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Grand challenges in mammal science

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Introduction

The class Mammalia, of which humans are but one relatively recently evolved species, is represented by a highly diverse monophyletic grouping of over 6000 species. Mammals inhabit most of the ecosystems across the planet, from hyper-arid deserts through to the polar ice caps. They exhibit a vast range of life histories, with a range in body mass from very small (around 2 grams, Kitti's hog-nosed, or bumblebee, bat, *Craseonycteris thonglongyai*) through to the largest animals known to have existed (around 96 000 000 g, the Antarctic blue whale, *Balaenoptera musculus intermedia*). Certain mammals are oviparous (the subclass Prototheria), while viviparous mammals can give birth to extremely altricial young that develop mostly in a pouch (the cohort Marsupialia), or young representing varying states of altriciality and precociality (the cohort Placentalia). Mammals are known to have over 20 senses that detect variations or stability in both the corporal and extracorporal environments, the information from which is processed by brains that range in size from 0.087 g (*Craseonycteris thonglongyai*) to 8000 g (the sperm whale, *Physeter macrocephalus*). These brains activate or inhibit muscles or glands, leading to the expression or suppression of behaviors relevant to survival and reproduction. The class Mammalia first appeared around 200-250 million years ago and has undergone major radiation and extinction events that has led to the appearance and disappearance of a vast number of species known only through the fossil record. Mammals, including humans, are not only a scientifically fascinating cohort of animals, but are an essential part of a healthy global ecosystem.

In general, we know a little about a large number of mammals (see for example the intensely researched and beautifully illustrated *Handbook of the Mammals of the World* edited by Wilson et al., 2009-2019); however, what we do not know far outweighs our current knowledge, in all spheres of the biological sciences as they relate to mammals. As part of an ongoing project, a number of colleagues and myself have gathered data on the average male and female body masses in mammal species, a basic biological, species and sex relevant parameter. Of the over 6000 mammal species, we could find reliable data on male and female body masses for only 1966 species (or ~32.8% of mammal species)!

Thus, for even this very basic trait that can be readily taken in the field with minimal equipment, we lack reliable data for over 4000 mammal species. In the growing field of genome science, genome assemblies are known for approximately 440 mammal species (or ~7.3% of known species) despite mammals being a major focus of this field (Hotaling et al., 2021).

Regardless of this apparent paucity, or depauperate knowledge in most mammals, for certain species, the "model" species, we have what appears to be an overabundance of exquisitely detailed information. For example, in non-subject-specific basic neuroscience journals, approximately 75% of the published pages present data on the nervous systems of the various strains of laboratory rat and mouse (45%) and human (30%) (Manger et al., 2008), i.e., 75% of research efforts in the basic neurosciences are dedicated to the nervous systems of ~0.05% of known mammal species. The basis for this extreme bias is due to the desire to translate both basic and experimental findings in the laboratory rodents to clinical and therapeutic practices in humans; however, translational research appears to be in a crisis due to a lack of success in ameliorating human maladies (e.g., Perrin, 2014; Schulz et al., 2016). One potential explanation for the weak translatability of rodent results is that we lack a clear understanding of what the similarities and differences between Murid rodents and humans truly are, at a fundamental biological level. We do not know enough about the independent evolutionary trajectories that these species have taken over the ~80 million years since they shared a common ancestor and what has remained fundamentally similar and what changes have occurred, from the molecular through to the behavioral levels. When we develop a better understanding of this evolutionary stasis *vs.* variation in these and other lineages, we may be able to use the fundamental similarities of these "model" mammals more effectively to understand human disease processes and develop therapeutics. Such understanding can only be derived through curiosity-driven research, allowing self-directed exploration, and encouraging creativity in scientists with an interest in mammalian biology; however, it would be erroneous not to indicate that the detailed understanding of these three species is not of use. Indeed, the detailed understanding of Murid rodent and human biology forms the requisite platform for the exploration and understanding of other species.

The study of mammals other than the commonly used laboratory species is never straightforward. As an individual who has been educated and employed in a number of institutions in high income countries (HICs), but having spent the majority of my career (20 years) in a lower-middle income country (LMIC), my experiences have led me to identify three crucial obstacles to undertaking curiosity-driven research on "non-standard" mammals: (1) The relevance to humans; (2) Geographical advantages and disadvantages; and (3) Ethical issues and red-tape.

Relevance to humans

All individuals that have conducted research on non-standard mammals have, at some stage, been asked at least once, if not regularly, about the relevance of their research to humans. The question of research relevance on mammals to societal issues is often posed by academic colleagues, university bureaucrats (whose main concern is metrics and funding), family members, and the lay public. Why are we spending our time and resources on these species when human problems need to be researched? The basic sciences, especially curiosity-driven research, are often side-lined for funding using this rationale – it is much easier for a politician (authorized to manage the public funding of science) to be elected to office by declaring that they will ensure funding towards, for example, cancer research, rather than indicating they will support the curiosity-driven endeavors of scientists. Thus, it is often difficult to convince both the lay and academic community of the intrinsic value of curiosity-driven research, despite curiosity (along with openness to learning and conscientiousness) being the major predictors of success (e.g., Von Stumm et al., 2011; Schattner, 2015).

