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How to choose your research organism

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ABSTRACT

Despite August Krogh's famous admonition that a ‘convenient’ organism exists for every biological problem, we argue that appeals to ‘convenience’ are not sufficient to capture reasoning about organism choice. Instead, we offer a detailed analysis based on empirical data and philosophical arguments for a working set of twenty criteria that interact with each other in the highly contextualized judgements that biologists make about organism choice. We propose to think of these decisions as a form of ‘differential analysis’ where researchers weigh multiple criteria for organismal choice against each other, and often utilize multidimensional refinement processes to finalize their choices. The specific details of any one case make it difficult to draw generalizations or to abstract away from specific research situations. However, this analysis of criteria for organismal choice and how these are related in practice allows us to reflect more generally on what makes a particular organism useful or ‘good.’

1. Introduction

In 2011, a group of biologists estimated that there are 8.7 million species currently living on Earth, give or take 1.3 million (Mora, Tittensor, Adl, Simpson, & Worm, 2011). But biologists do not study them all. In fact, many scientific commentators have been concerned that experimental biologists seem to focus their research on a very small fraction of extant species (Beery & Kaufer, 2015; Bolker, 2012). The decision to focus on a particular species (or handful of species) or even on a specific strain or variant is a common feature of biological research (Burian, 1993; Clarke and Fujimura, 1992; Hopwood, 2011). In this paper, we investigate the factors that guide the choice of organisms for biological research, focusing particularly on the interrelation of such criteria (see Table 1).

The most famous criterion for organism choice is usually attributed to the Nobel Prize winning physiologist, August Krogh (Green, Dietrich, Leonelli, & Ankeny, 2018). Dubbed Krogh's Principle by Hans Krebs in 1929, Krogh claimed that “[f]or such a large number of problems there will be some animal of choice, or a few such animals, on which it can be most conveniently studied” (Krebs, 1975; Krebs & Krebs, 1980; Krogh, 1929). The claim is popular amongst biologists, as can be seen through the over 160 citations to Krebs' paper on the Krogh Principle over the last forty years. Thanks to the Krogh Principle, the term ‘convenience’ has frequently been invoked when describing how researchers make such decisions, but this single term is overly broad (Green et al., 2018).

‘Convenience’ has frequently been understood as signposting practical and logistical choices in research design, which are made irrespectively of conceptual analysis and are meant to facilitate the day-to-day running of an investigation. In other words, the appeal to convenience has been interpreted by some researchers (and many philosophers) to involve the removal of as many practical obstacles as possible from research activities, so that researchers can pursue their studies without disruption or delays due to recalcitrant materials or unwieldy laboratory conditions (Gest, 1995; Robert, 2008). Interpreted in this way, ‘convenience’ has limited epistemic significance, and remains tied to technical aspects of the set-up and planning of research that some would contend are not central to science.

Appeals to convenience, we argue, are not sufficient to capture reasoning about organismal choice. As contemporary physiologists have noted: “The Krogh Principle, as it is now known, is often taken to be about more than ‘convenience’ when selecting the ‘best’ organism for the study of a certain physiological problem” (Andrews & Enstipp,

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Table 1
Criteria for organismal choice.

Cluster	Criteria
(A) Access	(1) Ease of Supply
	(2) Phenomenal Access
	(3) Ethical Considerations
(B) Tractability	(4) Standardization
	(5) Viability and Durability
	(6) Responsiveness
	(7) Availability of Methods and Techniques
	(8) Researcher Risks
(C) Resourcing	(9) Previous Use
	(10) Epistemic Resources
	(11) Training Requirements
	(12) Informational Resources
(D) Economies	(13) Institutional Support
	(14) Financial Considerations
	(15) Community Support
	(16) Affective and Cultural Attributes
(E) Promise	(17) Commercial and Other Applications
	(18) Comparative Potential
	(19) Translational Potential
	(20) Novelty

2016, p. 42). Here, the use of 'best' reflects more than simple logistical choices on the part of researchers. Reference to the terminology of convenience can also be interpreted as signposting significant strategic judgements around the design, realization, and interpretation of research on non-human organisms which have considerable implications for the type of knowledge obtained and the direction and organization of biological research as a whole. Our analysis of more specific criteria demonstrates that multiple criteria are at play within any one research project. Some of these criteria interact synergistically with each other, while others may be in tension or even direct conflict with one another. The extent to which researchers manage these types of tensions and strategize around the strengths and weaknesses of specific criteria contributes to the success of their employment of particular organisms in their research.

Our methods combine detailed analysis of scientific and historical literature on the Krogh principle enriched with insights from our own fieldwork and related historical and philosophical scholarship. We begin with an examination of more general scholarship in philosophy and biology on choice of research foci and components (section 2), drawing on the oft-time cited philosophical account by the population geneticist Richard Levins about "trade-offs" in model choice (1966) as a starting point for a broader reflection on the strategies and implications involved in the choices made when setting up a scientific project. We explore whether choices of research organisms are characterized by trade-offs similar to those Levins described in relation to model choice, such as generality, realism, and tractability. We contend that Levins' approach is insufficient for understanding the types of criteria associated with organismal choice, and that stark or generic trade-offs of the kind envisioned by him do not seem to exist in this domain.

Following a brief discussion on methodology (section 3), we identify and discuss twenty criteria for organism choice (section 4). This analysis shows how the kinds of values, assumptions, and expectations that enter into judgements about 'good' organismal choice are considerably more complex than a seemingly simple appeal to convenience as a pragmatic criterion. In section 5, we discuss how these different criteria can be synergistic or antagonistic with each other, and how commitment to one criterion (or a cluster of criteria) is often correlated with deemphasizing or devaluing others. We also contend that the ways in which each criterion for organism choice relates to others depends strongly on the specific research situation, making it impossible to produce a compact, generalizable matrix of trade-offs similar to the one envisioned by Levins. We propose to think of this as a form of 'differential analysis' where researchers weigh multiple criteria against each other, and often utilize multidimensional refinement processes to finalize their choices. We provide several examples which illustrate the diversity of situations in which choice criteria are evaluated and strategically prioritized. We conclude that although the specific details of any one case make it difficult to draw generalizations or to abstract away from specific research situations, this analysis of criteria associated with organismal choice and how they relate to each other in practice allows us to reflect more generally on what makes a particular organism useful or 'good.' These criteria also may prove useful in other scientific domains involving choices of research focus or material, and are critical to the scientific practices that result.

2. Philosophical perspectives on choosing research components

Judgements regarding theory choice (and what is considered to be a 'good' theory) appear to be useful analogs to judgements regarding organismal choice, so we begin this section with a selective review of the literature on theory and model choice for insights about the reasoning practices associated with assessing, evaluating, weighing, and comparing criteria for those choices. Numerous philosophers, historians, and social scientists have distilled different sets of defining values and norms for theory choice using various case studies. For instance, Thomas Kuhn (1977, p. 322) offers a list of five criteria for good theories (namely accuracy, consistency, broad scope, simplicity, and fruitfulness), and W. H. Newton-Smith (1981, pp. 226–30) provides a list of eight "good-making features of theories" (namely observational nesting, fertility, track record, inter-theory support, smoothness, internal consistency, compatibility with well-grounded metaphysical beliefs, and simplicity), while Lindley Darden (1991) expands the list further still. These lists, of course, could be expanded to include pragmatic criteria common in the organism-choice related literature to be discussed in more detail below (e.g., Burian, 1993; Clarke and Fujimura, 1992), such as cost and tractability, and social criteria, which include opportunism or political support for particular forms of research. Some of these criteria, such as simplicity, are considered epistemic by some philosophers (Laudan, 1986) and social by some sociologists (e.g., Bloor, 1981), although others have attempted to break down those distinctions (e.g., Longino, 1990; Solomon, 2001).

