A Living Foundry for Synthetic Biological Materials
A Synthetic Biology Roadmap to New Advanced Materials

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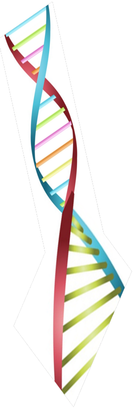

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1. Foreword

The UK has invested heavily in synthetic biology to establish platform technologies and capabilities for the manufacture of complex molecules that are too difficult, complex or expensive to produce using traditional manufacturing methods. The 2016 UK Roadmap *Bio-design for the Bio-economy* highlighted the substantial impact that synthetic biology could bring to the UK and global economies by developing frontier science and technology, and establishing a healthy innovation pipeline, a highly skilled workforce and an environment in which innovative science and businesses can thrive.

Synthetic biology is burgeoning in the UK. It has the explicit aim of integrating knowledge from chemistry, biology, computer science and engineering to design and construct new biological parts, devices and systems, and re-design existing biological systems for useful purposes. By using new platforms and technologies to harness biological genomic and metabolic resources synthetic biology has the potential to move from idea to product faster, cheaper and with greater precision than traditional manufacturing approaches. In part this is attributed to its foundation on the use and development of biology-based toolkits that are based on abstraction, standardisation and automated construction to change how we access and build biological systems.

Synthetic biology will transform the Industrial Biotechnology landscape, bringing bio-sustainable and affordable manufacturing routes to all industrial sectors including *Global Healthcare*, *Energy*, *The Digital Economy, Sustainable Manufacturing, Environmental Sustainability and Urban Development*. By adopting the enabling technology platforms of synthetic biology, we have the potential to grow UK industrial biotechnology for a sustainable circular bioeconomy[1] and to meet head-on many contemporary global societal *Grand Challenges*. Major recent investments by the UK Government have bolstered capabilities in synthetic biology, established new infrastructures and trained workforces equipped to drive forward anticipated outcomes from UK synthetic biology. It is now timely to consider how these investments can be harnessed to underpin sector specific challenges that extend across the innovation pipeline from basic discovery science to manufacturing and commercialisation. This Roadmap sets out a vision to achieve this for a new generation of *Advanced Materials – Synthetic Biological Materials*.

2. Executive Summary

Nurturing Emerging Capabilities for Synthetic Biological Materials

Society is on the cusp of harnessing recent advances in synthetic biology to discover new bio-based products and routes to their affordable and sustainable manufacture. This is no more evident than in the discovery and manufacture of *Synthetic Biological Materials*, where synthetic biology has the capacity to usher in a new *Materials from Biology* era that will revolutionise the discovery and manufacture of innovative *Synthetic Biological Materials*. These will encompass novel, smart, functionalised and hybrid materials for diverse applications whose discovery and routes to bio-production will be stimulated by the fusion of new technologies positioned across physical, digital and biological spheres.

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[1] A national Industrial Biotechnology Strategy to 2030. https://www.bioindustry.org/uploads/assets/uploaded/d390c237-04b3-4f2d-be5e776124b3640e.pdf

This Roadmap, which developed from an international workshop held in Manchester, United Kingdom, in 2017 (see acknowledgement and review[2]), sets out to identify opportunities in the new *Materials from Biology* era and to propose a mechanism to accelerate their commercial development. It considers requirements, early understanding and foresight of the challenges faced in delivering a *Discovery to Manufacturing Pipeline* for *Synthetic Biological Materials.* This challenge spans the complete production cycle from intelligent and predictive design, fabrication, evaluation and production of *Synthetic Biological Materials* to new ways of bringing these products to market. Pathway opportunities are identified that will help foster expertise sharing and infrastructure development to accelerate the delivery of a new generation of *Synthetic Biological Materials.* The UK has an opportunity to lead in this research field. In particular this roadmap identifies tangible benefits that can be brought to the area, from the leverage of existing UK investments in synthetic biology and advanced materials research, through a Hub and Spokes model of localised and distributed technologies, and a national coordinated approach to achieve this goal.

Roadmap Recommendations

1. **A Living Foundry for Synthetic Biological Materials.** An opportunity to interconnect and harness existing UK assets and capabilities in synthetic biology, materials science and allied disciplines, innovation and partner institutions to create a foundry concept that establishes a *Discovery to Innovation* pipeline to accelerate the discovery of new *Advanced Materials* and achieve rapid translation to market of *Synthetic Biological Materials.*

2. **Co-development to Meet 'Unmet Needs'.** Internationalise the UK Hub and Spokes model to facilitate academic, industrial and government co-development of research programmes to ensure early appreciation of unmet needs, commercial challenges and implementation of frontier science and technology to deliver these needs.

3. **Early Delivery of Next Generation Advanced Materials.** Identify areas of focus for early investments that can be delivered using the *Living Foundry* concept to demonstrate the power of *Synthetic Biology* methods in the delivery of the *Synthetic Biological Materials* paradigm.

4. **Industrial Challenges.** Coordinated foundry support would allow longer-term development to a point of pre-commercial demonstrator status, which will "de-risk" and lower investment barriers for industry and investors, supported through engagement and foresight benefit mapping in the early design process.

5. **Innovation and Training for Growth.** Embed a culture of continual innovation and training in the Hub and Spokes to ensure an expert workforce can meet the demands of growth in a burgeoning sector and that capability platforms can support increased demands for quicker and more predictable discovery and translation of *Synthetic Biological Materials* and further inward investment.

6. **Complete Ecosystem for Synthetic Biological Materials.** Within the Hub and Spokes infrastructure, develop an ecosystem for creative interdisciplinary *Synthetic Biological Materials* innovators of the future. This will retain and foster a depth of specialist scientific and technical knowledge, foresight and strategy implementation to meet commercial and business needs, support an 'ideas factory' for early co-development of programmes and, in working with partners, stimulate inclusive debate and knowledge of wider regulatory, acceptability and compliance issues.

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[2] Le Feuvre, R & Scrutton, N (2018). A Living Foundry for Synthetic Biological Materials: *A Synthetic Biology Roadmap to New Advanced Materials.* Synthetic and Systems Biotechnology. 3, 105-112.

3. Introduction

The Dawn of a New Era for Advanced Materials

Strong synergies exist between materials and chemicals sciences and their allied technologies, which have driven understanding at the atomic and molecular levels of the complex relationships between the chemical compositions, structures and macroscopic properties of materials. This has been the predominant agenda behind the development of new *Advanced Materials* to modify properties and enhance performance. The market pull is defined in the main by societal grand challenges. These include *The Digital Economy*, *Energy*, *Living with Environmental Change* and *Life-long Health and Well-being,* each placing demands on overall performance to suit new applications. *Advanced Materials* are at the core of *Systems Engineering* that relates to the design and management of complex systems over their complete life cycles, and its nexus with industrial engineering, manufacturing engineering, other branches of engineering and human-centered disciplines (e.g. project and risk management). Embedded in this is the need for *Sustainable Materials Management* and, increasingly, *Sustainable Materials Manufacture*, to reuse and sustain materials more productively, and affordably.

All this places great demand on the need to engineer new *Advanced Materials*. Whilst synthetic chemistry has, and continues to, advance core synthetic technologies to 'build' new materials through monomer provision, higher order polymerisation and functionalisation, synthetic biology is beginning to identify new ways of accessing chemical space. This opens up new chemical connectivities not accessible to the synthetic chemist and the rapid exploration of diverse (bio)-molecular structures. The conflation of synthetic biology and (combinatorial) synthetic chemistry, and exploration of potential connections with contemporary manufacturing platforms such as *Additive Manufacturing* (3D printing), defines a new era in the exploration of new *Advanced Materials* extending from basal materials with new (desirable) properties to complex and well-defined 3D mesostructures (3D topologies). Supplement that with developments in *Artificial Intelligence* (e.g. *Machine Learning*) to learn and predictively design new *Advanced Materials* in rapidly implemented (automated) iterative Design, Build, Evaluate, Learn cycles, and one has a powerful series of technology platforms with which to navigate the new *Advanced Materials* landscape.

