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## Cooperation: The Secret Society of Sperm

In the epic race for the egg, sperm have evolved cooperative teams that swim together. New research shows that some do even more: sperm seek out and swim with their relatives.

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and Tommaso Pizzari<sup>2</sup>

*“Help thy brother’s boat across, and  
lo! thine own has reached the shore”*  
Hindu Proverb

Evolutionary biology tends to emphasize the competitive side of sex. In pursuit of their reproductive interests, males will compete with females, females with females and males with males [1,2]. Nowhere is this focus more evident than in the study of sperm competition among the ejaculates of different males, arising in the many species in which females are sexually promiscuous [3]. Here, natural selection has produced all manner of byzantine traits that function to allow one male’s sperm to outdo another’s, such as fierce mate guarding, post-copulatory plugs and even genital scoops. But here, as for other aspects of the male–female union, one also finds evidence of cooperative behaviours in which one individual helps another to pass on its genes [4,5]. Of course, this is no reason to become misty eyed. A perfectly sensible response to strong competition is to join forces with others to form a stronger competitive unit. And this is what appears to have happened in the case of rodent sperm trains: fast-moving aggregates of sperm that in some species can out-swim loners [6]. A new study [7] on deer mice shows that — in addition to cooperative advantage — these sperm have evolved a second classic

feature of sociality: a preference for relatives.

Examples of sperm cooperation are not restricted to rodents and encompass a number of other weird and wonderful examples. Other cases of sperm training range from the paired sperm of the American opossum [8] to massive sperm trains in fishflies containing thousands of individual sperm [9]. In addition, the males of several invertebrate species produce sperm of different types (sperm heteromorphism): there are *eusperm* that fertilize eggs and one or more type of *parasperm* that — possibly analogous to the sterile workers of an insect society — have lost their

ability to fertilize and instead benefit the male by helping the eusperm along their way to the egg [10]. But why would natural selection favour the evolution of cooperative sperm that help one another to reach an egg? One answer is that sperm are simply slaves to a male’s interests. Natural selection on the male (diploid) genotype will favour maximizing his fertilization success, even if this means some sperm are sacrificed for the greater good. However, it is known that some genes carried by the sperm (i.e. the haploid sperm genotype) can also be expressed and thus might affect sperm behaviour [4,5,11]. This is important, as it means that there is the possibility for natural selection to act directly on sperm and shape their behavior against the interests of the male, should conflicts arise. Note for the gentleman reader: your sperm have the potential to rebel.

The potential for both haploid and diploid effects on sperm means that

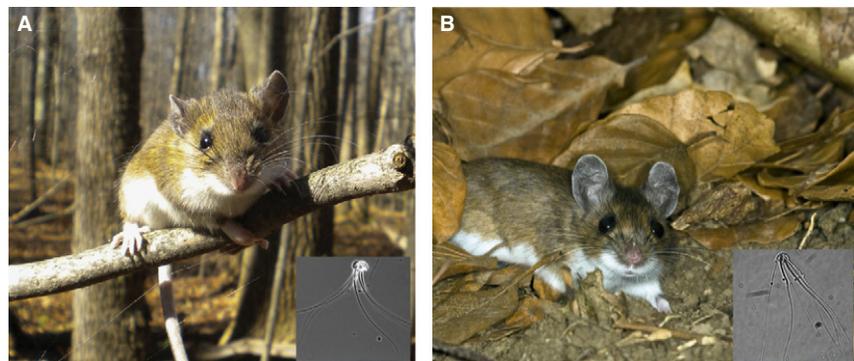


Figure 1. Deer mice and their sperm.

Two very similar species of deer mice that both have aggregating sperm (insets), which form trains and swim together. However, one species (A) has sperm that discriminate against unrelated sperm, while the other (B) has sperm that do not. (A) *Peromyscus maniculatus* is a promiscuous species with sperm that preferentially aggregate with related sperm when sperm are mixed in the laboratory. Photo by Evan Kingsley. (B) *Peromyscus polionotus* is monogamous and its sperm aggregate indiscriminately when mixed with sperm of a conspecific male. Photo by Shawn Carey. Both sperm train images by Heidi Fisher.