It is undoubtedly the case that evaluative judgments in scientific practice are typically multidimensional, be they in relation to the choice of research materials, or of theories or models. Scientific evaluation of a theory or a model can entail the mutual satisfaction of multiple criteria and/or trade-offs between different criteria. In his famous treatise on models in ecology, Richard Levins (1966; 1968) argues that one cannot have both generality and precision in any one model. He highlights how emphasis on a specific epistemic advantage of a chosen research entity (i.e., a particular model of population biology in his case) is unavoidably tied to simplifying assumptions and thus the devaluing of other features. Levins points to generality, realism, and tractability as traits of models that are necessarily in tension with each other, and which cannot be achieved in equal measure in any one choice. As he and many others building on his work have shown (Matthewson & Weisberg, 2009; Odenbaugh, 2002, 2006; Weisberg, 2006), increasing the generality of a chosen model by making it applicable to a larger set of cases necessarily decreases its descriptive value (its realism) as a representation of one specific case.

Even though they often are not as explicit as Levins, biologists have used a fairly consistent constellation of standards in their comparative evaluation of most theories, and philosophers of biology have done considerable work to enumerate those values and understand the ways in which they are used in scientific judgments (e.g., Lloyd, 1988 on confirmation; Darden, 1991 on assessment during cycles of scientific change; more generally on values in scientific practice, see; Longino, 1990; Lacey, 2004; Douglas, 2009). While there is a rich literature on the rise of certain organisms in biological research, philosophers, historians, and sociologists have taken a somewhat piecemeal approach to articulating the criteria that have been crucial to organismal choice in part because of their reliance on case studies of key organisms. In his reflections on the choice of experimental organisms, Richard Burian (1993) directs our attention to a number of features of this situation. Examples include how contingencies of evolution and circumstance make it difficult in many cases to know immediately whether a particular organism is a good choice for a particular investigation, and how the attributes of an organism can transform the researchers' perspectives on the investigative task at hand and lead them to questions that are better suited to the organism's features. Burian rightly emphasizes the multiple contingencies involved in finding and making an organism suitable for an investigative task. He notes that “the features that an organism should possess in order to be suitable for a given job are determined in good part by the problem at issue and by the available techniques” (p. 361, n. 20).

While Burian acknowledges the importance of issues including standardization and cost, he points to work by Doris Zallen (1993) for more detailed criteria. Zallen's careful analysis of the history of photosynthesis research leads her to articulate criteria such as the match between organismal properties and experimental equipment, the “ease of cultivation and maintenance of the organism,” the stability of the organism's properties, the ease with which multiple methods can be applied to the same kind of organisms, and the ease with which results can be generalized to other organisms (pp. 278–279). In the same special issue of the *Journal of the History of Biology,* Fred Holmes (1993) celebrates the “simplicity, ready availability, and capacity to survive severe injury” (p. 326) that made the frog the organism of choice for nineteenth-century physiology, while Bonnie Clause (1993) documents the power of standardization embodied in the Wistar rat. Developed from rich historical case studies, these early accounts of organismal choice stopped short of synthesis or generalization with regard to criteria. They did, however, recognize the complex interplay between different choice criteria, as well as illustrating diverse approaches to biological practice, including problem- or question-based research as compared to more descriptive strategies where a problem might emerge down the line.

At first glance, organismal choice using multiple criteria appear to inevitably involve trade-offs of a similar nature to those envisioned by Levins with regard to model choice. For instance, if one is interested in investigating fundamental biological processes shared by a broader class or taxon of organisms, an obvious candidate will be one of what have come to be recognized as the canonical “model organisms” (NIH, 2010). Relying on one of these organisms is likely to increase the generality of results, and particularly their applicability to higher level or more complex organisms including translation to humans, and at the same time can decrease the value of the organism in descriptive terms (what Levins calls ‘realism’) as a representation of one specific case (Ankeny & Leonelli, 2011). This sort of superficial adherence to Levins' trade-offs belies, we argue, a more complex set of judgements that involve what we call ‘multidimensional refinement processes,’ that is, the identification and comparison of various implications of the potential choices under consideration, embracing a range of factors including those that are more material (such as access and tractability), sociopolitical concerns (such as various economies), available resourcing (including epistemic resources such as previous theories), and future potential. This process of multidimensional refinement in turn involves a wide range of criteria utilized for choosing organisms, and a high degree of variability in terms of how such criteria are combined in any one instance of research organism choice. To illustrate this, we develop a analysis of the criteria involved in organism choice in section 4.

3. Identifying criteria for organismal choice: methodology

A brief description of the methods used to provide the empirical grounding for our analysis is necessary before we delve into it, particularly since some of the criteria that we identify as relevant to organism choice have not yet been discussed at length within the historical, philosophical, or sociological scholarship on the life sciences. Some interpretations of what counts as “convenience” (or more generally as criteria for “good” organismal choice) are explicitly discussed in published research by biologists, while others often can only be ascertained via observations of their scientific practices or presentations of their work in venues such as lab meetings or conferences, or via interviews or conversations with researchers about their practices (for a complementary account to ours on ‘good enough’ choices of animal models from a sociological perspective, see Lewis, Atkinson, Harrington, & Featherstone, 2013). Our starting point for this analysis was the collation and analysis of published biological literature that makes explicit reference to Krogh's principle and/or focuses on the issue of organismal choice, including both review papers and original research articles, starting from a list of over 160 articles obtained from a citation search in Web of Science. Cataloguing and assessing the various interpretations of Krogh's principle within that literature provided us with an initial outline of commonly utilized criteria. We were aware that many of these accounts of scientific methodology were retrospective reconstructions or pieces of methodological advice that may not reflect actual scientific practice or the range of circumstances in which these choices may in fact be made, but our aim was to explore the range of criteria biologists appeal to when clarifying or justifying their choice of organism(s). We enriched this initial taxonomy with other sources, including our own extensive fieldwork observing scientific practices or interviewing scientists[1]; informal, non-peer-reviewed source materials (e.g., grey literature shared within communities on experimental protocols); and the extensive previous historical and sociological scholarship on organism choice. We do not claim that our search was exhaustive or that it is perfectly descriptive of biological practice. We started from biologists' categories and refined them in light of our knowledge and experience as a diverse group of historians and philosophers of science to create a set of twenty criteria.

Our method explicitly aims to provide a philosophically useful account of criteria for organism choice that is both compatible with science in practice and allows us to develop deeper understanding of how conditions associated with research affect organismal choice, and in turn the outcomes of that research. The list of criteria that we have identified is not systematic in the sense of being grounded in a study of all existing scientific literature on the subject (as would be the case in a standard scientific systematic literature review), a task that in this case would be thankless given the amount of scholarship involved and the absence of any discussion of organismal choice in most biological publications. Instead, it provides a more expansive and empirically grounded list of criteria than has been proposed to date, that may usefully serve as a starting point for additional empirical investigations by scholars interested in organismal choice.

4. Twenty criteria for organismal choice

Our analysis has yielded twenty criteria for organismal choice. It may well be that additional criteria will be found through a different type of analysis of biological literature and practice, or via detailed focus on certain fields (such as those that are not experimental which tend to be less well-represented in the biological literature on organismal choice), and we thus see this paper as a step towards the further study of these issues. The criteria have been clustered together in order to allow the broader categories to serve as more accessible prompts for those who wish to utilize these criteria; these clusters are undoubtedly only one way amongst many to group the criteria and are not intended

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[1] When considered together, these fieldwork experiences encompassed ethnographic and interview-based research as well as collaborations within biology laboratories across Europe, the US, and Australia, carried out as part of several different projects over the last twenty years.

to be viewed as definitive or even necessary, but merely provided as a pragmatic device for the reader's convenience. The clusters clearly are not rigid, as many of the criteria have features that overlap with those in other categories; however, we believe that providing the criteria clustered in this manner allows a logical flow that helps to reveal important overlaps and discontinuities.

4.1. Access

The criteria in this section speak to issues of accessing organisms that are thought to be potentially useful for research or to provide access to the phenomena of interest. We include ethical considerations as a criterion which may regulate access to organisms or to some types of uses of particular organisms.

