Next steps for European synthetic biology: a strategic vision from ERASynBio
This Strategic Vision is published as a joint effort between the partners of the European Research Area Network for the development and coordination of synthetic biology in Europe (ERASynBio).

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For more information please visit: www.erasynbio.eu
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While modern molecular biology was born from the happy encounter of physics with life sciences that took place after WWII, contemporary synthetic biology stems from a similarly joyful marriage of biology with engineering – and vice versa – which explicitly or implicitly started with the new millennium on both sides of the Atlantic Ocean. Note that the use of the term engineering in biology is not new; since the onset of recombinant DNA technology of the late 1970s it has been applied to the action of rationally cutting and pasting DNA sequences. The entirely new angle of synthetic biology is that engineering stops being a metaphor to become a veritable methodology, both conceptual and material, for designing biological systems and objects with enhanced or altogether new-to-nature properties. The central dogma of molecular biology was that DNA makes RNA and RNA makes proteins.

Now, the tenet of synthetic biology is that parts make devices and devices make systems. Inconspicuous as this may sound at a superficial level, synthetic biology in fact brings about a fresh way of looking at living systems, not as complex objects to be thoroughly understood, but as sources of amazing building blocks that can be retrieved from their natural context, reshaped, standardized to fit a given specification and used for a purpose different from their original raison d'être. The transformative potential of this simple principle is extraordinary, perhaps only comparable to the development of the steam engine in the 18th century. If this invention marked the start of domesticating physical energy for humanity’s benefit that began our modern era, synthetic biology will enable a new type of industry – and ultimately a society where biological agents and materials (from fuels and environmental catalysts to intelligent fabrics and smart therapeutic agents) will take over many of the roles that are currently assigned to far more primitive and inefficient counterparts.

Synthetic biology has grown along not only with the rampant globalisation of the world economy, the omnipresence of the internet and the growing importance of social networks, but also with concerns about our planet’s sustainability, the public demand of higher ethical standards in the economic sector and the rising awareness of gender issues. This Zeitgeist demands new disruptive science and technology that allow our societies to enjoy a degree of prosperity while pursuing a fair share of the available natural resources. While synthetic biology can definitely contribute to this, we need to revisit many of the existing frames that impede the unleashing its full innovative power. One serious hurdle is the customary fragmentation of efforts in different European countries, which has to be overcome.

We must also challenge the over-emphasis – if not straight paranoia – of the Biotech sector regarding intellectual property issues. Sharing materials and knowledge is ultimately much more beneficial than not, and the young synthetic biology community has taken such sharing as one of its trademarks. Most current legal structures that deal with patents and other protection of knowledge come from the 19th century and have become a veritable burden to innovation and creativity in our time. This needs to change. A different issue is the social perception of gene technology, so badly damaged by the GMO controversy of the 1990s. In contrast to the mutual disrespect that marked this debate when it peaked in Europe 20 years ago, the present-day
synthetic biology community values social engagement as a clear benefit both for easing acceptance and for raising new scientific challenges. Finally, synthetic biology celebrates and encourages human and gender diversity as a pillar of imagination and inventiveness, thereby making a connection with other disciplines such as the arts, the social sciences and the humanities.

The report below constitutes a remarkable document that pinpoints and thoroughly substantiates what is to be done here and now for positioning Europe in a leadership role within the global synthetic biology landscape. The emphasis that permeates this exercise is exactly what this preface is about: transnational coordination, building capacities, sharing resources and facilities, networking (including brain-pooling!) and giving a free rein to creativity, all to the service of a better, more prosperous and sustainable society. The historical ambition of Europe is to become a peaceful, knowledge-based civilization, one of the dreams of the Enlightenment. If this report can contribute to this undertaking, the whole mission of the ERASynBio ERA-NET will have been thoroughly achieved.
Synthetic biology is a key enabling technology with the potential to fundamentally change the approach, tools and techniques of modern biological research and innovation, to the benefit of the bioeconomy and society as a whole.

In this Strategic Vision, synthetic biology is defined as the engineering of biology: the deliberate (re)design and construction of novel biological and biologically based parts, devices and systems to perform new functions for useful purposes, that draws on principles elucidated from biology and engineering.

Beyond this definition, synthetic biology represents a new approach to biological engineering through the convergence of expertise in biology, engineering, chemistry, physics and computer science. Due in part to this truly interdisciplinary nature, synthetic biology has the potential to enhance a myriad of industrial sectors including industrial biotechnology and bioenergy, chemicals, medicine, agriculture and environmental remediation, and research and development tools.

The field of synthetic biology has been widely recognised for less than 10 years. Despite this novelty, it has demonstrated real potential to contribute to grand societal challenges including lifelong health and wellbeing, energy and food security, and adaption to environmental change. Europe stands ideally placed to take advantage of the synthetic biology revolution, with world-class academic institutions and an innovative biotechnology industry; however the long-term potential of this field can only be realised through strategic international co-operation. In contrast to well-established life science or engineering disciplines, with long-standing and integrated national programmes, synthetic biology is at an early stage of development. This presents a remarkable opportunity to form a coherent and coordinated European and global policy framework, thus avoiding fragmentation and encouraging the sustainable and responsible development of the field.

To capitalise on these opportunities, a consortium of research funding and policy organisations have come together through the European Commission funded European Research Area Network in Synthetic Biology (ERASynBio). The ERASynBio project has 16 partners from 14 European Countries, with observers in Europe and the US. Together they have been working to enhance European and global synthetic biology by structuring and coordinating national efforts and investment, jointly striving to address a broad range of synthetic biology needs including: scientific, technical and societal research challenges; community building across the European Research Area; training and education; data and infrastructure; future industrial needs; and public engagement.

One of ERASynBio's primary objectives is to map existing activities in synthetic biology and, through consultation with leading researchers and other stakeholders, develop a strategic agenda to guide the emergence of the field within Europe. The ERASynBio Strategic Vision represents the culmination of these strategic activities, setting out an ambitious vision for the future of European synthetic biology and highlighting major opportunities and challenges over the next five to ten years. This vision is accompanied by a series of targeted recommendations designed to empower national and international funding organisations, policy bodies and other stakeholders. This strategic framework aims to support the development of this important research field and the enable the realisation of the economic and societal benefits of synthetic biology.
Summary of the vision and recommendations

Through its strategic activities, ERASynBio has developed a vision for synthetic biology where:

**World-leading and innovative European synthetic biology research will drive significant economic impact and address grand societal challenges**

through: networked, multidisciplinary and agile centres of excellence; a skilled, creative and interconnected workforce; cutting-edge and open underpinning technology; and a responsible and inclusive policy framework.

To achieve this future for synthetic biology, ERASynBio has developed a series of specific, measurable, attainable and timely policy recommendations drawn from the five major themes of the vision. The recommendations are broken down further in the ‘Realising the vision’ section on page 24, with each sub-recommendation apportioned to the stakeholders that will be the primary agents in its implementation.

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### Summary of recommendations

#### 1. Invest in innovative, transnational and networked synthetic biology research

Significant funding will be required to achieve the projected revolution in biological and biologically based technologies offered by synthetic biology. Increased spending through open peer-reviewed competition will be essential to maintain the cutting-edge nature of this discipline, but there is also a need for coordinated top-down actions to address European and global challenges within the field.

#### 2. Develop and implement synthetic biology in a responsible and inclusive manner

The ultimate success of synthetic biology will depend not only on the technological successes of natural scientists and engineers, but on the ability of the applied and industrial community to develop products and services that are needed by, and acceptable to, the public and other stakeholders. Achieving this will require a coordinated effort by members of the scientific, industrial and policy-making communities.

#### 3. Build a networked, multidisciplinary and transnational research and policy making community

Synthetic biology, perhaps more than any other related field, requires the interactions of researchers and policy makers from multiple locations and scientific backgrounds. Synthetic biology funders are currently in an exceptional position to bridge disciplinary and geographical barriers, and support a coherent European and global community.

#### 4. Support the future of synthetic biology by providing a skilled, creative and interconnected workforce

High-quality training at all levels will boost the absorptive capacity of the sector and increase the competitiveness of European and global synthetic biology. At the same time, creative educational approaches provide the opportunity to inspire the next generation of synthetic biologists.

