Institution: University of Bristol

Unit of assessment: UoA 5 Biological Sciences

a. Overview

Biological Sciences at Bristol encompasses research across a broad spectrum from molecules to cells to organisms to ecosystems. This activity is hosted across multiple schools at Bristol, but these units share common goals (understanding biological systems at multiple levels), research strategy (embedding mathematical theory and interdisciplinarity) and, to an increasing degree, core technology facilities. This submission, which covers our core biological research, comprises virtually all of the research hosted within the academic Schools of Biological Sciences (Faculty of Science) and Biochemistry (Faculty of Medical and Veterinary Sciences). Where it better reflects their research focus, a small number of researchers from these academic schools are being submitted through other UoAs, notably 4, 6, 7, and 8. The UoA 5 submission is driven by the 65 investigators (64.6 FTE) whose research goals embrace the Biological Sciences; it comprises both early career and established researchers and includes targeted recruitments, prestigious independent fellowship holders, and internally promoted exceptional staff. The UoA includes 57 HEFCE-funded staff and 8 Research Fellows, 7 of whom are Early Career Researchers.

Biological Sciences (referred to hereafter as Biology) delivers research across the full range of biology but, even where the proximate research is molecular or genetic, the ultimate goal is always to understand organisms in their natural, or managed, ecosystems. In addition to the academic staff, the School includes an average (in any year) of 35 research staff, 120 graduate students, and receives an average £4.9M annual research funding. Research in Biology spans the full range of biological disciplines, from genomics and cell biology, through whole organism biology and evolution, to population biology and ecosystems. Our research addresses major challenges in biological science, including translation of genomes into phenotypes, global change, evolution, loss of biodiversity, and food security

Biochemistry covers fundamental biomolecular research from structural and mechanistic biology to cells and organisms. In addition to the academic staff, the School includes on average 70 research staff, 60 graduate students, and receives an average £8.3M annual research funding. Biochemistry has key strengths in dynamic molecular processes within cells and their membranes, underpinned by broad expertise in a wide range of contemporary biochemical and biophysical approaches.

Research within the UoA is organized through 6 broad clusters that span diverse activities and exist to promote collaboration (locally, nationally, and internationally), cross-fertilization of ideas and translational activity. These clusters, Evolutionary Biology, Dynamic Cell Biology, Molecular Biosciences, Animal Behaviour & Sensory Biology, Plant and Agricultural Sciences, and Ecology & Environmental Change, have emerged or developed from the previous research strategies outlined in RAE 2008.

Both Schools address fundamental and applied biological questions and are united by a shared philosophy of systems and interdisciplinary approaches, often driven by mathematical theory. Across the UoA, investment in both emerging talent and state-of-the-art facilities has been crucial to our work. The UoA as a whole strives to foster a collegiate, high calibre research community, with strong research links to other Schools. Research is also at the heart of all our teaching programmes: undergraduates frequently co-author papers, some in the most prestigious science journals, e.g. from 2013 *Nature* (doi:10.1038/nature12031) and *Science* (doi: 10.1126/science.1230397).

b. Research strategy

Our fundamental ethos is scientific excellence. Multidisciplinary approaches and collaboration are embedded throughout our work. Our central tenet is that research questions are best addressed using multiple techniques applied across multiple dimensions, including both space (from molecular to ecosystem scales) and time (from molecular and cellular events occurring at the sub-second scale to environmental and evolutionary events at geological timescales).

Research in Biology seeks to understand the development, regulation, and evolution of biological complexity across these scales and, where appropriate, to apply and exploit this understanding to address global problems. These include food security, environmental change, and loss of biodiversity. We study diverse organisms (viruses, microbes, fungi, plants and animals) at all levels (genes, cells, organisms and ecosystems) because a diversity of study systems and scales of analysis brings coherence and synthesis to our research. It also stimulates wide collaboration across the University (e.g. with Mathematics, Physics, Psychology, Veterinary Science, Chemistry, and Earth Sciences) nationally and internationally. We have organized our priorities into four research clusters: Evolutionary Biology, Animal Behaviour & Sensory Biology, Plant & Agricultural Sciences, and Ecology & Environmental Change, exploiting the latest technologies in functional genomics and computational and mathematical analysis.

Biochemistry research is driven by a commitment to fundamental studies of the molecular processes that form the basis of life. Our strategy is centred on studies of the intricate networks of biomolecules that become organised within cells to form a living organism. We place a particular emphasis on the quantitative analysis of biomolecular mechanisms such that these systems can be harnessed and modified in a predictive manner. Our work exploits both *in vitro* and *in vivo* systems to fully understand health and disease, and to develop effective therapeutics. For strategic development, we operate as two overlapping research clusters: Dynamic Cell Biology and Molecular Biosciences. Core strengths include temporal and mechanistic studies of enzyme systems, protein:DNA interactions, membrane function including membrane protein folding, transporters and receptors, and the cellular dynamics by which membrane contents are delivered, assembled and recycled. Although fully coherent in itself, much of our research also informs and is further developed by surrounding research and clinical activity within Bristol including University wide thematic areas of neuroscience, cardiovascular research, and synthetic biology.

All activity in this UoA uses related technologies including genomics, bioimaging, proteomics, bioinformatics, mathematical modelling tools, and synthetic and chemical biology. These form a core feature of our research and are central to linking research clusters in Biology and Biochemistry with other University units conducting research across the 'Life Sciences'.