4.1.1. Ease of supply

Whether organisms are readily available (such as via strain centers) or rare and difficult to obtain can have a significant impact on organismal choice. Scarcity of organisms at a location or particular time of year can be limiting factors in research. For example in the early twentieth century, biologists studying the process of fertilization using amphibians had to wait for seasonal breeding periods when fertilized eggs were readily available. Later when it became possible to hormonally induce fertilization in the laboratory, temporal availability became less of a constraint (Rugh, 1968).

Whether one is searching for specimens in nature or ordering them through a supplier can make a significant difference for organism availability. Organisms can be obtained from commercial suppliers, as in mouse research (Rader, 2004), exchange networks and strain centers among laboratory groups as in the *Arabidopsis* and *C. elegans* research communities (Leonelli, 2007; Wood and the Community of *C. elegans* Researchers, 1988), or natural or wild settings (e.g., Abzhanov et al., 2008). The creation of marine stations in the early twentieth century, for instance, greatly facilitated research on a wide of range of organisms that were only available near the sea (Maienschein, Matlin, & Ankeny, 2019). Limited availability of organisms from wild or natural sources can make research on them highly localized and non-transferable. If it is important to study the organisms within their natural environment, research can be further restrained geographically and temporally.

4.1.2. Phenomenal access

Undoubtedly what researchers want to study (problem choice) constrains many of the choices that they make regarding research organisms, though not all biological investigations begin from a specific problem or question. There are many cases where researchers design their work around a specific research question concerning a particular phenomenon of interest, and thus look for an organism that provides access to that phenomenon in the sense of instantiating its typical features or providing insights that can be used towards understanding the phenomenon in question. For instance, Michel Milinkovitch and Athanasia Tzika (2007) point out that fruit flies have an “easy-to-score morphological variation” (p. 338) that made *Drosophila* a particularly useful organism for genetics. At the same time, it is significant that the easy-to-group morphological variations became a selling point after Thomas Hunt Morgan's fly lab identified them (Kohler, 1994) does not help explain why fruit flies were chosen in the first place. In another example, in the 1930s and the 1940s, Jean and Katsuma Dan used a variety of marine organisms to study cell cleavage. The Dans focused on these organisms because they provided insights into the cell division process, as the chosen organisms varied in the rate of division and provided uncommon visibility of phenomena involved in cell cleavage, such as astral rays (Dietrich, Crowe, & Ankeny, 2019).

Organism choice may become very restricted depending on the phenomena that one is trying to access. In embryology, some eggs have opaque shells that make observing the process of cell cleavage very difficult: hence if cell cleavage is the phenomena that a researcher wishes to investigate, organisms with more translucent embryos are a better choice. Specific questions regarding mammalian physiology may make choices between some organisms easy for researchers; mice provide phenomenal access to cancer genetics in a way that *Saccharomyces* may not, for instance. That being said, research models do not have to be isomorphic to the phenomenon of interest as long as effective comparisons be made (see criteria 18, comparative potential). Scientists working with zebrafish have pointed out, for example, that “the zebrafish intestine is analogous to the human intestine with segmentation of the small and large intestine” (Schwartz, de Jonge, & Forrest, 2015, p. 370), making them a reasonable organism choice if one is interested in issues related to the human digestive system. Notably since researchers can validate the use of an organism due to its analogous phenomenal access, a great many organismal choices can include many of the other criteria we list here.

4.1.3. Ethical considerations

Ethical considerations are clearly criteria that enter into organism choice and use, as different organisms have different moral standing and are subject to varying levels of ethical and legal regulation depending on the type of research and the locale in which it is to occur, among other factors. The most obvious example is use of non-human primates which many contend would be the most appropriate experimental organisms for behavioral and other types of research where the intention is to apply findings directly to humans, but where ethical (and financial) restrictions often enter into decisions.

Even more generally, humans might well be the most appropriate organisms on which to study human processes, but in many types of research, using human subjects is thought to be ethically unjustifiable, and hence mice and rats are extremely popular experimental organisms for biomedical research. Other species are problematic because of their availability due to being vulnerable or endangered; public perceptions regarding use of these animals for research, and particularly their degree of sentience and susceptibility to psychological and physical harm; or restricted access due to import or quarantine regulations (see e.g. the cases of monkeys and pigs analyzed in Koch & Svendsen, 2015; Svendsen, 2017). Concerted efforts by funders, regulators, and research institutions to use the three Rs (replacement, reduction, and refinement) as the key framework in animal experimentation in order to ensure what occurs is humane has led to support of alternative types of organisms, including increasing numbers of non-mammalian models including microorganisms and invertebrates, and even in vitro (e.g., cell and tissue cultures) or non-biological systems (e.g., computer simulations) where possible (Davies, Greenhough, Hobson-West, & Kirk, 2018).

4.2. Tractability

The criteria clustered under the heading of tractability each address dimensions of scientific practice. Some of these criteria focus on the ability of organisms to adapt to research conditions, such as whether the organism survive in captivity or respond to experimental treatment. Other criteria are more researcher-focused, such as what kinds of risks an organism poses for the researcher or what kinds of techniques can the researcher readily apply to the organism in question.

4.2.1. Standardization

In some cases, researchers require organisms whose features are stable enough to be reliably documented and compared across different laboratories by independent researchers (Hopwood, 2005, 2007; Logan, 2002; Robert, 2008). Complex techniques and methods have emerged to ensure that research organisms acquire and/or preserve certain characteristics across generations, giving rise to collections of standardized organisms as well as mutants and variants. The move towards standardizing organisms, most glaring in the case of model organisms, is typically accompanied by increasingly sophisticated standards for describing their characteristics, as exemplified by the recent revival of phenomics (Houle, Govindaraju, & Omholt, 2010) and morphology as fields of active research interest. As a result, some organisms come to "corner the market," in the sense that "so much begins to be known about a particular animal model—that is, they become so popular—that even more compelling potential models are no longer explored" (Burggren, 1999, p. 149).

There are other cases, by contrast, where what researchers value is the absence of standards. The degree of natural variation within a species has a significant role to play in its employment within research. These are situations where biodiversity and variability are themselves under scrutiny, requiring researchers to look for highly variable organisms that can help investigate either natural or induced variability within a laboratory environment. Fast-evolving microbial communities are a typical example here as are plant variants (e.g. Love & Travisano, 2013).

4.2.2. *Viability and durability*

Another possible interpretation of 'convenience' when it comes to research organism choices is connected to the logistics of conducting research. Here considerations of viability and durability as they affect generation cycles and physical robustness become important. As Jessica Bolker (2009) succinctly points out, "small size, rapid and robust development, and short generation time are also advantageous for many types of research" (p. 487). Many of the advantages that researchers have noted about *Drosophila* fall into this category. Fruit flies reproduce quickly, allowing researchers who were interesting in studying the transmission of traits from one generation to the next gather more information more quickly compared to organisms with seasonal generational cycles, such as maize. Similarly, high fecundity has typically been viewed as an advantage, as it allows for more individuals per generation.

However, just because an organism is small, has short generation periods, and highly fecund, it is not necessarily an easy choice for long-term experimental research. These attributes only become useful if they can be used in a laboratory setting. Organisms that are highly sensitive to captivity (e.g., where they have poor health and/or die quickly) or have problems procreating outside their natural habitat make it difficult for researchers to study them. For instance, John Gurdon and Nick Hopwood (2000) report the advantages of *Xenopus* to be "ease of maintenance…exceptional resistance to disease…a [short] life cycle…large numbers and size of eggs…and above all its year-round reproductive response" (p. 43). These qualities gave particular advantages over other amphibian species for studies of development. In comparison, *Rana pipiens*, a popular choice for researchers in the United States during the first half of the twentieth century, could not be bred in captivity or kept longer than a few months without deterioration. Later in the 1960s and 1970s, researchers using *Rana* had to contend with problems obtaining healthy specimens as wild populations experienced significant increases in rates of cancers. In comparison, the robustness of *Xenopus* became increasingly useful for researchers.

