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Peptide-based fibrous biomaterials: some things old, new and borrowed

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Bioinspired fibrous materials that span the nano-to-meso scales have potentially broad applications in nanobiotechnology; for instance, as scaffolds in 3D cell culture and tissue engineering, and as templates for the assembly of other polymer and inorganic materials. The field is burgeoning, and this review is necessarily focused. It centres on recent developments in the design of peptide-based fibres and particularly those using the α-helix and the collagen triple helix as building blocks for self-assembly. Advances include new designs in both categories, the assembly of more-complex topologies using fibres themselves as building blocks, and the decoration of the assembled materials with functional moieties.

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Introduction

An ability to design and assemble bioinspired fibrous materials from the bottom up would impact on both fundamental and applied science. The potential benefits to basic science include: improved understanding of biomolecular self-assembly in aqueous media; improved ability to predict natural biomolecular assemblies from sequence information alone; and increased confidence in engineering and designing natural and bioinspired materials *de novo*. The possible technological advances, and benefits to society in general, include the potential to create new self-assembled materials from first principles and to tailor these to specific needs; for instance, to generate minimal, self-assembled biocompatible scaffolds for cell-biological and biomedical applications such as 3D cell culture and tissue engineering; and, also, to make templates to seed the assembly of minerals (biomineralisation) and inorganic materials such as metals to make nanothin wires and interconnects, and polymers to expand the functionality of hybrid materials.

Given this backdrop, it is not surprising that considerable effort is being put into the design and assembly of biomaterials from many directions, taking different biopolymers (polypeptides, nucleic acids, lipids and polysaccharides) as inspiration. Nor should it come as a surprise that the task of programming and controlling the self-assembly of such materials is difficult. Many of Nature's scaffolds and templates are protein-based. Understanding of protein folding and assembly is improving, but it is far from complete. In addition, and although proteins are increasingly accessible through recombinant DNA technologies, the time required to engineer and prepare proteins can slow supramolecular and materials research. As a result, many supramolecular chemists and materials scientists involved in biomaterials design look to simplify the problem by working with smaller peptide units. However, what researchers gain in speed and efficiency of rounds of design and synthesis, they potentially lose in structural specificity and stability; peptide fragments tend to have less well-defined and long-lived structures than proteins. Having said this, whereas understanding sequence-to-structure relationships in whole proteins is challenging, there is a growing number of peptide folding motifs for which so-called 'design rules' are becoming available and understood. These motifs include the α-helical coiled coils and the β-structured amyloid-like assemblies and collagens.

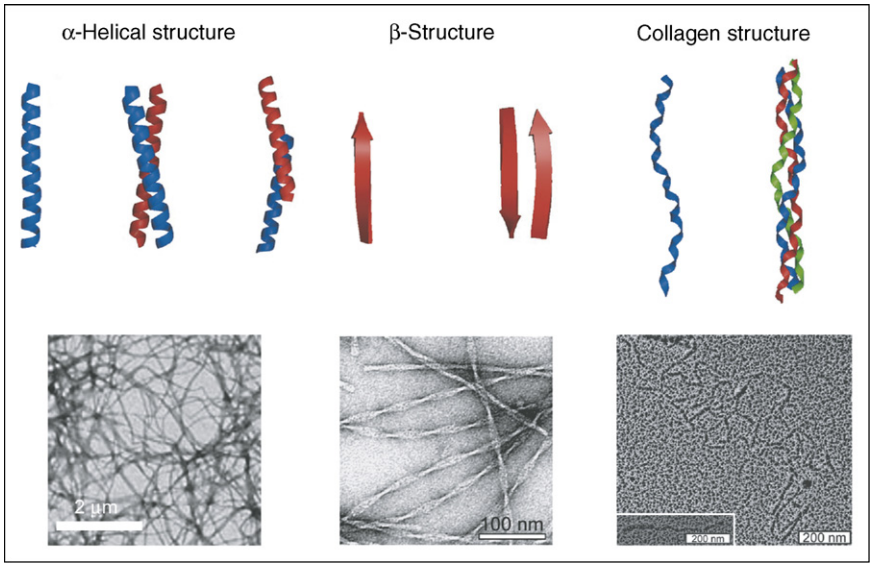
The amyloid field is vast and reviewed extremely well elsewhere. Therefore, here we review developments in the area of peptide-based biomaterials in the period January 2005 to June 2006, focusing on fibrous assemblies and materials based on the α-helix and collagens.

