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Commercializing synthetic biology: Socio-ethical concerns and challenges under intellectual property regime

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ABSTRACT **Synthetic biology also termed as 'genomic alchemy' represents a powerful area of science that is based on the convergence of biological sciences with systems engineering. It focuses on building, modelling, designing and fabricating novel biological systems using customized gene components that result in artificially created genetic circuitry. As discussed in the present study, synthetic biology is an elegant consequence of amalgamation of various branches of science. It is speculated that the resulting synthetic organisms can successfully provide solutions for the problems where natural biological systems have failed. These artificially synthesized organisms can be tutored to meet diverse applications such as production of various biodrugs and creation of tailor-made metabolic pathways. Evidently, this revolutionary technology has the potential to transform human life directly and indirectly. The article provides an insight into the tremendous commercialization ability of synthetic biology in various sectors (bioenergy, medicine, and so on) as demonstrated by various initiatives, collaborative projects with huge investments. It is noteworthy that synthetic biology tools and organisms can be used for saving, creating 'or' destroying life; hence the study further deals with the socio-ethical implications of this rapidly advancing field of biology and also assesses the challenging role of intellectual property regime in commercialization of synthetic biology.**

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INTRODUCTION

> There are only two ways we know of to make extremely complicated things. One is by engineering, and the other is evolution.
>
> Danny Hillis

The issues and concerns in modern society have necessitated biology to enter into a new and exciting era of developing effective and customized solutions. The realm of biological sciences has evolved from theorizing the fundamentals of life to applying established principles in association with new technologies in order to facilitate an interdisciplinary interaction between chemical, physical, engineering and computational sciences. Synthetic biology embodies this attempt towards developing new age technology, where multiple areas merge, complement and facilitate each other.

Research in the field of genetic engineering and DNA manipulation has paved the way for scientists to artificially engineer biological systems. In addition, these working models are speculated to have immense potential commercially. Synthetic biology is an impressive advancement in this field that has resulted from the interplay between several advanced engineering disciplines such as system design with novel inputs from genomics and proteomics. The possibility to construct and fabricate new biological parts and systems with success indicates the possible novel applications of biotechnology in human diagnostics and therapeutics.

Beginning from the first chemical synthesis of a gene by Har Gobind Khorana in 1970s and Marvin H. Caruthers of the University of Colorado in the 1980s, the foundation of developing and synthesizing single DNA strands by exploiting their natural chemistry has stood the test of time. By the mid-1990s, Willem Stemmer *et al* had modulated the polymerase chain reaction and were able to synthesize a large gene and vector system of approximately 2700 base-pairs,[1] leading to the evolution of high throughput designing of mechanisms of DNA manipulation with multifarious applications. By the year 2002, scientists were able to successfully develop functional artificial biological circuitry. The BioBricks foundation marked another milestone by providing open tools and standardized parts for biological engineering. Researchers today are working towards improving the power of DNA synthesis technology, and to counter bigger challenges such as inventing new languages and grammar that can enable the evolution of many new genetic 'programs'. These programs will be helpful in simulating useful behaviors, such as the production of fuel, food or medicines.[2]

Interestingly, technology evolves at a much faster pace giving man a limited scope and ability to comprehend and react to its progress as a consequence. This is particularly pertinent in the area of biotechnology, whose implications are not alien to social, ethical and legal ramifications. In order to approach technological advancement prudently, it is *prima facie* necessary to understand why society and legal systems find it difficult to respond and take cognisance of the pace at which it evolves. Synthetic biology being one of the most recent, powerful and prospective science arising from multidisciplinary research can possibly have more complex implications on the society. The present study deals with the raising concern of socio-ethical issues of synthetic biology. It also makes an attempt to gain insight into the role of intellectual property regime (especially patents) in commercialization of synthetic biology. Keeping these concepts in perspective, the earlier part of the study provides an insight into the ever-advancing field of synthetic biology and its dynamism. Role of various initiatives, projects involving universities, industry and funding agencies have been discussed with regard to commercial potential of synthetic biology. This is followed by the discussion on the implications of synthetic biology under the broad ambit of the possible social, ethical and legal concerns. It specifically tries to analyze the application of intellectual

property rights with respect to the patentability of inventions emerging within this area. The present work also deals with burning issues such as – how complexity in science can affect the legal system in terms of being multidisciplinary and applying social norms to bring about a transformation in perception of novel technology. The article concludes with outlining the areas where policy and law need further insights towards amending the socio-legal regime in order to encompass customized organisms.

UNDERSTANDING SYNTHETIC BIOLOGY

The term 'synthetic' according to the Oxford English Dictionary means anything which is unnatural, man-made or simulated. It relates to the creation of material or matter resembling the natural product by way of fabrication and combination of parts to form a connected whole. This approach forms the basic tenet that defines the entire scope of synthetic biology. It aims at artificial production of natural components of biological systems and assembling them together to create unique, tailor-made or customized life forms.

The term 'synthetic biology' was first coined by Barbara Hoom to describe a specific class of genetically engineered bacteria.[3] Although generally described as 'synthetic biology', this branch of applied technology associated with creating life artificially or synthetically has been ascribed a wide nomenclature including, 'Designer Biology', 'Intentional Biology', 'Constructive Biology', 'Natural Engineering', 'Synthetic Genomics' and 'Biological Engineering'.[4] Embodying the primary purpose of this area of science, Benner and Sismour in the year 2005 explained that, '[synthetic biology] attempts to recreate in unnatural chemical systems the emergent properties of living systems … [the] engineering community has given further meaning to the title … to extract from living systems interchangeable parts that might be tested, validated as construction units, and reassembled to create devices that might (or might not) have analogues in living systems'.[5]

Synthetic biology has developed from the advances made in biomimetic chemistry and genetic engineering. Biomimetic chemistry aims at the application of traditional chemical reactions to create molecular structures *in vitro* without requiring dependence on natural processes. The investigative and theoretical aspects of biomimetic chemistry have generated an in-depth understanding of the properties of molecules over the course of time. The conventional genetic engineering mechanisms, on the other hand, have facilitated scientists to manipulate and observe natural biological systems by tinkering with existing biomolecules, cells or organisms. These methods are, however, empirical and are not designed to accommodate complex molecular interactions.

Synthetic biology embodies a complex level research that has evolved from the well-established principles and traditional scientific methods. It is based on the premise that it is simulation and synthesis that aids both discovery and understanding of biological mechanisms, something that cannot be achieved by mere analysis.[6] Thus, it allows construction of artificial biological systems from scratch by either incorporating non-natural genetic parts into living systems or interchanging natural components to produce unnatural results from living systems. What differentiates synthetic biology from the traditional methods of genetic manipulation is that it does not involve mere alteration of existing genomes, but provides high throughput construction and engineering of organisms having genotypic characteristics that control synthesis of complex, biologically based (or inspired) systems that display functions that do not exist in nature.[7] Figure 1 indicates the disciplines of science and technology that have come together in developing such novel multi-functional organisms.