If, in 2015, I had to submit a funding application to examine the types of viruses and their loads in pangolins across the globe, based on the premise that these species and their environments are under severe pressure due to human activities, it is very unlikely such funding would be awarded – what is the immediate relevance? Seven years on and a Covid-19 pandemic later, such research appears to be much more "fundable" than in 2015. Any biologist will know that when viruses are under pressure, due to pressures on their hosts, they will evolve, adapt, and find new hosts, which appears to be what has happened to the covid-19 virus found in pangolins (Zhang et al., 2020). Rather than being proactive in funding curiosity-driven research, scientific funding is dispensed to researchers in a reactionary manner. This is a very important point in terms of the many potential emerging crises due to the pressure humans are putting on the world's environments. It is my personal belief that the funding priorities for science need extensive re-evaluation with the monotheistic view of human life above all else (God said to them, "Be fruitful and multiply, and fill the earth and subdue it; and have dominion over the fish of the sea and over the birds of the air and over every living thing that moves upon the earth" [Genesis 1:26–28]) potentially leading to global demise and human and animal suffering on an unprecedented scale.

Geographical advantages and disadvantages

The greatest diversity of mammal species is coincident with the biodiversity hotspots of the tropics (e.g., Ceballos and

Erhlich, 2006). These hotspots are primarily located in lower income countries (LICs) and LMICs; hence, the geographic regions that evoke the most interest in terms of mammalian biology are also the regions that can least afford to support scientific research. Only a very small fraction of the research investment of HICs has been directed towards the study of mammals in LICs and LMICs, most typically only with a collaborator from the HIC. Thus, the geographical advantage for the study of mammalian biology within LICs and LMICs is negated by the financial disadvantages of these countries and the minimal, sporadic, and condition-laden investment of research funding by HICs. Political instability and insecurity, high levels of governmental ineptitude and corruption, and resource depletion in LICs and LMICs by developed countries, have exacerbated the difficulties of undertaking meaningful scientific research in the regions of the world that can offer the most in terms of developing our understanding of mammalian biology.

Ethical issues and red-tape

The crucial need to reduce suffering and exploitation of animals used in scientific research, through appropriate and ethical treatment, is a necessary central tenet of any animal-based scientific research; however, there is a waning of the monotheistically-derived supremacy of humans over other animals in HICs (e.g., White, 2007; https://news.mongabay.com/2018/10/citizen-ape-the-fight-for-personhood-for-humans-closest-relatives/). Ethical standards are generally generated from the collective beliefs and values of the citizens of a specific country. Ethical standards for animal research are primarily developed in HICs, with scientific journals of good standing requiring these standards be met for publication; however, in the mammal rich LICs and LMICs adherence to these standards is often unachievable (due to intrinsic problems in these countries and their different ethical standards) and can vary dramatically. As a post-doctoral fellow at the Karolinska Institute I was told, while participating in a mandatory ethics course, that rather than work on the visual system of ferrets I should work on the laboratory rat visual system, as obtaining ethical clearance for rats will be much easier. Obtaining ethical clearance to research non-standard mammal models is far more difficult than for standard models (i.e., the "vermin" that have been specifically bred for use in research), and the HIC ethical standards are often imposed upon research in the LICs and LMICs, especially when the research is funded by a HIC. Added to these ethical issues are the governmental rules and regulations that are applied to research on free-living mammals. While these rules and regulations are necessary to reduce the potential for trafficking or commercial exploitation of species, especially endangered species, their implementation slows and frustrates genuine research on wildlife, especially in their natural habitat. It is unlikely that those intent on trafficking endangered animals and products will adhere to CITES and other regulations, and with the recent Nagoya Protocol the capacity for scientists to exchange biological material for collaborative research is again hampered (e.g., Alexander et al., 2021), especially with heightened suspicion regarding the movement of biological tissue after the Covid-19 pandemic.

What are the "grand challenges" we face as mammalian biologists?

The preceding outlines the obstacles to undertaking research on mammals, especially in the species-rich natural habitats of LICs and LMICs, but while these obfuscate research, we should not let this prevent research. Overcoming these obstacles are, in my opinion, some of the greatest challenges we face as mammalian biologists. Convincing funding agencies of the importance of quality, curiosity-driven, basic research that does not appear to have any immediate benefit to humans is likely to be one of the biggest challenges; however, given the failure rate of the translational research paradigm, it would be wise for us to hedge our investment in alternatives. If even only 5 – 10% of the budget spent on translational research was made available for curiosity-driven research, the advances in our understanding of mammals would rapidly increase and potentially lead to serendipitous findings that could greatly improve our understanding of human illnesses. Examples of this include the cancer resistance shown by naked mole rats (*Heterocephalus glaber*) (e.g., Liang et al., 2010) and African and Asiatic elephants (Abegglen et al., 2015). Increasing the availability of well-funded, equitable, research partnerships between researchers in HICs with colleagues in LICs and LMICs will raise the standards of science in LICs and LMICs and provide information crucial to the understanding of the wildlife under the auspices of the governments in LICs and LMICs. This should improve the potential for successful conservation projects. Lastly, streamlining the bureaucracy involved with mammalian research for genuine scientists will be extremely beneficial, allowing the researchers more time to do what they are trained to do, while adhering to understandably needed controls.

To help in overcoming these obstacles, high quality, curiosity-driven, basic science on mammals is deserving of an appropriate conduit for rapid publication, and it is my sincere hope that *Frontiers in Mammal Science* will be such a conduit. Deriving a broader collective understanding of mammals, from the detailed minutiae through to their importance in the health of both local and global ecosystems, is perhaps the biggest challenge we face. By encompassing a scientifically and phylogenetically diverse understanding of mammals, hidden clues of the complexities of their natural world may be revealed. By bringing together a broad range of scientific disciplines that are focused on mammals under one cover, it is hoped that *Frontiers in Mammal Science* will contribute to raising the profile of mammals in the eyes of the public in general, through developing our understanding of this fascinating class of animals and showing that they are crucial to the health of our planet and ourselves.

Author contributions

The work is solely that of the primary author.

Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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