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Organisms as technologies between lab and field: The case of precision toxicology

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ISHPSSB, Porto, 20 July 2025

Our arguments today

- Precision toxicology (PT) as a case of doing lab work *with the explicit and short-term prospect* of implementing at scale in the field
- AI plays a crucial role in mediating this transition
- To understand this: focus on use of model organisms in this domain
- Raises important questions around the relation between lab and field, and prospects for future intersections of such research

Towards Precision Toxicology

The goal of PrecisionTox is to improve chemical safety assessment to better protect human health and the environment by using non-traditional test species, multiple fields of knowledge, and powerful computational approaches to understand which chemicals are toxic and why.

Annual Meeting 2023

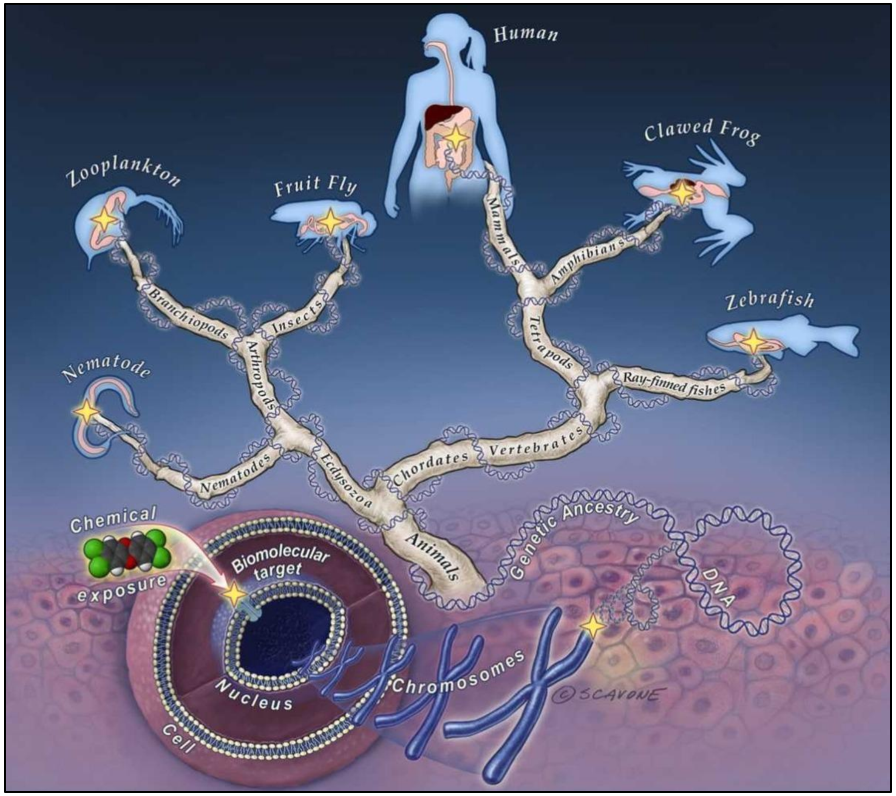
PRECISION
TOX

- Ideal space in which to investigate models due to diverse scientific sites (e.g., labs and real-world)
- Goal: to improve "chemical safety assessment using non-traditional test species, multiple fields of knowledge, and powerful computational approaches"

(Prec. Tox. Annual meeting 2023)

precision = focus on data-intensive and large-scale practices, enabled by high-tech data collection and AI-led analysis and multi-scale integration, to allow focus on variability to foster targeted and impactful interventions

Three Uses of Model Organisms



Source: www.sciencedirect.com/science/article/pii/S0378427423001807

- **As models of toxic effects:** e.g., nematode used as inexpensive and fast tracker for neurotoxicological impacts of chemicals on development
- **As 'sentinels':** more sensitive than humans to chemical exposures (even at sublethal levels) and evidence readily detectable effects
- **As bioremediators that become research targets** (e.g., filtering wastewater)

Ankeny, RA and Leonelli, S (forthcoming) Model organism futures in precision toxicology: Tracking the emergence of a research repertoire. *Biology & Philosophy*

