



## What's so special about model organisms?

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### ABSTRACT

This paper aims to identify the key characteristics of model organisms that make them a specific type of model within the contemporary life sciences: in particular, we argue that the term “model organism” does not apply to all organisms used for the purposes of experimental research. We explore the differences between experimental and model organisms in terms of their material and epistemic features, and argue that it is essential to distinguish between their *representational scope* and *representational target*. We also examine the characteristics of the communities who use these two types of models, including their research goals, disciplinary affiliations, and preferred practices to show how these have contributed to the conceptualization of a model organism. We conclude that model organisms are a specific subgroup of organisms that have been standardized to fit an integrative and comparative mode of research, and that it must be clearly distinguished from the broader class of experimental organisms. In addition, we argue that model organisms are the key components of a unique and distinctively biological way of doing research using models.

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### 1. Introduction

In the past ten years, particularly since the advent of the large-scale genomic sequencing projects associated with the Human Genome projects, the term “model organism” has become ubiquitous in contemporary biological discourse. It is extremely difficult to trace the precise point in history at which the actual term “model organism” was introduced; however it is clear that it was not in common use in scientific literature as recently as the late 1980s, based on a systematic review of the scientific literature using major search engines. The underlying concept of a “model organism” can be traced to a variety of sources, depending on how one defines it, as will be discussed in this essay.<sup>2</sup> In the most general terms, model organisms are non-human species that are extensively studied in order to understand a range of biological phenomena, with the hope that data and theories generated through use of the model will be applicable to other organisms, particularly those that are in some way more complex than the original model. They also have a

variety of experimental advantages; notably they are easy to breed and maintain in large numbers under laboratory conditions. The most widely acknowledged inventory of these organisms includes those that have been officially recognized by the U.S. National Institutes of Health as model organisms for biomedical research; their list includes thirteen species such as mouse, rat, zebrafish, fruitfly, nematode worm, and thale cress (NIH, n.d.; see also NCBI, n.d., NIH, 1999).

Currently the term “model organism” not only serves as a descriptor for organisms that have certain attributes, but it also has gained prescriptive power. Many research groups increasingly are experiencing pressures as a result of the popularity of the term, for instance due to competitive granting systems that force researchers to focus on these organisms or to rationalize any proposed research work on a particular organism by claiming that it is, in some sense, a “model organism” (e.g., Maher, 2009; Slack, 2009; Sommer, 2009). Some critics have argued that the model organism concept is “swamping out” contemporary biological research

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<sup>2</sup> For an early conceptual examination of model organisms as model systems, see Gest (1995). An exploration of how the term ‘model system’ maps onto the term ‘model organism’ is beyond the scope of this paper, particularly given the diverse definitions of model system.

agendas, making it difficult to pursue (or, more precisely, to get funding to pursue) any sort of biological research on organisms not considered to be model organisms (Gilbert, 2009). Thus perhaps not surprisingly, the term “model organism” is being used more frequently and to describe any experimental organism utilized to investigate a particular biological process or system. Examples of this tendency include the recent laboratory manuals on “emerging” model organisms ranging from honeybee and bat, to yam and tomato, finch to quail, snail, and even wallaby (Cold Spring Harbor Press, 2009, 2010).

However, should *any* experimental organism truly count as a “model organism”? The answer to this question has clear political and economic implications, to which we return in our conclusions. But the main focus of this paper is to provide an argument in favor of a particular characterization of the term “model organism,” against the backdrop of the use of organisms in experimental practice, with special attention to the sense in which model organisms serve as “models.” In what follows, we first examine the use of experimental organisms and the ways in which these can be viewed as serving as models. We then defend a more detailed and selective set of characteristics that apply not to all organisms that enter the biology lab, but more specifically to the group of organisms which became especially popular and central to biology during the second half of the 20th century, namely model organisms. We analyze the material, social, and epistemic features of these organisms<sup>3</sup> and the communities who adopted them, and conclude that this class of organisms can be clearly distinguished from the broader class of experimental organisms in several critical respects that relate to how they serve as representations. In addition, we argue that model organisms represent a unique way of doing research using models, and that it is distinctively biological.

## 2. A brief history of experimental organisms

It is undeniable that selective use of various species has been critical in many fields of biology for centuries.<sup>4</sup> The most commonly cited slogan associated with this experimental practice is ‘For a large number of problems, there will be some animal of choice, or a few such animals on which it can most conveniently be studied,’ dubbed subsequently the August Krogh principle (Krogh, 1929; see also Jørgensen, 2001). This principle was made more specific by Hans Krebs (1975) who noted that characteristics that often made experimentation easier included the organism being an appropriate size and having a convenient anatomical arrangement in relation to the process to be studied.

Which organisms prove to be useful (sometimes described as a “wise choice” or “the right organism for the job”) is a function of several features: these include not only their biological suitability and ability to be “tamed” to serve as standardized research materials, but also the questions or phenomena to be investigated, and the techniques and practices available that will allow the question of interest to be answered (e.g., Burian, 1993; Clarke & Fujimura, 1992). In some famous cases, the selection of particular organisms for certain research projects was somewhat fortuitous rather than carefully planned, as the choice was made primarily because the organisms were already in use or were in some other way familiar

to the researchers. For instance, much research with mice, rats, and frogs might fit this description. Researchers working on thale cress have actually referred to the initial choice of the plant as “fortunate,” since several of its advantageous features only emerged in retrospect (Sommerville & Koornneef, 2002).