Major strategic initiatives include extensive redevelopment of existing laboratory space to provide new facilities for cell biology and nanoscience and, most significantly, construction of a substantial new £56m building for Life Sciences. This enables integration of platform "-omics" technologies and leading experts that will serve to integrate activity across this UoA to address larger challenges in Biological Sciences. To support this strategy, significant new appointments have been made: Adams (Biochemistry), Beaumont (Mathematical Biology), Dodd, Franklin, and Whitney (Plant Sciences), Pisani and Vinther (Evolutionary Biology), Roberts (Sensory Biology), and Sumner (Animal Behaviour), all of whom use "-omics" technologies and associated computational analytical methods in their research. The new building will co-locate staff from this UoA with researchers from Earth Sciences (palaeobiology and phylogenomics), Mathematics (theoretical modelling and biostatistics), Computer Science (bioinformatics), Social Medicine (population genetics), and Chemistry (synthetic biology). A practical example of our strategy here is the relocation of genome sequencing equipment and bioinformatics capacity associated with the research labs of Day (School of Social and Community Medicine) and Edwards (Biological Sciences). Both are leaders in genomics and gene sequencing and although they work on very different organisms (humans and wheat) they share common technology and analytical ground. Underpinning and informing research across this UoA is the application of mathematical principles. Supporting the large data sets that these technologies generate will be Gough (Computational Genomics), Barker (Bioinformatics), and Beaumont (Biostatistics) who lead programmes that underpin the analysis of large genomic data sets. Synthetic biology forms a core of our future strategy. "BrisSynBio" brings together academics across 3 Faculties. Our emphasis is on harnessing understanding of biomolecular design, engineering, and assembly to provide new routes to synthetic biological systems, including: using self-assembled protein cages for the delivery of bioactive molecules to cells; reprogramming biosynthetic pathways in bacteria; and producing synthetic pathways for recombination in wheat.

The 6 research clusters that form this UoA provide a focus for individual research programmes, a basis for coherence in strategy, appointments and larger collaborative programmes, and help to define the capital equipment and facility needs. The clusters of Evolutionary Biology, Dynamic Cell

Biology, Molecular Biosciences, Animal Behaviour & Sensory Biology, Plant and Agricultural Sciences, and Ecology & Environmental Change also include members who are submitted to other UoAs to enhance the interdisciplinarity and opportunities for project and impact development from our research. Individuals frequently participate in more than one thematic area and there are no formal divisions.

Evolutionary Biology Evolution is the central unifying process underpinning our understanding of life. Bristol hosts the full spectrum of research needed for a deep understanding of evolutionary processes and principles, ranging from the origin of life, macroevolution and phylogenomics, comparative genomics, microevolution and population genetics, and theory. Within this new cluster, evolutionary biologists (e.g. Beaumont, Bridle, Genner, Hiscock, Houston, and Jones) will work closely with world-class palaeontologists (Benton, Donoghue, Rayfield in Earth Sciences, UoA 7), population geneticists (Day, Social and Community Medicine, UoA 2), computer scientists (Gough, UoA 11), and chemists (Mann, UoA 8). This presents an unrivalled opportunity for Bristol to establish a world-leading centre for evolutionary biology, capable of addressing some of the most important challenges in evolutionary biology: the origins of cellular and multicellular life, and the genomic basis of adaptation and speciation. Recent strategic joint appointments with Earth Sciences (Pisani and Vinther, submitted in UoA 7) strengthen the interface between palaeontologists and biologists.

Going forward our primary aim is to unravel patterns and processes underpinning the major formative episodes in evolutionary history, from the ancestral proteome and origin of cellular life, to the emergence of multicellularity and the three principal metazoan kingdoms: plants, fungi, and animals. The use of core genomic and proteomic technologies and closer integration with other clusters is a key part of this strategy.

Cluster highlights:

- Houston used evolutionary simulations to show that the equilibrium degree of cooperativeness depends critically on the amount of variation that is maintained in the population by processes such as mutation (*Nature*).
- Fawcett and Houston developed a new theory explaining the evolution of contrast effects, in which current behaviour depends on past conditions (*Science*).
- Robert has shown a high level case of evolutionary convergence between the auditory mechanisms of higher vertebrates and insects (*Science*).

Dynamic Cell Biology The cell is the fundamental unit of life in which biomolecules are organised. Our work across this large area particularly aims to understand mechanisms of membrane trafficking and regulation of dynamic complexes, within and between cells and at membranes, including the role of the extracellular matrix and cytoskeleton. Cell biology research incorporates many other activities within the University including epidemiology and clinical research, as demonstrated by closely integrated PhD Programmes and cross-theme activities with the Bristol Heart Institute and new Regenerative Medicine initiatives. There is close synergy with colleagues in Physiology & Pharmacology including joint appointments (e.g. Nobes and Martin) and the work of Kelly and Sheppard. Our cell biology research integrates heavily with core facilities in Proteomics and Bioimaging and managers of both facilities are submitted within this UoA. We play a prominent role in developing and applying advanced cell imaging techniques to study cellular function in relation to disease. The Bioimaging Facility is crucial to and acts as a catalyst for many of these research programmes; our goal is to continue to enhance capability in this area, notably in correlative light and electron microscopy, and the combination of technologies for molecular, cellular, and whole organism imaging. Ongoing industrial partnerships with Leica Microsystems and FEI drive development in this area, exemplified by a recent award of £630k through the BBSRC ALERT13 scheme. Increasingly work in this area extends to whole organism models, linking closely to the animal behaviour and sensory biology groups and more widely to medical and veterinary colleagues. Recent new appointments submitted through other UoAs (notably 1 & 4) integrate closely with this theme including Wuelfing (immunology) and Mellor (neuroscience).

Future research priorities in this cluster are directed at translation of fundamental knowledge of membrane trafficking, cytoskeletal dynamics, and cell migration to health and disease through the greater use of clinical samples, genomic and epidemiological information, and pluripotent stem cell technology. Genome Wide Association Studies using large cohorts will underpin this strategy, as

an example Adams has joint PhD student and published outputs with colleagues in Social and Community Medicine.

