Institution: University of Oxford

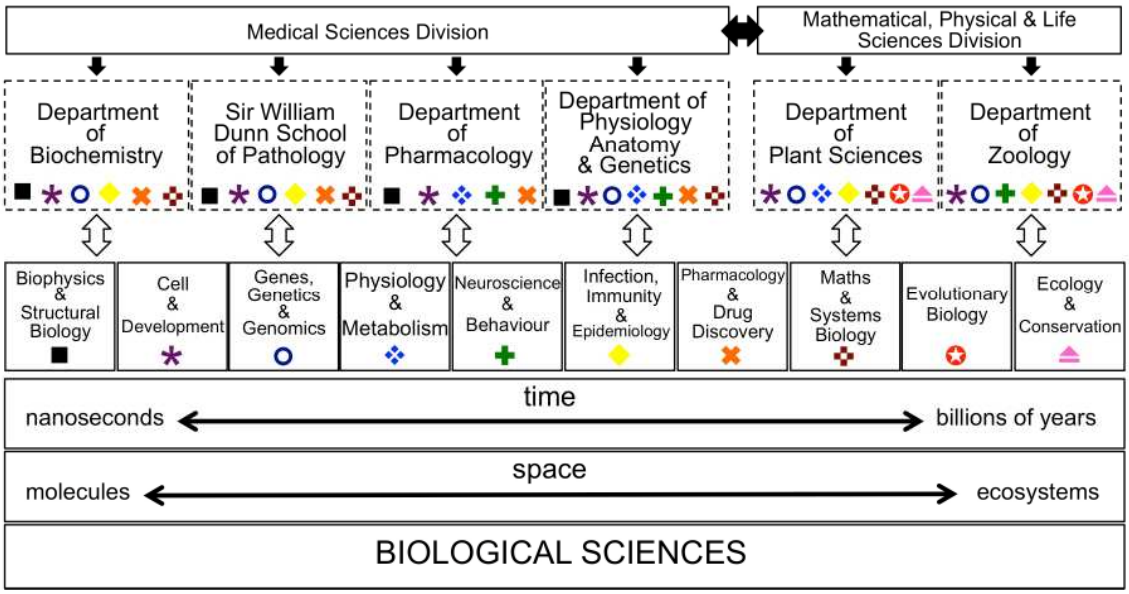
Unit of Assessment: UoA5 Biological Sciences

a. Overview

Aims. The University of Oxford's biosciences strategy is focussed on excellence in research and impact. Our strategy is underpinned by a strong commitment to inclusiveness and to sustainability through recruitment, training and early career support. Over 600 independent research groups are active across the spectrum of life sciences covered by REF Panel A. Research submitted to UoA5 is at the centre of this spectrum, pivoting to interface with clinical medicine on one side (UoA1, 2 & 4), and environmental and physical sciences on the other (UoA7-10). Across UoA5, research aims to understand biological processes, at scales ranging from molecules to populations, in spheres from human health to natural ecosystems, and at timescales from nanoseconds to billions of years. This breadth and depth of activity is founded on ten major thematic areas (Box 1).

Organisation. This submission returns 226 staff (223.8 FTE), 98% of whom are based in one of six departments that together occupy 58,000m^2 of space, employ ~450 postdoctoral research assistants at any one time, and admit ~130 graduate research students each year. The Departments are embedded in two of the University's four administrative Divisions: the Medical Sciences Division (MSD) and the Mathematical, Physical & Life Sciences Division (MPLS) (Box 1).

Box 1: Structural organisation showing divisional affiliations, departmental units, breadth of research across the submission, and the ten thematic groupings for research activities.



Distinctive Achievements 2008-2013. Research excellence across the breadth of biosciences, with strong links to clinical, environmental, physical and social sciences, is evidenced by:

- **Substantial advances in knowledge** through the publication of more than 5500 papers in ISI-indexed journals across ten major areas of bioscience.
- **Major capital expenditure** on new buildings and infrastructure exceeding £130M.
- **Investment in leadership** with appointments to 23 newly established or released Chairs.
- **Capacity building** through recruitment and mentoring of 68 new independent investigators.
- **Training of ~600 graduate research students**, 84% of whom entered bioscience careers.
- **Sustained success in obtaining external research funding** with over £260M awarded.
- **Initiation of more than 30 new research programmes** that align with national and international agendas on disease dynamics, regenerative medicine, health, food security and biodiversity.
- **External recognition** with 5 FRS, 9 FMedSci and 9 EMBO elections; 4 L'Oreal Women in Science Awards; 1 DBE, 2 CBEs and 1 OBE.

b. Research strategy

b1. STRATEGIC AIMS

Research in UoA5 strives to attain and sustain excellence across the **breadth of the biosciences**. Strategy is focused around ten aims that are implemented through a governance mechanism that focuses teaching, administration and subject-specific research in departments, whilst promoting and supporting interdisciplinary research through extensive interactions within and between the MSD and MPLS divisions. Necessarily, components of our research strategy relate to the strategy for impact.

Aim 1: Build Capacity by Investing in People

Our strategy for capacity building is based on recruiting, training and mentoring the best scientists. Success in these endeavours is illustrated by:

- **Recruiting leaders**: UoA5 invests in around four senior professorial appointments a year, using them to launch new research directions or to build capacity in existing strategic areas.
- **Academic staff development**: our commitment to the career development of all staff is evidenced by the 26 University Lecturers (ULs) who were awarded tenure during the REF2014 period, the 16 who received professorial titles and the 9 who were appointed to high-profile Chairs elsewhere.
- **Feeding the academic pipeline**: more than 7 senior research fellows join UoA5 each year, having secured prestigious fellowships that act as springboards for their independent careers. Over 90% establish a competitive research programme and are successful in obtaining further senior fellowships or tenure-track positions, either in Oxford or elsewhere.
- **Recruiting and training the best graduates**: applications for our graduate research programmes exceed capacity by over 5:1, requiring extremely competitive criteria to be met for acceptance. ~85% of these highly skilled students go into a biosciences related position after graduation, with 55% staying in academia and 10% going into the commercial sector.

Aim 2: Create a Dynamic Environment for Teaching & Learning Across the Subject Breadth

Research and teaching are intricately connected across UoA5, with a strong research base driving the highest standards of education, and with all undergraduates actively engaged in research. Over 90% of the individuals returned in this submission teach on a regular basis. The University centres teaching and learning around departments. This organisational structure ensures the stability of core subjects regardless of current trends, and retains breadth across the discipline. This strategy delivers:

- **Distinct strengths**: retaining critical mass in subject-specific areas provides internationally recognised cohorts of research excellence. For example, the Department of Zoology is a leading centre for research in whole organism biology, and the Department of Plant Sciences has one of the largest groups of plant scientists in any university in the UK.
- **Wide-ranging expertise**: there is a large community of senior scientists in UoA5 (86 professors) that is actively inspiring the next generation of researchers. Educating across an academic range from atoms to ecosystems, our research-led undergraduate courses are consistently rated one of the top each year nationally in student satisfaction surveys.

Aim 3: Invest Substantial Capital Funds in Facilities and Infrastructure

The University has a policy of investing capital to leverage funding from external sources, and has a commitment to provide the best research facilities. Examples over the REF2014 period include:

- **New buildings**: The New Biochemistry building opened in 2008, providing 12,000m^2 of state of the art laboratories for molecular and cellular research. The Oxford Molecular Pathology Institute (OMPI) building was subsequently opened in 2011, providing outstanding lab and office space for about 250 scientists. Plans to establish a Synthetic Biology Institute in OMPI are underway: this Institute will bring together biologists, chemists and physicists to synthesise novel compounds in a range of biological vehicles.
- **Technology platforms**: the University has invested widely in genomics, structural biology, mass spectrometry, bioinformatics and high-end imaging (details in section d). The most substantial investment (over £30M) delivered a new facility for *in vivo* animal research that ensures the highest quality care for animals, and provides state of the art procedure rooms.

Aim 4: Disseminate Knowledge Widely

The University provides a research environment where opportunities to disseminate, acquire and discuss new ideas are abundant:

- **Seminars**: over 300 bioscience seminars are held across the University each year, many by speakers from overseas institutions, with more than 10 prestigious named lectures held annually across UoA5. Reciprocally, UoA5 researchers collectively deliver at least 500 seminars at other institutions each year. In addition to external speakers, departments have internal seminar series where principal investigators (PIs), postdoctoral researchers and graduate students discuss their latest results in a constructive but challenging environment.
- **Depth and breadth**: UoA5 researchers participate in cohorts that are subject-specific (departments), cross-biosciences (institutes/programmes), and multidisciplinary (colleges). The network of interactions that is generated across the University as a consequence of these tri-partite alliances results in exceptional intellectual richness and diversity.
- **Outreach**: researchers in UoA5 deliver over 200 public seminars a year. The University Botanic Garden is particularly engaged with local schools, providing a conduit for information between researchers and teachers. In addition, the University Museum of Natural History provides a unique portal within UK universities for public engagement in biosciences, holding 'Science Saturdays' where Oxford researchers explain their research to the public, and an Annual Science Fair (more details in Impact Template).

