



Capacity building for the bioeconomy in Africa

*Harnessing fast, frugal and open
technologies for education and
sustainable development*



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EXECUTIVE SUMMARY

THE FIELD OF SYNTHETIC BIOLOGY IS INTRODUCING LOW-COST, BREAKTHROUGH TECHNOLOGIES FOR A WIDE RANGE OF PRACTICAL CHALLENGES INCLUDING DIAGNOSTICS, ENVIRONMENTAL CONSERVATION, MICROBIAL BIOPRODUCTION, CROP IMPROVEMENT AND HUMAN HEALTH. THESE ARE OF CRITICAL IMPORTANCE TO THE FUTURE WELL-BEING AND ECONOMIC DEVELOPMENT OF SUSTAINABLE SOCIETIES ACROSS AFRICA.

Synthetic biology offers new tools and approaches:

- Standardised, modular DNA parts and rapid assembly of genetic circuits for reprogramming biological systems.
- Cell free expression systems that do not require containment, and can be freeze-dried and stored at ambient temperatures to eliminate the need for refrigeration.
- Transient gene expression in contained hosts, and transgene-free genome editing to avoid the costs, resources and regulatory hurdles associated with the deployment of genetically modified organisms.
- Legal frameworks, repositories and open technologies for the open exchange of genetic materials.

These new technologies are relatively low-cost, but their adoption in Africa is limited by deficits in technical training, poor access to new research materials, inadequate laboratory facilities, and lack of strategic partnerships with other African and international research institutions.

The UK and Africa share a common goal with the need to develop improved synthetic

biology training in schools, universities, community labs and industry.

International efforts to develop open standards and protocols for DNA parts and tools will provide a major impetus for technology transfer to Africa.

We recommend that (i) biotechnology is fertile ground for UK-Africa exchange, and that (ii) capacity-building based on open technologies and exchange should be a major component of any funding initiative.

Synthetic biology can provide better solutions for: (i) rapid-response production of vaccines and biologics, (ii) point-of-use diagnostics and field biosensors, (iii) agricultural crop improvement using non-transgenic (genome editing) tools, and (iv) harnessing local biodiversity to build a sustainable bioeconomy.

In each of these applications, the development of practical solutions and social impact requires:

- Shared curricula for training and biotechnology education in resource-poor communities and institutes.
- Building local expertise through exchange and shared knowledge.

ENGINEERING BIOLOGY IN AFRICA

IMPORTANCE OF SUSTAINABLE TECHNOLOGIES AND THE BIOECONOMY IN AFRICA

New biological engineering approaches offer the prospect of breakthrough approaches to the reprogramming of living systems, and the rapid development of new sustainable production systems in the face of increasing global demand for sustainable and resource-efficient solutions to challenges of food production, materials, energy, health, climate change and environmental sustainability. In the process of transitioning from a fossil carbon economy, we are seeing the rapid growth of the bio-based economy in developed countries. Identified in the 2016 OECD Science, Technology and Innovation Outlook as one of the 10 key technology trends of the future, Synthetic Biology is a new field defined by the application of engineering principles to living systems for useful applications in health, agriculture, industry and energy. Internationally, there are large and ongoing investments in the field, which generally require substantial investment in laboratory infrastructure and the deployment of stably transformed, approved genetically modified organisms (GMOs) into the environment. Except in a minority of countries like South Africa where GMO

biosafety and regulatory frameworks are well established and specific GMO applications with emphasis on crop improvement may be well received (<http://www.biosafety.org.za/>), both of these issues can be highly problematic in the context of developing countries and can be circumvented through the application of recent low-cost, cell-free and transient synthetic biology systems.

BENEFITS OF THE NEW BIOLOGICAL TECHNOLOGIES

Cell-free and transient expression systems are easy to implement, relatively free of biosafety evaluation requirements and cheap to deploy. Underpinning this field is the open-source distribution of modular and standardised synthetic DNA components, which facilitates international exchange, knowledge transfer and innovation. These new technologies avoid complications, delays and regulatory uncertainties associated with uncontained use of GMOs, eliminate requirements for cold chain setups for transport and storage, and provide new options for high level collaboration on education, training and interdisciplinary research between UK and African scientists in low-resource environments. The promotion of open, low-cost, low-resource technology platforms allows for the in-country development of solutions

for local problems, while building capabilities in an emerging technology that will be valuable for education, research, innovation and economic development. These novel non-GM approaches offer new prospects for (i) low cost diagnostics and environmental sensors, (ii) programmable cell-free expression systems, (iii) vaccine production for rapid responses to emerging viral threats, (iv) biomining and bioproduction, (v) new breeding techniques in plants based on genome editing using CRISPR/Cas9, (vii) new opportunities for training and education in UK and Africa, and (viii) an opportunity to engage societies concerned about GM technology.

NEED FOR CAPACITY BUILDING IN AFRICA

The development of a thriving biological products-based economy (bioeconomy) in African countries is constrained by a general lack of funding, skills and infrastructure at multiple levels, from secondary school, undergraduate and postgraduate training to basic and applied research, pilot-scale testing and commercialisation. Concurrently, limited public and political understanding of biotechnology and its socio-economic benefits and risks also stultify the uptake of biotechnology in society and industry. A number of world-class African centres with

*NEW BIOLOGICAL
ENGINEERING
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REPROGRAMMING
OF LIVING SYSTEMS*

training and research capacity exist, generally in better-resourced countries, or where major foundation funding has been invested. However, these model centres are typically weakly connected to research institutions in neighbouring countries and the region as a whole. These challenges could be overcome in part through access to the latest low-cost, open-source, widely shareable and scalable synthetic biology technologies that can be applied to accelerate basic training and capacity building in biotechnology, while stimulating research addressing unique challenges of importance to the African continent. Fast, flexible and scalable Synthetic Biology technologies will be important components of an agile response to emerging challenges such as infectious diseases, and biotic and abiotic stresses impacting on food security in African countries, while supporting the growth of national bioeconomies.

RISKS OF INACTION OR EXCLUSION

The timing of implementing emerging biotechnologies will be critical for sustainable development of the African bioeconomy. The risks of inaction, exclusion or failure to adopt these technologies are profound. Long term negative impacts include: (i) losing a generation of talented young Africans who could otherwise contribute to building the African bioeconomy, (ii) African nations and scientists falling



behind the international scientific community, (iii) significant mortality and morbidity due to the inability of African countries to rapidly respond to emerging diseases (e.g. Ebola) and food security threats (e.g. novel crop pathogens). Rapid response to such emergencies will greatly depend on facility infrastructure and scale-up capabilities to achieve sufficient vaccine or therapeutic supply in a short time-frame, in addition to developing diagnostics for rapidly determining infection and disease spread.

We report the outcomes of a GCRF-funded workshop on Practical Synthetic Biology which includes a list of priorities for research and investment, synergies identified between UK and African role-

players, an assessment of technical and resource deficits, scale of investment required to address these deficits and, finally, recommendations for funding calls related to the development of capacity and infrastructure for the application of synthetic biology to address specific challenges faced in African countries.