Cluster highlights:

- Cullen defined the sorting nexins as critical determinants of endosomal function in development, metabolism, and neuroscience (*Nature Cell Biology x2, Developmental Cell, and Journal of Cell Biology*).
- Work from both Hanley and Henley defined molecular mechanisms of synaptic plasticity and neurotransmitter receptor dynamics (*EMBO Journal x3, PNAS, and Nature Neuroscience*).
- Martin has continued to develop animal models of wound healing including mouse, zebrafish, and *Drosophila* (*PLOS Biology and Current Biology x3*). In addition Martin and Bass defined the molecular mechanism by which signalling from the extracellular matrix following injury triggers cell motility to initiate wound healing (*Developmental Cell*).
- Nobes work on Eph receptors led to key findings on cell motility (*Nature Cell Biology*) and in the developing vasculature (*Nature*).

Molecular Biosciences Biochemistry in Bristol has a long and highly successful history of research in molecular enzymology and recognition, with a strong focus on the quantitative understanding of the dynamics of catalytic mechanisms and substrate recognition. With the development of new single-molecule techniques, FRET, AFM and other approaches to biomolecular studies, this traditional strength has now evolved to provide a broader range of techniques for exploring and exploiting key biomolecules in synthetic biology and other applications. This cluster has developed significantly since 2008 and now spans a broader remit encompassing mechanochemistry, synthetic biology, and structural biology. Representative research in this cluster includes: *de novo* protein design including enzymes and biomaterials; targeting metabolic enzymes for drug design; protein folding and chaperones; and an extensive range of systems acting on DNA and RNA, both individual proteins and assemblies involved in replication, recombination, DNA repair, transcription and restriction-modification. This cluster seeks to extend provision of advanced biophysical techniques to support this and other research groupings within and beyond this UoA through links with Nanoscience (e.g. atomic force microscopy with Miles) and Chemistry (e.g. computational enzymology with Mulholland). There is ever closer integration with the cell biology cluster and significant industrial links supported by technology development (e.g. membrane protein production (Collinson) and crystallography (Race)).

Future research priorities include artificial enzymes and designer membrane channels, improving natural product synthesis, molecular machines acting on nucleic acids, and targeting protein and lipid kinases for drug design. Chemical and Synthetic Biology underpin much of this developing activity. There is close integration with Biological & Organic Chemistry, such as the joint appointment of Woolfson (submitted in UoA 8, a dual Chemistry-Biochemistry appointment). New appointments of Anderson, Curnow and Race in this key area strengthen this overlap considerably. For example, Race collaborates closely with Simpson, Willis and Crump in Chemistry as well as Nobbs and Jenkinson in Dentistry. Close cooperation between several members of this UoA (notably Booth, Brady, Sessions, and Verkade) and colleagues in Physics (Miles, Antognozzi), Mathematics (Linden), and Chemistry (Woolfson) has led to significant grant support and high impact publications. Synthetic biology provides a cohesive centre for future activity across the entire UoA linking Race, Anderson, Booth, Jones, Sessions, Savery, Grierson, Roberts, Bailey, and Lazarus with colleagues across the life and physical sciences.

Cluster highlights:

- Dillingham and colleagues elucidated several key processes in the recombinational repair of double-strand breaks in DNA, primarily end-processing by the AddAB helicase-nuclease complex (*Molecular Cell*, *EMBO J*, and *PNAS* x2).
- Savery advanced significantly our understanding of how transcription systems overcome damage to the DNA template, by rescuing the RNA polymerase and recruiting DNA repair proteins (*Molecular Cell* and *Nature*).
- Szczelkun and colleagues exposed a revolutionary new mechanism for the translocation of proteins along DNA, triggered rather than driven by ATP hydrolysis: the scheme has major

implications for the roles for helicases in human health and disease (*Science* and *PNAS*).

- Collinson described the structure of the ubiquitous Sec-complex associated with a bona fide mimic of a pre-secretory protein in the native environment of the membrane (*Cell Reports*).
- Booth developed a lipid micelle method to allow subunit stoichiometry and ligand-binding properties of membrane complexes to be determined by mass spectrometry (*Science*).
- Collaborations involving Biochemistry (Booth, Brady and others), Chemistry, Mathematics, Nanoscience, Physics, Pharmacology and Physiology created novel three dimensional nanostructures from synthetic peptides and then characterised their tubular or spherical shapes: this work establishes a firm foundation for future work in synthetic biology and nanomaterials (*Nature Chemical Biology* and *Science*).

A coherent and major link between the *Dynamic Cell Biology* and *Molecular Biosciences* clusters is evident through our focussed work on Membrane Biology. Work in this thematic area focuses on fundamental chemical studies, asking functional questions about how proteins are inserted into and cross membranes, the function of crucial membrane channels and complexes, molecular recognition events during host-pathogen interactions, and the transport of macromolecules between and across membranes. Regulation and communication mechanisms within cells are primarily dictated through complexes formed on either cellular or organelle membranes. Bioimaging and proteomics act as cohesive technologies driving further collaboration, additionally with Plant & Agricultural Sciences. Close integration with National Health Service Blood and Transplant continues to drive considerable work in this area based around erythrocyte membrane biology (Toye, Lane, and Brady all receiving funding).

