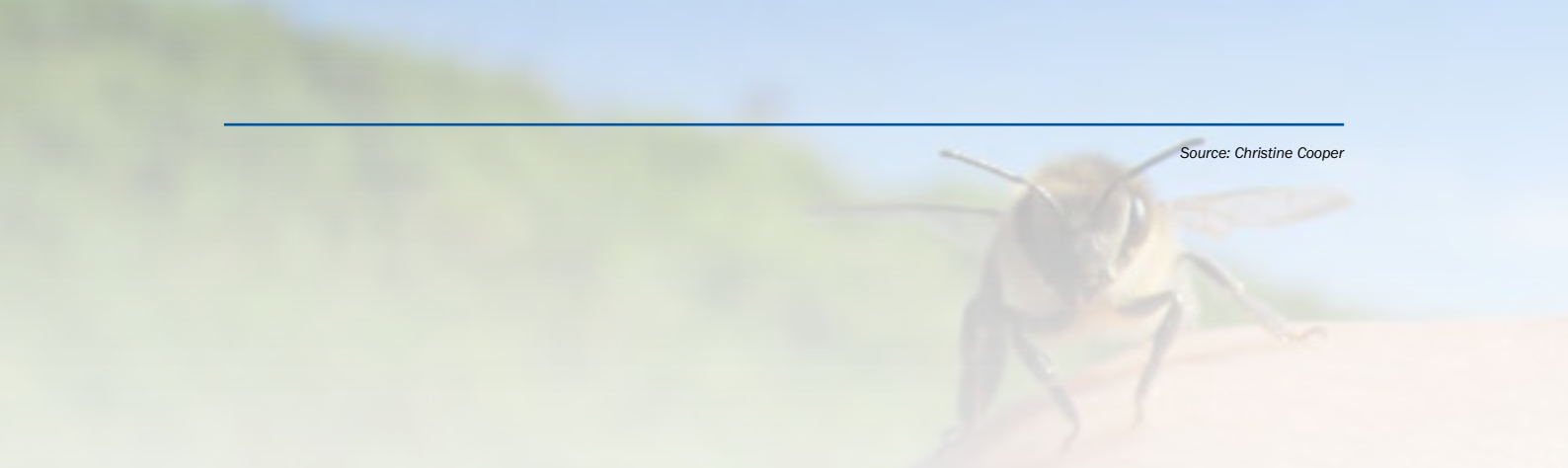


Source: Christine Cooper

D. POTENTIAL IMPACTS OF THE COMPONENTS, ORGANISMS AND PRODUCTS RESULTING FROM SYNTHETIC BIOLOGY TECHNIQUES ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY

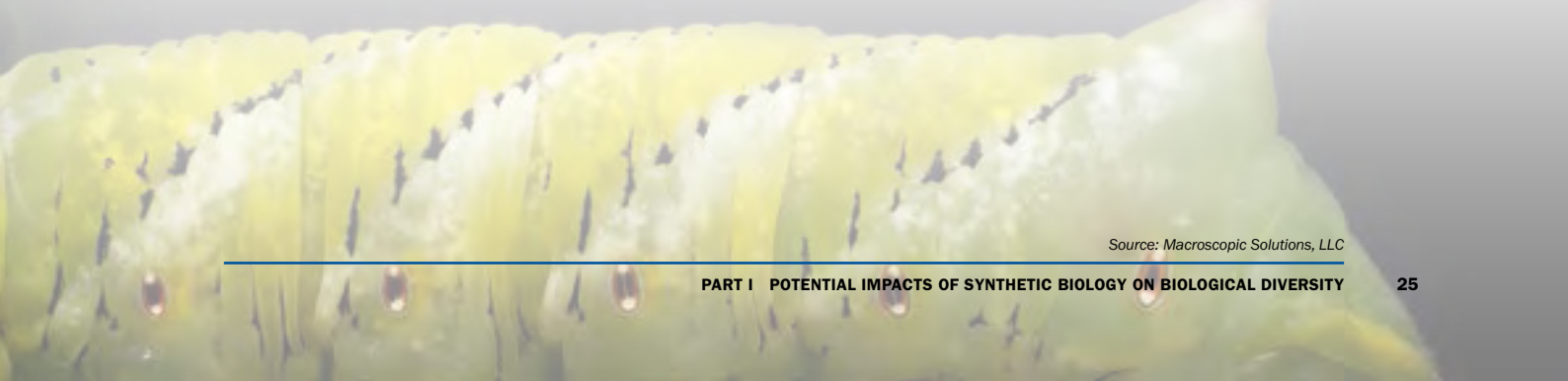
The conservation of biodiversity is one of three primary objectives of the CBD. The CBD's text defines *ex situ* conservation as "the conservation of components of biological diversity outside their natural habitats," and *in situ* conservation as "the conservation of ecosystems and natural habitats and the maintenance and recovery of viable populations of species in their natural surroundings and, in the case of domesticated or cultivated species, in the surroundings where they have developed their distinctive properties" (CBD, Art 2). The conservation of biological diversity occurs at all levels: genes, species and ecosystems.

Furthermore, in the context of the CBD, sustainable use is defined as "the use of components of biological diversity in a way and at a rate that does not lead to the long-term decline of biodiversity, thereby maintaining its potential to meet the needs and aspirations of present and future generations" (Art. 2). Sustainable use encompasses ecological, economic, social, cultural, and political factors (Glowka *et al*. 1994).

5. APPLICATIONS OF SYNTHETIC BIOLOGY AND THEIR POTENTIAL POSITIVE AND NEGATIVE IMPACTS

Although synthetic biology is often referred to as a coherent and single discipline presenting uniform benefits and dangers, the different areas of synthetic biology research represent different potential impacts, both negative and positive, on biodiversity-related issues.

This section discusses the potential impacts of components, organisms and products resulting from synthetic biology techniques on the conservation and sustainable use of biodiversity. A number of specific areas of current and potential applications of synthetic biology are described along with potential positive and negative impacts of these applications on the conservation and sustainable use of biodiversity. Table 1 at the end of this section summarizes examples of the potential positive and negative impacts of synthetic biology applications on conservation and sustainable use of biodiversity. Biosafety concerns of a more general nature are examined in section 6.



Source: Macroscopic Solutions, LLC

5.1. Bioenergy applications

Bioenergy applications, particularly through fuel production, are a significant focus of synthetic biology research (WWICS 2013a). As discussed above (section 4.2.1), biofuels produced using synthetic biology techniques are beginning to reach the stages of field testing, pilot runs, and relatively small-scale production. One area of research is to use synthetic biology tools to develop enzymes that break down a wider range of biomass more effectively, making it possible to utilize agricultural waste such as corn stalks and straw, and woody biomass (PCSBI 2010). Other approaches are to use synthetic biology to develop plants with more readily convertible biomass, or to engineer photosynthetic algae (including microalgae such as cyanobacteria) to produce more bio-oil (Georgianna & Mayfield 2012; PCSBI 2010). One goal of synthetic biology energy research is the production of consolidated bioprocessing platforms, such as *E. coli* engineered to both degrade biomass (without the external addition of enzymes) and convert biomass into biofuels (Bokinsky *et al*. 2011). The UKSBRCG (2012) describes synthetic biology research towards producing an artificial leaf that could convert solar energy into a carbon-based liquid fuel. The PCSBI (2010) describes synthetic biology research towards producing hydrogen fuel, from engineered algae to using starch and water via a synthetic enzymatic pathway. Synthetic biology tools are also expected to help design ways to harvest currently inaccessible hydrocarbons, such as coal bed methane (PCSBI 2010).

