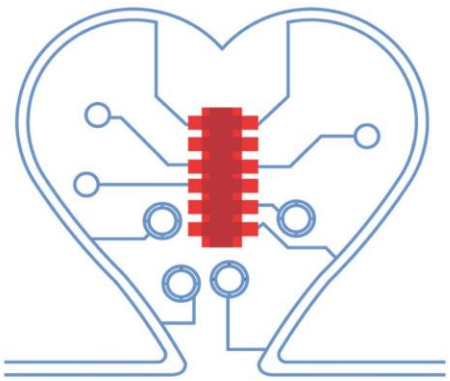

MEGAMORPH
FINAL REPORT

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IED esade UPC ATTRACT

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1. Abstract

Megamorph is a true breakthrough in the field of tissue engineering, utilizing a mechanical graphene-based technology to produce bio-grafts that are crucial for organ reconstruction purposes. Heart reconstruction is a significant challenge in medicine, with conditions such as CHDs and heart infarction being leading causes of death worldwide. Current solutions for heart bio/grafts are extremely primitive and do not provide a viable solution. Plastic grafts, which are currently used, need to be periodically changed and lack the same capabilities as real heart tissue, resulting in a high risk of multiple surgeries. This is why Megamorph's ability to create a bio/graft that becomes a real part of the heart, using the patient's stem cells, is such a game-changer. The simplicity and high modularity of Megamorph make it perfectly suited to provide a perfect solution to this yet unsolved challenge, offering new hope for better patient outcomes and quality of life.

2. Introduction

a. ATTRACT EU program

The ATTRACT Program is an initiative that aims to develop or create scientific innovations and products that will solve some of the existing problems in society or the industry of a specific field. In other words, these innovations can be called socially-aiming innovations that are based on science and research. ATTRACT has also added a major value to the field of entrepreneurship; as many entrepreneurs have been able to start their journeys based on the advanced and supportive tools of the program. The program is led by six major labs in Europe. These labs are CERN, ESO, ESRF, EMBL, European XFEL and ILL. Many major institutions and universities are partnering with the program such as ESADE Business & Law Schools and Aalto University.

ATTRACT program has launched two major phases. The first phase was in 2018. In this phase, 170 projects were chosen based on specific criteria or conditions and they were promised awards for the development process of the selected ideas. The second phase involved moving forward with the chosen projects in phase one. In other words, those ideas will be implemented in real-life applications to figure out how they can serve the market or the industry as future innovations. When the second phase ends, these products should be the targets of investors and entrepreneurs in different sectors of the market.

b. Megamorph technology

MEGAMORPH is a Graphene-based project that aims to provide revolutionary and creative solutions in many sectors. Examples of these sectors are education, medicine, aviation, transportation and the space sector. The project is based on the reflective display technology that is called Graphene MODulator (GMOD). The technology can reflect or produce different colours when applying a force, such as an electrical force, to the graphene surface or layer. The very small structures in these graphene layers are called " Pixels" and once the sunlight hits these tiny pixels, many shades of colours can be reflected. These pixels are expected to generate high-resolution displays and consume less power or voltage compared to the presented display technologies in today's market (IMOD Technologies). Other than optimizing the display

products, the technology is promising different solutions to other sectors. GMOD is considered to be an environment-friendly technology, as the materials that are used to construct the graphene layer are proven to be safe for the environment (Green Technology).

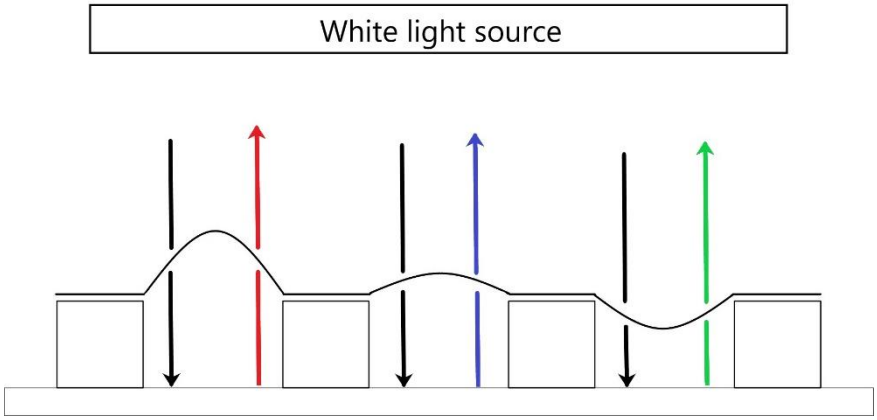


Figure 1 Simplified depiction of the functioning of Megamorph reflective-display

The presented picture provides a simplified depiction of the functioning of the Megamorph reflective display. By modulating a white light beam and reflecting various wavelengths, colours are produced. Understanding how the Megamorph reflective display works will help in making sense of the changes proposed in the applications.

3. Design Process

Our primary goal was to come up with new ideas for possible alternative uses of MEGAMORPH technology. We followed a methodical approach based on design thinking principles, with a focus on identifying societal needs and creating an exponential social impact. To achieve this, we gathered crucial insights and gained a deep understanding of our product and the problems it could solve.

Initial concerns

The initial concerns centred around the difficulty of discovering innovative ideas for a display technology that could experience exponential growth and significant social impact. We anticipated encountering obstacles in identifying an application for a display technology that was not already being addressed. Therefore, we decided to focus initially on gaining a deep understanding of the technology at hand and exploring its limits to uncover breakthrough applications.

First meeting

During our initial meeting, we gained a deep understanding of the display technology and how it worked. However, Dr Santiago Cartamil shared his expansive vision for MEGAMORPH technology. Rather than simply being a display technology, Dr Cartamil believes that the unique

properties of graphene can be leveraged for a multitude of different applications. Thus, he enthusiastically encouraged us to explore the full range of possibilities for his technology, highlighting its potential to revolutionize various industries.

