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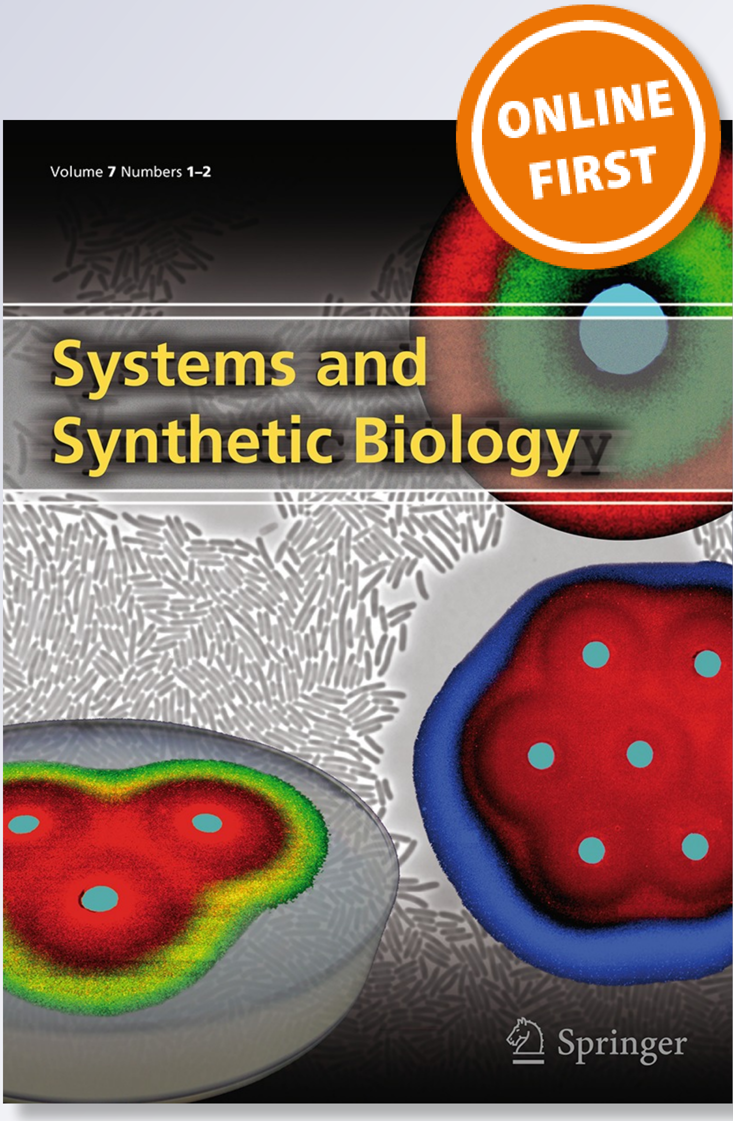

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RESEARCH ARTICLE

Do-it-yourself biology: challenges and promises for an open science and technology movement

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Abstract The do-it-yourself biology (DIYbio) community is emerging as a movement that fosters open access to resources permitting modern molecular biology, and synthetic biology among others. It promises in particular to be a source of cheaper and simpler solutions for environmental monitoring, personal diagnostic and the use of biomaterials. The successful growth of a global community of DIYbio practitioners will depend largely on enabling safe access to state-of-the-art molecular biology tools and resources. In this paper we analyze the rise of DIYbio, its community, its material resources and its applications. We look at the current projects developed for the international genetically engineered machine competition in order to get a sense of what amateur biologists can potentially create in their community laboratories over the coming years. We also show why and how the DIYbio community, in the context of a global governance development, is putting in place a safety/ethical framework for guarantying the pursuit of its activity. And finally we argue that the global spread of DIY biology potentially reconfigures and opens up access to biological information and laboratory equipment and that, therefore, it can foster new practices and transversal collaborations between professional scientists and amateurs.

Keywords DIYbio · Synthetic biology · iGEM · Health · Innovation · Biosecurity

Introduction

Biology is currently experiencing a profound technological metamorphosis as better tools and models are made for exploring and exploiting living systems. Synthetic biology, in particular, represents a major transition for the life sciences by aiming not only to understand but also to control the processes taking place in, or in connection to, a living cell. It is gathering in a synergistic way engineers and biologists to design and build novel bio-molecular components and devices, to *in fine* reprogram living organisms. Designer organisms are created to enable cheaper drugs, targeted therapies for diseases such as cancer, greener fuels and means for fighting strong biological pathogens (Khalil and Collins 2010). Synthetic biology is expected to bring about a new wave of innovations for responding efficiently to major and global health issues. As these promising biological technologies become easier to manipulate, achievements, such as plasmid refactoring, that were once only possible in leading laboratories are becoming routine for undergraduates, high school students, and even amateur biologists (that is, biologists who practice science as a "hobby", usually outside of scientific institutions). The international genetically engineered machine competition (iGEM) and the Do-it-yourself biology (DIYbio) community are challenging the limits of what we thought were

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possible with biotechnologies in the hands of junior/amateur scientists. Young students in the life sciences are now regularly working on ambitious projects like the creation of engineered bacteria that can sense arsenic in water (UANL_Mty-Mexico iGEM 2012 team) or target and destroy specific tumor cells in your body (Penn iGEM 2012 team). In times where there is urgency for better and especially cheaper biotechnology innovations, DIYbio and iGEM reveal that it is possible to realize biotech projects with limited experience and access to scientific equipment based on open-source biology. As promising as this could be, opening up access to the use of biotechnology outside traditional institutions presents its own set of challenge for safety and security (Schmidt 2008; Anderson et al. 2010; Gorman 2011).

