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Hierarchical structure of collagen composite systems: lessons from biology

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Abstract - Hierarchical structure in biocomposite systems such as in collagenous connective tissue have many scales or levels, have highly specific interactions between these levels, and have the architecture to accommodate a complex spectrum of property requirements. As examples, the hierarchical structure-property relationships are described in three soft connective tissues; tendon, intestine and intervetebral disc. In all instances, we observed numerous levels of organization with highly specific interconnectivity and with unique architectures that are designed to give the required spectrum of properties for each oriented composite system. From these lessons in biology, the laws of complex composite systems for functional macromolecular assemblies are considered. Finally, demonstrations of the application of these laws to simple synthetic composites are given including continuous multilayered polymeric materials, liquid crystalline polymers and "hard elastic" membranes. It is shown that structure-property relationships can only be described, and in some instances predicted, if these complex synthetic materials are accurately defined in terms of their hierarchical structure.

Soft connective tissues, designed to serve specific functions in the body of man and animals, are among the most advanced composite materials known made of macromolecular building blocks. By utilizing the same basic macromolecular design and only by varying the hierarchical structure, a wide range of tissues possessing very different properties are synthesized by the cellular organism. This article reviews our recent work on the hierarchical structure of soft connective tissues from the animal kingdom in hopes that these "lessons from biology" may provide polymer and materials scientists with new ideas for the design of high performance composite polymeric materials. Only with an appreciation and understanding of the unique structure-properties relationships in such biosystems can this be achieved.

All soft connective tissues have remarkably similar chemistry at the macromolecular and fibrillar levels of structure. This similitude extends through the collagen fibril which is the basic building block of all soft connective tissues. Differentiation in the hierarchical structure takes place when these fibrils are arranged in a particular architecture thus constructing a particular tissue for a unique function [1]. The hierarchical structure of a tissue reflects and depends upon the different stress states in which the tissue is required to function. Other requirements are also accommodated or coupled simultaneously such as the transport of water and the diffusion of the products of digestion. In each of these cases, the upper levels of the hierarchical structure or architecture are organized with specific mechanical and transport requirements in mind. Furthermore, the many discrete layers of the hierarchical structure must interact in such a way as to make the performance of these tasks possible [2].

The basic structural fiber in all connective tissues is collagen. It is often the most abundant protein in animals and is widely distributed in the structural elements of the body. The common elements in the structure of soft connective tissues begin at the molecular level with similarities in the amino acid sequences of this class of proteins. This similitude lays the groundwork for the development of a variety of tissues that share common chemical and physical properties. Collagens contain the amino acid hydroxyproline, which is not commonly found in other proteins. Along with proline and glycine, these three amino acids account for more than fifty percent of the total amino acid content in all collagen types. Addition of other amino acids or variations in the ratio of these amino acids differentiate between the different collagen types. Amino acids play a major role in determining the three dimensional conformation of the precursor to collagen, the tropocollagen molecule. This molecule is a coiled-coil of three helical polypeptides 290 nm in length (Fig. 1). Five of these molecules align longitudinally with an overlap of approximately one quarter the molecular length to form a microfibril of diameter 3.6 nm. This so-called quarter stagger combined with the gap between successive macromolecules is responsible for the characteristic 64 nm banding pattern observed in the electron microscope and by x-ray diffraction. The microfibrils are then assembled into collagen fibrils that may vary in thickness from 35 to 500 nm (Table 1). These basic building blocks are combined, oriented, and laid up to form higher ordered structures with a particular morphology to suit the requirements of a tissue.

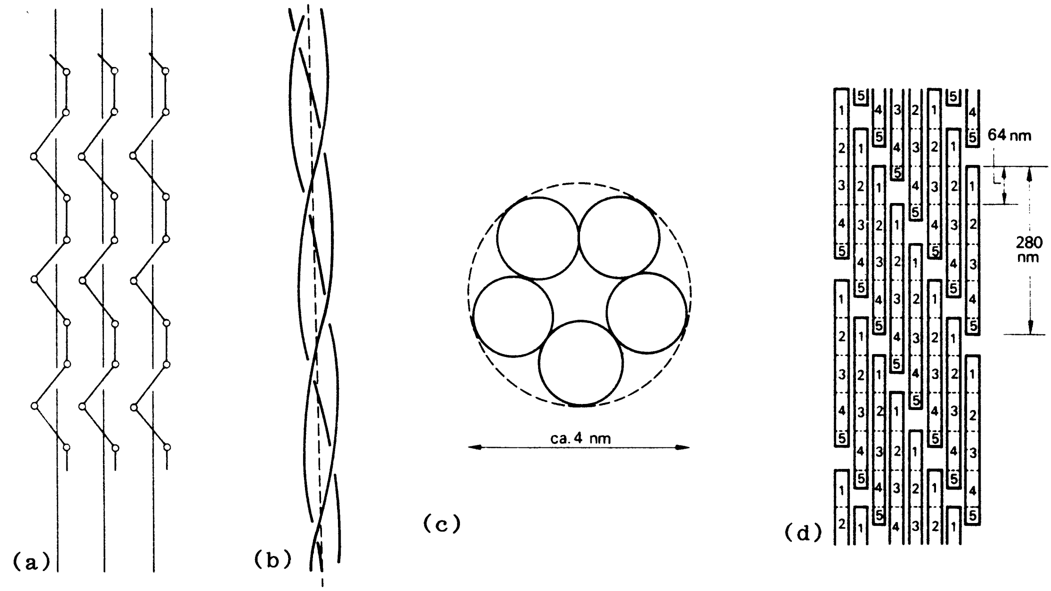

Fig. 1 Building blocks of the collagen fibril.
The association of amino acid molecules into the collagen fibril is illustrated schematically in these diagrams. (a) Three polypeptide chains, each coiled separately about a minor axis, form a coiled-coil (b) about a single central axis. This triple helical molecule is tropocollagen. (c) Five tropocollagen molecules aggregate to form a microfibril with diameter approximately 4 nm. (d) In a longitudinal section, the quarter staggered arrangement of the tropocollagen helices along the length of the microfibril is shown. This quarter stagger and the gap between the ends of the molecules gives rise to the 64 nm banding pattern observed in collagen fibrils. [Ramachandran, 1963; Smith, 1968; as quoted in Wainwright, Briggs, Currey, and Gosline, 1982]