First approaches

Following our meeting, our attention shifted towards comprehending the technology as an optical modulator and investigating potential applications for modulating non-visual light spectra, such as near-infrared and UV. This approach centred on utilizing the technology as an optical modulator. Additionally, we explored novel approaches that harnessed the graphene membrane as an ultrasound transducer. Our biggest concerns were the need for high technical knowledge to understand the technology and search for possible applications. This posed a significant challenge for our team.

The manner of work

The manner of work we designed for this project was to work individually with each of the team members in exploring different applications that we could come up with and sharing our ideas through our chat group and shared google drive folder. Additionally quick briefing and update once a week in a team meeting to discuss the current state of the project and future approaches, and coordinating the team to attend in pairs to the meetings with researchers. The UPC students also would advise IED and ESADE students in their technological comprehension of the technology. With this approach we intended to explore as much spectrum of possible approaches as possible, and in the future focus on the best candidate applications, thus promoting a natural selection of candidate applications.

This approach was proven to be ineffective after a few weeks. Because of its highly technical nature, non-UPC students found it difficult to understand and apply the technology in practical ways. Therefore, we completely changed our approach and focused on simplifying our understanding of the technology. This had a significant impact, as new and more practical approaches emerged, and team dynamics greatly improved.

Simplified notion

The simplification process presented the notion of understanding Megamorph as an electro-mechanical device that can bend a thin graphene layer.

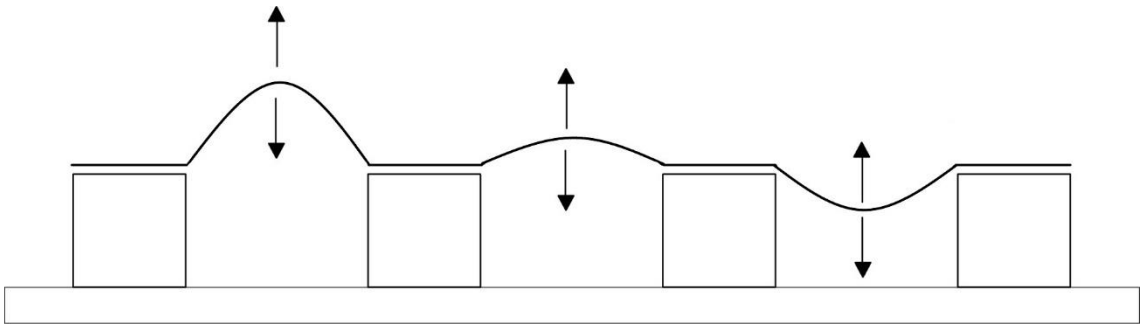


Figure 2 Simplified notion about the understanding of Megamorph

Thus, then we can exploit many of the unique graphene properties. Such as mechanical, biocompatibility, electrical and optical properties.

Final approach

After several iterations of the design thinking process, we decided to focus on the approach with the highest potential: utilizing Megamorph for tissue engineering, specifically for stem cell differentiation processes. This idea was first suggested by Professor Ramon Bragos, which we found incredibly interesting. Further investigation revealed a lot of backup research for this application, and the great *viability* of this hypothesis empowered this application ahead of the others. Also, the great impact that organ regeneration could have on society was a key factor in deciding to follow this idea.

Being a very niche and innovative application, we found it challenging to find researchers who could back up our hypothesis. We relied heavily on Professor Ramon Bragos, a former investigator in this field. However, we found many related papers that supported our idea. Our manner of working involved understanding tissue engineering, stem cells, and organ reconstruction, identifying potential areas where we could make the most significant impact, and finding researchers who could back up our hypothesis. We also focused on understanding the potential impact on society of having a reliable method for organ reconstruction.

CERN proposed applications

During our visit to CERN, we came up with three potential applications for Megamorph technology: stem cell tissue engineering, prosthetic interface, and drug administration and control patches. We discussed the technical feasibility of these ideas with Dr Santiago Cartamil. After the meeting, we decided to focus on our final approach.

Later in the document, we will discuss two feasible approaches. Due to time limitations and significant progress with our final chosen approach, we decided not to allocate resources to further explore these two potential ideas. Also, we will comment on a dead-end we encountered with the prosthe*tic interface* and explain why we did not pursue this approach any further.

Dead end: Prosthetic interface

During our exploration of Megamorph technology, we considered building a graphene-based nerve interface for limb prosthetics. This approach would use the high pixel density of Megamorph technology to create a high-resolution biosensor that could accurately capture the activation of individual nerves, allowing for more precise movements in the prosthetic and potentially creating the sensation of touch.

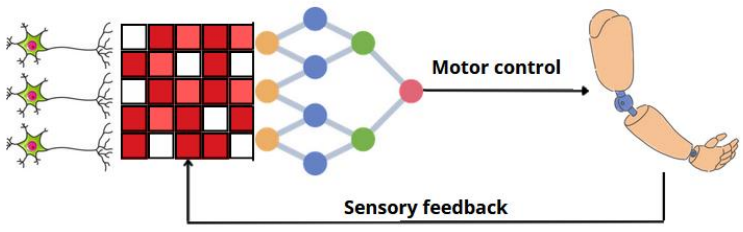


Figure 3 Scheme explaining the basic idea on nerve interface

We consulted with Mattia Bramini and Eloy Oppiso, researchers specializing in cell-graphene interaction and neuroscience, to validate this solution, and while it was technically feasible, there were physiological challenges to overcome in restoring neurological function associated with the lost limb. Ultimately, after discussing the idea with Dr Santiago Cartamil, we determined that a simple graphene transistor matrix would be better suited to this application than the Megamorph system. Therefore, we decided to abandon this idea and pursue a more suitable approach for the technology.

4. Final approach

a. Tissue engineering & stem cells

Stem cells

Stem cells are the body's raw materials, cells from which all other cells with specialized functions are generated. Under the right conditions in the body or a laboratory, stem cells divide to form more cells called daughter cells. These daughter cells become either new stem cells or specialized cells (differentiation) with a more specific function, such as blood cells, brain cells, heart muscle cells or bone cells. No other cell in the body has the natural ability to generate new cell types.