The usual list mentioned in historic discussions of biological organisms particularly well-suited for research purposes includes the sea urchin (and its eggs) for the study of a variety of developmental phenomena (e.g., see Ernst, 1997; Laubichler & Davidson, 2008; Maienschein, 1991); the investigation of *Planaria* (flatworms) for the study of inheritance (Mitman & Fausto-Sterling, 1992); the study of photosynthesis using *Chlamydomonas reinhardtii*, a unicellular green algae (Zallen, 1993); *Dictyostelium discoideum*, or slime molds, for the study of cellular differentiation and communication (Bonner, 1999; Sunderland, 2008); the sea slug *Aplysia* for neurobiological studies (Kandel, 2007); the use of pigeons, and in particular their breast muscle tissue, to study oxidative metabolism (Krebs, 1975); the dog to study physiology (Todes, 2001) as well as transfusion and other practices in hematology (Degeling, 2008); the mouse in fields ranging from physiology to immunology and oncology (Rader, 1998); the rat in nutrition, neurology, and behavioral psychology (Clause, 1993; Logan, 2001, 2002, 2005); and the tobacco mosaic virus in the molecular study of RNA (Creager, 2002), just to name a few.<sup>5</sup>

The guinea pig was an early example (starting in the 17th century) of the use of a specific organism to investigate particular phenomena, including anatomical structures, and later as an essential part of experimentation that led to the establishment of the germ theory, as well as the discovery of vitamin C, the vaccines for diphtheria and cholera, and various toxicological experiments (Bynum, 1990; Endersby, 2007; Guerrini, 2003; Löwy, 1992). In these research projects, the guinea pig was chosen because it was readily available; it also seemed to have the relevant characteristics needed to study the particular process or disease in question (e.g., unlike pigeons, guinea pigs acquire scurvy-like diseases when subjected to particular types of diets). Its long gestation and relatively low birth rates meant that it was displaced by the mid-1900s by mice and rats, particularly as genetic investigations became more prominent. Nonetheless in all of these experiments, the guinea pig was recognized as an acceptable proxy for higher level organisms, particularly human beings, especially in cases where testing of interventions or therapies at an early stage of development would be unethical.

Perhaps one of the most prominent examples of an experimental organism is the use of the frog for the study of muscle action and electricity, circulation, and respiration, among other phenomena (Holmes, 1993). Dating well back to Marcello Malpighi in the late 1600s (and perhaps arguably based on a basic recognition of the usefulness of particular experimental organisms as proxies which can be traced back to Aristotle), the frog is used because it is considered to be a more experimentally tractable and accessible version of a mammal than other possible experimental organisms (Holmes, 1993). In Malpighi’s research, although the frog’s lungs were much more structurally simple than those of mammals, the facts that they looked similar and had comparable basic structures particularly in relation to the circulatory system, meant that their

<sup>3</sup> This basic idea of a tri-partite characterization of model organisms is implicit in Gilbert (2009) but not explored in any detail by him.

<sup>4</sup> Although not part of our main argument here, it is important to note that in longer-range historical terms, the move to comparative biological approaches evidenced in contemporary model organism work could be viewed as a re-emergence of an alternative form of an existing research tradition that preceded the more “experimental turn” usually dated to the late 1800s and early 1900s (see e.g. Clarke, 1987; Logan, 2001). In addition, there were previously close links between a variety of disciplines or fields, particularly in terms of their “problem structures” (e.g., reproductive sciences, embryology, heredity, and evolution, see Clarke, 1991), which was in turn followed by the rapid growth of each of these disciplines that tended to move in separate directions. The emphasis in current model organism approach on unifying a range of disciplinary approaches also can be viewed within this broader historical context as a return to a pre-existing style of practice. On the “pre-history” of model systems and the basis of claims about universality in this era, see Churchill (1997); on related historiographic issues, see Laubichler & Geison (2001).

<sup>5</sup> For overviews of experimentation on non-human animals including discussions about techniques, disciplinary approaches, and the conceptual basis of the assumption that projections could be made from experimental organisms to other targets, particularly humans, see e.g. Asdal (2008); Bynum (1990); and Guerrini (2003).

structure and function could serve as proxies for studying the lungs in “higher level” organisms.

### 3. But aren't experimental organisms “models”?

So aren't experimental organisms a form of model? All experimental organisms indeed can be conceptualized as models in a very broad sense: they involve the choice of a certain organism that provides a means for experimental, controlled exploration of a particular biological phenomenon or a specific research question that it is hoped will serve as the basis for findings about that phenomenon which will apply or hold across a class of organisms. Here we wish to emphasize two critical dimensions that underlie the way in which experimental organisms serve as models: the concepts of “representational scope” and “representational target.”

We use the term “representational scope” to describe how extensively the results of research with a particular experimental organism (a specimen or token) can be projected onto a wider group of organisms (a type). The projection can vary in its scope, ranging from a single species for which the experimental organism is serving as a proxy (notably *Homo sapiens*), to a wider class of organisms such as a family or a kingdom (e.g. mammals, or animals) or perhaps even to all organisms. The extent of representational scope being assumed is closely related to the criteria for the selection of the experimental organism in the first instance, together with the question to be investigated. Admittedly the criteria by which claims of representational scope prove to be valid are often external to the research project, relying on a sort of promissory note or assumption on which the project hinges; nonetheless they are a critical part of such research.

Second, we utilize the term “representational target” to indicate the phenomena to be explored through the use of the experimental organism. By “phenomena,” we refer to the labels used by researchers to define concepts, entities, and processes related to their research interests. Our definition of phenomena is broadly inspired by the account provided by Jim Bogen and Jim Woodward (1988), yet for the purposes of our argument we do not wish to take sides on the debate surrounding their distinction between phenomena and data (e.g., Glymour, 2000; Massimi, 2007; McAllister, 1997). Whether understood as observable or unobservable, deeply theory-laden, or “mirroring” reality in an objective way, phenomena constitute for us the object of scientific claims. Thus, anything from “metabolism” to “UFO gene” constitutes a phenomenon and can become the representational target for an experimental organism.