Animal Behaviour & Sensory Biology Research in Animal Behaviour asks major questions about how animals make decisions, and the adaptive value of their decision rules. Research in Sensory Biology seeks to understand how animals perceive and react to the world around them, including mechanisms of vision (at all levels) and audition (particularly in insects and bats). Research in this cluster is strongly interdisciplinary and uses diverse physiological, biomechanical, neurological, molecular, theoretical modelling, and behavioural experiments in both laboratory and natural populations to link from the genetic foundations through to the evolution of behaviour and sensory systems. Bristol's strengths in these multidisciplinary areas of research are reflected in the University Centre for Behavioural Biology, incorporating members from this cluster with colleagues from Mathematics, Psychology, and Veterinary Sciences. Members of this Centre are world leaders in theoretical behavioural and evolutionary ecology, particularly the application of optimality and game theory. Researchers in Sensory Biology are also core members of the University Centre for Nanoscience and Quantitative Information (NSQI) and Robert was its first Director. Researchers in this cluster are also key members of the cross disciplinary Bristol Vision Institute, whose research interests span both the sciences and arts and link with external partners: the Bristol Eye Hospital, Bristol Robotics Laboratory, and the Machine Vision Laboratory at the University of the West of England.

Our strategic aims are to exploit fundamental discoveries to predict animal (including human) behaviour in a time of global change and uncertainty, and to use synthetic biology and nanoscience to develop artificial sensory systems for human exploitation.

Cluster highlights:

- Franks validated the theory that certain decision-making systems in vertebrate brains and honeybee societies might be similar at an algorithmic level (*Science*).
- Holderied discovered a new pollination syndrome where bats detect flowers by echolocation (*Science*).
- Ioannou published a powerful body of work demonstrating the complexities of group decision-making and collective actions (*Science* x2, *PNAS,* and *Current Biology*).
- Partridge and Roberts provided a mathematical framework that explains for the first time how multilayer stacks of transparent biological material can be both highly reflective over a wide spectrum and non-polarizing (*Nature Photonics*).
- Roberts provided the first demonstration of a fundamentally new type of optical tweezer and instigated a new field of optics (both *Nature Photonics*).

Plant & Agricultural Sciences A critical challenge for humanity is how to increase food production sustainably whilst preserving biodiversity in the face of climate change. The principal aim of research in this cluster is to address this grand challenge using the power of molecular genetics, genomics, and physiological approaches to improve our understanding of what limits plant growth and reproductive output with a view to increasing productivity without harming the environment. The Lady Emily Smyth Agricultural Research Station provides a focus for activity in this cluster. Researchers within the cluster are key members of the University's Cabot Institute, a multidisciplinary centre for research aimed at tackling the challenges of uncertain environmental change. Food security-related research is an increasingly significant area of research in the cluster; this includes work on cereal genomics (Edwards and Barker), and pollinators in agricultural ecosystems (Memmott), while Hetherington, Franklin, Dodd, Grierson and Edwards are working to improve water use efficiency of crops using genomics and systems biology-based approaches. This cluster is integrated in the University's Predictive Life Sciences network, which brings together scientists from biology, physics, chemistry, engineering, mathematics, and computer science to study systems biology and biological complexity more generally. The strategic appointments of Dodd, Franklin, and Whitney and major grant income have enhanced our capability in systems biology, pollination biology, cereal genomics and sustainable agricultural ecosystems.

Going forward, we are expanding functional genomics capability within the UoA and forging major collaborations with computer scientists and mathematicians in bioinformatics, and with chemists in synthetic biology. Bioinformatics and synthetic biology are identified as strategic areas for future appointments and for closer integration with Molecular Biosciences.

Cluster highlights:

- Edwards and Barker made significant contributions to sequencing and subsequent analysis of the wheat genome (*Nature*).
- Dodd showed that the plant circadian clock regulates photosynthesis genes in the chloroplast – this is the first time that a circadian clock has been shown to control the activity of an organelle in a eukaryotic cell (*Science*).
- Franklin provided the first molecular evidence of crosstalk between two different environmental signals (temperature and light) in a plant (*Current Biology*).
- Grierson showed how root hair length is controlled during plant root development, a finding that has major implications for optimising crop root architecture (*Nature Cell Biology*).

Ecology & Environmental Change Predicting, monitoring and managing biotic response to climate and habitat change represent the greatest challenge facing 21st century biology. A major focus here centres on how organisms, populations, and ecosystems react and respond to a changing world. The overarching aim of research in this new cluster is to address this challenge by understanding the processes that underlie the causes of the distribution and abundance of living organisms, and those that direct their evolution. Research here seeks to understand ecological relations between organisms (plant, animal or microbe) at individual, population and community levels, as well as between organisms and their environments. Research ranges from fundamental population genetics and evolutionary biology to applied ecology in different habitats, from tropical islands, marine and freshwaters to commercial farms, and urban landscapes. This understanding will allow us to better manage ecosystems, for example, to increase biodiversity in agro-ecosystems, to restore damaged natural ecosystems or control pests and pathogens in the midst of environmental change. We use molecular and physiological techniques to quantify genetic and phenotypic variation and response to environmental change and ecological approaches to determine the impact of change in the field. Our strategy going forward is to build upon our existing cross-disciplinary links with partners in the Cabot Institute to whom we will provide the biological expertise to help develop environmentally-sensitive approaches for the management, conservation, and exploitation of biodiversity in the face of global change.

Future priorities include the effects of land-use change on ecosystem service provision and the physiological, biochemical and molecular bases of adaptation and evolution. Applications of this research include: ecosystem management, wildlife conservation, environmental and biological control, and informing policy on conservation and agriculture.

