Examination and Discussion of the Technical, Ethical, and Social Benefits and Costs of Synthetic Biology

English 360 Section 001
Patrick Caveney
November 30th, 2012

Abstract

Synthetic biology is a new field of research focused on creating new organisms to solve human needs like the production of chemicals, fuels, and pharmaceuticals. This report gives an overview of the field and presents technical, ethical, and social challenges. Technical challenges covered include protein folding, genetic engineering, and metabolic engineering. Ethical challenges discussed include 'playing God,' and genetically modified foods. This report argues that both of these concerns are exaggerated. Social challenges discussed include rising food costs, newly created invasive species, and super viruses. This report argues that rising food costs and super viruses are genuine threats, but synthetic, invasive species are not.

Contents

List of Figures

Introduction

Synthetic biology is a new field that applies engineering design to biology. The ultimate goal of synthetic biology is to create designer organisms to fix human needs. The most obvious needs are chemical, fuel, and pharmaceutical production. Using biology to create these products is more efficient, clean, and resilient. Synthetic biology emerged from the study of genetics. Researchers in synthetic biology use knowledge gained from genetics to manipulate and create new organisms.

Definitions

Engineering has many inherent benefits. Everything that has been engineered today has calculable qualities. All the forces in a bridge are calculated, and the appropriate strength beam is selected. Every discipline of engineering has equations that are used to calculate these qualities. Bridges have equations. Circuits have equations. Equations were discovered through scientific inquiry, but they can be applied through engineering. Equations are used to predict what we expect to happen. Secondly, pieces in engineering applications are modular and can be moved around in a predictable manner. For example, a circuit board has many transistors, capacitors, and other electrical components. These can be shuffled around to suit different applications.

Engineering does have a few drawbacks. Technology is difficult to manufacture. Cars, bridges, planes, and circuit boards are difficult to design and make. Even though these examples can be calculated they are still complex. Technology must also be created in very special circumstances. Computers must be created in clean rooms because the smallest imperfections cause the system to fail. Cars must be created in many precise steps. Though, cars are more robust and tolerant to errors, they will still perform sub par if they have manufacturing errors. Engineered products can also never improve. Cell phones and computers wear down, but their circuit boards cannot grow more parts to make them faster. They must be replaced. Finally, engineered products cannot be repaired if they are damaged. If a car is damaged, it never quite goes back to the way it was before, even if the damaged parts are replaced.

Biology, on the other hand, can self assemble, is efficient, and stable. By its nature, biology can assemble itself. This is true for single cells replicating themselves and for humans who start as two cells and develop without any oversight. Self-assembly is very important at the scale that cells operate, the micro and nano scale. There is a lot of research in assembling nano motors and nano structures. While the research is important, it is not applicable if the structures cannot self assemble. To have any useful collection of nanostructures they must self assemble because to do otherwise would take too long. Biology is also efficient. Evolution ensures that only the most efficient organisms survive, so we know that what is alive today is more efficient than billions of years of other organisms. For example, the human brain only uses a few watts of energy, but a computer uses two orders of magnitude more. Sometimes evolution trades efficiency for reliability. For example, when DNA is being copied it is also checked. Obviously, checking it takes more time and energy, but it is worth the trade off. For the most part, organisms are efficient. Finally, biology is stable for a range of conditions. Organisms have been found that survive freezing and boiling temperatures, and mammals can survive over a range of a hundred degrees Fahrenheit.

Biology is not without its problems though. Organisms are a complex soup of chemicals, and there are great co-dependencies between molecules. The metabolisms, collections of all chemical reactions, of even the smallest organisms are very complex. The problem is that all these chemical reactions are occurring in the same place. Membranes can divide organisms, but for the most part, the molecules and chemicals are free to move. The second problem is that these molecules are not independent. They interact freely with one another, and changing one molecule can have unintended consequences. Every drug on the market today has side effects. These are the unintended consequences of adding a particular chemical to the complex metabolism of the body.

The goal of synthetic biology is to merge these two disciplines. The final goal is to make organisms that are calculable, and modular, but still efficient, stable, and self assembled.

