Institution: University of Warwick

Unit of Assessment: UoA5 Biological Science

a. Overview: This submission reflects the work of 41 members of the School of Life Sciences (SLS) and 6 members of the Warwick Systems Biology Centre (WSB). Work from SLS focusing on veterinary science and the plant and environmental science that underpins agriculture and horticulture (13 academics) is submitted separately to UoA6. SLS was established in October 2010 through the merger of the former Department of Biological Sciences (on Gibbet Hill campus) and of Horticulture Research International (HRI, at Wellesbourne). The merger was accompanied by rationalization of staff and resources across the two sites. Professor John McCarthy was appointed in October 2010 to lead an ambitious development programme for SLS, and Professor David Rand has led WSB since 2005. The Life Science development plan is being supported through investment in new academic positions, new facilities and new buildings. The latter include the *Warwick Phytobiology Facility* and the *Warwick Interdisciplinary Biocentre*. Our vision for research and training reflects the modern view of biology as an interdisciplinary science that increasingly incorporates quantitative methods and in which exciting discoveries are driven by the rapidly expanding repertoire of experimental and computational technologies. At the centre of our philosophy is therefore a commitment to an integrative approach that seeks to identify the core principles shared by all forms of life. The integrated nature of the Research Theme structure means that animal, plant and microbial science activities are associated with multiple Themes.

b. Research strategy

The overall strategy is to promote an ethos of research excellence within a framework that emphasises integrated, interdisciplinary, broadly systems-oriented approaches underpinned by a high degree of interconnectedness between research themes as well as extensive networking between our researchers, thus capitalizing on the collective skill base and synergies within the community. ***SLS has 6 integrative research themes:*** Development, Environment, Food Security, Infection Biology, Molecular & Cell Systems and Synthetic Biology & Biotechnology, all of which act to promote integrative and interdisciplinary research pursued by researchers working in our animal, plant and microbial communities. WSB complements the more experimental activities under the theme Molecular & Cell Systems in SLS. Our research translates into multiple cases of high impact in areas including Food Security, Biotechnology, Animal & Human Wellbeing, Environment and Big Data, a selection of which are included as Impact Case Studies in this REF submission. The continuing development of core technology capabilities, including computational facilities, genomics, proteomics, metabolomics, microfluidics, high-resolution imaging (EM, light microscopy, flow cytometry) and structural biology, underpins this strategy. The emphasis in the School's vision on the development and application of quantitative technologies maximises our interactions with the internationally acknowledged strengths of the University of Warwick in mathematics, computer science, engineering and the physical sciences. This research strategy also underpins the SLS strategy for training and education. In order to realise the SLS vision, we have made 14 new academic appointments in the period 2010-2013, as described in the People section. A unique selling point of WSB is the strength and breadth of the mathematical, statistical and bioinformatics skills that it brings to bear on biological projects.

Significant changes to research environment – A key component of the vision for SLS has been to achieve a significantly greater degree of integration in terms of staff environment, shared facilities, support structures, research and training activities. A major step in this direction has involved the construction of a state-of-the-art *Phytobiology Facility* on main campus, enabling the majority of the plant scientists to relocate from the (HRI) Wellesbourne site to refurbished laboratories on main campus. A cohort of crop science experts that makes intensive use of field-trials has remained as the recently formed Warwick Crop Centre at Wellesbourne. We have also significantly upgraded our Facilities for proteomics, genomics, imaging, microfluidics and computation through strong investment in equipment and infrastructure, as detailed below.

Completion of the first stage of our transformational life science strategy will lead on to stage two: the relocation of life science research into a major new building (the *Warwick Interdisciplinary Biocentre*) whose construction is due to start in 2014.

Evidence of strong research plans – It has been argued by Sir Paul Nurse FRS and others that biology is founded on a number of core principles, the most obvious being: 1. Determination of biological structure and function via expression of the genetic code incorporated into DNA; 2. The cell as the fundamental unit of life; 3. Evolution of life forms via natural selection. However, what is

missing is ('principle 4') a generic set of rules that explain how molecular components form progressively higher levels of complexity in terms of structures and functions that generate the diversity of extant phenotypic structures and behaviours, from the cellular to the organismal level. Elucidation of these emergent features of biological systems will be heavily dependent on the development and application of analytical/quantitative technologies. It is our strategy to build on capabilities and core technologies in areas including genomics, proteomics, metabolomics, biophysical methods (including structural biology), and computational biology, using them to enhance the insights gained from more traditional methodologies in genetics, biochemistry and physiology. Equally, our research reflects the diversity of life forms, covering microbes, plants and animals, and stretches from molecules to populations of multicellular organisms. There are multiple areas of impact from our research: e.g., we study how microorganisms cause disease and interact with the environment, we optimize the quality/yield of agricultural crops, and we develop novel methods/processes in biotechnology (especially in its new manifestation as synthetic biology).

The 6 integrative Research Themes in SLS are non-exclusive and promote interactions across the full range of organisms and systems that our community works on. As a highly interdisciplinary School, SLS collaborates extensively with the Departments of Chemistry (antibiotic biosynthesis, biodegradation) Computer Science (modelling, big data sets), Engineering (synthetic biology, microfluidics), Maths (systems modelling, epidemiology), Medicine (infection, 'omics, plant metabolites and health), Physics (synthetic biology, solid-state NMR), Politics (biopesticide use), Social Science (food security) and Warwick Manufacturing Group (biodegradation). Multidisciplinary work in WSB complements that in SLS and spans a broad spectrum from fundamental to translational, bringing together a broad range of expertise.

