

Is *Drosophila* the answer? The role of model species in biological research

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ABSTRACT

Biological research has been dominated by focussed effort on few model species and recent commentaries further discourage broadening the range of study species. It is undeniable that we now have unprecedented detail of information on the genetic, molecular and cellular biology of model species, but whether their biology can be broadly generalised is unclear. By channelling research into a limited range of species, we miss the opportunity to test theory on a wider range of species and the discovery of new biological phenomena. With new technologies and laboratory facilities becoming more affordable and accessible, establishing new species as models has never been more promising and important.

Key words: *Caenorhabditis*, *Mus*, *Danio*, *Drosophila*, biodiversity

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Introduction

Classic biological model species, such as the mouse (*Mus*), the worm (*Caenorhabditis*), the fish (*Danio*), and the fly (*Drosophila*) have been fundamental for biological research and discovery (Fields and Johnston 2005). Many of these species have enjoyed decades of research. *Drosophila melanogaster*, for example, started its research career in the early 1900s with Thomas Hunt Morgan (Columbia University), who was mostly interested in cytology and evolution (Kohler 1994). The research intensity surrounding these four classic model species is unrivalled. In the last five years (2008-2012), over 9,500 papers with *Drosophila* and over 1,500 papers with *C. elegans* in the title have been published (source: Web of Science). The consequence of this focused research effort is that we now have detailed information on the genetic, cellular, and molecular mechanisms in these model species. Recent commentaries predict that biological research will focus even more on a few selected species, and warn that this practice will restrict our vision and understanding of basic biological questions (Fields and Johnston 2005). In this essay I explore the attributes that make good model species, whether we can use the established model species to generalise across many species and highlight the potential of understanding variation by studying new systems.

What makes a good model species?

The precise reasons why the classic biological model species above were selected in the first place are obscure, and I suspect in part co-incidental rather than based exclusively on a *priori* reasoning. The foremost desirable traits, however, seem to be the ease with which the animals can be kept, reared, and manipulated in the laboratory (Maher 2009). According to Thomas Hunt Morgan one of the most endearing features of *Drosophila* flies was that they withstood the neglect and mistreatment by students (Kohler 1994).

Of course, many organisms are incredibly easy to keep in the laboratory and hence fit this general requirement for model species. As a consequence, the list of 'model' species is growing and some granting agencies (e.g. National Institute of Health, USA) provide a list of recognised model organisms for medical research (<http://www.nih.gov/science/models/>). In addition to the four already mentioned, the list also includes the rat (*Rattus*), yeast (*Schizosaccharomyces*), amoeba (*Dictyostelium*), the chicken (*Gallus*), and the frog (*Xenopus*). The implication of such lists is that funding will be linked to research on these species, further channelling research into few species.

The rationale for using a model species, with detailed knowledge of its biology and genetics, is that for some biological questions there will be a species that is best suited to study said phenomenon. Accordingly, a researcher may have a specific target of investigation, and selects a model species which is most suitable for addressing this particular question (Ankeny and Leonelli 2011). Thanks to the enormous research effort on model species, these have now become desired targets for many research questions that require detailed genetic, cellular or molecular knowledge. Of course, this practice eventually becomes self-fulfilling and channels research into already established models, thereby reducing the range of suitable study species. Recent high profile commentaries support this practice. For example, Leadbeater (2009) encourages the use of *Drosophila* to study social learning and a recent editorial in Nature (Vol 493, 17 January 2013), promotes the convergence of behavioural genetics research on a selected few intensely studied species. So, while many species may fit the desirable criteria for becoming a model species, the existence of already well-established model species seems to discourage broader species selection and canalizes research effort.

How representative are model species?

An assumption of model species is that they are representative of other species (Ankeny and Leonelli 2011). Thus, by studying one species, we are able to understand many other species. This assumption may be appropriate for some research areas in biology (e.g., cell biology, genetics) that focus on mechanism. However, evolutionary and behavioural biology is often concerned with explaining variation between individuals of the same species, as well as variation between species. Therefore, it is unlikely that a few model species can be broad representatives of behavioural and evolutionary phenomena.

This limitation becomes obvious when comparing the mating system of *D. melanogaster* with that of congeners. Male *D. melanogaster* transfer toxic molecules in their ejaculate that reduce female longevity. Females that mate less frequently have a greater lifespan. This selects against female promiscuity and males benefit as a less promiscuous female reduces sperm competition (Chapman *et al.* 1995). This discovery has sparked intense research interest in sexual conflict between male and female fitness optima. However, it is premature to assume that sexual conflict, as described in *D. melanogaster*, is present in most animals, or even in most *Drosophila*. In *D. simulans* for example, promiscuous females gain a fecundity benefit with no observable reduction in longevity (Taylor *et al.* 2009). From this simple example, it seems that to understand broad evolutionary and behavioural phenomena we have to diversify study systems.

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Model species snookered

Recent research suggests that the trait that makes established model systems so attractive for research may cause undesirable side effects. Species like *Drosophila* are often maintained in the laboratory for many generations. This is part of its appeal, as lengthy pedigrees and selection lines can be established and maintained easily and at relatively low cost. However, long-term laboratory populations evolve under reduced selection as there are no predators or parasites in the laboratory, and the environment is consistently benign. A recent meta-analysis on how dietary restriction affects longevity in animals has discovered that model species consistently show opposing relationships between diet and longevity compared to non-model species (Nakagawa *et al.* 2012). The authors interpret this difference as a result of the laboratory environment and if so, question the generality of the findings on model species. Whether behavioural or physiological traits of long-term laboratory populations are comparable to those of wild population is similarly unclear.

Diversity holds the future

Despite the progress, biological research has been made by focussing on a few select model species, and we now have the opportunity to look more broadly and test the generality of biological phenomena on a wider range of species. Genomic sequencing is now routine, facilitating the establishment of new model systems. Moreover, a balance is needed between uncovering more detail of one species versus discovering new phenomena and mechanisms in different species. This is particularly urgent at a time when we face catastrophic losses of species while searching for new biological resources to remediate anthropogenic impacts (Beattie 2013).