Three Uses of Model Organisms

Water fleas as 'canaries in a coal mine' offer key to managing chemical pollution

CURRENT PROTOCOLS

OVERVIEW | Open Access

Perspectives on the *Drosophila melanogaster* Model for Advances in Toxicological Science

Matthew D. Rand, Jason M. Tennessen, Trudy F. C. Mackay, Robert R. H. Anholt

First published: 28 August 2023 | https://doi.org/10.1002/cpz1.870 | Citations: 2

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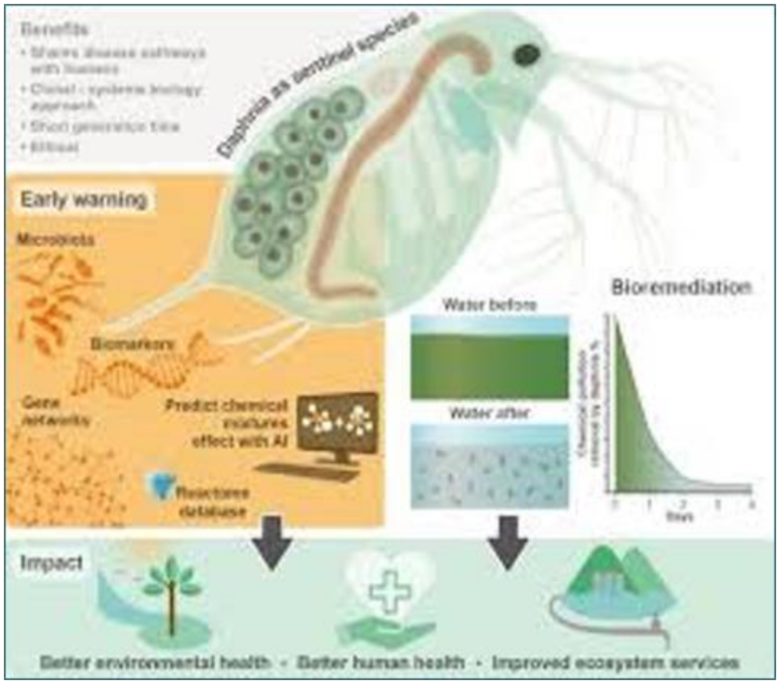

Source: mole-sept-2022.pdf (birmingham.ac.uk)

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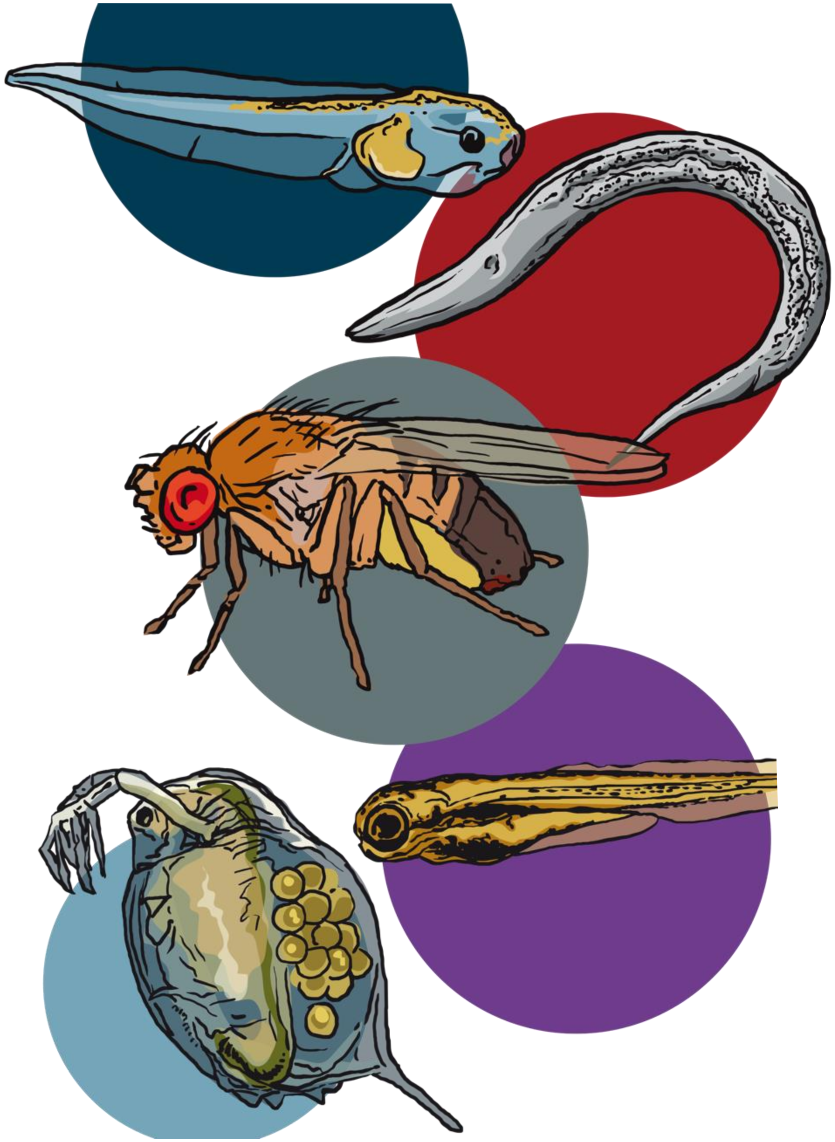
What are MOs modelling here?



