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Organ-on-a-Chip and Nanotechnology: Paving way to the future of bioartificial organs

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Abstract

This paper presents the idea of organ chips and the different types that can be available for various body organs. Three main aspects that go into creating this technology are microfluidics, microfabrication and microelectronics. These microfluidic devices that simulate organ responses have emerged as an eminent technology in the field of bioengineering that can be used for drug development, toxicology testing, disease modelling and for creating personalised medicine. Advancements in the field of biotechnology has helped it progress productively at a faster pace than before. This paper explores the idea of organ chips and how it's combination with nanotechnology can pave the way for development and practical application of bioartificial organs.

Keywords:

•microfabrication, microfluidic, bioartificial, nanobiological

1. Introduction

The organ-on-a-chip also known as OOAC technology dates back in the late 1990's when a professor from the Department of Biomedical Engineering at Cornell University- Michael Shuler coined the term "animal-on-a-chip" as part of his research. These are made just like computer microchips with the chips composing of a clear flexible polymer which is the size of a computer memory stick with hollow microfluidic channels lined with real living human cells. The three main branches that constitute the science behind organ-on-a-chip are microfabrication, microfluidics and microelectronics. Microfluidics is an interdisciplinary field involving engineering, nanotechnology, biotechnology, chemistry and physics that deals with behavior, control and manipulation of sub-millimeter scale fluids. Microfabrication is a technique that use semiconductor manufacturing processes such as ion etching, diffusion, oxidation, and sputtering and was earliest used for manufacturing Integrated Circuits. Microelectronics is a subfield of electronics and refers to the study and manufacture of small electronic components and designs and generally made from semiconductor materials. The advantages of this technology are various with uses such as helping and accelerating the process of drug testing and development, toxicology testing and creating physiological and disease models. This revolutionary technology eliminates the need for animal testing and predicts higher accuracy results of drug testing and environmental stimuli in body organs by mimicking the functioning of various body organs and organ systems.

2. Background and Approach

New medications and therapeutic approaches are generally developed using in vitro processes and animal testing. But animal testing raises ethical concerns. These tiny organ-on-a-chip models serve as a feasible alternative solution. Data published by FDAReview.org indicates that only about 1 in 10 drugs that enter clinical trials ultimately win Food and Drug Administration approval. It takes an average of 12 years for a drug to travel from preclinical research to the patient, according to California Biomedical Research Association with each drug amounting to at an average cost of $359 million. In this situation where 90% of these drugs do not even reach the market, there is a dire need for more efficient and cost-effective techniques. Specific treatment adapted to the patients and their characteristics could be developed from these organs on chips as well as specific disease models. Construction of OOC includes biomaterials, cells, and microscale technologies. These systems integrate microengineering, microfluidic technologies, and biomimetic principles to mimic functions of living organs such as critical microarchitecture, spatiotemporal cell–cell interactions, and extracellular microenvironments. Here, fluidic and electronic components are integrated on a single chip containing continuously perfused chambers lined by living cells that simulate tissue- and organ-level physiology. Earlier on, these miniatured devices were manufactured with silicon but polymeric devices can serve as a better substitute as formation of fluid channels are easier. Semiconductors and metals can be developed as the necessary components for detection of the electrical signals with materials such as semiconductor nanowires and carbon nanotubes being used as sensor components.

3. Discussion

- **Organ chips**

Evolution of the technology:

The evolution of Organ chip technology started with the microfabrication techniques in 1950's. By 1980's the concept of microelectromechanical systems or MEMS appeared where single chips incorporated electrical and mechanical functions for various applications. These MEMS microdevices are manufactured with the same microfabrication techniques as used in the manufacture of IC or Integrated Circuits. MEMS which is used for biomedical applications are referred to as BioMEMS and these mini devices help in analysis and manipulation of biological samples.