*OPEN, LOW-COST, LOW-RESOURCE
TECHNOLOGY PLATFORMS
ALLOW FOR IN-COUNTRY
DEVELOPMENT OF SOLUTIONS
TO LOCAL PROBLEMS AND BUILD
CAPABILITIES IN EMERGING
TECHNOLOGY.*

Workshop Methodology I

PRETORIA SYMPOSIUM

We chose the University of Pretoria (UP) as the chief institutional partner for hosting the meeting. UP and the Council for Scientific and Industrial Research (CSIR) in Pretoria and the University of the Witwatersrand (WITS) in Johannesburg, play prominent roles in promoting synthetic biology in Africa, hosting the only iGEM teams in sub-Saharan Africa, as well as hosting research activities, including an earlier technical training workshop with participants from Cambridge and Imperial College in 2016. UP co-funds the African Centre for Gene Technologies (ACGT), a collaborative structure of Gauteng-based universities and scientific councils.

UP is also home to the Future Africa campus, a major new investment that will bring together leading scientists, engineers, lawyers and societal experts. Future Africa aims to nucleate a new generation of transformation-minded science leaders in Africa (<http://www.up.ac.za/future-africa>), and will in future form the epicentre of a research precinct on the Hatfield Experimental Farm campus dedicated to bioeconomy-related research. The Future Africa initiative embraces an interdisciplinary approach to the continent's complex problems based on proper governance, human rights and the bioeconomy.

Participants were recruited for an open Symposium in Pretoria and strategically focused workshop at Bakubung. The 28 workshop participants represented 16 institutions (including universities, scientific councils, start-up companies, maker spaces, biotechnology-governing authorities and other biosciences platforms) with roughly equal numbers representing the UK, South Africa and the rest of Africa (Appendix 1). These included potential



collaborative partners such as UP, CSIR, University of the Witwatersrand, Stellenbosch University and Azargen Biotechnologies in South Africa, the BecA-ILRI Hub and Foondi Workshops in Kenya, the National Biotechnology Development Agency in Nigeria, the Pontificia Universidad Católica de Chile in Chile, and UK-based synthetic biology leaders and OpenPlant members such as the University of Cambridge, the Earlham Institute, the John Innes Institution, Imperial College London, the University of Edinburgh, and the Centre for Global Equality.

In order to introduce a wide range of South African researchers and potential partners to synthetic biology, an open symposium was held at the Encore Theatre in Pretoria on Friday 24th February, 2017. The symposium attracted 90 attendees including students, researchers, industry professionals, government departments, implementing agencies and science councils from twenty-three institutions as well as representatives from other African nations such as Kenya and Nigeria. The workshop opened with an introduction to the GCRF mandate and the workshop aims, followed by an introduction to the South African Bioeconomy Strategy by the Department of Science and Technology (Ben Durham, Chief Director of BioInnovations) and the University of Pretoria (Zander Myburg, Director: Forest Molecular Genetics programme).

Several UK speakers introduced synthetic biology principles, specific technologies with major transformative potential for the African bioeconomy, the role of open tools in synthetic biology and training and education initiatives in both the UK and Africa. These topics were expanded in two panel discussions focused on innovative applications and education with panellists from the UK and South, West and East Africa.

PRETORIA SYMPOSIUM

Panel: Practical applications for Africa

Panel:

Prof Lucy Ogbadu, Dr Musa Mhlanga, Dr Tsepo Tsekoa, Dr Lara Allen, Prof Zander Myburg, Prof Anne Osbourn, Dr Nicola Patron & Prof Jim Haseloff

The panel discussions included contributions from the audience. Major topics raised included access to technologies and freedom to operate while enabling value creation and economic growth

PRETORIA SYMPOSIUM

Panel: Shared training and education for Africa and UK

Panel:

Dr Kevin Land, Prof Bernard Slippers, Ms Marian Muthui, Ms Carol Ibe, Dr Eschar Mizrachi, Dr Fernán Federici, Ms Carol Ibe & Dr Jenny Molloy

Major topics included the importance of practical education and need for creativity in curriculum development, particularly in the African context of rapid growth in student numbers. There were clear unmet needs and a desire to more closely integrate scientific training with engineering, art, design, creativity and making.

PRETORIA SYMPOSIUM

SESSION 1

Global Challenges Research Fund

Dr Steven Hussey & Prof Jim Haseloff

The Bioeconomy in Africa

Ben Durham, Prof Zander Myburg

Reusable DNA parts and modular assembly

Dr Nicola Patron

Rapid prototyping and engineering of plant-based natural products

Prof Anne Osbourn

PRETORIA SYMPOSIUM

SESSION 2

Cell-free expression systems

Dr Fernán Federici

Africa-UK training

Ms Carol Ibe

Open tools for synthetic biology

Dr Jenny Molloy

Workshop Methodology II

BAKUBUNG LODGE RETREAT

The twenty eight strategic workshop participants (representing the UK, South Africa, Nigeria and Kenya) travelled to Bakubung Lodge in Pilanesberg National Park for in-depth discussions over three days following the open symposium. Initial sessions focused on introductions and discovering mutual connections and interests.

On considering the technologies presented in Friday's open symposium and current needs, the participants were divided into five multidisciplinary groups to propose a list of priority areas where synthetic biology might practically be applied to African challenges, basing their selection on the feasibility of the idea as a GCRF project and the potential positive impact on social and economic development as per the UK's overseas development aid (ODA) criteria. The areas were further prioritised by a dot-voting system.

Pathways to implementation were drafted in self-selected groups focusing on the top five ideas, taking advantage of the very wide range of expertise in the group. This included relevant contexts, barriers, bottlenecks and ideas of how to overcome them. The final workshop session built on these



pathways to identify the players that should be involved in implementing them, synergies between the represented UK and African groups, and the type of funding calls which might adequately address the identified needs.



BAKUBUNG WORKSHOP

Pathways to advanced, sustainable biotechnologies

This session took the ideas generated in the earlier session and identified pathways to implementation, including relevant context, barriers, bottlenecks and ideas of how to overcome them. Common threads from the focused discussions were drawn together to describe more general pathways to using synthetic biology and other biotechnologies that could contribute to a sustainable bioeconomy.

Objective 4

To identify a potential framework and pathways for implementation.

Objective 5

To estimate technical and resource deficits, and scale of investments required.

BAKUBUNG WORKSHOP

Breakaway sessions and report drafting

Unstructured time allowed participants to refine ideas from the earlier sessions and discuss them in greater detail. The participants then shared duties to generate the first draft of this report. Additional documentation and editing was coordinated online after the workshop.

BAKUBUNG WORKSHOP

Discussions on practical synthetic biology

This session aimed to stimulate discussion of the technologies presented in the Pretoria open symposium and generate prioritised views of key areas where synthetic biology might practically be applied to African challenges. The results framed discussions during the later sessions.