Source: https://precisiontox.org/project/

- effects of toxicity levels on more complex organisms and entire ecosystems
- “toxicity by descent”: Reframe evolutionary history in terms of organisms’ changing capacities to react to chemical stress (Coulbourne et al. 2022)
- decontamination and monitoring interventions

Under which conditions is modelling carried out? The case of *Daphnia*

Lab assays to detect heavy metals, pesticides, nanoparticles, pharmaceutical products:

- **Acute toxicity assays** exposing Daphnia to high concentration of substance over a short duration (24-48 hours): primary objective is to determine immediate effects and lethal concentrations (LC50) of substance on the organisms → **to identify immediate risks**
- **Chronic toxicity assays** with prolonged exposure of Daphnia to lower concentrations of a substance over an extended period (multiple generations) → **to assess longer-term risks (incl. developmental and ecological)**

(Ahmed 2023, Applications of Daphnia magna in ecotoxicological studies)

https://pennstatehealthnews.org/2025/01/revolutionizing-environmental-research-first-daphnia-histology-reference-atlas-published/

In silico, data-driven risk prediction: Scalable longitudinal monitoring of Daphnia

- track cohort until their natural deaths using a **computer vision algorithm that quantitatively extracts a representation** of the location and behavioral parameters of individual animals in culture tanks
- **machine learning** provides methodologies for analysis and practical use of collected multi-dimensional phenotypic information
- **major strength of ML:** identification of relevant patterns within complex, nonlinear data without need for *a priori* mechanistic understanding of underlying aging processes, and iteratively improvement of predictive performance of models

"We therefore used extracted features to train a supervised machine-learning algorithm to predict phenotypic age and compare to chronological age. We found that our predictive model was able to accurately estimate phenotypic age that might reflect animals' health states." (Cho et al. 2022)

Beyond lab-based measures of toxicity

Observations of *Daphnia* behavior, including swimming patterns, feeding, avoidance responses, can provide insights into sublethal, yet toxic, effects

- **Lab-based:** Reproductive and developmental assays
- **Prospects for field-based studies:** "Understanding the ecological role of Daphnia magna is essential for conservation efforts and ecosystem management. Research on its interactions with other organisms, response to pollutants, and adaptations to environmental stressors provides valuable insights into mitigating the impacts of anthropogenic activities on aquatic habitats" (Ahmed 2023)

Image: Daphnia behavior analysis - ViewPoint

Continuities

with MO research:

- the organisms themselves
- use of infrastructures, data collections, molecular methods
- large-scale omics data mining

with traditional toxicology:

- commitment to speed, low cost, rapid throughput, precise chemical screening in terms of impacts on health and environment
- embedding of regulatory/policy considerations from the start