Claims that there could be significant benefits for biodiversity from replacing fossil fuel energy sources with bioenergy are based on the premise that these approaches could reduce global dependence on fossil fuels and cut harmful emissions at a significant scale (PCSBI 2010). Through the CBD's cross-cutting programme on climate change and biodiversity, CBD bodies have documented and assessed the interlinkages between the two areas.[34] Synthetic biology tools may be used in designing "next generation" biofuels that, it is hoped, will overcome challenges of "first generation" biofuels made from food crops (Webb & Coates 2012).

Potential negative impacts could result from the increased utilization of biomass for synthetic biology applications. "Biomass" is generally used to refer to the use of "non-fossilized biological and waste materials as a feedstock" (ETC 2011). Much synthetic biology research aims at designing organisms that will use biomass as feedstock to produce fuels, chemicals, and pharmaceuticals at greater efficiencies than have previously been possible (PCSBI 2010). For example: Solazyme (see above) uses heterotrophic algae, i.e. algae that are able to feed on sugar for their energy source rather than utilizing sunlight to produce sugar through photosynthesis. The advantage of heterotrophic algae is that they yield more oil but the clear disadvantage is they have to be fed, in this case with sugar, which in turn has to be sourced from biomass grown on land. Some products, such as biofuels, are relatively low-value and high volume, and thus would require large amounts of biomass. As described in *CBD Technical Series 65: Biofuels and Biodiversity*, there are contradicting studies on the sustainability of utilizing waste feedstocks such as corn stover and straw (Webb & Coates 2012). A number of studies in ecology, agronomy, and environmental history find that biomass extraction from existing agricultural practices is already leading to a decline in soil fertility and structure (Blanco-Canqui and Lal 2009; Wilhelm *et al*. 2007; Smil 2012). Studies done in the US have found that removing corn stover from fields would require significant additional use of nitrogen, phosphorous and potassium fertilizers (Blanco-Canqui and Lal 2009; Fixen 2007). In addition to the potential loss of ecological functions of the soil biomass, there is also concern around the social impacts of increased biomass removal. Some civil society groups are concerned that, in part due to increased demand from synthetic biology, the tropics and sub-tropics will be targeted for their biomass and lead to economic and environmental and cultural injustice (ETC 2010; FOE *et al*. 2012; FOE 2010). They predict that communities will lose local access to resources, sustainable uses will be displaced, and environmental harm will be caused by establishing plantations in former forests, harvesting natural grasslands, and placing pressures on "marginal" lands such as deserts and wetlands (ETC 2010). While synthetic biology techniques promise to open up new sources of energy, such as algae and seaweed, the ETC Group has expressed concern that these uses will encroach on coastal and desert ecosystems and their traditional uses (ETC 2013). The US PCSBI noted: "On balance, many anticipate the potential efficiencies and attendant reduction in reliance on fossil fuels offered by energy production using synthetic biology would offset anticipated risks to the environmental ecosystem as it exists today. But considerable uncertainty remains" (PCSBI 2010).

As will be discussed in more detail in section 6, there are biosafety considerations related to the accidental or intentional release of organisms resulting from synthetic biology techniques used for bioenergy purposes. For example, microalgae resulting from synthetic biology techniques for bioenergy purposes

34 See: http://www.cbd.int/climate, accessed 13 Feb. 2014.

may have ecological impacts, particularly if grown in open ponds and thus with a higher chance of accidental release (Snow & Smith 2012). Moreover, micro-organisms may be used in small-scale decentralized bioreactors (e.g. for production of biofuels on farms), and this could be considered to constitute a new kind of category in-between contained use in large industrial fermenters and full deliberate release. Marris and Jefferson (2013) argued that there are blurred boundaries between contained use and deliberate release of genetically modified micro-organisms (GMMO), and "these boundaries are likely to be further challenged if and when the GMMO applications envisaged by synthetic biologists for environmental, agricultural and mining uses enter the regulatory system, because those applications cover a whole spectrum in terms of the nature, scale, and time-horizon of the release".

5.2. Environmental applications

Another area of synthetic biology research is in environmental applications, most of which would require environmental release or contained use[35] outside of the laboratory of organisms resulting from synthetic biology techniques. Scientists anticipate the use of engineered microbial consortia, in part using tools of synthetic biology, to enhance mining metal recovery and to aid in acid mine drainage bioremediation (Brune and Bayer 2012). Synthetic biology techniques are being used to design whole-cell biosensors that will indicate the presence of a target, such as arsenic in drinking water. French *et al*. (2011) describe their work growing out of an iGEM project to design an arsenic biosensor that would be suitable for field use in developing countries, using freeze-dried transformed *E. coli* that change color in the presence of arsenic. The arsenic biosensor work is now being further developed by the "Arsenic Biosensor Collaboration" (http://arsenicbiosensor.org). In another example of an environmental application, the 2011 European Regional Jamboree winning iGEM project involved engineering *E. coli* to secrete auxin, a plant hormone intended to promote root growth. The Imperial College (UK) team proposed pre-coating seeds with the bacteria, to be planted in areas at risk from desertification.[36]

Since recombinant DNA technology was first introduced, the use of genetically engineered micro-organisms for bioremediation and other environmental applications "has been a holy grail" – much desired but constantly out of reach (Skerker *et al*. 2009). Synthetic biologists see the failure to deliver the anticipated or desired benefits as due to the lack of sophistication of classic genetic engineering techniques (Marris and Jefferson 2013). As a result, synthetic biologists are generally optimistic about the potential for synthetic biology to succeed where previous modified micro-organisms for environmental release have failed (Garfinkel and Friedman 2012; PCSBI 2010; Schmidt and de Lorenzo 2012; Skerker *et al*. 2009). If so, synthetic biology could provide less toxic and more effective tools for bioremediation, which would positively impact local biodiversity.

If synthetic biology succeeds in producing microbes that are sufficiently hardy for release into the environment, such microbes may raise significant biosafety concerns depending on their potential to survive and persist (König *et al*. 2013), as well as on their potential to interact with their immediate environment causing adverse effects. Some of these micro-organisms might present significant challenges for the risk assessment approaches that are currently in use by regulatory processes (see section 6). The WWICS Synthetic Biology Project held several workshops on aspects of the safety of environmental release of organisms resulting from synthetic biology, identifying key areas of uncertainty and areas for research, and discussing what "safety" means in the context of synthetic biology (see WWICS 2013b for notes from workshops from 2000 to 2012). One question is how an organism designed for environmental release can be robust enough to accomplish its intended task but not persist and become problematic (Anderson *et al*. 2012). Those optimistic about the role of microbes resulting from synthetic biology techniques tend to acknowledge the possibility of invasiveness and unintended effects, but they also invoke the (not yet realized) promise of xenobiology and other orthogonal systems with built-in biological containment measures (Marris and Jefferson 2013; PCSBI 2010; Schmidt and de Lorenzo 2012; Skerker *et al*. 2009).

