Institution: University College London/Birkbeck College

Unit of Assessment: 5 – Biological Sciences

a. Overview

This unit comprises over 190 FTE academics, including those in UCL's Division of Biosciences, the researchers recently incorporated into UCL from the MRC Laboratory for Molecular Cell Biology (LMCB, previously affiliated with UCL Biosciences), and the members of Birkbeck's Dept of Biological Sciences who are part of the UCL-Birkbeck Institute of Structural and Molecular Biology. Within UCL Biosciences, researchers are located in the Research Departments of (i) Neuroscience, Physiology & Pharmacology (NPP), (ii) Cell & Developmental Biology (CDB), (iii) Genetics, Evolution & Environment (GEE), and (iv) Structural & Molecular Biology (SMB). Below, academics are described in groupings that mirror these Research Department titles.

The activity summarised in this UoA provides the core of our basic biological research, covering all biological scales from molecules, through cells and tissues, to whole organisms and populations. It generates outstanding, internationally-leading research, exemplified as follows:

- Our staff publish over 600 research articles per year in leading international journals, and 51% of the >700 papers submitted here are in the highest journals (the level of PNAS or higher)
- Research is funded by external grants providing £39.3M per year, and major one-off awards such as for the £140M Sainsbury-Wellcome Centre for Neural Circuits & Behaviour
- Research activity is sustained by vibrant programmes that train 400 post-doctoral staff and 460 PhD students
- Research is supported by outstanding infrastructure and has benefited from significant investment in equipment, facilities and estates, alongside a major programme of recruitment (49 group leaders since 2008) to maintain the strength of our research
- Researchers include 20 FRSs, 20 Academy of Medical Sciences Fellows, 12 EMBO members
- Our research-led teaching provides an education that ensures a focus on critical thinking

The buildings housing the UCL and Birkbeck academics in this submission are located within a few hundred yards of each other, providing an excellent physical basis for fostering interactions. Consequently there are numerous collaborations across departmental boundaries, including those stimulated by, for example, the common interests of academics in Cell and Developmental Biology and the LMCB, and by the formation of the Institute of Structural and Molecular Biology (ISMB) which is a highly successful collaboration between UCL and Birkbeck.

b. Research strategy

General approach

Our overarching research strategy is to recruit, train, support and retain the best investigators, students and support staff, and give them an outstanding environment in which their research can thrive. To achieve this, we recruit the best scientists working in important research areas, provide fellowship support and intensive mentoring for our junior personnel, and invest heavily in infrastructure to ensure access to cutting edge technologies. We provide funding and guidance for investigators wishing to translate their research for clinical and/or commercial benefits, or to engage with the public, and encourage innovative collaborations within or outside UCL/Birkbeck.

Mechanisms sustaining and developing our active and vital research culture

Constant self-assessment and improvement are needed if we are to remain at the international forefront of research. Issues addressed successfully during the REF period include the following.
(i) Newly emerging research areas require strengthening. This has been tackled through strategic recruitment of junior and senior researchers, and investment in key technologies.
(ii) The current funding environment is challenging. We therefore provide training for researchers in grant writing and interview skills, to best position them to obtain funds.
(iii) Recruitment is essential to invigorate research. We have recruited outstanding young

researchers across the UoA (see below).
(iv) We have facilitated inter-disciplinary research, by devising PhD programmes with supervisors from different fields, starting funding schemes for novel translational projects, introducing UCL-wide thematic research domains that foster interactions across disciplines, and developing the key partnerships described below.

Key partnerships

To foster inter-disciplinary work, both at the basic science and the translational level, UoA5 academics are developing partnerships with the following bodies.
Francis Crick Institute This £700M Institute will open in 2015 with 1250 researchers studying the biological bases of disease. UCL was chosen as the founding academic partner for the Crick because of its research excellence in Life and Medical Sciences. In the next 5 years we will invest in collaborations with the Crick (partly via strategic joint appointments, the first of which are Oates, Luscombe, Goehring, Margrie, Schafer and Yardimci), and allow researchers to move their labs there to apply our basic science approaches to address clinical problems.
Sainsbury-Wellcome Centre for Neural Circuits and Behaviour UoA5 academics played a key role in obtaining funding for this £140M institute, which will open in 2014. This centre will provide an outstanding focus for the use of interdisciplinary techniques to study how neural circuits control brain activity and behaviour.
UCL Centre for Drug Discovery This UCL-wide Centre is being developed to exploit the therapeutic potential of our basic biomedical and clinical sciences across a range of therapeutic areas including CNS and cardiovascular disease, inflammation, infectious diseases and oncology. The Centre will be focussed on the School of Pharmacy (which has recently become part of UCL), with significant contributions from medicinal chemists and UoA5 researchers.
MRC-LMCB University Unit Through the LMCB moving from MRC administration to UCL, a strategic alliance has developed allowing LMCB and UCL researchers to develop long-term research strategies as exemplified by the "Dynamic Cells" initiative described below.

Research grouping strategies

In the following we describe, for each of the research groupings identified in Section **a**, how our research strategy has operated since the RAE in 2008, and how it will evolve in the future.

(a) Neuroscience, Physiology & Pharmacology (NPP) Research Grouping

Introduction

UCL is active in basic neuroscience, physiology and pharmacology research at the very highest level, on a par with that in the very best institutions in the USA. The breadth of this research is such that it is divided between 4 submissions (to UoAs 1, 3, 4 & 5). Neuroscience, in particular, in which the majority of academics in this grouping work, is a major cross-cutting "research domain" (see below) at UCL, chaired from NPP, and there are strong collaborative links between research groups described here and teams in the other groupings of this UoA and in UoAs 1, 3 & 4.

This Research Grouping comprises 55 research groups. At the molecular level our research encompasses studies on receptors, intracellular signalling, ion channels and transporters. At the cellular level, it covers signalling within and between neurons, glia and other cells within and outside the nervous system. At the systems level, it includes the function of neuronal networks and their relationships to higher-order cognitive processing, as well as the function of organ systems such as the gut, respiratory system, kidney and heart.

Objective measurement of our research productivity in this research area

UCL possesses outstanding research expertise in neuroscience, generating 30% of England's contribution to the world's most highly-cited (top 20%) publications in this research area over 1995-2004 (RAND Corporation Working Paper WR-368-DH, April 2006, prepared for Dept of Health;

www.rand.org/pubs/working_papers/WR368.html). This contribution is more than twice that of the next highest contributors. Similarly for Physiology UCL generated 19% of England's contribution to the world's most highly-cited publications, again ahead of all other English universities (the RAND Pharmacology statistics are not interpretable because they are merged with Pharmacy). This demonstrates objectively that UCL constitutes the highest quality research base for neuroscience and physiology in England and presumably the UK. Confirming this 2006 analysis, Thomson ISI Indicators (access from Web of Knowledge) rate UCL as 2nd in the world and 1st in Europe for research in Neuroscience & Behaviour over 2002-2012.

This research grouping has 6 research-active Fellows of the Royal Society (Ashmore, Attwell, Brown, Colquhoun, Cull-Candy, and Wood who was added since 2008), 9 Acad Med Sci Fellows (2 since 2008) and 2 EMBO Members (both since 2008). Of the papers cited in this return, 49% are in Nature journals, Science, Lancet, NEJM, Cell, Neuron, Current Biology, PNAS or equivalent (i.e. at least at the level of PNAS). Further evidence of strength is the 39 five-year Programme Grants/Fellowships obtained from Research Councils, ERC and charities since 2008.

Research strategy over the last 6 years

Our RAE submission in 2008 listed a range of strategies for maintaining the excellence of our research in Neuroscience, Physiology & Pharmacology, which can be summarised under the themes of (i) encouraging interdisciplinarity and interactions between researchers, (ii) developing research in innovative areas by devising new experimental and theoretical methods, and (iii) recruiting the most outstanding researchers (which is dealt with in the People section **c** below). Here we review these strategies and the outputs that they have led to.