Cluster highlights:

- Memmott demonstrated that networks of species interactions within complex ecological communities differ in their robustness, with some more vulnerable to extinction than others (*Science*).
- Whitney identified iridescence in flowers, the structural mechanism used to produce it, and how bees learn to recognize it (*Science*).
- Whitney and Robert showed that flowers produce electrical fields that bees detect and respond to, thereby identifying a new attractant property of flowers (*Science*).

c. People, including:

i. Staffing strategy and staff development

During the review period we have made notable appointments to core funded posts as well as through prestigious personal fellowship awards. New appointments since RAE2008 include two at Professorial level: Adams and Beaumont. Adams strengthens our cell biology research and integrates closely with evolutionary biology through her studies on the origins of extracellular matrix proteins. Beaumont was appointed jointly with Maths strengthening already close links and supporting our interdisciplinary and quantitative approaches. Other new appointments include Dodd, Franklin, and Whitney (Plant Sciences), Pisani and Vinther (Evolutionary Biology), Roberts (Sensory Biology), and Sumner (Animal Behaviour), all of whom use functional genomics technologies and associated computational analytical methods in their research. Pisani and Vinther were joint appointments with Earth Sciences under our shared research theme of Evolutionary Biology. ERC Starter Investigator Awards (each >£1m) were secured by Curnow, Peel, and Whitney. We continue to attract exceptional researchers through prestigious fellowship awards (Anderson, Bass, Fawcett, Hammond, Ioannou, Franklin, Roberts and Whitney). We have actively sought to retain key junior staff through transition of existing holders of prestigious fellowships to future core-funded lecturer/senior lecturer posts (Anderson, Dodd, Curnow, Dillingham, Franklin, Ioannou, Race, Roberts, Sumner, and Whitney). Nine members of this UoA have been promoted to personal chairs in the review period: Collinson, Grierson, Kelly, Mellor, Nobes, Partridge, Savery, Stephens, and Szczelkun. Personal awards also form a key component of our large-scale funding. Booth, Henley, and Houston were awarded ERC Advanced grants of (>€2m); Martin was awarded a Wellcome Trust Senior Investigator award (£1.4m) with Dillingham securing a Wellcome New Investigator award (£1.2m). Our ability both to recruit and retain early career researchers has consistently been a driver of growth and excellence over the long term.

Recruitment and retention policies are also balanced to ensure equality and diversity, including (wherever possible) mixed gender shortlists, gender-balanced seminar programmes, and careful support of flexible working for all staff and postgraduate students. Members of staff are supported in their careers through mentoring and staff development projects (such as leadership, teaching, or management courses) and through compulsory annual staff review and development appraisals. Senior staff mentor new staff, in particular research fellows. All staff are encouraged to attend careers talks focussed on topics including research funding, industrial, communication and policy opportunities. Our success here is evidenced by the high proportion of research staff progressing to independent fellowships and that many of the current professorial staff previously held independent research fellowships at Bristol. Career development is supported through ongoing availability of postdoctoral fellowships. Our action plan in response to the Concordat to support the career development of researchers has been recognized by award of the HR Excellence in Research badge by the EU Commission in 2010.

Within the UoA we host regular research workshops, seminars and high profile colloquia given by major figures, including Nobel laureates and prestigious overseas speakers. Seminars and colloquia are often coupled with career development workshops for early career researchers. Many of our researchers organise major international research conferences and workshops. We also exploit public channels where appropriate to disseminate our work and work closely with the press and broadcast media to disseminate our work. One example is the 'Cabot Press Gang', established by a NERC/Cabot Institute Knowledge Exchange Fellow to work closely with the University Communications Office to promote our science to media. We engage directly with

funders (e.g. through the University's strategic partnerships with BBSRC and EPSRC), non-governmental organizations (e.g. conservation organizations), and industry (e.g. GSK, AstraZeneca) to shape and develop our research strategy.

ii. Research students

We benefit from diverse and vibrant Graduate Schools that oversee the multiple programmes, doctoral training centres and accounts that span the UoA. These are now integrated within the Bristol Doctoral College, a University-wide activity that provides a clear and visible focus (external and internal) for postgraduate research and training at Bristol, and the academic leadership required to maintain our position as a university of choice for the best PGR students from around the world. Postgraduate students benefit from a core set of taught courses, including an intensive three-week course on advanced statistics and experimental design, and transferable skills modules on communication and research technologies. They attend weekly seminars by visiting speakers and present their own research at regular sessions. PhD students have at least two advisors, with some second advisors from outside their School, which encourages good practice, collaboration and interdisciplinarity.

All of our postgraduate programmes aim to provide the highest standards in student recruitment, cohort building and interdisciplinary supervision. In 2008 we were awarded and began recruiting to our Wellcome Trust 4-Year PhD Programme in Dynamic Cell Biology. This was augmented by a second Welcome Trust 4-year PhD programme in Neural Dynamics operating alongside. Postgraduate recruitment across this UoA has been further strengthened through award of a BBSRC Doctoral Training Partnership (lead by Bristol, with Exeter, Bath and Rothamsted Research) to which this unit has recruited 17 students from the initial 2 annual intakes, and which succeeds a series of former BBSRC DTGs. The DTP forms a key component linking activity between all 6 research clusters by integrating quantitative training across all biological scales from atoms to organisms. CASE and other industrial studentships have contributed strongly to our translational work. For example, Halestrap has held collaborative CASE and direct funded studentships with AstraZeneca; a current CASE Studentship is directed towards developing cancer drugs. We have taught and supervised postgraduate students in the EPSRC Doctoral Training Centre in Complexity Sciences (the BCCS) since its inception in 2007, and currently host 4 BCCS PhD students. Additional students are funded by UK research councils (MRC, EPSRC, NERC and BBSRC, including 9 current CASE awards), charities, and, internationally, the European Research Council, foreign governments and overseas research agencies. These broad funding sources drive recruitment of ~40-50 postgraduate students per annum. We also host 10-40 Masters by Research students per annum, many of whom stay on for doctoral study. Most recently (Nov 2013) Bristol, was lead institution in a successful bid (through our formal alliance with the Universities of Bath, Exeter, and Cardiff, GW4 (Great Western 4)) for the largest NERC Doctoral Training Partnership in the UK (28 NERC-funded and 10 University-funded studentships).

