SYNTHETIC BIOLOGY

The dawn of a new industry

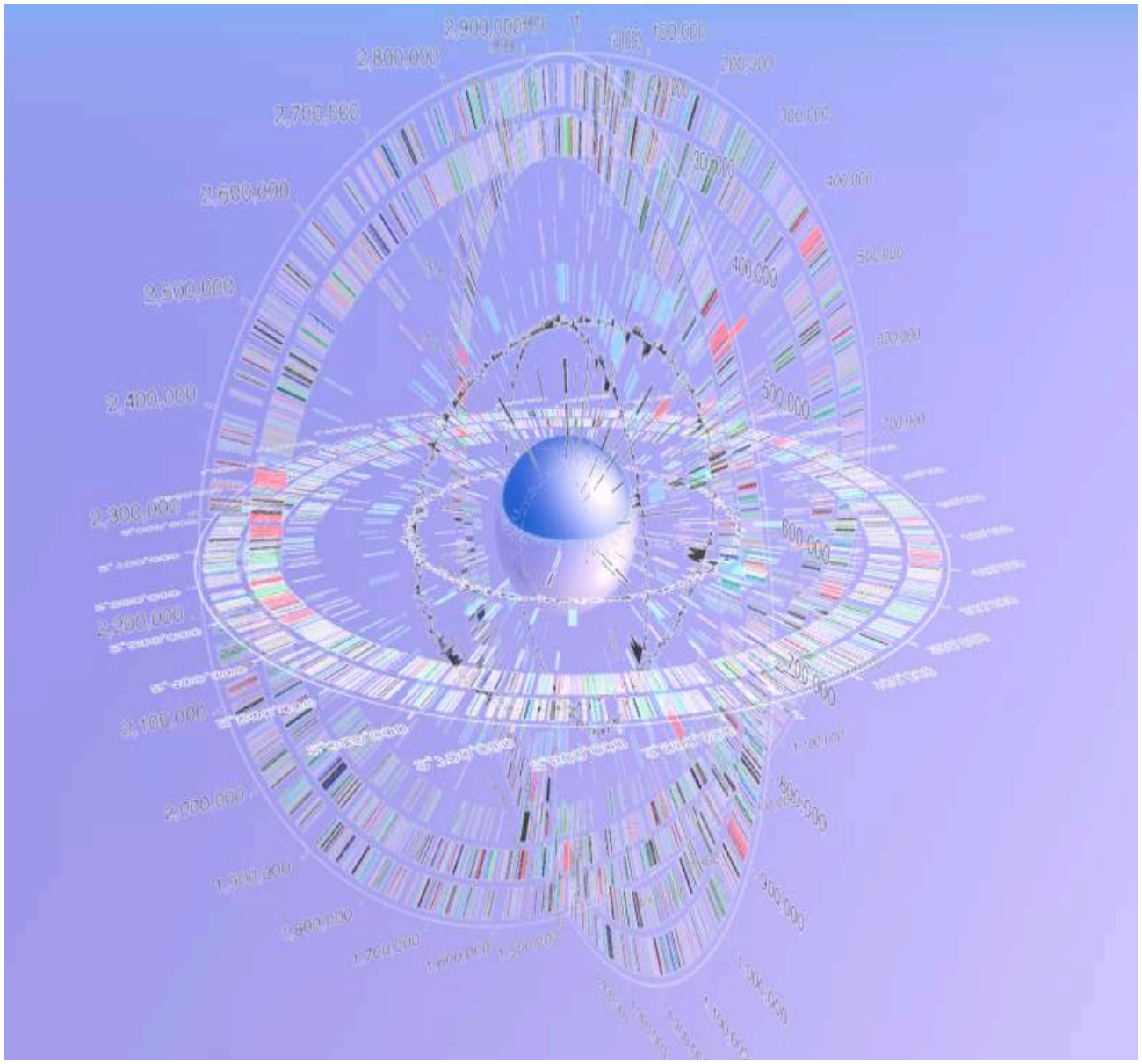

TABLE OF CONTENTS

1. INTRODUCTION

When examining current trends in genetic engineering it is evident that we are experiencing the birth of "Genomics". Scientists are talking about the radical implications of these new technologies and they mention things like curing genetic illness, preventing cancer and even producing energy. It is easy to get lost in all the possibilities and it is even easier to get anxious about the potential misuse and inherent dangers of genomics. As is the case with most new technologies, there is great deal of speculation coupled with countless unknown variables.

The purpose of this paper is to provide a guide to investors about the likely impact of the latest phase of technological advances and innovations in the genetic revolution: Synthetic Biology (SB) or Genome Synthesis. The wider impact of earlier phases of the genetic revolution has been thoroughly researched and will not be repeated here. Our analysis and discussion centre on the new technology, the creation of new markets and the organizational aspects of exploiting the technology.

We believe that any innovation or technology functions within a social environment. To provide a better understanding of the social context within which this new technology will function, the final part of our analysis will focus on the social system dynamics.

2. TECHNOLOGY OVERVIEW

Origins of the Genetic Revolution

Mankind has long recognized the concept of passing on traits from parent to offspring. However it wasn't until Mendel formulated his laws on hereditary traits in 1900 that the field of genetics slowly started to emerge and acquire a true scientific basis. An important milestone was the discovery of the structure of Deoxyribonucleic acid (DNA) by Watson and Crick in the 1953.[1, 2]

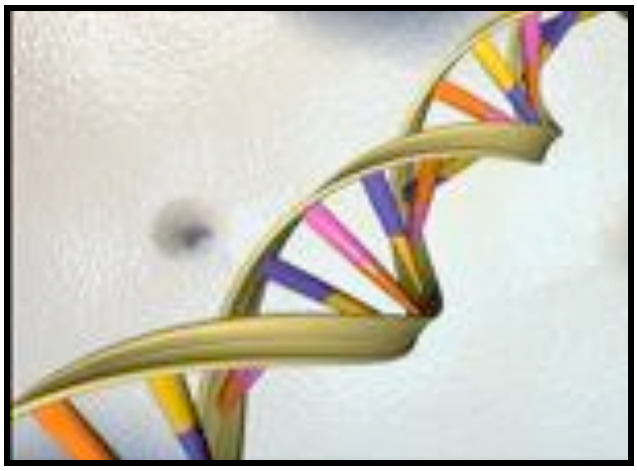

Figure 1: Double helix structure of DNA discovered by Watson and Crick[3]

