Engineering and Physical Sciences Research Council

EPSRC REVIEW OF MATHEMATICAL BIOLOGY

SUMMARY

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Summary of the EPSRC Review of Mathematical Biology

1. Introduction

The EPSRC Mathematical Sciences theme has undertaken a review of its mathematical biology portfolio. The aim of this activity is to consider the current position of mathematical biology in the UK and to consider what actions, if any, EPSRC may need to take to maintain the health of the discipline in the future.

Approximately ten years ago, it was noted at the Strategic Advisory Teams (SATs) Conference, and also by the Mathematical Sciences SAT, that new mathematics and computer science at the interface with life sciences was an area of increasing importance internationally and one which could lead to the development of new mathematical tools and techniques. In addition it was noted that there was a need to populate new theoretical biology with talented researchers with mathematical expertise to ensure that the discipline developed upon solid mathematical foundations.

Nevertheless, in 2010, the International Review of Mathematical Sciences (IRMS2010) noted that “the influx of researchers at the interface between fluid dynamics and the biological sciences is not as massive as in the US”. Furthermore, the review stated that “mathematics is already well integrated into some existing systems biology centres but UK strength in mathematical biology would be increased if this integration were more systematic. Separate Research Councils administer grants and funding in biology, and the Panel’s site visits indicate a widespread perception that in medicine and the mathematical sciences funding structures are often hampered by conflicting remits and criteria of EPSRC and BBSRC, leading to workarounds by researchers that consume time and energy better devoted to research. It may be helpful to have specific ‘high-risk’ funding programmes for mathematical biology.”

In view of the concerns raised in the IRMS2010, a key aim of this review is to establish whether research in the discipline has been adversely affected by its position at the interface of several research councils and, if so, to explore options available to EPSRC to ameliorate the situation.

The primary source of information for the review was key researchers within the mathematical biology community. In addition, input was obtained from Mathematical Sciences SAT members, relevant representatives of EPSRC as well as representatives of other Research Councils.

2. Definition of Mathematical Biology

Members of the community who participated in the review offered a broad range of views regarding the definition of mathematical biology, with many participants emphasising that the term includes a wide range of different topics within mathematics, statistics and computer science that are required to address biological challenges. Indeed, some participants felt that the expansive range of mathematical techniques required and used in a biological context meant that the term is so broad as to be of little use. However the converse view was also

expressed, with some participants suggesting that it may be better to consider the term biomathematics, which is perceived to be less exclusive and to cover a broader range of topics than mathematical biology. In general, however, most definitions of mathematical biology offered could be summarised as “the development and application of mathematical techniques to solve biological problems and to study biological systems”.

3. Current Position of Research in Mathematical Biology

Overview

Mathematical biology is very well represented in the UK, with research covering a broad range of areas of biology including, but not limited to, neuroscience, genetics, ecology, epidemiology and agriculture. Similarly, it was clear from discussions with the community that a very wide range of mathematical tools and techniques are required in mathematical biology including Bayesian techniques, stochastic processes, quantitative analysis, category theory, control theory, information theory, geometry, probability theory, graph theory, dynamical systems and non-linear models to name but a few. In short, there are opportunities for researchers in almost all areas of the mathematical sciences to contribute to the solution of biological problems.

Research in mathematical biology is by its nature highly interdisciplinary, usually involving collaboration with biologists and often with researchers from other disciplines such as computer science. Mathematical scientists active in this field felt that their aim was to develop projects where they are equal partners with co-investigators from other disciplines and where the mathematical techniques could be developed together with those other researchers. Most participants had a mathematical background and then specialised into specific fields of biology. There was a feeling that there were fewer barriers to mathematical scientists acquiring the specific biological knowledge necessary to research in this area than for biologists to gain the broad mathematical training required. However, respondents emphasised that this does not mean that mathematical scientists could learn the experimental skills necessary in biology and that it therefore remains of critical importance to build strong relationships with biologists as well as chemists and physicists.

Global Outlook

When asked to consider the global position of mathematical biology, the United States and the European Union were identified as the key areas of activity.

United States

The largest proportion of mathematical biology research globally is taking place in the United States (US). This research is funded from a range of sources including government funders such as the National Science Foundation (NSF) and the National Institute of Health (NIH) as well as private sector organisations such as Microsoft and IBM. In addition the federal government has committed $3bn over 10 years to the BRAIN project, an interdisciplinary effort to map activity in the human brain.

