A Review of 4D Printing for Biological Applications

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Abstract

4D printing in biomedical engineering is a relatively new and promising intersection of technologies where smart materials are used for biologically significant structures. These smart materials are simply ones that are able to respond to external stimuli, such as temperature, light, or moisture. For example, a 4D-printed object could be designed to expand or contract when exposed to temperature changes. This technology has the potential to revolutionize the way medical devices are designed and manufactured, as it allows for the creation of complex biological items. This process is currently being used in both tissue engineering and drug delivery, and many future medical uses are in development. Advances in the field allow for better material science in medicine, which has the knock-on effect of increasing both quantity and quality of life.

Keywords: 4D Printing, Biomedical Engineering, Biomaterials, Drug Delivery, Tissue Engineering

1. Introduction

All industries have experienced a Cambrian explosion of growth as a result of additive manufacturing, or 3D printing, particularly in the medical sector. The term "4D printing" refers to some advancements made to 3D printing that concentrate on a controlled change in material shape. These intelligent materials enable printed things to change shape fully in response to a particular stimulus in a particular setting. Certain potential use cases are impossible since 3D-printed things are very hard and frequently do not alter shape in a controlled manner. The solution to this problem is 4D printing, and the system can be optimized by using programmable material. Given this innovative technique, there are numerous ways it might be used in the biological sciences.

2. Materials and Mechanisms of 4D Bioprinting

There are two main points to target for full utilization of 4D printing: the material and the stimulus. Material choice is key in interactions with the outside environment, as a precise selection is needed to create an exact result without side effects. This creates a limited selection of materials, with the primary options being specific polymers that can respond to heat, water, light, a pH change, an electric charge, or a magnetic change. [1] Most conventional 4D bioprinting happens with a change in time. [2] In 4D printing, the choice of stimulus is influenced by both material availability and the object's environment [as shown in Figure 1].

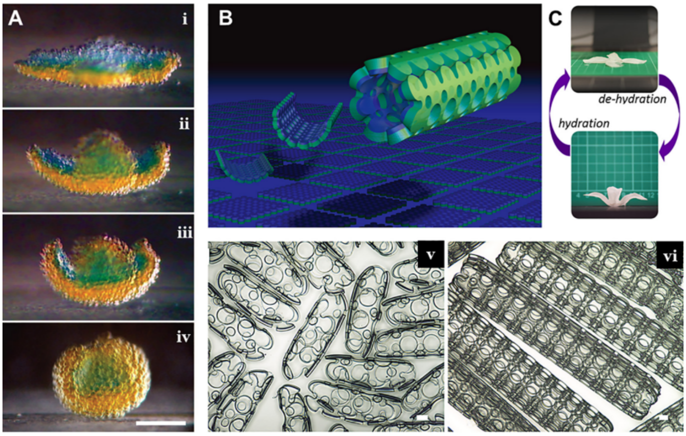

Figure 1. [3] An example of a folding liquid-responsive material. **A** is a material folding into a hollow cylinder with the presence of water over time; **B** is the self-assembly and folding of a hydrogel (a polymer that can absorb lots of water without structural damage); **C** is an example of how this material may dehydrate and hydrate.

Printing of these 4D biomaterials may happen with a traditional 3D printer, but material choice may interfere with the mechanisms of the printer. The creation of certain polymers, such as hydrogels, may require specialized lab equipment. [1], [4]

3. Current Uses

3.1 4D Printing in Tissue Engineering

The development, restoration, and regeneration of organs and cells that are damaged or missing is the focus of tissue engineering. Here, 4D printing has two applications: one is used to generate the materials for synthetic cells, and the other is used to build a scaffold to assist cell growth. As they may replicate the aqueous cytoplasm for cell interaction, certain hydrogels may be able to function similarly to some cells. [5] To fully comprehend the advancement of tissue engineering with enhanced bioprinting in this sector, more study is required. The scaffold is currently made using 3D printing or a time-consuming, costly approach that adapts standard manufacturing processes to match biological systems. Both have issues with biological interaction, including:

- difficulty of distributing cells uniformly inside the 3D scaffold (a cell organization issue)
- difficulty of controlling cell-cell organization inside the scaffold (a cell organization issue)

- technical barriers to end-users who are not specially trained for 3D biofabrication (a technological knowledge issue). [6]

All these issues are solved with 4D printing through advanced scaffolds that have strategic movements around physical barriers. Current methods involve creating a series of micro-patterns that can self-fold into a 3D scaffold. [6] Many types of smart materials can be used, but a strong material choice may be silk, as it can be manipulated through digital light processing to function as a smart material [as depicted in Figure 2]. [8] Utilizing a natural material circumvents a number of potential side effects associated with the implantation of a plastic with material-body interactions.

