**Session 1: Peptide Design**

**P1: Fibrils or globules? Tuning the morphology of peptide aggregates from helical building blocks**

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The aggregation propensity of helical oligopeptides formed exclusively by conformationally constrained amino isobutyric acid (U), has been studied in methanol and methanol/water solutions by optical spectroscopy (UV-Vis absorption, steady-state and time-resolved fluorescence), Infrared and Atomic Force Microscopy (AFM). The peptide investigated have general formula UnN, where n=6, 12 and 15, and N stands for a Naphthyl chromophore introduced with the double aim to serve as a spectroscopic probe and to analyze the effect of an aromatic group on the aggregation process. Spectroscopic experiments showed that the aggregation propensity in solution increases with increasing the length of the peptide chain, i.e. U6N<U12N<U15N. When the peptides were immobilized as a dried film on mica, the interplay of aromatic and inter-helix interactions, the latter being more and more important with the elongation of the peptide chain, determined the morphology of the resulting mesoscopic aggregates. AFM imaging revealed the formation of globular and fibrillar structures, the predominance of which was controlled by the helical content of the peptide building block.

**P2: Understanding the folding and stability of small alpha-helical peptides**

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We have designed a series of short alpha-helical peptides based on the general formulae (E4K3)h and (E4K3)h. We find that helix stability is determined by local charge effects at the termini and K-E sequencing is cooperative and more stabilising than E-K sequencing. A4(E4K3)hA4 and A4(K4E3)hA4 were designed with four terminal alanine residues to eliminate interaction of the charged amino acids with the δ+ and δ- charges which arise at the N and C termini of an alpha-helix respectively due to backbone hydrogen bonding. In all cases we find A4(E4K3)hA4 peptides to be more helical than their E-K counter-designs. Sigmoidal melt curves show cooperative folding only for the K-E designs. We believe that helix macrodipole theory is redundant for these systems, and helix stability is influenced by local effects at the termini. In the absence of terminal alanines, (E4K3)h is more helical than (K4E3)h. While we have found K-E sequencing to be more stabilising, this is outweighed by terminal effects in the case of (E4K3)h;

four N-terminal glutamates interact favourably with the N-terminal δ+ charge, and likewise four C-terminal lysines interact favourably with the δ- charge. This is supported by molecular dynamics simulations which show end-fraying for (K4E3)h. NMR spectroscopy highlights the different electronic environment of the terminal residues with respect to rest of the helix.

**P3: A new set of de novo designed heterodimeric coiled coils**

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α-Helical coiled-coil motifs are amongst the best understood peptide/protein folds. The basic coiled-coil motif is straightforward: sequence patterns of hydrophobic (h) and polar (p) residues – hhpphh, often denoted as achedf – direct the folding of amphipathic helices, which associate through their hydrophobic (a/d) faces to form helical bundles [1]. These principles facilitate the development of sequence-to-structure relationships for coiled coils, which can be used as rules to guide the successful de novo design of new peptides and materials.

Herein, we present a new set of de novo parallel heterodimeric coiled coils. The parallel orientation is directed by the combination of isoleucine and leucine residues at a and d positions, respectively. But in contrast to previous designs [2] we have also included two asparagine residues at the a-position of each coiled-coil helix. As found in previous studies [3], this additional design feature leads to higher dimer specificity and allows also the defined pairing of helices with different chain length. Heterospecificity is guided by complementary charge-charge interactions between e and g. Our study also includes the dependence of the coiled-coil stability on the length of the peptide chains.

The availability of such a set of peptides adds to our toolkit of peptide building blocks for potential applications in protein engineering, biomaterials design and synthetic biology [3].


**Session 2: Peptide Biomaterials & Tissue Regeneration**

**P4: Design of a functional octa-peptide to direct bone formation**

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Bone tissue is a highly organized and specialized connective tissue, which provides support to muscles and it is an important reserve of
minerals such as calcium and phosphorus [1]. The alveolar bone in the oral cavity, supports teeth [2] and is frequently affected by oral diseases such as periodontitis. This pathology is due to an exacerbated immune response induced by invasion of a myriad of microorganisms, which ultimately promotes a progressive destruction of soft tissues and alveolar bone [3, 4]. Today, biomaterials that are able to provide three-dimensional (3D) scaffolds for the culture of cells are being developed for cell culture and tissue engineering applications [3-5]. Peptide-based hydrogels is one class of biomaterials that is attracting considerable attention in both academia and industry. Such hydrogels are built from short amino acid sequences, that can spontaneously self-assemble into α-helix or β-sheet secondary structures, and go onto to form fibers that self-associate and become entangled to form a self-supporting matrix with structures similar to that of natural extracellular matrix [4, 6].

One type of peptide that has been well studied is the ionic-complementary octapeptide FEFEFKFK, where F, E and K are phenylalanine, glutamic acid and lysine respectively. It is known to self-assemble into a β-sheet rich fibrils, which in turn forms hydrogels under specific and controlled conditions [7, 8]. Recently, it has been shown that FEFEFKFK is able to support the 3D culture of bovine chondrocytes [9].

In this work, the ability of FEFEFKFK-peptide hydrogels to support the attachment, viability and proliferation of human osteoblasts is explored in order to promote bone cellular activity to form bone.

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P5: Characterization of a beta tri-calcium phosphate granular mixture in a hydrogel carrier for use in bone grafting
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The market of bone graft substitutes is ever broadening with many niche products being developed. βGel is a synthetic osteoconductive gel comprised of beta-tricalcium phosphate granules blended with a hydrogel carrier matrix. It is a void filler but has potential application in various circumstances. We hypothesise that by mixing βGel with autologous bone marrow or trabecular bone chips its osteogenic potential will be enhanced. However, the handleability of bone marrow/bone chips with βGel, the behaviour and metabolisation of cells after mixing with βGel need to be tested before clinical application. We have subjected the product to a variety of test methods including manual handling, compression analysis, X-ray microtomography, scanning electron microscopy (SEM), energy dispersive X-ray spectroscopy (EDX), and in vitro assays carried out with cell line and clinical samples. In doing the handleability, finer structure, and effects on in vitro cell metabolism have been evaluated. βGel was found to be easy to handle and to handle both in its native form and when used as a graft extender. Its micro-scale structure demonstrated the pseudo-porosity created by the dispersion of micron scale beta tri-calcium phosphate in the carrier. The in vitro tests showed βGel to be biocompatible with human bone marrow mesenchymal stem cells and fresh isolated human bone marrow/trabecular bone chips, and any effects to cell viability were found to be dose dependant. In conclusion, βGel can be easily mixed with bone marrow/bone chips at 1:1 and 2:1 ratio. However, further research is warranted to study the detailed cell viability/metabolism in the mixture and its clinical outcomes.

