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Using plastics in the body

Above: A scanning electron microscopy image showing large numbers of Staphylococcus aureus bacteria, which were found on a catheter. A catheter is a tube inserted into the body (often the bladder) to remove a fluid. The sticky-looking substance woven between the round bacteria is known as biofilm. This biofilm has been found to protect the bacteria from attacks by antibiotics. Research at Nottingham is aimed at developing plastics which will not allow such biofilms to grow.

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drug delivery

Polymers can be synthetic or natural, including polystyrene and acrylic; cotton, DNA and proteins. They are large, chain-like molecules that consist of many repeating subunits called monomers. The chemical composition of the monomers and the way that they are linked influence the polymer properties. This makes plastics very useful for medical applications since both the physical and chemical properties can be modified by changing the repeat unit, introducing combinations of different repeating units or changing the polymer length to suit the material's intended purpose.

Medical implants

Polymers have been used in medicine for several decades now as parts of artificial medical implants. One of the most widely used plastics today is polyethylene, used to make bottles, shopping bags, water pipes and toys. The same material, with longer chain length, is also used to make the weight-bearing surface of artificial knee implants as shown in ***Figure 1***. Polyethylene has an exceptionally low rate of wear, which means that these implants can last 30 years or more.

Figure 1 *A knee implant with a polyethylene articulating surface (white component) between the femoral (upper leg bone) and the tibial (lower leg bone) components*

Figure 2 *A replacement tri-leaflet heart valve made of various polymers. The leaflet is made of polyurethane whilst the frame of the heart valve is made of polyetheretherketone. The aortic valve is the gate between the main pumping chamber of the heart, the left ventricle, and the main artery of the body, the aorta. The aortic valve is able to open and close because it has leaflets (cusps). In a normal aortic valve there are three leaflets, and because of this it is called tri-leaflet.*

At present, polymers are used for medical products as diverse as catheters, replacement heart valves (***Figure 2***), artificial lenses to treat cataracts and sutures for stitches. Some products need polymers with specific properties such as good mechanical performance and biocompatibility or degradability.

At the University of Nottingham, we are researching using polymers in three different ways for medical purposes: polymer implants that aid bone repair; creating antibacterial surfaces for devices to prevent infections; and improving the delivery of medicines in the body.

Mending bones

We are developing new degradable plastic materials for the next generation of medical implants, with a focus on treating bone fractures. Our bones have the natural ability to regrow and repair when they break but sometimes we need implants such as bone plates to hold badly fractured bones in a fixed position to guide and support the healing process. The material used to make these bone plates must sustain the loads typically placed on bones and not cause any allergic reactions.

Currently, bone plates and screws are usually made of metal. However, metals are significantly stiffer than bone and tend to take the daily stresses that are placed on the bone as it heals. This can lead to porous and weak bones. The advantage of polymers over metals is that their stiffness is closer to that of bones, enabling the bone to recover to its original strength. Our new degradable polymer material aims to provide support to bones as they heal and then gradually dissolve within the body over the healing period. The degradable polymers break down into monomer units that are not harmful to the body. This means there will be no need for a further surgical procedure (operation) to remove the support after the fracture has healed.

Stopping infection

An important issue with any implant or medical device is the risk of developing a bacterial infection. The materials used to make medical devices have excellent mechanical properties, so they flex or provide support as required. However, these same materials are often very poor at preventing bacteria from attaching to them. This is particularly problematic, since bacteria can form biofilms when they attach to a surface (***Figure 3***). These ‘slime cities’ are communities of bacteria commonly associated with infections that provide protection for bacteria, making them up to 1000 times more resistant to the immune system and antibiotics.

