Environment template (REF5)

Institution: **University of Cambridge**

Unit of assessment: **UoA5**

a. Overview

Research in Biological Sciences at Cambridge is broad-ranging, encompassing animal, plant and microbial systems at scales ranging from atomic structures, through molecular, cellular and physiological processes to evolutionary, ecological and behavioural processes operating at the levels of populations and communities. In addition to supporting creative, investigator-led, basic research, Biological Sciences at Cambridge also has impacts on the pharmaceutical and biotechnological industries, on human and animal health and the clinic, as well as in conservation, agriculture and the environment. Research in this submission takes place within six academic departments (Biochemistry, Genetics, Pharmacology, Plant Sciences, PDN - Physiology, Development and Neuroscience - and Zoology), together with four research institutes (the Wellcome Trust-MRC Stem Cell Institute, the Wellcome Trust/CRUK Gurdon Institute for Cancer and Development, the Cambridge Systems Biology Centre and the Sainsbury Laboratory for Plant Development). These departments and institutes comprise the larger part of the School of the Biological Sciences. Other departments in the School are submitting to UoA1 (Pathology), UoA4 (Psychology) and UoA6 (Veterinary Science). Each department houses cognate research groups appropriate to the broader remit of the department, while the institutes provide additional dedicated accommodation for major areas of research with capital investment from external funders and the University.

In recognition of the evolution of closer integration between the traditional disciplines, we have developed a number of strategies to facilitate cross-departmental and inter-disciplinary research interactions. These include the merger of the former departments of Physiology and Anatomy into the Department of Physiology, Development and Neuroscience, as well as inter-departmental research institutes, PhD training programmes, seminar series and research facilities. In this submission we describe research in the School of the Biological Sciences based upon the following cross-departmental themes and sub-themes:

- **Conservation, Behaviour, and Ecology**: with sub-themes: Conservation; Behavioural ecology; Community ecology
- **Chemical and Structural Biology**
- **Developmental and Stem Cell Biology**: with sub themes: Stem cells and germ cells; Early development; Developmental mechanisms; Neural development
- **Evolutionary Biology**: with sub-themes: Palaeontology, Systematics and functional morphology; Population and evolutionary genetics; Genetic basis of animal diversity
- **Functional Genomics and Systems Biology**
- **Molecular Cell Biology**: with sub-themes: Cell cycle, chromosomes and gene expression; Cell signalling: receptors; Cell signalling: signal transduction
- **Neuroscience**: with sub-themes: Molecular and cellular neuroscience; Sensory neuroscience; Systems neuroscience
- **Disease Biology**: with sub-themes; Epidemiology; Microbiology; Molecular and cellular pathology
- **Plant Biology**: with sub-themes; Cell, molecular and development; Biochemistry, physiology and biotechnology

The structuring of our submission around research themes, rather than physical departments, reflects the dynamic interdisciplinary nature of our research. All themes comprise researchers from multiple departments or institutes. Likewise, many researchers are associated with multiple themes, although for the REF they are only listed under one theme. Reflecting successful development of our research strategy, the thematic structure is similar to our RAE 2008 submission, with the addition of Disease Biology helping to emphasise alignment with the

Biomedical Research Strategy developed jointly with the School of Clinical Medicine (Section 2.1.2). Moreover, the majority of the University's *Strategic Research Initiatives* and *Networks*, which coordinate interdisciplinary research across the University (Section 2.1.1), are Life Science-centred and align with our research themes. In the broader environment, the School has extensive links with the world-leading University departments of Chemistry, Physics, Mathematics, Computing, Engineering and the Clinical School, and with nearby major institutes, notably MRC-LMB, CR-UK Cambridge Research Institute, the Babraham Institute, the European Bioinformatics Institute (EBI), the Wellcome Trust Sanger Institute (WTSI), Microsoft Research and numerous Conservation NGOs. These links include graduate student training and generate many joint research projects and publications.

The 198 investigators returned to UoA5 includes 94.5% of our University tenured academic staff. This is a dynamic population of both young and established researchers, reflected in prestigious targeted recruitments, internal promotions, departure of staff to other high quality institutions, and recognition of excellence by national and international bodies. This is exemplified by numerous high impact publications (more than 296 in *Science/Nature/PNAS/Cell* between 2008-2013), as well as prizes and markers of esteem (Section 5) including the 2012 Nobel Prize for Physiology or Medicine to Professor Sir John Gurdon.

b. Research strategy

2.1 Organisation of research and strategic planning

Strategic Plan: our underpinning strategy is to foster sustained excellence and originality with critical mass, rather than comprehensive coverage of all areas. The School of the Biological Sciences is one of six Schools within the University to which responsibility for funding is devolved. The broad strategic direction of the School is set by the Council of the School and is formalised in a rolling five-year Strategic Plan that is reviewed and updated annually. All research areas are represented on the Council through Heads of Department or Institute who, in turn, engage with all staff through departmental staff meetings. Postgraduate students are statutorily represented on the Council. Additional members are co-opted to ensure coverage of all research areas. Cross-representation between the Councils of the Schools of the Biological Sciences and Clinical Medicine ensures co-ordination of the University biomedical strategy. The School strategic plan, relevant elements of which are highlighted in research themes (Section 2.4) and infrastructure (Section 4.2), addresses infrastructure, recruitment and estates strategy. The plan supports a dynamic research environment by complementary mechanisms: top-down, giving overall direction, and bottom-up allowing individual initiative. Major initiatives (e.g. the Sainsbury Laboratory) are prioritised by the Council of the School and are supported by substantial investments in recruitment, infrastructure and facilities. The priority given to these and to planned major initiatives (Sections 2.4, 2.5, 4.2 for details) has been guided by five key principles:

- flexibility in forming co-located and virtual Research Groupings to optimise the intellectual environment for high-quality research, drawing upon a range of disciplines including the clinical and physical sciences;
- integration of reductionist methods and systems approaches: encompassing scales from the sub-cellular and cellular, to organs, to whole organisms, and from individuals to populations and communities;
- translation of research for clinical and industrial exploitation and implementation of national policy;
- provision of high quality infrastructure to enable researchers in biological sciences to compete at the highest international levels;
- engagement with strategically important national and international priorities.

Two major strategic innovations since RAE 2008 are:

2.1.1. University-wide Strategic Research Initiatives and Networks: introduced from 2010 (http://www.cam.ac.uk/research/research-at-cambridge/strategic-research-initiatives-networks), these build upon existing areas of research strength by bringing together a critical mass of expertise from across the University. They address large-scale research challenges by strengthening internal, multi-disciplinary research collaborations, and provide a platform for large-scale funding applications, recruitments and international research partnerships. The

initiatives and networks are supported by University strategic funding for facilitators, workshops and short-term fellowships. Underscoring the importance of Biological Sciences within the University, seven of the current eight Strategic Initiatives: *Stem Cells, Neuroscience, Cancer, Infectious Disease, Conservation, Energy,* and *Food Security* are focused on the Life Sciences with major input from the Research Groupings in this submission. In addition, our researchers participate in five Strategic Networks (designed and funded to foster cross-disciplinary interactions): *Immunology*, *Metabolic Disorders*, *NanoForum, Sensors* and *Public Health*.

2.1.2. University Biomedical Strategy: the University's overarching approach in the biomedical arena is: "to pursue the highest quality biological, biomedical, clinical and population sciences research and translate this in a manner that delivers improvements of health and economic well-being". The joint Biomedical Strategy was developed by the Schools of the Biological Sciences and Clinical Medicine to support recruitment, enable critical mass, optimise infrastructure support, and promote engagement with key funders. The Biomedical Strategy helped to secure a Wellcome Trust Institutional Strategic Support Fund of £4.5M (Section 4.1). The 13 thematic areas of the Biomedical Strategy (*Developmental Biology; Stem Cell Biology and Medicine; Structural and Cell Biology, and its application to Medicine; Genomics and its application to Medicine; Application of Physical Sciences and Mathematics to Biomedicine; Cancer; Neurosciences and Mental Health; Infection and Immunity; Systems Medicine; Metabolic and Related Diseases; Cardiovascular and Respiratory Disease; Reproductive Biology and Medicine; Population Sciences - Epidemiology and Public Health*) reflect increasing collaboration with Physical Sciences, Technology and Social Sciences. The Cambridge UoA1 submission adopts the same thematic structure as the Biomedical Strategy. While UoA5 researchers are active in 10 of the 13 biomedical themes, our substantial non-biomedical activity meant that the biomedical themes were not suitable to structure our UoA5 submission.