P6: Cryopreservation of Cells using Peptidomimetic Macromolecules
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There is a real need for improvements in the cryopreservation of biological materials. Ice recrystallisation during freeze/thawing of cells is a major contributor to cell damage during cryopreservation [1]. Antifreeze (glyco)proteins (AF(G)Ps) are a naturally occurring class of proteins found in cold-acclimatised species that have a simple polymeric structure and display a strong recrystallisation inhibition (RI) activity (fig. 1) [2]. The isolation of AF(G)Ps in significant quantities is financially not viable and transgenic approaches would be complicated due to the essential glycosylation unit. Several studies have also indicated AF(G)Ps to be cytotoxic. We have developed several biocompatible peptidomimetic molecules that have comparable RI activity to AF(G)Ps [3]. We have thus far demonstrated their effectiveness at cryopreserving erythrocytes at concentrations 100x lower than existing cryoprotectants and continue to investigate their cryopreservation potential with numerous other cell types.

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P7: The development of a durable coating for Intra-osseous Transcutaneous Amputation Prostheses by covalently tethering RGD sequences in vitro
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etal Science, University College London

Osseointegrated transcutaneous implants are being developed for amputees so that they can attach their artificial limb directly to the skeleton avoiding current problems of soft tissue abrasion at the socket stump interface. In order to prevent infection a microbial seal is necessary which involves adhesion of the keratinocytes and dermal fibroblasts to the metallic alloy [1,2]. Fibronectin (Fn), is an extra-cellular matrix protein, RGD is the polypeptide sequence of Fn involved in the binding of fibroblast cells to the extra-cellular matrix [3]. We have previously shown that Fn can be covalently tethered to ITAP to create a more durable, bioinductive coating for human dermal fibroblast attachment [4]. However because of regulatory issues, sterilization protocols and the number of attachment sites the use of specific RGD sequences may be justified. We iodinated synthetic YRGD to investigate covalent peptide attachment and durability to titanium alloy surfaces with the aim of determining an optimal protocol for the development of a YRGD functionalized titanium alloy surface. These surfaces were then tested for cell adhesion by measuring the density of vinculin plaques in attached dermal fibroblasts. The attachment of the silanized RGD sequences was compared with adsorbed molecules and with fibronectin when incubated with fetal calf serum. Cell attachment to these surfaces was also quantified by measuring the density of vinculin adhesion plaques. Significantly greater bonding of YRGD to titanium alloy surfaces was found by increasing the concentration from 1mM, up to 7mM (p<0.0055) but there was no effect of increasing the concentration beyond this level. After challenging with FCS significantly higher levels of silanized peptides remained on the substrate surfaces (p<0.05) when compared to absorbed YRGD. These surfaces significantly enhanced
cell attachment when compared with a non-protein treated substrate.

Silanization of titanium alloys surfaces with YRGD sequences results in a more robust derivate d surface which, in vivo, enhances dermal fibroblasts attachment. It may be possible to use a YRGD function alized titanium alloy surface that will stabilize the skin seal at the transcutaneous portion of an implant which will enhance the resistance to infection.


P8: Protein Hydrogels As Tissue Engineering Scaffolds
Khairunnisa Nabilah Haji Ruslan & Aline Miller
Manchester Institute of Biotechnology, University of Manchester

More peptide and protein hydrogels are being studied due to their bet ter biological, biocompatible and biodegradable properties in comparison to the traditional polymer hydrogels. Under appropriate conditions, protein hydrogels can self assemble to form a fibrous network with a high water content that mimics the natural living environment of hu man cells. The hydrogel network allows cells to be embedded, trapped and possibly grow in numbers demonstrating the gel’s role as a scaffold in tissue engineering.

This research work focuses on developing, characterising and optimising hen egg white lysozyme (HEWL) hydrogels formed by physical and chemical denaturing methods. Strong gels were formed at pH 2 after 3 days of heating at 85°C without adding a reductant. In the presence of reducing agents dithiothreitol (DTT) and tris(2-carboxyethyl)phosphine (TCEP), there was a faster formation of strong lysozyme gels at pH 7 and pH 4 respectively. To study the properties and structure of these gels, several analytical techniques were used including micro differential scattering calorimetry (mDSC), Fourier transform infrared spectroscopy (FTIR), rheology, transmission electron microscopy (TEM) and powder diffraction. From these results, lysozyme gels with better controlled properties such as more responsive gels could be developed to optimise the process of tissue regeneration.

P9: Self-Assembling Octopeptide Hydrogel as a Scaffold for Cartilage Engineering
Anne Markey1,2, Iain Bruce1, Tim Woolford1, Sarah Cartmell2, Brian Derby2, Alberto Saiani2
1: Manchester Royal Infirmary; 2: School of Materials, University of Manchester

Tissue engineering of cartilage has many applications in the clinical setting. Chondrocytes require a 3D environment to facilitate the production of type 2 collagen and extracellular matrix. We have used an octopeptide hydrogel as a scaffold to provide a 3D environment in which to seed bovine chondrocytes. Optical microscopy was used to assess chondrocyte morphology and cell staining and fluorescence microscopy to assess viability. Glycosaminoglycan assays were used to quantify the production of extracellular matrix. The immunogenicity of the hydrogel was tested encapsulating monocytes within the gel and quantifying the production of cytokines using an enzyme linked immunoabsorbent assay. Furthermore, we have tested the mechanical strength of the gel over time with and without chondrocytes.

We have shown that chondrocytes are viable and maintain a normal morphology within the gel up to 42 days duration. The glycosaminoglycan assay was performed at 7, 14, 21 and 28 days (n=4). There was a statistically significant increase in glycosaminoglycan production over the time points (p<0.0001). Mechanical testing at 0, 7, 14 and 21 days has shown the gel to have stiffer properties at all time points when the chondrocytes are encapsulated within the gel.

This octopeptide hydrogel supports chondrocyte viability with maintenance of normal cell morphology. The production of glycosaminoglycans is a marker of cartilage production. Future work will include testing for collagen type and the use of human chondrocytes.

P10: The Development of Functional Peptide Scaffolds for Chondrocyte Culture.
Laura Szkelar1,2, Julie E Gough1, Aline Miller2, Alberto Saiani1
1: School of Materials, University of Manchester; 2: Manchester Institute of Biotechnology, University of Manchester

Molecular self-assembly has emerged as a powerful tool for the fabrication of molecular materials with a wide variety of properties. In recent years, considerable advances have been made in using simple oligopeptides as building blocks for the production of novel biomateri als.

