University of Sheffield | Materials - a SUBJECT that MATTERs

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Biomaterials

Modelling Brain Tissue

What is Materials Science and Engineering (MSE)?

MSE is defined as an ‘interdisciplinary subject, bridging the physics and chemistry of matter towards engineering applications and industrial manufacturing processes.’ The programme content spans from foundations in physics and chemistry to the mechanical, electrical, magnetic, and optical properties of materials, and the design, manufacture and applications of metals, alloys, ceramics, polymers, composites, and biomaterials.

MSE continues to establish itself amongst engineering disciplines and is offered as a degree course across the UK at the Universities of Birmingham, Cambridge, Imperial College London, Leeds, Loughborough, Manchester, Oxford, Queen Mary, Sheffield and Swansea, as well as Materials Chemistry being offered at St Andrews and Glasgow.

Key Learning outcomes

Brain cancer is particularly hard to treat and research resulting in extremely low survival rates…

The brain is an extremely complex environment- one which is difficult to replicate.

Glioblastoma brain tumours are physically located within the skull and surrounded by important normal brain tissue, making tumours difficult to access and remove. Even small increases in tumour size can have serious effects on cognitive function or patient survival. Treatment must therefore happen quickly, and effectively with little margin for error.

Tumours in other parts of the body usually have a clear margin of normal tissue surrounding them which can be removed alongside the tumour, making complete tumour removal more likely. This is generally not feasible for the brain, where the tumour will be surrounded by delicate brain tissue meaning risks to cognitive function and immediate patient survival must be considered. Further to this, 'stem' like glioblastoma cells that are then often left in this tumour margin can then lead to tumours reforming.

Read on to find out about why the 'Blood-Brain barrier also causes complications.

Key Learning outcomes

New materials are being designed that can be used to test drugs for the treatment of brain cancer and glioblastoma.

A way of accelerating research and treatment is through creating new materials that can be used to allow glioblastoma cancer cells to be grown in the lab. These materials should be able to be easily used by lab workers in clinical settings whilst still re-creating an environment that allows the cells being tested to mimic and behave as they would in a true living tissue (in this case the brain).

This will enable treatments to be accurately and efficiently tested to allow researchers to be able to quickly conclude whether the drug would reliably work against the tumour, and allow for personalised treatments specific to each patient.

To create these new materials, the brain tissue and its mechanical properties must be understood because cell behaviour is influenced by the stiffness of the environment it is found in. This is likely to be of high importance in the brain because the brain tissue is very soft.

GCSE Chemistry topics this episode could be taught alongside…

Bonds Structure and Properties of matter

Giant covalent molecules…

Graphene and fullerene (Link their honeycomb structure to that of the materials being researched) This is at a very different scale.

Materials Properties (relate to materials properties of brain tissue, it is very soft tissue)

GCSE Biology topics this episode could be taught alongside…

Cell Biology…

- Eukaryotes and prokaryotes
- Specialisation and differentiation
- Microscopy
- Stem cells

Principles of organisation (Cancer)

How does this episode go beyond the curriculum?

Materials properties of the brain- Brain tissue is **viscoelastic.**

Many materials exhibit viscoelastic properties, ranging from natural biological structures such as tissue, cartilage, and skin, to synthetic polymers and concrete.

Viscoelastic materials have both viscous and elastic properties meaning they can behave like a solid and a liquid.

Viscosity describes a fluid's resistance to flow. The higher the viscosity, the greater the force needed to generate a specific flow.

Viscoelastic materials can behave predominantly as viscous or predominantly as elastic depending on the size and rate of the applied shear stress. For example, toothpaste behaves as a viscous material when squeezed out from the tube but is mostly elastic when at rest on the toothbrush for it not to run off!

The Blood-Brain Barrier

The brain is taught at GCSE when learning about coordination and control. The brain is one of the most critical organs and our bodies have evolved to protect it from damage.

The brain is **protected from physical injury** by being surrounded by the skull, protective fluid (cerebrospinal – of the brain and spine) and a protective membrane called the meninges.

The brain also has a **‘blood–brain barrier’** which is talked about in this episode. This barrier between the brain’s capillaries (blood vessels), cells and other components that make up the brain, doesn’t provide protection against physical damage but provides a defence against disease-causing **pathogens and toxins** present in the blood.

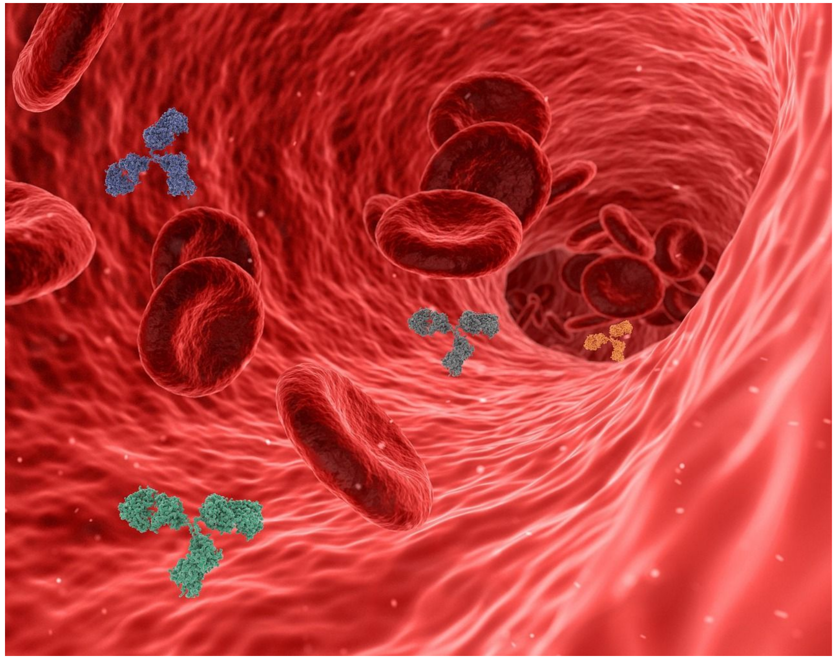
The key structure of the blood–brain barrier that creates the barrier preventing harmful pathogens entering the brain is the referred to as the **‘endothelial tight junction’.**