Assemblies based on the α-helix

The α-helix and the α-helical coiled-coil

The long-recognized α-helix (Figure 1), is a key building block of natural protein structures and, indeed, natural protein fibres [1,2]. The α-helix is a local or secondary structure element of proteins. It is formed by winding the polypeptide backbone into a right-handed helix with a periodicity of 3.6 amino acids per turn, and it is stabilized by internal backbone hydrogen bonding between the carbonyl oxygen atoms of residues, *i*, with amide hydrogen atoms of residues four along the chain, $i + 4$. This hydrogen-bonding pattern in itself, however, is not sufficient to stabilize the α-helix; stand-alone α-helices, although observed, tend not to be well-defined or long-lived structures. In proteins, α-helices pack together and gain additional stabilization through the hydrophobic effect and van der Waals' forces. As a result, α-helices

Figure 1



Protein structural motifs used as building blocks in designing self-assembling systems. To the left of each column: single peptide chains configured into an α-helix, a β-strand and a type II polyproline helix, respectively. To the right of each column: two helices married as blunt and sticky ended coiled-coil assemblies; two strands of a β-sheet; and three polyproline helices in a collagen triple helix. The α-helical, β-sheet and collagen structures were taken from the PDB entries 2ZTA, 1ICO and 1CGD, respectively. These quaternary structures can be used to produce higher-order assemblies. Examples of self-assembled fibres for each structural type are shown as transmission electron micrographs (adapted with permission from [22•,72••,77]. Copyright 2006, Wiley; 2006, National Academy of Sciences; and 2003, The American Chemical Society, respectively). The α-helical fibres comprise many protofibrils assembled from sticky-ended coiled-coil dimers and predicted to be approximately 2 nm in diameter. The protofibrils are not observed experimentally, however, as they bundle to form fibres 50 nm thick, and several microns long [22•]. The β-sheet-based fibres are bundles of 2–4 nm ribbons composed of twisted stacks of β-strands with hydrogen bonding parallel to the long axis of the fibres [77]. The collagen-like fibrils, which are approximately 20 nm long, are assembled from short sticky-ended building blocks made by covalently linking three strands that have the sequence patterns for a type II polyproline helix [72••].

tend to be amphipathic; that is, they have an apolar face — comprising hydrophobic residues (***H***) from the subset F, A, M, I, L, Y, V and W — and a polar face with hydrophilic residues (***P***) such as D, E, H, K, N, Q, R, S and T. Two or more such amphipathic helices can pack together to form globular structures in which the hydrophobic surfaces are largely buried from the aqueous media, leaving the polar faces exposed.

The α-helical coiled-coil represents an extreme of this type of helix–helix packing [3,4]. Most α-helical coiled-coil sequences are characterised by a seven-residue, or heptad, repeat of ***H*** and ***P***-type residues, ***HPPHPPP***, which is often denoted ***abcdefg***. Here, the spacing between hydrophobic residues averages to 3.5 residues. Thus, a hydrophobic seam is created along one side of the helix. However, because 3.5 falls short of the 3.6-residue helical repeat, the hydrophobic seam spirals slowly in a left-handed sense around the helix. The seams of two or more such helices can come together to form extended rope-like or fibrous structures known as coiled coils (Figure 1). This relatively precise definition of coiled-coil structures places restraints on the amino-acid usage in coiled coils, particularly at the ***H***, or ***a*** and ***d*** sites [5]. Moreover, the precise nature of amino acids at these sites strongly influences the architecture and topology of coiled-coil assemblies; that is, how many helices are in the bundle and whether they align parallel or antiparallel. These sequence-to-structure relationships gleaned from natural α-helical coiled-coil proteins constitute powerful rules for the design of novel coiled-coil-based fibrous structures [5]. Indeed, as highlighted below, the synthesis of such structures has been one of the notable successes in the field of assembling peptide/protein-based fibrous materials in recent years.