Today the field of human genetics is well established. Up until now, scientists knew the structure and function of DNA as well as how genes functioned and produced proteins. However an overall picture of the genome was missing. That changed with the completion of the Human Genome Project in 2003, which

[1] Reed, S.C. 1979. *A short history of human genetics in the USA*. American Journal Of Medical Genetics, 3(3), 282-295
[2] Stern, C. 1971. *The place of genetics in medicine*. Annals of Internal Medicine, 75(4), October, 623-629
[3] www.genome.gov [Online] Accessed 28 February 2008

sequenced the entire human genome, identified every gene and created a database for research purposes. As a result, the field of genomics was born - understanding genetic material on a large scale. This is widely recognised as the start of the genetic revolution.[4]

The Human Genome Project was just the beginning; the real benefits will come from identifying the function of each gene. This field is known as functional genomics and many believe it to be the second phase in the genetic revolution. This will permit physiological research on the molecular level; determining the 'normal' function of genes as well as detailed patho-physiological research of diseases and their relation to genes.[5] A secondary development is the emergence of bio-informatics, which uses supercomputers and advanced database management systems to manage the growing volumes of genomic information produced every year.

Evolution of Synthetic Biology (SB) or Genome Synthesis

The latest phase of innovation in the genetic revolution is technology that enables DNA synthesis; the process whereby strands of DNA are built *de novo*, using laboratory tools and techniques. In actuality the ability to synthesize DNA is not new, having been used for more than 20 years[6], however the techniques are only now being refined. Previously major obstacles included[7]:

- Error rate in the synthesis process
- Stability of lengthy DNA sequences
- Speed & Cost of the process

SB exists within an environment where new technologies and innovations tend to build upon one another. This process of *combinatorial engineering* has resulted in a complex system of SB enabling technologies which interact and depend on one another and empower further development.

SB has gone through one major cycle of disruptive innovation. The traditional method of synthesis, Recombinant DNA Technology, involved choosing required gene sequences from existing genomes, cutting the DNA into strands and then sorting them manually to obtain the desired template. Despite time and cost constraints it was a pioneering technology that established a new branch in genetics.

Recombinant DNA technology is being displaced by a new approach called SB. It started with the advent of Polymerase Chain Reaction, which allowed scientists to amplify specific DNA sequences.[8] The latest wave of innovation, allows scientists to choose the DNA strands from a computer database which are then assembled from scratch using computer guided synthesizers. This is done without any natural template using only the blueprint of the actual sequence. The required sequence is normally based on a known gene, but theoretically could be anything the scientist wants. This process is one of the main enabling factors for the latest achievements within SB and a driver for cost reductions. Foster's S-Curve (Fig. 2) illustrates the disruptive nature of Synthetic Biology over Recombinant DNA Technologies.

These new capabilities allow scientists to physically change an organism's DNA sequence or even create an entirely new organism. On January 25th, 2008 Dr. Venter at the J. Craig Venter Institute (JCVI) announced

[4] National Institute of Health. *Human Genome – Fact Sheet.* [Online] Accessed 3 March 2008 Available at: http://www.nih.gov/about/researchresultsforthepublic/HumanGenomeProject.pdf
[5] Bottles, K. 2001. *A revolution in Genetics: Changing Medicine, Changing Lives.* Physician Executive, 27(2), March, 58 -65
[6] Cello J, Paul AV, Wimmer E. *Chemical synthesis of poliovirus c DNA: generation of infectious virus in the absence of natural template*. Science. 2002 Aug 9; 297(5583): 1016-8.
[7] Biological and Environmental Research Advisory Committee. 2004. *Synthetic Genomes: Technology and impact.* Accessed 5 February 2008 [Online] Available at: http://www.sc.doe.gov/ober/berac/SynBio.pdf
[8] U.S. Department of Energy Office of Science - Office of Biological & Environmental Research. *Synthetic Genomes: Technologies and Impact*. December 2004 [Online] Accessed 2 March 2008. Available: http://www.science.doe.gov/ober/berac/SynBio.pdf

that they had successfully created a complete genome for a bacterium called *Mycoplasma genitalium*[9] with a sequence of 582,970 base pairs.[10]

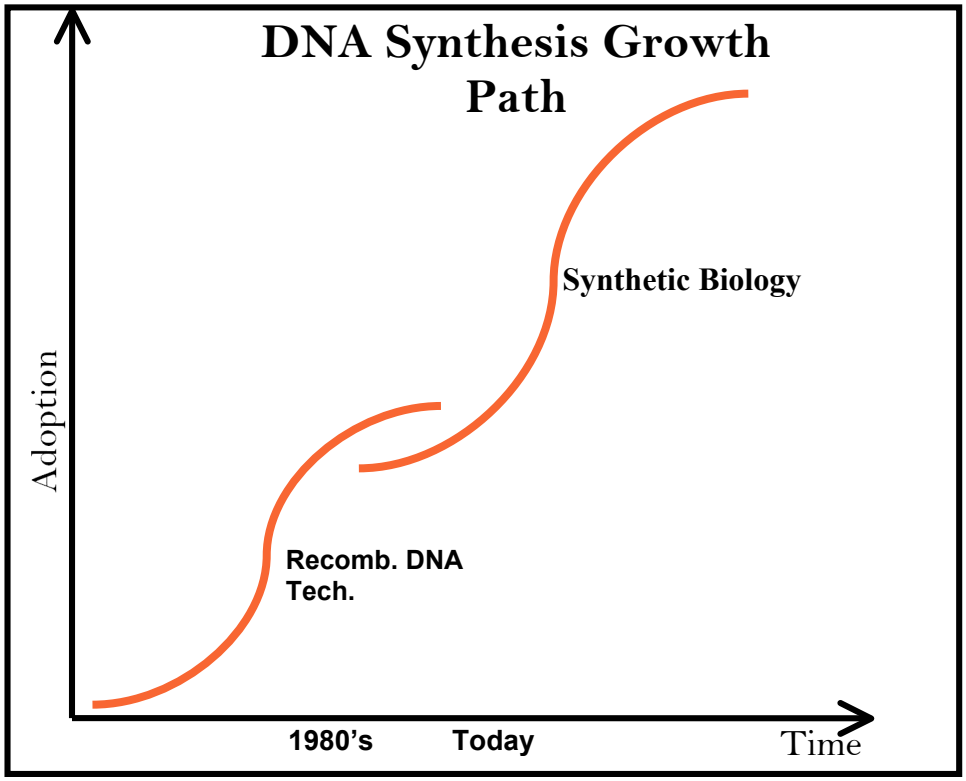

Figure 2: Illustration of disruptive nature of Synthetic Biology versus Recombinant DNA Technology[11]

In the wider context of genetic engineering, these new approaches to DNA synthesis must be viewed as enabling technologies and not necessarily disruptive. These techniques, however, provide a platform upon which several other processes can be built and in fact surpass the abilities of earlier technologies (Fig. 3).