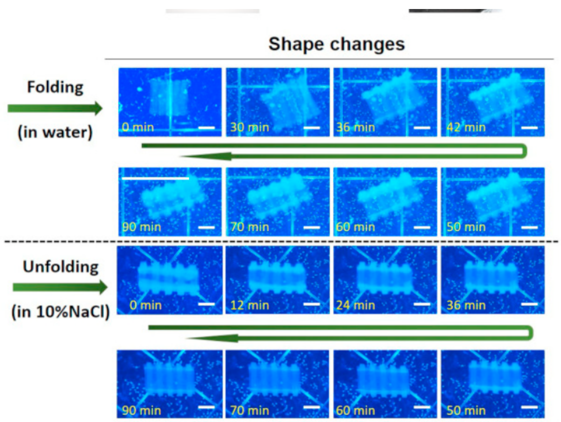

Figure 2. [8] How silk may fold from a series of sheets to a hydrogel. This hydrogel can be utilized for surgical assistance and rehabilitation and may also be used to assist transplants.

3.2 Drug Delivery and 4D Printing

Drug delivery is the process of delivering a drug to its target site in the body. These systems can be designed to release drugs at specific times and locations, allowing for more targeted and effective treatments. With 4D printing, drug delivery systems can be programmed to release drugs at specific times and locations. This could be used to create targeted drug delivery systems that can be tailored to the individual patient's needs. In addition, 3D-printed drugs have been developed, which means that an entire system of drug delivery can be created through additive manufacturing. [8] 4D printing here may happen by targeting different pH environments, a change in time, or through another physical change [as depicted in Figure 3].

4. The Future of 4D Bioprinting

The future of 4D bioprinting involves interactions in a number of subfields, with projects developing in biomimicry, regenerative systems, bone reconstruction, wound dressing, nanotechnology, textiles, and minimally invasive surgeries, to name a few. [9] Outside these cases, the central dogma of biology is itself an example of 4D printing. The self-assembly of proteins is categorized as a subsection of the field; however, amino

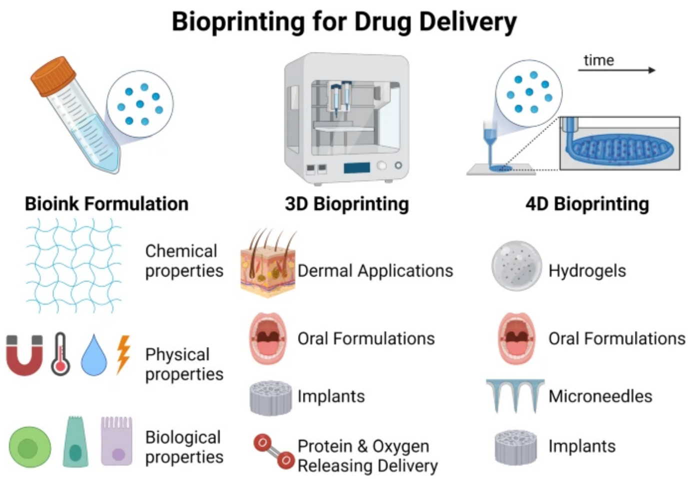

Figure 3. [9] Different ways that drug delivery and bioprinting can be utilized.

acids are readily available and cheap. With more research into the true process of protein assembly, the field of 4D bioprinting may be able to find cheaper and simpler materials to use. Right now, the field has two main issues: material supply and printing techniques. [10] With a high demand and low supply come high costs, and more progress is required before the field can be widely adopted.

5. Global and Ethical Impact

The global impact of 4D bioprinting lies in its potential to revolutionize the medical field by providing more personalized treatments and therapies. 4D bioprinting has the potential to enable personalized tissue and drug targeting. This could lead to improved patient outcomes and a reduction in healthcare costs. Cheaper technology at scale, especially in the medical industry, can globally level out discrepancies in class, race, nationality, and gender. There may be issues that come with utilization, as most of the work has happened in labs and clinical trials, but the potential for good will outweigh these speed bumps, and, as a result, a better world will be created for all.

6. Conclusion

Biological 4D printing is developing rapidly as the technology continues to improve. The structured change in shape given by a certain stimulant is very valuable, and as a result, nearly every medical subfield, from drug delivery to tissue engineering to other biomaterials, can be improved. The method of how the material is printed allows for certain processes to be used, which allow customization within an already versatile field. Advanced bioprinting can also target every stage of the healthcare process, from detection to therapeutics. Right now, the technique has not been fully utilized, but as familiarity with the tool grows and as issues begin to resolve, the medical field will start to use 4D printing in treatments. As this happens, lives will be saved across the world, providing a global benefit.

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