Examples of natural α-helix-based fibres include the intermediate filaments — which are coiled-coils and form structural components of the cytoskeletons in eukaryotic cells, and of certain extracellular and exoskelatal matrices — and certain viral coats.

Something old: established self-assembling fibre systems

A brief history

Several self-assembling fibrous systems based on designed linear peptides that adopt α-helical conformations were described before 2005. The first of these is by Kojima *et al.* from 1997 [6]. These workers describe a single-peptide system (the α_3-peptide) that assembles to

form fibres several microns long and 5–10 nm thick. Though lacking in detailed biophysical characterisation of the peptides and the fibres formed, this paper marks the start of the subfield.

We introduced a self-assembling fibre (SAF) system in 2000 [7]. This comprises two *de novo* leucine-zipper peptides designed to assemble in a sticky ended manner to render building blocks for elongated coiled coil-based fibrils (Figure 1). In practice, the targeted fibrils assemble further to form fibres. The mature fibres are typically ~50 nm thick and ~10 μm long. In recent years, we have built upon the SAF system in several ways: broadly and briefly, the standard linear SAF peptides have been supplemented with *special* peptides to introduce branches [8], kinks [9] and functional moieties [10] into the fibrous scaffolds.

Kajava and colleagues described an α-helical fibre-forming peptide (αFFP) system based on another coiled-coil building block, namely pentamers [11]. Unlike in the SAF design, the sticky ended building block is not set by specific side-chain interactions, rather in αFFP identical heptad repeats along a sequence gives the potential to form offset, and therefore sticky ended, building blocks, which then assemble into fibres. This works well to generate long thin fibres.

The final addition to this first set of self-assembling α-helix-based peptide fibres is from Conticello and co-workers [12] and is dubbed YZ1. This work uses a longer single coiled-coil peptide in which sticky end assembly is again prescribed by designed side-chain interactions.

Recent developments of these established systems

Of the four systems introduced above, further reports on all but the first [6] have been presented in 2005 and 2006. Regarding our own SAF system, we have described that the matured fibres assemble in a polar manner [13••]. That is, when fresh aliquots of a labelled SAF peptides are added to pre-assembled fibre, the new peptides add to the ends of the fibres and, moreover, the new peptide adds preferentially to one end. Furthermore, differently labelled peptides can be added sequentially to the growing fibres to build biomolecular barcodes. We have also demonstrated that different fibre morphologies and fibrous networks can be programmed semi-rationally by the addition of different non-linear *special* peptides [14•]. For example, kinked, multiply branched and segmented fibres can all be made, as can crosslinked fibrous networks (Figure 2).

In addition to the earlier follow-up papers detailing improvements to the design and more-detailed characterisation of fibres [15,16], Kajava and colleagues have recently reported that the αFFP system can be supplemented to incorporate the cell-binding peptide moiety, RGD, to support cell growth in culture [17•].

Conticello and colleagues have followed up their work on the YZ1 peptide with a new fibre design based on trimeric coiled-coils that incorporates buried histidine residues at three of the ***d*** sites in a six-heptad trimeric coiled-coil [18••]. This introduces a straightforward, but effective on-off switch for fibre assembly: the peptide forms helical assemblies at ~ pH 6 and above with fibres defined by transmission electron microscope (TEM) at pH 8.2, whereas no fibres are observed pH 4.