Aim 5: Promote and Strengthen Interdisciplinary Research

Interdisciplinary research is central to activities in UoA5, with initiatives cutting across departmental boundaries and facing outwards to clinical, physical, environmental and social sciences (details in sections b2 & e). Many are launched through the Oxford Martin School, which is a focal point for more societally relevant interdisciplinary activities in the University. Others are driven by individual PIs and supported by collaborating departments. Highlights of new and planned initiatives include:

- **Oxford Martin School Institutes**: five new interdisciplinary institutes and programmes were established over the assessment period to address key areas of global concern, for example the Oxford Stem Cell Institute and the Plants for the 21st Century Institute.
- **Oxford Network for the Environment** (**ONE**): ONE was established to harness research across the University on environmental problems. The network identifies clusters around Energy, Water, Food Security, Biodiversity and Climate Change, and provides a means for internal networking as well as showcasing and facilitating external contacts. This network links 300 academics across 28 departments and institutes.
- **Biosciences Forum**: in 2012, the Departments in UoA5 established the Biosciences Forum (chaired by the Pro-VC Research) to further co-ordinate interdisciplinary research. The Forum is currently working with colleagues in clinical and physical science departments to develop plans for a £100M Oxford Centre for Interdisciplinary Biosciences. The Centre will be an intellectual hub for biosciences research at the medicine/biology/physical sciences interface, with spokes extending to the science departments and biomedical research institutes in the University, to Diamond, and to the Research Complex at Harwell. This initiative will be realised in part by expanding the system of joint PI appointments between departments.

Aim 6: Expand and Develop the User Interface

The breadth of research across UoA5 leads to an equally broad user interface, spanning from the NHS and health-related industries, to international conservation agencies and energy companies. Interactions with users continue to be strengthened through public-private partnerships, multi-lateral and bi-lateral collaborations. The University is also arguably the driver of "open innovation" in UK academia (more details in Impact Template). Two prominent examples:

- **The StemBANNC Programme** brings together 23 academic partners and 11 pharmaceutical companies from across Europe to develop human induced pluripotent stem cell (iPSC) models of disease for drug discovery. iPSC lines are being generated from 500 patients (Parkinsons, Alzheimers, autism, schizophrenia, bipolar, diabetes) for phenotyping and storage. PIs from 9 Oxford departments are involved in the €52M programme.
- **Oxford Martin Programme for the Future of Food** brings together researchers from UoA5 and across the University to address critical issues in food security. Funded by £1.7M

from the Oxford Martin School, the programme integrates existing research, supports new interdisciplinary initiatives, and facilitates interactions between academia, government, civil society and the private sector. Working with UK government departments (Defra & DfID), and the United Nations Food and Agricultural Organisation, the programme has brought biological and social scientists together to develop policies in sustainable food production.

Aim 7: Protect Vulnerable Subjects

In the face of limited external funding opportunities, some universities cease to support key research areas. Oxford recognises the short-term nature of many of these funding trends, and through its department-based governance structure it is able to ensure that specialist skills that have been eroded elsewhere are retained. For example:

- **Taxonomy**: a paucity of funding over the last 20 years led many universities to shut down teaching and research in taxonomy. In contrast, our strategy ensured survival of the subject, and as the international community increasingly prioritised the need for an understanding of biodiversity, we were able to respond. Over the REF2014 period, taxonomists in UoA5 secured over £4M of external funding for global biodiversity assessments, with much coming from industry and international governments. Our researchers are now in the field in over 25 countries, training the next generation.
- **Bacteriology**: whilst research into bacteria as infectious agents has remained well supported, fundamental bacteriology has been largely neglected over the last decade. Our commitment to bacterial biochemistry, genetics and structural biology has positioned us to respond to the increasingly urgent need to understand fundamental bacterial processes in order to design novel antimicrobial agents.

Aim 8: Support Technology Development

Research across UoA5 is underpinned by technology platforms that are becoming increasingly sophisticated. Whilst some platforms can be operated as a service, cutting edge research requires the very best technology developers. Nationally, there is virtually no career structure for these individuals and UoA5 is therefore prioritising investment in this area. For example:

- **Imaging**: a multidisciplinary team that combines skills in physics, cell biology and microscopy, is being supported to develop correlative light and electron microscopy (with UoA1). Investment in these individuals is already reaping rewards, having given UoA5 researchers access to the most advanced super-resolution microscopy in the UK.
- **Mass spectrometry** (**MS**): in collaboration with UoA8, investment is being made to develop enhanced sensitivity and resolution of MS technologies. This investment will impact across UoA5, enabling advanced studies in microbial, plant and mammalian systems.

Aim 9: Respond Flexibly to Immediate Challenges

The University operates a highly devolved fiscal model whereby income passes directly to the divisions and departments that generate it. This financial autonomy at all levels of the University structure ensures rapid delivery of the environment and infrastructure required to carry new initiatives forward. Examples of emergency responses to national challenges include:

- **H1N1 & H5N1 Flu**: access to clinical material through the University's overseas units, and a rapid commitment of core expertise in epidemiology, virology and genetics, enabled UoA5 researchers in the Institute for Emerging Infections to be at the forefront of research and planning for avian and swine flu. Research informed government policy and WHO guidelines for treatment and containment.
- **Ash dieback**: over the last 20 years, UoA5 researchers have generated and maintained a collection of ash germplasm that contains the majority of genetic variation that exists for this species in Britain and Ireland. This population is now at the centre of the UK research programme to identify germplasm that is resistant to *Chalara fraxinea*.

Aim 10: Evolve to Address Unmet Needs

The REF2014 assessment period has seen an unprecedented emphasis on the need for scientific research to contribute to economic recovery, and to solve global problems brought about by ageing, disease and environmental change. Researchers, departments and divisions in UoA5 have initiated, or are developing, plans to deliver the science needed to tackle many of these issues.

Examples are illustrated in aims 5 to 7 above, in section e, and in the submitted Impact Cases and Template. Two additional highlights include:

- **Ageing**: applying strengths in evolutionary theory, UoA5 researchers are contributing to an ambitious programme on development, epigenetics and longevity determination. Funded by the EU (€12M), the Integrated research on DEvelopmental determinants of Ageing and Longevity (IDEAL) project involves researchers from 16 institutes in 8 countries. UoA5 researchers are investigating the role of phenotypic plasticity and epigenetic inheritance in life history trajectories, and assessing implications for health, disease and ageing.
- **Improving crop yields**: in response to calls for improved photosynthetic capacity in crop plants in the face of environmental change, UoA5 researchers are adapting knowledge gained from a research programme in plant developmental biology to crop plants. The University has invested in the required infrastructure, and Oxford researchers have played a central role in the formation of two international consortia that have secured over £20M funding from the Gates Foundation, DfiD, and the EU, to introduce C_4 traits into C_3 crops.

b2. RESEARCH THEMES

Collectively we carry out world-leading research across ten broad areas of biological sciences (Box 1), spanning the full range of scales from atoms to populations. This breadth is recapitulated within many of the themes. For example, programmes in both neuroscience and physiology span from molecules to populations. Over the assessment period, outputs in each of the ten areas have substantially altered the intellectual and/or technical landscape of the field. Examples of strategic appointments, transformative publications, and new initiatives that will underpin research over the next assessment period are outlined below.

Theme 1: Biophysics & Structural Biology (73 outputs returned)

New people:

- Two professorial appointments (**Sansom**, **Kleanthous**) secured new leadership and five junior appointments (**Higgins**, **McLain**, **Newstead**, **Schnell**, **Vakonakis**) renewed capacity in this area whilst establishing cell surface and membrane proteins as a new focus.

New insights:

- Structures of three proteins provided insight into how folded proteins can pass through membranes (**Berks**, **Lea** Nature 2012, **Schnell**, **Berks** PNAS 2013); how peptides and pro-drugs are transported across membranes (**Newstead**, EMBO J 2012); and how centrioles are formed (**Vakonakis**, Cell 2011).
- Proteins of the bacterial flagellar motor were shown to switch between the rotor and cytoplasm whilst the motor is still rotating (**Armitage**, PNAS 2010).

New initiatives:

- Biophysics research facilities have been upgraded in a joint venture with the Structural Biology Institute and Structural Genomics Consortium in UoA1, to enable structural characterisation of membrane proteins, protein complexes, and protein/ligand interactions.
- Strong links have been forged with groups at Diamond, building capacity in membrane protein structural biology and biophysics. These links were formalised with the 2013 renewal of the Wellcome Trust Doctoral Training Centre in Structural Biology, a joint programme between the University (UoA1, UoA5 & UoA8) and Diamond.

Theme 2: Cell & Developmental Biology (101 outputs returned)

New people:

- Seven professorial appointments (**Barr**, **Dolan**, **Freeman**, **Hassan**, **Jarvis**, **Raff**, **Riley**) built on existing strengths and positioned cancer biology and regenerative medicine as new foci. Five new group leaders were also recruited (**Agusti**, **Akiyoshi**, **Carr**, **Grüneberg**, **Vasileva**), most having secured independent research fellowships.

