Research Activities

My research extends across many fields within the theme of Soft Matter, in particular in the areas of peptide biomaterials and self-assembling copolymers. This work is truly interdisciplinary, and is conducted in collaboration with biologists and biochemists, physicists, chemical engineers and materials scientists.

The following brief summary gives a few examples of current activities and is not exhaustive. A full (reasonably up-to-date. usually!) list of publications (currently more than 300, h-index = 51) is provided on my webpage. This summary was prepared in Dec 2013.
Also, space does not allow a full list of our extensive range of national and international collaborations, which currently includes groups in Brazil, Finland, India, Israel, Italy, Spain, Switzerland, US.
We are regular users of central facilities for X-ray and neutron scattering experiments including DESY, Diamond, ELETTRA, ESRF, ILL, ISIS, MaxLab, SOLEIL.

(i) ***Peptide and Peptide Copolymer Self-Assembly***. We have projects on several classes of peptide and peptide conjugate including surfactant-like peptides, lipopeptides (peptide amphiphiles), polymer-peptide conjugates amyloid peptides. Surfactant-like peptides have potential applications in biomedicine including use as antimicrobial materials, which has been the subject of recent research. Amyloid fibril formation is responsible for/symptomatic of diseases including Alzheimer's, type II diabetes, BSE etc. We are investigating self-assembly of amyloid beta peptide fragments and conjugates of this to PEG.[1] We developed molecules that can bind to amyloid fibrils and disrupt fibrillisation.[2] The peptides and peptide conjugates are synthesized using an automated peptide synthesizer in our labs and characterized by multiple techniques including circular dichroism, FTIR and light scattering in our labs. We are also particularly interested in the self-assembly of peptide nanotubes, and

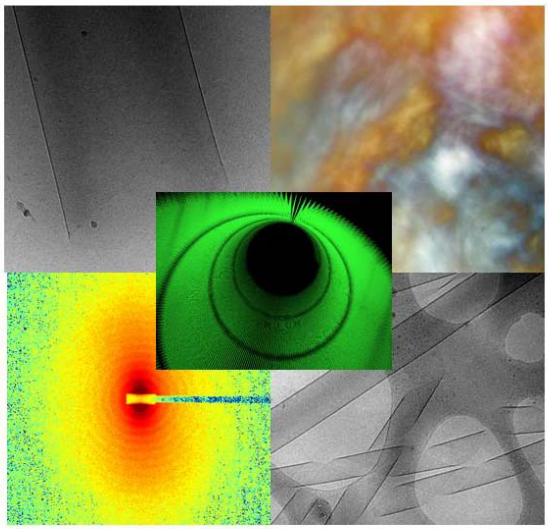

Fig.1 Peptide Nanotubes.

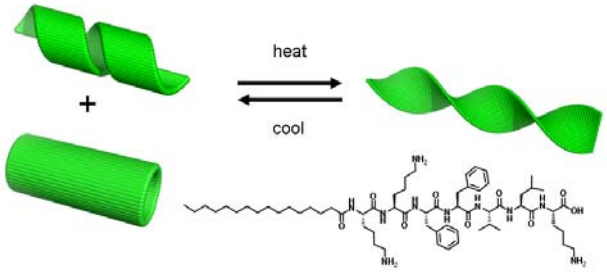

Fig.2. Schematic of thermo-reversible transition observed for the lipopeptide C_{16}-KKFFVLK.

their applications (Fig.1).[3] Fig.2 illustrates one recent example showing a thermo-reversible morphology transition observed for a lipopeptide containing an amyloid β peptide sequence.[4] This lipopeptide also exhibits enzyme-responsive self-assembly behaviour[5] and the development of enzyme-responsive functional biomaterials is another theme of our research.[6]
The self-assembly of natural bacterially-expressed lipopeptides incorporating cyclic peptides that show promising anti-microbial and anti-viral applications has recently been examined.[7]

(ii) ***Polymer/Peptide Conjugates***. In a series of recent papers, we have systematically investigated several aspects of the self-assembly of amyloid-PEG (poly(ethylene glycol) conjugates. This includes a study of the influence of PEG molar mass on self-assembly behaviour (see Fig.3 for an example of how the nanostructure can be tuned by changing PEG molar mass).[5] In other work we have uncovered novel lyotropic liquid crystal phase behaviour.[8-10] We also uncovered the mechanism by which PEG crystallization can be hindered by peptide fibrillization, depending on amyloid peptide fibrillization capacity.[11, 12] Another aspect of this research involves examination of bioactivity – examples include enzyme responsive materials[6] and conjugates incorporating cell adhesion motifs for tissue engineering[13] (see also next section). We have also investigated block copolymer micelles and vesicles as systems for drug delivery applications.