Fibre coarsening: thickening

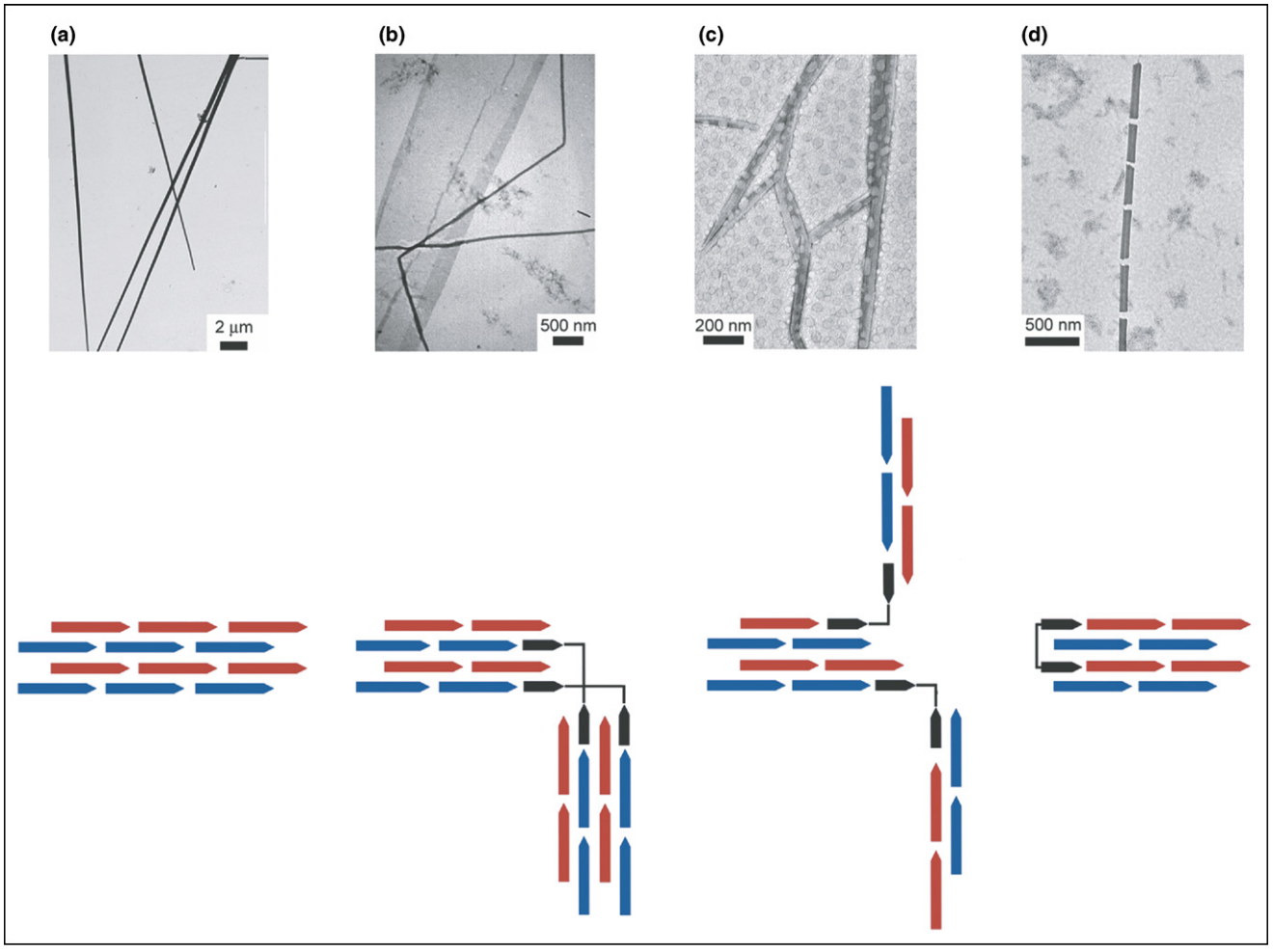
One intriguing feature of most, if not all, of the peptide-based fibres discussed above is that the intended fibrils assemble further to form thickened matured fibres. The extent of this coarsening varies from system to system. In comparison, β-amyloid-like assemblies (see below) tend to be of the order of 10 nm thick, which implies the packing of a small number of so-called protofilaments into so-called fibrils [19,20]. Whereas in our own SAF system, for example, the matured fibres can be up to 70 nm thick and involve hundreds of two-stranded coiled-coil fibrils. Some questions arise from these observations:

1. What drives the thickening process(es)?
2. Is thickening limited and can it be controlled?
3. Is thickening a failing or drawback of the design procedures and choice of building blocks?
4. Is the converse of point 3 true (i.e. is thickening actually useful)?

