Are *C. elegans* and *D. melanogaster* valid animal models for studies on aging?

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In a discussion about aging, two precise definitions are a necessary premise, because: "... 'ageing' is used with so many different meanings in so many different contexts that it is sometimes highly confusing when used without proper qualification." [1]
Many bird and mammal species - *H. sapiens* included - show an "increment of mortality with increasing chronological age in the wild" (IMICAW [2]), alias "actuarial senescence in the wild" [3]. This phenomenon is well documented [4,5] and is illustrated in Fig. 1 (A1 and A2).
Other animals show in natural conditions a constant mortality rate but, in artificial protected conditions, they display an age-related mortality increment starting from ages not existing in the wild. This "increment of mortality with increasing chronological age in captivity" (IMICAC [2]) is documented for well known species as the worm *Caenorhabditis elegans* [4] and the fly *Drosophila melanogaster* [6].
In fact, the longevity of *C. elegans* "under more natural conditions is reduced up to 10 fold compared with standard laboratory culture conditions" [7] and few individuals of this species remain fertile in the wild after 10 days [8]. *D. melanogaster* has a reported adult life span in the wild of 10-12 days [4]. For both these animals, the age-related increasing mortality described in Fig. 1 (B1 and B2) starts at ages non-existent in the wild and, so, it is only a laboratory artefact.

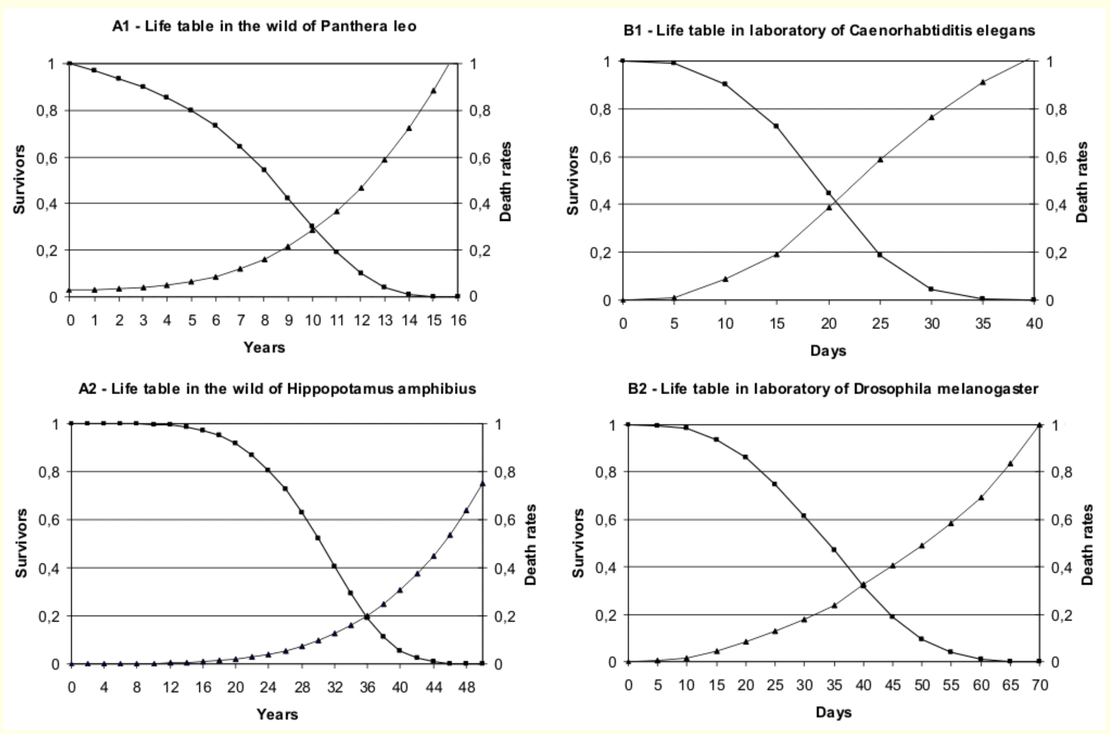

Fig. 1 - Life tables and death rates of: A1) lion (*Panthera leo*) in the wild, data from Ricklefs [5]; A2) hippopotamus (*Hippopotamus amphibius*) in the wild, data from Ricklefs [5]; B1) *C. elegans* reared in laboratory, data from Finch, fig. 6.1 [4]; B2) *D. melanogaster* reared in laboratory, data from Finch and Hayflick, fig. 10 [6].

