Journal of Simulation and Analysis of Novel Technologies in Mechanical Engineering
13 (3) (2021) 0053~0062
HTTP://JSME.IAUKHSH.AC.IR

Feasibility study of mechanical properties of alginates for neuroscience application using finite element method

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(Manuscript Received --- 02 Feb. 2022; Revised --- 24 Mar. 2022; Accepted --- 26 Mar. 2022)

Abstract
Alginate is a natural polysaccharide that is extracted from alga sources mainly laminaria. Alginate is readily processable for applicable three-dimensional (3D) scaffold materials such as hydrogels, microspheres, microcapsules, sponges, foams and fibers. Alginate hydrogels have been particularly attractive in wound healing, drug delivery, neuroscience and soft tissue engineering applications. As these gels retain structural similarity to the extracellular matrices (ECM) in tissues and can be manipulated to play several critical roles. The nervous system is a crucial component of the body and damages to this system, either by of injury or disease which can result in serious or potentially lethal consequences. In this research, the aim is to simulate nerve fibers in Abaqus simulation software by finite element method (FEM). Also, the use of a similar material such as alginate can be used to validate this simulation. Restoring the damaged nervous system is a great challenge due to the complex physiology system and limited regenerative capacity. Currently, most of neural tissue engineering applications are in pre-clinical study, in particular for use in the central nervous system, however collagen polymer conduits aimed at regeneration of peripheral nerves have already been successfully tested in clinical trials. In this study, due to the complexity of measuring nerve endurance, static simulation was used in Abaqus software and the results showed that paired strings are stronger than the number of individuals and the string plays a key role in the center.

Keywords: *Biocompatible materials, Hydrogel, Tissue engineering, Nerve regeneration*

1- Introduction
Alginate is a group of compounds that are generally considered safe by the Food and Drug Administration (FDA). The mechanical properties of alginate hydrogels are determined by the sequence and composition of its constituent monomer chains [1-3]. Alginate is used as the salt of sodium, and due to the addition of salts of divalent cations such as calcium and barium, etc., and special trivalent cations such as iron and aluminum, which cause ionic bonding and crosslinking of carboxyl groups of polymer chains [4-7]

the mechanical strength of alginate hydrogels depends on the tendency of the cations to alginate. Studies have shown that the chemical structure, molecular size and process of hydrogel gel formation play an important role in its properties such as swelling, stability, biodegradability, safety and biocompatibility properties [8-14]. Large proteins such as fibrinogen can easily pass-through calcium alginate hydrogels. Only cells and some high molecular weight enzymes such as catalase remain completely in the alginate hydrogel [15-21]. Alginate is biocompatible and harmless to the body and is used in the food industry as a thickener and stabilizer. This biocompatible hydrogel has been considered today due to its ease of preparation and its suitable properties for encapsulating cells. The alginate scaffold is formed by the cross-linking of calcium cations and can be degraded by the removal of calcium [22-28]. Alginate lattice congestion in hydrogels is related to the hardness of the alginate, which is directly affected by the cation concentration. The results of studies have shown that increasing the hardness of the hydrogel leads to a decrease in the permeability of the hydrogel and consequently a decrease in the viability and proliferation of encapsulated nerve stem cells [29-36]. It is used in the food, cosmetics and pharmaceutical industries [37-45]. The beneficial properties of alginate, such as biocompatibility and non-stimulation of the immune system, are probably related to its hydrophilic properties [46-51]. As cells are not damaged during the gel formation and ion crosslinking process, it is widely used to release drugs, encapsulate cells, and regenerate tissue [52-55]. Extracellular matrix (ECM) polysaccharides affect axonal conduction, function, synaptic evolution, and cell migration [56]. Therefore, polysaccharide scaffolds and polysaccharide-modified scaffolds, such as alginate, are crucial to the development of neural tissue engineering. Alginate polysaccharide sequences can act as functional groups in the ECM of the brain, which can modulate signal transduction pathways to guide cell migration and nerve growth. Alginate has been used to fill cavities in brain and spinal cord injuries in mice. It has also been used to stop astrogliosis in damaged central nervous system areas [54-55]. In this study, the aim was to predict the properties of neural neurons with the supports of Abaqus software and finite elements analysis (FEA) according to the existing variables worked for polymer alginate.