As the field of microfluidics gained more popularity and advanced significantly over the years, biomedical devices were improved by reduction in size and increased precision. This led to the LOC or Lab-on-a-Chip technology. These single chip devices outperformed conventional laboratory testing as these were cheaper, faster and efficient. They could handle extremely small fluid samples even lesser than a few picolitres and therefore required only micro-droplets of the fluids to be analyzed such as blood plasma, tears, saliva, urine and sweat. This increased the efficiency of the analysis and became important in the field of biomedical research. 2D cell-culture models were developed but these had limitations as they could not effectively mimic the biochemical environment experienced in a living organ. 3D models were developed to combat the limitations of the 2D model as they could provide a better simulation of the biochemical environment of the cells and could provide a better understanding.

Next step was the advancement of microfluidic cell culture and brought about the OOC or Organ-On-a-Chip technology. They are the next generation of 3D models that could mimic the smallest functional units of an organ and simulate the microenvironment of living organs more accurately as they possessed the unique characteristics of microfluidic systems such as laminar flow pattern of cells.

Organ chips exist for a variety of organs such as lung, heart, kidney, gut etc. Each of these represent and mimic the function of their corresponding organs and help learn about their functioning. By combining various such organ chips we could create connected chips to represent organ systems and form Human-on-chip. The chips contain vascular channels that can be linked using an automated instrument to transfer fluids between different types of organ chips to mimic flow of blood and monitoring the entire linked system. An AI system could be developed to link this computational model and experimental data to make quantitative predictions about drug behavior and responses. This can be applied to study diseases and to understand them better. Tumor-on-chips can be developed to study the proliferation of malignant cells and directly test treatments. By connecting different chips, the side effects of these treatments can be predicted and studied in advance. Relative size of the models matter when coupling organs on chips where such chip should be comparable in size to the ones connected to it to make effective inferences.
One of the main advantages of organ-on-chip technology is the ability to create disease models such as tumor-on-a-cell. One of the main compositions of a chip is the vascular fluid channel. An interesting enhancement over using fluids such as artificial blood would be to introduce nanobots to the fluid channel.

Figure 1: *Typical Organ-On-Chip device*

- **Nanobot technology:**

Evolution of the technology:

Nanotechnology is a field of science that deals with study and application of extremely small things such as atoms and molecules. A nanometer is only one-billionth of a meter which is so small that ordinary rules of physics and chemistry don't apply at these scales in the same way. For example, carbon nanotubes are very good candidates for electronic devices because of many properties they possess such as having better

thermal conductivity than diamond or being six-times lighter yet 100-times stronger than steel. Therefore products of nanotechnology may be much lighter, smaller, cheaper yet better functional and energy efficient. The term “nanobots” was first mentioned by the physicist Richard Feyman in 1959 when he talked about these helping to cure heart diseases and from there many scientists picked up on the idea and developed it further to make it an aspect of fiction no more.
Nanobots are robots built in the scale of nanometers that can be programmed to carry out a specific task. It is a technology of the present which is being researched and developed. Nanobots can be programmed for tasks such as targeted drug delivery, surgery and analyzing and storing cellular data. They can also be fitted with cameras that give us an insight and improve overall effectiveness of procedures. Integrating nanobot technology and organ chip technology, with a computational AI overseeing the functions of the nanobots, we can induce these bots into the fluid channels and control what we want their actions to be. For example in the case of tumor chips, these bots can be programmed to target the cancer cells and destroy them while also giving us additional data as to the in-depth working and responses of various cells in the chips. One main disadvantage of introducing nanobots into live human blood is that there is chance of cluster-formation but this can be rectified by using the simulation of these nanobots on organ chips and the data they returned combined with the predictive capability of the AI system to eliminate cluster formation and allocate precise target locations to each of the bots.

