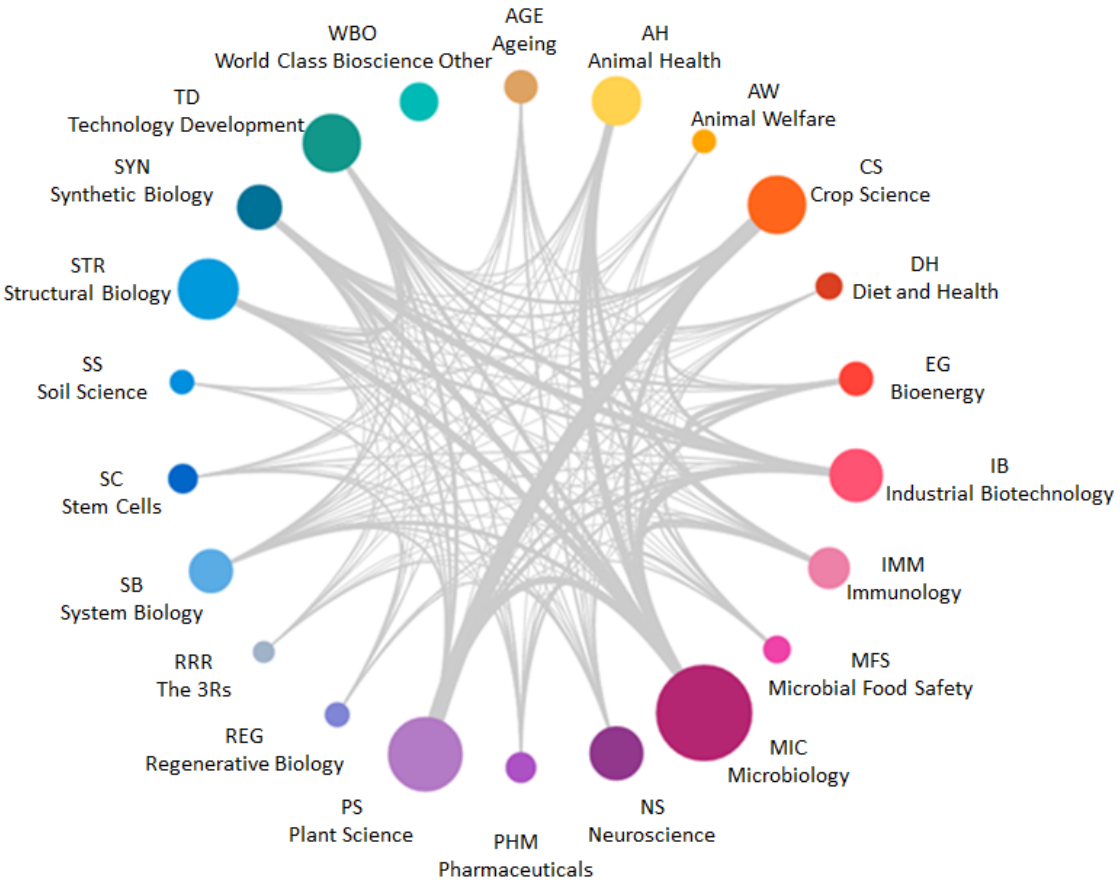
ANNEX 4

RESEARCH TOPICS

DEFINITIONS



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Ageing (AGE)
(sub-category of Bioscience for Health)

Research considered **directly relevant to Ageing** includes:

- Research on the molecular and cellular basis of ageing (in humans, animals and models systems e.g. yeast, not plants)
  - Cell senescence, replicative senescence; the mechanisms and regulation of apoptosis/programmed cell death; telomeres, telomere biology, maintenance and regulation; telomerase (including structure)
  - Mechanisms and effects of oxidative stress, free radical damage, reactive oxygen species (ROS), DNA damage and repair associated with ageing; mitochondria function and activity directly relevant to ageing (oxidative stress, superoxide release etc.)
  - Werners and Progeria (accelerated models of ageing)
- The genetic control of ageing, including understanding the primary mechanisms of ageing and the underlying genetic determinants of life span, longevity and reproduction potential; individual genetic and epigenetic variation
- Biomarkers of ageing (also potential biomarkers of health across the lifecourse)
- Cell, tissue and systems biology in ageing and health across the lifecourse:
  - Maintenance and regulation of homeostasis, homeostatic mechanisms in relation to maintaining health through life and understanding the processes leading to frailty
  - Effectiveness of the elderly immune system
  - Muscle-tendon-skeletal system including locomotion, balance, metabolism and effects of physical activity; also includes ageing muscle biology and dysfunction (hypertrophy and sarcopenia, but NOT sports science/injury); muscle satellite cells and regeneration; maintenance of bone health and age-related bone loss (NOT osteoporosis).
  - Reactive oxygen species as propagators of tissue ageing, effects of free radicals, mitochondria biology (see above)
- Diet and health:
  - The effect of ageing on responses to dietary constituents, for example, altered nutritional need to maintain physiological function
  - Altered food choice with age
  - Impact of diet on maintaining health during ageing, e.g. influence of nutrients on the health (and potential protective effects) of intestinal/gut, cardio-vascular, neural, musculoskeletal and other physiological systems
  - Dietary/calorie restriction effect on ageing/lifespan
  - Anti-oxidants, exposure to free radicals
- Relevant aspects neuroscience – age-related progressive decline in cognitive function and the cellular mechanisms associated with this, e.g.
  - Generic mechanisms of non-disease-associated neurodegeneration, (but NOT studies of neurodegenerative disease such as Alzheimers, dementia, Parkinsons*); neuronal damage and repair, neurogenesis; fundamental prion biology in relation to understanding normal ageing (but NOT including studies on TSE/BSE/Scrapie transmission and disease)
  - Preservation/maintenance of cognitive function with age
  - Age-related cognitive dysfunction and decline, long-term memory studies (NOT visual learning/behaviour unless looking at changes in learning ability with age)
  - Sleep (specific to ageing)
- Amyloidosis (the accumulation of misfolded proteins deposits in a tissue/organ which occurs during the normal ageing process). Includes mechanisms and function of amyloid fibrils and plaque formation (NOT studies of specific clinical conditions/diseases and structure/biophysical studies)
- Changes in angiogenesis during the normal ageing process – the growth of new blood vessels/vasculature associated with repair mechanisms of damaged tissue and wound

healing, and in response to physical activity (NOT that associated for clinical conditions, diseases or tumour biology)

- Stem cells and tissue engineering – only include studies that are relevant to ageing and involve tissue regeneration or transplantation e.g. bone, liver, wound healing (but NOT chronic wounds/ulceration), nerve regeneration.
- Relevant developmental biology but only if it includes some life course studies, i.e. developmental origins of optimal health. May include *in utero* studies, the mechanisms and effects of developmental factors and early life exposures on health during ageing (e.g. maternal influences, fetal or nutritional programming, imprinted genes)

Animal Health (AH)
(aligns with sub-category of Agriculture and Food Security)

Research considered relevant to **Animal Health** includes: all aspects of diseases[1] of farmed[2], lab and companion animals; diseases of wild animals[3] which can transmit to farmed, lab and companion animals (and where the possibility of transmission is included in the application); overseas diseases that could spread to UK livestock.

[[1]Diseases include infestations by "pests", i.e. internal (helminth) or external (arthropod) parasites, as well as infections by viral, bacterial, protozoal or fungal pathogens. [2]Farmed animals include: livestock, poultry, fish and bees; [3]Studies of vertebrate or invertebrate wildlife reservoirs or vectors of infection are only included if they focus on the role of wild animals in the transmission to and/or maintenance of disease in the target farmed species, and not on the nature or incidence of disease in the wildlife host *per se*.]

The following disease types are **included**:

- **TSEs** (Transmissible Spongiform Encephalopathies) research. Diseases include BSE and Scrapie. Includes research on yeast prions.
- **Endemic Diseases** representing a constant presence of disease or infectious agent within a given geographical area and/or population group. Includes research on: tuberculosis, Marek's disease, mastitis (including research on *Staphylococcus aureus* and *Streptococcus uberis*) and coronavirus.
- **Exotic Diseases** not native to a given area or population. Includes Bluetongue, avian flu, foot and mouth, and African swine fever.
- **Food-borne Zoonoses** - diseases that affect animals, which can be transmitted to humans through the food chain. Research includes food-borne bacteria and viruses, notably the pathogenicity of *Campylobacter*, *Escherichia* and *Salmonella*, where studies are at the animal level. It includes food-borne and other infectious diseases of zoonotic origin with implications for public health that are carried by farmed animals, but do not necessarily have a significant impact on animal health.
- **Parasitic Diseases** resulting from a number of microbial protozoan pathogens, including *Leishmania, Eimeria, Toxoplasma*, and *Cryptosporidia* and larger helminths, including nematodes.
- **Non-transmissible diseases** – physiological or metabolic diseases such as cancer in animals, metabolic disorders, immune disorders and reproductive disorders.

Also **includes**:

- research relating to animal welfare where the focus is a **welfare-related disease**, such as lameness or mastitis
- research on farmed animals that does not specifically relate to disease, such as: genetics and genomics of farmed animals; basic immunology of farmed animals; research into reproduction of farmed animals

Research considered relevant to animal diseases **excludes**:

- Studies of a disease-causing organism, but in a non-disease context
- Studies on non-disease-causing forms of an organism, particularly general studies on *E. coli*
- Diseases of humans or aspects of animal diseases transmitted to humans which do not focus on the animal, for example food-borne zoonoses where the focus is on the human host (e.g. pathogen-human interactions).
- General welfare research and studies on pain (included in Animal Welfare and The 3Rs).