Objective 1

To share knowledge of new technologies: (i) Cell-free synthetic biology (ii) Transient expression in plants (iii) Genome editing in orphan crops.

Objective 2

To identify key problems that might be addressed by application of these technologies, to include field applications, research capacity building and education.

Objective 3

To generate priority lists for research and investment.

BAKUBUNG WORKSHOP

Partnerships for implementation

This session aimed to identify pathways for implementation, including participants and extended networks and other partners who might be engaged, and to identify synergies between groups in the UK and Africa.

Objective 6

To identify synergies between UK and African groups and the potential for technical connections between southern and east Africa hubs.

Objective 7

To estimate technical and resource deficits, and scale of investments required.

IDENTIFICATION OF BOTTLENECKS AND OPPORTUNITIES

In order for the goals of the GCRF regarding positive social and economic impact on ODA-eligible countries to be most effectively and efficiently achieved, the following cross-cutting themes should be integrated into the implementation of specific technological solutions.

BOTTLENECK AND OPPORTUNITY I

Open Technologies

Open technologies allow for an unrestricted legal right to use, reuse and redistribute materials for all purposes, including commercial applications. Beyond legal aspects, open approaches provide mechanisms for organizing knowledge production that favour (a) universal versus restricted access e.g. availability of specific molecular tools unencumbered by intellectual property, (b) universal versus restricted participation e.g. greater involvement of beneficiaries in shaping projects using those tools, and (c) collaborative versus centralized production e.g. multiple partners working together for a common goal (Smith et al., 2008). For example, open designs for making lab equipment are intended to be documented in such a way that others can make the equipment locally, allowing social and professional communities to grow around the shared resource.

The workshop participants supported openness as an underpinning concept for GCRF calls, where all applicants should be required to justify their approach to sharing or protecting their work and how their strategy maximises ODA-relevant impact. Global challenges benefit more from unrestricted deployment of scientific knowledge and tools.

Openness has a range of potential impacts (see table opposite). Importantly, while the group were unanimous



OPENLY LICENSED OR PUBLIC DOMAIN TOOLS WILL ACCELERATE THE PACE OF INNOVATION

in the need to consider open approaches in synthetic biology for the African bioeconomy, they agreed that this is likely to form part of a two-tier strategy. Openly licensed or public domain tools will accelerate the pace of innovation, but at some point, investment and enterprise may require protection of specific applications - in order to best add value, create economic benefits and sustain activities. There are some situations where openness may impede deployment or run contrary to the needs of the beneficiaries (e.g. through precluding necessary investment in a technology or disadvantaging indigenous populations).

There are many examples of successful companies with intellectual property based on open technologies and a wide variety of business models that are not based on intellectual property as the key mechanism for capturing value, but instead rely on differentiation by quality, manufacturing, distribution channels and marketing, among other mechanisms. These approaches are well-suited for use in emerging bioeconomies.

Potential Impacts of Open Technologies

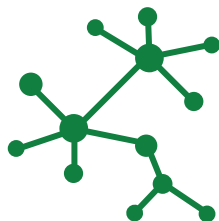
FREEDOM TO OPERATE



Enhance freedom-to-operate for entrepreneurs and companies without onerous and expensive licensing requirements, enabling value creation and small-scale, local enterprise.

OpenPlant and the BioBricks Foundation are collaborating to implement the Open Material Transfer Agreement (OpenMTA), a simple, standardized legal tool that enables open sharing of biological materials (<http://www.openmta.org>)

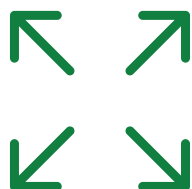
DECENTRALISED



Enable decentralised collaboration for pre-competitive innovation

For example, the Structural Genome Consortium shares open data on human proteins, de-risking high failure rate research for its funding consortium of pharmaceutical companies who then go on to formulate and commercialise promising therapies (Grundy et al., 2014).

SCALABLE



Enable opportunities for scalability of projects, particularly in small and under-resourced scientific communities.

Network is a cooperative grassroots research effort to address questions of global change through a network of forty grassland sites around the world (Stokstad, 2011).

ACCELERATED



Accelerate the pace of research through sharing and reduce time to translation and deployment.

For example, the Synaptic Leap and Structural Genome Consortium have demonstrably accelerated drug discovery research (Lee, 2015; Woelfle et al., 2011).

DE-RISKED



Reduce duplication of effort and inadvertent lock-in.

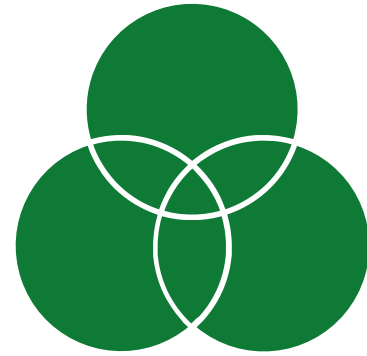
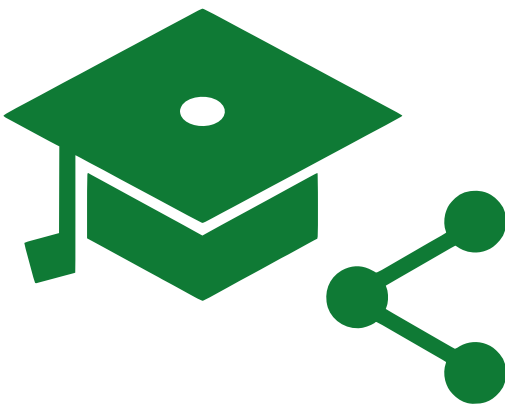
Working with patented underpinning technologies in research and development can require extensive negotiation, licensing or redesign at the stage of commercialisation or implementation.

BOTTLENECK AND OPPORTUNITY II

Education and Training

Modern biotechnology is exemplified by the growing field of Synthetic Biology, where formal engineering principles and practices are being incorporated into biology. Generally, the costs of biological fabrication and testing are low compared to other high technology industries, and living products, such as crops, pharmaceuticals and bioproduction systems, can be self-propagating. A number of parallels can be drawn between writing computer software and writing DNA code, where participation can be relatively cheap, the output can have a high value, and progress can be self-sustaining. However these are both knowledge-based activities, and success is directly linked to (i) availability of adequate education and training resources, (ii) opportunities to access these, and (iii) the ability to transfer skills and innovations from an educational system to market.

The Synthetic Biology field is providing new resources and approaches that offer prospects for dramatic improvements to teaching. For example, standardisation and modularisation of DNA engineering allows “de-skilling” and acceleration of complicated assembly processes, and new in vitro systems offer remote bioproduction and simple testing of DNA circuits without cold-chains, expensive laboratory equipment and containment facilities. The National Centre for Biotechnology Education (NCBE) in the UK has pioneered the co-development of pedagogy and accessible, cheap curriculum materials. Many African educational institutions suffer from underfunding and large student numbers, and would benefit from access to low-cost, state-of-the-art teaching materials. Just as



the biological components of the kits are becoming more modular and easier to use, there is an opportunity to develop modular curriculum elements that could be easier to implement in different educational and training environments.