2.2 Achievement and progress of strategic aims stated in RAE 2008

The major short and medium-term strategic objectives in our RAE 2008 submission focused on the Plant Biology theme, and included: laboratory refurbishment for Professor David Baulcombe and junior research teams; the Sainsbury Laboratory; the University Herbarium. A cross-theme interdisciplinary objective was the Physics of Medicine Building in West Cambridge.

• Laboratory refurbishment and redevelopment (£4.7M) in the Department of Plant Sciences provided major restructuring on the third and fourth floors resulting in wet and dry laboratory space for four teams, including Baulcombe and a newly recruited Lecturer, Ian Henderson. The new space accommodates up to 40 researchers and includes facilities for tissue culture, imaging, patch-clamping, handling of radioisotopes and hazardous chemicals and an air-conditioned room for a 96 node cluster with separate site back-up.

• The 11,000 m^2 Sainsbury Laboratory (£82M) was opened in 2011, with support (~£60M) for up to 10 group leaders and junior researchers for 5 + 5 years. The institute aims to develop an integrated understanding of plant development, setting the stage for a new synthesis that will draw on molecular, cellular, whole plant, and population biology to elucidate how plants are constructed. Attractive support packages, funded by the Gatsby Foundation, have helped to recruit internationally leading researchers with expertise in genetics, molecular biology, modelling and imaging. The Laboratory has state-of-the-art facilities for imaging, computational analysis, and plant growth. Experimental systems include model plant species, crops and bacteria. Professor Elliott Meyerowitz, FRS, was recruited as the Inaugural Director of the Laboratory (Jan 2011-Dec 2012); he is now a Distinguished Associate. Professor Ottoline Leyser, FRS, succeeded him as the Institute Director. Additional junior group leaders have been recruited, including James Locke, who was awarded the Merrimack CSB2 Prize in Systems Biology, 2013.

• The Cambridge University Herbarium (£3M) has been re-housed in a state-of-the-art facility in the basement of the Sainsbury Laboratory, co-locating >1M plant specimens, including Darwin's plants from the Beagle voyage, with the living plant collection on the Botanic Garden site. This has released research space in Plant Sciences (£1M) for a new lecturer – Dr Andrew Tanentzap.

• The Physics of Medicine Building opened in December 2008. It is aligned with the "Application of Physical Sciences and Mathematics to Biomedicine" theme of the joint Biomedical Strategy, and with a number of our themes (notably Developmental and Stem Cell Biology). Its

development has catalysed interactions between researchers in the Department of Physics and the Schools of the Biological Sciences and Clinical Medicine. The original interdisciplinary concept embodied by the Physics of Medicine Building has expanded with the formation of a Physical Biology Network to promote wider interactions. Physicists now work in different biological departments on joint projects; an annual "Physics of Living Matter" symposium highlights interdisciplinary research; and there is seed-funding for projects across the life and the physical sciences. These valuable cross-disciplinary interactions are increasing, attracting funding and promoting further inter-departmental collaborations. A key development has been the appointment of Professor Ben Simons (returned in UoA9) as the Herchel Smith Professor of Physics of Medicine; he is based, part time, in the Gurdon Institute and is a member of the Cambridge Stem Cell Centre.

Longer-term objectives in RAE 2008 included development of a Conservation Campus, upon which work has now commenced (Section 4.2.2), and the Downing Site redevelopment, which is progressing as a long-term estates plan (Section 4.2.2).

2.3 Mechanisms to disseminate and promote research

All departments have research seminar programmes with external speakers representing the forefront of their fields. These include annual prestigious named seminars (e.g. Anne McLaren Memorial Lecture). Additional seminar series and international symposia are organized by Strategic Research Initiatives (e.g. Cambridge Neuroscience; Cambridge Conservation Initiative). Numerous, less formal groupings (e.g. Stem Cell, RNA, Epigenetics, Evolution & Development, Evolutionary Genetics, and Cell Biology), hold seminars with researchers from across the University, WTSI, EBI, the Babraham Institute, Anglia Ruskin University, biotech companies, and often from London, Norwich and further afield. We host numerous visiting researchers, including 47 sabbatical visitors between 2008-13. Many sabbatical visitors hold visiting college fellowships, gaining added benefit from the interdisciplinary collegiate environment. Visiting researchers participate fully in the life of the hosting department and usually give one or more research seminars.

2.4. Major achievements of research groupings

Research highlights and achievements of our research themes are detailed below. To illustrate interdisciplinarity, we mention contributions of some researchers submitted by other UoAs; these are clearly indicated as such. Much of the forward planning in all research themes is based on a continued successful strategy of bottom-up investigator-led initiative. A number of themes, as indicated, also have more structured collaborative strategic goals.

2.4.1 Conservation, Behaviour and Ecology: activity in this theme falls squarely within the remit of the Conservation Strategic Research Initiative (established 2010). It covers a broad intellectual base, ranging from theoretical work modelling behaviour under different social and ecological conditions (Johnstone) to large scale surveys of major conservation issues that have direct policy impact (Sutherland) and the practical management of invasive species (Aldridge) (see impact cases studies).

In conservation, highlights include:

- study of the impact of agricultural development and deforestation on tropical biodiversity and, in particular, how alternative land use strategies can minimize biodiversity loss (Balmford, Gardner) concluding, controversially, that high intensity agriculture coupled with the preservation of pristine forest (land sparing) is more effective at preserving biodiversity than low intensity agriculture (land sharing) (see impact case studies).
- working with conservation practitioners including Rhys Green, RSPB senior scientist and Honorary Professor based full-time in the University. Field projects include reversing the precipitous decline of vulture populations in the Indian subcontinent caused by exposure to diclofenac. This has had a strong influence on the government policies of the four principal vulture range states (see impact case study – Rhys Green/SAVE programme).
- major projects with the UK Overseas Territories Conservation Forum, including rat eradication projects and population surveys of critically endangered species on oceanic islands (Brooke).

In behavioural ecology, highlights include:

- field and laboratory experiments on brood parasitic birds, revealing conflict and coadaptation (Hinde, Johnstone, Kilner), social transmission of host defences (Davies and Wellbergen) and

the role of genetic polymorphism in thwarting these defences (Thorogood, Davies).
- long term field studies of socially breeding mammals (Clutton-Brock), including the red deer of Rhum and the Meerkat populations at the Kuruman River Reserve, South Africa. Clutton-Brock's award-winning studies provide important understanding into how the diversity of animal societies affects the evolution of reproductive strategies and the operation of selection.

In community ecology, significant outputs have included:

- documenting the effects on canopy biodiversity of converting forest to oil palm and working with oil palm companies to monitor the effects of different management strategies on retained biodiversity (Foster).
- focusing on monitoring and management of invasive species, conducting survey work and working closely with e.g. water companies on the impact of zebra mussels in water treatment (Aldridge).

Future strategic plans focus on the development of the new Conservation Campus. This will bring together University researchers from biological and social sciences together with applied conservation researchers from a range of conservation NGOs to create a unique global campus to further conservation understanding, knowledge and expertise (Section 4.2.2).

2.4.2 Chemical and Structural Biology: work in this theme focuses on the molecular function of multi-subunit macromolecular complexes, particularly those involved in cell-signalling, protein-nucleic acid transactions, and assembly-line natural product biosynthesis; and in the engineering and directed evolution of enzyme catalytic function. Extensive collaboration occurs with researchers in other themes, notably Molecular Cell Biology, and in Chemistry, and there is increasing emphasis on integrative approaches to structural studies.

Research highlights have included:

- first high resolution NMR solution structure of a 7-helix trans-membrane receptor (Nietlispach),
- demonstration of how bacterial small RNAs guide RNase E to degrade target RNAs (Luisi),
- application of NMR-modelling approaches to single-cell chromatin conformation datasets to generate the first 3D models of chromosomal interactions in mammalian cell nuclei (Laue with Fraser, Babraham).

Other high-profile on-going programmes involve: fragment-based drug discovery, supported by strategic grants from the Wellcome Trust and the Gates Foundation (Hyvönen, Blundell); engineered biosynthesis of novel antibiotics and related natural products (Leadlay, Broadhurst); in vitro enzyme evolution using microdroplet compartmentalization (Hollfelder); super-resolution fluorescence microscopy to study the structure/assembly of protein complexes in live cells at near molecular resolution (Laue with Klenerman, Chemistry; see CAIC, Section 4.3).

Future strategic plans include increased use of cryoEM, using the new MRC LMB facility, and fluorescence and correlative microscopies for study of macromolecular assemblies. We envisage building on existing strengths in molecular enzymology and enzyme engineering to play a leading part in developing an internationally competitive activity in Synthetic Biology across the University (see Section 2.5). The Herchel Smith Chair of Biochemistry falls vacant in 2017 providing a valuable opportunity to recruit in this key area.