d. Income, infrastructure and facilities

(i) Income. Our income is derived from diverse sources including government research councils, major charities and industrial partners. In addition to the extensive support gained through early career awards (detailed above), major sponsors are the BBSRC, Wellcome Trust, MRC, and NERC. There has been distinct success with international awards, notably the European Research Council. Major grants active since 2008 include Edwards (BBSRC LoLa), Robert (EPSRC-Joint RCUK Research Grant), Roberts (US Airforce Office of Scientific Research), Memmott (BBSRC Pollinator Initiative), Halestrap (British Heart Foundation Programme grant), Martin (CRUK programme and MRC Programme grants), and Wellcome Trust Programme grants to Cullen, Martin, and Szczelkun. Research in the Plant and Agricultural Sciences cluster benefits from the Lady Emily Smyth endowment (~£11m in investments), which through its earnings (~£0.3m p.a.) supports research of agricultural relevance via pump-priming awards, PhD studentships, capital equipment, and Lady Emily Smyth Research Fellowships, which provide additional start-up and continuing funding for independent Research Fellows. Further income is generated from external use of our core facilities. University of Bristol postgraduate scholarships enable us to attract the very best UK and Overseas students.

(ii) Infrastructure. All areas of research in the UoA constantly move forward and diversify through innovative collaborative interdisciplinary science; for example taking new directions to increase knowledge in genomics, developmental biology, systems biology, and in commercializing therapeutics through spin-out companies. This is supported through provision and development of critical biological insight and technologies in cross-disciplinary ventures.

Our ambitious, collaborative, forward thinking approach has led to the University investing £56m in a major new infrastructure project, the Life Sciences building. With state-of-the-art technological infrastructure, the new building will act as a hub to bring together functional genomics technologies and researchers from disparate sites across the University. These technologies are at the heart of future research in this UoA as we exploit the power of genomics and metabolomics to address fundamental questions across the biological spectrum. This offers exceptional opportunities for research because critical technologies and associated computing capacity (bioinformatics) will be co-located for the first time.

Additional outside investment has enabled construction of new laboratory space for Cell Biology integrating significant activity in this UoA. Significant investment from MRC (£2.8m) and the University (£1.1m) for technology for *in vivo* imaging complements our existing bioimaging expertise and provides significant opportunities for researchers across this UoA.

Addressing RCUK aims This research structure will allow us to confront new challenges in molecular and cellular research and also critically to incorporate these new technologies into our "whole organism"-based biological research to deliver research hitherto deemed intractable in non-model organisms. This places us in an excellent position to address key strategic aims and priority research areas identified by RCUK including 'Food Security' and 'Basic Bioscience Underpinning Health' (BBSRC), 'Next Generation Science for Planet Earth' (NERC), 'Improving Human Health' (MRC), 'Transformative Research' and 'Living with Environmental Change' (BBSRC, NERC). Our integrated approach to these grand challenges is coordinated through University-wide infrastructures in the form of two cross-disciplinary Research Institutes. The Elizabeth Blackwell Institute for Health Research (EBIHR) and Cabot Institute for Environmental Research support our translational activity in healthcare and environmental research and policy making, respectively, as well as underpinning collaboration across disciplines. The work of these institutes is backed up by the *Research and Enterprise Development* (*RED*) team, who oversee a University-wide approach to impact.

Maximising Impact A key part of our ongoing strategy for translation of fundamental research is to ensure that staff from this UoA play a significant role in the EBIHR and Cabot Institutes. These University-wide institutes share similar translational agendas for research.

The EBIHR was established in 2012 (with Tavaré as its inaugural Director) to identify and nurture new opportunities for interdisciplinary research, in particular by exploiting expertise in the non-medical faculties, and translating that research into effective health outcomes. The organizational structure of the EBIHR includes key partnerships with bio-pharmaceutical companies, local hospitals and health groups. This helps develop collaborative links between biomedical research and patient-facing clinical research as well as with industrial partners. Access to clinician scientists, patient cohorts, and sample banks will be facilitated through this Institute. The EBIHR also provides an infrastructure (through Wellcome Trust strategic support funding and MRC Developmental Pathways Funding Scheme) for ongoing recruitment and development of new researchers, translational activities, and outreach events. Workshops also provide a showcase for our work and facilitate engagement with the biopharmaceutical industry. EBIHR is also identifying and supporting our best young non-clinical and clinical talent through a series of fellowship schemes, and creating an environment for effective collaboration with external partners within (e.g. Bristol Health Partners) and outside (e.g. other universities and industry) Bristol. In particular our goal is that these programmes will stimulate further crossover and researcher exchange between fundamental bioscience and clinical research labs. Expertise in genomics, food security, and population studies within this UoA also feed directly into the EBIHR. EBIHR also allows us to engage fully with major funders including the Wellcome Trust and Medical Research Council to address new and emerging areas of strategic importance to human health and clinical practice.

The Cabot Institute for Environmental Research provides a focus for our fundamental and responsive research on risks and uncertainty in a changing environment. It also provides an

infrastructure for environmental researchers to actively engage (e.g. via workshops) with policy makers, marine industries, fisheries scientists and conservation groups through links with (among others) DEFRA, the International Union for Conservation of Nature, Environmental Technology and Service Companies, the International Council for the Exploration of the Seas, and the Institute of Marine Engineering Science and Technology. Research interests include climate change, natural hazards, food, water and energy security, and future cities. This distinctive approach fuses rigorous statistical and numerical modelling with a deep understanding of interconnected social, environmental and engineered systems – past, present and future. To achieve its vision, the Cabot Institute stimulates linkages across disciplines and with industry and government, developing partnerships, enhancing knowledge exchange across sectors and building groups of shared interdisciplinary expertise.