35 *"Contained use", as defined in the Cartagena Protocol on Biosafety, article 3, paragraph (b), means any operation, undertaken within a facility, installation or other physical structure, which involves living modified organisms that are controlled by specific measures that effectively limit their contact with, and their impact on, the external environment.*

36 *See http://2011.igem.org/Team:Imperial_College_London, accessed on 5 June 2013. The team developed a bio-cotainment strategy ("Gene Guard") intended to prevent horizontal gene transfer, in response to concerns about the release of their organism into the environment. As French et al. (2011) explain, iGEM projects may not be as well-characterized as experiments reported on in peer-reviewed literature, but they are often based on highly creative ideas and can presage possible future applications in areas of synthetic biology. For this reason, they are often referenced when the powerful possibilities of synthetic biology are discussed. Dana et al. (2012) cite this project in their article on designing appropriate biosafety systems for synthetic biology.*

5.3. Applications to alter wildlife populations

Synthetic biology techniques are being explored for their potential to alter wildlife populations for conservational, health and agricultural purposes. Such potential uses of synthetic biology could have positive impacts on the health of humans, wildlife and ecosystems. The 2013 conference "How will synthetic biology and conservation shape the future of nature?" and an article in *PLOS Biology* (Redford *et al*. 2013) has sparked conversation between synthetic biologists and conservationists. At the conference, ideas for potential synthetic biology projects for conservation were identified, including adapting coral to temperature and acidity, attacking the fungus that causes white-nose syndrome in bats, and finding solutions to the crashing of bee populations.[37] Redford *et al*. (2013) suggest that synthetic biology applications in agriculture and bioenergy could alleviate pressure on ecosystems, aiding conservation. Furthermore, specific species or populations of wildlife may also be the target of synthetic biology applications to eradicate or control populations. For example, synthetic biology could be used to create "gene drive" systems that may be used to spread traits to control diseases borne by insect vectors, such as mosquitoes, by suppressing populations, potentially to the point of extinction (Weber and Fussenegger 2012) similar to what has been done by Oxitec to produce genetically modified mosquitoes with the aim of controlling dengue fever carriers.[38] Researchers have introduced a synthetic homing endonuclease-based gene drive system into mosquitoes in the laboratory, which could be used to increase the transmission of genetic modifications to wild populations of mosquitoes (Windbichler *et al*. 2011). Regarding the use of endonuclease-based gene drive systems to alter populations, Esvelt *et al*. (2014) hypothesize that this technique could also be used, for example, to restore vulnerability to pest and weeds which have acquired resistance to pesticides and herbicides by replacing the resistance genes with their ancestral forms, and to promote biodiversity by controlling or even eradicating invasive species. Concerns arising from the use of gene-drive systems to alter wild populations are raised by Esvelt *et al*. (2014) and Oye *et al*. (2014), who also propose possible risk management options before the development of any actual RNA-guided gene drives. As suggested by Oye *et al*. (2014), for emerging technologies that affect the global commons, concepts and applications should be published in advance of construction, testing, and release. This lead time would enable public discussion of environmental and security concerns, research into areas of uncertainty, and development and testing of safety features. It would also allow adaptation of regulations and conventions in light of emerging information on benefits, risks, policy gaps, and, more importantly, it would allow broadly inclusive and well-informed public discussion to determine if, when, and how gene drives should be used. There would also be biosafety considerations, including negative impacts on the health of humans, wildlife and ecosystems, relating to the use of organisms resulting from synthetic biology techniques designed for environmental release (section 6).

Popular press has given significant attention to the project of "de-extinction", which could involve synthetic biology techniques, along with advanced cloning and other tools of modern biotechnology. De-extinction was the subject of a day-long TEDx conference in Washington, DC (USA), and was the cover story of *National Geographic* in March 2013.[39] Research around the world is underway to restore extinct species such as the passenger pigeon, woolly mammoth, and the gastric brooding frog. Some (but not all) of the work towards bringing extinct species back to life involves techniques of synthetic biology, such as synthetic genome engineering. At the TEDx conference, George Church described innovations in DNA delivery and directed splicing into existing genomes to adapt the genomes of existing species to produce the physiological traits of the extinct species, such as tusks and woolly hair (Church 2013). It must be noted that de-extinction initiatives will only succeed if and when the decades-old challenges of cloning are overcome (Campbell 2004). Although de-extinction has not yet been achieved beyond viruses, conservationists and synthetic biologists are starting to discuss the potential impacts on biodiversity and ecosystems (Friese and Marris 2014).

Some conservationists anticipate positive direct and indirect ecological benefits from de-extinction. Stewart Brand, president of the Long Now Foundation, has argued that restoring keystone species such as woolly mammoths would help restore ecological richness as well as serve as flagship species to inspire ecosystem protection (Brand 2013a). Stanley Temple sees a potential use in reviving extinct alleles

37 *For an overview of the meeting, see Rob Carlson's blog "Harry Potter and the Future of Nature" at http://www.synthesis.cc/2013/05/the-economics-of-artemsinin-and-malaria.html, accessed on 5 June 2013.*

38 *Oxitec's ongoing field trials of OX513A Aedes aegypti: http://www.oxitec.com/health/our-products/aedes-agypti-ox513a/ongoing-field-trials-of-ox513a-aedes-aegypti/.*

39 *The webcast of the 15 March 2013 conference is accessible at: http://longnow.org/revive/tedxdeextinction, accessed on 15 March 2013.*

of species whose genetic diversity is dangerously low, or when "we've solved the issue that caused them to go extinct" (Temple 2013). Restoration of certain species could help restore ecosystems that rely on the ecological functions of those species (Seddon *et al*. 2014). Among possible indirect impacts, some are hopeful that the promises of synthetic biology and de-extinction will provide a new paradigm for biodiversity-advocacy, replacing crisis with a message of hope (Anderson 2013; Brand 2013; Burney 2013; Redford 2013). Kent Redford argues that conservation biology started as a "crisis discipline", and that after 30 years people have "stopped listening." His lesson from this is that "hope is the answer: hope is what gets people's attention" (Redford 2013). Similarly, David Burney describes his "poor man's Jurassic Park" efforts at re-wilding abandoned agricultural land as "trafficking in a very rare and valuable commodity in conservation: hope" (Burney 2013).

The use of synthetic biology for de-extinction projects and, more broadly, conservation projects also raises concerns. As discussed more fully in section 6, there is the possibility of direct negative impacts on biodiversity, such as organisms resulting from synthetic biology techniques becoming invasive or negatively affecting host ecosystems.[40] There is also concern about indirect impacts of the promises of synthetic biology and de-extinction such as co-evolution of other organisms (including pathogens, parasites, symbionts, predators, prey/food, co-inhabitants, commensalism, etc.) and diseases. A prominent concern among conservationists is that the hunt for synthetic biology solutions will divert focus, significant funds and other resources from other conservation efforts (Ehrenfeld 2013; Ehrlich 2014; Pimm 2013; Temple 2013). The editors of *Scientific American* warn that de-extinction "threatens to divert attention from the modern biodiversity crisis" (Editors, 2013). Stuart Pimm points out that his work with poor people in Brazil and Madagascar does not generate money for his university, unlike that of molecular biologists, and that de-extinction "can only perpetuate" the trend of university de-investment in ecology and field biology while "seduc(ing) granting agencies and university deans into thinking they are saving the world" (Pimm 2013). These concerns about diversion of resources from other conservation efforts are particularly keen because of the speculative nature of de-extinction projects and their high price tags (Ehrenfeld 2013; Ehrlich 2014). In comments to an earlier draft of this document, one organization noted that, outside of synthetic biology and conservation communities, publicity around de-extinction has prompted research policy communities to consider responsible conduct of research and prioritization of research areas. Another concern is that support for *in situ* conservation may decrease with the expectation that extinct species will be resurrected (ICSWGSB 2011; ETC 2007; Ehrenfeld 2013; Norton 2010; Pimm 2013; Redford *et al*. 2013; Temple 2013). Biologist David Ehrenfeld (2013) worries about what happens "when Members of Congress think it (extinction) is just a bump in the road?" Conservation biologist Stanley Temple (2013) notes the possibility that de-extinction research may have a de-stabilizing effect on conservation, leading to a net loss as less charismatic species are allowed to slip away. In an editorial in *PLoS Biology*, Redford *et al*. (2013) describe the potentially reduced willingness to conserve endangered species as a "moral hazard" of de-extinction research.