The US has several key institutes devoted to research in, or relevant to, mathematical biology, including the National Institute for Mathematical and Biological Synthesis (NIMBioS) in Knoxville, the Broad Institute in Boston and the Mathematical Biosciences Institute in Ohio. Furthermore, several of the US National Laboratories have active programmes of

research in mathematical biology. The major academic institutions active in the discipline in the US include California Institute of Technology, Cornell University, Harvard University, Massachusetts Institute of Technology, Princeton University and the University of Maryland amongst others.

Clearly, there is substantial breadth to mathematical biology research in the US distributed across a wide range of government, academic and private sector organisations. However, the United States has particular strength in computational biology, data analytics and systems biology.

European Union

Outside of the UK, Germany is the main focus of mathematical biology research in the European Union. There are several German groups who have focused strongly on systems biology with funding from the Bundesministerium für Bildung und Forschung (Federal Ministry of Education and Research, BMBF) and these groups are in the process of developing strong links with research groups in the United States. Additionally, biophysics is an area which is gaining increasing prominence in Germany with a particular focus on strong experimental research to complement the development of theory. France, Norway and the Netherlands are also important contributors to research in mathematical biology. In addition the European Union itself is an important source of funding for research in the area.

United Kingdom

The UK has a long tradition of strength generally in applied mathematics, and mathematical biology in the UK has been able to build upon these strong foundations to become a major contributor to the global research landscape in this area. Indeed the strength of the community in the UK is reflected in the number of UK institutions where mathematical biology is represented. The UK has particular strength in mathematical epidemiology and dynamical modelling and, although there are also strong groups in the US, the heart of the community in these areas lies in the UK.

Mathematical Biology at EPSRC

As discussed in further detail in Section 4, there is a multitude of funding routes open to UK researchers in mathematical biology. However, it is clear that EPSRC is a major source of funding for research in this area. Indeed, a keyword analysis of EPSRC's portfolio suggests that in the financial year 2013/14 EPSRC had a portfolio of active grants with some relevance to mathematical biology worth £144M. Indeed the size of the EPSRC portfolio relevant to Mathematical Biology has been remarkably constant since 2010/11, with the exception of 2012/13 when the value of the portfolio was somewhat larger than the average over the period. Under EPSRC's current taxonomy, mathematical biology research is classified under one or more of several Mathematical Sciences Research Areas depending upon the exact nature of the research involved. These Research Areas are most commonly Complexity Science, Continuum Mechanics, Non-Linear Systems, and Statistics and Applied Probability. Every EPSRC Research Area has a headline strategy associated with it of "Grow", "Reduce" or "Maintain", referring to the intended trajectory of funding in that Research Area as a proportion of EPSRC's overall portfolio. With the exception of Statistics and Applied Probability, which is a "Grow" area, all of the Research Areas most relevant to

mathematical biology have a headline strategy of “Maintain”. It is therefore reassuring that that the value of the mathematical biology research portfolio has remained stable of the period of the current EPSRC delivery plan.

A concern often raised regarding mathematical biology in particular, and interdisciplinary research in general, is that interdisciplinary proposals are less likely to be successful when considered alongside intradisciplinary research at EPSRC’s theme-based Standard Research Prioritisation Panels. We have therefore sought to determine the success rates for research in mathematical biology by financial year since 2010/11. Again it is important to bear in mind that since mathematical biology is not a classification area used under EPSRC’s current taxonomy, this data is based upon a keyword search and as such represents a best estimate of success rates in this area. However, notwithstanding this caveat, we find that the success rate of mathematical biology research by number of applications was above the EPSRC wide average in 2010/11, 2011/12 and 2013/14 and was identical to the EPSRC average in 2012/13. This provides some reassurance that research in mathematical biology is not adversely affected by its position at the interface of several Research Councils.

4. Funding Routes for Research in Mathematical Biology

It is clear that funding for research in mathematical biology in the UK comes from a very wide range of sources, including Research Councils, charitable organisations and industry. The most common sources of funding identified by the mathematical biology community are summarised below.

EPSRC

Twelve participants mentioned EPSRC, with many of them having had experience of EPSRC funding either for past or current projects. Participants viewed EPSRC as having a key role to play in developing core theory in mathematics that could be applied to biology but also to other disciplines. Specifically, the community felt that EPSRC is well placed to build core theory and tools whilst remaining sufficiently general in terms of the underlying techniques to facilitate links to other disciplines. There was, however, a desire for EPSRC to articulate more clearly which aspects of mathematical biology it supports and how it sees the future of mathematics in biology.