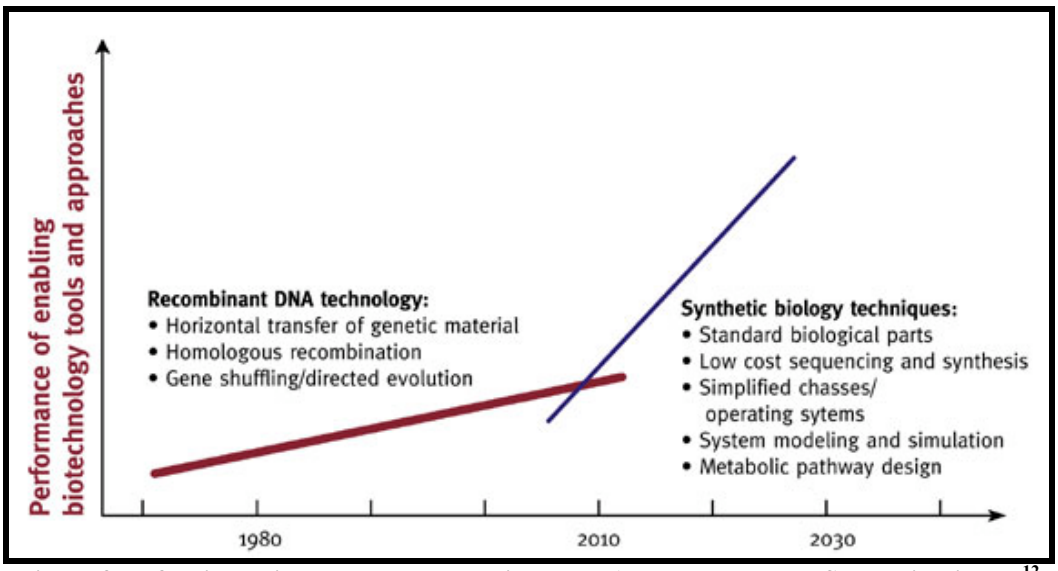

Figure 3: Inflection point between Recombinant DNA Technology and Synthetic Biology[12]

[9] JVCI. *Chemical synthesis of the Mycoplasma genitalium genom*. [Online] Accessed on 2 March 2008. Available at: http://www.jcvi.org/cms/research/projects/chemical-synthesis-of-the-mycoplasma-genitalium-genome/overview/

[10] Singer, E. 2008. Synthesizing a Genome from Scratch. Technology Review [Online] Accessed 5 February 2008 Available at: http://www.technologyreview.com/Biotech/20112/

[11] Own Compilation

Recent advances have led to the point where commercial application is a real possibility in the near future (Fig. 4).

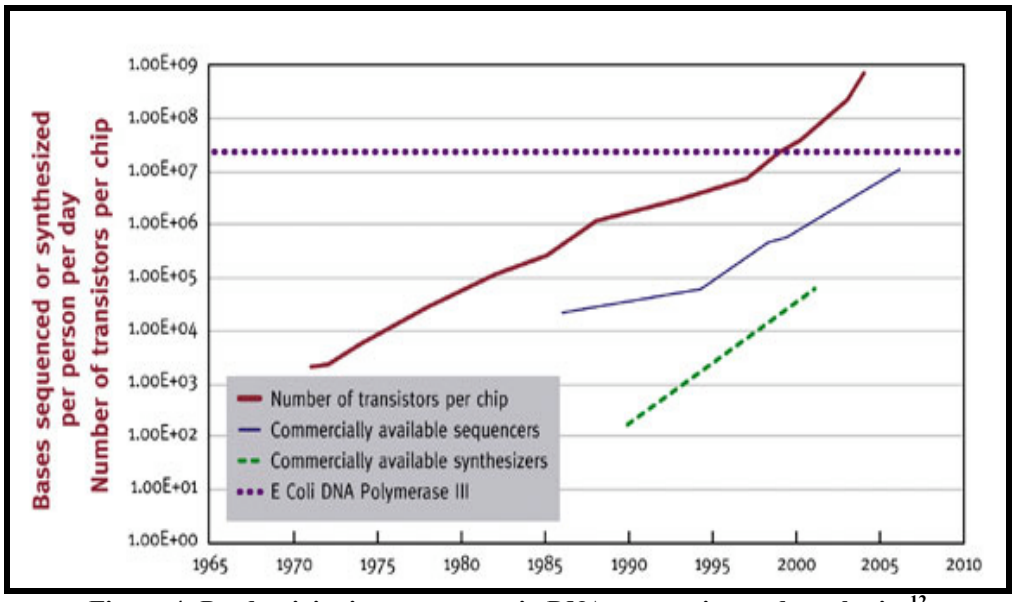

Figure 4: Productivity improvements in DNA sequencing and synthesis [12]

To put these performance improvements into context, over the past 10 years these trends have been observed[12]:

- Number of DNA base pairs sequenced/scientist/day increased 500 fold.
  - Doubling sequencing productivity every 24 months.
- Cost per sequencing of one base pair has reduced from $1.00 to $0.001.
  - An improvement of three orders of magnitude.
- Number of base DNA base pairs produced/scientist/day increased 700 fold.
  - Doubling synthesis productivity every 12 months.
- Cost to produce one base pair reduced from $30.00 to $1.00.