The unification of synthetic biology with other frontier sciences and technologies will usher in the new *Synthetic Biological Materials* era*.* In the main, the definition of *Biomaterials* has been associated traditionally with healthcare applications, for example in the development of biocompatible scaffold materials (tissue regeneration), structural biocompatible materials (prosthetics) and new materials for drug delivery (biomedical devices). This can be classified as *Materials for Biology*. With *Synthetic Biological Materials* the focus is more on *Materials from Biology* and the harnessing of new capability platforms (e.g. *Synthetic Biology*; *Additive Manufacturing*) in an integrated fashion with leading developments in more established fields (e.g. *Click Chemistry; Machine Learning; Automation; Miniaturisation of Materials Evaluation Platforms*). By bringing deeper biological thinking to *Advanced Materials* societal grand challenges can be met. Biology will bring sustainable and affordable manufacture of complex new materials that will impact not only in *Healthcare*, but also in other sector challenge areas (e.g. *Energy*, *Military*, *Advanced Manufacturing*, *Living with Environmental Change*, *Digital Economy* etc.). This will give rise to a wide range of new *Advanced Materials,* especially – although not exclusively – in the realm of soft materials that can be functionalised, elaborated and assembled hierarchically, and validated rapidly, for target applications.

THE OPPORTUNITY

By harnessing the power of synthetic biology existing materials discovery platforms and fabrication technologies would be augmented to widen the materials development space and define a new materials paradigm – *Synthetic Biological Materials*. This would enable delivery of next generation *Advanced Materials* with new and extended functional properties to address a wide range of unmet needs. By realising this opportunity, the UK would gain access to affordable and sustainable routes to the production of *Synthetic Biological Materials* able to meet many Global challenges*.*

4. Synthetic Biological Materials

Navigating a New Landscape to Advanced Materials

There are diverse potential application areas for *Synthetic Biological Materials* as a distinct, but major, contributor to the *Advanced Materials* landscape, impacting across multiple grand challenge themes – *The Digital Economy*, *Energy*, *Living with Environmental Change*, *Life-long Health and Well-being.* Using synthetic biology platforms the materials scientist can access a new design space not available with other platform technologies. That alone however is not sufficient. A requirement of any strategy for *Synthetic Biological Materials* is identifying unmet application needs (i.e. new materials performance properties) and to deliver routes to new bio-sourced components, with appropriate chemistries, that enable rapid assembly of new materials and the emergence of higher order functionality to satisfy those needs. Clearly, *predictive design* and *rapid evaluation* are at the core of any synthetic biology approach, alongside parallelised assembly of new materials through laboratory automation, high throughput characterisation and post production processing.

Industry Pull will identify 'hard-to-make' material targets and early wins for synthetic biology, but there is a need also to deliver a *Creative Push* to generate new ways of working that lead to transformative application solutions. This 'out-of-the-box' mode of operating will define proof of concept applications that will challenge convention and deliver solutions for contemporary problems faced by industry.

Any investment in *Synthetic Biological Materials* will be a relatively high-risk, high-gain venture. The substantial investment in synthetic biology made by the UK government provides some impetus for *Synthetic Biological Materials* but inertia remains, especially in uniting manufacturing and materials discovery communities to harness opportunities emerging from synthetic biology. Any strategy therefore must also provide for, and mobilise a skilled workforce from discovery science through to application, as well as the infrastructure to support it. The unifying concepts are therefore: platform technologies to support the delivery of *Synthetic Biological Materials;* a highly trained interdisciplinary workforce and academic/industry/government co-development that can implement and innovate these technologies; standardisation and interoperability of biological parts for new materials; sustainable materials manufacturing and management, and a common language and vision that places synthetic biology at the nexus of other disciplines, especially materials science, chemistry, computer science and engineering.

Clearly, a high-level strategy document cannot provide comprehensive appraisal of application areas and unmet needs. But, consideration can be given to exemplar areas where investment in *Synthetic Biological Materials* will facilitate step-change. For example, early challenge areas might include *Corrosion.* This destructive attack of a material by reaction (chemical and or electrochemical) with its environment causes serious problems with worldwide significance, in terms of contamination, reduced efficiency, safety and economics (costing $1.1 trillion in the USA alone i.e. 6% GDP). Next generation *Synthetic Biological Materials* could harness protective, biologically compatible coatings, by capturing the power of biological functions (e.g. biocides) 'out of context'.

In the field of *Bioelectronics* how signals can be effectively transduced (e.g. in coatings) to link capabilities (e.g. sensing) with other components, or modules, in complex materials is a major challenge. Here biology can provide new designs, genetically encoded in the form of redox polymers (proteins) or nanowires, for further elaboration to enable integration into new materials where signal transduction is an embedded function. Predicted examples of the impact of *Synthetic Biological Materials* in *Bioelectronics* are found in *Healthcare* where early detection/monitoring, rapid *in vivo* analysis, biomolecule to biosystem monitoring/management, and the design of scaled intelligent micro-bioelectronic systems are set to have major impact (e.g. cancer diagnosis and type II diabetes cost ~ $200 billion in direct medical costs in the US and heart disease afflicts 22 million US citizens costing $172 billion). Coupled with a wide range of industrial applications (*in situ* monitoring for industrial manufacture) this field is poised for exponential growth, and will impact in cross cutting ways e.g. medicine, health and well-being, forensics, homeland security, manufacture, and parallel diagnostics/miniaturisation. *Synthetic Biological Materials* can make substantial and unique contributions to all these challenge areas[3] and electroactive biopolymers[4] are beginning to show great promise attributed to the high tunability of chemical and physical properties that can be tailored to application. Here fabrication to form blends, composites or hybrids in the form of coatings or porous materials with improved conductive properties can drive diverse applications to satisfy unmet needs e.g. development of battery electrodes for improved storage capacity and charge/discharge rates, or rechargeable batteries for mobile electronic devices. Synthetic biology can be used to generate *Electro-genetic Devices* to provide bidirectional communication between electronic devices and biological systems. Self-assembly into well-ordered structures at the nanometer scale are sought by the electronics industry, whilst the fabrication of nanowires using peptide scaffolds could also provide templates for metallation. Extracellular electron transfer pathways that allow bacteria to communicate electrically between their intracellular chemical energy stores and extracellular solids, also present potential applications in biocomputing, bioenergy and biosensing.[5]

Optical Materials will undoubtedly emerge as important *Synthetic Biological Materials*. Natural biological systems have developed novel hierarchical photonic structures able to manipulate light propagation (e.g. structural colour, anti-reflection, light focus and chirality)[6] that are inspiring the design of new micro-structures and fabrication of smart optical devices for optical sensors, light-energy conversion and optical plasmonic material. Bio-templating methods have demonstrated success, but are not suitable for mass production, and reproducibility is poor. Biomimetic methods using engineering fabrication (e.g. nano-imprinting, 3D lithography and laser writing) are also promising but time consuming and expensive. Cross-discipline challenges should therefore provide the impetus and know-how to find bio-based nanofabrication solutions to build 3D photonic structures for real-world applications, where additional multi-functional natural properties (e.g. self-cleaning, directional adhesion, flexibility and fluorescence) will allow fabrication of multi-functional composite materials. These should find widespread application, especially in *The Digital Economy* and *Communications* sectors and specialised applications in the *Military.*