TABLE 1: Collagen fiber size and distribution in various tissues

	Diameter (nm)	Distribution
Rat tail tendon		
fetal	30	Normal (Broad)
adult	450	Broad (Bimodal)
Human periodontal ligament		
fetal	70	Normal (Narrow)
adult	40	Normal (Narrow)
Human intervertebral disc		
fetal	31	Normal
adult	40, 100-150	Bimodal
Human heart valve leaflet		
adult	30-50	Normal
Rat intestine (2 Years)	400	Normal (Narrow)
Rabbit Cornea	20-25	Normal (Narrow)

The collagen fibrils are surrounded by an extracellular matrix that maintains the integrity and architecture of the collagen. The primary component of this matrix is high molecular weight hyaluronic acid with a highly branched aggregate of proteoglycans. Proteoglycans consist of a core protein with numerous pendant mucopolysaccharide molecules. These mucopolysaccharides include chondroitin sulfates 4 and 6 and keratan sulfate. The amounts of these molecules and their ratios vary between connective tissues, with location within tissues, and with age. It is the ability of the proteoglycans to imbibe water which swells the matrix and supports the collagen fibrils. The mechanical properties of the matrix are regulated by its water content which, in turn, affects the properties of the composite tissue as a whole.

The overwhelming consideration in the arrangement of collagen fibrils to form connective tissues is its function in the body. This will be illustrated by three tissue types studied in our laboratories at Case Western Reserve University.

TENDON

Tendons connect muscle to bone around a joint thereby converting muscle contraction into joint motion. As such, the tendon is subjected almost exclusively to uniaxial tensile stresses oriented along its length. This situation requires that the tendon be elastomeric yet sufficiently stiff to efficiently transmit the force generated by the muscle. At the same time, it must be capable of absorbing large amounts of energy without fracturing. For example, absorbing the force generated about the knee joint in a fall. It accomplishes this through a unique hierarchical structure in which all levels of organization from the molecular through the macroscopic are oriented to maximize the reversible and irreversible tensile properties in the longitudinal direction without fracture.

In the tendon, collagen fibrils are organized into larger fibers. These fibrils are arrayed parallel to one another and oriented longitudinally between the muscle and bone. When the fibers are observed inbetween crossed polarizers in the optical microscope, they have an undulating appearance (Fig. 2). Further examination reveals the waveform to be a planar zig-zag or crimp rather than a helix [3]. That is, the macroscopic structure does not reflect the helical conformation of the collagen

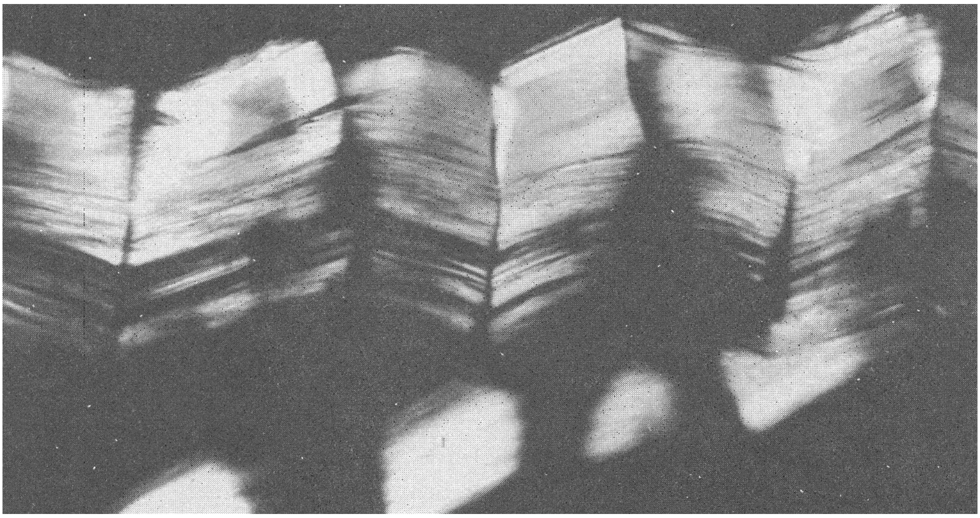

Fig. 2 The morphology of the collagen fibril in tendon. Viewed between crossed polarizers in the optical microscope, the collagen fibrils that make up the tendon have a wavy appearance. Upon further examination this waveform is characterized as a planar zig-zag. Adjacent fibrils are all crimped in register. It is this wavy conformation of the fibrils on the microscopic level of the structure that imparts a high degree of elasticity to the tendon, enabling it to be stretched repeatedly longitudinally without damaging the underlying structure on the nano- and molecular levels. [Baer, 1986]

