REVIEW

The role of β-sheets in the structure and assembly of keratins

R. D. Bruce Fraser · David A. D. Parry

Abstract X-ray diffraction, infrared and electron microscope studies of avian and reptilian keratins, and of stretched wool and hair, have played a central role in the development of models for the β-conformation in proteins. Both α- and β-keratins contain sequences that are predicted to adopt a β-conformation and these are believed to play an important part in the assembly of the filaments and in determining their mechanical properties. Interactions between the small β-sheets in keratins provide a simple mechanism through which shape and chemical complementarity can mediate the assembly of molecules into highly specific structures. Interacting β-sheets in crystalline proteins are often related to one another by diad symmetry and the data available on feather keratin suggest that the filament is assembled from dimers in which the β-sheets are related by a perpendicular diad. The most detailed model currently available is for feather and reptilian keratin but the presence of related β-structural forms in mammalian keratins is also noted.

Keywords α-keratin · β-keratin · Feather keratin ·
Reptilian keratin · Twisted β-sheets · Amyloid filaments

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Introduction

In the early 1930s, Astbury and co-workers studied the molecular structure of keratins using high-angle X-ray diffraction methods. They observed a meridional arc at a spacing of 0.51 nm in mammalian keratins such as wool, noting that this value was inconsistent with that expected from an extended polypeptide chain. Consequently, they proposed that the chain was folded. This led to the discovery of the α-helix and the coiled-coil α-helical rope. They also found that when wool was stretched to approximately double its original length in steam the original X-ray diffraction pattern (the α-pattern) was transformed into a second pattern resembling that obtained from silk. This they designated the β-pattern. In a further study, the chains in the β-form were shown to be antiparallel and packed together in sheets with three-dimensional regularity (Astbury and Woods 1933). The axial separation between residues (0.31 nm), however, was somewhat less than that seen in silk (0.334 nm). Later, a detailed pleated sheet model containing antiparallel chains was devised (Pauling and Corey 1951) and this was shown to be consistent with the intensities observed in the X-ray diffraction pattern of β-keratin (Fraser et al. 1969).

   Much has been learned about the β-conformation through the study of synthetic polypeptides (Fraser and MacRae 1973) and, in more recent times, a range of complex assemblies derived from the pleated sheet have been observed directly in both fibrous and globular proteins. These include the β-solenoid, the triple-stranded β-solenoid, the cross β-prism, the triple β-spiral and the spiral β-hairpin staircase (Kajava et al. 2006). To date, the only modification to the simple pleated sheet that has been shown to exist in keratins is the right-handed twist commonly observed in small sheets.

Avian and reptilian keratins

Although epidermal appendages such as the claws of mammals have similar functions and mechanical properties to those found in birds and reptiles their chemical compositions and molecular structures are quite different. In particular, mammalian hard keratins contain three disparate groups of proteins, each with many members (Gillespie 1990), whereas feathers contain only one type of protein with very few members (O'Donnell 1973). The first indication of differences in molecular structure was revealed in X-ray diffraction studies on feather keratin which indicated that the dominant secondary structure was based on the β-conformation (Marwick 1931; Astbury and Marwick 1932). Although the axial rise per residue (0.31 nm) was significantly lower than that observed in steam-stretched wool (0.334 nm) it was found possible to increase this to the "normal" value by stretching in steam, thereby adding credence to the designation of a β-type conformation.

Several models were suggested for feather keratin including a tubular β-helical structure (Schor and Krimm 1961). The crystallinity evident in high-resolution X-ray diffraction patterns, however, was not sufficient for classical crystallographical approaches to succeed; in addition the external interference between the filaments was too great for the pattern to be analyzed as the cylindrically averaged intensity transform of a helix. The external interference could be reduced, nonetheless, by selectively destroying the longitudinal and rotational correlation between filaments by mechanical treatments, thereby producing a 'simplified' X-ray diffraction pattern characteristic of a helical structure (Bear and Rugo 1951; Fraser and MacRae 1963). The helix had four units per turn and a pitch length of 9.5 nm. Using electron microscopy (Filshie and Rogers 1962) and infrared dichroism, it proved possible to develop a detailed model (Fraser et al. 1971). Individual molecules, each consisting of about 100 residues, were predicted to contain a β-favoring segment around 32 residues long that collectively formed the filaments observed in the electron micrographs. It was further proposed that each 32-residue segment folded into a four-stranded β-sheet that was twisted in a sense opposite to that of the helix and that the molecules associated in pairs to form antiparallel dimers. Axial polymerization of these dimers then formed the filaments. The concept of a *twisted* β-sheet in proteins, rather than a *planar* one, was unique at that time, but it was shown later that small twisted sheets are energetically more stable than planar ones and are now regarded as the norm.

Unfortunately, the observed intensities in the X-ray diffraction pattern obtained from feather keratin cannot be phased using the methods employed with crystalline proteins. Consequently, it is not possible at present to obtain electron density maps showing the positions of the individual atoms and so the structure cannot be solved directly. However, following the determination of the amino acid sequence of emu feather (O'Donnell 1973), the original model has been progressively refined by trial-and-error methods (Fraser and MacRae 1976; Fraser and Parry 1996, 2008) and its current status is shown in Fig. 1.

