

### Introduction

Synthetic biology is the deliberate design and construction of customised biological and biochemical systems to perform new or improved functions. It draws on a wide range of disciplines and methodologies to design molecules, construct genetic circuits and assemble simple organisms. Many in the scientific community consider that by applying the principles of systems biology, engineering and chemical design to biological systems, synthetic biology will lead to new applications of considerable societal value. Proof-of-concept has already been demonstrated in establishing less expensive ways of producing pharmaceuticals and other high-value chemicals and there are likely to be other early achievements in the generation and optimal use of biofuels. Further ahead there are possible applications of this biological toolbox in biomedicine, agriculture, land and water decontamination, biosensing, new materials, nano-machines and novel approaches to information processing.

However, in some respects synthetic biology has become a controversial area. Concerns have been expressed for the protection of human health and the environment, particularly arising from governance issues associated with biosafety (protecting legitimate users and the environment) and biosecurity (protecting against intentional misuse). Synthetic biology may itself provide the methodologies to engineer additional safety features, for example by creating functional dependency on exogenous regulatory molecules, or by installing systems that cannot interact with natural pathways. Nonetheless, various environmental and other non-governmental organisations have called for greater international oversight, including a moratorium on the release and commercialisation of synthetic organisms and their products.

### Previous work by academies

Member academies of IAP have explored many of the key biosafety and other issues relating to the contribution that synthetic biology could make to tackling societal objectives, what scientific and technical challenges must be overcome, and what else might prevent the field from realising its potential<sup>1</sup>. These issues continue to come under intense scrutiny and it is probably still premature to decide whether synthetic biology will be a truly revolutionary technology or a less radical, incremental advance. It is the purpose of the present IAP Statement, based on previous and ongoing academy activities, to emphasise that the advance of science must be connected to global policy development to ensure the appropriate, proportionate framework for supporting responsible science and its translation to innovation.

<sup>1</sup> For example: (i) Joyce, S, Mazza, A-M and Kendall, S (2013) Positioning synthetic biology to meet the challenges of the 21<sup>st</sup> Century. Summary report of the six academies symposium series, National Academies Press, [http://www.nap.edu/openbook.php?record\\_id=13316](http://www.nap.edu/openbook.php?record_id=13316); (ii) EASAC (2010) Realising European potential in synthetic biology: scientific opportunities and good governance, German National Academy of Sciences, <http://www.easac.eu/reports-and-statements/detail-view/article/synthetic-bi.html>

### Global environmental concerns: the Convention on Biological Diversity (CBD)

Recent consultation documents<sup>2</sup> explore implications of synthetic biology for the CBD in terms of potential impact on the conservation of biodiversity and precautionary strategies for physical and biological containment. Although many respondents to this CBD consultation considered the draft documents to be informative and a useful starting point for debate, significant concerns were also expressed about the text of the documents. IAP suggests that there should be clarity in defining synthetic biology and explaining what, if anything, is different from the genetic engineering technologies already in widespread use. This is crucially important because genetically modified organisms (GMOs) – in contained use, deliberate release and transboundary movement – are already subject to impact assessment and regulation. In particular, the Cartagena Protocol on Biosafety, an international agreement, aims to ensure the safe handling, transport and use of living modified organisms resulting from modern biotechnology. It is important to treat in a balanced and evidence-based way the potential risks and the potential benefits. Balance in the consultation can best be achieved by focusing on evidence that has been peer-reviewed, and by carefully keeping scientific literature in accurate context.

As this CBD discussion proceeds, under the auspices of the Subsidiary Body on Scientific, Technical and Technological Advice<sup>3</sup>, it is essential to take into account these concerns about underlying assumptions (in particular the assumption that current methodologies are unregulated) and the use of evidence (that has not been peer reviewed). In the view of IAP, introduction of a moratorium would be counter-productive. It is vital that global policy is not intentionally or inadvertently encouraged to introduce excessively cautious restrictions on synthetic biology, as that would deter the innovation that may help to deliver food and energy security, better health, environmental sustainability, or address other pressing societal priorities<sup>4</sup>. It is also important not to impede the fundamental research that will contribute to the better understanding of natural biological systems.

### Recommendations from IAP

Emerging technologies are often initially characterised by uncertainty and ambiguity, and the scientific community has an important responsibility to ensure that policy-makers and the public can realistically assess the assertions that often appear at such times. Academies stand ready to play their part in informing the synthetic biology debate based on accurate evidence about current progress and future possibilities.