New insights:

- Novel insights into cell division were revealed with the elucidation of how the cohesin ring holds sister chromatids together during mitosis (**Nasmyth**, Nature 2008); and the discovery that centrosome amplification in stem cells initiates tumorigenesis (**Raff**, Cell 2008).
- Understanding of the endomembrane system has been greatly enhanced with insights into

the activation mechanism of Rab11 GTPases (**Barr**, Dev. Cell 2012); insight into the role of lysosomal calcium signalling and its dysregulation in disease (**Platt**, Nature Medicine 2008; **Galione,** Nature 2009); and elucidation of the role of membrane trafficking in the regulation of growth factor and cytokine signalling pathways (**Freeman**, Cell 2011; Science 2012).

- Two publications changed our perception of growth regulation. The first revealed that growth is reactivated in dormant adult epicardial cells by the peptide thymosin beta4 (**Riley**, Nature 2011), paving the way for therapeutic treatment after myocardial infarction. The second showed that a single transcription factor is necessary and sufficient to induce and maintain growth in plant root hairs (**Dolan**, Nature Genetics, 2010), inspiring a strategy to engineer better nutrient uptake capacity in crops through constitutive induction of growth.

New initiatives:

- A major new imaging programme (Micron) was launched with a £3.9M award from the Wellcome Trust to **Brockdorff**, **Davis**, **Proudfoot**, **Raff** and **Robertson**. The programme is developing the most advanced super-resolution imaging systems in the UK, to facilitate the study of chromosome and RNA dynamics in single cells.
- With funding from BHF, **Riley** established a new programme in regenerative medicine that is investigating biological mechanisms that can repair damage in the heart. The programme is hosted in the Burdon Sanderson Cardiac Science Centre (led by **Paterson** and **Vaughan Jones**) to maximise synergies with research in cardiac physiology.

Theme 3: Genes, Genetics & Genomics (93 outputs returned)

New people:

- Five new investigators (**D**. **Ahel**, **I**. **Ahel**, **Esashi**, **Gullerova**, **Marques**) were recruited to expand capacity in this core area, and the appointment of **Mackay** to a newly endowed Chair in forest science provided leadership for a programme in tree genomics.

New insights:

- Understanding of gene regulation was significantly advanced by the discovery of a mechanism that co-ordinates gene transcription in convergent genes (**Proudfoot**, Cell 2008; Genes & Dev. 2011); by the identification of a DNA binding protein that recognises CpG islands (**Klose**, Mol. Cell 2010); and by the finding that desensitisation of a G-protein coupled receptor sustains calcium-dependent gene expression (**Parekh**, Nature 2012).
- Genome sequencing revealed the genetic basis of somaclonal variation in plants (**Harberd**, Curr Biol 2011), and the polished mouse genome sequence provided a robust foundation for future research in mammalian genetics and genomics (**Ponting**, PLoS Biology 2009).

New initiatives:

- The MRC Functional Genomics Unit is currently being reformed as an MRC University Unit, with £5.5M funding, and the unit's PIs (**Davies**, **Ponting**, **Liu**, **Webber**) are transferring to the University. The Unit has also been awarded £2.9M to host the MRC Centre for Computational Genomics Analysis & Training, which is running research projects in collaboration with other UK institutions.
- Genomics approaches to crop science were boosted through a KAUST Individual Investigator award for wheat research (**Harberd**, $10M) that has created a collaborative initiative between UoA5 and UoA1 (**Mott**).

Theme 4: Physiology & Metabolism (75 outputs returned)

New people:

- Research in cardiac science was reinforced by the recruitment of **Zaccolo** to a professorship plus **Swietach** and **Bub** as junior PIs, whilst the recruitment of **de Wet** and **Cantley** further enhanced the leading position of the ion channel diabetes team.

New insights:

- A major breakthrough in neonatal diabetes came with the finding that muscle dysfunction in patients is caused by a K_{ATP} channel mutation of neuronal origin (**Ashcroft**, Science 2010).
- Clinical trials showed that iron abrogrates the normal development of pulmonary hypertension in response to high altitude exposure (**Robbins**, JAMA 2009).
- Cardiac signaling groups provided insights to cellular microdomains for pH/Ca^{2+} buffering (**Vaughan Jones**, PNAS 2013), extra-mitochondrial domains and energetics (**Swietach**,

PNAS 2013) and cyclic nucleotide regulation (**Zaccolo**, Circ. Res. 2011).

New initiatives:

- With a £1.4M BHF award, **Tyler** has developed hyperpolarised magnetic resonance spectroscopy to enable the first human cardiac studies to be performed.
- Three new BHF programme grants have recently been awarded (**Vaughan Jones**, **Clarke**, **Zaccolo**).
- £6.4M from the Wellcome Trust renewed the OXION Ion Channels and Disease Initiative; a joint programme between Oxford, Cambridge, London and MRC Harwell led by **Ashcroft**.
- Research in cardiac science was boosted by renewal of the BHF Centre for Research Excellence award (**Galione**, **Paterson** with **Watkins** in UoA1, £6.1M).

Theme 5: Neuroscience & Behaviour (69 outputs returned)

New people:

- The recruitment of **Waddell** as a Wellcome Senior Research Fellow, and of **Becker**, **Biro**, **Goodwin**, **Gromak**, **Kohl**, **Mann**, **Oliver** and **K**. **Walker** as new investigators, strengthened research across the breadth of neuroscience and behaviour.

New insights:

- Significant insights have been made linking genetics and cell biology to behaviour, with the demonstration that individual behaviour may be traced back to transposon-induced genetic mosaics in the brain (**Waddell**, Science 2013); the discovery of neuronal network mechanisms underpinning memory and spatial learning (**Dupret**, Nature Neuro. 2010; Neuron 2013); the finding that descending projections from the cortex mediate auditory learning (**King**, Nature Neuro. 2010); the demonstration of functional presynaptic NMDA receptors in the hippocampus (**Emptage**, Neuron 2010), and the discovery of how memory and motivational-state information are integrated to drive behaviour (**Waddell**, Cell 2009).
- The identification of abnormal brain oscillations in a rat model of Parkinsons disease (**Magill**, Neuron 2012) and of compensatory mechanisms for hearing loss in infancy (**A**. **King**, Curr. Biol. 2013) have suggested a possible surgical solution for Parkinsons and a therapeutic approach for treating children with 'glue ear'.
- The demonstration that exosomes can deliver small RNAs to the brain in mice (**Wood**, Nature Biotech. 2011) has revolutionised approaches to the treatment of neuronal diseases with RNA drugs, by providing a non-immunogenic delivery method.

New initiatives:

- A total of £17.3M has been awarded to establish new programmes: £5M from The Gatsby Charitable Foundation for the Centre for Neural Circuits and Behaviour (**Miesenbock**); £4.4M from the Wellcome Trust for the Sleep and Circadian Neuroscience Institute (**Davies** with **Russell** in UoA1); £5M from the Monument Trust for the Oxford Parkinsons Disease Centre (**Wade-Martins**); and £2.9M from the Health Innovation Challenge Fund for the Centre for Translational Neuromuscular Science (**Wood** with UoA1).

Theme 6: Infection, Immunity & Epidemiology (81 outputs returned)

New people:

- Three new professorial (**Barclay**, **Fodor**, **Tang**) and five junior appointments (**Gluenz**, **Maloy**, **Moore**, **Smith**, **Vreede**) enhanced strengths in the cellular basis of infection and immunity, whilst the professorial appointment of **Pybus** at the interface of evolution and infection, and the recruitment of **Hay** (Wellcome Trust Senior Research Fellow) developed strength in epidemiology. The new focus on epidemiology attracted **Faria**, **Gray**, **Gething**, **Magiorkinis**, **Metcalf**, **Penman** and **Piel** on IRFs, building significant capacity in that area.

New insights:

- The structural elucidation of a complement/ligand interaction showed how *Neisseria meningitides* subverts the human immune response (**Lea** & **Tang**, Nature 2009), leading to informed vaccine design against this major pathogen (**Lea** & **Tang**, PLoS Pathogens 2012).
- Research into plant-pathogen interactions demonstrated that balancing selection maintains variation in plant defence proteins (**van der Hoorn**, PLoS Genetics 2012) and showed the protective role of heavy metals against bacterial disease (**Preston**, PLoS Pathogens 2010).
- Two studies substantially revised estimates of future disease threats, estimating a tripling of

the global burden of Dengue (**Hay**, Nature 2013), and showing that climate change is unlikely to increase the global distribution of malaria (**Gething**, Nature 2010).

New initiatives:

- The Programme for Vaccine Design was launched in 2012 with funding from the Oxford Martin School, aiming to integrate improved vaccine design with needle-free delivery technologies (**Gupta**, **Lea**, **Maiden**, **Smith**, **Tang** with UoA1).
- The Institute of Emerging Infections has been funded to expand its remit to understand chronic viral infections, particularly hepatitis C and HIV (**McLean**, **Pybus** with UoA1).

Theme 7: Pharmacology & Drug Discovery (57 outputs returned)

New people:

- Two professorial appointments (**Garland**, **Sitsapesan**) and the recruitment of **Dora** as a BHF Senior Fellow, established cardiovascular pharmacology as a new research strength. Five PI appointments (**El Andaloussi**, **Lei**, **Morgan**, **Tammaro**, **Vasudevan**) built capacity across the theme.

