Lecture 31 (12/07/20)

TODAY
•Reading: Chs4,6,8,10,14,16,17,18; 128-129, 189,311,377-380,555-557,561,621-622,639,662-663,679, 691-694

•Problems: –

NEXT (LAST!!)
•Reading: Ch13; 497-501, 507-514

•Problems: Ch13 (text); 5,6,9,10,22,24
Ch7 (study-guide: applying); **4**
Ch7 (study-guide: facts); *1-4,10-12*

•Additional Office hours – Thursday (12/10) & Wednesday (12/16) at 10:00-11 am

•Review session – next Monday 2-3 PM SCI109

•*Final Exam – Thursday 8-11 AM in LAW*

Carbohydrates

A. Definition
B. Roles
C. Monosaccharides
   1. Chirality
      a. One or more asymmetric carbons
      b. Linear and ring forms
   2. Derivatives: the chemistry of carbohydrates
   3. Polymerization
      a. The Glycosidic Bond
D. Oligosaccharides
   1. Glycoproteins & glycolipids
   2. O-linked
   3. N-linked
   4. Sequence determination-ABO
E. Polysaccharides
   1. Polymers of glucose
   2. Polymers of disaccharides

Vitamins & Cofactors

A. Water soluble
B. Fat Soluble

Metabolism

Announcements

•Additional Office hours – Thursday (12/10) & Wednesday (12/16) at 10:00-11 am

•Review session – next Monday 2-3 PM SCI109

•*Final Exam – Thursday 8-11 AM in LAW*

•Complete a course evaluation (detailed instructions under Announcements on website)
- Link to survey sent by email [BU.campuslabs.com/courseeval]. You can use any portable smart device (phone, tablet, laptop).
- Enter your BU login and Kerberos password. Complete the particular evaluation assigned to you for this course.
- Your individual evaluations are anonymous, and they will not be shared with the instructor. The instructor will receive only the average evaluation results for the entire class and anonymized comments, **after** the course has been completed and the final grades have been submitted.
- Comments in the text fields are valued and encouraged. Please try to answer all questions.
- You will have time from today until the site closes on next Monday (12/14) at 6 PM.

Carbohydrates

Polysaccharides

Carbohydrates

Polysaccharides

- The majority of natural carbohydrates are usually found as large polymers.
- These polysaccharides can be:
  - homopolysaccharides (one monomer unit)
  - heteropolysaccharides (multiple monomer units)
  - linear (one type of glycosidic bond)
  - branched (multiple types of glycosidic bonds)
- Polysaccharides do not have a defined molecular weight.
  - This is in contrast to proteins because, unlike proteins, no template is used to make polysaccharides.
  - Polysaccharides are often in a state of flux; monomer units are added and removed as needed by the organism.

Carbohydrates

Polysaccharides: Polymers of Glucose

Homopolymers of Glucose:

- Starch
- Glycogen
- Cellulose
- Chitin

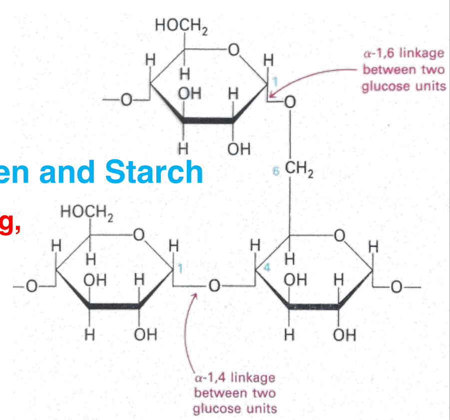
- Glycogen and Starch are the main storage polysaccharides for energy.
  - Glycogen and starch are insoluble due to their high molecular weight and often form granules in cells.
  - Molecular weight reaches several millions (~200 x 10^6)(can see in microscope).
- Glycogen is a branched homopolysaccharide of glucose.
  - Glucose monomers form $\alpha(1 \rightarrow 4)$ linked chains.
  - There are branch points with $\alpha(1 \rightarrow 6)$ linkers every 8–12 residues.
- Starch is a mixture of two homopolysaccharides of glucose.
  - Amylopectin is like glycogen, but the branch points ($\alpha(1 \rightarrow 6)$ linkages) occur every 24–30 residues.
  - Amylose is an unbranched polymer of $\alpha(1 \rightarrow 4)$ linked residues.