Benefits of the New Innovation

Functional knowledge of every gene, together with new synthesis abilities (Fig. 5), affords scientists the opportunity to create organisms with new characteristics that can be used to serve society in many ways[13] including:

- Manipulated bacteria that change biopolymers into biofuels or hydrogen
- Manipulated bacteria that clean up environmental contaminants
- Manipulated bacteria that scour carbon from the atmosphere
- Engineered bacteria to selectively kill cancer cells[14]

[12] Newcomb, J., Carlson, R. & Aldrich, S. 2007. Executive Summary - Genome Synthesis and design futures: Implications for the US Economy. [Online] Accessed 4 March 2008. Available at http://bio-era.net/research/doe_execsum1.html

[13] Biological and Environmental Research Advisory Committee. 2004. *Synthetic Genomes: Technology and impact* [Online] http://www.sc.doe.gov/ober/berac/SynBio.pdf

[14] Emily Singer. Tumor-Killing Bacteria - Scientists are synthetically engineering E. coli that can target and kill cancer cells. MIT Technology Review, June 2006 [Online] Accessed 20 February 2006 Available at: http://www.technologyreview.com/Biotech/16949/page1/

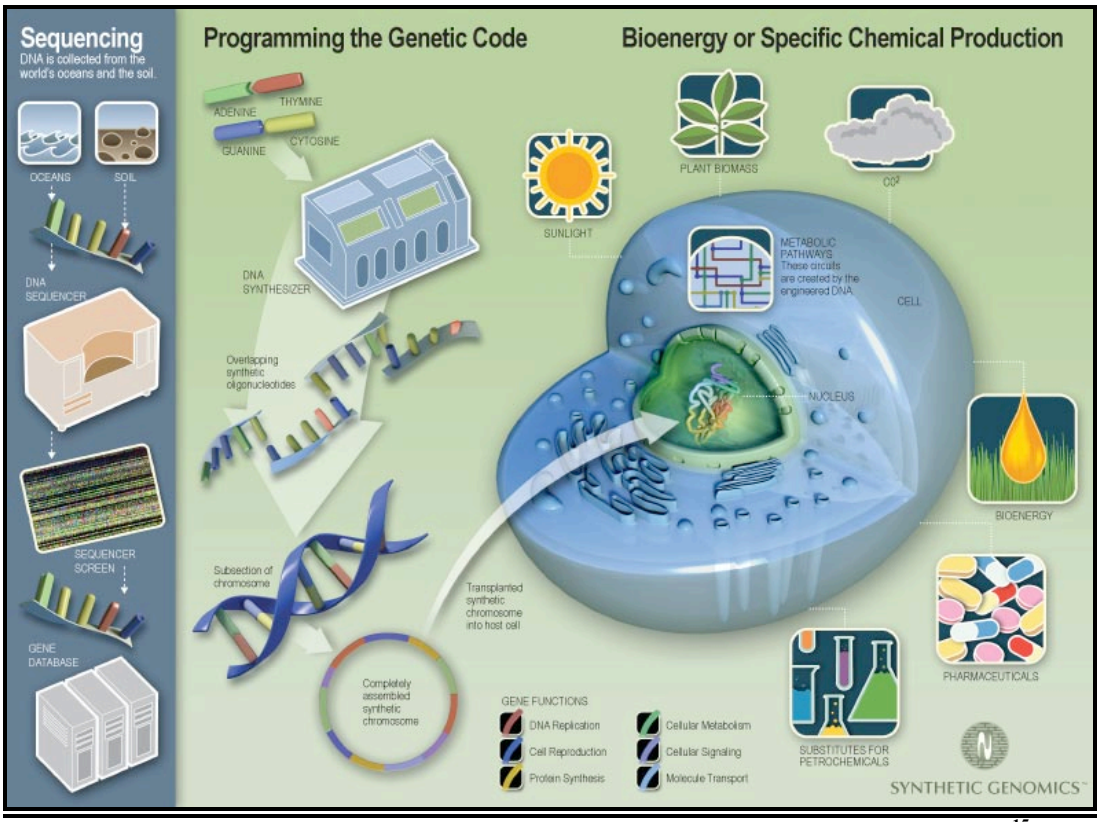

Figure 5: Illustration of the Genome Synthesis process and its possible applications[15]

Barriers to Adoption

The ability to modify or change genes is a powerful tool, which carries significant risk if not well controlled. These dangers create barriers to adopting the technology, they include: [13]

- Uncontrolled proliferation of genetically modified organisms
- Bio-terrorism: Creation of lethal pathogens, "superbugs", etc.
- Ethical considerations around use and application
- Lack of appropriate IPR

3. MARKET

Market & Value Creation

As a technological platform SB introduced new attributes currently not available to mainstream customers.[16] The potential for customized treatment programs for individual patients with decreased side-effects and increased potency is the Holy Grail for the pharmaceutical industry. However, the current state of technology is still unable to perform well enough on safety and costs facets. In the short-to-medium term incumbents must pursue niche markets while developing the ability to recognize market potential, as well as evaluating the extent of their abilities to appropriate, control and exploit opportunities.

NICHE MARKET: INDUSTRIAL APPLICATIONS

The first market to benefit from synthetic genomes is likely to be genetically modified (GM) foods. Although some sections of the western world are still hesitant to use GM crops, the developing world, which

[15] Synthetic Genomics. 2008. *The science of synthetic genomics*. [Online] Accessed 8 mach 2008. Available at: http://www.syntheticgenomics.com/science.htm
[16] Bower, *Disruptive Technologies*, HBR, 73

faces increasing food shortages, is embracing GM. In 2001 this market along was worth $21.6 billion with Monsanto Corporation controlling 80% of the market.[17]

With oil breaching $100 a barrel, oil companies are looking to more efficiently extract and process underground reserves. BP has already invested in Synthetic Genomics Inc. in hopes of modifying bacteria currently living in oil wells to convert 'heavy' crude into natural gas which is easier to extract and process.[18] The microbes could also increase extraction efficiency at non-conventional sites like the Canadian Oil Sands. As world energy demand shows no signs of slowing, the market for these microbes, as an oil production multiplier is extremely large.

As research efforts turn to alternative energy, synthetic genomes play a vital role in the development of bio-fuels. Currently it takes more energy to produce one unit of biofuel than energy extracted. Still, the biofuel industry stood at $22 billion in 2006, helped in part by generous government subsidies.[19] Microbes could be modified to increase the yield of hydrocarbons from plant material decreasing the need for subsidies.

Microbes modified with non-synthetic genes are already being used in the sequestration of heavy metals like mercury and greenhouse gasses. Unfortunately some pollutants are too complex for current microbes to breakdown; newly developed synthetic genes could give microbes the ability to tackle some of the worst pollution problems in a cost effective manner.

MAINSTREAM MARKETS: HEALTHCARE APPLICATIONS

In the near term, microbes could be modified with synthetic genes to allow greater production of essential enzymes and proteins that are used in many of the world's drugs. Cheaper production means greater availability of drugs to disease hotspots in the developing world.

