by around 45 Å [19], which might be sufficient to perturb the quaternary organization of the proximal coiled coil. Finally, the propagated conformational changes could in principle affect interactions with other binding partners, such as endosomal syntaxin 13 [20]. Understanding the full implications of the observed entropic collapse and underlying structural bases awaits further investigation.

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Ageing: Why Males Curtail the Longevity of Their Mates

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Male nematodes secrete pheromones that accelerate the somatic senescence of potential mates. A new study shows that this harm most likely is an unintended by-product of the males' aim to speed up sexual maturation and delay reproductive senescence of future partners.

Sexual reproduction requires a great deal of cooperation between the sexes. Nevertheless, males and females have different reproductive strategies, which often result in bitter conflicts between the sexes over all aspects of reproduction — from mating to parental care [1–3]. For instance, in the common toad (*Bufo bufo*) males compete so intensely over fertilization that females sometimes drown under the weight of struggling rival suitors [4]. This example suggests that females suffer as a result of male–male competition, and that male behaviour is subject to positive selection because,

under most circumstances, it increases male reproductive success. However, it is often not easy to provide direct evidence for the evolution of male harm to females, and yet more difficult to identify the exact mechanisms that males use to manipulate female reproductive decisions. Recent studies in nematode worms identified what appears to be a particularly spectacular case of male–female/hermaphrodite conflict: during mating, males induce a whole suite of physiological changes in their mates that literally results in body shrinking, rapid ageing and early death [5,6]. Remarkably, this post-mating collapse does not require mating *per se* — life shortening occurs via compounds that males secrete into the environment [6]. While the detrimental effects of these male pheromones on the lifespan of their sexual partners were clear, the evolutionary underpinnings of these effects were far less obvious [7]. How do males benefit from reduced longevity of females or hermaphrodites? In this issue of *Current Biology*, Aprison and Ruvinsky [8] show that male pheromones speed up sexual maturation and delay reproductive senescence of their potential sexual partners. But there is a catch — the price of fast development and increased late-life reproduction could be accelerated somatic senescence and early death.

Selfish Males Favour Female Germline over Soma

While most *Caenorhabditis* worm species reproduce as males and females by cross-fertilization, the favourite working model of nematode geneticists, *C. elegans*, reproduces primarily as a hermaphrodite. These hermaphrodites are essentially females that are capable of self-fertilization and they can also mate with males, which are usually present at very low levels except under stressful conditions. The hermaphrodites have a limited number of sperm and they exhaust their self-fertilization potential in a matter of days after producing 200–300 offspring. However, hermaphrodites can replenish their sperm supply by mating with males and can then start producing eggs again. The first startling discovery made by Aprison and Ruvinsky [8] was that hermaphrodites aged on plates with male scent were able to produce more offspring than control animals aged on plates lacking male scent when subsequently mated to males. Thus, while male scent causes rapid deterioration of the soma and expedites the death of hermaphrodites, it has the opposite effect on their reproductive function. It looks as if these ageing decrepit worms that had to live their lives in the presence of harmful male odour somehow remain more reproductively competent compared with their seemingly more fortunate counterparts that were spared the scent of males. How can this be?

Perhaps the best way to approach this question is to consider the reproduction–longevity trade-off and its role in the evolution of ageing and longevity. Ageing is characterised by progressive deterioration of reproductive and somatic functions. However, age-specific changes in reproductive performance and the probability of death do not necessarily occur in parallel. The wandering albatrosses (*Diomedea exulans*) are famous for their long life but they too succumb to the onslaught of time [9]. Nevertheless, female albatrosses show a striking increase in their reproductive performance just before they die [9]. While this ‘terminal investment’ may sound counter-intuitive, it is exactly what is predicted by classic life-history theory: organisms should increase their relative investment in reproduction as the probability of future reproduction diminishes [10]. The important take-home message is that organismal physiology and behaviour can be modified so that the reproductive output of the senescent individual remains high, even at the cost of further somatic deterioration.

