Demonstration

What Does a Brain Feel Like?

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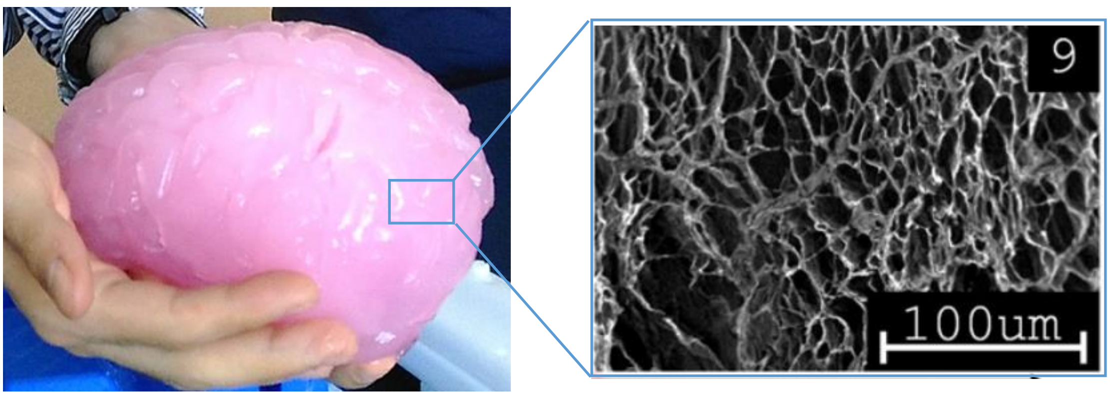
Abstract

We present a two-part hands-on science outreach demonstration utilising composite hydrogels to produce realistic models of the human brain. The blends of polyvinyl alcohol and Phytagel™ closely match the dynamic and non-linear mechanical response of real brain tissue in a range of strain rates considered adequate for surgery. The composite hydrogel is simple to prepare, biocompatible, non-toxic, and the required materials are widely available and inexpensive. The first demonstration gives participants the opportunity to feel how soft and deformable our brains are. A second demonstration allows students to perform a mock brain surgery on a simulated tumour. The demonstration tools are suitable for public engagement activities as well as for various student training groups. It encompasses concepts in polymer chemistry, materials science, and biology.

Keywords

Demonstrations, Public Understanding/Outreach, General Public, High School/Introductory Chemistry, Hands-On Learning/Manipulatives, Polymer Chemistry, Materials Science

Graphical Abstract

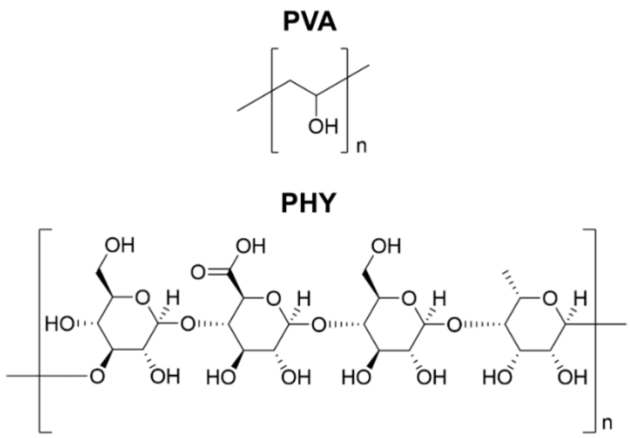


Introduction

Hydrogels are a group of polymeric materials that can swell to absorb huge amounts of water. They are formed through the cross-linking of hydrophilic polymer chains, resulting in three-dimensional polymer networks.[1] Hydrogels are 'smart' materials that are able to respond to the environment and have been used in a variety of areas ranging from pharmaceuticals to biotechnology.[2] Applications of hydrogels that many of us encounter every day include soft contact lenses[3] and diapers.[4]

Much like our own bodies, hydrogels are mostly made of water and can be highly viscoelastic: they exhibit both viscous and elastic characteristics when they are mechanically deformed.[5] As a result, hydrogels are ideal materials to use as surgical phantoms, since they have similar mechanical properties with a range of organic tissues. Phantoms are reproductions of human parts and organs that allow trainee surgeons to practice positioning of anatomical structures and hand-eye coordination.[6] They can also be used in prosthesis design, testing of robot-aided surgery systems, impact tests, and traumatic injury analysis.[6] If the phantom material is biocompatible, it can also be used for implants[7] and tissue engineering.[8] Unfortunately, most hydrogels have limited mechanical strength and are prone to permanent breakage during mechanical loading.[1] Composite hydrogels, which consist of a mixture of different polymers, can provide drastically improved mechanical properties.[7]

Recently, we have developed a composite hydrogel that closely matches the dynamic and non-linear mechanical response of brain tissue.[6] It consists of a blend of polyvinyl alcohol (PVA) and Phytagel™ (PHY), which is also known as gellan gum. PVA is formed from the vinyl acetate monomer, which is also used in PVA glue. PHY is a high strength, water-soluble tetrasaccharide that is commonly used as a gelling agent in plant and microbiological cultures.[9] The molecular structures of PVA and PHY are shown in Figure 1.



