Biotechnology and Biological Sciences Research Council

BBSRC Survey Report on the Use of Models in Research

SUMMARY: Between June 2020 and November 2021 BBSRC, in consultation with the Physiological Society, conducted a survey on the use of models in research to gain insight into how researchers currently use their experimental systems and models and how they expect to use them in the future, in order to better understand the area and ensure that the health of the disciplines is maintained and opportunities for improvements found. The survey was analysed and the report is included in Annex 2 along with the survey questionnaire in Annex 3.

Report by the Bioscience for and Integrated Understanding of Health (BIUH) team

BBSRC is a part of UKRI

BBSRC Survey on the Use of Models in Research

Executive Summary

This report provides a summary of the analysis of the BBSRC's Survey on the Use of Models in Research and the subsequent Expert Working Group discussion.

The survey was undertaken in June 2020. Following extensive analysis, in June 2021 the survey report was discussed and ratified by an Expert Working Group chaired by Professor David Paterson, President of the Physiological Society. For Working Group membership see Annex 1.

Introduction

The complexities of research across disciplines in animal and human biology necessitate a variety of approaches. Often a very large number of different experimental systems (e.g. cell culture, computational approaches and tissue slices) and species are used to investigate biological processes. The use of these model systems has been a vital part of both fundamental and translational scientific research.

498
responses were received

94%
of respondents were academic with a small number of non-academic responses received from industry, charity, and clinicians

★★★
The top three research areas of respondents were Neuroscience, Genetics and Cell biology

Survey Key Findings

The results from the survey are compiled into a report (Annex 2), the key findings from this report are summarised below. The survey questions are provided in Annex 3.

a) Current Use of Models

1. 15% of respondents used a single model and 83% of respondents used multiple models to answer their research question at the time of the survey.
2. Common reasons for choice of a model included its physiological relevance (21%) and availability of genetic tools (18%). The most important advantages of using a particular model cited were that they are the 'best model for research question', and 'expertise is available'.
3. 74% of respondents using a 'single' model use the whole organism, followed by computational/in silico models:
    a. The most common model species is the fly (18%) followed by mouse and zebrafish (both 17%), 'other' also features highly with yeast the most prominent model organism amongst this group.
    b. 50% of respondents have been using their model for more than 10 years.
4. The most common model when using 'multiple' models is the whole organism, followed by 2D cell culture and tissue/slice.
    a. The most common species are the mouse, human and fly combination of models, and the 'other' group also features highly with yeast ranking highest amongst this group.
    b. Of the respondents using multiple models, 80% use them to answer different aspects of their research question.
    c. 16% of respondents using multiple models are considering changing from one to the other, and the majority of these respondents are non-academic researchers.
    d. 35% of the non-academic respondents using multiple models are using six or more. None are using a single model.
5. 35% of respondents reported changing from one model to another. The most common reasons given for change included change of research focus (54%), the availability of genetic tools (49%), the availability of the model (36%), and a change of position (33%).

Survey Key Findings

b) Future Use of Models

6. The whole organism was considered the most popular model of choice for the future, followed by 2D cell culture and tissue/slice, with the use of organoid, computational/ in silico, and 3D cell culture all predicted to increase in use.
7. Respondents appeared confident in their current models of choice but suggested changes in regulations were preventing innovation within their research. There were some comments regarding regulatory bodies and whole organism usage, making the UK less competitive in the pace and scope of research due to higher costs and administrative burden of using whole organisms.
8. Respondents within the academic community reported working with a model for a long period of time, with the majority having worked on their current model for more than 10 years and not predicting changing from it in the future.
    a. 16% of all respondents are considering changing from one model to another, of which the majority of these are non-academic researchers.
9. Several challenges and barriers to an open model choice were identified:
    a. Training and expertise restrict the choice of models, as well as regulatory knowledge.
    b. Lack of validated novel models, lack of funding for validation studies, and the time required to investigate and establish new models prevent the switching of models. In addition, journals are unwilling to publish on novel and unvalidated models.
    c. Lack of availability of genomic information, and cost of the model, were highlighted as limiting factors of model choice.

The results from the survey were presented to an Expert Working Group which highlighted the key findings of the survey and identified the key trends surrounding the use of models. Based on these key findings, the Expert Working Group have made a series of recommendations for BBSRC to consider. The key discussion points and findings from the working group and their recommendations are presented below.

Working Group Key Findings & Recommendations

The working group discussions focussed on two themes within the report:

- Choice of model
- Animal research

a) Choice of Model

10. There is not a 'one model fits all' and it is likely that every research question may require a different model(s). In general, there appears to be a tendency to use the model that is available rather than the best model for the question and this approach can lead to poor reproducibility and translation. In addition, risk aversion means researchers tend to use the same model, 'stick to what they know', as changing models is perceived to be difficult due to validation concerns and associated costs, risk of failure, and funding insecurities.

Recommendation 1

BBSRC to ensure that peer review committees and panels are:

- Appropriately constituted to permit the effective and balanced evaluation of both traditional and novel models in research and innovation.
- Open to the higher perceived risk and increased time constraints when researchers are developing or switching to a new model.

11. Model availability is a serious limiting factor, preventing researchers from using the 'right' model for the research question. Often researchers are unaware of who to approach regarding training with a novel model, there is a lack of 'community' across the different model groups.
12. A lack of 'in-house' resources often impedes use of novel models and prevents the 'right' model being used. Researchers need to be able to access the necessary tools and technologies without the expensive establishment costs that would be incurred if they attempted to establish a novel technology from the start.

Recommendation 2

BBSRC working with the Physiological Society and NC3Rs to consider developing a cross-disciplinary and multisectoral engagement route that encompasses the entire range of models, including both animal and non-animal technology.

Recommendation 3

BBSRC, working with other funders, to encourage and enable researchers to share knowledge, expertise, and necessary tools, techniques, and methods, with a particular focus on cross disciplinary and collaborative working.

Working Group Key Findings & Recommendations

13. Health and disease are present in a complex state within the human body, they are often interacting with each other and other environmental factors. Up until now there has been emphasis on single-focus studies but this is changing, and model systems need to adapt. Currently, Non-animal Technologies are currently unable to study multi-morbidity as effectively as animal models.

Recommendation 4

Working with NC3Rs, BBSRC to:

- Assess the progress towards the recommendations of the 2015 Non-Animal Technologies roadmap.
- Support research into complex in vitro models and identify opportunities to accelerate their development and adoption across academia and industry.

14. Whilst further novel models may be useful, better validation and optimisation of current models is considered more important to ensure the 'right' model is being used for a particular research question.
15. Cross-cutting models spanning the remit of various UKRI councils (e.g. computational modelling) often struggle for support during validation stages as they 'fall between the gaps' of available funding schemes. An interdisciplinary approach when studying models would be beneficial to each discipline.

Recommendation 5

BBSRC, working with other funders, to progress support for model development and for validation studies.

16. Using multiple species to investigate common mechanisms and processes enables researchers not only to change model(s), but also to answer research questions from different perspectives. This enables investigation of the physiological relevance of a model, as integrated data analysis provides for comparison between different models.
17. Further work to understand how different models are suitable for different research aspects is needed. A large-scale evaluation of all the models in use could allow the development of a tool to enable researchers to select the most appropriate model for the research question.

Recommendation 6

BBSRC to consider support for Comparative Biology, and how it could be utilised for model evaluation and selection.

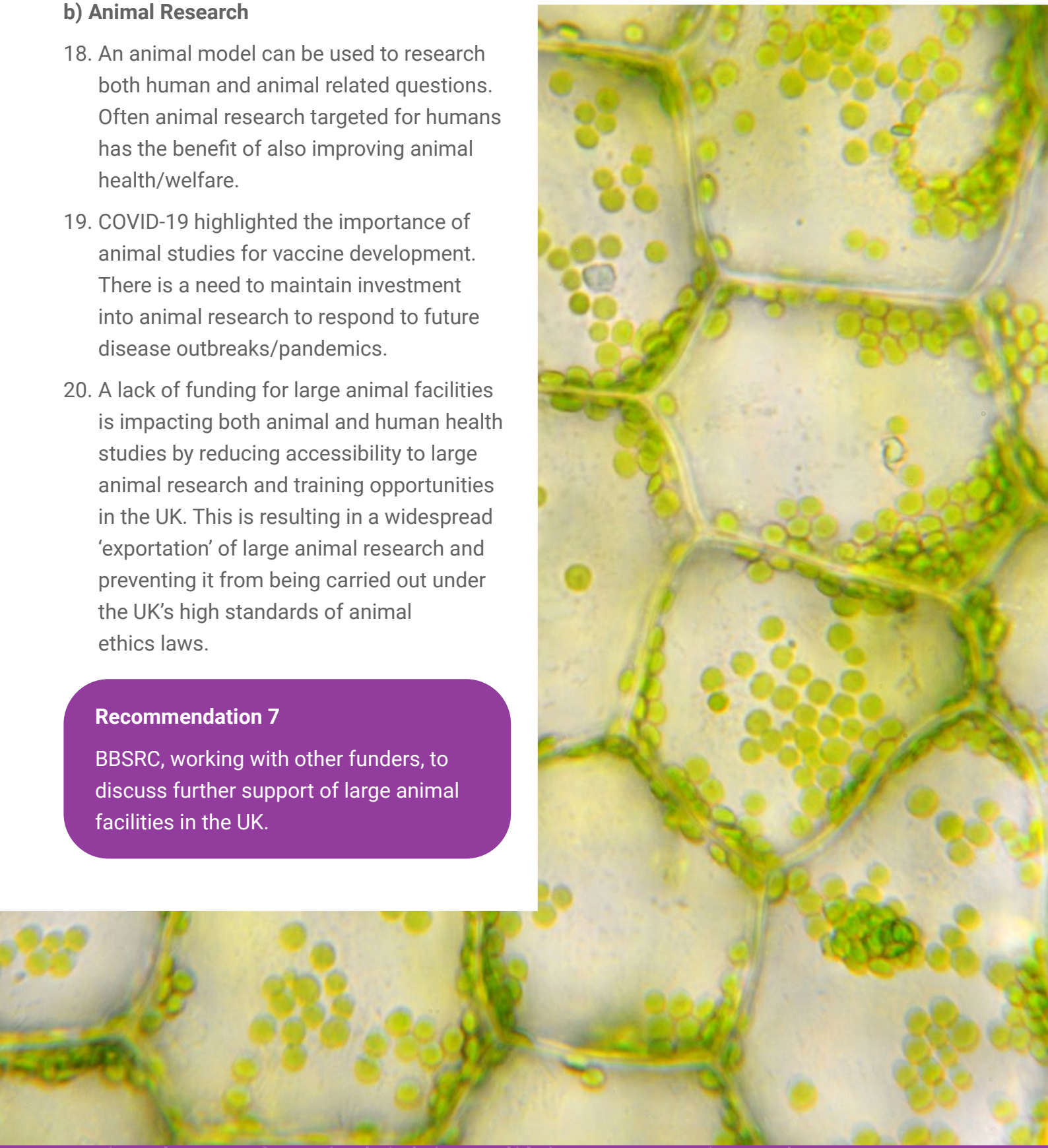
Working Group Key Findings & Recommendations

b) Animal Research

18. An animal model can be used to research both human and animal related questions. Often animal research targeted for humans has the benefit of also improving animal health/welfare.
19. COVID-19 highlighted the importance of animal studies for vaccine development. There is a need to maintain investment into animal research to respond to future disease outbreaks/pandemics.
20. A lack of funding for large animal facilities is impacting both animal and human health studies by reducing accessibility to large animal research and training opportunities in the UK. This is resulting in a widespread 'exportation' of large animal research and preventing it from being carried out under the UK's high standards of animal ethics laws.

Recommendation 7

BBSRC, working with other funders, to discuss further support of large animal facilities in the UK.



Annexe 1

Membership of the Working Group

Name	Organisation
David Paterson (Chair)	University of Oxford
Gareth Arnott	Queens University Belfast
Pelin Candarlioglu	GSK
Julian Dow	University of Glasgow
Malcom Macleod	University of Edinburgh
Andrea Münsterberg	University of East Anglia
Andy Philippides	University of Sussex
Stefan Przyborski	Durham University
Emma Robinson	University of Bristol
Hazel Screen	Queen Mary University of London
Kevin Shakesheff	Open University
Claire Stanley	Imperial College London
Elma Tchilian	Pirbright Institute
Andrew Trafford	University of Manchester

BBSRC:

Harry George, Portfolio Manager, Capability and Innovation
Louisa Jenkin, Senior Portfolio Manager, Bioscience for an Integrated Understanding of Health
Laura Pritchard, Senior Portfolio Manager, Capability and Innovation
Danielle Sagar, Portfolio Manager, Bioscience for an Integrated Understanding of Health
Sadhana Sharma, Head of Bioscience for an Integrated Understanding of Health
Luke Williams, Portfolio Manager, Bioscience for an Integrated Understanding of Health
Emma Dayman, Senior Policy Manager, Strategic Planning Evidence & Engagement

Observers:

Vicky Robinson, Chief Executive, National Centre for the 3Rs
Abigail Spear, Principle Scientist, Defence Science and Technology Laboratory
Stella Childs, MRC

Annexe 2

Background

In June 2020, BBSRC, in consultation with the Physiological Society, conducted a survey on the use of animals.

The survey was open throughout June 2020 to all researchers across the academic, industrial and third sectors. The survey was posted on BBSRC website and emailed to all BBSRC responsive mode research committees and the pool of experts. In addition, the survey was forwarded to various societies/networks of interest, strategic partner universities/ institutions, the Royal Society of Biology's science policy list and MRC. A copy of the survey questionnaire is in **Annex 3**.

498 responses were received. This report summarises the results obtained from this survey.

The report along with the working group's recommendations will be considered by the BBSRC's Bioscience for Integrated Understanding of Health Strategy Advisory Panel and help to inform future activities.

Annexe 2

Survey Report

Context of the survey

The complexities of research across the disciplines in animal and human biology necessitate a variety of approaches. Often a very large number of different experimental systems (e.g. cell culture, computational approaches and tissue slices) and species are used to investigate biological processes. Collectively these are referred to as models in this report. These models are necessary to enable the study of biological processes of target species, within a controlled environment. The use of model systems has been a vital part of both fundamental and translational scientific research.

For the purpose of the survey and this report the term 'model' includes:

- *in vivo*, *ex vivo*, *in vitro* and *in silico* experimental systems.
- Research where the species used is not the target species.
- Research where the species used is the target species for the research outcomes.
- Research where the species involved is used to investigate a general mechanism or process.

Overview of the survey

The survey was divided into 3 sections:

1. Introduction
To acquire general information about the respondent's research to provide context.

2. Current use of models
To learn the reasons why researchers, use the models that they do, and how these models help with their research. This section focussed on three aspects:

3. Previous use of models

4. Confidence of models

5. Difference in use of models

6. Future use of models
To ask questions on the future possibilities for the use of models in research. The section also questioned:

7. Barriers and challenges
8. Additional comments

Analysis of survey responses

There were 498 complete responses to the survey. Incomplete responses were not considered. Although the intended target of this survey was UK based researchers, 5 international responses were obtained and have been included in the survey analysis.

Annexe 2

1. Introduction

1.1 Respondents by sector

The majority of respondents were academic researchers but responses were also received from industry, clinicians and charities (**Fig 1**).

– *Of the 10 respondents who answered 'other', 5 were academic support staff, 2 industry/academic, 1 clinical/academic, 1 veterinarian and 1 from a government institution.*

1.2 Respondents by discipline

Respondents spanned a broad range of disciplines:

- Neuroscience was the most common discipline (16%), followed by Genetics (10.5%) and Cell biology (10%) (**Fig 2**).