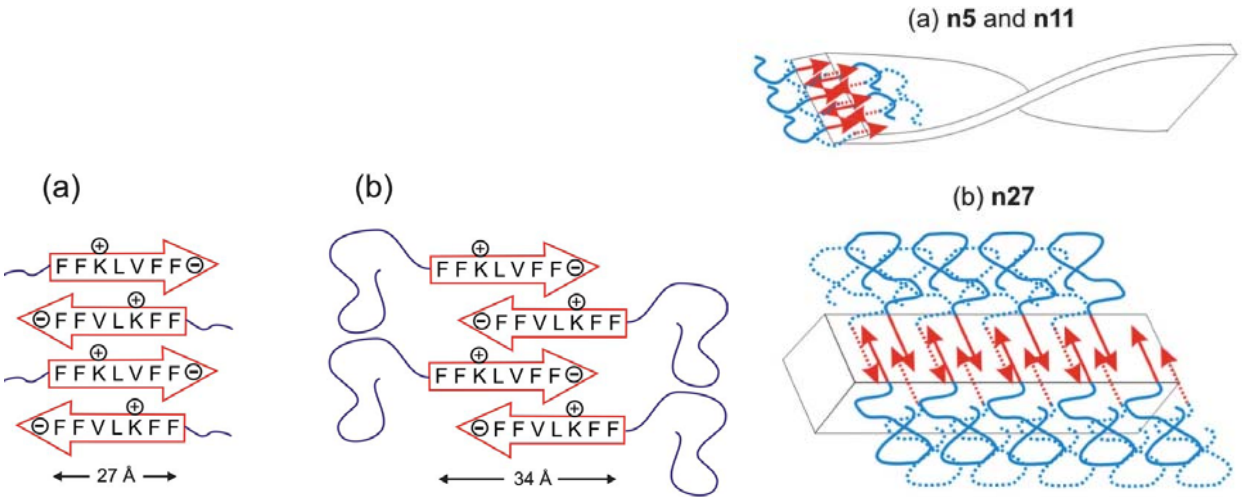

Fig.3. (a,b) Schemes for the packing of FFKLVFF β-strands based on X-ray diffraction for $(EG)_n$-FFKLVFF-COOH with (a) n=5 and n=11, (b) n=27, (c) Scheme for self-assembled structure based on stacking of β-sheets shown in (a) and (b).[14]

(iii) ***Regenerative Medicine***. We have discovered remarkable self-assembly by the lipopeptide Matrixyl™, C_{16}-KTTKS, which may relate to its application in cosmetics. This lipopeptide self-assembles into highly extended nanotapes.[15] This material is used as an active ingredient in commercial anti-wrinkle creams as the KTTKS pentapeptide, based on a sequence from the Pro-collagen peptide, has collagen-stimulating properties. We recently reported, in an ongoing collaboration with the Connon group at the University of Reading, the first peer-reviewed study on the activity of Matrixyl on fibroblasts including dermal and corneal fibroblasts.[16] Fig.4 shows results on collagen activity. This work generated immense media interest internationally, and has led to a number of ongoing collaborations with industry, including a leading multinational in the personal care products field, as well as several UK SMEs. We are currently extending this research towards the development of new materials for wound healing.

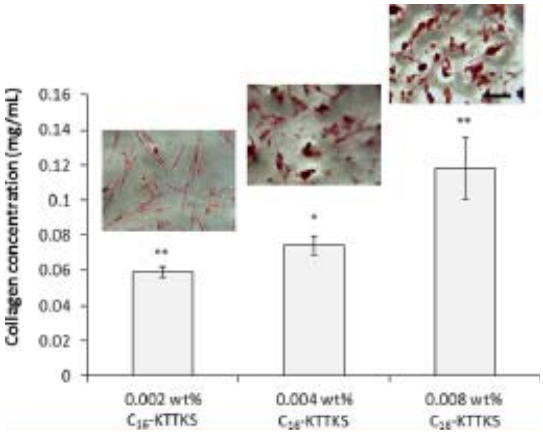

Fig.4. Collagen-stimulating activity of Matrixyl C_{16}-KTTKS. Collagen production assay on human corneal fibroblasts.