The mainchain coordinates are based on the original 'ruled surface' type of distortion used to introduce a twist into the β-sheet (Fraser et al. 1971). There is a current need for a more realistic set of atomic coordinates for the mainchain atoms probably based on the large amount of data on twisted β-sheets that has been collected from crystallographic studies. The reduced length of the axial repeat length observed in feather keratin provides a benchmark for selecting possible conformations of the twisted β-sheet and we have recently explored known structures which contain similar pairs of interacting twisted β-sheets. For example, Fig. 2 shows the mainchain in the β-sheet segments in the sugar-binding protein Congerin II (Kamiya et al. 2002). This contains a pair of twisted β-sheets packed together in a manner similar to that envisaged in the feather keratin dimer (Fig. 1b). The inclinations of the central chains in the front and rear sheets of Congerin II to what would be the fiber axis (z-axis) in feather can be calculated from the expressions

$$\cos \theta_a = \cos \theta_b = [a \cdot (a + b)]/|(a + b)| \qquad (1)$$

where a and b are unit vectors parallel to the intersecting red lines in Fig. 2, a · denotes a vector dot product, a + sign denotes a vector addition and || a magnitude. Similarly, the inclination to the fiber axis of the adjacent chain, also shown in red, is given by

$$\cos \theta_c = [c \cdot (a + b)]/|(a + b)| \qquad (2)$$

where c is a unit vector parallel to the direction of this chain.

The mean separation per residue along the length of the chain in the inner chains is 0.328 nm and that in the adjacent chain is 0.333 nm. These values are close to the 0.334 nm spacing observed in the extended planar β-sheets derived from stretched α-keratin. The inner chains are inclined at 14.3° to the z-axis and the adjacent chain is inclined at 20.3°. The mean axial rise per residue parallel to the axis in a twisted sheet with two inner and two outer chains would therefore be predicted to be 0.316 nm. Thus, a conformation similar to that observed in Congerin II, if present in feather keratin, would provide a plausible explanation for the observed axial spacing of 0.31 nm (Astbury and Marwick 1932).

Detailed studies of the twisted β-sheets in crystalline proteins have revealed that the ϕ and ψ values that characterize the progression of the chain from one residue to the next oscillate between two sets of values depending on the side of the sheet from which the sidechain projects, and that the values vary according to the lateral position of the chain in the sheet. These factors need to be incorporated into any
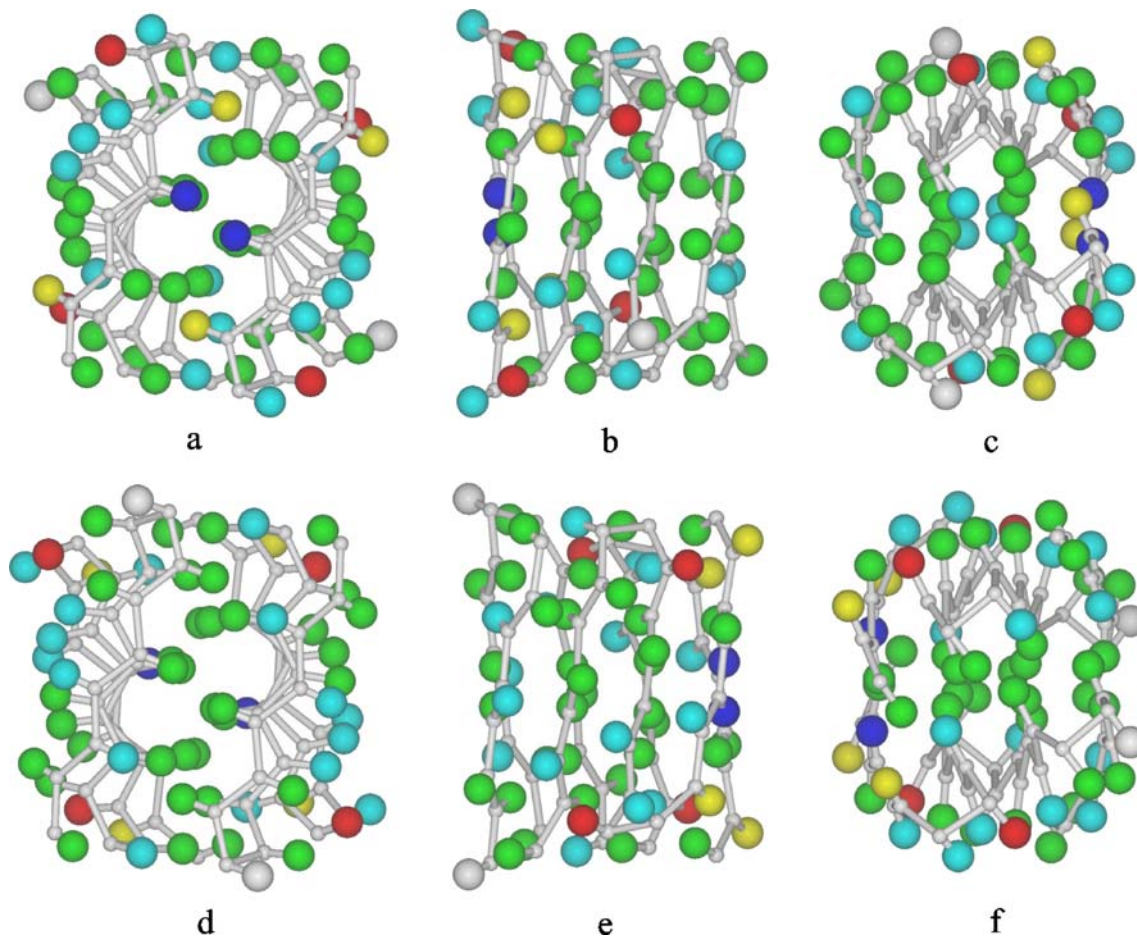
Fig. 1 Two models for the repeating unit in the feather keratin filament. The colored spheres delineate the approximate localities of the sidechains of emu feather (green, hydrophobic; pale blue, hydrogen-bonding; red, acidic; dark blue, basic; yellow, half-cystine; grey, glycine). The *upper views* correspond to *Structure A* and the lower views to a possible alternative *Structure B*. **a** and **d** are projections down the diad (*x-axis*), **b** and **e** are projections down the y-axis, and **c** and **f** are projections down the axis of the filament (*z-axis*)