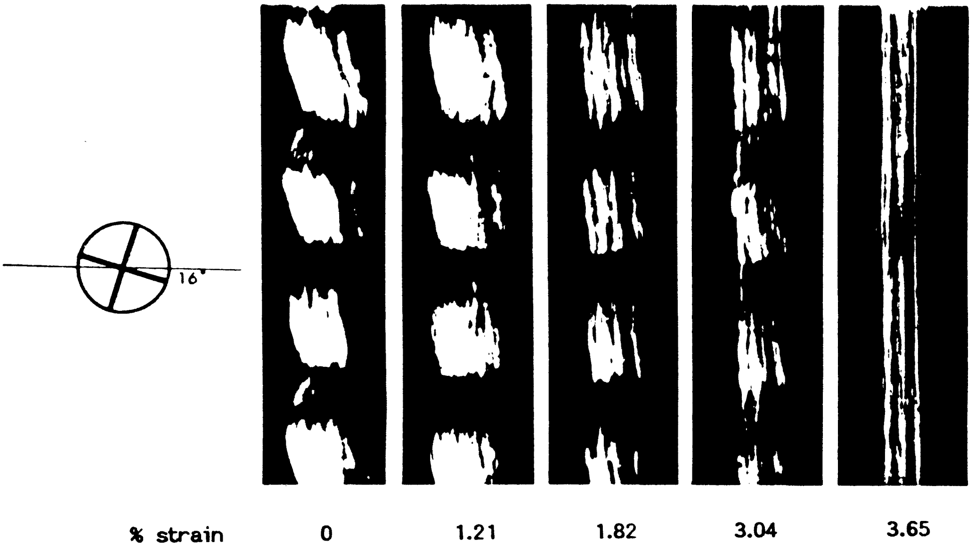

Fig. 3 Crimp straightening in the tendon.
The performance of the tendon in the toe region of the stress-strain curve is directly attributable to the wavy conformation of the collagen fibrils. In this series of photomicrographs, the progressive straightening of the planar zig-zag with increasing tensile strain is shown. The physiological loading range of the tendon is in this regime, so most loads are borne by this crimp waveform. [Diamant, Keller, Baer, Litt, and Arridge, 1972]

macromolecules. When the tendon is stretched along its length, this crimp waveform is gradually straightened (Fig. 3). It is the magnitude of this waveform that determines the reversible elastic properties of the tendon. As the tendon is pulled further, all the crimp in the collagen fibers is eventually pulled out. The waviness observed in collagen fibers in the rat tail tendon is also found in tendons from other species and in other connective tissue types (Table 2) [4]. This generality across species and tissue lines indicates the ubiquitousness of this crimp morphology and its importance in determining the mechanical response of all soft connective tissues. As the upper levels of structural architecture are varied to meet the mechanical and other environmental requirements of a particular tissue, so are the parameters of the crimp waveform altered to adjust the mechanical response of that tissue.

TABLE 2: Crimp parameters for various tissues

Source and age	Period (um)	Angle (deg)
Tendons:		
Rat tail (14 months)	200	12
Human diaphragm (51 years)	120	12
Kangaroo tail (11.7 years)	150	8-9
Human achilles (46 years)	40-100	6-8
Other tissues:		
Human periodontal ligament (8 years)	32	25
Human intervertebral disc (31 & 36 years)	12-16	20-42[a]
Heart valve leaflet	20	28-30
Rat intestine (3 month)	20	30-56
Rabbit cornea (adult)	14	(sine wave)

[a] The disc is a gradient structure and crimp parameters change with radial distance through the annulus fibrosus.

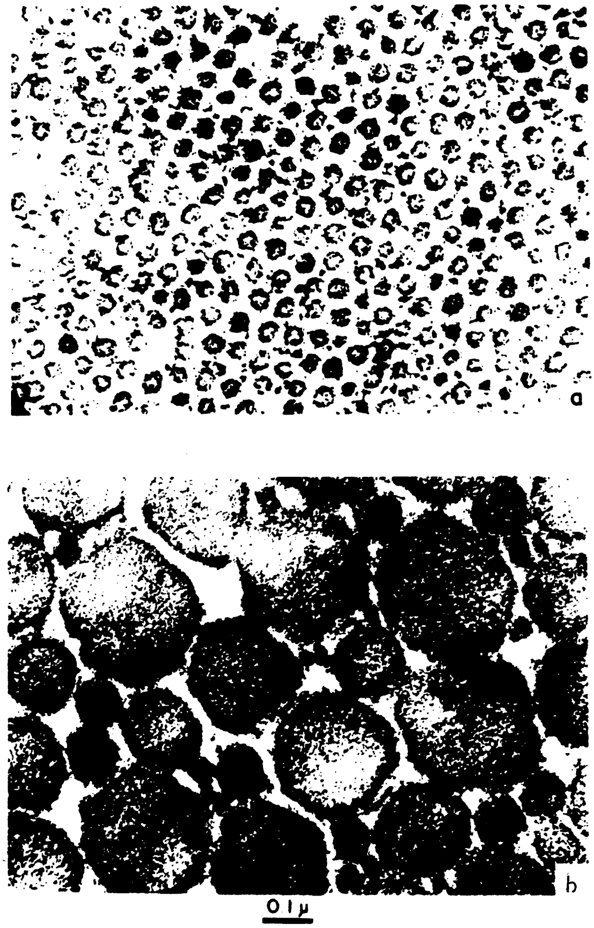

Fig. 4 Electron microscopy of collagen fibers in tendon. Transverse sections of undeformed rat tail tendon show the change in fibril size and distribution with age. (a) In the newborn rat, the fibrils are of uniform size, 30 nm in diameter. (b) At 30 months, there is a distribution of a fibril sizes up to 350 nm in diameter in this section. A longitudinal section (c) in a 24 month old rat reveals the 64 nm banding pattern of the collagen fibrils. [Torp, Baer, and Friedman, 1974; Kastelic and Baer, 1980]

Further examination of the structure of tendon for structural hierarchy reveals both the size distribution and the composite nature of the collagen fibrils. By cutting the tendon transversely. One observes that in young animals, the fibrils are of small diameter and they are all essentially the same size (Fig. 4) [5]. As the animal matures and ages, the fibrils get larger and the range of fibril sizes broadens considerably (Table 1). Interspersed between the fibrils is the matrix material discussed earlier. A longitudinal section through a tendon that has been extended to remove the crimp shows the 64 nm banding pattern that is characteristic of collagen and results from the staggered arrangement of the microfibrils. It is apparent that these soft connective tissues are a hierarchical structure constructed of many collagen fibrils that are themselves composite materials (Fig. 5) [6].