evolutionary explanations for sperm behaviour can become relatively complex, as one attempts to weave in the interests and power of all parties [5]. However, there is one thing on which the male and his sperm always agree: another male's sperm getting there first is bad. It is for this reason that sperm competition is expected to be a major determinant in the social evolution of sperm. All else being equal, in species with low risk of sperm competition, sperm are expected to be more individualistic and competitive with their own sibling sperm. If females mate with multiple males, however, there is the added possibility of sperm from another male reaching the egg. As a result, interfering with a sibling's swim becomes more risky. So much so that natural selection on sperm can even favour cooperative actions that reduce a sperm's own fertilization success in order to help siblings win over foreign genotypes. Such actions have been termed 'altruistic cooperation' in sociobiology to contrast to the easier-to-understand cases of cooperation that give mutual benefits [12]. This kin selection logic [13] led us recently to predict that cooperation, and particularly altruism, among sperm is most likely to evolve in species where females mate with multiple males and thus sperm competition is prevalent [4]. Of course, such sperm altruism is only beneficial if it is preferentially directed towards sperm from the same male [4]. Such a bias could, for instance, emerge passively if sperm aggregate before they encounter sperm of another male, such as shortly after mating. More intriguing though was always the idea that sperm might somehow recognize their kin. However, there was never any evidence that sperm make such discriminations. The new study on deer mouse sperm trains by Fisher and Hoekstra [7] changes this. They show that not only can sperm preferentially aggregate with siblings, but also that the behaviour is found in a species with high levels of sperm competition [7].

Fisher and Hoekstra [7] studied two species of deer mouse, which are very similar in most respects (Figure 1). However, one species, *Peromyscus polionotus*, is monogamous, while in the other, *P. maniculatus*, females will readily mate with multiple males in quick succession [7]. Sperm trains are formed shortly after ejaculation

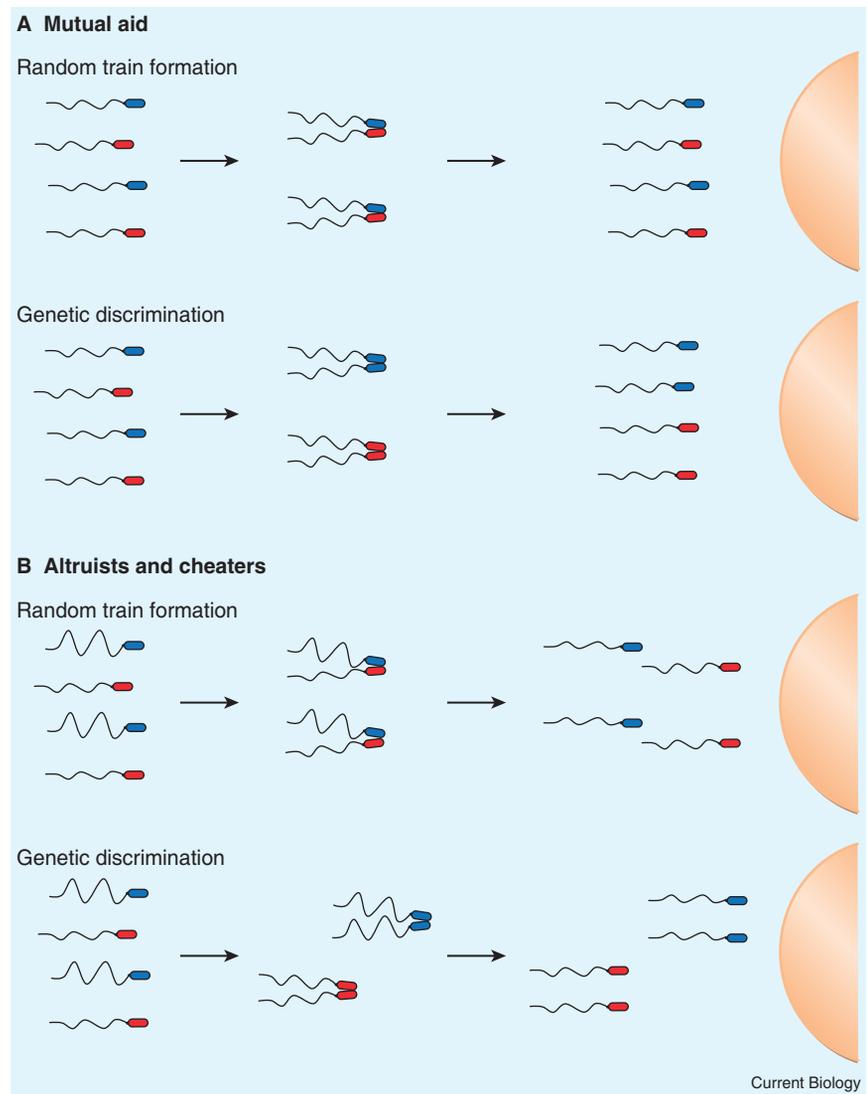


Figure 2. A hypothesis for the evolution of kin discrimination in sperm trains.