2- Physical characteristics

Many scaffolds used in soft tissue engineering generally fill the space normally occupied by the host tissue and act as a framework for the cells that will repair the lesion in the future. In addition to being able to withstand the load that enters the tissue naturally, the graft also needs to be able to provide the strength needed for the growth of cells on the scaffold [58-62]. Alginate ion bonds have a stronger mechanical strength when they are formed by adding divalent cations with a higher affinity for the polymer. The presence of these variables in the biomechanics of the scaffold makes it possible to create a suitable ECM for each tissue in accordance with the physiological characteristics of the tissue in question [62-64]. In most cases, cells cannot attach to hydrogels because they lack receptors, except for collagen, which is one of the proteins that make up the extracellular matrix. Because hydrogels are hydrophilic, ECM proteins cannot readily be absorbed on their surfaces [13]. The best way to modify hydrogel levels to provide cell binding receptors is to bind an ECM protein or a peptide sequence by covalent bonding to the hydrogel surface [14]. For this purpose, peptide sequences are mainly used. This sequence is naturally present in ECM proteins such as laminin, fibronectin and collagen. Numerous studies have been performed to prove that the peptide mentioned above can bind to alginate by covalent bonding, and it has been shown to improve the attachment of nerve cells [15-18]. Studies have shown that YIGSR and IKVAV sequences promote a greater number of neurites in each neuron as well as selective binding of neurons [16-21].

3- Mechanical simulation of central nervous system in the FEM

Alginate has been studied as a degradable scaffold *in vitro* and *in vivo* to guide nerve fibers [17]. The study showed that the arrangement of axons relative to each other in alginate scaffold after transplantation in the spinal cord injury area was parallel to the control group, while in the axon control group neurons grew in different directions. Therefore, the use of alginate can manage the major challenge of directing axon regeneration throughout the lesion site. But an important issue to consider when using alginate as a scaffold to repair nerve damage is the high rate of degradation of the substance in the body and it decomposes before axons can grow more than 2 mm at the site of the lesion [18].

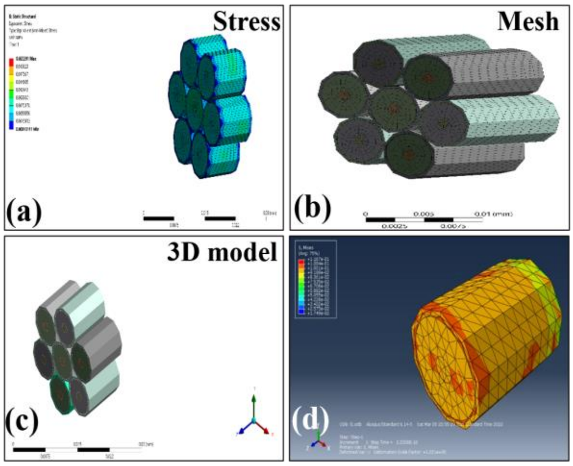

Fig. 1 Investigation of elastic properties of polymeric nerve fibers

Therefore, in order to use an alginate scaffold to repair nerve damage, a method should be used to reduce its degradation rate. Several researchers model becomes spinal cord injury [19-26]. Researchers showed the injection of this scaffold in a mouse. The model of spinal cord. Hemi section produces more neurofilament in the lesion region, On the other hand, another study showed that alginate may provide a suitable environment for increasing the length of spinal cord axons [25-36]. In one study, an alginate scaffold with a spongy structure was used, and nerve stem cells were isolated from the hippocampus and injected after culture, and finally the composite structure was transplanted to the injury site [52-54]. The obtained their results of the study showed that the motor symptoms improved, and the injured area was repaired histologically. Mesenchymal stromal cells (MSCs) have been shown to regulate the inflammatory environment of various tissues in the body, including the central nervous system. Until now, however, the success of direct use of these cells in the brain has been limited due to the depletion of these cells. In this study, the TET structure with the boundary conditions of the two closed sides was used and a force of 100 N was used.

