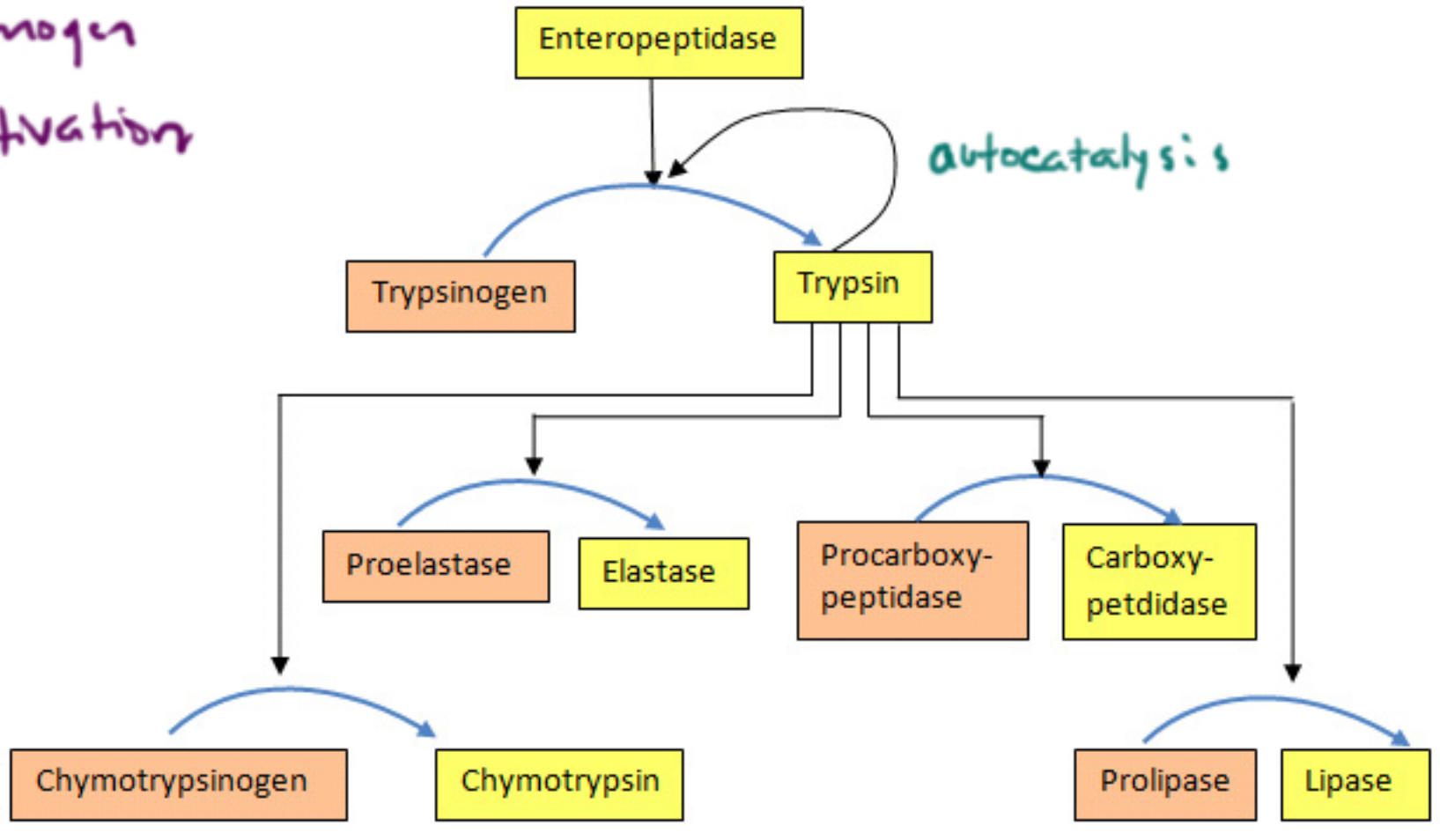