A notable development highlighted was that some researchers who would have previously seen EPSRC as their primary source of funding are increasingly seeking funding from BBSRC and ESRC, especially for research in those areas of mathematical biology which interface with the social sciences.

BBSRC

The Biotechnology and Biological Sciences Research Council (BBSRC) was identified by twelve sources and was seen as the obvious source of funding for mathematical biology research which is more focussed upon applications than on developing the underlying mathematical techniques. Although EPSRC can and does support mathematical sciences research which includes experimental components, the perception in the community was

that BBSRC was better suited to experimentalists. Conversely, there was a perception that BBSRC applications required a Principal Investigator with a biological background and was less suited to projects which contained a significant mathematical component even where the majority of the research fell within BBSRC's remit.

Many participants praised BBSRC for having a clear strategy towards quantitative biology, drawing together expertise in biology, mathematical modelling and data analytics.

MRC

The Medical Research Council (MRC) was mentioned by twelve participants. Although the MRC's Methodology Research Programme includes aspects such as biostatistics, bioinformatics and mathematical modelling, there is a perception in the community that MRC is not as welcoming to mathematicians as other Research Councils. Participants felt that MRC is more suited to projects which included substantial medical work.

European Union

EU funding was mentioned by six participants, particularly in relation to the study and prevention of diseases, with these projects tending to have a greater degree of international interest. A particular strength of EU programmes, such as the Future Emerging Technology Programme, is the ability to bring together disciplines and themes and to establish new links. Participants particularly valued the fact that the EU tended to have a large quantity of funding available and also that it accepts proposals for purely theoretical projects.

Charitable Foundations

The most commonly mentioned charitable foundation was the Wellcome Trust (mentioned by seven sources) although many participants felt that it was not an obvious choice for funding and was very much disease driven. Further charitable organisations highlighted as potential sources of funding included the British Heart Foundation, Cancer Research UK, the Leverhulme Trust, Marie Curie, the Nuffield Foundation, Parkinson's UK and the Royal Society. Participants were keen that the Research Councils continue to build and maintain relationships with these organisations.

Other Funding

Other governmental sources of funding included the National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs), the Scottish Government and the US National Science Foundation (in collaboration with groups in the US).

Industry was also mentioned by many participants as a potential source of funding, often leveraged with funding from governmental or charitable sources.

5. Challenges in Mathematical Biology

Participants were asked to identify the key scientific and operational challenges in mathematical biology based upon their personal experiences, perception and interaction with the wider community.

Scientific Challenges

On a scientific level, there were four key areas of relevance to Mathematical Biology which offered particular challenges; data analytics, multi-scale modelling, complexity science and uncertainty quantification.

Data Analytics

The storage, distribution and analysis of the large amounts of data generated in the course of biological research presents a particular challenge. The situation is often complicated further by the fact that these large datasets can contain a great deal of noise. There are therefore clear opportunities to advance the field of mathematical biology through the development of efficient tools and techniques for the handling and analysis of these large datasets.

A significant challenge which has arisen as a consequence of the increasing abundance and complexity of data is its incorporation into mathematical models of biological systems. It is becoming ever more important that such data is incorporated in models from the outset and can therefore help inform the design of the model. For example, there are many hundreds and thousands of genes, and the shear dimensionality of this data needs to be considered in the model from the outset with an analytical process to assess which kind of data is important before a particular system can be modelled. Currently, the mathematical techniques have not been developed to deal with such large data sets.

Multi-scale Modelling

It is often necessary in mathematical biology to develop models of systems which span multiple spatial or temporal scales, for example from cellular level to whole organism level, yet techniques which are used at small scales cannot be directly applied to larger scales and *vice versa*. Furthermore, there are few techniques available to enable robust models to be developed which are able to cope with multiple scale systems. The multi-scale nature of many problems in mathematical biology can consequently mean that macroscopic level prediction is very difficult.

Complexity Science

Several challenges in mathematical biology identified broadly fell into the category of complexity science and link closely with the challenges around data analytics and multi-scale modelling. These include, for example, the management and processing of complex, high dimensional data and its integration into models. In addition, the prevalence of networks in biology means that there is a significant need to develop improved mathematical and/or statistical techniques for modelling complex networks. Network models may also need to be able to span multiple scales effectively. For example, models of the brain must incorporate complex networks which range in scale from the microscopic to the whole organ.