This response of the elements of the hierarchical structure of the tendon is reflected in the shape of the stress-strain curve (Fig. 6). At small tensile deformations, the stress-strain curve is non-linear which is the case for all soft connective tissue. As the tendon is stretched further, the stress-strain curve becomes linear as a result of progressive straightening of the collagen fibers. This is referred to as the toe region of the curve. All normal physiological loads are confined to this non-linear toe region. When all the fibers are straight, the modulus is constant since the structure is uncrimped. In the linear region, the

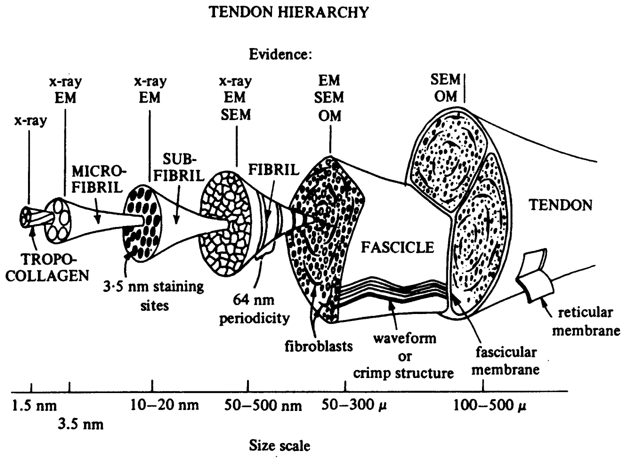

Fig. 5 Hierarchical structure of the tendon.
The hierarchical organization of connective tissues is illustrated in the tendon. Beginning at the molecular level with tropocollagen, progressively larger and more complex structures are built up on the nano- and microscopic scales. At the most fundamental level is the tropocollagen helix. These molecules aggregate to form microfibrils which, in turn, are packed into a lattice structure forming a subfibril. The subfibrils are then joined to form fibrils in which the characteristic 64 nm banding pattern is evident. It is these basic building blocks that, in the tendon, form a unit called a fascicle. At the fascicular level the wavy nature of the collagen fibrils is evident. Two or three fascicles together form the structure referred to as a tendon. It is this multi-level organization that imparts toughness to the tendon. If the tendon is subjected to excessive stresses, individual elements at different levels of the hierarchical structure can fail independently. In this way, the elements absorb energy and protect the tendon as a whole from catastrophic failure. [Kastelic and Baer, 1980]

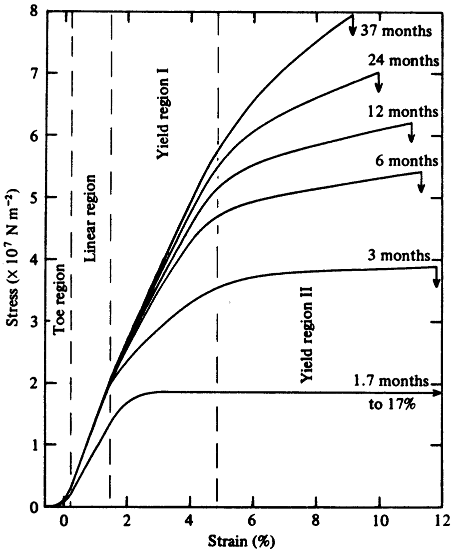

Fig. 6 Stress-strain behavior of rat tail tendon.
Stress response of the tendon is derived from the underlying architecture of the collagenous elements in the tissue. The stress-strain curve in tension is divided into three regions. In the toe region, the slope of the stress-strain curve (the modulus of the tendon) gradually increases with increasing length. This corresponds to a progressively straightening of the waviness in the collagen fibrils. Once all the fibers are fully straightened, the elements in the structural hierarchy are stretched elastically, giving rise to a region of constant modulus on the stress-strain curve. This behavior continues until individual elements at the sub- and microfibrillar levels begin to break or slip in relation to one another. The modulus then decreases with increasing strain until the tendon fails catastrophically. Differences in the hierarchical structure related to the age of the animal are manifested in all these regions. [Kastelic and Baer, 1980]

fully straightened collagen fibers are further pulled elastically. If the load is released, the tendon will entirely recover to its initial crimped morphology. At high strains, the tendon shows yielding and irreversible damage is imparted to the structure since the collagen fibrils begin to disassociate into sub- and microfibrils. Localized slippage and voiding between hierarchical levels account for the yielding observed at the macroscopic level. Thus, once the tendon yields, it cannot fully recover to its initial state. The hierarchical design distributes the remote stress locally by imparting damage efficiently throughout the different levels of structure thereby minimizing damage concentrations that could precipitate failure and fracture. This allows the damaged tendon to continue to function in a nearly normal way. The failure of these small structural elements also absorbs a tremendous amount of energy thereby preventing catastrophic failure. Ligaments behave in essentially the same manner as tendons except that they connect bone to bone around a joint. As such, their function is to provide a stabilizing force on the joint and prevent unnatural motions from occurring. Examined between crossed polarizers in the optical microscope, collagen fibers in ligaments have the same wavy morphology as in tendons.

