# IAP Statement on Realising Global Potential in Synthetic Biology: Scientific Opportunities and Good Governance

## 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[1]. 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

[1] *For example: (i) Joyce, S, Mazza, A-M and Kendall, S (2013) Positioning synthetic biology to meet the challenges of the 21st Century. Summary report of the six academies symposium series, National Academies Press, 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/detailview/article/synthetic-bi.html*

translation to innovation.

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

Recent consultation documents[2] 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[3], 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[4]. 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.

In the view of IAP, there is need for new global commitment: synthetic biology and what its boundaries are. There is need for 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-

[2] *Convention on Biological Diversity, New & Emerging Issues,* https://www.cbd.int/emerging

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

[4] *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

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[5] 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 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

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[5] *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 6 IAC and IAP, Responsible conduct in the global research enterprise, 2012, December 2013 pp46-49 http://www.interacademies.net/10878/19787.aspx*

of the scientific community. Individual academies, IAP and IAC[6] 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.

***7 May 2014***

*Signed by IAP -the global network of science academies (www.interacademies.net) IAP -the global network of science academies currently has a membership of 106 scientific academies from around the world; these include both national academies/institutions as well as regional/global groupings of scientists. For information, see the IAP Directory at:*

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# Summary Report on Synthetic Biology

## Academy of Athens

30 May 2014

## Introduction - Definition

**Synthetic biology** is an emerging field of interdisciplinary research that aims at the design and construction of novel organisms or biological systems that are not known to exist in nature or the re-design of existing natural systems to acquire specialized functions. Synthetic biology addresses societal needs in various fields such as medicine and healthcare, materials and chemicals, clean energy, pollution control, agriculture and food, security and others. Synthetic biology brings together several areas of research, including biology, engineering, informatics, physics, and chemistry. Scientists approach synthetic biology from different yet complementary perspectives, both conceptually and

[6] *IAC and IAP, Responsible conduct in the global research enterprise, 2012, December 2013 pp46-49 http://www.interacademies.net/10878/19787.aspx*

technically. For biologists, being able to assemble or construct a living system - or partial components - provides a means to better understand how this system works. For chemists, physicists and other natural scientists, synthetic biology offers an exciting platform on which to probe the functional properties of molecules and their interactions with the dynamic cellular environment. Engineers tackle synthetic biology as a unique and novel means to design and test novel tools for processing of information and transfer of energy. In all cases, the common aim of designing novel systems or re-designing components offers great promise for major scientific advances and innovative applications for the benefit of mankind.

While the idea of manipulating or engineering biological material so that it acquires novel characteristics is far from new, assembling whole living organisms from inanimate parts has proved all but fictional to date. In May 2010, the J. Craig Venter Institute achieved the synthesis and assembly of a complete bacterial genome and its transplantation to a recipient cell (of a different species) controlled only by the synthetic genome. Although the announcement spurred intense debate and often extreme reactions on the potential risks and benefits, it is clear that the achievement - though highly significant - does not in any way constitute "creation of life". In fact most scientists would agree that achieving such a goal remains far-flung in the foreseeable future. In practice, advances in the field are often of a technical nature and rely on bringing together components or tools already used in other fields, such as genetic engineering, chemical biology, nanotechnology and others.

## "Top-down" and "bottom-up" approaches

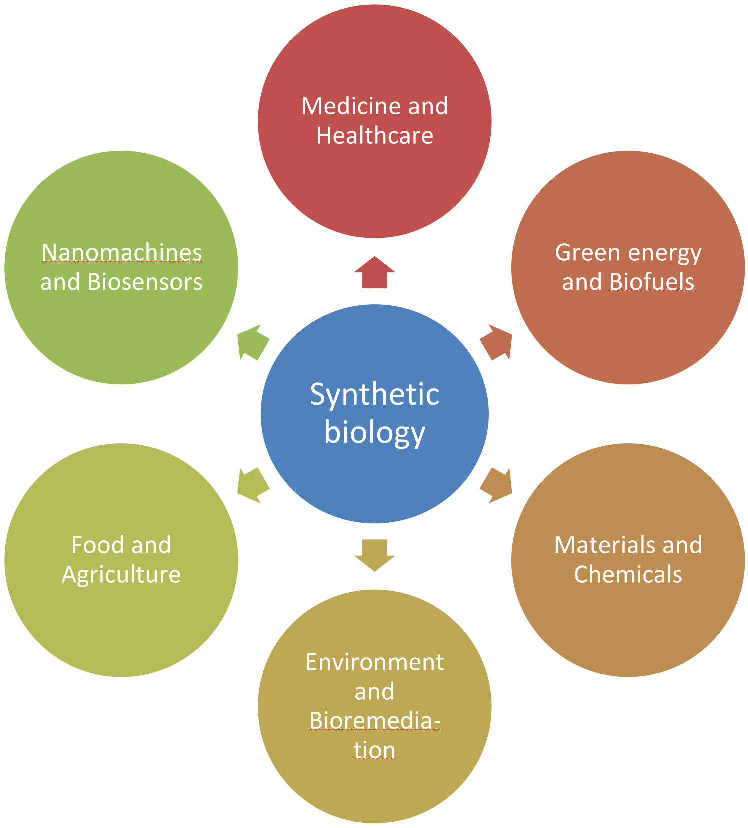
Synthetic biology approaches can be divided in "top-down" ones that aim to modify and re-design existing biological systems or components to produce novel or enhanced functions by removing or replacing unnecessary parts, and "bottom-up" ones that aspire to create novel biological systems from non-living material, an ambitious and yet unreached goal.