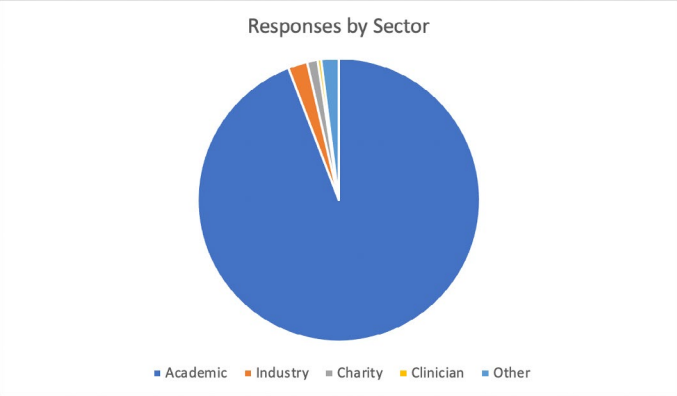
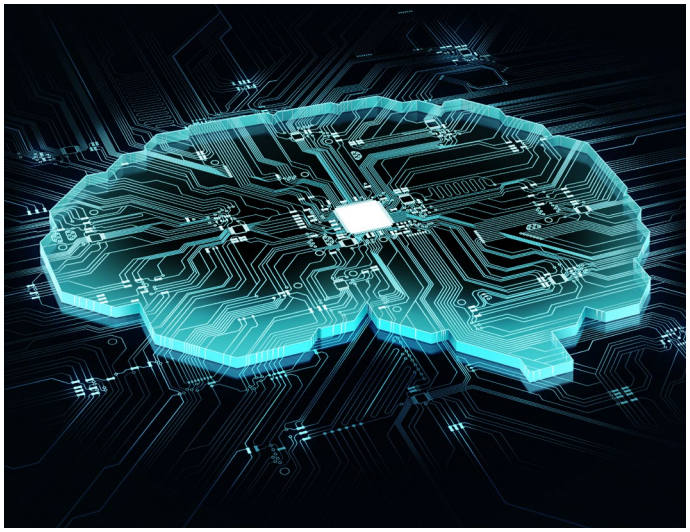


Figure 1 – Respondents by sector. Total number of respondents: 498



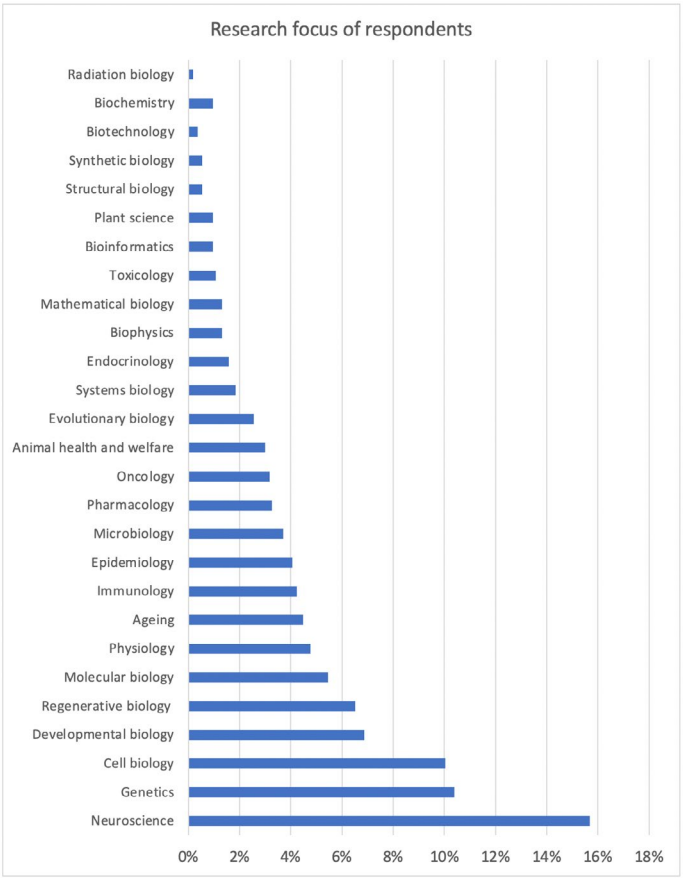


Figure 2 - Self-selected discipline or research focus of respondents. Please note percentages will not sum to 100% due to being able to select multiple options. Total number of respondents: 498; total number of options selected: 1135; percentages refer to respondent numbers.

2. Current Use of Models

2.1 Respondents were asked what number of models they currently use.

• Respondents mainly (74%) use between two and five models in their research **(Table 1)**

How many models do you use?	Responses	Percentage
None	12	2%
One	73	15%
Two to five	370	74%
Six to ten	43	9%

Table 1 - The number of models that each respondent currently uses in their research or have done over the previous year. Total responses: 498.

The small number of respondents who do not do not currently use any models were diverted to the future use of models in research section of the survey.

This question was primarily used to filter respondents into different pathways throughout the survey, those using one model and those using multiple models.

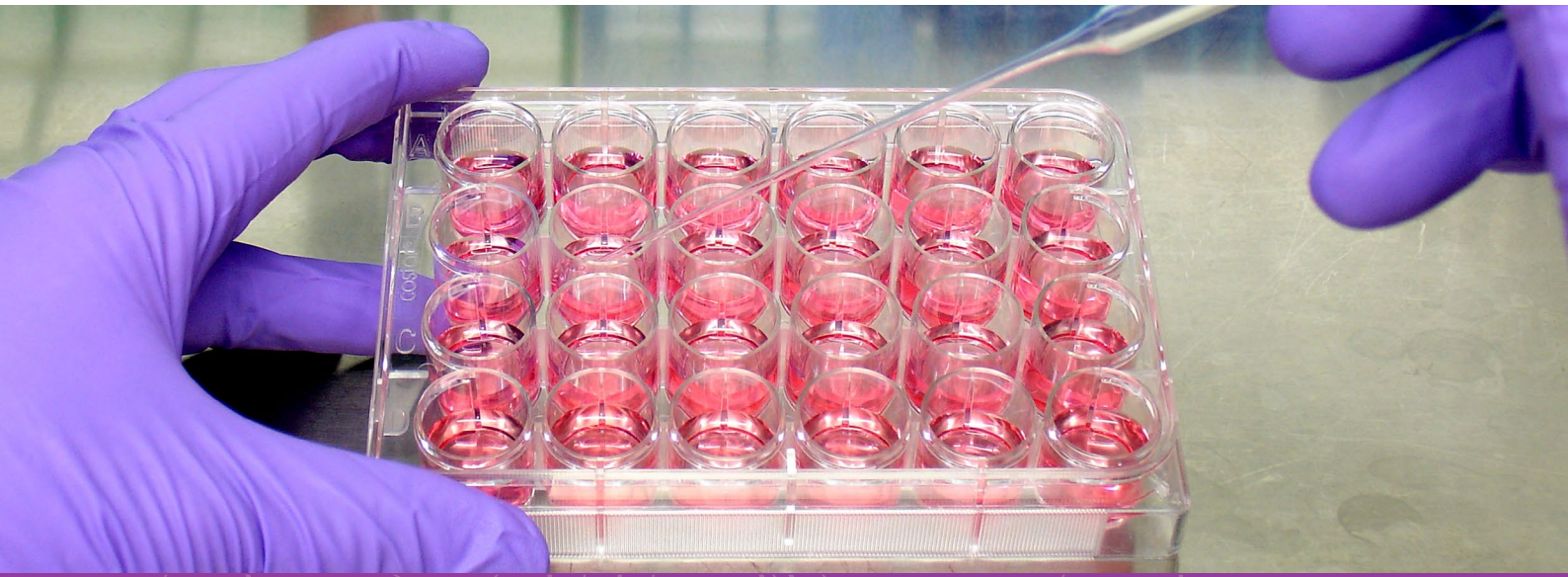
2.1.1 Single model usage

• Respondents using a single model in their research mainly use the whole organism **(Fig 3)**.

• Mouse, zebrafish and fly were the most popular species used **(Fig 4)**.

• Of the respondents who chose 'other' yeast was the most common (30%) **(Fig 4)**.

• 50% of respondents reported using their model of choice for longer than 10 years **(Fig 5)**.



Annexe 2

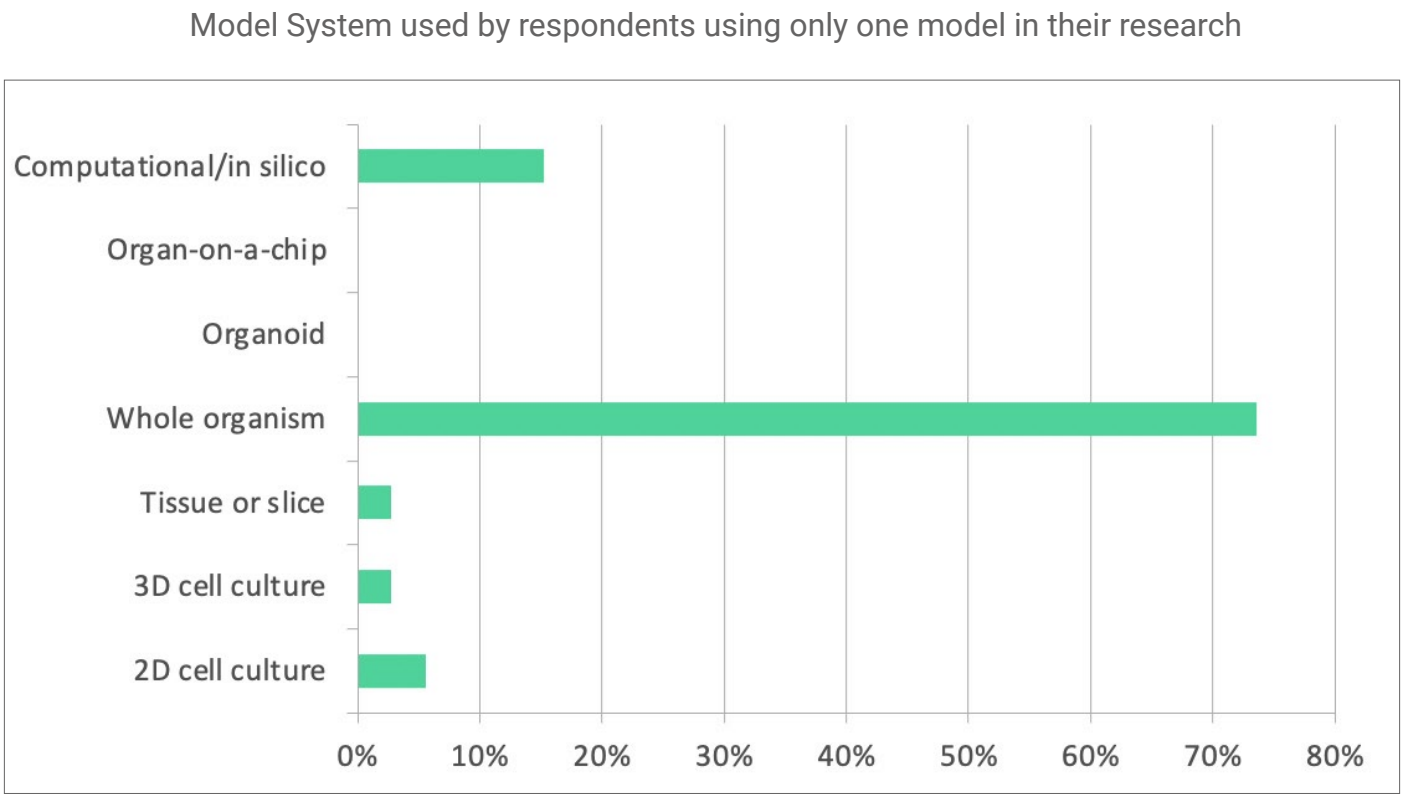
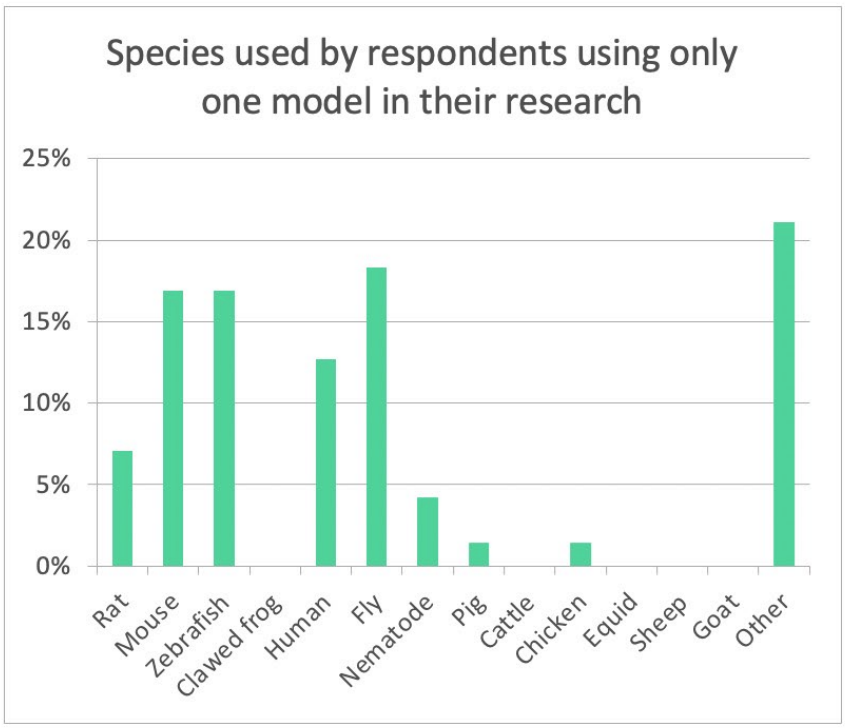


Figure 3 - Model systems used by researchers who only use one model in their research. Total number of respondents: 73.



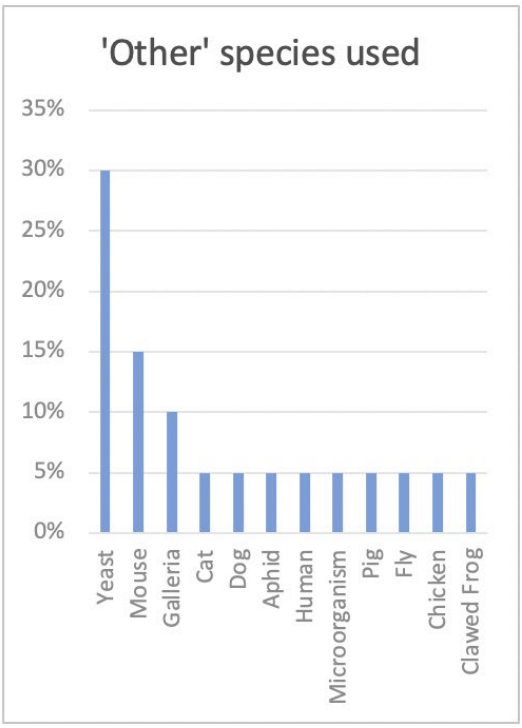


Figure 4 - Species used by researchers who only use one model in their research. Total respondents: 73.