INTERVERTEBRAL DISC

The intervertebral discs are interspersed between the vertebral bones in the spinal column. In this location, the disc is subjected to compressive loads generated on the spine by the weight of the body as well as torsion and bending loads during movement. Another design consideration is impact loading superimposed upon the body weight during activities such as walking or jumping. The disc is composed of two parts: a gelatinous nucleus pulposus containing a matrix of fine collagen fibers, hydrophilic proteoglycan molecules, and up to 88 percent water; and the annulus fibrosus, having concentric cylindrical layers of fibrous collagen arrayed around the nucleus like the layers of an onion skin (Fig. 7). The collagen fibers that comprise the annulus are inclined with respect to the spinal axis by the interlamellar angle. In successive lamellae, this angle

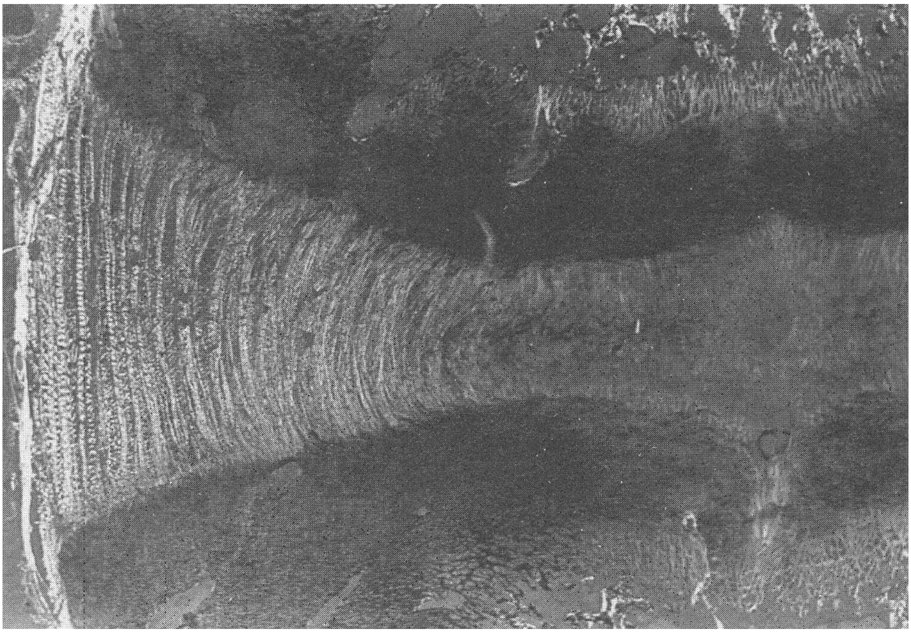

Fig. 7 Radial anatomy of the intervertebral disc.
A slice through the anterior of the disc cut parallel to the axis of the spinal column and photographed through the optical microscope in crossed polarized light reveals the complex collagenous architecture. The relationship between the annulus fibrosus, nucleus pulposus, and the cartilage endplates is shown. While the nucleus and cartilage exhibit little optical activity, the lamellae of the annulus are highly active. These lamellae are made up of large collagen fibrils, the cut ends of which are seen in this view. [Cassidy, Hiltner, and Baer, [1989]

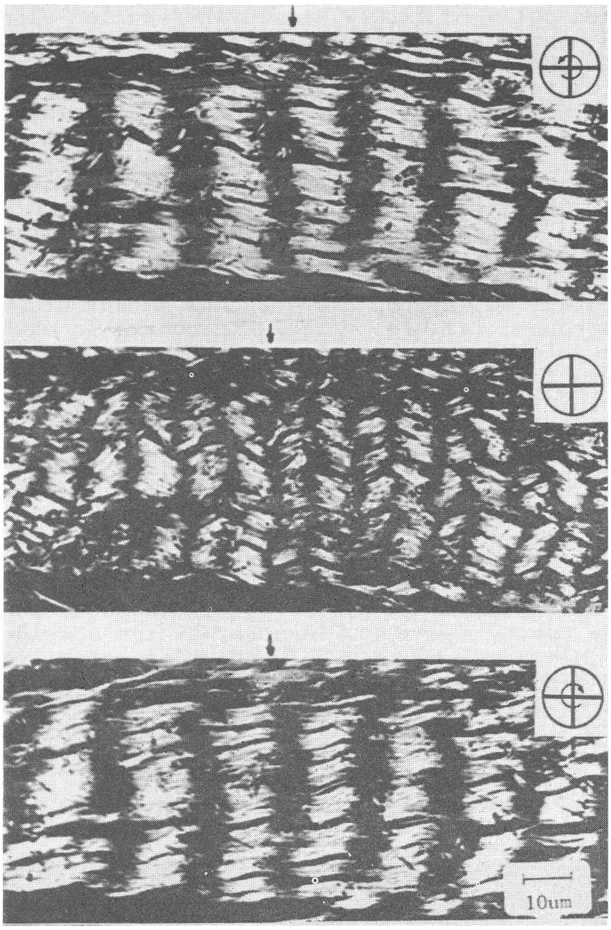

Fig. 8 Collagen fibril morphology in the disc.
The collagen fibrils that comprise a single lamellae are shown in crossed polarized light at high magnification in the optical microscope. Extinction bands are observed evenly spaced along their length. Upon rotation of the microscope stage, these bands approach one another and eventually merge. The behavior of these fibrils is identical to that of fibrils taken from the tendon and is characteristic of the planar zig-zag waveform observed in those tissues. [Cassidy, Hiltner, and Baer, 1989]

alternates like a layered layup in man-made composite materials [7]. This angle varies with radial distance through the annulus from ± 62 degrees at the periphery to ± 45 degrees in the vicinity of the nucleus thus imparting a structurally graduated architecture to the disc. The collagen fibers that make up these layers have the same planar crimped morphology as seen in the tendon (Fig. 8). The crimp parameters vary with radial distance through the annulus as well, with the crimp angle increasing from 22 degrees at the periphery to 42 degrees near the nucleus. The unique hierarchical organization of the disc utilizes the superior tensile properties of the collagen fibers of the annulus in resisting compressive forces oriented along the spinal axis as well as torsional and bending forces (Fig. 9). Examination of fixed discs in compression reveals that as the disc is compressed, the nucleus pulposus spreads outward laterally causing the lamellae of the annulus to bulge outward. Since the ends of the fibers are anchored to the vertebral bone, they are stretched in tension. This elongation of the crimped fibers again accounts for the observed shape of the stress-strain curve. The stress-strain curve of the disc in compression is similar to that of the tendon in tension, containing toe, linear, and yield regions.

