MATHEMATICS MATTERS

Tissue Engineering

We are all living longer. An ageing population means that the number of organ donors required is steadily increasing. However, a lower mortality rate also means there are fewer donor organs available. Scientists are trying to grow replacement organs in the laboratory and mathematics is playing a key role.

Imagine a world where if one of your organs is failing, a laboratory grown replica is ready to replace it. No more long waits on transplant lists and no need to altruistically leave your organs for others to use when you die. The threat of your body rejecting the tissue would also be greatly reduced. That's the dream for scientists and mathematicians working in the field of tissue engineering, a branch of regenerative medicine.

It's not a pipe dream either – they are already making headway. Functional, living heart valves have already been inserted into patients. The valves are biological, rather than artificial, they can grow and repair themselves just like normal heart valves. The same technology has also been applied to replacement tracheas (windpipes). Mathematics has played a fundamental role in ensuring the technique has come this far, and it continues to underpin the technology as it becomes ever more complex.

There are two ways such tissue can be grown, either in-vivo or in-vitro. Either inside the body, or outside. With the former, cells are inserted into the body and form new tissue by themselves using the body's available resources. However, this technique can be harder to experiment with in order to optimise the procedure. The alternative is to grow entire organs in the laboratory which can later be implanted into the patient.

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In order to grow an in-vitro replacement, scientists place tissue cells onto a 3D scaffold often made of porous biomaterial (similar in appearance to a pumice stone). This acts as a sort of skeleton around which the cells can grow. The scaffold is designed in such a way that it deteriorates as the cells grow, leaving behind a purely biological entity. This combination of cells and scaffold is called a construct. The construct is placed into a bioreactor – a device through which fluid is passed to provide the cells with the right nutrients and growth factors with which to thrive. The goal is to accurately mimic the way that the capillary system inside our bodies delivers this food naturally to our cells. And that's where the maths comes in.

Understanding how the fluid flows through the bioreactor is the key to creating the optimum set up. In principle, scientists could do this experimentally by testing all possible ways of delivering the fluid. However, these biological systems are so complex that it would be prohibitively expensive and time consuming to exhaust all the possibilities.

Institute of mathematics & its applications

By mathematically modelling the fluid flow instead, mathematicians can predict how the nutrients will be distributed. By creating a set of equations which relate the flow rate to the distribution of nutrients, mathematicians can give the biologists a much smaller range of possible alternatives that are likely to yield the most positive results.

Part of this work involves working with the equations of Darcy flow – those which describe the motion of a fluid through a porous material. They relate the amount of liquid flowing through the material to changes in pressure within the system. This mathematics is most often used in geology when modelling water flowing through sand or soil, but biological systems are harder to model because living things are more complex as they are constantly changing over time. The rate at which fluid flows through the construct affects how the cells grow, which in turn changes its porosity. This creates changes in pressure, which in turn affects the way the fluid flows and then again the way the cells grow. It can be a vicious cycle and modelling it mathematically is a challenge. It is also important to know how the waste products produced by the cells are transported. If they build up in sufficient concentrations they could inhibit further cell growth.

There are certain physical rules that can provide a leg-up. For example, two physical properties - mass and momentum - must always be conserved. That allows mathematicians to begin to write down some basic equations to try to encapsulate the essence of what is going on. The results of this basic model can then be compared to data coming from the lab. New terms (or other revisions) are added or taken away from the model to see if they improve the situation. If they do, the model is run again and iterations continue. If not, another alternative is tried. The ultimate goal is to optimise the way nutrients are distributed and limit the damaging effect of waste products. Knowing how this distribution depends on flow really helps.

This work is incredibly important. Fewer than 5,000 people die each year in a way that means they can become suitable organ donors. Yet more than 10,000 people are currently in urgent need of a new organ. On average a British adult has to wait more than 1,000 days for a new kidney and over a year for a new heart. By applying mathematics to the problem of creating replacement organs for those in need, we are inching closer to a day when organ donation is a thing of the past.

TECHNICAL SUPPLEMENT

Darcy Flow

Darcy's Law was originally derived through experiment by French engineer Henry Darcy (1803-1858). It is an expression of the conservation of momentum, and so was later derived directly from the Navier-Stokes equations which are in turn derived from Isaac Newton's Second Law of Motion.

It relates the volume flowing per unit time to the intrinsic permeability of the porous medium, the viscosity of the fluid and the pressure gradient. It is only valid for slow viscous flow – it seems to hold for any fluid with a Reynolds number less than ten.

References

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