# Biomimetic Hydrogel-Scaffold for Tendon and Ligament Repair

Lucas Chan, Luke Gailloux, Matt Levasseur, Edison Luke

March 9, 2025

**Abstract**

*Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetuer id, vulputate a, magna. Donec vehicula augue eu neque. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Mauris ut leo. Cras viverra metus rhoncus sem. Nulla et lectus vestibulum urna fringilla ultrices. Phasellus eu tellus sit amet tortor gravida placerat. Integer sapien est, iaculis in, pretium quis, viverra ac, nunc. Praesent eget sem vel leo ultrices bibendum. Aenean faucibus. Morbi dolor nulla, malesuada eu, pulvinar at, mollis ac, nulla. Curabitur auctor semper nulla. Donec varius orci eget risus. Duis nibh mi, congue eu, accumsan eleifend, sagittis quis, diam. Duis eget orci sit amet orci dignissim rutrum.*

## Introduction

Sample introduction for formatting testing.

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetuer id, vulputate a, magna. Donec vehicula augue eu neque. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Mauris ut leo. Cras viverra metus rhoncus sem. Nulla et lectus vestibulum urna fringilla ultrices. Phasellus eu tellus sit amet tortor gravida placerat. Integer sapien est, iaculis in, pretium quis, viverra ac, nunc. Praesent eget sem vel leo ultrices bibendum. Aenean faucibus. Morbi dolor nulla, malesuada eu, pulvinar at, mollis ac, nulla. Curabitur auctor semper nulla. Donec varius orci eget risus. Duis nibh mi, congue eu, accumsan eleifend, sagittis quis, diam. Duis eget orci sit amet orci dignissim rutrum.

## Hydrogel Structure and Composition

Hydrogels are 3D crosslinked polymer structures containing hydrohpilic functional groups, allowing them to absorb large quantities of water. Because of this, they are flexible and soft, and resemble many natural tissues (Ho et al., 2022). Recent advances in hydrogel technology have led to the development of implantable and injectable hydrogels with potential applications in drug delivery. By adjusting polymer composition, key properties such as swelling-deswelling rate, stiffness, and degradability can be fine-tuned to meet specific use case requirements. As biomedical applications of hydrogels continue to expand, their use in tendon and ligament repair presents a promising opportunity.

Hydrogel cross-linked chains can be formed using natural, synthetic, or semi-synthetic polymers. Natural polymers such as cellulose, chitosan, and collagen are inherently biocompatible and bioactive, but come at the cost of weak stability and poor mechanical strength. Being derived from natural sources, these hydrogels are generally safe to use in clinical applications, but have shown to be allergens in rare cases (Ho et al., 2022).

On the other hand, synthetic hydrogels are made of man-made polymers like polyvinyl alcohol (PVA), polyethylene glycol (PVG), or polyacrylamide (PAAM). Few of these synthetic materials have been shown to be biocompatible, but they offer superior mechanical strength and stability (Ho et al., 2022).

To achieve both the biocompatibility offered by natural hydrogels and the strength and mechanical properties offered by their synthetic counterparts, a common approach is to develop a hybrid, or semi-synthetic hydrogel chain. Hybrid hydrogels can either be made by chemically modifying natural polymers or by blending natural and synthetic components.

## Biocompatibility

The Janus Tough Adhesive has shown to exhibit high biocompatibility during testing, despite it containing the synthetic polymer polyacrylamide. To evaluate their performance and impact on natural tissues, Freedman et al. (2022) experimentally tested injured and healthy rats, and applied the JTA to the patellar tendon. For three weeks, potential swelling of the tendon and degredation of the gel were assessed by high frequency ultrasound. When a tendon becomes injured, its echogenicity—the amount of sound it reflects—decreases, because its collagen fibres become more disorganised and less densely packed (Hodgson et al., 2012). Researchers also found that injured tendons without application of the JTA had larger cross-section areas, indicating increased swelling as shown in Figure 1 below. A decrease in inflammation in the affected tendon therefore suggests that the JTA was effective and well-tolerated by the body.

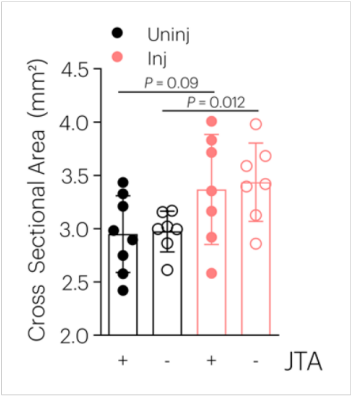


**Figure 1:** *Patellar tendon cross-sectional area ($mm^2$) after 3 weeks of treatment [Adapted from Freedman et al., 2022]*

Furthermore, in the patellar tendon, the JTA was found to have improved tendon relaxation (Figure 2), without impacting natural properties such as elastic mechanics, dynamic modulus, or linear modulus.