#### 5. Utilise open, cutting-edge data and underpinning technologies

For institutions that conduct synthetic biology research, access to novel data sets and the newest technologies will be essential to maintain and increase their competitiveness. Funding organisations and other stakeholders should do more to encourage effective use of data and new technologies and should also support the community in the development of the next generation of synthetic biology infrastructure.
An introduction to synthetic biology and its opportunities

Synthetic biology is the engineering of biology, the deliberate design and construction of novel biological parts, devices and systems to perform new functions. Synthetic biology offers the ability to engineer biological systems in a modular, reliable and predictable way, allowing biological units to be shared and reused in different contexts. This new approach promises to reduce the time, cost and complexity of developing biological systems and products, opening up new opportunities for a range of industrial sectors including industrial biotechnology and medicine, and thereby promoting economic growth and job creation.

Definition, scope and applications of synthetic biology

Synthetic biology is an innately multidisciplinary approach, bringing together expertise from biology, engineering, chemistry, physics and computer science. As with any rapidly evolving field, many different definitions of synthetic biology have been proposed and are in common use. The ERASynBio definition is drawn from recent reports developed by high-level scientific bodies including the European Academies Science Advisory Council1 and UK Royal Academy of Engineering2, as well as through consultation with leading European experts. Based on this, ERASynBio defines synthetic biology thus:

Several aspects of this definition can be elaborated upon to further demonstrate the scope and opportunities of this technology. The use of a `deliberate` approach allows synthetic biology practitioners to utilise rational design to develop highly complex and controllable biosystems as well as novel proteins and nucleotides with complexity beyond that which could be achieved through existing techniques. In addition, `engineering principles` such as modularity, abstraction and orthogonality simplify the design and build process; they allow engineered systems to work effectively within host chassis, including those with fully synthesised genomes, or simple protocell systems. While the ultimate goal of synthetic biology research does not have to be commercial output, the development of `new functions for useful purposes` is an important part of the synthetic biology approach, which sets it apart from other, more descriptive, biological research fields.

Synthetic biology for biomaterials

In one example of synthetic biology, Professor Dek Woolfson and his team at the University of Bristol are working on a toolkit of novel peptides and proteins for use as building blocks to assemble biomaterials and biological machines. They are producing modular parts so that biological structures can be designed and built from characterised catalogues rather than being crafted from scratch each time.

One application of this approach is a synthetic version of the extracellular matrix, which could be used in regenerative medicine to help generate tissues like skin, nerves or bone in vitro. Another application is the assembly of hollow spheres capable of carrying drugs or acting as novel vaccines.

1 Realising European potential in synthetic biology: scientific opportunities and good governance: http://www.easac.eu/fileadmin/PDF_s/reports_statements/Synthetic%20Biology%20report.pdf
A useful analogy for synthetic biology is that of the industrial revolution of the 19th century, where manufacturing transitioned from bespoke artisan approaches to affordable mass production. A number of factors converged to enable this shift, including a greater fundamental understanding of trade materials, the development of widely available standardised parts and the use of new machine tools.

A similar confluence of factors can be seen in the development of synthetic biology. Molecular biology – and newer fields like systems biology – began to unravel the enormous innate complexity of biological systems and offer clues about the effects of perturbation of these systems. At the same time, new tools and technologies including DNA sequencing and synthesis, biological modelling and the use of high-throughput robotic workflows have exponentially increased opportunities for the rational design of new biological parts, devices and systems, and enabled the development of biological standards. Over the last 10 years, innovative groups of scientists and engineers have embraced these new opportunities, producing the first biological logic gates and introducing orthogonal coding systems for novel amino acids. As the technology develops, it will continue to make biology easier to engineer, democratizing biotechnology and opening up the potential for new creative products and decentralized production models.

Figure 1 shows how the synthetic biology approach is supported by previous advances in a range of underpinning tools and technologies. It also shows the overlapping nature of the largest six disciplines that have, to varying degrees, applied the synthetic biology approach.
Impacts of synthetic biology

The first products developed using synthetic biology are already being made available on the market. Along with well-publicised examples in biofuels and therapeutics, synthetic biology is providing commercial solutions to problems as varied as uric acid detection and cattle fertility. However, this only scratches the surface of what is possible using this approach. A study from BCC Research suggests the sector will grow to $10.8 billion by 2016, while a report from McKinsey & Company suggests that the impact of this disruptive technology could reach at least $100 billion by 2025, offering huge economic growth and job creation for countries that can support a significant synthetic biology industry. The cross-cutting nature of this technology (as shown in Figure 1) offers enormous and wide-ranging commercial opportunities. In the longer term, this foundational nature gives synthetic biology the ability to have major impacts on a range of grand societal challenges, with a small number of promising examples shown below:

The ERASynBio project

ERASynBio is a European Research Area Network (ERA-NET) funded by the European Commission through the Seventh Framework Program. The project has 16 participating funding organisations from 14 European countries and observers in Europe and the United States (US). Together these organisations have been working to enhance European and global synthetic biology by structuring and coordinating national efforts and investments, striving to address a broad range of synthetic biology needs including: scientific, technical and social research challenges; community building across the European Research Area; training and education; data and infrastructure; future industrial needs; and public engagement.

The ERASynBio project started in January 2012 with a large-scale mapping exercise to provide an evidence base for its strategic activities and to benchmark European synthetic biology against the rest of the world. Alongside this activity, ERASynBio partners worked to address specific areas of need for the field. They explored the relevant ethical, legal, economic and societal considerations and synthesised them into recommendations on good governance, open dialogue and closer integration of social sciences. In parallel, they strengthened the scientific community and built critical mass by linking researchers, centres and technological platforms.

To address training and educational needs, ERASynBio partners mapped existing European training provision and interdisciplinary requirements, and ran the first of a set of advanced training summer schools focused on collaborative working and technological skills. Furthermore, they used an extensive survey to map the data and infrastructure requirements of the burgeoning European synthetic biology community, particularly the opportunities for enhanced management and sharing of synthetic biology data, and the needs of synthetic biology specific resources including biopart registries and host cell chassis.

As an important outlet for the transnational awareness and collaborations developed through this project, the ERASynBio programme brought together 12 funding organisations from Europe and the US, who provided €15 million of co-funding for the ERASynBio 1st Joint Call for transnational research projects: Building synthetic biology capacity through innovative transnational projects.

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<th>Societal challenge</th>
<th>Examples of synthetic biology impact</th>
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<td>Health and wellbeing</td>
<td>Synthetic biology could replenish the dwindling supply of novel antimicrobial agents available to clinicians. It enables the rational design of new antibiotics and the development of novel solutions such as engineered bacteriophages.</td>
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<tr>
<td>Energy &amp; climate action</td>
<td>Commercial scale bioethanol and biodiesel is already in production with use of organisms developed through synthetic biology. Greater efficiency and new engineered functions could lessen reliance on fossil fuels, while the use of CO₂ as a raw material for the chemical industry could further balance greenhouse gas emissions.</td>
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<tr>
<td>Food security</td>
<td>Development of photosynthetic biofuel-producing organisms could reduce competition between food and energy crops, while new crop varieties could increase nutrition and reduce losses to pests and environmental disasters.</td>
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<tr>
<td>Security</td>
<td>Synthetic biology has the potential to enable new biomaterials and biodetectors.</td>
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1 Biomedically relevant circuit-design strategies in mammalian synthetic biology: http://msb.embopress.org/content/9/1/691#sec-9
Synthetic biology in Europe

European synthetic biology is the product of a long history of scientific excellence, with pioneering research in molecular biology, sequencing and systems biology underpinning much of modern biotechnology. Today, Europe is home to some of the world’s foremost synthetic biology research, with expertise across the full spectrum of the field. Examples include the pioneering work at the D-BSSE in Basel, Switzerland, where a diverse synthetic network of combinatorial plug-and-play logic gates has been developed in mammalian cells. These genetic devices open the way to the assembly of tissue-like biocomputers for the design of complex human-machine interfaces, as well as diagnostic and new gene and cell-based therapeutic strategies. In an example of bionanotechnology, researchers in Ljubljana, Slovenia developed self-assembling tetrahedron polypeptide complexes. This provides a design platform for the construction of new polypeptide folds. These structures could be used for a range of applications, including the specific design of protein cavities and the arrangement of amino acid side chains for applications such as drug delivery or artificial catalysis. Multinational collaborations have also yielded exciting results. A team from France, Belgium and Germany developed a strain of *E. coli* with 98% of the thymidine bases in its genomic DNA replaced by the artificial chlorouracil base. This work provides proof of principle for the use of xeno nucleic acids in viable cells, and offers potential for a highly effective safety mechanism where synthetic organisms are totally dependent on laboratory-supplied nutrients.

