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A living foundry for Synthetic Biological Materials: A synthetic biology roadmap to new advanced materials

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A B S T R A C T

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. This article, which developed from an international workshop held in Manchester, United Kingdom, in 2017 [1], sets out to identify opportunities in the new materials from biology era. It considers requirements, early understanding and foresight of the challenges faced in delivering a *Discovery to Manufacturing Pipeline* for synthetic biological materials using synthetic biology approaches. 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 and the leveraging of existing investments in synthetic biology and advanced materials research to achieve this goal.

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1. 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 [2–4]. This opens up possible 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 meso-structures (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) [5]. 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 – defined as *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. Realising this opportunity would also provide access to affordable and sustainable routes to the production of synthetic biological materials. This would be an ambitious, high-risk and high-gain proposition, dependent on the emerging science of synthetic biology, but one that would deliver a new landscape for advanced materials and in a way that is fundamentally different to more traditional materials discovery and fabrication platforms. Through the engineering of biology, the synthetic biological materials paradigm would give access to i) rapid expansion of materials diversity, ii) hierarchical assembly of new multi-component, multi-functional materials (e.g. by uniting synthetic biology and materials fabrication platforms including additive manufacturing, spinning, coating technologies), iii) affordable and/or sustainable routes to production (e.g. fermentation on waste feedstocks) and iv) lessened environmental impact in next generation materials manufacture. This defines a large landscape for synthetic biological materials through the 'writing of DNA', and assembly of these biological 'parts' with other (e.g. non-biological) components. Synthetic biological materials will therefore span soft and hard materials, composites and other more complex multi-component and multi-functional structures.

2. 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 and functionalities, 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 [1] 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