4.2.3. *Responsiveness*

When Krogh (1929) originally highlighted that a large number of problems can be most conveniently accessed through specific animals of choice, he was referring to features of selected animals that make a biological process or mechanism more experimentally accessible. Among all possible choices, he argued, there will typically be a few organisms that provide better opportunities for the experimental manipulation of features of interest, or for non-experimental forms of interacting with the organism to elicit information about phenomena of interest. As an example, Krogh highlighted that the lungs of tortoises are well suited for studies of the respiratory system. Because the trachea for each lung are highly divided compared to mammals, these organisms make it possible to independently measure gas exchange in the two lungs. Experiments on tortoises and frogs were central to Krogh's demonstration of how gas exchange occur by diffusion alone, an insight that was later generalized also to mammals (Wang, 2011). Other historical examples occur in the case of the giant axon of the *Loligo* squid that provided empirical data for the Hodgkin-Huxley model, and the highly metabolic activity of pigeon breast muscle which allowed Hans Krebs to experimentally study the processes of oxidative metabolism (Krebs, 1975).

Features that ease experimental access can be purely practical or instrumental, such as a convenient size of a particular organ or organism: Krebs (1975) notes several examples in which "one of the decisive advantages is the mere size of the material, so that manipulations can become easier" (p. 225) including giant water bugs, the giant unicellular alga *Acetabularia,* and *Bufo marinus* (the giant Neotropical toad). But experimental access often is associated with specialized adaptive features that are more clearly displayed in specific organisms. In such cases, it is often stressed that distinct or extreme adaptations can give insight to "the limits to which organismal design can be driven and often best and most clearly illustrate the basic design principles at work" (Adriaens & Herrel, 2009, p. 1). For instance, the freshwater fish *Inanga* exhibits an extreme capacity to maintain sodium homeostasis across wide changes in water salinity and has been highlighted as an organism particularly well suited to study basic principles of ion transport and sodium regulation (Lee, Collings, & Glover, 2016). Organisms with extreme morphologies or capacities are thus often chosen as the experimental starting point for exploring more general relations between structure, function and environmental demands (see also criterion 18, comparative potential). Conversely, organisms that are well-recognized as canonical model organisms fail the test of experimental accessibility with regard to certain types of experimentation; for instance as noted by physiologist Kevin Strange, "It is safe to say that *C. elegans* violates Krogh's Principle when it comes to electrophysiology. Most somatic cells in *C. elegans* are quite small, and a tough, pressurized cuticle surrounding the animal limits access for study by patch clamp methods" (2002, p. 12). More generally, what experimental accessibility is taken to involve varies depending on the inquiry at hand, as demonstrated by the shifting status of organisms with large chromosomes (such as wheat or maize) depending on whether research focuses on sequencing or transposon activity.

4.2.4. *Availability of methods and techniques*

Having a well-developed set of tools for a particular organismal system can be a factor in the decision to adopt that system for laboratory or field research. For instance, as *Drosophila* was developed as an organism for genetic research in the first decades of the twentieth century, tools, techniques, and materials were developed that made the use of *Drosophila* easier and more consistent across researchers (Kohler, 1994). Simple matters, such as the size of bottles used to grow flies, the recipe for fly food, and the type of material used to make the bottle stopper, were routinized. Later as the *Drosophila* community grew, this technical information was communicated through the *Drosophila Information Service*, which shared technical information such as how to build a constant temperature growth chamber. The availability of this body of knowledge meant that new researchers had to invest less of their time and energy into the development of crucial organismal infrastructure, including development and maintenance of specialized mutant stocks. Similar configurations of techniques, skills and infrastructures characterize research on other key model organisms, such as *Arabidopsis* and *C. elegans* (Ankeny & Leonelli, 2011, 2012). At the same time, such a complex and sophisticated body of methodology, technologies, and analytic techniques is not always or even typically required when choosing organisms with which to work. Often researchers can make do with locally grown knowledge about how to handle an organism, as well as techniques and technologies enabling a smooth experimental interaction with it.

4.2.5. Researcher risks

Some research involves risk of danger and harm to researchers, organisms, and/or ecosystems. These risks of harm can hinder research on certain organismal systems. For instance, research on pathogens is crucial, but dangerous. The system of containment protocols and standards for disease organisms speaks to the risk to human researchers that can accompany some types of organismal research (Hunt, 2006). Research on venomous snakes likewise entails obvious risks that have to be taken into account when deciding to use them as research organisms (Altimari, 2000). The risk of harm to the organisms themselves should constitute an ethical concern, which we consider under our criterion A3, ethical considerations, in section 4.1.3.

4.3. Resourcing

The criteria in this section point to different kinds of intellectual resources that can facilitate research on a particular organism.

4.3.1. Previous use

The knowledge already available to researchers about a given organism—including about its physiology, genetics, and behavior—often plays a crucial role in shaping organism choice, in what in some cases might be described as allegiance to a given species. The acquisition of knowledge about an organism requires significant effort, much of which is not directly related to the investigation of the research questions at hand (e.g., learning how to feed the organism or how it reacts to specific laboratory conditions). This expertise helps to explain why researchers who have been trained in using a particular organism have tendencies to continue using it (Flannery, 1997, p. 244). Increasing familiarity with an organism thus increases the entrenchment of that organism within a given research community, as do the use of specific techniques, technologies, and conceptualizations.

A deep body of knowledge concerning a particular organism also increases the number of types of uses for which it can be deployed, as demonstrated by the many cases where advantageous features of an organism with respect to a specific research question only emerged in retrospect once it was already adopted as a preferred model (Ankeny & Leonelli, 2011). Hence applications of organisms that have been used for research purposes for several decades, such as the dinoflagellate *Oxyrrhis marina*, “appear to be rising exponentially across a number of fields” (Montagnes et al., 2011, p. 550).

4.3.2. Epistemic resources

Organism choice occurs against the backdrop of existing intellectual traditions, theoretical perspectives, and/or disciplines, and thus tends to conform—at least in some or most respects—to the background assumptions and conceptual commitments championed by the scientists involved in the research (this criterion hence echoes Kuhnian considerations, see e.g. Kuhn, 1977). The extent to which an organism fits such expectations, and thus the broader epistemic landscape within which the research is situated, is significant to the choice of organisms particularly since any rupture from such landscape needs to be justified and accounted for. A simple example can be found in the limited efforts to date to use plants to study certain kinds of phenomena: traditionally plants have been viewed as extremely simple and relatively inactive organisms that are largely stimulus-driven and have limited (if any) behaviors worthy of study. Thus, they have typically been thought to be poor choices for studying behavior, let alone cognitive activities. However, some researchers are choosing to use plants in novel ways by pushing back against these received views, for instance to study associative learning, and using positive findings to encourage others to rethink their assumptions about using plants for these types of research (Gagliano, 2017; Ruggles, forthcoming). Thus, while the criterion of epistemic resources recognizes the important role of theory in biological research practices, it also highlights the varied roles that background theories can play in organism choice. As one criterion among many, its significance may shift significantly depending on the situation, and be less decisive than sometimes predicated within the philosophical literature on modelling (e.g. Currie & Levy, 2015).

4.3.3. Training requirements

The amount of time needed to develop expertise and research competence can also be a factor in the choice of an organism. Well-developed systems may require review of a daunting amount of material associated with developing skills. Specialized manuals on organisms such as *C. elegans*, *Arabidopsis,* and *Drosophila* (see Sullivan, Ashburner, & Hawley, 2000) offer detailed descriptions of these systems. A new or relatively immature organismal system where very little is known and much needs to be developed before the system can be reliably manipulated requires much more extensive experience and training. Reflecting on her choice of a non-model organism, biologist Stefania Castagnetti reports, “For the new species, we have to start from scratch, figuring out simple things like their reproductive season, how to obtain mature eggs, how to treat the embryos. Even to film untreated embryos we have to figure out how to mount them. So for each animal, we have to start all over again” (Perillo, 2017).