Pluripotent stem cells, also called embryonic stem cells, have the ability to differentiate into all of the cells of the adult body, but the method to obtain them supposes an ethical debate. Adult stem cells are found in a tissue or organ and can differentiate to yield the specialized cell types of that tissue or organ. That means that depending on the location of the stem cell and the age of the patient, each stem cell has the potential to differentiate into different groups of differentiated cells.

For example, adipose tissue stem cells have been tested to have multi-lineage potentials, such as adipogenesis, osteogenesis, chondrogenesis, angiogenesis, myogenesis and neurogenesis. This means that a stem cell isolated from adipose tissue can go through a differentiation process and potentially differentiate into adipose tissue, but also into bone, cartilage, blood vessel, myocardium and neural tissue.

Stem cell differentiation is a complex and systematic process regulated by various environmental signals. Biochemical signal pathways controlled by growth factors and cytokines have traditionally been studied to understand the differentiation pathway. However, physical factors such as tissue stiffness and topology also play a role in determining stem cell differentiation, emphasizing the importance of mechanobiological pathways. These newly identified pathways provide clues to accurately design the microenvironment of stem cells to control the direction of differentiation. Various methods, such as micropatterned cell confinement, micro-/nanosized topographic substrates, and substrate stiffness, have been used to determine cell functions by changing cell adhesion through corresponding changes in external substrates.

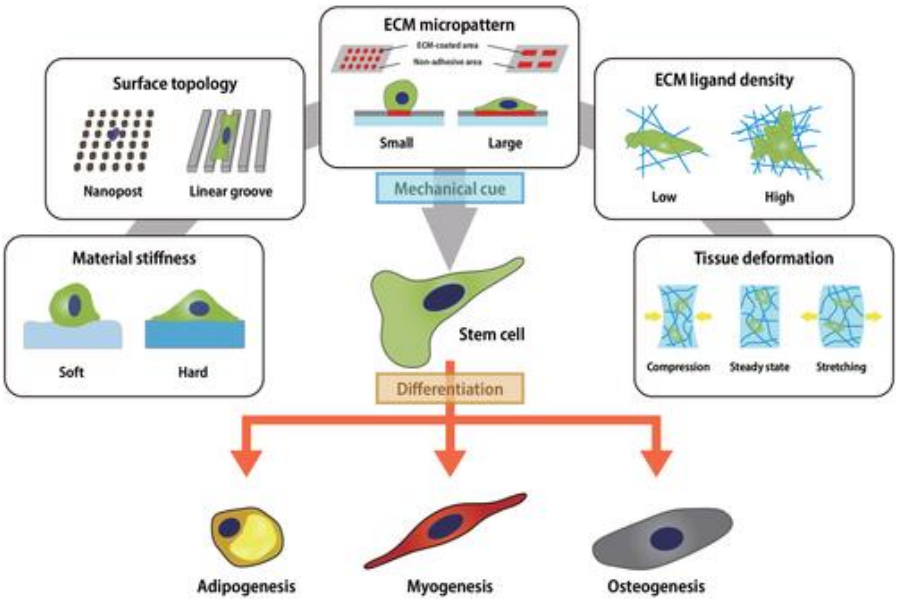


Figure 4 Stem cell fate changes induced by biophysical features of the microenvironment

Tissue Engineering

Tissue engineering is a practice that has evolved from the field of biomaterials. It refers to combining cells and biologically active molecules to form functional tissue to restore or improve the functionality of a patient's organ. In general, groups of cells form around them a thin structure called a scaffold, which besides providing physical support, forms a good medium for message exchange between cells. Each outside signal can start a chain reaction in the cell structure which determines their behaviour. By understanding how different cells respond to these signals, researchers can develop methods to manipulate the cell processes.

At the moment, tissue engineering plays a small role in patient treatment, as it is very experimental and costly. While complex tissues such as the liver, lung and heart have been created in the lab, they are a long way from becoming a common practice.

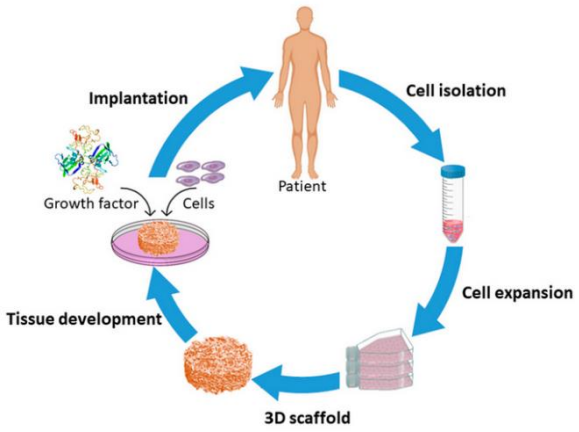


Figure 5 Tissue Engineering

However, during the past years, there have been some discoveries related to the methodology of tissue engineering:

- Discovery of methods to generate induced pluripotent stem cells, paving the way to personalized medicine.
- Finding that substrate stiffness can modulate the development of stem cells, using physical cues.
- Refined delivery mechanisms to enable biochemical cues such as growth factors.
- Increased understanding of the interaction between foreign bodies and the immune system.
- Advancement in biomaterials and scaffolds, which enable better fabrication of biomimetic structures.

b. The current state of technology

As previously mentioned, producing complex tissues such as the liver, lung, and heart remains a significant challenge in tissue engineering. Although current solutions exist, they often lack reliability and are too primitive and complex to be effective. As a result, these challenges remain unsolved.

In our study, we focused on the current technology for myogenesis processes, drawing on reliable sources such as Professor Ramon Bragos and the research of Dr Antoni Bayes, a renowned expert in the field. However, we believe that the potential of Megamorph extends beyond myogenesis and could become a general solution for tissue engineering.