2.4.3 Developmental and Stem Cell Biology: activity in this theme aligns with the University Strategic Research Initiative in Stem Cells (established 2010). Major contributions in development and stem cell biology have had both basic and biomedical impact with particular emphasis on the early embryo and on neural systems, in addition to technological advances as applied to stem cells in culture. In stem cells, germ cells and early development sub-themes, these have included:

- identification of important novel concepts in stem cell biology with wider implications for development, including determination of a 'naïve ground state' within the stem cell (A. Smith),
- quantifying the inter-relationships between cell states at the earliest stages of embryogenesis (Martinez-Arias & Zernicka-Goetz),
- identification of new principles of germline inheritance including the epigenetic mechanisms underlying the erasure and reestablishment of the pluripotent state (Surani),
- identification of a novel factor regulating the transcriptional programme in oocytes (Gurdon),

- uncovering novel mechanisms for regulating cell polarity in germ cells (St Johnston).

In the neural development sub-theme, these have included:

- identification of the insulin-mediated activation of quiescent neural stem cells (Brand),
- in vitro differentiation of a functional cortical neuronal circuitry (Livesey),
- the ability to rejuvenate remyelination in the CNS resulting in improved prospects for regenerative therapies in Multiple Sclerosis (Franklin, submitted in UoA6).

Major contributions to understanding, quantifying and visualising cytoplasmic events and signalling processes contributing to changes in cell identity, shape and movement during development have been made. These have revealed the importance of local translation, uncovered roles for new molecules and novel roles for old ones and have been facilitated by the development of new visualisation tools and, in particular, stimulating exciting advances in computational modelling (Harris, Holt, Adams, Sanson, Simons (UoA9)). These have allowed us to forge new links with researchers in the School of Physical Sciences. These advances are underpinned by the grouping's creative use of appropriate model organisms and developing cellular systems including *Drosophila, C. elegans, Xenopus,* zebrafish, mice and, in culture, mammalian stem cells and induced pluripotent cell lines.

Future strategic plans build on initiatives already underway, including investment in the new Stem Cell Institute at the Biomedical Campus (Section 4.2.2) and the pending senior appointments in this theme. Attention will focus on the integration of our strengths in basic research in developmental and stem cell biology with the more translational activities associated with UoA1, as well as our links with large national strategic initiatives; for example, the Wellcome Trust's investment in iPSC research at the Hinxton Campus.

2.4.4 Evolutionary Biology: many developments in evolutionary biology lie at the interface of traditional disciplines. In Cambridge, strength in developmental genetics and genomics complements the traditional evolutionary disciplines of comparative and functional morphology, and population genetics. Activity in this theme has been strengthened by the recruitment of Paul Brakefield as Director of the Museum of Zoology.

In Palaeontology, systematics and functional morphology, work has exploited the collections of the University Museum of Zoology particularly in the study of vertebrate evolution:

- Our understanding of the emergence of vertebrates on land has been transformed through studies of the earliest tetrapods - work leading to coordination of a major NERC project to study some of the earliest terrestrial faunas (Clack). Professor Clack's pre-eminence in this area was recognized by the award of the Daniel Giraud Elliot Medal (2008) of the National Academy of Sciences, USA.
- A significant recent investment supporting research in this subtheme has been the purchase of a dedicated microCT scanner to allow non-destructive 3D reconstruction of the internal structure of skeletal, fossil and foetal material from irreplaceable archival specimens (Asher).

The genetic basis of animal diversity: building on its strength in Drosophila developmental genetics, groups studying developmental diversity and morphological radiation in insects and other arthropods have made major contributions including:

- comparative studies that have elucidated the evolution, function and regulation of genes controlling segment patterning (Akam).
- studying the adaptive radiation and evolution of mimicry in butterflies demonstrating that the evolution of mimicry involves the introgression of key genomic regions between distinct species (C. Jiggins).

Highlights in Evolutionary genetics involve the use of abundant sequence data to follow the process of evolution in populations and across lineages, and include:

- identification of regions under selection during primate evolution (Scally, Mundy).
- tracing dynamics of population evolution in humans and domesticated animals (Manica).
- work on virus and pathogen evolution showing consanguinity effects on infectious disease susceptibility (Amos) and quantifying adaptive evolution in immune cells (Welsh, F. Jiggins).

Future strategic plans include redevelopment of the Museum of Zoology (Section 4.2.2).

2.4.5 Functional Genomics & Systems Biology: work in this theme underpins much of the School's Basic Biomedical Strategy in Genomics and is focused on the Cambridge Centre for

Systems Biology (CSBC), fostering collaboration across several departments. The CSBC has continued to drive the integration of the large-scale experimental technologies that facilitate systems research and provides access to these technologies for the wider Cambridge research communities. Research has been assisted by continual upgrades and acquisition of state-of-the-art mass spectrometers and development of novel proteomic methodologies in the Cambridge Centre for Proteomics (Lilley) (Section 4.3). Key research achievements include:

- identification of high-flux-control genes of yeast by a system-wide approach (Oliver);
- demonstration of epigenetic modulation of adult neurogenesis via an imprint switch (Ferguson-Smith);
- discovery of specific epigenetic chromatin signatures in introns and exons (Ahringer);
- elucidation of epigenetic mechanisms preventing transgenerational retrotransposition in plants (Pazskowski).

Highlights in large scale bioinformatics projects include:

- major contributions to modENCODE, the large-scale NIH project to define functional elements in model organism genomes (Russell, Ahringer, Micklem).
- development of a platform for integration of genome data for multiple organisms via the Intermine platform, in addition to model organism database coordination (Micklem).
- development of a platform for integrating phenotype ontologies, Phenomenet, which uses formal definitions of ontology classes to generate equivalences between phenotypes in species-specific ontologies (Schofield).
- establishment of a mouse programme for the cell-specific quantification of genome-epigenome variation in the EU initiative BLUEPRINT (Ferguson-Smith).

The School has initiated a major review of ***future strategy*** in this theme, which is a priority area for the next five years. This will be facilitated by proposed recruitment to an endowed Professorship in Genome Biology (funded by a KAUST donation) and expansion of the Systems Biology Centre to reflect the increased requirements for interdisciplinary and quantitative approaches to research in genome biology across the Biological and Physical Sciences and Clinical Schools and even within Humanities and Social Sciences. The strategic review will explore development of the discipline alongside other initiatives including Imaging, Physics of Medicine, and Stem Cell Biology, and will be underpinned by its integration with developments in infrastructure and training in genome informatics and computational biology.

2.4.6 Molecular Cell Biology: this is a core theme that is highly integrated across the School and interacts with many of the other themes. The cell cycle, chromosomes and gene expression sub-theme crosses over with global analyses of gene expression at the epigenetic and post-transcriptional levels in the functional genomics and systems biology, development and stem cell biology, and plant biology themes. The cell cycle and DNA repair work aligns with the Strategic Research Initiative in Cancer, and with related cancer research in the disease biology theme. Major achievements in this area include:

- The solution to the 30 year old problem of how the rapid division of early embryos slows down at the mid-blastula transition (MBT). The Zegerman group have shown that this is through the titration of 4 limiting replication factors. Altering the amounts of these factors can advance or delay the MBT, with profound effects on development.
- novel insights into regulation of the DNA damage response by ubiquitin and ubiquitin-like modifiers has led to the formation of a second spin-out company, Mission Therapeutics, based on the concept of synthetic-lethality to target cancer cells (Jackson, recognized as BBSRC Innovator of the Year 2009).
- demonstration that hyperedited inosine-containing RNA potently antagonizes the interferon response (Scadden).
- demonstration of the role of piRNAs in multi-generational epigenetic memory (Miska).

In the cell signalling theme, there is particular interest in the assembly and function of receptors, including Cys-loop (Lummis), Toll-like receptors (Gay), collagen receptors (Farndale), P2X (Murrell-Lagnado) and other ionotropic receptors (Edwardson). Major progress has been made in understanding signalling downstream of receptor activation, including compartmentalization of cAMP generation and utilization (Cooper), inositol trisphosphate (IP3) signalling (Taylor, Baylis) and kisspeptin signalling (Colledge), and work on intracellular trafficking and cell-cell interaction

(Brown, Gallop, Irvine, Jackson). Highlights in this topic include:

- demonstration that IP3-induced clustering of its receptors retunes their sensitivity to both IP3 and Ca2+ (Taylor),
- work showing that phosphatidylinositol 4-phosphate (PI4P) contributes to the pool of polyanionic lipids that define plasma membrane identity (Irvine).

Future work in this theme will benefit from continued investment in cutting-edge facilities and infrastructure, such as imaging and proteomics (Section 4.3). In particular, single molecule imaging methods will increasingly be used to address problems in cell signalling. Recruitment to the Sheild Chair of Pharmacology will allow us to build upon strength in cell signalling.