Synthetic Biological Materials will lead also to next generation *Synthetic Biomimetic Materials* and *Mineral Biomaterials.* The natural world has evolved a bewildering range of materials of desirable strengths, flexibility, adhesion, transparency, and reflectivity and conductance properties.[7] The challenge now is to build on a growing understanding of these materials to feed the development of new bio-inspired materials with improved functionality. Interactions between inorganic phases (simple salts or oxides), ions and biomolecules (e.g. proteins, lipids, carbohydrates or polyamides) provide complex structures with physical and mechanical properties that can support or withstand stress. The resulting composites have wide-ranging structures and properties that can serve as synthesis guides for controlled fabrication of materials with enhanced mechanical or other properties. Bringing the power of synthetic biology to diversify these materials further will facilitate deeper exploration of their properties and the creation of new composite materials for a wide range of application. A notable example is natural nacre (mother of pearl), which has superior properties to artificial materials of similar composition. The challenge here is to fabricate synthetic nacre in which the tiny aragonite slabs are held together using synthetic structures that mimic the structural and mechanical characteristics of their natural counterparts. Early reports to make synthetic nacre by predesigned matrix-directed mineralisation are now beginning to emerge.[8]

There is intense interest in developing *Smart Materials* (e.g. multiphase systems or membranes) with integrated biological functions, or the functionalisation of existing materials, that can self-assemble, self-repair or evolve to provide connective, responsive and controllable materials (e.g. expansion or

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[3] A Framework for Bioelectronics: Discovery and Innovation. National Institute of Standards and Technology (2009)

[4] Guarino et al. Electro-active polymers (EAPs): A promising route to design bio-organic/bioinspired platforms with on demand functionalities (2016) Polymers 8, 185

[5] TerAvest et al. Transforming exoelectrogens for biotechnology using synthetic biology (2015) Biotech. Bioeng. 4, 687-97

[6] Wu et al. Optical functional materials inspired by biology (2016) Adv. Optical Mater. 4, 195-224

[7] Wegst et al. Bioinspired structural materials (2014) Nature Materials 14, 23-36

[8] Mao et al. Synthetic nacre by predesigned matrix-directed mineralization (2016) Science 354, 107

motion). These materials will support diverse applications, especially in *Healthcare* (e.g. personalised medicines). The use of genetically tractable microbial cells to create multifunctional responsive interfaces (e.g. to moisture) where new functionality is added (e.g. fluorophores, colour or odours), or metabolically responsive to environmental cues towards wearable devices, would meet multiple unmet needs.[9] Here a *Synthetic Biological Materials* approach is powerful and enables assembly of responsive materials in a relatively facile and sustainable way that simply is not possible using other contemporary approaches.

Self-healing Materials have a built-in ability to automatically repair following damage without external problem diagnosis or human intervention. These materials could solve time-consuming and expensive repair of wear, tear and spontaneous damage. Whilst polymers embedded with self-healing adhesives that work through polymerisation and microcapsules exist, they have major drawbacks, e.g. 'single use'. The challenge is to create autonomous adaptive structures (e.g. thermoplastics) or self-healing polymer materials that utilise ion-dipole interactions. New materials are in development that use stretchable polymer chains linked by ion-dipole interactions between polymer polar groups and ionic salts. The resulting materials can stretch up to 50 times their usual size, and after being torn in two, can self-repair over the course of one day.[10] The creation of self-repairing materials capable of conducting electricity would have wide ranging applications, e.g. for use in touchscreens. Again, *Synthetic Biological Materials* platforms would facilitate rapid exploration of new components for *Self-healing Materials* and define routes to their affordable production through biomanufacturing.

Synthetic Biological Materials offers new opportunities for the development of *Micro-mechanical devices.* For example, bioengineering for biomolecular control (utilising DNA, RNA and other biomolecules for motion) to generate responsive structures and behavioural materials with expansion or motion towards biomolecular programmable robots is underway. Whilst development of helical coils of orientated polymer fibres that generate large, reversible changes in length as a result of thermal expansion under geometric constraint (winding / unwinding of helical constructs) could lead to actuators engineered to act as artificial muscle.[11] This provides motion through processes associated with intrinsic changes in constituent materials and could provide a solid-state alternative to mechanical machines (i.e. materials-based actuators).

In a similar vein, *Synthetic Biological Materials* platforms can support the discovery and development of *Multicomponent Responsive Materials* (e.g. turbulent drag reduction materials, responsive polymers and responsive interface materials) and '*SynBio-fy*' the more traditional field of *Biomaterials.* The latter covers a spectrum of research effort for materials engineered to interact specifically with biological systems. This might be for therapeutic or diagnostic medical purposes, including advanced formulation and fabrication for drug delivery systems and intelligent therapeutics that work harmoniously with the body for targeted or responsive delivery.[12] It includes the design and fabrication of polymer-based hydrophilic materials, or hydrogels, that allow incorporation of functional groups. By tailoring responsive polymers to applications in tissue engineering the properties of engineered scaffolds can be made responsive to a variety of physiological stimuli (e.g. pH, temperature, and salt conc.).

The above are examples of what might be achieved in the emerging field of *Synthetic Biological Materials,* and others will follow. The *Synthetic Biological Materials* agenda will be supported by the ability to define affordable and/or sustainable routes to biopolymeric materials and small molecule monomers through the bioengineering of extended metabolic space. Feedstock engineering can provide affordable routes to relatively low value monomers and there is already precedent from earlier investments in the synthetic biology of chemicals production, where bio-based production of monomers for a wide range of materials is already under development. Early exemplars include routes to terpene-based monomers, terephthalic acid and other materials components. Synthetic biology also

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[9] Wang et al, Sci. Adv. Mat. Bioinspired shape-memory graphene film with tunable wettability (2017) Sci. Adv. 3, e1700004

[10] Wang et al, Sci. Adv. Mat. A transparent, self-healing, highly stretchable ionic conductor (2017) Adv. Mater. 29, 1605099

[11] Haines et al. New twist on artificial muscles (2016) Proc. Natl. Acad. Sci. 113, 11709-16

[12] Shi et al. Electroconductive natural polymer-based hydrogels (2016) Biomaterials. 111, 40-54

opens up engineering of molecular chirality and order, or the inexpensive incorporation of stable isotopes (e.g. deuterium), which in solid materials can lead to enhancement of physical and functional properties. Harnessing and extending these capabilities will also augment the drive to expedite new routes to *Synthetic Biological Materials.*

Areas of Focus for Early Investments

In order to synergise synthetic biology, materials sciences and related disciplines in this burgeoning field, it is important to identify early challenges and consider exemplar areas where strategic investment would bring about a step-change in the early delivery of next generation *Advanced Materials*. Unmet challenges are wide-ranging and include applications in anti-fouling, coatings, bioelectronics, electro-genetic devices, optical materials, biomimetic and mineral based biomaterials, smart materials with added functionality, self-healing and multicomponent responsive materials. Identification of 'early wins' through interconnected challenge projects, with the potential to impact across multiple application areas, is crucial. This will address urgent unmet needs and catalyse additional growth to generate further 'co-development partnerships' with industry and government. Focus areas uniquely accessible to synthetic biology that would provide early impact across multiple application areas are identified below. These challenge themes are complementary; combined they would provide powerful new approaches to deliver diverse materials enabled through synthetic biology. These challenge areas embrace the need to 1) emphasise transformative fundamental research that will accelerate delivery of next generation biomaterial production methods; 2) drive molecule library development to produce large-scale repositories for immediate application; 3) develop small-scale rapid screening to predict and test performance and properties of individual molecules within the library; 4) ensure predictive key feature and functionality characterisation using deep learning applications in the discovery pipeline; 5) standardise data compilation and collection.