Also with the Connon group, we are developing new lipopeptide-based materials for regenerative medicine, specifically towards the development of a bioprosthetic cornea. The cornea contains layers of aligned collagen and achieving this morphology in a biomimetic material has been a key aim of our work. We recently developed an approach to achieve this using a template comprising stripes of a hydrophobic polymer, poly(tetra-fluoroethyelene).[17] Fig.5 shows representative images of cells aligned on such substrates which are coated with dual-function peptide amphiphiles which incorporate both a cell adhesion (RGDS)

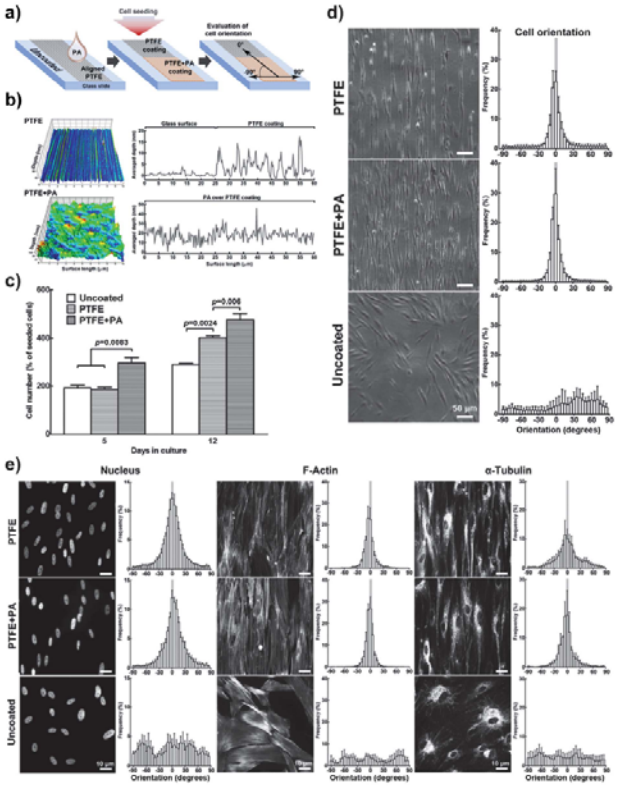

Fig.5. Alignment of human cornea stromal fibroblasts on peptide amphiphile-coated PTFE-stripe substrates.

motif as well as a matrix metalloprotease (MMP2) substrate.
Other activities in this area include the development of carnosine-based biomaterials.[18, 19] The dipeptide carnosine, βAH (beta alanine-histidine) found in many types of tissue, has a range of biological activities. The β- alanine βA residue can react directly with oxidized carbohydrates and lipids, and is therefore implicated in antioxidant properties for these species. The antioxidant properties of the dipeptide are also able to delay senescence of cultured cells. The histidine (H) residue in βAH has the ability to bind to transition metal ions or to inhibit glycation induced protein cross-linking. In particular, the prevention of cross-linking has a protective effect in inhibiting fibrillisation of α-Crystallin during the formation of cataracts. This property may also be important in the proposed application of βAH to treat Alzheimer's disease.

(iv) ***Polymer Nanotechnology***. Work in this area is supported by an EPSRC Platform grant at Reading (2008-2013). I have collaborated as part of this major grant with Prof Howard Colquhoun, Dr Wayne Hayes, Dr Barny Greenland and other polymer researchers at Reading on self-healing polymers[20], supramolecular urea/urethane polymers with applications in adhesives[21], bis-urea and related hydrogelators,[22] and polymers for drug delivery applications,[23] among others. In addition, I work with theorists, including Dr Zuowei Wang and formerly Prof Mark Matsen to model the self-assembly of amphiphilic polymers and block copolymers respectively.