Uncertainty Quantification

A key difficulty in developing a systematic approach to mathematical models in biology is determining the sensitivity of the model to changes in different aspects of the system. For example, robust methods of determining which parts of a biological system can be neglected

in developing models would greatly improve the efficiency of this process. The development of new techniques in uncertainty quantification would therefore be extremely valuable.

Operational Challenges

Links between Research Councils

The community continue to be concerned that research at the interface of mathematical sciences and the life sciences does not have a single "home" within the Research Councils. Instead, research in this area may be funded by EPSRC, BBSRC or MRC depending upon where the novelty of the research lies. Although the Cross Council Funding Agreement allows Research Councils to jointly fund grants which span the remits of two or more councils, these arrangements are not usually visible to the community at large or even applicants themselves in many cases. Poor communication of the policies and procedures in place to facilitate the funding of interdisciplinary research appears to be exacerbating existing concerns that such proposals are likely to be less successful even though EPSRC's data does not appear to support this view.

More generally, the community appreciated that EPSRC has an on-going dialogue with other research councils and there was a strong desire that these relationships should not only continue but also be developed further. Again, participants expressed concern that such dialogue often takes place "behind the scenes" and is not visible to the community. Increased communication regarding activities where Research Councils are working together would therefore be desirable. Several participants identified MRC as a research council with which EPSRC should encourage greater links; there is a belief amongst the community that activities led by MRC are often missing the mathematical underpinning even though there are myriad opportunities for mathematical sciences to contribute to solving grand challenges around human health and disease. Initial discussions with MRC suggest that they would be receptive to working more closely with EPSRC and are particularly interested in developing capability in the areas of data analytics and improved design of clinical trials.

Participants in the review were also keen that EPSRC develop closer relationships with non-RCUK funders active in this area, such as the British Heart Foundation, Cancer Research UK and the Wellcome Trust for example. EPSRC does currently have good working relationships with these funders but these relationships are typically managed by EPSRC's Healthcare Technologies theme and so are perhaps less visible to mathematical biologists who primarily interact with EPSRC *via* the Mathematical Sciences theme. We note that Cancer Research UK and the Wellcome Trust participated in a scoping workshop for the EPSRC Centres for Mathematical Sciences in Healthcare call which is jointly managed by Mathematical Sciences and Healthcare Technologies, and activities such as this provide a good opportunity to develop more direct links between the Mathematical Sciences theme and non-RCUK funders.

A number of concerns were raised by correspondents around the remit of the EPSRC Mathematical Sciences theme. In articulating this remit, EPSRC has often used the phrase "new mathematics", yet the community felt that in fact few new mathematical techniques are developed in applied mathematics in the short term. Rather, mathematical expertise is

required to adapt existing techniques to specific application areas and this process may in the longer term lead to the development of new tools and techniques. The phrase “new mathematics” has therefore led to confusion as to whether research in mathematical biology research falls within the remit of EPSRC. Clearly, the use of “new mathematics” as a short hand for the remit of EPSRC Mathematical Sciences has been unhelpful; a more accurate definition would be “research which has significant mathematical or statistical content, either *via* the development of new tools in mathematics or statistics, *via* novel combinations of existing mathematical or statistical techniques, or *via* novel applications of mathematics or statistics, and which inspires new ideas in both the mathematical sciences and application areas.” We would certainly anticipate that a large proportion of research in mathematical biology would fall within this expanded definition of EPSRC Mathematical Sciences remit, although it is important to recognise that research in mathematical biology will necessarily continue to span the remits of EPSRC, BBSRC and other Research Councils. Nevertheless all Research Councils are committed to ensuring that research does not “fall down the gaps”, and that applications are never adversely affected by crossing disciplinary boundaries.