5.4. Agricultural applications

There are hopes that synthetic biology tools and techniques will advance agricultural efficiency and lessen negative environmental impacts of agricultural production. The *UK Synthetic Biology Roadmap* predicts that "Synthetic biology has the potential to make food crops less vulnerable to stresses such as drought, saline water or pests and diseases; and/or to create new plants that can produce, in the field, large volumes of substances useful to man" (UKSBRCG 2012). In 2009, the RAE (2009) anticipated that, within 10 years, synthetic biology would be used to engineer new types of pesticides that are "very specific" and do not persist in the environment past their usefulness. The US PCSBI (2010) anticipates high yield and disease resistant feedstocks that can be supplemented with micro-organisms to minimize water use and replace chemical fertilizers. A columnist for *The Guardian* enthusiastically wrote that: "Current GM crops are the Ford Cortinas of agriculture, but synthetic biologists aim to make Ferrari plants that perform photosynthesis more efficiently by harvesting light from wider regions of the spectrum, or even capture nitrogen directly from the air so

40 *Redford et al. (2013) acknowledge the possibility of novel organisms becoming invasive or affecting the integrity of the host ecosystem. A professor of biotechnology, Subrat Kumar, recently wrote in Nature that the risk of a revived extinct species becoming invasive "are negligible compared with the scientific and social benefits of reviving the lost species" (Kumar 2013).*

Source: Macroscopic Solutions, LLC

they won't need nitrogen fertiliser" (McFadden 2012). There also hopes that the use of synthetic biology in agricultural production sectors will foster "sustainable intensification" and thus reduce land conversion into farmland and increase protection of wild habitats (Redford *et al*. 2013). There are hopes that synthetic biology can be used to design plants to serve as feedstocks for micro-organisms that would need less chemical pesticides and fertilizers, which could have positive ecological impacts (PCSBI 2010). These examples all relate to potential applications of synthetic biology to agriculture. Thus far, it is unclear whether there are commercialized agricultural applications of synthetic biology.[41]

Possible applications of synthetic biology for agriculture could also lead to negative impacts on biodiversity. As with other potential future applications of synthetic biology, many of the potential synthetic biology projects for agriculture would involve the release of organisms resulting from synthetic biology techniques. As discussed in section 6, this could lead to the possibility of negative impacts at an ecological level (such as organisms resulting from synthetic biology techniques becoming invasive, disrupting food webs or having other negative effects on non-target species) or through the transfer of DNA from vertical or horizontal gene flow (König *et al*. 2013; Wright *et al*. 2013). If and when these applications near commercialization, a rigorous, science-based evaluation of the potential impacts would be needed on a case-by-case basis (see section 8).

5.5. Applications to replace natural materials

Synthetic metabolic engineering and DNA-based device construction are being used to produce chemicals and molecules that are otherwise sourced from wild and cultivated plants and animals. Groups from industry and civil society have pointed to potential positive and negative impacts on biodiversity. Applications that are on the market or near commercialization are mostly the result of synthetic metabolic pathway engineering, and therefore are not universally recognized as resulting from synthetic biology techniques. Moreover, it should also be noted that these processes involve micro-organisms not meant to be intentionally released into the environment (although risks of unintentional release may still apply, as discussed in section 6).[42]

Molecules produced through synthetic biology could promote the conservation of plants and animals that are currently unsustainably harvested from the wild or through unsustainable cultivation. One possible example is squalene, an emollient used in high-end cosmetics and personal care products that has historically been sourced from the livers of deep sea sharks (ETC 2013a; WWICS 2012). In recent years, plant-based squalene, primarily from olives, became available as an alternative source to sharks. Unilever has already replaced squalene from sharks with the plant-based version in response to a campaign by Oceana to preserve deep sea sharks. Companies point to the price volatility and limited availability of the squalene sourced from olives, and some manufacturers continue to use deep sea sharks,[43] according to a French NGO (BLOOM 2012; Centerchem undated). In 2011, Amyris brought a synthetic biology-produced squalene to the Japanese market, marketed as Neossance™ squalane[44]. Using Brazilian sugarcane as feedstock, Amyris transformed yeasts to produce the hydrocarbon farnesene, which can be finished as squalene (WWICS 2012; Centerchem undated). Synthetic biology-produced squalene could potentially help to ease pressure on deep sea shark populations. Another example is palm oil, one of the industrial uses of which is to manufacture surfactants. The Biotechnology Industry Organization (2013) references concerns with the production of oil palm harming rainforest ecosystems, and points to industrial synthetic biology research to convert agricultural waste materials (soybean hulls) into surfactants.

The replacement of natural products with products resulting from synthetic biology could lessen the pressure on natural habitats but could also disrupt *in-situ* conservation projects. For example, Evolva and International Flavors and Fragrances, Inc. plan to market their vanillin, which is produced through fermentation in yeast (see section 4.2.2), as a natural product in the EU,[45] and hope to have a competitive advantage over other synthetic forms of vanillin, which are currently produced from

41 *As discussed in section 4.2.5, crops have been engineered with enzyme sequences in order to break down the feedstock for fermentation in making biofuels. Whether the techniques used to design and engineer the enzymes are indeed "synthetic biology" is a point of contention (BIO 2013; Lipp 2008; Schmidt 2012).*

42 *Many national biosafety frameworks regulate these micro-organisms under provisions for GMOs/LMOs destined for contained use.*

43 *According to Oceana's website: http://oceana.org/en/our-work/protect-marine-wildlife/sharks/learn-act/shark-squalene, accessed 21 March 2013.*

44 *Squalene is the natural compound, and squalane is the hydrogenated form of the compound. Squalane is more commonly used in cosmetics and as a lubricant.*

45 *On their website, Evolva states: "Recent EU regulatory changes have strengthened the competitive advantage of the proposed product. New EU rules state that only substances or preparations derived directly from an animal or vegetable material may be labelled "natural". Available at: http://www.evolva.com/products/vanilla, accessed on 21 March 2013.*

petrochemicals and paper pulp. While the developers of vanillin claim that their product offers the world a clear alternative to the petrochemical variety of vanillin without introducing a new environmental threat to rainforests and endangered species, the ETC Group warns that its large-scale production could negatively impact the many small-scale farmers involved in the production of cured vanilla beans (ETC 2013a). Vanilla orchids are commonly produced by inter-cropping with rainforest trees as 'tutors' for vanilla vines to grow on. ETC Group is concerned that this agro-ecological method of cultivation and livelihood for an estimated 200,000 people could be disrupted (ETC 2013a). ETC Group has also highlighted concerns over the key role of biomass as a base for synthetic biology industrial processes, as discussed above in section 5.1 (ETC 2013b). Related to this, ETC Group questions whether a switch from monoculture oil palm plantations to monoculture sugar plantations (for feedstock for synthetic biology processes) is an improvement for biodiversity (ETC 2013a).