procedure for predicting the atomic coordinates in twisted β-sheets of feather keratin.

Sequence comparisons across avian and reptilian keratins

Many data are now available for the β-keratins from both birds and reptiles. The distribution and variability of residues across the 32-residue segment (including the composition of the β-bends) have been analyzed (Fraser and Parry 2008; Alibardi et al. 2008; Table 1 and Fig. 3) and notable features include:

1. The conservation of a P-G-P motif that is part of one of the proposed hairpin turns and, as such, may provide the nucleation site for the β-sheet,
2. A preponderance of apolar residues on the inner face of the β-sheet (Fig. 4) and of charged and cysteine residues on the other,
3. The frequent occurrence of a charged residue in the first strand of the β-sheet thereby preventing the exposed edge of one sheet inappropriately bonding to the exposed edge of another sheet (Richardson and Richardson 2002), and
4. The unusual proline-rich sequences that are believed to play an important role in the formation of the three proposed hairpin turns.

The arrows in Table 1 show the original assignment of turn residue locations in emu feather (Fraser and MacRae 1976). The alignment of the other sequences is one of several alternative possibilities, maximizing the alignment of proline residues and is similar to that used in earlier studies. An alignment based on general sequence homology is similar except for the first few residues where there is a deletion located beneath the fourth residue of the emu sequence (F) in all the other sequences. The emu sequence was determined when methods were less reliable than those today and an independent determination is advisable.
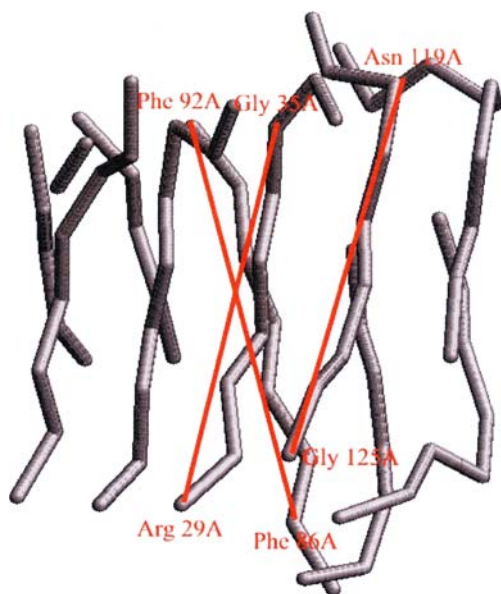
Fig. 2 The mainchain segments in the β-sheet "sandwich" in the sugar-binding protein Congerin II (Kamiya et al. 2002) provide a possible model for the geometry of the β-sheet sandwich in feather keratin

In fibrous proteins containing large β-sheets with repeating patterns of sidechains, such as *Bombyx mori* silk fibroin, complementarity of shape plays an important part in determining the way in which the sheets pack together. With smaller twisted sheets that lack such regularity, shape complementarity plays a less important part and the chain directions in pairs of sheets are commonly inclined to each other at an angle of around 30° (Chothia and Janin 1981). Because of the short lengths of chains involved, the maximum lateral displacement is only around ±0.2 nm and so a simple linear display of chemical properties such as that shown in Fig. 4 can be used to search for complementarity of chemical properties at the interface between the two sheets related by the diad. This reveals a concentration of hydrophobic residues in the inner region and a cluster of hydrogen-bonding residues towards the periphery.