Synthetic biology has a broader scope in terms of applicability as it attempts to recreate

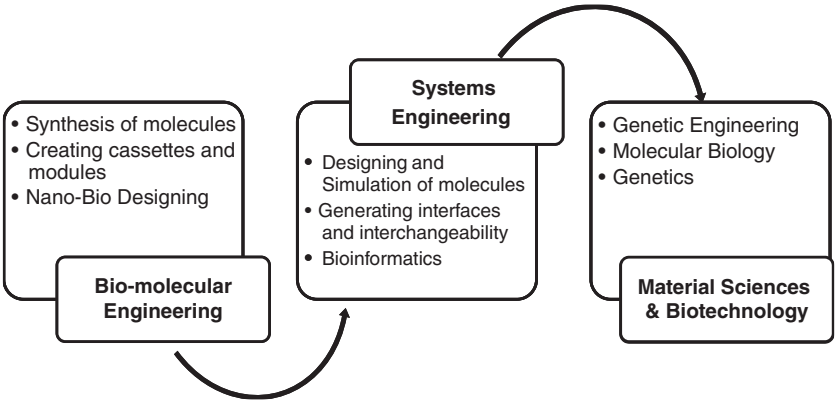

Figure 1: The interdisciplinary nature of synthetic biology.

the emergent properties of living systems, including inheritance, genetics and evolution in non-natural chemical systems.[8] Apart from merely understanding or explaining natural behavior, it has expanded the well-established knowledge base in science to generate tailor-made outputs. In common parlance it can be said that synthetic biology attempts to generate the building blocks of life.

The technology associated with synthetic biology is concerned with applying the engineering paradigm of systems design to biological systems in order to produce predictable and robust systems with novel functionalities that do not exist in nature.[5] It reflects amalgamation of the disciplines of systems biology, modular engineering and fundamental biology to resolve problems arising from traditional biotechnological methods. The engineering facet of synthetic biology typically deals with standardization and designing the modularity of parts in order to generate abstract design procedures of biological systems.

Systems biology further facilitates mapping of pathways, gene and protein interactions and logical 'circuitry' of natural organisms at the cellular, tissue and whole-organism level and the integration of this information into a computer model. Its primary goal is to attain a quantitative and predictive understanding of a biological system.[9] This is further facilitated by applied bioinformatics which allows simulation, thereby permitting not only new components to be incorporated into compatible living systems, but also enhances adaptation of existing genetic mechanisms to operate in novel living environments. Thus, synthetic biology allows scientists to develop custom-made and specialized mechanisms which are tailored to meet defined purposes and objectives.

VIABILITY OF SYNTHETIC BIOLOGY

Synthetic biology has the potential to revolutionize all fields of science and technology. Given its inherent nature and the capacity to accommodate and interface between disciplines, it may change the face of the life sciences industry, quite similar to the impact the information technology has on the computer industry. Many industry analysts and researchers believe that this field will be the impetus that will drive industry, research, education and employment in such a way that it would be possible to harness long-term gains within a shorter span of time. The primary objective of research in this area is to be able to counteract the imminent crisis in several areas including health care, food availability, environmental sustainability and energy.

Synthetic biology as a discipline in the era of modern science has gained focus in resolving issues such as the current global food and oil crisis, the rise in complex disorders and lifestyle dependant diseases. The rapid growth of synthetic biology has been partially because traditional mechanisms have either failed or have not been very successful in countering these problems. The wide range of areas where synthetic biological systems can be adapted is depicted in Figure 2. Synthetic biology provides a more objective and directed approach, thereby reducing the costs of development and commercialization within a short span of time. Although the initial investment in terms of finances for research and development in the area of synthetic biology may be large, however, once the platform is set, this area of modern science will prove to be an economically viable solution for the future. The broad spectrum of applications in different areas as illustrated in Figure 3 indicates commercial viability of the technologies developed employing synthetic biology.

The United States of America has gained the center stage for most of the synthetic biology research. The primary areas of focus include development and use for the generation of bio-energy and control measures against bio-terrorism. In this regard significant investment has been made by the Defence Advanced Research Projects Agency (DARPA) and the Departments of Defense (DoD) and Energy (DoE). DARPA is interested in DNA computing and the DoD has allocated US$3 million to Craig Venter's not-for-profit Institute for Biological Energy Alternatives.[10] Synthetic Genomics in the United States of America has made efforts towards developing efficient fuel that is environment friendly as well as cost effective.[11] This new technology will lead to the design and synthesis of microbial cells with far more superior capabilities in converting feedstock into fuels than even the most successful among the genetically modified natural cells.[12] In the European Union, there are collaborations amongst various universities for generation of biomolecular hydrogen (Engineered Modular Bacterial Photoproduction of Hydrogen) which is considered to be helpful in drug synthesis and manufacturing of biochemicals, waste treatment and production of other biofuels.[13]

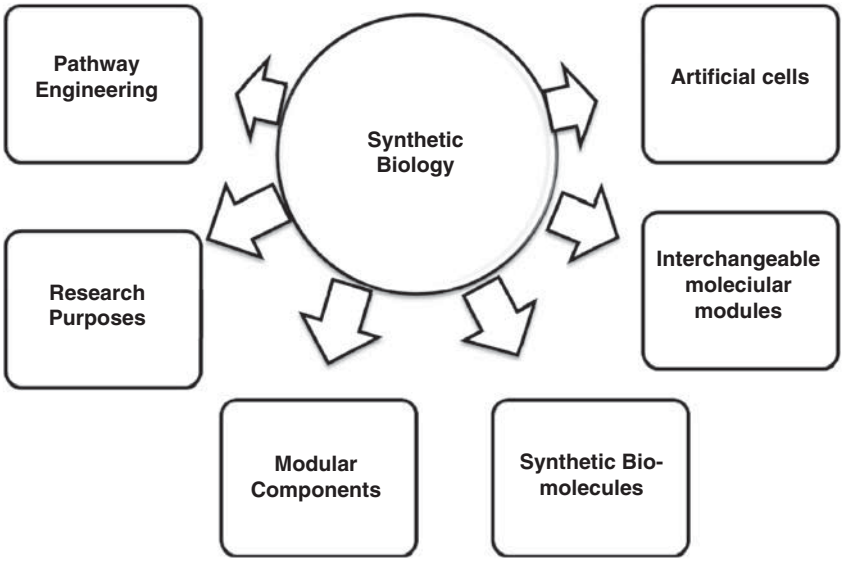

Figure 2: Potential scope of synthetic biology.

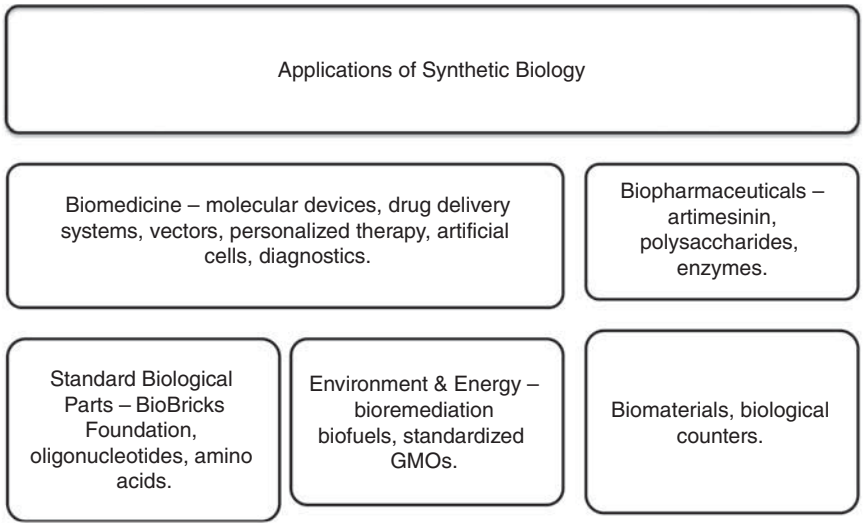

Figure 3: Areas of applicability.

