Designing & Manipulating Molecules for Tissue Engineering & Regenerative Medicine, 21-4-17

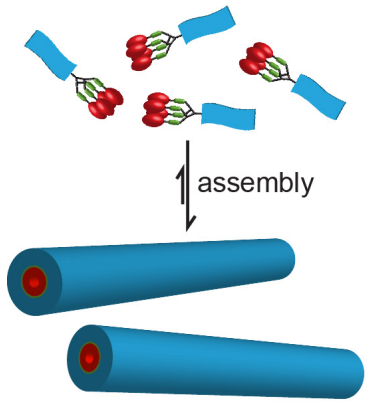
Professor Alvaro Mata first showed a picture of a salamander – an animal which can regrow a limb if need be. A range of simpler animals can do this - humans can cope with cuts and bruises.

Nature has surprising examples of material properties: the leaf of a lotus growing in the murkiest water is self-cleaning – it is super hydrophobic. A gecko can move across the underside of a leaf – it has myriad hairs on its feet which form hydrogen bonds (Van de Waals forces) with the leaf - the combined bonding being sufficient to take its weight.

A range of materials can be used for engineering tissue, both liquid and solid. Closing up wounds with sutures has been practiced for thousands of years. Metal inserts - gold and silver for instance, even glass – have been used. In the mid-20th century procedures had advanced to be able to develop biocompatible materials such as metal alloys, cellulose, polymethyl methacrylate, hydroxy-apetite, high strength polythene, nylon, and silicone – used for artificial hips etc.

Since then procedures have advanced from a 'boxing glove' level to being able to make macroscopic functional units. Molecular level materials can be produced, which can be bioactive, even smart - there are degradable polymer and hydrogel materials. Proteins are of nanometre dimensions, cells are micrometre, and tissues millimetre.

Peptide Amphiphiles (PA) are molecules made up of a hydrophilic end, a central section of sheet forming amino acids and a hydrophobic end; all fully biodegradable. In an aqueous solution the molecules self-assemble into nanofibers – the hydrophilic ends on the outside, the hydrophobic ends at the centre, with the central section forming hydrogen bonds to hold the assembly together. With a 4nm long PA, an 8nm diameter fibre is formed. The double arrow in the diagram shows that assembly is highly favoured over disassembly.



The outer end of the fibre presents a high concentration of the hydrophilic agent to the surroundings – very advantageous when the agent is a protein that is difficult to make/extract (and not necessarily one of the 20 proteins in the body, though one has to be careful not to cause rejection). The agent can be considered as a therapeutic bio-implant.

The outer end of the molecule may itself be a biologically active agent, or be combined with one. It can be designed to have positive, zero or negative charge, and to be sensitive to temperature, ph, or light – affecting the conditions under which self-assembly takes place – and whether a concentration of PA fibres assemble into a matrix.

A matrix can hold molecules, or even cells, ready for use by the body in an extra-cellular environment. For instance, bone marrow cells to support the formation of cartilage, bone etc. A small cranial hole in a rat has been bridged by this means.

Elastin is made of disordered protein, and allows tissue membranes in the body to resume their shape after stretching or contracting. At a PA interface with a solution of elastin like proteins (ELP) a membrane is spontaneously formed – depending the geometry of the equipment the membrane can form a tube or a balloon. Such tubes can be grown to useful lengths, and to have branches. Such elastin tubes, though not very strong are robust, and bring the possibility of engineering vessels and capillaries. Not to replace bodily tissues but to enable laboratory testing of drugs with a patient's fluids to ensure compatibility. This is particularly applicable to avoid disturbing the blood/brain barrier – or the membrane around an embryo.

Professor Mata closed by saying that this field of work is still young. Models for simulation and prediction are being improved, the uses of PAs are being developed and the range of uses extended. Artificial cells are being investigated.