

# Bacteria can be made to spin spider silk

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Biological and medical research is on the threshold of a new era based on better understanding of how large organic molecules bind together and recognise each other. There is great potential for exploiting the molecular docking processes that are commonplace in all organisms to develop new drugs that act more specifically without adverse side effects, and construct novel materials by mimicking nature.

A recent workshop on Biosupramolecular Chemistry organised by the European Science Foundation (ESF) strengthened Europe's platform for progress towards these goals by bringing together scientists in the relevant fields and identifying key research targets. The workshop also identified some applications close to fruition, including the engineering of bacteria to produce silks as strong for their thickness as spider webs.

It has been a longstanding challenge to emulate the mechanical properties of spider silk, which combines stiffness and tensile strength with the ability to become elastic under high strains to protect against destruction. A recent project led by Thomas Scheibel at the Technical University of Munich is close to a solution that could have a host of practical applications ranging from biodegradable fishing line to body armour.

The artificial spider silk production exemplified the expertise and skills required for successful applications in biosupramolecular chemistry, in this case by combining genetic engineering with sophisticated micro-manipulation techniques to optimise production of the desired material. Firstly genes were inserted into the bacteria to produce proteins as

similar as possible to spider silk. Then microfluidic approaches, dealing with fluids at very small scales, were used to fabricate the silk. Finally the mechanical properties were optimised further by substituting some of the amino acid components of the proteins.

Other applications of biosupramolecular chemistry are further off, but coming into range, according to the ESF workshop convenor, Professor Anthony Davis from Bristol University in the UK. But the most important aspect of the ESF workshop was the bringing together of scientists in two previously distinct fields, said Davis. “Our main aim was to get two groups of scientists talking to each other - the supramolecular chemists, and a group of biologists who might be termed ‘biomolecular engineers’,” said Davis. “Certainly this objective was fulfilled.” Supramolecular chemists study and manipulate the interactions between molecules in general, while biomolecular engineers specialise in exploiting the large organic molecules found in Nature.

Biological macromolecules include proteins comprising amino acids, complex carbohydrates made from simpler sugar molecules, as well as both RNA and DNA made from nucleic acids. Unlike small molecules, these large constructions exhibit multiple chemical properties at different parts of their surface, which means that interactions between them depend on geometrical features. It is the geometrical arrangement of the component parts, as much as their chemical identity, that determines how a macromolecule will behave and interact with other molecules both large and small. Some molecules will only react or bind with certain others, often temporarily, on a “lock and key” basis determined by the relative shapes of the surface. Such transient associations between large molecules (supramolecules) are very important in biology, for example in the binding between antibodies and antigens in the immune response, and also between an enzyme and its substrate, i.e. the compound it is acting upon.

These looser interactions between large molecules are called non-covalent because they do not involve sharing of electrons, but instead exploit variations in electrical charge distribution in their vicinity. Since each individual bond is weak, non-covalent bonding relies on the collective strength of multiple bonds and is therefore only a viable mechanism for joining larger molecules together.

As well as being important for temporary binding, non-covalent bonding forces are also essential for maintaining the structure of large proteins, and for the DNA double helix, on a longer term basis, by holding the components together. This is a very complex subject given the huge number of combinations of components involved, and so a significant advance reported at the ESF Biosupramolecular conference by Andrei Lupas from the Max Planck Institute for Developmental Biology in Germany was of a dictionary representing proteins by motifs, that is smaller coherent arrangements of its constituent amino acids, derived from studying their evolutionary history. Lupas showed how such a dictionary could be used to derive evolutionary relationships between proteins. This could have great application in evolutionary biology and also for determining the role of proteins whose function is as yet largely unknown, as well as understanding diseases where protein interactions go wrong.

Having identified many promising avenues of research, the ESF workshop is likely to be followed up by further meetings, according to Davis. "We hope to organise another meeting in 2009, and maybe keep going to create a regular series of symposia."

Source: European Science Foundation

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