One of the actual goals of iGEM, and of synthetic biology more generally, is to seek ways to make biology easier to engineer. One of the ways to do so is to formalize genetic information as genetic parts that compose genetic circuits and devices. This abstraction hierarchy enables scientists to visualize a genetic device as a set of simpler components, each identified by their functional characteristics and not anymore by their pure sequence (Shetty et al. 2008). Synthetic biology uses the same cumulative effect of standardization, decoupling and abstraction than for the design of electrical circuits. By using complexity and information management tools to modularize, abstract and understand biological systems (Rodrigo et al. 2012; Hillson et al. 2012), one can easily manipulate and prototype synthetic genetic systems on a laptop computer. One practical example of this modularization and standardization is the BioBrick toolbox (Shetty et al. 2008), allowing the development of prototypes of biological systems, without the need for considerable research and development processes. Based on "de-skilling" approaches, synthetic biology provides an increasing number of people the necessary skills to engineer biology, with the prospect to unleash more creative ways to use biotechnology. At times where participatory culture is hegemonic on the Internet, these are some of the key factors that explain the context in which the DIYbio community emerged 5 years ago. In this article we examine the organization, the projects, the spread, and the safety framework of DIYbio.

DIYbio is becoming a global movement, among others, by establishing supra-national networks and websites, a general ethical framework for its practitioners and dedicated laboratories across the world. Despite this, some argue that DIYbio will have little impact on global health issues in the near future. There are, however, possibilities opened up through DIY work on current health issues. A portable and cheap PCR device like *Amplino*, which can allow quick malaria detection in developing countries (see discussion below), or a biological blue ink, which is non-toxic, cheap and biodegradable, are but two examples of the kinds of contribution that DIYbio can make to global health issues.

We will, in particular, seek to answer the following questions: How has the DIYbio community organized itself and why has it spread all over the globe? What are currently the techniques and equipment that their members use and create? And what are the most representative projects being currently developed? By trying to answer these questions, we desire to provide a prism through which one can observe and understand the possible facets DIYbio exhibits today and the ones it may have tomorrow (i.e. via projects fostering cheaper and easier ways to perform medicine and thereby improve global public health). At the same time, this lens provides an understanding about how the development of this open science and technology movement is dependent on the acceptation of its philosophy by policymakers and society in general (and thus raises issues of governance, both on national and global level).

The DIYbio movement

Do-it-yourself biology is a rather recent phenomenon and can be described as the pursuit of biology outside of scientific institutions by amateurs, students, "hobbyists". As the "do-it-yourself" movement usually associated to home improvement, the idea is here also to build and create things oneself without the direct help of specialists. The first association in the field, DIYbio.org, was launched in 2008 in Boston. While the first meeting of the group brought together some 25 people, today the association counts over 2,600 members. Since its birth 5 years ago till January 2013, its members have produced more than 3,700 discussion topics on their mailing list, with a total of more than 25,000 messages of practical knowledge about biology. Thousands of people from around the world contribute to the informal Do-it-yourself biology (DIYbio) community. It is difficult to know precisely how many members the community counts because there are no formal requirements to join and dozens of online venues and physical spaces exist that serve the community in different ways. Yet, the movement has spread both within and outside of the US: DIYbio enthusiasts have already created 37 regional groups where they meet, share and create (Fig. 1). Recently, for example, we have witnessed the creation of DIY and hackergroups in Indonesia and Singapore (Kera 2012). If we follow the current trends on the creation of DIYbio community labs around the world, the number of amateurs and non-traditional biologists is likely to exceed tens of thousands in the next few years.

DIY bio is arguably becoming a global movement. While it started off in the United States in 2008, it has

Fig. 1 Location of known DIYbio laboratories (in January 2013). Fourteen countries are represented on four continents, representing 37 groups overall. 16 in Northern America, 13 in Europe, three in Asia, two in Oceania, two in Middle-east and one in Africa (Kenya)

spread around the world, above all in major Western cities. At the time of writing, the creation of a European network of do-it-yourself biology, called DIYbio.eu, is under way. The kick-off meeting was organized on the 1st of December 2012 in Paris and gathered almost fifty participants from several European countries. Various factors help to explain the spread of the movement: the presence of a central website (DIYbio.org) and its mailing list, the availability of cheap alternatives to laboratory equipment, reports on DIYbio in newspapers and academic journals (such as *Nature* and *EMBO reports*), the possibility of co-locating emerging DIYbio labs next to already existing hackerspaces, the meeting of young enthusiasts at iGEM jamborees, the collaborations between iGEM teams and DIYbio labs, etc. Technology, geeks and entrepreneurs oriented media, like *Make Magazine* and the Maker Fairez, also give to the DIYbio community a stimulating framework to blossom (Tocchetti 2012). It is through these various communication channels that DIYbio is able to move beyond regional, national and cultural boundaries. Although each regional group is distinctive in its focus and activities, generally the most common activities of regional DIYbio groups tend to be focused around education and learning about biotechnology through member-led seminars and workshops, guest lectures, and hands-on activities. The history of the development of the DIYbio community is closely linked to the long history of amateur science organizations (i.e. amateur astronomers have often been the discoverers of new celestial objects) and of community labs—the so-called hackerspaces, makerspaces or fablabs—where one can find the necessary knowledge, tools and support to develop one's own personal projects. Delfanti (2010) describes DIYbio as a "very interesting example of a direct translation of free software and hacking practices into the realm of cells, genes and labs". There are today more than 500 hackerspaces around the world and projects involving complex electronics, mechanics and informatics are routine in those places. Hackerspaces are recognized nowadays as places where citizen science can take place, and they share the common ambition to improve citizens' quality of life and freedom.