Current Research

Synthetic biology is being applied to a wide range of problems including production, agriculture, data storage, biosensors, and entertainment. Single celled organisms are being used to manufacture chemicals at the University of Tennessee and Chalmers University of Technology in Sweden (Trinh 2012, Chalmers 2012). The manufactured chemicals range from fuels to scents. Genetic engineering is being used in agriculture to increase crop yield and protect crops against disease (McFadden 2012). This application is a point of contention because we ingest the results and there is worry that genetically modified plants are not as safe as natural ones. Researchers at Harvard have recently used genetic engineering to store 700 terabytes of data in a single gram of DNA (Church 2012). This has large implications on long-term data storage such as library archives and video surveillance. Synthetic biological sensors are also being created to sense toxins and explosives (ScienceDaily 2012). This will provide an easy way to survey an area and sense attacks. Finally, synthetic biology is creating fun pets like fish that glow in the dark (GloFish). The fish have a gene from a glowing jellyfish. Designer pets will certainly become popular. They will be ok as long as the pets are not unethically treated.

Technical Challenges

Synthetic biology presents many technical challenges because of the messy nature of biology. Other engineering disciplines can isolate variables separate different parts of the system. In biology, chemicals and organisms are all mixed up. The main approaches to overcoming this challenge are researching protein folding, genetic engineering, and metabolic engineering.

Protein Folding

The main technical challenge facing researchers is that it is not possible to predict the shape, and thus the function, of proteins from the sequence of DNA. If this were possible researchers could produce designer proteins to use for any imaginable task. However, protein folding is too small and happens too fast to directly observe and is too complex and too slow for computers to model (Folding@home 2012). Proteins fold on the nanometer (one billionth of a meter) scale and the microsecond (one millionth of a second) scale. Computers use time increments 1000 times slower than proteins fold. Computer systems are too accurate. Current research is focusing on both modeling protein folding with computers and using people to creatively fold proteins. The purpose of these simulations is to find patterns in the protein folding that can be turned into rules of folding. Folding@home and Fold It are two major areas of research, and both allow everyone to participate in folding proteins. Folding@home is a program for any computer that runs when the computer is not in use by the owner. The computer is added to all the others on the network, and together they fold proteins. The purpose is to use computers that would otherwise be sitting idle, and it does not interfere with the normal function of the computer. Currently, there are 200,000 computers folding proteins with Folding@home. This many computers create a supercomputer to fold proteins that may cause human diseases like Alzheimer's (Folding@home 2012).

The second approach, Fold It is a collaborative game. The players try to fold proteins into the smallest shape possible. This method uses human creativity to fold proteins like origami. Players who fold the protein the furthest win, but anyone can jump ahead to the current leader's position and start from there. After all, the point of the game is to increase scientific knowledge (Fold It 2012).

Genetic Engineering

Genetic engineering is rewriting DNA. It is less of a problem now that is was in the early days of genetic research. This process is well understood, and relatively easy. Once DNA was discovered, the machinery involved in natural DNA manipulation was quickly researched. Organisms naturally change and copy their own DNA. So, by isolating the proteins organisms use to copy their DNA, researchers can copy DNA. The same goes for most all DNA manipulation processes. Genetic machinery is available from animals, plants, bacteria, and viruses. In high school biology we bought a gene, which had been isolated from glowing jellyfish, and injected it into E. coli. All of the machinery needed to insert a new gene into the E. coli bacteria was readily available. DNA in more complex organisms, mammals, is regulated in more complex ways, so changing the DNA does not always have predictable results.

Metabolic Engineering

Metabolic Engineering is like giving drugs to cells. The metabolism of a cell is the sum of all the chemical reactions that happen in the cell. As stated above, these reactions are happening all in the same space, so the metabolism of even simple cells is very complex. Some chemicals change how genes are expressed which, in turn, changes the products of the cell. A good example of this is yeast. Yeast naturally produces ethanol. If the proteins that create ethanol are created in excess, more ethanol will be made. This is analogous to giving people drugs to produce more insulin to cure diabetes. Like in humans, metabolic engineering in cells has side effects, limits, and unexpected results.

In the 1980's Richard Jorgensen and his colleagues tried to make purple petunias more purple. They started injecting different chemicals they thought would make more of the purple pigment. What they ended up with is a range of flowers with different patterns, some more purple, some white, and some striped (PBS 2005).