## Mechanical Properties of JTA-Hydrogels

In addition to biocompatibility, the mechanical properties of a given hydrogel decide whether or not a given hydrogel is functional. In particular, hydrogels must have sufficient toughness and adhesive strength (Freedman et al., 2022). In vivo, tendons must withstand a dynamic environment and bear strong forces (**ChenAdvancesApplicationHydrogel**); thus, a hydrogel must be able to withstand sufficient amounts of force without fracturing – that is, an ideal hydrogel should only deform plastically (Freedman et al., 2022). Furthermore, to promote optimal healing, hydrogels should be placed and remain near the relevant tendon. However, force generated by movement can lead to hydrogel displacement; Hence, adhesion is required to ensure immobility (Freedman et al., 2022). A variety of strategies can be implemented on a biochemical level to greatly increase the toughness and adhesiveness in order to create an adequate hydrogel for tendon repair.

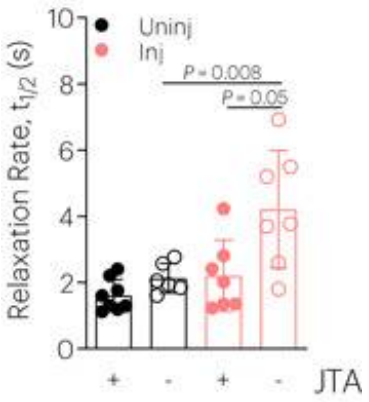


**Figure 2:** *Patellar tendon relaxation rate [Adapted from Freedman et al., 2022]*

### Mechanisms for Toughness in Hydrogels

In order to design a tough hydrogel, an analysis by Zhao (2015) found that tough hydrogels generally follow two principles; a tough hydrogel should dissipate significant amounts of mechanical energy upon crack propagation, and the original configuration of the hydrogel should be retained, even after large deformations. Simply put, tough hydrogels should have mechanisms to dissipate energy, and mechanisms to maintain elasticity.

### Fracture of polymer chains

A widely used method for energy dissipation is the fracturing of polymer chains (Zhao, 2015). As

a polymer chain is fractured, the mechanical energy stored within the chain is dissipated. Thus, to promote polymer fracturing, several polymer chains with short lengths are incorporated into the hydrogel. During a deformative event, these short chains can be ruptured to dissipate energy. Highly crosslinked polymers, such as polyacrylamide double network hydrogels, are notably effective in dissipating energy using this method (Zhao, 2015). However, it should be noted that hydrogels that rely on chain-fracturing to dissipate energy are susceptible to fatigue over multiple deformations (Zhao, 2015), highlighting the importance of a self repairing method, which will be discussed later.

## Reversible Crosslinking of Polymer Chains

Another mechanism to dissipate energy is to decrosslink polymer chain networks. Physical crosslinkers found in polymer networks are usually weaker than covalent crosslinking, allowing for energy to be more easily dissipated through decrosslinking. In addition, the mechanism of breaking physical crosslinkers has the advantage of being recoverable, meaning that this mechanism of energy dissipation can maintain stress-strain hysteresis over cyclic loading, or this mechanism allows for anti-fatigue hydrogels. However, recovered cross linkers are often not found in their original locations post deformation – Zhao et al. observed plastic deformations in ionically crosslinked alginate hydrogels – thus, a mechanism to maintain elasticity is critical.

## Interpenetration of long-chain networks

According to Rubenstein and Colby (2003), longer polymers allow for an increase in elasticity. Thus, long polymer chains can be interlaced with short-chain networks to form elastic interpenetrating polymer networks. Common polymer candidates for long-chain network elasticity include polyacrylamide, among other polymers.

## Hybrid crosslinking of physical and chemical crosslinkers

As mentioned earlier, the recovery of physical crosslinkers often leads to irreversible deformations. Thus, chemical crosslinkers can be used to maintain the elasticity, while physical cross linkers can be used to dissipate energy. Resultant hybrid polymer networks are effective in maintaining elasticity and dissipating energy, and are thus used for many tough hydrogels. Examples of polymer networks that are used for hybrid cross linking include alginate, chitosan, and polyacrylamide (Zhao, 2015).

## Application to the JTA

The proposed JTA hydrogel uses an alginate-polyacrylamide polymer network to ensure hydrogel toughness, which uses all of the above mechanisms in order to retain superior mechanical toughness. Due to its use of the above mechanisms, the proposed hydrogel has a fracture energy of 9000 J/m2, which is far superior to typical hydrogels, which typically have fracture energies around 10J/m2 . In comparison to human tissues, the proposed JTA hydrogel is stronger than cartilage, which has a fracture energy of 1000 J/m2, and slightly weaker than natural rubbers (10,000 J/m2) (Sun et al., 2013). Furthermore, in vivo load testing by Freedman et al. (20XX) demonstrated that the alginate-polyacrylamide polymer hydrogel maintained its mechanical integrity. Therefore, the tough matrix in our proposed hydrogel demonstrates sufficient mechanical toughness for tendon repair.