Demonstration

Figure 1. Molecular structures of polyvinyl alcohol (PVA) and Phytagel^{TM} (PHY) repeat units.

By exploiting the hybrid mechanical capabilities of binary polymer blends, we produced a composite hydrogel with similar porosity, elastic and viscoelastic properties to those of brain tissue. We used the composite hydrogel to create a life-sized human brain phantom, as shown in Figure 1a. PVA creates a porous solid network that provides the stiffness (see Figure 1b), while PHY enables realistic rate-dependent properties.[6] Tuning the PVA and PHY ratios allowed us to create a composite hydrogel that mimicked brain tissue at different displacement rates and for different loading conditions.[6] Similar to other composite hydrogels,[10] the interactions between the two polymer networks are not due to chemical bonds (cross-linkages) but rather to hydrogen bonds between the OH groups of neighbouring PVA and PHY chains,[6] as shown in Figure 2c-d. The synthesis procedure can also be modified to create a transparent composite hydrogel that can be used for non-invasive optical measurements within the samples.[11] The composite hydrogel has also been successfully used as ink in a 3D-printer to produce porous scaffolds for tissue engineering.[12]

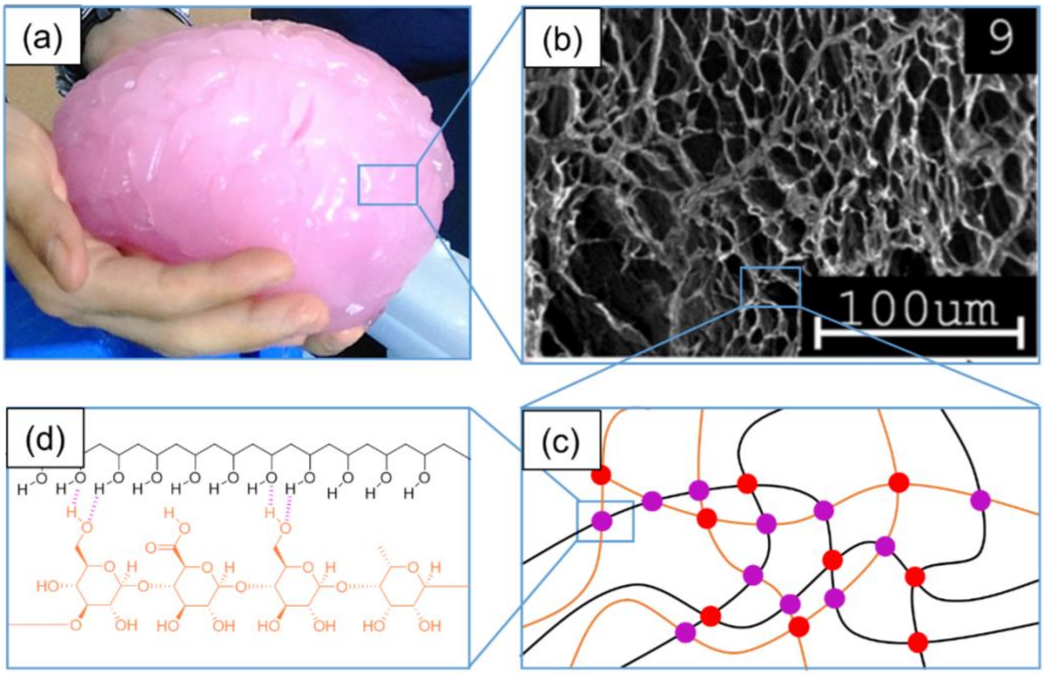


Figure 2. Life-sized phantom of the human brain (a). Scanning electron microscopy (SEM) image of the microstructure of the composite hydrogel (PVA 5.0 % + PHY 0.7 %) used in the first demonstration (b). Schematic showing cross-linkages (red) and hydrogen bonds (purple) in the polymer network (c). Schematic highlighting hydrogen bonds (purple) between PVA (black) and PHY (orange). UPDATE SEM IMAGE

In our previous study, we achieved the best match to the mechanical properties of porcine brain in compression, indentation, and shear tests by mixing PVA 6.0 wt% and PHY 0.85 wt% separate solutions in a 1:1 weight ratio.[6] Reducing the PVA concentration to 2.5 wt% reproduced the mechanical response of the brain tissue to cutting.[6] Different compositions have been devised that closely reproduce the mechanical properties of other organs such as the lungs and liver.[13]