More generally, the ‘disposable soma’ theory [11,12] posits that ageing evolves as an optimization of resource allocation between costly reproduction and somatic maintenance to maximize the organismal fitness. Because the organismal lifespan is inescapably curtailed by detrimental external forces, such as predation, parasites and environmental calamities, it makes little evolutionary sense to invest in near-perfect somatic repair and maintenance. Instead, the investment into the ‘disposable soma’ should be optimized, such that the soma can function for the expected lifetime determined by the external forces, while the rest of the energy is used to maximize reproduction. One of the important costs of reproduction is the maintenance of the germ cells, which enjoy a higher level of protection and repair than their somatic clones (reviewed in [13]). *C. elegans* hermaphrodites consist of 959 somatic cells and ~2,000 germ cells [14], so the costs associated with germline protection and repair are likely to be substantial. Indeed, somatic cells of germline-deficient mutants enjoy elevated levels of protection from proteotoxic stress, suggesting the freed-up resources may be reallocated to increase maintenance of the soma [15]. Therefore, it appears likely that boosting investment into the germline may in turn result in reduced investment in somatic maintenance and reduced longevity. Aprison and Ruvinsky [8] showed that male scent contains pheromones that result in an increase in the number of germline progenitor cells in worms aged on male-scented plates compared with control individuals that were aged on scent-free plates. Thus, male pheromones tinker with hermaphrodite physiology to increase the investment in germline maintenance, attenuate the loss of germline progenitor cells with age, and delay reproductive senescence, likely to the detriment of the soma. Interestingly, the researchers identified a particular blend of ascaroside pheromones in male scent that is sufficient to increase the number of germline cell nuclei in the gonad but does not produce a corresponding delay in reproductive senescence, suggesting that male scent contains additional, non-ascaroside components that are necessary for increased offspring production in ageing worms.

Accelerated Development

Aprison and Ruvinsky [8] found that male scent also had an effect on yet another life-history trait — time to sexual maturation. When young larvae were kept on the plates that were previously inhabited by males, they became sexually mature a few hours faster than their control counterparts. This level of difference in development time may sound trivial but it is likely to be crucially important in a nematode that takes only three to four days to develop. Early

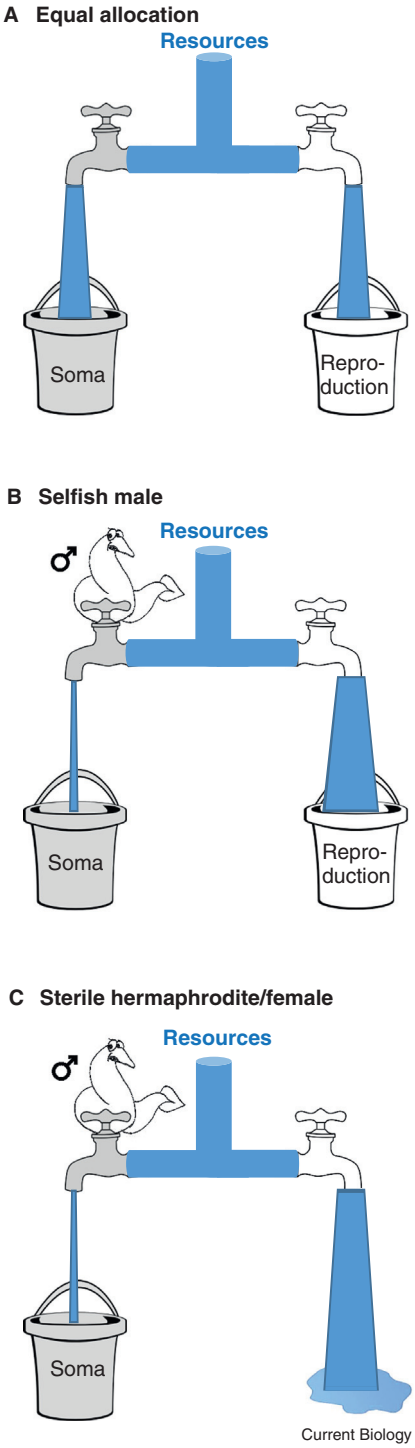

Figure 1. Selfish males influence resource allocation decisions of their mates.
Life-history theory posits that limited resources are allocated between somatic maintenance and reproduction in an organism. It is sometimes argued that changes in the level of somatic maintenance leading to either increased or decreased longevity in the absence of reproduction contradict the resource allocation hypothesis. For example, male nematodes cause somatic collapse and rapid death of their mates even when the latter lack a functional germline. However, the fact that males can reduce somatic maintenance in these sterile mutant hermaphrodites does not exclude the possibility that the soma–reproduction energy trade-off underlies the detrimental male effect. This cartoon depicts a hypothetical scenario where in (A) resources are being allocated between soma and reproduction in equal measure in a female or a hermaphrodite. (B) The selfish male tampers with the female nutrient-sensing signalling network to switch allocation from soma to reproduction. (C) However, when the reproductive system is removed in a sterile mutant, the reallocated resources are simply wasted.

maturation can speed up reproduction such that the offspring of early maturing individuals will have better access to ephemeral resources. Rapid maturation, however, can come at a cost to longevity [16,17]. There is ample evidence linking rapid growth to reduced lifespan, although it is still not clear whether growth rate *per se* (increase in mass per unit time), development rate (cell differentiation per unit time), or a combination of the two factors is responsible for the detrimental effect on longevity. Strikingly, rapid maturation is stimulated by different compounds in male scent than those that promote an increase in the number of germline progenitor cells in hermaphrodites. This further suggests that male scent is composed of several different signals that act on different aspects of hermaphrodite life history, such as germline maintenance and development time.