BOTTLENECK AND OPPORTUNITY III

Interdisciplinarity

Interdisciplinarity is pervasive in Synthetic Biology applications and should be strongly encouraged in GCRF funding proposals. An understanding of the social, political, economic and cultural contexts of project sites, along with their legal and regulatory environments, should be demonstrated at the outset. Responses to contextual opportunities and challenges identified should be integrated into the project design through interdisciplinary collaboration throughout the project lifecycle. Particular attention should be paid to the perspectives of end users, from problem identification to implementation. Examples might include:

- Collaboration with the social sciences to understand the perspectives of end users and other stakeholders before, during and after the intervention.
- Collaboration with disciplines making downstream use of the new technologies, such as the medical or agricultural sciences.
- Using new and traditional media and visual and performing arts to generate informed public dialogue about the opportunities and risks of the new technologies and to facilitate enhanced understanding.
- Identification of policy, regulatory and legal gaps and bottlenecks; and interdisciplinary collaborations to

devise mechanisms to address these.

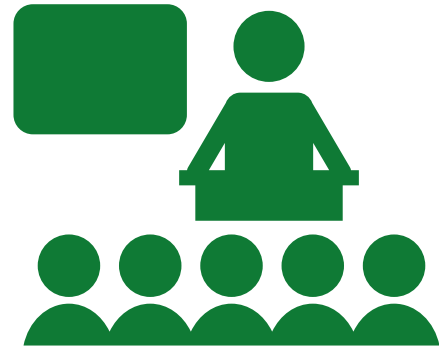
- Collaboration with other biological and physical sciences and engineering to address technological challenges.
- Collaboration with industrial designers who use a user-centred design approach to develop context-appropriate tools and devices.

We encourage reflection of this principle in the setup and scope of funding calls under the GCRF.

BOTTLENECK AND OPPORTUNITY IV

Linkages between institutional hubs in African countries

It is evident that facilities within African countries range from cutting-edge, high-value infrastructure hubs, to basic-level working spaces in a research or learning institution. Proposals to implement Synthetic Biology approaches therefore need to seek ways to address these differences both within and between countries. Proposals should not necessitate that all participating countries and institutions have the same facilities in order to be productive participants from the outset, and should seek to find mechanisms that enable the implementation of cutting edge technologies across the diverse existing resource spectrum. For example, good examples exist of practical training courses being conducted in low-resource environments, as well as experiments being performed with low-cost fabricated or purchased equipment.



New technologies also offer opportunities for distributed, parallel development across UK facilities and multiple African institutions. As a specific example, production of biomolecules (vaccines, biologicals, natural products and others) could leverage new DNA assembly and genetic cloning technologies using standard building blocks supplied to researchers for scaling from proof of concept to laboratory-scale production in microbial, mammalian or plant expression systems; or potentially in cell-free systems requiring fewer resources.

Despite these new opportunities, building capacity in multiple countries simultaneously remains challenging and proposals should articulate the role of regional hubs in knowledge exchange for systematically developing the continent-wide bioeconomy through the tools of Synthetic Biology. Regional hubs have the potential to bridge the gap between existing Centres of Excellence and countries that are much earlier in the development of their biotechnology capacity. As an example, South Africa has capacity to provide administrative and financial management skills as well as a regional scientific hub, working closely with other regional hubs such as Biosciences Eastern and Central Africa (BecA-ILRI Hub, Kenya). Proposals should also indicate how existing continental initiatives; such as the African Regional Universities Alliance (ARUA), UP's Future Africa Initiative, and the CSIR's Africa Strategy; will be engaged to build networks and roll out initiatives across the continent.

Regions have differing needs and priorities but proposals should also address cross-cutting issues pertinent to the continent, while remaining mindful of the diversity of cultures, languages, scientific strengths and capacity across different countries and regions.

BOTTLENECK AND OPPORTUNITY V

Stimulating public-private investment in capacity building

Establishing local facilities is an essential long-term goal for developing Synthetic Biology research expertise in the African context and expanding capacity at all levels, from basic labs through to integrated centralised facilities. Initial grant funding opportunities will need to be complemented or bolstered with additional funds for longer-term sustainability and impact. To support bioeconomy strategy development and implementation in several African countries, funding sources other than the GCRF will need to be leveraged. We propose that GCRF calls should favour proposals that seek to match GCRF grants with co-investment from external funds for facility and training capacity building, and/or through integration of proposed activities and upgrades with existing structures and programmes to mutually benefit the success of these structures and increase prospects for sustained co-funding by future investors.



BOTTLENECK AND OPPORTUNITY VI

Commercialisation and economic development

New breakthroughs that address challenge-driven projects need to be translated into commercial propositions, both to ensure that the technology is accessible to beneficiaries at scale and to capture economic value for Africa in a locally sustainable manner. Proposals should seek to capture economic value in creative ways and proposers of GCRF-funded projects should be supported as they seek to build appropriate value propositions. Two specific activities for GCRF support were identified:

- (i) Proposals seeking to develop capacity to progress technologies to Technology Readiness Levels (TRLs) 4 and 5. Examples would include a multinational manufacturing facility capable of taking research projects and performing quality assured pilot scale production. This is necessary to secure further investment for production scaling and subsequent commercial exploitation. All such facilities should be developed in Africa to ensure that value remains in African nations.
- (ii) Training in bioenterprise would help foster an entrepreneurial culture. Programmes that develop business models through real-world training by engaging with entrepreneurs and business mentors should be encouraged. These would also develop awareness of business skills in IP, business models, regulatory and quality requirements and finance.

CASES FOR IMPLEMENTATION

Workshop participants were in agreement that the combination of existing research capacity in synthetic biology in the UK and scientific excellence and research infrastructure in South Africa and select African countries could synergise to address Sustainable Development Goals in resource-challenged African regions.

Six research themes where synthetic biology might be able to provide solutions were prioritised for discussion in this report: (i) rapid-response production of vaccines and biologics, (ii) cold-chain free in vitro technologies for biosensing and bioproduction, (iii) capacity building for biotechnology research and educations, (iv) harnessing local biodiversity to build a sustainable bioeconomy, (v) improvement of commodity and orphan crops in Africa, and (vi) low-cost diagnostics and biosensors.

Given that responsible innovation is integral to the

practice of synthetic biology, all of the proposed research themes include mechanisms for knowledge exchange, capacity building and education in order to enable locally led, locally-appropriate solutions to deliver social and economic benefits.

The group noted that projects were only likely to produce practical solutions and achieve social impact if there was a significant focus on (i) building local expertise in the necessary technologies through knowledge exchange (ii) establishing the necessary facilities and distribution centre(s) of open-source tools and materials, and (iii) developing tools for training and education in biotechnology suitable for use in resource-poor regions or institutes.