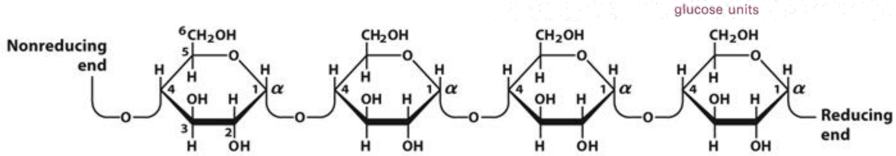
Carbohydrates

Polysaccharides: Glycogen & Starch

Glycosidic Linkages in Glycogen and Starch

(Glc-α(1→4)Glc)$_n$ with α(1→6) branching, where n≈10^6





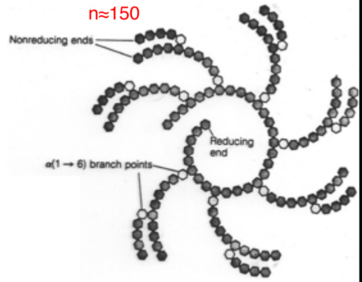
Non-reducing → reducing

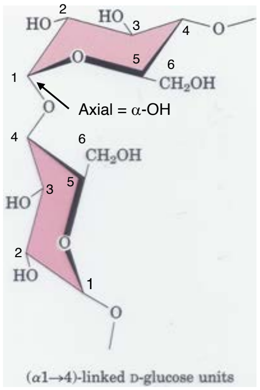
Haworth projections are not good to show the actual shape, which is helical!

Carbohydrates

Polysaccharides: Glycogen & Starch

I_2

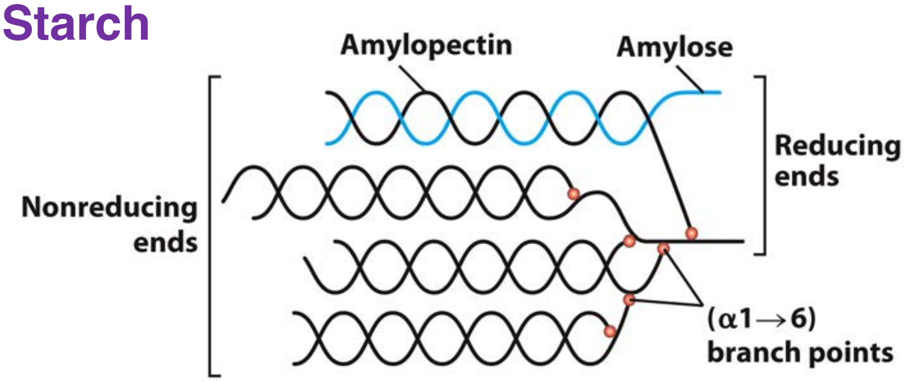




- Granules contain enzymes that synthesize and degrade these polymers.
- Glycogen and amylopectin have one reducing end but many nonreducing ends.
- Enzymatic processing occurs simultaneously in many nonreducing ends.

Carbohydrates

Polysaccharides: Glycogen & Starch



Mixture of **Amylose** and **Amylopectin** in Starch

Carbohydrates

Polysaccharides:

Homopolymers of Glucose:

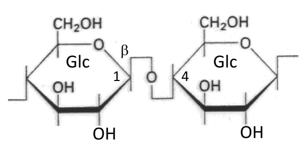
- Starch
- Glycogen
- Cellulose
- Chitin

- Cellulose is a linear homopolysaccharide of glucose.
  - Glucose monomers form $\beta(1 \rightarrow 4)$ linked chains.
  - Hydrogen bonds form between adjacent monomers.
  - There are additional H-bonds between chains.
  - Structure is now tough and water insoluble.
  - It makes up almost 50% of plant mass; in cell walls.
  - Cotton is nearly pure fibrous cellulose.
- Chitin is a linear homopolysaccharide of *N*-acetylglucosamine (GlcNAc).
  - *N*-acetylglucosamine monomers form $\beta(1 \rightarrow 4)$-linked chains.
  - forms extended fibers that are similar to those of cellulose
  - hard, insoluble, cannot be digested by vertebrates
  - structure is tough but flexible, and water insoluble
  - found in cell walls in mushrooms and in exoskeletons of insects, spiders, crabs, and other arthropods

Carbohydrates

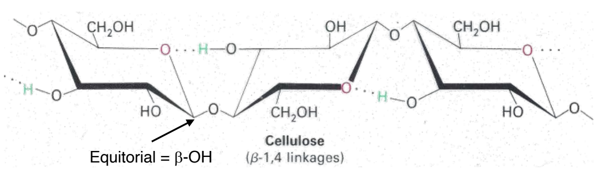
Polysaccharides:

Cellulose & Chitin

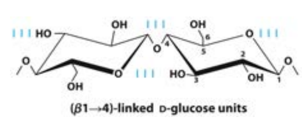


Glycosidic Linkages in Cellulose & Chitin

(Glc-β(1→4)Glc)$_n$ with NO branching,
$n \approx 10^4$



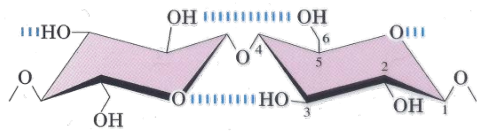
Notice that each chair is alternatively flipped