Myogenesis specific stimuli

To drive myocardiocyte differentiation in research settings, specific stimuli are required, including topographical cues that mimic the structure of heart tissue, as well as applied forces, stretches, contractions, and electrical signals. Additionally, a variety of biochemical factors are necessary to facilitate the cell signalling required to initiate the differentiation process. By providing these cues, researchers can simulate the working conditions of myocardiocytes and signal to stem cells that they may become part of the cardiac tissue, ultimately prompting the differentiation process. It's worth noting that further research may uncover additional or alternative stimuli that could enhance the differentiation process.

Bio-grafts

Tissue engineering offers a promising solution for reconstruction and regenerative medicine, known as Bio-grafts. This technique does not directly produce highly specialized tissue, Bio-grafts encourage some level of differentiation, and once implanted into the organ, they grow and remodel in parallel with the recipient organ. As the organ develops, the implant becomes a functional part of the body.

In heart reconstruction, current solutions involve the implantation of plastic-engineered grafts. Although sophisticated, these grafts cannot fully act as functional myocardium tissue and do not grow. Consequently, if the patient is still growing, the grafts need to be periodically replaced through surgery. The key advantage of Bio-grafts over transplants and prostheses is their compatibility. Since tissue is formed from cells from the same patient, there is a very low

chance of rejection and future issues. Furthermore, becoming a real part of the organ ensures that the patient will recover all functional tissue and avoid further surgeries.

Current technologies

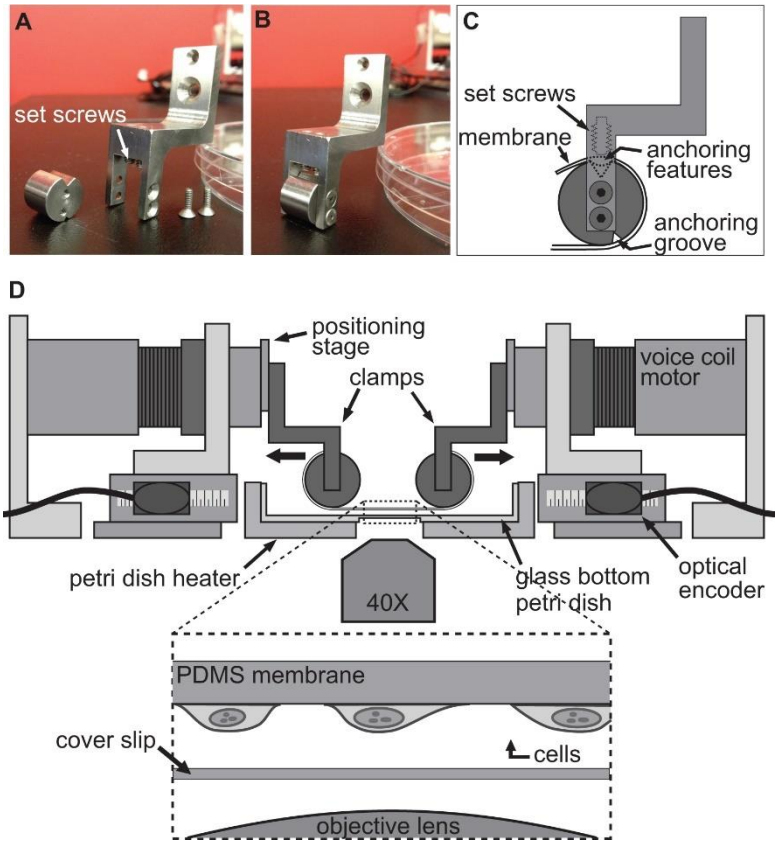


Figure 6 Current solution to induce stretching and contraction stimuli to start myocardiocyte differentiation

Based on the current state of technology, producing bio-grafts for heart tissue regeneration remains a complex and primitive process, as evidenced by the image. Current approaches primarily rely on applying macro-scale stretching stimuli, and a viable solution for producing functional heart tissue bio-grafts has yet to be developed. However, as we will discuss further in this report, the introduction of Megamorph represents a significant improvement over the current method. With Megamorph, it becomes possible to apply a greater variety of stimuli needed to initiate the differentiation process, including at the microscale level for specific cells. This represents a significant step forward in tissue engineering and holds promise for the development of more effective and efficient techniques for producing functional bio-grafts for heart tissue regeneration.

c. Proposed adaptation of Megamorph

Having discussed the challenges in tissue engineering, we can now explore how Megamorph technology could represent a significant breakthrough in this field. To this end, several modifications would be necessary to adapt Megamorph for tissue engineering.

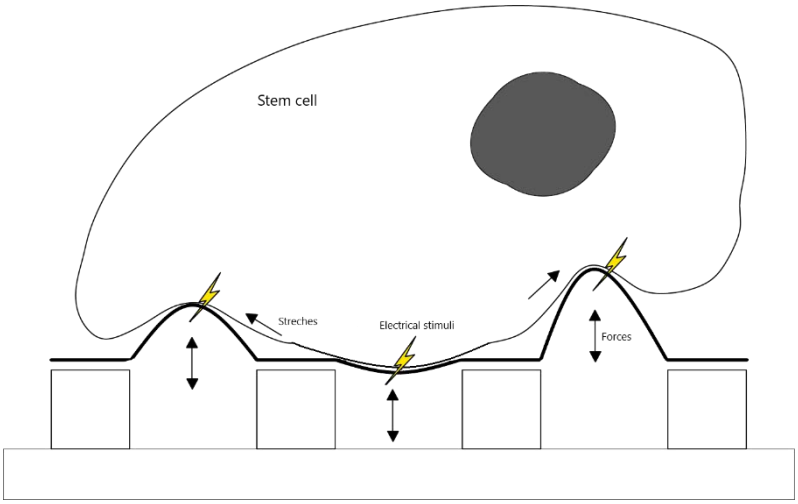


Figure 8 Proposed adaptation of Megamorph for Tissue Engineering

One of the main modifications would involve adding a second voltage differential to be applied to the pixel graphene surface individually, enabling the application of electrical stimuli. Additionally, the modification of the surface could mimic different layers and stiffnesses to induce topographical stimuli in stem cells, as well as the forces, stretches, contractions and electrical stimuli required for myogenesis.

