The Place of Computer Science Within Biohybrid Systems and Synthetic Organisms

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Introduction

Biohybrid systems and synthetic organisms are multi-disciplinary fields of science that focus on living systems and organisms. The definition of a bio-hybrid system is formed by coupling at least one biological component of a living system to at least one artificial, engineering component. A synthetic organism is a bit harder to define but it is generally a machine the replicates or takes inspiration from a living organism in some way.

The first time a bio-hybrid system was used was to support the smooth and cardiac muscles. To clarify, the cardiac muscle is the muscle around the heart that propels blood and leads to proper oxygenation of the blood and maintenance of each cell that comprises the human body. The smooth muscles are located around hollow visceral organs like the liver, pancreas, and intestines, and they use contractile force for shortening and propelling various contents across the lumen of the multiple organ systems(Carlsen 2014) The devices used were to help regulate the blood flow and the devices also had no random contractions or driving stimulus. An example of driving stimulus is an RC car, where the device is controlled by an outside controller. Moving on, another application for biohybrid systems was in insects. Insects were used because there is a much larger number of insects than humans and insects are more maneuverable and have a lower body temperature aids the electronics that are used in some systems. They also have a culture medium which supports the growth of microorganisms.

The first synthetically modified organism was from E. coli, Escherichia coli, which was first discovered in 1885 by Theodore Escherich. (Lim 2010) It is found in all over in nature, such as in raw meat like animals and intestines. In this case we are not focused on E. coli as a whole, but only on 0157:H7, whose full name is Shiga toxin-producing Escherichia coli 0157:H7. 0157:H7 was first recognized in 1982, a full 97 years after E. coli was discovered, hidden in some bloody diarrhea, one of the side effects of E. coli. It was one of the major contributors to the E. coli outbreak that made 73,000 people ill, hospitalized about 2,000, and killed sixty-one people(Rangel 2005). In comparison, E coli. As a whole infected 265,000 people and caused one hundred deaths. 0157:H7 is a strand that makes up about forty-percent of all E. coli while the other sixty-percent is classified as non-0157:H7. The way they modified it was that they changed the enzymes to make it immune to natural viral infections(Hayden 2016). They also changed its code to minimize potential bacteria and added a type of kill chain in case of an escape.

Biohybrid and synthetic organisms are on the cutting edge of the fields of both biology and engineering, but the contribution of computer science to this field is often overlooked. On the contrary, biohybrid systems and synthetic organisms provide an opportunity for research into creating hardware-based systems for onsite computing, software to aid in the management of experiments, simulations and genetic algorithms, optimization, and even an alternative to classical computing found in cellular computing.

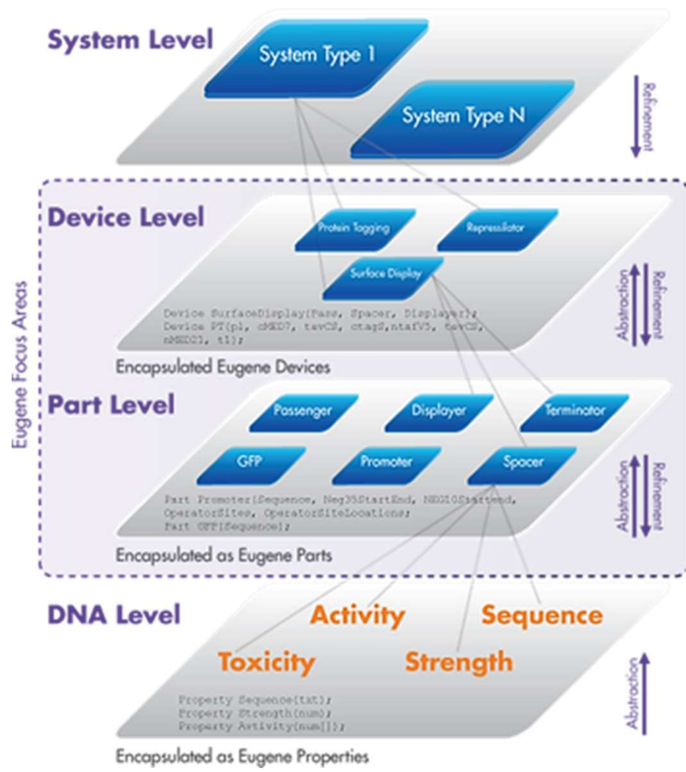
Literature Review & Discussion

Biotechnologies, including biohybrid systems and synthetic organisms, are where biology, computer science, and engineering all come together to face problems that stand in the way of the creation of these devices(Linshiz 2012). Although the need for biological knowledge is clear for the practical application of biotechnologies, the engineering and computer science contributions may be less clear. As will be discussed in analysis of other articles, the creation of biohybrid systems and synthetic organisms requires solutions to both engineering and computer science problems, so an interdisciplinary approach is the best way to face these issues(Linshiz 2012). Moving forward, the best way to advance the field may be through the work of interdisciplinary researchers, who are skilled in biology, engineering, and computer science, rather than teams of specialized researchers working together because of the inherent discontinuities that come with the current system(Linshiz 2012).