In the health-care sector, a partnership has been initiated between Fondazione Telethon (Italy) and French and Italian universities to develop methods for the treatment of diabetes and other complex diseases through the innovative use of novel biological delivery systems.[14] Also, the NEST Pathfinder Initiative in the European Union has a challenging project on developing a library of around one million hybridoma cells each expressing a different antibody and has been named as Hyblib System. The system intends to make the process of screening and selection of antigen-specific cells relatively easy. 'Smart drugs' are also being developed that will inherently detect infected cells and automatically activate in the specified sites. These programmed molecules will reduce the cost of drug delivery and also the undesired side effects.

As more synthetic biology-based research and development initiatives come into existence, the financial aspects in terms of investment from various public and private sectors are gaining momentum. It has become evident that investments with regard to the applied synthetic biology are on an exponential rise. This is indicative of the inherent potential and trust this novel technology has garnered among the scientific community and industry. Illustrating the quantum of investment is in the area of biofuel development which in the United States of America capitalized around $30 million in 2009.[15] Also, there has been large-scale funding with regard to development of novel drug molecules and delivery systems such as in the case of the anti-malarial compound artimesnin which is traditionally extracted from sweet wormwood plants (*Artemisia annua*). In April 2006, Professor Jay Keasling and his team at the University of California, Berkeley were able to successfully insert the genes for production of the compound by engineering a yeast strain to act as a factory of artemisinic acid.[16] In the year 2006, EraGen Biosciences, Madison, USA had a funding of $12 million for the development of oligonucleotides.[17] Collaborative efforts have been favored in order to cover the initial investment costs. The various organizations, universities and collaborative projects that are currently focusing on research in the areas of synthetic biology are illustrated in Figure 4. Examples of the areas in which collaborations and joint ventures are taking place around the world are presented in Table 1.

Key Players		
Industry – • Codon Devices. • EraGen Biosciences. • Synthetic Genomics. • Glycoform, UK. • Sangamo Biosciences. • Genomatica. • Genencor. • EngeneOS. • Amyris Biotechnologies.	University – • Massachusetts Institute of Technology. • Stanford University. • Scripps Research Institute. • Pasteur Institute, Paris. • Swiss Federal Institute of Technology, Zurich. • Joint BioEnergy Institute. • Ecole Polytechnique Paris. • Synthetic Biology Engineering Research Center (SynBERC). • Institute of Systems and Synthetic Biology, Imperial College London.	Collaborative Funding Agency- • National Science Foundation, USA. • Bill and Melinda Gates Foundation –collaboration between OneWorld Health, UC Berkeley and Amyris Biotechnologies. • EU's New and Emerging Science and Technology (NEST) program. • Defence Advanced Research Projects Agency (DARPA) and the Departments of Defense (DoD) and Energy (DoE).

Figure 4: Predominant organizations involved in synthetic biology research.

IMPLICATIONS OF SYNTHETIC BIOLOGY

The objective of researchers in developing synthetic systems has been to understand the natural world comprehensively and to apply the acquired insights towards beneficial applications. This capability has provided a new and powerful tool to engineer novel organisms. But along with such power comes the potential to be misused. The societal concerns about this type of emerging technology are broad in scope and include cultural, ethical and legal concerns about manipulating life, economic implications for the developed and developing regions, issues relating to ownership and intellectual property, concerns about environmental degradation and potential military uses and so on.[21] Figure 5 illustrates the complex inter-relationship of technology, society and legal systems that will stand in conflict with each other once synthetic biology is commercially applied.

Recombinant DNA methods work on an organism's genome and modify it in various ways, with results that are constrained by the original template. Synthetic genomics, on the other hand, permits construction of any specified DNA sequence, thereby enabling the synthesis of genes or entire genomes. With synthetic biology gaining momentum rapidly among the industry and academia, its implications cannot go unnoticed. While accepting the numerous applications in medicine, agriculture, industry, bioremediation and bioenergy sector, it will not be prudent to overlook or ignore the potential risks for society including possible unintended harmful consequences for human health or environment.[22] Every new technology carries an embedded risk which should be assessed at all the stages of technology development and synthetic biology is not an exception. Synthetic biology needs to establish itself within the social structure as a safe area of science that nurtures responsible practices and attitude. A code of ethics and standards therefore needs to be developed for biological engineering. Learning from gene therapy, we should imagine worst-case scenarios and seek to develop the right preventive mechanisms.[23] The necessity for regulation and policy control which are subsequently discussed, arises from the following premises:

- Synthetic biology ultimately results in live organisms that are self-replicating and capable of evolving into new strains.

Table 1: Collaborations and joint ventures

Name of projects/research	*Collaborating organizations*	*Name of projects/research*	*Collaborating organizations*
Engineered modular bacterial photo-production of hydrogen.	• Universidad Politecnica de Valencia (Spain) • University of Sheffield (United Kingdom) • Uppsala University (Sweden) • University of Porto (Portugal) • Weizmann Institute of Science (Israel)	Developing synthetic microbes to produce pharmaceuticals, fine chemicals, nutraceuticals, vitamins, flavors and Biofuels.	Amyris Biotechnologies, Emeryville, USA
A Biological Nanoactuator as a Molecular Switch for Biosensing.	• National Physical Laboratory (United Kingdom) • Ecole Normale Superieure (France) • Technology University of Delft (The Netherlands) • IMIC (Czech Republic) • EMPA (Switzerland) • INESC-MN (Portugal)	Design and construction of engineered genetic devices for partners in medicine, biofuels, agriculture, materials and other application areas.	Codon Devices, Cambridge, Massachusetts, USA
Biological Computation Built on Cell Communication Systems.	• Universitat Pompeu Fabra Barcelona (Spain) • Max–Planck Institut für Molekular Genetik (Germany)	Genetic diagnostic technologies based on expanded genetic alphabet.	EraGen Biosciences, Madison, USA
Engineering and Control of Biological Systems: a New Way to Tackle Complex Diseases and Biotechnological Innovation.	• Delft University of Technology (The Netherlands) • Institut National de Recherche en Informatique et en Automatique (France) • Genostar (France) • Swiss Federal Institute of Technology Zurich (Switzerland) • Boston University (United States) • Universita' degli Studi di Napoli 'Federico II' (Italy)	Developing minimal genome as chassis for energy applications.	Synthetic Genomics, USA
Human monoclonal antibodies from a library of hybridomas.	• Austria: Eucodis • Czech Republic: Academy of Sciences of the Czech Republic • France: French Institute of Health and Medical Research • Germany: Göttingen University	Develops biopharmaceuticals utilizing artificial amino acids.	Ambrx, USA in collaboration with Scripps Research Institute, San Diego, USA

Sources: European Commission,[18] Balmer and Martin[19] and Extreme Genetic Engineering: An Introduction to Synthetic Biology.[20]

- Once introduced into the environment, it is not practically possible for humans to control the outcome.
- The technology still being in the nascent stage cannot accurately predict and control its impact.
- Self-regulation is an area which has not been explored as yet.
- The possibility of open access to such organisms can work in a retrogressive manner when misused.
- Legislature and policy makers are yet to understand the quantum of risk these organisms/systems possess.