To advance metabolic engineering, current researchers are trying to remove all unnecessary metabolic pathways. That is, they are trying to make cells as simple as possible to reduce the unintended consequences. One of the primary goals of synthetic biology is a minimum viable cell. This cell would include only the things needed to survive and nothing else. The cell could then have chosen functions added to it like modular parts on a robot. The simple cell would also be well documented, so any changes added to it could be reconciled with the existing minimal structure. Dr. Trinh at the University of Tennessee has done something similar with yeast. To make yeast more efficient at producing ethanol, he removed all the metabolic functions that are not needed for the yeast's survival or ethanol production (Trinh 2012). Hopefully this method will create simple productive cells.

Ethical Concerns

Along with all its technical challenges, synthetic biology introduces ethical concerns. The most debated are 'playing God' and genetically modifying foods. 'Playing God' is a criticism with many new technologies, and it is really a fear of unlocking more power than we can control. Genetically modified foods also stem from a fear of the unknown. The question is whether or not to allow these foods, and, if so, to what extent should they be regulated.

Playing God

The first ethical concern is 'playing God'. This notion is mostly the view that humans are encroaching on powers beyond our knowledge and beyond our control. It has always thought to be dangerous to reach for the god's powers. The Greek god Prometheus was forever tortured by having a vulture eat his liver every day for giving people fire. Stories like these taught people that they should not be too ambitious and avoid power they cannot control. Researchers have always been careful, but sometimes large leaps are needed. When scientists first tested a nuclear reactor under Chicago during World War 2, they were unsure if the chain reaction could be contained or if it would consume the city. Every now and then our equations and predictions fail and we need to gather experimental data to further our knowledge.

The best argument against 'playing God' is that every technological advance has been met with the same criticism and synthetic biology is no different than any other advance. Adam Rutherford of the Guardian states, "Yet there is almost no aspect of human behaviour that isn't some form of manipulation of the environment for our own purposes." (Rutherford 2012). And, he goes on to mention how unnatural farming and breeding are. The same argument can be applied to modern medicine, electricity, and automobiles. Arthur C. Clarke is famously quoted as saying, "Any sufficiently advanced technology is indistinguishable from magic." And, given that powers of gods tend to be magical it is no surprise that people resist technology as being from the gods.

Genetically Modified Foods

Genetically modified foods are another debated ethical concern. The number of genetically modified foods is growing in the United States.

