

Reaffirming the value of model organisms in training scientific minds

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As biomedical research prioritizes human models and translational promise, classic model organisms are increasingly dismissed. Here we argue that they have a lasting value, both in enabling discovery and in cultivating scientific thinking, by training researchers in systems reasoning, integrative thinking and independent inquiry.

Model organisms, in particular non-mammalian model organisms, such as yeast, *Caenorhabditis elegans*, *Drosophila* and zebrafish, have long stood at the centre of biological discovery, enabling insights into gene regulation, cell signalling, development and physiology, owing to their simplicity and experimental accessibility. These model organisms have revealed core biological mechanisms, driven technological innovation and shaped conceptual frameworks with broad applicability beyond themselves. The advantages of these model organisms include genetic tractability, short generation times, optical accessibility, and low experimental cost. These features have made them indispensable tools for systematic experimentation, hypothesis-driven inquiry, and identifying fundamental biological principles. In what follows, the term ‘model organisms’ refers to non-mammalian model organisms, unless stated otherwise.

However, in recent years, model organisms have been facing increasing scepticism. The emergence of technologies, such as gene editing, organoids, multiomics and artificial intelligence (AI), has led to questioning whether evolutionarily distant species can continue to meet the demands of studying biological complexity and clinical relevance. The advantages of model organisms, such as standardization, genetic accessibility and experimental efficiency, may be perceived as diminishing in relative importance, as comparable capabilities are becoming available in other organisms. These concerns are not limited to animal models. In plant biology, for example, *Arabidopsis* has seen reduced support with the perception that it is ‘done’, despite its continued relevance¹.

Although such perceptions are difficult to directly quantify, they are reflected in a noticeable decline in funding support for model organisms. By analysing US National Institutes of Health (NIH) R01 funding – the main source for investigator-initiated research support in the USA – we noted a decline in support for model organisms from 2000 to the present. The relative share of R01 grants allocated to yeast, *C. elegans* and *Drosophila* has steadily decreased in recent years (Fig. 1). This trend aligns with a previous analysis of NIH and US National Science Foundation (NSF) funding records, which identified a decrease in funding allocated to *Drosophila* research from 2003 to 2013². These patterns suggest that the research communities focused on these

organisms may either be shrinking or encounter increasing difficulty in securing support. This trend is consistent with shifting priorities that increasingly emphasize human relevance and translational outcomes, as formalized in recent NIH policies [prioritizing human-based research technologies](#) and [aligning funding mechanisms with this initiative](#).

In light of these perceptions and funding trends, it is timely to reconsider what makes model organisms valuable. This Comment challenges questions about their continued relevance and argues that their greatest impact lies not only in past discoveries but also in how they help to shape scientific thinking.

Model organisms as frameworks for scientific thinking

The contributions of model organisms to our understanding to biology are well established, from determining fundamental mechanisms and enabling technical innovation to revealing conserved principles and informing translational applications^{3–5}. However, one critical dimension remains underappreciated – their unique capacity to train scientific thinking and cultivate independent inquiry. By enabling an efficient transition from hypothesis to mechanism and from data to insight, model organisms help build the intellectual foundations that sustain innovation. Although there is certainly value in using more complex organisms in scientific training, model organisms provide a uniquely coherent and efficient platform to develop core research capacities.

What makes a model powerful is not merely its simplicity and conservation, but also its capacity to support discovery across scales and contexts. Such model organisms enable early-career scientists to pursue open-ended questions, refine hypotheses in real time, and engage in the full breadth of research, from design to synthesis. More than experimental tools, model organisms serve as cognitive frameworks that foster systems-level reasoning, hypothesis-driven thinking and scientific autonomy. The scientific capacities of questioning, reasoning and testing, which are cultivated through work with model organisms, are indispensable across all research fields.

Scientific training with model organisms

Building systems thinking across biological scales. Model organisms provide an exceptional platform for cross-scale, integrative biological research. They enable scientists to address a single question across several levels of organization – from molecules and cells to tissues and whole organisms. By revealing how individual components interact within broader systems, these models help to cultivate systems thinking, fostering the ability to identify causality and reconstruct biological processes across scales. For example, in our own work, we have used *C. elegans* to study the spatiotemporal dynamics and systems-level regulation of embryonic development, leveraging its transparency, invariant lineage and technological advancement. These features allow even a single researcher to trace gene expression dynamics across all cells, identify key genes, and examine their functions from single-cell behaviours to tissue-level patterns and whole-organism phenotypes⁶.