Despite its breadth, our definition of phenomena as targets of a model can be clearly distinguished from our concept of representational scope: while the representational target describes the conceptual reasons why researchers are studying a given organism, the representational scope defines the extent to which researchers see their findings as applicable across organisms. Our use of the notions of representational scope and representational target broadly parallels the account of models found in the “models as mediators” account defended by Mary Morgan and Margaret Morrison (1999). The notion of mediation is used to suggest that a model serves ‘both as a means to and as a source of knowledge’ (Morrison & Morgan, 1999, p. 35): models constitute the meeting point between knowledge and reality, thus providing ‘the kind of information that allows us to intervene in the world’ (Morrison & Morgan, 1999, p. 23). In this same sense, experimental organisms are models that mediate between theory and the world. The theory or question to be investigated is the representational target and the “world” that the model represents can be defined in terms of its representational scope. Such scope may be quite delimited, for instance to understanding the phenomenon in question within a cer-

tain group such as mammals, or much broader. So in the case of the frog, the frog is a tool used to study and hence to represent the phenomenon of respiration (the target of interest) and it is also taken to be representative of how respiration works in mammals (the representational scope of the research).

It must be noted that although our interpretation is in broad agreement with Morgan as well as Evelyn Fox Keller about the need to focus on how models are used in practice, it does not map easily onto a distinction used by Morgan as well as Keller with regard to the representational functions of organisms. They both draw a distinction between the notions of “representative of” versus “representative for.” In Morgan's account (2003, p. 230; see also her 2007), the distinction captures a difference in the scope of the representation: “representative of” indicates a narrow, endogenous scope, while “representative for” stands for broad exogenous scope (e.g., the laboratory mouse is representative of mice and may be representative for humans). This distinction is compatible with our account with regard to the concept of “representational scope”: it does not apply to what we call the representational target. Keller's account (2000) differs from Morgan's insofar as it focuses on the purposes for which a model is used (which she calls “representative for,” as opposed to being “representative of” specific phenomena) (cf. also Bolker, 2009). Again, however, Keller's account does not capture the difference between the target and the scope of the model, which we believe to be crucial to distinguish when considering the epistemic functions of organisms in the lab.

Before moving onto an analysis of the difference between experimental and model organisms, it also is important to note that both the representational scope and the representational target of an organism can vary during the process of research. Indeed, Hans-Jörg Rheinberger (1997) as well as Morgan (2003, see also her 2005) and Keller (2002) point to a model's ability to “surprise” researchers and lead them in unexpected directions as one of the main attractions of working on real organisms in the lab. Experimental organisms are simultaneously samples of nature and artifacts: they are systems that have been engineered and modified to enable the controlled investigation of specific phenomena, yet at the same time they remain largely mysterious products of millennia of evolution, whose behaviors, structures, and physiology are for the most part still relatively ill-understood by scientists. Through this hybrid status as both natural and artificial objects, experimental organisms facilitate exploratory research by enabling biologists to ask questions without necessarily having clear expectations about what answer they will obtain or even about what questions will end up being the focus of inquiry (on the theoretical issues associated with this type of “exploratory experimentation,” see Burian, 1997; O'Malley, 2008).

Coming back to our analysis of experimental organisms, we can now see how they can be characterized as functioning as scientific models in the laboratory. On the one hand, they model a range of organisms beyond themselves, a range that varies depending on the context and which defines their representational scope. On the other hand, they model specific phenomena that constitute their representational target. The investigation of phenomena typically involves asking questions that are phrased within certain disciplinary approaches and pursued using the techniques associated with those disciplines; accordingly, the representational target of experimental organisms tends to be well-defined and characterized along specific disciplinary lines. For example, a frog can constitute a model for how respiration works, which in turn involves reference to physiology and anatomy as the main disciplinary approaches guiding the use of the frog in the laboratory.

Model organisms also serve as models that can be described within the “models as mediators” account: they share the same characteristics that are present in experimental organisms, notably

that they are tractable systems that allow close study of particular biological processes in laboratory settings where variations have been eliminated or closely controlled such that more general conclusions can be drawn about how these processes work and what the theories underlying such processes might be. In this sense, model organisms are part of the more general class of experimental organisms. However, the “models as mediators” account is very permissive, and potentially applies to an enormous range of types of representations, both physical and biological. Although this breadth is one of its main strengths, this account does not provide a systematic study of variability among models. This gap is arguably due in part to the fact that it overlooks a crucial feature of the research context in which models are employed, namely the epistemic goals envisaged by the investigators.<sup>6</sup>

All scientists make specific choices about what they wish to achieve when pursuing a particular research project, and such choices inform the whole research process, including the selection and use of assumptions and techniques. As we argue in later sections of this essay, the epistemic goal that is shared by researchers who pursue model organism work is that they are seeking to contribute to the construction of integrative models for whole, intact organisms, using a variety of disciplinary approaches, with the long-term hope of contributing to large-scale comparative work across these organisms.<sup>7</sup> Hence, as we argue in the next three sections, both the representational scope and the representational target of model organisms differ from those of experimental organisms. This difference is critical to emphasize because it is what makes model organisms into a distinctive, contemporary type of model with an associated set of scientific practices that are specific to the biological and biomedical sciences.

#### 4. The material features of model organisms

Key examples of popular current-day model organisms include the yeast *Saccharomyces cerevisiae*, the bacterium *Escherichia coli*, the fruitfly *Drosophila melanogaster*, the nematode worm *Caenorhabditis elegans*, the plant *Arabidopsis thaliana*, and various mouse strains.<sup>8</sup> In most of these histories, the model organisms were developed as a form of resource materials, in concert with a range of specific research techniques and practices. The usual historic narrative associated with model organisms is that they are organisms that were specially selected as research materials because they were viewed as easy and relatively inexpensive to gather, transport, maintain, and manipulate experimentally. Of course not all of the important biological characteristics for these organisms were evident when they were first obtained in the field (in their “wild” form), but rather they come to be expressed (or even induced) in the processes of manipulation and experimentation in the laboratory setting.

More specifically, model organisms have particular experimental characteristics that are closely related to their power as genetic tools: they typically have small physical and genomic sizes, short generation times, short life cycles, high fertility rates, and often high mutation rates or high susceptibility to simple techniques for genetic modification. Furthermore, they have been developed

using complex processes of standardization that allow the establishment of a standard strain which then serves as the basis of future research.<sup>9</sup> The standard strain, often paradoxically referred to as “wild type,” is a token organism developed through various laboratory techniques (ranging from cross-breeding to genetic manipulation) so that it possesses features valued by researchers and can be reproduced with the least possible variability across generations, for example through cloning (on such processes in the neurobiology of *C. elegans*, see Ankeny, 2000).