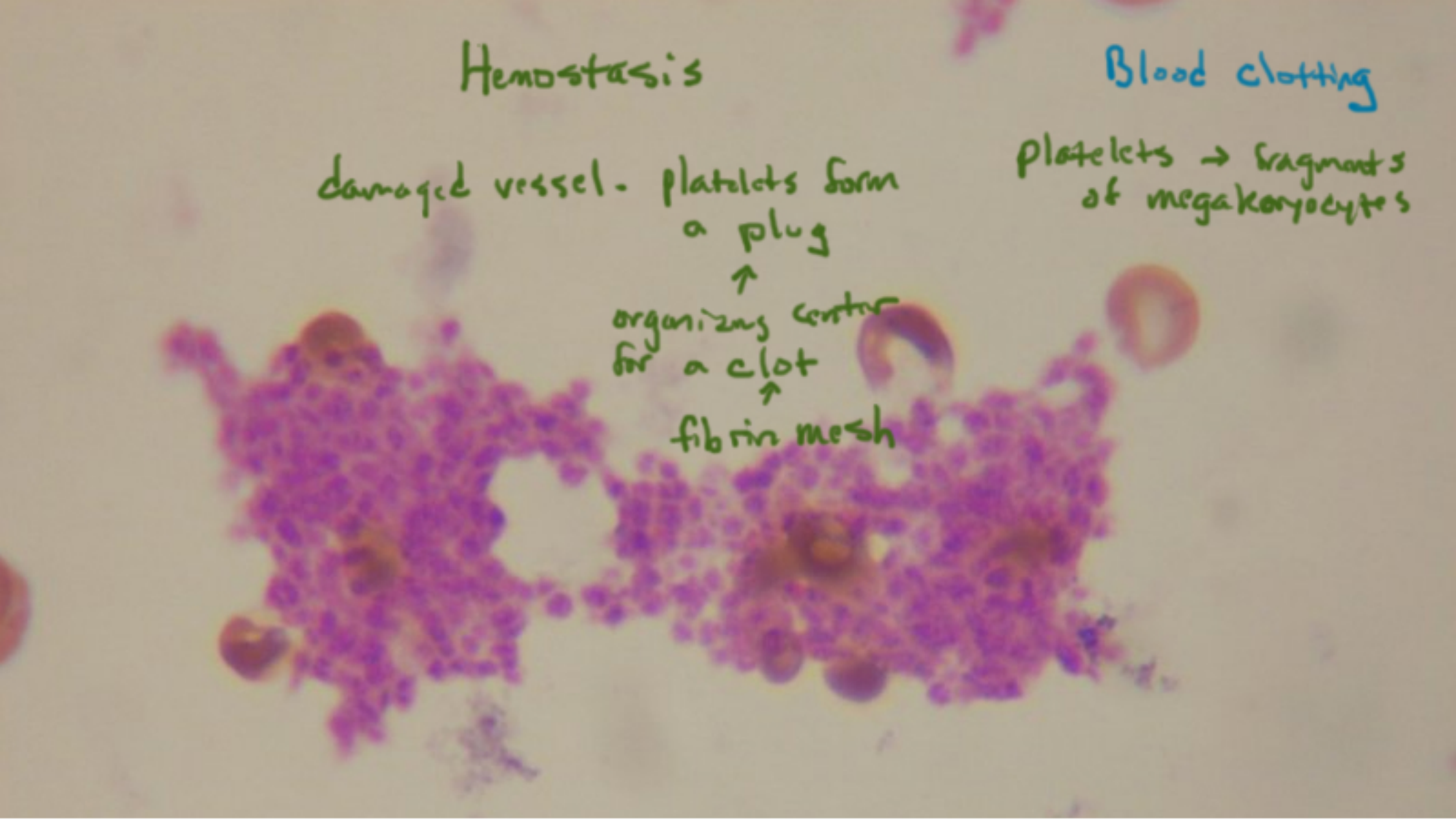
Blood Clotting and Collagen