EXISTING RESEARCH CAPACITY IN SYNTHETIC BIOLOGY IN THE UK AND SCIENTIFIC EXCELLENCE AND RESEARCH INFRASTRUCTURE IN SOUTH AFRICA AND SELECT AFRICAN COUNTRIES COULD SYNERGISE TO ADDRESS SUSTAINABLE DEVELOPMENT GOALS IN RESOURCE-CHALLENGED AFRICAN REGIONS.

CASE FOR IMPLEMENTATION I

Rapid-response production of vaccines and other biologicals in plants

A significant number of challenges faced by agriculture, medicine and industry in Africa may be addressed through increased access to biological production platforms. Plant-based transient production provides significant potential for fast, low cost, scalable and high yield production of materials such as vaccines, antibodies and small molecules for therapeutic and industrial applications (e.g. biocatalysts, biorefining, waste stream processing) (Merlin et al., 2014). Importantly, plant platforms are easier to implement in low-resource environments compared to other systems (Peyret and Lomonossoff, 2015).

Agroinfiltration of the leaves of *Nicotiana benthamiana* (a relative of tobacco) is an established and cost-effective platform for transient heterologous production of high yields of proteins and other biological molecules in a short amount of time. The method has also been scaled for both translational research and commercial production of high-value products (e.g. Leaf Systems, UK; Medicago,



Canada; and Kentucky Bioprocessing, USA). Plant transient expression has been used for some time in South Africa (e.g. CSIR and University of Cape Town) and therefore expertise and capacity exist. Combined with knowledge transfer, training and the provision of open tools (e.g. plasmids, DNA parts and assembly techniques), these platforms could be further scaled and replicated in other African regions to enable the production and commercial development of biological products of local importance and interest. The rapidity and scalability of transient heterologous production allows the ability to respond rapidly to disease outbreaks (e.g. through capacity for production of vaccines and therapeutics), create spin-

off enterprises, and establish strategic commercial partnerships. For commercialisation, use of foundational open tools provides freedom to operate while retaining the possibility of patenting novel developments to secure investment.

The current barriers to the wider implementation of plant expression systems in Africa, particularly in resource-scarce regions, include a lack of access to the necessary tools, infrastructure, technologies and expertise and high upfront cost for use at translational and commercial scales. Lack of local production chassis for natural products is an interesting area for Synthetic Biology exploration through identification of local plant species with novel traits (e.g. metabolic pathways, orphan genes).

CASE FOR IMPLEMENTATION II

Cold-chain free in vitro expression systems for field use

While synthetic biology approaches could be applied to solve problems in diverse areas such as diagnostics and bioproduction, the timescales for deregulation and release of bioengineered organisms are uncertain, particularly in the many African countries where regulatory processes are not yet in place or GMO technology is contested (Adenle et al., 2011). Additionally, while there is a strong demand for low-cost materials and resources for teaching applied sciences such as biotechnology, the lack of underlying infrastructure in the low-resource environments of many African countries means that maintaining a typical molecular biology laboratory is fraught with challenges. For practical training in synthetic biology in African schools and universities to succeed, and to stimulate the establishment of bio-maker spaces to facilitate informal education and innovation, there is a requirement for non-GM, rapid, cheap and safe materials.



Cell-free expression systems can be used for the development and optimization of synthetic gene networks. They have already been leveraged for the rapid screening of gene constructs and the application of the paper-based platforms for programmable in vitro diagnostics of human pathogens (Pardee et al., 2016), and can be coupled to existing microfluidics expertise at the Council for Scientific and Industrial Research (CSIR) in South Africa.

This technology has the potential to overcome the bio-containment issues inherent with the use of live cells as biological chassis since living cells are not required. As a consequence, deploying tools outside of the laboratory environment (e.g. point-of-use biosensors for diagnostic applications) is more likely with cell-free systems with their vastly reduced regulatory burden and cell-free applications are therefore more likely than cell-based systems to achieve social impact in the short to medium term.

The avoidance of living cells also makes cell-free systems particularly well adapted to education in low-resource environment (Garamella et al., 2016), where cell extracts and reagents can be stabilized for storage at ambient temperatures, negating the need for cryostorage and reliable electricity supply that are required for living cells. They are likely to be an effective and affordable system for implementation in African training and education programs fashioned on competition models such as iGEM (www.igem.org).

CASE FOR IMPLEMENTATION III

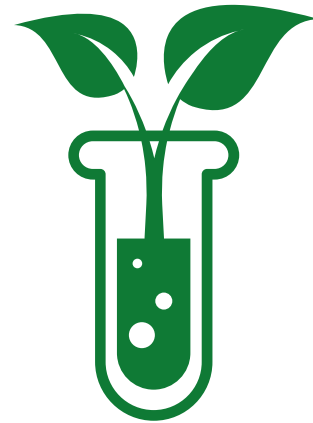
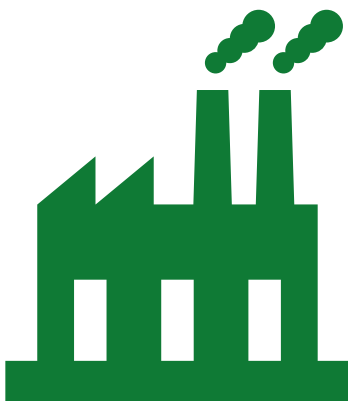
Capacity building in Africa for biotechnology education and research

Capacity building is a key requirement for developing partnerships in African research institutions and developing the African bioeconomy through Synthetic biology. Academic research capacity is generally underdeveloped in low- and middle-income countries (LMICs). Broad expansion of academic capacity to established and limi-

ted-resource research institutions is important to achieve impact (Van der Stocken et al., 2016). Access to standard biological reagents and laboratory equipment required for synthetic biology research are limited due to relatively high costs (e.g. international import costs, unfavourable currency exchange rates and price markups by local distributors). This drives up operational costs and is slowing the evolution of the continent's bioeconomy. Furthermore, the training capacity to implement basic molecular biology techniques (e.g. DNA manipulation and cloning) and use new synthetic biology tools (e.g. high-throughput DNA construct assembly, cell free systems, plant transient expression systems) to investigate biological problems is generally lacking (Vicente-Crespo et al., 2016).

There are currently no established African facilities that develop and manufacture materials and reagents required for synthetic biology such as basic molecular biology reagents and enzymes. Similarly, there are no facilities that make or supply open-source laboratory hardware (e.g. 3D-printed gel tanks, pipettes, microscopes) or biological parts and cell-free expression systems available to regional education and research institutions. The establishment of national or regional suppliers of low-cost, reliable, basic molecular biology consumables and equipment, together with strategic investment into facility upgrades, would significantly enhance the continent's capacity in Synthetic Biology at all levels, from educational labs to high-throughput, centralised bioeconomy research facilities.