An application of computer science within the biotechnologies world, although not strictly in devices themselves, is in the creation of a cloud service for the scientific community(Linshiz 2012). This proposed cloud would feature experiments planned out to a high level of abstraction, provide a database for storing experimental results, and provide security for researchers(Linshiz 2012). The implementation of cloud computing and services is a difficult undertaking and must be overseen by experts(Ranjan 2015), but might revolutionize the way biological experiments are carried out. This provides a great opportunity for computer scientists to not only work in the same field as biologists but also provides an opportunity to diversify the skill set of all parties involved in this endeavor.

Another facet of biotechnologies that involves the work of computer science is in the robotic equipment in laboratories. For example, there are machines that are specialized for handling the liquids that are used during many biological experiments that are aimed to make the manual tasks associated with these experiments less dependent on the researcher themself(Linshiz 2012). Unfortunately many of these machines go under utilized in laboratories because of the inability of the researchers to adjust the program being run on the machine to fit specific tasks(Linshiz 2012). This results in these machines going unutilized in many contexts in which they would be incredibly useful and the only reason for this being that there is no one with the skills to adjust these machines present. This further accentuates the need for interdisciplinary researchers to be working in this field, with a special emphasis on the need for computer science expertise.

This lack of integration with computer science and therefore lack of progress with the aid of laboratory robotics, lead Linshiz to also discuss the creation of a high level language that is to be used in laboratories. The language Eugene, which is a script-based graphical design language designed to work with CAD tools, has since been released for the specific purpose of aiding the design of biological systems. The way Eugene works is that the elements of a project are defined in layers of abstraction, DNA are the smallest components which are used to form parts which are used to form devices which are finally used to form systems(Bilitchenko 2011). This framework allows for both bottom-up and top-down design perspectives(Bilichenko 2011), and integration with other simulation software to aid in the design process. Eugene is also a statically typed language like Java and in fact requires the use of Java to run(Bilitchenko 2011). The creation and use of Eugene shows a shift toward integrating computer science within the field of biotechnologies. This shift could allow for more



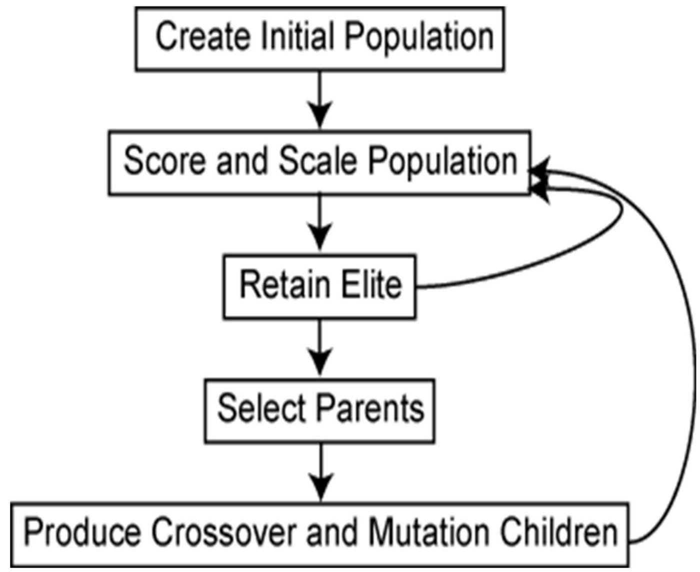
A diagram depicting the levels of abstraction within the Eugene programming language, https://www.cidarlab.org/eugene seamless cooperation, like that described by Linshiz, and allow individual researchers to take a more holistic perspective on their projects.

