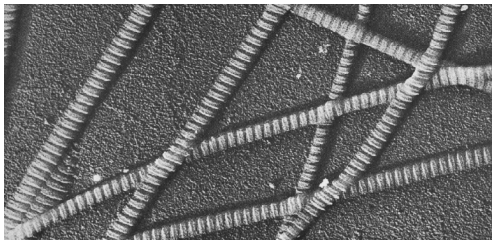
ME 482 Experimental Tissue Mechanics

Professor A. Wagoner Johnson

Collagen Structure and synthesis
Monday, 8/29/2016



Collagen Fibrils (Cowin and Doty)

Recommended reading:

Cowin and Doty, Tissue Mechanics, Ch 10: Collagen

Papers on next slide may also be useful

Additional resources on collagen

MOLECULAR STRUCTURE OF THE COLLAGEN TRIPLE HELIX

By BARBARA BRODSKY AND ANTON V. PERSIKOV

Department of Biochemistry, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Piscataway, New Jersey 08854

ADVANCES IN PROTEIN CHEMISTRY, Vol. 70
DOI: 10.1016/S0065-3233(04)70009-1

This paper discusses some diseases caused by mutations of collagen and lots of detail about bonding, stability, etc. etc.

There are 1000 different collagen mutations that lead to disorders!

Building Collagen Molecules, Fibrils, and Suprafibrillar Structures

David J. S. Hulmes
Journal of Structural Biology **137**, 2–10 (2002)
doi:10.1006/jsbi.2002.4450

Nice resource for proteins:
resources.schoolscience.co.uk/unilever/16-18/proteins/Protch1pg1.html

Today

Collagen

- Structure
- How it is made by cells
- How it assembles
- Length scales (emphasis on length scales in this class…)

Suprafibrilar architectures of collagen are different for different connective tissues

Figure 10.22. Light micrographs. Samples viewed in a polarizing microscope at the same magnification.

skin (top) type I collagen fibrils are organized into a wicker work or cable-like structure

annulus fibers from the **intervertebral disc (middle)** – note orientation less directional than tendon

tendon (bottom) type I collagen fibrils in the tendon are oriented along one axis

Each tissue illustrates a difference in the orientation of the component fibrils, their width, and their geometric distribution.

All x 380, bar = 25 µm.

Cown and Doty

Collagen structure - AA sequence

What 2 things do you notice about the AA sequence?
These are hallmarks of a collagen molecule.

Amino acid sequence of collagen

Gly-Ala-Hyp-**Gly-**Pro-Hyp-**Gly-**Ala-Hyp-**Gly-**Ala-Hyp-**Gly-**

Pro-Val-**Gly-**Pro-Ala-**Gly-**Lys-Ser-**Gly-**Asp-Arg-**Gly-**Glu-Thr-**Gly-**Pro-Ala-**Gly-**

Gly-Ala-**Hyp-**Gly-**Pro-Hyp-**Gly-Ala-**Hyp-**Gly-Ala-**Hyp-**Gly-

Pro-Val-Gly-**Pro-**Ala-Gly-Lys-Ser-Gly-Asp-Arg-Gly-Glu-Thr-Gly-**Pro-**Ala-Gly

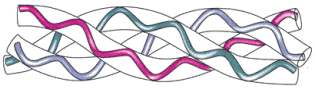
Table 9-1. Amino Acid Content of Collagen[a]

Amino acids	Mol/100 mol amino acids
Gly	31.4–33.8
Pro	11.7–13.8
Hyp	9.4–10.2
Acid polar (Asp, Glu, Asn)	11.5–12.5
Basic polar (Lys, Arg, His)	8.5–8.9
Other	Residue

[a] From M. Chvapil, *Physiology of Connective Tissue*, Butterworths, London, 1967.

Structural parameters for α-chains and superhelix –

Cowin & Doty



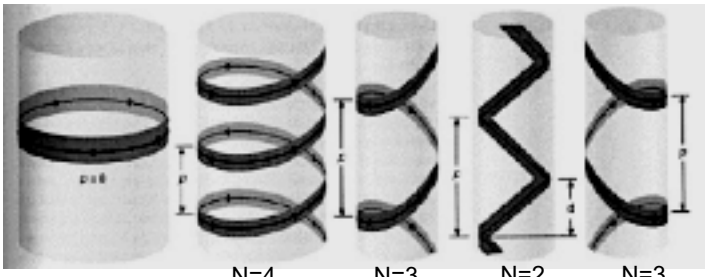
http://resources.schoolscience.co.uk/Unilever/16-18/proteins/Protch5pg1.html

allrite.com

Type	Chain composition	Distribution
I	$[\alpha1(I)]_2\alpha2(I)$	
II	$[\alpha1(II)]_3$	*Part of HW*
III	$[\alpha1(III)]_3$	