While there are stories of laboratories being set up in people's private closets or garages (Alper 2009; Wolinsky 2009), most of the active DIYbio members gather in regional biology-oriented community labs like Genspace in New-York, Biocurious in California, La Paillasse in Paris (France) and Madlab in Manchester (UK), to cite a few examples. In contrast to academic laboratories, the places where DIYbio is carried out usually allow access to everyone, regardless of their academic and socio-cultural background. DIYbio communities do not require that practitioners possess academic degrees, and monthly fees vary between zero and a couple of hundred euros. In addition, mailing lists and websites are freely accessible. One of the highest constraints for an amateur is the access to lab equipment and an efficient way to overcome this limitation is thus to put all personal facilities in a common place. We will see below how non-professional people can get access to necessary laboratory hardware by recycling old material or by manufacturing themselves cheaper replicas. By definition, amateur groups are not working at the frontiers of science and technology. In fact, in two articles published in *Nature* we read that "Most biohackers are hobbyists who delight in crafting their own equipment and who tackle projects no more sophisticated than those found in an advanced high-school biology lab" (Anon 2009) and that one can "have a hard time seeing the cutting edge, fundamental research reaching the hobbyist laboratory" (Sawyer 2011). Even though modern scientific challenges like synthetic biology are much discussed, the practice of DIY synthetic biology is very modest at this time. Instead, when doing wetlab work, DIY practitioners tend to focus on getting basic molecular biology protocols to work in their own settings. It is clear that individuals in the community do want to do more complex wetlab work, demonstrated by the presence of "Synthetic Biology crash courses" in DIYbio labs like Genspace or Biocurious. Recently, a survey realized by the University College of London 2012 iGEM team asked biohackers across the world whether they wish to work with BioBricks. It appeared that 75 % of them answered positively (iGEM UCL 2012). In general, however, DIY biology practitioners are currently foremost working towards creating and tinkering with scientific hardware, software and experimental protocols. And it is by creatively designing and redesigning equipment and protocols that DIY biology can foster new scientific practices (i.e. OpenPCR project, Quick and Dirty DNA barcoding, Biological ink project…).

DIYbio, a new substrate for biotech innovation

The motivation in DIYbio to redesign equipment and open up access to biology is intrinsically linked to the existence of synthetic biology and the iGEM competition, which have both offered amateurs an image of biology as something powerful and easy to engineer, even for novices, and as a means to attain better knowledge of their environment, their health and their bodies. In a larger spectrum, and to cite Ellen Jorgensen (Genspace.org): "In a DIYbio lab you can work on a project without having to justify it is going to make a lot of money, or that it is going to save mankind, or even that it is feasible, you just need to follow safety guidelines". In fact, innovation in hackerspaces is fundamentally driven by personal or social ambitions. Amateurs are now able to manipulate the same tools than professional researchers, what would keep them out of actual cancer research in the future, or of trying to develop their own "biotools" like biosensors and bioremediation-directed bugs, in an attempt to make their own life and the life of their community easier and safer? In Table 1, we tried to gather the most representative ongoing projects within the DIYbio community that are focused directly or indirectly on resolving health issues (even if in their early stages of development). We did find two types of projects, those involving forward genetic engineering and the use of biomaterials (e.g.Biological blue ink) and those focused on passive analysis of genetic data (e.g. BioweatherMap).

For instance, the idea to build a Yogurt biosensor is a project popularized by Meredith Patterson, a computer programmer based in the US, who worked on a project where genetically modifying lactic ferments (e.g. *lactobacillus bulgaricus*) would sense melamine contamination in milk and trigger a visual response (Ledford 2010). This project was actually motivated by the massive melamine contamination from baby milk that happened in China in 2008 (Ingelfinger 2008). In France, a DIY project of biological blue ink, made using non-toxic pigments produced by bacteria, is proposing a non-polluting and biodegradable alternative to modern inks (Lapaillasse.org). The use of biomaterials will probably be the easiest route for amateurs and designers to produce innovative biotechnologies.

An amusing example of applied genetic analysis is the unusual implementation of DNA barcoding that the german Sascha Karberg used to investigate who was the owner of the dog excrements he frequently found in front of his door. He compared genetic signatures from the proof to the ones from his neighborhood dogs to find the culprit. Another example is Bioweathermap, a research project launched by Jason Bobe (Co-founder of DIYbio.org), George M. Church and Rob Knight. The project aims to monitor and study bacterial strains present in various surfaces in a house, in a city or a country, using metabarcoding (Hajibabaei 2012), so as to represent the distribution of microbial life according to the nature of the place and according to time. In the same way, the Genspace DIYbio laboratory is planning to improve the taxonomic classification of wild plants in Alaska with the Barcoding Alaska project. Similar projects using crowd participation could be used to monitor the evolution of global epidemics, such as flu, by sequence mapping the mutations of the virus in different parts of the world.