5.6. Applications for chemical production

A significant potential use of synthetic biology is the engineering of plants and microbes to produce raw materials that are currently produced using synthetic chemistry (Garfinkel and Friedman 2010; Philp *et al*. 2013). For example, some bioplastics, such as polylactic acid plastics, use synthetic biology techniques and are made from biomass such as sugar cane instead of petroleum (Philp *et al*. 2013). DuPont produces bio-based 1,3 propanediol by fermenting corn sugar with a "patented micro-organism" that converts glucose to propanediol.[46] Consolidated bioprocessing (CBP) aims to engineer what would be several processing steps into the functions of one microorganism, resulting in cost savings (Philp *et al*. 2013; Garfinkel and Friedman 2010). Synthetic biology is also being explored for new industrial processes, such as research into harvesting reserves of hydrocarbons with microbial digestion (PCSBI 2010).

Industry and civil society have predicted positive and negative impacts on biodiversity from the application of synthetic biology to produce chemicals. Such products and processes may result in decreased use of non-renewable resources and "less impactful manufacturing processes in general" (Garfinkel and Friedman 2010). Civil society groups have expressed concern that, as synthetic biology companies shift their focus from biofuels to the smaller but more lucrative markets of chemicals, the "same polluting companies" are taking the lead in developing bioplastics (ETC 2010; ICSWGSB 2011). The ETC Group questions whether the use of synthetic biology is leading to "greener" products or industrial processes. They point to the use of synthetic biology and biomass to produce products with similar problems as the non-synthetic biology versions, such as bio-based PVC (which still requires chlorine in its production) and many bio-plastics (some of which cannot compost, or would do so only in industrial composters) (ETC 2010). In a review article, König *et al*. (2013) note that some methods of producing biodegradable plastics may have more environmental impacts such as the release of carcinogens and eutrophication than fossil-based polymers.

6. GENERAL BIOSAFETY CONCERNS

This section focuses on biosafety concerns related to the accidental or intentional release of organisms resulting from synthetic biology techniques that are applicable to all types of applications seen in section 5 above. These include concerns related to ecosystem-level impacts, gene flow, and the emergence of unpredictable properties.

6.1. Ecosystem-level impacts

Unintentional or intentional release of organisms resulting from synthetic biology techniques to ecosystems outside of a contained laboratory or production facility could negatively impact biodiversity. One set of concerns center on the possibility of such organisms' survival and persistence. For example, organisms resulting from synthetic biology techniques could displace existing species because of fitness advantages (intentional or otherwise) and become invasive (Redford *et al*. 2013; Snow and Smith 2012; Wright *et al*. 2013). The International Civil Society Working Group on Synthetic Biology (ICSWGSB 2011) expresses concern that organisms resulting from synthetic biology techniques could

46 *See: http://www2.dupont.com/Renewably_Sourced_Materials/en_US/proc-buildingblocks.html, accessed on 23 Feb. 2014. The ICSWGSB (2011) identifies this process as using synthetic biology techniques. Esvelt & Wang identify DuPont's work on propanediol as a "great example of genome-level metabolic engineering" (2013).*

Source: Macroscopic Solutions, LLC

become a new class of pollutants if they persist, for example algae that continues to produce oils or organisms engineered to break down sugarcane degrading sugar in the local environment. Even if the organisms did not persist for long periods, they could disrupt ecosystems and habitats, for example, if algae engineered for biofuel production escaped containment and bloomed (Redford *et al*. 2013; Snow and Smith 2012; Wright *et al*. 2013).

Notwithstanding that risk assessments must be carried out on a case-by-case basis, there is disagreement within the scientific and policy communities over the degree and probability of harm that organisms resulting from synthetic biology techniques that are intended for contained use could cause if released (RAE 2009; Lorenzo 2010; Snow 2011; Zhang *et al*. 2011; Dana *et al*. 2012; Snow & Smith 2012; Tait & Castle 2012). A common argument is that an accidental release of organisms resulting from synthetic biology that are intended for contained use would likely not lead to survival and propagation because engineered changes generally lead to reduced fitness (Garfinkel and Friedman 2010; Lorenzo 2010; RAE 2009; Moe-Behrens *et al*. 2013). On the other hand, the limit of detection for relevant microbes may be too high (i.e. a large population of microbes is needed in order to be detectable) to extrapolate their extinction, and microorganisms that have been released into an environment may have long lag times before they develop into a population that is large enough to be detected or to cause an ecological change. For example, it was popular for some decades to speculate that the rise of antibiotic resistance in medically relevant bacteria would disappear if the associated antibiotics were temporarily withdrawn. This did not turn out to be the case. After resistance levels fell below detection and the drug was reintroduced, resistance emerged unexpectedly rapidly. Assumptions that resistance rendered these bacteria less fit in the absence of the antibiotic also turned out to be frequently incorrect (Heinemann *et al*. 2000). Snow (2011) and Snow and Smith (2012) point out that (i) the majority of research in synthetic biology uses microbes as hosts, (ii) microbes have a particularly high potential for rapid evolutionary change, and (iii) modified microbes resulting from synthetic biology techniques that seem innocuous or weak might survive due to mutations. Ecologists and commentators urging caution point out that organisms resulting from synthetic biology techniques cannot be retrieved once released (Dana *et al*. 2012; Snow and Smith 2012; FOE *et al*. 2012). Wright *et al*. (2013) note that even genetically modified microorganisms that may be programmed to "self-destruct" pose an environmental risk, as their DNA can potentially be scavenged by other organisms after they have died (see section 6.2 below).

Some anticipated future applications of synthetic biology would require the intentional release of organisms resulting from synthetic biology techniques into the environment (Anderson *et al*. 2012), which may present additional complexities and types of potential negative impacts. Many synthetic biologists are aiming to design microorganisms that are sufficiently hardy for release into the environment (section 5.2). Belgium's Biosafety and Biotechnology Unit notes that "risk assessors and regulators have relatively little experience considering the potential risks [sic] posed by the intentional release of micro-organisms," and that environmental microbiology is more complex that of higher organisms (Pauwels *et al*. 2012). They go on to say that it is still "premature" to address potential challenges since they consider environmental applications of synthetic biology to still be several years away (Pauwels *et al*. 2012). Marris and Jefferson (2013) also note that regulatory agencies in the United States, Europe and elsewhere, which have been conducting risk assessment for crops resulting from modern biotechnology, have very little experience of risk assessment for genetically modified micro-organisms. Rodemeyer, writing for the WWICS Synthetic Biology Project, further notes that regulatory agencies have had "relatively little experience considering the potential risks [sic] posed by the eventual evolution of genetically engineered microorganisms intended for non-contained use"; most GMOs/LMOs that have been intentionally introduced into the environment are annual food crops, therefore, evolution has not been seen as a relevant risk factor (Rodemeyer 2009). Risk assessment of microorganisms resulting from modern biotechnology is among the topics identified by a group of experts established by the Parties to the Cartagena Protocol on Biosafety for the development of guidance (CBD 2014).