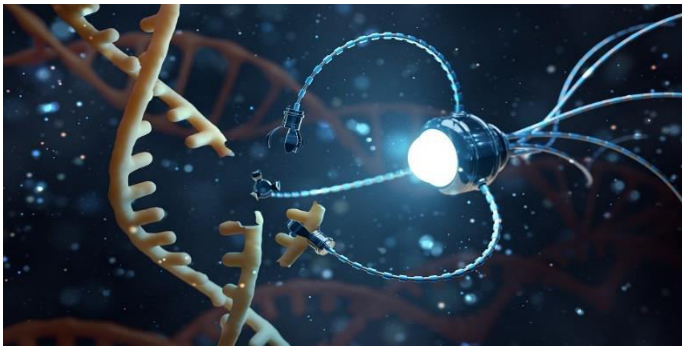

Figure 1: *Visualization of a nanobot*

4. Futuristic approach

The combination of both of these technologies give birth to a futuristic hybrid child with the advantages of both but without the individual disadvantages. Nanobots can be tested on organ chips and can also be programmed for repair and restoration of faulty components of the chips and damaged tissue hence increasing the ease of maintenance. The computational data recorded and stored gives a massive leap to the field of nanotechnology and helps in giving an insight as to how it would function in a real human body as well as pinpoint any corrections or modifications to be made in their programming. They can demonstrate a very similar working simulation in the artificial chips like that of their working in the real human body and increase our understanding of these and in turn could advance the technology even quicker. Using this technology, we move to the realization of the more futuristic concept of bio artificial organs.

Although thinking about an artificial organ replacing a real organ seems far away in the future, it is not. As the world of technology grows, things that may have seemed like fiction some time back are being brought to life. Bioartificial organs are basically a mixture of man-made organ devices and real human tissues to replace a real organ. These can augment a specific or multiple functions or provide life support while the host awaits a transplant. Rather than using completely artificial implants that may or may not fail in a real host body and may not function as required, the more optimal approach would be to use nanobiological devices which are basically nano devices integrated with artificially created living tissues that interact with the cells and the tissues of the body and carry out specific tasks. These artificially created tissues can be lab-grown tissues or 3D bioprinted tissues which are made by depositing materials known as bioinks to create tissue-like structures using a layer-by-layer method.

A completely artificial implant such as the Organ chips may fail inside a human body but rather than using it as such, it can be used to pave way for bioartificial organs that can successfully be implanted into the human body with nanotechnology enhancing it’s potential of carrying out functions, repairing and maintenance of cells and tissues and payload delivery of drugs to target sites. They can successfully replace a fully biological organ and eliminate the dire urgency of transplantation and shortage of organ donors. Essentially these would be the next generation of portable and implantable bioelectronic devices. Futuristically it may even function better than a real organ and with higher efficiency and increase lifespan by eliminating chances of organ damage and failure.

5. Conclusion

Organ chip technology has many benefits over conventional testing methods such as in-vitro testing and animal testing. These chips help drug, disease and toxicology testing to be much more efficient as they can be personalized and customized according to the various requirements and significantly reduce time and cost. Nanotechnology is an ongoing advancement in the field of bioengineering. Nanobots can perform many functions on a nano level inside our body with ease if they are programmed correctly. These can be combined with organ chip technology to create an interdisciplinary technology that utilizes the benefits of both these but do not carry the limitations of the same. In a scenario where a person needs a replacement for an organ, the problems he faces are the lack of availability of the organ, the difficulty in finding a match and also the chance of whether the body may accept the new replacement. Bioartificial organs inspired by OOC chips with the computational data and feedback provided by nanobots can be useful in such situations. Made with nanodevices, these can integrate nanobots and lab-grown or 3D printed tissue. Rather than using fully artificial devices like artificial pacemakers, these bioartificial organs would not face the problem of being rejected as they can be personalized and grafted with the tissues of the host body. These would also be more durable and less prone to malfunctions and damages as the nanobots can be programmed for surgery, repair and to store valuable data for feedback. This would make it a suitable replacement for real body organs much longer than fully mechanical devices while waiting for a transplant. This technology may even create a future where these bioartificial organs can sustain and function just like a live human organ and can be a permanent replacement solution that may even be more durable and efficient as well. With further research and developments, this may pave the way to many possibilities and unlimited applications in the future.

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