Despite the existing uncertainties associated with the field of synthetic biology, efforts have been already initiated to address the socio-ethical issues that may arise in future when commercialization of the synthetic biology will be achieved to its fullest extent. The Laurence Berkeley National Laboratory as well as

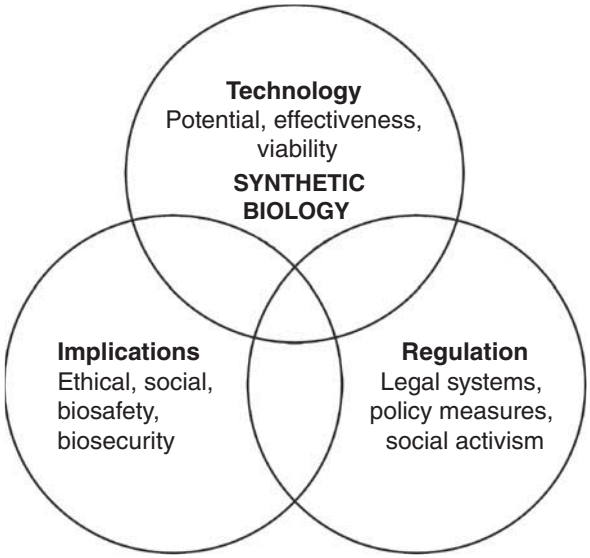

Figure 5: The promises and issues pertaining to synthetic biology.

Massachusetts Institute of Technology have developed programs on synthetic biology that include exploration of the associated ethical issues. Within Europe, the European Commission has established SYNBIOSAFE to create a framework for safety, ethics and public opinion on synthetic biology. It has been observed that strong policy measures and creating more public awareness can strengthen and help in containing the use and misuse of the technology. The ethical and social considerations cannot be severed from legal implications. They are intimately associated and reflect on the complexity of law trying to encompass larger social obligations. Therefore, the following sections are an attempt to provide an insight into various socio-ethical and legal concerns that may arise with the development of synthetic biology. An effective intellectual property regime, plays a crucial role in commercial success of synthetic biology; therefore, special emphasis has been laid in the present study on the related patentability issues.

Biosafety and biohazards

The primary concern of any responsible government and socially conscious industry is to ensure that application of a novel technology associated with biological materials does not turn the products into biohazards. Many studies exist on the impact of the introduction of genetically engineered plants and animals into the environment and the potential dangers of human consumption of genetically modified foods.[24] One of the main reasons to focus on the potential of such organisms as biohazards is that the control over behavior and function of the organisms by the technology practically ceases after their release into the environment. These organisms can exploit their innate ability to actively interact with wild organisms pre-existent in nature once they are introduced into the environment. This mixing known as an 'adventitious presence' generally refers to the unintended presence of genes, traits or seeds in a crop or other consumable material.[25]

It is also important to note that the functioning of the biotechnology products cannot be clearly defined because they arise in the highly complex milieu of living organisms, where interactions among hundreds of biochemical pathways are involved. Often, scientists cannot accurately predict the potential effect of a product when released into the market. It perhaps raises the highly

essential issue of the liability of damage caused to an individual. Toxicity or allergic reaction studies of the products carried out in the laboratory are not ideal indicators of the effects they might have once they are released into the environment as the functioning of a particular product is affected by other factors associated with the environment. Also, the effects may not only differ from environment to environment, but also from an individual to individual. Hence, it is not possible for a laboratory data to accurately predict the potential risk posed by the products of synthetic biology.

To illustrate the prior experience from genetically modified plants, in the year 1993 Pioneer Hi-Bred International developed a soybean variety with an added gene that translated into increased levels of amino acid methionine, derived from Brazil nut. Investigations revealed that the genetically modified soybean produced immunological reactions with people suffering from Brazil nut allergy as a result of the methionine gene introduced into the genome of the plant.[26] Recombinant vaccines and therapeutic proteins have also revealed the unpredictability of the effects of genetically engineered products in relation to human health. Reports indicate that patients using recombinant human insulin rather than animal insulin exhibit 'loss of warning' of hypoglycemia.[5] When using animal insulin, patients may sweat, become hungry or perceive other warning signs before a hypoglycemic attack; however while using human insulin some patients may not experience these physiological signals.[5]

In light of the past experience with genetically modified organisms, concerns related to organisms and biological systems developed through synthetic biology become obvious. These artificially engineered organisms are undoubtedly novel and substantially different from those that exist in nature. However, they still retain the inherent nature of self-replication and evolution. They are also subject to environmental and genetic pressure. According to Eckard Wimmer, 'An engineer's approach to looking at a biological system is refreshing but it doesn't make it more predictable. The engineers can come and rewire this and that. But biological systems are not simple … And the engineers will find out that the bacteria are just laughing at them'.[27] This can possibly result in unexpected interactions with the environment and other naturally occurring organisms. The intensity of the same cannot be quantified because the engineered organisms are themselves a combination of genetic elements that can behave differently in different environments.

Further, their integration into natural systems can contaminate the natural gene pool. This has a long-term effect as the expression of such genes cannot be perceived apparently. These interactions can be also spread over time and area, whereby, the containment and immediate counteraction is virtually impossible. Established risk assessment methods may not be adequate to deal with the much more complex changes brought about by synthetic biology, which involves engineering of the entire biochemical pathways. This challenge may require important changes to the methods and procedures used to assess the environmental risks posed by the novel organisms created by synthetic biology.[28]

Measures of control and regulation need to be accessed to prevent any risks from the use of the organisms by humans. In the year 1975, a meeting at the Asilomar Conference Center in Pacific Grove, California focused on the possible environmental and health risks of the powerful new gene-splicing techniques, the need for containment guidelines and the necessity for scientists to behave responsibly.[29] These concerns have to be reiterated in the case of synthetic biology where synthetic constructs are generated from hundreds of sources or more. More recently, concerns have been raised by the Canadian Erosion, Technology and Concentration (ETC) Group in 2007 against Craig Venter's Minimal Genome Project, which has sought patent for the engineered organism *Mycoplasma*

laboratorium. The group claimed that 'The same minimal microbe could be harnessed to build a virulent pathogen that could pose grave threats to people and the planet'.[30] The concern accentuates with an increasing large number of pathogenic viruses and bacteria being engineered. In 2002, a team of researchers at the State University of New York led by Eckard Wimmer reported the assembly of an infectious poliovirus constructed in the laboratory directly from nucleic acids.[31] In 2006, a viral 'fossil' of a human endogenous retrovirus was reconstructed using a variety of synthetic techniques.[32] The possibility to reengineer extinct and indigenous strains of organisms further heightens the issue of uncontrolled release and containment.

Synthetic living systems need not be always constructed from scratch but with the library generated by the BioBricks foundation, they can be designed by combining elements. This brings in a new dilemma as such organisms will lack clear genetic pedigrees and could express properties arising from complex interactions among the constituent genes. Accordingly, the risks associated with the accidental release of such an organism from the laboratory would be extremely difficult to assess in advance, including its possible spread into new ecological niches and the evolution of novel and potentially harmful characteristics.[33] Also, risk assessment of this nature cannot be made effectively as animal models may not reveal similar results as human hosts. The proposed applications in the area of biosensing, agriculture and bioremediation would necessarily involve testing and use of synthetic microorganisms in the open environment. The synthetic organism might damage or disrupt some aspect of the habitat into which it is introduced resulting in deterioration of the natural ecosystem(s).