Annexe 2

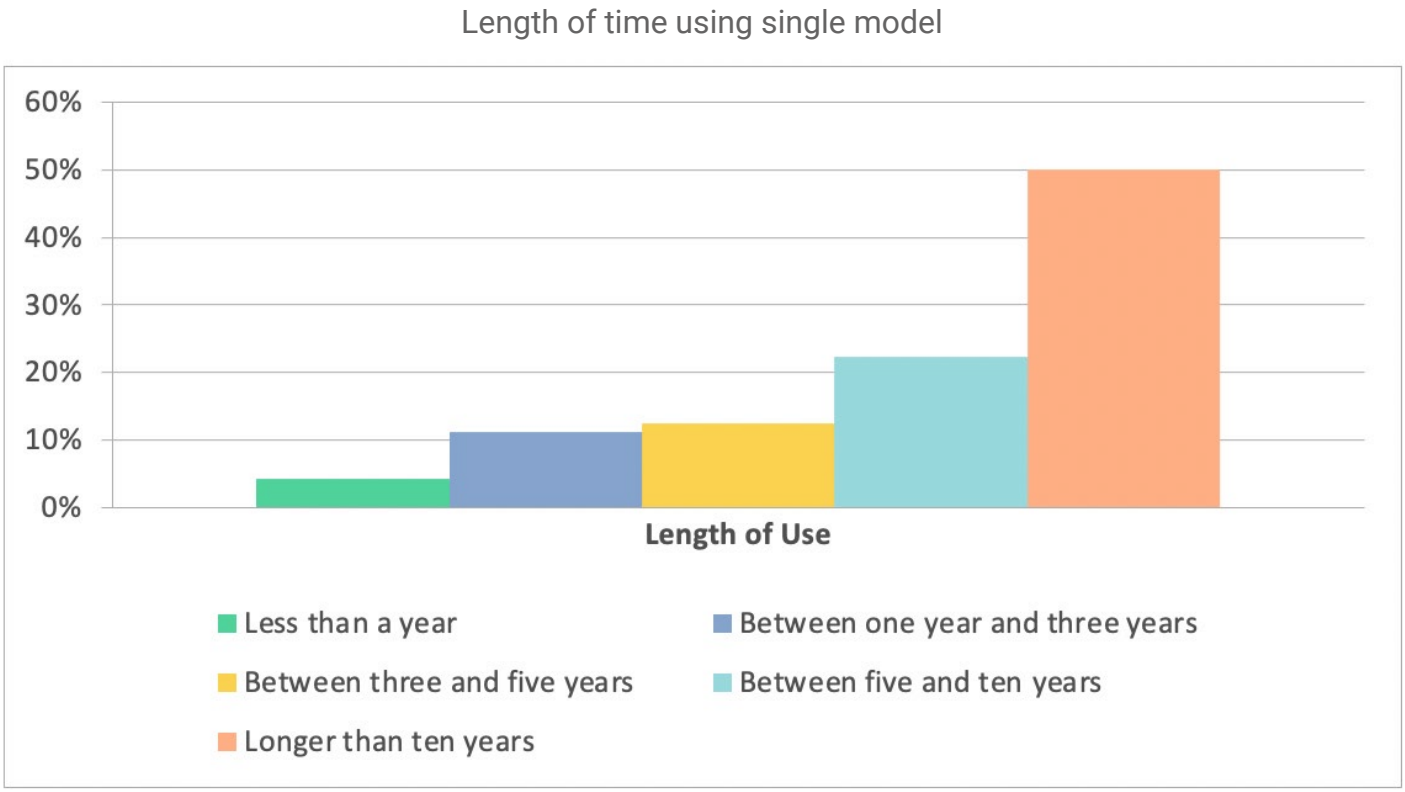


Figure 5 - The length of time that researchers have been using their single model in their research. Total number of respondents: 73.

2. Current Use of Models

2.1.2 Multiple model usage

- 74% of respondents use multiple models. Only 6 respondents chose to use the full selection of nine additional models. The majority of respondents use no more than 2 additional models, with only 6 respondents chosing to use the full selection of 9 additional models.
- Respondents using multiple models mainly use the whole organism **(Fig 6)**.
- Amongst the additional models, 2D cell cultures and tissues/slices were also popular **(Fig 6)**.
- Mouse, human and fly were the most popular species used **(Fig 7)**.
- Respondents who chose 'other' commonly indicated yeast **(Fig 8)**.
- 60% of respondents reported working on their primary model for more than 10 years **(Fig 9)**.
- Respondents reported a varied level of experience with their additional models **(Fig 9)**.

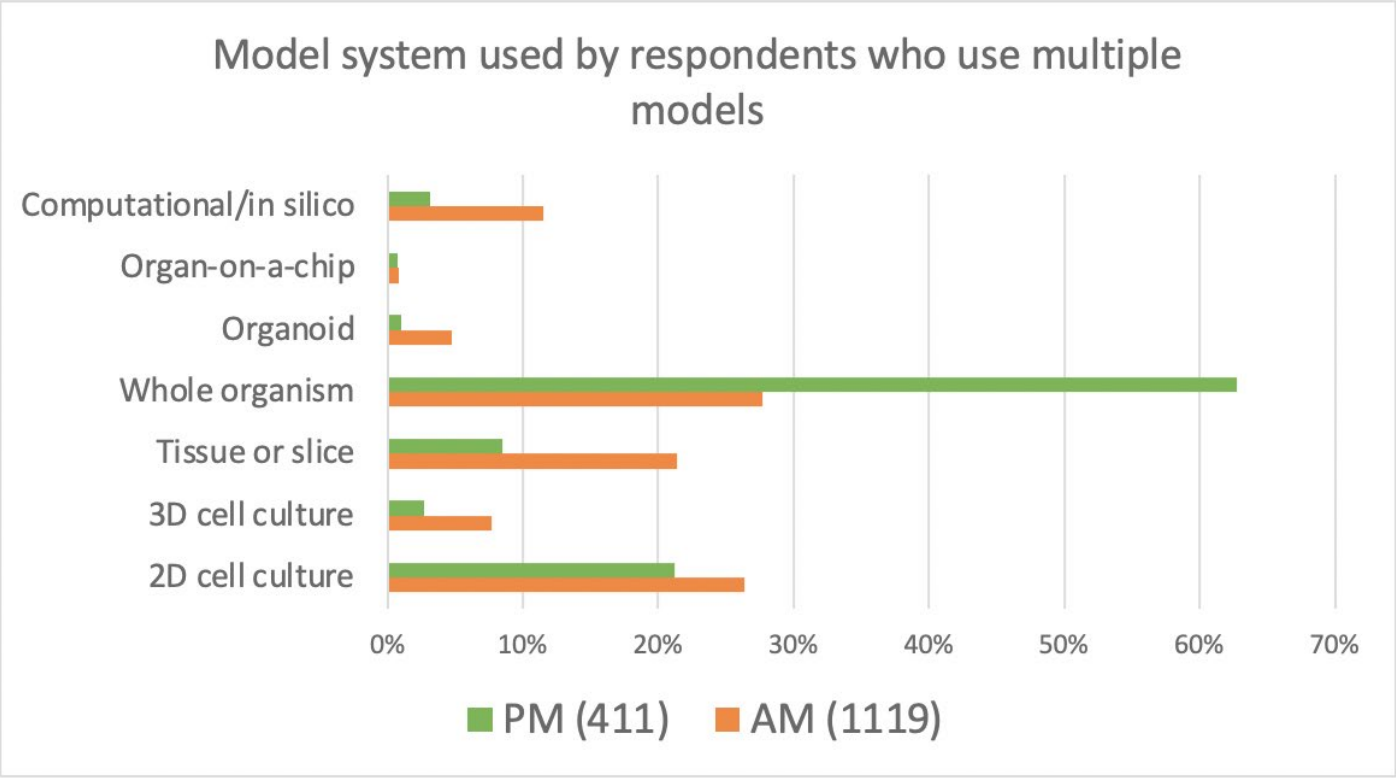


Figure 6 - Experimental systems used by researchers who use multiple models. PM is Primary Model; AM is Additional Model. The numbers refer to the number of respondents. Total respondents: 412.

2. Current Use of Models

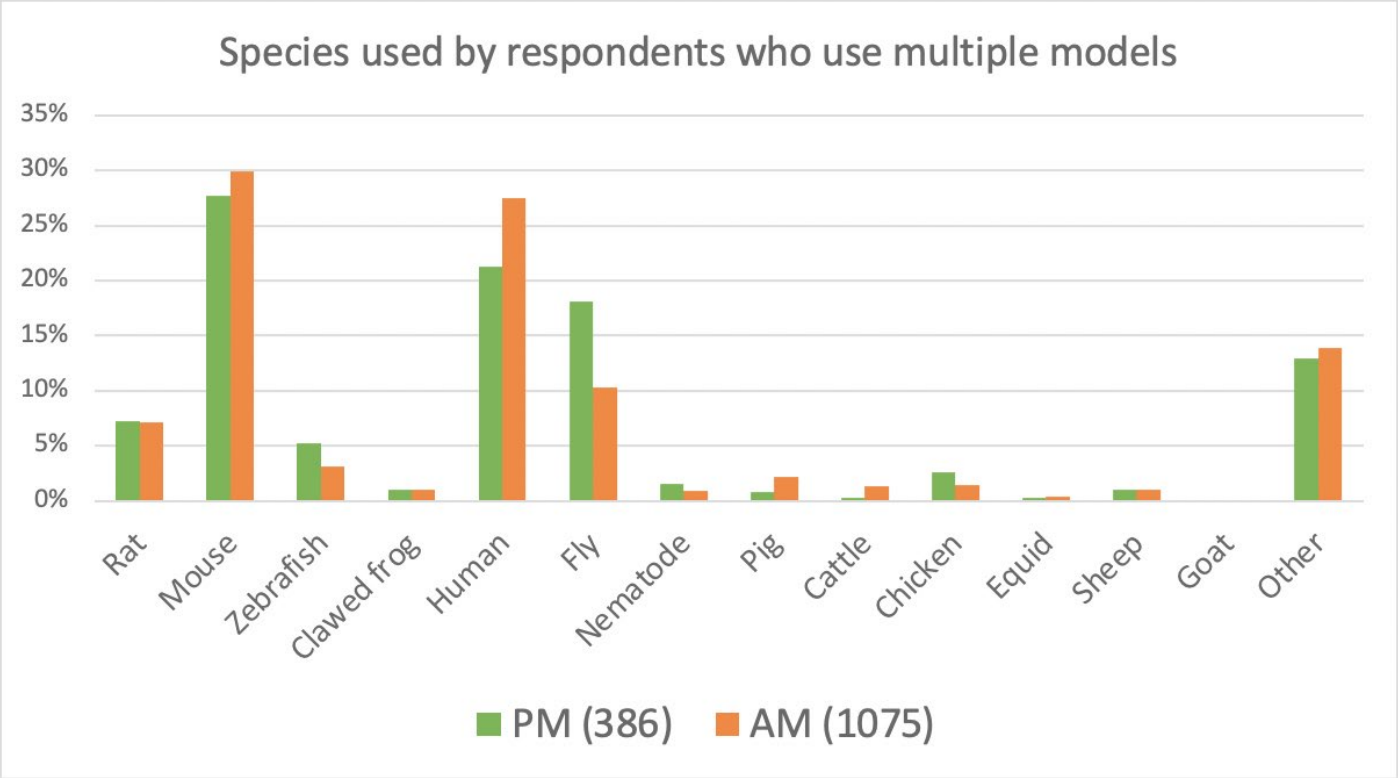


Figure 7 - Species used by researchers who use multiple models. PM is Primary Model; AM is Additional Model. The % refer to the number of respondents. Total respondents: 412. Please note the numbers may not match the previous figure on experimental systems as other species may be used.

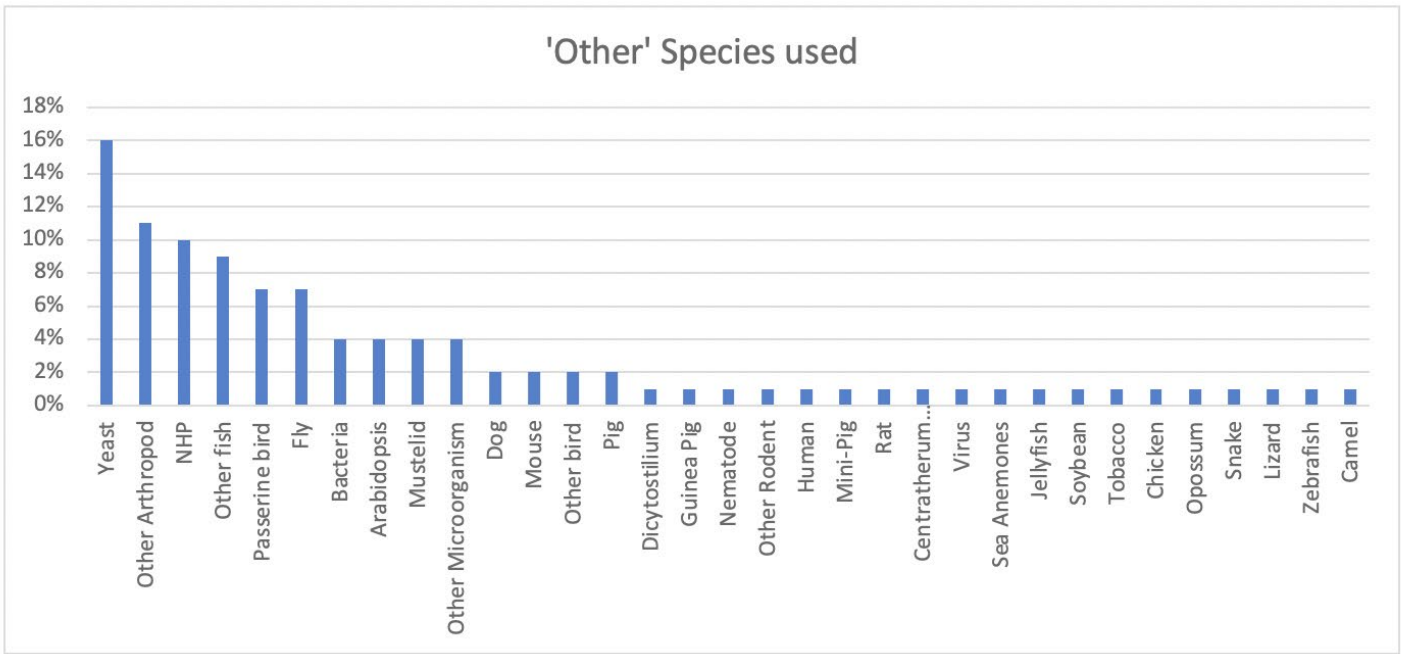


Figure 8 - Species used by researchers who use multiple models and selected other.

Annexe 2

2. Current Use of Models

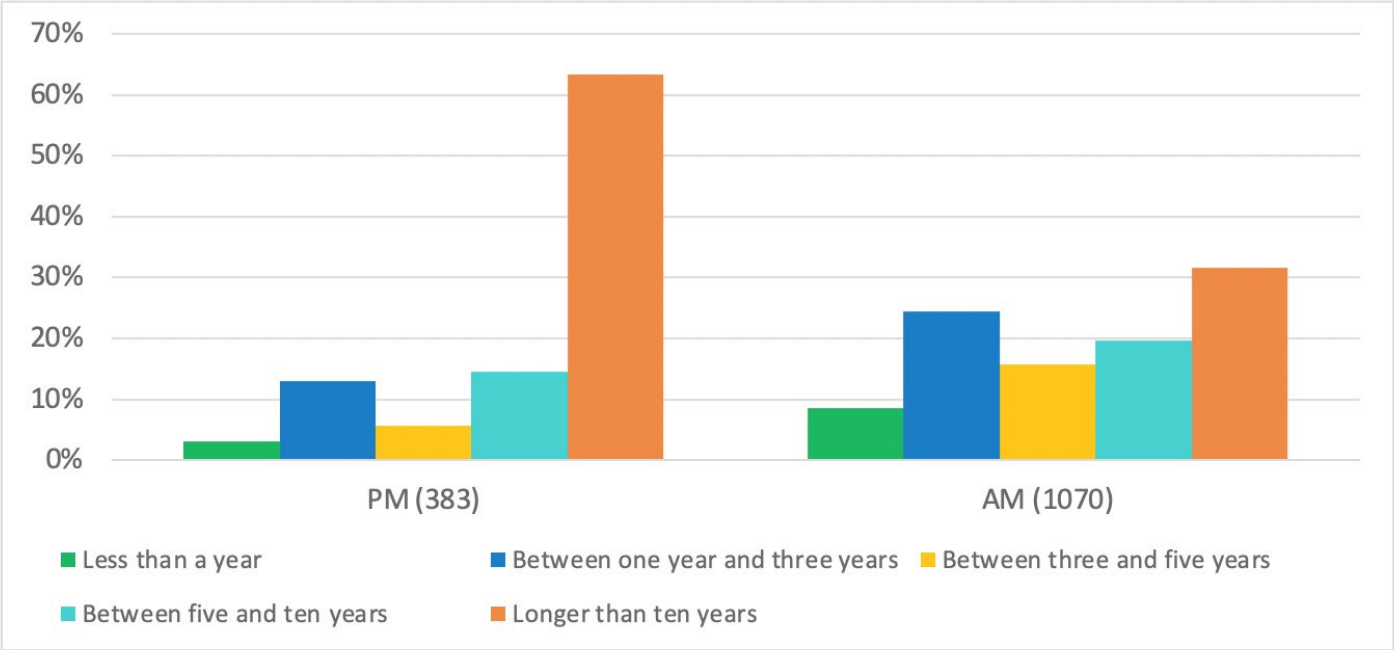


Figure 9 - Length of time model used by researchers who use multiple models. PM is Primary Model, AM is Additional Model. The numbers refer to the number of respondents. Total respondents: 412. Please note the numbers may not match the previous figures.

Although only a small number of non-academic responses were obtained, they indicated the following:

- Industrial researchers indicated using models for Cell Biology and Human Disease research.
- Charity or NGO researchers used models for Cell Biology and Genetics research.
- On average, non-academic respondents used more models in their research, none solely relying upon a single model, and 35% using six or more. This contrasts with 16% of academic researchers who use a single model and less than 8% using six or more.