New insights:

- A new drug was discovered for bipolar disorder using *in silico* techniques (**Churchill** & **Vasudevan**, Nature Comm. 2013); polyunsaturated liposomes were shown to act as antivirals against HIV and hepatitis (**Zitzmann**, PNAS 2010) and the mechanism by which influenza A evolves drug resistance was identified (**Schnell**, PNAS 2009).

New initiatives:

- The MRC Anatomical Neuropharmacology Unit is being reformed as an MRC University Unit with an award of £7M. Transfer of the unit's PIs (**Somogyi**, **Bolam**, **Capogna**, **Dupret**, **Magill**), along with the appointment of **Minichiello** to a Readership, will create one of the largest groupings of neuropharmacologists in the UK, with particular expertise in the chemical anatomy of neuronal circuits, *in vivo* electrophysiology and optogenetics.
- A £24M Target Discovery Institute (TDI) opened in 2013 that will use large-scale screening methods to identify potential drug targets (led by **Ratcliffe** in UoA1). The addition of TDI to existing strengths in UoA5 will deliver research that spans from target discovery, through early stage validation, to the analysis of how new drugs regulate biological activities.
- An MRC stratified medicine award (£3.6M) (**Platt** co-PI) has brought together a consortium of academic scientists, major industrial partners and patient advocacy groups to improve the outcome of treatment for Gaucher disease by better targeting and timing of therapy.

Theme 8: Mathematical, Computational & Systems Biology (53 outputs returned)

New people:

- The professorial appointment of **Poole**, and the recruitment of five junior PIs (**Angel**, **Bayer**, **Biggin**, **Dushek**, **Kelly**, **van der Hoorn**) has built capacity in this emerging research area.

New insights:

- Sophisticated modelling revealed how a checkpoint behaves as a bistable switch to create a point of no return in mitotic progress (**Novak**, PNAS 2011); and how genetic regulatory networks underpin self-organising properties in leaf development (**Tsiantis**, PNAS 2011).
- Large-scale metabolic flux analyses provided network models that can be used to predict the behaviour of plant metabolism (**Ratcliffe** & **Sweetlove**, Plant Physiol. 2008, 2010).

New initiatives:

- A $7M programme funded by the US National Science Foundation and BBSRC (**Poole** lead PI), aims to use a systems understanding of plant-microbe interactions in the rhizosphere to develop synthetic symbioses that will deliver biologically sourced nitrogen to crops.

Theme 9: Evolutionary Biology (60 outputs returned)

New people:

- The professorial appointment of **West** catalysed growth in social and experimental evolution, attracting **Foster**, **Griffin**, **K. King**, **Maclean** and **Wigby** as new PIs, whilst the recruitment of **Aboobaker**, **Daley**, **Katzourakis** and **Uller** built capacity in the evolution of genomes and developmental mechanisms.

New insights:

- Genome level discoveries showed that splicing variations at the binding site of the IGF2 receptor provided a molecular mechanism for the evolution of parental conflict (**Hassan**, Science 2012); provided major insights into early vertebrate evolution through analysis of the amphioxus genome (**Holland**, Genome Res. 2008); uncovered a 100 million year co-evolutionary history of cryptic retroviruses infecting mammalian genomes (**Katzourakis**, Science 2009); and demonstrated that Y chromosome degeneration in plants is retarded by purifying selection in the haploid phase of the lifecycle (**Filatov**, Curr. Biol. 2011).
- At species and population levels, the evolution of sex determination in lizards was shown to be governed by the environment (**Uller**, Nature 2010); and relatedness within families was revealed to be the major driver of the evolution of cooperative behaviour and paternal care in vertebrate societies (**Griffin**, Nature 2010; PLoS Biology 2013).

New initiatives:

- Three ERC Advanced Investigator awards with a combined value over €7M (**Dolan**, **Holland**, **Langdale**) built on existing activities and has created one of the largest cohorts of 'evodevo' researchers in the UK, aiming to link genotypic and phenotypic evolution.
- Three ERC awards (total >€5M) (**Foster**, **Maclean**, **West**) have created a research cluster using experimental evolutionary approaches to understand adaptation and cooperation.

Theme 10: Ecology & Conservation (57 outputs returned)

New people:

- Strategic expansion of research in evolutionary and community ecology was realised by the appointment of **Coulson**, **Hector**, and **Willis** to Chairs, and by recruitment of eight new PIs (**Durham**, **Jeffers**, **Leimu-Brown**, **Macias-Fauria**, **Seddon**, **Tobias**, **Turnbull**, **S**. **Walker**).

New insights:

- Analyses of long-term bird population data elucidated the mechanism of population viability under climate change, enabling quantitative predictions to be made (**Sheldon**, Science 2008, PLoS Biology 2013); predictions of population dynamic responses to climate change were also achieved through a synthesis of developmental processes, genetic transmission, selection and environmental variation (**Coulson**, Science 2009, 2011; Nature 2010).
- The uniquely successful conservation of a threatened butterfly was shown to be dependent on detailed ecological understanding of its ecosystem (**Thomas**, Science 2009).

New initiatives:

- The Biodiversity Institute was established in 2011 with £3.5M funding from the Tasso Leventis Foundation and the Oxford Martin School. The Institute is acting as a focus for biodiversity research across the University, with UoA5 researchers interacting with social scientists to develop the frameworks, structures and novel technologies needed to implement biodiversity science into management and policy.

c. People, including:

c1. STAFFING STRATEGY AND STAFF DEVELOPMENT

c1.1 Staffing Strategy

Our staffing strategy is based on three criteria:

- **Excellence**: excellence in research and teaching is our overriding criterion for academic recruitment, and the University is committed to hiring the best academic staff, irrespective of gender, racial origin or nationality. Both the recruitment process and responsibility for staff development are devolved to departments. Each department identifies priority areas for appointments in the University's annual strategic planning round, with emphasis placed on those that address core teaching needs, actively support new initiatives, build upon existing research strengths or open new areas of multidisciplinary and collaborative research. Joint appointments between departments are a priority over the next five years.
- **Visionary leadership**: UoA5 has introduced a system of fixed-term stints for Heads of Department (HoD) in order to retain vitality in leadership roles. Five new HoDs have been appointed since 2008: Biochemistry (**Nasmyth** to 2011; **Sansom**); Dunn School of Pathology (**Waldmann** to 2012; **Freeman**); Pharmacology (**Galione**); Physiology, Anatomy and Genetics (**Davies** to 2011; **Robbins**); Plant Sciences (**Langdale** to 2012; **Dolan**); Zoology (**Harvey** to 2011; **Holland**).

- **Empowerment of young scientists**: great emphasis is placed on supporting young researchers and providing them with the intellectual and physical environment needed to develop their own careers: over 30% of the submitted staff are Early Career Researchers (ECRs). This commitment is recognised by the hundreds of postdoctoral research assistants that come from all over the world to join groups in UoA5. Of the 467 that are currently employed, 60% are from the UK and 40% from overseas.

c1.2 Staff Profile

Tenured and tenure-track staff are appointed to Statutory Chairs, Research Professorships (RSIV) or University Lectureships (ULs). Statutory Professors and ULs are appointed both by the University and a college. There is no requirement for RSIV post-holders to be simultaneously appointed to a college, however, many choose to take advantage of a college affiliation. ECRs are either appointed to fixed term Departmental Lecturer (DL) positions or join the University having secured their own Independent Research Fellowship (IRF) from external funding bodies. DLs and IRFs have the same status as tenured/tenure-track academic staff with regard to space allocation, access to facilities and input to policy. Postdoctoral research assistants (PDRAs) are recruited on externally funded grants awarded to academic staff.

Across the UoA overall numbers of academic staff have remained rather constant since RAE2008 (Table 1). However, there has been much turnover with 23 professors and 68 new group leaders recruited, 22 retirements and ~60 PIs moving on elsewhere. There are 65 (29%) female staff submitted, 33 (15%) of whom are tenured/tenure track as compared to 20 (9%) in the previous submission; two women (**Davies**, **Langdale**) have been both HoD and Associate Head of Division over the REF period; and three are Directors of Institutes (**Armitage**, **McLean**, **Willis)**.

Table 1	Professors	Readers	Lecturers	Snr. Res. Fellows	IRFs	Total
RAE 2008	62	7	77	13	60	219
REF 2014	86	0	43	7	90	226

c1.3 Starting at Oxford

Statutory Chairs and RSIVs receive generous start-up packages (up to £1M) to enable them to move their research programme to Oxford with minimum disruption. HoDs and Departmental Administrators provide guidance about procedures that are specific to Oxford and all new Professors attend an induction meeting hosted by the Pro-VC (Research). Further integration into the University takes various routes depending on individual academic interests and synergies.

A more proactive and supportive approach is taken to help ULs establish themselves in Oxford. All new ULs are given start-up packages that provide them with the best possible opportunity to initiate their research programme. These packages can include dedicated equipment, technical support and graduate studentships. Crucially, each new UL is assigned a mentor who regularly reviews their progress and helps them with the goal of achieving tenure in 5 years. Mentors are normally senior academics with experience of both departmental and college expectations. In consultation with the HoD, the mentor ensures that teaching, examining and administration loads are kept to a minimum for the first three years, after which time a formal mid-term review of progress is held. All new ULs attend courses held by the Oxford Learning Institute on all aspects of academic practice, including graduate supervision, grant writing and lecturing. Annual appraisals with the HoD provide an opportunity to discuss progress, to highlight successes and to raise any concerns that the Department or College can address. 26 ULs were awarded tenure over the assessment period.