This research is supported by a wealth of expertise in underpinning technologies. The multi-state funded European Molecular Biology Laboratory has the fourth highest citation impact in molecular biology and genetics in the world, and the highest impact outside the US. As part of this centre, the European Bioinformatics Institute provides the world’s most comprehensive range of freely available molecular databases. This institute is a pivotal partner in ELIXIR, a project which has seen a commitment of over €340 million for the next generation of European infrastructure, tools and training for biological data.

Europe has also enjoyed considerable success in international synthetic biology events such as the student International Genetically Engineered Machine (iGEM) competition, with European teams taking 1st, 2nd and 3rd place at the world championship finals in 2012 and 2013. Furthermore, Europe played host to the world’s largest synthetic biology meeting – the SBx series – in 2007 and 2013.

National and transnational public funding

ERASynBio completed the first stage of its comprehensive mapping activities in December 2012, gathering detailed information on: relevant funding organisations, national and transnational funding programmes, funded synthetic biology projects, relevant strategies and reports, policy contact points and active companies. These data provide an important evidence base for this Strategic Vision and for future strategic planning in synthetic biology.

These mapping exercises captured just over €310 million of public research funding allocated for synthetic biology since 2004. Funding in 2013, and from non-ERASynBio countries in Europe, places the likely total European investment at around €450 million – a significant figure for any emerging scientific discipline and a reflection on the growing recognition of synthetic biology across Europe.

A number of interesting patterns emerged from the mapping data; as shown in Figure 2, funding is unevenly distributed within Europe, with higher investment in the UK, Switzerland and Denmark leading to the development of world-leading synthetic biology centres. Secondly, the data revealed the relative importance of national and transnational support mechanisms. A total of €106 million was awarded through transnational mechanisms including the European Commission Framework Programme, ERA-NETs and bilateral initiatives. The Seventh Framework Programme provided €86 million and while the European Research Council and Knowledge-Based Bio-Economy theme were the greatest contributors, the cross-cutting nature of synthetic biology allowed researchers to gain additional support from themes on Information and Communication Technology, energy, nanoscience and socio-economic sciences. The remaining synthetic

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* The International Genetically Engineered Machine (iGEM): http://igem.org/Main_Page
biology funding was invested on a national basis, underlining the clear need to align national strategies with one another and with the broader transnational landscape.

Finally, the data underlined the diverse range of activities within the European synthetic biology portfolio, with all six of the disciplines from Figure 1 supported. In particular it highlighted strengths in metabolic engineering, which accounts for 30% of funded projects – double that of the next most popular approaches (regulatory circuits and bionanoscience). Minimal genomes and protocell approaches were used in a comparatively small proportion of the portfolio, but there are significant numbers of projects focused on other areas of the field including biosafety, ethics and intellectual property, emphasising the broad and vibrant science base that Europe has to build upon.

Strategy and policy activities

Synthetic biology has been the subject of a range of strategy and policy activities in Europe. It was identified as a priority area for the European Commission in 2005 through the ‘New and Emerging Science and Technology Pathfinder’ initiative. As part of this programme the Symbiology, Symbiosafe and Emergence projects were launched to investigate funding, ethics, safety, security, education, infrastructure and standards, and the Toward a European Strategy of Synthetic Biology (TESSY) project produced a roadmap of measures and milestones for successful European synthetic biology. Since then, transnational European synthetic biology reports have been published by the European Academies Science Advisory Council and the European Group on Ethics in Science and New Technologies. Several national stakeholders have conducted their own strategic activities, with a small number producing official reports and strategies. In the UK, the Biotechnology and Biological Sciences Research Council, Engineering and Physical Sciences Research Council and Technology Strategy Board have been active in synthetic biology policy development since 2007. They have conducting a series of basic, applied and industrial research calls and led a large-scale public dialogue exercise. In July 2012 they published a synthetic biology roadmap to provide strategic direction for the development of a cutting-edge, economically vibrant and responsible UK synthetic biology industry, with oversight for the recommendations being managed by a Synthetic Biology Leadership Council (SBLC). The SBLC is jointly chaired by industry and government, with a membership that includes key stakeholders to ensure a responsive, well directed and informed implementation of the roadmap.

In France, the Parliamentary Evaluation of Scientific and Technological Office published a report in 2012 on the challenges of synthetic biology. This led to the establishment of the Observatory of Synthetic Biology to consider developments, opportunities and challenges, and to determine the appropriate conditions for a dialogue with society. Several other countries have also produced scientific reports, while others will utilise the strategic activities of the ERASynBio project as their primary strategic activity.

Commercial activities

Europe already hosts a large number of companies that could exploit synthetic biology approaches, including some of the world’s largest biotechnology, pharmaceutical, chemicals and research technology companies. The ERASynBio mapping activities captured 148 European companies engaged in synthetic biology research, ranging from small and medium enterprises and academic spin-offs to large multinationals. The distribution of these companies within Europe broadly matched the distribution of funding shown in Figure 2, with over 45 active companies in the UK and around 30 each in Switzerland and Austria. Figure 3 shows the primary area of R&D interest for these companies. The high uptake within the red and white biotechnology sectors demonstrates the significant opportunities for European industry to use synthetic biology to help address societal challenges, especially in energy security and lifelong health and wellbeing.

![European companies engaged in synthetic biology by sector](http://www.rcuk.ac.uk/publications/reports/syntheticbiologyroadmap/)

*Other companies include bioinformatics and service providers.
The global synthetic biology context

A recent study identified synthetic biology publications from 682 organisations in 40 countries\(^1\). The greatest publication output comes from the US, and while there is an equivalent output from Europe as a whole, the US continues to lead a significant proportion of high profile synthetic biology projects. This is due in part to the earlier adoption of synthetic biology approaches by US scientists and engineers, supported by proactive prioritisation and investment by national funding organisations and industry. In addition, coordination activities including the Synthetic Biology Engineering Research Centre (SynBERC) project have helped to link the community and develop strong synthetic biology centres.

There are several areas of complementary strengths between European and US synthetic biology, with significant demand from both sides to work together. A number of transatlantic coordination programmes have been developed including the Six Academies series (UK-US-China) and three UK-US calls for joint synthetic biology projects. At the transnational level, the EU-US Task Force on Biotechnology Research\(^{12}\) established a synthetic biology working group in 2010 to consider standardisation needs, ethical, legal and social issues, and the contribution of synthetic biology to the biotechnology industry. The ERASynBio 1st Joint Call provided a crucial mechanism to fund EU-US scientific collaborations. The second call in 2014 will further enhance transnational collaborations by both funding high quality joint projects and implementing some of the recommendations within this Strategic Vision.

In the longer term, there is a need for European synthetic biology stakeholders to engage with their counterparts in emerging economies, particularly China that has identified synthetic biology as a key priority area\(^4\). Replicating EU-US collaboration at a global scale will present a number of challenges, not least of which is the identification of areas of mutual benefit and the building of new working relationships. Despite these challenges, global co-operation by researchers, policy makers and industry will be essential for synthetic biology to fulfil its potential in an ever more interconnected scientific landscape.

Developing the ERASynBio Strategic Vision

This Strategic Vision represents the culmination of all the strategic activities of ERASynBio so far. It is informed by the European reports listed above as well as international reports and strategies such as Organisation for Economic Co-operation and Development (OECD) report on Future Prospects for Industrial Biotechnology\(^{14}\).

The themes discussed in these papers were further developed using the results of the comprehensive mapping activities, with a strong steer from the outcomes of the ERASynBio 1st Strategic Conference. This two-day meeting, held in January 2013 in Basel, brought together 85 leading experts from research, funding and policy organisations around Europe to debate the current synthetic biology landscape and future vision for the field. The meeting provided a qualitative assessment of the effectiveness of existing synthetic biology funding, governance activities, community building, training and education, and infrastructural support. Conference attendees produced short, medium and long-term landscapes for a number of important areas of the field, including important underpinning technologies, likely development areas for the basic science areas of synthetic biology and applied / industrial opportunities. They also identified and ranked the policy levers, underpinning technologies and future applications most likely to contribute to the development of the field (all available as an annex to this document).

These outputs were complemented by strategic papers – produced by a number of ERASynBio partners – on governance and dialogue, training and education, and data and infrastructure. A first draft of the paper was refined at a second strategic conference, where a small number of ERASynBio partners and leading experts agreed the final themes and recommendations for the Strategic Vision.