The adoption of cutting edge Synthetic Biology tools and standard approaches would significantly enhance research capabilities; because much smaller reagent sets are required and the reagents are often non-proprietary. Synthetic Biology approaches are often cheaper than traditional molecular biology (e.g. Golden Gate Cloning and Gibson Assembly DNA assembly methods, compared to Gateway®). Furthermore, by combining the supply of inexpensive, locally manufactured reagents and open-source DNA parts with workshops to coach trainers, best practice can be shared effectively across African universities and research institutes. Co-ordinating the supply of reagents and open-source parts with UK-led training workshops for current and potential customers will accelerate knowledge transfer and technology uptake at facilities where Synthetic Biology research is relevant and needed. These could take place in the UK. However, greater reach would



be achieved if UK scientists provide local workshops co-ordinated with the distribution of open components and tools. A combination of locally made and distributed tools, technologies and training would provide a powerful mechanism to build and sustain the African bioeconomy through practical application of Synthetic Biology.

CASE FOR IMPLEMENTATION IV

Harnessing biodiversity for a sustainable bioeconomy

The Convention for BioDiversity (CBD) and the recent supplementary agreement known as the Nagoya Protocol on Access and Benefit Sharing, recognise the sovereign rights of nations to derive benefits from their biodiversity. The CBD has already recognised eight biodiversity hotspots in Africa. Three are in South Africa, in whole or in part, and the South African plan for developing a sustainable bioeconomy emphasizes harnessing the country's unique biodiversity to create jobs, industry and revenue, aiming to create a skilled local workforce and facilitate translation into sustainable businesses.

The advanced technologies and expertise available in the UK for metabolite analysis, genomics, data mining and pathway (re)construction using metabolic engineering offer an excellent training opportunity for African scientists to become skilled in these areas, so complementing their interests in particular indigenous flora and their traditional uses. This would build skills that could support authentication of the quality of traditional medicines and open up opportunities and lead to new areas of innovation. As all such work is required to be compliant with the CBD/ Nagoya Protocol and national laws such as the South African Biodiversity Act (2004, 2006), a social science stream should be integrated into any such initiatives. In particu-

lar, translational research of African native species raises concerns of, for example, the inequitable exploitation of indigenous knowledge, or the possibility of irresponsible bioprospecting of sensitive fauna and flora that could lead to their decimation for financial gain.

While knowledge exchange to allow local populations to harness their biodiversity may be an achievable short-term goal in South Africa, which has scientific infrastructure as well as relevant laws and treaties (see <http://www.wipo.int/wipolex/en/profile.jsp?code=ZA>), it would be hard to replicate in African nations without similar regulatory frameworks. However, initiatives like Future Africa could be leveraged to establish a conduit for inclusive knowledge exchange with the wider African scientific community and core activities such as training and capacity building would enable fair and equitable access to the necessary knowledge, skills and expertise in Synthetic Biology to allow scientists across Africa to harness the unique biodiversity of their local environs to create sustainable bioeconomies that have the potential to solve local problems in health and industry and that achieve global impact.



CASE FOR IMPLEMENTATION V

Improvement of commodity and orphan crops in Africa

The African continent is exceptionally diverse in terms of climate (e.g. temperate, cold, arid, semi-arid, warm subtropical, Mediterranean, tropical savannah, monsoon), rainfall (less than 10 mm to over 3000 mm per annum), vegetation type (e.g. desert, grassland, fynbos, savanna, rainforest, afro-montane), orphan crop cultivation (e.g. cassava, finger millet, amaranth, okra, fava bean) and adoption of subsistence vs. commercial agriculture models. These factors necessitate the genetic improvement of commodity crops for regional cultivation through breeding with local germplasm and the accelerated improvement of orphan crops.

African workshop participants therefore expressed a strong desire for training in, and tools for, genome engineering that can be used to rapidly engineer and fix desirable traits into crops using programmable nucleases (e.g. CRISPR/Cas9) without integrated transgenes, as demonstrated in barley and Brassicas (Lawrenson et al., 2015) and wheat (Zhang et al., 2016). Such techniques are attractive because it is believed that the regulatory burden for transgene-free targeted mutagenesis is likely to be far less onerous than for transgenics and there is hence more likelihood of achieving positive social impact in the medium-term.

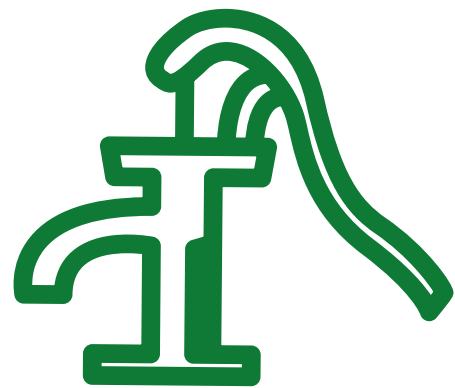
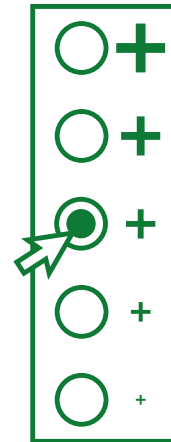
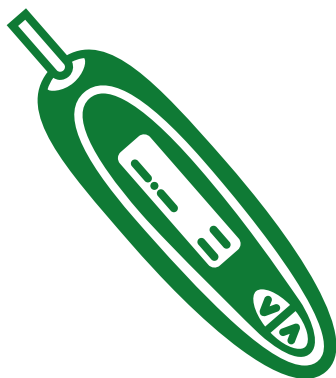
However, research needs to be informed by a sound knowledge of the socio-economic factors surrounding the cultivation of commodity and orphan crops in Africa, particularly on edible species (e.g. the feasibility and likely impact of genome editing, traditional or molecular breeding, and genetic modification), as well as farmers' experience with local pests and diseases. Recognition of the importance of investigating the unique needs of end-users in different regions, is demonstrated by the establishment

by the Bill and Melinda Gates Foundation of an Agricultural Development Strategy that considers farmer-based knowledge and feedback to ensure their needs are addressed. In projects such as the Next Generation Cassava Breeding Project, researchers are supplementing regional germplasm from other geographical sources in breeding programmes, training future plant breeders and holding awareness-promoting workshops to inform stakeholders and communities of new agricultural approaches. The implementation of relevant and high-impact genome editing, precision breeding and other genetic improvement projects for African crop systems requires a similar level of socio-economic evaluation of the issues faced by local farmers, before during and after interventions.