It has been shown that at a critical concentration the octapeptide FEFKEFK (F- phenylalanine, E- Glutamic acid, K- Lysine) can self assemble into β-sheet rich fibres leading to the development of a dense fibrillar network and a self supporting hydrogel .

Degenerative diseases of cartilage affect a high proportion of the population. Such diseases cause pain and disability, reduce the quality of life and put strain on the healthcare system. Current treatment options focus on preventative medicine and pain management but these are not sufficient for the long term treatment of many patients. The focus of current research is to produce ways of culturing chondrocytes on a large scale or producing replacement cartilage . Here we have developed a simple protocol for the encapsulation of chondrocytes for 3D cell culture applications.

Rheology was used to characterise the mechanical properties of the hydrogels. Peptide / cells were plated in transwells with subsequent gelation of the materials, upon addition of NaOH, leading to encapsulation of the cells into a 3D network. This system was evaluated for the 3D cell culture of Bovine Chondrocytes (BC’s). Microscopy showed that cells were uniformly distributed within the gel matrix. Cell counting and live/dead staining showed proliferation of BC’s over 14 days.

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P11: Self-assembled peptide gels for intervertebral disc tissue engineering
Simon Wan
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Lower back pain (LBP) affects 80% of people in their lifetime and costs the UK economy £12 billion annually [1]. While aetiology varies, intervertebral disc (IVDs) degeneration is strongly associated with LBP in over 40% of cases [2].

IVDs are found in between the vertebrae of the spine where they act as shock absorbers and allow movement. They consist of the tough fibrous annulus fibrosus (AF) which surrounds the gel-like nucleus pulposus (NP). With age, the NP dehydrates and deteriorates which accelerates disc degeneration and can cause LBP. Current treatments for LBP are symptomatic however a cell-based therapy has the potential to be curative.

Nanofibrous self-assembling peptide hydrogels were investigated as scaffolds for NP tissue engineering due their biocompatibility, ease of modification and injectability.

3D cell culture was carried out as it better replicated the native NP environment. Fluorescence imaging showed that encapsulated cells maintained their characteristic rounded morphology, crucial in retaining cell phenotype, for the duration of cell culture with above 80% cell viability. A colourmetric assay showed evidence of cell proliferation. In conclusion, preliminary results indicated that the hydrogels successfully mimicked the native NP environment which suggests that they could be used in NP tissue engineering.

**Session 3: Peptide Interactions with Materials & Nanomaterials**

**P12: Drug-layered double hydroxides nano-hybrids: Role of layered double hydroxides as nano-reservoir and nano-vehicle**

**Khalid Ahmad.Alamry**

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Drug delivery has attracted great attention due to their clinical, medicinal and wide range of technical applications. A large number of drug deliveries with various bioavailabilities have been discovered but the potential for pharmaceutical prospects are still limited. Thus development of drug delivery with safe and controlled bioavailability is of great interest due to medical point of view. Recently, increasing attention has been directed the development of bio-inorganic hybrid systems in the drug delivery for the controlled release of biochemic-
als. Bio-inorganic systems can allow safe and controlled delivery of various bioagents into targets with high efficiency. In this proposal, we will make an attempt to synthesis layered double hydroxide (LDH) nanoparticles and further develop innovative nano-drug deliveries by intercalation of various drugs into the interlayer of LDH. Both LDH and drug-LDH nanohybrids will characterize by using field emission scanning electron microscopy (FESEM), energy dispersive spectroscopy (EDS), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), and UV-visible absorption spectroscopy. The drug contents will study by thermogravimetric analysis (TGA) and elemental analysis (CHN). Drug-LDH nanohybrid will apply in a formulation for the oral administration and the drugs release profile will study by simple deintercalation of drugs by various anions using UV-visible and HPLC.

**P13: Carbohydrate recognition on membrane surfaces - Interaction of Peptide based Carbohydrate receptors and artificial Glycolipids**

**Sebastian A. Berg & Bart Jan Ravoo**

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Carbohydrates play a crucial role in various recognition processes in nature and are present on all mammalian cells in form of the glyco-
lix. They are, for example, involved in the inflammatory process, they determine the blood type, mediate cell-cell adhesion and recognition and are involved in cell-cell communication. Furthermore the glyco
calix is subject to various dynamic processes due to cell growth and function and different infections or malign transformations of cells lead to a change in its structure [1].

Thus artificial carbohydrate receptors are of great interest to study carbohydrate-receptor interactions and for medicinal applications e.g. drug delivery. In a previous work it was shown that dimers of cyclic tripeptides are able to specifically bind different carbohydrates in solution with binding constants of up to 5000 M⁻¹ [2]. In this project the interaction of membrane bound carbohydrate receptors and carbohydrate receptors is investigated.

Liposomes, consisting of phosphatidylcholine, are decorated either with artificial glycolipids or with peptide based amphiphilic car-
bohydrate receptors. Upon mixing of these two kinds of liposomes the interaction of the carbohydrates and the receptors lead to agglutination which can be monitored by dynamic light scattering and measurements of the optical density.

These new membrane bound carbohydrate receptors pose various new possibilities for studying multivalent carbohydrate-receptor interactions and for application e.g. targeted drug delivery or cell binding studies.


**P14: Fibroblast Response To Surface Chemical and Nano-Topographical Cues**

**Folashade Kufoniji & Paul Roach**

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Modern biomaterials are engineered to repair, replace or augment healthy tissue in order to restore function to damaged body parts. Al-
though mechanical properties derived from the material bulk are well established, attention has turned towards the surface of biomaterials in order to more easily integrate these materials into the body. Many researchers have shown differences in physical cell responses toward their environment, e.g. cell morphology or migratory characteristics are well used discriminators to identify healthy cell-material interaction. Cells naturally secrete proteins in order to moderate their environ-
ment, a natural mechanism used to repair wounds or communicate signals to other cells to promote healing. However, little is currently understood about the cellular mechanisms related to their interaction with biomaterial surfaces. By further understanding these processes advanced biomedical coatings may be developed that allow control over specific cell responses to direct healing processes. Here we investigate the so-called ‘secretome’ and characterize cell responses to differences in chemical and nano-topographical cues.

3T3 fibroblasts have been shown to adhere, proliferate and have distinct morphology depending upon the surface chemistry and nano-
topography on which they reside.

