Getting stuck in

Nature produces a wide variety of glues that outperform all synthetic adhesives. Michael Gross looks into this sticky subject

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Glue is something we buy in plastic bottles or tubes, and apply to 'clean, dry surfaces'. How then do mussels and barnacles stick to the hulls of ships and to the steel structures of piers exposed to seawater? If we leave a glue container open for a couple of hours, it dries out and becomes unusable. But carnivorous plants expose glue drops to the air waiting for an insect to stick to them, remaining sticky for as long as it takes. Clearly, nature knows a lot about gluing things together that we haven't mastered yet.

Thus, it would make sense to find out more about nature's glues. But where to begin? There is a bewildering array of sticky materials in many different species of plants and animals, sharing few general principles other than being sticky. Patrick Flammang from the University of Mons, Belgium, who chairs a European collaborative project on natural adhesives – Biological adhesives: from biology to biomimetics – admits that the field is difficult to survey. 'The diversity of biological adhesives is huge,' he says, 'but at the same time it represents an opportunity to look for adhesives with novel interesting properties.'

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Sea cucumbers expel sticky spaghetti-like tubules to trap attacking organisms

Caught in a trap

Charles Darwin marvelled at the phenomena of carnivorous plants that snare insects for additional nutrition, publishing a book on them in 1875. Many of these plants use glue for this purpose, as it prevents the bugs escaping while the plant digests them.

In his book, Darwin described a plausible evolutionary path from the use of sticky leaves for defence only, via the accidental uptake of nutrients from trapped insects degraded by bacteria, to the secretion of digestive enzymes enabling the plant to 'eat' the prey. Darwin also described the first practical application of such plants – people in Portugal used them to keep houses free of insects.

Given this illustrious history, surprisingly little is known about the molecular details and mechanisms of action of the carnivorous plant glues. They can be organised into two major groups: water soluble and more fat soluble.

Several carnivorous plant families, including *Droseraceae* and *Lentibulariaceae*, produce water-based polysaccharide glue. The house plant cape sundew (*Drosera capensis*), for example, has long leaves covered in hundreds of very fine hairs, with a tiny droplet of polysaccharide solution crowning the tip of each hair. When an insect gets stuck on these, the leaf curls to enclose it from all sides, allowing for more efficient digestion. This plant's glue is a viscoelastic aqueous solution of a polysaccharide based on a repeating dimer of glucuronic acid and mannose. Other sugars including arabinose, xylose and galactose are found in its side chains and end groups. There is nothing else present in the glue before an insect gets caught, only after capture does the plant leaf secrete digestive enzymes into the fluid.

The glue from the Portuguese sundew (*Drosophyllum lusitanicum*), which Darwin obtained through contacts in Portugal and described in detail, has a similar composition and is slightly acidic as it contains ascorbic acid. It smells of honey and is strongly hygroscopic (it can collect water from fog). In a recent review article, Wolfram Adlassnig and colleagues from the University of Vienna, Austria, concluded that the glue of these species would be an interesting material for pharmaceutical applications, as 'it is non-toxic, remains stable under varying environmental conditions, and even exhibits antibiotic properties'.[1] However, other than its use for fly catching, no applied research has been reported yet.

A sticky mess

Any marine predator that approaches a sea cucumber may end up looking like they have had a nasty accident with a bowl of spaghetti. Sea cucumbers carry a bizarre defence weapon in their posterior body cavity consisting of sticky white threads, known as smooth cuverian tubules. One end of each thread is attached to the animal's respiratory tree (its lungs), while the other floats freely in the fluid that fills its body cavity, the coelomic fluid. When the animal feels threatened, it will point its backside towards the disturbance and contract its entire body. The contraction causes the spaghetti-carrying cavity to burst open, and the fluid to erupt into the cloaca (the posteria opening). The free ends of dozens of those spaghetti will be expelled via the cloaca and shot at the hapless adversary.

The animal then pumps these tubules (still connected to the respiratory tree) full of water, which extends them to a multiple of their original length. When they hit a surface (eg the suspected predator), the inflated tubes instantly develop strong adhesive properties. In the last phase of the attack, the tubes detach from the respiratory tree and the animal can take flight, leaving behind a frustrated predator tangled up in a sticky mess.

The black sea cucumber (*Holothuria forskali*) is the most studied of these animals. The material left on the trapped predators once the tubules are removed has been found to contain a mixture of 60 per cent protein and 40 per cent carbohydrates. Flammang's group has studied the amino acid composition of the protein portion and found that it is rich in glycine and other amino acids with small side chains, and in charged and polar amino acids.[2]

In short

- **Natural adhesives currently outperform all synthetic glues**
- **The wide range of natural glues share few general principles other than being sticky**
- **More fundamental research is needed before scientists can understand the secrets of their success**
- **Natural and bioinspired glues are being considered for medical applications such as surgical adhesives and diabetes treatments**

'Polar and charged amino acids are important for adhesive interactions with the surface. Different side chains (polar, positively charged and negatively charged) increase the number of possible interactions with the surface (Van-der-Waals, electrostatic etc),' explains Flammang. 'Small side chain amino acids are characteristic of the so-called elastomeric proteins, proteins that can deform considerably without breaking (eg elastin). This is important for the cohesive strength of the glue.'

While marine adhesive proteins from different groups of organisms can vary widely in their sequences, most of them share these fundamental aspects of their amino acid composition.

Unlike the adhesive plaque proteins of mussels, the protein component does not appear to contain the modified amino acid 3,4-dihydroxyphenylalanine (Dopa). However, phosphorylation of another amino acid – serine –previously observed in mussel glue and tube worm cement, is present.