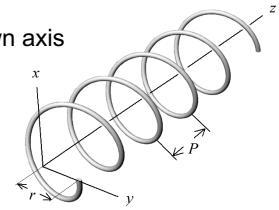
Nice resource on collagen: http://www.ncbi.nlm.nih.gov/books/NBK21582/

Parameters describing a helix



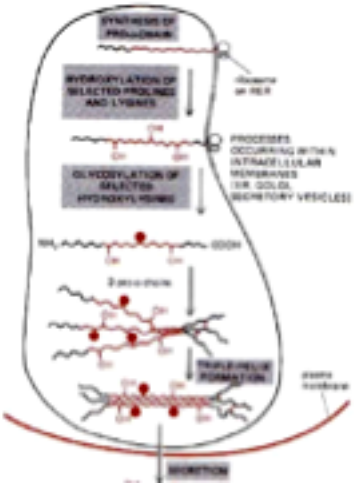
Ring n=5 | N=4 (right hand) | N=3 (right hand) | N=2 (flat ribbon) | N=3 (left hand)

- Rt hand helix – CW turn moves helix away when look down axis
- Lft hand – CCW “..””
- Pitch (P) is linear distance between turns
- N – number of AA residues/turn
- D= rise/residue
- P=D x N



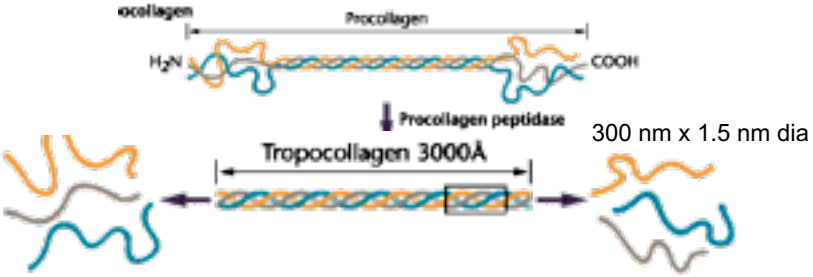
fizyka.phys.put.poznan.pl/~pieransk/CPHelices.htm

Synthesis of tropocollagen *begins* inside the cell



Procollagen molecule (superhelix) is secreted

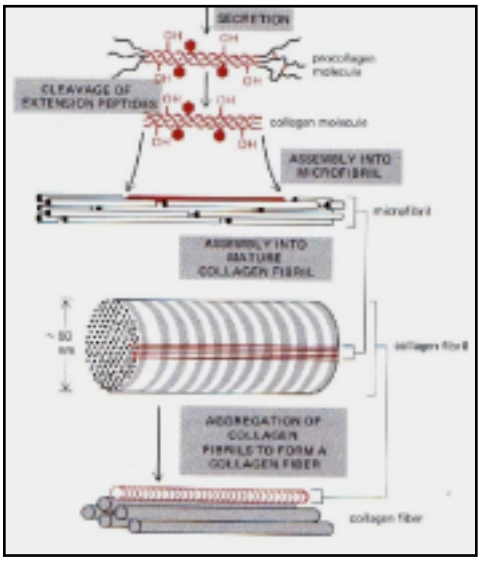
Terminal ends are cleaved by collagenase enzyme



N=3 (right hand)

Procollagen molecule is secreted

Tropocollagen assembles into fibrils and fibers



The fibril arrangement results in a characteristic striped pattern in fibrils, visible by electron microscopy (EM)