Session Slides with Notes

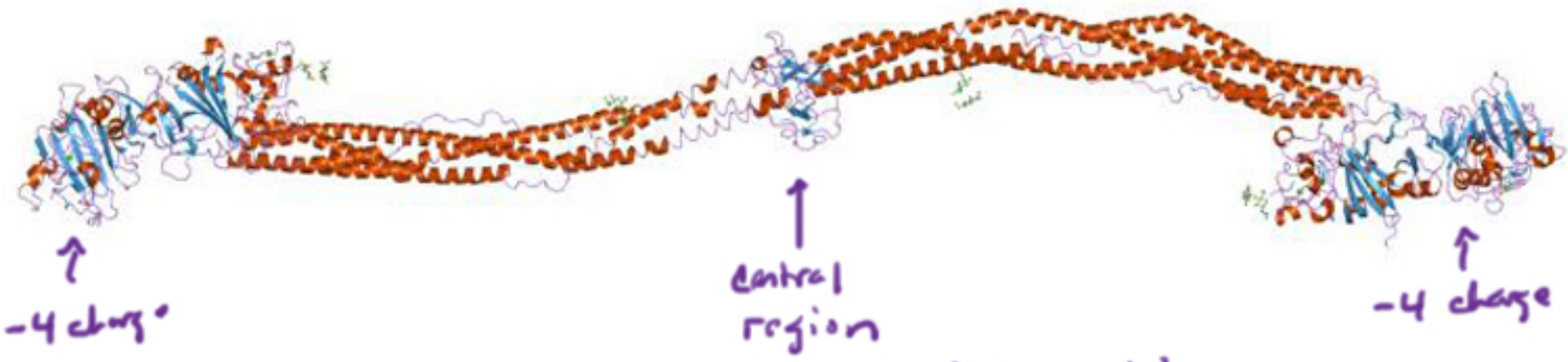
Zymogen activation




Hemostasis
damaged vessel. platelets form a plug
organizing center for a clot
fibrin mesh
Blood clotting
platelets → fragments of megakaryocytes