6.2. Gene flow

Altered DNA could be transferred from organisms resulting from synthetic biology techniques to other organisms, either by sexual or horizontal gene flow/transfer. Sexual or "vertical" gene flow occurs when genes from one organism are passed on to populations of the same species or a related species through reproduction (Hill *et al*. 2004). This can occur through pollen exchange, particularly if an engineered crop is in close proximity to wild relatives, as may occur in centers of biodiversity (Rhodes 2010). Gene flow into an ecosystem can also occur via seed dispersal and vegetative

propagation. An example from the past decades of genetically modified crop use is the reported presence of transgenes in landraces of maize (Quist and Chapela 2001; Piñeyro-Nelson *et al*. 2009) and of recombinant proteins in wild populations of cotton in Mexico (Wegier *et al*. 2011).

Genes from organisms resulting from synthetic biology techniques could also transfer to unrelated species through horizontal gene transfer (HGT). HGT is a naturally occurring phenomenon that may happen in three ways: 1) transformation, in which naked DNA is picked up and incorporated by an organism; 2) conjugation, through DNA transfer from one organism to another by plasmid; and 3) transduction, through DNA transfer from one organism to another by virus (Snow and Smith 2012; Hill *et al*. 2004). Much is not understood about HGT, including its frequency and mechanisms of transfer, but recent research has found that HGT plays a role not just in the evolution of bacteria and archaea, but also in the evolution of eukaryotic genomes (Rocha 2013; Schönknecht *et al*. 2013). HGT is common among microbes (Hill *et al*. 2004; Rocha 2013). HGT from symbiotic algae to animals has been observed, in the uptake of an algal nuclear gene by a sea slug to become photosynthetic (Rumpho *et al*. 2008). HGT thus represents a potential mechanism for the transfer of altered genetic material, which is possible even if the original organism produced through synthetic biology has died (Wright *et al*. 2013). Gebhard and Smalla (1999), for example, have shown that DNA from genetically modified sugar beet could persist in soil for two years. The potential for HGT, taking into account the potential persistence of the modified genetic elements in the environment, is an important consideration in the risk assessment of organisms resulting from modern biotechnology and synthetic biology.

The transfer of genetic material from an organism resulting from synthetic biology techniques to another organism may change biodiversity at a genetic level (genotype) and may spread undesirable traits (phenotype). Some scientists, commentators, and civil society groups have expressed concern that the spread of novel DNA may result in undesirable traits in other organisms, such as those encoding antibiotic resistance (commonly used as a marker in synthetic biology and classic genetic engineering) or the production of enzymes that break down cellulose (ICSWGSB 2011; Tucker and Zilinskas 2006; Wright *et al*. 2013). Even if no undesirable phenotypes are detected, the spread of synthetically designed DNA into other species is considered by some to be "genetic pollution" (FOE 2010; ICSWGSB 2011; Marris and Jefferson 2013; Wright *et al*. 2013). There is disagreement whether genetic pollution *in itself* is harmful. Marris and Jefferson (2013) identify synthetic biologists and environmental NGOs as generally assuming that the transfer of genetic material needs to be prevented, while the European regulatory system does not consider the transfer of genetic material as an adverse effect in itself, but a potential mechanism by which adverse effects could occur.

It is also important to note that unpredictable consequences and ecological harms may result from HGT *into* modified organisms. HGT from wild organisms into modified ones may, for example, inactivate biological containment devices or complement engineered auxotrophies, allowing the modified organisms to survive in areas where they are not intended to go (see section 7.2).

6.3. Emergence of unpredictable properties

The scientific community speculates that synthetic biology could result in radically different forms of life, with "unpredictable and emergent properties" (RAE 2009; Garfinkel and Friedman 2010; Mukunda *et al*. 2009). However, there is no agreement over the significance of such unexpected possibilities. Pauwels *et al*. (2013) explain that, even if the sources of genetic sequences are known and understood, it may be difficult to assess how all of the new circuits or parts will interact or to predict the possibility of unexpected emergent properties. Similarly, Schmidt and de Lorenzo (2012) explain that: "It is paradoxical that such an impressive ability to synthesize DNA does not match our much more limited knowledge to forward-engineer genetic devices with more than 20 genes or biological parts. This places the synthetic biology field in a territory where designing new-to-nature properties will still rely for some time on trial-and-error approaches where emergence of unexpected, perhaps undesirable traits might certainly occur". Dana *et al*. (2012) reflect a concern that "no one yet understands the risks that synthetic organisms pose to the environment, what kinds of information are needed to support rigorous assessments, or who should collect such data".

In discussions of the danger of unforeseen results in synthetic biology, a common example is an experiment in 2000 using classic genetic engineering technology. An engineered mousepox intended to induce infertility was unexpectedly virulent, killing all of the unvaccinated mice and half of the vaccinated mice (Jackson *et al*. 2001, cited or described in: Douglas and Savulescu 2010;

Garrett 2011; Mukunda *et al*. 2009; Schmidt & de Lorenzo 2012; Wilson 2013). Some scientists question how "unexpected" the increased virulence was (Müllbacher & Lobigs 2001) (although the researchers who inadvertently developed a lethal mouse virus continue to insist that, even if increased virulence could have been predicted, it was still surprising that immunized mice were susceptible to the virus (Selgelid & Weir 2010)). Although not a result of synthetic biology techniques, the mousepox case is raised in the context of synthetic biology as an example of the potential for producing more pathogenic products (Douglas & Savulescu 2010; Schmidt & de Lorenzo 2012; Wilson 2013) and the possible limits of predictive knowledge (Garrett 2011; Mukunda *et al*. 2009). One commentator noted about the mousepox case: "While the problem of unforeseen results is not unique to synthetic genomics, the combining of multiple sources of DNA sequence (not just, say, a bacterial vector and a specific gene as is exemplified by standard recombinant DNA techniques), particularly when this can occur very rapidly, may be of some concern" (Fleming 2006).

7. STRATEGIES FOR CONTAINMENT

Containment strategies to prevent the unintentional release of organisms resulting from synthetic biology techniques and/or exposing the environment to such organisms may be physical (e.g. physical barriers) or biological (e.g. inhibited ability to reproduce or survive outside of contained system) (Schmidt and Lorenzo 2012). Both physical and biological containment strategies are being explored as means to reduce the risks and potential negative impacts of organisms resulting from synthetic biology techniques.

7.1. Physical containment

The UK Healthy and Safety Laboratory noted that research and production of organisms resulting from synthetic biology under contained use conditions could be used to develop evidence on how to regulate future applications that may involve intentional release, in a step-by-step approach (Bailey *et al*. 2012). Future uses of synthetic biology may straddle the line between containment and release. For example, French *et al*. (2011) consider their prospective arsenic biosensor that may be used in a contained device - but outside of a laboratory - as raising less concerns than biosensors that are designed for direct introduction into the environment. Moreover, the level of containment of organisms developed through synthetic biology will also influence the likelihood of their accidental environmental release. For example, because of their need for exposure to sunlight and carbon dioxide (WWICS 2013), algae that are grown in open ponds may be more prone to accidental release than organisms contained in laboratory facilities.