Firstly, thickening, at least to some extent, may well be inevitable for fibres of the types described above [7]. This is because identical chemical moieties will be presented regularly on the outer faces of the nascent fibrils through helical repetition of identical building blocks. In such arrangements, if two such moieties have some affinity for each other, however small, they will tend to zipper up via complementary patterns along the lengths of the fibrils. In this way, nascent fibrils (or other multi-peptide units) will be brought together to make thickened fibres through an avidity effect (or crystallization). Regarding limiting and controlling this process, some thought has been put into this for both the amyloid and coiled-coil systems [21,22•,23••]. For instance, if the geometry of the fibrils (or peptide units) being recruited to fibres is compromised at all upon binding, then coarsening will be arrested when the deformation energy outweighs the uncompromised binding energy. Alternatively, the thickness of the matured fibres might be determined earlier in the assembly process: for instance, this could be determined by the number of peptides co-assembled in non-fibrous aggregates, or nucleators. Resolution of this issue awaits detailed combined kinetic and structural studies of the coiled-coil-based fibrous systems described.

Whether thickening is a useful aspect of these systems depends on the particular applications in mind for the

Figure 2



Morphologies introduced by different non-linear special peptides in the SAF background. **(a)** Standard SAF preparation. **(b)** With a branching special peptide added. **(c)** With a cross-linking special peptide added. **(d)** With a special peptide that interrupts fibrillogenesis. Modes of assembly are schematically shown for each case. Standard SAF peptides (blue and red arrows) form a sticky-ended dimer that propagates longitudinally into protofibrils that by bundling together form fibres. For simplicity, only two protofibrils are shown. Special peptides are depicted as black arrows. Adapted with permission from [14]. Copyright 2005, The American Chemical Society.

fibres. For instance, thickening may be a disadvantage for making templates for nanothin wires [24,25], but an advantage for making more stable scaffolds for tissue engineering where the nanoscale precision is less important [22•].

This subject of fibre maturation has been addressed by several groups working on coiled-coil-based systems. For instance, the design of nanofilaments and nanoropes reported by Fairman *et al.* [23••] is for a leucine-zipper peptide, dubbed CpA, and in this respect is similar to the SAF and YZ1 systems. However, in CpA two 'phased' hydrophobic faces are created by inserting two alanine residues between the second and third heptads of a four-heptad sequence. (Note that similar structures found in Nature have been referred to as bifaceted [26].) CpA has another unique features — namely, Cys at the first ***a*** site to promote polymerization — but otherwise borrows from the N-terminal half of the natural GCN4 leucine-zipper sequence [27]. The aim, in part, is to address the issue of thickening by using non-covalent interactions to concomitantly favour axial and disfavour, or at least regulate, lateral modes in the assembly of fibres. The resulting fibrous structures are indeed thinner compared with the SAFs and YZ1; however, they are also much shorter. Heterogeneity in the length of the nanoropes, and some of the less-regular morphologies observed are possibly related to poor inter-associations and stabilities of the coiled-coil protofilaments [23••].

Recently, we have shown that the thickness, stability and other properties of the SAFs can be engineered to some extent through rational redesign [22•]. Briefly, the first-generation SAFs, which comprise two complementary

four-heptad leucine zippers form fibrils that assemble to matured fibres ~45 nm thick and tens of microns long [7]. In a second-generation SAF design, further thickening is promoted through additional favourable electrostatic interactions on the fibril surfaces, producing fibres that are ~70 nm thick. In a third-generation redesign, the initial step in fibrillogenesis (i.e. formation of the sticky ended heterodimer) is promoted by increasing the lengths of the interacting peptides to five heptads each; otherwise, the design is like the second-generation SAFs. Consistent with this, the third-generation fibres are more stable than the second-generation, and only slightly thinner at ~60 nm on average.