Fibrinogen - 2%-3% of plasma protein

↑
soluble precursor



-4 charge

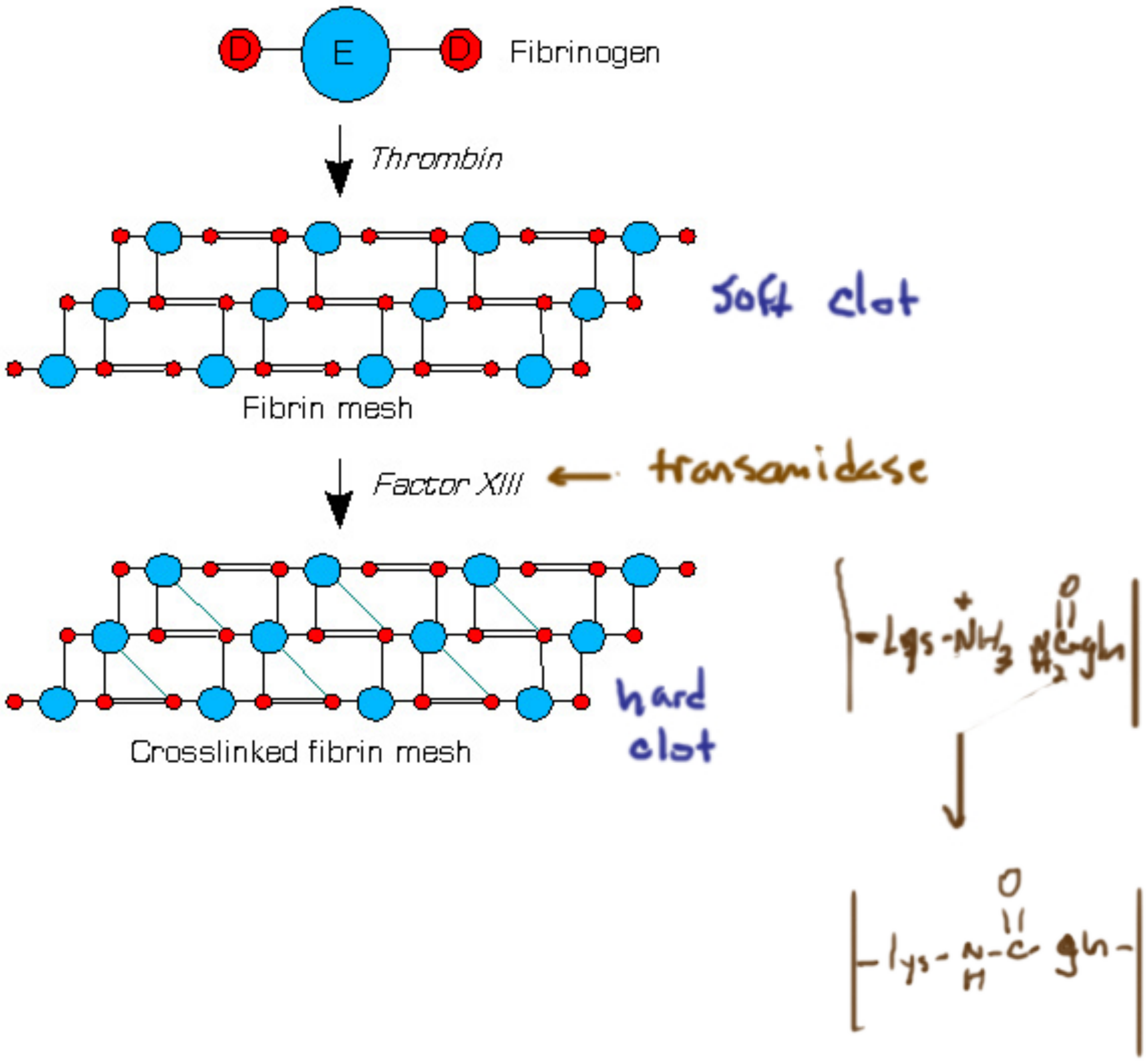
central region

-4 charge

-8 charge with fibrinopeptides

+5 charge without them

cleaved by thrombin


D
E
D
Fibrinogen
Thrombin
Fibrin mesh
Soft clot
Factor XIII
transamidase
Crosslinked fibrin mesh
hard clot