Dramatically changing and improving the very nature of healthcare would be the ultimate goal of synthetic genome technology. The world pharmaceutical market was worth $400 billion in 2001; the potential value that could be captured by synthetic genomics is immense.[20] The first target segment would be genetic deficiencies that result in debilitating or fatal diseases. Gene therapies for this segment are already fast-tracked through regulation and this will likely continue in the future.

BUILDING MARKETS: THE VALUE NET

Human capital is critical bottleneck to early stage industries. Complementors like the DOE/ NIH (fig. 6) are funding university scholarship, but it will take years to build critical mass. Meanwhile, potential SB markets are not being ignored by competing technologies. Miniaturization and nanotechnology are already improving yields in energy production. Furthermore the healthcare industry is still devoting the majority of its resources to conventional technologies.

[17] BBC, *Seeds of Contention*, April 2001.
[18] Kanellos, *Oil giant BP invests in microbe specialist*, CNET, 2007.
[19] Department of Energy, *Genome Synthesis and Design Futures*, 2007.
[20] IMS Health, *World Review*, 2001.

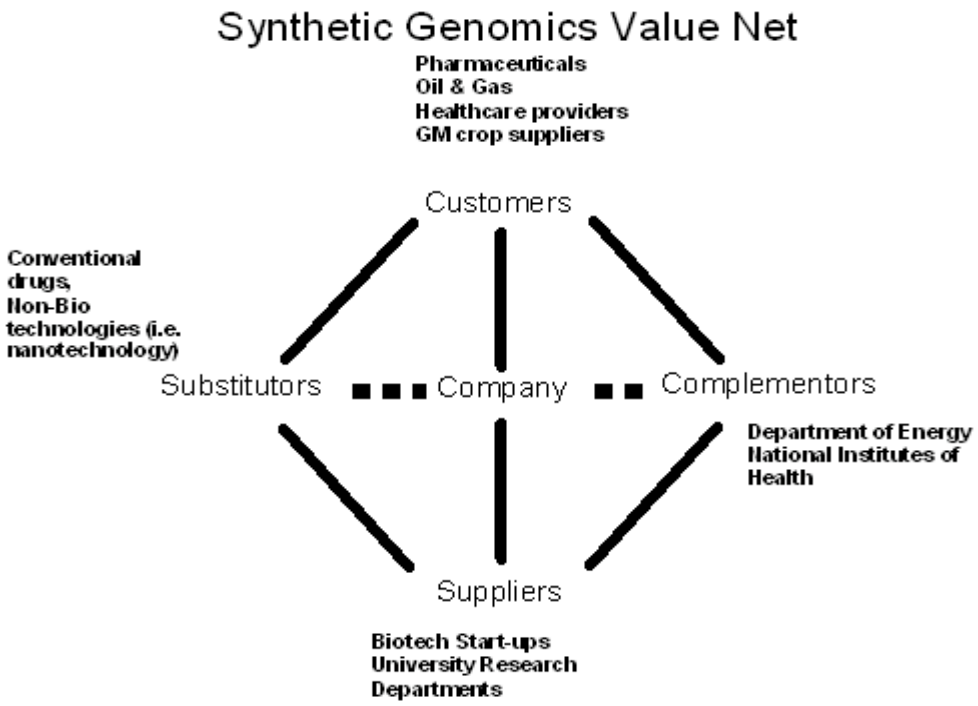

Figure 6: SG Value Net

Intellectual Property Implications

In 1980, Diamond v. Chakrabarty provided a precedent for the ambiguous state of intellectual property rights (IPR) currently faced by stakeholders. The ruling stated that "anything under the sun that is made by man" could be subject to IP protection.[21] With respect to genetic engineering and its nascent sub-area, synthetic biology (SB), legal frameworks such as US or European IP laws are not yet able to incorporate the challenges of this new field; moreover our research suggests that advances in SB are occurring faster than legislators can adjust corresponding legislation. Auspiciously the development of legislation, urgently required by potential investors, has already begun.[22]

Consider for example the current US patent law, which applies to technology and process innovations in the field of SB. According to scientific and judicial opinion, the current framework of the US Patent and Trademark Office (PTO) is insufficient for dealing with SB.[23] Traditional criteria for patents such as novelty, non-obviousness and enablement are satisfied by almost every innovation in the field; while non-traditional but applicable criteria such as the moral utility doctrine, where SB innovations have to demonstrate "at least one beneficial application to society"[24] are subject to interpretation by US courts. Besides being subject to interpretation, the moral judgment of an SB invention receives different treatment internationally, e.g. the European Patent Office (EPO) states it "…will not grant patents against public or morality"[25], which appears somewhat stricter than the US approach.

The situation described above raises important questions for potential SB investors with respect to appropriability, control, and exploitation. Will it be possible to protect SB processes and technologies through patents to ensure commercial exclusivity? Will it be possible to freely use basic genetic sequences for synthesizing a new drug or will such sequences become proprietary IP of a company and therefore be

[21] US Supreme court, 447 U.S. 303 (1980)
[22] e.g. Iwasaka K., "Chakrabarty to Chimeras: The Growing Need for Evolutionary Biology in PatentLaw", Yale Law Journal, April, 2000
[23] Arjun Bhutkar, *Synthetic Biology: Navigating the Challenges Ahead*. J. BIOLAW & BUS., Vol. 8, No. 2, 2005.
[24] Arjun Bhutkar
[25] European Patent Convention (EPC), article 53(a)

protected? Definitive answers to these questions are urgently required to clarify the underlying legal framework.[26] Based on the answers, investors and companies can then further define their future IP strategies ("block", "run" or "team up".)[27]

The basic issue that legislators have to rapidly solve is the dichotomy between openness and IPR. Too much restriction (i.e. overly broad patents), bears the danger of suppressing further innovation in SG, though IPRs also stimulate research due to profit opportunities.[28]

	Openness	Restrictions (e.g. copyrights, patents)
Before research is finished	No incentive for research, because of limited commercial opportunities	Incentive for research due to commercial exclusivity
After research is successfully finished	Broad usage because publicly available; stimulates further innovation	Possible costs (royalties, license fees etc.) reduce utilization

Table 1: Openness vs. Restriction

One possible and currently discussed approach is to create a so called "commons", similar to how software is offered as open-source under 'copyleft' licenses (e.g. GNU).[29] Such licensing models could theoretically allow for usage of basic components such as sequences, while still recognizing existing copyrights and imposing requirements on further usage. However, our research suggests that the discussion of applicability of such models to SG has just started and has yet to address the concerns of potential investors and business models implications. Other approaches currently discussed include mandatory licensing and social patent legislation.[30]

Overall, no matter how future IPR legislation develops, the scientific community and political leaders are demanding that basic innovations, which are either required by or the result of SB, must remain publically available to ensure further R&D. Their main intention is to consider the overall public good[31], to support scientific advancements on a large-scale[32] and, presumably, to retain a certain level of public control. For commercial investors, this limits the scope of potentially attractive investment opportunities, especially with respect to the "low hanging fruits" of fundamental SB technologies. Future developments in SG, as well as in related fields, have to be carefully observed by investors since IP legislation could be subject to amendments, which may not always be investor friendly.