We have undertaken major projects on the nanoscale self-organization of block copolymers in the melt, solution and crystalline states and in thin films.[24-27] The technological use of soft materials is expanding rapidly in areas ranging from coatings to personal care products to foods, detergents, adhesives and optoelectronics. In one example, we prepared novel thermoresponsive nanoparticles with potential applications in photothermal cancer therapy (Fig.6). Thermoresponsive PNIPAM (polyN-isopropylacrylamide) based materials have been one theme of our activities in this field.[28-31]

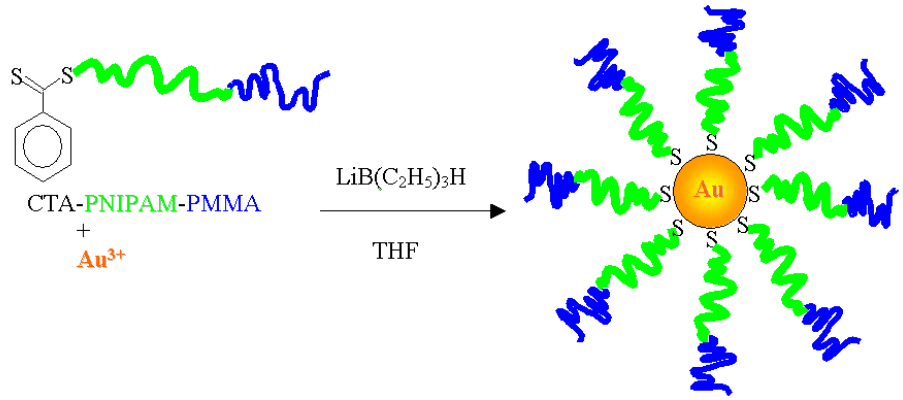

Fig.6 Synthesis Scheme of Gold Nanoparticles, templated by a block copolymer containing a thermoresponsive PNIPAM block. PNIPAM = poly(N-isopropylacrylamide), PMMA = poly(methyl methacrylate).[32]

In a recent EPSRC-funded project, in collaboration with Prof Matsen (Dept of Applied Mathematics) we investigated the microphase separation of block copolymers on surfaces, both flat and spherical. Tethered films of polystyrene-block-poly(methyl methacrylate) copolymers of varying composition and molecular weight were investigated using atomic force microscopy and the observed structures compared with theoretical predictions. Although the experimental results were in qualitative agreement with the theory, there was significant quantitative variation. This was attributed to the presence of solvent in the films prior to and during annealing, a hypothesis supported by new preliminary calculations reported here. Solvent exchange experiments (where a good solvent for both polymer blocks was gradually replaced by aselective solvent), were also performed on the films. This procedure generated textured films in which the structure was defined by miscibility of the polymer blocks with the second solvent.

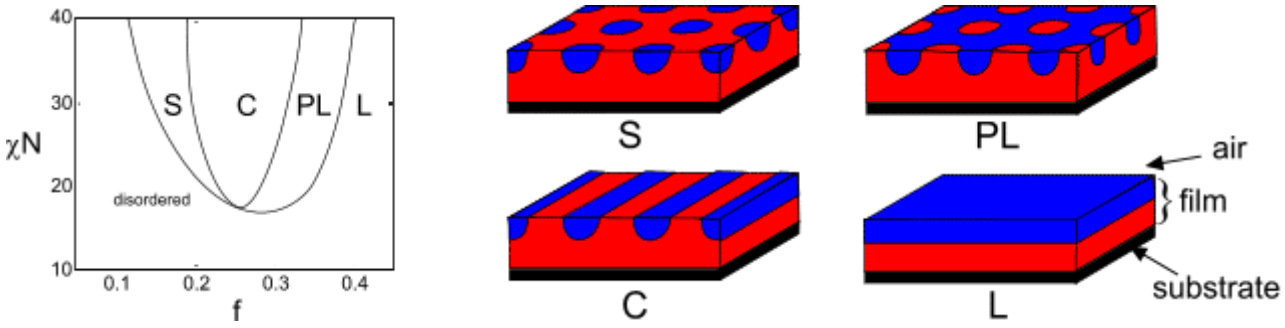

Fig.7. Theoretical phase diagram of a diblock-copolymer brush on a flat substrate with schematic diagrams of the four ordered phases. Here *f* denotes the volume fraction of the non-grafted block forming the blue domains.[33]

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