Misuse and bioterrorism

While appropriation of the artificial systems may possess tremendous potential for improving the quality of life in various areas, misappropriation of the synthetic life reflects the unforeseen risk of containment coupled with the difficulty in detecting illegal biological activity. This raises issues relating to biosecurity and control of bioterrorism. According to the Central Intelligence Agency, United States of America, 'The same science that may cure some of our worst diseases could be used to create the world's most frightening weapons'.[34] In the United Kingdom, similar concerns have arisen about synthetic biology with the Ministry of Defence highlighting the field as one that may impact future military capabilities and in the year 2006 the Defence Science Advisory Council agreed to examine the military opportunities and threats arising from the field.[35] While an international consensus on the issues relating to biosecurity is yet to be reached, the Convention on 'Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction' under the United Nations' Biological Weapons Convention bans development, production, stockpiling and transfer of 'microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes'.[36]

In the opinion of the experts such prohibition is desirable as the processes, techniques, equipment and know-how needed for advanced bioagent development possess dual use nature; it will be extremely difficult to distinguish between legitimate biological research activities and production of advanced biological warfare agents. The prospects for the creation of biological weapons based on synthetic biology still remain contentious and uncertain. The technology which underlies the development of advanced biological agents is likely to advance very rapidly, causing a diverse and elusive threat spectrum. However, a more fundamental problem has been raised about the level of awareness within the

scientific community regarding potential military uses of the technology. Most proposals for governance and oversight depend on scientists being aware of and reporting potential misuses.

The National Research Council's (NRC, United States of America) Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology has recently made policy recommendations for scientists and the US Government that deals with the conduct, review and publication of a broad scope of biotechnology-related research. The committee speculates that the resulting diversity of new biological warfare agents could enable such a broad range of attack scenarios that it would be virtually impossible to anticipate and defend against; as a result, there could be a considerable time lag in developing effective bio-defence measures.

As described in the above sections, the evolving science of synthetic biology has the capacity to provide solutions for many unsolved problems and benefit mankind; however, there is a very thin limiting line which if ignored may lead to gross misuse of the technology and its tools for destructive purposes. Thus, judicious use of synthetic biology will aid the researchers and investors alike to reap its benefits in financial terms. As is the case with all other novel technologies, intellectual property regime can play a vital role in economic viability and the commercial success of synthetic biology. The section below explores the challenges that synthetic biology may pose for its protection under intellectual property regime especially in the area of patents.

Intellectual property rights and synthetic biology

The need to innovate, explore and invent in order to have a comfortable and quality life has always been a matter of importance to humans. As societies evolved and civilizations progressed, the need to develop a technology intensive industry has gained significance. Along with this necessity, came the requirement of recognition and proprietorship, and this was the genesis of the concept of intellectual property. Intellectual property rights epitomize the balancing act between public welfare and private rights. They seek to provide the incentive to innovation while ensuring that the public at large secure the benefits of the developments.

Like other novel fields of technology, synthetic biology is also making an attempt to create a niche for itself in, the realms of intellectual property law. The necessity to do so can be inferred from the philosophy of intellectual property right protection. Thomas Jefferson first provided an insight into the free nature of ideas and the exclusive rights conferred to the creator by society at its will, which itself would allow for the moral and mutual instruction of man, and improvement of his condition.[37] Patent protection has been considered to promote technological development by offering inventors exclusive rights for a limited period as an incentive for their research efforts. The United States Patent law is based on the principle that 'the productive effort fostered by patent protection will have a positive effect on society through the introduction of new products and processes of manufacture into the economy, and the emanations by way of increased employment and better lives for our citizens'.[38] In the case of synthetic biology this has a definite impact given the quantum of research, convergence of diverse areas and the potential scale of application. Every stage within the construction and modelling of the organism involves a large amount of ingenuity and human intervention.

Scope of protection

Being an interface between varied technology areas, one dilemma that can possibly arise is what kind of protection may be secured for such inventions. Synthetic biology ultimately aims at designing complete synthetic systems composed of multiple synthetic organisms working synchronously to achieve a complex

objective. The mode of achieving such targets requires the interplay between functional genomics, systems engineering, bioinformatics and conventional molecular biology. As a result, the scope of subject matter has expanded to include computer hardware and software, engineering models, high throughput devices, novel genomic constructs and methods to customize genetic information. The categorization of patents granted in respect of synthetic biology covering diverse subject matter is illustrated in Figure 6. Issues that relate to the large number of options to protect various facets of developing an organism *de novo* are also apparent. Possibility of protection of synthetic biology tools and products under multiple areas of intellectual property regime such as copyright (for software protection), patents or tradesecrets (for products and processes) and designs (for bioreactors etc) will result in overlapping of rights. Such superimposition may lead to issues relating to enforcement and establishing the rights conferred.

Further, protection of information under intellectual property regime stands in conflict with the increasing prominence of the open source software and open source biology. The Massachusetts Institute of Technology has developed the Registry of Standard Biological Parts otherwise known as the BioBricks Foundation that promotes open access to software and biological standard parts developed. Such open source inventories would negate the ability to protect copyright in, synthetic biology associated software and patenting of the genetic components as they would be under the creative commons licence. In addition, regarding the copyright regime, the elements of synthetic biology are not discussed as copyrightable subject matter in the US copyright statute. Also, there are internal restrictions of copyright law, which do not cover functional articles or methods of operation as protectable subject matter.[39]

'Click-wrap licenses' offer an alternative way of protecting the softwares that cannot be copyrighted under the described circumstances. Also described as 'web-wrap', 'click-proceed' or 'click-through' agreement,[40] 'click-wrap license agreements' came into existence at the rapidly evolving online forum of electronic commerce. The concepts of click-wrap license agreement are similar to those of shrink-wrap license agreements. The users are generally asked to review the terms of the agreement and to indicate assent by clicking on the button at the end of the license.[41] While these kinds of agreements are enforceable through contract law, they will impede the progress of technology and work as an anti-thesis to allow these softwares to be available for further research. The efforts to develop a system that will allow further research to take place and provide for adequate protection against misappropriation, therefore, need to be addressed.

Patentability issues with synthetic biology

Synthetic biology raises issues relating to the scope of patent law to confer effective

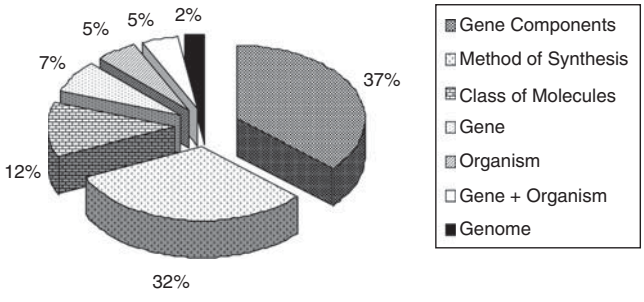

Figure 6: Distribution of claimed subject matter in granted patents.

protection. The organisms which are engineered are composed of multiple constructs that are artificially simulated and synthesized into a single organism. The question raised in *Diamond* v. *Chakrabarty*[42] is reiterated – whether life forms are patentable. Under the US law 'whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title'.[43] Considering that genetically modified organisms are regarded as products of 'manufacture' or 'compositions of matter' under the US patent law, there is necessity to establish that there must be transformation where a new and different article must emerge 'having a distinctive name, character or use' from the starting material.[44]

Legal precedence has been established where the US Supreme Court has held that where the patentee produced a new bacterium with markedly different characteristics from any found in nature having the potential for significant utility, his discovery would not be considered as nature's handiwork, but his own. Accordingly, such organisms form patentable subject matter under 35 USC §101.[45] A contrasting view came from the Canadian Supreme Court which held that there is the necessity to cautiously deal with patents on living organisms, 'the unique concerns and issues raised by the patentability of plants and animals necessitate a parliamentary response. Only the legislature has the institutional competence to extend patent rights or another form of intellectual property protection to plants and animals and to attach appropriate conditions to the right that is granted'.[46]

In relation to synthetic biology, the inventions seeking patent protection will require the applicant to establish that the organism would have little chance of developing naturally and that it was only through the intervention of human interest and technology that such an organism has come into existence.[10] When claiming a whole organism, the applicant will have to provide evidence as to the absolute novelty of the same as well as that the skill involved was not obvious to a person of ordinary skill in the art. This may be difficult as most of the organisms that are developed are either through the combination of existing synthetic constructs or by way of improvement over pre-existent models.