Given its central importance to our strategy, we have been growing our capability in ***Molecular & Cell Systems***. Plant systems biology has been a strength for some years, featuring work on transcription networks (Beynon, Buchanan-Wollaston, Gifford), but we have now added systems-oriented research into the control of gene expression in microbial and mammalian systems (McCarthy, Kreil, Hebenstreit, Soyer) as well as cell signalling (Ntoukakis), and have strengthened our capability in bioinformatics (Kreil, Allaby, Hebenstreit). Gene expression noise, which plays diverse roles in biology, is also a focus of activity (Hebenstreit, McCarthy, Soyer). WSB has ongoing programmes in transcriptional noise/regulation (Rand) and signalling (Bretschneider, Ott, Rand) in collaboration with groups in SLS and elsewhere. In the area of molecular/cell biology, we have strengths in protein and membrane trafficking (Frigerio, Jones, Roberts), protein folding (Freedman), macromolecular assemblies (Smith), proteomics approaches (Jones, Scrivens), and membrane protein structural analysis (Cameron). Related complementary research in WSB includes modelling and quantitative imaging to study cell motion and cytoskeleton dynamics (Bretschneider, Burroughs), development (Bretschneider), T and NK cell signalling and activation (Rand) and circadian clocks (Rand, Ott). Machine learning and Bayesian statistics are used to reverse engineer gene regulatory networks by integrating 'omics and bioinformatics data (Burroughs, Wild, Savage, Ott, Rand), provide integrated analysis of such heterogeneous data (Wild, Savage), segment and analyse complex images (Bretschneider), analyse/predict regulatory structures in promoters (Ott), and reconstruct fine-scale stochastic dynamics of genes and proteins from single cell time-lapse images (Rand). *Examples of high-profile papers published in this area* during the review period include: 6 in *PNAS* (plant nitrogen responses, plant circadian clock, stochastic modeling, chaperones and toxins, model for clathrin disassembly), 2 in *Plant Cell* (plant stress transcriptional networks, evolution of plant regulatory elements), 2 in *Nature* (transporter mechanisms), 3 in *Science* (plant immunity signaling, symporter/antiporter mechanisms), 1 in Cell (plant photoperiod circuits), 4 in *Molecular Systems Biology* (control of gene expression, temperature compensation, clock plasticity) 1 in *PLoS Biology* (transcriptional bursting). *Additional examples of key achievements:* McCarthy defined the first *in vivo* rate control map for eukaryotic protein synthesis. Beynon leads a major systems biology programme on plant stress responses involving Warwick, Essex and Exeter. Cameron has determined the structures of a series of medically significant membrane transporters.

An important part of the manifestation of emergent features of biomolecular systems becomes evident during organism development, which is underpinned by differentiation and the formation of cell patterns. We have accordingly added to our research capability in ***Development***, which features work by Moffat, Hebenstreit, Nezis, Mortimer, Squires and Pires da Silva (animal systems) as well as Jackson (plant systems) and McCarthy (fungal systems). Neuroscience is another

aspect of development studied in SLS, and we have maintained a strong presence in this area (Frenguelli, Dale, Pankratov) with collaborative theoretical activity in WSB (Richardson). *Examples of high-profile papers published in this area* during the review period include: 6 in the *Journal of Neuroscience* (synaptic transmission, activity and plasticity, neuronal regulation), 2 in *PNAS* (plant developmental plasticity, circadian rhythms), 2 in *Plant Cell* (circadian clock, regulation of flowering), 2 in *Current Biology* (regulation of cytokinesis in *Drosophila*, sexual plasticity in nematodes), 1 in *Nature* (the genome of *Tetranychus urticae*), 1 in *Science* (behavioural immune responses in *Drosophila*), and 1 in *New Phytologist* (root development). *Additional examples of key achievements:* Nezis discovered the first selective autophagy receptor in *Drosophila*, Dale and Roper established a new mechanism of CO_2 sensing mediated by carbamylation of β-connexins; Frenguelli identified MSK1 as a key signalling component underpinning positive early life environmental effects promoting synaptic plasticity in the brain.

In the ***Environment*** theme, we have renowned expertise in the study of microbial communities in the marine environment (Christie-Oleza, Scanlan, Schäfer, H.), in soil (Schäfer, P., Wellington) and in biogeochemical cycles (Schäfer, H., Chen), whereby metagenomics, proteomics, metabolomics and computational biology are playing an increasingly central role. Moreover, we have leading experts in the ecology of marine environments (Sheppard) and of estuarine systems (Purdy). *Examples of high-profile papers published in this area* during the review period include: 1 in *PNAS* (nutrient cycling and biogeochemistry), 10 in *ISME Journal* (nutrient cycling in the oceans and terrestrial systems, niche specialisation, pathogen ecology), 1 in *Science* (impacts of climate change on coral reefs), 1 in *Genome Biology* (genomic mosaics of marine bacteria), 3 in *Environmental Microbiology* (sulphur cycle, antagonistic coevolution, niche specialisation). *Additional examples of key achievements:* Scanlan discovered the vital role of eukaryotic picoplankton (*Prymnesiophyceae*) in carbon cycles; Chen elucidated the role of microbial catabolism of small methylated amines in terms of oceanic influence on global climate.

Food Security is a theme that spans plants through to animals, and molecular processes through to animal health, and is the focus of our submission to UoA6.