Mass spectral investigation of culture media highlights differences associated with cell-surface interaction. A number of key differences were found showing contrasting behaviour of cells corresponding to characteristic secretory signals. Further investigation is currently underway to further characterize the chemical signals released by the cells in response to their surrounding and understand the internal cel-
lar mechanisms that are activated during this process.

Surface charge seems to play a major role in determining cell secretion response.

Methyl surfaces (-CH₃) showed the highest number of cells adhered yet the lowest number of spreading cells after 1, 2 and 24 hours in culture. Amine surfaces (-NH₂) showed the lowest number of attached cells, although those that had adhered spread well. This may be due to the high density of positively charged species presented at the surface (experiments carried out at pH 7.4) interacting with cell membranes. These results suggest differences in cell response characteristics due to both wettability and substrate charge.

Differences in cell secretions were observed for cells cultured on all surfaces. Very interestingly principle component analysis identified these differences not only from cells cultured for 24 hours, but also from those presented over the substrates for 30 minutes.

Further investigation to identify the nature of differences in secreted molecules is on-going, using MALDI-TOF-TOF, but may drive the design of novel materials to initiate desired cellular responses.
This study revealed that chitlac in solution is degraded by lysozyme spectrofluorimetry and electrothermal atomic absorption spectroscopy. FRCs [2]. The degradation of the lactose-modified chitosan (chitlac) was obtained via strong electrostatic interactions on dense and porous bone substitute materials in craniofacial reconstruction [1]. An antimicrobial, non-cytotoxic silver–polysaccharide nanocomposite in solution and as coating on fibre reinforced P16: Degradation of silver–polysaccharide nanocomposite in solution and as coating on fibre reinforced composites by lysozyme and hydrogen peroxide Sara Nganga1, Andrea Travani2, Ivan Donati3, Matteo Crosera3, Sergio Paolotti2, Pekka K. Vallittu1
1: Department of Biomaterials Science, University of Turku, Finland and Biotcity Turku Biomaterials Research Program, Turku Clinical Biomaterial Centre - TCBM, Turku, Finland; 2: Department of Life Sciences, University of Trieste, Italy; 3: Department of Chemical and Pharmaceutical Sciences, University of Trieste, Italy Glass-fibre-reinforced composites (FRCs), based on a bifunctional methacrylate resin, are under current investigation to serve as durable bone substitute materials in craniofacial reconstruction [1]. An antimicrobial, non-cytotoxic silver-polysaccharide nanocomposite coating was obtained via strong electrostatic interactions on dense and porous FRCs [2]. The degradation of the lactose-modified chitosan (chitlac) coating was investigated in vitro in conditions simulating in vivo inflammation. Analysis methods applied were capillary viscosimetry, spectrofluorimetry and electrothermoluminescence absorption spectroscopy. This study revealed that chitlac in solution is degraded by lysozyme similarly to native chitosan. In contrast, the chitlac coating, bound to implant surfaces, showed no signs of degradation within seven days of exposure to lysozyme or one day to hydrogen peroxide (H₂O₂), the silver nanoparticles incorporated in the chitlac coating were shown to be not significantly leaching from the material [3].


P17: Host-guest interactions and aggregation studies between Cucurbit[8]uril and Amyloidβ(1-42) Silvia Sonzini and Oren A. Scherman
Melville Laboratory for Polymer Synthesis, Department of Chemistry, University of Cambridge; ss2005@cam.ac.uk Alzheimer’s disease is an important illness that affects an ever increasing number of individuals. This disorder seems to be correlated to the abnormal production of Amyloid β peptides that form aggregates and fibrils evolving into senile plaques [1]. Consequently, several major efforts have been made to both find a treatment as well as to gain a deeper understanding of the protein conformations responsible for toxicity. Cucurbit[n]uril (CB[n]) analogues are macrocycles with a hydrophobic cavity and a polar rim, which are known to bind to molecules bearing aromatic moieties such as phenylalanine and tryptophan residues [2]. Cucurbit[8]uril (CB[8]) is capable of binding two of these residues simultaneously on account of its larger cavity [3].

Herein, we report mass spectrometry and circular dichroism binding studies on Amyloid β (1-42) and CB[8] suggesting how these binding phenomena are capable of significantly speeding up the aggregation of Amyloid β. We postulated that the F19 and F20 residues, which are crucial residues for the oligomerisation of Amyloid β (1-42), [4] could act as binding sites for CB[8]. To further validate this hypothesis we carried out a series of biophysical studies on shorter peptides that mimic the 17-22 fragment of Amyloid β (1-42). Isothermal titration calorimetry (ITC) and 1H-NMR suggested that CB[8] preferentially binds to F19 and F20 over the other aromatic residues in the peptide. These data provide further insights that are valuable for the development of specific stabilisation strategies of Amyloid β (1-42) dimer and eventually leading to new Alzheimer’s treatments.

yet to be characterised in this way due to their inherent insolubility in aqueous solutions. Our research aims to unlock the mechanisms at the molecular level through which these membrane proteins control biomineralisation by studying the hydrophobic loops linking their transmembrane helices using both free peptides and constrained stem loop coiled coil scaffolds. This will hopefully pave the way for the production of tailor-made magnetic nanoparticles using biomimetic components and gentle reaction conditions.

**P19: Reversible Aggregation of Human Insulin through Supramolecular Host-Guest Interactions with Cucurbit[8]uril**
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The formation of ordered, amyloid-like structures in proteins has been associated with several diseases such as Alzheimer’s, Parkinson’s and type II diabetes, and is now thought to be a generic feature of protein aggregation [1]. There is considerable interest within the pharmaceutical industry in maintaining the integrity of protein-based drugs such as insulin during transport, however little is understood about the initial stages of aggregation.

Cucurbit[n]uril (CB[n]) homologues are a series of macrocyclic host molecules comprising a polar portal region with a hydrophobic cavity, capable of binding molecules containing an aromatic moiety such as phenylalanine [2]. Smaller CB[n] homologues, where n = 5, 6 or 7, can bind one guest, however, the larger cavity size of CB[8] allows it to accommodate a second guest simultaneously [3].

Herein, we report an investigation into the effects of complexation between human insulin and CB[8] in aqueous solution. We show by isothermal titration calorimetry (ITC) that the N-terminal phenylalanine residue of human insulin acts as a suitable guest, binding to CB[8] in a 2:1 molar ratio. Additionally, dynamic light scattering (DLS) confirms that the resulting aggregation process is temperature-dependent yet remains fully reversible in the presence of CB[8].