A final intriguing observation from the redesigned SAFs is that the second- and third-generation fibres, but not the first, show striations in negative-stain transmission electron microscopy reminiscent of patterns observed in natural fibrous assemblies such as collagen and fibrin [28,29]. For the designed SAF system, the distance between striations matches the expected lengths of the component peptides folded into α-helices and aligned with the long axes of the fibres. This suggests nanoscale order in the fibres above that originally designed, and that these features can be tuned by using peptides of different lengths [22•].

Some things new

More coiled-coil-based self-assembling peptide systems

Over the past 18 months, three new coiled-coil-based self-assembling peptide systems have been introduced. The aforementioned report from Fairman and co-workers describes a system in which a bifaceted peptide is used as a building block for fibre assembly [23••].

Lazar *et al.* showed that engineered helix-turn-helix fragments of apolipoprotein I assemble to form α-helical fibres [30••]. The characterisation of these assemblies is very thorough, which is critical as this is the first experimentally confirmed report of fibres in which the α-helical building blocks align perpendicular to the long fibre axis; in all of the aforementioned systems the α-helices are aligned along the long axis.

Koksch and colleagues have described a short coiled-coil-based peptide, VW19, which switches from the unfolded state to both α-helix and β-sheet-based fibrous assemblies depending on pH and peptide concentration [31]. As well as providing an unusual example of peptide-based fibres, this system adds to the growing set of design peptides that switch conformational state in response to changes in conditions [32–36]. This is an important and emerging field that is beyond the scope of this review, but which has recently been reviewed by others [37,38].

A final example of α-helix-based fibrillogenesis comes from Chakrabartty's group [39•]. They constructed a small library of 15 short peptides based on the sequence AKAxAAxxKAxAAxxKAGGY, where x is either Ala or Ile. The design aims to impart high potential α-helicity, solubility and an ability to associate via hydrophobic interactions. This simplicity distinguishes these so-called 'KIA' peptides from the more-rationally designed coiled-coil-based assemblies described above. Nonetheless, the peptides fold: one forms a native-like, four-helix bundle; 10 make molten-globule assemblies; only two are unstructured, and the remaining peptides, KIA6 and KIA13, form helical filaments [40]. One of these, KIA13, has been studied in detail [39•]. This peptide effectively has two coiled-coil heptads. α-Helical structure and fibres are induced by high concentrations of salt (up to 1 M), which presumably masks the Coulombic repulsion between the positively charged peptides. Fibrillogenesis is reversible and, interestingly, is inhibited by another of the KIA peptides, KIA16.

Assemblies based on β-structure

β-amyloid-like structures

The penultimate example of peptide VW19 [31], which forms both α-helix and β-sheet-containing fibres, provides a link to fibrous and gel materials based on β-structure. The best known of these are the amyloid-like materials. Although these structures have generally proved refractory to high-resolution structural studies, the general description of the core structure is now well established and accepted [19,20] (Figure 1): short peptides, or even large segments of whole protein chains, fold or *misfold* predominantly into β-strands that are hydrogen bonded into β-sheets; the β-sheets are paired to form protofilaments, which pack to form matured fibrils. Except for the fibres formed from fragments of apolipoprotein [30••], the assemblies described in the previous section have α-helical units that lie parallel to the long axes of the fibres. However, in amyloid-like structures, the corresponding β-strand units lie perpendicular to this axis. A final property — which also seems to be distinct from all of the α-helix-based fibre systems, and is certainly so for the SAFs characterised in our own laboratory — is that amyloid-like systems tend to gel. It is possible that this is due to shorter persistence lengths of amyloid fibres, which leads to entangled fibres and networks, matrices and gels.