In the area of ***Infection Biology***, we study viruses that cause disease in humans (Anderson, Burgert, Easton, Evans, Hollingsworth, Leppard), bacterial infections of humans (Dowson, Fullam, Wellington) and animals (Wellington, Green, Purdy), drug targeting (Dowson, Roper) and host-pathogen interactions in plants (Schäfer, P., Ntoukakis). Computational modelling is utilized by our epidemiologists (Medley, Courtenay, Nokes, Keeling, Green) to study infections in humans and animals, an area that we have recently strengthened through a further joint appointment (Hollingsworth) with the Dept of Maths and the Liverpool School of Tropical Medicine (LSTM). WSB collaborates with LSTM (joint bioinformatics programme and research students; Wild, Savage, Rand) and with Cardiff on various aspects of T cell biology, including a BBSRC LoLa on degeneracy and cross-reactivity and a programme on sequencing T cell repertoires. *Examples of high-profile papers published in this area* during the review period include: 3 in *Science* (pandemic influenza, host-parasitoid interactions, plant immunity), 2 in *PNAS* (adenovirus-cell interactions, host-parasitoid interactions), 2 in *J. American Medical Association* (bacterial infection in cystic fibrosis, viral pneumonia), 1 in *Science Translational Medicine* (antibiotic structure), 2 in *Clinical Infectious Diseases* (respiratory syncytial virus in children) as well as 10 papers in the *Journal of Virology* (covering a breadth of virus infection biology). *Additional examples of key achievements:* Nokes's work on respiratory syncytial virus gives us a world lead in the development of associated vaccination programmes.

Synthetic Biology represents an exciting domain of research growth that is strongly supported by the UK government. Research utilizing synthetic biology as a strategy to enhance understanding of naturally evolved biomolecular systems in yeast has been ongoing since 2010 (McCarthy), but our strategy has been to build critical mass (through the appointments of Corre, Jaramillo and Soyer) in the bioengineering of novel synthetic gene circuitry, design of circuitry and artificial evolution at the single cell level, metabolic pathways (including those generating antibiotics) and microbial communities with a variety of applications. This strategy has been coupled to two new bioengineering appointments in the Department of Engineering. We are a partner in: the only UK Innovation Knowledge Centre in synthetic biology; a BBSRC Network in Industrial Biotech & Bioenergy (£1.7Mio), and an EPSRC bid for a synthetic biology DTC (still pending). WSB has grant-funded projects in photosynthesis and bioenergy. *Examples of high-profile papers published in this growing area* during the review period include: 5 in *PNAS* (antibiotic production, engineering

synthetic riboregulation, translational regulation, engineering riboswitches, design of transcriptional networks), 4 in *Molecular Systems Biology* (stochasticity of gene expression and bistability, evolution of signalling networks), and 2 in *PLoS Computational Biology* (evolution of metabolic networks, and bistability of signalling networks). *Additional examples of key achievements:* Soyer is PI on a bioenergy sLoLa and Corre is Co-I on a sLoLa on antimicrobial drug discovery; Jaramillo's technology advances give us unique capacity in the UK to utilise microfluidics in synthetic biology.

University Research Centres – In order to further promote interdisciplinary research in key growth areas, SLS has taken a leading role in establishing the *Warwick Centre for Integrative Synthetic Biology (WISB)*, the *Warwick Centre for Infectious Disease Epidemiology Research (WIDER)* and the *Warwick Global Research Priority* on *Food*.

The multiple Impacts of our Research – A notable feature of our research community is its capacity to deliver strong impact in multiple areas (as illustrated by our Impact Case Studies). This feature, of course, fits well with government policy on maximizing the translation of the excellent science in the UK into economic growth. The Impact areas of our research include Food Security, Biotechnology (including Synthetic Biology), Big Data (the Knowledge Economy), Human/Animal Wellbeing, and the Environment, and this bodes well for the sustainability of our research activities.

Capacity building – Since its creation, SLS has been in a phase of continuous recruitment, making a large number of new appointments (see below) in order to build capacity across the six research themes and to consolidate our own particular research profile. In doing this, we have both built on established strengths within the School and responded to the changing landscape of national and international research opportunities and priorities. Thus, the establishment and growth of new themes in *Molecular & Cell Systems* and *Synthetic Biology & Biotechnology* is in line with the current trends in modern bioscience. These are highly inter- and multi-disciplinary areas that complement and feed into the other themes. Moreover, both themes overlap with research in WSB.

There are a number of emerging areas of research growth where we anticipate the visibility of the outcomes to develop particularly rapidly over the coming two years. These include fundamental underpinning work in the computational and experimental aspects of single cell biology, noise in biological systems, developmental biology, and synthetic biology. We have made multiple recruitments from Europe and the USA to drive forward new developments in these areas. We are also looking forward to multiple commercial and medical impacts from recent discoveries related to viral infections, crop quality and yields, bioenergy, and to antimicrobial drug discovery.

Research student recruitment - During the period of this research assessment, we have attracted PhD students to multiple schemes of interdisciplinary training. Most prominent among these were the following 4-year programmes: EPSRC-funded Molecular Organisation & Assembly in Cells (MOAC, extended in 2013 for another 4 years), NERC-funded DTP, EPSRC/BBSRC-funded DTC in Systems Biology (joint between WISB, SLS and Warwick Medical School), and BBSRC-funded DTP. Moreover, a further CDT has been funded by EPSRC in 2013 (*MathSys*, run by Warwick Complexity Centre, WIDER and WSB). In parallel we have recruited students to three-year PhDs, many of them funded by external (international) funding and/or competitive University scholarships. In addition, we have initiated a number of international partnership schemes that support further PhD students at Warwick, including programmes involving Monash University (Melbourne, Australia) and Nanyang Technological University (Singapore). These will be joined by new multinational training programmes with Boston University/Harvard/MIT (synthetic and systems biology) and with São Paulo University (USP, Brazil; synthetic biology and biotechnology). In the latter case, we have established an agreement that enables USP students benefiting from *Science without Borders* funding to pursue PhD training at Warwick without the need to find any further funding. Overall, the development of this combination of new schemes will lead to significant further growth and internationalization of our PhD (and Masters) training programmes.