The following areas would be especially attractive for early investment in *Synthetic Biological Materials* and would build on existing investments and infrastructures available in the UK. The themes below are interrelated and provide a framework for early delivery of new *Advanced Materials.*

- *Small molecule monomer libraries* to produce a large-scale, shared repository of generic small molecule building blocks for multiple applications. This is needed to speed up delivery of parts (e.g. functional components) and polymeric building blocks for subsequent diversification and hierarchical assembly (polymeric scaffolds and decoration/tailoring). Here computational approaches will provide the ability to search extended metabolic spaces and facilitate iterative design, build, test and learn (DBTL) cycles to new monomeric building blocks using existing HTP automated metabolic engineering infrastructures available in the UK (e.g. SYNBIOCHEM). This would provide sustainable synthetic biology routes (metabolic modules) to a wide range of monomers used in diverse polymeric materials. These include: sustainable polymers derived from terpene monomers (e.g. pinene; limonene; menthol; α-methyl-γ-butyrolactone and others) to provide platform scaffolds for further (hierarchical) modification; terephthalic acid, diamines, furan dicarboxylic acid, lactides and succinic acid (base monomers for many currently used polymers); long chain monomer precursors (oleic acid, ricioleic acid and derivatives), epoxidised / functionalised fatty acids.

  Deliverables: *A comprehensive repository and 'know how' for use of these building blocks would be established from both internal DBTL programmes and optimisation of externally available strains to these monomers <u>for immediate application</u>.*

- *Biopolymer building blocks* with, for example, signal transduction and sensing capabilities for bioelectronics and optical properties engineering. These would be protein modules, elaborated to interface with other components (scaffolds, surfaces and other bespoke molecules) that, for example, transmit electronic signals from one part of a material to a distal region to facilitate signal transduction. Protein nanowires can be built through diversification of natural protein components (e.g. multi-heme proteins; metalloprotein domains) and functionalised genetically (conventional amino acid substitution and orthogonal incorporation of non-proteinogenic amino acids into biopolymers) using synthetic biology platforms. This would provide a repository of self-assembling components that can form nanowires functionalised to form hybrid/composite materials; components engineered to form linear/branched/networked structures; components functionalised to interface (e.g. through Click chemistry or by adapting a process used by nature) with other materials components, biopolymers and surfaces; nanowire components that are readily interfaced with other components for capture and monitoring (e.g. electrical, optical, fluorescence signals). Similarly optically responding protein biopolymers (e.g. reflectins; phytochromes, to name but a few) can be likewise functionalised to generate higher order composite materials.

Deliverables: *A comprehensive repository and 'know how' for use of nanowire/optical building blocks would be established from both internal DBTL programmes and external sources to use for immediate application in new materials discovery and applications programmes. These would include electrical communications/storage (e.g. bio-computation, batteries), sensor technology (e.g. protein nanowires in layered composites), sensing/camouflage/protection coatings (e.g. transparent coating/two-photon absorbing coatings) and biomedical applications (bio-sensing/delivery systems).*

- *Rapid higher order assembly and fabrication of materials from component scaffolds.* Higher order fabrication of materials with novel properties will necessitate further development of instrumentation and characterisation platforms such as spinning techniques and interfacing with 2/3D printing (e.g. in layers), miniaturisation and high throughput (HTP) capabilities. Establishing new routes to spinning synthetic biological material polymers, assembling layered materials through *Additive Manufacturing* and self-assembling novel and diverse components (e.g. through Click chemistry to form novel coatings) are early targets to drive higher order assembly of new materials. New coatings could be rapidly assembled through use of laboratory automation and functionalised scaffolds/components building blocks. This would enable rapid integration of optical or sensing chromophore components (e.g. development of tunable, photon absorbing optical limiting materials to prevent laser dazzle for transparent sensor protective coatings, or camouflage coatings with reflectins). Protein based scaffolds could also provide the basis for nanowires for subsequent functionalisation and diversification. An early objective would therefore be to establish rapid and robust fabrication routes to such higher order materials.

  Deliverables: New technology routes to the higher order assembly of diverse materials using a number of miniaturised/automated platforms including Click chemistry (for immediate delivery of functional coatings); additive manufacturing (e.g. for higher ordered layered materials); novel spinning approaches (for new biopolymer fibres e.g. bio-Kevlar; silks etc.). This would provide an infrastructure and 'know-how' to rapidly assemble new Synthetic Biological Materials from constituent components.

- *Robust production chassis for affordable production of Synthetic Biological Materials.* Despite exciting advances in the scale and scope of metabolic engineering, major limitations of laboratory (e.g. yeast, *E. coli*) and industrial strains (e.g. bacillus, yeast) have prevented affordable development of sustainable bio-based manufacture at scale. Materials components fall into the high volume/low cost category and robust production chassis are now urgently required to drive affordable production. Development of *robust industrial* production strains that can be grown in non-sterile environments, with reduced water demand, and reduced capital investment in establishing production facilities offers the potential to develop sustainable and affordable bio-production platforms and distributed manufacture in challenging environments for both small molecule and biopolymer-based materials. For example, some industrial strains have been adopted for the high volume commercial production of bioplastics but not adopted more widely as a production hosts for other materials. Early objectives would be to migrate production platforms into new robust strains for affordable and sustainable production at scale. This would require establishment of a comprehensive synthetic biology repository of tools and resources for production of materials in these new hosts.

> *Deliverables: A repository of tools and resources to enable scaled production of Synthetic Biological Materials in robust industrial production strains. This would facilitate early migration from other microbial production platforms to enable affordable and cost effective production of materials and their components (e.g. through distributed manufacture), with less reliance on a skilled workforce, without major capital investment and in challenging environments (e.g. in coastal regions, arid environments or in military theatre).*

The above describes interconnected early focus areas that would have the broadest impact and also guarantee early wins for *Synthetic Biological Materials*, both in terms of new materials discovery that cuts across multiple application areas and also affordable and sustainable manufacture of the building blocks for these materials. Thus the delivery of cross-cutting and integrated projects based within these themes would provide a capability pipeline of discovery research that could be rapidly translated for focused and broad range applications. These general frameworks would provide early exemplars/areas for translation that could tackle *Grand Challenge* areas and unmet needs in co-development programmes with industry and government agencies. They are also areas where international collaborations and industrial partnerships would be particularly fruitful. These challenge areas would run iteratively within the first 5 years. *Given the mature state of UK assets in support of this field it is envisaged that early wins for new materials discovery with properties suitable for application would emerge from Y2 onwards. The development of this coordinated ecosystem will provide UK growth for the global bioeconomy*

Integrated Delivery Platforms for Advanced Materials

To accelerate discovery and delivery of *Synthetic Biological Materials,* integration of interdisciplinary and advanced platform technologies would be required to form a pipeline capability that is able to progress smoothly from early target building block design, through to material fabrication and scaled-up production. The early consideration of multiple technology components, described below, will be important.

Embedding *AI/Machine Learning* at every stage of the DBTL cycle will facilitate *accelerated* delivery. *Predictive Design* driven by *Machine Learning* using more limited experimental datasets will accelerate the delivery of new materials with desirable properties and needs to work alongside more established Design areas such as *Multi-scale Modelling.* Application of iterative rounds of intelligent Design, Build, Test and Re-design with the development and adoption of 'higher-level' language and abstraction towards Design will enable further understanding of complex systems. Leveraging frontier developments in *AI, Data Analytics, Machine Learning and Deep-deep Learning* will synergise this approach and will define new routes to *in silico* exploration of new materials, their structures and functional properties.