While the constant struggle to establish whether this category of inventions would be liable to obtain patent protection, the number of applications being filed in this regard before the USPTO and WIPO-PCT is continuously increasing. Table 2 adduced herein is an indicative of the patenting trends in the area of synthetic biology. The trends in the number of patents granted in this regard as depicted in Figure 7 indicate the potential viability of this technology area. The data secured from the USPTO, EPO and WIPO show that diverse subject matter areas have been claimed. These extend from methods of building synthetic DNA strands,[47] compositions and methods for protein design,[48] genes or parts of genes represented by their sequencing information[49] to the methods of engineering biosynthetic pathways. Some of the granted patents also include entire genomes[50] as well as the engineered organisms.[51] Some patents incorporate broad concept-level patents on the computer systems and software that are used routinely.[52] These patents indicate the possibility of obtaining multiple patents over a single invention and also the expansion of scope of a single patent by claiming broad components.

The resultant issues

The issues pertaining to conferring intellectual property protection to synthetic biological systems gained momentum with Craig Venter filing a US Application No. 2007/0122826, published on 31 May 2007 and PCT application WO/2007/047148, published 27 April 2007, naming almost 100 designated countries for a set of essential genes and a

Table 2: Patent data of granted patents and filed applications over the last 10 years collected from the USPTO, EPO and WIPO

Title	*Patent number/application number*	*Inventors*	*Category*
Diterpene-producing unicellular organism	US 7,238,514 B2	Matsuda *et al* (Assignee: William Marsh Rice University)	Organism
New bacterium with a genome genetically engineered to be at least 5 per cent smaller than the genome of its native parent strain, useful for producing a wide range of commercial products.	US 6, 989, 265	Frederick Blattner *et al* (Assignee: Univ. of Wisconsin)	Organism
Method for incorporating into a DNA or RNA oligonucleotide using nucleotides bearing heterocyclic bases	US 5,432, 272	Steven Benner	Method of synthesis
Gene Synthesis Method	US 6,110, 668	Strizhov *et al* (Assignee: Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V.)	Method of synthesis
Method for *in vitro* evolution of polypeptides	WO2005030957 (A1); US2007105117; ES2300808 (T3); EP1668126 (A1); EP1668126 (B1); JP2007507210 (T)	BERTSCHINGER JULIAN; HEINIS CHRISTIAN (Applicant(s): ETH ZUERICH [CH]; BERTSCHINGER JULIAN [CH]; HEINIS CHRISTIAN [CH])	Method of synthesis
Methods for identifying a biosynthetic pathway gene product	WO05033287A3	Keith K. Reiling *et al* (Assignee: University of California)	Method of synthesis
Method for enhancing production of isoprenoid compounds	US2006/0079476A1	Jay Keasling *et al*	Method of synthesis
Methods for assembly of high fidelity synthetic polynucleotides	WO06044956A1	Noubar Afeyan *et al* (Assignee: Codon Devices, Inc)	Method of synthesis
Polynucleotide synthesis	US2006-0127920A1	George Church, Jingdong Tian (Assignee: Harvard)	Method of synthesis
Compositions and methods for protein design	WO06076679A1	George Church, Brian Baynes (Assignee: Codon Devices, Inc)	Method of synthesis
Biosynthetic polypeptides utilizing non-naturally encoded amino acids	WO06091231A2	Ho Cho *et al* (Assignee: Ambrx, Inc)	Method of synthesis
Method for carrying out the selective evolution of proteins *in vitro*	CN 101258244 (A); DE102005037351 (B3); US2008233616 (A1); WO2007017229 (A2); WO2007017229 (A3); EP1913140 (A2)	MICHAEL LISS (Assignee: GENEART AG, Germany)	Method of synthesis
Recognition of oligonucleotides containing non-standard base pairs	US 6,037,120	Steven Benner	Method of synthesis
Evolution-based functional genomics	US2005-0038609A1	Steven Benner	Method of synthesis

Table 2: *Continued*

Title	*Patent number/application number*	*Inventors*	*Category*
Method for the complete chemical synthesis and assembly of genes and genomes	US 6,521,427	Glen Evans (Assignee: Egea Biosciences; subsidiary of Johnson & Johnson)	Method of synthesis
Synthetic Bacillus Thurigenensis cryic gene encoding insect toxin	US 6,043,415	Strizhov *et al* (Assignee: Ramot Univ. Auth. for Applied Research and Industrial Development Ltd., Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften e.V)	Individual functional component
Modular Genomes for Synthetic Biology and Metabolic Engineering	US 2007/0243617 A1	Robert A Holt	Genome
Hybrid Bacillus thuringiensis gene, plasmid and transformed Pseudomonas fluorescens	US 5,128,130	Gilroy *et al* (Assignee: Mycogen Corporation)	Genes, Organism
Synthetic insecticidal crystal protein gene	US 5,380,831	Adang *et al* (Assignee: Mycogen Plant Science, Inc)	Genes, Organism
Synthetic plant genes	US 5,500,365	Fischhoff *et al* (Assignee: Monsanto Company)	Genes
Compositions and methods for non-enzymatic ligation of oligonucleotides and detection of genetic polymorphisms	US 7,033,753	Eric T. Kool (Assignee: University of Rochester)	Gene Components and Mechanism
Artificial DNA base pair analogues	US 5,126,439	Harry Rappaport (Assignee: Temple University)	Gene Components
Backbone-modified oligonucleotide analogs	US 5,378,825	Cook; Philip D. , Sanghvi; Yogesh S. (Assignee: ISIS Pharmaceuticals, Inc)	Gene Components
6-O-substituted guanosine derivatives	US 5,412,088	Jones; Roger A. , Fathip; Reza , Gaffney; Barbara L. (Assignee: Rutgers, The State University (New Brunswick, NJ)	Gene Components
DNA sequences useful for the synthesis of carotenoids	US 5,589,581	Misawa *et al* (Assignee: Kirin Beer Kabushiki Kaisha, Japan)	Gene Components
Synthetic DNA sequence having enhanced insecticidal activity in maize	US 5,625,136	Kozeil *et al* (Assignee: Ciba-Geigy Corporation)	Gene Components
Gapped 2' modified oligonucleotides	US 5,955,589	Cook; Phillip Dan, Monia; Brett P. (Assignee: Isis Pharmaceuticals Inc)	Gene Components
Oligonucleotides with non-standard bases and methods for preparing same	US 6,001,983	Steven Benner	Gene Components
Precursors for deoxyribonucleotides containing non-standard nucleosides	US 6,140,496	Steven Benner	Gene Components