On releasing the protein guest from the CB[8] host by increasing temperature, the insulin was shown to aggregate irreversibly in a manner comparable to the native protein, via controlled temperature incubation at 70°C [4].

**P20: Magnetite templating Peptides from proteins in M. Magneticum**
Jonathan P Bramble¹, Andrea Rawlings¹, Arnout P Kalverda², Sarah S Staniland¹
¹. School of Physics and Astronomy; 2. School of Molecular and Cellular Biology, University of Leeds
First discovered by Richard Blakemore in the 1970s [1], magnetotactic bacteria (MTB) are aquatic prokaryotes that swim parallel to the earth’s magnetic field. All magnetotactic bacteria contain magnetosomes, which consist of biominaleralised, nanometre-sized, magnetic mineral crystals, encapsulated in a membrane [2], normally arranged in a linear chain within the cell. There is sufficient torque on this chain from the geomagnetic field to orientate the bacterium.

The process of magnetic nanoparticle (MNP) formation is complex and consists of several steps. Here we are concerned with the iron accumulation by the bacteria and its mineralisation inside the magnetosome. Known as ‘biologically controlled mineralisation’, this process is under genetic control, leading to specific proteins controlling the shape and size of the MNPs for a given bacterial strain. There are a number of proteins associated with the magnetosome membrane which are believed to precisely template the formation of the MNPs [3,4].

We aim to obtain an understanding of the role of magnetosome membrane specific proteins in biominaleralisation. This will be achieved through biochemical, structural and computational modelling analysis of specific proteins, peptides and mutants, as well as iron binding assays and detailed analysis of MNP formation in vitro using these protein targets.

**P21: Reducible Polypeptide Vectors for Gene Delivery**
Bohumi Savaš¹, Jon Preece¹, Anna Peacock¹ and Richard Burrows²
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Gene delivery is the process of transporting a particular gene safely and efficiently into the nucleus of a target cell. It is one of the most important processes involved in gene therapy. The gene carrier, which is called a vector, must be utilized for successful gene delivery. Fig. 1 shows a schematic of the gene delivery process using a non-viral vector [1].

A range of peptides were synthesised by combining varying amounts of arginine, lysine, histidine and cysteine residues and these were then oxidatively polymerised to form reducible polypeptide vectors. These vectors are promising as they can bind DNA extracellularly to form polyplex nanoparticles. These polyplexes will then be transfected into different cell lines to measure their transfection efficiency and toxicity.

A recent study by Borrows et al. [2] has indicated an association between decreased caveolin-1 expression and renal fibrosis, which can lead to long term graft failure in a kidney transplant recipient. The aim is to develop the vector for use to deliver the CA V1 gene to upregulate caveolin in the grafted kidney, so as to prevent renal fibrosis.

**Session 4: Dynamic Peptide Systems & Self-assembly**

**P22: Influence of a Pluronic Copolymer on the Self-Assembly of a Collagen Stimulating Peptide Amphiphile**
A. Dehsorkhi¹, V. Castelletto¹, I. W. Hamley¹, P. Lindner²
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Peptide amphiphiles (PA) or lipopeptides are attracting a considerable amount of attention due to their importance in biomedical applications [1]. These fascinating class of self-assembling PAs have been found to form high aspect ratio nanostructures in aqueous solution [2, 3]. The PA C₁₆-KTTKS has been shown to stimulate collagen production [4]. However its mechanism of action is not fully understood,
therefore there is a need to examine the self-assembly in order to shed some light on this matter. In formulations, C₁₆-KTTKS is mixed with surfactants therefore we have investigated the influence of a non-ionic surfactant, Pluronic P123 on the self-assembly of C₁₆-KTTKS. Previous work reveals that C₁₆-KTTKS self-assembles to form nanotapes [5]. A combination of microscopic, spectroscopic and scattering techniques have been employed in order to characterize the nanostructures. We have observed that the addition of P123 can instigate a change of morphology from nanotapes to cylindrical nanofibers [6]. The β-sheet superstructure is disrupted by P123 as revealed by circular dichroism however the local β-sheets are intact as suggested by FTIR and XRD. The preferred self-assembled nanostructure is dependent on the order of mixing. Self-assembly of these mixtures exhibits slow kinetics towards equilibrium. Heating above the lipid chain melting temperature assists in disrupting trapped non-equilibrium states.

**P24: Using Molecular Dynamics simulations to understand and predict peptide self-assembly**

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Nanostructure formation by self-assembly of small peptide molecules is a notoriously tricky concept to model in silico. This is due to the large number of individual molecules required to form a self-assembled structure that is large enough for obtaining statistically relevant information. With the advance of computational power however, simulations of sufficient size are becoming available, although appropriate methods are still in development.

Here, we will discuss two of such computational approaches to understand and predict the properties of self-assembled nanostructures of peptides: 1) atomistic simulations using the CHARMM force field and 2) coarse grain simulations for the screening of new biomaterials consisting of small (di)peptides using the MARTINI force field. The atomistic simulations performed are consistent with experimental data showing π-stacked β-sheets for Fmoc-dipeptides and can correctly predict self-assembly for monomers in various ionization states, even in mixed-molecule structures. Our coarse-grain screening protocol and scoring method correctly predict whether aggregation (an indicator of the ability to self-assemble) will occur for almost all known examples of dipeptides in literature. Interestingly, extended simulations can even give insight into the supramolecular structure of a particular peptide. Overall, the procedure shows good promise for the discovery of new bio-inspired materials.

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hydrogels which resulted in enhanced supramolecular order of peptidic self-assembly and modulation or inversion of supramolecular chirality. The rheological measurements suggested that the addition of protein fractal structures can modify or tune the rheological behaviour of hydrogels depending upon the peptidic sequence selected. Recently, we have incorporated light harvesting complexes from purple bacteria in these hydrogels and found that the gel environment provides remarkable structural and functional stabilization of these complexes. This will enable us to harvest light and then trigger charge separation reactions which can potentially be used by other enzymes like hydrogenase to produce hydrogen fuel.