Megamorph's outstanding resolution allows for the application of individual stretches to individual stem cells, with a pixel size of around 1 micron, which is precise enough to accommodate stem cells that are approximately 10 microns in size. The simplicity of this approach is also noteworthy compared to previous methods. By utilizing graphene's biocompatibility, we can avoid stem cells refusing contact surfaces and use graphene to input the required electrical stimuli.

It's important to note that while this research has focused on heart tissue engineering, Megamorph technology could potentially be a general solution for tissue engineering. With the ability to create and tune different stimuli profiles for specific differentiation processes, Megamorph could hypothetically enable the creation of various tissue types from a given group of stem cells. As such, the potential of Megamorph technology extends far beyond heart tissue bio-grafts and could represent a significant breakthrough in tissue engineering more broadly.

d. Social Impact

Heart disease is a major health concern worldwide, and tissue engineering offers a promising solution for many illnesses related to myocardial tissue. Two major illnesses that could have a significant social impact if cured are myocardial infarction and congenital heart defects (CHD).

Myocardial infarction

Myocardial infarction, commonly known as a heart attack, results in the permanent loss of cardiomyocytes and scar tissue formation, leading to irreversible damage to the heart's function. MI remains a major clinical problem and the leading cause of mortality in the world, with approximately 1 million people suffering from MI each year in the United States alone. While existing therapies can lower early mortality rates and reduce the risk of further heart attacks, there is a need for treatment to improve clinical conditions by replacing damaged heart tissue.

Congenital Heart Defects

CHD is an umbrella term for abnormalities in the heart's structure that occur before birth. Valve defects, atrial and ventricular septal defects, and heart muscle abnormalities can range in severity from minor to life-threatening. CHD is the most common congenital anomaly in newborn babies, with approximately 4600 babies born with CHD every year in the UK. These heart defects can lead to the underdevelopment of other organs due to the lack of oxygen or blood flow, making it essential to treat them at a young age.

CHD is a leading cause of birth defect-associated infant illness and death, with about 95% of babies born with non-critical CHD expected to survive to 18 years of age. However, about 4 in every 10 adults with CHD have a disability, with cognitive disabilities being the most common type. There are an estimated 2800 adults with CHD per 1 million population, with more than half having moderate or high complexity defects.

Current solutions for CHD are limited and mainly reserved for the most severe cases, requiring surgery and the use of prostheses that need to be periodically changed and have a high risk of failure.

Social Impact calculations

Calculating the total impact in both cases is a daunting task, and further research is needed to fully understand the potential benefits. However, due to the unknown investment and cost of these procedures, and the fact that this is a new and revolutionary approach to regenerative medicine, it offers a solution to current unsolved problems that were previously deemed impossible. As a result, there are no existing solutions to compare it to, making social impact calculations highly improbable.

As previously discussed, this technology has the potential to impact millions of people. Currently, there is no feasible approach to heart reconstruction after MI or CHD, and the improvement in life quality for patients could be life-changing for most of them.

In the case of MI, the loss of cardiac function can result in a high risk of causal death. A heart attack can greatly affect a patient's life, but by replacing damaged heart tissue, significant improvements in life expectancy and quality of life could be achieved.

In the case of CHD, it is estimated that 2.1 million adults have the condition only in the EU, with more than half experiencing moderate or high complexity defects. Preventing newborns

from developing these defects and significantly curing existing ones could have an incredible impact on the life expectancy and quality of life of millions.

5. Alternative feasible applications

In this part of the report, we will discuss more in-depth the different possible applications we investigated: what were they, what graphene property was it exploiting and the reasons why it was discarded or executed. We will only discuss those ideas that were most investigated and thought into, preliminary ideas will not be discussed.

a. Biosensor for drug monitoring

The inspiration for this idea stemmed from the possibility of using infrared technology to detect blood glucose levels in individuals with diabetes. However, upon further investigation, we quickly realized that accurate readings of blood glucose levels using near-infrared technology are still an underdeveloped field of study, and we could not find any reliable information to support its feasibility. While we did come across evidence of multiple applications for near-skin infrared readers, at the time of the project, we were only focused on mechanical applications. Thus, we decided to abandon this idea and did not pursue it any further.

Our proposed application is a patch that can be attached directly to the skin and contains an infrared source. By modifying MEGAMORPH (as shown in the figure), the patch can monitor the substances contained in sweat and transmit relevant data to a mobile phone app for processing and display.

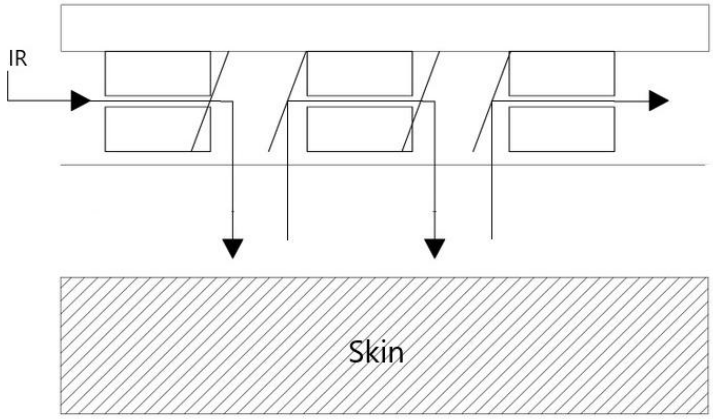


Figure 9 Basic depiction on the proposed modifications

Our intended use case is for doctors and nurses to track medication adherence in patients who have difficulty taking their medications, such as those with Alzheimer's, bipolar disorder, multiple personality disorder, or elderly patients. Proper medication management is crucial for these patients, and the patch can help track whether the appropriate medications are being taken at the appropriate times. This technology can also be used as a bandage-like material, allowing doctors to monitor medication adherence without the patient's knowledge.