The calculated length of the β-sheet is very close to that of the unit height of the helix, indicating that the ends of dimers must be in close contact. The nature of this interface, which is important in axial polymerization, is more difficult to investigate since there is no requirement that the twist of the sheet is exactly 90° in the unit height. If it was, in fact, 90°, and allowing for the fact that the hand of the helix is opposite to that of the sheet twist the situation at the interface would be as illustrated in Fig. 5. The proximity between hydrophobic sidechains on the upper surface of a dimer and those on the lower surface of the dimer above will contribute to the stability of the polymer as will hydrogen-bonding residues. However, there

will be repulsion between the negatively charged residues in position 9. Assignments of structural positions in the first and fourth chains are subject to some uncertainty (Fraser and Parry 2008). Also, the β-sheets constitute only about one third of the residues in feather keratin and it is likely that the residues adjacent to the 32-residue segment will also be involved in polymerization.

Amyloid-like filaments from feather keratin proteins

Another manifestation of the β-pattern reported by Astbury et al. was one in which the high-angle X-ray diffraction pattern indicated that the polypeptide chains were oriented perpendicular to the fiber axis. This was termed the cross-β pattern (Astbury et al. 1935). The original observations were made on denatured globular proteins but subsequently the cross-β pattern was observed in low-molecular-weight synthetic polypeptides (Fraser and MacRae 1973) and in the naturally occurring egg stalk of the green lacewing fly *Chrysopa flava* (Parker and Rudall 1957).

Keratins are extensively crosslinked by disulphide bonds formed between cysteine residues during the final stages of biosynthesis. Feather keratin can be solubilized by cleaving the disulphide linkages and chemically modifying the cysteine residues. X-ray diffraction patterns obtained from oriented films of these derivatives were found to be of two distinct types. In the first, the original filamentous structure appeared to have been restored (Rougvie 1954), suggesting that the disulfide linkages were not involved in the assembly process. In the second, the X-ray pattern was of the cross-β type suggesting that polymerization occurred via the hydrogen bonds of the β-sheets, so that the chains became oriented perpendicular to the fiber axis (Filshie et al. 1964). Electron microscope studies of the latter revealed the presence of filaments around 4 nm in diameter that were twisted around each other in pairs (Fig. 6, lower micrograph) and assembled into ordered sheets (Fig. 6, upper micrograph). The filaments bear a close resemblance to the cross-β structures commonly referred to as amyloid filaments.

Other β-sheets

The β-sheets thus far described have been confirmed through high-angle X-ray studies. However, there are segments of the amino acid sequence in mammalian, avian, and reptilian keratins for which there is a high expectation that the polypeptide chain will also adopt an extended conformation. In these cases, the orientation of the sheets is probably such that their contribution to the X-ray diffraction pattern cannot easily be recognized.

Table 1 An alignment of sequences in the β-sheet segments of avian and reptilian keratins that maximizes the coincidence of proline residues

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         ↓↓    ↓↓↓↓    ↓↓↓↓    ↓↓↓↓    ↓↓ *
    PCLFRQCQDSTVVIEPSPVVVTLPGPILSSFP  emu feather (Dromaius novaehollandiae)ᵃ
    PC VRQCEASRVVIQPSTVVVTLPGPILSSFP  seagull feather (Larus novaehollandiae)ᵇ
    PC VRQCQDSRVVIQPSPVVVTLPGPILSSFP  chicken feather (Gallus domesticus)ᶜ
    PC VRQCQDSRVIIEPSPVVVTLPGPILSSFP  turkey vulture bristle (Cathartes aura)ᵈ
    PC VRQCPDSTTVIQPPPVVVTFPGPILSSFP  chicken scale (Gallus domesticus)ᵉ
    PC VRQCPDSTVVIQPPATVVTFPGPILSSFP  chicken claw (Gallus domesticus)ᶠ
    VL VDTGSTTDVHVQPGGCSLTIPGPRLISYS  goanna claw (Varanus varanus)ᵍ
    PSCINQIPPAEVVIQPPPVVMTLPGPILSATG  gecko skin 1-2 (Tarentola mauritanica)ʰ
    PSCINQIPPAEVVLQPPPVVVTLPGPILSATG  gecko skin 3 (Tarentola mauritanica)ʰ
    PSCINQIPPAEVVIQPPPVVMTLPGPILSATG  gecko skin 4 (Hemidactylus turcicus)ʰ
    PSCINQIPPAEVVIQPPPVVLTLPGPILAATG  gecko skin 5 (Hemidactylus turcicus)ʰ
    PSCINQVPASEVTIQPPAVIVTIPGPILSASC  snake 2-3 and 4 (Elaphe guttata)ⁱ
    PSCINQIPASEVTIQPPAVVVTIPGPILSASC  snake 5 (Elaphe guttata)ⁱ
    PKPINQIPPAEVVVQPPACVLTIPGPILSASC  wall lizard 1 (Podarcis sicula)ⁱ
    PC VRQCQDSQVVINPSPVVMTLPGPILSNFP  turtle 1 (Pseudemys nelsonii)ʲ
    PC VRQCPDSEVVIQPSPVVVTIPGPILSNFP  turtle 2 (Pseudemys nelsonii)ʲ
    AC IRQCPDSRAVIQPPPVVVTLPGPILSSFP  crocodile 1 (Crocodylus niloticus)ʲ
    AC IRQCPDSRVVIQPPPVVVTIPGPILSNCP  crocodile 2 (Crocodylus niloticus)ʲ
    AC IRQCPDSRVVIQPPPVSVTIPGPILSNFP  crocodile 3 (Crocodylus niloticus)ʲ
         ↑↑    ↑↑↑↑    ↑↑↑↑    ↑↑↑↑    ↑↑ *
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The arrows show the original assignment of turn residue locations in emu feather (Fraser and MacRae, 1976). The alignment of the other sequences is one of several alternative possibilities. That shown maximizes the alignment of proline residues and is similar to the one used in our earlier studies