Table 2: *Continued*

Title	*Patent number/application number*	*Inventors*	*Category*
Polynucleotide compositions encoding broad-spectrum .delta.-endotoxins	US 6,242,241 B1	Malvar *et al* (Assignee: Monsanto Company)	Gene Components
Chimeras of sulfur-linked oligonucleotide analogs and DNA and RNA	US 6,444,798 B1	Steven Benner	Gene Components
Selected polynucleotide and polypeptide sequences of the methanogenic archaeon, methanococcus jannashii	US 6,503,729	Bult *et al* (Assignee: The Board of Trustees of the University of Illinois, The Institute for Genomic Research, Johns Hopkins University)	Gene Components
Nucleotide sequence of the mycoplasma genitalium genome, fragments thereof, and uses thereof	US 6,537,773	Fraser *et al* (Assignee: The Institute for Genomic Research, Johns Hopkins University, The University of North Carolina at Chapel Hill)	Gene Components
Nucleotide sequence of the *haemophilus influenzae* Rd genome, fragments thereof, and uses thereof (genome recorded on computer-readable medium – useful for identifying commercially important nucleic acid fragments by homology searching)	US2005/0131222A1	Robert D. Fleischmann, J.; Craig Venter *et al* (Assignee: Human Genomes Sciences, Johns Hopkins Univ.)	Gene Components
Methods for preparing oligonucleotides containing non-standard nucleotides	US 6,617,106	Steven Benner	Gene Components
Biosynthesis of isopentenyl pyrophosphate (in a host microorganism, useful for pharmaceutical purposes)	US2003-0148479A1	Jay Keasling *et al*	Class of molecules
Biosynthesis of amorpha-4, 11-diene (in a host cell, useful as pharmaceuticals)	US2004-0005678A1	Jay Keasling *et al*	Class of molecules
Method for the production of 1,3-propanediol by recombinant *Escherichia* coli strain comprising genes for coenzyme B12 synthesis	US 7,074,608	Nigel Dunn-Coleman *et al* (Assignee: Dupont; Genencor)	Class of molecules
Biosynthesis of isopentenyl pyrophosphate	US 7,172,886 B2	Keasling *et al* (Assignee: The Regents of the University of California)	Class of molecules
Biosynthesis of amorpha-4,11-diene	US 7,192,751 B2	Keasling *et al* (Assignee: The Regents of the University of California)	Class of molecules
Genetically modified host cells and use of same for producing isoprenoid compounds	WO06014837A1	James Kirby *et al* (Assignee: Univ. of California)	Class of molecules

Table 2: *Continued*

Title	*Patent number/application number*	*Inventors*	*Category*
Filed applications			
TRICHODERMA REESEI PHYTASE ENZYMES, NUCLEIC ACIDS ENCODING SUCH PHYTASE ENZYMES, VECTORS AND HOST CELLS INCORPORATING SAME AND METHODS OF MAKING AND USING SAME	Publication number: US 2005/0130148 A1	Nigel Dunn-Coleman *et al*	
SYNTHESIS OF SELENIUM-DERIVATIZED NUCLEOSIDES, NUCLEOTIDES, PHOSPHORAMIDITES, TRIPHOSPHATES AND NUCLEIC ACIDS	Publication number: US 2003/0055016 A1	Zhen Huang	
SELF-PROCESSING PLANTS AND PLANT PARTS	Publication number: US 2008/0045702 A1	MICHAEL B. LANAHAN *et al*, Syngenta Biotechnology	
Installation of genomes or partial genomes into cells or cell-like systems	US2007-0269862A1	John Glass; Lei Young; Carole Lartigue; Nacyra Assad-Garcia; Hamilton Smith; Clyde Hutchison; J. Craig Venter	
Synthetic Genomes	US2007/0264688	J. Craig Venter; Hamilton Smith; Clyde Hutchison	
Synthesis of Error-Minimized Nucleic Acid Molecules	US2007-0128649/ WO2007-065035	Lei Young	
Minimal Bacterial Genome	US2007-0122826/ WO2007-047148	John Glass; Hamilton Smith; Clyde Hutchison; Nina Alperovich; Nacyra Assad-Garcia	
Method for *In Vitro* Recombination	US2007-0037196/ WO2007-032837	Daniel Glenn Gibson; Hamilton Smith	
ESCHERICHIA COLI STRAINS THAT OVER-PRODUCE L-THREONINE AND PROCESSES FOR THEIR PRODUCTION	Publication number: US 2006/0205044 A1	John N. D'Elia *et al*	

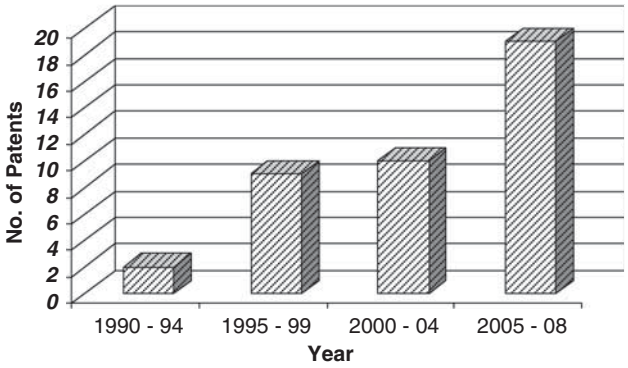

Figure 7: Trends in grant of patents in relation to synthetic biology.

synthetic 'free-living organism that can grow and replicate' that is made using those genes, named as *Mycoplasma laboratorium*.[53] The issue that has been raised in case of Venter's application relates to the claim over a non-existent organism. This does not seem to be plausible under the existent law as the requirement of 'reduction to practice' forms the essential pre-requisite for protection. Such questions exhibit the need to address the dilemma of the scope of patenting system in relation to technology's ever-growing potential. Experts believe that the claims pertaining to protection of an entire organism in case of synthetic biology would require close examination. This is because broad and far-reaching claims over synthetic genomes can surreptitiously expand the scope of the patent to actually claiming biological pathways or complete organisms. This would stand completely in violation of the fundamental rule of patent law that substances already existing in nature are not liable for patent protection.

Most patent applications dealing with synthetic biology present issues that are invariably related to the nature of the claims. Further, the national patent laws require the written description to be clear, concise and specific.[54] The claims of a patent define the metes and bounds of a patentee's right to exclude.[55] It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude'.[56] However, in some cases the claims not only extend to the synthetic components created, but also to mechanisms for their production, that are otherwise known. The difficulty is that broad patents may restrict collaboration and stifle development in the field and narrow patents may over-complicate the process, meaning that hundreds of patents have to be negotiated to produce a system from standardized parts.[5]

Ambiguous or abstract claims also raise issues related to the establishment of traditional criteria for determination of patentability, that is, novelty, utility and non-obviousness. In determining novelty, the proof should actually shift to the burden of proving that such an organism could not be generated naturally and that natural selection would actually work against the organism but for the intervention of human interest and technology.[57] In terms of determining utility, it cannot be guaranteed that the organism will function essentially as it was designed to function once it is introduced into the environment or host. Interactions among various components could actually defeat the purpose for which the organism was engineered. Therefore, examination practices with regard to such invention will need to be more intensive and subjective to the nature of commercial application of the claimed organism or gene construct.