P26: A controllable and efficient ‘active colloidal engine’
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A controllable and efficient ‘active colloidal engine’ utilising enzyme-driven peptide self-assembly is explored, exploiting our previously reported self-assembling aromatic peptide system.1 In detail, the enzyme alkaline phosphatase is driven by the supramolecular assembly of the dipeptide derivative Fmoc-FY into fibre structures, similar to actin-polymerization driven motion used in biology. The phosphorylated peptide (Fmoc-FpY) forms 5nm in diameter sphericial micelle structures in water, above a critical micelle concentration of 5mM. In the presence of alkaline phosphatase the phosphate group of the tyrosine side chain is cleaved resulting in β-sheet fibre networks of unphosphorylated dipeptide. This micelle to fibre transformation has been characterised using spectroscopic; light scattering and chromatographic techniques. Visualisation of enzyme motion is achieved by conjugation of the enzyme to a fluorescing quantum dot via a carbodiimide coupling reaction and observation is achieved by single particle tracking fluorescence microscopy. Without the peptide substrate present the enzyme is expected to exhibit Brownian motion and upon addition of the peptide, fibre formation is proposed to guide and direct the enzyme motion. Understanding the control of nanoscale motion is vital for applications including nano-separation, targeted transportation of ‘cargo’ for construction, and controlled self-assembly.


P27: Synthetic Viral Capsids Self-assembled from Viral Peptide Fragments
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Recently, application of plant viruses to nanotechnology have attracted much attention due to their fascinating nanostructuring abilities. However, it remains difficult to rationally design artificial nanoparticles. Peptide fragments such as viral capsids and clathrin, provide excellent models for the study of self-assembly and modulation or inversion of supramolecular chirality. Self-assembly in biological systems, such as viral capsids and clathrin, provide excellent models for the study of self-assembly and modulation or inversion of supramolecular chirality. However, it remains difficult to rationally design artificial nanoparticles. Peptide fragments such as viral capsids and clathrin, provide excellent models for the study of self-assembly and modulation or inversion of supramolecular chirality.

In this paper, we report that a synthesized viral β-annulus peptide (24 residues) showed spontaneous self-assembly into hollow nanocapsules (synthetic viral capsid) with the size of 30-50 nm in water (Figs). The hollow structure was revealed by small angle X-ray scattering measurement. It was revealed that and Pro residue and 8-mer sticky-end (VTRQLVGS) at C-terminal are essential for the formation of nanocapsules. Mutation of Pro residue of 24-mer β-annulus peptide to Ala afforded fibrous assembly instead of nanocapsule.

We also report self-assembly of Ni-NTA-modified β-annulus peptide into the stable nanocapsules and their complexation with His-tagged green fluorescent protein (GFP). GPC analyses of Ni-NTA-modified β-annulus peptide and His-tagged GFP revealed that the peptide nanocapsules complexed with His-tagged GFP.


P28: Making Bacterial Toxins into Virus-Like Particles for Therapeutic Drug Delivery
James Ross
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Synthetic Biology, the re-design and controlled self-assembly of natural systems into non-natural functional products is a quickly developing field. Protein-protein interactions, among other areas, show great promise for manipulation. In nature protein-protein assemblies mediate many cellular processes and exhibit complex and efficient functions. It is thus rational to assume human guided biomolecular assemblies could house equally complex functionality and could help address our needs for such devices as molecular diagnostic tools and therapeutic drug delivery systems. The goal of our project is the design and production of a capsid-like protein cage of dodecahedral symmetry and diameter of 15 nm or 32 nm, with an internal cargo-holding space. We will use a combination of current computational methods to find increases in interaction energies, then use novel experimental strategies to test our designs and optimise the simulations via a feedback loop. These methods should be appropriate for generic application to the design of self-assembling protein systems. The dodecahedral particle will be assembled from Cholera Toxin B-subunit, a natural homopentamer with an inbuilt cell targeting and endocytosis triggering mechanism. Future applications could therefore use our capsid as a drug delivery vehicle to transport protected therapeutic agents to targeted cell types.

P29: Peptide-Polyoxometalate Hybrids for Biomimetic Nanostructured Materials
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Polyoxometalates (POMs) are a large family of metal-oxygen clusters commonly made of V, Mo and W in high oxidation states. POMs display a variety of properties which make them promising for a wide range of applications such as catalysis, medicine and nanotechnology. Organic-inorganic POM hybrids are a subset of the POM family which combine POMs with tunable organic ligands. Hybrid POMs combine the properties of both organic and inorganic moieties, and therefore can be used for formation of vesicular assemblies, surface patterning and as photosensitized materials. Very short peptides are known to display interesting self-assembly features, especially di-peptides. This micelle to fibre transformation has been characterised using spectroscopic; light scattering and chromatographic techniques. Understanding the control of nanoscale motion is vital for applications including nano-separation, targeted transportation of ‘cargo’ for construction, and controlled self-assembly.

P31: Silk: a model system for shear controlled denaturation
Maxime Boulet-Audet, Fritz Vollrath, and Chris Holland
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Silk protein solutions self-assemble to form multi-scale hierarchical structures producing a solid insoluble fibres exhibiting remarkable mechanical properties [1] and biocompatibility. These properties come from a controlled denaturation induced by shear stress during spinning. Silk peptides can therefore be used as a model system for understanding the denaturation phenomenon occurring for other proteins as well.

By providing shear stress, rheology thus became the leading technique to mimic silk’s natural spinning process whilst measuring its flow properties [3]. Besides, further insights beyond bulk rheological properties can be obtained by combining with structural analysis. With this in mind, we have developed a new tool to measure the flow properties as well as the molecular structure by coupling rheology and infrared spectroscopy. As a result, our platform has revealed the temporal relation between gelation and protein conformational change during spinning. In addition, our tool can be used to determine the quality of silk artificial analogues compared to “gold standard” native feedstocks. The feedstock characterisation is the key to unlock access to the affordable and sustainable silk industrial production for making silk based biomedical devices for regenerative medicine [2].


Poster Abstracts
P33: α-Helical peptide hydrogels as functional biomaterials

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Hydrogels have been tested in vitro as potential tissue-engineering scaffolds. These materials can influence cellular activity and act as a native tissue mimic. Here we present self-assembled α-helical peptide hydrogels (Banwell et al. 2009) specifically designed to provide a temporary support to cells. We have decorated these scaffolds with the cell adhesion motif, RGDS, to promote increased cellular proliferation and differentiation producing a functional scaffold.

Self-supporting hydrogels were formed from the undecorated and RGDS-decorated system. Electron microscopy revealed a network of interconnecting fibres, whilst CD spectra recorded data consistent with predominantly α-helical structures in both the undecorated and RGDS-decorated hSAFs. Cell studies showed high cell viability with increasing amounts of cytoplasmic projections visible, indicative of strong cellular attachment to the gel surface. Quantitative data supported the cell proliferation seen, with the assessment of metabolic activity showing an increasing number of cells present on the gel over 14 days, comparable to commercially available matrigel.