2.4.7 Neuroscience: Cambridge Neuroscience, established as a Strategic Research Initiative in 2010, has cross-cutting research programmes in several sub-themes. Four of the sub-themes are represented in UoA5. The cognitive and clinical aspects are submitted in UoA4.

Development: In addition to the major achievements outlined in the Developmental and Stem Cell Biology theme (Section 2.4.3), major achievements in this sub-theme include:

- the developmental mechanisms that control the diversification of sensory neurons shed new light on the evolutionary trajectory of sensory systems since tetrapods moved onto land (Baker).
- pioneering work showing that local protein synthesis and degradation is necessary for axon guidance, branching, synapse formation and axon degeneration (Holt).

Molecular and Cellular: key achievements include:

- screening of Drosophila for drugs used to treat neural degenerative diseases such as Alzheimer's with implications for the next generation of therapies (Crowther and O'Kane).
- comparative research into NMDA receptors in the substantia nigra has led to deeper understanding of neural chemistry underlying some neurological and psychiatric diseases (Jones).
- the characterization of neurochemical and cellular mechanisms underlying state changes in the brain, such as shifting from solitary into swarming mode in the locust (Ott).

Sensory: Members study fundamental mechanisms involved in sensory transduction including audition, vision, and olfaction (Laughlin, Hedwig, Matthews). Some breakthroughs include:

- the discovery that the extremely fast light responses in Drosophila photoreceptors are due to the mechanical gating of stretch-sensitive trp channels (Hardie).
- Demonstration of the mechanism by which the species-specific temporal features of male song are mirrored in the response properties female auditory neurons (Hedwig).

Systems neuroscience: Systems Neuroscience is an area of growing strength in Cambridge. Particular achievements in this area include:

- finding that climbing fibres input to Golgi cells in the cerebellum induces long-term changes in their temporal firing properties – a new route of cerebellar motor learning (Edgley);
- the discovery of functioning mechanical gears that precisely synchronise left and right leg extension better than the nervous system could in a jumping insect (Burrows);
- optogenetic research showing left right asymmetry in the mechanisms of learning in the hippocampus, the behavioural consequences of which can now be investigated (Paulsen).

Future strategic plans focus on "The Neurobiology of Natural Behaviour", an initiative already endorsed by the School and Cambridge Neuroscience. The vision is of a physical centre with focused ambition yet strong interdisciplinarity, and will seek to unravel the mechanisms whereby nervous systems encode ethologically appropriate, evolutionarily adaptive behaviours. A combination of advanced imaging, molecular engineering, optogenetics, computation, and sophisticated ethological approaches will be used to revolutionize our understanding of animal brains. Our first faculty member in this area (Gonzalez-Bellido) has shown how target-selective neurons in dragonflies create a neuronal population vector that predicts the position of rapidly flying prey with high accuracy. More appointments in this exciting area are forthcoming.

2.4.8. Disease Biology: research within this theme encompasses diseases of humans, animals and plants, ranging from mathematical modelling of the spread of infectious disease to elegant switchable mouse models of cancer. Activity in the theme aligns with University Strategic

Research Initiatives in Cancer (2011), Infectious Diseases (2010) and Food Security (2011).

Recent highlights in Epidemiology of human and plant diseases include:

- Mathematical modelling of host-virus evolution to predict the likelihood of development of mammal-to-mammal transmissible H5N1 avian influenza A strains (D. Smith).
- Development of stochastic, spatio-temporal models and coupling with economic models to predict disease spread and effectiveness of control at landscape and regional scales (Gilligan).
- First theoretical framework to identify epidemiological effectiveness of biological control of fungal pathogens (Cunniffe).

Work in Microbiology encompasses prokaryotic and eukaryotic micro-organisms and includes infectious diseases, as well as much activity that relates to the Molecular Cell Biology theme. Highlights include:

- Characterization of a bacterial altruistic anti-phage mechanism involving non-coding RNA inhibition of a toxic endonuclease (Salmond).

The Molecular and Cellular Pathology subtheme has been substantially enhanced by strategic recruitments at professorial level of Gerard Evan (molecular oncogenesis) and Randall Johnson (tumour microenvironment), and appointment of Erica Watson (foetal development), Marc de la Roche (Wnt signalling) and Walid Khaled (molecular architecture of breast cancer) as Lecturers. Highlights include:

- Demonstration of how hypoxia in tumour cells and associated stromal fibroblasts is a critical force in driving tumour angiogenesis, inflammation and metastasis, and of how interplay between isoforms of hypoxia-inducible factor dictates the onset and spread of metastasis in breast cancers (Johnson).
- Use of novel models of switchable mouse genetics to toggle Myc on and off in lung, pancreas and mammary cancer models validate Myc as an effective therapeutic target for most, perhaps all, cancers (Evan).
- Use of a mouse model deficient in folate metabolism to demonstrate that the consequences of folate deficiency in human pregnancy include epigenetic instability and multigenerational developmental defects (Watson).

Future plans include, in the Cancer initiative, development of: a dedicated graduate programme in Cancer Biology; shared facilities for imaging cells, animals and patients; genetic and pharmaceutical platforms for assessing new cancer therapeutic targets (including a pre-clinical "Mouse Hospital"); and support for international collaborations. Activity in cardiovascular biology, currently spread across research themes, will benefit from a new Strategic Research Initiative in cardiovascular biology (November, 2013), strengthening links with the Clinical School.

2.4.9 Plant Biology: Plant Biology has been one of the major areas of recent strategic development within Biological Sciences at Cambridge, with major investments in new buildings and infrastructure and a series of senior level appointments. Researchers in this theme are active in three of the University's Strategic Research Initiatives: Global Food Security (2011), Energy (2011), and Conservation (2010). Major research achievements in this theme include:

- understanding fundamental carbon concentrating mechanisms in enhanced photosynthesis and identifying key features that are present in all plants irrespective of the efficiency of photosynthesis (Griffiths and Hibberd). The findings will shape a new generation of crops for sustainable food production and biofuels.
- major advances in understanding the regulation and function of the plant circadian clock including demonstrating that sugar is a regulator of the circadian clock of Arabidopsis (Webb), attracting industrial interest because of potential impact for improving crop plants.
- the discovery that movement of small RNAs between cells can establish epigenetic marks in recipient cell types (Baulcombe). This has implications for the behaviour of hybrids and stress tolerance in plants. The epigenetic landscape also appears to influence recombination frequency during meiosis in plants with relevance for variation (Henderson).
- finding that mechanical stresses and changes in elasticity can influence the outgrowth of early organ primordia, and also act as a cue for the positioning of the organ via hormone

polarization or patterning (Meyerowitz and Braybrook).

- co-discovery of the DNA binding code of plant pathogen TAL effectors, giving rise to numerous studies on their function and their application as activators, repressors and nucleases (TALENs) in animals and plants (Schornack).
- Industrial Biotechnology and Biofuels - including the use of algae for biofuels and development of the novel concept of synthetic ecology that exploits the mutualistic interaction of algae and bacteria to optimize culture systems (Alison Smith). Also, understanding the use of the plant cell wall as a feedstock for lignocellulosic ethanol production identifying enzymes to produce individual hexoses and pentoses that can be fermented (Dupree). Groups in this theme have also pioneered the use of photosynthetic organisms to generate electricity directly in "biophotovoltaic devices" (Smith, Howe, Davies, Fisher).
- high-tech spectral imagery developed, to reconstruct forest canopy images with relevance to forest dynamics/disturbance and recovery, and climate change via carbon sequestration. The work is relevant to REDD+ and carbon credits with implications for biodiversity, monitoring and ecosystem services with links to the Cambridge Conservation Campus (Coomes).

Future strategic plans include recruitment of six new group leaders (funding already in place), two at professorial level, to attain the full complement of 12 research groups in the Sainsbury Lab, as well as significant contribution to new activity in Synthetic Biology (Section 2.5).