(i) Maintaining interdisciplinarity and interactions between researchers, including those in clinical departments Three innovations have ensured that productive interactions thrive between researchers doing complementary research. Firstly, we have consolidated the merger, initiated just prior to RAE 2008, of our original departments of Physiology, Pharmacology and Anatomy into research departments of Neuroscience, Physiology & Pharmacology and Cell & Developmental Biology, which has brought researchers doing related research more into contact with each other. Secondly, to maintain interactions between researchers in the same field but in different faculties (such as basic and clinically oriented neuroscience researchers) a "Domain Structure" was devised (see www.ucl.ac.uk/slms/domains). The Neuroscience domain has been outstandingly successful at bringing together researchers from different faculties, as exemplified by the cross-faculty committee set up to devise our successful bid for the £140M Sainsbury-Wellcome Centre for Neural Circuits and Behaviour, and the annual UCL Neuroscience Symposium which showcases a broad range of neuroscience research from across the faculties and regularly attracts a capacity audience of 900 attendees. Thirdly, we are involved in developing the £700M Francis Crick Institute, which will promote the application of basic physiological, pharmacological and neuroscientific techniques to solving clinical problems.

(ii) Devising new experimental and theoretical methods As proposed for RAE 2008, we have made development of new techniques a major component of our research strategy, as follows.
(a) In response to the recognition that our outstanding electrophysiological work would benefit from a structural dimension, we are in the process of developing new tools and recruiting scientists to work at the interface of structural biology and ion channel/transporter function.
(b) To combine basic cellular and systems neuroscience with computational modelling, in order to take the understanding of neural circuits controlling behaviour to a new level, we have devised new techniques linking modelling with *in vivo* and slice recordings from the same cells (Mrsic-Flogel & Hofer, this led to papers in Nature 2011, 2013, Nature Neuroscience 2011), fostered experiments linking single neuron physiology to behaviour (Hausser, Nature 2013, Nature Neuroscience 2010, 2013, Neuron 2011, Science 2010), developed high volume electron microscopy to examine mammalian neural circuit wiring at high resolution (Roth, Science 2009, Nature 2010), and made a major input into the proposal for the Sainsbury-Wellcome Centre.
(c) We have developed new animal models of disease including neurodegenerative disorders (Kittler, Neuron 2009), pain (Wood, Science 2008, Neuron 2010, Nature 2011, Nature Comm

2012), alcoholism (Smart, Nature Commun in press), hyperekplexia (Sivilotti, Nature 2008) and ADHD (Stanford, mouse patented and available through Charles River), and new models of cardiovascular and respiratory control (Gourine, Science 2010).
(d) We have developed innovative imaging techniques to follow the movement of single synaptic molecules or organelles in real time using genetically encoded or quantum dot fluorescent tagging (Kittler, Neuron 2009, PNAS 2010, Molec Psychiatry 2011) and to probe membrane structure using scanning ion conductance microscopy (G Moss, Nature Methods 2009).
(e) We have developed innovative computer programmes to analyse the behaviour of large ensembles of neurons (Silver, Neuron 2010, Nature 2009, PLoS Comput Biol 2010; the programmes NeuroConstruct and NeuroML are freely available at www.neuroconstruct.org/ and www.neuroml.org/), and have extended programmes to analyse single channel currents (Colquhoun & Sivilotti) which are free at www.ucl.ac.uk/Pharmacology/dcpr95.html.
(f) We have promoted the development of new chemical tools for studying neuronal function, including a photoactivatable GABA antagonist (Baker in UCL Chemistry and Smart).
All of these developments, which together span the molecular to the systems level, are now coming to fruition in terms of research grants obtained and papers published.

Research strategy for the future

Over the next 5 years four key strategic developments are planned to help us maintain our research excellence in neuroscience, physiology & pharmacology.

(i) Developing molecular and cellular neuroscience We will continue to invest in our world-leading basic neuroscience research to study how single protein and cell activity in the nervous system contribute to normal function and to disease. This strategy includes recruiting young innovative researchers [Macaskill (Nature Neurosci 2012, Nature 2013, Wellcome fellow), Gielen (Neuron 2008, Nature 2009, HFSP fellow), Rancz (PNAS 2010, Nature Neurosci 2011, Nature 2012, Wellcome fellow), Sullivan (NSF fellow), Beato (PNAS 2009, Royal Soc Fellow), Gold (PNAS 2011, Biosciences Fellow)] who use novel technology to approach these issues, such as targeted mutations, structural biology, optogenetic control of cell activity, light uncaging of molecules, single molecule tracking (in part via interactions with physical scientists in UCL's London Centre for Nanotechnology), serial section electron microscopy and super-resolution imaging (being established in the LMCB, in collaboration with the National Physical Laboratory, with a £1.6M grant from the MRC). We plan to recruit 2 further groups in the next year.

(ii) Developing methods to understand neural circuits and behaviour From 2014, the Sainsbury-Wellcome Centre will provide a unique focus for the use of interdisciplinary techniques to study how neural circuits work. Our systems neuroscience strategy is for researchers in Neuroscience, Physiology & Pharmacology (Hausser, Wellcome PRF; Silver, Wellcome PRF; Cacucci, ERC Young Investigator; Gourine, Wellcome SRF; Martini, EMBO fellow; Khan, Marie Curie fellow; Bianco, Wellcome Dale fellow) to collaborate with and in some cases physically relocate to the Sainsbury-Wellcome Centre. This will promote interactions with staff in the Centre who have computational neuroscience expertise, facilitate access to cutting edge specialised equipment there, and free space on the main campus to develop new initiatives.

(iii) Enhancing structural neuroscience We wish to enhance our structural work on ion channels and transporters, since this is a key area in which UCL Neuroscience lacks expertise. We are now planning a joint appointment with the Institute of Structural and Molecular Biology (see below), anticipating that this will facilitate the recruitment of an outstanding scientist.

(iv) Developing translational research We will develop a 'UCL Centre for Ion Channels in Health and Disease', to link work on ion channels, synaptic physiology and neuronal networks to translational work. This is based on the considerable unmet clinical need in neurological and psychiatric disorders which results mainly from a lack of knowledge of basic mechanisms, not from a lack of translational effort (indeed many Pharma companies have stopped neurology operations because the basic science is insufficiently advanced to support translation). Our pharmacological experts will also make a significant input to the UCL-wide Centre for Drug Discovery, and we will

trial a new modality for interacting with industry (described in section **e**).

(v) Expanding pain research We will develop our pain research portfolio which is expanded to include studies of human sensory physiology [Ianetti (PNAS 2011), Moayedi (IASP fellow)] and (with UCLH) pain in neonates/infants [Fitzgerald (PLoS 2008, Lancet 2010, PNAS 2012)]. Animal models are being developed to identify new drug targets (Dickenson, Wood, Smart, Dolphin). This research forms part of the Wellcome Trust Pain Consortium's recent renewal.

(b) Cell and Developmental Biology (CDB) Research Grouping

Introduction

This research grouping comprises activity in the Research Department of CDB and the newly established MRC LMCB University Unit (most of whose researchers were affiliated to CDB prior to the recent transfer to UCL). Our research ranges from molecular cell biology and embryology through to biological timing and "evo-devo". The department comprises 69 research groups, producing work of the highest international standard.

Our research exploits all of the major model organisms, including yeast, *C. elegans*, *Drosophila*, zebrafish, *Xenopus*, chick and mouse. There is an emphasis on neural development, although stem cell biology, cell division and differentiation, cell fate and gene expression are studied in the widest context. At the integrative cell biology level, research groups explore tissue morphogenesis and regeneration/wound healing, bone formation, and the establishment of neuronal connections. Other groups study learning and memory, sleep regulation and circadian rhythms. Our strengths in developmental neuroscience complement the functional neuroscience within NPP, and our work on evo-devo and human evolution complements the broader genetic research in the Genetics, Evolution and Environment research grouping (see below). We are home to the major university core imaging facility, including a large suite of confocal, 2 photon and other microscope systems including fluorescent slide scanners and luminescent imaging systems, and soon to include a super resolution microscope facility.

Objective measurement of our research productivity in this research area

Research in cell and developmental biology at UCL is amongst the best in the UK, and internationally. In Anatomy and Morphology, UCL contributed 19% of England's contribution to the world's most highly cited publications (RAND Corp. Working Paper WR-368-DH www.rand.org/pubs/working_papers/WR368.html), as well as 12% to cell biology, 12% to developmental biology and 12% to biochemistry & molecular biology. With its extensive imaging facilities, CDB also contributes to UCL's 53% of England's highly cited papers on neuroimaging.