What is new? (1)

with respect to MO research:

- use or organisms as research target, medium/instruments, detection tools for broader environmental effects
- focus on organism as responsive to broader, highly variable environment
- increasing attention to individual and environmental variability
- novel goals (e.g., addressing pollution, climate change)

Prospect: Realistic field conditions subject to rapid and unpredictable change

What is new? (2)

with respect to traditional toxicology:

- *Going beyond* what is toxic to humans: focus on non-human responses to environmental stressors (and what they may signify for human health)
- New organisms (beyond rodents): much cheaper and more tractable for later analysis
- Diverse uses of organisms, including for bioremediation
- Opportunity for novel theoretical contributions to evolutionary ecology

Prospect: Field as laboratory as well as instance of 'wild' (uncontrolled) environment

So what is the ‘field’ for PT? (1)

For now:

- laboratory studies importing samples from the wild from more complex aquatic ecosystems
- tracking multi-generational exposure to uncover eco-evolutionary effects
- in silico studies powered by data-intensive AI

“The research findings revealed that traditional toxicity assessment setups may not fully provide a base to capture the complexity of occurring toxicity. Therefore, the study proposes deviations from standard test protocols and emphasizes the need for holistic models that consider multiple factors to accurately assess toxicity risks in aquatic environments” (Paylar 2023)

So what is the ‘field’ for PT? (2)

Future prospect: release of MOs in the wild (uncontrolled field conditions)

- crucial for bioremediation
- permits study of MO behavior and broader ecological/developmental impacts of environmental exposure

“Expanding the use of *Daphnia* beyond its current applications in regulatory toxicology has the potential to improve both the assessment and the remediation of environmental pollution” (Abdullahi et al. 2022)

Conclusions: How may the emergence of PT shape researchers' relationships to the field?

What could PT involve in terms of

- preparing the field?
- preparing *for* the field?
- managing the field?
- interpreting field results?

More and new collaborations with field-based researchers!

(cf. work with Emma and Daniele on pest-plant interactions:

Cavazzoni E, Leonelli S, Giannetti D, Patelli N, Vaccari G, Maistrello L, Pinotti MC, 2025 Monitoring Technologies for Pest-Plant Interactions: The Need for Transdisciplinary Research Design. EMBO Reports)

Thank you for your attention!

Philosophy of Open Science

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How living things help us to understand our world

- Ankeny, RA and Leonelli, S (in preparation) Repertoires: Making Sense of Scientific Change in Theory and in Practice. *Monograph*.
- Ankeny, RA and Leonelli, S (forthcoming) Model organism futures in precision toxicology: Tracking the emergence of a research repertoire. *Biology & Philosophy*
- Ankeny, RA and Leonelli, S (2020) Using Repertoires to Explore Changing Practices in Recent Coral Research. In: Matlin, K., Maienschein, J and Ankeny, R *From the Beach to the Bench: Why Marine Biological Studies?* University of Chicago Press, pp. 249-270.
- Ankeny, RA and Leonelli, S. (2016) Repertoires: A Post-Kuhnian Perspective on Scientific Change and Collaborative Research. *Studies in the History and the Philosophy of Science*.