2.5 Future initiatives

Future plans are driven by existing strengths and emerging opportunities. We will build on and lead the University Strategic Initiatives in Stem Cells, Cancer, Neuroscience, Conservation, Infectious Disease and Global Food Security. In addition to infrastructure plans (Section 4) and theme-specific plans (Section 2.4), we have identified three new cross-cutting priority areas:

- Physical and Mathematical Approaches to Cell Biology: it is proposed to provide dedicated space to allow theoreticians and experimenters from the mathematical and physical sciences to work closely with biological scientists in order to introduce and test new approaches to cell biology. The proposal will build on developments led by Simons (Physics and Gurdon Institute) and Martinez-Arias (Genetics) arising from Physics of Medicine, and the WT ISSF Internship scheme to attract postdoctoral physical scientists to work in biological labs. It will also link closely with Cambridge Systems Biology for bioinformatics and related experimental expertise and the Cambridge Advanced Imaging Centre (Section 4.3).
- Researchers in UoA5 have been early and prominent participants in the new field of Synthetic Biology. Interdisciplinary research activities are growing, with the appointment of new faculty (e.g. Locke, Schornack, Sainsbury Lab), and development of a range of partnerships with industry including Ceres, DNA2.0 and Microsoft Research (Haseloff, Ajioka (UoA1), Locke). The range of current activities includes Leadlay's engineering of novel bioactive molecules by modified assembly line biosynthesis (see impact case study), development of a parts registry for algal biotechnology (Alison Smith), and of arsenic biosensors for field use (Ajioka, UoA1). Cambridge has promoted open technologies for research, providing the first UK iGEM team, and initiating the OpenLabTools programme, supported by the Raspberry Pi Foundation. From November 2013, a new Strategic Research Initiative in Synthetic Biology, led by Haseloff, will allow us to expand the network of interdisciplinary collaborative activity with the Schools of Technology and Physical Sciences and with a wide range of outside organisations including: Autodesk, GSK, the BioBricks Foundation, NASA, OECD, National Institute for Agricultural Botany, Joint BioEnergy Institute LBNL, Woodrow Wilson Center and the John Innes Centre.
- The School of the Biological Sciences is driving a new initiative on Cambridge and Africa, with a well-established joint programme of applied research in infection and immunity with further plans to include research in food security.

c. People:

3.1 Staffing strategy and staff development

We aim to attract and retain the very best staff; to promote a sustainable staff structure with an appropriate balance of senior, mid- and early-career researchers and support staff; and to nurture career development and progression for all categories of staff. We expect all academic staff to be active in teaching and research and our staffing strategy is consequently driven by both teaching and research needs. The filling of all academic posts is agreed by the Council of

the School in line with the School strategic plan. Search committees for lectureships have representation from at least two departments and, where appropriate, seek advice from management committees of strategic initiatives and networks. New professorial appointments occur by electoral board, chaired by the Vice Chancellor, with participation of experts from outside Cambridge. Key professorial appointments, by research theme, between 2008-13 include: *Evolutionary Biology*, Michael Akam, FRS, to the Chair of Zoology; Paul Brakefield, FRS, from University of Leiden to the Directorship of the University Museum of Zoology; *Functional Genomics and Systems Biology*, Anne Ferguson-Smith to the Balfour Chair of Genetics; *Molecular Cell Biology*, Eric Miska to the Herchel Smith Chair in Molecular Genetics; *Neuroscience*, Ole Paulsen from the University of Oxford to the Chair of Physiology; *Disease Biology*, Gerard Evan, FRS, from the University of California San Francisco, to the Sir William Dunn Chair of Biochemistry; Randall Johnson from the University of California, San Diego, to the Chair of Molecular Physiology and Pathology; *Plant Biology*, Elliott Meyerowitz, FRS, from Caltech to the inaugural Directorship of the Sainsbury Laboratory (Jan 2011-Dec 2012); Ottoline Leyser, FRS, from the University of York to the Directorship of the Sainsbury Laboratory; Beverley Glover to the Directorship of the Botanic Garden.

In addition to established academic staff, we currently sponsor 34 independent research fellows supported by competitive externally funded fellowships from Research Councils, the Royal Society, the Wellcome Trust, Cancer Research UK and other biomedical charities. Since the last RAE, 22 early career researchers have been supported by Cambridge College Junior Research Fellowships. These fellowships are highly competitive, typically attracting >100 applicants across all disciplines, and often provide the first step on an independent research career. The Centre for Trophoblast Research also offers senior postdoctoral workers (currently 5) the opportunity to make the transition to independence via Next Generation Fellowships. One of these, Erica Watson, will be taking up a Lectureship in October 2013. The Herchel Smith Fellowship Fund for 4-5 senior postdoctoral fellowships pa. also facilitates the transition to independent research. Research fellows are encouraged to gain experience of undergraduate and postgraduate teaching as part of their career development.

During the assessment period > 30 Early Career Researchers and Research Fellows moved onto more senior group-leader positions in universities and research institutes in the UK and internationally (over thirteen countries). We view this as a positive outcome of our vibrant training environment. Examples include: Matthew Higgins and Swidi Ott (both RS-URFs), appointed to lectureships at the Universities of Oxford and Leicester, respectively; Lora Heisler (WT-SRF) to a Chair at the Rowett Institute, University of Aberdeen. Senior researchers recruited to leadership positions include; Jim Smith, Director of MRC NIMR; Jordan Raff, Cesar Milstein Professor of Molecular Cancer Biology, University of Oxford; Fiona Watt, Director of the Centre for Stem Cells and Regenerative Medicine, King's College, London.

Staff support and development: the University is committed to the principles of the Concordat to support Career Development of Researchers, and has received the European Commission HR Excellence in Research Badge in recognition of its work to foster career development for researchers. New Lecturers are given a clear outline of their expected contributions in research, teaching and administration. Training is provided in the form of the Pathways in Higher Education Practice scheme. New appointees have a mentor, usually a senior academic in the same department, and are initially given a lighter teaching load to allow them to establish their research programme. They are required to attend a training course on supervising graduate students in science. A competitive annual promotions procedure allows academic staff to apply for promotion to Senior Lecturer, Reader or Professor. Evidence is sought from international experts and final decisions are made by a Committee chaired by the Vice-Chancellor. In the six exercises since 2008, there have been 53 promotions of our staff. Staff have biennial appraisals to discuss progress, training and development needs. Identified needs can be met from the range of courses offered by the Personal and Professional Development programme. All University Teaching Officers (including part-time) are entitled to one term of sabbatical leave on full pay for each six terms of service, with no requirement to raise external funding for replacement teaching. Staff make use of this entitlement to refresh their research outlook and expertise, often at overseas universities. Central support facilities available to staff and students include Occupational Health, the Disability Resource Centre and the Counselling Service.

Postdoctoral researchers now comprise the largest staff group (37%) in the University. In

response to this growth, the University has initiated a major property development in North West Cambridge (NWC). In the first £300M phase, due to open in 2015–16, high-quality sustainable housing will be provided for over 600 postdocs and their families. Professor Chris Abell has been appointed to a new post of Director of Postdoctoral Affairs to develop strategy and act as an advocate for the entire postdoctoral community and to spearhead fund-raising for further NWC facilities. The University's Employment and Career Management Scheme, launched in 2011, provides a framework for induction, probation and appraisal of contract research staff. It provides researchers with clear role descriptions for each level of a research career, guidance on pay progression and information on promotions criteria. An initial induction meeting and Career Management Review (CMR) are held between the contract researcher and their PI to identify development needs and make arrangements for mentoring and appraisal. Further CMRs are held biennially. Online guidance on CMRs is provided for both PIs and researchers, along with a self-assessment tool for researchers. Postdocs have access to a bespoke Life Sciences programme run by the University Careers Service. The programme involves online careers advice, one-to-one sessions with a dedicated Life Sciences adviser, and regular seminar series on careers options and opportunities within and beyond academia. *"Postdocs Of Cambridge (PdOC)"* is a University Society for early career researchers (ECRs). Through its website, the society offers guidance to ECRs on opportunities within and outside Cambridge. It organises monthly social and networking meetings and seeks to represent postdocs in matters of career development and employment conditions. Departments and institutes organise additional support. Examples include annual postdoc retreats (Gurdon Institute) with discussions on career development and progression; teaching experience via a Postdoctoral Teaching Fellowship scheme (Biochemistry); annual postdoc research symposia and postdoc-led Masterclass and Techniques colloquia, with review and discussion of hot topics in Biological Sciences (PDN).

Equality and diversity: the University benefits from a highly diverse population of numerous nationalities. All our departments and institutes comply with the University's Combined Equality Scheme (CES) which was devised in response to the Equality Act (2010). The Dignity@Work policy sets out procedures for dealing with harassment, bullying and other inappropriate behaviours drawing on specialist advisors. In 2009, the University appointed three Equality Champions (around Gender, Disability and Race) who are available to members of protected groups and who provide overall leadership in diversity issues. In 2011-2012, the University was ranked 11th on the Stonewall list (the highest for any UK HEI) and won an Employee Engagement award from the Employers Network for Equality and Inclusion.