Anticipating Reproduction

Male scent accelerates development, sexual maturation and somatic ageing, while increasing the number of germline cells and delaying reproductive ageing of hermaphrodites. It is exciting to speculate that these effects are causally linked: for example, rapidly maturing hermaphrodites can suffer from an increased number of developmental errors, and investment in germline maintenance can result in fewer resources being allocated to costly somatic maintenance. However, at present, we do not yet know if this is indeed the case. Earlier work suggested that the detrimental effects of male scent on hermaphrodite/female longevity are unrelated to investment in reproduction because mating decreased the lifespan of germline-deficient *glp-1* mutants, which do not pay the costs of germline maintenance and egg production [5]. However, this observation may not constitute a strong argument against the resource reallocation theory [18,19] (Figure 1). Male pheromones can directly affect cell metabolism in a way that anticipates increased investment in reproduction because such a response would occur naturally in a wild-type individual that possesses a functional germline. Such a change in metabolism would be lost on a germline-deficient mutant that will suffer the decrease in lifespan following reduced investment in somatic maintenance without the corresponding increase in reproductive output. However, because natural selection operates on the physiological response to mating in a wild-type worm rather than in a germline-deficient mutant, we cannot conclude that the post-mating somatic collapse of germline-deficient worms argues against reallocation of resources from soma to reproduction: the freed-up energy from reduced somatic maintenance could simply be wasted in worms that lack a reproductive system (Figure 1).

Outlook

Much remains to be learned about the relationship between reproduction and somatic ageing, and about the role of germline-to-soma and soma-to-germline signalling in mediating this relationship. In sexually reproducing organisms, this relationship is further complicated by the evolutionary conflicts of interest between the mating individuals. Aprison and Ruvinsky's study [8] makes an important contribution by showing how selfish males can interfere with the physiology of their mating partners to shift their life history towards rapid sexual maturation, increased germline maintenance and improved late-life reproduction — all at the cost of longevity. Nevertheless, a selfish act does not always result in the reduction of fitness of the recipient, and natural selection optimizes fitness rather than longevity. One reason for the lack of female/hermaphrodite evolutionary response to male manipulation of the

reproduction–survival trade-off could be that it does not reduce their Darwinian fitness. Future studies should focus on the economy of sexual interactions in *Caenorhabditis* worms to provide a definitive test of whether females and hermaphrodites pay the ultimate evolutionary price of increased male fitness.

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Axonal Degeneration: RIPK1 Multitasking in ALS

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A recent study reports that microglia and oligodendrocytes promote motor neuron degeneration by inducing inflammation and necroptosis in a manner dependent on receptor-interacting kinase 1 (RIPK1). These findings could be significant for our understanding of the neurobiology and treatment of neurodegenerative diseases like amyotrophic lateral sclerosis.

Amyotrophic lateral sclerosis (ALS), also called Lou Gehrig's disease in the USA, is the most common paralytic disorder in adults [1]. To date, there is no cure for ALS and, even when the cause is known, as in rare familial cases of the disease that are linked to mutations in particular genes, the mechanisms responsible for neurodegeneration remain enigmatic [1]. Studies in human post-mortem tissues from ALS patients and from mouse models of ALS have led to two insights about the neurobiology of this disease, however [2]. First, while damage to motor neurons is responsible for ALS paralysis, denervation of the neuromuscular junctions consistently precedes and exceeds the extent of loss of motor neuron cell bodies [2], raising the idea that the ALS clinical picture results, first and foremost, from the degeneration of nerve terminals. Second, several lines of evidence support a role for glial cells in the demise of neighboring motor neurons, suggesting that the neurodegenerative process of ALS relies, at least in part, on non-cell-autonomous mechanisms [3]. In a recent study published in *Science*, Ito *et al.* [4] provide an exciting new twist in the biology of ALS whereby the reader is presented with the notion that two types of glia, namely microglia and oligodendrocytes, provoke the destruction of motor neuron axons via