Animal Welfare (AW)
(aligns with sub-category of Agriculture and Food Security)

Research considered relevant to **Animal Welfare** includes dedicated research that aims to improve the conditions and management of farmed, laboratory*, companion and other managed animals (e.g. zoo animals) through improvement to procedures and husbandry which minimise pain, suffering, distress or lasting harm.

[*Includes the refinement (welfare) of the use of experimental animals in research, thus overlapping with the research topic The 3Rs (replacement, refinement or reduction of the use of animals in research).]

Relevant research includes:

- The basic behavioural, neurobiological, immune, metabolic, physiological and tissue responses of animals to their environmental conditions
- The consequences of human intervention, genetic selection and management for the normal function of animals
- The incidence and alleviation of disease, pain and mental disorders
- Measures of welfare, including developing and validating new measures
- Welfare related health/disease (e.g. foot rot, lameness, mastitis, postweaning multisystemic wasting syndrome)
- Housing, husbandry and environmental impacts on welfare
- Relevant behaviour, cognition and perception
- Pain and nociception
- The impact of early life challenges on development and long term health and welfare
- The influence of production traits on animal welfare.

It should be noted that although all animal disease research has welfare implications, this research topic aims to capture research where the main driver is to understand animal welfare. The majority of animal disease research is excluded from this research topic, although we accept that a significant part of animal disease research has welfare implications.

Bioenergy (EG)
(sub-category of Industrial Biotechnology and Bioenergy)

Bioenergy is a renewable form of energy generated from materials derived from biological sources.

Research includes:
Biofuels (fuels which have been derived from biomass). Includes projects aimed at increasing understanding and further exploitation at various levels:

- improving the growth rates and yields of biological material to be used for biofuel production;
- addressing the logistical and scale issues of producing and processing biomass feedstock;
- scientific and technical aspects (including biological conversion, concentration and recovery processes) associated with using biological sources for energy;
- social, environmental and economic aspects of biofuels production.

- Basic, strategic and applied research into the development and scale-up of sustainable replacement liquid transportation fuels at all points across the bioenergy pipeline:
  Biomass growth→ Biomass composition →Biomass deconstruction→ Biological conversion→ Fuel and associated value-adding chemical co-products
- Translation of research into biofuels and associated value-added co-products.
- Development and/or improvement of enabling technologies relevant to the biorefinery concept[1].
- Use of alternative feedstocks, such as algae or municipal waste, or adopting synthetic biology approaches to produce alternative biofuels.
- Growth and development of biomass crops (plants and algae) for direct combustion and electricity generation, fermentation to produce biofuels, or for isolation of oils.
- Underpinning 'solar' research such as basic research into photosystems and light harvesting complexes in plants and photosynthetic bacteria where the work is carried out in the context of bioenergy production; excludes fundamental studies on photosystems.
- The production of enzymes capable of degrading lignocellulose, and the direct generation of fuels from microbes and other organisms.
- Replacement of fossil-fuel derived lubricants with plant oils.
- Capture of heat from growth of organisms.
- Bio-derived gases including anaerobic digestion.

[1]This approach, in which all components of the feedstock are used to make multiple products (chemicals, heat and fuel), improves the economic feasibility and resource efficiency/ sustainability of biofuel production.

Crop Science (CS)
(sub-category of Agriculture and Food Security)

Crop plants are defined as plants (including algae and cultivated mushrooms) grown to be harvested as food (cereals, vegetables, oils), livestock fodder, or for any other economic purpose. Such purposes include: use of trees for wood and paper production; extraction of non-food plant oils; use as materials (e.g. cotton); use for extraction of bio-pharmaceuticals; production of energy crops (such as for biofuels).

Includes:

- All research involving crop plants or crop plant cells, including managed grass/clover/pasture and grazing crops
- Crop breeding, including by genetic modification
- Study of diseases (viral, bacterial or fungal) and invertebrate pests of direct relevance to crops, including studies of crop pests and pathogens not directly involving the crop (e.g. combating resistance of insect pests to insecticides, or the study of crop pathogens on model plants or in isolation)
- Influences of the environment on crop plants (e.g. climate change, drought)
- Soil-crop interactions and studies on the rhizosphere that directly involve crop plants
- Pharming – use of crop plants to produce biopharmaceuticals
- Studies on pollinators only where direct interaction with a crop is being studied

Excludes:

- Post-harvest processing of foods
- Influences of foodstuffs on health, unless the research relates to crop improvement to benefit health
- Studies on pollinators where there is no direct interaction with a crop (e.g. studies of flight paths, bee diseases)
- Soil science that does not directly involve a crop plant
- Most studies on non-crop model plants (e.g. *Arabidopsis thaliana*, *Brachypodium distachyon, Medicago truncatulum*), with the exception of research looking at interactions with a crop pest or pathogen
- Research on general farming practice and land management not specifically involving crop plants