<sup>2</sup> Convention on Biological Diversity, New & Emerging Issues, <https://www.cbd.int/emerging>

<sup>3</sup> Meeting documents, 18<sup>th</sup> meeting of SBSTTA, Montreal 23-28 June 2014, <https://www.cbd.int/doc/?meeting=sbstta-18>

<sup>4</sup> Previous IAP work on societal priorities includes: (i) Response to the Report of the High-Level Panel of Eminent Persons on the post-2015 development agenda, <http://www.interacademies.net/10878/22347.aspx> and (ii) Letter from Rio-2013 on the role of science academies in grand challenges and integrated innovations for sustainable development and poverty eradication, <http://www.interacademies.net/File.aspx?id=21458>

In the view of IAP, there is need for new global commitment:

- *Preparing researchers for work in synthetic biology* Research funders worldwide need to support the underpinning scientific disciplines, develop integrative multidisciplinary initiatives and promote translational research across the diverse range of synthetic biology approaches. These currently include: minimal and rearranged genomes, xenonucleic acid polymers and engineering of genetic codes, artificial biological machines, metabolic engineering and cell factories (including recent advances in conditional synthesis of high-value chemicals in micro-algae, plant cell cultures or entire plants), bio-robots, regulatory circuits and bionanoscience. Responsible research and testing of outputs must embrace awareness of environmental dimensions, for example the prospect of gene transfer or evolution of novel organisms. It is equally critical to prepare the next generation of skilled researchers. Synthetic biology is often a popular topic with students. The iGEM (International Genetically Engineered Machine, see <http://igem.org>) competition has proved very effective in introducing young students, increasingly from high schools and colleges in Asia and Africa as well as from Europe and the Americas, to the principles and practices of synthetic biology. The potential for academies and the young academies to support such initiatives and to incorporate collective learning about the relevant ethical and social issues, as well as the experimental and business techniques for emerging technologies, should be considered further. If it is to be successful, synthetic biology research must also embrace the social sciences and the humanities. Interdisciplinary centres need to be organised where common languages from members of different disciplines are spoken.
- *Engaging with the public and clarifying ethical and social concerns* Further work is needed to ascertain where there may be regional variation in concerns and what should be addressed at the global level. The scientific community must proactively communicate a balanced account of progress, opportunities and uncertainties while, at the same time, raising public awareness about the established regulatory frameworks that evaluate effects on health and the environment. Recent interactions between synthetic biologists and conservationists<sup>5</sup> provide a useful model for sharing good practice in understanding mutual interests.
- *Considering alternative models for owning and sharing research outputs* The current situation in synthetic biology reflects its different origins, in biosciences (where there is a tradition of proprietary ownership and patenting) and in engineering and software development (where there is a tradition of open sources and sharing of standard parts). A culture of greater openness is stimulated by initiatives such as the BioBricks Foundation (see <http://biobricks.org>) making its registry of devised regulatory and structural elements available for use. New routes to sharing protected information may also be possible, for example by using patent pools. Patent offices must be careful when requested to grant broad patents that might unreasonably deter competitiveness and slow down the translation of research into products.
- *Determining how synthetic biology should be regulated* There is continuing need for clarity in defining what constitutes

synthetic biology and what its boundaries are. There is reason to expect that the greater precision embedded in synthetic biology makes it less, not more, difficult to regulate, manage and audit, compared to older technologies. It is important to find the right balance between scientific self-governance and statutory regulation. Predictable and proportionate regulation worldwide should be based on the validated procedures already in place in many countries. Experience gained through the contained use of GMOs helps to provide a growing evidence base on how to regulate and mitigate any risks. Many of the efforts to design new environmentally benign production systems are contained and, thus, separated from environmental interactions. According to a previous analysis by academies (see footnote 1(ii)), existing legislation for biosafety is adequate for current purposes, providing the regulations and review mechanisms are properly managed. Nonetheless, developments are diverse and dynamic, requiring continuing monitoring of the advances in science and technology together with the setting of clear criteria for assessing the benefit-risk for novel organisms.

- *Disseminating guidelines and calling for scientific responsibility* Maintaining biosecurity brings challenges beyond those of biosafety: for biosecurity the core defence rests on the responsibility of the scientific community. Individual academies, IAP and IAC<sup>6</sup> have produced relevant material advising on individual scientific responsibilities and institutional codes of conduct that helps to promote both biosecurity and biosafety. These guidelines should be disseminated widely. It is also important that all of the global research community, including the do-it-yourself (DIY) community of amateur biotechnology researchers, support the development and follow the recommendations of these codes of conduct.

In conclusion, IAP recommends continuing collaboration worldwide between the various groups supporting researchers, those regulating and enabling synthetic biology, and those who will be the users and beneficiaries. Because of the uncertainties and fast pace of change, it is challenging to scan the horizon for probable developments. However, academies of science are well placed to undertake this activity that is critically important for future preparedness. We must collectively ensure that policy development worldwide is sufficiently flexible to encourage research and manage innovation, including those applications not yet envisaged, while suggesting sensible practices to mitigate any risks.



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<sup>5</sup> For example, (i) Redford K, Adams W and Mace G, Synthetic biology and conservation of nature: wicked problems and wicked solutions, PLoS Biology 2013, 11, e1001530; (ii) Griggs J, The odd couple, New Scientist 7 December 2013 pp46-49

<sup>6</sup> IAC and IAP, Responsible conduct in the global research enterprise, 2012, <http://www.interacademies.net/10878/19787.aspx>