This research grouping has 7 research-active FRSs (Burnstock, Ish-Horowicz, O'Keefe, Wolpert, Zeki, and Richardson and Stern added since 2008), 9 Acad Med Sci Fellows (1 since 2008) and 4 EMBO Members (2 since 2008). Of the papers cited in this return, 58% are in Nature journals, Science, Lancet, NEJM, Neuron, Cell, Current Biology, PNAS or equivalent (i.e. at least at the level of PNAS). Further evidence of strength is provided by the 24 five-year Programme Grants/ Fellowships obtained from Research Councils, the ERC and Charities since 2008.

Research strategy over the last 6 years

During the period of this assessment, CDB has put in place mechanisms to ensure that our research evolves and strengthens over the next ten years. This has included building further strength in areas already considered strong (clocks, oscillators and rhythms), filling weaknesses in otherwise strong areas (invertebrate model organisms) and rebalancing the age profile through recruitment of junior investigators. Here we review these strategic approaches and their outcome.

(i) The clocks, oscillators and rhythms programme We have a long-standing programme of research in biological timing and have targeted recruitment and investment to further strengthen

this area. We have recruited Rihel (Science 2010, PNAS 2010) who studies sleep in fish, Stanewsky (Neuron 2009, Curr Biol 2013) who studies circadian rhythms in flies, and Oates (PLoS Biol 2012, joint with NIMR/Crick) who studies the rhythmic generation of somites.

(ii) Strengthening research in invertebrate model organisms CDB has an outstanding international reputation for developmental biology research, but we were concerned by our relatively limited use of invertebrate genetic model systems as, for studies of gene function, cell and tissue development, we want to use models best suited to the research questions, rather being limited by the available organisms. We have therefore recruited a senior Drosophila biologist (Stanewsky, see above) and two junior *C. elegans* biologists (Poole, PLoS Genet 2011, Development 2010; Barrios, Nature Neurosci 2012) and will invest in core infra-structure to enable further recruitment and integration of model organism research across departments.

(iii) Recruitment of outstanding junior investigators Our strong international reputation has often been based upon the research of senior faculty and the imbalanced age profile of PIs was a significant risk for the future. To address this we have recruited outstanding junior investigators to internal and external career development fellowships, e.g. Rihel (see above, UCL Excellence Fellow & ERC Award), Paluch (PNAS 2012, ERC Award), Poole (Wellcome CDF), Wills (Science 2010, Royal Society Fellow), Barrios (Nat NSci 2012, UCL Fellow), Barnes (Nat Genet 2008, Wellcome CDF), Barry (Nature 2012, PNAS 2012, UCL Excellence and Henry Dale Fellow), Chubb (PNAS 2012, Curr Biol 2010, Wellcome Senior Fellow), Mao (Gene Dev. 2011; UCL Excellence Fellow), Mercer (Science 2008; MRC LMCB funding) and Stefan (Cell 2011; MRC LMCB funding). Mentoring and career development for these fellows is a high priority for us.

Research strategy for the future

Over the next five years we will invest in four key strategic areas, which build on the recruitment occurring in the last 6-year period. Much of this development will be based around the construction of a new £35 million building to house the Institute of Cell and Molecular Dynamics, which will integrate efforts across the Division of Biosciences and LMCB. This additional space, combined with extensive renovations within the Department of Cell and Developmental Biology, will allow for development and expansion of the following strategic themes.

(i) Dynamic cells We will construct a state-of-the-art imaging facility which will support the latest imaging approaches, from macroscopic light sheet imaging, through advanced confocal and super-resolution techniques, to high throughput EM. This core facility will provide a focus for technology innovation to drive new techniques for cell and developmental biology. Dr R Henriques (Nature Methods 2010) has been recruited to lead this programme. Together with Dr A Lowe (SMB), and collaborators at the National Physics Laboratory (Teddington), this will provide the nucleus of a national resource for imaging instrumentation and development. This resource will allow us to strengthen existing links and build new partnerships, e.g. with the Crick Institute (we have already made joint appointments in this area: Oates, Goehring & Luscombe). Improved imaging resources will facilitate work on membrane trafficking, cell migration, morphogenesis, tissue differentiation and viruses, driven by groups such as Baum (Dev. Cell 2013), Wilson (Neuron 2009, Dev Cell 2013), Paluch (Nature 2011), Stern (PLoS Biol 2008), Tada (PLoS Biol 2011), Mayor (Nature 2008), Marsh (Dev Cell 2012), Mercer (Science 2008, PNAS 2010) and Oates (see above). At the cell biological level, Salinas (PNAS 2011) will use the new technologies to explore details of synaptogenesis and Stanewsky, Rihel and Whitmore (EMBO J 2008) will obtain high-resolution time series data relating to sleep and circadian clock function.

(ii) A computational-biomathematical hub The BBSRC funded nationwide SysMIC (Systems training in Maths, Informatics and Computational Biology) is an e-learning program established by Thomas (J Cell Biol 2010) and new recruits Barnes (Nature Genet 2008, Nature 2010 (x2), PNAS 2011) and Baier (Phys Rev E 2012). It will be expanded to include areas of interest for the biotech/pharma industry, promoting its national and international significance, and will be linked with the highly successful CoMPLEX Mathematical Biology PhD programme organised by GEE. The academic aspects of this computational programme will be greatly expanded to include

genomics and systems approaches to cell biology and neuroscience. This will complement the investment in GEE-based population/ecological and genomic computational studies (see below).

(iii) Functional genetics in health and disease Over recent years we have invested heavily in genetic model organisms. Our work on zebrafish will be greatly expanded over the next 5 years, with the construction of new animal housing, behavioural and drug screening facilities and the recruitment of several new groups using zebrafish to study central questions in developmental biology that will benefit from our new imaging facilities. Following the recruitment of Stanewsky (see above), we are constructing a £0.5M fly facility to support fly groups in the LMCB including Baum (Dev Cell 2012, 2013, Nature 2012), Pichaud (PNAS 2012, Curr Biol. 2010) and Mao (Genes Dev 2011), and facilitate recruitment of two more fly groups. The third model system we will develop is *C. elegans*, building on the recent recruitment of Poole and Barrios (see above).

(iv) Stem cells and regenerative medicine CDB hosts a Centre for Stem Cells and Regenerative Medicine. The recruitment of Tedesco (Science Translat Med 2011, 2012) is the first step of a much larger commitment over the next five-year period. This initiative will cross multiple departments and faculties, linking to the Cancer Institute and medical departments. By recruiting researchers working on how cells build tissues (Mao, see above), bridging research on stem cells to that on morphogenesis and whole body function, we aim to move developments in basic science rapidly towards translation into clinical therapies.

(c) Structural & Molecular Biology (SMB) Research Grouping

Introduction

Research activity in structural biology and biochemistry occurs in a virtual Institute of Structural and Molecular Biology (ISMB, www.ismb.lon.ac.uk/), created in 2003 to strengthen links between researchers in UCL (in the Research Dept of Structural and Molecular Biology) and Birkbeck College (Biological Sciences). It is allied with the Chemical Biology section of UCL's Dept of Chemistry (returned separately) and has a strong computational biology component. The ISMB occupies 3 adjacent sites: the recently refurbished Darwin building at UCL, the extension building at Birkbeck and the Chemistry building at UCL, and is structured around 6 programmes covering a broad range of structural and molecular biology: Structural Biology, Biophysics, Structural Bioinformatics & Chemo-informatics, Proteomics, Biochemistry & Cell Biology and Chemical Biology. Overall this research grouping comprises 60 research groups, and has become a world-leading centre for structural and molecular studies of macromolecular machines.

Objective measurement of our research productivity in this research area

There is no ranking survey for Structural Biology but, from the number of Structural Biology papers in high (Nature, Science, Cell) or high & medium (Molecular Cell, EMBO J, Nature Struct Molec Biol, PNAS) impact journals, the ISMB ranks co-first among UK teaching biochemistry departments and 3rd if research Institutes (ICR, CRUK, LRI, LMB) are taken into account.