Staff have generous maternity and paternity leave entitlements, options of career breaks for up to two years and/or flexible working, and two workplace nurseries. A newly introduced Returning Carers Scheme, open to men and women, provides grants of up to £10,000 to individuals after periods of parental or carer's leave to assist their return to research. Within our UoA, 21% of tenured staff are women, compared to ~40% of PhD students and ~46% of postdocs. A number of mechanisms are being used to address the gender imbalance among tenured staff. The University's Women in Science, Engineering and Technology Initiative (WiSETI) promotes and supports women from undergraduate to professorial level in STEM disciplines at Cambridge. WiSETI organises a CV mentoring scheme for women applying for promotion, career development seminars for early career scientists, and talks from women scientists working in policy, industry and academia. Encouragingly, of the 51 academic promotions since 2008, 18 (35%) were for female staff. The WiSETI committee led the successful process to renew the University's Bronze Athena SWAN award in 2013. Four departments and institutes in this UoA have applied for Bronze or Silver awards in November 2013. In response to the 2012 School Staff Survey, and the Athena SWAN scheme, a series of workshops has been instituted including, for example, training to avoid unconscious gender bias in recruitment.

3.2 Research Students

Recruitment: we aim to recruit the highest calibre graduate students, focusing on PhD training, with a minority (<10%) of one-year M.Phil research students. We have a thriving community of >490 PhD students from >70 countries, many funded through competitive schemes, such as the Cambridge International Scholarship Scheme, Cambridge Commonwealth Trust, Cambridge Overseas Trust, the Gates Trust and the Islamic Development Bank. During the assessment period, 712 PhD degrees were awarded. In addition to department-centred doctoral training, we

have a number of interdepartmental 4-year PhD programmes that include first-year rotation projects designed to give a broad experience of the subject area:

- BBSRC Doctoral Training Partnership. This flagship programme has four main research areas: Basic Biosciences Underpinning Health, Bioenergy and Industrial Biotechnology, Food Security and World Class Underpinning Bioscience. The programme includes a three-month professional internship. 31 new students will be joining the programme in October 2013.
- The Wellcome Trust PhD programme in Developmental Biology admits six students per year.
- The British Heart Foundation PhD studentship programme in cardiovascular research. The programme admits 4-5 students per year with an emphasis on interdisciplinary research.
- The Wellcome Trust PhD Programme in Stem Cell Biology admits 4-5 students per year.

We have 3-6 studentships per year from the University's MRC Doctoral Training grant and we participate in international collaborative graduate programmes, including the Herchel Smith Fund, providing four life sciences PhD studentships annually, including support for a conference with Herchel Smith funded students at Harvard and the Howard Hughes Janelia Farm Graduate Programme (2-3 students per year) in which students spend time in both Cambridge and Janelia Farm. During the assessment period, 49 CASE or equivalent collaborative studentships have been held with a range of industrial partners.

Training and support: all research students are affiliated with a department and a college. The departments and institutes provide the research training environment, while the Colleges provide pastoral care and a uniquely vibrant interdisciplinary social environment. Students are advised to spend 10 days/year undertaking training and to keep a skills development log. The **Graduate School of Life Sciences** provides training support for all life sciences graduate students across the University and associated institutes, providing access to a wide range of courses including a basic training schedule for PhD students wishing to pursue academic or non-academic careers. The programme includes induction events, presentational courses, writing classes and a range of subject-specific classes, developed by particular departments, but open to all research students to enhance their breadth of knowledge and the scope of interdisciplinary study. Additional courses are available in: statistics through the University Statistics Clinic; courses provided by the University Computing Services; the 'Rising Stars' public engagement programme run by the Office of External Affairs and Communications. Training in business and entrepreneurship is provided by: the Centre for Entrepreneurial Learning; The Cambridge University Technology and Enterprise Club, a student-run organisation, hosting talks, workshops, mentoring and networking sessions; the i-teams Cambridge scheme, in which multi-disciplinary teams of students work with researchers and industry mentors to investigate potential markets for University produced technology. The success of this approach is demonstrated by the award to a Cambridge team with UoA5 PhD students Alap Chavda and Anastasia Kamenska of the £1,000 top prize in the 2012 Biotechnology Young Entrepreneurs Scheme (YES).

Research students are fully integrated into the research life of their departments and benefit from a rich programme of research seminars and symposia (Section 2.3). For example, the Conservation science group plays a leading international role in graduate education, through the Student Conference on Conservation Science, launched in Cambridge and now mirrored at sites in Bangalore, New York, Australia and Beijing. Over 14 years, this annual conference has brought 2,300 delegates from 119 countries to network and learn new ideas in Cambridge.

Assessment: PhD students are assessed at the end of their first year by a dissertation on their work to date and future plans. An oral examination is held with two academics independent of the supervisor. Students present seminars to their Department, usually in their first and third years. Supervisors review academic performance, identify appropriate training courses and submit termly reports (available to the student) to the Department and University, in which any problems are highlighted. Independent advisors provide additional feedback and support as needed. The PhD dissertation is examined by two examiners, one of whom is external to the University; their reports are forwarded to the student and supervisor after the oral examination.

d. Income, infrastructure and facilities

4.1 Income

Our current portfolio of grants includes over 450 awards (57% UK charities, 24% Research Councils, 15% EU and 4% Overseas, UK Government and Industry) with a value in excess of £300m. Changes since RAE 2008 include 7.4% average growth in research income, well in

excess of inflation, and an increase in number of >£1M grants e.g. Brindle, £5.3M, Wellcome Trust Strategic Translation Award and CRUK (Section 5.3). The Wellcome Trust (WT) remains the major funder (current grants £112M; >60% of charity income), followed by BBSRC (£42M) and MRC (£21.5M). We continue to diversify funding sources with significant growth in EU funding and major grants from the Gates foundation (Hibberd, Gilligan, D. Smith, Blundell, Oliver, total £3.9M) in drug discovery and epidemiology. We successfully renewed core grants for the Gurdon (£11.6M) and Stem Cell (£6.5M) Institutes, negotiated the first five year core support grant from the Gatsby Foundation (£24.4M) for the Sainsbury Laboratory, and The Centre for Trophoblast Research endowment was renewed (£5m over 5 years). Other strategically important awards with significant research support, providing investigators with intellectual freedom to develop new areas, include the following: WT Principal Research Fellowships (Johnson, St Johnston; £9.9M total); MRC Professorial Fellowship (Austin Smith £2.4M); Royal Society Professorial Fellowship (Baulcombe, £0.8M); WT Senior Research Fellowships, £11.44M (Ahringer, Lummis, Pellegrini, Hendrich, Zernicka-Goetz). WT Senior Investigator Awards (Ferguson-Smith, Gay, Gurdon, Harris, Lawrence, Livesey, Surani, Taylor, £15.4M total) and a New Investigator Award (Sanson, £0.57M). ERC Advanced Investigator (Baulcombe, Brakefield, Clutton-Brock, Evan, Holt, C.Jiggins, Leyser, Martinez Arias, total €17m) and Starting Investigator schemes (Burdakov, Carazo Salas, Frye, Gallup, F.Jiggins, Kilner, Miska, Rasler and Wigge, total €14m). Cambridge UoA5 has also supported 27 RS URFs since RAE 2008.

In conjunction with the School of Clinical Medicine, we have secured a Wellcome Trust Institutional Strategic Support Fund award of £1.5m per annum, for a 3-year pilot period (2011-14). The award is equally matched by other institutional funds to support key strategic research themes through: Recruitment/ start up packages for new academic staff; support for strategic platform technologies; an internship programme to embed mathematical and physical sciences approaches within biomedical research groups; bridging funding for exceptional grant-funded staff/ fellows. Awards include £650k to support the professorial appointments of Eric Miska and Anne Ferguson-Smith and £50k start-up packages for six new University Lecturers.

Strategically important income is also provided by University and College endowments. Examples include: the Newton Trust, administered by Trinity College, provides support to supplement external funding (~£1.9M since Jan 2009); King's College funded four year fellowships in interdisciplinary research in food security and in economic epidemiology. King Abdullah University of Science and Technology (KAUST, $10M) provides flexible funding that is being used for leverage in bioscience and bioengineering. The Gatsby Foundation provides start-up packages (£200k over 5 years) for 5 Career Development Fellows in the Sainsbury Laboratory.

4.2 Infrastructure

We are housed in thirteen buildings in central Cambridge on the New Museums, Downing, and Tennis Court Road sites and the nearby Botanic Garden. Each building accommodates 100-200 researchers, local administrative and teaching units. A rolling programme of refurbishments aims to optimise research space within the physical constraints of our older buildings, many dating from 1900-1940, and consistent with teaching needs (Section 4.2.1). Our building and refurbishment projects are carried out within the context of the University's Environmental Policy: "In achieving excellence in teaching and research, the University of Cambridge aims to manage its activities, buildings and estates to promote environmental sustainability…".