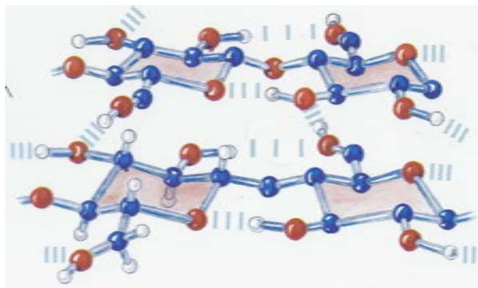
THE most abundant biological molecule in the world: ~300 trillion kg

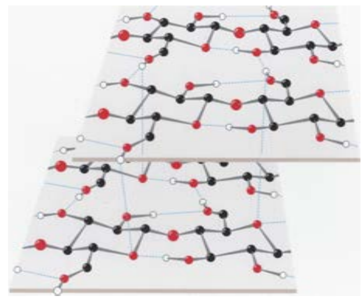
Carbohydrates

Polysaccharides: Cellulose & Chitin

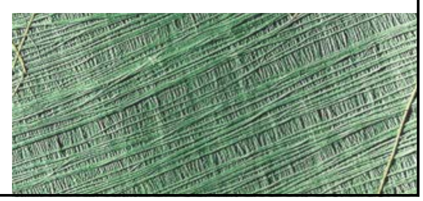


(β1→4)-linked D-glucose units





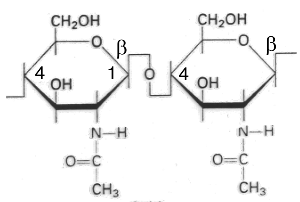
- The fibrous structure and water insolubility make cellulose a difficult substrate to act upon.
- Most animals cannot use cellulose as a fuel source because they lack the enzyme to hydrolyze $\beta(1\rightarrow4)$ linkages (β-Amylase).
- Fungi, bacteria, and protozoa secrete cellulase, which allows them to use wood as source of glucose.
- Ruminants and termites live symbiotically with microorganisms that produce cellulase and are able to absorb the freed glucose into their bloodstreams.
- Cellulases hold promise in the fermentation of biomass into biofuels.



Carbohydrates

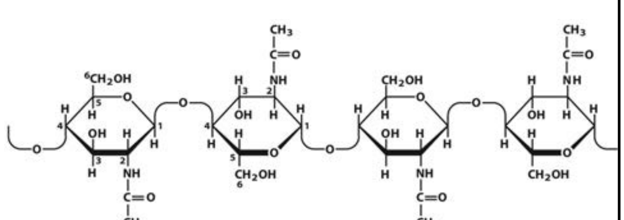
Polysaccharides: Cellulose & Chitin

A Sally lightfoot crab. The exoskeleton of this arthropod is rich in chitin, one of the most abundant biopolymers on earth.



Chitin

$(GlcNAc–\beta(1\rightarrow4)–GlcNAc)_n$

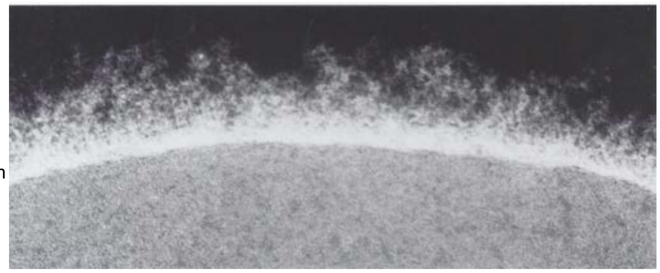


Carbohydrates

Polysaccharides: Polymers of Disaccharides

First, need to describe the Extracellular Matrix (ECM)

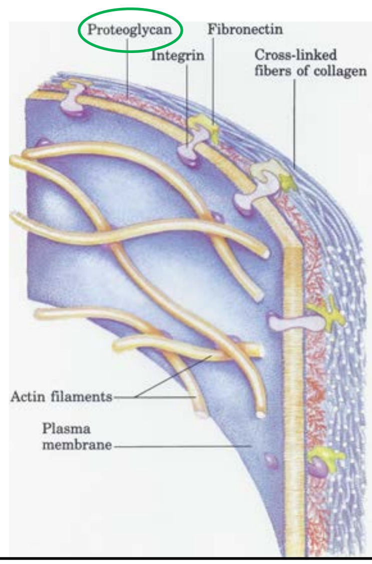
- Material outside the cell
- Strength, elasticity, and physical barrier in tissues (varies tremendously)
- Main components
  - proteoglycans
  - collagen & elastin fibers
- Proteoglycans
  - Different glycosaminoglycans are O-linked to the “core protein.”
  - Linkage from anomeric carbon of xylose to serine hydroxyl
  - Our tissues have many different core proteins; aggrecan is the best studied.