4. ORGANIZATIONAL ANALYSIS

Analysis of Organizational Capabilities

Early organizational structures within the SB industry are both dynamic and convoluted; from early investors with broad ranging interests, to national governments interested in garnering a piece of future innovation. This presents both challenges and opportunities for incumbents and newcomers alike. The companies that will eventually capitalize on the market need to have capabilities in two areas:

[26] „Synthetic Biology: Applying Engineering to Biology", Report of a NEST High-Level Expert Group, European Commission, EUR 21796, 2005
[27] Afuah, A., Innovation Management, OUP, 1998
[28] Rai A, Boyle J (2007) Synthetic biology:Caught between property rights, the public domain, and the commons. PLoS Biol 5(3): e58. doi:10.1371/journal.pbio.0050058
[29] Rai A, Boyle J (2007)
[30] Rai A, Boyle J (2007)
[31] Cho M.K., et. al., "Ethical considerations in synthesizing a minimal genome", Science 286: 2087, 1999
[32] Arjun Bhutkar

- Funding: To do proper research, to push through regulations & withstand litigation
- System Builders: Able to connect investors, governments, researchers & universities

At this stage, innovation must move forward under an explorative approach with a high tolerance for failure. Although close governmental links are important, some degree of distance and flexibility is crucial. Further development requires an organization that understands highly complex biological systems and is able to overcome significant technical hurdles, in the face of early-investor scrutiny.

SB is part of a complex system of technologies; each building and complementing the other. In order for an organization to remain at the forefront of market innovation, it will have to develop a network of system builders in complementary spaces.

Incumbent Organizations

Currently, two U.S. companies, JVCI (together with Synthetic Genomics) and Amyris Biotechnologies have taken the lead in developing SB applications.

JVCI is the private sector leader with significant commitment from the U.S. government (DOE & NIH). It was formed in 2006 by Dr. Venter and Dr. Hamilton Smith, who have managed to build an organization with a number of key capabilities, which increase its chances of successfully exploiting the technology. The most important of these is Dr. Venter himself, who received a Nobel Laureate in the field of genomics and synthetic biology. He not only brings a wealth of experience from his involvement in the Human Genome Project, but more significantly the contacts and resources he has developed over the course of a groundbreaking scientific career. Investment from the DOE[33] and the NIH[34] seems to be less driven by an interest in commercialization and instead by a desire to explore the technology and applications.

Drs. Smith and Venter stand at the centre of another company called Synthetic Genomics (Fig. 6), serving as the commercialization arm for innovations developed in the JCVI. With BP as a main investor[35], Synthetic Genomics has the resources necessary to develop SB in profitable markets such as bio fuel; however it will be crucial for them to hire a cadre of systems builders that can move government regulations forward.

Amyris is a newer player in SB but has raised close to $100M in venture capital[36]. Furthermore, they have been working with the University of California, Berkeley and poached significant executives in the industry.

Both incumbents are closely tied (scientifically) with similar funding. The winner of the SB race will be the company who is best able to leverage their network of resources to overcome roadblocks and institutional voids.

[33]Scripps Institute of Oceanography. 2006. *Leading Department of Energy Genome Scientist to Direct Joint Marine Microbial Metagenomics Cyberinfrastructure Initiative*, April 27, Accessed 10 March 2008. Available at: http://scrippsnews.ucsd.edu/Releases/?releaseID=730

[34] NIH News. 2007. *NIH-Funded Scientists Solve Genetic Code of Parasitic Worm that Causes Elephantiasis*, September 20, Accessed 10 March 2008. Available at: http://www.nih.gov/news/pr/sep2007/niaid-20.htm

[35] Synthetic Genomics. 2008. *FAQ on BP/Synthetic Genomics Deal*. [Online] Accessed 9 March 2008. Available at: http://www.syntheticgenomics.com/press/SG-BP_FAQs.htm

[36] Amyris Biotechnologies. 2008. *Press Releases and Announcements.* [Online] Accessed 8 March 2008. Available at: http://www.amyrisbiotech.com/news.html

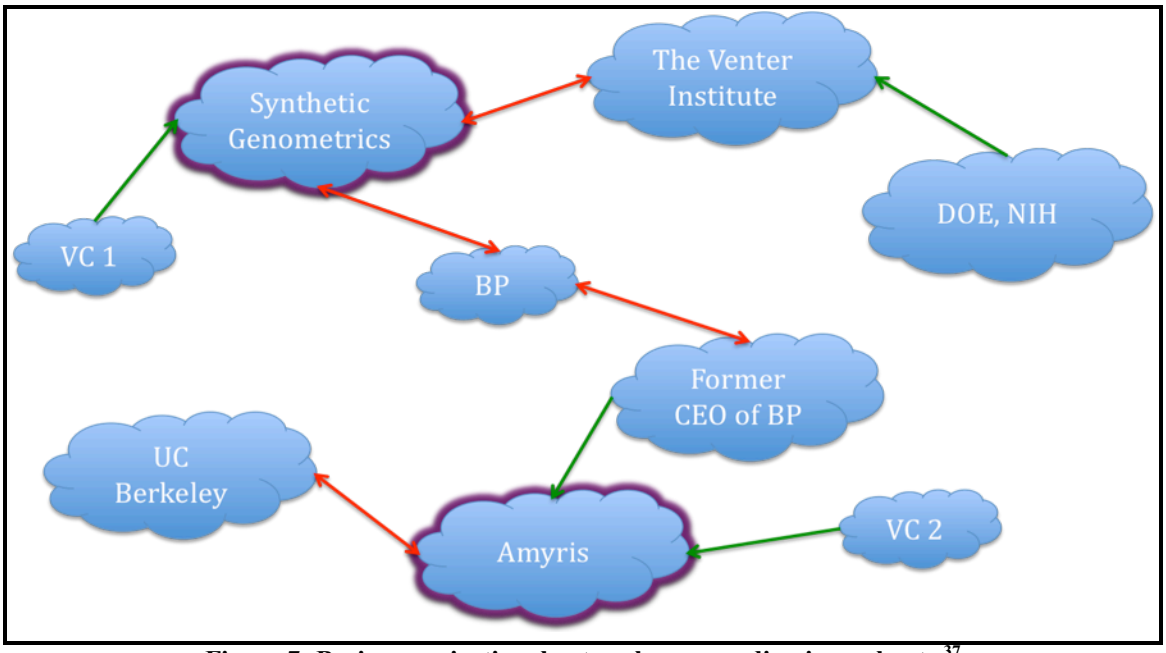

Figure 7: Basic organizational network surrounding incumbents [37]