Here we begin to see one of the specialized features of model organisms: these processes of standardization are essential because model organism research hinges on (eventually) developing a detailed *genetic* account of the standard organism in terms of sequence, gene function, and phenotype. This characteristic is not an in principle requirement for the development of a model organism, but rather one derived from the historical context in which model organism research was developed. Throughout the 20th century, genetics keeps playing a prominent role in biological research and thus has come to define how biologists understand two notions of central importance for developing widely-representative models: (1) the idea of the “pure line,” which is crucial for the purposes of experimental control over what strains are used and for reducing variability, and for which genetic analysis acts as a defining measurement (see Rheinberger & Müller-Wille, 2010); and (2) the idea of “comparability” across species, which has become closely associated to the principle of genetic conservation. This reductionist approach to understanding standardization and cross-species comparison was not strictly necessary for the conceptualization of the category of model organisms and their use, and yet, for reasons that were at least partly contingent, the classical tradition of genetic analysis ended up playing an important role in shaping the experimental practices and concepts used to investigate and standardize organisms (see e.g. Weber, 2007 for the case of *Drosophila*). However, this genetically-based approach became perhaps the most popular one in organismal biology between the 1950s and 1990s and thus shaped the ways in which researchers conceived of model organisms as well as the resources used to study them.

Consequently, it is now widely accepted that model organisms should be tractable using both forward-genetic approaches (identifying genes based on mutant phenotype) and reverse-genetic approaches (functional analysis of a gene of known molecular identity) (see Barr, 2003). Many experimental organisms do not fit this criterion: although *Xenopus* is very useful for studying embryonic development, its generation time is nearly three years, which basically rules out genetic analysis of the sort required for model organism work. In contrast, it is clearly not an essential requirement for all experimental organisms to be genetically tractable: whether this is necessary is a function of what research question is under investigation. For example, some research groups will invest considerable efforts in organisms that are not tractable (genetically or otherwise) according to conventional definitions because they are nonetheless viewed as biologically interesting. As developmental biologist Scott Gilbert notes about his work on shell development in red-eared terrapins, they are a ‘horrible

<sup>6</sup> The key role played by the researchers’ goals in the construal and use of models has been emphasized by other authors in the philosophy of science, for example Keller (2002); Leonelli (2007a); and Weisberg (2005).

<sup>7</sup> We do not mean this point to be taken literally as indicating that every researcher who works on any type of model organism has these goals in the forefront of his or her mind at every moment in the lab; in many cases, the espousal of such goals is largely a working ideal or perhaps mere rhetoric used to pursue research funding. Indeed, it may well be the case that the Human Genome projects have helped to bring this integrative vision to the fore and make it canonical within these communities. However, as we discuss in later sections, this overarching, idealized goal nonetheless is a defining characteristic of current-day model organism research.

<sup>8</sup> The literature in the history and philosophy of science on the development of and research with various model organisms is now voluminous but notable contributions for the themes discussed in this essay include the essays in the collection edited by Clarke & Fujimura (1992); articles in the 1993 special issue of the *Journal of the History of Biology* on experimental organisms edited by Burian; Ankeny (1997); Ankeny (2001a, 2001b); de Chadarevian (1998); Kohler (1994); Leonelli (2007b, 2008); and Rader (2004).

<sup>9</sup> For more detailed arguments on the historical, epistemic, and social processes involved in constructing standard specimens of organisms, see e.g. Kirk (2010); Kohler (1994); and Leonelli (2007b).

system to use if one wants. . . to have research material at any given day' (as quoted in Maher, 2009, p. 698). Similarly for other more "non-traditional models," obtaining the organisms on which to do work involves considerable efforts in the field, let alone growing, maintaining, and manipulating them. Nonetheless, researchers continue to use their organisms of choice because they think they are particularly well-suited for the questions of interest: Gilbert's turtles have characteristics that make them extremely useful for studying transitions from one cell type to another, due to the fact that they convert soft tissue into bone.

Many experimental organisms do, of course, undergo processes of standardization. However these are not a defining, generic feature of experimental organisms, since how standardized the organism is in genetic or other terms is also a function of the question under investigation. These questions differ radically across experimental organisms taken as a group: for instance if one is interested in variations in behaviors of pigeons, the standardization of specific "pigeon types" will not be a critical part of developing the experimental organism; by contrast, using frogs for the study of respiration required trying to find organisms with similar morphologies and size, so that their lungs could be studied as though they belonged to the same token animal.

In summary, the most important criterion of the selection and development of experimental organisms is the way in which they enable the study of specific questions; experimental tractability is also relevant, but will be diversely defined depending on the question of interest and is often subsidiary to it. In the next two sections, we show how this feature is in direct contrast to model organisms that operate under a set of shared assumptions about the goals of research, which typically involve attempts to generate complete knowledge of the fundamental processes at work in these organisms, including the molecular, cellular, and developmental processes; in this sense the model organism is understood as a test tube for achieving a full understanding of all biological processes.

## 5. Building the infrastructure to support a model organism

The material features necessary for pursuing integrative research on model organisms may arise casually in the first instance, but they also require the establishment and maintenance of a range of infrastructures enabling cross-disciplinary communication and the exchange of standardized materials and instruments, as well as specific social structures in order for the models to retain their epistemic value. Model organism research has depended critically on building infrastructure around each model organism, including both stock/strain centers and cyberinfrastructure such as community databases for communication of results within and across communities of researchers. Hence the second essential feature which contributes to the characterization of a model organism is the distinct infrastructure that surrounds these organisms, including the social structures built to enhance co-operation among researchers, and the community ethos which is associated with model organism work (for a discussion of this in the early *Drosophila* community, see Kohler, 1994).