While it has not been demonstrated experimentally, one can imagine that the toe, linear, and yield regions of the stress-strain curve for a disc in compression correspond to the same morphological requirements and

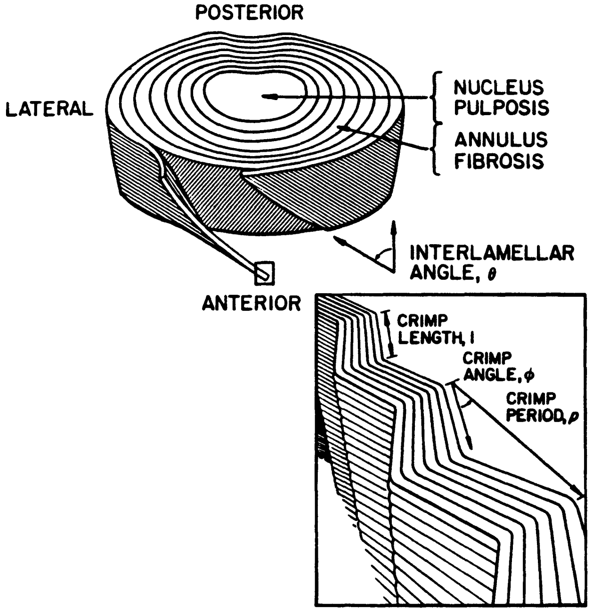

Fig. 9 Hierarchical structure of the intervertebral disc
In the intervertebral disc, collagen fibrils are organized into lamellar sheets in the annulus fibrosus which surround a galatinous and highly hydrated nucleus pulposus. The thickness of lamellae vary with location and are thicker at the anterior and lateral aspects of the disc than at the posterior. Within lamellae, fibrils are parallel and inclined with respect to the axis of the spinal column by an interlamellar angle which alternates in successive lamellae. This angle decreases from the edge of the disc inward. At higher magnification, the fibrils have a planar zig-zag waveform. The crimp angle is largest in fibrils close in to the nucleus and decreases toward the periphery. The orientation of the collagen fibrils in the annulus give the disc strength and stability in tension, bending, and torsional motions. Based upon optical microscope observations of the morphology of the collagen fibrils, the levels of structural hierarchy below the fibrils are assumed to be identical to that of the tendon and intestine. [Cassidy, Hiltner, and Baer, 1989]

changes in the collagen fibers that are present in tendon. The biaxial layup of the fibers in the annulus also stabilizes the disc in torsion and bending. In torsion, the collagen fibers in the lamellae oriented in the direction of twist are stretched while the balance are unloaded. In bending, the biaxial layup of the fibers prevents the disc from buckling on the flexion side while resisting excessive bulging on the extension side.

The high water content of the disc plays a vital role in determining the time dependent mechanical response of the disc in compression [8]. If the disc is compressed and held, as it is when the body weight presses the spine during stance, water is squeezed out of the disc. This water loss and the concomitant decrease in disc height is responsible for the "shrinkage" in height that people experience during the course of a normal day's activities. This water is transported out of the disc through cartilage endplates separating the disc from the vertebral bones and into the general circulation. When the load is released, the water is reabsorbed by the disc in the same manner. The stress relaxation and creep responses of the disc in compression are the result of this transport process, rather than the molecular reorganization normally associated with time dependent mechanical phenomena in materials.

INTESTINE

The intestine is a semipermeable flexible tube in which mechanical break up of food is accomplished and through which the products of digestion diffuse into the circulation. As this process takes place, the walls of the intestine are stretched in both the longitudinal and the radial or hoop directions. While this requires a design with adequate tensile strength in these two directions, movement of nutrients across the wall of the intestine demands that efficient routes exist for diffusion to take place. The intestine fulfills both these requirements through an innovative hierarchical structure. The intestinal wall is a layered structure with four distinct layers. Two layers contain smooth muscle cells oriented in the longitudinal and circumferential directions to macerate food particles; another is a covering that isolates the intestine from the other organs in the body cavity.

The predominant structural member of the intestine is the submucosa, which contains the majority of the collagen fibrils. Fibrils are arranged in layers oriented biaxially around the lumen. In successive layers the fibrils are oriented at ±60 degrees to one another forming helices of opposite sense arrayed at ±30 degrees to the longitudinal axis winding around the intestine (Fig. 10). This biaxial winding of the collagen fibrils prevents buckling of the intestine as it winds through the body cavity while the multiple layers of helically wound fibers gives maximum resistance to internal bursting pressures. Within each layer the collagen fibrils are planar crimped as in the tendon. The hierarchical structure of the intestine below the level of the fibrils is identical to that of the tendon (Fig. 11) [9].