Another pertinent issue relates to monopoly and the open access of standardized parts created by this technology. In order to facilitate ease of access to developed parts, the database of the BioBricks foundation allows sharing, using and improving the modules of biological systems. However, most of the biological functions encoded by parts of BioBricks are already covered by patent claims.[58] This is also important wherein multiple patents over a single invention and small modifications thereof, can lead to the creation of patent thickets which would in effect restrict access and further development of the technology.

Scope of patenting in different jurisdictions

While the US law permits the grant of patents over 'anything under the sun, made by man', the European Union and India have laid down strict exceptions to grant patents over life forms. Article 52 of the European Patent Convention, 1973 contains the general principles of patentability. Article 53 states that European patents shall not be granted in respect of:

(a) inventions the publication or exploitation of which would be contrary to 'ordre

public' or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States;

(b) plant or animal varieties or essentially biological processes for the production of plants or animals; this provision does not apply to microbiological processes or the products thereof.

The possibility of rejection of a patent application arises only when the new technology is at the risk of harming higher life forms.

In India, Section 3(j) of the Patents Act, 1970 stipulates that plants and animals in whole or in part thereof (other than microorganisms), including essentially biological processes for production or propagation of plants and animals shall not be considered as patentable subject matter. This Section would require an objective analysis as to whether the genetic modules generated can be considered to govern fundamentally biological processes which occur naturally, but are claimed because they are a part of an artificially synthesized system. In addition, Section 3(1) of the Patents Act, 1970 excludes methods of treatment of humans and animals. In accordance to this, components of an artificially developed drug delivery system could be rejected for functioning as a therapeutic mechanism of treatment, even though they satisfy the patentability criteria. Artificially generated living cells that are generated by the combination of standard elements would stand barred by Section 3(f) that refers to mere arrangement, rearrangement or duplication of independently functioning devices. The interpretation of this Section will require the determination whether the standardized cassettes that are developed and their inter-operability will be considered as devices. Even while possibilities of protection need to be explored, Indian jurisdiction is not open to patenting with regard to computer software *per se*. In addition, as described earlier, living organisms whether in whole or in part also cannot be patented, thereby, posing an impediment to securing patent protection for synthetically engineered organisms in India.

Inter-relationship of socio-ethics and intellectual property regime

The concept of intellectual property protection is intrinsically associated with issues such as morality and ethics and have been raised before the judiciary several times.[59] It has been strongly argued that the genetic alteration of life forms is immoral and leads to commercialization of life, which stands in contravention to nature's purpose. In addition, some views propound that technology has commoditized life forms, thus placing the future of humanity at the will of research. Such approach would amount to the unauthorized exploitation of natural resources including invasion of privacy of person and property. The ethical debate in regard to patenting also extends to the fact that monopolization of biological material can lead to decrease in access of such material to the public.

The aforementioned perspectives have gained ground with the inclusion of a statutory bar under the patent legislations in different parts of the world. For example, Article 53 of the European Patent Convention, 1973 specifically excludes 'inventions the publication or exploitation of which would be contrary to "ordre public" or morality'. This is supplemented by Rules 23 (d) and (e) of the Implemental Regulations to the Convention of the Grant of European Patents. In India, under the Patents Act, 1970, Section 3(b) mandates that, 'an invention the primary or intended use or commercial exploitation of which could be contrary to public order or morality or which causes serious prejudice to human, animal or plant life or health or to the environment' as not eligible for patent protection. The legislative intent for the inclusion of such provisions can be inferred from the role of the State that plays as a *parens patriae* thereby, liable to

provide for all the requirements to establish and enforce the rights of its citizens. From the concept of *laissez faire*, the functions of the State have become more focused at social justice, wherein the emphasis lies on the role of the State as a vehicle of socio-economic regeneration and welfare of the people.

Synthetic biology has already raised criticism in terms of man playing God's role. Commenting on Craig Venter's project, the Economist in 2004 stated, 'if Dr Venter can take the final step of kicking the new, wholly synthetic genome into reproductive life, he will not only have made a great technological leap forward, he will also have erased one of the last mythic distinctions in science – that between living and non-living matter'. The further monopolization over the same and uncertainty of the possible implications could stand as impediments in its development.

Another factor that has ethical ramifications is in relation to the necessity to evolve a balance between the monopoly rights conferred by intellectual property rights and the access to the public. The development of technology is an expensive affair and, therefore, affects the price of the final commodity in the market. The conflict of interests between the patentee and the consumer has always been a matter of concern. The attempt to provide and facilitate more research in this regard comes from the creation of the BioBricks foundation by Massachusetts Institute of Technology. From a consumer's point of view, another issue pertains to the capacity of the technology to gain confidence and market. So far, none of the products generated through synthetic biology have actually reached the common man. The level of awareness with regard to its market potential and scope is therefore yet to gain support from the consumers.

CONCLUSION AND RECOMMENDATIONS

The issues discussed in this article come from the traditional understanding of the conflict between new technology and the closely associated society. Debates about biosafety, bioweapons and the ethics of engineering life have been taking place right from the first synthesis of artificial DNA. The factor that makes these issues more critical in the case of synthetic biology is the rapid rate at which the scientific community is pursuing towards engineering life. The era of biomolecular engineering also marks the maturity of a series of powerful technologies, which are converging with other developments in computing, materials science and nanotechnology. Furthermore, the application of synthetic biology can successfully provide solutions to the gravest of problems faced in the modern world.

Attempts to control and regulate activities related to biotechnology and the associated products have been made at an international as well as the national level. Some of such attempts include 'Cartagena Protocol on Biosafety' which legally binds its parties to regulate trans-boundary movements of living modified organisms. The Codex Alimentarius Commission (Codex) is the joint body under the auspices of the Food and Agriculture Organisation and the World Health Organisation responsible for compiling the standards, codes of practice, guidelines, recommendations and developing principles for the human health risk analysis of genetically modified foods. Countries such as United States of America have developed organizations and research laboratories such as the US Army Biological Warfare Laboratories (USBWL) to develop containment measures for biological warfare.

These steps take cognisance that it is essential to understand the uncertainty, risks and benefits of new technology. Further there is need to facilitate its use through a mechanism which is socially acceptable and least damage prone. Finally, there is a need to regulate and address concerns over who should own or control the application of technology. This reflects that science, technology, regulatory frameworks and social

implications must evolve together to secure the welfare and safety of mankind. In respect of the technology and applications of synthetic bioengineering, focus should be placed upon:

(a) Instilling confidence among the public and making them aware of the potential benefits so as to garner support, avoid excessive public anxiety and overzealous claims.
(b) The scientific community must take upon themselves to be more socially conscious and take a lead in debating the implications of their research.
(c) The technology must have a nexus with its ultimate purpose. Stringent regulations in terms of access and availability of components and products need to be developed.
(d) Allowing public participation in determining policy measures can help evolve a unique legal system wherein technology is allowed to progress while maintain a balance with social interests.
(e) A review of existing controls and regulations, and the development of new measures in the specific areas relating to biosafety, environmental release and biosecurity need to be addressed.
(f) Risk assessment and containment will not only provide the means to avoid hazards but also to be prepared to counter them.
(g) In relation to intellectual property rights, the possibility of developing specific guidelines in light of the complex technologies used can prevent exclusive rights on the essential processes of creating life.
(h) To mitigate the risks involved with synthetic biology a concerted effort needs to be made by the national governments, funding organizations, the scientific community and the end consumers of the technology.

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