Being a very young community, what innovation, currently taking place in independent laboratories, could have the potential to bring cheaper and easier ways to perform medicine and improve health care from users' perspectives for example? The current promise of the DIYbio approach is not particularly relying on the cutting-edge nature of its projects, but rather on the following aspects (Table 2): (1) Full corpus of scientific protocols are re-written to become cheaper to perform (sometimes more than 10× to more than 100× cheaper) and handled more easily by amateurs with more accessible or local components. (2) Essential pieces of scientific equipment are re-engineered in order to make them open-source, simpler to assemble and cheaper to buy. For some members of the community, some of the hardware innovation even became the first step into the world of entrepreneurship and start-ups, like for the open-PCR, the Dremelfuge and the Genelaser open-source

Table 1 Most representative DIYbio and DIYbio-related on-going projects directly or indirectly targeted toward resolving health issues

Categories	Projects	Description	References
Genetic engineering and biomaterials	Synthetic Biology crash courses	Using GFP or pigment-synthesizing enzymes to color bacteria	http://www.indiebiotech.com/?p=152
	The Glowing plant project	Inserting luciferase gene into a plant to make it glow	http://www.kickstarter.com/projects/antonyevans/glowing-plants-natural-lighting-with-no-electricit/posts
	The biological blue ink	Using blue pigment-producing bacteria to make a non-toxic biodegradable ink alternative	http://www.lapaillasse.org
	Genomikon DNA assembly	Easy sequential ligations on a solid support	http://2010.igem.org/Team:Alberta
	Hacking Yogurt into biosensor	Engineer lactic ferments into biosensors (e.g. for Melamine detection)	http://www.indiebiotech.com/?p=152
	Biosynthesis of insuline and thyroxine	Engineer bacteria into synthesis plant for insuline and thyroxine	http://www.indiebiotech.com/?p=135
	First public biobrick	Antifreeze protein for making bacteria more robust to freeze/thaw cycles	http://2012.igem.org/Team:University_College_London/HumanPractice/DIYbio
	Nitrogenase directed evolution	Nitrogen fixation bioprocess for ammonium synthesis	http://wiki.biohackers.la/Nitrogenase_Directed_Evolution
Monitoring, sequencing and genomics	Quick and dirty DNA barcoding	Fast and cheap DNA barcoding	http://www.lapaillasse.org/news/1063/la-version-quick-and-dirty-du-dna-barcoding/
	Bioweather map	Geographic and temporal distribution patterns of microbial life	http://bioweathermap.org/
	Barcoding Alaska	Barcoding alaskan vegetal species	http://genspace.org/project/Barcoding%20Alaska
	Barcoding of fishes - "Sushigate"	Identification of mislabeled fish species in restaurants	http://phe.rockefeller.edu/barcode/sushigate.html
	Genelaser	Kit for extracting specific genes from your genome for sequencing	http://cofactorbio.com/genelaser
	Buccal Bioweather map	Identification and description of the buccal microbiome	http://groups.google.com/group/diybio/browse_thread/thread/62ff122b0e0272bd/c845f7cbbfcc4bbe?lnk=gst&q=health#c845f7cbbfcc4bbe
	Animal feces barcoding	Identification of specific dog feces' owner	https://www.globalscreen.de/programmes/show/117066
	Hack your genome	Tools for analyzing personal genomic data	http://sciencehackday.pbworks.com/w/page/47743279/sfhacks2011#hack_22
	OpenSNP	Open-source sharing of personal genomic and phenotypic data	http://opensnp.org/
	Personal genome project	Open-source sharing of personal genomic and phenotypic data	http://www.personalgenomes.org/
	Patients like me	Open-source sharing of personal medical files	http://www.patientslikeme.com/

Table 2 DIYbio alternatives for major experimental steps and lab equipment needed to realize synthetic biology projects