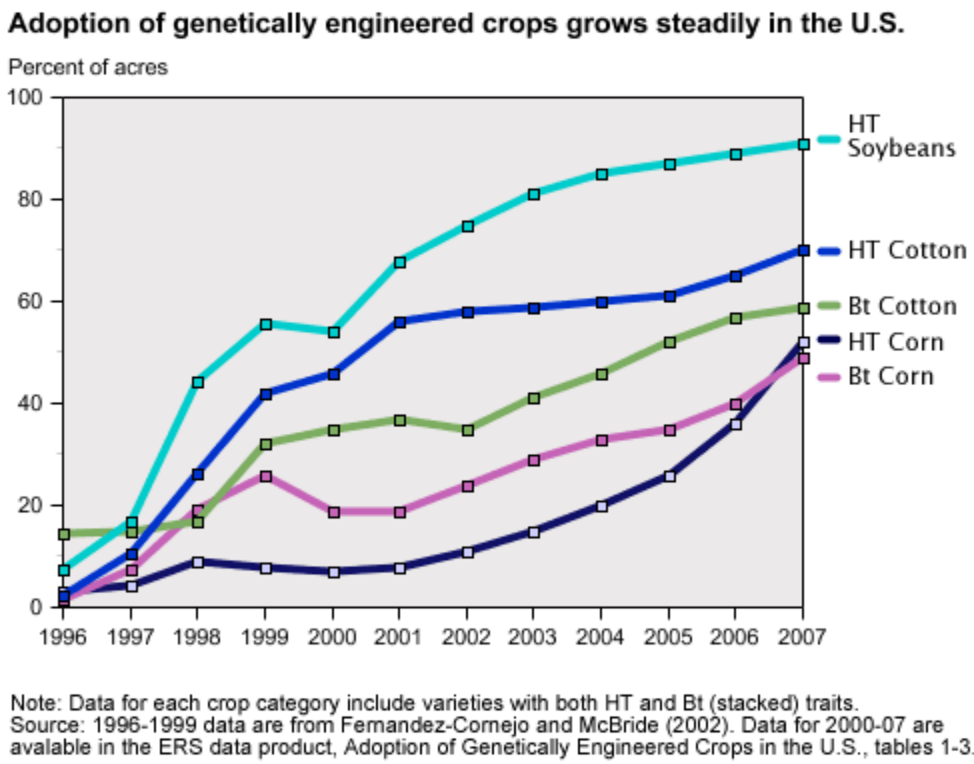

Figure 1. Growth of Genetically Engineered Crops in the United States. *Source: Alexis Madrigal, "Have You Eaten Your Genetically Modified Food Today," Wired, last modified September 11, 2007, accessed November 10, 2012, http://www.wired.com/wiredscience/2007/09/monsanto-is-hap/.*

Figure 1 shows the growth in herbicide tolerant (Ht) crops and insect resistant (Bt) crops in the United States since 1996. A movement called Just Label It is organizing to force companies to label if their food products contain genetically modified (GM) foods. This would be similar to the mandate to provide nutrition labels. According to their website, over 90 percent of the population supports labeling of GM food in multiple studies. Interestingly, they also claim that over 90% of Republicans, Independents, and Democrats support GM food labeling (Just Label It 2012). Their real issue with GM food is that it is unproven and untested in the way that drugs currently are. People are consuming what are essentially new species, species that our bodies have not had millennia to adapt and evolve to consume. The genetic makeup of current GM food is not too different from the original species, but it is noticeably different. Artificial selection, only planting seeds from the best plants, is another form of genetic engineering, and it has been around almost since farming. The difference is that our bodies have been able to adapt over the long time these crops have been modified. Just Label It's concern is that these new foods may be toxic or cause allergies or have other side effects. This concern is valid, and these foods should be investigated, but no more than other food.

I must disagree with their analysis of the market but applaud them for bringing the problem to the public's attention. If it were true that 90% of people wanted their food labeled, then companies would step up and label their food as GM or GM-free to appeal to the consumers. Of course, labeling food as such may drive away consumers, they may want to pay more for GM-free food, or they may not care as long as the food is cheap. Anyway, the first companies to label their food would be applauded if the public consensus were that GM food should be labeled. Adding more government regulation would shut down small businesses that are researching these foods, and the innovations they produce would be lost.

Social Concerns

Synthetic biology presents many social concerns that must be investigated before the field can progress. These concerns affect the large population, and they include increasing food costs, creating super viruses, and creating new invasive species. Rising food costs are always an issue, and they are compounded by synthetic biology. Super viruses are a very hazardous concern, and small outbreaks have already occurred. Invasive species already threaten ecosystems. Synthetic species may pose a greater threat.

Food Costs

Food costs are a serious concern. Everyone eats, and increasing foods costs affect the poor first and hardest. The concern here is using synthetic organisms to convert corn to ethanol drives up the price of corn because of the increased demand.

Figure 2. Food and Agriculture Organization (FAO) of the United Nations Food Price Index. *Source FAO, "FAO Food Price Index," last modified 2012, accessed November 17, 2012, http://www.fao.org/worldfoodsituation/wfs-home/foodpricesindex/en/.*

In Figure 2 from the United Nations shows the international price of food rising. Even the real price, which is inflation adjusted, is rising. Adding synthetic biology to this already growing problem is unacceptable. One of the main problems here is that in the United States, the

Environmental Protection Agency (EPA) requires a set number of gallons of ethanol to be produced from corn every year. This is in an effort to reduce our carbon impact and global warming. While these goals are great, achieving them at the expense of starving the poor is not acceptable. The EPA mandate forces the production of ethanol from corn, which raises corn prices for people trying to eat corn, and its derivatives, and for people trying to burn it. This program raises food prices all the time, but the problem is exacerbated during times of poor corn harvests. This is currently the case. The EPA has refused to waive the mandate even though they acknowledge the impact of the drought this year (EPA 2012). Part of the problem is that the mandate calls for a set number of gallons of ethanol from corn (7.5 billion gallons). If the mandate instead called for a percentage of corn to be converted into ethanol the food price would be less affected by the mandate in times of poor harvest. Tim Worstall, a contributor to Forbes, says, "40% of the US corn crop is converted into ethanol." (Worstall 2012). If this could be lowered to a more reasonable level, food prices could be restored to a level more in line with a low income.

