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In Shortly about Biomaterials

Sinisa Franjic*

Independent Researcher

***Corresponding Author:** Sinisa Franjic, Independent Researcher.*

ABSTRACT

The science of biomaterials combines knowledge from medicine, biology, chemistry, tissue engineering and materials science. They are obtained in the laboratory from other natural or artificial materials, and must meet certain characteristics and standards in order to be used for biomedical purposes, or implanted in living organisms. Biomaterials are today indispensable in various medical applications, forming a structure that enhances, enhances or replaces the natural function of a structure within the organism.

Keywords:*Biomaterials, Biomedical Engineering, Tissue Engineering, Health*

INTRODUCTION

The ultimate goal of the research and development of materials (other than drugs) for applications in medicine, which we call biomaterials, has always been to emulate natural materials [1]. Since the natural target for biomaterials, i.e. our body's tissues and organs, is exceedingly complex, it is not surprising that in many instances the laboratory-made materials cannot match in their performance the natural entities they are meant to augment or replace.

This is obviously different from the development of materials for industrial applications, which usually perform better than their natural counterparts (if the latter exist), and also evolve relatively fast, unhindered by biological constraints. For too long, an acceptable end-performance in the short term was the main requirement from a biomaterial, with little attention paid to changing its bulk and/or surface properties through the manipulation of composition and/or structure, in order to maximize the clinical outcome. Over the past six decades or so, however, the progress in bringing the properties and functionality of biomaterials close to those of their biological targets has been remarkable.

MICROARRAY

A microarray is an orderly arrangement (grid pattern) of sample molecules (i.e. probes with known sequences) immobilized on a particular substrate (e.g. glass, silicon, etc.) at microscopic length scale [2]. The probe can be a DNA, protein, antibody/antigen or enzyme. Therefore, an artificially synthesized grid pattern of probes can be used to recognize unknown complementary gene sequences, amino acid sequences within proteins, other biological entities by using antigen-antibody binding kinetics or selective enzymatic activity on substrates in order to recognize levels of these substrates in biofluids. Microarrays find wide usage in clinical diagnostics of diseases, genome sequencing for sensing and therapeutics work, drug discovery, environmental and toxicological research and so on. In summary, the microarrays are comprised of two main elements i.e., (a) a probe molecule and (b) an analyte which needs to be detected. Further, any microarray should have a signal transduction step enabling the user to read out chemical kinetics happening at the surface. Thus patterning of the probe molecule becomes a fundamental issue and patterning further necessitates an organizing step which should be able to send and bind such probe molecules into different regions. Thus, the interaction of the binding surface to the probe molecule is a very important step in fabricating a microarray.

Employing the same array platform also enables the detection of unlabeled DNA targets in a complex environment [3]. A randomly addressable bead array was fabricated in which each microsphere was functionalized with molecular beacons. Molecular beacons are hairpin-shaped structures in which the 5′ and 3′ nucleic acid ends are complementary to each other, which keeps a fluorophore and quencher in proximity. As the complementary DNA target hybridizes to its complementary pair on the molecular beacon, the fluorophore and quencher are separated, resulting in an increase in

fluorescence upon target hybridization. The molecular beacons employed were designed to be complementary to different wild-type and mutated genes of the cystic fibrosis transmembrane conductance regular region. This DNA biosensor was capable of making quantitative measurements with a detection limit of approximately 100 pM. There was a linear relationship between the initial rate of beacon fluorescence vs. target concentration, enabling unknown target concentrations to be determined.

SCAFFOLDS

Since the introduction of the concept in 1988, tissue engineering, a technique invented to reconstruct living tissues by associating the cells with biomaterials that provide a scaffold on which they can proliferate three-dimensionally and under physiological conditions, has emerged as a potential alternative to tissue or organ transplantation and has thus attracted great attention in science, engineering, and medicine [4]. To meet the diverse needs of tissue engineering, scaffolds made from various materials have been tested in this field. Although certain metals are somewhat good choices for medical implants due to their superior mechanical properties, their lack of degradability in a biological environment makes them disadvantageous for scaffold applications. Inorganic/ceramic materials such as HAP or calcium phosphates, being studied for mineralized tissue engineering with good osteoconductivity, are also limited due to poor processability into porous structures. In contrast, polymers have great design flexibility because their composition and structure can be tailored to meet specific needs. Degradable polymers frequently used for tissue engineering applications are linear aliphatic polyesters such as PGA, PLA, and their copolymers (PLGA), which are fabricated into scaffolds. These polymers are among the few synthetic polymers approved by the FDA for human clinical applications. The drawbacks of these polyesters include their hydrophobicity and lack of functional groups, which limits cell adhesion, an important factor when constructing polymeric scaffolds. Another drawback is their slow hydrolytic degradation.