CASE FOR IMPLEMENTATION VI

Low-cost diagnostics and biosensors

The Convention for BioDiversity (CBD) and the recent supplementary agreement known as the Nagoya Protocol on Access and Benefit Sharing, recognise the sovereign rights of nations to derive benefits from their biodiversity. The CBD has already recognised eight biodiversity hotspots in Africa. Three are in South Africa, in whole or in part, and the South African plan for developing a sustainable bioeconomy emphasizes harnessing the country's unique biodiversity to create jobs, industry and revenue, aiming to create a skilled local workforce and facilitate translation into sustainable businesses. The advanced technologies and expertise available in the UK for metabolite analysis, genomics, data mining and pathway (re)construction using metabolic engineering offer an excellent training opportunity for African scientists to become skilled in these areas, so complementing their interests in particular indigenous flora and their traditional uses. This would build skills that could support authentication of the quality of traditional medicines and open

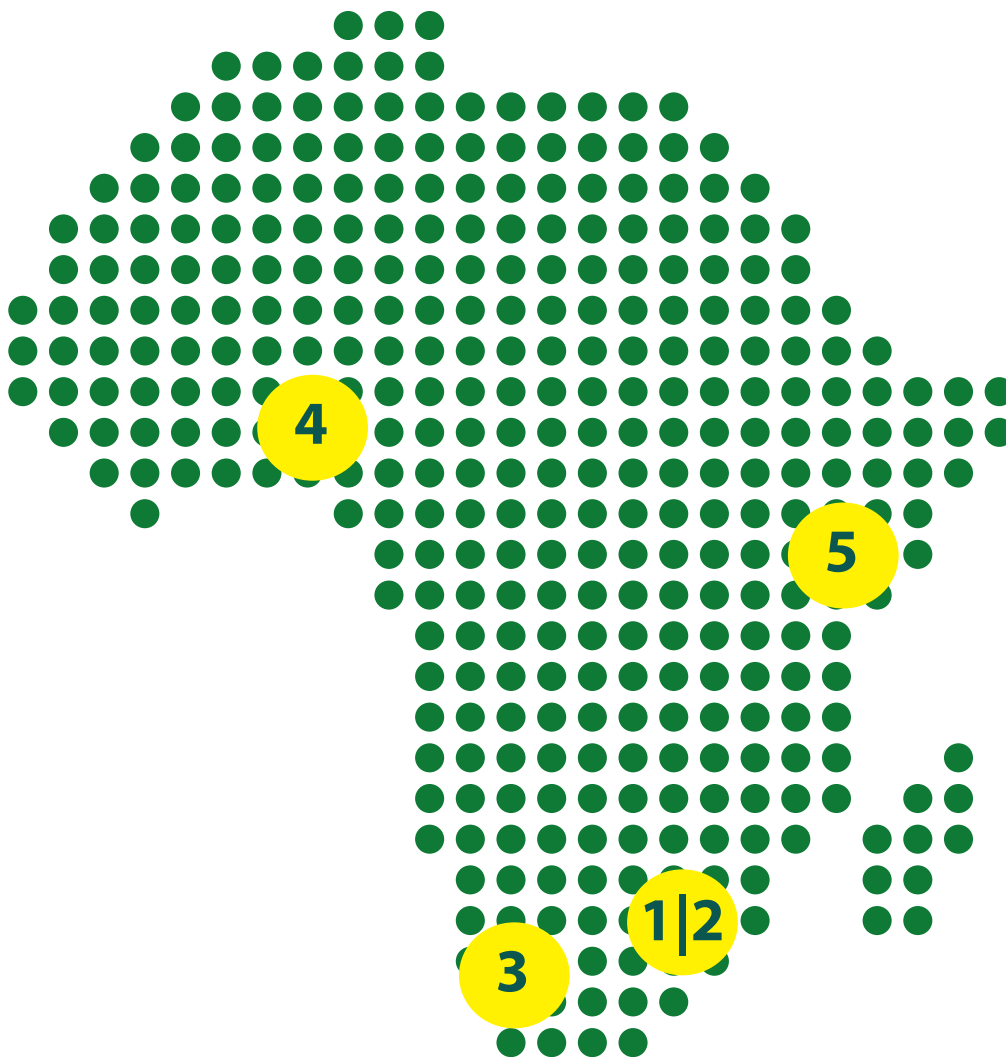


up opportunities and lead to new areas of innovation. As all such work is required to be compliant with the CBD/ Nagoya Protocol and national laws such as the South African Biodiversity Act (2004, 2006), a social science stream should be integrated into any such initiatives. In particular, translational research of African native species raises concerns of, for example, the inequitable exploitation of indigenous knowledge, or the possibility of irresponsible bioprospecting of sensitive fauna and flora that could lead to their decimation for financial gain. While knowledge exchange to allow local populations to harness their biodiversity may be an achievable short-term goal in South Africa, which has scientific infrastructure as well as relevant laws and treaties (see <http://www.wipo.int/wipolex/en/profile.jsp?code=ZA>), it would be hard to replicate in African nations without similar regulatory frameworks. However, initiatives like Future Africa could be leveraged to establish a conduit for inclusive knowledge exchange with the wider African scientific community and core activities such as training and capacity building would enable fair and equitable access to the necessary knowledge, skills and expertise in Synthetic Biology to allow scientists across Africa to harness the unique biodiversity of their local environs to create sustainable bioeconomies that have the potential to solve local problems in health and industry and that achieve global impact.

STRATEGIC PARTNERS AND SYNERGIES

High-impact outcomes are most likely to arise from collaborations between leading institutions in the UK and Africa that combine complementary expertise and capabilities towards a common challenge. There is strong interest in forming such strategic partnerships.

During discussions at the workshop, a number of potential synergistic partnerships were considered as examples of possible GCRF-supported collaborations. These include the following examples, which by no means represent an exhaustive list.



SOUTHERN AFRICA

South Africa was host to the workshop and has a national bioeconomy strategy and emerging centres of national and regional excellence.

EAST AFRICA

The BecA-ILRI Hub in Kenya serves as the focal point for our interactions with East African Bioscientists and there are numerous linked initiatives.

WEST AFRICA

Nigeria hosts the International Centre for Biotechnology which could serve as a platform for partnerships with the UK in research and training.

1

BIOPRODUCTION FACILITIES

Scaling up of microbial expression systems to 1000L fermenters is possible at the CSIR's Biomanufacturing Industry Development Centre (BIDC), and large-scale plant expression for early commercialization can be facilitated by Norwich's Leaf Systems International. If Good Manufacturing Practices conditions are a requisite for research projects proceeding to advanced TRL levels, an African facility specifically aimed at this purpose would be required.

2

PRECISION PLANT ENGINEERING

A Precision Plant Growth and Phenotyping Facility linked to a Bioeconomy Africa building dedicated to plant-based biomass bioengineering is planned to be integrated with the Future Africa campus currently being constructed at UP (<http://www.up.ac.za/future-africa>). Around 20% of the multidisciplinary research positions planned for the Bioeconomy Building will be reserved for international visiting scientists from Africa and the rest of the world, who can be accommodated at the adjoining Future Africa precinct. Synthetic biology and chemical engineering are envisaged as enabling components of the plant lignocellulose engineering focus of the facility.

3

MOLECULAR BIOLOGY TRAINING

At Stellenbosch University, the Institute for Wine Biotechnology (<http://www.sun.ac.za/english/faculty/agri/wine-biotech>) and the Institute for Plant Biotechnology (<http://www.sun.ac.za/english/faculty/agri/plant-biotech>) are the most likely candidates for participation in various aspects including skills training and capacity building. They also have a history of training researchers from Africa, such as a cohort of students from Gabon, in molecular biology. There is a Central Analytical Facility (<http://www.sun.ac.za/english/faculty/science/CAF/about-us>) at Stellenbosch University with genomic, proteomic and metabolomic services.