Endothelial cells line the interior of all blood vessels. In the capillaries that form the blood–brain barrier, endothelial cells are wedged extremely close to each other, forming the tight junctions.

The **tight gap** only allows selective molecules, and some gases to pass freely through the barrier into the brain tissue. Molecules, such as glucose, which are too big to fit through the gap can only pass through the barrier if they are bound to transporter proteins (these act like special doors that open only for certain molecules).

There are other components of the blood–brain barrier surrounding the endothelial cells that don’t prevent things entering the brain, but that communicate with the cells that form the barrier to monitor how much is allowed to pass through.

Alongside protection, the barrier also helps maintain **vascular homeostasis**, where levels of hormones, nutrients, and water are kept relatively constant in the brain. The brain environment is complex and so fluctuations in these components could disrupt functioning.



Key definitions

Glioblastoma

A fast-growing, aggressive brain tumour.

Glioblastoma is a type of cancer that starts as a growth of cells in the brain or spinal cord.

It starts in cells called astrocytes that support nerve cells, growing quickly to invade and destroy healthy tissue.

Tissue Engineering

A field of biomedical engineering where living tissue can be produced outside of the body through materials development, biochemical manipulations, cell culture, and genetic engineering.

The goal is often to construct functional replicas that restore, maintain, or improve damaged tissues or whole organs.

Chemotherapy drugs

Cancer treatment that stops the growth of cancer cells, either by killing the cells or by stopping them from dividing, preventing them from growing and spreading in the body.

There are many different types but they all work in a similar way.

However, they can also affect healthy cells in the process which leads to side effects.

Stem Cells

Stem cells are cells that have not undergone differentiation.

A cell which has not yet become specialised is called undifferentiated and so can differentiate to form many different types of cells. Stem cells from human embryos and adult bone marrow can be cloned and made to differentiate into different cells, e.g., nerve cells.

Endothelial Tight Junction

The seal between two cells in the epithelial membrane providing a semipermeable barrier to ions and solutes.

They act to regulate the transport of water, ions, and molecules, serving as an important barrier in blood vessels and maintaining vascular homeostasis.

PolyHIPE (Poly High Internal Phase Emulsions)

PolyHIPEs are emulsion templated porous polymers.

This means they are a synthetic highly porous material prepared by the polymerization of high internal phase emulsions.

Put simply- they often look like honeycomb-like the inside of a malteaser!

Questions to think about

What are the materials properties of the brain?

Imagine the consistency of blancmange!

- Soft
- low stiffness
- low linear viscoelastic strain limit
- strain-rate sensitive (increasing stiffness with increasing strain rate)

Why do we not want to grow cells on a flat surface? What type of materials do we want to use to grow our cells on instead?

Growing cells on a flat surface results in a different drug response to what would be observed in a patient.

We want to use a polyHIPE material that changes the behaviour of the cells, so we can test chemotherapy drugs and obtain better data that is accurately related to patients.

We currently use polystyrene for this but it is still a basic and stiff material. We therefore want to develop new materials for this purpose, for example a gelmer or collagen based material which is softer.

Discussion Topic…

Why does the blood-brain-barrier create a challenge for research?

The blood–brain barrier is very effective at preventing unwanted substances from accessing the brain, and as learnt in the episode, this creates a challenge for research. Most potential drug treatments are unable to naturally pass through the barrier which makes disorders difficult to treat.

One possible way around the problem is to “trick” the blood–brain barrier into allowing the drug to pass through. This is done using the same method that is used for the transportation of larger molecules across the barrier, where the drug is bound to a molecule that can passes through the barrier via a transporter protein.

Discussion Topic…

Why is it not possible to conduct research using real living systems such as mice?

- It is unethical or deemed 'cruel'.
- There are other methods to carry out medical research.
- Their immune system does not reliably replicate a human immune system.
- Could produce misleading safety and efficacy data.
- 9/10 drugs that appear promising in animal studies go on to fail in human clinical trials. There are more efficient ways of conducting scientific research. [1]

Additional Resources

Cancer Research video: Brain Tumour Facts
https://www.youtube.com/watch?v=fVWw2m6hx44

Nature Communications Article: brain tissue Biomaterials that might be helpful
https://www.nature.com/articles/s41467-020-17245-x

STEM learning- 'Exploring tissue engineering' resources
https://www.stem.org.uk/resources/community/collection/515068/catalyst-magazine-live-exploring-tissue-engineering-teacher

REFERENCED FACTS

[1]https://aavs.org/animals-science/problems-animal-research/#:~:text=Nine%20Out%20of%20Ten%20Drugs,end%20up%20failing%20in%20humans.