This research grouping has 3 FRSs (Saibil, Brockes, and Waksman who was added since 2008), 1 Acad Med Sci Fellow (added since 2008) and 3 EMBO Members. Of the papers cited in this return, 44% are in Nature journals, Science, Lancet, NEJM, Neuron, Cell, Current Biology, PNAS or equivalent (i.e. at least at the level of PNAS). Further evidence of strength is provided by the 11 five-year externally funded Programme Grants/Fellowships obtained since 2008.

Research strategy over the last 6 years

Since 2008 we have improved our research competitiveness, and increased our reputation as a leading international centre for structural biology, by adding technological infrastructure to allow new kinds of experiment, by renovating space allowing the recruitment of dynamic new staff in novel research areas, by introducing a new focus on "macromolecular machines", and by developing new computational techniques for data analysis. Together, these strategies have led to

the development of a strong collaborative, multidisciplinary base at the interface of structural, computational and chemical biology. Here we review these strategies and their outcome.

(i) Adding technological infrastructure We have invested in state-of-the-art infrastructure, including £0.76M to refurbish and equip our X-ray crystallography facility, £1.6M to update our NMR facility, £1.9M to upgrade our high resolution EM facility, £0.26M to equip a new single molecule biophysics lab and £0.45M for a new mass spectrometry laboratory. This was achieved in part with Wellcome Trust funds (including £0.6M for an 800 MHz NMR magnet and £0.5M for a direct electron detector for EM). We have invested heavily in electron tomography coupled to correlative fluorescence imaging, and are building a super-resolution STORM microscope that, with the Dynamic Cells initiative in CDB, will dramatically advance light based microscopy facilities. We have also developed new facilities for electron paramagnetic resonance, molecular biophysics, and analytical mass spectrometry and proteomics. Development of NMR and other spectroscopic techniques, applied to ever larger assemblies, has been essential to capture the states through which macromolecular machines cycle to function. Advances facilitated by these new facilities include one of the first applications of EPR to the monitoring of conformational changes in membrane embedded nano-machines (Kay, & Waksman, Nature 2011), application of single molecule fluorescence approaches to investigate the nuclear pore complex (Lowe, Nature 2010), study of the interplay between ligand binding and receptor clustering in membranes (Tomas, Nature Chem 2010), further development of the novel technique of synchrotron radiation circular dichroism spectroscopy (Wallace, PNAS 2010), and development of new NMR techniques to study the mechanism of folding of nascent protein chains as they emerge from the ribosome tunnel (Christodoulou, PNAS 2009). The availability of such a wide array of techniques has made the ISMB one of the premier research centres in the field of protein science, and have led to ISMB researchers determining the structures of some of the largest macromolecular complexes currently investigated worldwide (Waksman, Cell 2008, Nature 2009, 2011, 2013; Saibil, Nature 2010, PNAS 2012, Nat Struct Mol Biol 2012; Moores, Cell 2012; Werner, Molecular Cell 2011; Orlova, Science 2009; Christodoulou, PNAS 2009).

(ii) Recruitment of talented scientists We have recruited 12 new group leaders, including Christodoulou (PNAS 2009), Thalassinos and Hansen (Nature 2011) to push NMR and mass spectrometry technologies to investigate large macromolecular complexes, and Raleigh (Nat Chem Biol 2011, Nat Chem 2012), a world-leader in the biophysics of folding intermediates and aggregation. Pinheiro (Science 2012) was recruited to strengthen synthetic biology. For super-resolution microscopy and single molecule biophysics, we recruited Lowe (Nature 2010). Boucrot (Science 2010, Cell 2012) was recruited to continue his seminal work on intracellular membrane traffic during endocytosis and cell division, and Vaughan (Mol Cell 2008) to work on Hsp90. We have strengthened our microbiology by hiring Cabreiro (Nature 2011, Cell 2013) to work on microbiota, Arnvig to work on regulatory RNAs of *Mycobacterium tuberculosis* (PLoS Path 2011), Osborne (Mol Micro 2013) working on malaria, and Hayward (Traffic 2012) to study *Chlamydia*.

(iii) Introducing a new research focus on "macromolecular machines" The challenges of Structural Biology have changed considerably since the last RAE. High-throughput structural genomics has transformed work targeted to single proteins while pushing technology to the point where structure determination is no longer rate-limiting once crystals have been obtained. This revolution has redefined the work of X-ray crystallographers: the new frontiers are in determining the structure of macromolecular assemblies. The increasing size of the macromolecular complexes being handled has led to increasing use of high resolution EM allied to atomic resolution X-ray crystallography. Now that determining the structure of single proteins is no longer a challenge, structural biology research has evolved towards the biophysical and cell biological characterization of macromolecular complexes. A key part of our strategy has therefore been to develop a major focus on "macromolecular machines", encompassing the necessarily large spectrum of approaches required to understand their mechanisms. This has resulted in the publication of a range of important papers on nanomachines (Werner, Molec Cell 2011; Christodoulou, PNAS 2009; Waksman, Nature 2009 & 2013; Orlova, Science 2009; Boucrot, Cell 2012; Lowe, Nature 2010; Saibil, Nature 2010, PNAS 2009, Cell 2012; Kay, Nature 2011).

(iv) Developing new computational techniques Computational advances have been crucial to our progress. Orengo developed new algorithms to explore structural and functional divergence in superfamilies (PLoS Comp Biol 2009, Structure 2010, NAR 2011) and predict functional families (NAR 2009) and networks (PLoS Comp Biol 2010). Topf developed computational techniques that use experimental data to define the structure of macromolecular assemblies (Structure 2008, NSMB 2008, Cell 2012). Thalassinos developed new programmes for the analysis of proteomics and mass spectrometry data (Anal Chem 2009, Int J Mass Spectr 2012). Wallace explored the limits of circular dichroism and developed algorithms to interpret spectra over extended synchrotron wavelength ranges. Finally, Nobeli developed new approaches to investigate protein-ligand interactions (Nature Biotech 2009, BMC Bioinfo 2012) and Martin has designed state-of-the-art predictors of pathogenic mutations (BMC Genomics 2013).

Research strategy for the future

Structural biology is undergoing a revolution: researchers at the forefront of this field have progressed beyond determining individual protein structures to tackling large, multicomponent, macromolecular complexes including those embedded in membranes. The sheer size of these complexes requires investigation using complementary approaches at a range of resolutions, spanning classical structural biological techniques such as X-ray crystallography, NMR and single particle cryo-EM, to visualization directly *in situ* using electron tomography and fluorescence imaging. Based on this, our strategy for the next 5 years has several strands.

(i) Institute for Mechanisms of Molecular Machines (IM^3) To build on our reputation in the structural and molecular biology of macromolecular machines, we will create a new world-class Institute for Mechanisms of Molecular Machines (IM^3) jointly between UCL and Birkbeck. This Institute is planned to lead the field in multi-scale analyses of macromolecular machines, spanning the entire resolution range from high resolution with X-ray crystallography, cryo-EM, NMR and EPR, to low resolution with super-resolution fluorescence microscopy and single molecule detection in cells, medium resolution tools being provided by electron tomography. IM^3 will also underpin research for other strategic objectives in UCL Biosciences, notably “Dynamic Cells” (see CDB above) and the “UCL Centre for Drug Discovery” (see NPP above). The IM^3 initiative provides an excellent opportunity to link with cell biology to visualize the biological nanomachines that drive cell biological processes and cellular behaviours. Because macromolecular nanomachines are the main drivers of cell biological processes, they are also prime targets for designing inhibitors of these processes. Consequently, defining the myriad of protein-protein interactions between proteins that form the multi-megaDalton workhorses of the cell will provide fertile ground for drug design.

(ii) Imaging at all resolution levels We need to be able to work from low resolution imaging of ultrastructure to high resolution X-ray crystallography. The ISMB is building a super-resolution STORM microscope (Lowe) that will complement other super-resolution approaches being developed in the LMCB/CDB (see above), and is at the cutting edge of NMR (Christodoulou, Hansen), X-ray crystallography (Waksman) and EM (Saibil, Orlova, Moores). It will remain a pioneer in developing EPR (Kay), ensemble and single molecule FRET (Werner and Lowe), mass spectrometry (Thalassinos), IR spectroscopy (Rich) and structural bioinformatics (Orengo).