Experimental steps	Necessary equipments/consumables	DIYbio solutions	Saving ratio	References
Cell culture	Incubator—$130	Styrofoam insulated box with heating pads, computer fans and a thermostat—recycled material—$10	13×	http://hackteria.org/wiki/index.php/DIY_Incubator
	Bioreactor—$3,000	Aquarium air pumps connected to plastic bottles with fluorescent tubes—recycled material—$100	30×	http://hackteria.org/wiki/index.php/Algae_Culture_at_Home
Microscopy	400× optical microscope with camera—$130	Webcam optical microscope 400×—$10	13×	http://hackteria.org/wiki/index.php/DIY_microscopy
Centrifuges	Benchtop centrifuge—$2,000	Dremelfuge (requires 3D printer, drill)—$100	20×	http://www.thingiverse.com/thing:1483
Water bath	Water bath—$400	Home-made water bath (aquarium heater + bucket)—$40	10×	http://hackteria.org/wiki/index.php/DIY_Water_Bath
Magnetic stirrer	Magnetic stirrer—$70	DIY magnetic stirrer—$10	7×	http://hackteria.org/wiki/index.php/Magnetic_stirrer
Spectrophotometer	Spectrophotometer—$150	DIY spectrophotometer—$10	15×	http://publiclaboratory.org/tool/spectrometer
Sterile work	Autoclave—$1,000	Pressure cooker—$70	14×	http://cathalgarvey.posterous.com/an-analysis-of-what-diybio-has-and-what-it-ne
		Microwave—$50	20×	Sanborn et al. (1982)
	Glove box—$10,000	DIY Glove box—$500	20×	http://www.p2pfood.net/wiki/index.php/DIY_Glove_Box
	Sterile hood—$2,000	Custom sterile hood—$200	10×	http://hackteria.org/wiki/index.php/DIY_Sterlisation_Hood
Electrophoresis	Gel box—$400	Home-made plastic gel box—$25	8×	http://citizensciencequarterly.com/?p=3084&preview=true
		Pearl gel box kit (with UV ztransilluminator)—$199	7×	http://www.pearlbiotech.com/
	UV Transilluminator—$1,000	DIY UV transilluminator—$100	10×	http://www.instructables.com/id/UV-Transilluminator/
	Blue light transilluminator—$1,000	The blue note project—$30	33×	http://www.lapaillasse.org/news/1078/le-bluenote-project-prototype-2/
	Power supply—$1,000	DIY power supply—$40	25×	http://wiki.biohackers.la/index.php?title=Electrophoresis_Power_Supply&redirect=no
PCR	Thermocycler—$2,500	Open PCR—$500	5×	http://openpcr.org/
		Lava Amp—$300-$500	5×	http://www.lava-amp.com/
		Thermotyp—$400	6×	http://speakscience.org/
		Personal PCR—$199	7×	http://cofactorbio.com/personalpcr
		Bulb PCR—$25	100×	http://russelldurrett.com/lightbulbpcr.html

Table 2 continued

Experimental steps	Necessary equipments/consumables	DIYbio solutions	Saving ratio	References
DNA purification	Miniprep kits—$1 per miniprep	DIY buffers + Regeneration of silica columns—reusable 10–20 times—$0.2 per miniprep	5×	Siddappa et al. (2007)
DNA digestion/DNA ligation/PCR/DNA assembly	Enzymes—Taq polymerase $0.3 per Unit	DIY purification of recombinant proteins—Taq polymerase $0.001 per Unit	300×	Grimm and Arbuthnot (1995)
Make cells competent + transformation	Long protocol using Ice and CaCl2 salts—ice difficult to procure	Fast one-step method using PEG-3,350 (laxative) + $MgSO_4$ (Epsom salts)—easy to find	1×	Chung et al. (1989)
Transformation	Gene-gun—$17,000	DIY Gene-gun—$200	85×	http://arkiv.radio24syv.dk/video/6997330/3-planet-fra-solen-uge-36-2012
Sequencing	1 single read—5$	No cheaper alternative	1×	http://www.gatc-biotech.com/en/index.html
Quantitative PCR diagnostics	qPCR—$10,000	Amplino—$200	50×	http://www.amplino.org
Bioprinting	Non existing commercial solutions	Hacked inkjet printer for printing layers of bacteria	N/A	http://biocuriousmembers.pbworks.com/w/page/48912717/Bioprinter%20Project

The DIYbio community has proposed numerous substitutes to make biology cheaper to perform for amateurs

projects (see Tables 1, 2). DIY projects in biology are now a reachable goal in most places around the world. To prove that cheaper medical diagnostic can be made with local and easy-to-procure components, is already an important innovation by itself for developing countries. Building their own material and setting up their own protocols can help emerging countries to reduce their dependency on imported, expensive and difficult to maintain machines from developed countries, which is a major hindrance for the development of medical care centers and of technological innovation incubators.

An interesting example here is Amplino, a project developed by three Dutch DIY biologists and that won 40.000 euros with the first prize at a Vodafone Mobile competition. The idea behind Amplino is to build a quantitative PCR diagnostic system that is open-source and much cheaper (less than $250) and easier to use than a conventional solution. Amplino can be used in developing countries as a diagnostic tool to detect malaria in less than 40 min by using a single blood drop. In areas in which biotechnology is usually unaffordable and not used for health purposes, disruptive technologies like the Amplino are expected to fill an important niche for global health improvement.

Resources and practical knowledge for DIYbio projects can be found freely on the web, be it on open-source platforms for information sharing like the OpenWetWare database (an MIT initiative), the websites protocol-online.org and instructables.com or directly on the DIYbio google group as all threads are searchable, and of course on the wiki (equivalent to lab notebooks) of all DIYbio regional communities. This sets a cornerstone for anyone who is looking to go into biological tinkering by his/her own means. It also sets an ethical and security framework for laboratory work as best practices are shared and projects are developed in an open and transparent way.

The reasons behind the fact that the DIYbio community has not yet been able to carry out successfully synthetic biology projects are of three kinds: (1) Funding. Prime biological material like synthetic DNA sequences and enzymes still cost too much as basic components. (2) Administrative. Existing regulations for the use of recombinant DNA techniques to create genetically modified organisms (GMOs) vary between different countries or federal states (in the USA for example). Usually one needs to obtain a license for being able to conduct such manipulations but legislation is absolutely not adapted for proposing amateur-specific licenses. Access to raw genetic material such as BioBricks and chemicals such as pure ethanol (one of the key solvents in biology) is still prohibited to amateurs at the present day. (3) Scientific. Even though DNA assembly standards and computer-aided-design (CAD) softwares enable fast prototyping of biological systems (Carothers 2013), achieving the engineering of robust and optimized solutions is very hard, even for large companies, like Amyris, who possess the money, the okay from regulators and the technicians. However as progress in CAD software permits greater predictability in the design process, and as the cost of consumables and equipment incrementally decreases, it will also encourage a larger crowd of amateurs to turn to genetic engineering.