The assembly of binary (or higher order) materials, where properties only emerge, on mixing or assembly of components, is an essential consideration. Important drivers will be *rapid* generation of materials diversity, scalability of synthesis, synthesis of biological and chemical stability, modular synthesis and production of composites. Total integration of *all* synthetic methodology embracing chemical, biological and nanotechnology approaches, will be required for rapid design and assembly of new materials. *Additive Manufacturing* is an emergent domain defined as the design, fabrication, assembly and measurement of bio-elements into structures, devices, and systems, and their interfacing and integration into larger scale structures *in vivo* or *in vitro*. Innovation in this space will be required to drive *Synthetic Biological Materials* into the fabrication of more complex hybrid materials that will enable new properties and functions to emerge. Future infrastructure investment will therefore need flexible, adaptive manufacturing capability to design and manufacture a range of *Synthetic Biological Materials*.

Rapid diversification of basal materials and layering to form composites and other higher order structures, exploiting *Additive Manufacturing,* will be enabled by genetic encoding of non-canonical amino acids in synthetic biology platforms which would support further diversification by efficient chemical tagging of small molecules, other biological components, surfaces or non-biological polymers/mineral surfaces. This would require expertise in the bioengineering of metabolic and regulatory parts, pathways and production systems, for example those for chemicals and proteins, and for feedstock engineering. The challenge here will be to drive existing capabilities for parts, pathways and chassis engineering towards more complex hierarchical assembly of new materials by interfacing with technology platforms established in other disciplines, including synthetic and materials chemistry, and engineering.

Accelerated discovery of natural biological materials would be required to explore the diversity of materials and provide access to new materials properties currently lacking. Recent advances in next generation sequencing are key here, and would considerably reduce the time constraints in identifying new biological materials. Research programs would need to embrace these new technologies to give access to the potential power of vast libraries of biological materials (natural and synthetic) and to deliver these new biopolymers into artificial systems through further chemical/biological elaboration, and/or through the assembly of new composites.

The required evaluation platforms present major challenges, because of the sheer diversity of new *Synthetic Biological Materials* that will emerge from 'Design', 'Build' and 'Production' platforms. Here we have an opportunity to harness leading national infrastructures (e.g. the Henry Royce Institute and other materials Centres throughout the UK), and to establish more generic parallelised and miniaturised approaches to the evaluation of general properties. The demands on evaluation of new *Advanced Materials* properties will be extensive, encompassing a variety of sub-themes including structural (size, strength, flexibility, shape etc.), functional (e.g. conductivity, programmable, light responsive, visco-/poro-elasticity etc.), compound properties through inventive combinations and arrangements of component materials (emergent properties), biocompatibility, biological and chemical stability, and the ability to self-assemble or nucleate hierarchical complexity and anisotropic behaviour. A comprehensive 'Evaluation' capability platform that harnesses state-of-the-art analytical tools for *Synthetic Biological Materials* characterisation would be of benefit (e.g. built at the Henry Royce Institute locally or through its partner networks). The platform technologies for evaluation of physical properties would typically include: HTP rheology, tensile testing, small/wide angle X-ray scattering, light scattering, thermal characterisation and structural analysis through a suite of imaging and spectroscopy approaches. Likewise surface analysis would require a suite of specialised methods.

There is a pressing need to establish new sensitive high throughput evaluation methods to support the production and characterisation of building blocks delivered through *Synthetic Biology* approaches. *High content analysis* through quantitative cell analysis (e.g. '*Cellomics*') is needed to assess biocompatibility and toxicity of expressed building blocks designed and synthesised in the production platforms. This uses state-of-the-art bioimaging methods and informatics with a workflow involving three major components: image acquisition, image analysis, and data visualisation and management. These processes are generally automated and all three of these components depend on sophisticated software to acquire qualitative data, quantitative data, and the management of both images and data, respectively. High content analysis would contribute to the *active learning* that runs throughout the pipeline, providing data on biocompatibility that can inform the design and synthesis of next generation building blocks. Critical to the evaluation and *active learning* programmes will be access to HTP sequencing, to map sequence-property relationships, which through *active learning* can then be further optimised.

Similarly, miniaturisation of parallel evaluation methods would be required to assess and sort (filter) desirable properties for the diverse range of *Synthetic Biological Materials* produced. This might include rapid read out of Infra-Red signatures to assess the folded nature of biopolymers, or optical/fluorescence properties of assembled materials components using automated screening/evaluation methods, or micro-rheology. Picodroplet technology would be especially powerful for rapid sorting of building blocks at the front end of the production platform. Here DNA writing to encode building blocks could include extended sequence to encode auto-fluorescent protein tags or peptide extensions that could be tagged with small molecule fluorophores. Picodroplet microfluidic technology processes (e.g. fuse, split and sort) and analyses (using fluorescent detection methods) would allow interrogation of tens of millions of strains per day (i.e. ultra-high throughput screening). This would allow generic screening and identification of 'folded' *versus* unfolded/unstable building blocks at a frequency > 150 s^{-1}. Each clone could be sequenced to identify components with desirable predicted properties that are then synthesised in the same way and tested in an iterative loop i.e. *Active Learning*. In this way, the Hub would pioneer the rapid expansion and provision of stable bio-based modules for further combinatorial assembly.

Ultimately selected building blocks would be needed in high-yield to drive functional elaboration and application. At the laboratory scale stable building blocks could also be encoded with suitable tags (e.g. polyhistidine, biotin tags and similar) at the DNA writing stage**.** These would enable high throughput recovery from expression hosts in 96- or 384-well format using automated liquid handling platforms incorporating magnetic bead recovery of biosynthesised products. The design possibilities are endless – tags can be retained, cleaved and even positioned at various points in the encoding DNA sequence (N and C-terminal, or within exposed internal loops of a biopolymer). For medium scale production, methods could be transferred to automated affinity chromatography platforms where sequentially or in parallel production optimisation is scouted with minimal operator intervention.

In due course the optimised components would need to be manufactured at larger scale. This would be achieved through fermentation of host strains that enable scale-out/scale-up at laboratory scale (typically 10-50L scale) following scouting of optimised production conditions in automated fermentation or mammalian cell culture platforms. Production could be coupled to established downstream processing to generate building blocks (mg-g scale) providing material that will support hybrid synthesis and assembly of complex biomaterials. Production chassis might need to be engineered to use available, affordable or waste feedstocks (e.g. CO_2, SynGas, lignocellulosic, glycerine and other wastes), and these feedstock pathways would need to be leveraged from the existing capabilities in *Synthetic Biology Centres* across the UK. This is especially the case for higher volume/lower value products where the economics of production and recovery of new components would be important factors. Any investment infrastructure would need to innovate in the production area to lower such costs, for example by lowering barriers to capital investment to production. This might be achieved through expression in robust industrial hosts that are less dependent on high cost infrastructure for cell growth, or expensive media for cell propagation. In selected cases expression of building blocks could be achieved in mammalian or yeast cell lines, with new opportunities emerging in genome editing. This would allow targeted biological post-translational modification (e.g. glycosylation) of building blocks that could contribute to novel functional properties.