Newcomers

Contrary to intuition, in the field of SB, smaller start-ups with scarce resources are not the organizations capable of capitalizing on this opportunity. SB requires significant risk capital, extensive government/regulatory connections and a host of eminent scientists – all of which the incumbents have.

On the other hand, there is growing concern that the early investment by the U.S. in SB will quickly disintegrate in a regulatory quagmire. A very realistic scenario involves another nation with considerable resources and lax regulations taking the lead in SB by leveraging early technologies (funded by the U.S.) to drive further development and commercialization. There already exists multiple smaller laboratories[38] around the world producing short DNA sequences, but at this stage they do not have the expertise or resources to compete with incumbents. Nevertheless under the right circumstances these small operators could very well take the commercial lead.

China has already expressed interest, along with other countries in the Asia Pacific region, in encouraging a new wave of scientific innovation and commercialisation.[39] With rising global powers investing vast resources, we can easily envision the locus of SB research shifting from the U.S. to overseas laboratories.

5. A COHERENT PICTURE OF THE FUTURE SYSTEM

Despite detailed analysis in the previous sections, unpredictable advances in multiple related fields are constantly improving technologies. This results in complex interactions that may shape the future of SB, its markets and the nature of organizations likely to embrace the technology. Although the potential impact of SB is promising, it is still in early phases of development, thus its exact future impact is hard to envisage. Subsequently it is quite difficult to accurately describe the nature of the resulting system in order to structure a coherent investment thesis. However, the context in which these changes are taking place is more stable in

[37] Own Compilation
[38] ETC Group. 2007. Extreme Genetic Engineering: *An Introduction to Synthetic Biology.* [Online] Available at: http://www.etcgroup.org/upload/publication/602/01/synbioreportweb.pdf Accessed 8 March 2008
[39] http://content.nejm.org/cgi/content/full/355/12/1191 (Online) Accessed

relative terms, since society as a whole is only changing incrementally. We can thus speculate about the future of SB in terms of the current social environment.

Willis Harman in his book "*An Incomplete Guide to the Future*" described six principles for evaluating future social systems and speculating about potential futures. We used his principles to guide our questions during formal interviews with industry experts, who were asked to comment on the impact of SB technology and how it may relate to potential markets and organizations. The six principles along with some of our respondent's key responses are summarized below.

Continuity within Systems

Social systems have the tendency to change smoothly between different states; they do not change in discontinuous jumps. Even disruptive events, by human observation, have little impact when looking at the grand scheme of events. This idea was echoed by one of our respondents when she was asked if SB will ever overtake the current dominant technology: "*Probably not. There are other more proven processes, so they probably won't replace existing treatments. Status quo is almost always preferred in biotech*."

Self-consistency within Systems

A social system can be subdivided into different parts which interact and build on one another. Such a system is internally self consistent in that some parts are required for other parts to function. When asked about system-wide consistency within SB one responded noted that: "*...there isn't really any infrastructure to support this technology...if treatments are time sensitive as in radiopharmaceuticals...you'd need a particle accelerator to produce them at your facility or somewhere very close by. Plus as mentioned before it's a rarefied field, more human resources need to exist to make it commercially successful."*

Similarities among Systems

A lot of technological developments have similarities in their growth, adoption into society and application. For instance, in the semiconductor industry faster CPUs followed similar developmental routes to their predecessors. This view was shared by one responded who also cautioned that this development was: "*...Largely dependant on what the company/institution decides to do with it, and if they continue to pass new versions/products through the pipeline before there is a commercial need*."

Cause-effect Relationship in Systems

Social systems exhibit factors that have an apparent cause-effect relationship. An example can be taken from economics where supply and demand have an indirect statistical relationship. Not so subtle causal relationships were echoed during discussion: "*Development will take a very long time...the medical device/drug path is very convoluted...I could spend days talking about FDA regulation. Even new medical devices are met with a lot of scepticism...Societal backlash/long standing controversy will be very likely...look at the GMO argument that's been going on for ages."*

Holistic Trending within Systems

A social system acts as an integrated whole and any one part of it can not contradict the rest of the system. Social trending seems to have been a reoccurring theme in all of our discussions: "*There will be a lot of controversy especially in the ethics side of things but it also depends on what the labs decide to develop first. Legal is going to pop up when new classifications for regulation/new CSR issues emerge."*

Goal Seeking of Systems

Social systems, although sometimes appearing aimless, have specific goals that guide them. These goals are not necessarily declared but they guide the individual or organizational actions to steer the system to a

desired future. By carefully observing the system and discovering its goals, it is possible to speculate on the possible futures of that system. Despite extreme scepticism among some industry insiders all agree upon the overall system goal: "*Revolution in medicine and the treatment of diseases on the molecular level!"*

6. RECOMMENDATIONS & CONCLUSION

Investment Opportunities

Conventional venture capitalists have a 5-7 year exit window during which they wish to recoup their investment, yet the SB market is far from certain and may not significantly materialize for many years to come. Nevertheless risk capital convergence (hedge funds, private equity, and venture capital) has given rise to a new breed of firms with longer exit horizons, for whom SB investments may prove attractive. Investors wishing to enter the market at this point in time are advised to focus their efforts on sourcing deals which further enable platform development. Potential areas for investment include:

- Device manufacturers developing next generation sequencers
- Chemical/Solution providers creating formulas which enhance existing processes
- Software vendors creating tools enabling SB information & project management

To help guide investment decisions we have developed four scenarios which track the likely development of SB technology through the year 2025 (Appendix I). These scenarios attempt to help investors understand SB market dynamics and in the process mitigate downside risk in their investment portfolio.

