3D printing of tough hydrogels creates complex, viable cellular environments

2015-08-26

When it comes to synthetic hydrogels, finding the perfect mixture of toughness and ease of fabrication has been elusive. Although tough hydrogels have been created to withstand a high mechanical load, they cannot be easily printed by a three-dimensional (3D) printer owing to their relatively complicated compositions or fabrication processes. 3D printing is essential in the hydrogel field as it allows for rapid prototyping as well as ease of constructing complex structures. In a recent study published in *Advanced Materials*, researchers at the Massachusetts Institute of Technology (MIT), Duke University, and Columbia University have combined two commonly used materials to create a printable gel that is tough enough to stand up to intense stresses.

Although 3D printers have already been used to print hydrogels, those gels have not been ideal, says Xuanhe Zhao, a professor of mechanical engineering at MIT and lead author on the study. A major point of concern is the toughness of the material. For biomedical applications, hydrogels would have to display high fracture toughness to sustain significant mechanical loads applied internally and externally. While progress has been made in designing raw materials that have such tough characteristics, crafting them into useable and functional microstructures has proven a challenge.

“There is no technique to print these robust hydrogels into 3D complex microstructures,” says Zhao. He also points out that the existing fabrication processes of robust hydrogels with or without printers are mostly toxic to cells, meaning even if microstructures could be printed, they would not be functional for fields like tissue engineering.

Seeing both the toxicity and printing challenges as major barriers in the field of tissue engineering, Zhao and his team decided to tackle both problems at once. They fabricated a new gel by combining two materials, sodium alginate mixed with calcium ions and poly ethylene glycol (PEG). Both materials have been widely used in gels for cell encapsulation, so the team knew that the combination will be very likely to be benign to cells. However, research has shown that when used alone neither alginate nor PEG approach the necessary toughness threshold needed to create truly functional, load-bearing hydrogels. When put together, though, they formed a material with remarkable mechanical properties.

The sodium alginate utilizes the calcium to create reversible ionic crosslinks. These Ca^{2+} crosslinks allow alginate to dissipate mechanical energy. The PEG created covalent crosslinks, which allow it to maintain elasticity even under large deformations.

“The combination is quite surprising,” says Jonathan Butcher of Cornell University who is a tissue engineer but is unaffiliated with the current research. Butcher has worked with both PEG and alginate before, and so was intrigued by the results. “Overall the material is tougher than what we would have expected. It appears to be stiffer, appears to be stretchier than either one by itself. It’s very interesting.”

When the material was printed into complex microstructures, the performance was impressive. After a 500% deformation, the material was able to recover 70.5% of the fracture energy lost during deformation. With current printing technology, microstructures as complex and intricate as vascular beds full of blood vessel-like structures could be printed, for supplying necessary nutrients to a growing tissue, says Zhao.

A major question does remain: can this new tough hydrogel be used as scaffolding to grow tissues. Both PEG and sodium alginate are biocompatible, so in theory they should be able to encapsulate and support cells. Initial tests with human mesenchymal stem cells did show a survival rate of over 80% over the course of several weeks. However, Butcher is unsure if the cells will actually be able to function in the environment.

“The cell viability is quite remarkable,” says Butcher. “But you want the cells to be able to spread and remodel the matrix material. [The article] shows rather rounded cells that become spread when you stretch the materials. But it’s not like the cells are spreading on their own.” Butcher suggests that further tests and tweaks may be needed to see if this tough gel can also play host to actual tissue engineering in a dynamic environment.