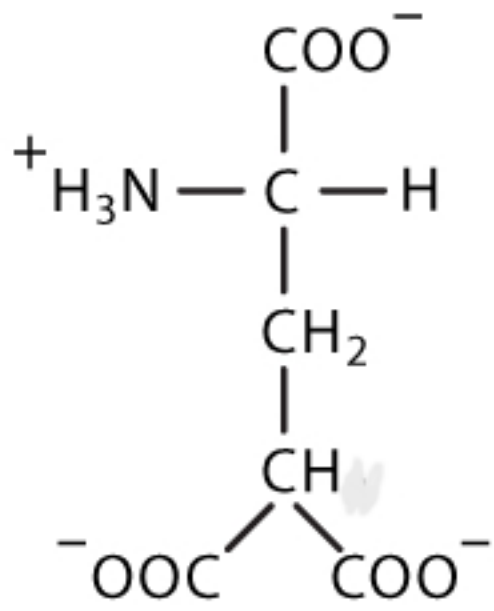
Prothrombin (FII)

zymogen

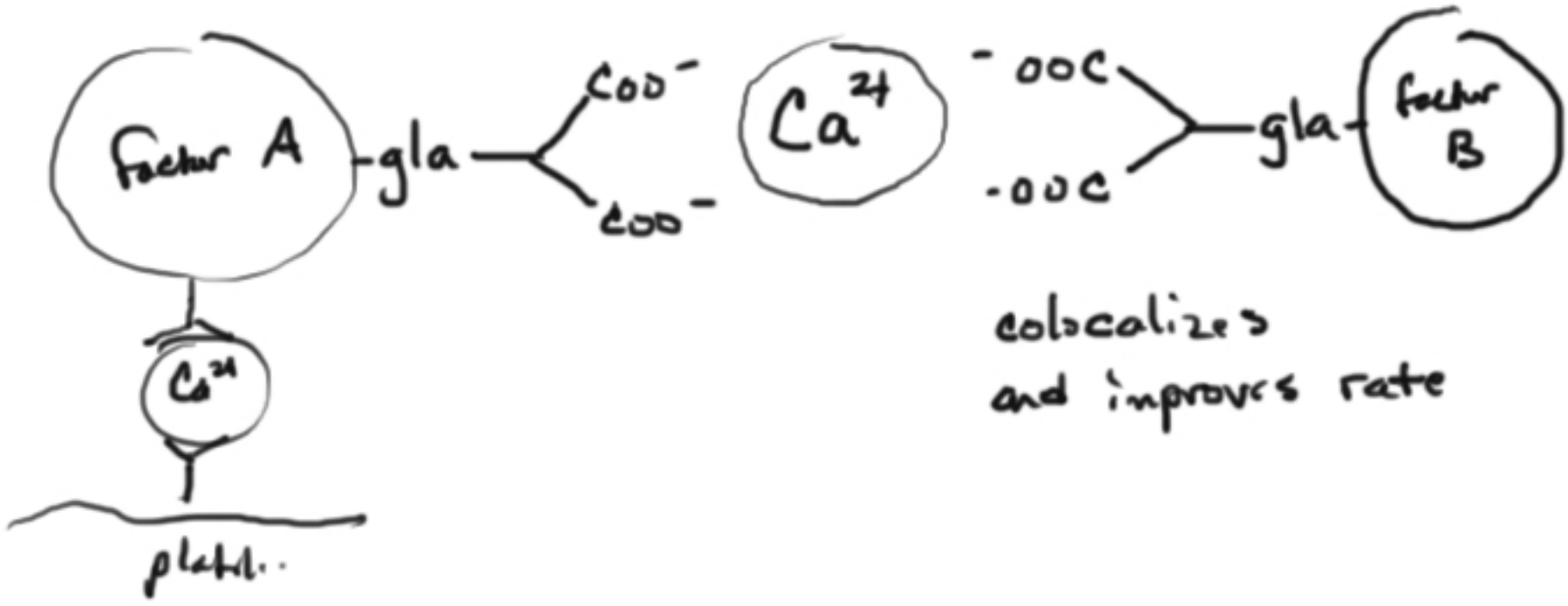
↓ Factor X (Stuart factor)