Another problem is finding room to grow all the biomass, from food or not, needed for synthetic biology production. Viable land is not unlimited; growing plants people do not eat, like switchgrass, takes up space that may be used to grow food. Friends of the Earth, an organization pushing for government regulation on synthetic biology, points out that small farms around the world sustain families and small communities (Friends of the Earth). If the lands that these small farms are on are so valuable to synthetic biologists, then can't the local farmers make money selling biomass to the biologists? I think this problem can be a benefit to both parties. The scientists can get the biomass to feed to their synthetic organisms and the farmers can get money to do with what they want. It may be that the scientists do not pay enough to justify the switch for the farmers. In that case the farmers are well within their rights to keep planting what they are now. However, if the land is as scarce as predicted, the farmers could make quite a bit of money.

Invasive Species

New, synthetic invasive species may pose a large risk to the environment and natural ecosystems. Already we have seen the effects of species like kudzu, Asian carp, and Africanized bees on American habitats. The risk is that a new synthetic organism would overtake local species. Friends of the Earth is an organization that is trying to place government regulations on synthetic biology, in part, to protect the environment. They give an example of disseminating an organism to clean up an oil spill but accidentally introducing an invasive species. This species, once released, would not be containable (Friends of the Earth). David Biello argues in Scientific American, "Most such creations today [synthetic organisms] are too ungainly to survive in the wild." (Biello 2010). This is quite likely the case. Popular lab organisms like mice have been breed for very specific purposes and traits. Unlike the wild, the lab is not a competitive environment, so weak mice can survive. If lab mice were released into the wild they would most certainly die. The same is true of organisms like the yeast Dr. Trinh is creating with metabolic engineering. To make the organisms simpler, he is removing natural processes that do not produce ethanol. These extra processes allow the yeast to survive in the wild where it could face any number of problems. In the lab, its environment is controlled, so survival traits become unnecessary. As the trend in synthetic biology is to create simpler organisms, it is unlikely that these lab created organisms will take over ecosystems.

Super Viruses

Super viruses are the most serious social problem facing synthetic biologists. The worry is that scientists cannot predict every result of their work and may accidentally create an unstoppable virus, or published papers may lead to the purposeful creation of an unstoppable virus. The scary part is that small laboratory leaks have already happened. Spiegel, a German news outlet, reports that in 2001 a 100% fatal smallpox virus for mice was accidentally created. They also report that a lab leak in 1977 may have lead to the "Russian flu." Also reported was that SARS infected a laboratory researcher, and could have lead to an outbreak (Hackenbroch 2012). These serious cases could have been a lot worse. Spiegel also reports how Ron Fouchier, a virus researcher, "performed only a few targeted manipulations on the genetic material of the ordinary H5N1 virus and, to make the virus even more dangerous, he repeatedly transmitted it from one laboratory animal to the next." (Hackenbroch 2012). His results were withheld from publication out of fear terrorists could follow his steps. The problem here is that his work could allow other researchers to develop a cure or early detection system for the deadly version of the virus. A federal committee, National Science Advisory Board for Biosecurity (NSABB), prevented the publication. NSABB is charged with developing "outreach, education, and training" programs; advising "publication, communication, and dissemination" of results; and "fostering international engagement." (NSABB 2012). Blocking potentially deadly results fits their goals. But, blocking advancements in science is the opposite of what they need to be doing. So, information cannot be released to anyone, but perhaps an agreement could be made to release the information to select researchers who are working on virus detection.