This final paper sets out an ambitious vision for the future of European synthetic biology, accompanied by a series of targeted recommendations to empower national and international funding organisations, policy bodies and other stakeholders. As an important first step towards the vision, the Strategic Vision will inform the development of the ERASynBio 2nd Joint Call for transnational research projects. The call will build on the existing European strengths in synthetic biology, while also addressing gaps and opportunities identified in the mapping exercise. It will break down international barriers to synthetic biology research, maintaining and enhancing Europe’s position as a world-class environment for this emerging research field. In the longer term, the vision will inform national and trans-national policy development and guide investments in synthetic biology.

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\(^2\) Science & Technology in China: A Roadmap to 2050: Strategic General Report of the Chinese Academy of Sciences

\(^3\) EU-US Task Force on Biotechnology: http://ec.europa.eu/research/biotechnology/eu-us-task-force/index_en.cfm

\(^4\) Future Prospects for Industrial Biotechnology
The ERASynBio vision for European synthetic biology

ERASynBio and its partner organisations envision a pivotal role for synthetic biology in the future of the European bioeconomy, as well as a vital role in addressing societal grand challenges. However, it is important to recognise that the European and global synthetic biology landscape is rapidly changing and, as such, it would be unfeasible and unproductive to attempt to develop a detailed long-term vision for the field. This Strategic Vision attempts therefore to set out the broad themes that will contribute to a vibrant research environment over the coming five to ten years, after which time further reviews will be required to determine any changes to the trajectory and opportunities for the field.

As previously stated, synthetic biology has the potential to fundamentally change the approach, tools and techniques of modern biologically based technologies. Based on ERASynBio’s strategic activities, the greatest economic impacts are envisioned in:

- Industrial biotechnology and bioenergy
- Medicine
- Ecology and agriculture
- Materials science

In turn, the greatest societal impacts are expected on:

- Lifelong health and wellbeing: meeting the challenges of the ageing population in Europe and the widening gap between lifespan and wellbeing.
- Energy security, living with and avoiding environmental change: ensuring access to affordable and sustainable energy for a growing population, while mitigating the effects of climate change.
- Global food security: providing the world’s growing population with a sustainable and secure supply of nutritious food from less land and using fewer inputs.

During the development of this vision, five thematic areas were consistently identified as key to the development of a European synthetic biology research base capable of delivering on these opportunities:

- **Theme 1**: World-leading and innovative synthetic biology research
- **Theme 2**: Responsible research and innovation
- **Theme 3**: A networked, multidisciplinary and transnational community
- **Theme 4**: A skilled, creative and interconnected workforce
- **Theme 5**: Cutting-edge open data and technology

Based on these opportunities and themes, ERASynBio has developed a vision for synthetic biology where:

World-leading and innovative European synthetic biology research will drive significant economic impact and address grand societal challenges through: networked, multidisciplinary and agile centres of excellence; a skilled, creative and interconnected workforce; cutting-edge and open underpinning technology; and a responsible and inclusive policy framework.

The move from the current position in synthetic biology towards the vision will require the concerted effort of a number of actors including synthetic biology researchers, national funding organisations, the European Commission, ERASynBio and other international coordination bodies, and the public and other stakeholders.

The following sections investigate in more depth the needs and opportunities of each of the themes. Each section informs a series of specific, measurable, attainable and timely policy recommendations designed to enhance the value of current and future investments and enable synthetic biology to fulfil its full potential.
Next Steps for European Synthetic Biology: a strategic vision from ERASynBio

Theme 1: World-leading and innovative synthetic biology research

Synthetic biology is projected to enable extraordinary economic growth and job creation by revitalising existing industries and fueling innovative new sectors. These projections derive from the understanding that disruptive synthetic biology technologies offer solutions for a number of grand societal challenges. However, with these opportunities come significant technological challenges. This means that in globally competitive markets, only those regions that are prepared to offer concerted and strategic investments stand a chance of realising the full economic and societal benefits.

Within Europe, national funding organisations have provided the bulk of financial support for synthetic biology; however this national funding varies considerably between states. Some countries have proactively invested large sums of money in the field with the clear goal of developing a synthetic biology community. In other countries, well-resourced experts, funded through general basic science or biotechnology calls, have adopted some or all of the approaches of synthetic biology in a bottom-up manner. In yet another group of countries, there has been little top-down support or bottom-up adoption of the technology.

In addition to this internal fragmentation, there is a clear disparity in synthetic biology prioritisation between Europe and other world leaders in the field. The US continues to provide significantly more support to synthetic biology, building on their existing position as world leaders in the field. In addition, emerging economies – especially China – have made synthetic biology a clear funding and policy priority.

Broad support for basic synthetic biology research

For future European synthetic biology to be world-leading, and for Europe to capitalise on the opportunities presented by synthetic biology, enhanced national and transnational funding will be imperative. A range of scientific and applied areas were identified as important in the ERASynBio mapping activities, including opportunities to enhance photosynthesis and produce new biomaterials, high value compounds and antimicrobials. However, to ensure innovation and creativity, the overall recommendation was that investments should be directed, not towards specific topics, but into sustainable support for broad foundational topics and approaches through bottom-up and open peer-reviewed calls.

It is therefore important that, while synthetic biology emerges, additional funding is effectively channelled into research that demonstrably exploits synthetic biology approaches. This clear delineation of synthetic biology will embed the technology and build a clearer identity for the community (described further in Theme 3), and accelerate the uptake of community resources and new infrastructure (Theme 5). As the sector becomes established, tangible opportunities will be clarified and funders will be able to assess whether support should be preferentially channelled towards specific societal and / or industrial challenges.

For national funding bodies, this Strategic Vision provides recommendations to guide synthetic biology funding policy, and offers clear exemplars from Europe and the US. Future transnational support for synthetic biology should come both from national funding bodies, through Europe-wide activities such as ERASynBio, and through other instruments of the European Commission. In addition, funders should look beyond Europe, to engage with other world-leading countries in a collaborative rather than competitive manner.

The start of the €70 billion Horizon 2020 programme represents a pivotal moment for transnational synthetic biology funding. Bottom-up actions such as the European Research Council are likely to continue to support innovative synthetic biology research, but the European Commission could go much further, acting as a major driving force for European and global synthetic biology through its top-down calls. This kind of prioritisation by the European Commission will require national policy makers and researchers to make a coordinated case for the potential benefits of synthetic biology, especially the opportunities for industry and the bioeconomy.

Developing multidisciplinary networks of synthetic biology excellence

The added value of conducting synthetic biology research within linked multidisciplinary environments has been highlighted during several of ERASynBio’s strategic activities. Synthetic biology in the US is heavily concentrated within a small number of well-funded institutes (predominantly in Boston and California). The critical mass of researchers and their links through the
SynBERC project has shaped global synthetic biology research, providing a focus point for researchers and attracting some 20 industrial partners.

Much of the most successful European synthetic biology has also benefited from a critical mass of researchers working as part of focused programmes. As an example, investments by the UK Research Councils at Imperial College London have supported the growth of the Centre for Synthetic Biology and Innovation (CSynBI). Large-scale grants to CSynBI and its network of collaborators are supporting the development of platform technologies and an Innovation and Knowledge Centre (SynbiCITE), which is specifically designed for the industrial translation of research. This provides a pipeline from basic science to industry, which is only possible within an integrated mission-focused environment.

It is notable however, that the majority of European synthetic biology research is not conducted within linked programmes of this kind. There is a clear opportunity therefore to enhance the field in Europe by promoting the development of a series of linked multidisciplinary networks of synthetic biology excellence. Along with the potential research benefits, these networks would perform a number of other services critical to the development of the field. Cohesive networks would promote multidisciplinarity by providing a greater opportunity for the mixing of scientists and engineers, both within the networks and in other European and non-European institutions. Through effective branding they would increase visibility, acting as a hub for industry and promoting synthetic biology to a wider audience. The larger number of experts present in a synthetic biology network would provide greater opportunities for training and education at all levels of the academic career ladder. Importantly they would also promote the shared use of large-scale technologies and promote the uptake of data and measurement standards within the field.

These kinds of networks have already proved feasible and effective on a national level. The German Virtual Liver Network has created a strong foundation for multiscale modelling within the German systems biology research community. Over the coming years, it aims to contribute to the creation of an infrastructure that adopts these approaches routinely as part of the establishment and eventual practice of systems medicine. In the UK, the Networks in Synthetic Biology have helped to build a group of mission-focused, but cohesive, multidisciplinary synthetic biology communities. Collaborations built through this programme have seeded excellent and sustainable research communities, some of which have gone on to develop into large-scale – and internationally competitive – physical research centres, funded through a €49 million call in 2013.