These preliminary data show that the scaffolds may be suitable for cell delivery and tissue engineering purposes.


P34: Fabrication of Stable Biocatalyst Networks for the Cascadable Manufacture of Fine Chemicals

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A fibril rich hydrogel network has been formed via the dissolution of the self-assembling peptide, VKVKVEVK in water. The biocatalytic enzyme; pentaerythritol tetrinate reducctase (PETNR) can reduce specific substrates such as the carbon-carbon double bond of small enones. These biotransformations occur optimally at physiological pH. By encapsulating VKVKVEVK tagged PETNR within VKVKVEVK hydrogels, hydrogels with biocatalytic ability are produced. The PETNR-hydrogels formed remain active towards ketoisophorone, RGDS, to promote increased cellular proliferation and differentiation producing a functional scaffold.

The system is optically transparent, permeable to surfactants, and fully reversible upon pH change. FTIR showed that peptides form antiparallel β-sheets under physiological conditions, and electron microscopy demonstrated that gels are comprised of small flexible fibrils as thick as the length of a single peptide, alongside larger interweaved and twisted fibres that are up to 100 microns in length and appear to comprise fibrils neatly aligned along their long axes. Rheology also showed that gel stiffness can be tuned via a number of factors such as concentration, pH and temperature over a very wide range (50 Pa - 100 kPa). Surfactant- and dye-modified hydrogels were found to be resistant to proteases and dilution, and released their cargo only upon addition of the correct enzyme [5]. However, this system suffered from slow response times and low sensitivity, caused by low gel permeability, and the potential for the 5CB layer to become dewetted due to sample disturbance.

To combat these limitations a novel optically transparent binary-component amyloid-based hydrogel with tunable gel permeability was designed. Modified peptides were successfully incorporated within its structure to provide a large and accessible reservoir of surfactant, that being in contact with the surface of the liquid crystal layer prevented dewetting from occurring. Initial results are promising; each component peptide remains a non-viscous solution at > 100mM at pH 1-14, while a hydrogel forms rapidly at a total peptide concentration of > 4mM at pH 4.9, in the presence of a wide range of salts and buffers. The system is optically transparent, permeable to surfactants, and fully reversible upon pH change. FTIR showed that peptides form antiparallel β-sheets under physiological conditions, and electron microscopy demonstrated that gels are comprised of small flexible fibrils as thick as the length of a single peptide, alongside larger interweaved and twisted fibres that are up to 100 microns in length and appear to comprise fibrils neatly aligned along their long axes. Rheology also showed that gel stiffness can be tuned via a number of factors such as concentration, pH and temperature over a very wide range (50 Pa - 100 kPa). Surfactant- and dye-modified hydrogels were found to be resistant to proteases and dilution, and released their cargo only upon addition of the correct enzyme, leading to a visible change in liquid crystal orientation or colour release, respectively. Response time and sensitivity were found to have been significantly improved.


P35: A Novel Hydrogel-LCD Sensor for Screening Protease Activity

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Proteases are involved in several disease states such as cancer, HIV and Hepatitis C [1]. Current methods for their detection involve methods such as fluorimetric [2] or SERRS-based detection [3], requiring the use of specialised equipment and trained personnel. Often this involves transporting samples to a specialised laboratory, further increasing the cost and time required for analysis. Therefore there is a need for low-cost, portable devices that can perform these tasks on-site.

When in contact with an octadecyltrichloro silane (OTS)-coated glass slide 4’-n-pentyl-4-cyanobiphenyl (5CB) liquid crystals align parallel to the interface in aqueous solution and appear bright when viewed through crossed polarisers due to twisting of incoming plane polarised light. When a surfactant is absorbed at this interface twisting no longer occurs, causing the liquid crystals to appear dark [4]. In previous work, surfactants anchored via a peptide sequence to immobilized PEGAs gels were shown to be released into an aqueous solution that was in contact with a 5CB layer to effect a light to dark transition only in the presence of the correct enzyme [5]. However this system suffered from slow response times and low sensitivity, caused by low gel permeability, and the potential for the 5CB layer to become dewetted due to sample disturbance.

To combat these limitations a novel optically transparent binary-component amyloid-based hydrogel with tunable gel permeability was designed. Modified peptides were successfully incorporated within its structure to provide a large and accessible reservoir of surfactant, that being in contact with the surface of the liquid crystal layer prevented dewetting from occurring. Initial results are promising; each component peptide remains a non-viscous solution at > 100mM at pH 1-14, while a hydrogel forms rapidly at a total peptide concentration of > 4mM at pH 4.9, in the presence of a wide range of salts and buffers. The system is optically transparent, permeable to surfactants, and fully reversible upon pH change. FTIR showed that peptides form antiparallel β-sheets under physiological conditions, and electron microscopy demonstrated that gels are comprised of small flexible fibrils as thick as the length of a single peptide, alongside larger interweaved and twisted fibres that are up to 100 microns in length and appear to comprise fibrils neatly aligned along their long axes. Rheology also showed that gel stiffness can be tuned via a number of factors such as concentration, pH and temperature over a very wide range (50 Pa - 100 kPa). Surfactant- and dye-modified hydrogels were found to be resistant to proteases and dilution, and released their cargo only upon addition of the correct enzyme, leading to a visible change in liquid crystal orientation or colour release, respectively. Response time and sensitivity were found to have been significantly improved.

P36: Manipulating the Mechanical and Structural Properties of Peptide Hydrogels
Jonathan Gibbons
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Peptides that self-assemble into fibrils to form hydrogels have great potential as scaffolds in 3D cell culture. It is thought that interactions between the cells and the scaffold play an important role in cell survival and proliferation, and the mechanical and structural properties of the scaffold may affect the degree of these interactions.

Two octapeptides have been designed to carry monomer charges of +1 and +2 respectively at physiological pH. Gels were prepared of both peptides at pH values where each carries a charge of either +1 or +2 and the mechanical and structural properties compared. It was observed that the elastic modulus of gels formed by the +1-charged peptides was ca. one order of magnitude higher than those of the +2s. A variety of analytical techniques (including FTIR, TEM, WAXD and SANS) were then used to ascertain what structural differences exist between the peptides in the two charge states. It was found that at +2, both peptides form fibrils that remain largely distinct from one-another, whereas at +1 bundling of the fibrils to form larger fibres occurs.

Session 7: Peptide Nanostructures for Opto / Electronic Applications

P37: Electro-conductive peptide amphiphile hydrogels: exploiting aromatic stacking interactions
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Hydrogels are composed of an extensive three dimensional structure, incorporating a high quantity of water within. These materials can be classed as chemical [1], or physical [2], the former being composed of polymer, whilst the latter relies solely on intermolecular interactions in order to influence the self assembly of smaller molecules.