α - Thrombin

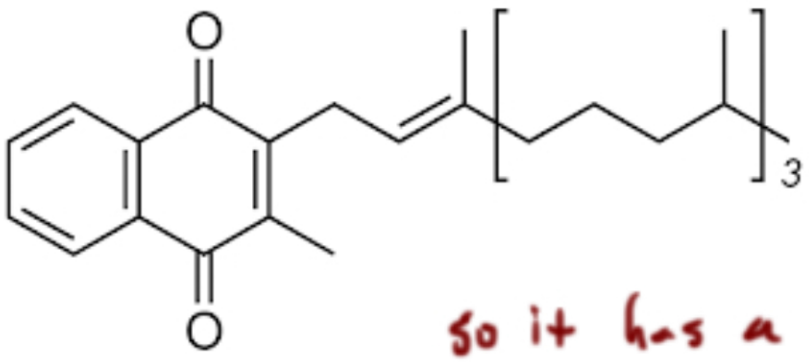
Many clotting factors possess γ carboxy glutamate



synthesis requires vitamin K

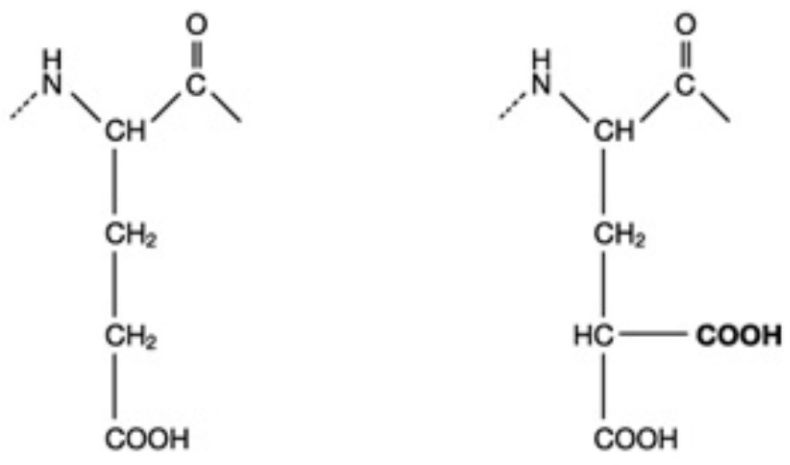


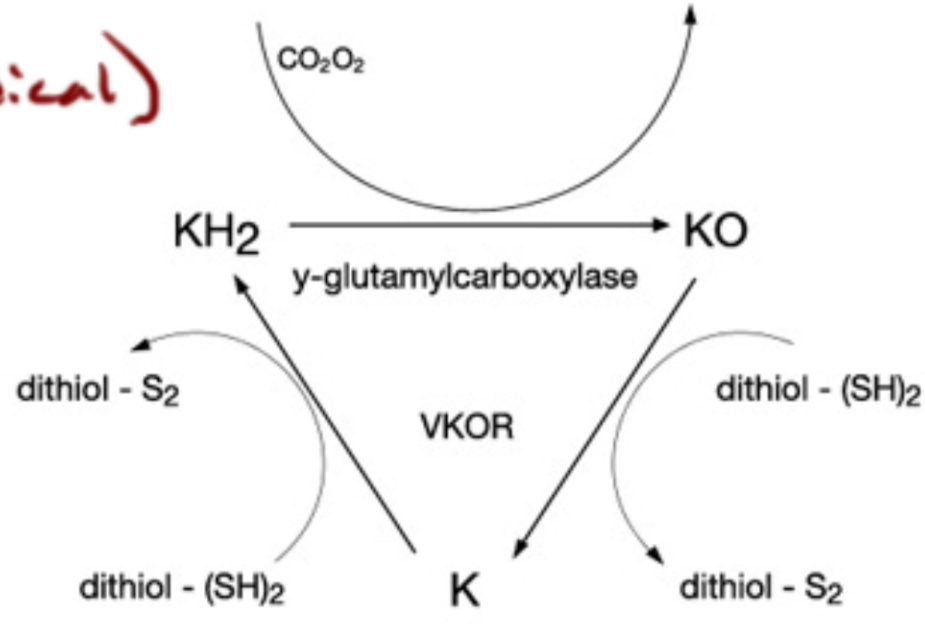