Examples of **"top-down" approaches** include the identification of minimal genomes, which aims at defining and characterizing the minimal components of a genome that are needed for a biological system to survive. This requires systematic reduction of genomic parts to produce a minimal set that allows the system to function. Another example is metabolic engineering and the design of orthogonal systems, which involve the modification of biosynthetic pathways in a cell to yield desired products that do not occur naturally or to change the coding capacity of a cell to produce artificial biomolecules.

Examples of **"bottom up"** approaches involve the creation of "synthetic cells" de novo, with the objective to achieve protocells that self-assemble, self-repair, reproduce and evolve. It is around this ambitious and challenging approach that most controversy revolves regarding the ability to create new life and its ramifications.

## Applications

The methodological approaches described above have a plethora of potential applications in diverse fields such as the development of cheaper drugs and targeted therapies, green fuels, biosensors, biofuels and biomaterials, as well as solutions for bioremediation, food production, and others (Scheme 1).




***Scheme 1.*** *Fields of application of synthetic biology methodologies*

A successful application of synthetic biology is the development of the **anti-malaria medicine** Artemisinin. Researchers managed to engineer the pathway of production of an Artemisinin precursor in yeast cells. This precursor could then be easily converted to the final product (which was previously isolated from plants in an expensive and unreliable manner depending on crop success). Similar innovative yeast-based platforms are currently being used to produce fuels and other chemicals (lubricants, polymers, healthcare and cosmetic products), including the conversion of sugar into yeast-derived cellulosic alcohol fuel.

In another application engineers used thermophilic bacteria and fermentation of cellulosic sugars to produce energy products that include **second generation bioethanol**. This innovative platform is based on proprietary microorganisms that can produce ethanol from a wide range of non-food lignocellulosic feedstock. The technology offers promise for the development of better strains that can be used in the production of more renewable fuels. Similarly, yeast and bacteria were engineered to transform sugar into **hydrocarbons** identical to those distilled from oil.

Synthetic biology can also be applied to address **environmental issues**.  For example, an E.coli strain was engineered to degrade atrazine, a herbicide widely used to prevent weeds in maize and sugarcane. By generating an atrazine-sensitive riboswitch, scientists enabled the response to occur only in the presence of the herbicide.

## Ethical considerations

Although synthetic biology is still in its infancy and most of the described applications so far are falling within the area of genetic engineering and biotechnology, critics have already raised several issues, both practical as well as ethical.

***Biosafety***

One issue raised revolves around biosafety. Accidental - or even deliberate - release of self-replicating organisms that consist partly or entirely of artificial components does indeed constitute a significant possible risk to the environment. However this type of risk is not unique to synthetic biology applications. In fact extensive and active debate is currently going on in the context of genetically modified organisms (GMOs) that are used in agriculture and extensive regulatory legislation is in place both in Europe and internationally. Additional risks associated specifically with synthetic biology are not envisioned at this point, although the scientific community should continuously re-assess and re-evaluate the adequacy of the legislative framework and its implementation in the context of new technological and conceptual developments.

***Biosecurity***

A second issue often raised in relation to synthetic biology is the risk related to biosecurity and the possibility that products of such research may be misused to cause harm, for example through the dissemination of synthetic pathogens. While this type of risk is also not limited to synthetic biology products, and expands to the criminal use of any genetically modified system, the main argument against this notion is that such risk is negligible as there is a plethora of naturally occurring pathogens that could be used instead for such harmful purposes, rather than undertaking the challenging task of creating a new one.