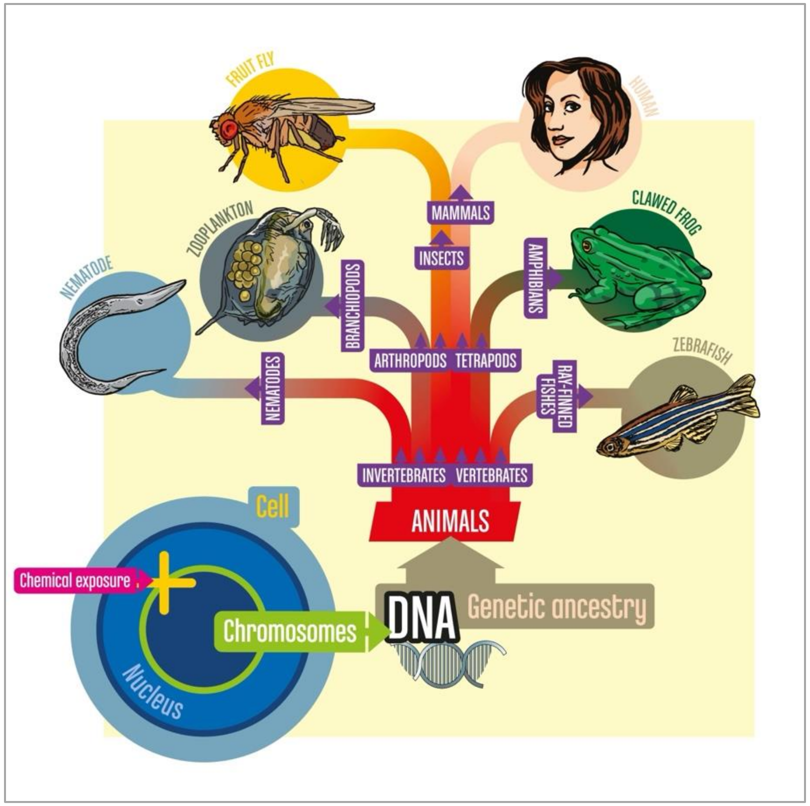
SUBMITTED ABSTRACTS

This paper explores an emerging set of scientific practices associated with the use of model organisms in toxicological bioremediation both as tools and as representations. Organisms such as Daphnia are developed and used as technologies to monitor and assess chemicals in polluted waters, and hence serve as sentinel species and diagnostic agents. They also can be used for bioremediation for instance to reduce hazards in chemical mixtures contained in waterways in the environment. At the same time, organisms thus instrumentalised are studied to assess which strains are most well-adapted to chemical pollution – with the ultimate goal to develop models for reduced chemical sensitivity that can be projected onto and investigated in other organisms, notably humans. Hence in this domain, these organisms bridge the field and the lab through the simultaneous use of novel data-intensive approaches appropriate in complex real-world settings and of traditional practices and understandings associated with model organisms from the lab. We argue that such organisms can be viewed as material technologies that nevertheless retain their representational power, and provide an important example of a type of hybridity that will be increasingly common as field-based research leverages the knowledge, data, and technologies created in lab settings.

Using DEKI to track scientific change

- Modelling practices and assumptions continuously change, with implications for what counts as good science – how to track this process?
- DEKI used as we propose highlights how *plausible modelling is grounded on specific commitments*, which are historically evolved and motivated to support use of specific key in matching properties of model with properties of target
- Tracking of repertoires fosters better understanding of how keys are chosen, justified and changed over time and space
- In turn, tracking of keys in turn helps understanding of how repertoires absorb new elements, are challenged and evolve

Model Organisms in Precision Tox



- Five model species (‘NAMs toolbox’)
- Aim is to produce comparative data about evolutionary origins of biomolecular interactions predictive of adverse health effects
- Key goal is to identify conserved toxicity pathways and understand their significance to human health, including variations in individual susceptibility
- Highly interdisciplinary and porous domain: overlaps in methods/concepts with medicine, environmental science, marine biology, chemistry, and numerous other fields

Source: https://precisiontox.org/project/

What do MOs represent?