It is widely acknowledged among microbial biologists and ecologists that physical containment is never fail-proof (Moe-Behrens *et al*. 2013; Schmidt and Lorenzo 2012; Snow 2010; Wright *et al*. 2013; Marris and Jefferson 2013). One of the conclusions that Schmidt and de Lorenzo (2012) draw from decades of research and use of recombinant DNA is that "it is naïve to think that engineered organisms have never escaped the laboratory. They often have, and massively". Synthetic biologists Wright *et al*. (2013) call it prudent to include some form of physical containment, but caution that "failure in [the physical containment] is a matter of when, not if". The disagreement is thus largely not about whether engineered organisms will escape physical containment, but rather over the degree of concern this should elicit and the appropriate responses.

There is significant disagreement over how stringent physical containment measures should be for synthetic biology, stemming from disagreement over the seriousness of the threats posed by organisms resulting from synthetic biology techniques (EGE 2009; FOE *et al*. 2012; Garfinkel *et al*. 2007, Marlière 2009). Requiring synthetic biology research to take place only in BSL 3 or 4 laboratories would significantly restrict synthetic biology research to a few laboratories (Garfinkel *et al*. 2007). *Principles for the Oversight of Synthetic Biology*, collaboratively drafted by civil society groups and endorsed by 111 organizations, calls for the strictest levels of containment of synthetic biology (FOE *et al*. 2012). They do not specify a specific Biosafety Level, but more generally call for physical, geographical and biological confinement strategies that prevent the release of organisms resulting from synthetic biology techniques into the biosphere (Ibid.). Tucker and Zilinskas, experts in nonproliferation policy, declared "it would be prudent to [...] treat synthetic microorganisms as dangerous until proven harmless. According to this approach, all organisms containing assemblies of BioBricks would have to be studied under a high level of biocontainment (Biosafety Level, BSL, 3 or even 4) until their safety could be demonstrated in a definitive manner" (Tucker and Zilinskas 2006). On

the other hand, the US Presidential Commission for the Study of Bioethical Issues (PCSBI 2010) found that the *NIH Guidelines*' existing guidance on the BSL for any specific experimental agents and designs were adequate for synthetic biology at its current stage of development. The Center for Genetics and Society published an open letter signed by 58 civil society groups who consider that the "Commission's recommendations fall short of what is necessary to protect the environment, workers' health, public health".[47]

The Cartagena Protocol on Biosafety, in article 3(b), defines contained use as "any operation, undertaken within a facility, installation or other physical structure, which involves living modified organisms that are controlled by specific measures that effectively limit their contact with, and their impact on, the external environment". The Cartagena Protocol does not elaborate on how these measures are to be implemented but, at their seventh meeting, the Parties to the Protocol will deliberate on the development of tools and guidance to facilitate the implementation of the Protocol's provisions on contained use of LMOs.[48]

7.2. Biological containment

In reference to the need for containment, researchers sometimes note that engineered organisms generally have reduced fitness, referencing past experience with genetically modified micro-organisms (Bassler 2010; WWICS 2011; de Lorenzo 2010). However, some synthetic biologists see synthetic biology as providing tools that could result in hardier organisms, and lack of fitness does not discount the possibility of the transfer of genetic material to other organisms. Therefore, among synthetic biologists and in policy discussions, a commonly suggested response to the limitations of physical containment and the possibility of organisms successfully designed for environmental release is that synthetic biology be used to design organisms with "built-in safety features" (RAE 2009; Marlière 2009; Moe-Behrens *et al*. 2013; PCSBI 2010; Wright *et al*. 2013). In 2009, synthetic biologist Philippe Marlière argued that most experts see physical containment as "a futile tribute to superstition", and that biological containment was the "surest if not simplest way to avoid risks of dissemination and contamination" (Marlière 2009). There are four general areas of research that aim to develop built-in biological containment: induced lethality; horizontal gene transfer prevention; trophic containment; and semantic containment.

The idea of engineered induced lethality (also referred to as "kill switch" or "suicide gene") is frequently raised as a solution to the problem of survival and persistence (PCSBI 2010; Venter 2010), but there are significant constraints to its effectiveness. The US Presidential Commission for the Study of Bioethical Issues (PCSBI) frequently mentioned "suicide genes or other types of self-destruction triggers" as a way to reap the benefits of synthetic biology while avoiding potential harms (PCSBI 2010). This is also a popular suggestion among iGEM teams as a way to respond to biosafety concerns (Guan *et al*. 2013). However, as recently discussed by Wright *et al*. (2013), Schmidt and de Lorenzo (2012), and Moe-Behrens *et al*. (2013), kill switches in microbes are prone to failure. The selective pressure acting to inactivate or lose suicide genes (i.e. through mutation) is expected to be stronger than for other genes, precisely because the suicide genes are expressly designed to kill the host cell. Moreover, while suicide genes are intended to be active only under certain conditions, there may be varying amounts of "leaky" expression, which means that the selective pressure is present even under normal conditions where the host cells are intended to thrive. Wright *et al*. (2013) corroborate this notion by writing that "dependency devices based solely on toxins seem designed for failure due to their inability to withstand mutation over time".

Trophic containment is another suggested biological barrier where auxotrophic organisms are designed to be unable to synthesize a compound that is required for its survival and that cannot be found outside a controlled environment (Marlière 2009; Moe-Behrens *et al*. 2013; PCSBI 2010; Wright *et al*. 2013). Once auxotrophic microbes escape, they die without the necessary compound. There are some drawbacks to auxotrophic containment. The compound required for survival might be available in the environment to which it escapes (Moe-Behrens *et al*. 2013). Even if the compound is not present in the environment, organisms may parasitically rely on metabolites from other organisms, or gene transfer could revert the containment by introducing the necessary gene (Moe-Behrens *et al*. 2013; Wright *et al*. 2013). Moe-Behrens *et al*. note that only a few of the genetic safeguard approaches, including engineered auxotrophy, have met the recommended limit of engineered microbe survival of less than 1000 cells per 2 litres (Moe-Behrens *et al*. 2013). A related method of containment that is being explored in influenza research involves modifying the influenza virus to express specific micro-RNA target sites. This was found to attenuate influenza pathogenicity in

47 Available at http://www.geneticsandsociety.org/article.php?id=5517.

48 Document UNEP/CBD/BS/COP-MOP/7/15 on "Contained use of living modified organisms" is available at http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=5193.

different species that express the specific micro-RNA (Langlois *et al*. 2013). It is hoped that a similar approach could add extra precaution when studying other pathogens (Devitt 2013).

Another containment strategy is preventing horizontal gene transfer (HGT); this is also still in development. Scientists from UC Berkeley's Department of Bioengineering suggest that synthetic biology organisms could eventually be engineered to prevent HGT, through strategies such as deleting certain plasmid sequences, producing phage-resistant strains, and mutating specific genes in order to prevent the uptake of DNA from the environment (Skerker *et al*. 2009). Skerker *et al*. (2009) express confidence that HGT can be understood sufficiently enough to be prevented. Other synthetic biologists acknowledge that minimizing the uptake of 'free' DNA via transformation (as opposed to conjugation or transduction) continues to be challenging (Wright *et al*. 2013). Ecologists and social scientists identify HGT as a key area for risk research (Dana *et al*. 2012; Snow and Smith 2012).

