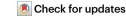
# Biologists should embrace Earth's biodiversity as a library of solutions

## Jason R. Gallant



Biological research focused on canonical research organisms can yield profound insights, but it can also obscure evolutionary context and hinder understanding of biodiversity itself. Biology researchers should tap the underutilized potential of Earth's biodiversity by matching the biological question to the organism best suited to answer it.

A pillar of modern biological and biomedical science has been the deep investigation of questions in a narrow set of 'canonical' research organisms (CROs), which include mice, frogs, zebrafish, flies, roundworms and yeast. These CROs rose to prominence owing to their ease of husbandry, genetic tractability and — crucially — the formation of large, active research communities that enabled the rapid development and sharing of tools and techniques. CROs have yielded profound insights into genetics, cellular and developmental biology, neuroscience and many other research areas.

As biology grapples with complex 21st-century grand challenges<sup>1</sup> such as understanding the brain, connecting genotype to phenotype, and maintaining biodiversity on a changing planet, reliance on a handful of organisms is no longer sufficient. The sustained dominance of CROs has blurred distinctions between general study systems and models of specific phenomena<sup>2</sup> – which encourages the misguided assumption that CROs apply universally. As Maslow warned "If the only tool you have is a hammer, it is tempting to treat everything as if it were a nail". Nearly 80% of therapeutic agents that are successful in mice fail in human trials<sup>4</sup>, often owing to fundamental differences in physiology. Highly inbred laboratory strains represent only a sliver of natural genetic<sup>5</sup> and microbial<sup>6</sup> diversity. CRO research communities often ignore the ecological, social and evolutionary context of organisms, which limits insights into variation, resilience and evolution. And because CROs are intentionally simplified and decontextualized, they offer little traction for understanding the origins, maintenance and consequences of biodiversity itself - a foundational challenge in biology. The US National Institutes of Health has even proposed shifting priorities towards "non-animal research methods", citing the translational limitations of CROs7.

Rather than eliminating animal-based research, it should be diversified beyond the canonical few organisms. Relying predominantly on traditional models overlooks the enormous biological innovation that can be found among roughly 8.7 million species: life has evolved innovations — disease resistance, novel metabolic pathways<sup>8</sup> and unique symbioses — that can offer solutions to urgent problems<sup>9</sup>. This logic is rooted in Krogh's principle, which states that "for many problems, there is an organism in which it can be most conveniently studied"<sup>10</sup>.

Crucially, this 'convenience' does not refer to ease of use or availability of tools (as with CROs) but to the fact that some organisms exhibit exaggerated, specialized or uniquely evolved versions of biological processes. These specializations often make the relevant phenomenon easier to observe, manipulate or understand than in generalist or less derived systems. For example, researchers studying diabetes turned to the Gila monster because this lizard maintains stable blood sugar during extended fasting, which yielded exendin-4 (now used to treat type 2 diabetes)<sup>8</sup>.

In the past two decades, technological advances — including genome sequencing, CRISPR–Cas9 editing and computational biology — have enabled researchers to choose the right organism for the right question. Still, major structural barriers deter researchers from developing nontraditional model systems.

One barrier is the entrenchment of CROs in biology education and research communities. CRO communities benefit from databases, optimized protocols and peer networks — assets that discourage the exploration of potentially more suitable species. Education must emphasize biodiversity, evolutionary biology and interdisciplinary thinking. Trainees should routinely ask 'What's the right organism for this problem?' Community building among researchers of different taxa is essential. In two decades of work with noncanonical species, I have observed common challenges — unknown life histories, husbandry difficulties and reagent shortages. Yet researchers often operate in isolation. Meetings focused on nontraditional models, such as Aquatic Models for Human Disease Conferences<sup>11</sup>, would promote cross-taxon problem solving and community cohesion.

Similarly, institutional support must evolve to facilitate the adoption of novel organisms. One powerful approach would be the establishment of centralized academic hubs or institutes that are dedicated to leveraging biodiversity to solve 21st-century biological problems. These centres would develop innovative, species-agnostic training programmes and tools that are tailored to the needs of emerging model systems. They could also house 'incubator' programmes designed to launch, nurture and sustain new model organism research efforts. Most current facilities are optimized for CROs, which creates substantial logistical barriers for researchers working with unconventional species. Purpose-built institutes could lower these barriers to entry by providing flexible, modular vivaria that are capable of supporting a broad range of aquatic and terrestrial organisms - from microorganisms and plants to invertebrates and vertebrates. Funding could involve partnerships among federal agencies, universities, technology transfer offices and industry partners, and tap into the commercial potential of discoveries made through these novel biological models.

Dedicated funding mechanisms should be established specifically to develop novel model organisms. Currently, biological sciences funding disproportionately supports CROs, which reinforces their dominance and limits opportunities for researchers who study nontraditional species. This imbalance is exacerbated, at least in the

USA, by grant review panels that are dominated by CRO researchers. Existing programmes can also be adapted to explicitly reward model diversity and reduce implicit biases. For instance, grant review panels could include experts familiar with unconventional systems — similar to recent National Institutes of Health efforts to incorporate specialists in non-animal research methods  $^7$ . This approach does not seek to create additional canonical organisms but instead promotes a flexible funding environment that encourages researchers to select organisms uniquely suited to specific biological questions, embracing Krogh's principle.

Finally, the community needs flexible, species-agnostic informatics platforms that can support any organism and be deployed easily and inexpensively. Existing databases — often built around a handful of model species using outdated systems — limit interoperability and collaboration, which leaves researchers who study other organisms at a disadvantage. Successful community efforts such as SequenceServer<sup>12</sup> and JBrowse<sup>13</sup> demonstrate how simple, accessible tools can transform research, and already serve hundreds of genomics communities worldwide. The next generation of platforms should go further by embracing modern approaches that take advantage of cloud providers (for example, Google Cloud, AWS (Amazon Web Services) and Microsoft Azure). Such systems would reduce operating costs and offer scalable, on-demand access to data and tools — enabling researchers to share results, connect across communities and accelerate discovery in both traditional and emerging model research organisms.

The next frontier of biology will not be found simply by doing more with the same few organisms. It will come from embracing Earth's biodiversity as a library of solutions — one that modern genomic tools have finally made accessible. The limiting factor is no longer technical; it is structural. By investing in the people, infrastructure and institutions that enable a broader range of model organisms, a more flexible, innovative and powerful research ecosystem can tackle the grand challenges¹ of 21st-century biology.

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Published online: 10 November 2025

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### Competing interests

The author declares no competing interests.