4

FOOD SECURITY AND TROPICAL DISEASE

A West African facility known as the International Centre for Biotechnology is a UNESCO category II centre hosted by Nigeria at the premises of the University of Nigeria Nsukka. The centre, when fully operational, is intended to advance teaching and research in biotechnology with a focus on food security and tropical diseases and could serve as a platform for partnerships with UK institutions in capacity building for sub-Saharan African scientists in synthetic biology.

5

LIVESTOCK DISEASE RESEARCH AND CAPACITY BUILDING

The BecA-ILRI Hub (<http://hub.africabiosciences.org>) is a facility established through the New Partnership for Africa's Development (AU/NEPAD) African Biosciences Initiative (ABI) to provide a common biosciences research platform, research-related services and capacity building opportunities to the region and beyond. Located in Nairobi, Kenya, and hosted and managed by the International Livestock Research Institute (ILRI), the Hub serves African scientists and innovations in different areas related to the following technology platforms/research areas: molecular biology and genomics, golden gate technologies, nutritional and diagnostics platforms, tissue culture and transformation.

RECOMMENDATIONS FOR GCRF CALLS

FOCUS AREAS AND GENERAL THEMES

The group concluded that a main focus of future GCRF calls should be capacity building for the African bioeconomy. Following UNICEF's Principles for Innovation and Technology in Development, which include the use of open standards, open data, open source, and open innovation (see: https://www.unicef.org/innovation/innovation_73239.html), emphasis should be placed on the development of open tools, co-funded facilities and resources, enabling technologies and training in Africa in order to address urgent needs in medicine, agriculture and industry.

Our priority areas for call topics relating to capacity development include:

1. Teaching and training resources to support fast and frugal innovation in bioengineering in low-resource environments
2. Adoption of cell-free expression systems for rapid prototyping
3. Transient plant-based expression for production of vaccines and bioeconomy-related biologicals
4. Responsible harnessing of plant and microbial biodiversity in synthetic biology
5. Low-cost and instrument-free diagnostics

BUDGET AND SCOPE OF FUNDING

We discussed the nature of calls that would adequately address these topics and considered that funding multidisciplinary networks focusing on clearly articulated challenges relating to capacity building for the African bioeconomy would be an appropriate mechanism and that calls of up to £10 million would be an appropriate scale. Due to the identification of interdisciplinarity as key to the success of the prioritised projects, we strongly encourage consideration of cross-council funding such as joint calls with the Economic and Social Sciences Research Council and Engineering and Physical Sciences Research Council.

There was discussion of the type of calls and whether separate calls are required for exchange and coordination activities or whether a larger combined call is preferable. There was no

consensus, but the following types of proposals are expected and required:

- Research projects
- Research coordination networks
- Capacity and capability strengthening
- Partnership building and research

Infrastructure development is highly challenging, thus building on available local infrastructure is critical. We recommend that GCRF calls consider this including:

- Investment in knowledge transfer at existing premier national and regional research facilities to produce reagents and open-source hardware tools (including quality-control processes, SOPs).
- A realistic purchasing remit to provide suitable lab and/or engineering equipment, where necessary, for reagent and tool production.
- Market research and development of relationships with local research institutions to establish demand and distribution requirements. Building partnerships with local suppliers may assist with distribution challenges.
- Middle-income countries with better-developed infrastructure and established or developing research facilities (e.g. South Africa, Kenya, Nigeria) may be more suitable targets for developing regional Synthetic Biology infrastructure.

Based on our discussion of underpinning concepts, the group would like to see all proposals i) demonstrating consideration of Responsible Research and Innovation principles, ii) justifying their approach to sharing and intellectual property rights to maximise impact for the intended beneficiaries, iii) demonstrating how the proposal builds on existing networks, facilities and frameworks to mitigate risks of ineffective collaborations, lack of dissemination or lack of knowledge of beneficiary needs, and iv) detailing the risks to the project above that are specific to the context of addressing global challenges and planning mitigation measures.

BIOLOGICAL ENGINEERING...HAS THE POTENTIAL TO ADDRESS MAJOR CHALLENGES FACING AFRICA.

CONCLUSIONS

Biological engineering through synthetic biology, and in particular new, rapid and non-GM tools, has the potential to develop the bioeconomies of several African countries and address major challenges facing the continent. In identifying and prioritising key applications of current synthetic biology technologies, there was a consensus among the participants of the scoping workshop that local expertise, training tools, capacity building and facility development are core focus areas that will achieve practical solutions with social impact.

Knowledge exchange between UK and Africa-based institutions, local production and distribution centres for open-source tools and materials, as well as cost-effective educational tools for synthetic biology training and interdis-

ciplinary innovation in resource challenged regions or institutions were regarded as key opportunities, among others.

The participants favour leveraging GCRF-funded projects to increase knowledge and open materials transfer and develop local capacity for cell-free and transient bioproduction systems with co-funded infrastructure at leading African and UK institutions.

It is intended that new strategic and synergistic partnerships between such “anchor” institutions across the African continent will facilitate the transfer of skills, synthetic biology materials and expertise to less-equipped regions to achieve the maximum impact.



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Dr Steven Hussey	Lecturer in Genetics and Group Leader	University of Pretoria/FABI, SA
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Prof Zander Myburg	Professor of Genetics and Head of Forest Molecular Genetics Programme	University of Pretoria/FABI, SA

In memoriam

DEAN MADDEN (1960-2017)

Dean was Director of the National Centre for Biotechnology Education (NCBE) at the University of Reading. The Centre, which was founded in 1986, develops low-cost molecular biology resources for schools and colleges, which are sold to 30 countries worldwide. Dean worked at the University since 1990 and was responsible for developing most of the resources sold by the NCBE, including the first genetic modification kit that could legally be used in European schools and bioinformatics teaching materials. He coordinated a 12-nation European Union-funded project 'Volvox', aimed at the electronic exchange of educational materials. He recent began to devise synthetic biology teaching materials that can be used within schools, while adhering to the restrictions that apply to genetic modification within the EU. Dean was formerly head of biology in a state secondary school in the UK and was awarded a fellowship to develop teaching materials at the University of Newcastle-upon-Tyne. He held an Honorary Doctorate from Gothenburg University. Dean developed some extraordinary teaching resources, which can be found at the NCBE website: <http://www.ncbe.reading.ac.uk>. These type of resources, in combination with new and open synthetic biology tools, provide powerful tools for promoting education in low-resource environments. Dean had embarked on exciting new collaborative projects funded by OpenPlant and was due to join us in Bakubung, before his sad and untimely death shortly before the workshop. He is much missed.

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**MORE BACKGROUND INFORMATION ABOUT THE WORKSHOP IS AVAILABLE AT:
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