colocalizes and improves rate



↑ benzoquinone like CoQ

so it has a semiquinone (stable radical) form

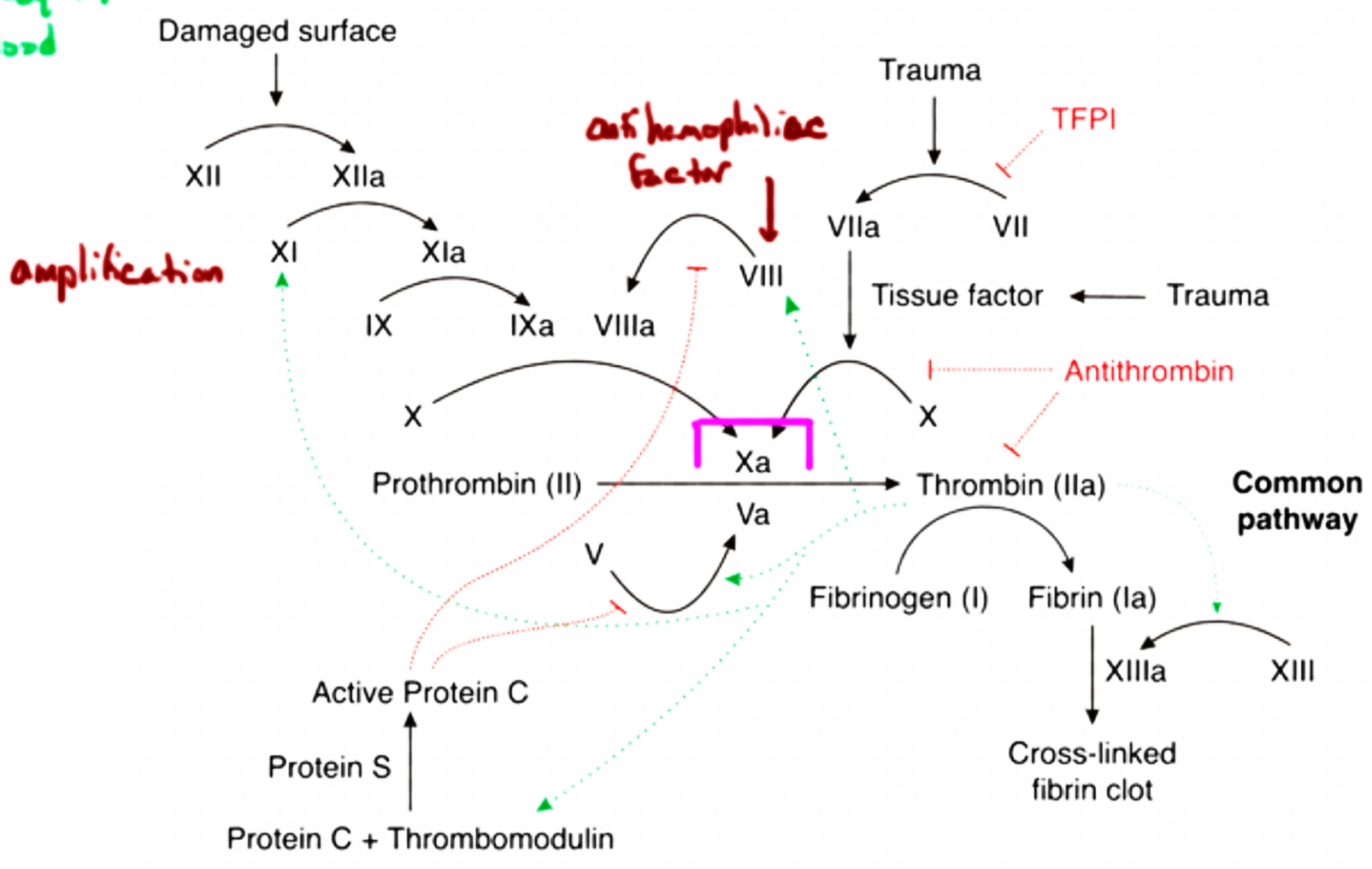




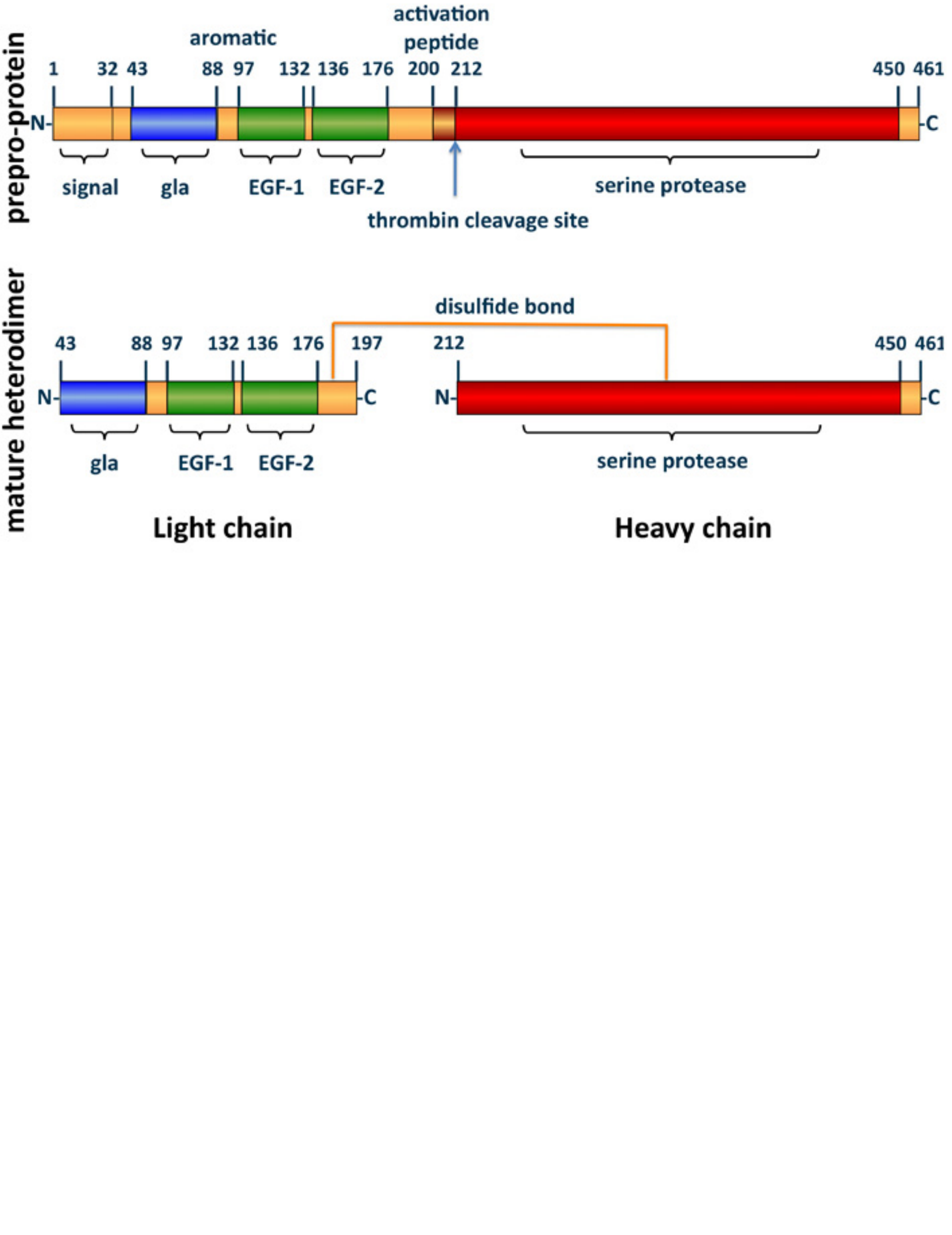
Warfarin and Coumadin are vitamin K competitive inhibitors

