted in Figure XX and XX, female-based modifiers can evolve that act to further facilitate the sperms action in disrupting driver.

Discussion

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.

OUTLINE

YB: 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. show that such alleles:

1. can't be balanced,

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.

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 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.

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