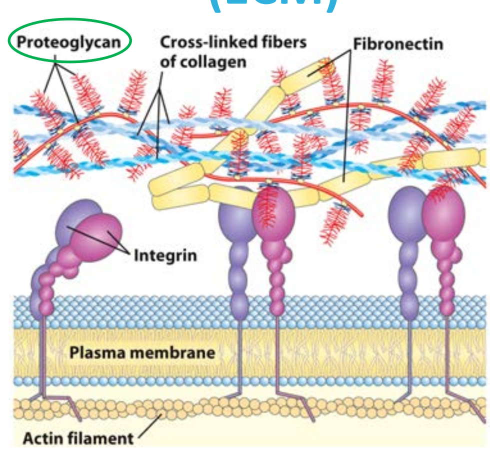


Carbohydrates

Polysaccharides: Polymers of Disaccharides

Extracellular Matrix (ECM)





Carbohydrates

Polysaccharides: Polymers of Disaccharides
Glycosaminoglycans
(the carbohydrate part of proteoglycans)

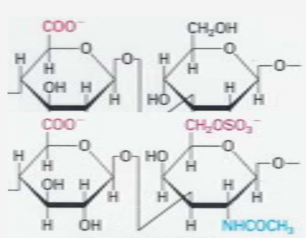
- Linear polymers of repeating disaccharide units (sugarX-sugarY)$_n$
- One monomer (sugarX) is either sugar acid or Gal
  - uronic acids (C6 oxidation)
  - Most have sulfate esters
- One monomer (sugarY) is either:
  - *N*-acetyl-glucosamine (GlcNAc) or *N*-acetyl-galactosamine (GalNAc)
  - Also sulfate esters
- Extended hydrated molecule
  - Negatively charged
  - minimizes charge repulsion
- Forms meshwork with fibrous proteins to form extracellular matrix
  - connective tissue
  - lubrication of joints
- Form huge ($M_r > 2 \cdot 10^8$) noncovalent aggregates (Hyaluronan and Aggrecan).
  - They hold a lot of water (1000× its weight) and provide lubrication.
  - Very low friction material
  - Covers joint surfaces: articular cartilage
    - reduced friction & load balancing

Carbohydrates

Polysaccharides: Polymers of Disaccharides
Glycosaminoglycans

Major components of the polysaccharide portion of mucopolysaccharides (proteoglycans)

Usual molecular weight of poly-saccharide chain	Component sugars	Location of sulfate	Linkage	Major Source



Chondroitin 6-sulfate

[a]The attachment of hyaluronic acid to protein has not been demonstrated unequivocally.

[b]This linkage of L-iduronic acid, identical to the β-linkage of D-glucuronic acid. However, iduronic acid is of the L rather than D configuration, which results in this bond being designated as α rather than β.

Carbohydrates

Polysaccharides: Polymers of Disaccharides

Glycosaminoglycans

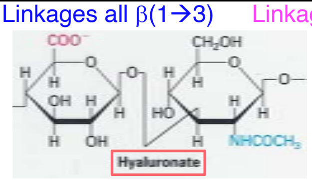
Major components of the polysaccharide portion of mucopolysaccharides (proteoglycans)

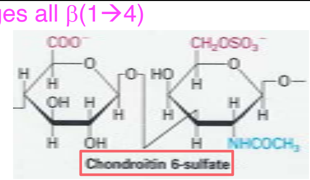
	Usual molecular weight of polysaccharide chain	Component sugars	Location of sulfate	Linkage	Major Source
Hyaluronic acid[a]	1 - 3 x 10^6	*N*-acetylglucosamine glucuronic acid	-	β-(1→4) β-(1→3)	synovial fluid, vitreous humor of the eye, umbilical cord, cock's comb
Chondroitin 4-sulfate (chondroitin sulfate A)	2 - 5 x 10^4	*N*-acetylgalactosamine glucuronic acid	4	β-(1→4) β-(1→3)	human cartilage, aorta
Chondroitin 6-sulfate (chondroitin sulfate C)	2 - 5 x 10^4	*N*-acetylgalactosamine glucuronic acid	6	β-(1→4) β-(1→3)	heart valves
Dermatan sulfate (chondroitin sulfate B)	2 - 5 x 10^4	*N*-acetylgalactosamine iduronic acid glucuronic acid	4	β-(1→4) α-(1→3)[b] β-(1→3)	skin, blood vessels, heart valves
Heparin	1 - 3 x 10^4	glucosamine glucuronic acid iduronic acid	3,6,N 2	α-(1→4) β-(1→4) α-(1→4)[b]	lung, mast cells
Heparan sulfate (heparitin sulfate)	2 - 10 x 10^3	glucosamine *N*-acetylglucosamine glucuronic acid iduronic acid	N ? 3,6 2	 α-(1→4) β-(1→4) α-(1→4)[b]	blood vessels, cell surfaces
Keratan sulfate	5 - 20 x 10^3	*N*-acetylglucosamine galactose	6 6	β-(1→3) β-(1→4)	cornea of the eye, nucleus pulposus, cartilage

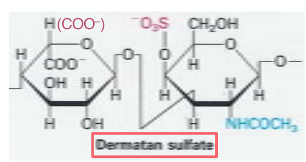
[a]The attachment of hyaluronic acid to protein has not been demonstrated unequivocally.