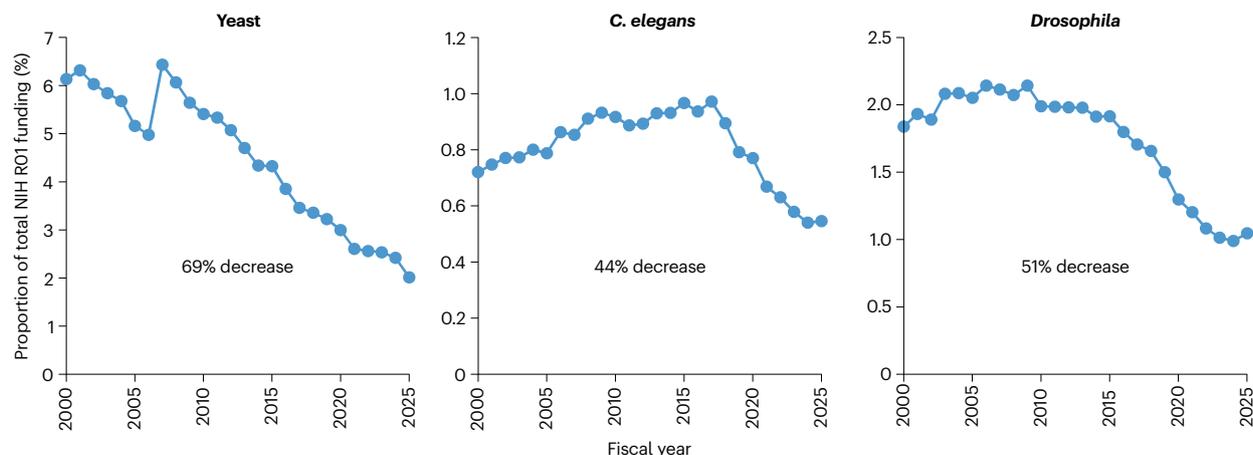


Fig. 1 | Decline in NIH R01 funding for yeast, *C. elegans* and *Drosophila*. Proportion of R01 grants from 2000 to 2025 (projected), based on keyword searches for organism names in project titles or abstracts from NIH RePORTER. Percentages indicate the projected 2025 decrease relative to each organism's highest level since 2000.

Furthermore, in zebrafish, transparent embryos enable the real-time monitoring of cell movement and physiological function, such as heartbeats or blood flow⁷. This type of cross-scale resolution is difficult to achieve in complex organisms and fosters a systemic view of biology by helping researchers connect molecular, cellular, tissue and organismal levels, and reason across the causal relationships that link them.

Developing conceptual reasoning via networked inquiry. Model organisms support in-depth mechanistic inquiry and also provide powerful platforms to investigate 'one-to-many' and 'many-to-one' regulatory relationships, forming interconnected networks of biological understanding. For example, early *Drosophila* screens identified key developmental regulators such as *hedgehog* and *wingless*, which were later found to act in diverse processes including cell fate decisions, polarity and regeneration³. Conversely, neurogenesis exemplifies many-to-one regulation, in which several pathways coordinate to drive a common developmental program. This enables researchers to trace how regulatory logic is reused across distinct processes, and how diverse pathways converge within a single organism, insights that are difficult to achieve in more complex or less tractable models. Such flexibility cultivates scientific breadth and the ability to synthesize connections across fields, by engaging with networks of inquiry that few systems foster as effectively as model organisms.

Training integrative reasoning within rapid hypothesis–test cycles. Model organisms uniquely support a rapid, iterative dialogue between theory and data that drives scientific progress. Their short life cycles and experimental responsiveness enable a fast transition from hypothesis to prediction to empirical test. In zebrafish embryos, injecting mRNA or inhibiting gene function can yield observable developmental phenotypes within hours to days, which facilitates rapid functional testing and hypothesis refinement. In yeast, the well-characterized metabolic network and facile genetics enable high-throughput hypothesis testing and regulatory model refinements through iterative experimental cycles. These organisms thus enable frequent loops of prediction, validation and revision, training researchers to build, test and improve conceptual models in real time. This helps to develop technical proficiency, and also fosters cognitive agility, the capacity to identify

logical gaps, adapt hypotheses, and construct coherent explanatory frameworks, as well as an appreciation that scientific knowledge is not linear but evolves by recursive reasoning and disciplined iteration.

Cultivating scientific autonomy through end-to-end research. Scientific competence lies not in mastering techniques, but in completing full research cycles, from posing questions, designing experiments, to generating and interpreting data, and constructing conceptual models. Model organisms make this possible at an individual level, whereas in more complex organisms, research is often distributed across several teams, limiting opportunities for individual researchers to experience the entire workflow. For instance, a single student working with *Drosophila* or *C. elegans* can design genetic crosses, visualize tissues, analyse behaviour, and validate molecular mechanisms, experiencing the full trajectory of scientific inquiry firsthand. This level of autonomy nurtures essential scientific instincts, such as identifying meaningful problems, linking data to mechanisms, and making conceptual leaps. It is the difference between working on one puzzle piece and considering the whole picture. Although both have value, only the latter trains researchers to be able to navigate complex systems.

Thus, model organisms not only train 'hands' but also cultivate independent thinking and help to develop scientific maturity (Fig. 2).

Model organisms shape scientific leaders

Model organism training has shaped generations of scientists, giving rise to at least three distinct types of scientific leader who have advanced biology in different but equally transformative ways.