Overall, our patch has the potential to improve medication management for patients with complex medical needs, helping them stay on top of their medication regimens and reducing their risk of medical issues.

b. Drug patch

Building on the idea of drug control, we came up with the concept of administering the correct amount of medicine directly to the patient, without the need for the patient to remember to take it. To achieve this, we proposed a modification for Megamorph technology. Our idea involved creating a small hole in the graphene layer of each pixel, which would be small enough for the surface tension of the liquid drug to prevent it from escaping. By inducing the contraction of the graphene layer, acting as a pump, the liquid drug would be administered to the patient.

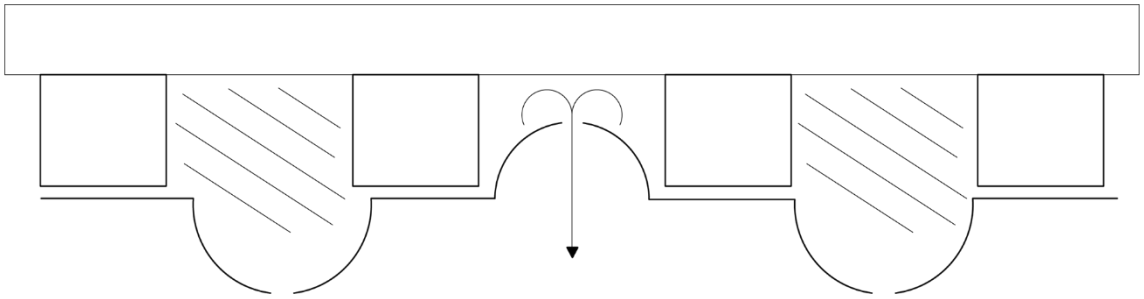


Figure 10 Proposed modification for the drug patch

Several concerns arose with this idea. Firstly, the drug would need to be topically administered and absorbed in significant amounts to make this method of administration feasible. However, this approach could have significant benefits, including incredibly precise dosage, the ability to administer different medicines to different areas, and programmability. For example, a single patch could deliver exact amounts of multiple medicines over many days, eliminating the need for patients to carry a medicine box with pills for each day of the week. This technology could greatly help patients with difficulties in taking their medication, which is a significant concern among doctors and nurses.

While we ultimately decided not to allocate resources towards further developing this idea, we strongly encourage others to investigate this approach. We did not have the opportunity to seek confirmation from patients, doctors, or nurses, but we did look for backup papers that could hold our first hypothesis in this approach.

6. Conclusion

a. Student reflection

As a team, we can all agree that working on this project was a challenging but ultimately rewarding experience. It provided us with the opportunity to push ourselves outside of our comfort zones and grow both personally and academically. The project required technical and engineering knowledge, as well as creativity and people-focused skills to build something usable with a positive impact on society.

For some of us, it was our first time working on a project that required an in-depth understanding of technical knowledge and methodologies. However, we found that there was beauty in understanding how things work and how we could apply our knowledge to make a difference. We also had the chance to work with people from different countries, universities, and cultures, which allowed us to better understand the perspectives and points of view of each team member. This, in turn, improved our ability to work within a group and compete with other groups in a friendly and supportive environment.

One of the most significant takeaways from this project was the importance of considering the needs of our customers and patients when designing a solution. We learned that any product that does not serve a clear need in the market or society might not succeed, no matter how creative it is. This was emphasized in the provided lectures on how to find socially-adaptable innovations, which completely changed our perspective on how we can start future businesses or products.

Working in a multidisciplinary team was also a great learning experience. It allowed us to see the problem from multiple different perspectives and not get stuck in the technical details. We also had the chance to develop our interpersonal skills through constant group work and reaching out to researchers for interviews. For many of us, this was a significant learning experience, as we were not used to doing this before enrolling in this project.

Although we faced some difficulties along the way, such as time constraints and technical issues, we were able to come up with innovative solutions and complete the project successfully. We made mistakes, had lots of iterations and ideas, and learned from them to improve our work. As a team, we worked seamlessly, and were easy-going, and hard workers, which allowed us to complete the project to the best of our abilities.

Overall, this project provided us with a great learning opportunity that allowed us to apply the knowledge and skills we have acquired throughout our studies and provided us with valuable experience in real-world problems. We feel proud of the work we have done and are excited to see how it could make a positive impact in the field.

b. Conclusions

In conclusion, the potential social impact of Megamorph technology in tissue engineering is significant, particularly in the treatment of myocardial infarction and congenital heart defects. Current solutions for these conditions are limited, and Megamorph technology offers a promising solution that could improve life expectancy and quality of life for millions of people worldwide.

While other potential applications for Megamorph technology were explored, such as biosensors for drug monitoring and drug administration and control patches, they were

ultimately deemed unfeasible or not pursued further. However, they offer potential for future research and development.

Overall, Megamorph technology has the potential to be a game-changer in the field of regenerative medicine and could have a significant positive impact on society. Further research and development are needed to fully realize its potential and bring it to market, but the possibilities are exciting, and we look forward to seeing where this technology will take us in the future.

7. References

Attract project & Megamorph

Megamorph. ATTRACT Project phase 2. *https://attract-eu.com/projects/megamorph/*

The Technology. MEGAMORPH. *https://megamorph.eu/the-technology/*

Cartamil-Bueno, S.J., Davidovikj, D., Centeno, A. et al. Graphene mechanical pixels for Interferometric Modulator Displays. Nat Commun 9, 4837 (2018). https://doi.org/10.1038/s41467-018-07230-w

Stem cells basics & differentiation

Zakrzewski, W., Dobrzyński, M., Szymonowicz, M. et al. Stem cells: past, present, and future. Stem Cell Res Ther 10, 68 (2019). https://doi.org/10.1186/s13287-019-1165-5

Stem Cell Basics | STEM Cell Information. (n.d.). https://stemcells.nih.gov/info/basics/stc-basics#:~:text=Pluripotent%20stem%20cells%20have%20the,of%20that%20tissue%20or%20organ.