Conclusion

In conclusion, this report has presented technical, ethical, and social concerns with the emerging field of synthetic biology. The technical concerns discussed are protein folding, genetic engineering, and metabolic engineering. The most challenging are protein folding and metabolic engineering. Genetic engineering has been mostly established and is routine by now. The ethical concerns discussed are 'playing God' and genetically modified foods. 'Playing God' is not a concern to worry about as this argument has been brought up against may other technological advances, which we have overcome. Genetically modified foods are a legitimate concern because modified species have genes to which our bodies may have not natural defenses. However, enacting tough regulations is a heavy-handed approach, which will stifle innovation. The social concerns discussed are increasing food costs, invasive species, and super viruses. Rising food costs is a major ethical concern, but it is one that is largely being mishandled. Rising food costs could be collaboratively approached and all parties could be better off. Invasive species is not a very large problem because most lab creations are simple and lack the defenses needed to survive, let alone thrive, in the wild. Finally, super viruses are a real concern, and some small outbreaks have already occurred. This concern needs much more care, thought, and planning so as not to hold back the whole synthetic biology field. Synthetic biology is a new and exciting field. There are many questions to be answered, which will require the collaboration of disciplines across academia and industry to solve.

References

University of Tennessee, “Dr. Cong Trinh Faculty Page,” accessed November 10, 2012, http://www.engr.utk.edu/cbe/faculty/Trinh/default.html.

Chalmers University of Technology, “Sys2bio,” accessed November 10, 2012, http://www.sysbio.se/.

Johnjoe McFadden, “Synthetic biology:the best hope for mankind’s future?,” *Guardian*, last modified March 29, 2012, accessed November 10, 2012, http://www.guardian.co.uk/commentisfree/2012/mar/29/synthetic-biology-best-hope-mankind.

George M. Church, Yuan Gao, and Sriram Kosuri, “Next-Generation Digital Information Storage in DNA,” *Science* 337 (2012): 1628, accessed November 10, 2012, doi: 10.1126/science.1226355.

ScienceDaily, “Most Complex Synthetic Biology Circuit Yet: New Sensor Could Be Used to Program Cells to Precisely Monitor Their Environments,” last modified October 9, 2012, accessed November 10, 2012, http://www.sciencedaily.com/releases/2012/10/121009131505.htm.

GloFish, “GloFish,” accessed November 10, 2012, http://www.glofish.com/

Fold It, “Solve Puzzles for Science,” last modified November 29, 2012, accessed November 15, 2012, http://fold.it/portal/.

Folding@home, last modified 2012, accessed November 15, 2012, http://folding.stanford.edu/English/HomePage.

“RNAi,” PBS Nova, last modified July 26, 2005, accessed November 15, 2012, http://www.pbs.org/wgbh/nova/body/rnai.html.

Adam Rutherford, "Synthetic biology: 'playing God' is vital if we are to create a better future for all," Guardian, last modified July 27, 2012, accessed November 15, 2012, http://www.guardian.co.uk/commentisfree/2012/jul/27/synthetic-biology-playing-god-vital-future.

Just Label It, last modified 2012, accessed November 15, 2012, http://justlabelit.org/.

EPA, "Renewable Fuel Standard," last modified November 28, 2012, accessed November 15, 2012, http://www.epa.gov/otaq/fuels/renewablefuels/index.htm.

Tim Worstall, "Drought, Climate Change, Corn Prices, Ethanol and Biofuels," last modified July 20, 2012, accessed November 15, 2012, http://www.forbes.com/sites/timworstall/2012/07/20/drought-climate-change-corn-prices-ethanol-and-biofuels/.

Friends of the Earth, "Synthetic biology," accessed November 15, 2012, http://www.foe.org/projects/food-and-technology/synthetic-biology.

David Biello, "Creation of Life," *Scientific American*, 302 (2010): 42, accessed November 15, 2012, doi: 10.1038/scientificamerican0610-42.

FAO, "FAO Food Price Index," last modified 2012, accessed November 17, 2012, http://www.fao.org/worldfoodsituation/wfs-home/foodpricesindex/en/.

Veronika Hackenbroch and Gerald Traufetter, "Controversy Brews Over Scientists' Creation of Killer Viruses," last modified February 17, 2012, accessed November 15, 2012, http://www.spiegel.de/international/spiegel/containing-super-flus-controversy-brews-over-scientists-creation-of-killer-viruses-a-815782.html.

Alexis Madrigal, "Have You Eaten Your Genetically Modified Food Today," Wired, last modified September 11, 2007, accessed November 10, 2012, http://www.wired.com/wiredscience/2007/09/monsanto-is-hap/.

National Science Advisory Board for Biosecurity (NSABB), "About NSABB," last modified April 4, 2012, accessed November 15, 2012, http://oba.od.nih.gov/biosecurity/about_nsabb.html.