Finally innovation is needed for development of new production platforms. These might involve the production of biological layers/sheets for hard and soft materials, the spinning of polymer fibres using innovative spinning technologies and the production of materials *in situ*. This development of production and fabrication platforms for hybrid materials would require wide interdisciplinary collaboration. Whilst the generation of materials, rather than production of new precursor chemicals and biological modules, would require revolutionary approaches to cellular production. Challenges would be around *Formulation of Materials* and how to insert *Synthetic Biology* steps to improve and functionalise materials. Here activity will need to integrate expertise, for example, the 2D nano community has extensive knowledge in the area of graphene-layered hybrid materials, as does the electronics industry in related materials. Formulation of nanoparticles from atomic precursors, the organisation of molecules on the surface of nanoparticles, and materials built from nanoparticles, could provide uniformity and control of one length scale profoundly affecting material properties.

It is clear that to take advantage of this burgeoning interdisciplinary field and deliver a new paradigm of *Synthetic Biological Materials* with wide-spread applications, will require convergence of expertise, co-development of novel platforms and interdisciplinary, international and inter-sector collaborations coordinated through an innovation pipeline.

EARLY INVESTMENT PRIORITIES

- Emphasis on basic discovery science for next generation *Advanced Materials* production
- Diverse molecular libraries to form a large scale repository of components to enable rapid assembly, evaluation and application
- Small-scale rapid screening to predict and test performance and properties of molecular libraries and emergent materials
- Predictive key feature and functionality characterisation using deep learning
- Standardised data compilation and collection

An Innovation Pipeline for Synthetic Biological Materials

An *Innovation Pipeline* for *Synthetic Biological Materials* should extend from the discovery, development, testing and fabrication of new *Advanced Materials* through to industrialisation and commercialisation. A supporting strategy should seek to establish and integrate existing expert capabilities, resources and infrastructures in order to achieve this vision. This is a major challenge but in the UK excellent progress on the back of substantial public sector investments has provided an interconnected national eco-system for synthetic biology and materials science from which to leverage resources, capabilities and partnerships. These include:

- £300M of public investment to establish a network of nationwide *Synthetic Biology Research Centres* (SBRCs) that drive early stage discovery science, each contributing distinctive and complementary fields of expertise towards synthetic biology.
- A national industrial centre for synthetic biology *SYNBICITE* (http://www.synbicite.com) designed as a translation engine bridging university-based research and industrial exploitation, focusing in particular on entrepreneurial activities.
- A public sector investment of £235M in the national *Henry Royce Institute for Advanced Materials* (http://www.royce.ac.uk) that will grow a world-leading research and innovation base in *Advanced Materials* science fundamental to all industrial sectors.
- A UK government commitment to *Building our Industrial Strategy* to shape a modern industrial nation as part of the plan for post-Brexit Britain in which 10 central pillars define a connected strategy to invest in science, research and innovation that takes UK discovery science through to commercialisation (http://www.ukspace.org/wp-content/uploads/2017/03/Industrial-Strategy-Ten-Pillars-One-Pager.pdf).
- Confluence with each of the *Eight Great Technologies* identified by the UK government to build UK research strength across multiple sectors to provide growth potential in the UK economy (https://www.gov.uk/government/publications/eight-great-technologies-infographics).
- Alignment with major international bilateral programmes and partnerships (e.g. US-UK; http://www.rcuk.ac.uk/international/offices/us/engaging-with-the-usa/), and also global programmes (e.g. *Global Challenges Research Fund*; http://www.ukcds.org.uk/funding/funding-landscape/gcrf) designed to ensure that the UK takes a leading role in addressing problems faced by developing countries (http://www.ukcds.org.uk/funding/funding-landscape/gcrf).
- The UK's strong academic foundational sciences and strengthening foundation industries (i.e. producers of materials, chemicals etc) that are key to rebalancing the UK economy and boosting exports and is reflected in the UK's government commitment to strengthen the UK manufacturing economy through its post-Brexit *Industrial Strategy* (http://www.ippr.org/publications/strong-foundation-industries).

The above combine to provide a 'top down' national framework from which to drive the new *Materials from Biology* paradigm from the 'bottom up'. These strategic investments have shaped national infrastructures and created energised workforces with the necessary skills that provide us with the opportunity to drive *Synthetic Biology Materials* towards delivery of commercial applications.

KEY FACTS

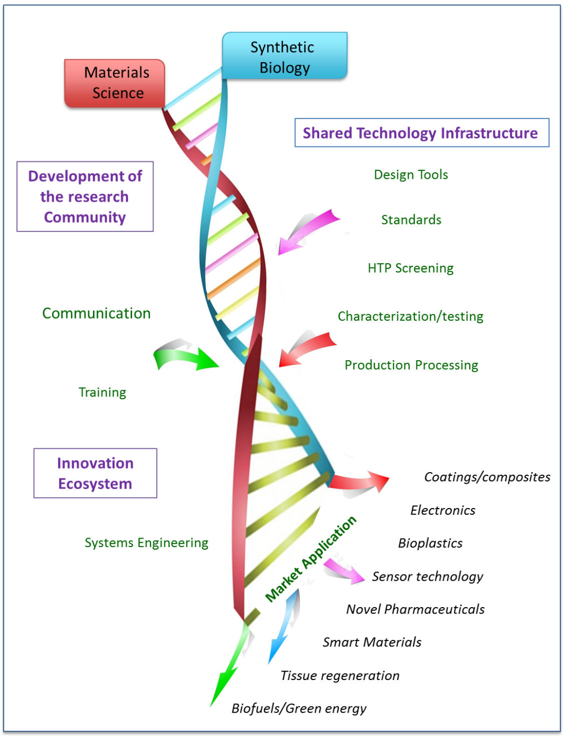
- Global market for *Advanced Materials* estimated as €316 billion by 2030 and €1098 billion by 2050
- The EU bio-economy supports 17 million jobs, and contributes *ca* €2 trillion annually
- *Advanced Materials* underpins one third of all UK manufacturing
- *Advanced Materials* have strategic importance for economic growth across all Grand Challenge areas

5. Delivering the New Paradigm of Synthetic Biological Materials

Hubs, Spokes and Coordination of Resources.

Driving *intersectorial*, *interdisciplinary* and *international* connectivity (abbreviated here as *I-Con*^{3}), and the leveraging of existing investments in synthetic biology, materials science, allied science and technology areas, are the major challenges in delivering the *Materials from Biology* vision. This is alongside a need to establish early stage partnerships with industry to define unmet needs in *Advanced Materials* and to maintain continued engagement from early-stage discovery and development through to manufacturing delivery and commercialisation.

The unification of existing, and leveraging of new UK and international investments will best be achieved through a Hub and Spokes *Living Foundry* model in which the impetus and coordination to deliver the *Materials from Biology* vision is driven from a flourishing Hub. This Hub model would connect/integrate existing and emerging Spokes to provide complementary additional essential resources and synergise devolved cultural and training perspectives required to deliver the vision.