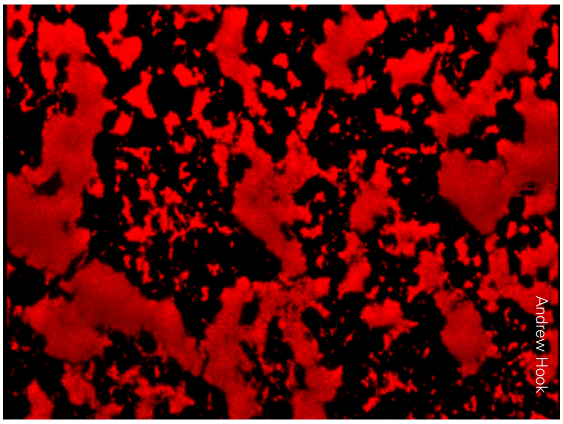

Figure 3 *A microscopy image of a bacterial biofilm; image dimensions are 640´640 micrometres.*

We are developing new polymer coatings that can be applied to current medical devices to prevent bacterial attachment and biofilm formation, leading to a reduction in device-associated infections. We needed an efficient way of finding one that would work. To do, this we and our collaborators at MIT (Massachusetts Institute of Technology) developed a chip that had thousands of very small samples of different polymers that we could use to screen an entire polymer library in a single experiment (***Figure 4***). Using this chip we successfully identified new materials that are resistant to bacterial attachment. The particular polymers that best prevented biofilm formation would not have been predicted from the current knowledge of how bacteria stick to surfaces. The polymer works by weakening the interaction that bacteria makes with a surface, which then disrupts the biofilm formation process.

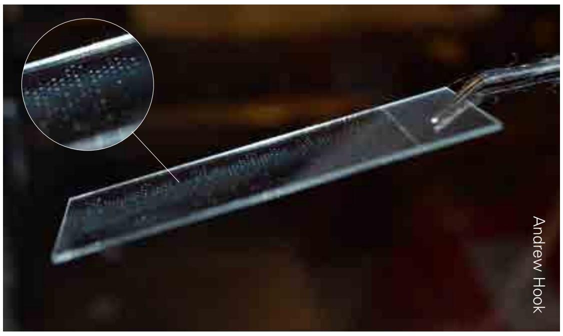

Figure 4 *This slide is the chip developed that has thousands of very small samples of different polymers that could be used to screen an entire polymer library in a single experiment. The tiny dots you see are each of the different polymers printed on as spots.*

Targeting medicines

We are also looking use polymers to improve way we administer medicines. The current typical treatments for are tablets to swallow or directly into the bloodstream. However, while the medicine itself might be very effective, these approaches can be an inaccurate way of dispensing the treatments into the body. This is due to the low control over where the medicine goes or and the uncertainty of the drug dosage in the targeted area.

Figure 5 *The author Amanda Pearce preparing a formulation of polymer nanoparticles loaded with the chemotherapeutic drug docetaxel. They are blue because they also have a fluorescent dye included for tracking by microscopy. Photo by Amanda Pearce*

Many diseases require the drugs to reach an exact location, such as a specific organ or a tumour. A patient with a tumour in their liver could receive an injection of a chemotherapy drug, which will travel throughout the entire bloodstream and may end up in the liver, but it can also end up in other organs or blood cells too. The result of this is a low dose to the tumour, which means repeat treatments are needed to deliver a high enough dose to the tumour. This can then cause severe drug side effects and make the patients even more ill.

Alternatively, we can use polymer carriers to help deliver the drugs (***Figure 5***). We first take a water-soluble and biocompatible polymer and make it into a nanoparticle – spheres around 100 to 200 nm in diameter. The nanoparticles can then be loaded up with the drugs to be delivered. This prevents the drugs from going into the rest of the body where they are not needed, therefore reducing the side effects. The nanoparticles can also be 'decorated' on their surface with targeting groups allowing specific delivery to the required location.

Summing up

Polymer physics and chemistry provide a great opportunity to develop polymers that aid our bodies to repair or replace lost function. Every day new polymers, devices and medical treatments are developed around the world in an effort to keep everyone fit and healthy!

Amanda Pearce, Andrew Hook and Gabriel Choong are scientists at the University of Nottingham. Amanda researches new polymeric materials to be used for the targeted delivery of chemotherapy and antimicrobial drugs. Andrew is developing new polymers resistant to bacterial attachment to prevent medical device associated infections. Gabriel was part of the team researching new materials to help bones to heal.