An ideal scaffold used for tissue engineering should possess the following properties: 1) Be biocompatible, so that the scaffold can be well integrated into host tissues without resulting in any immune response; 2) It should be porous with appropriate pore size, size distribution and mechanical function, to allow cell or tissue growth and the removal of metabolic waste; 3) It must be mechanically able to withstand local stress and maintain the pore structure for tissue regeneration; 4) Very importantly, the scaffold should be biodegradable. Synthetic scaffolds are considered important components of a successful tissue engineering strategy. Hybrid three dimentional porous scaffolds of synthetic and naturally derived biodegradable polymers are particularly promising because they combine the advantages of the two types of materials. They should maintain sufficient mechanical strength while providing specific cell-surface receptors during the tissue remodeling process that stimulate both in vitro and in vivo cell growth. PLA-based hybrid materials have been successfully tested clinically for that purpose so far, and tests on other tissues including bladder, cartilage, liver, adipose, and bone tissues have also been reported.

A prerequisite of classical tissue engineering approaches is a suitable biomaterial scaffold or substrate with an architectural design, chemical, mechanical and physical makeup comparable to that of the native tissue [5]. Prior clinical practices of delivering cell suspensions directly into a defect site have proven to be problematic—if not ineffective—due to insufficient retention within the defect and subsequent flushing into the surrounding tissue. Consequently, the implementation of naturally derived vehicles, composed of more durable materials found readily in the body and more specifically within the tissue region of interest, are an attractive option for mimicking the native host tissue in the form of three-dimensional (3D) prefabricated scaffolds that retain the delivered cell population.

ENGINEERING

In the field of biomedical engineering, reverse engineering is used to reconstruct physical models in the form of computer data (virtual models) without the assistance of conceptual drawings, specifications, or technical drawings of the product design [6]. This involves the phase of data collection which is achieved through the scanning of physical components by medical imaging techniques. Due to the demands of production time and complexity, rapid prototyping can then be applied to fabricate geometries matching those of the human body, which is often irregular, complex, and unique in shape. With rapid prototyping

replacing some of the conventional manufacturing processes, the efficiency of the whole process of production can be boosted.

A straightforward flow of product development can be started from a product idea fulfilling market demands, followed by product specification definition, prototype drafting, fabrication, assembling, and detail optimization. Such a product development flow is categorized as "forward engineering" which generally translates a high level form of design (such as logical designs and data) into a low-level form of structures (such as physical element). Sometimes, there are cases in which physical parts are required without any technical details of the product; in which cases, traditional forward engineering development approaches cannot fulfill the requirements. In some biomedical applications such as prosthesis manufacturing, custom implanted fixation devices need to be shaped and fabricated based on the bone damage pattern of a patient. However, the forward engineering approach is not applicable as the device shape and other details are determined by the patient's body status rather than market needs or any expected specifications. Furthermore, forward engineering normally requires a long duration of product development time which cannot generate the necessary implant device on time.

The search for artificial replacements for failing human organs is long and filled with great successes [7]. Today, hemodialysis is routinely used to replace kidney function, artificial hip prostheses allow millions of people to walk, and artificial lenses provide cataract sufferers with clear vision. There are many disappointments as well; despite decades of serious effort, there is still no proven artificial heart, liver, or pancreas.

Over the years, some materials have been demonstrated to be biocompatible after implantation, although the degree of compatibility can vary significantly depending on the site of implantation and the function of the material at that site. Biomaterials are now used routinely in diverse medical applications—from contact lenses to artificial hearts. Frequently, the materials used in biomedical applications are polymers or metals.

Ceramics

Ceramics are defined as the art and science of making and using solid articles that have as their essential component, inorganic nonmetallic materials [8]. Ceramics are refractory, polycrystal line compounds, usually inorganic, including silicates, metallic oxides, carbides and various refractory hydrides, sulfides, and selenides. Oxides such as Al2O3, MgO, SiO2, and ZrO2 contain metallic and nonmetallic elements and ionic salts, such as NaCl, CsCl, and ZnS. Exceptions to the preceding include covalently bonded ceramics such as diamond and carbonaceous structures like graphite and pyrolized carbons.

Ceramics in the form of pottery have been used by humans for thousands of years. Until recently, their use was somewhat limited because of their inherent brittleness, susceptibility to notches or micro-cracks, low tensile strength, and low impact strength. However, within the last 100 years, innovative techniques for fabricating ceramics have led to their use as "high tech" materials. In recent years, humans have realized that ceramics and their composites can also be used to augment or replace various parts of the body, particularly bone. Thus, the ceramics used for the latter purposes are classified as bioceramics. Their relative inertness to the body fluids, high compressive strength, and aesthetically pleasing appearance led to the use of ceramics in dentistry as dental crowns. Some carbons have found use as implants especially forbloodinterfacingapplicationssuchasheartvalves.Duetotheirhighspecificstrengthasfibersandtheir biocompatibility, ceramics are also being used as reinforcing components of composite implant materials and for tensile loading applications such as artificial tendon and ligaments.