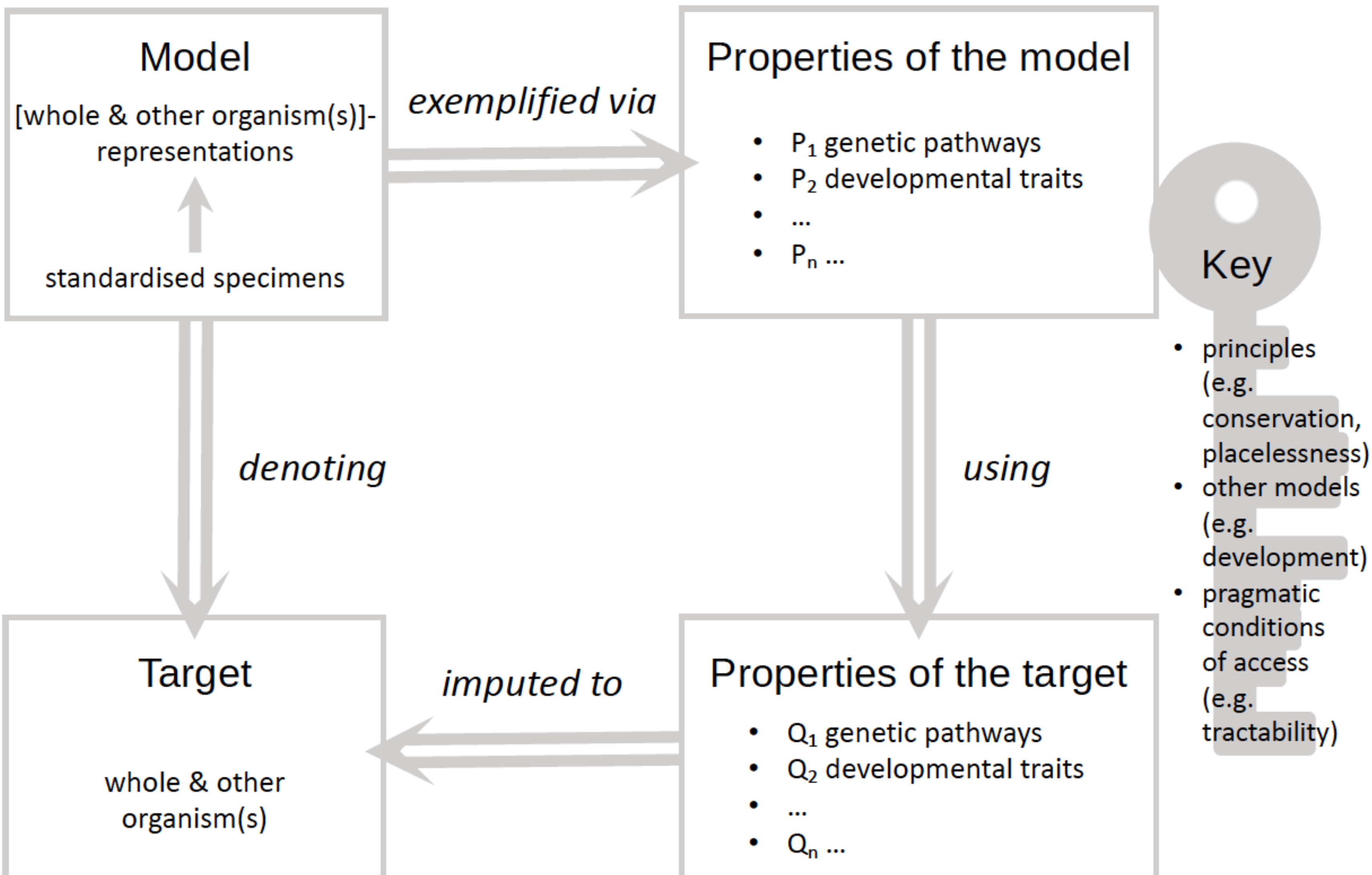
- Artefacts *and* samples of nature, key components of a distinctive way of doing research
- Help create knowledge that can be projected beyond its immediate domain
- Projection occurs in terms of
  - range of organisms being represented ('representational scope')
  - type of phenomena MOs are used to study ('representational target')
- Distinctive representational power stems from the simultaneous attribution of wide representational scope ***and*** wide representational target

(Ankeny & Leonelli 2011, 2020)

How do MOs represent?

- Specimens (displaying broadly similar phenotypic properties) constitute the material object that functions as a model
- Crucial assumption: selected properties of the object represent properties of assumed target, exemplified by specific properties of the model
- Object is thus interpreted as a type of representation for the intended target (‘standardised specimens’ are a ‘whole and other organism(s)’-like representation)
- Researchers impute these properties to their target, thus solidifying the representational relationship between model and target

How do MOs represent?



(Ankeny and Leonelli 2020, application of Frigg and Nguyen 2018)

How do MOs represent?