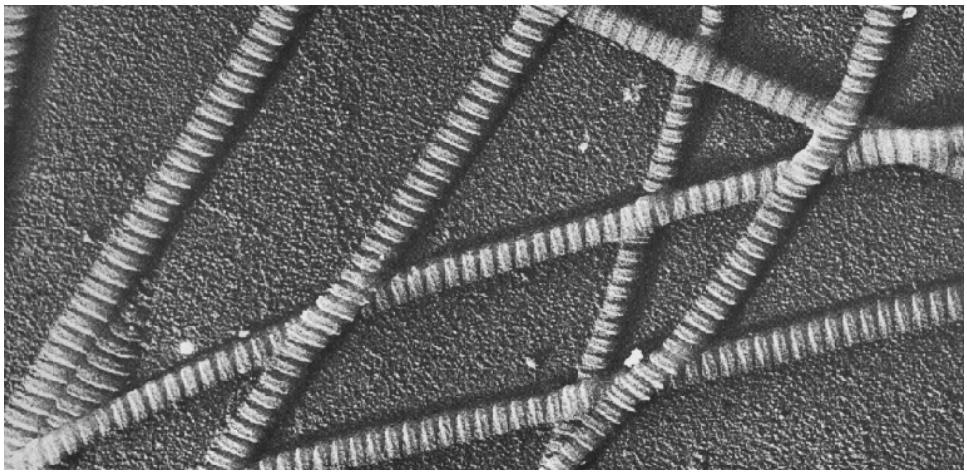
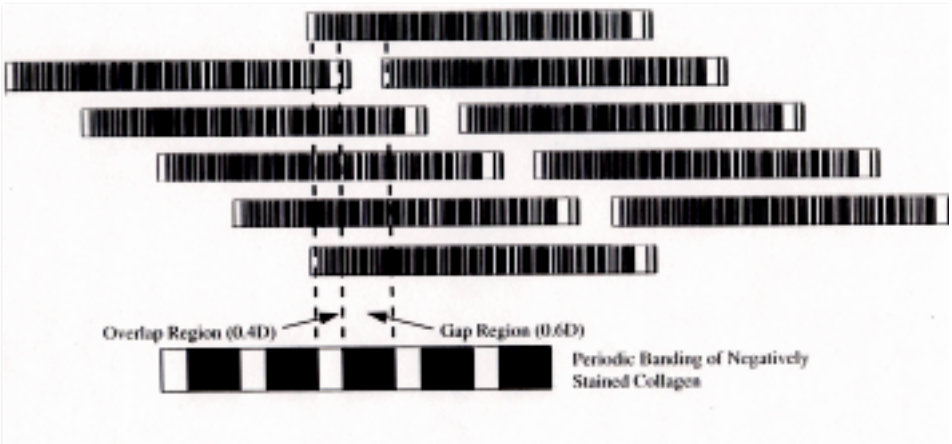


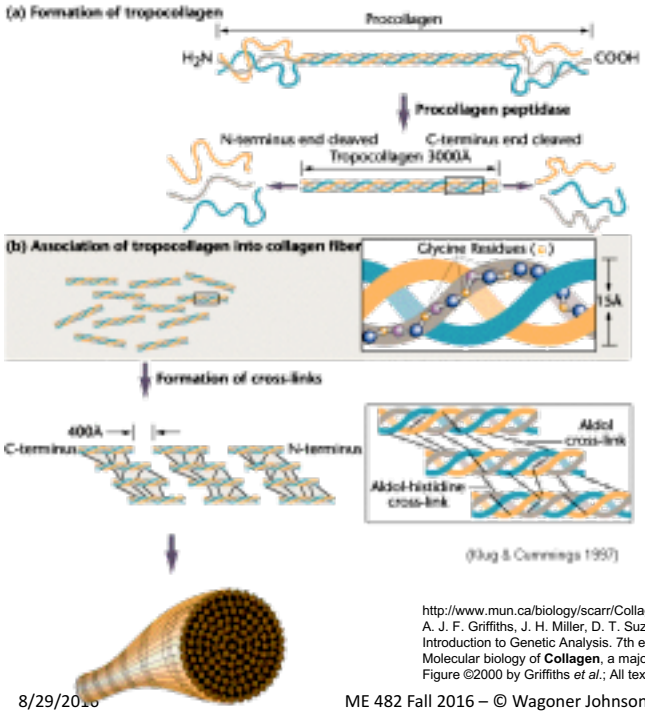
Figure 10.25 Collagen fibrils, Cowin and Doty

The packing of tropocollagen yields a periodic overlap region and a gap region that appears as light and dark bands in EM



Negative stain in EM = stain goes into holes, is electron dense
D=67nm

Figure 10.26 Cowin and Doty
Quarter stagger packing pattern of type I collagen molecules in tendon.



Summary of collagen fibril formation

http://www.mun.ca/biology/scarr/Collagen_structure.html
A. J. F. Griffiths, J. H. Miller, D. T. Suzuki, R. C. Lewontin, and W. M. Gelbart (2000). An Introduction to Genetic Analysis. 7th ed. W. H. Freeman, New York NY.
Molecular biology of **Collagen**, a major structural protein
Figure ©2000 by Griffiths *et al.*; All text material ©2005 by Steven M. Carr