DLs and IRFs are often assigned space alongside established researchers so that they have immediate access to facilities at start-up. They are also assigned mentors who offer confidential support, including advice on workload management, initiation of an independent research programme and managing a research group.

c1.4 Career Development

Departments use central university support structures to co-ordinate and facilitate individual career

development programmes. Support is provided by Personnel Services, the Oxford Learning Institute (personal and professional development), Research Services (grant applications and contracts), and the Careers Service. The University's work to support career development has been acknowledged by the European Commission's HR Excellence in Research Award.

Recognising that needs differ between individuals and career stages, different approaches are taken to support tenured/tenure-track academics, ECRs and PDRAs. In all cases, the aim is to enable the development of personal and professional skills that will enhance individual career trajectories and aspirations. Examples of approaches to support specific groups include:

c1.4.1 Tenured/Tenure-Track Academics

- Staff are appraised on an annual basis: Statutory Chairs by the relevant Head of Division; RSIVs and ULs by the HoD. The appraisal process allows staff to articulate personal and professional development needs, and provides a formal conduit to respond to them.
- The University operates a 'Recognition of Distinction Exercise' that awards Professorial Titles for research excellence. Since 2008, 16 ULs in UoA5 have received the title.
- All academics are entitled to one term's sabbatical for every six terms of service.
- Academic Leadership courses are run by the Oxford Learning Institute for incoming HoDs, and for others who wish to develop general leadership skills. All five new HoDs attended.

c1.4.2 Early Career Researchers

- ECRs are appraised annually by the HoD to assess their training needs.
- Skills training courses on career development for ECRs are run by both Divisions (MSD: 'Building a Successful Career in the Sciences'; MPLS: 'Preparation for Academic Practice'). These courses cover the skills required to get and keep an academic job, including grant writing, people management and teaching.
- ECRs are encouraged to teach on courses offered across the UoA, and to do so they receive training for lecturing, tutorial and small group teaching. Most of the ECRs submitted have taught over the assessment period, although the loads are generally very light.
- The University's John Fell Fund distributes £5M for research each year and is particularly supportive of applications from ECRs (36 ECRs in UoA5 received a total of £1.2M over the assessment period).
- Mentors and other colleagues review grant applications, advise on job applications and carry out practice interviews. Since 2008, 30 ECRs have successfully moved to academic positions or senior fellowships either within Oxford (14), at other institutions in the UK (12) or at institutions outside the UK (4). Two others moved to positions in industry.

c1.4.3 Postdoctoral Research Assistants

- PIs implement the University's Code of Practice for the Employment and Career Development of Research Staff, the key means of achieving national Concordat principles.
- At the start of a PDRA contract, PIs set up a meeting to clarify the job description, the degree of freedom for pursuing the research objectives, expectations about outputs and progress, and to discuss the individual's own aspirations and skills. After this, regular informal meetings are the norm but in addition, departments have introduced annual PDRA appraisals, providing a formal mechanism to develop and monitor career progression plans.
- PDRAs who wish to pursue an academic career are encouraged to attend the Divisional courses that also cater for ECRs (c*1.4.2*). Around 30 senior PDRAs attend each year.
- Considerable support is provided to individuals who wish to apply for personal fellowships, in the form of feedback on applications and practice interviews. 495 applications were submitted over the assessment period and 111 were awarded.
- Departments run a series of seminars in collaboration with the Careers Service that highlight the range of career opportunities for PDRAs.
- All PDRAs are encouraged to teach and they are provided with relevant training to enable them to do so. PDRAs are also encouraged to present their research at national and international meetings, and to assist PIs in preparing grant applications.

c1.5 A Vibrant, Inclusive and Flexible Working Environment

Across the UoA there is a culture that is inclusive and flexible. Teamwork is highly valued,

individual strengths are recognised, and there is a commitment to advancing the careers of everyone, regardless of gender or role. Both formal and informal flexible working arrangements are common. We aim to provide a family-friendly environment where both women and men feel able to take the time they need for family, regardless of whether that time is spent with children, partners or aging parents. This ethos is as relevant to support staff as academic staff, and processes are in place to enable all staff to balance a successful professional career with a fulfilling personal life. For example, there are generous maternity, paternity, parental, and adoption leave terms and a comprehensive range of university childcare services. Women returning from maternity leave have reduced teaching loads so that they can focus on research. 12 staff returned in this submission had maternity leave during the assessment period; more than 50 staff (PIs and PDRAs) took paternity leave, and 52 children currently benefit from the childcare facilities.

Each department has an Athena SWAN panel involved in implementing and monitoring the impact of strategies to provide equal opportunity to all staff, with a particular focus on women's careers. Two departments hold Athena SWAN Silver awards (Plant Sciences, Zoology); two hold Bronze awards (Physiology, Anatomy & Genetics, Biochemistry); while Pathology and Pharmacology are preparing applications for November 2013. Athena SWAN panel meetings are embedded in the regular cycle of departmental meetings, providing a robust conduit for information flow, and allowing contributions from all stakeholders to inform strategy. Examples of initiatives arising from the Athena SWAN process include the switch to core working hours to ensure that departmental meetings and seminars are held between 9.30 and 16.00. 11 senior academics in UoA5 have acted as mentors in 'Ad Feminam' the University's scheme to mentor women for leadership roles and two women have received mentorship through the scheme since its start in 2011. The University recently established the Vice-Chancellor's Diversity Fund (£1M), to further promote and encourage representation of women and ethnic minorities in senior research and academic posts.

c1.6 The Added Value of Oxford Colleges

Colleges create a stimulating intellectual environment, providing opportunities to meet academics from other disciplines and to develop research synergies. These interactions are particularly valuable for junior researchers who are developing their research portfolio, but can also lead to the initiation of major cross-disciplinary projects by senior researchers. For example, the Global Ocean Commission has been established at Somerville College, bringing together research in marine biology and international policy, to provide management solutions for threats to healthy marine environments. Many academic staff receive college research allowances (~£1250 a year), graduate students receive travel grants, and externally funded IRFs have been successful in gaining college junior research fellowships (~30 across the UoA during the REF period). These fellowships often provide additional stipend and a research allowance. Many colleges operate 'subject families' or 'research clusters' whereby fellows, graduate students and undergraduates operate as a co-ordinated unit to support teaching and research in that subject.

c2. RESEARCH STUDENTS

c2.1 Strategic Oversight

Responsibility for the strategic direction, policy, procedures and oversight of postgraduate training in UoA5 lies with the Graduate Studies Committees (GSC) and Educational Policy & Standards Committees of both MSD and MPLS, acting within the University's overarching framework. The GSC comprises Directors of Graduate Studies (DGS) from each department plus Directors of the Doctoral Training Centres (DTC) (see c2.4 below). Implementation of these policies is currently delivered in two strands, primarily as a consequence of the recent switch by RCUK away from quota studentships to doctoral training programmes. Students can thus enter either into a subject-based departmental programme or into an inter-departmental programme that is often strategically focussed. In both cases, students train as a cohort, and are a member of a Graduate School.

c2.2 Graduate Schools

Both MSD and MPLS launched Graduate Schools in 2012 to better support doctoral training. The Schools were launched with three main aims: improve the recruitment process; provide full funding for students; and deliver a first class training experience in a rich and vibrant research environment. Progress towards these goals includes:

- A website for prospective students with clear and comprehensive information on the application process, funding opportunities, and research opportunities.
- An annual funding competition based on academic merit, drawing together funding from multiple sources to ensure timely awards to the most able candidates. This process incorporates the University's flagship Clarendon Scholarship scheme that is highly competitive, being awarded to less than 3% of students. Since 2008, more than 50 students in UoA5 have received full or partial Clarendon Scholarships.
- Provision of training in transferable, research and specialist scientific skills offered through the MSD Skills Training Programme and the MPLS Graduate Academic Programme. Over 100 courses and events are offered each year.
- Dissemination of information to students on events and activities across the University, as well as the outstanding services and facilities the University provides for all students.

c2.3 Student Numbers

Each year, around 130 postgraduate research students are admitted across the UoA. With most students on 4-year courses leading to a DPhil, the cohort at any one time is always above 500. Of this cohort, around 70% are home/EU students and the remainder are from overseas. 20-30 students a year are also admitted for the MSc in *in vivo* pharmacology, with funding from MRC, Pfizer, GlaxoSmithKline and the British Pharmacological Society.

c2.4 Graduate Courses

c2.4.1 Doctoral Training Centres: The DTCs provide academic oversight through senior Academic Directors, and training resources for 14 inter-disciplinary structured doctoral programmes (Table 2). Since 2012, this has become the major route for graduate entry. A total of 402 students entered via DTCs between 2008 and 2012, 150 of which from the 2008-2011 starters ultimately joined groups in UoA5. From 2014-18, an additional 24 students will enter each year to a recently awarded NERC doctoral training programme (totalling £10M) in Environmental Science.