- Crucial assumption: properties of the model singled out by researchers, such as conserved evolutionary pathways, can *plausibly* be attributed to the target
- What makes this possible is commitment to a *key:* allows comparison of properties of the model (P) and properties of the target (Q)
  - helps to avoid confusion between the object that embodies the model (the organisms and their properties $P_{1,}$ $P_{2,\,..}$) and the phenomenon being investigated (specific clusters of properties attributed to a wide range of organisms and to organisms as intact wholes)

What makes MOs into *plausible* representations/models?

- Plausibility: degree to which researchers deem the use of a specimen as a model for a given phenomenon or group of organisms to
  - be acceptable to their peers;
  - fit within an epistemic space (Rheinberger 1997, 2010) and system of practice (Chang 2012, 2022)
  - make it possible to rationalise and justify commitment to that organism

- Necessarily *dynamic*
  - encompassing a spectrum of plausibility which can vary from low to high, and evolves in tandem with practices and conceptual underpinnings

- *Choice of key depends on what is plausible*, which in turn depends on association with a *repertoire* (blueprints for specific ways of doing science, Ankeny and Leonelli 2016, 2020) encompassing
  - habits/assumptions built into model organism (and other relevant) communities
  - physical and abstracted/attributed features of the model (as it becomes standardised)
  - acceptable goals and conditions for research

Components of MO repertoire (1)

CHARACTERISTICS OF THE ORGANISM	**Natural or intrinsic**	Tractability in the lab Length of life cycle Fertility rates and ease of breeding Size of organism Ease of storage Size of genome Physical accessibility of features of interest
	Induced/uncovered through experimental interaction and transfer to lab	Mutability of specimens Response to lab environment (food, light, temperature, cages, routine) Availability of standardised strains
	Attributed to or projected onto the organism by researchers	Representational scope (how extensively the results of research with the organism can be projected onto a wider group of organisms) Representational target (number of phenomena that can be explored via the organism) Power as genetic tools Ability to serve as the basis for comparisons to other organisms Multi-disciplinary usefulness (capacity to fit different research domains, e.g. genomics, development, and physiology) leading to cross-level integration

Components of MO repertoire (2)

CHARACTERISTICS OF THE COMMUNITY	**Conceptual commitments**	Evolutionary conservation Holistic, inter-level approach to organisms Focus on organisms in isolation from environment
	Available technologies	Well-developed community databases Fit with available instruments and tools (e.g., sequencing techniques)
	Shared skills and practices	Commitment to free exchange of materials, data, and knowledge Ability to move across biological subfields (and related instruments, terminologies, and standards) Public relations skills in attracting funding and attention from outside the scientific community
	Institutional organization	Charismatic leaders with strong organisational and scientific skills Efficient and accessible stock centres Common communication venues and institutions (e.g., steering committees, journals, community databases, organism-focused conferences)
	Dependable funding sources	Long-term support from governmental funding Strategies to secure that funding