4.3.4. Informational resources

The adoption of an organism for research can be strongly influenced by the presence of databases, newsletters (Kelty, 2012), and/or journals dedicated to the study of a given species. Researchers often ask themselves whether there are resources that make information available about their organism of choice, or at least groups of people that they can approach to acquire more knowledge about it. The importance of informational resources has been increasingly recognized by funding bodies around the world, which are often confronted with difficult choices around which of such resources to fund (and thus, which organism to support as a better for particular types of research). For example, “The National Institutes of Health (NIH) directly support database development when there is significant demand. Consider the phenomenal success of GenBank (www.ncbi.nlm.nih.gov) or the significance of FlyBase (flybase.bio.indiana.edu) to the Drosophila community. Both of these resources are a testament to the influence that a well-supported database can have on promoting and shaping research” (Halanych & Goertzen, 2009, p. 477). Repositories that are not focused on particular species but do enable researchers to compare different species in relation to a common set of questions, are also highly valued and influential in the choice of organism. An example is the study of human craniofacial anomalies via non-human animals, where “data repositories such as FaceBase (https://www.facebase.org/) are crucial for advancing the field. Broad screening of animal models (such as the mouse) can efficiently link gene identification to cellular function” (Liu, 2016, p. 169).

4.4. Economies

The criteria in this section speak to the financial, institutional, social, and moral or affective economies in which organisms may be positioned. We cluster criteria that range from the financial to the emotional because in part these criteria represent ways to consider different kinds of costs and benefits for different parties.

4.4.1. Institutional support

The institutional contexts for researchers also can play a role in their choice of organism. Some institutions have invested heavily in facilities for particular organisms, therefore incentivizing and sometimes even requiring researchers to use those organisms. Historically both the Jackson Laboratory in Bar Harbor and the Wistar Institute in Philadelphia are good examples of the institutional commitments to mice and rats, respectively, that would have significantly influenced organismal choices for researchers (Clause, 1993; Rader, 2004). Even on a smaller scale, researchers hired into new institutions could also be incentivized to use established breeding colonies, networks, or laboratory infrastructures for a particular organism rather than using resources to create the infrastructure needed for a new organism. In an institution that may not have many resources, a researcher may choose an organism precisely because it does not require much institutional investment, particularly in locales where regulatory and compliance costs can be high, such as for the use of genetically modified organisms which in many countries requires the adoption of expensive and logistically challenging containment and security measures.

The priorities of even larger institutional structures also can play a role in organism choice. Large funding agencies may explicitly favor the use of particular organisms or decide to focus on projects that achieve particular goals. The former is best exemplified in the official U.S. National Institutes of Health designations in 1999 of thirteen model organisms. Whether NIH actually favored projects using these organisms is up for debate, but many researchers had the impression that their work was more likely to get funded if they used one of the listed organisms (Peirson, Kropp, Damerow, & Laubichler, 2017). In the latter case, organismal choices for researchers can also be canalized when funding institutions set topical priorities, such as occurred in the Human Genome Project. Similarly, the U.S. Department of Health and Human Services 2015 BRAIN Initiative devoted tens of millions of dollars towards research to map the human brain and incentivized researchers to ask specific questions about phenomena.

4.4.2. *Financial considerations*

Given the above-mentioned specificity of material conditions, technologies, and conceptual tools required to do research with any one species, it is no surprise that a significant criterion affecting the choice of organisms relates to the associated financial costs. Research budgets are rarely as large as researchers would wish them to be and include considerable capital expenditure such as equipment and staffing for laboratories. Whenever choosing an organism, researchers need to consider whether some of these costs are heightened or diffused by available standardized organisms and related tools. In some cases, the presence of already developed culture facilities or chromosome libraries can help researchers economize; in others, the costs associated with standard mutants (e.g., the oncomouse), containment facilities for such mutants, or relevant technologies (e.g., next-generation sequencers) will outstrip the advantages of choosing a particular organism.

Research costs can also vary widely from organism to organism. Mammalian systems, for instance, require a much more complex, expensive, and extensive physical infrastructure than the average fruit fly or zebrafish lab. Following NIH guidelines for rate setting practices, most major U.S. research universities publish schedules of animal husbandry per diem rates which are revealing: for instance at the University of Michigan, the per diem rate for a mouse is $0.44, while for a pig is $17.42.[2]

Arguments around emerging model organisms provide particularly useful examples for analyzing arguments about the financial requirements of selecting organisms that do not have established track records of use in research: for instance, “increased resources from funding agencies will have to stretch to support the development of new community resources (e.g., transgenics or culture facilities) and the creation of preliminary tools (e.g., EST collections or bacterial artificial chromosome libraries) for emerging model systems, making it even more important that choices be made with care” (Abzhanov et al., 2008, p. 359).

4.4.3. *Community support*

Organism choice and use is strongly shaped by the availability of a community which can provide various forms of support for the research being pursued (Leonelli & Ankeny, 2012), particularly amongst those earlier in their careers. In addition to informational resources, communities provide a location for presenting research and recognized methods for peer review and feedback, especially through those communities which are primarily focused on a single organisms or group of organisms and convene regularized conferences, as well as steering communities, oversight groups, and so on which provide institutional structures that support and justify the research. Community support also results in stronger pooled resources becoming available for informal and sometimes more formal exchange, such as strains, materials, methods, data, findings, and techniques. The existence of a community organized around a particular organism also tends to lead to greater recognition more broadly in biology, including amongst funders (Leonelli, 2019).

4.4.4. *Affective and cultural attributes*

When the American Elasmobranch Society asked its members for reasons why they studied sharks, one responded “Because sharks are cool!” (Ferry & Shiffman, 2014, Appendix 2). Self-professed ‘shark huggers’ have more than an intellectual attachment to their organisms. Like other ‘charismatic megafauna,’ sharks are linked to a powerful symbolism (in this case around strength, speed, and danger) that has become entrenched in many cultures around the world. It also colors researchers' interactions with these creatures as well as the ways in which such interactions are narrated both within and outside the research community, for instance in the widespread discourse around sharks being ‘less dangerous than people’ and the emphasis by conservation biologists on the falsity of some of the cultural stereotypes associated with the animal. They also, and relatedly, elicit an emotional connection from researchers. In the words of another elasmobranch biologist, “I enjoy (get personal happiness) from interacting with elasmobranchs more than any other taxa.” It is not only people who work with charismatic organisms that form attachments to their research organisms. Research communities form strong loyalties to many different types of organisms ranging from microbes to weeds, which may be grounded in familiarity with these organisms as well as the value attributed to them within the broader ecosystem. The intense emotional link between marine biologists and coral reefs, whose threatened extinction has come to symbolize the threat posed by human-made climate change on the planet, is a case in point (Braverman, 2016). These connections can also be a source of tension as attachment to organisms may lead researchers to treat them more as pets than research subjects, raising not only questions of objectivity, but about the ethical status of research organisms (Herzog, 2002; Lehman, 1992).

4.5. *Promise*

This final cluster of criteria is comprised of forward-looking criteria. These criteria speak to the promise of potential of an organism to produce a commercial reward, to be compared to studies in other organisms, to be used in a medical context, or to lead to novel findings.