Until the advent of full-scale work on the Human Genome projects in the 1990s, communication within each community focused on a particular model organism was strongly valued, yet the means to achieve it were limited: they consisted primarily in newsletters, annual meetings focused on research on each organism, personal contacts, and laboratory exchanges. Despite the practical focus on the mechanisms for communication during this period, the ethos of sharing (particularly of data and techniques) was nonetheless firmly established in many of these communities (e.g., see Rhee, 2004; Sulston, 2002; Sulston & Ferry, 2002). The value of

model organism research but also the advantages of the collaborative communities associated with such research were clearly recognized by governmental funding bodies in the 1980s, leading to the awarding of large-scale funding to the genome sequencing projects in the 1990s, as well as "community resources" such as stock centers (e.g., *C. elegans* and *Arabidopsis*) and community databases such as Flybase, The Arabidopsis Information Resource (TAIR), and WormBase. This infrastructure contributed significantly to the abilities of these communities to foster communication and collaboration, and hence to further their research efficiently and effectively. Without cyberinfrastructure and communal access to standardized specimens, the exchange of information about model organisms and their use for comparative purposes would be impossible to realize on the appropriate scale, given the large-scale integrative goals of many contemporary biological research programs. Due to their capacities for bringing results, people, and specimens together, community databases and stock centers have come to play a crucial role in defining what counts as knowledge of organisms in the post-genomic era (Leonelli & Ankeny, submitted for publication; Rosenthal & Ashburner, 2002).

Furthermore, these communities have a strong ethos of sharing resource materials, techniques, and data and of making materials and data available across the community almost immediately. This philosophy was highlighted in the notorious debates within the U.S.-U.K. Human Genome Project over public versus private approaches to sequencing, where many of the key players on the public side had their origins within model organism communities (Sulston & Ferry, 2002). This requirement of open sharing of data became a critical part of the public Human Genome Project, and more generally served as a model for rules governing data sharing in publicly-funded research (NIH, n.d.). Researchers within the Arabidopsis community refer to this as the "share and survive" ethos (Rhee, 2004): it is strongly argued that restricted availability to model organisms (and the surrounding techniques and data) would impede research, since they are unique research resources which provide fundamental data and because further studies are highly dependent on previous results (perhaps more so than in other research domains). Hence a key defining component of what it means to do model organism research is that researchers participate in sharing data and other resources, and hence are active participants in the broader community which shares the common epistemological goals to be discussed in the next section.

Here we see three additional distinctions between what makes something a model organism rather than just a member of the larger class of experimental organisms. First, research groups who use various organisms for research and experimentation do not tend to have strong social ties simply because they work on the same organism. We do not see unified research communities of "pigeon people" coming together annually to meet and exchange data as we do see "worm people" or "weed people," nor do we see identity politics of the type that leads individuals in the mouse community to envision themselves as "mouse people" (Rader, 1998). In contrast, communication about such research is most likely to occur in disciplinary groupings (such as within research societies and journals focused on behavior or neurobiology in the case of pigeons).

Second, the rules that bind work with other types of organisms more broadly construed as experimental organisms are considerably less well-articulated than those which have been promulgated for (at least publicly-funded) work with model organisms (Bevan & Walsh, 2004; Marshall, 2001). Many biological researchers have implicit shared values for communication and collaboration; some journals and societies have explicit requirements for data being made publicly accessible; and various regulations and laws govern ethical conduct of research particularly with non-human animals. However these values are not typically tied to being an identified

researcher within a particular community: in other words, the communities which are associated with particular model organisms have themselves become models for certain behaviors within science.

Finally, the expectations for participation in model organism communities are considerably different than those which govern the more general biological research community. Those who participate actively in model organism communities are expected to contribute material to the stock centers, support the community databases by providing data and other information, and perhaps even assist in the curation of such databases, in exchange for being critically dependent on the specialized information and resources available through the database and the strain center. In contrast, although strain centers and community databases are accessible to the wider biological research community (and in many cases even to the general public), there is limited direct contribution back to the community databases and the strain centers, and very limited engagement of the specialized nomenclature and terminology specific to any one model organism. Hence the material practices of model organism research are defined much more clearly than those associated with research on experimental organisms, and in turn what constitutes a model organism is dictated by the norms that are essential parts of the practices used to work on this class of organisms.

## 6. The epistemological features of model organisms

Model organisms share two key epistemological characteristics which in large part derive from the communities' shared research goals; we believe these characteristics also are the crux of critical differences between model and experimental organisms. First, model organisms are always taken to represent a larger group of organisms beyond themselves, and hence rely on very particular types of claims about their (potential) representational scope. In their ideal form, model organisms are thought to be a relatively simplified form of the class of organism of interest, particularly in light of principles of genetic conservation which indicate that smaller genomes might be the smaller and more compact form of more complex, higher genomes, and hence they may be the most appropriate models for these fundamental processes of interest. The actual relationships between the model organism and this larger group often are very ill-articulated in the earliest stages of model organism work, and do not necessarily hinge on particular claims about genetic conservation or precise knowledge of the phylogenetic placement of a particular organism in relationship to others. As various authors have noted, perhaps most forcefully Jessica Bolker (1995), many model organisms do not in fact fulfill these idealized criteria and have proven to be taxonomic outliers (see also Gilbert, 2009). For instance, both the nematode *C. elegans* and the fruitfly *D. melanogaster* are highly specialized organisms, and hence their genes are often very divergent at the sequence level from the homologous genes in the mammals for which they are intended to serve as a model. It is also important to note that the extent and degree of genetic conservation in various organisms was not well understood until after a number of the key model organisms were already being developed.

Nonetheless this concept is a critical epistemological feature which shapes which organisms are selected as a research focus, and how they are developed for research. Model organisms are models precisely because they serve as the basis for articulating processes that it is thought will be found to be common across all (or most) other types of organisms, and particularly those processes whose molecular bases can be articulated. This goal is shared by all research groups who claim a focus on model organisms as model organisms.<sup>10</sup>

Those using experimental organisms also rely on claims about their representational scope in a general sense: although of course it is hoped that research on pigeons or dogs might reveal something about behavior that is generalizable, for example, the anticipated scope of this claim is much more narrow in part because much of this research does not rely on articulating fundamental and conserved genetic and other processes. It is perfectly acceptable for an experimental organism to possess representational scope extending only to its own species, as in the above-mentioned case of specific turtles being used by Gilbert to understand turtle biology. Furthermore, the precise representational scope in each instance of a use of an experimental organism differs: the extent of the intended projection from the original organism to a wider class of organisms is a function of each particular context of use and especially of the processes of interest and the research question to be answered.