(iii) Facilities. This UoA is highly active in ensuring continued investment in core facilities for *Bioimaging*, *Proteomics*, and *Functional Genomics* and drives the intellectual and technological development of these areas across the University. These facilities act as key hubs for research across the UoA with users from all 6 research clusters. They are also all now established as high profile regional and national resources used by many external researchers. Facility managers for Bioimaging (Jepson and Verkade) and Proteomics (Heesom) are research active and returned within this UoA. The academic leads for the Bioimaging, Proteomics, and Functional Genomics Facilities (Stephens, Cullen, and Edwards, respectively) are all included in this UoA. The importance of these facilities to our research is reflected in the significant investment during the review period. Over £2.8m of investment has been made in the Bioimaging Facility, including extensive redevelopment, acquisition of new technology, and full physical and functional integration of existing light and electron microscopy facilities. We have always been at the forefront of implementing new imaging technologies. As a result, the Bioimaging facility is now a node within Euro-BioImaging and the host of a prestigious European Molecular Biology Organization course in correlative light/electron microscopy.

Quantitative mass spectrometry, high-throughput capillary DNA sequencing, high-density-microarray facilities, and next generation sequencers (Illumina, Ion Proton, and Ion PGS) make our Proteomics and Functional Genomics Facilities the focus of much interdisciplinary activity. Further investment in transcription profiling and next generation sequencing (£1.0m) and state-of-the-art mass spectrometry (~£1m) has enhanced our capability in these key areas.

The *Animal Services Unit* provides outstanding facilities for maintaining model organisms used by this UoA including an extensive and newly equipped zebrafish facility, a new £1.5M aquarium facility for other species, as well as major facilities for rodent and large animal work.

The *Advanced Computing Research Centre* provides access to high performance computing for all researchers, along with full training and support. The centre includes a £7 million super-computer facility called BlueCrystal, which was introduced in 2008 and is used by more than 600 researchers across the University. This underpins significant work in molecular modelling, proteomics, bioinformatics, and synthetic and systems biology. The *Research Data Storage Facility* provides integrated resilient, long-term petascale storage to all researchers ensuring best practice in data management and sharing.

Research governance The University has robust policies regarding research governance including infrastructure, data storage and management, use of animals and human tissue in research, grant management and regulatory issues. Written policies (available to all staff and students online) are augmented by on-site training in research ethics. These areas are underpinned by the activity of *Research and Enterprise Development* (RED), a group of more than 80 staff with specialist skills and training, who work with academics and researchers to help sustain and grow research activity while ensuring best practice in governance.

Public Engagement We collaborate actively with the *University Centre for Public Engagement* to deliver extensive outreach and public engagement activities. Examples within the review period include contributions to local and national science events and festivals (e.g. Cheltenham Science Festival, and Bristol Festival of Nature – the largest Natural History festival in Europe), public lectures, broadcast and print media, school visits, and open days for schools to visit and get hands-on experience of experimental bioscience. The University Botanic Garden (of which Hiscock is Director) was built in 2004 as a major vehicle for diverse public engagement activities and its achievements have been recognised with many awards.

e. Collaboration or contribution to the discipline or research base

Collaboration This UoA is proactive within the University in coordinating major funding bids, most recently in the form of regional cooperation through a formal alliance (Great Western 4 - GW4) with the Universities of Bath, Exeter, and Cardiff. Key examples include the BBSRC and NERC doctoral training programmes and Food Security Land Research Alliance which span multiple Institutions to unite individual research strengths and maximise cross-institutional working and cross-disciplinarity with each member organization. UoB is also a BBSRC strategic partner university which informs strategy and planning in both directions.

Interdisciplinary working is embedded in our working method and this integration is reflected by the submission of some staff to other UoAs (Gibson, Pisani, Rands, Vinther, Wall, Woolfson). Our researchers are important drivers of major University-wide initiatives: Robert is former Director of the Centre for Nanoscience & Quantum Information, overseeing the completion of and move into these state-of-the-art low vibration facilities. Cuthill was a founder member of, and is on the management team that runs the Bristol Vision Institute, coordinating research in human and animal vision, artificial vision systems, and imaging. This provides strong links with Psychology (Cuthill, Partridge), with emerging collaborations in the field of evolutionary psychology (Cuthill, Houston), animal cognition (Radford, Whitney), and the Bioimaging facility (Stephens, Verkade, and Jepson). Dynamic Cell Biology and Sensory Biology clusters also have multiple links with photonics and nanoscience groups in Physics (Banting, Robert, Partridge, Roberts, Stephens, Toye, and Whitney). Halestrap was until recently Director of the Bristol Heart Institute. Houston and Cuthill were founder members of the Centre for Behavioural Biology. Grierson is lead academic for life sciences within the Bristol Centre for Complexity Sciences. University-wide research themes in Cell Biology and Molecular biosciences are led by Cullen and Booth respectively. Brady, Cullen, Grierson, and Lane each direct doctoral training programmes.

These activities lead directly to full engagement with external collaborators worldwide. The effectiveness of our extensive network of national and international collaborations can be evidenced by multiple high profile publications that result from this strategy (e.g. Savery with Darst (New York) and Strick (Paris); Dillingham with Sanchez-Moreno (Madrid); Nobes with Adams (London); Booth with Robinson (Cambridge); Cullen with Korswagen (Utrecht); Szczelkun with Seidel (Dresden); Franks with Seeley (Cornell) and Visscher (Riverside); Ioannou with Couzin (Princeton); Roberts with Cronin (Maryland) and Marshall (Queensland); Dodd with Azuma and Tanaka (Tokyo); Holderied with von Helversen (Erlangen) and Simon (Ulm); Edwards with Bevan (John Innes Centre) and Hall (Liverpool); Hetherington with Gray (Sheffield) and Hussey (Durham); and Grierson with Leyser (Cambridge).