Diet and Health (DH)
(sub-category of Bioscience for Health)

Includes:

- The study of **diet** for the maintenance of human health.
- Includes **relevant** aspects of:
  - dietary components and effects (diet, digestion, absorption/uptake, nutrition, vitamins, food antigens and minerals (not synthesis)
  - gut biology and interaction (.e.g. GI tract health & transport, epithelial barrier function; mucosal immunity; commensal bacteria)
  - disease prevention through diet (e.g. antioxidants/bioactives and their protective effects; prevention of obesity and malnutrition)
  - neuroscience (gut-brain interactions, psychology, satiety, appetite, food choice, flavour, dietary effects on cognition and mental health)
  - the influence of maternal diet on the developing foetus and/or future life course (e.g. through epigenetic modification; placental nutrition)
  - food applications (neutraceuticals, including probiotics and prebiotics);
  - effects of food structure, processing and modification on health-related food properties

Excludes:

- Animal diet and health (unless the study is a model for human diet and health)
- Generic (not related to nutrition) foetal programming research
- Food-borne zoonoses and food safety
- Pre farm-gate food production
- Food labelling, production, manufacturing, structure and nutrient composition when not directly related to health properties (or taste / perception / choice with a view to health outcomes).
- All cell biology which is not specifically related to immediate dietary events.
- Studies on lipid metabolism and insulin control at the intracellular level when it is not directly related to dietary events.

Immunology (IMM)

Includes:

- Immunological research, from molecular, cellular, tissue and organ levels through to systems level and specific forms of the immune response.
- Animal immunology and normal human immunology in terms of the immune system as a body system
- Fundamental immunology (lymphocyte function and signalling) and immune responses against infection.
- Applying new knowledge and technologies to develop effective means of inducing protective or therapeutic immunity developing models for studies of novel vaccines.
- Developing new formulations to allow delivery of antigens to the immune system.
- Investigations into cellular and humoral immune responses, including mucosal immunity, interactions with other physiological systems, effects of ageing, and immune mechanisms leading to allergy and inflammation.
- Immune responses in response to infection.
- Intracellular and transmembrane signal transduction mechanisms, cell-cell signalling processes, and specialised cell function, including molecular immunology and lymphocyte functioning and signalling.
- Immunity and host resistance relating to foodborne zoonoses, including development of vaccine strategies for zoonoses.
- Interaction of diet and nutrition with the immune system.
- Immunological research at the biochemical level examining protein structure and interactions; substrate specificity, protein folding and protein-protein interactions of the immune system.

Industrial Biotechnology (IB)
(aligned to sub-category of Industrial Biotechnology and Bioenergy)

Industrial Biotechnology is the use of biological resources for producing and processing materials, chemicals and energy; these resources include plants, algae, marine life, fungi and micro-organisms. The following list describes prominent examples of IB areas.

- **Biocatalysis and metabolic engineering**: Biocatalysis refers to the use of either isolated enzymes or whole cells to carry out chemical reactions. In the IB area, biocatalysis has become a recognised method for performing specific reactions that yield high-value compounds with desired stereochemistry or to produce platform chemicals that are fed into manufacturing processes. Metabolic engineering describes the alteration or overhaul of cellular metabolic systems to change the yield or identity of biological products/metabolites. This includes transfer of specific enzymes or entire metabolic pathways from rare or genetically intractable organisms to those that can be readily engineered (like *E. Coli* or yeast strains).
- **Bioenergy**: Bioenergy is a renewable form of energy generated from materials derived from biological sources. Refer to the separate Research Topic entry for a fuller description of bioenergy research.
- **Non-food crop/non-food application**: Research in this category focuses on the use of crops for purposes other than food supply. Examples include cotton or flax for textile production, seed oils for industrial uses as solvents or lubricants and the residues of food-crops (especially straw) for downstream non-food applications.
- **Bioremediation and waste treatment**: Bioremediation is the use of biological resources to remove or reduce the prevalence of selected substances from the environment. Research in this area is often directed at using biological processes to overcome environmental problems, such as contamination or waste treatment.
- **Process design**: Projects in this area aim to develop new equipment for biological processing which can be used by industry. This includes bioreactors as well as the processes which are upstream or downstream of this central fermentation/conversion unit, such as product pre-treatment or separation units. Projects in this category usually have a clear industrial relevance.
- **Recombinant Biologics**: Recombinant biologics are therapeutic peptides and proteins produced or extracted from biological systems. Biologics often replicate the effects of substances already present in the body, such as signalling proteins and monoclonal antibodies. As these are medical products, they would not normally be captured by UKRI-BBSRC remit; however, projects relating to the production of these substances using biological resources are in-scope for IB due to the potential for technology transfer to other sectors.