Accelerating the applied and industrial use of the technology

While synthetic biology is yet to reach mainstream commercial use, its truly disruptive potential makes a strong case for a coordinated portfolio of European actions to build an enabling research and development ecosystem. There are however a number of challenges to the commercialisation of the technology, many of which are not unique to synthetic biology. To attract greater investment from industry, synthetic biology needs to demonstrate an acceptable proximity to market and potential mechanisms of return on investment. However, many of the funding organisations that supported the emergence of the field are unable to direct resources toward research outside academic institutions, leaving a gap in support for precompetitive commercial research.

Bridging this funding gap will require dialogue between relevant funders and ultimately the development of joint calls such as those between the UK Research...
Councils and UK innovation agency (the Technology Strategy Board). At the European level, there are already a number of European Commission funded commercialisation mechanisms that could be utilised for synthetic biology, including Public Private Partnerships\(^9\), European Technology Platforms\(^20\) and the Knowledge and Innovation Communities\(^21\).

Beyond these types of interaction, there are a great number of national and international policy levers that can be used to encourage the commercialisation of emerging research fields. Many of these are beyond the scope of ERASynBio and its partner organisations. Therefore, considerable additional work – involving significant input from industrialists, regulators and public funders of commercial research – will be required before specific European recommendations in this area can be formulated. For the purpose of this Strategic Vision, the UK Synthetic Biology Roadmap, which was specifically designed to address these commercial needs – albeit at a national level – provides a useful frame of reference for the development of European actions in this area (details in the box to the right).

A recent ERASynBio workshop on intellectual property rights echoed these sentiments. The invited experts noted the need for novel intellectual property models, especially those that draw on the experiences of relevant established sectors, such as the pharmaceutical and telecommunications industries. The ultimate aim should be to facilitate sharing within the community without destroying the possibility for economic return on research effort.

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### Key areas from the ‘Developing technology for commercial use’ theme of the UK Synthetic Biology Roadmap

**Seeing the opportunity:** An opportunity exists to bring those at the cutting edge of science together with innovators in business to find the best fit between commercial opportunity and scientific potential, and to help them to work together to develop their ideas: to energise the new product supply chain, and to inform the science base.

**Creating the industrial translation process:** It is essential to develop processes whereby industrialists and academic researchers can more effectively collaborate to define application projects and requirements in terms of industrial techniques, market potential and societal benefits.

**Accelerating the journey to market:** Each organisation along the value chain has to evaluate the impact a new technology may have on its operations. One of the best ways to speed up this process is to create ‘demonstrators’ that show what is on offer in a compelling way. Helping innovating organisations to produce demonstrators of various kinds will advance the technology more quickly to market.

**Reducing the commercial and technical risk:** This can be done by bringing people from different organisations and with different capabilities together to work jointly on collaborative projects. These organisations can find better solutions to problems, and share the research and development costs, reducing the burden on any individual one of them.

**Building a community of practitioners:** When businesses cluster together they can collectively be more effective. A characteristic of synthetic biology is the need for multidisciplinary centres. Establishing a wide network of academic, industrial and other organisational interests will benefit from the presence of a backbone of potentially several multidisciplinary centres.

**Intellectual property:** At a fundamental level, the concept of ‘ownership’ of living organisms and components raises ethical and legal issues that are approached differently in different jurisdictions. At a technology level, there needs to be a balance between that which may reasonably be protected and that which would encourage greater enterprise through being made available as open source.

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\(^{9}\) A synthetic biology roadmap for the UK: http://www.rcuk.ac.uk/publications/reports/syntheticbiologyroadmap/
Theme 2: Responsible research and innovation

Synthetic biology combines the complexity of nature and living things with the principles of engineering. The combination has enormous potential and offers many exciting possibilities. At the same time, it is also breaking new ground and much is unknown. The field is likely to impact on all of our lives; society stands to benefit significantly if the promise of synthetic biology can be realised, but it will also shoulder the consequences if things go wrong. It is critical that synthetic biology is mindful of its context in society, continues to develop responsibly and that society has a significant role in guiding the application of the technology. This will allow the field to be responsive to societal needs and ensure that the impact of the technology. This will allow the field to be responsive to societal needs and ensure that the impact of the technology. This will allow the field to be responsive to societal needs and ensure that the impact of the technology.

This theme is built on a foundation of work in responsible research and innovation, which can be described as the process of “taking care of the future through collective stewardship of science and innovation in the present”22. Responsibility in synthetic biology has been reported upon by the European Group on Ethics in Science and New Technologies, the US Presidential Commission for the study of bioethical issues23 and the UK Synthetic Biology Roadmap Coordination Group. Other cross-cutting responsible research and innovation papers also influenced this theme. These include the Nuffield Council report on Bioethics Emerging Biotechnologies: technology, choice and the public good24 and documents associated with the international Open Government Partnership.

Applying the principles of good governance

The need for good governance in synthetic biology applies at all stages of the research process, from research funding – and the planning of research – through implementation, application and dissemination. It also involves people and organisations at all levels, from governments, funders and institutions to individual researchers. This is particularly important for synthetic biology, where the novelty of the field and uncertainties associated with that novelty demand foresight and early consideration of potential downstream impacts.

Considerable effort is directed toward defining the principles of good and open governance. Here, the three principles from the international Open Government Standards project25 are particularly useful in describing the need for governance to be transparent, participative and accountable. In the context of ERASynBio, this means that the process for research and research funding should be clearly articulated, and the research outcomes should be made available and accessible. A wide range of stakeholders, including individuals that represent the public interest, should be involved meaningfully in ERASynBio. The goal is to have ERASynBio and other subsequent projects become exemplars of good governance. Alongside this, the organisations and individuals funded through ERASynBio should be encouraged to think about the long-term implications of their work.

Integrating ethical and social questions

As mentioned above, good governance demands early consideration of the downstream impacts of synthetic biology, including the social and ethical aspects of the research and its outcomes. Apart from the sense that this is the ‘right thing to do’, it is also a chance to identify and maximise potential opportunities, and to identify and manage potential issues.

Social and ethical questions are often related to the purpose and motivation of doing research, and understanding the balance of the risks and benefits of an application. Also important is the exploration of the alternatives to a synthetic biology approach, and asking whether the outcomes will be for the ‘common good’. The UK’s Synthetic Biology Dialogue26 identified some useful questions that researchers and research funders could use as a starting point for considering these issues (see box overleaf).

Whilst it is important that scientists themselves reflect on what they are doing, and consider social and ethical questions, there is also an important role for the social sciences. Rather than mandating the participation of social scientists for all synthetic biology projects, funders should support the productive inclusion of social scientists whenever the research raises profound or novel ethical, legal or social considerations.

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22 Developing a framework for responsible innovation; Stilgoe et al, 2013
24 Emerging Biotechnologies: technology, choice and the public good
25 The Open Government Standards project
Broadening participation

Social scientists are not the only group who can make valuable contributions to synthetic biology. One of the principles of good governance is ‘participation’, as different groups of people bring different perspectives that can help researchers and research funders think about synthetic biology in new ways. Engaging with a wide range of people early and throughout the research process can help ensure that the research and its outcomes are in line with societal expectations. This includes ensuring that synthetic biology does not over-promise and that exciting novel applications are seen within the context of long-term research and innovation.

Funding organisations should support open and meaningful dialogue involving a range of actors including economists, policy makers, industry, media, users, non-governmental organisations, public groups and legal experts. This would be delivered most effectively through local mutual learning and engagement projects that link together to maintain a more continuous discussion. Critically for mutual learning, there must be a meaningful exchange of information and viewpoints, and scope for real impacts on future policy, research direction and regulation.

Developing balanced regulations

In Europe, synthetic biology is subject to both to the European Commission and national regulations for genetically modified organisms. These provisions provide sufficient safety and environmental protection for existing synthetic biology research, but do not effectively balance the risks and benefits of the field. The long-term potential of synthetic biology is such that it may eventually challenge this framework. More research will be required to determine both the potential risks to workers, consumers and the environment, and the scope for the responsible adoption of existing rigorous regulations on a sectoral basis, such as in healthcare. A potentially challenging area for the regulation of synthetic biology is the DIYbio movement, where practitioners conduct biological research outside of normal research environments. Similar movements in other fields, such as IT, played very significant roles in economic development, education, and democratization of the technology. Synthetic biology could greatly benefit from this approach. Nevertheless, communication with schools and clubs will be required in order to spread understanding of relevant regulations, and reduce the risk of malicious use.

Any changes to regulation should be designed in a manner which effectively addresses long-term impact and sustainability. They need to provide safety and security without stifling economic development through over-regulation. Furthermore, they must balance intellectual property protection with the need for open and accessible data use. To achieve these balances will require thorough and inclusive dialogue and mutual learning. Research funding and policy organisations should remain engaged in these activities to support the needs of the synthetic biology community and to communicate regulatory impacts to researchers.