Conclusion

Given the embryonic state of SB many mainstream market-driving forces have yet to solidify. Moreover the underlying international IP system is ill equipped to deal with the intricacies of SG, as such a good deal of our analysis has focused on the need for patent reform in order to enable forward momentum by encouraging outside investment.

While there is no doubt about the future potential of SB, many uncertainties remain. Investors are encouraged to comprehensively evaluate their risk tolerance and preferred exit horizons before allocating significant funds to this sector.

APPENDIX

Scenario Development

From an investor's point of view, the main criteria for investment focus upon the commercial viability of SB technology. In our TMO Analysis we identified two emerging themes upon which the success of the technology will depend. They are New Markets and Intellectual Property Rights.

Based on our analysis the viability of the technology itself seems likely and even with the technology in an early phase of development, some commercial products with very narrow market applications have already been produced. The wider adoption of the technology will, however, heavily depend on the establishment of appropriate markets. Even with viable technology, the absence of markets will ultimately be disastrous from an investment point of view. The failure to establish an appropriate market could, for instance, be due to social rejection, too strict regulations or even the lack of effective system builders.

The second emerging theme was intellectual property rights. Appropriate property rights are critical to ensure the development of technology and we can use the pharmaceutical industry as an example. In order to develop the technology to a point where it can be commercialized, significant investment is still required. The promise of a healthy return will thus be very important to attract private investment. From a private investor's point of view, a guarantee in the form of appropriate IP laws will thus be a determining factor whether to invest or not.

To further explore the investment decision we have developed four scenarios. The scenarios are plausible narrative states of possible futures of the system surrounding Synthetic Biology and it aims to help the potential investor contextualize his/her decision making, and to develop a better understanding of the complex interaction among all the factors involved.

It is important to note at this stage that we believe the benefit from Scenario Planning comes from the actual process of creating the scenario, and not merely the end scenarios themselves as presented here. By engaging in the actual process different stakeholders voice their beliefs thereby provoking thoughtful debate about the subject at hand. [40] Nevertheless, we believe that by offering these four scenarios the investor can engage with the possibilities and reflect on the processes involved for a scenario to develop in a certain way.

To construct our scenario we used the two emerging themes from our TMO analysis, namely legislative and market creation issues. We used these two themes as axes to create four scenarios – each of the themes in a positive or a negative mode. The four scenarios presented below are:

- A quick death
- An expensive toy
- Free for all
- The dawn of a new industry

The scenarios are from the point of view of an early investor and narrated from a 2025 perspective.

[40] Senge, P., et. Al. 1994. The Fifth Discipline Fieldbook - Strategies and Tools for Building A Learning Organization, Doubleday, New York

2025 Investment Scenarios

	Lack of property rights	Property rights enforced
Inability to create markets	**A quick death:** From about 2010 to 2020 we noted good but incremental progress in the technology. The problem was that, despite some public gains and useful products, nobody was willing to buy our products on a large scale. There were, of course, the niche markets (some GM crops and limited applications for very rare genetic diseases) but we never seemed to get institutional or large corporates to buy in and invest further. We were hoping for the large pharmaceuticals to come on board by 2015, but they were slow because of general public discourse. An announcement of the creation of a synthetic insect in 2015 met with severe public resistance. To make matters worse, legislative bodies never really took note of the importance of IP rights in this domain. The general view point from legislators were that genetic codes are naturally occurring phenomena and that we can not gain copyright just by manipulating it. Because of the combined effect of a lack of markets and of IP rights, risk capital never got involved on a large scale and the whole industry is now in decline. Currently Synthetic Biology is the domain of universities and the DOE still has ongoing interests to try and develop bio-fuels.	**An expensive toy**: We observed good progress throughout the period of 2010 to 2020. By 2020 the creation of a small insect jolted the legislative body into action - they mostly wanted to regulate the industry properly because of public safety fears. Through pressure from some of our large investors, this opportunity allowed us to gain crucial property rights for our technologies. In the years following this remarkable achievement, the topic persistently stayed in the media and, more often than not, the media coverage was negative. It mostly highlighted the dangers like terrorism and cataclysmic ecological disasters. Because of established IP laws, a number of large pharmaceuticals, energy companies and risk capital firms started to invest. The investment resulted in even better achievements. By 2025 the public debate, at least in the US and EU, reached a climax after the announcement of a synthetic mammal. The public wholly rejected the technology and most of its related products. Public acceptance was only achieved for small niche markets. Currently there is a large number of organizations with very expensive labs and no real prospects of creating viable markets. Investors stand to loose a large amount of money.
Appropriate markets created	**Free for all:** The technology behind synthetic biology continued to make steady progress during early 21st Century, and remarkably achieved to produce a synthetic insect by 2020. The public gradually accepted the technology, but there were pockets of resistance. Because of the extraordinary commercial potential, we noted that risk capital became involved much earlier and invested long before traditional VC's or Private Equity firms. Legislative bodies somehow never got on board with enforcing property rights, despite lobbying from various investment groups. Changes in legislation was undertaken in the US and some EU countries, but for the most part these were not tight enough and not enforceable globally. Copying of ideas and technologies never really became a large scale problem and as a result investment never slowed down. About five years ago we noted a sudden increase in copying of technologies and innovations. This may have happened because of the first biologically engineered insect. This announcement signalled to companies just how powerful the technology was and they quickly commercialized the technology to make large profits. Currently there are a multitude of products and services available, some better than others and it seems that as soon as companies come up with good ideas, it gets copied by others. As a result investment in research has slowed dramatically and international legislative bodies are rushing to rectify the problems.	**The dawn of a new industry**: During 2010 to 2020 the technology gradually improved. The result was a much publicized creation of a small insect in 2020. Since then legal bodies were jolted into action after they realized the potential societal benefits and risks associated with this technology. Legislation introduced strict regulatory measures, but at the same time introduced proper IP protection. Critically, society never rejected the idea of a synthetic insect or other organisms for that matter. There were some resistance to the technology from various groups, but it never reached a critical mass to stay in the public domain. It was noted between 2008 and 2025 that various synthetic biological products were accepted in various niche markets, such as GM crops and they gradually became acceptable in the wider public. Although it had limited application at that stage, some medical application gained public acceptance as well. From 2020 onwards we noted a flurry of risk capital coming on board and large corporations like pharmaceuticals and energy companies invested significantly. Markets gradually grew as public acceptance improved and as a result of the efforts of various start-up companies. Currently there are a few large organizations and multiple smaller start-up companies producing and selling synthetic biological products.