In addition to its primary application as a realistic surgical phantom,[6] the model brain can be used as an engaging demonstration tool. Here we outline a two-part demonstration using slightly different PVA-PHY composite hydrogels. In the first part, we produce a life-sized phantom of a human brain that students can touch and manipulate. In the second part, we show how the composite hydrogel can be used for mock brain surgery with a simulated tumour. The composite hydrogel is inexpensive, simple to prepare, and its constitutive components are widely available, biocompatible, and non-toxic. The demonstrations complement recent suggestions for applications of hydrogels[3,14,15] and other environment-sensitive polymers[16,17] in chemical education. The main purposes of these demonstrations are:

1. To provide evidence that our brains are much softer and more fragile than most people expect.
2. To enable students to touch, manipulate, and perform mock brain surgery on realistic synthetic brain tissue.
3. To show how the mechanical properties of a material are determined by the molecules from which they are made.
4. To show how chemistry can be used to convert a common household material (PVA glue) into a useful functional material.

Pre-Demonstration

The Materials

PVA (146,000-186,000 g mol^{-1}, CAS: 9002-89-5), PHY (CAS: 71010-52-1), and deionised water were supplied by Sigma-Aldrich UK. Red or pink food dye was used to colour the composite hydrogel. For the negative brain mould required for the first demonstration, we used CS2 silicone rubber from Easy Composites Ltd. UK. For the second demonstration, glitter pompom balls (25 mm diameter) purchased from Amazon UK were used as simulated tumours.

For these demonstrations, we use slightly different blend compositions to those in our previous study.[6] For the life-sized brain phantom, we use 5.0 wt.% PVA and 0.7 wt.% PHY, which still matches the stiffness of brain but is much tougher so that it lasts longer during hands-on demonstrations. For the surgical training demonstration, we use 2.5 wt.% PVA and 1.1 wt.% PHY since this composition more closely mimics the surgical cutting and penetration forces of brain.[6]

General Procedure

The procedure consists of three stages; preparing the composite hydrogel, casting the life-sized brain phantom, and casting the surgical training phantom. To make the composite hydrogel, PVA and PHY powders were added to separate solutions of deionised water in two different conical flasks of suitable size. A magnetic stirrer bar was placed inside each flask. The two separate solutions were heated to 90 ^{o}C under constant stirring using a magnetic stirrer hot plate until the PVA and PHY powders were completely dissolved (approx. 60 min), resulting in completely transparent solutions.[6] Care was taken to avoid excessive evaporation during the process; if using a conical flask, the screw cap should be loosely fitted and if using an open flask, aluminium foil should be fitted to cover the flask opening. The two solutions were then mixed together in a single flask (1:1 weight ratio) and stirred at 70 ^{o}C for 30 min. The masses required for each constituent material are shown in Table 1.

Table 1. Calculated weights for composite hydrogel constituents of the two different compositions

Composition	**Total solution weight (g)**	**PVA powder weight (g)**	**DI water weight for PVA (g)**	**PHY powder weight (g)**	**DI water weight for PHY (g)**
5.0 wt% PVA 0.6 wt% PHY For life-sized brain mould	1400.0	35.0	665.0	4.2	695.8
2.5 wt% PVA 1.1 wt% PHY For surgical training	500.0	6.2	243.8	2.8	247.2

To make the life-sized brain phantom, the 5.0 wt% PVA 0.6 wt% PHY solution was poured into the silicone mould and allowed to cool down to room temperature (approx. 30 min). Further guidance on how to obtain a reusable life-sized brain mould can be found in the Supplementary Information.

To make the phantom for the surgical training demonstration, the 2.5 wt% PVA 1.1 wt% PHY solution was poured into a clear plastic container of > 500 mL capacity. The glitter pompoms (approx. 16 for every 500 g of solution), used to simulate tumours for resection, were placed inside the solution and lightly pressed down to ensure submergence.

The composite hydrogel containers were then stored in a freezer (approx. -25 ^{o}C) for 18 h and subsequently thawed at room temperature for 6 h before the demonstration. The frozen life-sized brain phantom should be placed into a 60 L clear glass fishbowl and tap water should be added until fully submerged. The demonstration may begin when the composite hydrogels are fully thawed. The hydrogel will remain fresh for up to 3 days after thawing when stored in a refrigerator at < 4 °C. We recommend that the preparation should begin 2-3 days before the demonstration to give the frozen hydrogel sufficient time to fully thaw.

The Demonstration

1. Feeling a Brain

The demonstration of the life-sized brain phantom stimulates the tactile response of real brain tissue to the audience. The audience should be encouraged to take turns to lightly touch and hold the brain phantom submerged in water with their bare hands, as shown in Figure 3. Paper tissues should be provided for the public to dry their hands after participation.