(iii) Promoting interactions between different disciplines Most appointments in the ISMB have been joint between Birkbeck and UCL, to harness the joint power of Birkbeck’s reputation in crystallography and EM, and UCL’s excellence in cellular/molecular biology and biochemistry. UCL’s 0.5 FTE contribution is usually from Biosciences, but for a recent appointment (Lowe) the faculties of Medical Sciences and of Mathematics & Physical Sciences also contributed. Dr. Lowe is also jointly appointed to the ISMB and the London Centre for Nanotechnology, due to the involvement of physics and nanotechnology in this research. As research in structural biology becomes more multidisciplinary, we anticipate more appointments of this nature.

(d) Genetics, Evolution and Environment (GEE) Research Grouping

Introduction

GEE's research strengths are diverse and fall into four groupings, as follows.
(i) Ageing Research: an immense strength where researchers, located in the Institute of Healthy Ageing, use a range of model organisms (mouse, worm, fly, yeast) to study the biology of ageing.
(ii) Evolutionary Biology: for which we are a leading international centre, with activity in sexual evolution, ecological genetics and comparative evolutionary biology.
(iii) Human Genetics and Computational Biology: where research has undergone a massive renewal through initiatives led by the UCL Genetics Institute, which has recruited in statistical genetics, bioinformatics and computational expertise, linking us to many biomedical researchers.
(iv) Environmental and Biodiversity Research: for which we have created a new centre to develop innovative studies of biodiversity loss, environmental change and limits to adaptive change.

Objective measurement of UCL's research productivity in this research area

This research grouping has 4 Fellows of the Royal Society (Steve Jones added since 2008, Mace, Partridge, Yang), 1 Acad Med Sci Fellow and 3 EMBO Members (2 since 2008).

Of the papers cited in this return, 50% are in Nature journals, Science, Lancet, NEJM, Cell, Neuron, Current Biology, PNAS or equivalent (i.e. at least at the level of PNAS). Further evidence of research strength is provided by the 2 Wellcome Trust strategic awards to the Institute of Healthy Ageing (Partridge/Gems), 3 Royal Society Wolfson Research Merit Awards (Bahler, Yang and Telford), and 9 five-year Programme Grants/Fellowships obtained from Research Councils, the ERC and charities since 2008.

Research strategy over the last 6 years

GEE has been completely transformed since 2008. We have made a huge effort to regenerate research activity through a large number of new appointments, and of the researchers entered into the REF, 17 are new members of staff, giving GEE a young and dynamic air. The department has grown to 42 research groups, as well as a number of junior research fellows.

(i) New buildings and infrastructure In 2010 the whole department was bought together into a single location in newly refurbished space on the main UCL campus, adjacent to other departments in Biosciences. The £12M refurbishment included one floor of shared space with the Dept of Computer Science (CS), to provide space in which computational scientists from GEE/SMB and CS can work together. UCL also provided a new building for the Centre for Biodiversity and Environment Research (see below). These new buildings and infrastructure have entirely re-energized the department, allowed it to meet the high demands of excellent recruits, and provided the infrastructure needed for contemporary research.

(ii) Ageing research GEE houses the world-renowned Institute of Healthy Ageing (IHA, funded by the Wellcome Trust: £3.4M for 2007-12; renewed for 2013-18 by a £7M Strategic Award, with external links to Imperial and the EBI). The IHA has flourished under the Directorship of Linda Partridge (Nature 2009, Cell Metabolism 2010), whose joint appointment with the Max Plank Institute in Köln allows significant research synergies. Over the REF period, appointments of young IHA researchers have been made to cover the full range of model organisms and a diverse porfolio of research on ageing, including: Foukas (PNAS 2010) who studies mammalian cell signalling pathways sensing nutrient availability; Piper (Nature Methods 2008, Nature 2009), a Royal Society URF, who uses flies to investigate metabolic controls of ageing; Schuster (Mol Syst Biol 2010), an MRC Career Development Fellow, who brings bioinformatics skills; and Alic (Aging Cell 2011), a Biosciences Fellow, looking at how transcription factor activity drives the plasticity of adult physiology and lifespan in flies. The Chair in Systems Biology was filled by Bähler (Nature 2008) from the EBI who analyses transcriptome regulation, non-coding RNAs and genomic variation in ageing and under stress, in fission yeast. He is supported by Jeffares (PLoS Genet 2010), a Senior

Research Fellow using bioinformatics to study pathogen transcriptomics.

(iii) Evolutionary biology We have strengthened existing excellence by appointments to extend our coverage in new technologies. Mank (PNAS 2012) was appointed Chair of Evolutionary and Comparative Biology, studying genome and transcriptome evolution of sex chromosomes, and Raihani (Science 2010) extends our interests in the evolution of cooperative behaviour in animal and human societies. The prominent science writer Nick Lane (Royal Society Prize for Science Books 2010, Nature 2010) returned to full time research on the Provost's Venture Research Prize Fellowship. He leads an interdisciplinary team studying the origins of life and fundamental traits of eukaryotes, working alongside the theoretician Kuijpers (PNAS 2011) studying the evolution of sexes and the germ/soma distinction associated with multicellularity.

(iv) Human genetics and computational biology The UCL Genetics Institute has been a powerhouse in the development of statistical and bioinformatic approaches for clinical and human population genetics, and in the rejuvenation of human genetics. Three new biostatisticians have been appointed, as follows. Balding (Am J Hum Genet, 2012), an expert in Bayesian modelling of genetic associations, was appointed Chair of Statistical Genetics. Plagnol (Nat Genet 2009, Nature 2010) uses genetic data to investigate molecular mechanisms underlying associations with disease, and Hellenthal (Nature 2011) is developing genome-wide association methods. We also appointed: Luscombe (Nature 2012, Science 2012, Cell 2013) as Computational Biology Chair (a joint appointment with CRUK, to be located at the Francis Crick Institute), who analyses genomic scale data on how regulation of gene expression affects evolution; Balloux (Curr Biol 2010, Science 2011) as Chair of Computational Systems Biology, who is interested in reconstruction of infectious disease epidemics in humans and wildlife and has links to the Dept of Infection & Immunity and the Inst of Zoology; Davis (Mol Psych 2012, 2013) who uses twin-based analysis to look for genetic and environmental hotspots in cognitive abilities; and Dessimoz (Nature 2013) a joint appointment with Computer Science with expertise in reconstructing the tree of life, as well as development of algorithms and user/programming interfaces.

(v) The Centre for Biodiversity and Environmental Research (CBER) UCL has given £1.5M for building work and 4 new posts to found the CBER. We appointed Mace (PLoS Biol 2010, Science 2010), an international leader in the study of ecosystem change with multiple links to international policy leaders, as Director. Kate Jones (Nature 2008), who studies wildlife disease macroecology and human emerging diseases, was appointed Chair in Ecology and Biodiversity. She has forged links with Statistical Sciences, developing new technologies for monitoring biodiversity. Two lecturers have joined CBER, Collen (Science 2010) who is developing biodiversity indicators to understand extinction risk, and Pearson (Science 2013) who studies the distribution of species at large spatial scales, and how distributions change over time, as well as Freeman, a CoMPLEX 2020 Research Fellow joint with Microsoft Cambridge, who is developing computational systems to collect behavioural, ecological, and spatial data in sea birds.

(vi) Maintaining interdisciplinarity In the last 6 years we have developed a strongly interdisciplinary mentality, linking with Computer Science, CoMPLEX (a £7M EPSRC-funded PhD programme and post-doctoral fellowship scheme linking biological and physical sciences), the Environment Institute, several Biomedical departments, as well as with the Institute of Zoology, Natural History Museum, London School of Hygiene & Tropical Medicine, Francis Crick Institute and Microsoft/University of Oxford post-doctoral training centre.