Contribution to the discipline Many of our studies target a fundamental understanding of living processes and we actively seek to disseminate this emerging knowledge into translational outcomes. Our work underpins a diverse range of translational activity both here at Bristol and elsewhere. Examples include discoveries in cell and molecular biology that are being directed into therapeutic programmes (e.g. Bass, Martin, & Nobes – promotion of wound healing; Halestrap – mitochondria as a target for cardioprotection; both Brady and Tavaré have worked closely with industry on developing enzyme inhibitors for treatment of infectious diseases and cancer). Molecular marker data from wheat (Edwards) is informing targeted wheat selection by commercial breeders. Further direct engagement is expected to arise in the future as our research moves increasingly to integrated studies reaching beyond the molecular and cellular level. An analysis of the research links between the unit and other departments reveals not only the high volume of collaborative research, but also a diversity of connections. Thus, there are collaborations with Chemistry on proteomics, enzyme structure and function, and synthetic biology (notably Anderson, Bailey, Brady, Lazarus, Race and Verkade), with Mathematics on economic modelling of behaviour (Houston, Cuthill) and mathematical, agent-based and network modelling of biological systems (Grierson), with Physics and Psychology on camouflage (Cuthill), with Earth Sciences to develop new models of joint strain (Hammond), and with Computer Science via bioinformatics development (Barker, Beaumont), modelling of social organisation (Franks, Houston), and artificial vision (Cuthill, Roberts). Other activities exemplify how the strategic organization of the unit with fluid boundaries allows rapid developments in new priority areas, for example Booth, Brady, Sessions and Verkade have been integral to synthetic biology work within Chemistry (*PNAS* and *Science*). Close links with clinical colleagues are also evident (Nobes, Adams, Hammond, Race, Halestrap,

Tavaré and Toye). We engage directly with industry for example through links to AstraZeneca and GlaxoSmithKline for pharmaceutical work, and Leica Microsystems and FEI for microscopy. Our Bioimaging Facility has been pro-active in the organization of both UK and European future strategies for Bioimaging which have fed directly into UK and EU funding agency programmes.

Many members of the unit serve on and chair major national and international grant panels, strategy boards, and advisory boards, e.g. the ERC (Booth, Grierson, Martin), UK Research Councils (Brady, Bridle, Collinson, Cullen, Cuthill, Edwards, Grierson, Hetherington, Hiscock, Martin, Memmott, Radford, Stephens, Viney), HEFCE RAE2008/REF2014 (Brady, Hetherington), Wellcome Trust (Banting, Martin), Juvenile Diabetes Research Foundation and Diabetes UK (Tavaré), British Heart Foundation (Halestrap), NC3Rs (Cuthill) and Royal Society (Adams, Anderson, Cuthill, Mellor, Race). Members of the UoA also serve (or served during the review period) as trustees or board members of professional societies (including Adams, Booth, Cuthill, Dillingham, Grierson, Hanley, Hetherington, Hiscock, Holderied, Lane, Mellor, Memmott, Nobes, Savery, Stephens, Verkade), and as Editor-in-Chief or editorial board members of >40 journals.

Multiple prestigious Fellowships, Prizes, Medals, and Awards evidence our achievements:

- Houston was elected FRS (2012), awarded the Association for the Study of Animal Behaviour Medal (2013), and the Hamilton Award from the International Society for Behavioural Ecology (2008).
- Halestrap, Martin and Henley were elected Fellows of the Academy of Medical Sciences.
- Martin was elected an EMBO Member.
- Hiscock was elected Vice-President of the Linnaean Society of London (2013).
- Cuthill was President of the Association for the Study of Animal Behaviour (2007-10).
- Sumner and Whitney were awarded the L'Oréal-UNESCO Fellowship for Women in Science in 2008 and 2011, respectively.
- Personal research fellowship awards active during the review period include: Booth (Leverhulme), Peel (ERC), Stephens (MRC), Toye (Wellcome) , Bass (Wellcome), Hammond (ARC), Dodd, Franklin, Race, Dillingham, and Anderson (all Royal Society), Ioannou (Leverhulme), Roberts (BBSRC), Whitney (Lloyd's of London Tercentenary Trust). Martin and Dillingham have secured Wellcome Trust Investigator awards.
- In 2010, the Biochemical Society honoured 3 members of the unit: Dillingham the Colworth Medal and Prize, Cullen the Morton Lecture, and Halestrap the Keilin Memorial Lecture.
- Memmott was awarded the British Ecological Society President's Medal (2011).
- Edwards was awarded the Royal Agricultural Society Research Medal (2011).
- Robert received a Royal Society Wolfson Merit Award in 2008, and Cullen and Booth are current holders of this award.
- Franklin and Whitney won the Society of Experimental Biology (SEB) President's Medal in 2010 and 2012, respectively. Franklin was also awarded the Federation of European Societies of Plant Biology Award (2010).
- Anderson awarded the Inorganic Biochemistry Young Investigator's Award by the Royal Society of Chemistry (2012).
- Roberts and Partridge were awarded the Rank Prize (2011).
- Dodd was awarded the Daiwa Adrian Prize (2013).
- Viney awarded the CA Wright Medal of the British Society for Parasitology (2013)
- Ioannou won the New Investigator award from the Association for the Study of Animal Behaviour (2013).

Interactions with our research collaborators, other Universities, professional societies, industry, charities, and governmental agencies ensure that our research contributes substantially to research outcomes, policy making, and strategy at national and international levels.