[b]This linkage of L-iduronic acid, identical to the β-linkage of D-glucuronic acid. However, iduronic acid is of the L rather than D configuration, which results in this bond being designated as α rather than β.

Linkages all β(1→3) Linkages all β(1→4)





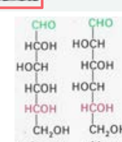


GlcUA – GlcNAc

GlcUA – GalNAc

C6/C4-sulfate

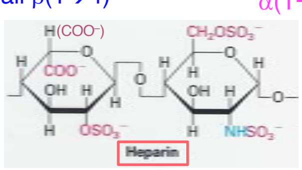
L-IdoUA (C5 epimer of D-Glc) & C4-sulfate only

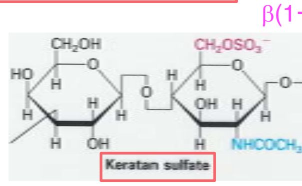


– (SugarX – SugarY)$_n$ –

GlcUA(IdoUA) or Gal GlcNAc or GalNAc or GlcN

Linkages all β(1→4) α(1→4) β(1→3)





GlcUA – GlcN

L-IdoUA GlcNAc

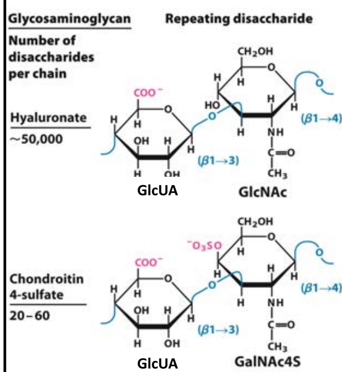
Sulfate everywhere, including GlcN

Gal – GlcNAc

C6-sulfate

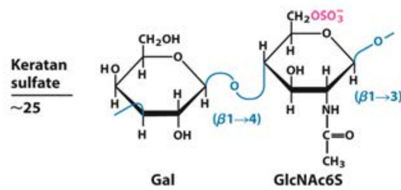
Glycosaminoglycans

– (SugarX – SugarY)$_n$ –
GlcUA(IdoUA) or Gal   GlcNAc or GalNAc or GlcN



GlcUA – GlcNAc

GlcUA – GalNAc (C6/**C4**-sulfate)

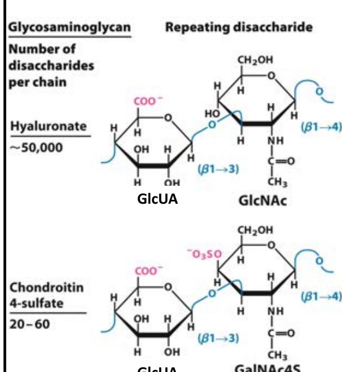


Gal – GlcNAc
C6-sulfate
Linkages all β, and opposite of Hyl & CS
alternate (1→4) & (1→3)

IdoUA

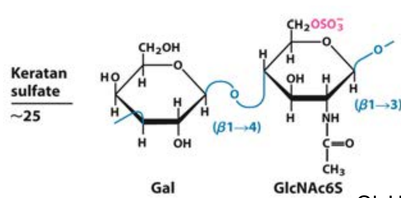
Glycosaminoglycans

– (SugarX – SugarY)$_n$ –
GlcUA(IdoUA) or Gal   GlcNAc or GalNAc or GlcN



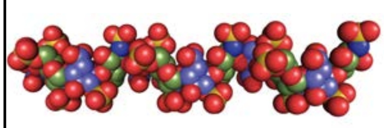
GlcUA – GlcNAc

GlcUA – GalNAc (C6/**C4**-sulfate)