Research strategy for the future

We have identified four key areas for strategic development, as described below. We are also building new Masters programmes (in existence: Genetics of Disease, Stratified Medicine, Biodiversity; in planning: Ageing) in each research theme as feeders for PhD programmes (BBSRC, NERC, CoMPLEX) that support departmental research.

(i) Developing functional genetics in health and disease The Institute of Healthy Ageing has been a remarkable success under the leadership of Partridge. We will appoint a senior person with

similar drive and insight to promote functional genetics research. This initiative will link with other groups in UCL in Biosciences (see related CDB strategy above) and clinical departments.

(ii) Strengthening research on origins and comparative biology We plan to strengthen our research in comparative biology, evo-devo and early eukaryotic origins through Reader and Chair appointments in experimental and computational approaches. In this important area the questions are profound but the approaches often difficult. New technologies in genomics, genome engineering and transcriptomics are opening up for non-model organisms, and allowing real progress. The work is highly interdisciplinary, and needs to be connected to biochemists and engineers in order to study the origins of membranes, energetics and complex life. We already have considerable and diverse talent, and now need to build greater critical mass.

(iii) Expanding computational biology and mathematical modelling We already have strong links with the mathematical, computational and statistical sciences through CoMPLEX (see (vi) above), whose former Director Pomiankowski is now head of GEE. In partnership with CDB and SMB, we will invest further in bioinformatic, statistical and computational skills, as demand for mathematical and modelling expertise is expanding, and expand our joint space with SMB and Computer Science for computational biologists.

(iv) Growing the Centre for Biodiversity and Environmental Research We expect CBER to grow considerably over the next 5 years, and new space for the centre has been planned in outline. We need to appoint experimentalists working on natural systems to complement our existing expertise. CBER will also expand our links to the Institute of Zoology and Natural History Museum, and other London Universities and Institutes who are natural partners for this activity.

c. People

1. Staffing strategy and staff development

Overall strategy for outstanding staff and a sustainable staff structure Our overarching strategy is to recruit, train, support and retain the best investigators, and to maintain a good balance of junior to senior investigators. Over the REF assessment period, UoA5 has recruited 18 Professors/Readers and 18 Lecturers. Of the 14 new Professorial appointments, 8 are under the age of 45, while 11 of the lecturers were 35 or under when recruited, showing a commitment to promoting leadership from a young age and to hiring outstanding young scientists. We have also recruited 27 Senior or Junior Career Development or Marie Curie Fellows on external or UCL funding, with an average age of 36.5 years, 19 of whom were 35 or under when recruited.

Career development support for research assistants, postdoctoral researchers, and early career researchers, and support of the Concordat All staff (both in UCL and Birkbeck, including those paid on research grants) in UoA5 have undergone a constructive career appraisal every second year (annually from 2013) to provide advice on career development. This appraisal includes discussion of any training needed to enhance performance and career development, and consideration of which courses could be taken to expand their skills and career prospects. Particular attention is paid to the development of new junior PIs. These are assigned a mentor who advises them on obtaining grants, publication, teaching and promotion strategies, and they are given a lower teaching load in the first 2 years of appointment as a Lecturer. Early Career Workshops also support the careers of junior staff members: these cover a wide range of topics to help junior researchers to progress within their field of research.

Evidence of commitment to equal opportunities Equal opportunities are supported from the highest level, with UCL Council having members specifically assigned to gender, disability, age, race, religion and belief, and lesbian, gay, bisexual & transsexual equality (indeed UCL is a Stonewall top 100 employer for LGBT staff). UCL policy is that those interviewing job applicants must be trained in equal opportunities issues and at least 25% of interview panels should be women. UCL has just renewed, and Birkbeck has obtained, an institutional Athena SWAN bronze award (for promotion of women in STEM subjects), and within UoA5 the LMCB holds a silver Athena Swan award. In UoA5 21% of professors are female, significantly higher than the 12% of

UK Biosciences Professors who are women (HESA data 2010/11). For the REF, in this UoA 12% of male and 8% of female researchers were not submitted (not significantly different, p=0.55).

Strategy for career progression of staff UoA5 follows UCL/Birkbeck procedures for staff promotion and pay increments, based on the appraisal process described above and on one off applications for pay increases or promotion. Post-docs and technicians can apply for accelerated increments or re-grades based on achievements over and above those expected of them. Academic staff can apply through the annual promotions round for progression to Senior Lecturer, Reader or Chair, either with the support of their Head of Department or via an independent application. Part-time working is available for those who want it, e.g. after childbirth, and sabbatical terms are available to academic staff every 7 years. A large range of courses foster career development, e.g. courses.grad.ucl.ac.uk and www.ucl.ac.uk/hr/osd/timetable/.

Institutional support for careers of staff As detailed in the departmental strategy sections above and section **d** below, UoA5 has made a large investment (£37M since 2008) in research platforms and refurbishment to support the needs of researchers. It has also invested in its administration and technical structure since 2008 to provide a comprehensive support system to the academics and junior members of staff, with 5 administrative teams supporting Finance, HR, Estates, Teaching and IT activities. Technicians now provide core support to twelve facilities as opposed to individual labs. Standards of ethics and safety in research are maintained by centralised services (ethics.grad.ucl.ac.uk/ and www.ucl.ac.uk/estates/safetynet/).

2. Research students

4 year and 3 year PhDs

UCL has set up structured 4 year PhD programmes (funded by the Wellcome Trust, MRC, BBSRC, British Heart Foundation and Wolfson Foundation), with supervisors in this UoA, in different research areas: Molecular Cell Biology; Developmental & Stem Cell Biology; Structural, Molecular & Chemical Biology (with Birkbeck); Neuroscience; Pain; Macromolecular Machines (with Birkbeck); Neurodegeneration; Medical Research; Cardiovascular Research; Bioscience & Bioengineering; Maths & Physics in the Life Sciences and Experimental Biology (CoMPLEX). Together these offer 64 PhD places/year, many of which are in UoA5. These programmes are complemented by CASE and other industry-funded awards (10 per year in UoA5 over the REF period) and 30 per year 3 year PhD positions funded by grants or research councils in UoA5.

4 year PhD programme student outcomes

The 4 year PhD programmes provide UCL with high quality students because of their coordinated recruitment in which the best students are selected from a large number of applicants (e.g. the 4 year PhD in Neuroscience regularly receives over 400 applications for the 6 places available each year), and as a result ~90% of the accepted students have 1st class degrees. The 4 year programmes funded by the Wellcome Trust can also take non-EU students, further increasing the pool of excellent students from which applicants are chosen.

The 4 year programmes provide the students with numerous benefits, including:
(i) 3 rotation placements in different labs to experience different supervisors and techniques;
(ii) promotion of interdisciplinary work by working between different labs (some programmes require that a student be supervised by 2 academics with different areas of expertise);
(iii) provision of general courses (e.g. statistics, ethics, experiment design, presentation skills);
(iv) a wide range of discipline-specific courses.
Surveys of the students show them to be very satisfied with the programmes' structure.

The first year training provided by the UCL 4 year PhD programmes has been shown to increase the productivity of the students: analysis for students on the Neuroscience programme has shown (see Student Outcomes tab at www.ucl.ac.uk/npp/NeuroscPhD/) that:
(a) 5 years after starting the programme, 4 year students have published 1.8-fold more papers than

3 year students in the same departments at the same time;
(b) 9 years after starting the programme, 4 year students have published 1.9-fold more papers than 3 year students in the same labs (this controls for supervisor differences);
(c) 9 years after starting the programme, 4 year students have published 1.9-fold more papers than equally excellent students who we offered a place to but who rejected our offer.
About 80% of the students go on to post-doc positions, 95% use their science training in their first post-PhD position, and the earlier cohorts are now starting to obtain permanent academic posts.

The quality of the 4 year PhD students, and the fact that in their first year they rotate around labs in different departments so that many supervisors and other students meet them, has contributed significantly to producing a high quality research culture among all graduate students in this UoA.

Recruitment, progress monitoring and subsequent careers of students

All the 4 year PhD programmes and some 3 year PhDs go through a multi-stage recruitment process in which applicants respond to an advertisement. Out of the large number of applicants (see above) a shortlist is drawn up by a committee and these students then visit the programme for interview. UCL/Birkbeck policy dictates that all interviewers have had training to guarantee equal opportunities for women and ethnic minority applicants. Although there are year-to-year variations because of the small numbers accepted to each programme per year, the gender ratio for the accepted applicants generally matches that in the applicant pool.