The UK Synthetic Biology Dialogue

In 2010, the UK Research Councils, with support from the UK Government’s Sciencewise-ERC, published findings from a public dialogue around synthetic biology.

The dialogue sought to explore participants’ hopes and concerns in relation to synthetic biology in order to inform funders work in the field. Stakeholder interviews from 41 organisations fed into a series of workshops held with a total of 160 members of the public in four locations around the UK.

The findings showed that participants supported synthetic biology and were enthusiastic about the possibilities it presents but that their support was conditional. People highlighted the following important questions that should be considered for synthetic biology proposals:

- What is the purpose?
- Why do you want to do it?
- What are you going to gain from it?
- What else is it going to do?
- How do you know you are right?
The truly global and multidisciplinary nature of synthetic biology is well recognised. In Europe, the small number of established multidisciplinary synthetic biology centres are well linked through ongoing research collaborations and international conferences such as the SBX.0 series. However, ERA SynBio community building activities have highlighted the urgent need to link smaller European institutions and those research and industrial groups still in the process of adopting the synthetic biology approach.

There is also a clear need to build stronger links between individual researchers, especially those from different scientific or industrial backgrounds. Continued acceleration of the field will require close interaction of engineers, biologists, chemists, physicists and computer scientists. Social scientists, industry representatives, economists and policy makers will likewise have an essential role in ensuring that synthetic biology produces economically viable products that meet societal needs in a responsible manner.

Linking European synthetic biology
A common challenge for European researchers is to develop meaningful transnational collaborations with their counterparts in academia and industry. Small-scale networking and mobility grants are available from several sources, including ERA SynBio, the European Commission, national funding organisations and charities. In addition, transnational research funding from ERA-NETs and the European Commission, especially the networks envisioned in Theme 1, will provide significant transnational links. These connections could be enhanced by broadening the networks to include outside partners through cross-project activities, such as grant holder’s workshops, and through targeted support for areas of specific need including academic-industry collaborations.

Web portals are another important community networking tool, as they provide a low barrier to entry for interested parties. The website for the International Wheat Initiative has around 450 subscribers from research and policy organisations, while the UK Synthetic Biology Special Interest Group maintains a website on the Connect portal with over 700 members. Both these sites have community message boards and social media features to enhance community building. They also provide information on policy activities, research breakthroughs and funding opportunities. In addition to these functions, there is the prospect of utilising the data generated through the ERA SynBio project. The Alfred P. Sloan Foundation-funded ‘Synthetic Biology Project’ hosts an interactive map of active synthetic biology laboratories and a resource of this kind could be used to link European groups and showcase European research to the rest of the world. A longer term goal, highlighted by ERA SynBio’s strategic activities, is the opportunity for an international society of synthetic biology. This could act as a focal point for the community and encourage bottom-up responses to major challenges in the field, such as standardisation.

Theme 3: A networked, multidisciplinary and transnational community

Promoting multidisciplinary teams
Multidisciplinarity is one of the defining features of synthetic biology; it encourages new perspectives and creativity, broadens expertise without compromising on depth of understanding, and enables greater impact from fundamental research. To break down the language and cultural barriers that this mode of working presents will require strong support for interdisciplinary networking, research and publication. Particular emphasis will be required to nurture the mutual understanding of needs and priorities in academic and industrial sectors.

Focused synthetic biology centres will play an important role in multidisciplinarity, as they will have the resources and breadth of mission to successfully integrate researchers from a range of backgrounds. They should be encouraged to share expertise in this area more broadly within the synthetic biology community, supporting sectors which experience significant financial barriers to multidisciplinary working such as SMEs.

At the funder level, it is important that researchers are not only given the option to work in multidisciplinary teams, but also that these are actively rewarded. Funders should utilise the continued drive to leverage research spending as a stimulus to promote greater communication, and overcome the remit and assessment challenges associated with multidisciplinary research. In addition, multidisciplinarity should be made a key component of the linking efforts described above.

27 The International Wheat Initiative website
28 The UK Synthetic Biology Special Interest Group: https://connect.innovateuk.org/web/synthetic-biology-special-interest-group/synbio-sig
Breaking down the barriers to transnational research

Transnational joint projects are essential for the development of an integrated European and global synthetic biology community. Strong participation in the synthetic biology-specific calls in the Seventh Framework Programme and the ERASynBio 1st Joint Call demonstrates community demand to work internationally. As described in the Theme 1, Horizon 2020 represents a significant funding opportunity especially if the field receives a level of prioritisation proportionate with its level of potential economic and social impact.

There is also a need to break down the barriers to collaborative research between Europe and the rest of the world. A number of European funders have supported bilateral synthetic biology funding activities, while strong US participation in the ERASynBio 1st Joint Call suggests that ERA-NETs represent a viable option for global funding. Funders should also consider creative funding methods such as Sandpits or Ideas Labs.

ERASynBio’s remaining activities will be guided by this Strategic Vision; however this fruitful transnational programme will end in December 2014, leaving a gap in support for transnational development and coordination. Given the successes of the project so far, a clear case should be made for a follow-up activity. ERASynBio partners should carefully consider the aim, mechanism and optimal membership for such a follow-up activity and – where possible and strategically justified – broaden the project to include non-ERASynBio and non-European partners.

A transnational, multidisciplinary project in action

In 2009, five transnational synthetic biology projects were funded through member state contribution to the European Science Foundation. The SYNMOD project, led by Professor Oscar Kuipers, University of Groningen, successfully integrated molecular geneticists, biochemical engineers and social scientists from five European countries.

The project aimed to use a synthetic biology approach for the design and production of novel antibiotics. A modular synthesis pathway was designed and assembled within a reduced complexity bacterial chassis. Thousands of novel molecules were then produced and tested in a microfluidics system.

Social scientists within the consortium examined the safety and ethical implications of the project and engaged the public through approachable videos, a bio-art exhibition and a smartphone game app.
Theme 4: A skilled, creative and interconnected workforce

The rapid growth of synthetic biology presents an urgent need for highly trained researchers, industrialists and policy makers, with the novelty and multidisciplinarity of the field presenting particular challenges. High-quality postgraduate training is the point of greatest need, but accessible training at all educational and research levels will be required to boost the absorptive capacity of the sector and increase the competitiveness of European and global synthetic biology. At the same time, creative educational approaches will be required to inspire the next generation of synthetic biologists and develop future leaders in the field.

Supporting high quality and creative educational approaches

Synthetic biology training needs to provide an environment which attracts the very best researchers to the field. Promotion of synthetic biology could start as early as secondary school, with formal training offered as part of higher education courses in engineering and biological sciences. Europe has seen a rapid rise in institutions advertising taught undergraduate or postgraduate programmes which include synthetic biology. Courses are currently offered by around 50 institutions including highly regarded master’s courses at Imperial College London and Universities of Basel, Freiburg and Strasbourg. In addition, student-focused activities such as the iGEM competition have been recognised as a successful method of promoting enthusiasm for synthetic biology amongst students, principle investigators and the public, while providing valuable training for the participants.

Training through genome building

The Build-a-Genome course is an intensive laboratory training programme at Johns Hopkins University that introduces undergraduates to synthetic biology.

In addition to lectures that provide a comprehensive overview of the field, the course contains a unique laboratory component in which the students contribute to an actual, on-going project to produce the first eukaryotic cell with a fully synthetic genome.

This course laid the foundations for the Synthetic Yeast 2.0 project, an international programme to develop yeast with a fully synthetic engineered genome.

Global coordination support from the NSF funded Science Across Virtual Institutes (SAVI) mechanism enabled participation from partners in the US, China, India and the UK.

European students have been highly successful in iGEM and, as the field expands, funders should encourage development of - and participation in - new creative training opportunities such as maker faires or the Build-a-Genome course described in the box to the left. There is a particular need for financially accessible mechanisms that support collaborative project-based learning. While seed money from funding organisations will be important, there are also opportunities to leverage corporate sponsorship. Other much-needed training tools include approachable synthetic biology textbooks and web resources, such as massively open online courses (MOOCs) or the OpenWetWare wiki platform.

In the short-term, research funders should also learn from the educational approaches of other related fields such as systems biology. A long-term goal should be the establishment of a recognised education structure which provides broad transferable skills and allows students to progress in research careers and / or move into other professions. To address the broader implications of synthetic biology, all training should include sociological aspects, potential dual use issues, intellectual property rights, and regulatory literacy. Where possible, training should include time within a variety of academic, industrial or even non-science environments, such as work with artists and designers.