Microbial Food Safety (MFS)
(sub-category of Agriculture and Food Security)

Microbial Food Safety describes the production, transportation, handling, preparation, storage and consumption of food in ways that prevent food-borne illness. Also includes contamination of food with microbial toxins.

Includes:

- Research relating to microorganisms that potentially cause illness in humans via the contamination of food sources (food poisoning). Relevant microorganisms include*: Salmonella, Campylobacter, Shigella, Listeria Clostridium*, entero-hemorrhagic bacteria such as *E. coli* O157:H7 (EHEC, ETEC, VTEC, etc.), enteric viruses. Research should include that where the emphasis is on the interaction of the microbe with the human or farmed animal host.
- Research relating to fungal contamination of grain and other foods with mycotoxins (e.g. ergot, aflatoxins), or contamination of foods with bacterial toxins.
- Processing of food to inactivate/delay growth of microbial components, e.g. pasteurisation and sterilisation. Food preservation, storage and handling methods to prevent unwanted microbial growth and spoilage (e.g. salting, chilling, freezing, desiccation) – including products that are modified by desirable microbes (cheese, yoghurt, etc.).
- Monitoring of the food supply chain to allow traceability of microbial contamination; development of methods for detection of specific microbes or their toxins.
- Microbial safety relating to specific diets, for example, baby foods, maternal diet.

Excludes:

- Studies of potential food-borne microbes outside the context of microbial food safety, e.g. *E. coli* physiology.
- Contamination of food with agents other than microbes or microbial products.
- All prion / TSE research.

Microbiology (MIC)

Includes:

- Research involving significant use of any types of microorganisms e.g. bacteria; fungi; viruses; archaea; protista, and other microorganisms.
- Research where unidentified microorganisms or complex mixtures of microorganisms are studied (e.g. metagenomics).
- Research on interactions of microbes with animals or plants. This includes:
  - Interactions, pathogenicity and host immune response (where this is to understand the microbe);
  - Processes of the rhizosphere and rhizological interactions with plants; and
  - Interactions with the gut or rumen (including pathogenic and commensal interactions).
  - Interactions of microbes with each other.
- Cellular processes of microbes, including: microbial physiology, metabolism, genetics, protein studies, differentiation, reproduction, persistence, antimicrobial resistance or sensitivity, quorum sensing.
- Studies with pharmaceutical or industrial biotechnology applications, including:
  - Virus-based gene therapy vectors;
  - Research into the development of novel or improved antimicrobials or vaccines;
  - Bioenergy, bioremediation and degradation using microbes;
  - Use of microbes for 'omics' scale studies; and
  - Other industrial applications including the development of **new** laboratory tools utilising microbes.
- Ecology and evolution of microbes (noting interface with NERC remit here).
- Studies involving research into microbial aspects of food production, safety or standards.
- Use of microbes for the provision of resources, including: development or maintenance of microbial cultures or libraries; significant development of microbes for general lab use e.g. culture facilities.

Excludes:

- Research on animal/human TSEs (studies on prions in yeast are included as the host is a microbe).
- Helminths and nematodes.
- Use of existing microbe technology as a routine lab tool e.g. yeast 2 hybrid, *E. coli,* expression systems.
- Using microbes to probe immune function/host response without an aim to further understand the microbe or its interaction with the host.

Neuroscience and Behaviour (NS)

Includes:

- The study of the structure and function of the nervous system, the entire nerve apparatus, composed of a central part, the brain and spinal cord, and a peripheral part, the cranial and spinal nerves, autonomic nervous system, ganglia, nerve endings and peripheral nerves in humans and animals including invertebrates.
- Cell biology and genetics (neuro-transmission, synapses, development, hypothalamic/pituitary effects)
- Mental processes including cognition, behaviour, learning, memory and psychology
- Transmission (impulse, sensitivity, pain)
- Neurodegeneration (degeneration resulting from the normal ageing process, or other neurodegenerative diseases including encephalopathies)
- Stem cell / tissue engineering (regeneration, plasticity).

Excludes

- Research on transmissible spongiform encephalopathies and prions should only be included where it addresses neuroscience or behavioural aspects.