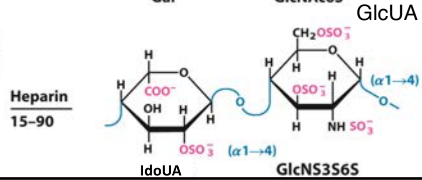


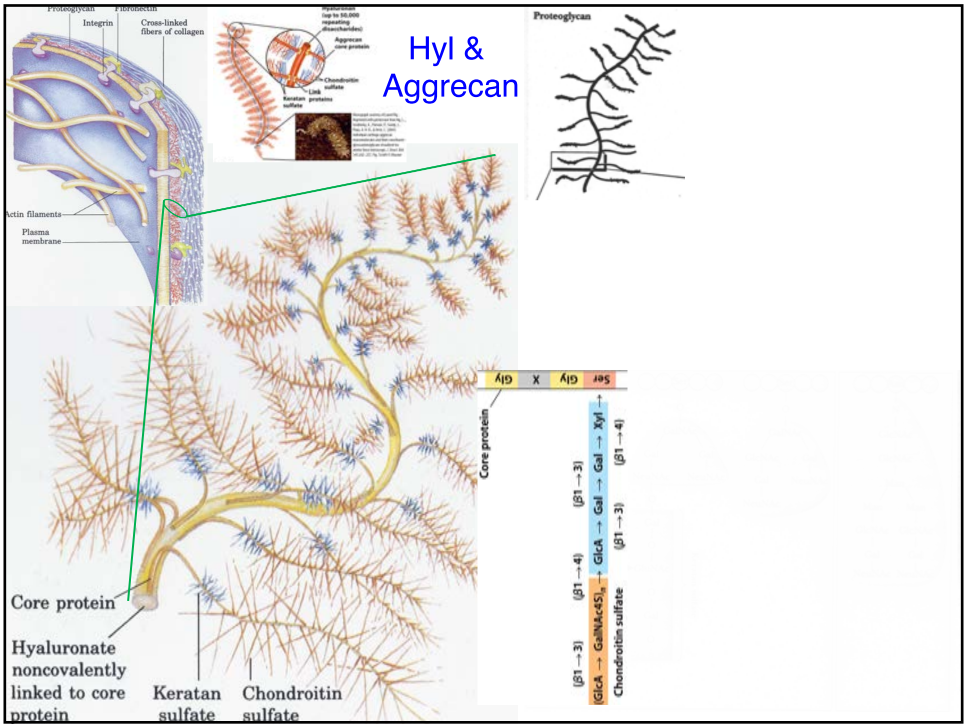
Gal – GlcNAc
C6-sulfate
Linkages all β, and opposite of Hyl & CS
alternate (1→4) & (1→3)

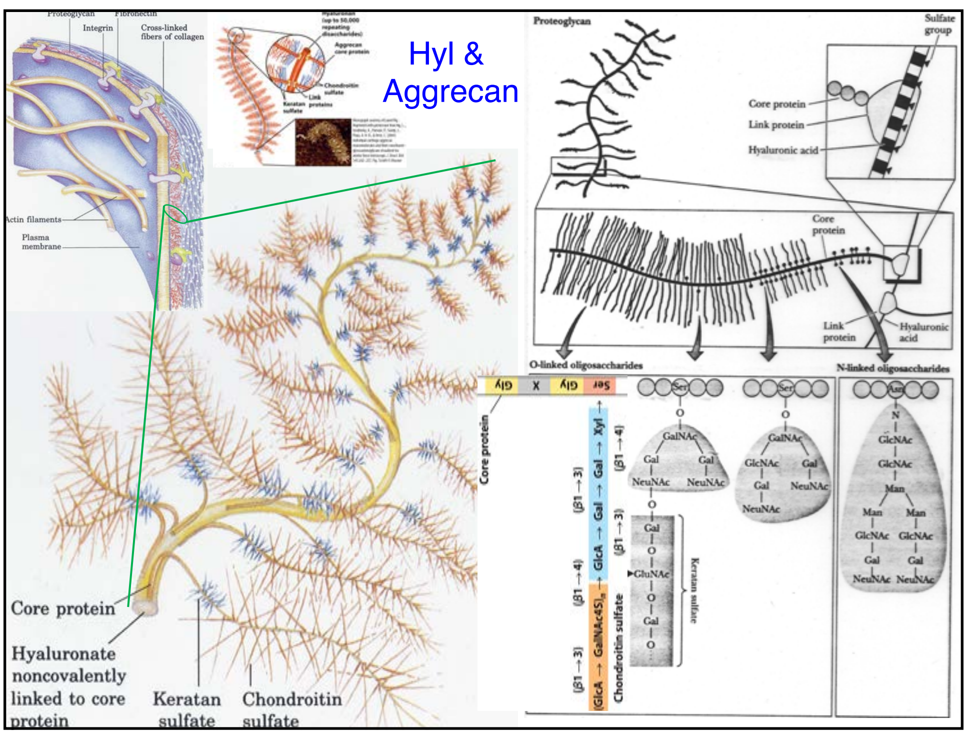
GlcUA or IdoUA – GlcN
Sulfate everywhere, including GlcN
Linkages all (1→4), alternate α & β