Embedding multidisciplinary skills

As discussed in Theme 3, multidisciplinarity is essential for the continued advance of synthetic biology. At the same time, the breadth and pace of development is such that no one can feasibly be an expert in all areas. The primary need therefore is to provide skills to

29 MRes in Systems and Synthetic Biology at CSynBI
30 Universities in Basel, Freiburg and Strasbourg offer a joint synthetic biology Masters programme
31 Maker Faire has been used by funded synthetic biology researchers and DIYbio practitioners: http://makerfaire.com/
single-discipline specialists that enable them to operate effectively in multidisciplinary teams.

The consultation exercises by ERASynBio identified a clear need to balance specialist and multidisciplinary training. There was agreement that the principles of multidisciplinarity should be developed during undergraduate studies, while postgraduate synthetic biology training should be intrinsically multidisciplinary. This training should be provided by researchers with direct experience in ‘wet-lab’ biology, engineering design and modelling, and expertise in the ethical, legal and societal aspects of the field.

A small number of high-quality multidisciplinary training courses are offered by the European Molecular Biology Laboratory and US Cold Spring Harbour Laboratory. In addition, the 1st ERASynBio summer school provided a two-week, hands-on multidisciplinary training environment for students from 11 ERASynBio countries. The summer school participants received lectures from leading synthetic biology figures and were challenged to work on a real synthetic biology project using systems engineering principles. Multidisciplinary training should be further encouraged through conferences, workshops, retreats, summer schools and exchange visits.

For established researchers, discipline hopping (where researchers with a track record in one area immerse themselves in a complementary field) is another mechanism to foster creativity and multidisciplinary skills. Funders should support these experiences as well as encouraging the use of existing mechanisms such as the Human Frontiers Science Program Cross-Disciplinary Fellowships.

Developing training centres and fellowships to increase educational capacity

A number of European institutes offer PhD programmes to work on their existing research projects. Currently, coordination of these programmes is limited and primarily depends on the availability of active synthetic biology projects. The UK Research Councils addressed this need through two new high-quality Centres for Doctoral Training in synthetic biology. Over the next four years, these centres will build the next-generation synthetic biology community by providing cohorts of students with both depth within core disciplines and the ability to work in cross-disciplinary synthetic biology collaborations. Training in these centres will integrate broader societal and business contexts, with a particular focus on awareness of responsible innovation and industrial exchange.

There are barriers to developing centres of this kind on a European level, not least the diversity of funding mechanisms for postgraduate courses. Nevertheless, the rewards for supporting strategically focused training within multidisciplinary centres were clearly identified during ERASynBio’s strategic work. The linked networks described in Theme 1 could provide one opportunity to satisfy this need, and educational activities should be clearly highlighted in the ERASynBio 2nd Joint Call. In addition, funding organisations should support cross-cutting training for all the transnational projects funded through ERASynBio.

Alongside the need to increase the number of students graduating with relevant PhDs, is the need to support early-career synthetic biology researchers on their journey up the academic career track. Funding organisations should consider specifically highlighting synthetic biology as a priority area in fellowship schemes to develop future leaders in the field. In addition, they should support short travel fellowships to boost multidisciplinary skills and creativity, and media training to enable early career researchers to act as advocates for the field.

32 Cross-Disciplinary Fellowships: http://www.hfsp.org/funding/postdoctoral-fellowships
33 UK Research Council funded Centres for Doctoral Training in Synthetic Biology
The emergence of synthetic biology was made possible by the advancement of underpinning technologies including DNA sequencing and synthesis, systems engineering and computational design, and systems biology and modelling. ERASynBio’s strategic activities identified the vital role for infrastructure in the current synthetic biology landscape, and the defining role for underpinning technologies for the future of the field.

Promoting effective data management and sharing

Enhanced use and sharing of data would be of clear benefit to synthetic biology through increased efficiency, collaboration and accountability. However, the current culture within the community remains mixed. There are a number of clear exemplars of best practice, with some groups rapidly making considerable amounts of their data available for the wider community. Significant barriers remain for the majority of the community, most notably the need to balance openness against protection of intellectual property (as described in Theme 2) and the resource requirements associated with open data.

Many of these issues are not specific to synthetic biology. Large-scale European activities are already underway through EUDAT34 and the SIM4RDM ERA-NET35. In addition, a report from the European High Level Expert Group on Scientific Data (Riding the Wave: How Europe can gain from the rising tide of scientific data)36 used data from several ERASynBio countries to develop a vision and recommendations for European data use. There is a particularly important role for scientific journals – including new synthetic biology specific journals such as ACS Synthetic Biology - in providing options for, and enforcing, the timely and open release of data.

Supporting standardisation

Standardisation of components and processes is a fundamental necessity for a wide variety of industries and related research areas. Their implementation provides significant economic returns, which can account for as much as 25% of GDP growth in developed countries37. Synthetic biology faces similar challenges to other emerging industrial fields. There is an urgent need to develop standards for data exchange, design, fabrication, automation, documentation, characterisation, measurements, operation and safety. If deployed effectively, synthetic biology standards will increase sharing, community building and adherence to safety standards. In addition, they have the potential to provide common expectations of biopart performance, increasing compatibility and reducing duplication of work.

A number of synthetic biology standards have already been developed including the BioBrick standard, the Synthetic Biology Open Language (SBOL), DICOM-SB and JBEI-ICE. Standard uptake however remains low, due in part to the significant challenges associated with standardising the intrinsic complexity of biological systems. Despite these challenges, the emerging position of the field offers a timely opportunity to use interoperable tools and standards to enhance research and development – something that was successfully achieved in the field of systems biology. The widespread use of synthetic biology standards will require basic-science investment, researcher coordination and an interaction with industry standards agencies. The British Standards Institute (BSI) is already assessing how standards in synthetic biology may be supported; however further coordination with the International Organization for Standardization (ISO) and the European Committee for Standardization (CEN) will be required to develop truly global synthetic biology standards.

Developing biopart registries and software

Accessible registries of rigorously characterised and interoperable bioparts would be an incredibly valuable resource for the global synthetic biology community, increasing scientific reproducibility, widening access and driving innovation. A variety of repositories are available, but their use remains low, with the majority of researchers favouring personal or lab-based registries. Quality control within existing public registries along with background-specific requirements has led to a proliferation of new registries, risking fragmentation within the area. Funders should work to promote access to bioparts and reduce duplication of biopart and registry development effort.

The importance of the multidisciplinary interaction between computer and natural sciences is demonstrated by the array of software tools available for synthetic biology. While this variety indicates the vibrancy of

34 The EUDAT European Data Infrastructure project
35 The SIM4RDM ERA-NET project
37 The economic impact of standardization, technological change, standards growth in France, AFNOR
this research area, it again presents challenges for the interoperability of synthetic biology data and underlines the need for appropriate and accepted data standards. Furthermore, there is a need to appropriately use both open source and open access software to balance commercialisation and openness.

In addition, it would be beneficial to exploit the large amount of work already completed in systems biology, especially for directly transferrable processes such as standards and modelling of systems and biopart functionality. There are opportunities to link synthetic biology with large-scale existing European actions in this area, including the ELIXIR and Infrastructure for Systems Biology Europe projects from the European Strategy Forum on Research Infrastructures.

Supporting host chassis and physical infrastructure

Host chassis have a large impact on the functionality of synthetic biology bioparts and therefore represent an important community resource. Both broadly applicable model systems and industrially relevant backgrounds will be important. There is particular demand for freely available, robust, easy to manipulate and reliable chassis, as well as chassis in novel backgrounds including photosynthetic and thermophilic microorganisms.

Development of new chassis is resource intensive, and underpinning research of this kind often falls poorly in open grant funding calls. Funding organisations should therefore direct chassis developers towards technology development schemes such as the UK Bioinformatics and Biological Resources Fund, which has funded the Yeast 2.0 chassis. Alongside this, actions are also required to make existing chassis more widely available, including links to existing collections such as the UK National Collection of Yeast Cultures.

As shown in Figure 4, synthetic biology research is underpinned by a broad range of physical infrastructure. Access to these technologies varies considerably, with the greatest need arising from technologies that are not being routinely outsourced, including high-throughput strain generation and automated robotic workflows. In addition, faster, cheaper and more accurate DNA synthesis was consistently identified as an important opportunity to increase the pace of synthetic biology research.