2.2 Respondents were asked which species is being investigated using their model

- Researchers using single or multiple models are mainly conducting human research **(Fig 11 and 12 respectively)**.
- Researchers often use one species to model another, with a common example being rodent models of human diseases.
- Respondents who selected 'other' were most often conducting research with more general application to multiple species, with yeast and bacteria featuring strongly.

2. Current Use of Models

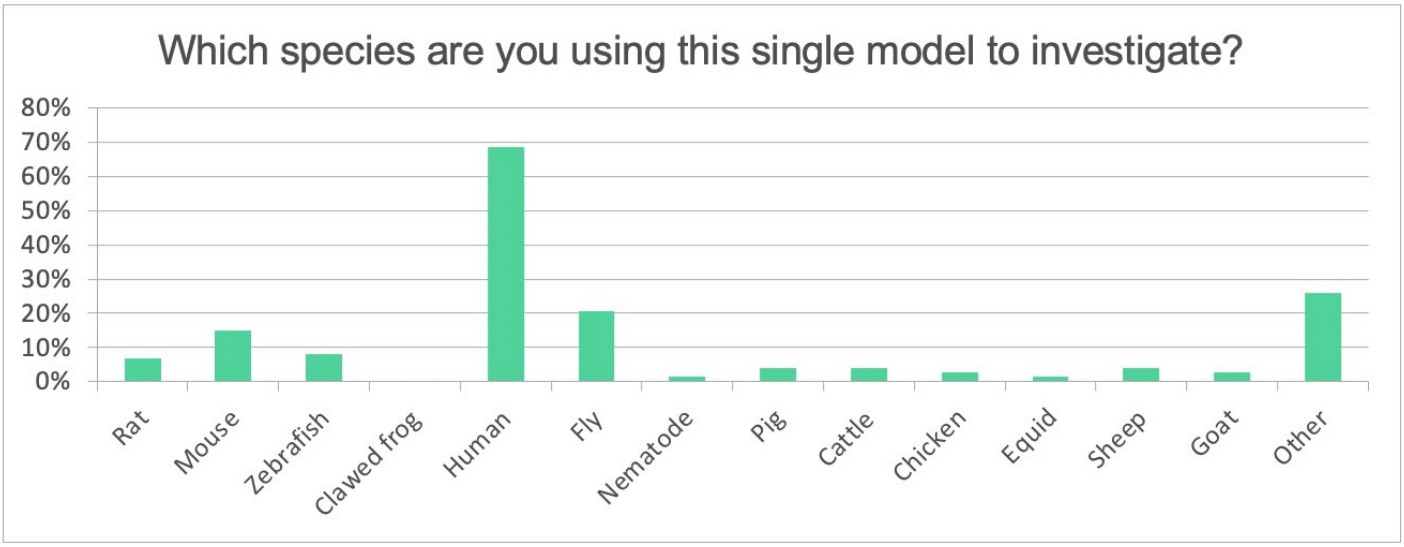


Figure 11 - Target species for research involving a single model. Answers do not sum to 100% because multiple selections are possible. Total respondents: 73; total responses: 121. Numbers may not match the previous figures.

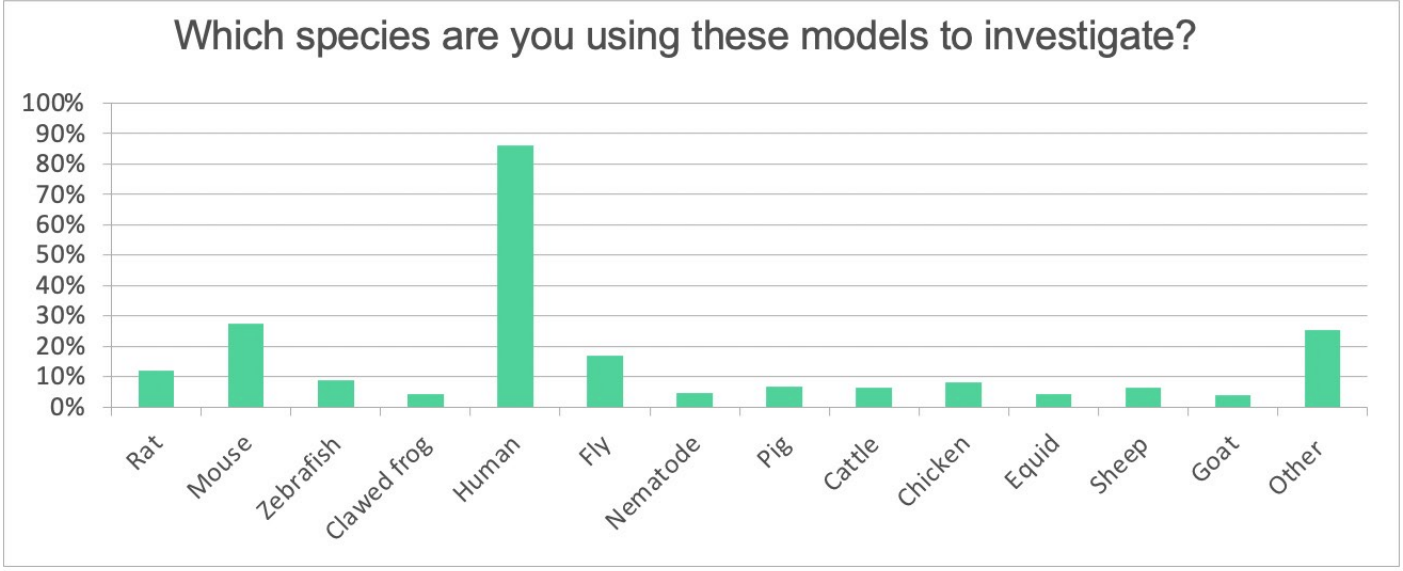


Figure 12 - Target species for research involving multiple models. Answers do not sum to 100% because multiple selections are possible. Total respondents: 413; total responses: 916.

Annexe 2

When considering target species, some respondents indicated that humans were the ultimate beneficiary of research as captured in the comments below:

"I find it interesting to research any species for its own right; but it is true that ultimately, if I think of "benefit" of anything I do, I mostly hold in mind us humans."

"This is a strange question; I don't use flies or mice to model any species. Discovery science does not directly benefit a species, and what benefits a species might be deleterious to another. For example, we have made findings in flies relevant to malaria which might benefit humans by harming mosquitoes. If the question is whether my research will generate wealth or improve human health the answer is hopefully yes, eventually, our research provides the first stepping stones."

2.3 Respondents using multiple models were asked to consider why they are using multiple models?

- 80% of respondents said this was necessary as models are required to recapitulate different aspects of their research question **(Fig 13)**.
- 16% of respondents are considering changing models and are therefore using both simultaneously. The majority of these respondenst were non-academic researchers **(Fig 13)**.

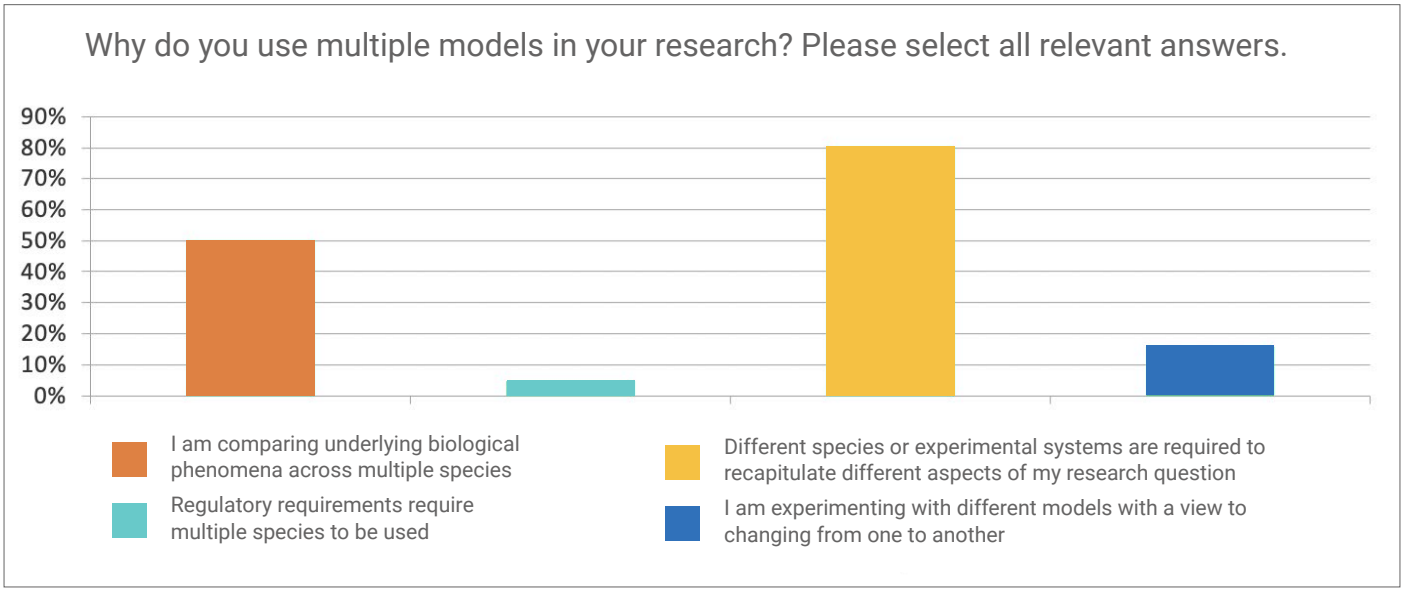


Figure 13 - Reasons why researchers use multiple models. Please note percentages do not sum to 100% because multiple options can be selected. Total respondents: 411.

Some of the most common reasons for using multiple models are in the comments below:'

"They all offer different angles on the research questions my lab is interested in."

"The most appropriate model (least sentient) needs to be used depending on the questions asked."

"Its not reasonable to perform large drug screens on mice, so cell culture or zebrafish are used, nor is it possible to quickly assess multiple gene effects in mice, so flies are used. Ultimately, interesting or relevant therapies are tested in mouse models but not before they have been assessed in at least two other models."

3. Previous Use of Models in Research

3.1 Respondents provided information about the need to change models, and highlighted some of the barriers or challenges experienced.

- **35% of the 486** respondents said they have changed models.
- Most respondents changed models due to a change of research focus (54%), and the availability of genetic tools (49%). Other significant reasons included the availability of the model (36%) and a change of position (33%) **(Fig 14)**.
- Within 'other' the majority reported changing models due to improved results or physiological relevance, with only 2 respondents reporting to have changed models to enable translation and greater clinical applications.

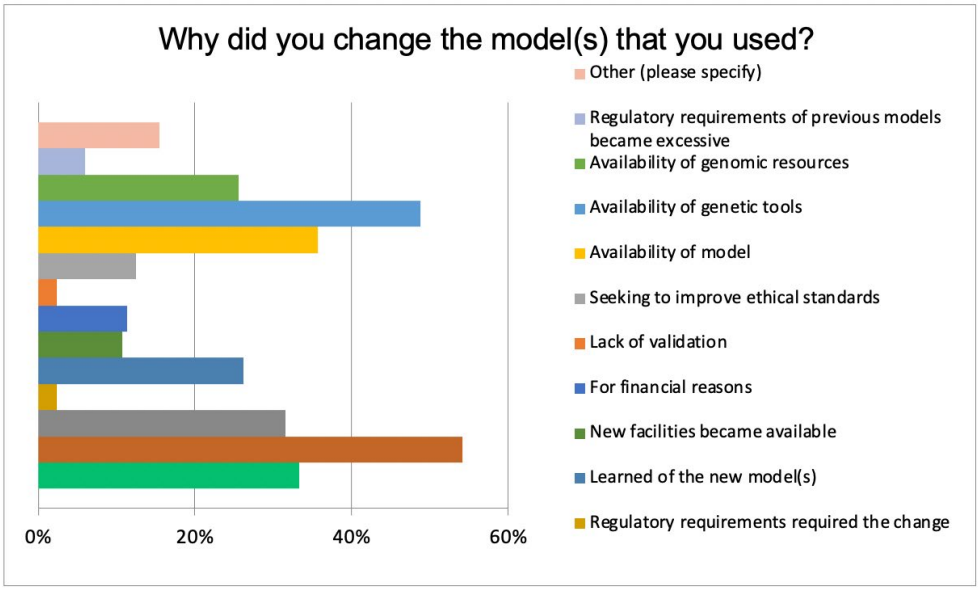


Figure 14 - Why respondents changed from models. Please note percentages will not sum to 100% due to multiple selections. Total respondents: 168.

4. Confidence of Models in Research

4.1 Respondents were asked to consider their confidence in the models they use. To keep responses as simple as possible, respondents were specifically asked to refer to their primary model only.

- All respondents showed a high confidence level (>4.0) in all aspects of their model **(Fig 15)**, with the appropriateness from an ethical perspective ranking as the highest factor.

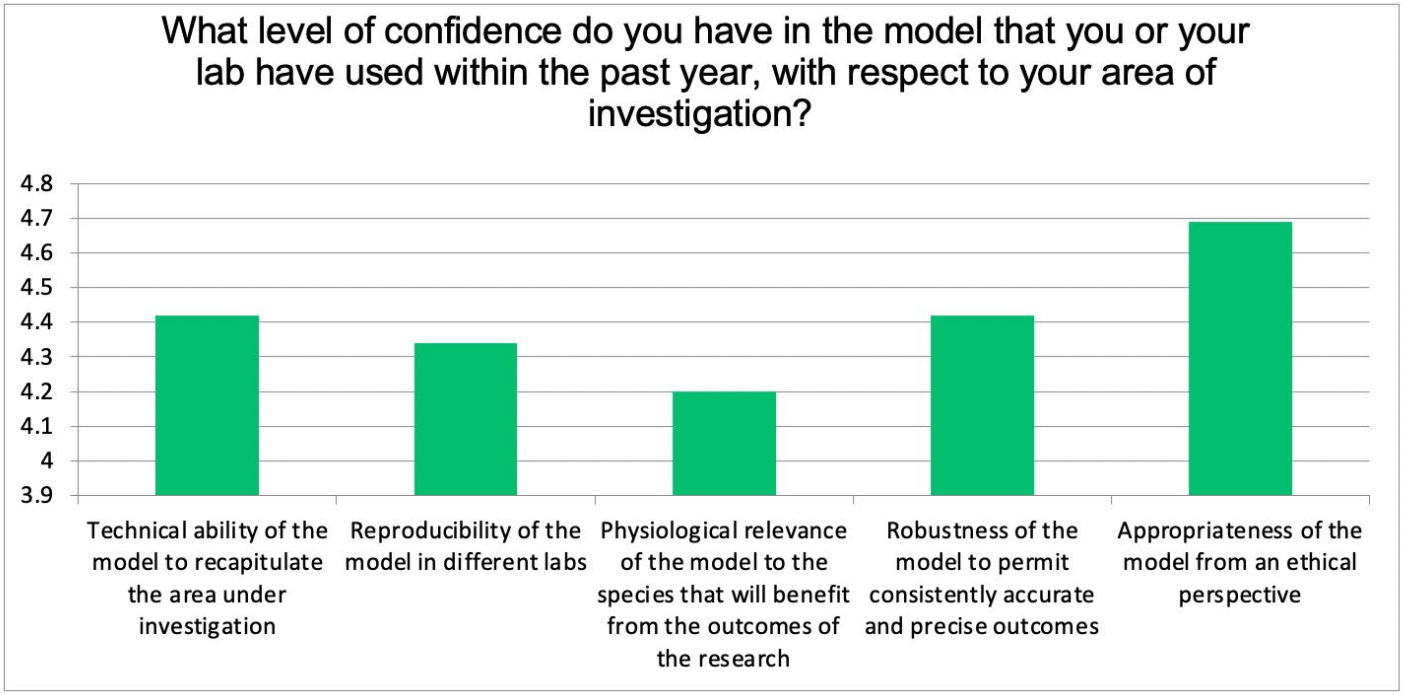
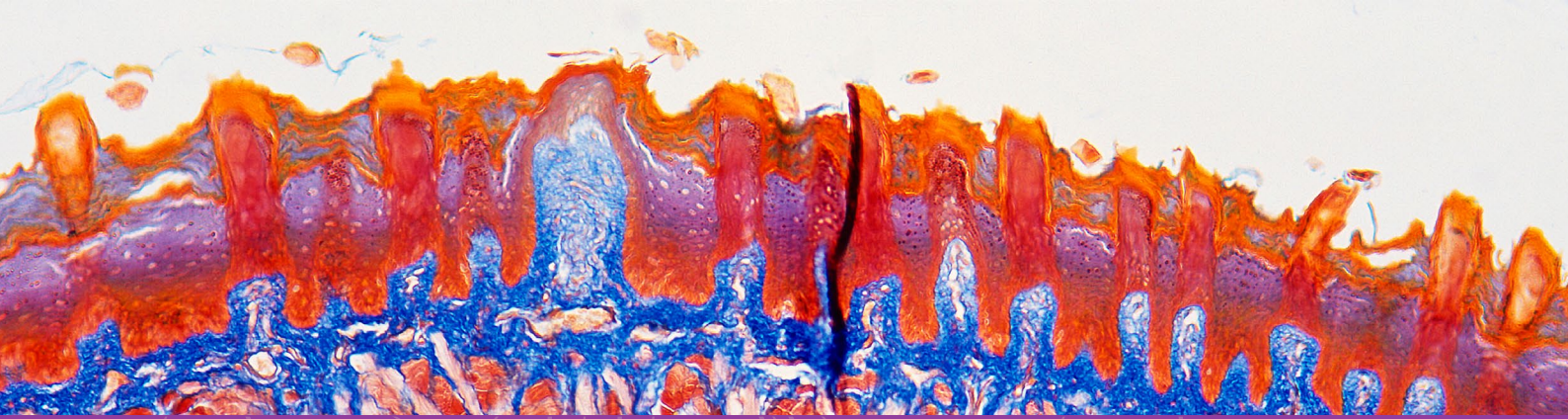


Figure 15 - Weighted average of responses regarding the level of confidence in key areas of respondent's models. A weighted average of 4.0 reflects a high confidence in the model. Respondents were asked to consider their primary model only. Total Respondents: 486. Numbers may not match the previous figures.



