Discussion on the Evolution of Ageing

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Amitabh Joshi's article -Evolution, Fruit flies and Gerontology (*Resonance*. Vol.1. No.11. pp.51-63) is fascinating. But I suspect a subtle circularity in the arguments regarding evolution of ageing. The argument, as presented, seems to be critically dependent on the assumption of cessation of reproduction after a certain age or atleast decrease in reproductive success with age. Why anyone should stop reproducing much before death is a really perplexing question from the evolutionary point of view. But we know that this is common in many species including humans. If you say that individuals stop reproducing because they grow old, it is ridiculous, since we are set to explain why they grow 'old'. If we fail to find an ageing independent explanation for the cessation of reproduction, the further sequence of arguments collapses.

Perhaps cessation of reproduction is not so crucial for antagonistic pleotropy to work. Cumulative survivorship may alone be responsible for the difference in the strength of selection at young and old ages. This can drive the evolution of ageing. Cessation of reproduction can then be looked upon as a part of, or an effect of ageing and not the cause.

Author's Reply

Watve has highlighted what appears to be circularity in the logic of the argument regarding the evolution of ageing as a consequence of the fact that the power of natural selection acting on a gene decreases with the age at which the gene is expressed. The apparent circularity, however, is not in the theory but, I suspect, a consequence of the example I gave, of a lethal gene acting at late ages in humans. Watve has correctly pointed out that, in such a case, the pattern of decline in reproductive output with age has already been established and that, therefore, the reduction in reproductive output with age is a consequence and not a cause of ageing.

The basic issue that I think needs to be clarified is what the current thinking about life-history evolution is. In the original article I could not devote much time to this topic because I wanted to focus upon genetic theories of the evolution of ageing. So, let us start at the beginning and ask "What is an organism's life-history?". From an evolutionary view point, the life-history of an organism refers to the timing and distribution of reproductive output, given that the organism survives to a particular age. For example, the life-history of an organism tells us at what age it would normally begin to reproduce, for how long it would continue to be reproductively active, and whether the distribution of offspring during the reproductive phase of its life is uniform or, say, concentrated more towards the earlier part of the reproductive time span. Of course, if a particular individual organism died at some relatively early point in life, the potential reproductive output it would have had will not be realised. Thus, one can differentiate between *potential* reproductive output at a given age, which is conditional upon the individual first surviving to that age, and *realised* reproductive output, which is the number of offspring actually produced at the given age.

Let us now consider how we would expect life-histories to have evolved in the course of the evolution of life forms. First, let us imagine a stage very early in the evolution of life. If any genetically variant individual could produce more offspring than others, this would tend to increase the representation of its descendants in the population over generations. *More formally, all else being equal, there would have been strong natural selection for increased total reproductive output.* Now, it is not unreasonable to assume that there is a limit to how many offspring any individual can produce in its lifetime (this limit, of course, may vary from species to species). Therefore, we assume that most species would have evolved so as to reach their maximum total reproductive output fairly early in their evolutionary history, as a result of the very strong selection they would have been experiencing for increased total reproductive output.

Now, given that species would have attained their maximum reproductive output at some relatively early point in their evolution, the next issue to consider is how the distribution of their reproductive output over their life-span may have evolved. Let us consider here a scenario where we have individuals of a species that has a uniform distribution of offspring over a fixed life-span (this is a little artificial, but I am considering an extreme case in order to be conservative). For example, let us say individuals of this species lived exactly 10 years and produced 10 offspring each year. I will argue that even in such a species, where there was no post-reproductive life (i.e. individuals reproduced until their death), and where the probability of survival to a given age did not decline gradually with increasing age, *natural selection would favour the evolution of a life-history wherein reproductive output was increasingly concentrated in the earlier part of the life-span.*