iGEM as model for DIY synthetic biology

One aspect that must be mentioned is the potential future capability of DIYbio enthusiasts to conduct more mature synthetic biology projects. The level of skills needed to create innovative biotechnology projects like in the iGEM competition is relatively low, considering that undergraduate students, and now high-school students, are the main contributors to their team's projects. Indeed, the abstraction hierarchy that characterizes the BioBrick standard have permitted very easy and intuitive-enough manipulation of genetic information. The financial means, the equipment and the knowledge that an iGEM team uses for developing its project is comparable to what a bio-hackerspace could manipulate too. Therefore it is reasonable to look at how iGEM teams perform today in the objective to foresee what amateur biologists could create in their community labs over the coming years. We thus explored all 764 different iGEM projects developed since the beginning of the competition in 2005, we retained only the ones whose goals were directed toward resolving health issues, be it directly or indirectly (overall 329 projects), and we classified them in Table 3 (see supplementary table 1 for the detailed classification) according to their final application: Health and Medicine, Environment quality, and Food and Energy. In the category health and medicine, we can find projects whose goals are to find new ways of fighting against cancer or infectious diseases using engineered bacteria or a possible new generation of vaccine against HIV. Projects about environment quality include, for example, students who have engineered biological systems to sense various kinds of pollutants in water and soil, and ways to recapture them for the purpose of depollution. Among the projects dedicated to food, there were iGEM teams who proposed to enhance the nutritional quality of plants or to release vitamins and protective molecules in the gut through edible bacteria. And in the category energy, we can find projects seeking solutions for producing biofuels, bioplastics or new technologies to remediate biological waste into usable energy. As a matter of fact, an increasing number of iGEM teams collaborate with DIYbio community labs (like Genspace in New-York) or strategically design their project with the aim to give more affordable tools for genetic reprogramming of bacteria to amateur biologists. For example, the 2012 iGEM teams of Edinburgh and University College London proposed new bacterial chassis and alternatives to the use of antibiotics as selective markers. For an iGEM team, human practices are important elements of the project development; it pushes the questioning of the technological framework students use during the competition and act as a form of positive governance. This aspect of iGEM resonates with the transparent and open nature of DIYbio. In 2012, the french Evry iGEM team was hosted several times by La Paillasse to debate openly on the "Chassis" metaphor that Synthetic Biology uses. Such collaborations between iGEM teams and DIYbio practitioners are, we argue, a way to outline where future innovations enabling cheaper and safer biological tinkering potentially lie.

What might be achievable in the future?

Looking at this relatively large number of iGEM projects can help us to assess the potentiality of synthetic biology outside traditional research institutions. We consider the capability of current iGEM teams to be sufficiently similar to the one of future DIYbio communities (not least since the number of collaborations between iGEM teams and DIYbio labs has been increasing over the past few years). Strategies to assemble DNA sequences are what currently limit the price and the pace at which they can develop

Table 3 Number of iGEM projects since 2005 that were targeted toward resolving directly or indirectly health issues

Categories	Sub-categories	Number of iGEM projects (years 2005–2012)
Health and medicine	Medical diagnosis	30
	Medical cure for cancer	17
	Medical cure for infectious diseases	19
	Medical cure—others	62
	Vaccines and antiviral treatment	4
Environment quality	Environment monitoring	71
	Depollution	33
	Environmental prevention	7
	Control of GMO dispersion	5
Food and energy	Food	27
	Energy (biofuels/bioplastics and bioremediation)	42
DIYbio (since 2009)	Working with DIYbio groups	7
	Mentioning DIYbio in the aspirations for their project	5

designer genetic systems. In order to realize designer genetic systems, nowadays one has access to various technologies and methodologies to assemble synthetic DNA pieces.

A telling example is the BioBrick 3-antibiotics assembly, which has been popularized by the iGEM competition and which uses a "classical" approach where specific restriction enzymes and ligases cut and link respectively BioBricks together. On the one hand, this process has the advantage to work with any BioBricks or BioBrick-compatible DNA sequences. On the other hand, it can only handle 2–3 BioBricks at once and needs a long iterative process that limits the pace at which the final construction can be assembled. For about $100, the BioBrick DNA kit is the best starting DNA assembly kit available today, even though they are only shipped to academic laboratories for the moment. However, due to a high demand from the amateur community, a registry of open and free BioBricks is more than to be expected in the near future, which is illustrated by active discussions on the DIYbio.org mailing list and during the DIYbio Europe summit. To get DNA bricks, community labs can use either gene synthesis or tap into their relationship with institutional labs. In recent years, new strategies enabling the manipulation of custom sequences for assembling any pieces of DNA together were created (Gibson and SLIC assembly methods) (Hillson 2011), giving the means for a total customization of the final construction, while with BioBricks people are condemned to deal with scars in between each ligated parts. The so-called Gibson methodology was the one used for the assembly of the first synthetic chromosome (Gibson et al. 2008). Both Gibson and SLIC use the same basic principle of creating, through the use of an exonuclease, necessary hanging cohesive ends on each DNA pieces that will auto-assemble and permit the formation of unique and specific couples in your DNA soup. One could see the process as the assemblage of a chain where each link recognizes and assembles specifically with a set of 2 unique and different neighboring links. The DNA complexes can then either be re-ligated beforehand (Gibson) or immediately transformed (SLIC) into the cell. The clever aspect of those two methodologies is that people can assemble together a lot more different DNA pieces at once than before (between 5 and 10), and even use strategic assembly for reducing the cost of making large libraries (Yehezkel et al. 2011).