There continues to be a strong appetite for schemes to encourage interdisciplinary working. Specifically, the community emphasised the potential role of fellowships in encouraging researchers to develop interdisciplinary links and were very supportive of EPSRC’s New Connections from Mathematical Sciences Fellowship priority area. It was felt that this was an opportunity that should be promoted and encouraged amongst the Mathematical biology community. Funding opportunities from other EPSRC themes were not specifically mentioned by participants and this could reflect a lack of awareness of such opportunities. For example, it is likely that some researchers in Mathematical biology could take advantage of the Healthcare Technologies theme’s Diagnostics and Therapeutics Fellowship priority areas which specifically identify the development of models to improve the diagnosis and treatment of disease as areas of interest. Consequently there is an opportunity to promote such schemes from other EPSRC theme’s more widely to Mathematical Scientists, especially those already working at interdisciplinary boundaries. To this end we have initiated a regular feature in the Maths@EPSRC newsletter which highlights upcoming and open calls from across EPSRC which may be of interest to mathematical scientists.

Although EPSRC’s Mathematical Sciences theme continues to explore opportunities for jointly managed activities with EPSRC’s Challenge themes, it is unlikely in the short term that EPSRC will be in a position to develop new standing schemes specifically to facilitate interdisciplinary working. Nevertheless, EPSRC’s Standard Research scheme is designed to be flexible and can accommodate a range of activities including interdisciplinary research, networks, workshops and overseas travel to develop new collaborations. There is clearly an opportunity for EPSRC to do more to increase awareness of the range of activities which can be supported through the Standard scheme.

Networking and Collaboration

It is clear from discussions with participants that the social challenge of forming new interdisciplinary collaborations cannot be underestimated. As an example, participants felt that biologists often don’t fully appreciate what mathematicians can offer them and explaining the relevance of mathematical sciences to biology remains a difficulty. Similarly, mathematical scientists working in more fundamental areas of research are often reluctant to

engage in multi-disciplinary projects. It is therefore clear that greater communication between mathematical scientists and biologists will be essential to maintaining the health of the discipline. More fundamentally it was felt that a cultural change was needed such that cross-disciplinary collaboration becomes the accepted mode of operation rather than a last resort. Clearly such a cultural shift is not something which can be achieved in the short term or by any individual party. However, many participants felt that interdisciplinary working needed to be established earlier in the people pipeline, and schemes such as EPSRC's New Connections from Mathematical Sciences Fellowship priority area, which is open at the Postdoctoral and Early Career stages, should make an important contribution to this goal.

Skills and Training

Access to high quality PhD students continues to be highly valuable to the community in mathematical biology but competition for funding in this area is very strong. Unfortunately, although "New Mathematics in Biology and Medicine" was a priority area in the recent Centres for Doctoral Training (CDT) exercise, there was no successful application under this priority. However, many CDTs funded under other priority areas have projects available in mathematical biology, including:

- **Mathematics for Real-World Systems – University of Warwick**
- **Systems Approaches to Biomedical Science – University of Oxford**
- **Fluid Dynamics across Scales – Imperial College London**
- **Fluid Dynamics at Leeds – University of Leeds**
- **Data Science – University of Edinburgh**
- **Doctoral Training in Synthetic Biology – University of Oxford**
- **Mathematical Analysis and its Applications: Maxwell Institute Graduate School in Analysis & Applications – University of Edinburgh**
- **Next Generation Statistical Science: The Oxford-Warwick Statistics Programme – University of Oxford**
- Neuroinformatics and Computational Neuroscience – University of Edinburgh
- Life Sciences Interface – University of Oxford
- Systems Biology – University of Warwick
- MASDOC – Mathematics and Statistics – University of Warwick
- Warwick Complexity Science – University of Warwick
- Bristol Centre for Complexity Sciences (BCCS) – University of Bristol

(N.B. Several of the above CDTs are collaborative efforts between more than one institution. Where this is the case only the lead institution is shown. Those centres shown in **bold** were funded as part of the recent 2013 CDT exercise.)

However, it is clear that continued access to flexible funding for PhD students *via* Doctoral Training Partnerships and CASE awards will continue to be important to the health of mathematical biology in the UK.

More generally, there was broad agreement regarding the need for more multidisciplinary talent and consequently that improved communication between disciplines is becoming increasingly important. One suggestion by which such increased communication might be achieved was to identify individuals, particularly at a senior level, who can fill a translational role between different disciplines such as biology and pure mathematics. Indeed, such

translational figures could be vital in maintaining the health of the chain from pure mathematics to applied mathematics to end users of the research and would play an important role in developing the strength of these links.