[a] O'Donnell (1973)
[b] O'Donnell and Inglis (1974)
[c] Presland et al (1989): the same sequences is present in duck (*Anas platyrhynchos*) and pigeon (*Columba livia*)—Arai et al. (1986)
[d] Sawyer et al. (2003)
[e] Walker and Bridgen (1976)
[f] Inglis et al. (1987)
[g] Whitbread et al. (1991)
[h] Toni et al. (2007a)
[i] Toni et al. (2007b)
[j] Dalla Valle et al. (2008)

An additional β-sheet in chicken leg scale

The molecular weights of chicken scale and feather keratins differ significantly from one another (about 15 and 10.5 kDa respectively) and this is almost entirely accounted for by the presence in scale, but not in feather, of a fourfold repeat (residues 77–128) of a 13-residue, glycine–tyrosine-rich motif (G-Y-G-G-S-S-L-G-Y-G-G-L-Y). X-ray diffraction studies of powdered scale keratin corresponding to this particular region (Stewart 1977) have indicated a β-structure. The 52-residue segment (Fig. 7) is located C-terminally with respect to the 32-residue β-favoring motif discussed earlier (residues 25–56). The latter lacks tyrosine residues and contains but a single glycine, thereby illustrating the very non-uniform distribution of the glycine and tyrosine residues in scale keratin. In fact, in scale, the bulk of both residue types lies in the C-terminal half of the chain (29 glycines and 20 tyrosines are found in residues 77–155 and only seven glycines and two tyrosines occur in residues 1–76).

Secondary structure prediction techniques suggest that the 52-residue, fourfold repeat will adopt an eight-stranded, antiparallel, twisted β-pleated sheet conformation with the β-turns each having a G-Y-G-G sequence (Gregg et al. 1984). This would give rise to rows of highly interactive tyrosine residues, especially in the turn regions. Glycine–tyrosine-rich proteins play an important part in mediating the properties of mammalian keratins but virtually nothing is known about the way in which they interact with the filaments. A similar situation exists as regards the glycine–tyrosine rich segment in avian scale keratins although some possibilities have been discussed (Fraser and Parry 1996).

An additional β-sheet in lizard claw

The first reptilian hard keratin to be analyzed in detail was from lizard claw (*Varanus varius*). A 32-residue segment of similar composition and sequence to that found in feather keratin was also found to be present in this reptile (Fraser and Parry 1996). In addition, a second "ghost" segment was also observed in the sequence, though its degree of similarity with the feather repeat was less well-developed. It is not yet clear whether this second segment represents a structurally significant feature of reptilian keratins.

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AFILMVWY    Hydrophobic
NQST        Hydrogen Bonding
HKR         Basic
DE          Acidic
C           Cysteine
P           Proline
G           Glycine
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Avian Feathers and Scales

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  ↓↓     ↓↓↓↓      ↓↓↓↓       ↓↓↓↓      ↓↓
PCLFRQCQDDTVVIEPSPVVVTLPGPILSSFP    emu feather
PC VRQCQADRVVIQPSTVVVTLPGPILSSFP    seagull feather
PC VRQCQDDRVVIQPSPVVVTLPGPILSSFP    chicken feather
PC VRQCQDSRVIIEPSPVVVTLPGPILSSFP    turkey vulture
PC VRQCPDDTTVIQPPPVVVTFPGPILSSFP    chicken scale
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Comparison of Avia and Reptilia

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  ↓↓     ↓↓↓↓      ↓↓↓↓       ↓↓↓↓      ↓↓
PC VRQCQDDRVVIQPSPVVVTLPGPILSSFP    chicken feather
PC VRQCPDDTTVIQPPPVVVTFPGPILSSFP    chicken scale
GVLVDTGSTTDVHVQPGGCSLTIPGPRLISYS    goanna claw
PSCINQIPPAEVVIQPPPVVMTLPGPILSATG    gecko skin 1-2
PSCINQIPASEVTIQPPAVVVTIPGPILSASC    snake 5
PC VRQCQDSQVVINPSPVVMTLPGPILSNFP    turtle 1
       Δ        Δ ▲      Δ   ▲▲▲ ▲
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↓ Suggested turn residues in emu feather
▲ Invariant across all the above sequences
Δ Large hydrophobic in all the above sequences