An important class of physical hydrogels are those based on short peptide amphiphiles, which have been capped at the N-terminus with an aromatic moiety. In this instance, supramolecular assembly is governed by a combination of aromatic stacking interactions, and the propensity of the peptide to form a beta sheet type arrangement, as observed by FTIR and CD.

One possible strategy for augmenting the properties of these systems is via the replacement of Fmoc, with alternative aromatic functionalities [3]. The incorporation of more extensive aromatic stacking has been shown to induce a redshift in the fluorescence emission spectra; indicative of charge transfer throughout the supramolecular structure, and introduces the possibility of electronic conductivity [4].

In addition, the inclusion of different fluorophores has allowed for the more effective monitoring of co-assembled systems; where at lower concentrations, the characteristic fluorene and pyrene emission profiles gradually begin to emerge from the broad supramolecular excimer emission.

In the longer term, the aim is to more extensively characterise these systems in terms of their electro-conductive [5] properties, and intercalate with other aromatic species in order to facilitate donor-acceptor [6,7] behaviour. These constructs could potentially have future opto-electronic [6,8] or cell culture [9] applications.


P38: Superfast Supramolecular Light-Harvesting Hydrogels Formed by Enzyme-Triggered Self-Assembly
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The fabrication of functional supramolecular architectures that are capable of displaying good electrical conductivity is a challenge in bio-nano-electronics [1,2]. Recent reports have demonstrated that the enzyme-driven dynamic peptide library (eDPL) can be used to identify the most stable self-assembling peptides from component mixtures through enzyme-assisted self-assembly of short aromatic peptides [3]. The ultimate aim of this research is to exploit eDPL to achieve the most stable conductive nanomaterials from a library of several self-assembling precursor components based on the charge transfer interactions between donors and acceptors.

In particular, thermodynamically controlled thermolysin-assisted molecular self-assembly of aromatic Fmoc substituted short dipeptides has already been reported [4].

In this contribution, we show that the thermolysin-assisted reversed hydrolysis can also be extended to the non-Fmoc containing aromatic short dipeptides Nap-xy-z (Figure 1a) that forms superfast supramolecular hydrogels. We have already observed unprecedented enzyme-assisted superfast gelation behaviour for the amide derivatives, Nap-YF-NH2, Nap-YNL-NH2, Nap-FF-NH2 and Nap-FL-NH2 that form supramolecular hydrogels within couple of minutes after the addition of enzyme to the corresponding precursor components. These hydrogels were characterised by various techniques such as rheology, fluorescence spectroscopy, FT-IR spectroscopy, UV-vis spectroscopy, transmission electron microscopy (TEM) and atomic force microscopy (AFM).

However, the enzymatic reversed hydrolysis of Nap-S and Nap-T with various amide combinations did not form any hydrogels presumably due to the lack of thermodynamic driving force. Furthermore, the methyl ester derivatives of Nap-S, Nap-T, Nap-Y and Nap-F did not form any hydrogels although there is a significant conversion of reactants into products in some cases.

Fig. 1: (a) Thermolysin-catalysed reversed hydrolysis of Nap-thio substituted amino acid derivatives. (b) Optical images of Nap-xy-NH2 hydrogels.


Late Posters

P39: Self-healing hydrogels
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Hydrogels are polymeric networks, capable of absorbing large amounts of water and biological fluids. This makes them ideal candidates for use as injectable materials in the controlled release of drugs and in tissue engineering. Crosslinks are required for hydrogel stability, but the current crosslinking methods disrupt bio-degradation and lack adaptation to environmental influences. Our goal is to develop synthetic calcium-crosslinkable polymers, by adopting the calcium-binding features from biological macromolecules. For this purpose, several calcium binding peptides were synthesised, including the binding domains of the Ca2+-binding messenger protein Calmodulin. These peptides were functionalized to star-shaped PEG, to create calcium binding polymeric networks. We will also develop thermo-sensitive calcium-releasing microcapsules. In this way, triggerable
hydrogels can be created, in which we can control and time the release of calcium. These hydrogels hold promise as injectable biomaterials, which are able to assist in unique self-healing processes such as the repair of bone tissue.

P40: Cell penetrating peptides with switchable activity
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In the last twenty years, a large number of cell penetrating peptides (CPPs) have been reported. Because CPPs are able to pass cell membranes, they are promising tools for the cellular delivery of bioactive molecules. Synthetic oligoarginines form a well known family of CPPs. They are active when composed of six or more arginine residues. Despite their promising characteristics, most CPPs cannot distinguish which type of cell they are about to enter, limiting their application in drug delivery. To overcome this problem, we aimed to develop oligoarginine peptides, that can be activated by an external trigger.

To do so, we created a fluorescein-labeled series of inactive, ‘too short’ oligoarginines, consisting of three to five arginine residues and a cysteine on their C-terminus. These peptides can be activated by disulfide linkage to a complementary series of Cys(Arg)3-5 peptides. In this way, we determined whether the peptides are indeed active upon disulfide linkage, and if they lose their activity again after reduction. The internalization of these peptides into HeLa cells was studied by flow cytometry and fluorescence microscopy techniques.

P41: Computational Study of Catalytic Peptides
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The amide bond is remarkably stable under physiological conditions, yet living systems critically rely on its rapid formation and hydrolysis to assemble and disassemble proteins and peptides, a task carried out by highly efficient enzymes. The de novo design of mimics of enzymes that enable effective amidolysis without relying on cofactors has been a longstanding challenge. We have developed methodology that enables the self-selection of amidolytic oligopeptides from sequence libraries based on their function (i.e. catalytic turnover). This is achieved using phage display in combination with precursors that, upon catalytic amide condensation, form powerful gelators that encapsulate amidolytic catalysts, enabling their facile removal by centrifugation. We have demonstrated, that the resulting highly flexible oligopeptides have the ability to spontaneously fold into catalytic triads that enable catalytic hydrolysis of proteins. It is remarkable that the peptides selected from our in vitro experiments, which do not rely on a rigid binding framework, give rise to the same catalytic solution that resulted from evolution, yet with a much simpler molecular architecture and an emphasis on creating a catalytic, rather than a binding system. Our results provide new insights into enzymatic catalysis and present a new approach to discovery of catalysts. Moreover, the simplicity of the systems presented, may point to a role of catalytic peptides in the emergence of life at the molecular level.