***Philosophical and religious considerations***

The attempts to create animate matter out of inanimate material has also been met with some concern. While similar reproaches have been associated with virtually all major advances in modern biology and biotechnology (including recombinant DNA technologies, mammalian cloning, in vitro fertilization etc), it is of particular relevance to synthetic biology due to the magnitude of the task at hand and its relation to fundamental aspects of life inciting ontological, theological and philosophical considerations. Crossing the boundary between the animate and the inanimate - or even the effort to achieve this - has incited lively discussions between political, cultural and religious groups of various perspectives, even though this endeavor is not even remotely close to culmination at this point. A solid regulatory framework overseeing this type of research will be key in order for synthetic biology research to flourish in the context of conceptual considerations regarding the definitions, risks, and benefits of producing "artificial life".

## Recommendations

While activities in this field so far mostly constitute **incremental technological advances** in existing fields such as biotechnology and bioengineering, and thus do not warrant specific measures to be taken specifically with regard to synthetic biology, nevertheless pro-active deliberation of potential concerns should be dealt with to ensure that research efforts and the development of beneficial applications are not hindered. To that end the following measures should be encouraged and implemented.

### *Support for research*

Serious investment, as well as transparent coordination, evaluation and support for interdisciplinary research should be implemented to allow this highly innovative field to flourish. Local efforts should be **aligned with international activities** to maximize global benefits and minimize potential risks. Advisory bodies and policy makers must be updated and informed in order to incorporate synthetic biology concepts in upcoming strategic development plans for research, technology and infrastructures.

### *Education*

Synthetic biology should be incorporated in the curricula of schools and universities, providing accurate information and broadly disseminating findings and applications of synthetic biology to diverse groups, thus **developing scientific literacy** specific to this field to tomorrow's citizens and scientists. Furthermore, **ethics education** must be strengthened at all levels, both in the medical and biology communities, as well as in related fields such as engineering, informatics and natural science, to address the evolving ethical issues that synthetic biology presents, thus fostering **responsible and accountable research**.

### *Society*

**Active public debate** and democratic deliberation regarding ethical and practical considerations for synthetic biology must be encouraged. This should involve experts that can provide **accurate information** on advances in the field, so that the debate is based on factual observations rather than fictional assumptions. Public engagement will help shape perceptions, address hopes and fears, and **increase awareness and acceptance** of synthetic biology research and technological activities. This will help citizens and other stakeholders to realize possible benefits and will allow them to make informed and balanced decisions.

### *Legal framework*

A **robust and balanced regulatory framework** must be developed and continuously re-assessed, to allow innovative research to proceed while at the same time respecting safety and ethical considerations. Continuous risk assessment and evaluation of harm vs. benefit, will aid in gaining confidence in these new technologies and in realizing their potential applications to address global challenges.

## Conclusions

In summary, synthetic biology is an emerging field with enormous potential for scientific advances and technological innovation offering possibilities for significant benefits to society. While - historically - groundbreaking technological advances have been demonized due to safety and ethical implications associated with their applications, the advancement of scientific knowledge has almost never stopped because of such limitations or exclusions. However, active debate on the global potential of synthetic biology must be endorsed - based on accurate scientific information - so that a robust ethical and legislative framework is established to address social concerns, as well as biosafety and biosecurity risks.

**Considering that the new 'IAP Statement on Realising Global Potential in Synthetic Biology: Scientific Opportunities and Good Governance' is in complete accordance with the above, the Academy of Athens endorses the IAP statement.**

**The Academy of Athens is actively involved with global scientific challenges and aims to raise awareness and shape opinions to enable global citizens to evaluate upcoming developments in these fields.**

## Related publications


- IAP Statement on Realising Global Potential in Synthetic Biology: Scientific Opportunities and Good Governance. May 2014.
- A Synthetic Biology Roadmap for the UK. July 2012.
- Synthetic Biology: An Introduction. EASAC January 2011
- New Directions - The Ethics of Synthetic Biology and Emerging Technologies. Presidential Commission for the Study of Bioethical Issues. USA December 2010.
- Time to settle the synthetic controversy. Nature, 509:135, 2014.
- Realising European potential in synthetic biology: scientific opportunities and good governance. EASAC policy report 13. December 2010.