Fig. 3 Comparison of representative examples from the database of sequences of avian and reptilian keratins (see Table 1 for references). The residue letters are colored to indicate their special property (see *key at top of the diagram*). Patterns of proline and large hydrophobic residues are evident as is the constancy of a PGP sequence. Greater variability occurs in the early part of the segment and the alignment of the sequences in this region is less certain. The alignment shown maximizes the coincidence of proline residues (Fraser and MacRae 1976)

β-sheets in mammalian keratin

In each of the examples below, there are no X-ray diffraction data that provide experimental evidence for the existence of β-sheets. In every case, the conformation is predicted on the basis of the amino acid sequences and each must, therefore, be treated with caution until supported by experimental data.

1. In the tail region (C-terminal domain) of the Type II trichocyte keratin chain the sequence immediately adjacent to the coiled-coil rod domain is predicted to adopt a four-stranded antiparallel β-pleated sheet (Fig. 8; Parry and North 1998). The first (S-S-S-R) and second β-bends (S-G-S-R/A) have near identical sequences as do the third (A-P-C-S) and fourth (A-P-C-G). One face of this putative structure would be composed almost entirely of apolar residues whereas the other would contain predominantly cysteine and charged residues. Since the companion (parallel, in-register) Type I chain lacks this feature, the most likely partner for the β-pleated sheet would be one from the same chain in different molecule. The apolar faces would be expected to come together to stabilize the assembly. The topology

of the intermediate filament makes it most probable that the partner would arise from an antiparallel rather than a parallel molecule within the filament structure itself.

2. The head region (N-terminal domain) of the Type II trichocyte keratin chain contains a fourfold contiguous repeat of nine residues (G-G-F-G-Y-R-S-X-G). This too is thought to adopt a β-pleated sheet conformation but in this case, there is not a clear chemical sidedness to the two faces (Parry et al. 2002). It would still be expected, nonetheless, that this sheet would interact with the same region emanating from a second molecule. Some similarities with the 13-residue repeat in scale keratin are worth noting, most notably the high glycine and aromatic residue content in both motifs.
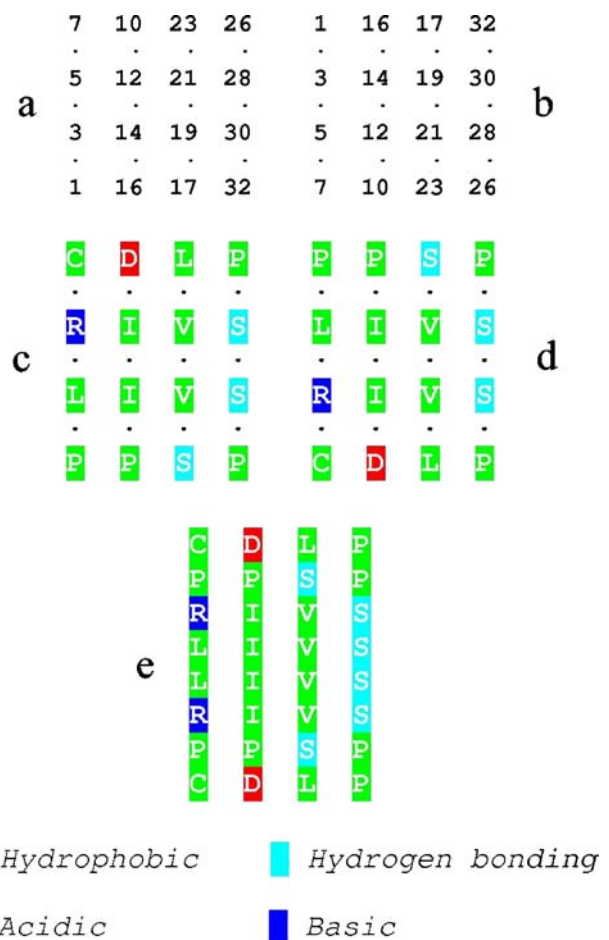