Sobhani A, Khanlarkhani N, Baazm M, Mohammadzadeh F, Najafi A, Mehdinejadiani S, Sargolzaei Aval F. Multipotent Stem Cell and Current Application. Acta Med Iran. 2017 Jan;55(1):6-23. PMID: 28188938.

Khanlarkhani N, Baazm M, Mohammadzadeh F, Najafi A, Mehdinejadiani S, Sobhani A. Multipotent Stem Cell and Reproduction. J Stem Cells. 2016;11(4):219-229. PMID: 28296874.

Shi L, Yang X. [Differentiation potential and application of stem cells from adipose tissue]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2012 Aug;26(8):1007-11. Chinese. PMID: 23012940

Rodriguez AM, Elabd C, Amri EZ, Ailhaud G, Dani C. The human adipose tissue is a source of multipotent stem cells. Biochimie. 2005 Jan;87(1):125-8. doi: 10.1016/j.biochi.2004.11.007. PMID: 15733747.

Stem cell differentiation stimuli & cell signalling

Han, B., Kim, K., Lee, G., & Kim, H. (2020). Mechanical Properties of Materials for Stem Cell Differentiation. Advanced Biosystems, 4(11), 2000247. https://doi.org/10.1002/adbi.202000247

Petzold, J., & Gentleman, E. (2021). Intrinsic Mechanical Cues and Their Impact on Stem Cells and Embryogenesis. Frontiers in Cell and Developmental Biology, 9. https://doi.org/10.3389/fcell.2021.761871

Bursac, Nenad. "Cardiac tissue engineering using stem cells." IEEE Engineering in medicine and Biology magazine : the quarterly magazine of the Engineering in Medicine & Biology Society vol. 28,2 (2009): 80, 82, 84-6, 88-9. doi:10.1109/memb.2009.931792

Rajala, Kristiina et al. "Cardiac differentiation of pluripotent stem cells." Stem cells international vol. 2011 (2011): 383709. doi:10.4061/2011/383709

Balafkan, Novin et al. "A method for differentiating human induced pluripotent stem cells toward functional cardiomyocytes in 96-well microplates." Scientific reports vol. 10,1 18498. 28 Oct. 2020, doi:10.1038/s41598-020-73656-2

Patel, Anjali et al. "Regulation of Myogenic Activity by Substrate and Electrical Stimulation In Vitro." BioResearch open access vol. 8,1 129-138. 30 Jul. 2019, doi:10.1089/biores.2019.0016

Ma, Ruilian et al. "Electrical Stimulation Enhances Cardiac Differentiation of Human Induced Pluripotent Stem Cells for Myocardial Infarction Therapy." Antioxidants & redox signaling vol. 28,5 (2018): 371-384. doi:10.1089/ars.2016.6766

Geuss LR, Suggs LJ. Making cardiomyocytes: how mechanical stimulation can influence differentiation of pluripotent stem cells. Biotechnol Prog. 2013 Sep-Oct;29(5):1089-96. doi: 10.1002/btpr.1794. Epub 2013 Sep 12. PMID: 23956196.

Tissue engineering and regenerative medicine

Tissue Engineering and Regenerative Medicine. (n.d.). National Institute of Biomedical Imaging and Bioengineering. https://www.nibib.nih.gov/science-education/science-topics/tissue-engineering-and-regenerative-medicine#:~:text=The%20goal%20of%20tissue%20engineering,limited%20use%20in%20human%20patients.

Stoltz JF, Zhang L, Ye JS, De Isla N. Organ reconstruction: Dream or reality for the future. Biomed Mater Eng. 2017;28(s1):S121-S127. doi: 10.3233/BME-171633. PMID: 28372287.

Brown, Patrick T et al. "Stem cell-based tissue engineering approaches for musculoskeletal regeneration." Current pharmaceutical design vol. 19,19 (2013): 3429-45. doi:10.2174/13816128113199990350

Roshanbinfar K, Esser TU, Engel FB. Stem Cells and Their Cardiac Derivatives for Cardiac Tissue Engineering and Regenerative Medicine. Antioxid Redox Signal. 2021 Jul 20;35(3):143-162. doi: 10.1089/ars.2020.8193. Epub 2020 Nov 12. PMID: 32993354.

Ikada, Yoshito. "Challenges in tissue engineering." Journal of the Royal Society, Interface vol. 3,10 (2006): 589-601. doi:10.1098/rsif.2006.0124

van Laake, Linda W et al. "Heart repair and stem cells." The Journal of physiology vol. 577,Pt 2 (2006): 467-78. doi:10.1113/jphysiol.2006.115816

Roura S, Gálvez-Montón C, Mirabel C, Vives J, Bayes-Genis A. Mesenchymal stem cells for cardiac repair: are the actors ready for the clinical scenario? Stem Cell Res Ther. 2017 Oct 27;8(1):238. doi: 10.1186/s13287-017-0695-y. PMID: 29078809; PMCID: PMC5658929.

Tremblay D, Cuerrier CM, Andrzejewski L, O'Brien ER, Pelling AE. A novel stretching platform for applications in cell and tissue mechanobiology. J Vis Exp. 2014 Jun 3;(88):51454. doi: 10.3791/51454. PMID: 24962250; PMCID: PMC4186581.

Myocardial infarction

Madigan M, Atoui R. Therapeutic Use of Stem Cells for Myocardial Infarction. Bioengineering (Basel). 2018 Apr 6;5(2):28. doi: 10.3390/bioengineering5020028. PMID: 29642402; PMCID: PMC6027340.

Congenital Heart Defects

Avolio E, Caputo M, Madeddu P. Stem cell therapy and tissue engineering for correction of congenital heart disease. Front Cell Dev Biol. 2015 Jun 30;3:39. doi: 10.3389/fcell.2015.00039. PMID: 26176009; PMCID: PMC4485350.