Table 2	Yrs active	Funder	# students (into UoA5)
Genomes, Development, Evolution	2008	BBSRC	4 (4)
Molecular Biology & Chemical Biology	2009-12	BBSRC	25 (13)
Interdisciplinary Bioscience	2012-	BBSRC	11 (n/a)
Cardiovascular Science	2005-	BHF	19 (11)
Medicinal Chemistry	2006-10	CRUK	7 (7)
Systems Biology	2008-	EPSRC	82 (42)
Life Sciences Interface	2008-	EPSRC	70 (4)
Systems Approaches to Biomedicine (Industrial)	2009-	EPSRC	44 (10)
Chromosome & Developmental Biology	2008-	Wellcome	25 (19)
Genomic Medicine & Statistics	2008-	Wellcome	26 (9)
Infection, Immunology & Translational Medicine	2008-	Wellcome	26 (2)
Neuroscience	1996-	Wellcome	25 (9)
OXION: Ion Channels & Disease Initiative	2009-	Wellcome	13 (7)
Structural Biology: from Molecules to Cells	2000-	Wellcome	25 (13)

c2.4.2 Direct Entry: Each department continues to admit students for subject-specific programmes that have historically been funded by RCUK doctoral training grants or other directed awards. Despite RCUK's move towards multidisciplinary graduate programmes, the Departmental cohort based programmes remain popular with students who have focussed research interests. These programmes attract overseas students who gain prestigious individual scholarships (e.g. Rhodes). Scholarships from Oxford Colleges and from philanthropy are also available to a small number of home/EU students. 528 students entered via this route in the 2008/9 to 2012/13 academic years.

c2.5 Training

Whether entering directly into a department or into a DTC, all students are trained in an environment in which there is a critical mass of experts and resources. Induction programmes help integrate students into that environment as rapidly as possible, and events such as student symposia reinforce the cohort. Each student also belongs to a college. The College provides independent academic and pastoral support, libraries and computing facilities, access to travel

funds and other bursaries, and a diverse intellectual environment.

All research students have a supervisor who is responsible for their scientific training, assesses their training needs, and identifies the appropriate courses that they should attend. They are often assigned a further supervisor where their research would benefit from additional scientific expertise. The University has a "Code of Practice for Supervision of Research" under which supervisors must advise, guide and support research students in all aspects of their research project; have regular meetings; and encourage them to participate in the wider Oxford community. A termly reporting system ensures close monitoring and support of students' progress, with input from students, supervisors and DGSs. The academic milestones of Transfer of Status and Confirmation of Status, where student progress is evaluated by independent assessors, also ensure progression is kept on track.

c2.6 Industrial Training

Direct engagement by whole cohorts of graduate students with industrial research is mediated through the Systems Approaches to Biomedical Science industrial DTC. Around 12 students have been admitted each year to this course since 2009 and each student works closely with industry. The companies currently involved in the iDTC are linked to the following industrial sectors: Pharmaceutical; Biomedical and Imaging Technology; Health Related IT; and Biotechnology and Health Related Informatics.

Further industrial partnerships were forged through the 37 industrial RCUK CASE awards (26 BBSRC, 6 NERC, 4 MRC and 1 EPSRC) that were secured over the assessment period, with many associated with small and medium enterprises (SMEs). Outputs from these partnerships include the adoption of molecular dynamics simulations as a mainstream drug design tool in the investigation of G-protein coupled receptors, and the use of membrane transport proteins as drug targets (**Biggin**, with Evotec & UCB).

c2.7 Destination of Students

598 DPhil students graduated between 2008 and 2013, 87% within 4 years of starting on course. The first destination of these students after graduation is shown in Table 3. Notably 84% continued in bioscience careers, building substantial national and international capacity.

Table 3	Number (%)
Academic research	332 (55%)
Industrial research	53 (10%)
Medicine	52 (8%)
PGCE	10 (2%)
Scientific publishing	17 (3%)
Other biosciences related	37 (6%)
Other	65 (11%)
Unknown	32 (5%)
Total	598

d. Income, infrastructure and facilities

d1. INCOME

External grant income exceeded £50M per annum over the assessment period, an increase of 35% compared to the previous assessment period. Notably, a strategy to diversify funding sources in the face of the UK's economic downturn has seen significant increases in funding from the EU (up 194%) and from overseas (up 328%). As outlined in sections b2 and e, much of the awarded grant income has contributed to the development of strategic large-scale programmes, but substantial individual awards have also been secured: 38 staff hold senior fellowship or equivalent awards and 37 junior staff have been awarded Royal Society University Research Fellowships or similar intermediate awards. The range of funding sources is shown in Table 4 (annual average £).

Table 4	BIS/RCUK	UK Govt.	EU	Charities	Industry	Overseas	Total
RAE2008	£14.8M	£1.3M	£1.7M	£17.5M	£2.7M	£0.7M	£38.7M
REF2014	£15.8M	£1.0M	£5.0M	£25.2M	£2.4M	£3.0M	£52.4M

d2. BUILDINGS

The six Departments in UoA5 occupy buildings in close proximity that together comprise approximately 58,000m^2 of laboratory and office space. Activities in each building are underpinned by experienced technical support teams that ensure health, safety and regulatory compliance; continuity of expertise and specialised animal health and plant growth care. Over £100M has been invested over the REF period in the physical construction or refurbishment of these buildings:

- Biochemistry researchers moved into an outstanding 12,000m^2 building in 2008 (£55M).
- The new Oxford Molecular Pathology Institute building (£30M) was completed in 2011.
- The Pharmacology building was completely refurbished and a new animal quarantine facility with 'Gold Standard' procedure rooms was installed (£2.5M).
- Refurbishments were completed to provide the Centre for Neural Circuits and Behaviour with state of the art facilities for sensing and imaging neuronal activity (£10M).
- The Plant Sciences building was completely refurbished to provide extensive transgenic plant growth facilities and modern research laboratories (£5M).

d3. SHARED FACILITIES

Research across UoA5 is enhanced by the provision of shared facilities for *in vivo* animal research, molecular biosciences and whole organism biology. By sharing the large-scale equipment and facilities needed for all of these technologies, we ensure that the equipment is the most advanced available and that the supporting expertise is retained in the University. In brief, facilities comprise:

d3.1 *In vivo* Animal Research

d3.1.1 Biomedical Research Facility for Animal Research: A new facility to house animals was completed in 2008 at a cost of over £30M. The building is state of the art in terms of animal health and hygiene and has full Home Office Regulatory approval. Veterinary Services staff work in the building to ensure the highest quality support and care for animals.

d3.1.2 Magnetic Resonance Imaging: The UoA has two high-field (11.7T & 7T) pre-clinical systems for *in vivo* imaging (MRI/MRS). These have been complemented by two hyperpolarisers that enable the *in vivo* assessment of metabolic function on a second by second basis. Development work on these systems has enabled installation of the first hyperpolariser for clinical use in the UK.

d3.2 Facilities for Molecular Biosciences Research

d3.2.1 Genomics and Bioinformatics: UoA5 researchers benefit from the infrastructure and expertise provided by the University's Wellcome Trust Centre for Human Genetics (WTCHG). The Centre has the largest capacity for next-generation sequencing in the UK after the Sanger Centre and its scientists are at the forefront of developing technologies underpinning genomics research. For example**,** the read-mapper *Stampy*, the variant-caller *Platypus* and the *de novo* assembly algorithm *Cortex* were all developed at WTCHG.

d3.2.2 Protein Characterisation: Biophysics facilities are available for all aspects of characterisation of proteins and their interactions, both during and subsequent to protein purification:

- Facilities available include CD, SPR, SEC-MALS, analytical ultracentrifugation, DEER spectroscopy and AFM fluorescence spectroscopy. All are widely used by groups from UoA5, UoA1, UoA8 and UoA9.
- Mass spectrometry and proteomics facilities are available to aid protein identification and quantification. These include 'standard' proteomics facilities and more advanced resources that have been developed jointly with researchers in UoA8.

d3.2.3 Structural Biology: Structural biology continues to be a major strength of Oxford biosciences, with co-ordination of expertise and facilities across UoA5, UoA1 and UoA8.