Fig. 4 The distribution of sidechains in the interior of the model for the feather keratin dimer shows a preponderance of large hydrophobic residues but also opportunities for hydrogen bond formation towards the edges. The half-cystine residue (*7*) has been shown as hydrophobic since this aspect of its character is important here. Also evident are the negatively charged residues (*5*), which may prevent unwanted lateral aggregation (Richardson and Richardson 2002). **a** Residues on the inner surface of the Up component of the dimer and **b** the inner surface of the Down component viewed from the same direction. **c** and **d** show the nature of the residues in emu feather and **e** shows the two surfaces superposed
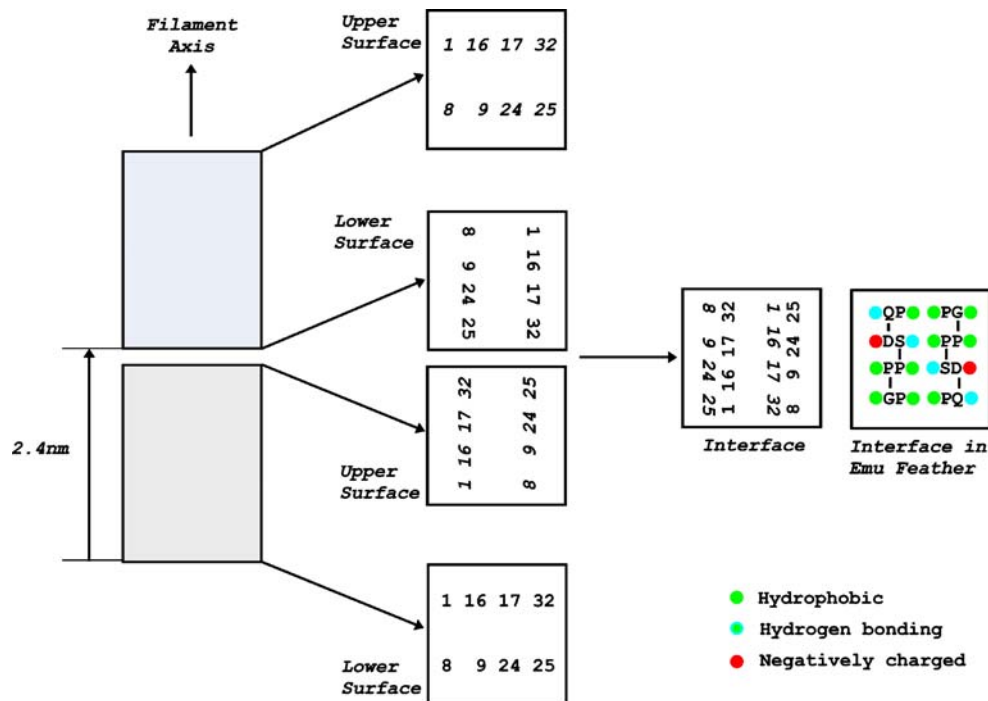
Fig. 5 The area of contact between successive repeating units along the length of the feather keratin filament. The repeating units (*shaded*) are spaced at axial intervals of 2.4 nm and the left-handed helical symmetry means that when viewed down the filament axis, there is a 90° rotation about the filament axis in a clockwise direction between successive repeating units. Each repeating unit comprises a pair of twisted β-sheets related by a perpendicular diad and the distribution of residues in the upper and lower surface of each of the repeating units (viewed down the axis) is shown on the right. Allowance must be made for the fact that the β-sheets have a right-handed twist (i.e., a counterclockwise rotation when viewed down the filament axis) and the phasing in the end views has been adjusted appropriately. A right-handed twist of 90° was used although there is no requirement that that it be exactly this value and is likely to be slightly less. The upper surface of the lower repeating unit and the lower surface of the upper repeating unit are combined to show the residues that populate the interface between the two repeating units in emu feather. The majority of these residues are hydrophobic, with some having hydrogen-bonding potential. Two negatively charged sidechains occur near the periphery. Parts of the remainder may also contribute to the interactions regulating end-to-end polymerization

3. The two-stranded rod domain of keratin intermediate filament molecules consists of long segments of α-helical coiled-coil structure (1A, 1B, 2A, and 2B) interrupted by short, non-helical linkers known as L1, L12, and L2. Of these, a portion of L12 has a repeat of the form (apolar-hydrophilic)$_4$ (Parry and Fraser 1985). As such, the possibility has been raised this might form a pair of parallel β-strands with an apolar aspect (Conway and Parry 1988) and that a mini β-sheet could be formed with the same region in an oppositely directed molecule in the A$_{12}$ mode of aggregation. Predicting the conformation of such a short piece of sequence is extremely difficult and the model postulated must remain very speculative.

Summary

We have drawn attention to the diverse ways in which β-sheets contribute to the structure of keratins. The formation and subsequent interactions between small β-sheets in both
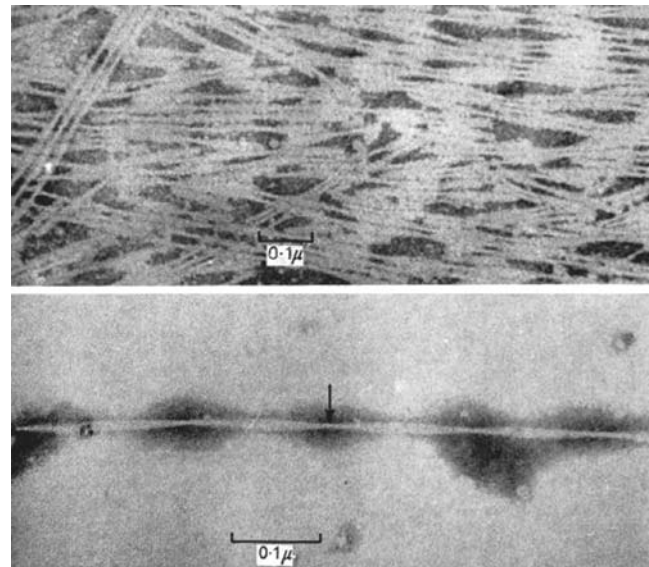