4.2.1 New buildings and refurbishments, 2008-2013

The **Sainsbury Laboratory** is the principal new building (Section 2.2). Opened in 2010, this landmark building was awarded the 2012 RIBA Stirling Prize. The School has invested >£16M within UoA5 for strategic building refurbishment since 2008 including: laboratory refurbishments to improve facilities for the incoming Regius Professor of Botany (Baulcombe), other existing groups (Davies, Webb) and new research fellows in Plant Sciences (Section 2.2); laboratory refurbishment to house the incoming Sir William Dunn Professor of Biochemistry (Evan), to improve research facilities and relocation of 10 groups; major refurbishment to improve support for research groups in association with the new Professor of Genetics (Ferguson-Smith). New zebra fish (£1M) and behavioural suites (£3M) have also been completed.

4.2.2 Future building plans include a series of ambitious developments:

The Arup building and Zoology Museum: work on the Conservation Campus (£60M) started

in Sept. 2013, with projected completion in Oct. 2015. Formally launched by Sir David Attenborough in April 2013, the refurbished Arup building (13,400 m^2), adjacent to the Department of Zoology, will house 500 University and NGO staff. The project will also involve complete refurbishment of research and exhibition facilities in the Museum of Zoology and adjoining laboratories in the Department of Zoology for Akam and Brakefield, and for the new Prince Philip Professor of Evolution and Ecology (succeeding Clutton-Brock). The Conservation Centre will bring together applied conservation scientists from seven NGOs (BTO, RSPB, TRAFFIC, Tropical Biology Association, IUCN, Birdlife International, Fauna and Flora International), together with basic and applied researchers from the biological and social sciences in six University Departments. The Museum refurbishment will enhance the use of collections in the teaching of Zoology and completely renew the public displays and outreach activity while showcasing our research.

Stem Cell Institute: a new building with 8000m^2 of research space is planned on the Biomedical Campus, with a planned start date in the first quarter 2015. The projected cost is £60M, with £8M committed by the Wellcome Trust and MRC. The new Institute will unite 30 leading research teams with expertise in embryonic, adult and induced pluripotent stem cell biology and will allow fundamental and translational stem cell research to be integrated at one location. Research scientists will work alongside technology specialists and clinicians to develop new therapeutic approaches underpinned by a strong base of fundamental stem cell biology. Key areas of research will include pluripotency, haematopoiesis, epithelial tissues, and neural and cardiovascular stem cells. Following relocation, the current WT Stem Cell Biology building is earmarked to accommodate up to two new planned initiatives (Sections 2.5, 2.4.7).

[Text removed for publication.]

Downing Site Redevelopment: the long-term estates plans for redevelopment of the main Biological Science site over 15-20 years include three new buildings of total capacity 12,450m^2. This will facilitate: realignment of research groupings that are prevented by the constraints of our current buildings; development of cross-School support services and a modern teaching block.

4.3 Research facilities

There has been a major change since RAE 2008 in consolidating and providing high-quality facilities and technical support for key resources. This extends from planned major investment with £150M committed for animal facilities (Section 4.2.2) through School investment of £3.9M supported by the Wellcome Trust, Newton Trust, Wolfson Foundation in rationalising imaging, proteomics, metabolomics, structural biology, bioinformatics training with on-going reviews to optimise provision of DNA sequencing, computing resources and support. Major bids for equipment are now reviewed at School level to optimise strategic use. The University has introduced schemes to support purchase of equipment through providing matching funding to partner with RCUK/ other sponsors' contributions. In the spirit of the Wakeham Review, we are developing a comprehensive inventory to promote sharing of equipment and services. The University also participates in the Science and Engineering South Equipment Sharing Project. Major innovations that set the model for improvement of resource to researchers across multiple themes are summarised below.

The recently completed **Cambridge Advanced Imaging Centre (CAIC)** (£8M from the School, the Wolfson Foundation and the Wellcome Trust) provides a University hub for the development of, and access to, state-of-the-art imaging facilities. The Centre, led by Harris, was developed as part of a strategic review to coordinate integration, access and development of microscopy facilities across the University. The strategy involves core facilities for advanced microscopy at hubs where physical scientists and biologists work together to develop cutting-edge microscopy that is widely available to the scientific community at Cambridge. The central CAIC hub is in PDN, with complementary hubs in the Gurdon Institute and Sainsbury Laboratory. CAIC provides an opportunity to build new generations of microscopes (led by Kaminski, Chemical Engineering and Biotechnology, and Klenerman, Chemistry) that are flexibly designed to improve sensitivity, resolution and speed in tackling dynamical imaging challenges in developmental biology and neurosciences. The facility already has or soon will have: state-of-the-art Transmission and Scanning Electron Microscopes, Multiphoton Confocal Microscope with adaptive optics, Far-field Individual Molecule Localization with Total Internal Reflection Fluorescence microscope, Gated Stimulated Emission Depletion microscope (g-STED) with Reversibly Switchable Optical

Fluorescence Transition, Light Sheet Fluoscence Microscope (LSFM) to work with embryos, High Resolution LSFM, Capture Microscope and two standard confocal microscopes. The facility has initial 300Tb storage, and the support of three dedicated staff.

The **Cambridge Centre for Proteomics** (CCP) houses a range of mass spectrometry instrumentation for protein identification, absolute and relative quantification and analyses of post-translational modifications. A University strategy for biological mass spectrometry ensures complementary development of the CCP and facilities at the Cambridge Institute for Medical Research, the CRUK Cambridge Institute and the MRC-LMB. The CCP benefits from the research programme of its director (Lilley) and has expertise in proteomic method development, bioinformatics and biostatistics for quantitative proteomics. Combined with a rolling programme of instrument upgrade, this facilitates service access to state-of-the-art technology and methodologies, and transfer of these to the other local proteomic facilities. The Metabolomics Facility provides NMR and mass spectrometry analysis of lipid and soluble metabolites. Researchers in structural biology access major synchrotron facilities such as Diamond and Grenoble, complemented by upgraded in-house facilities: crystallography facility (upgrade 2011-12, £1M Wellcome Trust) with X-ray diffraction system, 3 crystallization robots and automated crystal imaging; biomolecular; NMR facility (upgrade 2010/11, £500K Wellcome Trust), with 800, 600 and 500 MHz Bruker NMR spectrometers, all with cryoprobes, and an additional 500 MHz spectrometer; a new Biophysics Facility houses a range of instrumentation for analysis of biomolecular structure and interactions.

Given the rapid development of DNA sequencing technology and the successful establishment of technological platforms utilised across the research themes, our strategy for sequencing and the associated informatic support is under review. In particular, a high priority is being given to the expansion of capital infrastructure for computational biology and bioinformatics and the integration of cross-School facilities into a unified core that includes the purchase of an additional Illumina HiSeq machine. The DNA Sequencing facility in Biochemistry continues to provide traditional sequencing services along with next generation sequencing (NGS) via Roche 454 Genome Sequencer FLX, and Illumina MiSeq. Genomics services in Systems Biology and Pathology provide a MiSeq facility and a range of array services for transcriptome, genotyping and DNA methylation analysis. These are all associated with the development of tools and analysis pipelines for custom integration of high throughput genome wide datasets and the application of computational approaches to address hypothesis-driven questions and theoretical modelling applications arising from them. Researchers in UoA5 have also invested in Illumina sequencing facilities at the CRUK Cambridge Institute and the Babraham Institute, and there is considerable collaborative research with members of the Wellcome Trust Sanger Institute and EBI. Other specialist facilities include: flow cytometry (Stem Cell Institute, Pathology, Clinical School Cell Phenotyping Hub); fermentation facility for systems biology and recombinant protein expression; various model organism facilities (*Drosophila*, Zebrafish); an array of very high performance plant growth facilities at the Sainsbury Laboratory and Botanic Garden. Support services are available in bioinformatics and computational biology within departments and at School level. For high performance computing, researchers have access to the ~1000 core resources of CamGrid and, from 2014, the £20M West Cambridge Data Centre. Research is supported by the University Library, a legal deposit (copyright) library with >2M volumes, access to 21,000 full-text electronic journals, ~400 databases and a growing collection of e-books.

e. Collaboration and contribution to the discipline or research base

Collaborative, interdisciplinary research is an established part of our research culture, which has been further strengthened by our Strategic Research Initiatives and Networks (Section 2.1.1), and very recently by an agreement with the São Paulo Research Foundation to provide seed-funding for collaborative projects involving researchers in the School of Biological Sciences and Brazil. Our researchers contribute to the discipline and research base in many ways. We can only summarise some examples here.