- There are excellent facilities for macromolecular crystallography, with robots for crystallisation trials on proteins, recently enhanced for membrane proteins.
- Oxford has world-class protein NMR facilities for both solution NMR (including a 950 MHz magnet that is a national facility) and more specialist solid state NMR for membrane proteins (housed in **Watts**' laboratories on the Rutherford Appleton Laboratory site).
- There are good electron microscopy facilities (SEM, TEM, sample preparation) across

UoA5, and also ready access to state of the art electron cryo-microscopy and tomography within the Oxford Particle Imaging Centre that forms part of UoA1.
- Computational structural biology enables modelling and simulation methods to enhance and integrate experimental structures, forming links through to cellular behaviour. Dedicated world-class facilities and expertise for biomolecular simulations are available via the structural biology group in UoA5 (**Biggin**, **Sansom**).

d3.2.4 Cellular Imaging: Advanced cellular imaging plays a key role in extending our structural and biophysical understanding of individual proteins and their complexes to a detailed understanding of their dynamic localisation and behaviours within living cells.
- At a basic level, there are extensive (more than 30) multiphoton, TIRF, and other confocal microscopes distributed throughout UoA5. Some of these microscopes are provided by the manufacturer (e.g. Nikon) to advance technology development.
- Micron's multidisciplinary advanced bioimaging unit houses bespoke TIRF microscopes that have been developed (with UoA9) to enable single molecules to be imaged with sensitivity and speed of acquisition greater than for commercially available instruments.

d3.3 Facilities for Organismal Biosciences Research

d3.3.1 Wytham Woods & Field Station: Wytham Woods, a 385ha tract of semi-natural woodland is one of the most intensely monitored ecological survey sites in the world, having been the focus of numerous long-term projects. Because Wytham is one of the 12 terrestrial sites of the Environmental Change Network (managed by NERC), monitoring data of international importance exist for numerous physical and biological variables. Also located on site is the John Krebs Field Station, which provides greenhouse, aviary and enclosure facilities for a wide range of research in organismal biology; immediately adjacent is the University Farm, currently leased to the Food Animal Initiative, and used to develop and test approaches to animal welfare on farm animals.

d3.3.2 Oxford University Herbaria: The Herbaria comprise some 800,000 specimens that are used by members of the University and others around the world for research in plant systematics and taxonomy. Online databases have been developed to broaden access to the collections: BRAHMS is a searchable database of herbaria specimens, and the Virtual Field Herbarium is a diverse collection of images and data aimed at helping researchers identify tropical plant species.

d3.3.3 Organismal Biophysics: Unique facilities include a virtual reality flight simulator for insects which is used to measure vision-based control responses, and a low-speed low-turbulence wind tunnel equipped with 6-component force-moment balance and high-speed cameras, which is used to measure the control responses and aerodynamics of insects.

d4. SHARING MORE WIDELY

d4.1 Across the University

In 2012 the University launched a new online searchable database of its research facilities and major equipment (1,200 items each worth over £10K), which was developed with EPSRC funding. All researchers, including graduate students, have access to the database and hence to the vast array of equipment available, The database is one way in which the University has sought to respond to the report of the RCUK Task Group (chaired by Sir Bill Wakeham) urging higher intensity use of assets. We have also recently moved to fund large items of new equipment through a joint MSD/MPLS committee that administers the University's Wellcome Trust Strategic Equipment Grant. This approach ensures best use of both funding and equipment.

d4.2 Nationally

The following examples illustrate our participation in UK-wide initiatives to share facilities:
- Oxford researchers (**Ashcroft**, **Davies**) use the MRC Mouse Genetics facility at Harwell, sharing information and access to mutant populations and phenotyping screens.
- OXION hosts core microarray and proteomics facilities in Oxford that are shared with Cambridge, London and MRC Harwell.
- Extensive use is made of the Diamond beamline, and a joint endeavour is developing correlative microscopy between super-resolution and X-ray microscopies of cells.
- EPSRC funding was used to participate in the South East England Science & Engineering

Consortium with Cambridge, Southampton, UCL and Imperial, to facilitate sharing of managed research facilities and large-scale equipment.

d4.3 Internationally

d4.3.1 Large-scale Equipment: Researchers in the physical sciences have been sharing large items of equipment on an international basis for a long time, but a similar requirement in the biosciences is relatively new. Oxford researchers are central to the new European INSTRUCT Project that brings together groups with expertise in structural biology and its associated cell biology. INSTRUCT provides members with access and training in shared state of the art sample preparation and structure determination technologies. It recognises that the next generation equipment for structural biology will cost more than a synchrotron beamline and thus no single country will be able to posses the equipment or deliver the expertise across all technologies.

d4.3.2 Biological Resources: The capacity to generate biological resources can be limited either by scarcity of samples or by technological limitations. There are a number of cases where Oxford has either generated resources, or shares those that have been generated by others. For example:

- Oxford has established a partnership with a world-leading transcriptomic centre at the Karolinska Institute in Sweden to share advanced mouse miRNA arrays to acquire data on the role of extracellular RNAs in the pathogenesis of neuromuscular disease (**Wood**).
- To enhance the global capacity for monitoring microbial diversity, UoA5 researchers (**Maiden**) have developed two publicly accessible online databases: *Neisseria.*org provides an electronic resource for individuals interested in research and clinical aspects of *Neisseria*, especially *N. meningitides* and *N. gonorrhoea*; and PubMLST.org hosts an ever expanding collection of multi-locus sequence typing data for a range of microbial genomes.

d5. CENTRAL UNIVERSITY SUPPORT

d5.1 Research and Legal Services

Research and Legal services teams facilitate research across the University and knowledge exchange with external users. The teams also ensure compliance with the University's Code of Practice and Procedure for Academic Integrity in Research. During the assessment period, over 2300 grant applications, 1250 successful awards (with a combined value over £305M), 950 materials transfer agreements and 900 other inter-institutional contracts were processed for UoA5.

d5.3 Libraries

The Radcliffe Science Library (RSL) subscribes to over 20,000 journals and all university members can access them either on the University network or remotely. Online provision of science titles is more extensive than for any other UK university. The RSL also houses more than 1M volumes of printed materials and is one of the UK's largest science libraries.

d5.4 Computing

Core computing support is provided for all staff in addition to high performance computing facilities. The Oxford Supercomputing Centre has a number of conventional clusters, a large shared-memory system and two small GPU clusters. The University is also a partner in an EPSRC funded (£3.8M) supercomputing consortium with Bristol, Southampton and UCL.

d5.5 Technology Transfer

Isis Innovation Ltd, a wholly owned subsidiary of the University, is the main vehicle through which technology transfer support is provided (further details in the Impact Template). During the REF2014 period, Isis handled 243 invention disclosures and 152 patent applications for UoA5, with a total of 89 patents granted across 26 legal territories.

e. Collaboration or contribution to the discipline or research base

e1. COLLABORATION AND INTERDISCIPLINARY RESEARCH

All of our major collaborative and interdisciplinary projects are PI-initiated, often large-scale, endeavours that both nucleate and drive interactions within the University and beyond. Administrative support is in place to ensure that PIs can focus on the science in both the application and delivery phases of such projects. The effectiveness of our approach is evidenced

by the substantial number of projects that UoA5 researchers are involved in, both with Oxford researchers in other UoAs and with other institutions. Some of the recently initiated large-scale collaborations that have been led by Oxford researchers have been highlighted in section b; other examples of both long-standing and new programmes are given below.

e1.1 University-wide Collaborations

UoA5 researchers actively participate in extensive collaborative networks across the University, interacting with researchers in most UoAs covered by main panels A and B, and with UoA17, UoA19, UoA21 & UoA24. Many examples have been articulated in section b, others include:

- Research in structural biology is co-ordinated across the University, and with Diamond, through interactions between the Structural Biology Institute (STRUBI) (led by **Jones** & **Stuart** in UoA1), Structural Genomics Consortium (SGC) (led by **Bountra** in UoA1), researchers in UoA5 (led by **Sansom**) and chemical biologists in UoA8 (led by **Bayley** & **Schofield**). The fundamental objective of all of the constituent research programmes is to understand biological mechanisms in terms of underlying macromolecular structure and dynamics. These studies translate into research in a wide range of diseases, and also provide fundamental insights into potential mechanisms of pharmaceutical intervention.
- The Oxford Centre for Integrative Systems Biology (OCISB) provides a focus for systems biology approaches to research. OCISB facilitates close collaboration between experimental, mathematical, and computational biologists, bringing together researchers from UoA5 (led by **Armitage**), UoA10 (**Deane**, **Maini**), UoA8 (**Schofield**) and UoA11 (**Cardelli**, **Gavaghan**). Research is focussed on the dissection and quantitative understanding of regulatory networks in both bacteria and in eukaryotes.
- Genomics research across the University links strong computational research (UoA10 & UoA11) via model organisms (UoA5) to patient populations (UoA1 & UoA4). The combined strength of bioinformatics in UoA1 (**Donnelly**, **Mott**, **McVean**) and biological applications of genomics in UoA5 (e.g. **Davies**, **Harberd**, **Holland**, **Mackay, Ponting**) delivers an extensive research portfolio in disease genomics, whilst also delivering research in areas as diverse as evolution and cell biology.
- Cardiovascular research is co-ordinated across UoA1 and UoA5 under the umbrella of the BHF Centre of Research Excellence Award that brings together 37 PIs based in 10 departments (**Watkins** in UoA1 lead PI). Research spans from molecules to populations and covers the spectrum from basic to clinical research. Collectively, research projects cover developmental biology, epidemiology, clinical trials, cardiac imaging, human genetics, cardiovascular electrophysiology, cardiovascular pharmacology, and disease.
- Neurosciences research across 14 departments in UoA1, UoA4, UoA5 and UoA10 is co-ordinated by the University's Neuroscience Oversight Committee (chaired by **Kennard** in UoA4). This strategic approach delivers outputs in both basic and clinical neuroscience, linking the function of genes and cells to systems and behaviour. Translational research spans the whole arena of neuroscience and includes the use of genetics, stem cells, drug discovery, biomarkers, gene therapy, brain stimulation and visual prostheses.
- Research in infection, immunity and epidemiology is reinforced by activities in the Jenner Institute, an initiative that brings together over 20 PIs in UoA1 and UoA5 to develop innovative vaccines against major global diseases (led by **Hill** in UoA1). The Jenner Institute has a strategic alliance with the BBSRC Pirbright Institute, giving it a unique focus on diseases of both humans and livestock.
- A number of collaborations bring engineers and zoologists together to use machine learning and pattern analysis to assess complex animal behaviours. A recent BBSRC funded project (£738K) aims to develop optic flow measurements in flocks of broiler chickens as a tool to monitor bird welfare (**Maiden**, **Smith** with **Roberts** in UoA15).