All PhD students at UCL carry out their PhD under the auspices of the Graduate School (www.grad.ucl.ac.uk/) which provides the following quality control mechanisms for monitoring student progress (similar procedures apply to Birkbeck students). Every PhD student is assigned a mentor (and in some departments a PhD committee) not directly connected with the work but who the student can consult in the event of problems arising – as a result, in the rare cases when the student-supervisor relationship goes wrong, an intervention can be made to help the student make the best of the situation, if necessary by introducing an additional supervisor. The mentor or PhD committee, together with the departmental Graduate Tutor, is also responsible for assessing the student's progress at the crucial upgrade viva at the end of the first year of PhD work. For students on the 4 year PhD programmes, there is frequent contact with the PhD Programme committee, who assess progress at the end of each first year lab rotation (the students have to present their work as a conference talk and as a small research paper to improve their communication skills), and also assess the student's plan for their PhD at the end of that first year. All students also have to fill in an electronic log (roughly every 3-6 months), which allows the departmental Graduate Tutor to monitor their progress. Together, these measures result in 64% of 3 year PhD students and ~85% of 4 year students finishing their PhD within one year of the end of their funding.

Throughout their PhD, UCL and Birkbeck students can take a vast range of courses put on by the Graduate School (courses.grad.ucl.ac.uk/list-training.pht). These cover 4 broad areas: Knowledge and intellectual abilities (137 courses relevant to this UoA); Personal effectiveness (90 courses); Research organisation & governance (53 courses); and Communication influence & impact (109 courses). From 2008-2013, PhD students in this UoA took up over 3000 places on these courses. Of these courses, 45 are relevant to progression to a career (academic or otherwise) after the PhD, and since 2008, 385 PhD students in UoA5 took part in these courses. PhD students also have access to the UCL Careers Advice Service: 539 PhD students attended courses led by Careers Service counsellors and 87 students were booked onto industrial employer led events.

Interactions of PhD students with industry

The Graduate School courses mentioned above include 21 devoted to promoting a pro-business attitude among PhD students. These include Bright Ideas Awards, supporting the development of new student-led businesses emerging from UCL, and an Enterprise Society which encourages the commercialisation of cutting-edge postgraduate research (it won the "Enterprise Society of the Year Award" in 2012), at which 200 students regularly attend events such as "launching 6 ventures in 48 hours" and an "entrepreneurial networking party". PhD-specific careers consultations were

introduced in late 2011 with 35 booked by UoA5 PhD students to June 2013. In addition to these courses, to promote PhD student-led start-up companies, the UCL Student Business Hatchery provides comprehensive training for students to get into business (www.ucl.ac.uk/advances/students) and helps businesses get off the ground by offering free office space for business startups led by UCL students or recent alumni (www.ucl.ac.uk/advances/students/hatchery). Interaction with industry has also been provided by the 50 partly industrially funded PhD studentships (37 CASE and 13 other) in UoA5 since 2008.

d. Income, infrastructure and facilities

The UoA5 research environment is excellent, with academics located in good to outstanding laboratory space in adjacent buildings. Much of the estate has undergone, or will undergo, major renovation as part of a strategy to improve infrastructure at UCL (www.ucl.ac.uk/masterplan) and Birkbeck. Since 2008, £8.2M million has been invested in renovations to the Darwin Building and ongoing work is transforming many parts of the nearby Anatomy and Medical Sciences buildings. This will culminate in a £35M new building situated between CDB, NPP and the LMCB. As part of this development, a major new imaging facility is planned to establish an international centre for molecular, cellular and tissue level imaging within UoA5. A £20M building is also planned for the Institute for Mechanisms of Molecular Machines in SMB. These investments will ensure that almost all research in UoA5 is conducted in new or renovated state of the art laboratories, offices and interaction areas. In parallel, the UCL Sainsbury-Wellcome Centre for Neural Circuits and Behaviour (SWC) will be complete in 2014 and the Crick Institute in 2015. SWC scientists will work within the UoA5 remit and there will be considerable UoA5 activity within, and in partnership with, the Crick. Joint senior academic appointments between UoA5 Groups and the Crick already include Oates, Schaefer, Luscombe, Yardimci, Margrie and Goehring.

Superb core facilities provide UoA5 researchers with access to state-of-the-art equipment and expertise for their research. For instance, the two main Core Imaging Facilities in CDB and the LMCB have 14 highly trained technical staff (6 HEFCE- and 8 MRC-funded) and provide users with a wide range of confocal, multi-photon, time-lapse, laser ablation, high-throughput imaging, EM and other microscopes, as well as training in and access to various image processing and analysis software. Ongoing investment will bring several super resolution imaging platforms to these core facilities in the coming months and light sheet imaging will be developed in the coming year. This expansion in imaging is being coordinated with the recruitment of academics (including Lowe and Henriques) who can develop and exploit the platforms, and benefits from the LMCB's ongoing collaboration with the National Physical Laboratory. Aligned with the imaging facilities, the £2M LMCB Translational Research Resource Centre provides access to robotics and high throughput screening for small molecule, siRNA and cDNA screens. Two similar platforms are being developed in CDB to expand capacity and provide whole animal screening platforms for fish embryos and other small animals. To support molecular techniques across the UoA, there are 5 major Molecular Biology core facilities run by 7 University support personnel as well as comparable facilities within the LMCB. These provide access to all standard molecular biology equipment as well as many more specialist approaches such as NMR, analytical ultra-centrifugation, Biacore surface plasmon resonance instrumentation, EPR, X-ray crystallography and high resolution cryo-electron microscopy.

The UCL Fish Facility is a state of the art resource run by a manager (who won the 2013 PMI European Technician of The Year Award) and 4 core staff. It provides researchers with access to several hundred genetically distinct fish lines, and also supports zebrafish research in other HEIs (on many hundreds of occasions over 2008-13). Investment of over £2M will expand the Facility to enable large-scale small molecule and genetic screens as well as supporting new recruits working with this model organism. In addition to these and other core facilities, researchers have outstanding IT and specialist workshop lab support as well as finance, personnel, estates and general administrative support.

For core facilities to function effectively, they require huge investment. In the early phase of the assessment period, the CIF scheme provided major funding for internal equipment. To maintain this after termination of the CIF scheme, UCL annually invests several million pounds in research

platforms through its internal peer-reviewed competition (assessed by Vice-Deans for Research) for Capital Equipment Funding (CEF). When possible this funding is matched by external grants (such as Wellcome Trust Multi-User Equipment grants), enabling major equipment purchases each year. Over the REF period to date, about £4.3M from CIF/CEF plus £3.7M matching funding has been invested. For instance, a £1.6M MRC award in 2012/13, matched with £0.5M of UCL CEF funding, will bring super-resolution imaging to Biosciences, and a UCL investment of £1.3M has enabled purchase of two Leica SP8 confocal/multiphoton microscopes and two high throughput microscopes for the core imaging facility. In structural biology, the purchase of 800MHz NMR equipment funded by £1M from UCL and a £0.6M Wellcome Trust infrastructure grant will considerably increase our capability. In the last two years, further support for capital equipment has come from the annual allocation of £1.5M provided through the Wellcome Trust Institutional Strategic Support Fund. This also supports people, through start-up funds and Fellowships for junior investigators, and translational research through small project grants.