The *Living Foundry* Hub would:

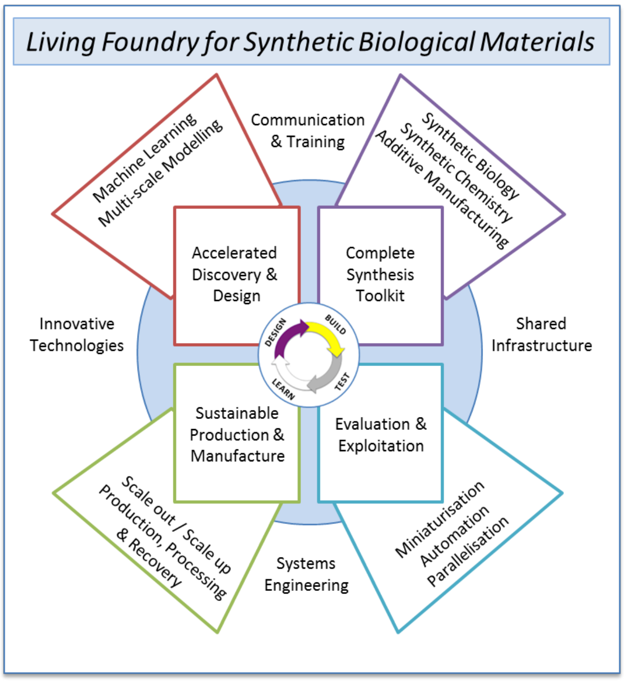
- ➢ Provide a communication portal to: unite UK and international expertise across materials science, synthetic biology and related disciplines; synergise activities towards exemplar programme delivery, and to facilitate and drive the *Materials from Biology* vision.
- ➢ Be a focus for new science and shared technology platforms, not available in the Spokes, required to deliver the *Materials from Biology* vision and be a delivery centre for early stage *Synthetic Biological Materials,* their fabrication and evaluation.
- ➢ Hold responsibilities as a point of contact for external stakeholders, clients, partners and the coordination and sourcing of expertise from the spokes/external groups engaged with the *Materials from Biology* vision.
- ➢ Be responsible for people training, client relationship management, project management and the implementation/coordination of programmes between the Hub and satellite locations from early stage development through to product delivery.
- ➢ Act as a generator and repository of biological parts/components for *Synthetic Biological Materials*, provide infrastructures for data management (open/shared/confidential) to support Foundry activities and to embed infrastructures for standardisation and interoperability across all Hub and Spokes activities.

- Be a catalyst for new *Advanced Materials* development to accelerate the Foundry's '*Discovery – Innovation Pipeline*' by working with stakeholders at all stages from discovery to manufacture and commercialisation. This will require early understanding and foresight of the challenges, adoption of *Systems Engineering* approaches, and understanding of *Sustainable Materials Management* and *Sustainable Materials Manufacturing.*

Located close to both synthetic biology and material science infrastructures (e.g. North West, UK), the Hub would have a central facilitating role to deliver the *Materials from Biology* vision. The Hub would nurture and develop the Living Foundry by harnessing leading UK expertise across existing Synthetic Biology Research Centre's, the National Henry Royce Institute for Advanced Materials (itself a Hub and Spokes model), and the National Industrial Centre for Synthetic Biology (SynbiCITE), such that they can collectively support the merger/integration of the disciplines and share and develop technology platforms.

A Hub and Spokes *Living Foundry* model would harmonise national capabilities and resources to develop world-class science and technology for *Synthetic Biological Materials.* It would allow centralised coordination for skills development, resource utilisation, and operational efficiency and unify operational processes across the Spokes. By capitalising on secured national/international investments the model would also ensure a lower cost for technology implementation in establishing the *Materials from Biology* vision. The Hub and Spokes model provides the best opportunity of leveraging and networking existing resource so that the vision delivers bespoke *Advanced Materials* within the first 2-5 years of operation from design/discovery technology platforms (predominantly in the Hub) through to production, detailed evaluation, translation and application/device construction (predominantly in the Spokes), and ultimately to market (through early partnerships with stakeholder industries and Government departments). The UK is well positioned to deliver this vision.

Platform Capabilities for the Living Foundry Concept



A *Living Foundry* for *Synthetic Biological Materials* should place advanced technology platforms at the core of the Hub to accelerate delivery of new *Advanced Materials*. These platforms define the technology pipeline that facilitates both rapid diversification of existing materials and exploration of novel *Advanced Materials*. The vision is to construct materials from standardised components, and to build higher order structures where emergent properties will be discovered. Iterative synthetic biology cycles of Design, Build, Test and Learn (DBTL cycle) are at the core of the approach and interfaced with other technology platforms from other disciplines (e.g. *Click/Combinatorial Chemistry; Additive Manufacturing; Miniaturisation; Automation*) that enable modular and hierarchical assembly of new materials. The Hub would work in partnership with the expertise and technical capabilities in the Spokes and wider community towards the development of standards and metrology for registries of standardised materials parts, and work on big data and statistics to build understanding of performance, including the creation and maintenance of shared databases for standards. These should be developed through partnership with other UK/overseas stakeholders that have expertise in these areas, for instance the *Department of Defense Science & Technology Enterprise* (USA) and *National Institute of Standards and Technology* (UK).

In short, the Hub would need to be committed to gather information and to *learn and work with other communities* to ensure delivery of *Synthetic Biological Materials* and their hierarchical integration into new *Advanced Materials*.

Suggested Operational ACTIONS to Deliver Early Science and Technology Developments

Formalise the *Living Foundry* concept for *Synthetic Biological Materials* using the proposed Hub and Spokes model using assets *already available within the UK* and integrate new science and shared technology platforms, not available in the Spokes or other national centres, for synthetic biology, materials science or allied disciplines.

1. Operationalise the *Living Foundry* concept through funded cross-cutting research programmes as a framework for early delivery of basic discovery science to support rapid translation of new and emergent *Advanced Materials*.
2. Ensure accelerated delivery of new materials by providing a high degree of automation across the pipeline and embedding machine learning across the DBTL cycle.
3. Establish a repository of new parts, devices and systems for *Synthetic Biological Materials* and implement a *Data Management* infrastructure and *Standardisation Framework* for this repository.
4. Establish routes to rapid translation and sustainable manufacture of new materials as part of the *Living Foundry* concept to ensure new materials discovery can support identified unmet needs through industry-academic-government co-development programmes that can be brought to market quickly.
5. Embed a programme of continual innovation in the *Living Foundry* to capture new capabilities in line with the stated objectives of the foundry (i.e. rapid delivery and predictable design, fabrication and sustainable production of new *Advanced Materials*).

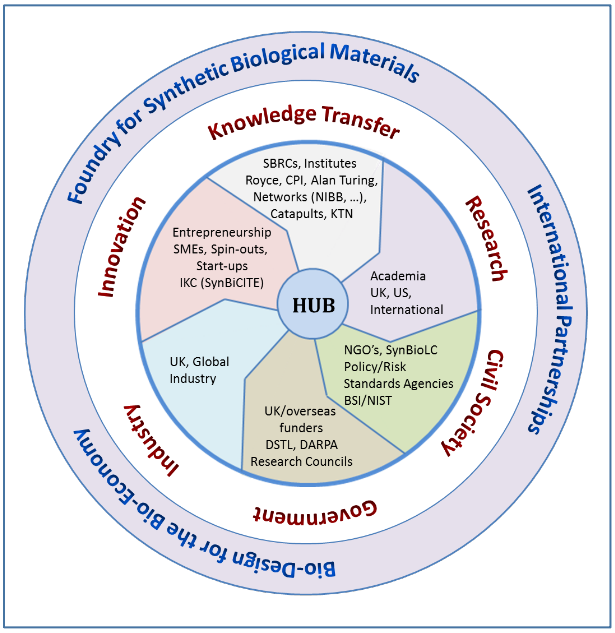
Delivery Timeframes for Suggested Operational Actions

- Formalise Hub and Spokes; merging and coordination of capabilities from UK assets; operationalise technology innovation programmes and early science programmes; drive new bi-lateral (US/UK) international projects that capitalise on the *Living Foundry* concept (Y1)
- Phase 1 of components repository established from external and internal programmes (Y2)
- Phase 1 co-development projects initiated (Y1) and completed (Y2)
- Review outcome of Phase 1 developments and ideas workshop to drive Phase 2 bi-lateral (US/UK) projects. To be repeated periodically to grow new *Advanced Materials* programmes
- Technology development for higher scale materials fabrication initiated (Y1), completed (Y3), again building unique US/UK partnerships
- Early sustainable production platforms for first generation materials components initiated (Y1), completed (Y3)
- Additional (Phase 2) co-development projects; expansion of repository with new component parts; further technology development for *Living Foundry*/fabrication (Y3-5)