The literature on amyloid-like assemblies is both broad and deep. For these reasons, and also because amyloid-based assemblies tend to gel, we deemed this area beyond the scope of this review. Nonetheless, the assembly of amyloid-like structures is fascinating, and there are many potential applications of the fibrils and gels that they form. Excellent recent reviews cover the second topic [41–44]. A few recent developments are noteworthy here, however. For example, Schneider and colleagues demonstrate that the primary physical properties of their peptide materials can be regulated by conformational changes in

peptide building blocks [45]. Their design features a short β-sheet sequence including a β-turn insertion. This insertion has a key proline residue, which, depending on its stereochemistry, sets the conformation of the peptide. This supports or discriminates specific hydrogen bonding to favour gel formation or laminated fibrillar precipitates. Along with other groups led by Zhang [46] and by Aggeli and Boden [47], these researchers are using *de novo* designed β-structured peptides to assemble fibrillar materials and reversible gels, and testing them as supportive scaffolds for cell growth, and as injectable lubricants [48–50]. Other β-structured fibrous assemblies include β-helices and silks. Again, we do not cover these structures here, but direct the reader to recent reviews [51,52].

Some things borrowed: peptide conjugates and hybrid fibrous materials

Of particular note in the context of this review, however, is the work of Mihara and colleagues [44]. The group has successfully engineered amyloid-like peptides that assemble into discrete fibres that do not gel [53]. In this work, peptide **FI** (PKFKIIEFEP) and variants of this — in which the hydrophobic residues are systematically replaced with F, I, V and Y — form twisted fibrous ribbons microns long and reminiscent of amyloid. However, the fibres are considerably thicker (at ~80–130 nm) than typical amyloid-like assemblies.

Most recently, the group has combined the **FI** design with their previously developed concept [54•] — which is analogous to those introduced by others [10,55,56] — to decorate fibrillar structures with functional moieties. In the foregoing work, another peptide, **β16**, designed as an α-to-β structural switch [44], is derivatized with biotin through an N-terminal, hydrophobic, 6-aminohexanoic acid spacer. Mixtures of the naked and derivatized peptides produce co-fibrils that can be regularly decorated with streptavidin modified with nanogold particles. In the new work, **FI** and related peptides are conjugated to biotin via the same hydrophobic spacer or a polar linker. Unlike in the work with **β16**, mixtures of **FI** and biotinylated **FI** do not render decorated co-fibres. However, both of the conjugated peptides alone formed 'fibres' that can be decorated with anti-biotin antibodies carrying gold nanoparticles [54]. Interestingly, the modifications to the **FI** peptide change the morphology of the fibrous structures: whereas the unmodified peptide form twisted ribbons ~ 100 nm thick [53], the biotin–spacer–peptide conjugates form well-defined nanotubes that are thinner (50–70 nm) and are clearly hollow [54•] with inner diameters of 20–35 nm.

Before moving on from the decoration of amyloid-like assemblies, recent work from Baldwin *et al.* is also worth noting [57•]. This team have fused the genes for an amyloid-forming SH3 domain and metalloporphyrin-binding cytochrome b_{562}. Acid-induced fibrillogenesis of the fusion protein produces fibrils typical of amyloid in their structural and tinctorial properties. Furthermore, haem-binding and the resulting redox properties of the cytochrome can be reconstituted in these assemblies.

Another type of protein chimera in which the two components are maintained in their correctly folded states involves the fusion of a Dps protein and one of the aforementioned β-helix structures, namely that from the tailspike of bacteriophage T4 [58]. This 'ball-and-spike' construct, although not directly related to the work otherwise presented herein, holds promise for the construction of protein-based biomaterials in general along the lines suggested by Yeates and colleagues [59].

The tubular structures formed by the **FI** conjugates [54], along with fibrillar structures reported by others, share morphological similarities with nanofibres formed by the peptide amphiphiles described by Stupp and co-workers [60], and dipeptides from Reches and Gazit [24]. These designs have advanced in several ways in the past 18 months. For instance, the Stupp nanofibre architecture is shown to tolerate various conjugated derivatives including the RGD motif, biotin, inorganic materials and peptide-nucleic acids [55,56,61,62]. These moieties are introduced using orthogonal chemistry to allow branched nanofibre-forming components as applied in our laboratory to otherwise linear polypeptides [8–10,14•]. The nanofibres have been further developed as biocompatible scaffolds to mimic the extracellular matrix for tissue engineering [63–65]. Reches and Gazit have further characterised their dipeptide-based nanotubes, and built on them in several exciting ways particularly in the area of electrochemical biosensors [66–69].