The crimped morphology in conjunction with the biaxial orientation of the collagen fibers gives rise to the shape of the stress-strain curve in tension and to the anisotropic nature of the mechanical response. At low tensile strains, a similar toe region exists as in the tendon. However, in the intestine, there are two deformation mechanisms at work due to the requirement of simultaneous biaxial expansion. A limited reorientation of the fibers, as evidenced by a decrease in the angle between fibers in adjacent layers, takes place along with the progressive straightening of the crimp in the fibers. The biaxial layup of the fibers also causes an anisotropic mechanical response in tension. If the intestine is stretched along different orientations

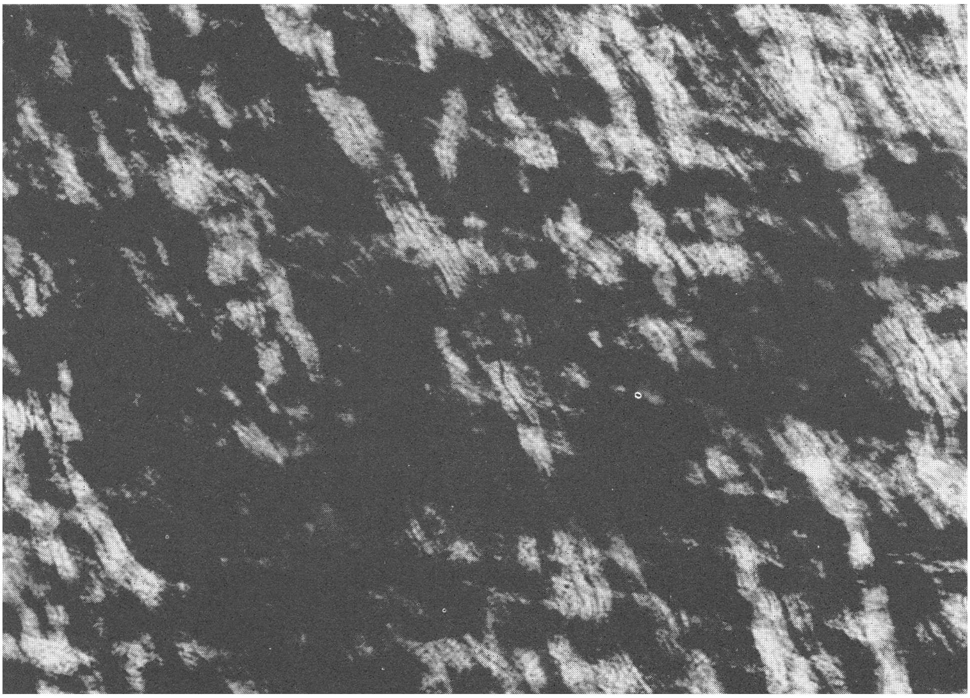

Fig. 10 The biaxial crimped layered structure of collagen fibers in the intestine.
Collagen fibers in the intestine have the same planar crimped morphology observed in the tendon. The parameters of the waveforms (crimp angels, period) are different, however, with the greater extensibility required in the intestine being reflected in a large crimp angle. [Hiltner, Orberg, and Baer, 1983]

with respect to the longitudinal axis, different stress-strain responses are observed (Fig. 12). Intestine is the stiffest and least extensible at ±30 degrees to longitudinal, in alignment with the fibers in one set of layers, while the greatest extensibility is at 90 degrees to the longitudinal axis. This is suited to the function of the intestine which necessitates changes in the diameter of the

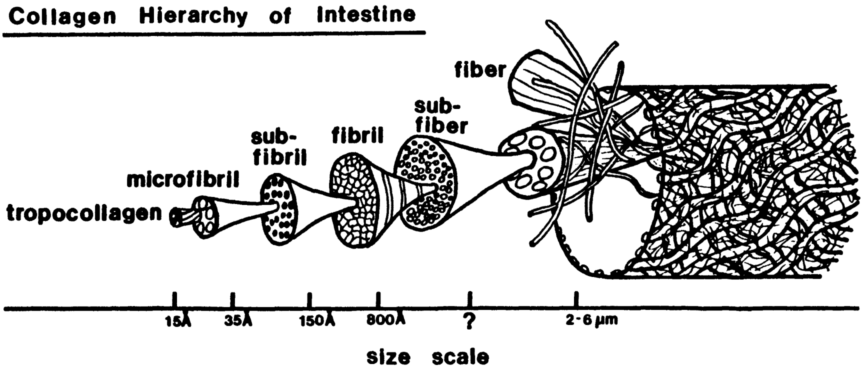

Fig. 11 Hierarchical structure of the intestine.
The hierarchical organization of the intestine is identical to that of the tendon from the molecular through the fibrillar level. The two tissues differ only in how the collagen fibrils are arranged into the highest levels of structure. Note that in the intestine no fascicles are present. Instead the collagen fibrils aggregate into fibers which are then wound around the intestine in a helical fashion. [Hiltner, Orberg, and Baer 1983]

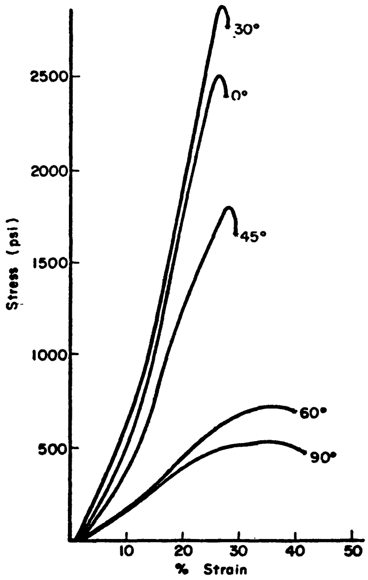

Fig. 12 Stress-strain behavior of the intestine in tension.
The tensile properties of the intestine vary with orientation as would be expected in a tissue made up of biaxially oriented fibers. the greatest modulus and least extensibility occur when the intestine is stretched parallel to the fibers in the layers (30°). The properties along the longitudinal direction (0°) are only slightly less than in the fiber direction. The greatest extensibility and least modulus are found perpendicular to the long axis in the hoop direction (90°). These properties represent a structural adaptation to the function demands of the intestine. Digestion of food requires the ability to accommodate changes in the diameter of the intestine as food passes through and for rapid diffusion of nutrients through a permeable wall. At the same time, changes in the length of the intestine must be minimized in order for the peristaltic action of the smooth muscle to operate efficiently. The arrangement of collagen fibrils in the intestine enables these demands to be met.

intestine as food passes rather than changes in length. Once fully straightened, the collagen fibers are strong and inextensible, effectively resisting bursting.