5.1 Peer review and strategic contributions to research strategy

All our researchers are expected to engage as 'good citizens' in external peer review. Most exceed these minimal expectations. Among >170 editorial board memberships are internationally prestigious journals such as *Cell* (Baulcombe, Surani), *Science* (Brakefield, Ferguson-Smith), *PLoS Biology* (Harris, Martinez-Arias), *Cancer Cell* (Evan), and *e-LIFE* (Ahringer, Baulcombe, Brand, Ferguson-Smith, Pines). Glover is Editor in Chief of the Royal

Society's open access journal *Open Biology*. During the assessment period, 47 individuals served on committees of national funding agencies including research councils and major Charities (69 memberships in total), and 31 on other international funding bodies (40 memberships in total) including the European Research Council (St. Johnston, Ahringer, Akam, Brakefield, Luisi). Amongst major advisory/strategy roles, Blundell is Chair of BBSRC Council (2009-15), Baulcombe a member (2009-14), and Gilligan chairs the Defra Science Advisory Council (2011-14). Brakefield and Evan are members of the REF 2014 UoA5 committee.

5.2 Membership and contribution to academies

Many of our researchers are elected members of prestigious national and international academies including the Royal Society (29 total, 8 elected 2008-13), the Academy of Medical Sciences (15 total, 5 elected 2008-13), and the European Molecular Biology Organization (29 total, 9 elected 2008-2013). Elections to overseas academies since 2008 include: Academia Europea (Austin Smith, 2010), US National Academy of Sciences (Leyser, 2012), the Indian National Academy of Sciences (Baulcombe, 2011), the American Academy of Arts and Sciences (Clack, 2009) and the Dutch Academy of the Arts and Sciences (Brakefield, 2011). Significant contributions to the work of academies include: Thomas, Biological Secretary and Vice-President of the Royal Society (2008-); Leyser, RS Council member (2012-13) and a member of the working group that prepared the RS 2011 State of the Nation Report on school to university transition in STEM subjects; Baulcombe, RS Council member 2008-9, chaired the working group that prepared the Reaping the Benefits report on biological science and sustainable crop production; Leadlay, represented the RS in co-organising three complementary symposia on Synthetic Biology in London, Shanghai and Washington and co-authored a widely circulated European Academies (EASAC) report on Synthetic Biology. Other contributions include EMBO (Austin Smith, membership committee; Bray, Fellowship committee; Ferguson-Smith, Young Investigator Award Panel); Nuffield Council on Bioethics (Leyser, member Report on Biofuels).

5.3 Collaboration with Government, government agencies, the NHS and industry

Such collaborations often lead to impact beyond academia; additional examples are given in our Impact Statement and case studies. Selected examples are listed here: Clutton-Brock has advised Defra on badger dynamics and control, Dicks on ecosystem services indicators for pollination. Sutherland serves on Natural England Science Advisory Board, Defra Review of England's wildlife network. In Epidemiology, Derek Smith is Director of WHO Collaborating Centre for Modelling Evolution and Control of Emerging Infectious Diseases and a Member of the WHO influenza vaccine strain selection committee that recommends the vaccine strains for 350 million doses of vaccine per year. He has advised the US and Dutch governments on the risk of A/H5N1 avian influenza virus evolving to become human-to-human transmissible. Outputs from Gilligan's epidemiological models have been used by the UK Government to set policy for the ash dieback disease; variants of the models are also used to inform disease control and sampling strategies for Defra (Sudden Oak Death) and USDA (Sudden Oak Death and Citrus diseases) with $4.3M support from the Gates Foundation to apply the models to global threats from wheat diseases and cassava viruses in Africa. Gilligan chaired the UK Government Taskforce on Plant Biosecurity leading to a national risk register and contingency plans for invading plant pests and pathogens. In collaboration with GE Healthcare, Brindle has developed metabolic Magnetic Resonance Imaging and hyperpolarized ^{13}C-labelled cell substrates as a tool for monitoring tumour responses to treatment (see impact case study). In a three-way collaboration (GE Healthcare, University of Cambridge, Addenbrooke's NHS Trust), the ability of a clinical hyperpolarizer to detect treatment response in lymphoma, glioma and breast cancer patients is being tested. The Cambridge Partnership for Plant Sciences (Griffiths, Alison Smith) links University and industrial research. The Bioenergy initiative (Howe, Dupree, Alison Smith) brings together plant scientists, biochemists, conservation scientists, engineers, chemical engineers and economists, to develop sustainable, ethically and socially responsible forms of bioenergy. The Dupree research group on lignocellulose bioenergy leads one of six research hubs in the BBSRC Sustainable Bioenergy Centre and has an on-going association with Shell Global Solutions (providing 14 postdoc-years). Many of our researchers sit on the Scientific Advisory Boards (SABs) of companies and research institutes. Examples include: Blundell, SAB UCB Celltech; Dupree, SAB for the US Department of Energy Joint Bioenergy Institute, California; Ferguson-Smith, SAB NIMH Silvio Conte Center, Harvard University, USA; Pines, SABs Cell Biology Unit, Institut Curie, Paris and Institute of Biochemistry, ETH, Zurich;

Brakefield, SAB Netherlands Centrum of Biodiversity Naturalis.

5.4 Contribution to research networks and community resources

Our researchers contribute in various ways to research community resources and projects. For example, Laue has led the Collaborative Computing Project for NMR (CCPN), which develops software for the biomolecular NMR community in academia and industry (see impact case study). Laue has also led a community-wide discussion and engagement with funders to develop a national strategy for UK biomolecular NMR infrastructure. Micklem plays a leading role in developing open source community resources such as the data warehouses Intermine, Flymine, metabolicMine, modMine: http://www.micklemlab.org/resources. Other significant contributions to community resources are listed in the Functional Genomics & Systems Biology theme (Section 2.4.5). Our researchers have engaged with numerous multi-PI collaborative grants such as EC Networks of Excellence involving academic and industrial partners including: EPIGENOME, EpigeneSys, BLUEPRINT (Ferguson-Smith, Surani); EURASNET (C Smith); SIROCCO (D Baulcombe coordinator – 23 groups on small RNAs in plants and animals); EnAlgae (Alison Smith, Howe); Austin Smith and other members of Stem Cell Institute have been involved in numerous networks including NeuroStemCell, BetaCellTherapy, EuraTrans, SyBoSS, Eurostemcell, EuroSyStem, BLUEPRINT, EpiHealth. Collaborative interdisciplinary working is also promoted by joint appointments. S. Jackson is an Associate Faculty member at the Sanger Institute; Griffin has a 50% appointment with MRC Human Nutrition; Brindle has a 50% appointment with CRUK Cambridge Institute; Fisher has an 80% appointment at Microsoft Research (20% Biochemistry).

5.5. Prizes represent a measure of recognition of contribution to the discipline; these have included early and mid career as well as established scientists in this UoA. Foremost amongst senior personnel is the Nobel Prize for Physiology or Medicine for Sir John Gurdon in 2012 who was also awarded the Lasker Prize in 2009. Other senior awardees include: Baulcombe (Lasker Prize, Basic Medical Research Award, 2008; Harvey Prize for Science and Technology; Wolf Prize for Agriculture, 2010; Balzan Prize 2012); Austin Smith (Prix Louis-Jeantet for Medicine, 2010); Jackson (BBSRC Innovator of the Year, 2009; Royal Society Buchanan Medal, 2011); Leadlay (Smets Prize Chair, 2010; Humboldt Research Prize of the Alexander von Humboldt Foundation, Germany, 2011-2012; Inhoffen Medal of the Helmholtz-Zentrum für Infektionsforschung (HZI) awarded for excellence in natural products research, 2012); Hardie (Rank Prize in Optoelectronics, 2012); Holt (Remedios Caro Almela Prize for Research in Developmental Neurobiology 2011); Martinez-Arias (Waddington Medal, British Society for Developmental Biology, 2012); Fowden (Joan Mott Prize of the Physiological Society, 2008); Ferguson-Smith (2010: Aaron E Szulman Prize Lecture, University of Pittsburgh); Burton (Wim Schellekens Foundation Visiting Professor, Universities of Maastricht and Nijmegen 2013); Clack (Daniel Giraud Elliot Medal, National Academy of Sciences, USA, 2008); Akam (Zoology Medal, Linnean Society, 2009); Irvine (J.R. Vane Medal, British Pharmacological Society, 2010).

Prizes for early career research include: Miska (Hooke Medal, British Society for Cell Biology, 2013); Ralser (Wellcome Trust, Wellcome-Beit prize, 2010); Nichols (NC3Rs prize 2009; Suffrage Science Award, 2013); Gardner (British Ecological Society Founders Prize 2012); Locke (Merrimack-CSB2 Prize in Systems Biology, 2013).