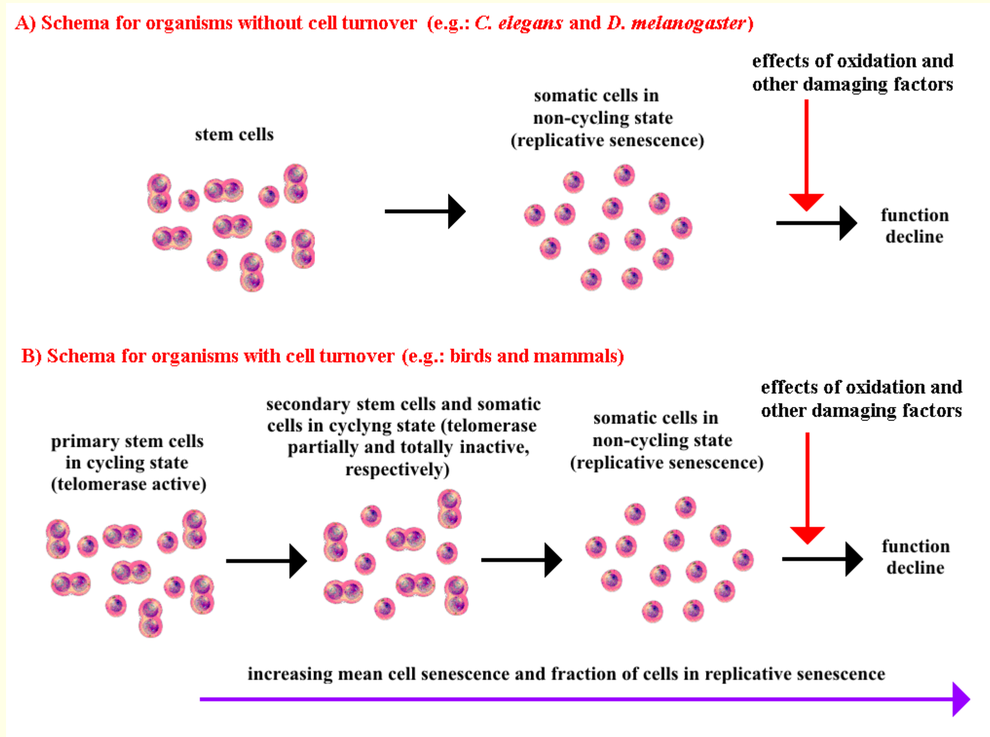

Fig. 2 – Comparison between organisms with and without cell turnover

C. elegans and _D. melanogaster_ are common animal models for studies on "aging". There are strong arguments against the reliability of these models for an effective explanation of the age-related mortality increase observable in natural conditions for other species.