The first includes pioneers who made foundational discoveries using model organisms and transformed modern biology, from identifying key regulators of the cell cycle to discovering microRNAs. Notably, 18 scientists working on *C. elegans* and *Drosophila* have been awarded 10 Nobel Prizes. In addition, research in yeast has contributed to 5 Nobel Prizes since 2000, including groundbreaking work on autophagy and vesicle trafficking.

The second group consists of researchers whose research remains within model organisms and who continue to drive innovation by building tools, developing theoretical frameworks, and pushing the boundaries of fundamental biology. At least 36 out of 273 current Howard

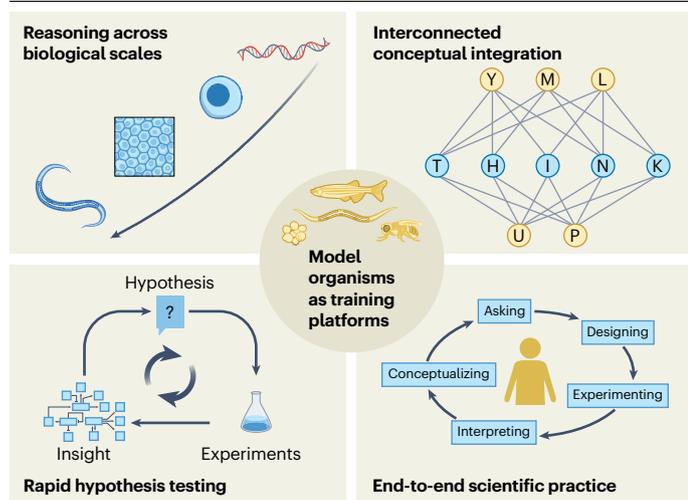


Fig. 2 | Model organisms as platforms for training scientific minds. Model organisms train scientific minds by enabling systems-level reasoning, conceptual synthesis, fast hypothesis testing, and independent research practice, shaping both discoveries and discoverers.

Hughes Medical Institute Investigators (~13%) conduct research using yeast, *C. elegans* or *Drosophila*, whereas researchers working with these models likely make up only ~4% of the broader US life sciences community. This value is based on PubMed queries of US-affiliated papers published since 2000: of approximately 1,150,000 articles containing ‘gene’ or ‘cell’ in the title or abstract, only 49,000 contained these organism names (4.25%). Although indirect, this provides a reasonable estimate of the representation of such research groups in the broader field. The resulting approximate threefold overrepresentation underscores the immense influence model organism research has on high-impact scientific recognition.

The third group includes scientists who began their careers in model organisms before transitioning to broader biomedical research, highlighting how early training in model organisms equips scientists for complex challenges. For example, John Sulston’s work mapping the complete *C. elegans* cell lineage and sequencing its genome^{8,9} laid the foundation for practices adopted in the Human Genome Project. C. David Allis started with pole cell studies in *Drosophila*, later turning to *Tetrahymena*, where he discovered histone acetyltransferases and helped to establish the field of epigenetics¹⁰. Michael Wigler’s early work on oncogenes in yeast set the stage for breakthroughs in cancer genetics¹¹. Christiane Nüsslein-Volhard made landmark discoveries in embryonic patterning through genetic screens in *Drosophila*, and later extended her work to zebrafish, establishing it as a key vertebrate model¹². Kathryn V. Anderson, who began her career working on *Drosophila*, is widely recognized for her pioneering application of forward genetics to discover genes essential for mouse development¹³. What unites many of these scientists is not just intellectual brilliance, but early immersion in environments that emphasized conceptual rigour, experimental iteration, and systems-level thinking, hallmarks of model organism training.

Model organisms still matter

In an era increasingly focused on human relevance and clinical translation, model organisms may seem peripheral. However, this perception

overlooks their deeper value, not only in what they model but in how they shape the scientific process itself. Overlooking this dimension risks weakening the very foundations of both scientific discovery and training. Clearly, human-relevant organisms, organoids and translational systems are essential. Equally important, however, is the cultivation of researchers with abstract reasoning, integrative thinking and independent problem-solving skills. These capacities are particularly well nurtured in model organisms, which provide environments that support both experimental practice and conceptual depth.

The training value of model organisms also extends to the grassroots. Programs that use *Drosophila* and *C. elegans* have empowered high-school and undergraduate students to engage in hands-on research, develop experimental and analytical skills, and build scientific confidence and identity^{14,15}. These programs also help to spark curiosity and foster lasting interest in science.

Importantly, model organisms are not static. Emerging models such as tardigrades, planarians and killifish are expanding the fields of stress, regenerative and ageing biology. Their rise reflects the evolving definition of model organisms and their continued role in training researchers to tackle new questions with creativity and rigour.

Although no longer in the spotlight, model organisms remain among the most effective environments for scientific training. Neglecting these organisms would not only limit what we study, but how we learn to study it. As such, model organisms are not the destination, but often where the journey toward deep biological insight begins.

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Competing interests

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Additional information

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