5. Differences in the Use of Models in Research

5.1 Respondents were asked if there were alternative models available for their research.

- 68% stated that there were alternative models to those that they were currently using, 27% stated there were no alternatives and 5% were unsure.

5.2 Respondents were then asked to consider the advantages for their model of choice.

- The most common advantage was Physiological Relevance (21%) **(Fig 16)**. Availability of Genetic Tools (18%) was ranked second. Cost, Ethics, Speed and Expertise are also important considerations.
- The most important advantage was 'it is the best model for my research question' followed by 'the model enables us to address new biological questions' and 'there is expertise available to use the model' **(Fig 17)**.

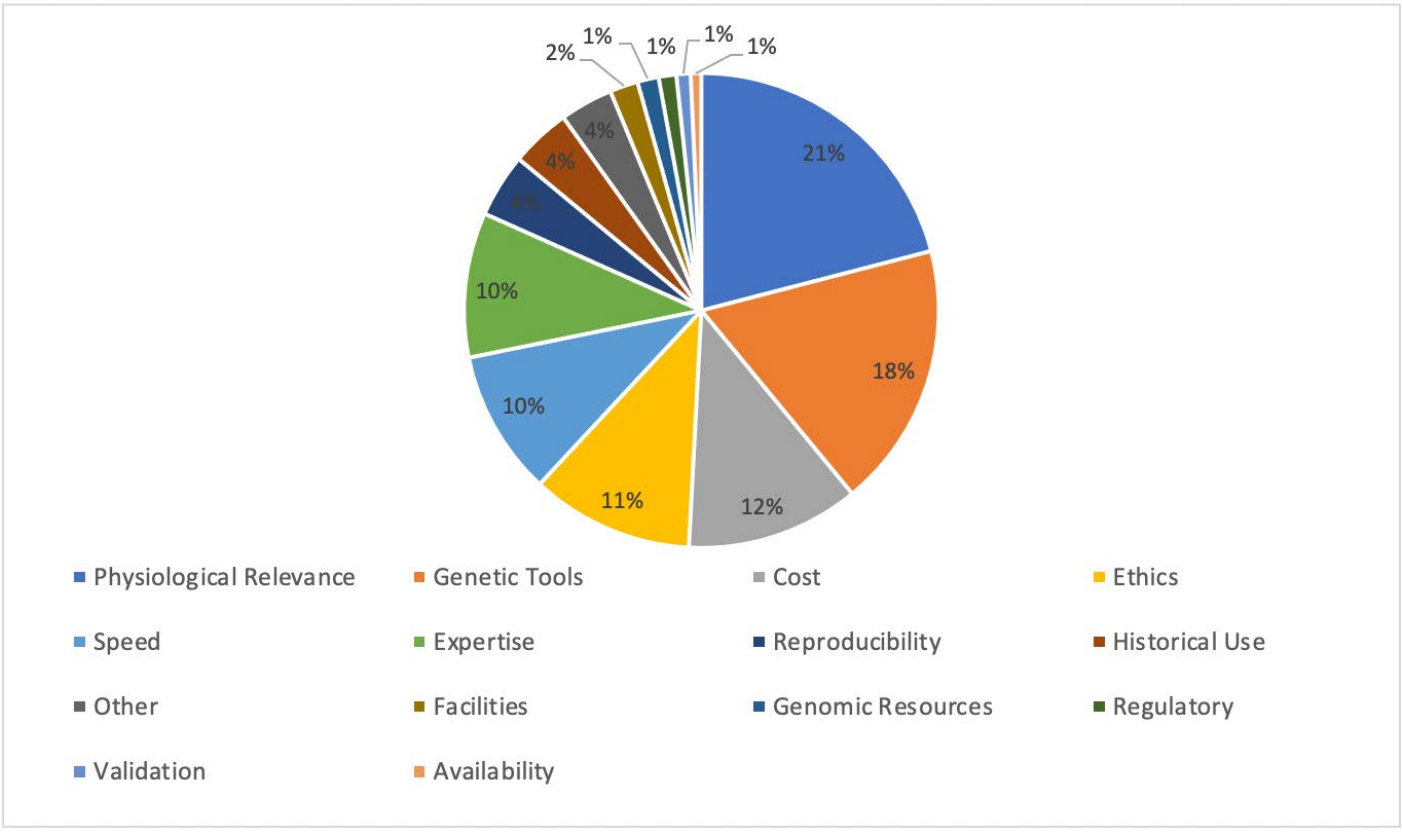


Figure 16 - Advantages given for the current use of models. Total respondents 318; total themes provided: 415.

Annexe 2

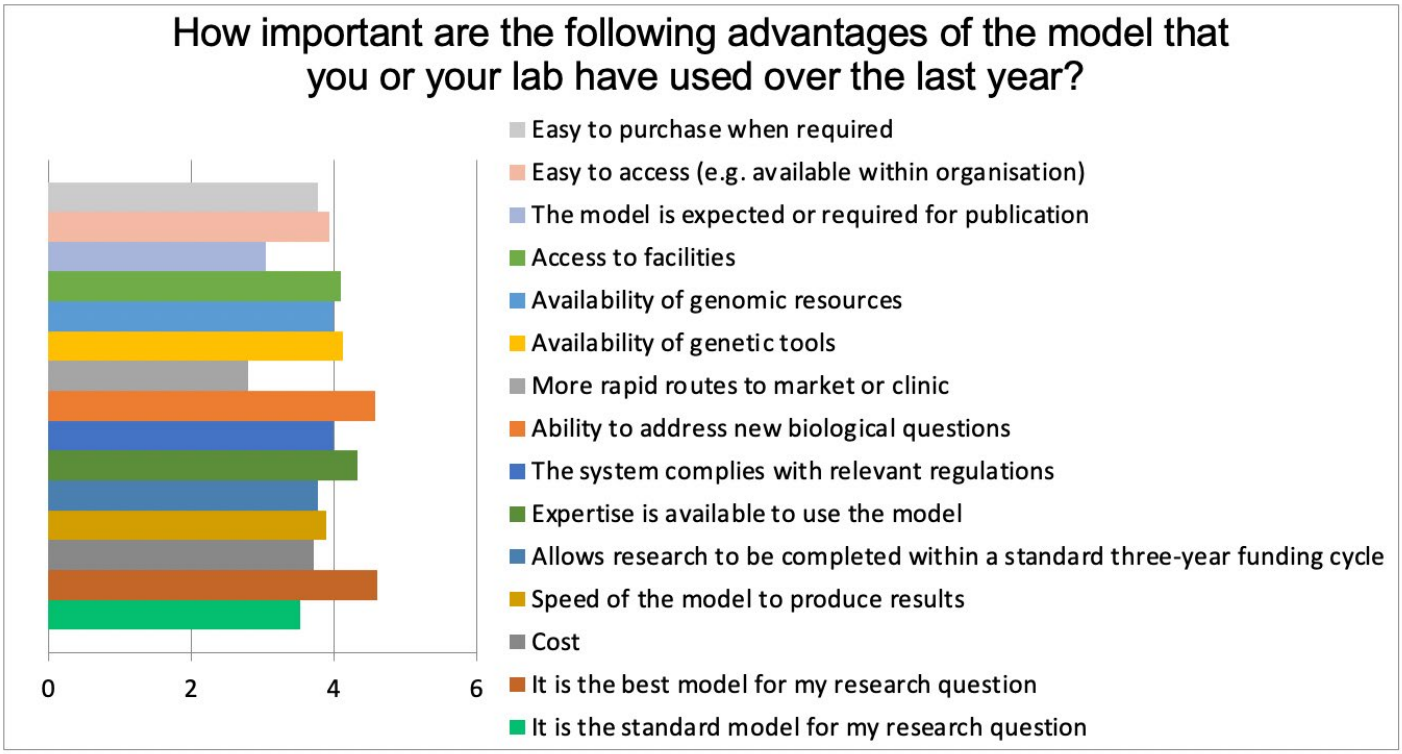


Figure 17 – Weighted average of responses as to the importance of the advantages of the model (primary or single model) that respondents currently use. Total respondents: 486.

5.3 Respondents were asked to consider how their model usage compared to that of their peers.

- 78% agree or strongly agree that their peers use the same models to answer related research questions.
- Respondents considered the different expertise and research questions being investigated to be the main reasons for any differences in model choice.

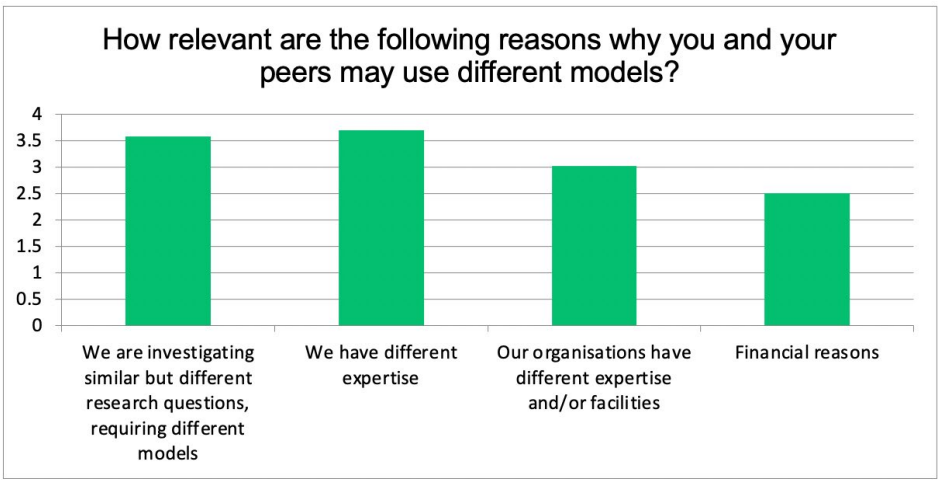


Figure 18 - Weighted average of responses as to why peers may use different models to those that the respondents use. Total respondents: 105.

6. Future Use of Models in Research

6.1 Respondents were asked what models they anticipated using within the next five years.

- Whole organisms remain the primary model of choice for future research (59%) **(Fig 19)**.
- 2D cell culture, tissue or slice, and computational/in silico were also favoured choices. There is a notable increase in the use of organoids (14% to 27%) compared to a decrease in 2D cell cultures across all models.

6.2 Respondents were asked what species they anticipated using over the next five years.

- Mouse and human were the most favoured species **(Fig 20)**.
- Yeast was common within the 'other' category.
- Species selection appears to be fairly stable.

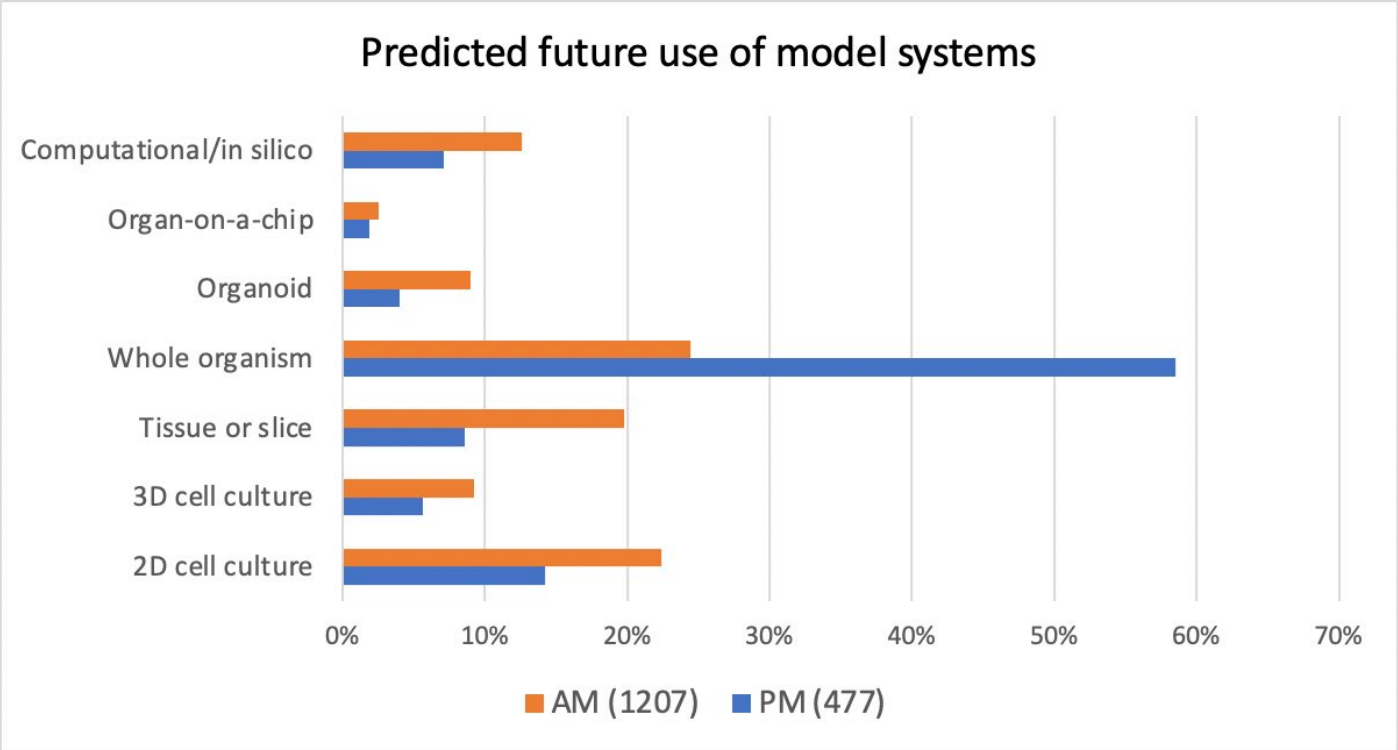


Figure 19 - Intended model systems to be used over the next five years. PM is primary model, AM is additional model. Please note that this question was asked of all respondents regardless of the number of currently used models. Total respondents: 479; numbers in brackets are the number of responses.