Promoting a vibrant research culture – We have established multiple mechanisms for promoting active and internationally successful research. These include:

The 6 interdisciplinary research theme leaders organize and facilitate interactions across SLS to support a vibrant research culture and to stimulate collaborative research; we run multiple international seminar series that attract excellent speakers from across the globe; we mentor via the respective research themes and via regular 1:1 review meetings between academic staff and the Head of School to review progress in research and to discuss potential areas where additional support could be of assistance; Assistant Professors on probation receive support and advice

managed through a special programme led by the Deputy Head of School; SLS has appointed a Research Strategy & Development Officer, responsible for managing new processes that enhance research excellence, including an internal grant reviewing system (which is helping PIs optimize the quality of their applications), and an SLS research pump-priming scheme that helps PIs generate preliminary data for new grant applications; a workload model in SLS provides a valuable mechanism to balance contributions to research, teaching and administration for each academic in a fair and logical manner. This mechanism also ensures that new appointees (particularly Assistant Professors) are introduced progressively into teaching in a way that helps them build and maintain high quality research activity; for more senior staff, we offer regular opportunities for study leave, during which they can focus intensively on research; finally, we provide extensive support for existing staff (and for external candidates) that wish to apply for Research Fellowships.

c. People, including:

i. Staffing strategy and staff development

SLS has appointed 14 new members of academic staff since October 2010, and will make 2 more appointments within the next six months. Further appointments will be made after that in response to anticipated retirements. So far, we have made 6 appointments at Assistant Professor level: Hebenstreit, Mortimer, Ntoukakis, Chen, Corre (joint with Chemistry), and Hollingsworth (joint with Maths and LSTM); 5 appointments at Associate Professor level: Pires da Silva, Jones, Nezis, Schäfer P. and Cameron; 3 appointments at Professor level: Kreil, Jaramillo and Soyer. One further Professorial appointment and 1 Assistant/Associate Professor appointment are underway. Our recruitment strategy has been to build on current research strengths, and to establish new areas of expertise that complement existing ones. These appointments therefore contribute to developing a strong and balanced research (and teaching) programme in SLS that promotes interdisciplinary interactions and networking. At the same time, we are ensuring that our appointments contribute to an appropriate balance of levels of experience across the academic staff cohort. Maintaining a balance of junior and senior PIs in the respective themes will of course also lead to sustainability in terms of succession and viable groupings within the community. The above appointments have so far been accompanied by start-up investments totalling >£1.4Mio.

We actively encourage and support ***Research Fellowship*** holders. Current staff with Research Fellowships during the assessment period include: McCarthy (BBSRC Professorial Research Fellowship); Schäfer H., Chen, Christie-Oleza (NERC Fellowships); Fullam (Leverhulme Early Career Fellowship); Ntoukakis, Corre (Royal Society University Research Fellowships); Lloyd, Fulton (Birmingham Science City Fellowships); Correa, Bull (SLS Research Fellowships); Rand (EPSRC Senior Research Fellowship); Savage (MRC Career Development Fellowship). With ongoing support and encouragement from the School, these numbers will continue to expand.

Fit to Research Strategy – Our recruitment strategy will continue to play a central role in the realization of our research strategy, since the selection of new appointees will be guided by the priority of securing a balanced set of themes, each manifesting an internationally leading profile in terms of scholarship and research performance. Selection of new recruits will also be guided by the principle of maximizing coherence through complementarity between research themes and by the principle of maintaining an appropriate balance of research training expertise.

Athena SWAN - SLS has been awarded the Athena SWAN Bronze Award in recognition of its commitment to ensuring equal opportunities for career progression and is now working towards a Silver Award. The University of Warwick has been awarded an institutional Silver Award.

Wellcome VIP Fellowship scheme - This scheme has funded a number of short-term fellowships over the assessment period. These Fellowships are used to kick-start the academic careers of young researchers by providing a bridge between postdoctoral and academic positions.

HR Excellence – In 2013 Warwick received a HR Excellence in Research Award in recognition of the institution's implementation of the 'Concordat to support the career development of researchers'. Existing policies have been improved and new initiatives introduced, including induction programmes, mentoring schemes, and transferrable skills programmes.

ii. Research students

Training of Research students – Our training programmes incorporate a diversity of taught modules that provide training in research and transferable skills, and incorporate experimental as well as computational skills. Students on each of our training programmes work within their respective cohorts, all of which promote an ambitious research and training culture. Warwick is the lead on a successful BBSRC DTP (£4.2Mio) with Birmingham and Leicester that started Oct

2012. Other major training programmes include the MOAC EPSRC-funded Doctoral Training Centre (DTC), a pioneering programme established in 2003 to catalyse research and training across the physical/life sciences interface; and the Systems Biology DTC, a multi-disciplinary centre funded by EPSRC and BBSRC that provides state-of-the-art training in the mathematical, statistical and computational skills required to underpin systems biology research.

Total PGR student numbers have increased from 111 FTEs in 2010/11 to 125 in 2012/13 and during the REF period 194.84 were successfully graduated. We are prioritising development in this area and expect to continue to grow these numbers via success in DTP-type competitions and by reaching out to scholars from abroad, for example Brazil, Singapore, Australia and the USA. All PGR students receive an Apple Macbook to ensure that they are well equipped for data analysis and that they are able to access the excellent range of PGR skills training available at Warwick.

Industrial CASE studentships provide postgraduates with a valuable opportunity to undertake a period of research with an industrial collaborator. This not only benefits the student, through providing opportunities for the development of new skills and knowledge, but can also help to initiate longer-term collaborative research projects. Between the 2008/2009 and 2011/2012 academic years 15 of our PhD graduates had completed industrial CASE studentships as part of their studies. The cross-sectoral knowledge transfer facilitated by these industrial collaborations has resulted in non-academic impacts as well as publications in high-impact bioscience journals. Examples include: Sequencing of strains of *C.diphtheriae*, the causative agent of diphtheria, as a tool for characterising and monitoring different strains (PI: Dowson; Industrial partner: Micropathology Ltd; Publicn: Bolt *et al* (2010) *J Clin Microbiol* [see also REF2]); A study to evaluate rapid diagnostic tests for canine visceral leishmaniasis (PI: Courtenay; Industr. partner:Pfizer; Publicn: Quinnell *et al* (2013) *PLoS Negl. Trop. Disease*; DOI: 10.1371/journal. pntd.0001992).