4.5.1. *Commercial and other applications*

The potential to use research on organisms (or even the organisms themselves) as products or as part of various technologies or applications in some cases shapes research choices. Examples abound, such as exploring materials produced by various organisms as exemplars that can be used via biomimicry and other techniques to produce novel products like bee, ant, and wasp silk (for a review, see Liu & Jiang, 2011). Zebrafish may well be the ‘Rosetta stone’ of biology due to its role in molecular biological research (Gest, 1995), but in fact it is highly valuable in economic terms allowing tests of the effects of effluents among other applications (Vascotto, Beckham, & Kelly, 1997). Similarly, there are historical examples of organisms doubling up as commercially viable technologies, such as the use of *Xenopus* in pregnancy testing in the 1950s. As summarized by Kurt Schwenk, Padilla, Bakken,

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[2] Animal Husbandry Rates, University of Michigan. https://animalcare.umich.edu/business-services/rates. Accessed on March 11, 2019.

and Full (2009), "The vast diversity of functional solutions to environmental problems embodied within organismal systems and perfected through natural selection over evolutionary time provides a rich resource for human needs. New sources of food, structural materials, energy, microbial processes, waste and energy conversion, problem-solving algorithms, and engineering design remain to be discovered, characterized, and developed. Organismal biologists can take a leading role in this process and in organizing and directing the data so that it is maximally beneficial" (pp. 9–10). A glaring example of this tendency is to be found in contemporary plant science, where attention to the study of commercially relevant crops is increasing at the expense of research on economically irrelevant plants like *Arabidopsis* or less profitable crops like Bambara groundnut.

In addition, the potential for an organism to serve as a cornerstone of public engagement which in turn leads to support financial and otherwise can be critical to organismal choice. For instance in conservation biology, focus on 'charismatic species' goes well beyond its affective dimension but has considerable impact on the ability to finance research and build related endeavors such as tourism: in the case of elasmobranchs (skates, sharks, and rays), researchers surveyed reported that it is "easier to engage the public and therefore educate them about conservation issues" (Ferry & Shiffman, 2014, Appendix 2), and similar considerations apply to work on coral reefs (Braverman, 2016).

4.5.2. Comparative potential

Insights into relations between structures, functions, and environmental constraints can be obtained by comparing organisms that are hypothesized to display variation across a particular dimension. The comparative method has for instance been central to insights in renal physiology, where the kidneys of very diverse species (mammals, birds, reptiles, amphibians, and fishes) have been compared to identify functions of common structures such as renal tubules and Bowman's capsule. The strategy has often been to observe a particular physiological structure in an 'exaggerated form' among a specific species, and to explore the generality of the structure or principles in a variety of other species (Dantzler, 1987). Through such comparisons, physiological adaptations to specific environmental challenges often become visible. Comparing the kidney morphology of desert rodents to aquatic freshwater mammals for instance reveals that these differ with respect to the length of the kidney structure called the loop of Henle, which upregulates urea concentration through osmotic gradients along the loop (Campbell & Reece, 2005; Schmidt-Nielsen, 1983).

The aim of the comparative method is not only to map biological diversity, but also to identify variations over characteristic types of solutions that respond to more general "constraints on being alive" (Wouters, 2007, p. 66). This heuristic is in line with August Krogh's recommendations as he stressed that the ideal of generality in physiology could only be reached by studying physiological features "throughout the myriad of organisms" and "in all their essential modifications" (Krogh, 1929, p. 202; see also; Jørgensen, 2001). From a comparative point of view, organism choice is thus guided by an interest in understanding the solutions that make possible the survival of organisms under different environmental conditions, but also in understanding why there is unity in diversity in terms of shared physiological or biochemical principles (Somero, 2000).

4.5.3. Translational potential

Organisms are often chosen because of the potential of translating insights from experimental studies to the biomedical domain. Most commonly, organisms are chosen because of their physiological or genetic resemblance to humans, the presence of similar mechanisms in both species, or due to high rates of incidence of a given disease of interest. These features are often highlighted when justifying why mice and rats currently make up the majority of vertebrate models in animal experiments (Beery & Kaufer, 2015). Similarly, animals that are highly sensitive to heavy metals or endocrine disrupting chemicals, such as zebrafish, have been widely used to study potential impacts of chemical compounds on human health and environmental effects (Dai et al., 2014); species of yeast are routinely used to model cell deregulation in oncology (Leonelli, 2018; Pray, 2008).

In some contexts, however, organisms are chosen for biomedical research because of the lack of sensitivity to environmental expose or due to the absence of a specific disease. Such organisms are often highlighted as *negative models* of human physiology, as they offer some advantages that are complementary to organisms chosen because of similarity (Alstrup & Wang, 2016). For instance, mice do not develop Alzheimer's disease unless specific human genes are incorporated in their genome; thus transgenic Alzheimer's mouse models are explored in an attempt to provide a controlled replication of the disease pathology and explore possible targets of reversal (Elder, Gama Sosa, & De Gasperi, 2010; Oddo et al., 2003). Negative models are also chosen in the hope that these allow for insights to possible defense mechanisms. The naked mole rat is an example of an increasingly popular experimental organisms in cancer research, because, despite its longer lifespan compared to other rodents, it rarely develops cancer. Studies of biochemical processes within the cells of the naked mole rats have suggested a set of potential "anti-cancer mechanisms" that potentially can be exploited in biomedical treatment (Rankin & Frankel, 2016; Tian et al., 2013). Translational potential of experimental organisms can thus stem from similarities as well as differences to human physiology (Perlman, 2016).

4.5.4. Novelty

Novelty is another potential criterion for organismal choice: in a space tightly occupied by ever-growing groups of biologists, particularly in association with heavily used, more well-established research organisms, some researchers seek novel options as they are viewed as providing opportunities for new findings or diverse types of comparisons to other species. Clearly there are trade-offs here, as although a lightly used or otherwise overlooked species may offer greater opportunities for discovery, it is likely to lack well-developed techniques and methods or a community of fellow users to appreciate or take up findings, particularly compared to traditional model and research organisms. Some have termed this the "inverse Krogh principle," namely "choosing to study a species that has been most appropriate for stimulating new questions rather than providing definitive answers" (Kram & Dawson, 1998; after; Dawson & Taylor, 1973), in this case with specific reference to the use of the red kangaroo to study locomotion as a way of opening up a new research space via focus on a novel organism.

More poetically, others cite the medieval similes of the "world as a book" or the "treasure house of nature" as pointing to biodiversity as critical for insights and learning, for instance in a biologist recounting his own experience as "the sole PhD student working on hybrid poplar in a department where virtually everyone else was studying Arabidopsis" (Robischon, 2014, p. 195). A more general recent trend focuses on 'emerging model organisms,' ranging from leeches to wallabies, which are organisms that typically have been relatively underexplored except within particular research groups or fields, but which are being argued to be useful for particular types of studies (CSHL, n.d.). Finally, some emphasize 'non-consensus' models (e.g., Rosario-Ortiz et al., 2008), thus explicitly embedding an aspiration for these organismal choices to become more established and agreed upon more widely in the future as useful models.

5. Practical applications of criteria for organism choice: strategies in designing biological research

Organism choice involves complex judgements based on consideration of multiple criteria, a situation which may not always be explicitly discussed by scientists, although it is sometimes mentioned by researchers attempting to articulate their methodological strategies. For example, Anneliese Beery and Daniela Kaufer (2015) claim that "The choice of the best animal models for advancing understanding of normal and abnormal human functions is constrained by disciplinary traditions, expedience, cost, ethical and political consideration, and institutional resources" (p. 117). Having identified a diverse range of criteria for choosing (or rejecting), and using (or abandoning) research organisms, we now turn to a discussion of how these criteria are used in relation with each other.

In any instance of organismal choice, not all of the criteria will be used; of those used, not all will be given equal weight. In fact, many research situations require scientists to prioritize a cluster of criteria over others. Such decisions are not merely grounded in claims about contingency, for instance, when a researcher disregards the poor viability of his or her chosen organism because it was inexpensive to use. If a scientist's goal is to increase our knowledge of some phenomenon, then phenomenal access and ease of supply typically will have more weight than other criteria. In some cases, these criteria cannot be fulfilled, and research on specific phenomena or organisms is not possible. For instance, before the invention of submersibles, research on predation among deep ocean fish was limited by the lack of access to those organisms. Limits on material supply made this research impossible. In an analogous fashion, research on predation in fish requires the availability of fish (a condition that can be easily met), but the fish must also engage in predatory behavior, so not every species of fish will suffice as an object of study.