e1.2 Collaborations Between UK Institutions

Most PIs have at least one collaborative project with a PI from another UK institution. These interactions often generate synergies within a discipline or innovate at the interface between disciplines. The effectiveness of these collaborations is seen in the 31% of submitted outputs that are co-authored with PIs from other UK institutions. Examples of participation in larger UK

consortia include:

- eMonocot: a project to develop novel bioinformatics tools for taxonomists, 2010-2013, £2M NERC, with Kew and the Natural History Museum London (**Godfray** co-PI).
- SAFE: Biodiversity, ecosystem functions and policy across a tropical forest modification gradient, 2013-2018, £2.3M NERC, with Aberdeen, CEH (Wallingford and Edinburgh), Kent, Open, QMUL (**Lewis** lead PI).
- BALI: Biodiversity and land-use impacts on tropical forest ecosystem function, 2013-2018, £4.6M NERC, with Aberdeen, Cambridge, CEH (Lancaster), Edinburgh, Liverpool, York and Natural History Museum London (**Hector** co-PI with **Mali** in UoA17).

e1.3 International Training Networks

Training graduates in international cohorts cements collaborative interactions between the PIs involved, and our lead in Marie Curie Initial Training Networks demonstrates the value that we place on such programmes. Examples include:

- CardioNeT: Translational Training network on the Cellular and Molecular Bases of Heart Homeostasis and Repair, 2012-2016, €4.5M, 9 academic and 3 industrial partners, 7 countries (**Riley** co-PI).
- PlantOrigins: Plant Developmental Biology – Discovering the Origins, 2010-2014, €3M, 5 academic and 1 industrial partner, 4 countries (**Dolan** co-PI).

e1.4 International Collaborations

The extent and effectiveness of our international collaborations is evidenced by the fact that over 50% of the submitted outputs were co-authored with PIs from overseas institutions. New collaborative ventures were launched through opportunities presented by the European Union FP7 framework programme, and by other international initiatives. Examples not already highlighted in section b include:

- EDICT: European Drug Initiative on Channels and Transporters, 2008-2011, €15M FP7, 25 academic and 2 industrial partners, 12 countries (**Ashcroft**, **Sansom** co-PIs). **Aim**: to determine the structures of clinically significant membrane protein channels and transporters for the initial development of drugs.
- EFACTS: European Friedreich's Ataxia Consortium for Translational Studies, 2010-2014, €6M FP7, 13 academic partners, 7 countries (**Wade-Martins** co-PI). **Aim**: to adopt a translational research strategy for the recessive neurological disease, Friedreich's ataxia.
- EpiGenSys: System Biological Determination of the Epigenomic Structure-Function Relation, 2010-2013, €1.9M FP7, 5 academic partners, 3 countries (**Cook** co-PI). **Aim**: to use systems biology approaches to address fundamental epigenetic mechanisms both spatially and temporally.
- GENCODYS: Genetic and Epigenetic Networks in Cognitive Dysfunction, 2010-2015, €11.6M FP7, 13 academic and 2 industrial partners plus a patient network, 8 countries (**Ponting** co-PI). **Aim**: to use a systems biology approach to gain insight into common mechanisms leading to cognitive impairment.
- Health-TIES: Healthcare Technological Innovations and Economic Success, 2010-2013, €3M FP7, 18 academic and industry partners, 5 countries (**Hassan** co-PI). **Aim**: to promote innovation in healthcare technology.
- International MDEX Consortium: Advances in Oligonucleotide-Mediated Exon Skipping for DMD and Related Disorders, 2011-2015, €3.9M, 10 partners in UK and France (**Wood** PI). **Aim**: to develop and test treatments for Duchenne Muscular Dystrophy.
- NIH Consortium: Exosome-mediated drug delivery for Huntington's disease, 2013-2018, $5M NIH, 4 academic partners, US and UK (**Wood** co-PI). **Aim**: to develop RNAi based therapies for Huntingdon's disease.
- Mapping Determinants of Arrhythmia in Structural Heart Disease, 2014-2019, NZ $5M (£2.63M), 2 partners at University of Auckland (**Paterson** co-PI). **Aim**: to map the determinants of arrhythmia (abnormal electrical rhythm) in structural heart disease.
- ECOFOR: Biodiversity and Ecosystem Functioning in degraded and recovering Amazonian and Atlantic Forests, 2013-2018, £3.4M NERC/FAPESP, 5 UK & 2 Brazilian partners (**Tobias** co-PI). **Aim**: to investigate the contribution of rainforests in Brazil to biodiversity

conservation, and to the provision of critical ecosystem services such as carbon storage.

e1.5 Collaboration with Industry

Many of the projects in section e1.4 involve industrial partners, but major collaborations with industry are underway in the STEMBANCC project outlined in section b2 and in a second FP7 Innovative Medicine Initiative (IMI) project in which Oxford researchers are playing a leading role:

- COMPACT: Advances in Drug Delivery across Biological Barriers, 2012-2017, €26M FP7 IMI, 23 academic and industrial partners, 11 countries (**Wood** co-PI).

Examples of other large scale collaborations with industry include:

- Development of protein variants as vaccine candidates for the prevention of meningococcal disease, 2009-2014, £1.87M, Novartis (**Lea** & **Tang**).
- Phase ll trials of Aleglitazar in patients with diabetes, 2012-2016, £876K, Roche (**Clarke**).
- Biodiversity assessments in Brazil, 2011-2014, £1M, BP Biofuels (**Langdale** co-PI).

e2. OTHER CONTRIBUTIONS TO THE RESEARCH FIELD

e2.1 Collective Contributions

Researchers across UoA5 collectively make a diverse, wide-ranging and substantial contribution to the research base through peer review, as members of grant panels, through membership of committees of learned societies, as editors or editorial board members for journals, and through service on advisory boards for charities, institutes and companies. Individual examples of such contributions are far too numerous to cite but indicative numbers are given in Table 5.

Table 5	# people	# of organisations
Member of Funding Body Committee	75	31 (13 countries plus EU/ERC panels)
Member of Learned Society Committee	64	45 societies
Journal Editor	48	52 journals
Journal Editorial Board Member	105	102 journals
Advisory Board for Charitable Foundation	40	51 charities
Industrial Advisory Board or Consultancy	35	42 companies
Keynote Lectures at Conferences	107	703 lectures

e2.2 Individual Contributions

Substantial individual contributions to the discipline, and recognition of such, include:

e2.2.1 Leadership Roles on Boards of Scientific Organisations. **HFSP Council**: Armitage; **Deputy Chairman of the Wellcome Trust**: Davies; **Council of the Royal Society**: Ashcroft, Freeman, Nasmyth, McLean; **Society of Biology Council**: Garland; **NERC Council**: Godfray.

e2.2.2 Figurehead Roles. **Freeman**: Chair, British Society Developmental Biology; **Garman**: President, British Crystallographic Association; **Godfray**: President, British Ecological Society; **Hay**: President, Royal Society Tropical Medicine & Hygiene; **Kleanthous**: Chair, Biochemical Society; **Raff**: Chair, British Society Cell Biology; **Robertson**: Chair, British Society Developmental Biology; **Scotland**: President, Systematics Association; **Thomas**: President, Royal Entomological Society.

e2.2.3 Notable Prizes. **L'Oreal-UNESCO Women in Science Award**: Griffin 2008, Seddon 2009, Biro 2010, Aschroft 2012; **Royal Society Croonian Lecture**: Ashcroft 2013; **Royal Society Rosalind Franklin Award**: Gupta 2009; **Royal Society Gabor Medal**: McLean 2011; **JR Vane Medal**: Garland 2011; **The Brain Prize**: Somogyi 2012, Miesenbock 2013; **Linnean Medal for Zoology**: Holland 2012; **Genetics Society Medal**: Hodgkin 2011.

e2.2.4 Election to Learned Societies. **FRS**: Harberd, McLean 2009; Grafen, Kacelnik 2011; Armitage 2013. **FRSE**: Macdonald 2008. **FMedSci**: Nasmyth 2009; Galione 2010; Bolam, King, Platt, Tang 2011; Miesenbock, Parekh, Ponting 2012. **EMBO**: Barr, Dolan, Harberd, Mellor 2009; Armitage, Davis 2010; Raff 2011; Novak, Ponting 2012.

e*2.2.5 Honours*. **DBE** Davies 2008; **CBE** Macdonald 2010, Godfray 2011; **OBE** Thomas 2011.