Investment in undergraduate students. We actively encourage our best undergraduates to get involved in research. This we achieve by offering them a wide range of third-year research projects and by giving them the opportunity to engage in research placements during the summer vacation. As with the PGR students, our philosophy is to prepare our undergraduates for the new world of bioscience, in which both experimental and computational skills are increasingly required. Our state-of-the-art Interactive Computational Learning Suite, which contains 120 iMacs coupled to an interactive network, is a valuable asset in the realization of this strategy. *We will also start 4-year undergraduate Masters of Bioscience degrees in 2014, which include a 7-month project.*

d. Income, infrastructure and facilities

Research Income. The overall trend is that of an increase in research income *per capita*, starting at ~£158,000 *per FTE* in 2008/9 and peaking so far at ~£223,000 *per FTE* during the review period. There will inevitably be some fluctuation year-on-year, but our strategy for growth (supported by recruitment) will generate accelerated improvement in these numbers over the coming years. These are pleasing results because the development of our research income has been complex and unusual, largely because of the major changes in staffing and institutional funding status associated with the incorporation of HRI into the University of Warwick (including a reduction in the number of academic staff from 94 (2008) to 65 (2013). There was a sharp reduction in research income in 2010 associated with the merger of the former School of Biological Sciences with HRI, which saw a number of PIs move to other institutions and a number of PDRAs and technicians leave, resulting in a slower rate of drawdown on existing grants. In addition, the portfolio of funding has undergone a metamorphosis – most significantly, funding of plant science by Defra has been progressively withdrawn [for example, leading to a loss of approximately £5Mio ring-fenced funding over four years]. However, the HRI-derived community has been successfully adjusting its funding profile to favour BBSRC, and this trend continues.

Examples of recent major grants that reflect the School's drive towards a more multi-disciplinary approach are as follows: Vegetable Genetic Improvement Network (VeGIN): An interactive network of researchers and industry leaders working together to address how genetic improvement of key crop varieties can contribute to a sustainable increase in food production to meet the twin challenges of food security and climate change (£2Mio, Buchanan-Wollaston, DEFRA); Studying stochasticity in eukaryotic gene expression using novel tools of synthetic biology modelling and analytical science: A four-year project to study how multiple steps in a model signalling and expression pathway determine its noise characteristics using synthetic biology, systems biology, analytical science and computational modelling to analyse contributions to noise generation of steps in the pathway (£1.4Mio, McCarthy, BBSRC); TranSys: a systems approach to defining

membrane protein networks and applications (£1.6m, Robinson, FP7 Marie Curie Initial Training Network); How the brain senses CO_2 (£1Mio, Dale, MRC); GARNet: Genomic *Arabidopsis* Research Network and MASC: Multinational *Arabidopsis* Steering Committee (£1.3Mio, Beynon, BBSRC); The Potential Impact of Vaccination on RSV and Other Respiratory Virus Pneumonia in the Developing Country Setting (£1.8Mio, Nokes, Wellcome Trust); Engineering synthetic microbial communities for biomethane production: a five-year project that brings together an interdisciplinary team of engineers, microbiologists, evolutionary biologists, synthetic biologists, and bioinformaticians to understand natural microbial communities and engineer synthetic ones. (£4Mio, Soyer, BBSRC sLoLa); PROMYS: Funded through the FP7 Knowledge-Based Bio-Economy Programme to develop, validate and implement a novel synthetic biology platform technology known as ligand responsive regulation and selection systems - biological devices that integrate biological sensing modules within larger regulatory networks to control cellular programmes. This project includes three industrial partners. (£723k, Jaramillo, EU FP7); EVOPROG: A collaborative synthetic biology project to programme bacteriophages and bacteria to compute combinatorial optimisation algorithms by constructing and using a high-throughput droplet device for the directed evolution of biomolecules *de novo*, integrating for the first time *in silico* and *in vivo* evolution (£979k, Jaramillo [Coordinator], EU FP7).

Substantial grants involving SLS and WSB include: Elucidating signaling networks in plant stress responses (£2.7Mio(SLS)/£1.4Mio(WSB), Beynon, BBSRC SABR); Global control of rhythmic gene expression by transcription factor LHY (£720k, Carré, BBSRC); Comparative Cell-specific Profiling to understand the Molecular Basis of Nodulation (£813k, Gifford, BBSRC); Negative feedback control of neocortical activity (£940k, Richardson, BBSRC); Unravelling of the mite *Varroa destructor* on the interaction between the honeybee and its viruses (£800k, Evans, BBSRC). Other substantial recent grants to WSB include: Systems medicine of chronic inflammatory bowel disease (SysMedIBD; £754k, Rand, EU); Systems Biology analysis of biological timers and inflammation (£4.1Mio, White (Manchester), Rand, Ott, Bretschneider, BBSRC sLoLa).

Research support allocated by the University of Warwick – A wide range of additional types of funding (including from the Research Development Fund, Institute of Advanced Study, Higher Education Innovation Fund, SLS Pump-Priming Fund, and BBSRC Sparking Impact Fund) has been awarded to our community by the University, totalling £930k over the review period.