Annexe 2

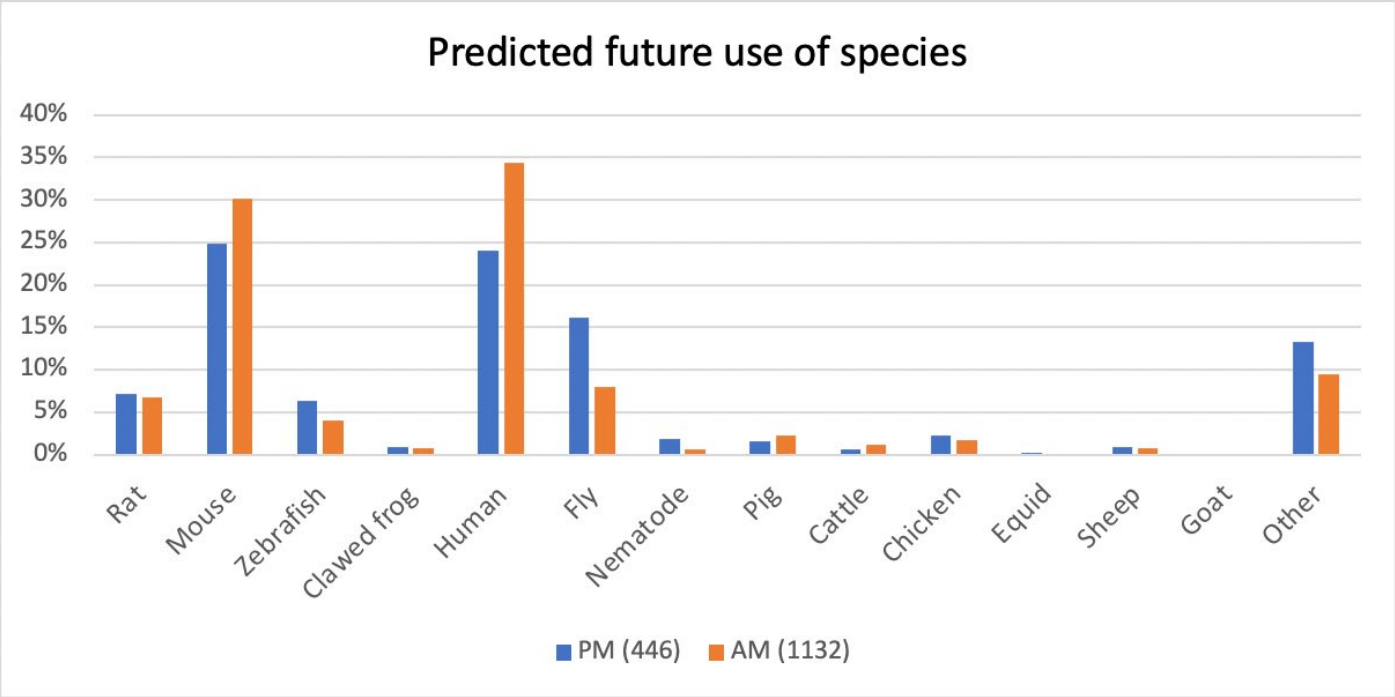


Figure 20 - Intended species to be used over the next five years. PM is primary model; AM is additional model. Total respondents: 446; bracketed numbers indicate number of responses.

6.3 Respondents were asked which options are most important to their future research plans.

- Respondents considered 'validation' to be the most important area of further work, narrowly followed by 'comparison of *in vivo* and other systems to identify similarities and differences.' **(Fig 21)**.

Whilst further novel models may be useful, better validation and optimisation of current models are going to be the most important.

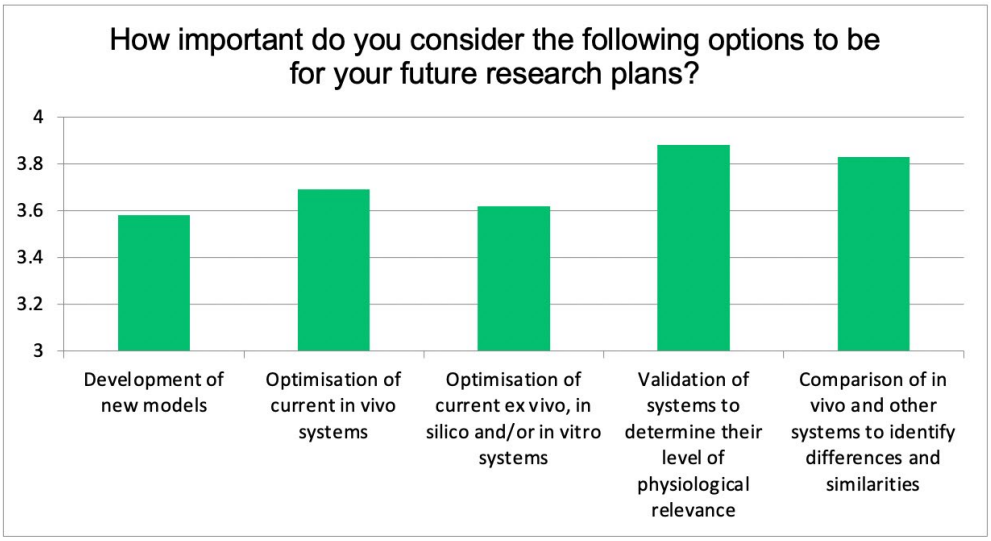


Figure 21 - Weighted average of responses to what areas respondents would consider most important for their future research plans. Total respondents: 498.

7. Barriers and Challenges

It should be noted that the responses shown here have a substantially lower weighted average than other questions which asked respondents to rate statements. This is because approximately 20% responded negatively to all statements, with a further 10% responding that none were applicable.

7.1 Respondents were asked to consider what barriers were preventing them from using the models of their choice.

The majority of respondents indicated that they are content with their choice of model. Although cost was the most common barrier preventing researchers from using their preferred model, there was a broad coverage across the potential barriers **(Fig 22)**.

7.2 Respondents were asked to consider what advantages would most likely be obtained if these barriers were removed.

- The most substantial advantage noted by respondents is being able to run new experiments to expand investigations to new areas **(Fig 23)**.

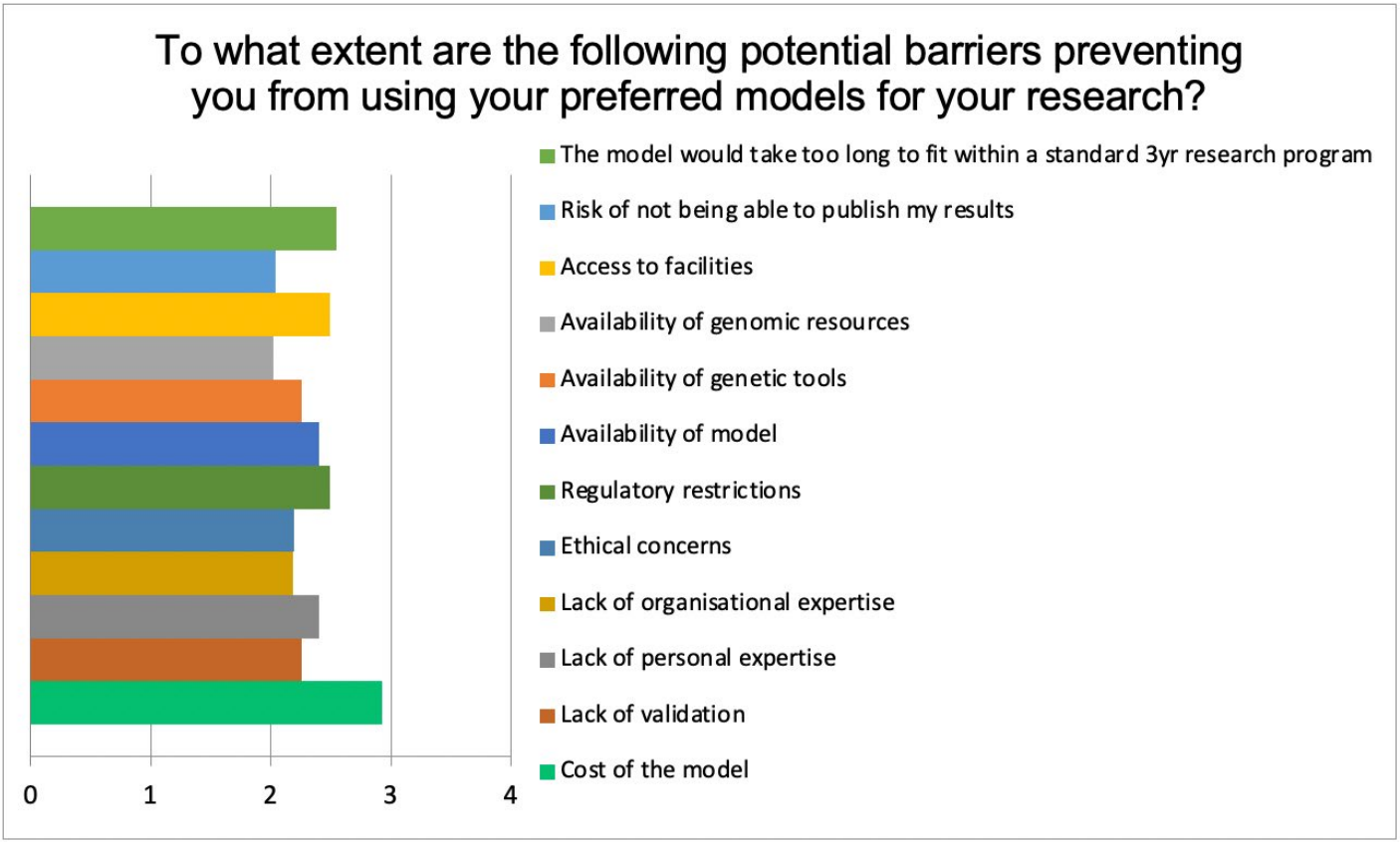


Figure 22 - Weighted average of responses to indicate which key areas were preventing researchers from utilising their preferred models. Total respondents: 498.

Annexe 2

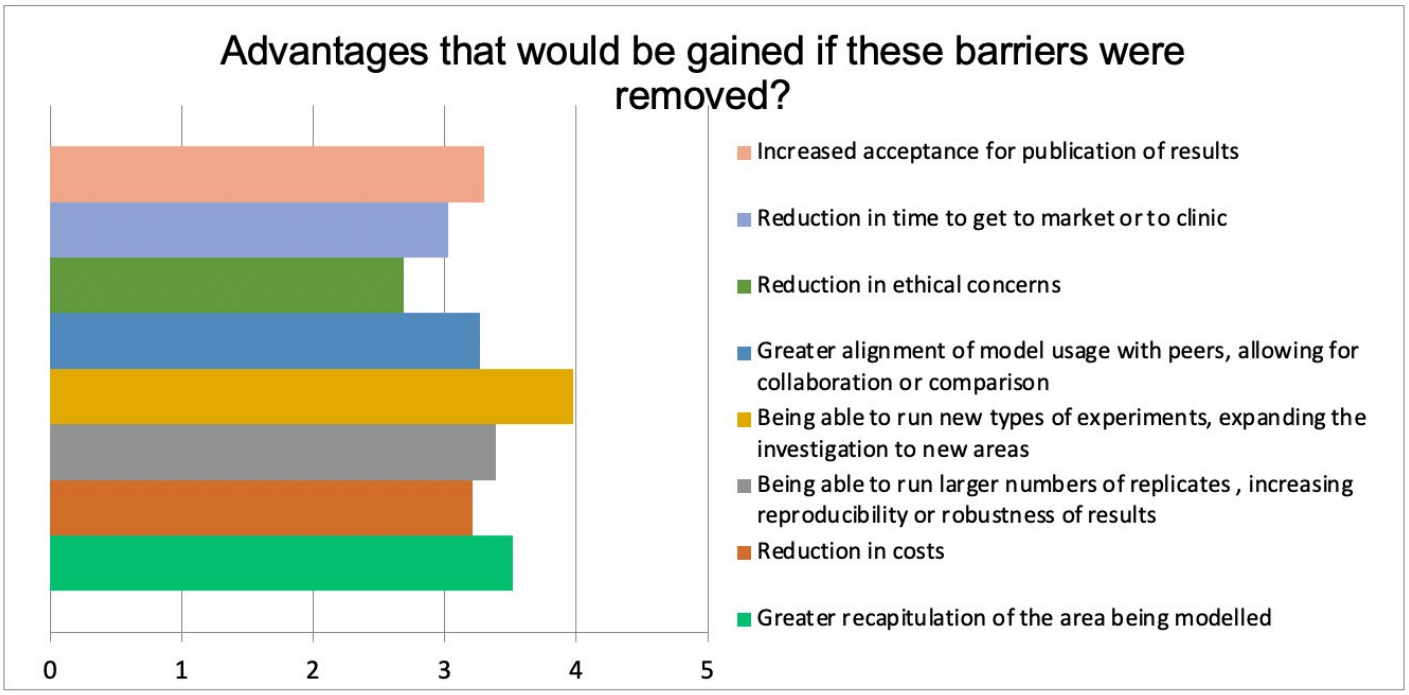
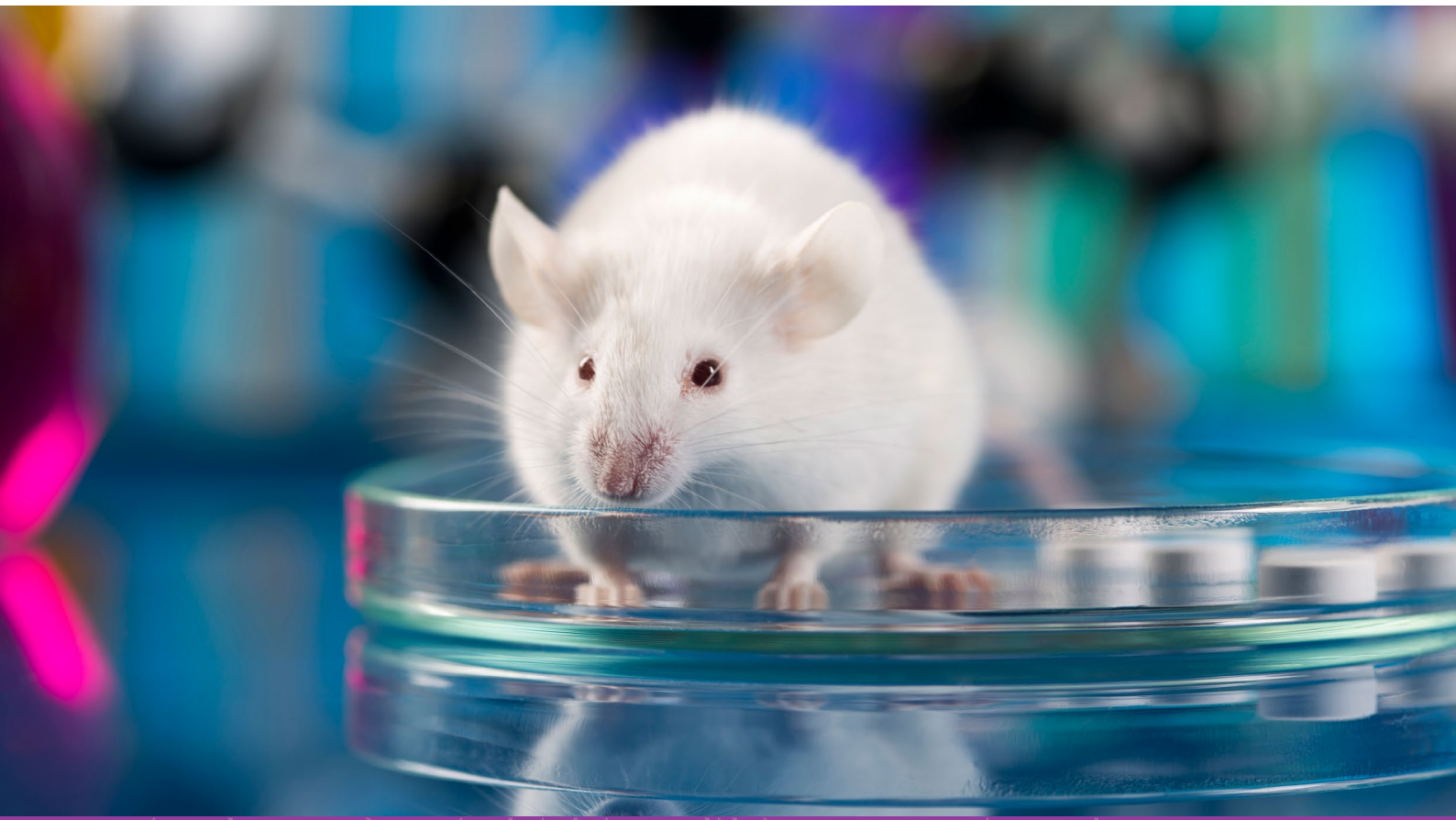


Figure 23 - Weighted average of responses to the question 'how substantial are the advantages that would be gained if these barriers were removed?'. Total respondents: 498.