A Connected People Resource for I-Con^3

The *Living Foundry*, with its organisational heart in the Hub, would act as the nerve Centre for wider coordination and engagement across the Spokes and external partners. The identification and recognition of interdisciplinary expertise and capabilities at Spoke institutions will be an important early coordination goal. The Hub would require strong *strategic leadership* across academic, industrial, commercial and creative sectors to drive the *Materials from Biology* agenda. Strong partnerships with industry and government agencies would need to be generated, maintained and developed requiring commercial, as well as scientific and technical leadership, and supporting activities leveraged (where possible) from industry and Spoke partners. Strategic leadership for these activities would require a Hub Commercial Director to work alongside the Hub Academic Director and a Director of Operations. Knowledge and support from Hub technology experts would be needed to innovate and drive the operation of the *Discovery – Innovation Pipeline* technologies and to coordinate scientific teams associated with research programmes that exploit core facilities of the Hub.

The I-Con^3 principle would act as a nucleating point for scientific dialogue and exchange of ideas, strategic intelligence and development of new programmes and collaboration through implementation and joint working. This would provide a connected and collaborative community with expert capabilities and understanding of the broad scientific landscape to connect interdisciplinary expertise and infrastructures. There would be a pressing need to develop strong connections to existing complementary centres such that the Foundry would provide a bond that links and synergises capabilities. These would be regional and national academic centres of excellence (e.g. Manchester Institute of Biotechnology, Henry Royce Institute, International Centre for Advanced Materials, Materials Innovation Factory, Materials and Engineering Research Institute Manchester, Imperial College, Cardiff, Newcastle, Birmingham), national Synthetic Biology Research Centres and the Synthetic Biology Leadership Council, other national research institutes (e.g. Chemical Process Institute, Biologics Manufacturing Centre Darlington) and Networks (e.g. RCUK Networks in Industrial Biotechnology and Bioenergy; Institute of Materials Minerals and Mining). The Hub would also need to be connected internationally (e.g. National Science Foundation funded Materials Research Science and Engineering Centres, USA) to fully develop the vision.



The Hub would nucleate complementary activities (and avoid duplication) to generate a complete *Innovation Ecosystem* and would be an engine room for technology acceleration and commercial development. It would embed sector-specific commercial planning, business assessment, life cycle analysis, affordability analysis and related activities into its working practices, and leverage expertise through academic, commercial and other external partnerships relevant to its mission. This would provide early foresight of challenges that extend across the innovation pipeline from basic discovery science to manufacturing and commercialisation. The Hub's responsible accelerator platform would build strategic links and partnerships with existing community frameworks working across the TRLs including: Innovate UK and Knowledge Transfer Networks; Catapults (e.g. 7 HVM Catapult Centres, particularly the Advanced Manufacturing Centre at Sheffield and National Composite Centre at Bristol) and Innovation Knowledge Centres (e.g. Cambridge Innovation Knowledge Centre, and the Leeds Medical Technologies Innovation and Knowledge Centre). It would engage a broad spectrum of industrial partners from SME's through to global conglomerates and foster a culture of entrepreneurship that nurtures/supports the establishment of spin-out and start-up companies relevant to the *Synthetic Biological Materials* sector. It would also work closely with regulatory bodies and testing/data standards agencies (e.g. British Standards Institute and National Institute of Standards and Technology).

As a *Living Foundry* portal, the Hub would also provide a channel for wider stakeholder engagement for governance frameworks and policy. This would include local and national institutes, non-government organisations (e.g. International Centre for Trade and Sustainable Development; Intrac for Civil Society; Overseas Development Institute), Government departments (e.g. BEIS), Military and

Defence organisations (e.g. DSTL, ONR/AFOSR/RDECOM, and DARPA), Venture Capitalists, UK/Overseas funding agencies and the general public.

The Hub would need to take a lead in *training* next generation scientists in all its activities supported by an I-Con^3 Centre for Doctoral Training in *Synthetic Biological Materials* that would drive *intersectorial*, *interdisciplinary* and *international* training and research programmes. This would ensure sustained growth of a capable workforce in the *Materials from Biology* sector to underpin future development of the science base and growth in the *Advanced Materials* economy. Through its national and international networks and close working with related Centres for Doctoral Training, training will cover the whole innovation pipeline and would also benefit from access to specialist entrepreneurship training activities (e.g. SynbiCITE Lean Launch Pad, iGEM and Biotech YES).

The Hub would provide a catalyst for generating new ideas and coordinate/drive their implementation. This would be achieved, for example, through 'ideas workshops' to consider unmet *Advanced Materials* needs, working with stakeholders to innovate and showcase capabilities from discovery science through to market delivery. The Hub would therefore conceptualise, capture and maximise the capabilities of the innovation pipeline in *Synthetic Biological Materials*.

Suggested Strategic ACTIONS Forging New Partnerships:

1. Build value for national and international partnerships by ensuring a broad spectrum of understanding across different scientific and business communities and foster communication, partnerships and collaborations for synergistic co-development of novel approaches and technologies.
2. Build an expert workforce through skills training and skills development required for inter-disciplinary challenges associated with delivering the *Materials from Biology* paradigm.
3. Create a national and internationalised, *Living Foundry* Hub and Spokes infrastructure that facilitates academic, industrial and government co-development of programmes to ensure early appreciation of unmet needs, commercial challenges and implementation of frontier science and technology to deliver these needs.
4. Develop a supportive business environment for the sector specific challenges of *Synthetic Biological Materials* by alignment of existing responsible research and innovation, and policy and regulatory developments with sector specific commercial activities in the Hub.
5. Develop and implement an inclusive strategy to achieve I-Con^3 for the *Synthetic Biological Materials* sector and ensure this meets the mutual needs and capabilities of the sector, generating value for both the UK and globally.
6. Stimulate inward investment in the *Materials from Biology* sector from the above actions and review periodically to ensure barriers are removed so as to maximise the capability of the innovation pipeline.

6. Conclusions

The UK is a world leader in the fields of synthetic biology and advanced materials and it has made unprecedented investments in these separate fields in recent years. Unification of these fields will create major opportunities for new materials discovery, their sustainable and affordable manufacture and application to unmet needs for industry. The timing is now right to harness national and international capabilities in the foundational sciences and industries through coordination and new investment to underpin sector challenges that will accelerate the translation of new *Advanced Materials*. This will contribute to major growth in the UK and global economies and address major societal concerns in global *Grand Challenge* areas. The UK is uniquely positioned to capitalise on these developments and to take a global lead.

Acknowledgements: The authors are grateful to all colleagues who contributed to the discussions at the Manchester workshop in 2017 whose views were used to inform this Roadmap for *Synthetic Biological Materials*. The authors also acknowledge funders of the workshop including Office of Naval Research Global (ONRG), Defence and Science Technology Laboratory (DSTL) and the University of Manchester's Centre for Synthetic Biology (SYNBIOCHEM grant BB/M017702/1).

This report formed the basis for a review which has now been published: Le Feuvre, R & Scrutton, N (2018) A Living Foundry for Synthetic Biological Materials: *A Synthetic Biology Roadmap to New Advanced Materials.* Synthetic and Systems Biotechnology. 3, 105-112.