Heparin segment



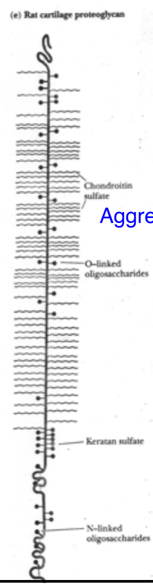

Proteoglycan
Fibronectin
Integrin
Cross-linked fibers of collagen
Actin filaments
Plasma membrane
Hyaluronan (up to 50,000 repeating disaccharides)
Aggrecan core protein
Chondroitin sulfate
Link proteins
Keratan sulfate
Hyl &
Aggrecan
Proteoglycan
Core protein
Hyaluronate noncovalently linked to core protein
Keratan sulfate
Chondroitin sulfate
Gly X Gly Ser
Core protein
(GlcA → GalNAc4S)n → GlcA → Gal → Gal → Xyl →
(β1 → 3) (β1 → 4) (β1 → 3) (β1 → 3) (β1 → 4)
Chondroitin sulfate


Proteoglycan
Fibronectin
Integrin
Cross-linked fibers of collagen
Actin filaments
Plasma membrane
Hyaluronan (up to 50,000 repeating disaccharides)
Aggrecan core protein
Chondroitin sulfate
Link proteins
Keratan sulfate
Hyl &
Aggrecan
Proteoglycan
Sulfate group
Core protein
Link protein
Hyaluronic acid
Core protein
Link protein
Hyaluronic acid
O-linked oligosaccharides
N-linked oligosaccharides
Ser
GalNAc
Gal
NeuNAc
GluNAc
Keratan sulfate
GlcNAc
Asn
Man
Core protein
Hyaluronate noncovalently linked to core protein
Keratan sulfate
Chondroitin sulfate
Gly X Gly Ser
Core protein
(GlcA → GalNAc4S)n → GlcA → Gal → Gal → Xyl →
(β1 → 3) (β1 → 4) (β1 → 3) (β1 → 3) (β1 → 4)
Chondroitin sulfate

Carbohydrates

Polysaccharides: Proteoglycans = Polymers of Disaccharides (glycosaminoglycans) + proteins

a.k.a. - mucopolysaccharides

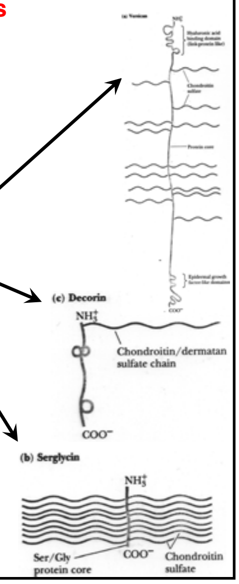


Some Proteoglycans of Known Sequence

Proteoglycan	Glycosaminoglycan	Protein M_r	Number of Amino Acid Residues
Secreted or extracellular matrix proteoglycans			
Large aggregating cartilage proteoglycans (Aggrecan)	CS/KS*	220,952	2124
Versican	CS/DS	265,048	2409
Decorin	CS/DS	38,000	329
Intracellular granule proteoglycan			
Serglycin (PG19)	CS/DS	10,190	104
Membrane-intercalated proteoglycans			
Syndecan	HS/CS	38,868	311

*CS, chondroitin sulfate; DS, dermatan sulfate; HS, heparan sulfate (an analog of heparin); KS, keratan sulfate. These glycosaminoglycans are polymers consisting of the repeating disaccharides: glucuronic acid N-acetylgalactosamine (CS), iduronic acid N-acetylgalactosamine (DS), iduronic acid N-acetylglucosamine (HS and heparin), and galactose N-acetylglucosamine (KS). DS, HS, and heparin also contain some disaccharide units in which the uronic acid is glucuronic acid instead of iduronic acid. These glycosaminoglycans and CS are generally bound to the hydroxyl group of a serine residue to give the sequence (disaccharide) nGlcUA-Gal-Gal-Xyl-O Ser. Keratan sulfate has a different linkage region and can be either O- or N-linked. The sugars in the repeating disaccharide unit are sulfated to various degrees. By comparison, hyaluronic acid is a polymer of glucuronic acid and glucosamine that is not sulfated and does not attach covalently to a protein core.

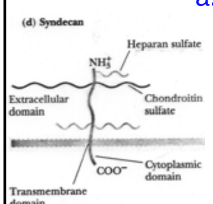
Adapted from Ruoslahti, E., 1989. *Journal of Biological Chemistry* **264**:13369–13372.