In the case of model organisms, representational scope tends to be much broader: the most commonly shared sense in which these organisms are "representative" relates to their use in the Human Genome projects and for biomedical research, and hence model organisms are often claimed to be representative more generally of processes that it is hoped will be shared by higher level organisms but especially human beings.<sup>11</sup> But what is clear is that these organisms are not being studied because they are interesting in their own right (though they may well be) but primarily because of the value they can have for investigating processes in a manner that will be generalizable beyond the specific model organism itself: in other words, 'the fish is a frog. . . is a chicken. . . is a mouse' (Kimmel, 1989, as paraphrased in Grunwald & Eisen, 2002, p. 721).

The second key epistemological feature which characterizes model organisms is that they have a very specific representational target: model organisms serve as models for whole, intact organisms,<sup>12</sup> in other words for a range of systems and processes which occur in living organisms, including genetics, development, physiology, evolution, and ecology. This approach allows pursuit of one key goal of this type of research, which is ultimately to allow large-scale, comparative work across species integrating a range of disciplinary research approaches. This goal is achieved using a specific strategy, which is to first gather resources and build infrastructure on individual whole organisms integrating a range of disciplinary approaches, and then to do work on comparisons between these organisms using the original organism as a reference point. So for instance as is well-known, a number of homologous genes have been identified across a range of model organisms, although of course questions remain in many cases about the correlation between sequence and function. Nonetheless researchers conceptualize identification of these homologs as a key step in producing knowledge about the molecular basis of phenotypes across these organisms, and particularly of variations

<sup>10</sup> It is worth noting that some research on organisms typically considered to be model organisms occurs which is *not* explicitly model organism research: for instance, there are projects that focus on the agricultural aspects of *C. elegans* as well as its relevance for parasitology which may draw on the data available via model organism work but which do not explicitly aim to contribute to its main goals. For an early discussion of the relevance of *C. elegans* genomic sequencing to other nematodes, see Blaxter (1998).

<sup>11</sup> This point is illustrated by a joint statement by model organism biologists issued after the 2006 meeting of the Genetics Society of America, where they note that 'few, if any processes at the level of genes are known to be unique to humans, although the cellular and organismal physiology certainly differ. Consequently, we argue that the key aspects of most human disorders ultimately can be modeled in organisms in which the compromised process are controlled by closely related genes, thereby offering the potential for rapid and inexpensive genetic analyses' (Spradling et al., 2006). Even the plant *Arabidopsis* has been claimed to have contributed substantially to the understanding and treatment of human diseases, as reviewed in Jones et al. (2008).

<sup>12</sup> See also arguments in Rubin (1988).

including those that cause disease (e.g., the gene *BRCA1* which is associated with human breast cancer whose homolog has been found in variant forms in *C. elegans* and the mouse), and also for gathering information about the evolutionary histories of these organisms and in particular speciation.

Another example of the fruits of such a research strategy can be found in the elucidation of the mechanisms associated with programmed cell-death, which is a regulated process which generally confers some sort of advantage during an organism's life cycle. Using *C. elegans*, Sydney Brenner, Robert Horvitz, John Sulston, and others identified key genes regulating the processes of cell death in this organism (for an overview, see Wood et al., 1988). It was subsequently shown that corresponding homologous genes exist in higher species, including human beings, and that the basic morphological and biochemical features of programmed cell death are conserved in both the plant and animal kingdoms. In these sorts of programs, understanding molecular and developmental processes in the intact, model organism is the initial focus of research which then serves as a building block or platform (e.g., *C. elegans* Sequencing Consortium, 1998) for a more general investigation of developmental processes together with molecular and other processes across a range of organisms.

This epistemological feature is clearly distinct from the sense in which experimental organisms model a particular representational target: experimental organisms are models for specific phenomena, to be investigated through a particular discipline or perspective with its accompanying set of techniques and practices. Experimental organisms need not be as versatile as model organisms in order to be useful and successful for particular types of research; for instance even if it would be extremely difficult to study dogs in genetic terms due to their relatively large genome size and long generation times, these limitations make them no less valuable for the study of behavior.

In short, although both experimental and model organisms are models in the sense of being representative of a larger class of organisms, they are distinct types of models because of the fundamental difference in the breadth of their representational scope and, most importantly, their intended representational target. Experimental organisms tend to be models for particular phenomena, while model organisms are models for organisms as wholes, used not just to explore specific phenomena, but aimed at developing an integrative understanding of intact organisms in terms of their genetics, development, and physiology, and in the longer run of evolution and ecology, among other processes.

It might be objected that while the broad research goal of model organism communities is indeed to understand the organism as a whole, any one research group tends to focus on specific aspects of the organism, in much the same way as with experimental organisms. It is of course true that model organisms are used as resources for a variety of particular experimental projects, which may vary enormously in scope. Indeed, the epistemic power of model organisms consists precisely in their abilities to serve as resources that can be used in such a variety of ways. To understand how these two aspects might be reconciled, it is important to distinguish the ways in which model organisms are produced as resources for a community of scientists from the ways in which they are used in specific experiments. These two processes are tightly intertwined historically, but they can be differentiated analytically in terms of their epistemic goals. What singles out model organisms is the goal to make them usable models for a variety of

different purposes, which involves 'preparing' organisms for experimental use by standardising specimens and accumulating as much knowledge as possible about all of their traits. The ability to pursue specific experimental goals constitutes both the practical means and the desired outcome of constructing this kind of resource as well as an holistic understanding of the organism in question.