Such practices are today possible because of the increasingly cheaper price for DNA synthesis and sequencing (Carlson 2010). So one can imagine to manufacture, like Soma et al. (2012), a synthetic genetic construct to express a set of five enzymes in bacteria to produce a high value organic chemical (i.e. Isobutanol) by implementing an extrageneous metabolic pathway within a living cell that uses an abundant natural source of energy (i.e. cellulose). Seven thousands nucleotides (7,000 nt) should be quite representative of the DNA sequence length for such a construction. The current cheapest method would be to fragment a given DNA sequence into 14–16 parts and to order them at $99 a piece (gBlocks fragment—Integrated DNA Technologies, Inc) and to assemble them using the Gibson methodology. Manufacturing such a de novo sequence would cost between $1,500 and $2,000 in total, additional cost comprised, which is almost affordable for most community laboratories. However if one reuses genetic information or DNA from previous plasmids or constructions through PCR amplification, then the price can dramatically decrease. We should also keep in mind that DNA synthesis and sequencing costs will continue to decrease at fast pace and it may be soon possible to order an entire synthetic chromosome of 1 million nucleotides for the same price. As a matter of fact, the company Cambrian Genomics announced a new disruptive gene synthesis technology called "DNA Laser Printing", that is high-throughput while its synthesis efficiency is theoretically of 100 %, removing the costs of error correction. If they succeed to bring this technology on the market, it could decrease the cost of DNA synthesis by at least an order of magnitude.

In terms of financial issues, public micro-funding through crowdsourcing platforms like Kickstarter has made it possible for DIYbio associations such as Biocurious ($35,000) to set up their own laboratory. In the future, we might thus see community labs apply to public grants like the ones of the European Commission or to private calls such as Grand Challenges in Global Health by the Bill and Melinda Gates Foundation in order to fund their health-related and science popularization projects. In fact, Madlab gets funding from the Welcome Trust through the Manchester University, and Biologigaragen (Copenhagen, Denmark) is benefiting from the StudioLab FP7 European project to install a biohacklab in a medical museum. In conclusion, even if most DIYbio amateurs have not yet turned towards resolving specific health issues, their philosophy and methodologies are offering a new path for alternative developments in biotechnology, ones that could potentially yield benefits for improving people's quality of life on a larger scale.

Biosafety, biosecurity and public fears

There are undoubtedly new biosafety and biosecurity threats associated with the synthetic biology era (PCSBI Synthetic Biology Report 2012). And it creates some legitimate fears in the public. The point we'll try to address here is not about synthetic biology itself, but how DIY biology is trying to make sure that nothing harmful can be created. Safe practices are by all means necessary for efficient spreading of amateur work in biology and democratization of science in general.

Media have been writing about people carrying out biotechnology experiments in their kitchen, hidden from any kind of regulation. This is not a very reassuring image, especially considering that security, safety, and terrorism are high on the agenda in a number of countries. In fact, several cases of people being harassed by the authorities for pursuing biology or chemistry related activities outside of regulated laboratories have been reported. One revealing example is the story of artist Steve Kurtz (Wohlsen 2011), who uses biotechnological material in his performances. Having discovered at wake-up that his wife had died from cardiac arrest, he had called the police who, discovering his material, called in the Joint Terrorism Task Force. Suspected of bioterrorism, all his equipment, and even the body of his wife, was seized for analysis by the FBI. It turned out that Kurtz's wife had died from a natural cause and charges were eventually dropped against him a couple of years later (Wolinsky 2009). While this story has widely circulated, and while the FBI today closely watches—and even organizes conferences with—the international DIYbio community, there haven't been any reported cases of security or safety threats stemming from DIY bio practitioners. To use the words of Jason Bobe, co-founder of DIYbio.org, the DIYbio and iGEM communities are very well-positioned to develop a positive culture around citizen science and to "set the pattern" for best practices worldwide for biotechnologies by establishing a code of ethics, developing norms for safety, and creating shared resources for amateurs (Kuiken and Pauwels 2010).

By setting up community labs that are official and public, that are insured and that foster documented adherence to safety regulations, Biocurious (Sunnyvale, USA) and La Paillasse (Paris, France), among others, are showing a way to build spaces where regulation can be commonly followed and more easily enforced to practitioners. This should play a role in facilitating DIYbio's social legitimacy and regulatory framework. Ellen Jorgensen (Genspace.org) summarized this by stating that the press had a tendency to consistently overestimate biohackers' capabilities and underestimate their ethics. Nonetheless isolated biohackers would still be hard to reach and it is mainly for this reason that DIYbio.org has set up in 2012 a Question and Answer platform on biosafety, which is a great example of what global governance can be in the case of DIYbio. This unique free web service enables amateurs to submit questions to professional biosafety experts and members of the American biological safety association. The issues of safety, security and social acceptance are also what motivated the DIYbio community to organize in summer 2011 its first international congresses gathering all regional groups throughout the world. The goal of those congresses (one European and one American) was to elaborate collectively a code of ethics for the community. Among all propositions, the most frequent were Transparency, Safety, Open-access, Education, Respect and Responsibility. On the draft code of ethics from the European delegation we read, for instance, that practitioners should "adopt safe practices", "emphasize transparency" and "respect humans and all living systems". While such general frameworks are arguably an important starting point, DIYbio still needs to find an active and, above all, binding way to deal with regulatory and safety issues. In particular, local and national regulations and legislation need to be taken into account. Some new regulations probably need to be created *ad hoc*, in order to provide a more robust framework, especially since there still are uncertainties about which scientific practices can and cannot be carried out outside of traditional research sites.