Fibrils then form fibers

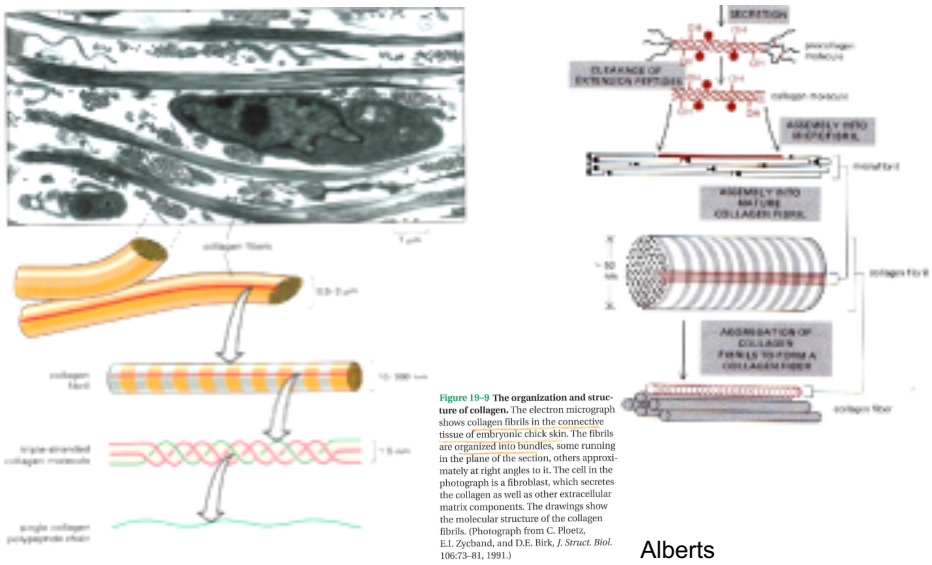


Figure 19–9 The organization and structure of collagen. The electron micrograph shows collagen fibrils in the connective tissue of embryonic chick skin. The fibrils are organized into bundles, some running in the plane of the section, others approximately at right angles to it. The cell in the photograph is a fibroblast, which secretes the collagen as well as other extracellular matrix components. The drawings show the molecular structure of the collagen fibrils. (Photograph from C. Ploetz, E.I. Zycband, and D.E. Birk, *J. Struct. Biol.* 106:73–81, 1991.)

Alberts

Summary table of sizes of structures for collagen
(you need to know columns 1-3 and will be asked on exam)

Structure	length	diameter	other
Amino acid chain	~300nm	0.15	Rise per amino acid residues 0.291 nm Residues/turn 3.33 Distance between glysines, or rise per turn, or pitch = ~3.3x.291 ~ 1 nm
Tropocollagen (superhelix)	~300 nm	1.5 nm	Pitch (rise per turn) ~ 8.6 nm Rise per residue ~.286 nm Residues per turn ~30
microfibril	?	3-4 nm	5 tropocollagen strands in staggerd array
fibril	?	10-300 nm	Striated appearance with 67nm period
fiber	?	1-10 μm	

Brief assignment due in class ***Friday, Sept. 2***

- Fill in the information (next page) for your assigned fiber forming collagen (I, II, III, V, XI).
- Find and very briefly describe a disease that results from a mutation from your "assigned" collagen.
  - Those assigned to collagen I or II need to describe TWO diseases!
- We will take a little time to report to your groups (A-G) on Friday.
- Take notes, and turn in your assignment with your notes individually.
  - The coll assigned to you must be detailed. The information for the others can be brief.
- **Cite your sources.**

Classes of collagen: ~28 known types of collagen.

You need to know Types I, II, III well.

- Fiber forming collagens include Types I, II, III, V, and XI – these are in the homework!
- All about the same length
- 3 alpha chains in form of triple helix
- Synthesized as a procollagen molecule
- Aggregate into staggered arrays, microfibrils of 5 collagen molecules, then aggregate into fibers

Type of Collagen	Location
I	• Where do you find it? In what tissues? • What are the collagen chains? • What disease is associated with mutations in this form of collagen? What does it do?
II	
III	
V	
XI	

	Col	Student Name		Col	NAME
	I	Anderson, Zachary C		I	Meyer, Joel I
	II	Bettinardi, Michael		II	Misurac, Rachel A
A	III	Bruno, Peter A	D	III	Muckatira, Sameer
	V	Chen, Mingze		V	Olbrich, Curtis E
	XI	Dupont, Gabriella R		XI	Pullen, Brendan R
	I	Edwardson, Elizabeth		I	Rappleye, Michael F
	II	Goldsmith, Sam W		II	Salehpour, Zaynab
B	III	Greenwell, Erik J	E	III	Schilling, Amelia J
	V	Halvorsen, Samuel C		V	Schuh, Sarah A
	XI	Hayani, Zayd		XI	Scully, Samuel W
	I	Kothari, Konik R		I	Secor, Erica J
	II	Kwiatkowski, Brandon		II	Shanley, John F
C	III	Lam, Peter D	F	III	Sherwin, Jeremiah M
	V	Livingston, Elizabet		V	Son, Jong Hyun
	XI	Lund, John R		XI	Thompson, Nicholas A
				I	Volkman, Kimberly M
				II	Westjohn, Cameron Y
			G	III	Xu, Yuchen
				V	Yan, Chenxi
				XI	Zhang, Zhichao
			A	I	Zhao, Yida
			B	II	Zhang, Yijie