## 7. Consequences of "tightening" our usage of the term "model organism"

As was discussed at the start of this essay, the term "model organism" has come to be used increasingly to describe any experimental organism used to investigate a particular biological process or system. We have argued that this type of reference is problematic inasmuch as the usage of the term "model organism" implies a series of very particular biological, epistemic, and socio/political commitments which are not actually adopted within many research programs in experimental organismal biology, even ones that focus on single organisms. Indeed, we wish to argue that, given the plurality of goals of interest within the life sciences, not all biological research needs to be centered on model organisms. The use of experimental organisms for the investigation of specific questions within well-defined contexts is just as important as the use of model organisms for integrative and comparative research. There is thus no obvious justification for the recent efforts to transform several experimental organisms that are popular within specific disciplines for answering certain kinds of questions into model organisms; for such organisms to have a likelihood of success as model organisms, a range of features would be required that are typically not in evidence in such organisms.

The temptation of transforming experimental organisms into model organisms arises in part from the fact that there is no straightforward "boundary" between these two categories of models. As we have highlighted, model organisms often have begun their scientific careers as experimental organisms; the process of obtaining a model organism from an experimental one is gradual and multifaceted. Thus, while we believe it useful to stress the epistemic differences between the two types of models, we are aware that model organisms themselves can be viewed along a continuum, with some fitting the idealized set of criteria articulated above more precisely than others for a range of historic, sociopolitical, and other reasons. For instance, the fact that *C. elegans* and *Arabidopsis* are relatively new model organisms (compared to, say, *Drosophila* or mouse) means that they have in fact been actively chosen with the type of integrative and comparative research outlined above in mind and also conceptualized as model organisms in the earliest stages of research on them, rather than having evolved more organically from a previous incarnation within another type of research program.<sup>13</sup> Perhaps the most striking example of the selection of model organism with a limited previous experimental history is zebrafish, which was consciously chosen, then promoted and established specifically as a model organism relatively late in the process of the emergence of model organism research (1990). It was selected because of its anticipated abilities to serve as the basis for comparative research across a range of organisms and with a full awareness of the requisite components for doing successful model organism research, deriving in part from close observation of how research on *C. elegans* and *Arabidopsis* had been structured (Endersby, 2007; Grunwald & Eisen, 2002).

<sup>13</sup> Both *C. elegans* and *Arabidopsis* were used previously for biological research prior to being adopted as the focus of model organism research programs; however the continuity to these earlier lines of research was rather weak for a variety of reasons which are not central to our argument here. On *C. elegans*, see Ankeny (2001b), and on *Arabidopsis*, see Leonelli (2007b). Gilbert (2009) does not see model systems as normally resulting from integrative tendencies. Rather, he sees model systems as arising from the needs of one methodological perspective (such as genetics) and modified secondarily and often superficially to the needs of other perspectives (see Félix, 2004; Keller, 1996; and Schilling & Webb, 2007).

Other organisms commonly recognized as model organisms are weaker in one or more of the requisite components, while still likely fulfilling the general characterization of model organisms as espoused above. For instance there are claims that both the mouse and the rat communities have not quite succeeded in implementing the typical model organism community values and sharing ethos (Anonymous, 2009). This gap likely is due in part to the commercial and clinical natures of many of the research settings in which these organisms are used which run counter the idea of non-proprietary exchange of information and materials, as well as to their long histories as experimental organisms which resulted in more diversified (as well as more fragmentary) communities (Anonymous, 2009; Rosenthal & Ashburner, 2002). Yet other organisms sometimes recognized as model organisms reflect limitations which are both biological and social. For instance, the chick has been relatively limited in its development as a genetic system and does not have stocks which are highly standardized; similar issues have affected the use of *Xenopus* (Maher, 2009).

Finally, there are model organisms which instantiate in an extreme way both the motivations behind model organism research and some of the biological advantages (e.g., the relatively small size and compact nature of the genome), but are limited in their representational abilities. These organisms might be argued to include organisms associated with minimal genome projects such as the pufferfish, microorganisms such as the bacterium *Mycoplasma genitalium*, and perhaps even (controversially) *Escherichia coli*. They have limited comparative value because of their extreme simple structures and physiology as well as limited higher-level processes; they also do not have extensive communities surrounding them.

## 8. Are model organisms a distinct type of “model”?

Philosophers of science have tended to distinguish different varieties of material models depending on how accurately they represent their target system.<sup>14</sup> Models that more faithfully mirror their target, such as the scale model<sup>15</sup> of a car in a wind tunnel that is used to measure wind resistance, are referred to as “true” models (Achinstein, 1968, ch. 7) or “replicas” (Hesse, 1966). These are seen as different from models that portray only some of the characteristic features of their target system, which are often called “idealized” or “simplifying” models.<sup>16</sup> An example of a simplifying model is the material model of an atom constructed out of the typical balls and sticks. There are a number of key differences between the model and the target system being modeled: nonetheless, these simplifying models serve as appropriate and useful models because any non-analogous features are not critically relevant to understanding the structure of process under investigation.

However we maintain that the philosophical distinction between true and simplifying models does not help us to understand the key representational features at stake in the case of the category of experimental organisms. Some experimental organisms may well be “true” models in cases where they mirror their target in most features (even those beyond the process or system of interest), but many will be a form of simplifying model. The key feature which is common to the class of experimental organisms is the fact that the details of the representational scope of these models (in terms of the extent of the possible projection from organism to lar-

ger groups) are determined according to the specific contexts of use. As discussed above, experimental organisms can be described within the “models as mediators” account, inasmuch as they are tractable systems that allow the study of particular biological processes in laboratory settings where variation can be eliminated or controlled so that more general conclusions can be drawn about how these processes work. In some research contexts, they are treated as representing solely the class of organisms (i.e., the type) from which the token organism has been taken, as in the case of a single platypus being investigated to achieve a better understanding of platypus biology more generally. In other contexts, experimental organisms are studied to understand processes which are thought to have much wider representational scope (as in the above-mentioned case of the study of circulation and respiration using the frog). Experimental organisms are thus similar to material models of phenomena as used in other sciences: they are models for a specific phenomenon (their representational target) but have a high degree of variability in terms of their representational scope.