Pharmaceuticals (PHM)
(aligned with sub-category of Bioscience for Health)

Pharmaceuticals related research includes the development of novel therapeutics, including antibiotics and other drugs, including those for dental purposes. It includes biomedical or pharmacological research (for example on stem cells, ageing, neuropathological and other human illnesses) only where the research demonstrates a clear aim of relevance to the pharmaceutical industry

Includes:

- Research on drug development and delivery such as:
  - identification of targets for therapeutic intervention
  - analysis and regulation of specific drug targets and drug transporters
- effects and interactions of drugs with cells and cell components including enzymes, receptors, drug transporters
  - understanding the mechanisms of drug resistance, prevention and combating drug resistance
  - technology development for drug design.
- Development of biomaterials for medical devises that have antimicrobial properties.
- Underpinning bioscience and technology development to improve bioprocessing, scaling up of manufacture of novel drugs
- Technology development for replacing animal use in drug testing.
- Gene therapies

Excludes:

- Research on veterinary medicine (including foodborne zoonoses) or animal welfare. It also excludes underpinning biomedical or pharmacological research, for example on stem cells, ageing, cancer and other human illnesses.
- Studies on regenerative medicine (unless there is a secondary pharmaceutical application to the research).

Plant Science (PS)

Includes:

- Most research classified as Crop Science, including: crop breeding; study of crop diseases and invertebrate pests (including in isolation from the plant); influences of the environment on crop plants; soil-crop interactions; rhizosphere studies directly involving crop plants; pharming – use of plants to produce biopharmaceuticals; studies on pollinators directly interacting with crop plants.
- All research involving plants or plant cells, including non-crop plants such as model organisms (e.g. *Arabidopsis thaliana*, *Brachypodium distachyon, Medicago truncatulum*) and non-food crops such as willow.
- Other (non-plant) photosynthetic organisms, including unicellular (e.g. *Chlorella*) and multi-cellular green algae (e.g. seaweeds), mosses and ferns.
- Studies on chloroplasts.

Excludes:

- Research solely on cyanobacteria or other photosynthetic bacteria.
- Soil science, except where the research involves studies on soil-plant interactions.
- Research on mushrooms, although this is included in Crop Science.

Regenerative Biology (including Tissue Engineering) (REG) (sub-category of Bioscience for Health)

This area includes projects whose driver is providing underpinning research leading to the repair, replacement or regeneration of cells, tissues, or organs, ultimately for clinical applications.

Includes:

- Research on stem cells and their reprogramming where they are used for the purpose of tissue engineering or regeneration.
- All tissue engineering research, including the development of 3D cell culture, tissue scaffolds & matrices, and the maintenance of tissue structure and function, and the generation of tissue models for research or pharmaceutical testing.
- Growth factors and regulatory molecules involved in cellular communication that determine cell fate and differentiation, where the aim of the research is to develop an understanding of techniques for regenerative medicine.
- The development of biomaterials or biomimetics; artificially engineered biological materials or units designed to replace natural human biological materials or units; development of biodegradable polymers, soluble molecules and related materials.
- Development and application of improved wound healing technology, including fundamental studies on understanding wound healing.
- Fundamental studies on understanding nerve regeneration.
- Underpinning research that will enable the generation of patient-specific cell types (e.g. derivation of iPS (induced pluripotent stem) cells).

Excludes:

- Gene therapy, except where coupled with regenerative medicine.
- Fundamental studies on stem cell differentiation and reprogramming, unless with a specific aim of regeneration.
- Basic studies on developmental processes such as bone growth or basic morphological studies, unless directly informing regeneration.
- Whilst fundamental studies on understanding wound healing are included, normal biological processes that include cell regeneration/cell turnover are excluded (e.g. epithelial cells, gut mucosa).

Soil Science (SS)

Soil science includes research on soil processes whether agricultural, biological, biophysiochemical or geochemical and includes water and gas fluxes, plant-soil interactions and bioremediation.

Research of primary relevance includes:

- Research on soil structural composition (including soil microbiology)
- Soil fertility
- Interactions with liquid/gas systems
- Nutrient cycling
- Peat and compost
- Biogeochemical cycles
- Modelling of soil systems
- Nutrient availability from perspective of soil (i.e. not specifically looking at a particular plant system)
- Sequestration when looking at the effect on the soil
- Tilling
- Soil sub-structure
- Effects of roots on soil structure
- Effects of fertiliser on soil (and not primarily the plant)
- Plant-soil interactions where >50% of the research is focused on the soil system

Other relevant research includes:

Research involving some soil systems (at least 10-20%) but where another system is the primary focus of the research:

- Research primarily on plant science which contains some elements of soil interactions (including rhizosphere research)
- Bioremediation
- Nutrient availability from perspective of plant (including fertiliser)
- Root research
- Soil ecology
- Sequestration from the perspective of the plant
- Effects of land use/ management on soil

Excludes:

- Research on the rhizosphere/roots which does not involve interactions with natural soil systems, i.e. hydroponics, or modelling of plant-root systems which does not include soil factors in the model.
- Research on soil microbes/nematodes outside the soil ecosystem (e.g. *C. elegans* model work; lab-based microbial biotransformations).

Stem Cells (SC)

Stem cells are relatively undifferentiated cells that retain the ability to divide and proliferate throughout postnatal life to provide progenitor cells that can differentiate into specialized cells.