Tissue Engineering

Tissue engineering, a relatively new field in biomedical engineering, consists of the manufacture of biological tissue either ex vivo or in vitro (outside the body), or the incorporation of new advancements to aid in the repair and growth of existing tissues in vivo (inside the body) [9]. In ex vivo applications, bioartificial tissues (those composed of both synthetic and natural materials) are used as an alternative to organ transplant or developed to study tissue behavior in vitro. Some important issues within the field include cell isolation, control of cell organization and function, upscaling to full bioartificial tissues, and biomaterial fabrication.

While the most well-known tissue engineering feats have been in epithelial tissues, clinical trials are also currently under way for reconstruction of cartilage, bone, neural, and

liver tissues. Grafts are used for treatment of every type of skin damage, including burns, pressure sores, venous stasis ulcers, and diabetic ulcers. Polymeric tubes are implanted to assist in nerve regeneration due to central and peripheral nervous system damage or disorders.

Tissue engineering also covers joint replacements, including connective tissue recreation and bone grafts. Artificial heart valves implement bovine and porcine tissues along with bioartificial substances. Organ failure is treated with innovations in the field as well, with treatment for everything from liver cancer to breast reconstruction. Blood transfusions and dental surgery advancements are just two more examples of the wide range of applications of tissue engineering technologies.

The success of a tissue engineering project depends on a lot of different areas [10]. The type of cells used, the use of growth factors, and the materials that the cells are seeded on and in the scaffold are all extremely important for the viability of the developing tissue. One area of equal importance is the structure of the scaffold used to house the cells. The architecture of the scaffold influences the chemical species that the cells are exposed to through the diffusion of materials through its pores. It can control the metabolic activity of the cells by subjecting cells to surfaces that are on par with the size of the seeded cells or much larger than the seeded cells. The architecture can limit or allow cell and tissue infiltration through pore size and pore interconnectivity. If a scaffold is too porous the mechanical strength may be compromised, leading to premature failure. In light of the importance of scaffold architecture a variety of techniques have been developed to produce a wide range of architectures to give cells different surfaces and pore sizes to ensure regenerative tissue success. In this section, we will discuss several techniques that create commonly used scaffolds in the area of tissue engineering.

3D Technology

There are many definitions for 3D printing [11]. To simplify, it can be described as fabricating physical 3D object based on virtual 3D mesh, by successively printing layers on top of one another. In medical scenario, “physical 3D object” is usually an anatomical model, and “virtual 3D mesh” is a computer representation of anatomical structure. The crucial part of clinical 3D printing, however, is the process that leads to creating that virtual model based on medical imaging. This process, called segmentation, has been widely explored in computer vision for decades, which led to partial automatization. Several open-source software packages are available to speed up segmentation process with access to semiautomatic algorithms, e.g., thresholding or region growing. Having said that, segmentation is still considered one of the main bottlenecks of 3D visualization and 3D printing processes.

It is important to notice that although 3D printing is available for about a decade now, clinical evidence is still relatively sparse. The most published research consists of case studies, as the personalization of 3D printing comes most useful in rare and complex cases. The first meta-analyses have been published very recently, virtually only in orthopedic surgery. Systematic reviews have been performed for most medical fields, however, and have shown that models are accurate and helpful. Having said that, those conclusions are drawn usually just from physicians’ reports and with no quantitative data to support it. In-hospital 3D printing labs are still located in almost only large university hospitals, often with industry support. There is a slow change toward more desktop, user-friendly, and accessible machines, and the process itself is simplifying, helping the expansion of the technology. It is still most likely that smaller, rural hospitals will never need 3D printing services.

Fabrication

It is evident that professionals from different disciplines must share thoughts and work interactively together to develop novel technologies and to shape the future of bio fabrication field [12]. The cooperation among life scientists, material scientists, and engineers of different specializations is absolutely essential for speeding up this emerging field. Further more, multidisciplinary research groups that include scholars and researchers not only from biology, biotechnology, biomedical engineering, regenerative medicine, healthcare, chemistry, and materials sciences but also from computer science, automation engineering, and mechatronics are those seeked to move beyond the frontiers of biofabrication.

In addition to the multidisciplinarity research groups, individuals from universities, companies, governmental agencies, and non profit organizations must interact to create a proactive innovation culture for bio fabrication. Of course, the development of joint efforts

among professionals with different skills, attitudes, and values is a challenging issue as it involves a multitude of stake holders often distributed across both public and private organizations. Indeed, coordination and cooperation are often prerequisites on biofabrication teams surpassing the individual as the fundamental unit. Thus, interdisciplinarity or even transdisciplinarity seems to be then extstep in biofabrication despite it still requires the members of teams to learn how to share their knowledge and protocols across the disciplinary boundaries and move beyond disciplines.

CONCLUSION

Biomaterials are materials used in medicine and dentistry to compensate for tissue loss. They can be obtained from living beings or they can be synthesized in a laboratory. One of their most important characteristics is biocompatibility. Raw materials for the production of such biomaterials can be metals and their alloys, various types of bioceramic and glassy materials, combinations of composite biomaterials, polymers, bioderivatives and nanoparticles.

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