There is a clear need to support infrastructure and new technologies as they emerge and are embraced by the synthetic biology community. However, long-term provision of capital and staff resource can be challenging for funding organisations. There is therefore a clear need to leverage the activities of national and international funders, especially the European Commission. A positive first step would be to review the location and use of existing large investments to demonstrate impact, monitor uptake and effectively target future funding; this would be complemented by the training and networking activities described in Themes 1, 3 and 4.

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39 The international Yeast 2.0 project
40 UK National Collection of Yeast Cultures: [http://www.ncyc.co.uk/](http://www.ncyc.co.uk/)

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### Figure 4. Use of and access to physical infrastructure for synthetic biology

Data from the 191 responses to the ERASynBio infrastructure survey in July 2013.

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- Yes (outsourced, international provider)
- Yes (outsourced, national provider)
- Yes (in house provision)
- No (not required)
- No (unable to access)
Realising the vision

Through consultation with leading synthetic biology researchers and other stakeholders, ERASynBio has developed a vision for synthetic biology where world-leading and innovative European synthetic biology research will drive significant economic impact and address grand societal challenges. This will be achieved through: networked, multidisciplinary and agile centres of excellence; a skilled, creative and interconnected workforce; cutting-edge and open underpinning technology; and a responsible and inclusive policy framework.

As shown in Figure 5, the move from the current position towards this vision will require the concerted effort of a number of stakeholders including synthetic biology researchers, national funding organisations, the European Commission, ERASynBio and other international coordination bodies, and the public.

In this section, ERASynBio describes specific, measurable, attainable and timely recommendations drawn from the five major themes of the synthetic biology vision. These recommendations do not represent a definitive solution to all the challenges faced by synthetic biology and are not designed to replace existing activities in the field.

They are instead designed to utilise the unique transnational position of ERASynBio and its partner organisations to enact positive change within the research communities that they support. In particular, these recommendations are designed to complement and build upon the substantial national investment that will occur over the next five to ten years, providing a coherent European and global framework and tackling issues which cannot be managed at a national level.

As participants in the preparation of this Strategic Vision, the ERASynBio partners will aim, wherever possible, to implement these recommendations. They will work with other stakeholders to promote the field, enabling synthetic biology to fulfil its potential to contribute to the bioeconomy and to help address grand societal challenges.
Recommendations

1. **Invest in innovative, transnational and networked synthetic biology research.**

Significant funding will be required to achieve the projected revolution in biological and biologically based technologies offered by synthetic biology. Increased spending through open peer-reviewed competition will be essential to maintain the cutting-edge nature of this discipline, but there is also a need for coordinated top-down actions to address European and global challenges within the field.

1.1 Given its future potential to contribute across many areas of the bioeconomy, synthetic biology should be given a high priority and afforded significant support by national funding organisations and through the Horizon 2020 programme. Funders, researchers and other stakeholders should work together to ensure that synthetic biology is positioned as an area of high strategic importance, and that there are sufficient calls and support measures for the sustainable development of the field in academia and industry.

1.2 A major opportunity to add value to investments in synthetic biology is by linking high-quality synthetic biology research into larger multidisciplinary networks. ERASynBio partners, the research community and other stakeholders should work together to support the development of a linked series of networks that can act as a focal point for the global development and application of synthetic biology.

1.3 Relevant stakeholders should support the acceleration of the technology to market. This complex process will require the coordinated efforts of many stakeholders currently outside of the ERASynBio programme, including large industry, small and medium enterprises, regulators and public funders of industrial research. Bringing together these actors should be a major aim of any international action that follows on from ERASynBio.

2. **Develop and implement synthetic biology in a responsible and inclusive manner.**

The ultimate success of synthetic biology will depend not only on the technological successes of natural scientists and engineers, but on the ability of the applied and industrial community to develop products and services that are needed by, and acceptable to, the public and other stakeholders. Achieving this will require a coordinated effort by members of the scientific, industrial and policy-making communities.

2.1 The ERASynBio project and any transnational follow-on actions should work within the principles of good governance. Culture change towards the principles laid out in this Strategic Vision is a long term goal; however there is an opportunity for ERASynBio to set the benchmark for transparency, participation and accountability in its policy activities. Achievement of this benchmark should be monitored and could be presented in the form of an online checklist.

2.2 Organisations and individuals funded through ERASynBio and any follow-on projects should be required to demonstrate that due consideration has been given to the full range of potential ethical and social issues associated with funded projects, including environmental and other risks. Participation of social scientists should be encouraged and synthetic biology researchers should have easy access to relevant expertise through cross-cutting activities, even where projects do not raise specific social or ethical considerations.

2.3 Research funders should encourage and support open and meaningful dialogue with a range of stakeholders including a variety of publics. This should be conducted primarily through local mutual learning and engagement projects that link together to maintain a more continuous discussion.

2.4 Regulation of synthetic biology will require discussion of intellectual property legislation, safety regulations and controls on the synthetic organisms themselves. Funders should remain engaged in these discussions at both national and international levels, promote the open involvement of other stakeholders and be prepared to fund risk assessment activities in awarded projects.
3. **Build a networked, multidisciplinary and transnational research and policy making community.**

Synthetic biology, perhaps more than any other related field, requires the interactions of researchers and policy makers from multiple locations and scientific backgrounds. Synthetic biology funders are currently in an exceptional position to bridge disciplinary and geographical barriers, and support a coherent European and global community.

3.1 Synthetic biology funders should support new and existing links between synthetic biology researchers from a range of disciplines through travel, exchange visits, workshops, retreats and conferences. In addition, they should promote the development of a cohesive network of ERASynBio grant holders. ERASynBio and any follow-up action should take advantage of web-based networking solutions, especially where the data and researcher network generated by the ERASynBio project can be utilised.

3.2 For European synthetic biology to be world-leading, broad multidisciplinary teams need to be the norm. Applications to the joint funding calls should be required to demonstrate multidisciplinarity, and ERASynBio partners should work with appropriate additional funders to ensure that all aspects of synthetic biology (including industrial synthetic biology) can be supported. In addition, the outcomes and examples of best practice from the ERASynBio interdisciplinary workshop should be widely promoted.

3.3 Synthetic biology funders and policy makers should prepare further bids for transnational support mechanisms to build on the achievements of ERASynBio and enact transnational activities recommended in this Strategic Vision. They should consider how best to broaden the project to include non-ERASynBio and non-European partners.

4. **Support the future of synthetic biology by providing a skilled, creative and interconnected workforce**

High-quality training at all levels will boost the absorptive capacity of the sector and increase the competitiveness of European and global synthetic biology. At the same time, creative educational approaches provide the opportunity to inspire the next generation of synthetic biologists.

4.1 Funding organisations should promote the development of high-quality synthetic biology training, with particular emphasis on areas of need such as high-quality masters and PhD programmes and training hubs within centres of research excellence. Where ERASynBio partners are unable to directly support these kinds of activities, they should work the relevant national and international funding bodies.

4.2 Funding and policy organisations should gather and disseminate information on relevant training and educational opportunities as part of the broader community building activities within Theme 3. They should further this approach by supporting the release of freely available educational material, including protocols, presentations and videos.

4.3 Synthetic biology funders and other stakeholders should support innovative multidisciplinary training and educational courses, including student exchanges, summer / winter schools and competitions. They should also promote student and early-career participation in conferences and workshops.
5. Utilise open, cutting-edge data and underpinning technologies.

For institutions that conduct synthetic biology research, access to novel data sets and the newest technologies will be essential to maintain and increase their competitiveness. Funding organisations and other stakeholders should do more to encourage effective use of data and new technologies and should also support the community in the development of the next generation of synthetic biology infrastructure.

5.1 Synthetic biology funding organisations should work to link synthetic biology with relevant existing activities. Funders should try to achieve the aims and recommendations set out in the ‘Riding the wave’ report on data management and sharing. They should actively engage with large ongoing projects, including the ELIXIR and Infrastructure for Systems Biology Europe projects from the European Strategy Forum on Research Infrastructures Roadmap.

5.2 Funding organisations should use mechanisms such as the ERASynBio 2nd Joint Call as a lever for cultural change within the synthetic biology community. They should promote open data use and increased software, biopart and host chassis sharing, as well as widening the use of data and models from systems biology.

5.3 National funding organisations should consider reviews of key physical infrastructure and technologies to determine gaps in provision for synthetic biology. Partners should then explore how they can use national and international programmes to encourage efficient use of these technologies and prioritise infrastructure provisions for synthetic biology research. In addition, the development and uptake of novel underpinning technologies should be encouraged to support the next generation of synthetic biology research.
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