Data and Statistics on Congenital Heart Defects | CDC. (2020, December 9). Centers for Disease Control and Prevention. https://www.cdc.gov/ncbddd/heartdefects/data.html

Giraldo-Grueso, M., Zarante, I., Mejía-Grueso, A., & Gracia, G. (2020). Risk factors for congenital heart disease: A case-control study. Revista Colombiana De Cardiología, 27(4), 324–329. https://doi.org/10.1016/j.rccar.2019.11.008

Near-infrared for noninvasive monitoring

Ibrahim, N.F.A.; Sabani, N.; Johari, S.; Manaf, A.A.; Wahab, A.A.; Zakaria, Z.; Noor, A.M. A Comprehensive Review of the Recent Developments in Wearable Sweat-Sensing Devices. Sensors 2022, 22, 7670. https://doi.org/10.3390/s22197670

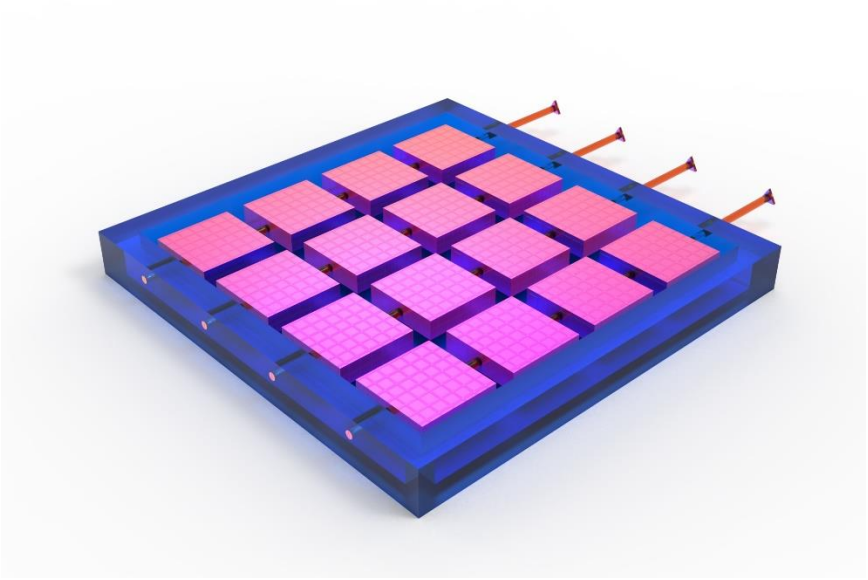
Hina, Aminah, and Wala Saadeh. "Noninvasive Blood Glucose Monitoring Systems Using Near-Infrared Technology-A Review." Sensors (Basel, Switzerland) vol. 22,13 4855. 27 Jun. 2022, doi:10.3390/s22134855

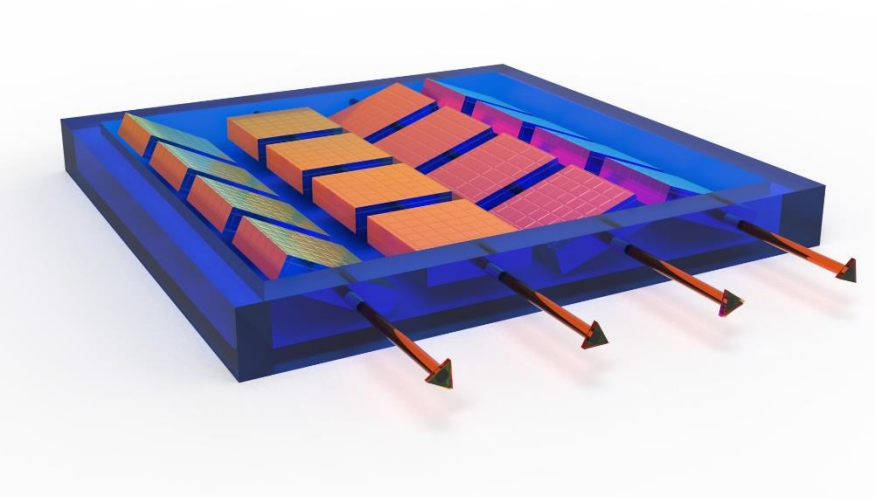
Sultana, N., Dewey, H. M., & Budhathoki-Uprety, J. (2022). Optical detection of pH changes in artificial sweat using near-infrared fluorescent nanomaterials.

ROYAL SOCIETY OF CHEMISTRY, 1(6), 1189–1197.
https://doi.org/10.1039/d2sd00110a

8. Appendices

The following images are renders of the prototype we created to explain how can you model a surface with pixel-moving parts:





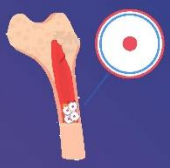
MEGAMORPH

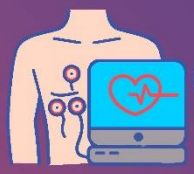
Saving the children, the easy way

Congenital Heart Disease (CHD) refers to heart abnormalities present at birth. It affects 1 in 100 newborns, with 1 in 4 cases being critical. Disabilities affect 4 in 10 cases. Early intervention is crucial to prevent further complications during organ development. However, current solutions are limited and carry a high risk of failure.

The ultimate solution for repairing CHD lies in tissue engineering. By utilizing stem cells from the newborn, we can create a graft that repairs damaged hearts, providing a permanent fix.

The remarkable feature of this graft is that it grows with the recipient's organ and becomes a fully functional part of the body. Unlike current grafts, which have no functionality and always require replacement as the child grows, this approach uses the patient's own stem cells, reducing the risk of rejection and future complications.





Megamorph offers a breakthrough in producing the desired grafts by inputting the necessary stimuli for stem cell differentiation. Unlike current approaches, which are primitive and complex, Megamorph's simplicity is a game-changer.

Cardiac cells require specific stimuli, including mechanical forces, stretches, and electrical signals, to differentiate effectively. Megamorph's ability to produce these stimuli makes it a total solution for CHD and many other heart diseases.

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