Semantic containment would require creating organisms that "cannot communicate with the extant biochemistry of the existing live world" (Schmidt and Lorenzo 2012). Xenobiology is the main area of research exploring the creation of orthogonal biological systems. By introducing unnaturally occurring nucleotides or an alternate backbone besides ribose or deoxyribose into the nucleic acid of micro-organisms, a cellular information system that retains the original functions but cannot be read by naturally occurring enzymes (Marlière 2009; Schmidt and Lorenzo 2012; Wright *et al*. 2013). Orthogonal systems based on xenobiology "offer significant hope for microbial cells designed to have minimal genetic interaction with nature" (Wright *et al*. 2013), but synthetic biologists acknowledge that they are years (possibly decades) away from achieving truly orthogonal organisms resulting from synthetic biology techniques, l*et al*one demonstration of containment (Moe-Behrens *et al*. 2013; Wright *et al*. 2013). Furthermore, xenobiology organisms' effects on natural organisms are unclear. Recent research suggests that alternative backbone nucleic acids can bind with natural DNA and RNA, with toxic effects (Moe-Behrens *et al*. 2013; Sutherland *et al*. 2013).

According to Wright *et al*. (2013), "The current consensus in the synthetic biology research community is that multiple biosafety mechanisms will be needed to ensure system redundancy in case of component inactivation". The same authors also note that the higher the complexity, the more prone it may be to failure; thus, safety components must be chosen carefully.

Civil society groups, conservation biologists, and social scientists have urged that biological containment strategies based on synthetic biology not be relied upon as biosafety measures until thorough risk assessments have been carried out (King 2010; FOE *et al*. 2012; Snow 2010; Sutherland *et al*. 2013). The 111 organizations endorsing *Principles for Oversight of Synthetic Biology* called for the restriction of xenobiology research within laboratories (FOE *et al*. 2012). The ICSWGSB calls on the CBD COP to recommend that Parties not approve biocontainment strategies based on synthetic biology "for field testing until appropriate scientific data can justify such testing, and for commercial use until appropriate, authorized and strictly controlled scientific assessments with regard to, *inter alia*, their ecological and socio-economic impacts and any adverse effects for biological diversity, food security and human health have been carried out in a transparent manner and the conditions for their safe and beneficial use validated" (ICSWGSB 2011). These groups are responding to what they perceive as overly optimistic expectations of many synthetic biology commentators for the promise of built-in biosafety.

7.3. Social aspects of containment

Because containment strategies occur within social and institutional systems, the effectiveness and types of containment depend on the conditions of use and characteristics of the users of synthetic biology technologies (Marris and Jefferson 2013). As noted in comments made by one Party on an earlier draft of this document, this requires dialogue between synthetic biologists, regulators, and social scientists.

As a converging field, synthetic biology has attracted people from outside of the life sciences. While this is generally seen as a positive trend, it also represents potential challenges for containment. Many newcomers to the biology laboratories have potentially not had formal biosafety training, and therefore may not know or be able to follow proper protocols for human and environmental safety (Schmidt 2009; NSABB 2010). Professionals attracted to synthetic biology, such as chemists, physicists, engineers, and computer scientists, "may not have been sensitized to the ethical, social and legal norms of the traditional life sciences research communities" (NSABB 2010). Others are early in

Source: Macroscopic Solutions, LLC

their careers in laboratories. For example, the annual iGEM competitions involve college and high school students in synthetic biology experiments (Guan *et al*. 2013).[49]

Some experiments in synthetic biology are carried out by amateur biologists, sometimes referred to as "bio-hackers", or the do-it-yourself biology (DIYbio) community (Ledford 2010; Schmidt 2009; Guan *et al*. 2013). There is contention over how many people are engaging in modern biotechnology outside of formal laboratories and the sophistication of the research and synthesis they are able to do (Bennett *et al*. 2009). Some civil society groups have expressed concerns that such independent researchers have neither the knowledge nor the tools to properly dispose of wastes or prevent release into the environment and have urged that DIYbio and bio-hackers be individually licensed in addition to their laboratories being licensed (EcoNexus 2011; FOE 2010).

Beyond the matter of laboratory safety practices, there is a broader concern that synthetic biology practitioners lack an understanding of ecosystem and biodiversity science. At the US PCSBI hearings, the President of the Hastings Center, Tom Murray, stated:

> "As the relative participation of biologists, familiar with the complexities and the non-linearities of biological systems diminishes, so may an appreciation of consequences of intentional or unintentional perturbations of, for example, eco systems. It is just not the way they think about it. Biologists are trained or at least particularly whole organism biologists even microbial biologists do think about whole organisms and think about environments and ecosystems. That is less true about some molecular biologists, and probably less true about some of the other people that are now coming into synthetic biology…. Why is this important? We need to make sure the people who are on the leading edge of synthetic biology understand the complexities of the systems they will eventually purport to tinker with" (Murray 2010).

8. ADEQUACY OF CURRENT METHODOLOGIES FOR ENVIRONMENTAL RISK ASSESSMENT

Perspectives on the adequacy of environmental risk assessments and regulatory structures designed for GMOs/LMOs resulting from classic genetic engineering in addressing organisms resulting from synthetic biology will depend, in part, on the perceived novelty of synthetic biology. Writing for the WWICS Synthetic Biology Project, Michael Rodemeyer noted that near-term products "derived from well-understood bacterial hosts and natural genetic sequences" and intended for contained use are "likely comparable in risk to currently produced genetically engineered organisms" (Rodemeyer 2009). Similarly, national government reports - such as the US Presidential Commission on the Study of Bioethical Issues (PCSBI 2010), the Belgian Biosafety and Biotechnology Unit (Pauwels *et al*. 2012), and the UK Health and Safety Laboratory (Bailey *et al*. 2012) and UK Synthetic Biology Roadmap Coordination Group (UKSBRCG 2012) - express the view that their regulatory regimes and risk assessment methodologies for genetically modified organisms sufficiently apply to the current and near-term results of synthetic biology techniques. Most of these documents also, however, stress that regulators need to continue to monitor developments in the field, implying that changes may be necessary depending on how synthetic biology develops (Bailey *et al*. 2012; Pauwels *et al*. 2012; UKSBRCG 2012). Rodemeyer (2009), for example, notes that risk assessment will be challenged as the complexity of organisms increases as novel gene sequences are more significantly modified, and as genetic components are assembled from a greater variety of sources. From the perspective of the ICSWGSB (2011), current developments of synthetic biology techniques already demand new risk assessment procedures and regulatory responses. The ICSWGSB (2011) argue that, as current risk assessment methodologies have a strong element of comparison with the risks posed by the recipient or parental organism,[50] they are inadequate for organisms produced using synthetic biology techniques that have no analog in the natural world.

49 iGEM notes that the teams work in BSL1 or BSL2 laboratory spaces at high schools, universities, or similar institutions. The teams are required to follow all applicable laws and university biosafety rules.

50 Among the general principles for risk assessment, Annex III of the Cartagena Protocol on Biosafety states that "risks associated with living modified organisms [...] should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment."

Source: Macroscopic Solutions, LLC