Moving away from the general application of computer science within the field of biotechnologies, computer science is directly involved in many cutting edge biohybrid devices. Specifically, Organic Mixed Ionic-Electric Conductors are integral to the advancement of computer science within this field(Zhang 2022). These devices are intended to be used as part of systems placed within the body that will detect biosignals and interpret them(Zhang 2022). In order for devices to be both safe and effective inside the body, they must be durable, flexible and low voltage(Zhang 2022). Creating systems that hold up to these standards are not only an engineering problem but also a computer science problem because the materials that are traditionally used to create computers are not always practical for use in biohybrid contexts. The goal of these devices is to be able to perform that of an EKG and similar monitoring devices, so as to be able to read in a signal and classify it into categories based on the person they are monitoring(Zhang 2022). The way to achieve this is to create a hardware based neural network that will read in these signals through a sensor and then use a classification array to determine whether the signal is normal or if it is signifying a medical event(Zhang 2022). As of right now materials that can work for these devices within the confines of being safe for human implantation have not been developed(Zhang 2022). The reason for this is that there are not very many viable materials that can act as n-type semiconductors which are integral to the system, requiring both p and n-type semiconductors(Zhang 2022). A proposed solution to this problem is the creation of an ambipolar material that can act as both a p and n-type semiconductor(Zhang 2022). As of yet this has not yet been achieved, therefore on site computing for these devices is still out of reach, so these devices still rely on outside sources for computing(Zhang 2022). Although the hardware constraints are a challenge that needs to be overcome through the field of engineering, it is still important to consider the role that computer science is playing within the system. Since the current design is unachievable, it is important for those working on it to take an interdisciplinary approach and make changes on both sides. The solution may lie in trying to change the computing design to fit the materials, or change the materials to fit the computing design, or, most likely, changing both to better fit the constraints of the other.

Similarly, there has been research into electrochemical neuromorphic organic devices(ENODes) that are meant to mimic neuronal and synaptic function(Burgt 2017). This research comes as a replacement to memristors that face limitations with noise interference, non-linearities, as well as high voltage and currents that can be harmful in bio-hybrid context(Burgt 2017). These devices are neuromorphic systems that are made out of lightweight and flexible arrays that have been put through neural network training simulations for classifying handwritten digits and have yielded ninety-three to ninety-seven percent accuracy in each of these simulations(Burgt 2017). This success is very promising, and could be employed in the biosensing contexts(Burgt 2017) discussed for the OMIECs but there are even more contexts in which this device could thrive. One of the projects this device is hoped to be a part of is in the development of neuroprosthetics(Burgt 20217). Specifically they are seeking to develop interfaces between the brain and machine and combine that with neural sensing training(Burgt 2017). This opens up a very large opportunity for new research in computer science. Interactions between the human brain and implanted machines may be the most varied field within biohybrid systems and may also be the most sensitive. The brain is a robust and complicated organ that is also very susceptible to damage, so knowledge of those risks and how best to mitigate them is required for working in this field. That is an issue that must be dealt with from an engineering perspective but must also be supported by the creation of computing systems that can work within the confines of a bio-hybrid system with the even narrower confines of working within a system that is designed to interface with the brain.

Synthetic organisms are the other side of biotechnologies that provides exciting opportunities for computer scientists to contribute to this growing field. Synthetic organisms are machines that seek to emulate or are inspired by organic processes. One of the most interesting applications of this concept is the work of the Biorobotics institute in Italy. The goal of their research is to make a swimming machine that is inspired by the locomotion of batoid fish, such as the manta ray(Cacucciolo 2014). Batoid fish are quick and efficient in their locomotion through the water and fill a diverse set of ecological niches, so they were chosen as the inspiration behind the design of the machine with the goal of it being efficient and highly adaptable(Cacucciolo 2014). The design of this machine relied heavily on computer science with the design being created virtually and then being run through a WeBots simulation with a genetic algorithm provided by MathLabs to find the optimal design given their desired criteria(Cacucciolo 2014).

Genetic algorithms are an important part of the design process for many things but lend themselves quite well to synthetic organisms. Genetic algorithms take inspiration from natural processes to find the best solutions to problems(Herrera 1998). There are a few different kinds of genetic algorithms that deserve to be covered in detail but that is outside the scope of this paper. It is worth looking into the Genetic Algorithm that was used in this design process that was based on the process of natural selection.



A diagram depicting the basic workigns of a genetic algorithm, https://www.mathworks.com/help/gads/what-is-the-genetic-algorithm.html

This Genetic Algorithm is based on the process of natural selection where organisms compete with each other and the ones that are the most fit are the most successful and are propagated through the generations(Herrera 1998). In the case of the genetic algorithm a set of possible solutions to an issue, in the case of the swimming machine it is possible designs, called chromosomes, are given a fitness score(Herrera 1998). The chromosomes with the highest fitness score are the elite and are made to be a higher proportion of the gene pool which have their traits crossed over with each other to form the next generation of new solutions(Herrera 1998). This new generation will also have new solutions added to it called mutations, which are created when one of the traits of a solution is arbitrarily altered(Herrera 1998). After generations of this taking place the best solutions will begin to appear(Herrera 1998). There is no guarantee that the optimal solution will be found by a genetic algorithm but it can reliably produce good solutions to problems(Herrera 1998). Early on in the development of Genetic Algorithms it was difficult for them to operate on complex chromosomes but were reliable when working with things like vectors, matrices, floats and so on(Herrera 1998). There have since been bounds in the development of these algorithms to work on more and more complex solutions to problems and this provides a very interesting avenue of research for any computer scientist that is interested in the optimization of algorithms and real world problems and those with knowledge and interest in biology.