Improvements to Physical Infrastructure – A priority has been to integrate the former HRI community with the main campus SLS community, generating a coherent School on one site. The first stage of this process (completed Feb 2013) involved refurbishment of laboratory space on Gibbet Hill coupled to construction of a ***Phytobiology Facility*** (£4.8Mio), providing state-of-the-art plant cell culture and glasshouse facilities on main campus for plant scientists relocating from Wellesbourne. The second stage is construction of the ***Warwick Interdisciplinary Biocentre*** *(to which the university has already committed £25Mio in its Capital Plan).* This new building will function as a leading centre of quantitative, broadly systems-oriented bioscience and synthetic biology and will be a focus of interdisciplinary research located in close proximity to the Schools of Chemistry, Physics, Engineering, Computer Science and Maths (WIB; University Estates plan; http://www2.warwick.ac.uk/services/estates/projects/timeline). Construction of the WIB will represent a major step-change in the quality of the research environment, providing purpose-built laboratories, facilities and shared spaces of a standard appropriate for a world-class *interdisciplinary* bioscience community.

Research support and governance – Research activity within SLS is supported by multiple mechanisms and structures. A Research Committee, attended by the research theme leaders, reviews research progress and strategy on a regular basis, and develops and implements policies designed to promote research activity and excellence. This committee is also attended by our Research Strategy & Development Officer and by the School's Education Strategy & Communications Officer, since it is our philosophy to ensure that research excellence is reflected in teaching excellence. In addition, research excellence is promoted by a rigorous internal grant reviewing system (which maintains a grant success rate of approximately 30% with the Research Councils), an internal research pump-priming system (which provides grants to enable PIs to generate preliminary data for grant applications), and a departmental workload model that ensures that academic staff have adequate time to pursue (and manage) their research. The WSB PIs work in an interactive team; staff development is assessed on a 6-monthly basis and there is a transparent system for balancing workloads appropriately and preparing staff for promotion.

Equipment - The research environment has been enhanced through a ***total of £10.4Mio*** of (partly SRIF/CIF) investment. The larger items have included: a Genix X-ray beam delivery system, a Becton Dickinson 4 laser influx cell sorter, 3 Conviron walk-in controlled environment rooms, a Zeiss LSM710 confocal microscope, a Solexa genome analyser, an interactive computational training suite, modification of Gibbet Hill labs to accommodate colleagues from Wellesbourne, a photon scanning microscope X2, a DeltaVision Elite microscope, two protein crystallisation robots, a Micro crystal imaging system, a Waters Synapt G2 mass spectrometer with Acquity system and Xevo mass spectrometer with Acquity system. We have also invested >£1Mio in equipment and refurbishment for our new Biological Mass Spectrometry Facility, which will house a new Orbitrap Fusion Mass Spectrometer and a new Triple Quadrupole Mass Spectrometer as well as Liquid Chromatography systems for nano and standard flow applications. A state-of-the art controlled environment and glasshouse Phytobiology Facility Building (£4.8Mio) was also completed in 2013.

Research facilities - We have a number of excellent core facilities available for general use. These include (indicating the number of support staff associated with each): Wellesbourne glass and field trials, total replacement cost is around £10Mio (10 staff); Wellesbourne controlled environment facilities replacement cost around £3Mio (1 staff); Animal house equipment and building replacement cost around £5.9Mio (4 staff); Genomics, equipment replacement cost around £730K (1 staff); Imaging facility (EM and confocal) equipment replacement cost around £1.7Mio (1 staff); Proteomics facility, equipment replacement cost around £1.1Mio (1 staff).

We also have three dedicated mammalian tissue culture facilities, three category 2+3 containment suites, media (bespoke) and glassware kitchens with a total of 6 staff for research and teaching activities. SLS also has an in-house IT support team of 3, and an instrument repair and plant maintenance workshop with 3 staff. We also have 4 chief technicians providing research lab, health and safety and equipment support. Our imaging facility (1 staff) was enhanced in 2012 by the purchase of a Typhoon Phosphorimager (£101k) and a Deltavision wide field microscope (£193k), and new flow cytometry equipment will also be added shortly. Following the appointment in 2013 of Alex Jones to spearhead the redevelopment and re-integration of our Biological Mass Spectrometry Facility, this important technology will be more widely incorporated into our research. This appointment is accompanied by new investment in mass spectrometry technologies of around £950k. Another key resource is the 4-person bioinformatics team shared between WSB, SLS and Warwick Medical School. This supports primary 'omics and sequence data analysis, development/implementation of databases, user interfaces/workflows for interrogating and linking different data types and software development.

e. Collaboration or contribution to the discipline or research base

We play an active role in multiple partnerships with other Schools, including: Chemistry, Computer Science, Engineering, Maths, the Medical School and Warwick Manufacturing Group. Our partnerships with other institutions in the UK include the Liverpool School of Tropical Medicine (LSTM) and the following plant research institutes: JIC, East Malling, IBERS, Rothamsted. Our partnerships with other institutions abroad include CUSP (New York); Singapore (NTU); the FioCruz Institutes in Brazil (Recife and Curitiba); the University of São Paulo, Brazil; Kenya Agricultural Research Institute, Africa; Monash University, Melbourne; Boston University and Harvard, Boston. A major new initiative has been the establishment of a Transatlantic Synthetic Biology Research Triangle involving Warwick, São Paulo and Boston University / Harvard.

Strategic partnership – The University of Warwick is one of only 9 strategic partners of the BBSRC. This relationship was forged primarily on the basis of SLS's profile as a leader in research areas (plant systems biology, plant-pathogen interactions, *Brassica*, horticulture and synthetic biology) that are relevant to Food Security and Biotechnology.