It has been argued that the "de-skilling" implied in synthetic biology may encourage the design of criminal bioweapons by facilitating their creation (Tucker 2011). Such an argument relies on the idea that it will be possible to engineer organisms without having the whole basic practical knowledge currently necessary in lab practice. It may therefore be easier for criminals devoid of this knowledge to create lethal organisms. Several objections may be advanced against such arguments. First, even though BioBricks are useful for rapid prototyping and testing of conceptual ideas, living organisms are too complex to be entirely captured by such an abstraction. It is indeed much more easy to spoil a genetic function than to optimize it, especially in the case of virulence. In order to optimize an artificial organism, it will probably be necessary to go back to the lab to tweak the DNA in more subtle ways—therefore needing more sophisticated tacit knowledge of experimental biology (i.e. directed evolution methodologies). Another counter-argument is that if in the future biological processes are well standardized, automated and commercially available, it is likely that various security features will be deeply embedded in the structure of the components. To stick to the computer metaphor, it is much more difficult to manipulate the internal working of computer RAM in Basic or in Javascript (high-level programming language) than in C or Assembly language (low-level programming language). Also, these "commercial biotechnological toolkits" will probably be based on some standard genetic operating system, a minimal genome that should be intrinsically weak. Even if there is currently no reason to panic, we cannot evidently predict for sure what the technological threat will be in 20 years from now.

Conclusion

In this article, we have shown how the DIYbio community has developed a consciousness of its responsibilities when it comes to deal with biological samples. Regional DIYbio groups are working toward making their activity the most secure, transparent and respectful as possible. Even though synthetic biology is opening up new paths to biological weapons, one could remark that the 2nd paragraph of the US national strategy for countering biological threats even states that garage biology is good and necessary for the future physical and economical security of the USA (National Strategy for Countering Biothreats 2010). Now one of the main challenges for the DIYbio community will be to prove that it can be trusted on the long-term when dealing with safety and security in order to better interact with the public and scientific institutions.

Bill Gates recently told Wired magazine that if he were a teenager today, he would be hacking biology: "If you want to change the world in some big way that's where you should start—biological molecules." (Wohlsen 2011). The DIYbio community is currently drawing interesting promises toward making biology easier and cheaper to use. At the same time, synthetic biology, though still stammering, is permitting the deepest control we ever had on biological systems. Together they have the potential for global development and advances in global health.

As the DIY biology community is growing and spreading across the world, several issues are concurrently raised. We have shown that DIYbio labs and practitioners are working on a large variety of projects geared towards making scientific equipment cheaper, more available, more mobile, more usable. This equipment holds the potential to make synthetic and molecular biology more accessible and, in doing so, it holds the potential to empower citizens and to reshape the relationships between biology and society. DIY biology, we can argue, is both a scientific endeavor and a socio-political movement. It is a movement that is to be open and that can provide citizens a counter-power to participate in the societal choices concerning the use of these technologies and therefore represents, it has been discussed, "a material re-distribution, a democratisation, and an alternative to established, technoscience" (Meyer 2012).

By allowing scientific equipment to enter people's homes and by building community laboratories accessible to amateurs, DIY biology thus also raises questions about its regulation. The ways in which DIY biology is "governed" or "regulated" takes a distinctive form: rather than being top-down it is bottom-up; rather than being defined by institutions or policy makers, it is collectively and openly negotiated by a large group of people; rather than being illegal, undercover or anti-establishment, DIYbio groups (at least the official ones) want to be transparent and do collaborate with professionals and public authorities. The elaboration of a code of ethics is to date perhaps the most explicit example of the community's wish to find a "soft" yet binding way to create a common set of values and principles for its members. The question remains to what extent a global set of ethical principles will and can be adapted and adopted in local contexts.

Governance is a double-edged sword: on the one hand, there is a need for regulation to protect people's safety and the environment. On the other hand, too much regulation might push some people underground so that eventually the movement might become even more difficult to control (Wolinsky 2009). The regulation and governance of DIY biology calls for a balancing act: to collectively set ethical standards without alienating individuals, to establish a global set of principles that makes sense in local contexts, to be close enough to authorities, yet far enough to avoid loosing the counter-cultural and innovative edge that DIYbio stands for.

Finally, we want to stress that DIY biology enables new partnerships between amateur and professional scientists. Hence, besides seeing DIY biologists as people who are hacking, tinkering with scientific equipment and having fun while doing so, why not conceive them as actors that can be fruitfully integrated into research activities? After all, biohackerspaces are spaces of intellectual freedom and they have the benefit of being open to a wide range of actors and social backgrounds and sorts of collaborations. DIY biology certainly has the potential to provide the key means for rethinking modern and traditional biology by both moving biotechnology out of the laboratory and moving it into people's everyday lives.

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