6. Recent and Continuing Developments

At the end of 2012, EPSRC commissioned an independent review of the importance of engineering and physical sciences to the health and life sciences. This review was conducted by a group led by Professor Patrick Maxwell, Regius Professor of Physic and Head of the School of Clinical Medicine at the University of Cambridge. The report was published in May 2014 and concluded that engineering and physical sciences research, including mathematics, statistics and computer science, has played a major role in advancing health and life sciences. Furthermore the review made a number of key recommendations:

1. Funders and research organisations should actively foster work at the interdisciplinary interface. This should build on experience of successful approaches in the UK and overseas, which suggest that while there is no simple recipe, creating the right scientific environment is critical and that important ingredients are inspirational leadership, a clear mission, flexible funding and an organisational culture which encourages 'non-silo', 'trans-discipline' thinking.
2. Effectiveness at the [interface of engineering and the physical sciences and the health and life sciences] depends in part on focussing effort on the right challenges. Funders and research organisations should play a major role in identifying and defining important challenges, assembling effective teams to tackle these challenges and providing sufficient support for them to do so. However, these challenge-driven approaches should not exclude support for curiosity-driven research.
3. The UK should build human capacity that can operate effectively across discipline boundaries in order to maintain our leading role in health and life sciences. As well as focusing on high quality doctoral level training for interdisciplinary research, research organisations and funders need to work together to maximise career opportunities for EPS and HLS trained researchers within interdisciplinary environments.
4. The role of engineering and physical sciences should be integrated into the UK strategy for life sciences. Government departments such as BIS and the Department of Health need to ensure that they fully engage with relevant stakeholders in developing and delivering a shared vision for this interface.
5. As part of the process to promote and encourage interdisciplinary research at the EPS/HSL interface, we recommend that key stakeholders give detailed thought to how interdisciplinary research and the environment in which it occurs can best be measured.
6. Key stakeholders should review activity and opportunity at the EPS/HLS interface on a regular basis. These reviews should challenge the status quo and aim to catalyse more effective coordination between EPS and HLS.

Although the Maxwell review was carried out independently from the review of mathematical biology, the recommendations above reflect many of the concerns raised by the mathematical biology community, especially with respect to ensuring the health of the people pipeline at cross-disciplinary interfaces, encouraging interdisciplinary research and the need

to ensure that research in the engineering and physical sciences, including the mathematical sciences, is fully integrated into health and life sciences research. EPSRC has long recognised the need to encourage greater links between disciplines and to ensure that we build leadership which spans traditional disciplinary boundaries and indeed these are key strategic priorities of EPSRC's Mathematical Sciences theme.

During the review of mathematical biology, a number of specific concerns were raised by the community with respect to the strength of EPSRC links with other Research Councils. We believe that there are well established mechanisms, such as the Cross Council Funding Agreement, to facilitate investigator-led research which spans disciplinary boundaries. The efficacy of such mechanisms appears to be borne out by the strong success rates observed for proposals in mathematical biology over the current EPSRC delivery plan period. Furthermore, EPSRC has taken a proactive role in developing activities to fund research at key cross-disciplinary interfaces including that between mathematical sciences and the health and life sciences. Nevertheless, we recognise that there is a need to give greater consideration to engaging with other funders at an early stage when developing strategic activities at interdisciplinary interfaces and have been implementing this strategy wherever appropriate. By way of example, a number of other funders were involved in the scoping and design stage of the EPSRC Centres for Mathematical Sciences in Healthcare call which was open for outline proposals at the time of writing. These included the two other research councils with interests at the interface of mathematical sciences and the health and life sciences; BBSRC and MRC. Similarly, when invited to do so, we have actively participated in activities led by other funders, recently including a BBSRC workshop on multi-scale biology. We will continue to take a proactive approach to engaging with other Research Councils and other funders more generally. We also recognise that there is also an issue of perception with respect to the links between Research Councils. A great deal of communication between Research Councils takes place without being advertised publicly. It is often necessary that such discussions are conducted privately, at least initially, but we undertake to make our interactions with other funders clearer wherever appropriate.