To see why this should be so, consider the following example. Suppose a mutant individual arises in this population. This mutant still produces the same total number of 100 offspring, but produces these offspring at the rate of 20 offspring per year during the first 5 years of its life. Now imagine a population in which there are 10 individuals initially, of which one is the mutant type. For simplicity, assume reproduction to be asexual. So, the initial frequency of the mutant in the population is 0.1. After 1 year, the population will consist of the original 10 individuals plus their offspring. The normal individuals will have produced 9 x 10=90 offspring, whereas the mutant will have produced 20 offspring. The frequency of the mutants in the population after one year has, thus, increased from 0.1 to about 0.167 (21/120). In a similar manner, the frequency of the mutants will increase each year until, gradually, the population will consist almost entirely of the mutant individuals. At this point the life-history will have evolved from one where reproductive output was uniformly distributed to one where reproduction is concentrated early in life, and there is a post-reproductive period.

Natural selection will tend to favour the evolution of life-histories in which reproductive output is concentrated relatively early in life.

As I said earlier, the preceding example was a little artificial. But the incorporation of more reality into the argument only makes the conclusion stronger (this is what I meant when I said I was being conservative). In reality, organisms do not live up to a fixed time and then die. In fact, the probability that an organism is still alive at any given time tends to decrease with time (why this is so was explained in the original article). Thus, even though an organism may have a high potential reproductive output till a relatively late age, its realised reproductive output tends to decrease with age as a consequence of the declining likelihood that it will still be alive to realise its potential reproductive output at more and more advanced ages. Indeed, this is also a point raised by Watve. Whatever the exact contributory causes may be, I think it will be reasonably clear that, by and large, natural selection will tend to favour the evolution of life-histories in which reproductive output is concentrated relatively early in life. At this point, the stage is set for the evolution of ageing via the two mechanisms I discussed in the original article, namely antagonistic pleiotropy and mutation accumulation.

One additional point that I would like to stress here is that *although decreased reproductive output with age is a part of the syndrome we call ageing, there is a lot more to ageing that just decreased reproductive output.* This is a distinction that is not clearly made by Watve and the lack of this distinction further adds to the perception that the argument is tautological i.e. organisms age because they stop reproducing at later ages, and they stop reproducing at later ages because they have aged. In fact, natural selection first drives the evolution of a life-history in which reproductive output is concentrated relatively early in life. Once this has occured, genes with effects that are harmful only at relatively advanced age are no longer weeded out of the population by natural selection. This is because the organism has already passed on copies of such genes to its offspring as the harmful effects of the genes are not manifested until most of the organism's reproduction is over. Such genes then tend to rise to high frequencies in populations, either through selection because they also have beneficial effects early in life when those effects really matter, or through random genetic drift. The expression of these genes late in life produces the syndrome of degenerative effects that we typically call ageing. One among the many degenerative effects of these genes may be a further decline in reproductive output at later ages. Thus, it is difficult to clearly say whether decreased reproduction at later ages is a cause or a consequence of ageing. In fact, I would argue that it is both a cause and an effect of ageing; indeed, it is a positive feedback cycle of sorts. Feedback cycles are very common in biological systems, whether one is focussing at the molecular or populational level, and *I would, consequently, argue that causation and effect in biological systems are very often circular rather than linear, and that this is one of the features that separates biology from physics.* Our views on linear cause and effect relationships derive ultimately from Greek philosophers who based their thinking primarily on their observations of physical systems.

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One last point that I would like to touch upon in the context of Watve's query is that of examples and analogies. As I see it, the confusion in the original article seems to have stemmed partly from a simple example that I thought may help readers not well versed in evolutionary biology. However, when I teach evolutionary genetics, I prefer not to use examples of this kind, because I feel that the analogy between the example and reality is usually not complete. In fact this is why, when writing technical papers, evolutionary geneticists often prefer to use the language of mathematics. Our subject has, perhaps, more than its fair share (among sub-disciplines of biology) of subtle and abstract concepts, and mathematics is admirably concise, precise and unambiguous as a medium for expressing potentially confusing ideas. I would welcome comments from teachers and students regarding whether they find simple examples from everyday life useful or a source of confusion when trying to understand (or teach) concepts that could, alternatively, be developed more rigorously using formal mathematical models.

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