Collaborative grant funding – Our researchers have ongoing collaborations with a range of partners, both within the UK and beyond. In many cases funded projects are multi-disciplinary in nature and bring together wide-ranging expertise from researchers in academia and industry. Examples of collaborative grants include: Plant Responses to Environmental STress in *Arabidopsis* (PRESTA): a five-year collaboration between the Universities of Warwick, Essex and Exeter (Beynon, BBSRC/EPSRC Systems Approaches to Biological Research); TranSys: a systems approach to defining membrane protein networks and applications (£1.6m, FP7 Marie Curie Initial Training Network, Robinson); GARNet: Genomic Arabidopsis Research Network and MASC: Multinational Arabidopsis Steering Committee (£1.3Mio, Beynon, BBSRC); Engineering synthetic microbial communities for biomethane production: a five-year project involving the University of

Exeter, Newcastle University, Imperial College London, The Genome Analysis Centre, and Anaerobic Analytics (£4Mio, Soyer, BBSRC sLoLa); PROMYS: An EU funded project that includes *three industrial partners*. (Jaramillo, EU FP7); TeamCanUK: A collaboration between Canadian and UK researchers on antibiotic resistance (Dowson, £2.2Mio, MRC/CIHR); Tuberculosis epidemiology and novel transmission routes in rural Tanzania (Wellington, US$599,389, NIH USA).
National/International resources – We provide resources to industry and researchers on national and international levels. Examples include: *Genetic Resources Unit (GRU):* An internationally recognised collection of seeds and genetic material from a range of vegetable crops and their wild relatives, e.g. *Allium* and *Brassica*, to facilitate conservation, characterization, documentation and research on these important species. GRU collaborates with other international organisations, including Nordic Genebank and the Food and Agriculture Organization of the UN.
Indicators of wider influence – Participation in (inter)national committees/bodies includes:
External Scientific Committees: Royal Society Synthetic Biology Committee, Chair of Royal Society of Chemistry Chemistry-Biology Forum and of the Governing Council of the John Innes Centre (McCarthy); PRESTA, *Brassica* and resources (Buchanan-Wollaston); advisory capacity to government with respect to epidemiology (Keeling); advisory capacity with respect to bovine Tuberculosis (Wellington); Science Advisor to the Commissioner of the British Indian Ocean Territory (Sheppard); Nuffield Council on Bioethics working party review on biofuels (Barker); UK Government Advisory Committee on Pesticides (Bending); Scientific Advisory Board of the British Neuroscience Association (Dale); Advisory Committee on Dangerous Pathogens: Transmissible Spongiform Encephalopathies Risk Assessment sub-group and Spongiform Encephalopathy Advisory Committee (Medley); Research Advisory Board for Diabetes UK (Squires); Chair of the Education, Training and Policy Committee of the Society of Biology (Freedman); NC3Rs Expert Working Group on Epilepsy Models and Advisory Committee Epilepsy Research UK (Frenguelli); Joint Committee on Vaccination & Immunization for Dept of Health 2009, 2010, and Quantitative Modelling Standing Capacity for Defra (Keeling); NERC Science Advisory Committee for Environment & Human Health Programme 2011 and MRC UKCRC Translational Infection Research Initiative Scientific Advisory Panel 2010 (Wellington); Chair UK Plant Sciences Federation Advisory Committee (Beynon); Board of Directors of iPlant NSF $50m Grand Challenge Programme USA 2008-2011; Scientific Council of Interdisciplinary Research Institute, CNRS, Universités Lille; Advisory Board of Centre for Computational Systems Biology, Fudan University, China 2010-present; International Centre for Math Sciences Programme Committee, 2009–present; Jury of Prix De Leeuw-Damry-Bourlart, a top Belgian science prize (Rand).
Learned Societies: Fellow Royal Society Chemistry (McCarthy, Scrivens); Director British Neuroscience Association (Frenguelli); Faculty of 1000 (Keeling, Hebenstreit); Fellow Linnean Society London (Sheppard); Fellow Wissenschaftskolleg zu Berlin (Soyer); Member Scientific Committee Bacterial Genetics & Ecology (BAGECO; Wellington); Fellow Society of Biology (Beynon); President of International Society for Seed Science (Finch-Savage).
Research Funding Panels: Chair of BBSRC Grant Reviewing Committee A and BBSRC Animal Health Research Club (Green); 2014 REF panels (Green, Frenguelli); Chair of Royal Society Research Grants Panel F 2008 (McCarthy); BBSRC Pool of Experts (Bending); NERC Biomolecular Analysis Facility Steering Committee 2010-present (Scanlan); NERC Peer Review College (Schäfer, H., Sheppard, Scanlan, Wellington); NSF Grant Review Panel and Fulbright Foundation Review Panel (Pires da Silva); Marie Curie Evaluation Panel 2010-2012 (Purdy); Wellcome Trust Pathogen Biology & Disease Transmission Panel (Keeling); Kentucky Science & Engineering Foundation (Nezis); MRC Infection & Immunity Board (Dowson); BBSRC Committee B (Beynon and Carré); Wellcome Trust Immunity & Infection Committee and Fellowship Interview Panels (Medley); BBSRC Integrative Systems Biology Strategy Panel 2009–present; International Review Panel, Helmholz Initiative on Systems Biology, Germany; Expert Panel, Systems Biology–FORSYS, German Federal Ministry of Education and Research 2008; Evaluation Panel BMBF priority FORSYS/FORSYS-Partner 2011; Review Panel, SULSA Award for Systems Biology, Cell Biology and Translational Medicine, Scottish Funding Council, 2008; Board of External Reviewers Freiburg Zentrum für Biosystemanalyse (ZBSA); MRC: Systems Immunology Panel, 2013 (Rand).
Organization of international conferences/workshops: including *Systems Biology workshop* in Venice (Buchanan-Wollaston); *International Conferences on Systems & Synthetic Biology* (2010, 2012; Spain; McCarthy); *International Conference on Industrial Microbiology* (Purdy); Director of FEBS *Advanced Courses in Systems and Synthetic Biology*, Greece (2008, 2010, McCarthy);