One of the ways in which UCL maintains a vital and sustainable research environment in the life and medical sciences is through the three branches of the Life and Medical Sciences Research Support Centre (RSC www.ucl.ac.uk/slms/research_support_centre). One branch supports all activities related to Platform Technologies and core equipment as described above. The second branch comprises the Translational Research Office (TRO), whose 6 personnel help academics to enhance translational research within UCL. Such guidance is of particular importance to UoA5 investigators, many of whom have had little experience with translational research. The TRO also has funding schemes to develop translational research which have promoted activity in this area for UoA5 investigators. For instance, two UoA5 investigators have had £50K pilot projects supported through the Therapeutic Innovation Fund (with one project leading to a further award of £316K from the BBSRC) and in the 2012 round of the Confidence in Concept Scheme, 3 UoA5 investigators received awards of ~£100K to pursue small molecule drug discovery projects. The third branch of the RSC comprises the Research Coordinators. These are senior academically trained personnel, often with a background in the research funding sector, who provide a wide variety of support services to academics, particularly with respect to supporting research initiatives that cut across different disciplines. They have played key roles in coordinating major funding applications involving multiple labs and, in some cases, multiple institutions; they organize grant writing workshops and mock interviews; they facilitate events that encourage academic interaction; and they administer internal funding schemes. Their activities, together with increased mentoring of junior academics by more senior academics, has enabled UoA5 researchers to maintain excellent funding in a very challenging period for funding for basic biosciences research.

The activities of Research Facilitators are aligned with those of the Research Domains (www.ucl.ac.uk/slms/domains), which are interdisciplinary networks of investigators that encompass the breadth of research in areas of strength across the University, irrespective of affiliation. For example, the Neuroscience Domain (www.ucl.ac.uk/neuroscience/) involves more than 450 academic group leaders across the university. The coordinator of this domain, who is in UoA5, guided by a strategy committee from across the University, has to understand the diversity of neuroscience research and bring together investigators with common or related interests to stimulate research and take advantage of research funding opportunities. For instance, the neuroscience coordinator and strategy committee put together the successful UCL application for the Sainsbury Wellcome Centre for Neural Circuits and Behaviour, which will bring £140M in infrastructure and research to support activities largely within the UoA5 remit.

Research grant income to UoA5 was £171 million for 2008-13 (plus £140M for the Sainsbury-Wellcome Centre) with annual income increasing from £31.2M for 2008/09 to £39.3M for 2012/2013. Two academics received Wellcome Principal Research Fellowships, 20 received MRC or Wellcome Senior Fellowships or Investigator Awards, 19 received ERC Investigator awards, 43 received Career Development Awards and 38 obtained 5 year programme grants.

It is well-recognised that the continued success of research in UoA5 biosciences is dependent upon recruitment of, provision of funding for, and mentoring of outstanding junior investigators. UCL has funded the Excellence Fellowship Scheme to recruit, worldwide, the very best junior investigators at

the point at which they are ready to start independent research. In UoA5, six such fellows have been recruited and several others through related internal fellowship schemes. The quality of the candidates appointed ensures that they are likely to obtain prestigious external fellowships and this has indeed been the case for four of the Excellence Fellows. As mentioned above, we now invest much effort in mentoring junior academics to ensure that they make a successful transition from fellowship funding to a permanent position, and most are offered permanent positions upon acquisition or renewal of major Fellowships.

UCL Governance Policy (www.ucl.ac.uk/ras/acs/resgov) requires that UCL's vision as a world class centre of research, acquiring and disseminating knowledge to benefit the world, is underpinned by a commitment that research is conducted in accordance with the highest professional standards. UCL has established a Research Governance Committee to address all issues related to governance strategy. Allied to research governance is UCL's open access mandate (www.ucl.ac.uk/library/publications-policy.shtml) which supports open access to research literature and provides, through UCL Discovery (discovery.ucl.ac.uk) public access to UCL's published research. All UoA5 research adheres to these policies.

e. Collaboration or contribution to the discipline or research base

Contribution to the discipline

- UoA5 has 20 research-active Fellows of the Royal Society (names are given above) with 5 of them receiving an FRS since 2008 and 1 (Partridge) serving on the Royal Society Council, 20 Fellows of the Academy of Medical Science (4 of them since 2008), and 12 members of EMBO (6 of them since 2008).
- 33% of UoA5 academics served on national (e.g. Research Council) or international grant panels since 2008, including for the Wellcome Trust (Attwell [panel co-chair], Christodoulou, Partridge, Saibil, Silver, Wilson [panel chair]), MRC (Balding, Cull-Candy, Cutler, Duchen, Marsh, Partridge, Salinas, Wilson), BBSRC (Bahler, Orengo, Luscombe, Purton, Srai, Telford), EPSRC (Partridge), NERC (Fowler, Mace [Council & panel], Mank, Pomiankowksi), ERC (Cossu [Panel Chair], Cull-Candy, Hausser, Mace, Moores, Partridge, Riccio, Saibil, Salinas, Smart), Royal Society (Ashmore, Beato, Cull-Candy, Ketteler, Saibil, Smart, Stern), DFG/Acad Sci (Germany: Mace, Partridge), CNRS/INSERM/ANR/Pasteur (France: Cramer, Cull-Candy, Kittler, Marsh, Silver, Stern), Spanish Ministry (Stern), Finnish Academies (Luscombe, Mank), NWO (Netherlands: Pomiankowski), NSF (USA: Mallet), Austrian Science Fund (Sivilotti), Telethon Italy (Wilson), Scientific Council of UNESCO Venice (Zeki).
- Mace serves on the UK Government Natural Capital Committee.
- Our expertise has been recognised by the award of numerous prizes; examples from various disciplines are: Linda Partidge - Darwin-Wallace Medal of the Linnean Society of London and a DCBE for services to science; Georgina Mace - Ernst Haeckl Prize, of the European Ecological Federation; Judith Mank - Dobzhansky Prize for Evolution; Kate Jones - Philip Leverhulme Prize for Zoology; Trevor Smart - Gaddum Medal of the British Pharmacological Society; Sonja Hofer - Eric Kandel Young Neuroscientist Prize; John O'Keefe - Gruber Prize; Josef Kittler - Lister Prize; Jeremy Brockes - Newcomb Cleveland Prize for best paper published in Science; Semir Zeki - the Erasmus Medal of Acadamia Europae; Steve Wilson - Remedios Caro Almela Prize in Developmental Neurobiology; David Attwell - Kenneth Myer Medal for Public Lecture; Nick Lane - Royal Society Prize for Science Books.
- 30% of UoA5 academics took leading roles in learned societies since 2008.
- 47% of UoA5 academics served on editorial boards of journals since 2008.
- 60% of UoA5 academics were involved in organising conferences since 2008.
- 39% of UoA5 academics have been conference programme chairs since 2008.
- 38% of UoA5 academics gave invited keynote lectures since 2008.
- In response to the ageing of the population, a national and international priority for health and social policies, UCL has developed the Institute of Healthy Ageing.
- Some UoA5 members produced reports of national or international significance, including Steve Jones' Review of Impartiality and Accuracy of the BBC's Coverage of Science (www.bbc.co.uk/bbctrust/assets/files/pdf/our_work/science_impartiality/science_impartiality.pdf) and Linda Partridge's Academy of Medical Sciences Report on Rejuvenating Ageing Research.

Collaboration

- 81% of UoA5 members took part in collaborative research, and 53% in inter-disciplinary research since 2008, while 31% collaborated with industry or other research users.
- 35% of UoA5 members took part in collaborations for PhD research training since 2008, including for a Wellcome-funded Pain PhD Programme between UCL, King's College London, Imperial College and Oxford, and a BBSRC-funded Biosciences PhD between UCL, Birkbeck, KCL, LSHTM and the Royal Vet College.
- Mechanisms for promoting collaboration include the Research Facilitators (see section d) who bring groups together to respond to funding calls, the UCL European Office (www.ucl.ac.uk/research/europe) which fosters interaction with other EU groups when applying for EU funding, the Research Domain structure (sections b & d) which promotes interactions between researchers in different departments, and the Grand Challenge studentships and some PhD programmes that require supervisors from 2 distinct disciplines.
- As described in our REF3A, effective collaboration with industry is indicated by the award of 50 PhD studentships (37 CASE and 13 other) partly funded by industry, and the award of 24 grants from industry, and we are developing a new modality for interacting with industry, in which academics can propose projects to a joint industry-UCL committee that selects projects for pump-priming funding by industry, with UCL providing basic science and clinical expertise. To trial this idea, a pilot arrangement like this is being set up with Eisai.
- Indices of the success of our mechanisms promoting national and international collaborations are the involvement of 11 UoA5 members in collaborative BBSRC LoLa awards and Wellcome Strategic Awards, and 52 in EU FP7 partnerships.