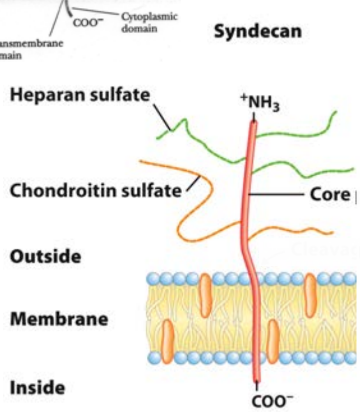


Carbohydrates

Polysaccharides: Proteoglycans = Polymers of Disaccharides (glycosaminoglycans) + proteins

a.k.a. - mucopolysaccharides





Sulfated glycosaminoglycans attached to a large rod-shaped protein in cell membrane

- syndecans: protein has a single transmembrane domain
- glypicans: protein is anchored to a lipid membrane

Interact with a variety of receptors from neighboring cells and regulate cell growth

Carbohydrates

Polysaccharides: Proteoglycans = Polymers of Disaccharides (glycosaminoglycans) + proteins

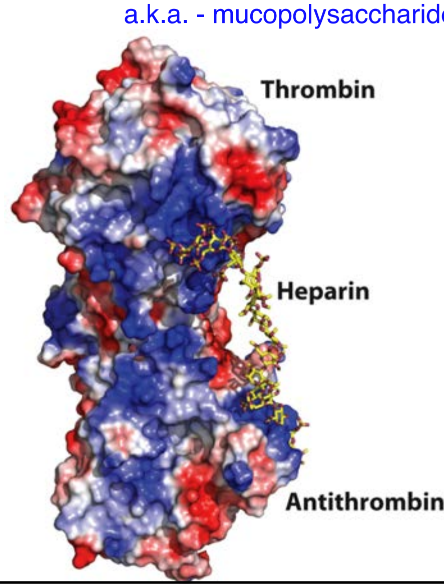
a.k.a. - mucopolysaccharides

- Some integral membrane proteins are proteoglycans.
  - syndecans
- Other integral membrane proteins are receptors for extracellular proteoglycans.
  - Integrins (which then interact with Actin)
- These proteins link cellular cytoskeleton to the ECM and transmit signals into the cell to regulate:
  - cell growth
  - cell mobility
  - apoptosis
  - wound healing
- In chondrocytes, huge amounts of cartilage proteoglycans are produced (Aggrecan)
  - Resilience
  - Plasticity
  - Cushioning
  - Due to reversible hydration
- Heparin is linear polymer, 3–40 kDa.
  - Heparan sulfate is <u>heparin-like polysaccharide but attached to proteins</u>.
  - Highest density of negative-charge of any biomolecule
  - Prevent blood clotting by activating protease inhibitor antithrombin III
  - Binding to various cells regulates development and formation of blood vessels.
  - Modulates growth and development by binding growth-factor receptors
  - Important role in cancer metastasis
  - Can also bind to viruses and bacteria and decrease their virulence

Carbohydrates

Polysaccharides: Proteoglycans = Polymers of Disaccharides (glycosaminoglycans) + proteins

a.k.a. - mucopolysaccharides



Heparin

Prevent blood clotting by activating protease inhibitor antithrombin III

TABLE 7-2	Structures and Roles of Some Polysaccharides			
Primer	**Type**[a]	**Repeating unit**[b]	**Size (number of monosaccharide units)**	**Roles/significance**
Starch				Energy storage: in plants
Amylose	Homo-	(α1➔S4) Glc, linear	50–5,000	
Amylopectin	Homo-	(α1➔S4) Glc, with (α1➔S6) Glc branches every 24–30 residues	Up to 10^6	
Glycogen	Homo-	(α1➔S4) Glc, with (α1➔S6) Glc branches every 8–12 residues	Up to 50,000	Energy storage: in bacteria and animal cells
Cellulose	Homo-	(β1➔S4) Glc	Up to 15,000	Structural: in plants, gives rigidity and strength to cell walls
Chitin	Homo-	(β1➔S4) GlcNAc	Very large	Structural: in insects, spiders, crustaceans, gives rigidity and strength to exoskeletons
Peptidoglycan	Hetero-; peptides attached	4)Mur2Ac(β1➔S4) GlcNAc(β1	Very large	Structural: in bacteria, gives rigidity and strength to cell envelope
Hyaluronan (a glycosaminoglycan)	Hetero-; acidic	4)GlcA (β1➔S3) GlcNAc(β1	Up to 100,000	Structural: in vertebrates, extracellular matrix of skin and connective tissue; viscosity and lubrication in joints

[a]Each polymer is classified as a homopolysaccharide (homo-) or heteropolysaccharide (hetero-).
[b]The abbreviated names for the peptidoglycan, agarose, and hyaluronan repeating units indicate that the polymer contains repeats of this disaccharide unit. For example, in peptidoglycan, the GlcNAc of one disaccharide unit is (β1➔S4)-linked to the first residue of the next disaccharide unit.