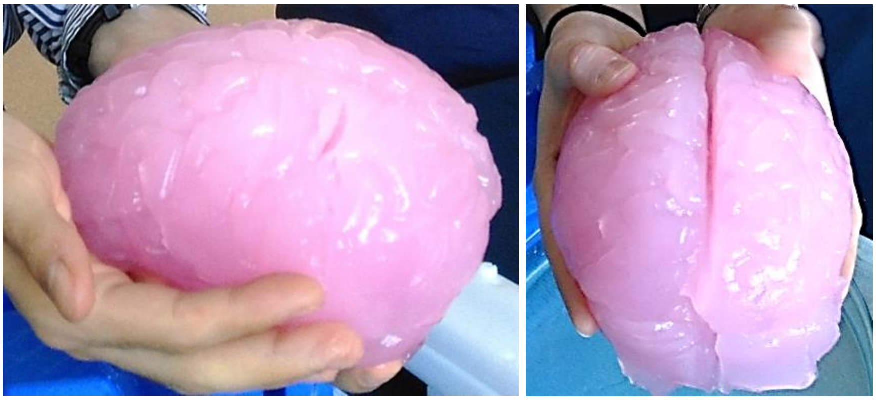


Figure 3. Experiencing what the brain feels like. CHANGE TO IMAGE OF FEELING BRAIN IN FISHBOWL

2. Cutting a Brain

The surgical training demonstration showcases how the composite hydrogel can be used to help surgical trainees practise dexterity and gain familiarity with the delicate forces required during open operations. In particular, participants can practice resecting tumours from highly sensitive anatomical regions of the body. The aim for the participants is to use mock surgical tools such as tweezers, small nail scissors, and safety scalpels to remove the mock tumours that were cast-moulded into the tissue phantom, as shown in Figure 4. Participants should be encouraged to cause the 'least damage' to the surrounding material that is mimicking the brain. Surgical gloves can be provided for the participants to more closely mimic a surgical scenario, although this is not necessary since the hydrogel is not hazardous.

Figure 4. Surgical training using a brain phantom.

Hazards

PVA and PHY are not classified as hazardous substances, although normal lab practice should be followed. All solutions can be disposed of down the sink. The solid hydrogel material can be disposed of as general waste. If broken, the brain material may represent choking hazard. The tools for the second demonstration (e.g. scissors) are sharp and should be used with care.

Results

This demonstration was originally developed and performed at outreach events at Imperial College London. It has since been implemented at schools, universities, and outreach events across Europe by the Enhanced Delivery Ecosystem for Neurosurgery in 2020 (EDEN2020) consortia. These events include; *New Scientist Live* (ExCeL, London, UK), *European Researchers' Night* (Natural History Museum, London, UK), *Great Exhibition Road Festival* (London, UK), *Natural History Museum Lates* (London, UK), *Maker Faire Rome* (Rome, Italy), and *Meet me Tonight* (Milan, Italy). Some examples are shown in Figure 5. Tens of thousands of students, parents, and teachers have viewed the demonstration at these events. This demonstration has prompted thoughtful and engaging discussion about the underlying science of the demonstration as well as the work that the presenters do as scientists and engineers.

Figure 5. Demonstration of composite hydrogel brain at New Scientist Live 2019 at ExCel London (left) and European Researchers' Night 2019 at the Natural History Museum (right).

Summary and Perspectives

The two-part demonstration detailed in this contribution involves a polymeric material whose mechanical properties mimic that of the brain and can therefore be used as a surgical training tool. This demonstration provides a unique first-hand and tactile experience for a wide range of audiences. The primary aim is to educate young students in basic polymer science and engineering and show them how these everyday materials are usefully applied in real life situations to inspire them to pursue further studies in STEM fields. The demonstration can be easily scaled up for larger classes and events by simply making larger volumes of the hydrogel used in the surgical training application. Furthermore, the procedure may be appropriately modified to become a brain phantom for testing robotic surgical tools or a medical surgical training tool by embedding a secondary hydrogel mass, dyed a different colour for example, inside the life-sized brain phantom to more accurately mimic a tumoral mass. Therefore, there is an extensive scope of impact that can be achieved by utilising the composite hydrogel material as a mechanically accurate, cost effective and easily procurable presentation tool during brain mimicking demonstrations.

The team is currently working on the design of a dynamic lung phantom as training tool for lung surgeries and educational purposes, which can reproduce the respiratory cycle and the organ deformations realistically, besides mimicking lung tissue's stiffness.

Supporting Information

A detailed description on how to obtain or create a life-sized brain mould. File to 3D-print brain for negative mould. Videos showing the two demonstrations.

Acknowledgements

Demonstration

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