Organizer/Chair UK *Molecular Microbial Ecology Group Meeting* 2010 (Schäfer, H.); Diamond Course Co-organizer (Cameron); Organizer/Chair Neuron-Glia interactions, Fukuoka, Japan 2009 (Dale); Director Translation UK 2009 (Anderson); Advanced Course on Practical Proteomics, India 2010-2013 (Scrivens); Co-organizer Microbiology of Oceans at SGM, Edinburgh 2010 and XIVth International Symposium on Phototrophic Prokaryotes, Portugal 2012 (Scanlan); Organizer Isaac Newton Institute (Soyer); Leader iGEM team Paris and Co-Chair 1st and 2nd *European Conferences on Synthetic Biology* (Jaramillo); EPSRC Symposium Complexity and Systems Biology, Warwick 2009-10 (Wild, Burroughs).

Prestigious presentations: Numerous, including Plenary Lectures at Purines 2008, Copenhagen and Purines 2011, Bonn (Dale); 3rd EMBO Workshop Microbial Sulfur Metabolism, The Netherlands 2012 and Gordon Research Conference, Maine 2010 (Schäfer, H.); Plenary at Brazil Marine Science Society and Keynotes (2x) UN Maritime University Conference, Sweden (Sheppard); Keynote 13th ISMAS Workshop on Mass Spectrometry, Mumbai 2008 and Plenary International Workshop on Atomic, Molecular & Ionic Processes, Lisbon 2008 (Scrivens); Plenary Brazil Annual Genetics Conference 2012 (McCarthy); Plenaries American Society for Microbiology Meeting, Boston 2008 and Applied & Environmental Microbiology Gordon Research Conference, Massachusetts 2013 (Scanlan); Plenary IV International Workshop Seed Ecology, Shenyang 2013 (Finch-Savage); Annual Science Faculty Lecture, Strathclyde University, 2009, Opening Keynote Lecture, 2009 International Conference on Molecular Systems Biology, Shanghai, China, AstraZeneca Lecture (Plenary), 11th International Conference on Systems Biology, Edinburgh, 2010, Keynote Lecture, Gordon Conference on Chronobiology, Italy, 2011, Invited Plenary Lecture, ICSB 2014 Melbourne (Rand); Invited keynote lecture Society Experimental Biology 2014 (Wild).

Editorial roles: Assoc. Editor *Integrative Biology* (McCarthy); Editor *J. Virology* (Evans); Assoc. Editor *PLoS One*, Assoc. Editor *Archaeological and Anthropological Sciences* (Allaby); Editorial Board Member *Frontiers in Terrestrial Microbiology* (Chen); Assoc. Editor *Purinergic Signalling,* (Dale); Board Reviewing Editor *Scienc*e, Handling Editor *Mathematical Biosciences* (Medley); Editorial Board *Journal Cytology & Histology*, Nezis; Assoc. Editor *Microbiology* and *FEMS Microbiology Ecology* (Purdy); Editor *Marine Pollution Bulletin* (Sheppard); Editor *Epidemics* and *American Naturalist* (Keeling); Editorial Board *J. Phycology* (Scanlan); Editorial Board *Microbial Drug Resistance* (Dowson); Editorial Board *J. Biological Engineering* (Jaramillo); Editorial Board *J. of Royal Society: Interface*, Assoc. Editor & Editorial Board *Bulletin Mathematical Biology* (Rand); Review Editor *Frontiers in Systems Physiology*, *Current Proteomics*, *Current Bioinformatics* (Wild).

Responsiveness to national and international priorities – Our research is strongly aligned with the national research priorities of Food Security, Industrial Biotechnology, Big Data, Environment (Climate Change), Human/Animal Wellbeing. Indeed, over the REF review period, we have increased our capabilities in these Impact Areas through new recruitment to our 6 Research Themes. The most significant change is that we have built critical mass in Synthetic Biology & Biotechnology, thereby creating one of the UK's major Centres in Synthetic Biology.

Commitment to working with Industry and Other Commercial Funders – SLS has multiple research partnerships with industry, including: ***Syngenta*** – Mapping/analysis of genetic loci controlling QTs in broccoli (PI: Buchanan-Wollaston); ***Basilea*** – bacterial metabolism and peptidoglycan synthesis (PI: Roper); ***Waters*** – development of novel mass spec techniques via the Warwick/Waters Centre for Biomedical Mass Spec & Proteomics, and an industrial CASE PhD studentship (PI: Scrivens); ***Sarissa Biomedical*** – spin-out company producing microelectrode biosensors for rapid point-of-care clinical diagnosis (PI: Dale; see Impact Case Study WSLSA5.4); ***Elsoms Seeds*** – A Knowledge Transfer Partnership to implement genetic Marker Assisted Selection technology in the development of new commercial crop varieties (PI: Barker); ***AHDB*** - biological control of plant diseases using insect pathogenic fungi with dual activity against plant pathogens (PI: Chandler); research on the incidence and control of numerous plant pathogens (PI: Clarkson); control measures for insect pests that damage crop species (PI: Collier); ***Unilever*** – the role of microbial adaptation in the biodegradation of chemical pollutants and how data from lab-based research can be extrapolated to the field (PI: Bending); ***Rijk Zwaan*** - Manipulation of bolting time for improved quality and greater sustainability in lettuce production (PI: Jackson); ***Bacmine SL*** (Spain), ***Evolva SA*** (Switzerland), ***Biosyntia*** (Denmark) – Industrial partners in the PROMYS EU-funded project to develop new synthetic biology platform technologies (PI: Jaramillo); **Microsoft Research** – Analysis of the relationship between topological and biochemical features in signalling systems and response dynamics (PI: Soyer).