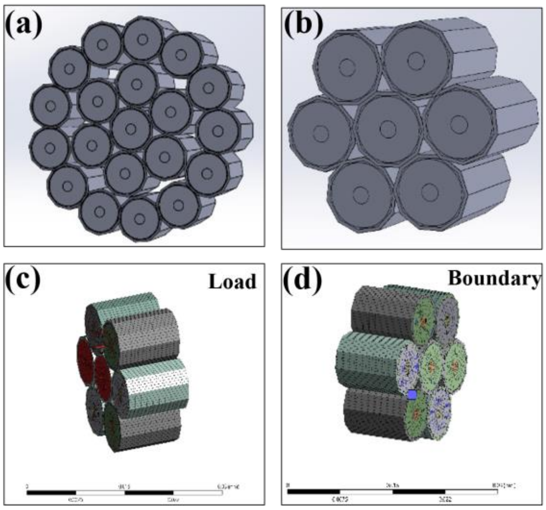

Fig. 2 Investigation of Von Mises Stress (VMS) of simulated nerve fibers in Abaqus software with a force of 100 N

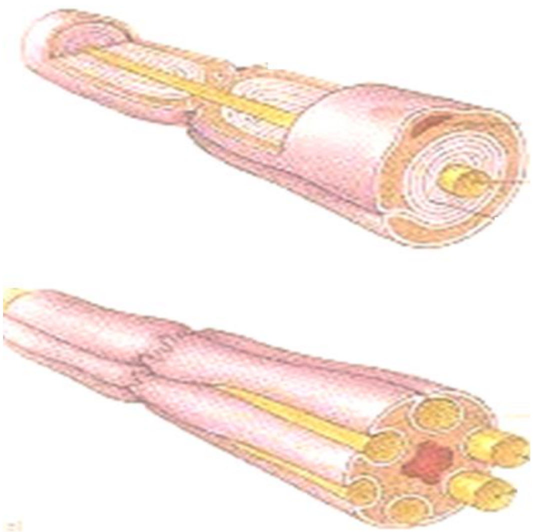

Fig. 3 Myelin formation in the nervous system begins from the embryonic period until puberty [26]

In the study of finite elements analysis, it can be found that most of the stress concentration occurs in the center. It is also shown in Fig. 1(d) that a single string in the center and on the edges contains the most stress. Fig. 2 (a-d) shows the surface of the filaments with 20 strands and the cross section of the cross-section, while the stress level boundary shown in Fig. 2 under load shows well that the fibers in the center withstand the highest stresses. In neuroscience, the methods of neuroimaging, computed tomography (CT), positron emission tomography (PET), operative magnetic resonance imaging (FMRI), and the study of the inside of the brain. The application of artificial intelligence and machine learning in biological data and neural imagery opens new frontiers for bioinformatics: Increasing the understanding of the umbilical cord. Advances in this field can eventually lead to the development of automated diagnostic tools as well as the precise medicine that may be taken into consideration by considering a specific treatment method. Prior to the advent of machine learning algorithms, bioinformatics algorithms had to be handwritten to solve problems such as predicting protein structure. The obtained results of this study show that the stem cells encapsulated in alginate have the ability to be used as an improved carrier for transplantation and also this method has a therapeutic effect on inflammation of the nervous system [21-36]. Transplantation of encapsulated mesenchymal stem cells with alginate improves cellular pathology after brain injury [22-24]. Razavi et al. [37] studied the safety, regulatory issues, long-term biotoxicity, and the processing environment of hydrogels. Fig. 3 shows the myelin formation in the nervous system begins from the embryonic period until puberty

4- Conclusion

The use of a similar material such as alginate can be used to validate for this simulation. Restoring the damaged nervous system is a great challenge due to the complex physiology system and limited regenerative capacity. Currently, most of neural tissue engineering applications are in pre-clinical study, in particular for use in the central nervous system, however collagen polymer conduits aimed at regeneration of peripheral nerves have already been successfully tested in clinical trials. This material can be used in many medical applications, especially in the fields of wound healing, drug transfer, cell culture *in vitro* and tissue engineering. Alginate has effective properties such as biocompatibility, cheapness and availability of raw material and the possibility of applying simple changes to prepare alginate derivatives with new properties. Mammalian cells do not have receptors for alginate polymers, which make alginate gels relatively ineffective. One way to create cell adhesion is to use cell adhesion molecules such as laminin, fibronectin, and collagen with alginate. Alginate decomposition can be controlled by manipulating its molecular weight and composition. According to the strategy of using molecules with different chemical structure, different molecular weights, it is possible to design and fabricate alginate scaffolds suitable for use in various tissues, including nerve tissue. Alginate scaffold can play an important role in neural tissue engineering as it maintains a structural similarity to the ECM in tissues. However, the use of this hydrogel as a cell scaffold *in vivo* in humans requires further studies. n this study, due to the complexity of measuring nerve endurance, static simulation was used in Abaqus software and the results showed that paired strings are stronger than the number of individuals and the string plays a key role in the center.

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