Fig. 6 Amyloid-like filaments regenerated from a purified fraction of solubilized fowl feather (Filshie et al, 1964). X-ray diffraction studies suggest that feather keratin dimers in this preparation are aligned with the polypeptide chains oriented perpendicular to the axis of the filament giving a cross-β structure
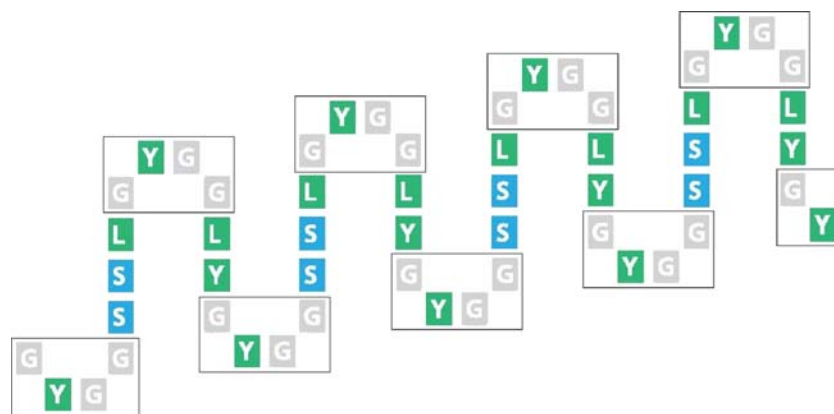
Fig. 7 Diagrammatic representation of the potentiality for β-sheet formation in the 52-residue segment in chick scale keratin that comprises four consecutive 13-amino acid residue repeats

fibrous and globular proteins appears to play an important role in the assembly of the molecules into well-defined aggregates. The characteristic right-handed twist, and the commonly observed partitioning of different residue types
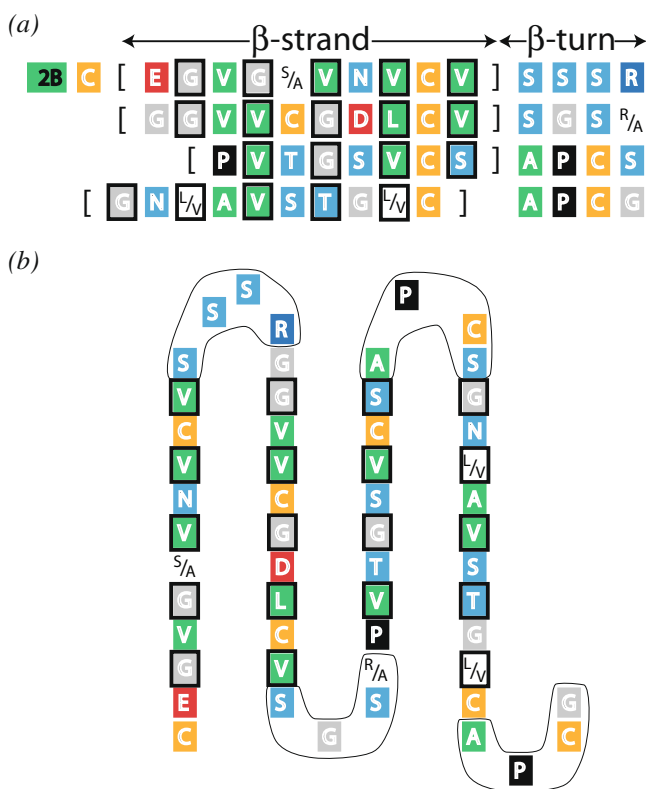

(a)

(b)

Fig. 8 a The consensus sequence of the first 57 residues in the tail domain of Type II trichocyte keratins laid out to illustrate the potentiality for four β-strands and four connecting β-turns (Parry and North, 1998). One face is predominantly occupied by apolar residues and the other by cysteine and charged residues (amongst others). The apolar residues are *boxed*. **b** Schematic diagram of the proposed four-stranded antiparallel β-sheet. The β-turns are *ringed*. Figure modified from Parry and North (1998)

on the two faces through sequence regularities, provides a versatile mechanism for introducing a high degree of specificity into the assembly process. Assembly will be mediated by both shape and chemical complementarity, and also through the pairing of sheets, whereby sequence regularities internalize the hydrophobic residues and shield them from the aqueous environment.

Apart from the results obtained with experiments on the reassembly of solubilized feather keratin derivatives, there is little direct experimental evidence to support the involvement of interactions between β-sheets as being involved in the polymerization of fibrous proteins molecules. However, evidence from crystallographic studies of β-sheet rich proteins suggest that interactions between β-sheets will prove to play an important role in the higher levels of assembly in fibrous proteins.

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