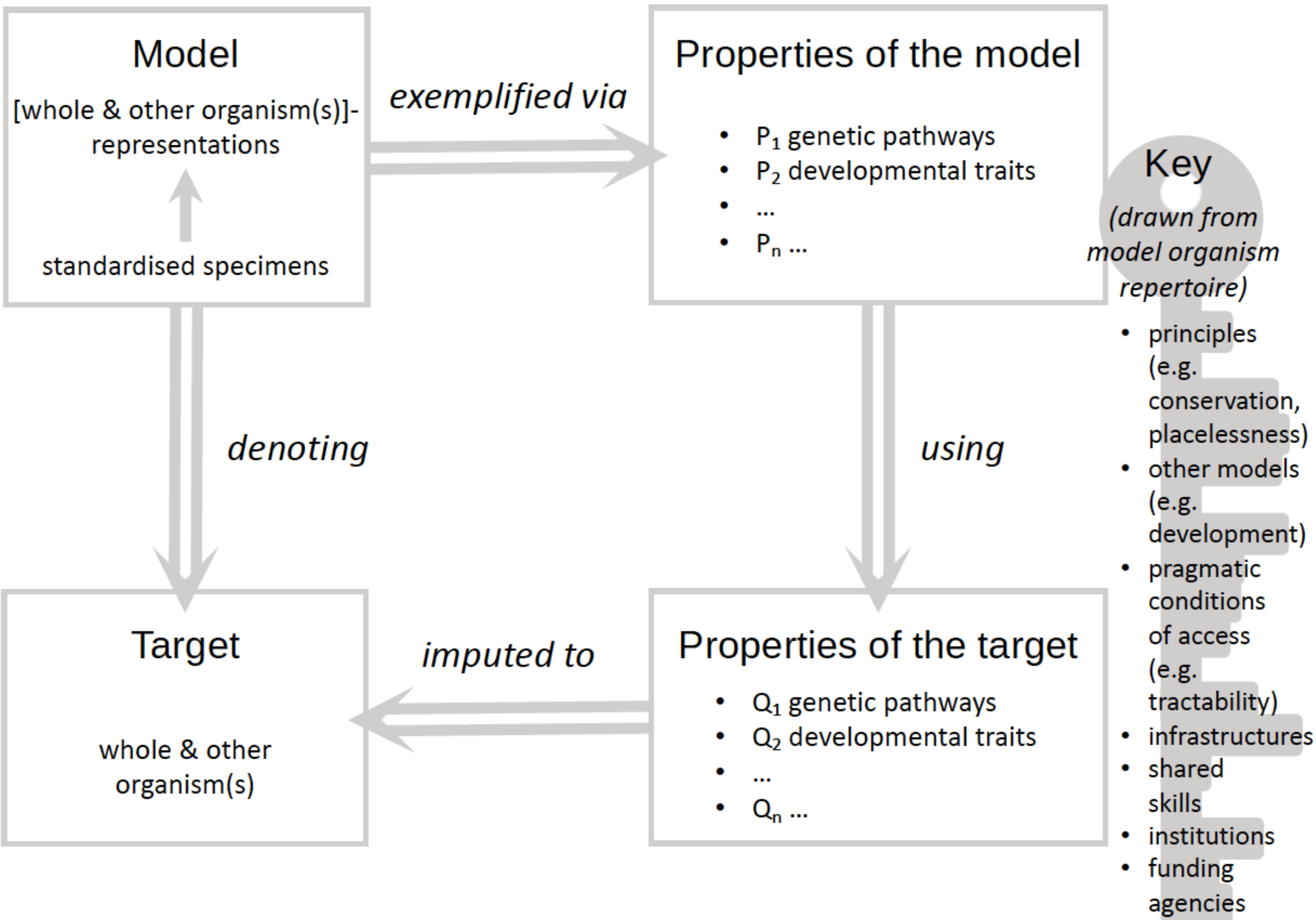
Components of MO repertoire (3)

CHARACTERISTICS OF THE BROADER LANDSCAPE	**Fit with political and social goals**	Vision of basic molecular research as grounding innovation in medicine and agriculture
	Intellectual property regime	Free or otherwise well-regulated exchange of materials, techniques, and data

Thus MO repertoire includes

- the concept of *one* 'model organism' as reference for other species
- production, use, dissemination of standardised strains
- relevant know-how, expertise, protocols, instrumentation, (critically) large-scale data collections
- ethos of sharing data and techniques prior to publication
- establishment of infrastructures including databases and stock centres
- long-term, blue-skies funding (via the HGP)

MO Repertoire: the key for MOs to plausibly function as models



(Ankeny and Leonelli 2020, application of Frigg and Nguyen 2018)

What happens when the key starts to look less plausible?

Problems with MO repertoire, e.g.:

- How to understand **biodiversity**? Implausible and increasingly unnecessary restriction to one species (and often one strain/variety/ecotype)
  - Increasing emphasis on cluster of variants of same species, comparisons between wild and domesticated samples
  - Next-gen methods allow for faster analysis of broader set of organisms, e.g. precision agriculture
- How to understand **health x environment** interactions?
  - Analysis of environmental stressors requires broader repertoire including cross-species comparisons and sensibility to ecosystem interactions