8. Further Comments

Respondents were then invited to provide further insight into the potential barriers which were preventing them from using their preferred models, or areas which were frustrating their progress.

8.1 Regulatory Challenges

The responses for this question were grouped into categories for analysis, see below.

Animal Research	29	Research Organisation	4
Home Office Licensing	23	Funding	3
Human Tissue	15	Regulatory Acceptance	2
Standardisation	4	Clinical Translation	1

Table 2 - The major problems noted by respondents with respect to regulatory concerns. Total respondents: 88.

- Concerns regarding the regulatory process surrounding *in vivo* research is making the UK less competitive, e.g. the amount of administrative work involved (refer to comments box below).
- Difficulties navigating the Home Office licensing process, Animal Welfare Ethical Review Bodies, Home Office Inspectors, and primary legislation such as the Animals (Scientific Procedures) Act 1986 (as amended).
- Lack of understanding of novel models leading to a delay in getting necessary approval.
- Access to human tissue, particularly brain tissue, is challenging. However, it can be circumvented by collaborating with clinical colleagues, but it was acknowledged that establishing collaborations or networks to facilitate this can be challenging.
- Administrative burden preventing innovation.

Some example respondent comments are provided below:

"Home office regulations are extremely bureaucratic and take a lot of investigator time. In turn, they can stifle innovative research."

"Getting permission to work with laboratory animals is a long, complicated and expensive process. It is extremely difficult to conciliate the need of performing innovating research and plan all the experiments in detail years in advance."

Annexe 2

"Regulations in place are justified and necessary. Their removal may speed up research but could not be justified."

"Organoids would be generated from human patient iPSCs so ethical approvals are required. This takes significant time and curbs my use of the model"

"The use of mouse models is absolutely essential and remains a corner stone for research in immunology, complemented by excellent research using human volunteers, epidemiology and other methods. There is a real concern that the regulatory burden and cost of animal research in the UK is making us less competitive and attractive. A few years ago, there were attempts to streamline Home office approval processes, but this seems to have been reversed such that it now often takes more than a year to have a licence approved."

8.2 Training and Expertise Needs

Respondents were asked to outline issues they may have encountered with training and expertise and highlight any potential solutions. The responses for this question were grouped into categories for analysis, see below.

Availability	38	Animal Facility	3
Time	13	Regulation	3
Collaboration	12	Novel Species	2
Funding	11	Whole Organism	2
New Technology	7		

Table 3 - The major challenges noted by respondents with respect to training and expertise concerns. Total respondents: 98.

Key training barriers identified are:

- Challenge to find people with relevant expertise, particularly with novel technologies.
- Lack of awareness of who is available to collaborate with.
- Lack of open sharing of materials and methodologies.
- Lack of time to give or receive training.
- Lack of funding which permits training to be received, rather than producing immediate results.
- Lack of long-term lab members (aside from PI) to gain/provide training.

Annexe 2

Some example respondent comments are provided below:

"Transgenics in chickens are nowhere near as advanced as in mice and flies; more training there would be great."

"It takes a long time for people to get back to you and there is no clear way to find trainers on specific techniques."

"Organ on chip expertise is concentrated in a few labs and it is difficult to collaborate as they are focused on their own work or only want to link up with clinicians who can gift them samples rather than basic scientists who they see as competitors. Funding is difficult unless you have preliminary data."

"There is a lack of *in vivo* training of students with the removal of funding training schemes that used to be provided by the BBSRC."

"The new models are technically challenging. It would require significant training to use them. There are a few groups with expertise UK wide (more world wide), but time to train is an issue since the postdoctoral contract is fixed term."

"Conditions for organoid culture differ between tissue type, which prevent introduction of this technique to my research. List of experts or training course funded by UKRI would be helpful."

"This is primarily an issue of time, expertise and resource available. My own expertise as a more experienced researcher becomes limiting as I have less time available to develop my own skills to pass this on. A solution to this would be the funding of more scientific officers over the longer term to retain skills and experience within a research lab (or group of labs) as well as to enable them to develop their own skills and continue their professional development."

Annexe 2

8.3 Validation of model

Respondents raised the following concerns:

- Lack of validation studies are preventing uptake of novel models.
- Lack of research funding for validation of models.
- Lack of interest from research journals regarding novel models and their validation.
- Difficult to maintain interest in developing new models as there is a preference to seek the most novel model rather than improve previously discovered or used models.
- Lack of harmonisation across different laboratories, with each one seeking its own model or models and limited collaboration.

Some example respondent comments are provided below:

"Publishing with a new 3D culture model is difficult in highly-rated journals. This makes persuading people to fund or to adopt the techniques difficult, making validation and acceptance of the model harder."

"Some novel areas are very attractive (organs on a chip) but they are not sufficiently validated to trust the results."

"What has worked elsewhere may not work the same way in a new lab. Validation of a model for multiple different diseases is very time and resource intense and doesn't offer anything in the way of publishable data so can be difficult to fund or justify in terms of both costs and time in a grant."

"Advancing the models themselves is favoured over standardized use of those models for other research questions."

"There is not time, money or willingness to validate complex models thoroughly. The UK Home Office is unwilling to grant licences for 'model development', so there is pressure to generate high quality results from the outset."

"The model I would like to use (zebra fish) has never been used to study what I want to. Without resources I cannot develop the system, and I cannot get resources without the preliminary data."

Annexe 2

8.4 Availability of Models

Respondents were asked to outline any issues they have encountered with availability of models and to suggest any potential solutions. The responses for this question were grouped into categories for analysis, see below.

Funding	20	Time	4
Expertise	9	Animal Purchase	3
Human tissue	9	Novel Model	2
Characteristics	8	Uptake	1
Regulation	7		

Table 4 - The major challenges noted by respondents in the availability of models. Total respondents: 81.

Key concerns regarding the availability of models are:

- Difficulty of obtaining the large amount of research funding required to maintain specialist/niche models, including facility costs and retention of necessary expertise.
- Difficulties of obtaining human tissue.
- Lack of models for specific research purposes due to lack of physiological relevance or characteristics of available or established models.
- Regulatory restrictions hampering access to models.
- Lack of model availability due to poor sharing of expertise.

Annexe 2

Some example respondent comments are provided below:

"Few UK academic groups have the expertise we need 'on tap', and those that are tend to be too busy. There are no longer any funds to support technical staff to do routine PK or biodistribution experiments in UK academic labs, and it takes too long to train students in this area (time to get a licence and be fully trained in the UK PhD timeframe)."

"A basic challenge with non-traditional model species is sourcing the animals (you can't just order a Frogfish from your laboratory supply company). For the fish species I'm interested in, I'd love to work with aquariums or marine labs to source animals ethically and responsibly--right now I don't have the connections or resources to do that."

"Would like to move to organoid or organ-on-chip, but no experience, no availability within university, no funds to set-up. Technology access programmes, start-up funds potential solutions."

"Live human cardiac tissue is very rare."

"Models are sometimes available from the UK, however they are more likely to come from abroad due to the specific line required. This increases cost and takes far too long in most cases."

"If you don't have a surgical team interested in research this work can't be done."

8.5 Tools, Technologies and Facilities Needs

Respondents were asked to consider the key challenges in the broad area of tools, technologies and facilities. This was the area with the strongest response of challenges to the use of models in research. The responses for this question were grouped into categories for analysis, see below.

Animal Facilities	27	Time	6
Tools	24	Research Organisation	6
Cost	21	Collaboration	5
Equipment	13	Genomics	5
Expertise	9	Regulation	4

Table 5 - The major challenges noted by respondents in the area of tools, technologies and facilities. Total respondents: 132.

Annexe 2

Key issues noted in this area were:

- Lack of availability of large animal facilities and/or containment level three facilities.
- Availability of any required animal model in the broadest sense, from human tissue and non-human primates through to rodents, flies and snails, depending on the respondent.
- Specific problems regarding access to human tissue, regulatory concerns with respect to non-human primates and genetic modification of non-human primates.
- Constraints broadly due to the availability of genomic information and regulatory speed.
- Lack of funding in the tools needed to start using novel models as universities are unwilling to invest in areas outside of what they already do. If researchers do not have access to the relevant specialist facilities or the tools required to utilise a given model, then they are not able to use that model.

Some example respondent comments are provided below:

"Pigs and sheep used for research are typically sourced from commercial vendors and costs of animal facilities available in our organisation are very high. This makes the planning of large scale and labour-intensive experiments very challenging. The sheep genome is only partially completed, and annotation is poor. The pig genome is more advanced, however detailed understanding of some genomic features lack experimental validation. Finally, IVF technique in the pig is very inefficient. Thus, all experiments aimed at genetic modification require the use of *in vivo* produced zygotes. This makes the experimental setup much more complex than in sheep, where embryos can be produced *in vitro* regularly, from abattoir material."

"Relatively few organisations produce and share knowledge in these areas so investment in specialist scientific communities and establishing expert core facilities are key."

"Access to on-campus facilities to house and care for non-traditional model species has been a major barrier. Because this is new, exploratory research that's never been done before, the University views it as too risky to invest in support infrastructure. This is a major obstacle to working with a new model species. Maybe there could be more flexibility to share facilities between Universities (current regulations make this quite burdensome) or sources of funding to build/maintain campus facilities."

Annexe 2

"Mainly access to equipment is very limited as either it very expensive or not present, especially if state-of-the-art quality is expected. It is very difficult to acquire new equipment and it takes a long time. There are hardly any equipment grants out there and they as well take time to write and be granted. This almost always exceeds the 3-year period of a project."

"Maintaining our facilities is always challenging as is costing technical support. The resourcing issue long term is the challenge here. This might require fundamental structural changes to the support system."

8.6 Other Comments

Finally, all respondents were offered the opportunity to provide further feedback on any areas they considered BBSRC should be aware of.

Key considerations for:

BBSRC

- Respondents felt that changes could be made to the research funding system to better support the use of a diverse range of models.
- Training and skills for early career researchers e.g. What models are available/ Where to gain expertise/ How to write grants around models?
- Funding is needed for support/technical staff to assist research teams in their use of novel models and pass on training to newer lab members.
- Further funding for facilities and infrastructure is required to improve national capability.
- BBSRC and other UKRI councils appear to have limited engagement in this area but need to have better communication with all stakeholders e.g. regular discussions to identify how the research community is using/ wants to use models, and what support they need to realise this.
- The research community encourages the support of a diverse and broad portfolio of models, rather than a focus on a select few models of importance.

Annexe 2

Key Funding Bodies

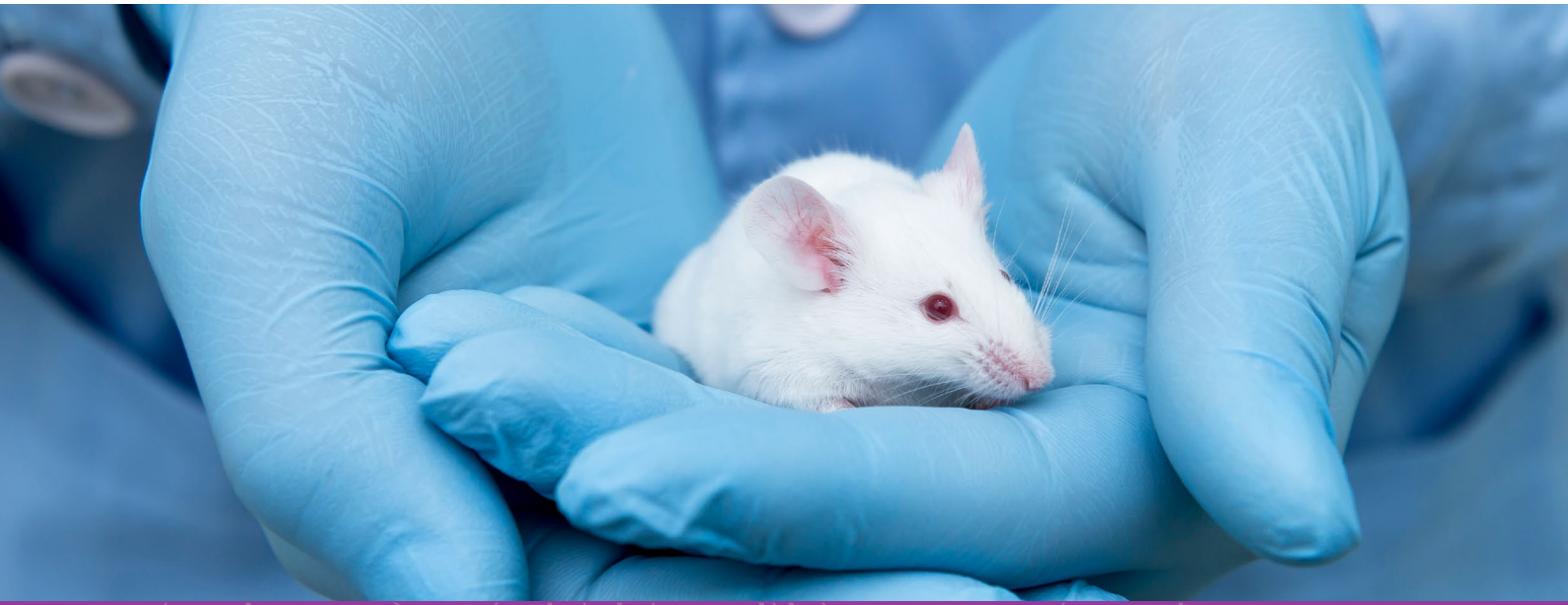
- A more joined up approach for animal research and animal facilities could reduce cost and improve regulatory burdens.
- The use of animals in the UK has a high cost and administrative burden, if funding bodies do not account for this then the UK could lose its competitiveness.
- Often novel models are not taken up due to a lack of resources available to validate the model, more validation specific funding is required.

Some example respondent comments are provided below:

"Co-funding for high-skilled research experimental officers at universities would greatly help. This provides continuity and career structures for staff to support model maintenance and new model development which PhD students can't really do. Currently we try to do this work with PDRAs on short-term contracts, and this is wasteful as PDRAs move on and expertise is lost."

"There is a lack of a nationwide policy on provision of suitable animals for research, and it is dependent on the policy of individual organizations that can change their policy for reasons disconnected from their research consequences."

"There is limited amount of funding dedicated solely to development of models (without other expected outcomes than having a working and efficacious model that could be used widely for many purpose)."



Annexe 2

"As you will see from the models that I listed, they are not the 'conventional animals' researchers use in the stem cells developmental biology arena to study human development and physiology. However, I have invested a great deal of my career to develop them (in particular the pig) because of the significant similarity with the human embryo and the answers it has offered with regards to conserved developmental mechanisms that are highly divergent in the mouse. Developing a national resource that can cater for people needs of embryos has been a long-term aim of my research.
The advantage of the pig is its dual relevance, for research but also for agriculture. Sourcing these animals needn't be difficult nor costly. Setting up infrastructure equivalent to that of other countries (China or USA) to provide animals for researchers is highly achievable. The impact of this research to enhancing the understanding of human development will be significant. The UK is one of the few places in the world carrying out this kind of work, however it lacks sufficient scale and facilities. I collaborate with researchers in different Universities across the UK that acknowledge the significance of these models, however they are limited by access. A strategic, long term perspective for developing these systems is of paramount importance to maintain the UK's leading position in this area of research."

"Animal model research is instrumental to our progress in science/medicine. We should not stick to the models we know but expand. CRISPR will make this easier. A sole human focus is not optimal in discovering the basic biology we need to make large leaps in our understanding of disease and fundamental aspects of life."

"I think it is utterly damning (and typical) that the most significant model organisms in terms of our elucidation of basic eukaryote (human!) molecular biology (trivial things like gene regulation, DNA repair, cell cycle etc.) were omitted from the list of models here. The two yeast models: S. cerevisiae and S. pombe have been, and remain fundamental, tractable and CHEAP. Please continue to fund work in these models."