The use of the simulation with a genetic algorithm allowed the researchers to find a fairly generalist design of their swimming machine that can perform well in different environments(Cacucciolo 2014). These types of simulations have many applications but are especially useful in the fields of biohybrid systems and synthetic organisms. Progress in this field can come from advances in biology and engineering, but the advances in design simulation and optimization can have a profound effect on the quality of these machines which makes the impact of computer science on this field impossible to overlook.

Research into making these batoid swimming machines has progressed even farther and the latest design has mixed the concepts of synthetic organisms and biohybrid systems. The concept of a biohybrid system has been taken even farther into a biohybrid robot, which is when biological material, usually muscle, is used with an artificial scaffolding to create a machine that is more adaptable and more receptive to stimuli(Guix 2021). How this relates to swimming robots is that in 2016 a soft swimming machine made using cardiac cells was created that was based on the locomotion of a stingray(Park 2016). Not only is the creation of better swimming robots important for the field of robotics, but creating a machine that can integrate with a species population could revolutionize the study of animals(Romano 2021). Similarly to everything else in the field of biohybrid systems and synthetic organisms, this area of research is both exciting and connected to computer science in the need for simulation and optimization. Also, the possible application of new kinds of sensors can open the door to more biohybrid implants that will need systems and interfaces created by computer scientists.

One of the most interesting fields within biohybrid systems and synthetic organisms, and is the most relevant to computer science, is cellular computing. Cellular computing is the concept of using living biological cells as the medium for which human defined computations are performed(Grozinger 2019). One of the ways cellular computing has been viewed is within the framework of a genetic circuit which uses organic cells to approximate the operation of a classical computer(Grozinger 2019). The perspective of seeing the cell and the systems cells form as machines have been popular metaphors for understanding biological systems, and was reinforced in by the work on modifying the genome of E. coli which was described as a set of boolean instructions(Grozinger 2019). There is actually a new perspective that suggests that traditional computing perspectives based on combinatorial logic may be limiting the application of cellular computing and, by proxy, the entire field of synthetic biology(Grozinger 2019). One of the main applications of cellular computing is that it has been shown to excel in finding all possible graphs from a set of vertices. Cellular computing has been shown to not be very feasible when scaling up the amount of vertices and therefore the amount of calculations needed to be done(Grozinger 2019). Cellular computing, like quantum computing, may be the next frontier in computer science but there is much work that needs to be done in order to achieve a viable cellular computer that is powerful enough to be a useful tool. I believe this will require interdisciplinary knowledge even more so than the earlier discussed applications because of the intense knowledge of cellular biology that is needed to understand these systems and the computer science knowledge that is needed to develop a new form of computing. I think this is the most exciting new avenue for computer scientists with an interest in biology to pursue.

Although the field of biohybrid systems and synthetic organisms is making large strides towards achieving viable versions of these products, there is still a long way to go before that is realized. Many biohybrid systems face challenges with foreign body responses and electronics degradation over time within the body, which is standing in the way of these devices(Luo 2018). Synthetic organisms, like all robotics, still has a long way to go before it can fully be applied in biological research, but with advances in simulations and genetic algorithms there is a lot of potential for progress in this field. Cellular computing is incredibly interesting but is yet to find its niche within the broad field of computing, but it will be very exciting what becomes of it.

Conclusion

In conclusion, creating synthetic organisms is a recent achievement along with bio-hybrids. Both have had a rough start, one was E. coli, the other was human testing, but both have come so far in 20+ years that they have been around starting with altering a common disease and human testing to finding ways to create and cure deadly viruses and gathering data from how a new bio-hybrid fish effects a school of normal fish.

The field of Biohybrid systems and Synthetic organisms is incredibly wide and varied with an incredible amount of progress yet to be made with the aid of computer science. The development of new hardware-based systems, development of new algorithms for simulations, and even a new form of computing are all frontiers that computer scientists can, and sometimes must, study through the lens of biohybrid systems and synthetic organisms. This field also provides an avenue for computer scientists who are also passionate about the fields of biology and engineering to not only use their knowledge and passion but also have the chance to take an interdisciplinary approach that might be needed to make the next leaps in this field. Biology and engineering may be able to take biohybrid systems and synthetic organisms a long way, but they will never be practically viable machines without the work of computer scientists producing better hardware-based systems, better genetic and optimization algorithms, and cellular computing may be the future of biohybrid systems.

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