Virtually all connective tissues, whether soft or hard, have hierarchical structural designs arranged at discrete levels of structure. For example, the cornea has mechanical requirements similar to that of the intestine. Collagen fibers must contain the pressures generated internally in the eye by the vitreous. However, its distinguishing characteristic is its transparency to light in the visible region of the spectrum. Both these functions are accomplished using a layered structure as in the intestine. The principal structural layer is the stroma which makes up ninety percent of the corneal thickness. The stroma is a layered structure with approximately 200 lamellae between 2 and 3 μm thick. Within these lamellae, the collagen fibrils are parallel to the surface of the cornea and extend entirely across it. Within lamellae, the fibrils are parallel to one another while in successive lamellae, fibrils make large angles to one another (Fig. 13). This lamellar structure and cross-ply orientation provide enhanced reinforcement for the eye when compared to an isotropic arrangement of collagen fibrils. The arrow distribution of fibril thicknesses, uniform packing scheme, and the highly ordered arrangement of the fibrils in the lamellae permits the stroma to perform its mechanical function while passing visible light undisturbed.

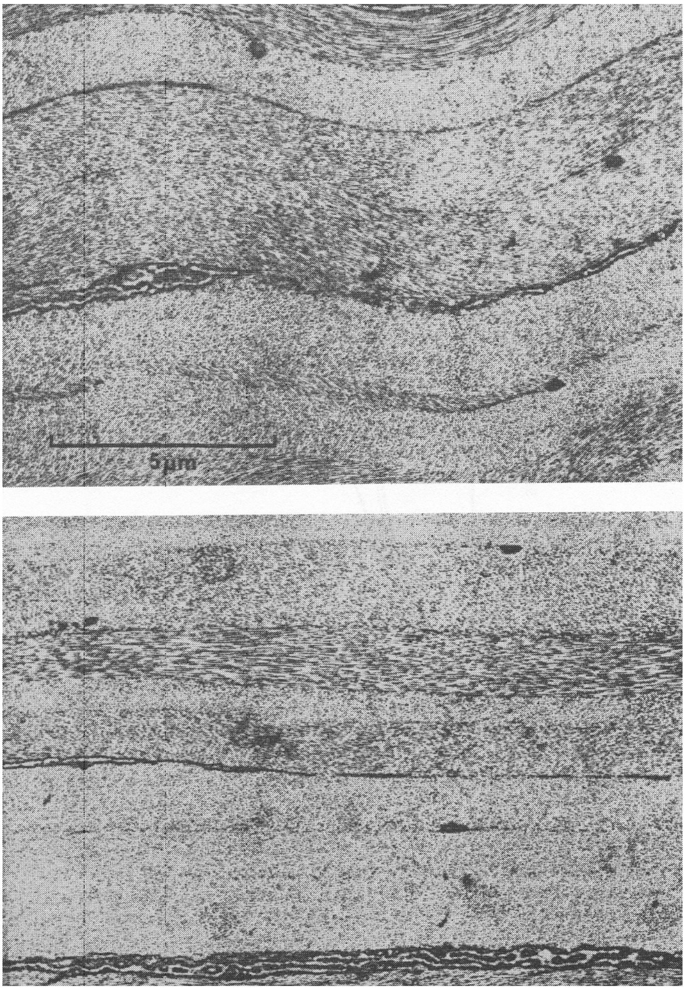

Fig. 13 Collagen fiber layup in the cornea.
Electron micrographs of the central rabbit cornea show the wavy morphology of the collagen fibers extending through the thickness of the stroma. Note also the layered structure of the stroma, the uniform fiber diameter, and the variation in the orientation of the fibers in each layer. [McCally and Farrell, 1982]

GENERAL COMMENTS

It is tempting to suggest that all connective tissues follow at least three "Laws for Complex Assemblies." Starting with a very similar macromolecular design (the fibrous protein, collagen, and the ground substance, mucopolysaccharide), the hierarchical structures are assembled into distinct and totally different systems both in their morphology and their function.

First, the macromolecules associate into discrete levels of organizations. Usually these are in the form of fibrils which are themselves composed of smaller subfibrils and microfibrils. The fibrils are subsequently arranged in layered structures reflecting the specific functional requirements of the overall composite system. The minimum number of discrete levels or scales observed thus far in biocomposites are four. That is, structural levels at the molecular, at the nano, at the micro and at the macro scale are the minimum required components within an ordered hierarchical biocomposite system.

Second, these levels are held together by highly specific interactions between surfaces. Considerable evidence exists for surface to surface interactions due to intermolecular bonding at specific active sites, and for epitactic arrangements of a crystallographic nature. Whatever the nature of the interfacial mechanism, strong interfacial interactions are required having chemical and physical specificity.

Third, the highly interacting fibers and layers are organized into an oriented hierarchical composite system which is designed to meet a spectrum of property or function requirements. This law of architecture, stipulates that as the complexity of the overall system and its uses increases, the system is capable of a higher degree of adaption in difficult and unexpected environments. The so-called "intelligent composite system" results from a complex architectural arrangement which is designed to serve highly specific functions.

At the very least, the analysis of complex behavior in natural polymeric systems in terms of hierarchies is an approach that interrelates our understanding of structure at various scales. Such an approach may prove invaluable in the design of new advanced polymers. Structural hierarchy is more than a convenient vehicle for description and analysis. Important and difficult questions that remain to be addressed include the physical and chemical factors that give rise to relatively discrete levels of structure and the relations that govern their scaling [2].

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