Currently, Flammang's team is analysing peptide fragments of the glue proteins. The goal here is to identify the genes, allowing them to produce the pure proteins for more detailed analysis. The group has also applied sugar-binding proteins known as lectins to analyse the distribution of carbohydrates in the cuverian tubules.

There is more work to be done, and the detailed molecular structure and adhesive mechanism of the black sea cucumber glue still remains elusive.

Get it off me

While the sea cucumber is a glue producer we may want to emulate in technology, interest in other marine adhesives is directed towards the question of how to stop them from sticking to things. Organisms such as barnacles, mussels, bacteria and algae find the steel structures that humans immerse into their habitats – ship hulls and piers for example – very appealing to settle on.

This can cause significant problems. On ships, even simple slime films consisting of bacteria and diatoms (a group of algae) can increase fuel consumption by up to 15 per cent. Antifouling coatings releasing heavy metals like copper or tin had some success, but were banned due to their environmental impact. Silicone-based coatings, which should stop organisms from forming strong adhesion, such that they are washed away by water movement, have failed to stop diatom-based biofilms from growing.[3]

Nicole Poulsen and Nils Kröger from the Georgia Institute of Technology in Atlanta, US, have just launched a project to identify the glue molecules of diatoms. 'Diatom glues aren't very well characterised at the molecular level,' Kröger says. 'Lectin binding studies point to the presence of carbohydrates, and the saw-tooth fingerprints you get in force-distance plots when you stretch the material in AFM [atomic force microscopy] experiments suggest the presence of protein domains.' What exactly makes the diatoms stick and how one can stop them from doing so remains to be explored.

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Barnacles and mussels are able to stick to structures immersed in seawater

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Northern spadefoot toad 'couples' glue themselves together during mating

Sticking together

Humans may have notions that love, mortgages, children and other shared interests keep couples together, but the northern spadefoot toad (*Notaden melanoscaphus*) of northern Australia – and three other species of the same genus – play it safe, using glue to make that special bond.

These frogs (they are frogs, not toads as their name suggests) are so well-rounded that they can't cling on to each other with their short limbs during mating, like many other frog species do. Instead they use glue to stick together for the duration.

Michael Tyler from the University of Adelaide, Australia, tested the adhesive power of the northern spadefoot toad secretions by using it to stick two full, cold, wet beer cans together – lengthwise in one experiment and bottom-to-top in another. In both cases the frog glue was strong enough to carry the weight of a full can. He also found that the glue can bind glass, plastics and even 'non-stick' Teflon surfaces, no matter whether they are wet or dry, hot or cold.

Another team of Australian scientists, led by Lloyd Graham at CSIRO Molecular and Health Technologies in Sydney, found that the glue – which can be harvested from living frogs by electrical stimulation – is protein-based. It contains a range of proteins of different sizes, which are rich in

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glycine, proline, and glutamine or glutamic acid.[4]

'Having demonstrated that the glue will adhere vertebrate tissues and that it is non-toxic, the potential for this glue to be used for surgical repairs is virtually unlimited,' Tyler enthuses. 'Orthopaedic and ENT [ear, nose and throat] surgeons are very keen to be able to use this product following the success of our animal studies. To proceed we now need the collaboration of a major pharmaceutical company to underwrite the next stage of development.'

Other frog species (as with the sea cucumbers) use glue purely for defence, as Alan Cooper from the University of Glasgow, UK, experienced during his research into their foam nests (*Chemistry World*, July 2009, p40). 'Several tropical frogs exude a sticky secretion from their skin as a defence response when attacked – usually to discourage snakes and other predators. I got caught out by this once in Malaysia when I grabbed a nice looking frog – it immediately puffed itself up in my hand and exuded a sticky goo that took hours to wash off,' Cooper reminisces.

Other glue manufacturers in the animal kingdom include spiders (*Chemistry World*, December 2010, p42). Their glue, made up of glycoprotein, behaves like a viscoelastic solid. This means that the material is viscous at high extension rates, so an insect flying into the web will get stuck in it. At low extension rates, when the prey is struggling to get free, the material responds elastically, making it impossible for the insect to detach itself.

Medical adhesives

The northern spadefoot toad secretion is not the only natural glue being considered for surgical applications. The hope is that biological – or bioinspired – glues will be functional under physiological conditions, non-toxic, and ultimately biodegradable.

Biomaterials scientist Phillip Messersmith from Northwestern University at Evanston, Illinois, US, has developed a glue inspired by the chemical principles used by marine mussels. The natural process involves proteins with the modified amino acid Dopa, carrying a catechol group as a side chain. Introducing this group into the synthetic polymer polyethylene glycol, the researchers can make a biomimetic glue. Dixon Kaufman's group at the same university has successfully tested this adhesive in an animal model for a new diabetes treatment, gluing islet cells to liver surfaces.[5]

To enable more biomedical applications to benefit from the natural variety of glues, more fundamental research is still needed. 'It is certainly true that there is limited molecular understanding of natural adhesive systems and that this impedes efforts to mimic biological adhesives,' says Messersmith. 'Each organism has its own features and peculiarities, evolved under very strict environmental conditions – therefore it is difficult to make generalisations across species. Even "simple" biological adhesive systems are exceedingly complex and may require years of research to understand sufficiently to allow for mimicry.'

Byssal threads from a mussel inspired the development of a medical adhesive

'Even "simple" biological adhesives may require years of research to understand sufficiently to allow for mimicry'

A team effort to improve fundamental knowledge, with the ultimate aim of bringing innovative bioinspired adhesives to market, is exactly what Flammang is hoping to achieve with his project. 'Our goal is fostering collaboration across disciplines, which is important in order to develop biomimetic adhesives for various applications,' he says.

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References

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