The importance of building leadership in interdisciplinary fields of research was emphasised by the community during the course of the review. Building leadership is one of EPSRC's strategies as outlined in the recently refreshed Strategic Plan. In the Mathematical Sciences theme, ensuring the health of the people pipeline is a key strategic priority. This means not only building leadership in the core of the discipline but also supporting research leaders who can help to establish new links between mathematical sciences and other disciplines. One of the ways in which we have sought to achieve this is by introducing the "New Connections from Mathematical Sciences" fellowship priority area which is intended to provide flexible support to outstanding researchers working at the interfaces of mathematics and other disciplines. Furthermore, researchers at the start of their academic career can apply for funding for interdisciplinary projects *via* EPSRC's First Grant scheme. This scheme allows researchers to apply for funding up to £125,000 (calculated at 100% full economic cost) over two years without being subject to direct competition from senior colleagues. We will continue to explore opportunities to build leadership at strategically important interfaces with the mathematical sciences, including the interface between mathematical sciences and the health and life sciences.

A number of key scientific challenges were identified by the community as requiring particular attention over the next five to ten years. These included data analytics for large data sets, multi-scale modelling, complexity science and uncertainty quantification. Several of these themes have been taken forward in a variety of activities being developed by EPSRC. For example, the broad area of "big data" has recently been the subject of a great deal of activity, both within EPSRC and outside. Recent EPSRC activities in this area have included the Making Sense from Data call for outline proposals which lie at the interface of Mathematical Sciences and Information and Communication Technology as well as a planned ICT Perspectives on Big Data workshop in early March 2015. In addition the need for further research into methods of integrating data into mathematical models was recognised in the recent call for Centres for Mathematical Sciences in Healthcare. More broadly, mathematical sciences will form an integral component of the planned Alan Turing Institute for Data Science. Complexity science (particularly in the area of networks) and multi-scale modelling were also both identified as areas of potential focus in the Centres for Mathematical Sciences in Healthcare Call.

Opportunities for networking and collaboration are critical to facilitating excellent quality research and this is especially true in the mathematical sciences. The importance of such activities is recognised in EPSRC's Standard Research scheme which is always open for applications for funding for networks and workshops. In addition, EPSRC encourages collaboration in and between a wide range of disciplines, including at the interface of mathematical sciences and the health and life sciences, through running managed activities. For example, following a sandpit in September 2012 jointly organised between EPSRC's Mathematical Sciences and Healthcare Technologies themes, we funded the Predictive mOdelling for hEalthcare technologies through MathS (POEMS) network which includes a strong component of mathematical biology.

7. Conclusions

Although a number of challenges, both scientific and operational, remain for the mathematical biology community it is important to be clear that the discipline in the UK is in a position of considerable strength. This strength is reflected in the global position of UK mathematical biology research; the UK is a major world player in the area and leads the world in several sub-disciplines of mathematical biology. The quality of UK mathematical biology research is reflected in the success rates of proposals to EPSRC. For the majority of the period of EPSRC's current delivery plan, the success rate of EPSRC mathematical biology proposals by number has been at or above the whole-EPSRC average. There remain substantial scientific challenges to be addressed and there are consequently considerable opportunities for mathematical sciences to have a major impact in the development of the health and life sciences. EPSRC will continue to do all that it can to ensure that the UK has the mathematical capability and the cross-disciplinary leadership to realise that impact.

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EPSRC Response to the Review of Mathematical Biology

In EPSRC's Review of Mathematical Biology, some participants raised concerns that support for the discipline may be affected by its position at the interface of three Research Councils (BBSRC, EPSRC and MRC). As explained in the Summary of the Review, the Research Councils have clear policies in place to manage interdisciplinary research at the interface of two or more Councils (full details of the Cross Council Funding Agreement are available at http://www.rcuk.ac.uk/funding/fundingagreement/). Following on from the review, EPSRC undertook a data exercise to look at the success rates achieved by proposals in Mathematical Biology at EPSRC. Averaged annual success rates were initially determined for the four year period running from financial years 2010/11 to 2013/14. These data have now been updated with the provisional values for 2014/15.