What, then, distinguishes model organisms as a specific type of models compared to the general class of experimental organisms? First of all, model organisms are tied to a very specific type of representational target: they are explicitly models for whole organisms, to be investigated using a range of disciplinary approaches with the intention of integrating these approaches to develop an understanding of the whole, intact organism. Hence the epistemic goal shared by members of the model organism communities clearly has shaped the way in which model organisms are not only viewed, but also used as models.

Further, and partly as a consequence of this first point, model organism research programs share a specific interpretation of the extent of the representational scope of their model organisms. Their common goal is to use single organisms to represent a much wider class of organisms or even all living organisms in some cases, which means that the representational scope of these organisms is much wider and potentially inclusive than the representational scope assigned to other experimental organisms. In sum, model organisms are models for whole organisms, whose potential representational scope extends to all living beings.

This type of model is arguably distinctive to the biological sciences, since the type of understanding sought through the model cannot be pursued in isolated systems or non-intact organisms. As research aims to articulate processes in living things, it is necessary to use intact organisms to study it, so that they can incorporate all the dimensions characteristic of living creatures: crucially, as mentioned above, development, genetics, physiology, ecology, and evolutionary history. A scale model which only reflected one (or a few) key attributes of the target system would not be sufficient to pursue the types of questions which are of interest in model organism research. It is also questionable whether non-living entities could, even if a metaphorical sense, be studied in terms of their development, evolutionary history, or genetic make-up.<sup>17</sup> Further, findings of non-analogous features (when making comparisons across model organisms) are much more fundamentally problematic than in work with experimental organisms or other types of material models, since model organism work proceeds from the assumption that organisms can be compared to each other at the most basic level. Finally, the ways in which model

<sup>14</sup> Sources on material models in the biological sciences are numerous, and include Griesemer (1991); and de Chadaverian & Hopwood (Ed.) (2004).

<sup>15</sup> For a detailed discussion of scale models particularly in engineering, see Sterrett (2006).

<sup>16</sup> For a discussion of this distinction and an overview of the modeling literature in general philosophy of science, see Frigg & Hartmann (2006).

<sup>17</sup> We do not have space to engage in an extensive discussions about the philosophical issues associated with the relationships between animate and inanimate objects, what counts as a living entity, and what is the appropriate system in which to study “life.” These are important topics within contemporary philosophy of biology (e.g., see Dupré & O’Malley, 2009; Lewens, 2004) and it would be extremely interesting to discuss further the relation between these issues and the modeling strategies (and associated ideas about what constitutes life, functional integration, and organismal individuality) promoted through model organism research.



organisms represent the world is peculiar if not unique. As we mentioned above, these organisms are not actually “natural,” given the amount of standardization to which they are subjected in order to serve their representational function, but rather an idealization of the natural. So they are samples of the world in a material sense, but at the same time they are a (large) step away from what could be conceived as the “wild” or the “natural.”

Rather than being generic tools for experimental interventions, model organisms in fact represent a unique “way of doing” science, in John Pickstone’s terms (2001). They involve a set of essential practices that emerged in relation to a set of distinctive epistemic goals, which in turn are finely tuned to the study of the very special objects that these models are taken to represent. Model organisms in this sense are the right tools for a very specific type of scientific job, that of investigating life. And these tools can be meaningfully used only in the broader context of a “right way to do biology,” which includes a range of experimental practices such as molecular sequencing but also social norms such as collaboration and open sharing of resources; institutions and infrastructure that can support the implementation of such norms (e.g., community databases and stock centers); and, perhaps most importantly for our purposes, an epistemic commitment to pursuing integrative and comparative accounts of life by focusing on individual organisms as the main unit of analysis.

### 9. Postscript: are model organisms a dying breed, or where to from here?

It has been claimed that the individual model organism approach is on the decline, and is being supplanted by systems biology and comparative genomics (e.g., Davis, 2004). We argue that this understanding of the potential power of model organisms and the goals of model organism research is overly limited, and does not take account of the long-term goals of such work, which in fact are explicitly related to comparative genomics and more generally to pursuing comparative biological questions using a range of disciplinary perspectives eventually including ecological and environmental approaches, which in fact form the very basis of system-biologic approaches.<sup>18</sup>

In addition, recognizing the epistemic value and characteristics of model organism work also involves recognizing that this type of research can be a very inappropriate strategy for certain types of research questions or programs<sup>19</sup> where the processes of interest are much more delimited or can be usefully studied in isolation. This limitation was recognized long ago by many biologists, and has strong resonance with historic debates in developmental biology over whether it was better to study a number of different organisms at once with one research question in mind, or to focus and obtain more in-depth information about one organism (Gilbert, 2009; Sunderland, 2008).

Currently there is no adequate understanding among researchers, science administrators, or historians/philosophers of science of the implications of using the term “model organism” and the deep epistemic commitments that necessarily accompany it. By invoking and analyzing the term, we do not intend to endorse the idea that integrative, comparative research necessarily needs to start with a strict focus on individual organisms and a gathering of resources on a massive scale. Rather, we wish to acknowledge that this idea has already been implemented on a wide scale by scientists and science administrators, and that in order to make use of those efforts, we need to understand the epistemic and social characteristics of this form of “big science.” In order to make wise use

of those resources already developed, researchers now find themselves committed to carrying out this specific, long-term vision about what is the right way to do biological research with all of its accompanying epistemic assumptions. Thus we hope that our arguments regarding the appropriate characterization of the key features of model organisms provides clarity to the recent debates around the claim that too much funding has been invested in the best-established model organisms (e.g., Davies, 2007). As pointed out by researchers within these model organism communities (e.g., Ledford, 2010), sudden cuts of funding for model organism research will run counter to the long-term goals of such research and potentially undermine all the efforts underlying this research to date.

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<sup>18</sup> It is notable how many projects in system biology have emerged from the study and integration of data available on model organisms.

<sup>19</sup> For the example of the naked mole rat as a “boutique” system which may nonetheless prove to be useful, see Sedivy (2009).

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