Includes:

- Research on model organisms and humans.
- Research on the following stem cell types: adult; embryonic; foetal; haematopoietic; mesenchymal; multipotent, pluripotent, totipotent, epithelial; and neural stem cells.
- Cell biology and genetic aspects, including the molecular signals and mechanisms controlling the balance between self-renewal and differentiation of stem cells; also analysis of transcriptional changes, protein expression and nuclear reprogramming.
- Production of induced pluripotent stem (iPS) cells from differentiated cells.
- Engineering aspects, including the use of stem cells in cell-based therapies and tissue engineering applications; also the development of bioreactors and culture systems to maintain cell populations.

Excludes:

- Research involving stem cells in plants.
- Routine use of embryonic stem (ES) cells to produce transgenic animals, unless studying some aspect of stem cell biology.

Structural Biology (STR)

Structural Biology is a branch of molecular biology concerned with the architecture and shape of biological macromolecules, especially proteins and nucleic acids

Includes:

- Studies into how the primary structure of a protein molecule defines its tertiary structure, including the requirement for additional factors for correct folding, (e.g. the involvement of chaperonin molecules and heat shock proteins);
- Analysis of quaternary structure – assembly of multi-subunit molecules;
- Databases of protein structure and structural motifs;
- Structural bioinformatics – information deduced from patterns in the protein sequences of molecules from different organisms or protein family members that give rise to a particular molecular shape or fold;
- Computer-based protein structure prediction and molecular dynamics;
- Analysis of protein structural motifs, e.g. zinc finger proteins;
- Prediction of membrane topology of integral membrane proteins through hydrophobicity analysis;
- Macromolecular assemblies, e.g. studies on the structure of viruses, ribosomes or multienzyme complexes;
- Re-folding of denatured proteins and other molecules;
- Structural genomics – to determine the three dimensional structure of all proteins of a given organism, experimentally and/or using computational approaches;
- Protein engineering informed by knowledge of structure, including the creation of novel activities in enzymes;
- Structure / function studies, e.g. where structural properties are inferred by generation of mutations and analysis of effect on function;
- Use of analytical methods for structural studies, including: X-ray crystallography, NMR spectroscopy, ultra-fast laser spectroscopy, electron microscopy, cryo-electron microscopy, Dual Polarisation Interferometry, circular dichroism (CD), atomic force microscopy (AFM) and Synchrotron radiation.

Synthetic Biology (SYN)
(sub-category of Exploiting New Ways of Working)

Synthetic Biology is an emerging area that can be described as the design and construction of novel biologically based parts, devices and systems, as well as redesign existing natural biological systems for useful purposes. It incorporates the principles of engineering (e.g. modularity, abstraction and orthogonality) into classical biotechnology. Synthetic biology is sometimes referred to as the 'operational engineering' of biology, an approach that, when fully developed, will standardise, systematise and accelerate bio-based industrial production. Specific areas of application include, but are not limited to, industrial biotechnology, bioenergy, bioprocessing, novel materials and biosensors. Within this context, UKRI-BBSRC is keen to encourage proposals in the following areas[1]:

- Minimal genomes: understanding the minimal number of parts needed for life, to serve as a basis for engineering minimal cell factories for new functions.
- Orthogonal biosystems: expanding genetic information storage and adding coding capacity. Regulatory circuits: designing synthetic gene circuits that may be based on standard biological parts
- Metabolic engineering: engineering biosynthetic pathways to yield useful products and overcoming / removing elements that block production.
- Protocells: bottom-up chemical design approaches to create new cells.
- Bionanoscience: utilising and exploiting synthetic molecular machines based on cellular systems.

Proposals may be focused on a specific scientific question, sector, or industrial outcome, or aimed at underpinning technologies/research.

[1] *Realising European potential in synthetic biology: scientific opportunities and good governance* European Academies Science Advisory Council (2010) (http://www.easac.eu/fileadmin/PDF_s/reports_statements/Synthetic%20Biology%20report.pdf)

Systems Biology (SB)
(sub-category of Exploiting New Ways of Working)

Systems Biology is an approach by which biological questions are addressed through integrating data collection activities with computational/ mathematical modelling activities to produce a better understanding of biological systems (or sub-systems).