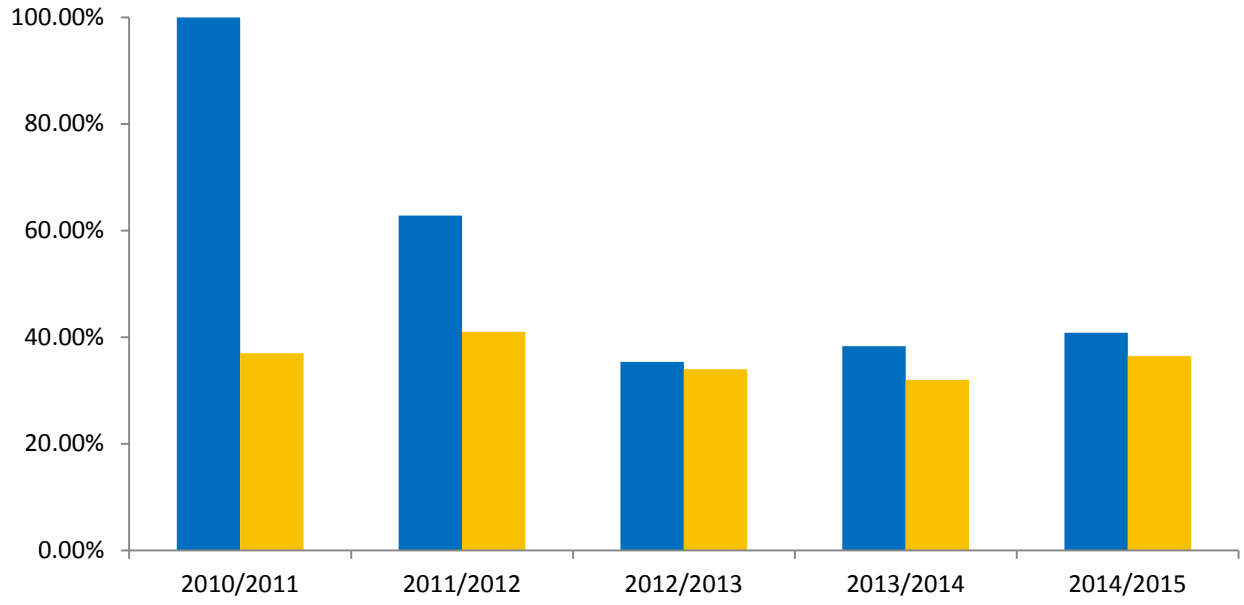

Figure 1 - Success rates by number for proposals received by EPSRC in mathematical biology (blue) and for all proposals received by EPSRC (yellow). Note that these data have been updated as of March 2015 and the values for 2014/15 are therefore provisional.

The data clearly indicate that Mathematical Biology has achieved success rates at or above the EPSRC wide average over the period investigated.

Any applicant wishing to make an application at the interface of Mathematical Sciences, Biology and Medicine, but unsure of the most appropriate council to apply to, should consider submitting a remit query (http://www.epsrc.ac.uk/funding/howtoapply/basics/remit/remitqueries/). All Research Councils are committed to ensuring that there are no gaps between Councils' remits and that interdisciplinary and multidisciplinary research is effectively supported by the Councils, either independently or in partnership.

As a general guide the three councils working at this interface describe their remits as follows:

BBSRC: BBSRC's Strategic Plan emphasizes the importance of exploiting new ways of working and the need for multidisciplinary research in the biosciences. BBSRC encourages and supports projects involving mathematical and statistical approaches across the breadth of our scientific remit and research portfolio. This includes (but is not limited to) projects that address key strategic priority areas for BBSRC, including systems biology and data driven bioscience. Projects submitted to BBSRC may be led by mathematicians/statisticians where appropriate but the key driver of projects

is expected to be biological (as opposed to mathematical or biomedical). This broadly encompasses (1) research that uses mathematical or statistical methods to understand biological systems and processes relevant to BBSRC's scientific remit and/or (2) the development of mathematical or statistical tools or methods that have clear 'end user' relevance to BBSRC's research community. BBSRC Remit Queries: remit@bbsrc.ac.uk

EPSRC: EPSRC Mathematical Sciences funds research which has significant mathematical or statistical content, either via the development of new tools in mathematics or statistics, via novel combinations of existing mathematical or statistical techniques, or via novel applications of mathematics or statistics, and which inspires new ideas in both the mathematical sciences and application areas. Remit Queries: http://www.epsrc.ac.uk/funding/howtoapply/basics/remit/remitqueries/.

MRC: MRC has a strong history of supporting the development and application of new mathematical, statistical and computational techniques as a cornerstone of modern biomedical/health research, from understanding of biomolecule and cellular structure and function, through to clinical trials methodology and informatics approaches in population science.

MRC supports multidisciplinary research which develops and applies such methods, where their use will underpin or lead toward advances in understanding of disease, medicine or impact on human health. MRC works closely with the other Research Councils (including co-funding) on research straddling the Councils' remits and encourages the mathematical community to engage with biomedical science. MRC Remit Queries: rfpd@headoffice.mrc.ac.uk