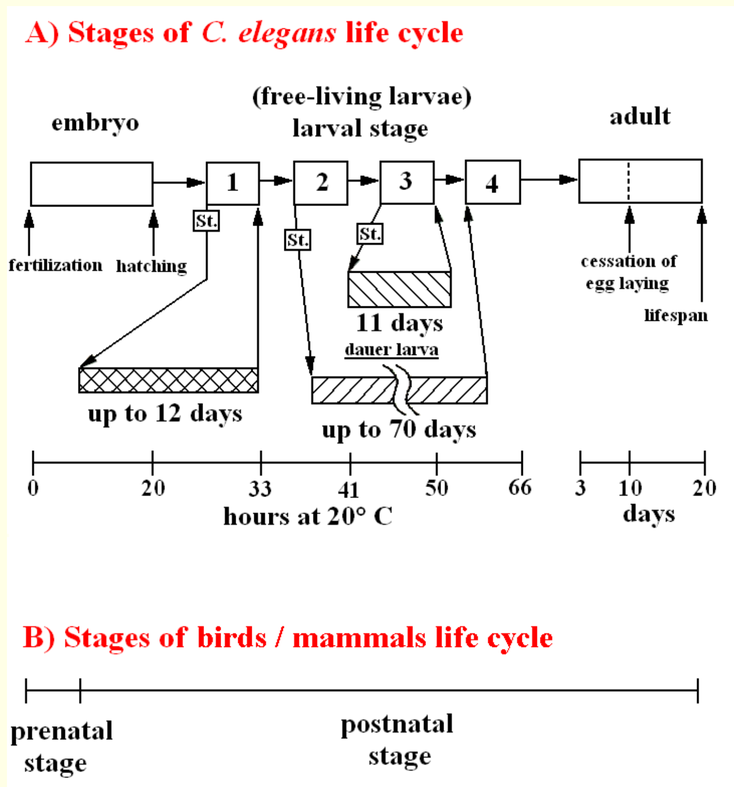

Fig. 3 – A) Stages of *C. elegans* life cycle (redrawn from [4]). The lifespan reported in the figure is in laboratory conditions, while it is reduced up to 10 fold in the wild [7]; B) Stages of bird / mammal life cycle. For studies on "aging", the equivalence between adult stage of *C. elegans* and postnatal stage of birds / mammals is not at all a self-evident assumption.

As *C. elegans* and *D. melanogaster* are easily available in laboratory, many studies on "aging" have used these two species as animal models [9,10]. But:
1) is IMICAC a phenomenon that can be compared to IMICAW?
2) are these two species reliable animal models for studies on IMICAW?

Most likely, the answer is negative for three main reasons:
I) By definition, IMICAW exists in the wild and therefore is influenced by natural selection. On the contrary, by definition, IMICAC is non-existent in the wild and therefore cannot be influenced by natural selection. This means, in principle, that IMICAW, and not IMICAC, could be modeled by natural selection and that the two phenomena are radically different in their evolutionary determinants and mechanisms.
This argument could be contested with the assumptions that IMICAW does not exist in the wild and/or is not determined or influenced by natural selection [11] but these prejudice are contradicted by natural observations [4,5] and theoretical arguments [2,12].
II) *C. elegans* and *D. melanogaster* (and in general the adult insects) are composed by cells with no turnover [4,13], while lion, hippopotamus and man (and, in general, birds and mammals) - species that show the IMICAW phenomenon - have cells and tissues with turnover (Fig. 2). If, as it seems likely, the slowdown and later the stopping of cell turnover, and the correlated cell senescence, are pivotal elements in the fitness decline of animals as lion, hippopotamus and our species [14,15], it is rather doubtful to use experiments on animals with no cell turnover to explain the fitness decline in animals with cell turnover.
III) Animals as *C. elegans* and *D. melanogaster* have life cycles thoroughly different from those of bird and mammal species (for *C. elegans*, see Fig. 3). Studies on "aging" that use these animal models implicitly assume that their adult stages are equivalent to the postnatal stages of birds / mammals for the extension of their results to bird / mammal species. But this assumption is not proved and seems quite doubtful.

This is a basic problem, certainly of extreme weight for those interested in the explanation of aging mechanisms. However, in renowned texts on the topic, the problem is not considered [9], and it is frequent that, in very influential journals, experiments modifying – in laboratory conditions and at ages non-existent in the wild - the life table of our dear worm or of our beloved fly are presented as meaningful advances in the understanding of human aging [10,16,17]!

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