Methods for integrating data into models should be relevant to the system under investigation but may include a combination of mathematical, statistical and computational modelling, visualisation tools and network inference. Models should capture complex biological behaviour by integrating the necessary components and interactions and thereby simulate the biological system in a way that enables useful predictions to be made. Systems approaches are most relevant when there is a clear biological endpoint. Model development and validation should proceed iteratively, using relevant data to improve the knowledge of the system. We are particularly interested in encouraging the development and adoption of systems approaches at multiple scales and using multiple approaches, with the ultimate goal being to generate '**digital organisms**'. A digital organism represents all biological processes, pathways and interactions, within a specified organism in the form of mathematical or computational models underpinned by quantitative data. Such tools will enable realistic predictions of behaviour to be modelled across levels of biological hierarchy (macromolecule, cell, tissue, organ, organism). Initially models could be developed to describe an organism's disparate biological properties and functions; however models would need to be able to be integrated with each other in order to provide a more holistic and mechanistic understanding of the organism. The ultimate goal is for models to be able to account for all biological functions experienced by the organism. Grant proposals utilising systems approaches can feature any part of our remit. Proposals require strong multidisciplinary partnerships between bioscientists and researchers in the physical sciences, engineering and information technology disciplines. Tools and technology platforms for systems biology are also relevant. Proposals should ensure that they are designed as much as possible/practical with the end users in mind.

Includes:

- Research which demonstrates full integration of experimental biology with modelling approaches.
- Study at various levels of biological organisation which may include: the cell, the organelle, the tissue, the organ, the organism, and higher biological hierarchy such as an ecosystem.
- Dynamic studies of biomolecular complexes *in vivo* or *in vitro*.
- Systems biology of animals, plants, microbes (including bacteria, yeast and viruses) and environmental systems.
- Tools and technology platforms for systems biology.

Excludes:

- Projects which do not demonstrate full integration of experimental biology/data analysis with modelling approaches.
- Projects in which data is used to generate a theoretical model as the end-point of the project without further iteration.

Technology Development (TD)
(sub-category of Exploiting New Ways of Working)

This area of focus aims to encourage the development of novel bioanalytical and / or biological tools and technologies, the types of approach that would appear on a biologists 'wish-list', and where there are currently 'technological gaps'.

Includes:

- The process of the creation of new technologies that underpin basic biological research, or the radical modification of existing technologies to allow for new applications. Such technologies include:
  - Methodologies, e.g. biomolecular characterisation;
  - tools, e.g. chemical biology tools, bionanotechnology tools, toolkits for synthetic biology
  - infrastructure;
  - instrumentation, e.g. bioimaging and functional analysis
  - information technology, e.g. for predictive modelling of biological systems**;**
  - software, e.g. informatics for biology and 'omics' technologies, including sequencing
- Includes the generation, rather than application, of technologies for biological research. Often this will apply to basic (underpinning) biological research rather than research with a clear industrial application.

Excludes:

- Projects that are making minor, incremental modifications to existing technologies.
- Projects focused on the **application** of an **existing** technology.
- Projects on technologies where the impact of the technology and/or the resulting research enabled by them is likely to be limited
- Projects focused on generic technologies with principal applications in non-bioscience disciplines.

The 3 Rs (RRR)
(Replacement, Reduction and Refinement of animals in research)

The principles of the 3Rs, replacement, refinement and reduction, were originally developed by Professor William Russell and Rex Burch, and are now widely accepted internationally as criteria for humane animal use in research and testing.

Research relating to the 3Rs includes research involving studies where the stated aim from the outset is to develop procedures or methodologies designed to replace, refine or reduce the use of animals in research or improve the welfare of experimental animals. However, BBSRC wishes to embed these principles in all the research within its remit involving animal use. It encourages grant applicants, including those whose research does not involve animals but could contribute to reduction and replacement, to consider opportunities to address the 3Rs. Applications that do not exclusively address improvements in the 3Rs will fit this priority if they aim to generate information relating to the 3Rs as part of a larger or related study.

The 3Rs are defined as:

- **Replacement** - Methods which avoid or replace the use of animals defined as 'protected' under the Animals (Scientific Procedures) Act 1986 (i.e. all vertebrates plus *Octopus vulgaris*) in an area where they would otherwise have been used. Examples of replacement approaches include:
  - Absolute replacements - techniques which do not involve animals at any point, such as computer modelling, *in vitro* methodologies (e.g. tissue engineering), use of human volunteers
  - Relative replacements, which replace the use of 'protected' animals with other species e.g. invertebrates, larval forms of amphibians and fish until the stage where they become capable of independent feeding.

  The use of organisms such as *C. elegans* or *Drosophila* as models of mammalian systems or the use of human trials should not be automatically considered as replacement unless it develops (directly or indirectly) a novel model for the replacement of protected animals.

- **Refinement (welfare)** - Improvements to scientific procedures and husbandry that minimise actual or potential pain, suffering, distress or lasting harm and/or improve animal welfare in situations where the use of animals is unavoidable. Examples could include reducing stress by developing new approaches such as training animals, use of non-invasive techniques or enrichments that improve living conditions.

- **Reduction** - Methods that minimise animal use and enable researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same number of animals, thereby reducing future use of animals. Examples could include: improved experimental design and statistical analysis, data and resource sharing and use of techniques such as imaging which require smaller numbers of animals or provide a greater amount of useful information.