New collagen-based assemblies

It is reasonable to bracket collagen-type assemblies [70] with the amyloids because their backbone geometries are similar (Figure 1): both fall in the top left-hand corner of the Ramachandran plot. There are notable and important differences between the two structures, however. As mentioned, amyloid-like structures are made of β-strands hydrogen bonded into β-sheets. Though they are not often described as such, β-strands are in fact helices with 2 residues per turn and a rise per residue of ~3.3 Å. Collagens are based on the polyproline type II helix, which is left-handed. Through small changes in the backbone torsion angles, this structure has three residues per turn and a slightly decreased rise per residue of ~3.1 Å. To complete the comparison, the α-helix is right handed and has 3.6 residues per turn, and a rise per residue of 1.5 Å.

As with β-strands, and unlike α-helices, stabilization by intrahelix hydrogen bonding is not possible in the polyproline type II helix. In collagen, three such helices assemble to form a tight left-handed superhelix

(Figure 1) with a ~10 nm pitch. Some of the backbone CO and NH groups form interchain hydrogens, leaving the others solvent exposed. The tightness of the superhelix restricts the centre-most positions to glycine, and collagen sequences are characterised by tandem triplet repeats comprising proline-hydroxyproline-glycine ('POG'). Because collagen is a major component of the extracellular matrix and connective tissue, the creation of new collagen-based materials self-assembling is a clear target for the development of novel biomaterials for tissue engineering [71]. However, the synthesis of proline and glycine-rich sequences is non-trivial, and, until recently, no rational self-assembly strategies have been presented to make extended fibrous structures from such peptide building blocks.

Two groups have adopted the sticky ended concept used in recombinant DNA technology, as exemplified in the aforementioned SAF system for peptides [7], to present an elegant solution to the second problem noted above [72••,73•]. In essence, both groups create a sticky ended building block for collagen assemblies by cross-linking three POG-based sequences together with staggered disulfide bridges. The folding and assembly of the fragments are probed and confirmed using a range of biophysical methods. The work of Kotch and Raines is the more developed. They observe assemblies directly by AFM, which highlights some structures > 400 nm, which is larger than natural collagens. Hartgerink and colleagues take a different tack to the same problem [74••]. This group use chemical ligation to generate large polymers of POG-based peptides. These assemble into collagen-like structures and networks as demonstrated by CD spectroscopy and electron microscopy. As with the work of Kotch and Raines, the resulting fibres are very extended, in this case up to microns in length. Finally, Su and colleagues have pursued approaches to modify and functionalise collagen fibres and networks [75,76]. Here, short POG-based peptides are synthesized and tagged with fluorophores and other moieties. These are then incorporated into collagen assemblies by an annealing process of heating and cooling.

Summary, scope and perspectives

It is an exciting time for biomaterials research. Specifically for soft, fibrous materials, we are witnessing rapid development and expansion of the field. This was once the province of synthetic polymer chemistry and, to a lesser extent, naturally derived biomaterials. Over the past decade, however, synthetic and overexpressed peptide and protein precursors have been introduced as the raw materials of fibrous biomaterials. For example amyloid-like materials, which are based on β-structure, designed α-helix-based assemblies and, most recently, self-assembling collagen-like materials have all been reported. Because of their inherent solubility in water (at least of the building blocks), biocompatibility and natural functions, such materials bring exciting possibilities for working with biological systems and towards biomedical applications. Furthermore, the ability to append peptides and proteins with other active moieties, whole proteins and materials is fostering the development of functional and hybrid materials. Potential applications for these in bionanotechnology include the construction of nano-to-meso scale objects, templating inorganic materials including nanothin wires, and as scaffolds for the adhesion, growth and differentiation of cells (i.e. cell and tissue engineering).

Acknowledgements

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