That said, adherence to these criteria need not be absolute. Biologists regularly engage in what we term 'multidimensional refinement' as they adjust the criteria which they are considering; their research goals, questions, and methods; and consider the wider context and circumstances of their research. Faced with the impossibility of studying predation in deep ocean fish, biologists could have modified the goals of their research to focus on a related problem, such as predation in freshwater fish where material is readily available and the phenomenon of predation can be discerned amongst the many different species that are available. This kind of refinement, we assert, is commonplace, even if it is seldom explicitly discussed in the methods section of published papers (which typically focus on the logical reconstruction of the argument proposed, rather than the chronological development of the research that underpins it). Even ethical criteria, which are seen by many as providing a hard constraint on some forms of contemporary research, can be subject to refinement. Widely accepted practices of replacement, refinement, and reduction in research involving animals explicitly encourage minimizing ethically significant harms by replacing, for instance, vertebrate for invertebrate organisms (Davies et al., 2018). At the same time, the ethical principles informing this practice have changed considerably over time, and their practical implementation can differ across research environments.

While Krogh appealed to a criterion of convenience for organismal choice, our list suggests that appeals to 'convenience' typically cover several distinct criteria, often with complex relationships to each other; how criteria are used is contingent and variable. In the context of making a choice from among a range of organisms, we propose that criteria can play a range of roles: for instance, they can constrain choice; they can confer an advantage or disadvantage to a particular organism or set of organisms; multiple criteria can act in synergy with each other to confer a greater combined advantage; and multiple criteria can antagonistically combine to confer a greater disadvantage to an organism or set of organisms.

Criteria which act as constraints on choice limit the available set of possible organisms. Ethical (or financial) considerations, for instance, may be invoked to prohibit research on certain kinds on primates. In this context, the criterion of ethical (or financial) considerations acts as a constraint on the choice.

Some criteria may confer an advantage or disadvantage to some organisms in a particular situation. For a herpetologist, cobras and garter snakes may both be attractive research subjects, but the risk to the researcher of handling cobras and the safeguards that their home institution may require could confer an advantage to the garter snake. In these kind of cases, multiple criteria are employed in a choice between a range of organisms. Choice can be predicated on a single criterion or applied singly to organisms. When multiple criteria are used, they can have different weights and researchers can use different decision procedures to maximize or minimize certain payoffs or costs. Because our focus here is on the criteria for choice, we leave discussion of different decision strategies for another paper.

Multiple criteria can also combine to produce a synergetic effect: their combination can amplify the advantage conferred beyond the sum of the individual criteria. Similarly, for some combinations of criteria in some circumstances, the criteria could interact antagonistically, producing greater disadvantages than the sum of the individual criteria. Possible synergies include relationships between know how, familiarity, and standardization; between community support and informational resources; or between translational potential, financial considerations, institutional support, and commercialization. For instance, financial considerations, institutional support, and commercial potential could interact synergistically to produce a greater incentive to use a particular organism. This feedback would be created when a university stands to share in the profits from the commercialization of some research and offers more space or financial support for that line of research. Conversely, criteria such as previous use and ethical considerations could act antagonistically. For instance, the success of zebrafish is said to be due in part to the limited ethical considerations associated with it, as compared to other vertebrate species. [3]

In the philosophical discussion of Levins's criteria for model choice, trade-offs between criteria play a central role. The idea behind a trade-off is that criteria that are in a trade-off cannot both be fully realized at the same time. Possible trade-offs between criteria for organism choice might include previous use and novelty: a very well-studied organism may be judged to be unlikely to yield an original new result. Unlike the trade-offs in model choice which are grounded in logical relations between the criteria, however, the potential trade-offs in organismal choice are themselves contingent: there are not logical trade-offs that are obligatory regardless of the research context.

We view trade-offs between criteria for organism choice as non-generalizable, because they depend as much on practical and situated considerations as they depend on conceptual considerations about how results obtained through the organism can be interpreted. Researchers seek to satisfy multiple criteria in any given decision. So ethical and financial considerations are not 'trump cards' that are the final arbiters about organism choice for scientific research. Rather, doing ethical research within a budget meets multiple goals: it instantiates a simultaneous solution to intersecting problems through the consideration and weighting of a range of factors and criteria, which are all heavily context dependent. Thus, the importance of determining advantages and synergies among criteria over trade-offs is particularly significant. While it is important to determine which criteria are in tension with each other in a given research situation, it is also productive to think about how different criteria may mutually coexist and/or reinforce each other.

Virtually all the criteria listed above require that researchers identify and evaluate potential implications of choosing a particular organism before finalizing that choice. On the one hand, this process can resemble a form of risk assessment (Abt, Rodricks, Levy, Zeise, & Burke, 2010), particularly when considering possible ethical concerns or the epistemic implications of choosing a particular organism (such as the projectability of results to other species). On the other hand, it can be thought of as akin to a feasibility study (Bowen et al., 2009), where scientists are concerned with the possibility that research may be impeded by material that fails to allow phenomenal access or institutional

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[3] We are grateful to Reuben Message for pointing out this example.

constraints and are attempting to assess what type of organism may fit the available set-up. As has been noted in relation to risk assessment and feasibility studies, the interpretation and practical application of criteria for organism choice can vary significantly across contexts of inquiry, with different combinations of factors determining a shift in how each criterion is understood and implemented, a situation that explains the historical shifts in the use and status of certain organisms even within the same research programs and groups (see e.g. Kohler, 1994; Rheinberger, 1995).

Each research situation tends to involve different types of tensions and utilize diverse combinations of criteria differently. In what follows, we sketch two case studies to illustrate the usefulness of tracking how different criteria are used in synergy or against each other through the development of research programs around specific organisms, thus exemplifying the process of multidimensional refinement which our approach makes visible and accessible to historical and philosophical analysis. These cases are necessarily oversimplified, and we hope that others will find these criteria useful for more detailed and complex analyses.

5.1. Choosing embryos

Our first case exemplifies the way in which our approach facilitates the study of an individual's reasoning around model choice develops over time. Like many areas of biology, the field of developmental biology has gone through several shifts in research organism popularity. For example, in the middle of the twentieth century the frog species *Xenopus* gained in popularity whereas the use of urodeles, specifically salamanders and newts, declined. The latter had become particularly important to the field after the famous experiments of Hans Spemann's group in the 1920s. Spemann and his students were especially adept at performing microsurgical manipulations of salamander and newt embryos, which led to a cascade of experimental work on induction in embryogenesis. In the 1970s, however, the frog *Xenopus* pushed out salamanders and newts as the preferred objects of study (Gurdon & Hopwood, 2000).

Historically there are lots of reasons why this occurred. Lancelot Hogben created an important experimental colony of *Xenopus,* a frog species from South Africa, in the 1930s and it grew in popularity because it was commonly used for pregnancy testing in the early and mid-twentieth century (Hopwood, 2011). However, availability of the new organism does not justify why it became popular for developmental biologists to use. The reflections of Pieter Nieuwkoop, an embryologist whose career spanned from the 1940s through the 1980s, offers more insight into this change.