"Determining appropriate sample sizes and use of statistics remains very important and is thankfully much more recognised now than even a few years ago. Nevertheless, research committees spend a lot of time on power calculations etc which are not useful for discovery science when a type of experiment is not already being done routinely. We all need to work smarter and be more agile to remain relevant and competitive."

Annexe 2

"*In vivo* models will continue to be a major cornerstone of comparative biology and physiology, allowing deep mechanistic insight that impacts upon our understanding of disease and pathology, in both humans and animals. We need a joined-up approach across all funders from the BBSRC to Wellcome to MRC to assess the needs and requirements for animal facilities that will maintain our international competitiveness. It is clear that we are falling behind in this area. The major funders should convene a working group to develop a joined-up national strategy for animal research and animal facilities to support key areas of comparative *in vivo* biology, disease mechanism studies and genomic medicine, delivering a joined-up and internationally competitive landscape for model organism research in the UK."

"I consider that it is very important for BBSRC to continue to support resources such as the Tick Cell Biobank that generate new models for use in a wide range of veterinary, medical and agricultural research areas in UK and worldwide. The skills and expertise required to develop relatively "niche" models such as arthropod cell lines are held by few people, while the new models may then be used by a much broader range of scientists."

"The generation of new and better models requires long-term investment and the freedom to accept risk of failure, for which the current UKRI policies suggest far too little appetite"

"The development of new models to address research questions should be heavily supported. Additionally beginning and completing such a study in the standard 3 year window is impossible. There should be some leeway in terms of funding for this type of research."

"BBSRC focuses too much on applied work with immediate (and already demonstrated) results. While this is of course of value, the importance of laying groundwork and doing fundamental research is overlooked, and the researchers are pushed to look to financial support elsewhere. BBSRC can't hope that great applications will be coming out without a proper investment into the fundamental mechanisms, new tools (including genetic tools), etc. In addition, BBSRC has a tendency to go very low-risk, and to fund projects that are already 50-70% done. This is simply wrong and does not give a chance for new ideas to develop."

Annexe 3

Survey on the Use of Models in Research

Below is the full survey as provided to the research community.

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Introduction

UKRI-BBSRC is consulting the research community (including academic, industrial and other researchers) on their current use of experimental systems or models for human and animal research, as well as their future perspectives.

For the purpose of this survey the term 'model' includes:

- *in vivo, ex vivo, in vitro* and *in silico* experimental systems
- Research where the species involved is used to represent a different species
- Research where the species involved is used as it is the target species for the research outcomes
- Research where the species involved in used to investigate a general mechanism or process

This survey contains 30 questions, but you are more likely to answer 20 to 25, depending on your responses. It will take approximately 20 minutes to complete. We thank you in advance for your input.

All information submitted to UKRI-BBSRC will be treated in confidence. Non-attributable comments from the survey comments may be used in subsequent activities, e.g. included in internal and external publications on this topic.

If you have any questions about this survey, or experience any problems filling it out, please contact: bfh@bbsrc.ukri.org

Annexe 3

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Introductory Questions

In this first section you will be asked to provide contact information and general information about your research to provide context.

Annexe 3

1. UKRI-BBSRC carries out the processing of personal data in accordance with the General Data Protection Regulation (GDPR).

The information you provide as part of this survey will only be used by UKRI-BBSRC and its partner, Survey Monkey, for the purpose of informing the review of this area. We would like to use your contact details to:

· Provide updates on the review, including requesting further community input and provision of a copy of the final report.

Would you be happy to be contacted again for these purposes?

The personal data you have provided will be collated and anonymised prior to analysis and will not be attributable to individuals. Information gathered will be used by UKRI-BBSRC, alongside data gathered through other exercises, to provide a dialogue that facilitates strategy development.

The personal data provided will be retained on our systems for as long as is required to carry out processing for the purposes outlined above.

By providing your information you are consenting to its use as detailed above. You can access a copy of the UKRI Data Protection Policy at: https://www.ukri.org/files/termsconditions/ukri-data-protection-policy-pdf/

- [ ] Yes, I would be happy to be contacted again for these purposes, including to provide additional information.
- [ ] No, I do not wish to be contacted further.
- [ ] Yes, I would be happy to be contacted again, but only to receive a copy of the final report.

2. What are your details?

First Name	
Last Name	
Job Title	
Organisation	
Email Address	

Annexe 3

3. Which of these options best describes you?

- ○ Academic Researcher
- ○ Industrial Researcher
- ○ Charity/Non Governmental Organisation Researcher
- ○ Clinician or Allied Health Professional
- ○ Other (please specify)

Annexe 3

4. Which of the following would you say are the general area(s) and/or discipline(s) of your research? **Please pick at most three options.**

- ☐ Cell biology
- ☐ Soil science
- ☐ Reduction, refinement and replacement of animals in research
- ☐ Endocrinology
- ☐ Physiology
- ☐ Psychology
- ☐ Immunology
- ☐ Animal welfare
- ☐ Neuroscience
- ☐ Tissue engineering
- ☐ Biochemical engineering
- ☐ Biological catalysis and enzymology
- ☐ Chemical biology
- ☐ Ageing
- ☐ Epigenetics
- ☐ Evolutionary biology
- ☐ Population biology
- ☐ Structural biology
- ☐ Stem cells
- ☐ Developmental biology
- ☐ Genetics
- ☐ Microbiology
- ☐ Crop science
- ☐ Imaging
- ☐ Industrial biotechnology
- ☐ Synthetic biology
- ☐ Bioenergy
- ☐ Non-human animal health
- ☐ Regenerative biology or medicine
- ☐ Non-human animal disease
- ☐ Human disease
- ☐ Human health
- ☐ Food, nutrition and health
- ☐ Technology development
- ☐ Methods in research
- ☐ Epidemiology
- ☐ Cell and gene therapies
- ☐ Radiation biology
- ☐ Pharmacology
- ☐ Toxicology
- ☐ Oncology
- ☐ Infectious disease
- ☐ Mental health
- ☐ Antimicrobial resistance
- ☐ Non-communicable disease
- ☐ Genomics
- ☐ Bioinformatics
- ☐ Systems biology
- ☐ Mathematical biology
- ☐ Molecular biology
- ☐ Biophysics
- ☐ Plant science

Annexe 3

5. How many types of model have your or your lab used in the previous year? Please do not count individual strains or cell lines separately. For example whole flies, fly tissues and computational models of a fly would be three.

- [ ] None
- [ ] One
- [ ] Two to five
- [ ] Six or more

Annexe 3

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Current Use of Models

This section contains questions on your current use of models, the reasons why you use the models that you do, and how they help with your research.

6. In order to explore the variety of models used in research, could you indicate the combination of experimental system and species in the model that you or your lab have used in the last year, and for how long you have been using these models? **If the necessary options are not available in the dropdown menus, please note them below.**

	Experimental System	Species	Length of use
Model			

Other (please specify)

7. How do you use this model in your work? Could you briefly indicate its relevance by outlining the general types of experiment that you use it for?

Annexe 3

8. Which species are you using this model to investigate, i.e. which species will benefit from the outcomes of your research?

- [ ] Rat
- [ ] Mouse
- [ ] Zebrafish
- [ ] Clawed frog
- [ ] Human
- [ ] Fly
- [ ] Nematode
- [ ] Other (please specify)
- [ ] Pig
- [ ] Cattle
- [ ] Chicken
- [ ] Equid
- [ ] Sheep
- [ ] Goat

Annexe 3

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Current Use of Models

This section contains questions on your current use of models, the reasons why you use the models that you do, and how they help with your research.

Annexe 3

9. In order to explore the variety of models used in reserarch, could you indicate the combination of experimental system and species in the models that you or your lab have used in the last year, and note how long that you have used each model for? **If the necessary options are not available in the dropdown menus, please note them below.** Please note which model you have selected as your primary model, as subsequent questions will ask you to consider this model.

	Experimental System	Species	Length of use
Primary Model			
Additional Model 1			
Additional Model 2			
Additional Model 3			
Additional Model 4			
Additional Model 5			
Additional Model 6			
Additional Model 7			
Additional Model 8			
Additional Model 9			

Other (please specify)

Annexe 3

10. Why do you use multiple models in your research. Please select all relevant answers.

- [ ] I am comparing underlying biological phenomena across multiple species
- [ ] Regulatory requirements require multiple species to be used
- [ ] Different species or experimental systems are required to recapitulate different aspects of my research question
- [ ] I am experimenting with different models with a view to changing from one to another

Other (please specify)

11. How do you use these models in your work? Could you briefly indicate their relevance by outlining the general types of experiment that you use them for?

12. Which species are you using these models to investigate, i.e. which species will benefit from the outcomes of your research?

- [ ] Rat
- [ ] Mouse
- [ ] Zebrafish
- [ ] Clawed frog
- [ ] Human
- [ ] Fly
- [ ] Nematode
- [ ] Pig
- [ ] Cattle
- [ ] Chicken
- [ ] Equid
- [ ] Sheep
- [ ] Goat

Other (please specify)

Annexe 3

Biotechnology and Biological Sciences Research Council

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Current Use of Models

This section contains questions on your current use of models, the reasons why you use the models that you do, and how they help with your research.

13. Prior to using the model(s) that you have detailed above, did you or your lab use different models?

- [ ] Yes
- [ ] No

Annexe 3

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Current use of models

This section contains questions on your current use of models, the reasons why you use the models that you do, and how they help with your research.

14. Why did you change the model(s) that you used? **Please select all relevant answers.**

- ☐ Changed position or organisation
- ☐ Altered focus of research project
- ☐ New expertise became available
- ☐ Regulatory requirements required the change
- ☐ Learned of the new model(s)
- ☐ New facilities became available
- ☐ For financial reasons
- ☐ Lack of validation
- ☐ Seeking to improve ethical standards
- ☐ Availability of model
- ☐ Availability of genetic tools
- ☐ Availability of genomic resources
- ☐ Regulatory requirements of previous models became excessive

Other (please specify)

Annexe 3

15. What level of confidence do you have in the model that you or your lab have used within the past year, with respect to your area of investigation? **For this question if you have used multiple models, then please refer to your primary model.**

	Very Low	Low	Moderate	High	Very High	N/A
Technical ability of the model to recapitulate the area under investigation	○	○	○	○	○	○
Reproducibility of the model in different labs	○	○	○	○	○	○
Physiological relevance of the model to the species that will benefit from the outcomes of the research	○	○	○	○	○	○
Robustness of the model to permit consistently accurate and precise outcomes	○	○	○	○	○	○
Appropriateness of the model from an ethical perspective	○	○	○	○	○	○

16. Are there other models that are appropriate for your area of research?

- ☐ Yes
- ☐ No
- ☐ Don't know

Annexe 3

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Current use of models

This section contains questions on your current use of models, the reasons why you use the models that you do, and how they help with your research.

17. Please briefly outline what these models are and why you chose the model(s) that you have, instead of these alternatives.

18. How important are the following advantages of the model that you or your lab have used over the last year? **For this question if you have used multiple models please refer to your primary model.** If you would like to add further comments regarding other models that you have used, please use the text box.

	Not important at all	Slightly important	Somewhat important	Important	Very important	N/A
It is the standard model for my research question	○	○	○	○	○	○
It is the best model for my research question	○	○	○	○	○	○
Cost	○	○	○	○	○	○
Speed of the model to produce results	○	○	○	○	○	○
Allows research to be completed within a standard three-year funding cycle	○	○	○	○	○	○

Annexe 3

	Not important at all	Slightly important	Somewhat important	Important	Very important	N/A
Expertise is available to use the model	○	○	○	○	○	○
The system complies with relevant regulations	○	○	○	○	○	○
Ability to address new biological questions	○	○	○	○	○	○
More rapid routes to market or clinic	○	○	○	○	○	○
Availability of genetic tools	○	○	○	○	○	○
Availability of genomic resources	○	○	○	○	○	○
Access to facilities	○	○	○	○	○	○
The model is expected or required for publication	○	○	○	○	○	○
Easy to access (e.g. available within organisation)	○	○	○	○	○	○
Easy to purchase when required	○	○	○	○	○	○

Other (please specify)

Annexe 3

19. How far do you agree that your peers use the same models to answer related research questions?

Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
○	○	○	○	○

Annexe 3

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Current use of models

This section contains questions on your current use of models, the reasons why you use the models that you do, and how they help with your research.

20. How relevant are the following reasons why you and your peers may use different models?

	Not relevant at all	Slightly relevant	Moderately relevant	Relevant	Very relevant
We are investigating similar but different research questions, requiring different models	○	○	○	○	○
We have different expertise	○	○	○	○	○
Our organisations have different expertise and/or facilities	○	○	○	○	○
Financial reasons	○	○	○	○	○

Other (please specify)

Annexe 3

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Use of Models in Research

Future Use of Models

The third and final section of the survey contains questions on the future possibilities for the use of models in your research and more broadly.

Annexe 3

21. Which models do you anticipate that you or your lab will use in the next five years? **If the necessary options are not available in the dropdown menus, please note them below.**

	Experimental System	Species
Primary Model		
Additional Model 1		
Additional Model 2		
Additional Model 3		
Additional Model 4		
Additional Model 5		
Additional Model 6		
Additional Model 7		
Additional Model 8		
Additional Model 9		

Other (please specify)

Annexe 3

22. To what extent are the following potential barriers preventing you from using your preferred models for your research?

	Very low extent	Low extent	Moderate extent	High extent	Very high extent	N/A
Cost of the model	○	○	○	○	○	○
Lack of validation	○	○	○	○	○	○
Lack of personal expertise	○	○	○	○	○	○
Lack of organisational expertise	○	○	○	○	○	○
Ethical concerns	○	○	○	○	○	○
Regulatory restrictions	○	○	○	○	○	○
Availability of model	○	○	○	○	○	○
Availability of genetic tools	○	○	○	○	○	○
Availability of genomic resources	○	○	○	○	○	○
Access to facilities	○	○	○	○	○	○
Risk of not being able to publish my results	○	○	○	○	○	○
The model would take too long to fit within a standard three-year research program	○	○	○	○	○	○

Other (please specify)

Annexe 3

23. How substantial are the advantages that would be gained if these barriers were removed?

	Very low	Low	Moderate	High	Very high	N/A
Greater recapitulation of the area being modelled	○	○	○	○	○	○
Reduction in costs	○	○	○	○	○	○
Being able to run larger numbers of replicates , increasing reproducibility or robustness of results	○	○	○	○	○	○
Being able to run new types of experiments, expanding the investigation to new areas	○	○	○	○	○	○
Greater alignment of model usage with peers, allowing for collaboration or comparison	○	○	○	○	○	○
Reduction in ethical concerns	○	○	○	○	○	○
Reduction in time to get to market or to clinic	○	○	○	○	○	○
Increased acceptance for publication of results	○	○	○	○	○	○

Other (please specify)

Annexe 3

Biotechnology and Biological Sciences Research Council

Use of Models in Research

Future Use of Models

The third and final section of the survey contains questions on the future possibilities for the use of models in your research and more broadly.

24. Based upon your response above, you have indicated that regulatory concerns are a major problem in this area - please briefly outline the issues that you have encountered and any potential solutions.

25. Based upon your response above, you have indicated that training and expertise are major problems in this area - please briefly outlne the issues that you have encountered and any potential solutions.

26. Based upon your response above, you have indicated that the validation of the models is a major problem in this area - please briefly ouline the issues that you have encountered and any potential solutions.

27. Based upon your response above you have indicated that the availability of the models is a major problem in this area - please briefly outline the issues that you have encountered and any potential solutions.

28. Based upon your response above you have indicated that the availability of tools, technologies or facilities is a major problem in this area - please briefly outline the issues that you have encountered and any potential solutions.

Annexe 3

29. How important do you consider the following options to be for your future research plans?

	Very low importance	Low importance	Moderate importance	High importance	Very high importance	N/A
Development of new models	○	○	○	○	○	○
Optimisation of current in vivo systems	○	○	○	○	○	○
Optimisation of current ex vivo, in silico and/or in vitro systems	○	○	○	○	○	○
Validation of systems to determine their level of physiological relevance	○	○	○	○	○	○
Comparison of in vivo and other systems to identify differences and similarities	○	○	○	○	○	○

Other (please specify)

30. Do you have any further comments that you would like UKRI-BBSRC to consider?

Thank you very much for completing this survey. We appreciate that your time is valuable, and are grateful for your assistance with our research. **Please ensure that the survey is submitted before leaving the page.**