(A) Mutual aid, where the behaviour of one sperm cannot be exploited by another sperm, does not favour kin discrimination. (B) Altruism, where the behaviour of one sperm can be exploited by another sperm, favours kin discrimination. With random train formation, blue sperm that altruistically invest energy early in swimming are exploited by red sperm that save energy for the final swim to the egg (or possibly to avoid an early acrosome reaction [14]). Kin discrimination allows the blue sperm to form fast swimming all-blue trains that outcompete red sperm trains. The probability of meeting an exploitative sperm genotype will increase with multiple mating by females. The idea that sperm in trains can in principle exploit one another is supported by the anecdotal observation that non-swimming sperm are carried along in sperm trains (Heidi Fisher, personal communication).

when each sperm cell attaches onto neighbouring sperm. In general, rodent sperm-trains swim collectively for a certain period of time (60–90 minutes) in buffer before splitting up, which may indicate a final solo dash for the egg. Previous work in other rodents has shown that, as predicted, adaptations for train formation appear more pronounced in species with intense sperm competition [6]. In addition, there appear to be costs associated

with swimming in trains. While the trains can out-swim single sperm, train formation renders most sperm essentially infertile by the time they split up [14]. This is where Fisher and Hoekstra [7] entered the picture. First, they mixed the color-labeled sperm of the two species together. The mixed species trains showed a clear segregation. Second, they mixed the sperm of two males of the same species. The sperm of multiply-mating

*P. maniculatus* preferentially aggregate with sperm from their own male, even when the two males involved are brothers, while sperm from the monogamous *P. polionotus* show no discrimination.

How do *P. maniculatus* sperm discriminate? The mechanism is unknown but one candidate would be a hypothetical polymorphic locus expressing a homophilic binding protein (a protein that prefers to bind to copies of itself over other variants). If correct, the lack of discrimination in *P. polionotus* might be explained by a lack of variability at the recognition locus. Broadly consistent with this, mixing the 'indiscriminate' *P. polionotus* sperm with 'discriminate' *P. maniculatus* sperm gives seemingly identical patterns of segregation as mixing sperm from two *P. maniculatus* males [7]. This suggests that adding *P. maniculatus* sperm to *P. polionotus* may make *P. polionotus* sperm discriminate, as predicted by the homophilic binding model — if *P. polionotus* were not discriminating in the presence of *P. maniculatus*, one would expect less segregation than in a pure *maniculatus* mix. This model also predicts that there is discrimination within each *maniculatus* ejaculate that cannot be detected. There are, of course, other possibilities including more active mechanisms for joining or leaving groups, or a recognition system based upon paternal effects, whereby male (diploid) genotype rather than sperm genotype determines binding affinity.

Whatever the mechanism, it is clear and amazing that sperm have found a way to preferentially aggregate with their siblings. But, why discriminate? The answer is less obvious than it might appear [15]. While altruism — which reduces lifetime reproductive success — is expected to be tightly linked to kin association [16], the same is not true for cooperation involving mutual gain (Figure 2). The simplest explanations for sperm discrimination, therefore, require that there is some way in which sperm are altruistic. Knowing that many sperm flounder after trains break up [14] is not proof of altruism because this fate may befall all sperm with equal probability [4, 15]. An altruistic behaviour in the eyes of natural selection must statistically bias a sperm's fate in a sperm train. One candidate for altruism, and accordingly

the evolution of discrimination, is variation in sperm swimming effort (Figure 2B). But this is speculative, at best. Clearly, there is much about sperm sociality that we have yet to understand [4]. Nevertheless, the discovery of kin discrimination in sperm suggests a new synthesis in which the study of sperm competition can inform kin selection theory and vice versa. Studies that bridge the fields of sexual selection and social evolution are frustratingly rare, but sperm trains present fertile ground for the future.

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## Thymocyte Selection: Chemokine Signaling Is Not Only about the Destination

The development and function of lymphocytes depend upon their precise migration in response to chemoattractant cytokines, or chemokines. Two recent reports suggest that, during thymic  $\beta$ -selection, the binding of the chemokine CXCL12 to the receptor CXCR4 on thymocytes provides not only directional but also developmental cues.

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and Harald von Boehmer\*

T-lymphocyte development is a spatially complex process in which bone-marrow-derived hematopoietic precursors migrate via the bloodstream to the thymus, where they progress through sequential developmental stages and checkpoints in distinct thymic microenvironments, before exiting the thymus to perform immune functions (reviewed in [1–3]). While it is not surprising that thymic

development should depend on chemokines — chemoattractant cytokines that entice lymphocytes and their precursors to specific locations in the body (reviewed in [4]) — recent complementary results from two groups [5, 6] demonstrate that the chemokine CXCL12 (also known as stromal cell-derived factor 1 or SDF-1) is pleiotropic, and not only acts as a traffic warden, ushering T-cell precursors to environments where necessary factors are present, but also provides developmental cues.