In 1996, Pieter Nieuwkoop reflected on the advantages and disadvantages of salamanders as he tried to come to terms with the rise of *Xenopus* in developmental biology. Overall, he understood that good research organisms needed to fulfill several criteria. The “the adequate experimental animal,” he said, included “good local availability, easy adaptation to laboratory conditions, proper length of breeding season, relatively easy manipulation of eggs and embryos, adequate speed of embryonic development, not too long a generation time, proper histological differentiation of embryo and larva, etc.” (Nieuwkoop, 1996, p. 617). We see here five of the criteria (ease of supply, phenomenal access, standardization, viability and durability, and responsiveness) coming to the fore in ways that, far from competing, reinforce each other. The criteria of previous use, epistemic resources, and training requirements are also emphasized in Nieuwkoop's account. What's interesting is that he realizes that the standards for fulling these criteria changed over time. He acknowledged that *Xenopus* offered some initial advantages, namely, it “can be reared very easily under laboratory conditions, while breeding can be initiated experimentally by gonadal hormone injection throughout the entire year.” However, “it is certainly the last fact that led to its preference over all other anuran species,” because there were real problems with using the organism for the types of research that dominated the field from the 1930s–1950s. Namely, if one was interested in experimental morphology, as Nieuwkoop was—research that necessitated transplantation of embryonic tissues—then salamanders and newts offered real advantages over *Xenopus*. In this regard, *Xenopus* had “serious limitations” due to the size of their eggs and the “double-layered nature of the totipotent animal moiety of the *Xenopus* blastula/gastrula and neurula stages.” (Nieuwkoop, 1996, p. 618). In other words, there was deep problems with phenomenal access for researchers in the mold of Spemann and many other experimental embryologists during the 1940s and 1950s.

The disadvantages of *Xenopus* became less so as the field became more focused on the molecular aspects of development in the 1960s and 1970s. Once genetics and biochemistry became the focus of research, having physical access to the morphological development of the embryo became far less of a barrier. Instead, the year-round breeding and ease of laboratory husbandry offered significant advantages over urodeles, which possessed limited periods of fertilization, creating serious temporal constraints on experimental work. The ease with which this limitation could be overcome in *Xenopus* was a major source of appeal for researchers who wanted to conduct year-round molecular studies.

For a researcher like Nieuwkoop who came of age doing transplantation experiments, the small size of *Xenopus* eggs and the difficulty of following processes of gastrulation and neurulation visually were strikes against understanding its morphological processes of development. But these features were not limitations for biochemical or genetic research. Nieuwkoop's complaint about the rise of *Xenopus* is not that it is inappropriate for the uses to which it is put, but that its acceptance marks a shift in the kinds of problems undertaken in experimental embryology. His perspective on the adoption of *Xenopus* highlights a shift in what is considered to be an adequate conceptual fit, as well as a strong synergy between responsiveness, ease of supply, and phenomenal access, which however arguably limited the comparative potential of the research produced using the organism. In 2009, the *Xenopus* Community issued a white paper report that noted the significant levels of funding awarded to *Xenopus* research, yet noted that limitations in informatics infrastructure, genome sequencing, training centers, and stock centers placed *Xenopus* at a disadvantage compared to other model organisms (Dietrich, Ankeny, & Chen, 2014; Xenopus Community, 2009). These financial and institutional factors were perceived to be important to supporting the continued choice of *Xenopus* as a research organism.

5.2. Settling on a “satellite organism”: the choice of Thellungiella

As a second case, we consider the much less prominent example of using salt cress *Thellungiella halophila* (also published under a newer designation, *Eutrema salsugineum*) to research salt tolerance in plants (Inan et al., 2004; Yang et al., 2013). The case exemplifies the usefulness of our account towards tracking how organism choice emerges from complex and dynamic social interactions, rather than the reasoning of an individual researcher. This type of situation has typically proved more difficult for philosophers and historians of science to analyze, and yet is by far the most common within the life sciences, where organism choice tends to be the concern of groups and even whole fields (part of what Strasser, among others, calls a “moral economy”; Strasser, 2019).

The choice of salt cress was certainly related to phenomenal access: given its ability to survive in environments characterized by extreme salinity and cold temperature, the plant enables researchers to study the functioning of osmolytes and ion channels within responses to abiotic stress, which are in turn crucial to understanding plant growth in dry or drought-prone areas (Inan et al., 2004). Even more important, however, was its comparative potential with the well-established model organism *Arabidopsis thaliana,* which is phylogenetically related and physiologically similar to salt cress and yet displays less tolerance to salinity, making it possible to exploit some of the knowledge already available about *Arabidopsis* to study a characteristic (salt tolerance) that *Arabidopsis* itself does not exhibit. *Thellungiella* was praised for its short life cycle, which is "very similar to that of Arabidopsis, and it shares important morphological and phenological attributes with Arabidopsis that are necessary for rapid efficient genetic analyses" (Inan et al., 2004, p. 1720), as well as its responsiveness, which paralleled characteristics to which plant researchers working with *Arabidopsis* were already accustomed: "[m]ore than any other reported halophyte, salt cress offers simplicity and efficiency for genetic analyses. It represents an outstanding case of a trait-specific genetic system that also provides the needed powerful molecular genetic tools developed for the Arabidopsis system" (p. 1720). Indeed, plant researchers list *Thelungiella* as an 'Arabidopsis satellite system,' that is, a plant that is "phylogenetically as close to Arabidopsis as possible and therefore amenable to laboratory use and to the methods developed for Arabidopsis but with special features not found in *A. thaliana"* (Chang, Bowman, & Meyerowitz, 2017, p. 332). Here we see a convergence between the criteria of comparative potential and training requirements, previous use, and informational resources: researchers working on salt cress can avail themselves of a rich trove of knowledge and resources associated with *Arabidopsis,* which are likely (though this is open to empirical scrutiny) to apply to *Thelungiella* as well. Last but not least, *Thelungiella* was viewed as valuable towards producing more drought tolerance plant varieties, which gives it an edge over *Arabidopsis* in terms of commercial and translational potential.

These characteristics engender a high level of synergy among several criteria for organism choice, and are manifested through an assessment of the value of salt cress in relation to its role in the broader landscape of plant science and its applications. This was in tension with at least some interpretations of the criteria of novelty and institutional support. At the time at which it was chosen, *Thellungiella* did not have a reference genome, which would only be published in 2013 (Yang et al., 2013). This put researchers at a disadvantage in comparison to organisms with more dedicated resources. Using Arabidopsis as comparator was not a straightforward way to address this gap, since the very validity of the comparison would need to be assumed rather than demonstrated at the start of the research program. Nevertheless, researchers decided to accept the risk, thus choosing to trust the potential link to a powerful model organism in order to be able to work with an economically valuable species.

6. Conclusion: unpacking 'good' organismal choice

As noted above, the criteria involved in choosing organisms for biological research outlined here are not intended to be exhaustive. What is more critical to our argument is the ways in which such criteria are refined in concert (or conflict) with other criteria and placed in synergy with others. Choosing organisms involves making strategic choices about which of these criteria to emphasize. Through analysis of cases, we have shown that such trade-offs tend to happen at the level of specific research instances, making it impossible to provide a generic table of the type generated by Levins in the case of model choice. Nevertheless, this analysis of criteria for organismal choice and how they relate to each other in practice does allow us to trace the development of research trajectories and the role of organisms within them. It also allows us to reflect more generally on what makes a particular organism useful, or perhaps to what biologists sometimes refer in shorthand as 'good.' At a minimum, it must be tractable and offer access to the phenomenon that biologists wish to study. From an epistemological perspective, the organism must 'match' the entity that it seeks to represent in ways that are relevant for the question(s) being addressed (whether the entity is only organism's own species, a broader group or taxon, or some other target group such as humans). The challenge is to determine which aspects of biology need to match to consider the organism under study and that which is being represented to be 'the same kind' with respect to the causes, qualities, or mechanisms involved in the thing being studied. The less that we know about the phenomenon to begin with, the more difficult this choice process is (Steel, 2008).

Articulating such requirements helps to clarify the factors on which scientists should focus when they choose and assess organisms for particular kinds of research. In addition, identifying misalignments or potential choices that prove not to be useful (e.g., an organism that can easily yield answers in terms of genetics is not particularly useful if one wishes to study a disease that turns out to have critical environmental causes) helps us to understand why organism-based research sometimes fails to yield the expected or envisioned outcomes, particularly when applying the results of basic research to humans for clinical purposes (Von Herrath & Nepom, 2005; La Follette & Shanks, 2016).

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Appendix A. Supplementary data

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