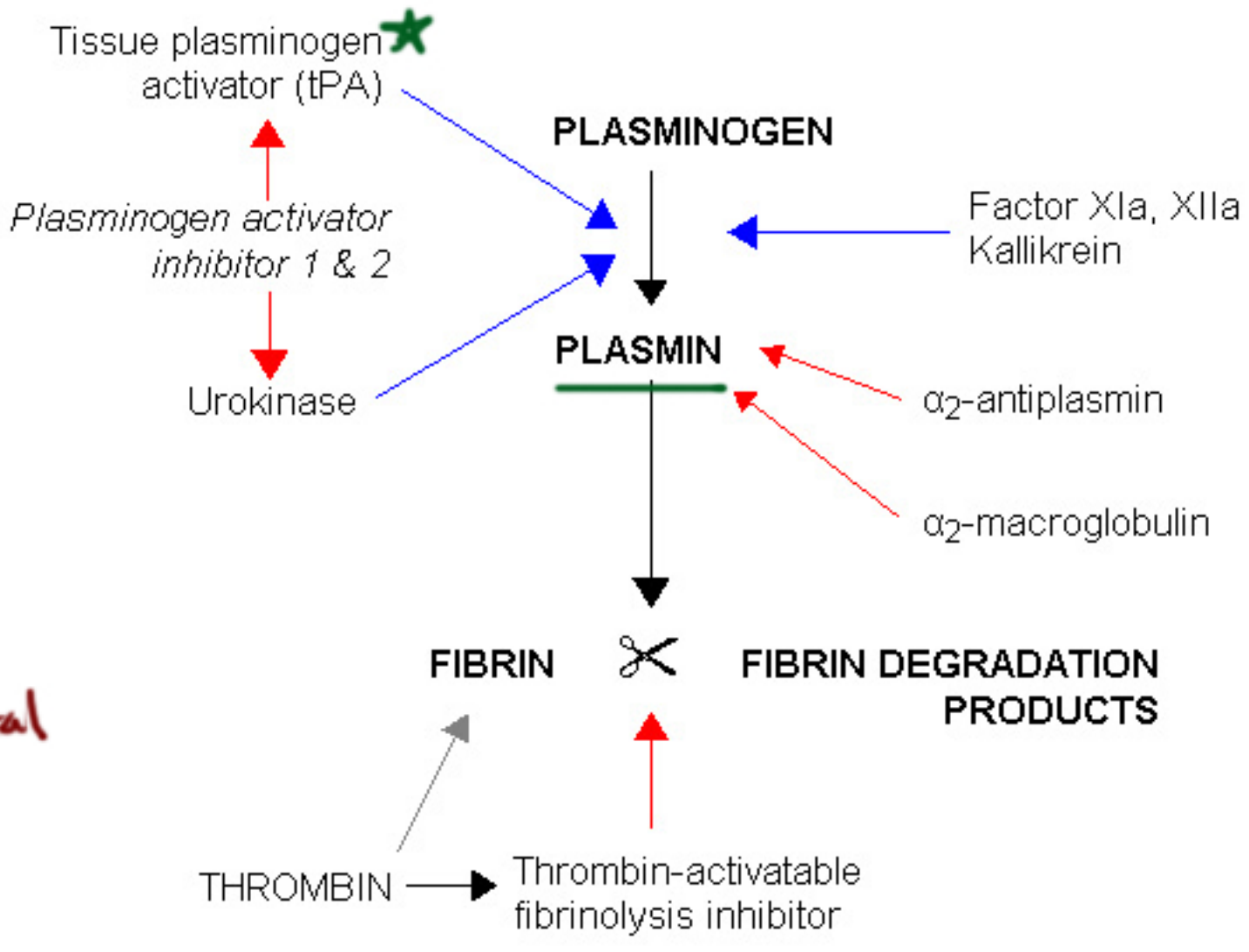
everything necessary is already in the blood

requires tissue factor

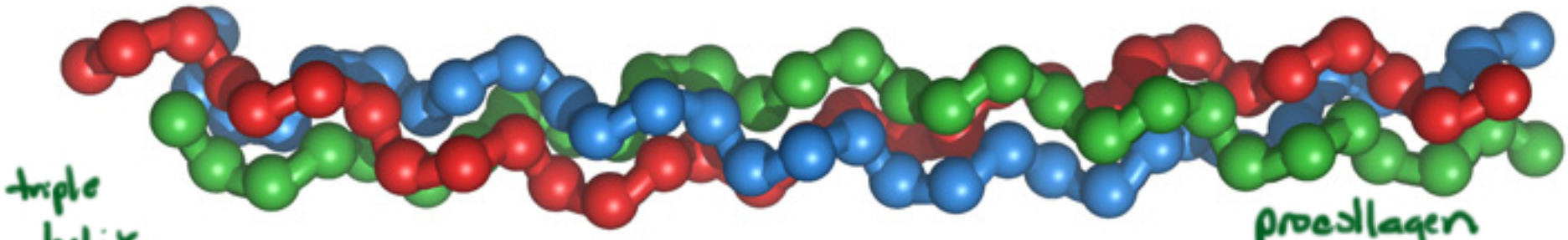


Don't worry about nitty gritty details


prepro-protein
activation
peptide
aromatic
1
32
43
88
97
132
136
176
200
212
450
461
N-
-C
signal
gla
EGF-1
EGF-2
serine protease
thrombin cleavage site
mature heterodimer
disulfide bond
43
88
97
132
136
176
197
212
450
461
N-
-C
gla
EGF-1
EGF-2
serine protease
Light chain
Heavy chain

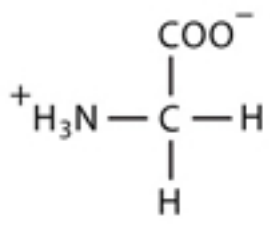


Supplemental



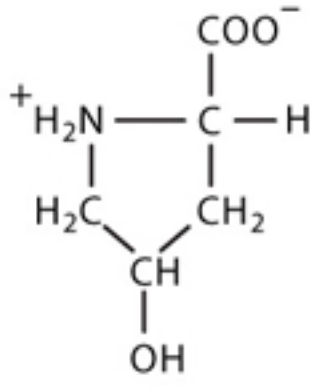
triple helix

procollagen

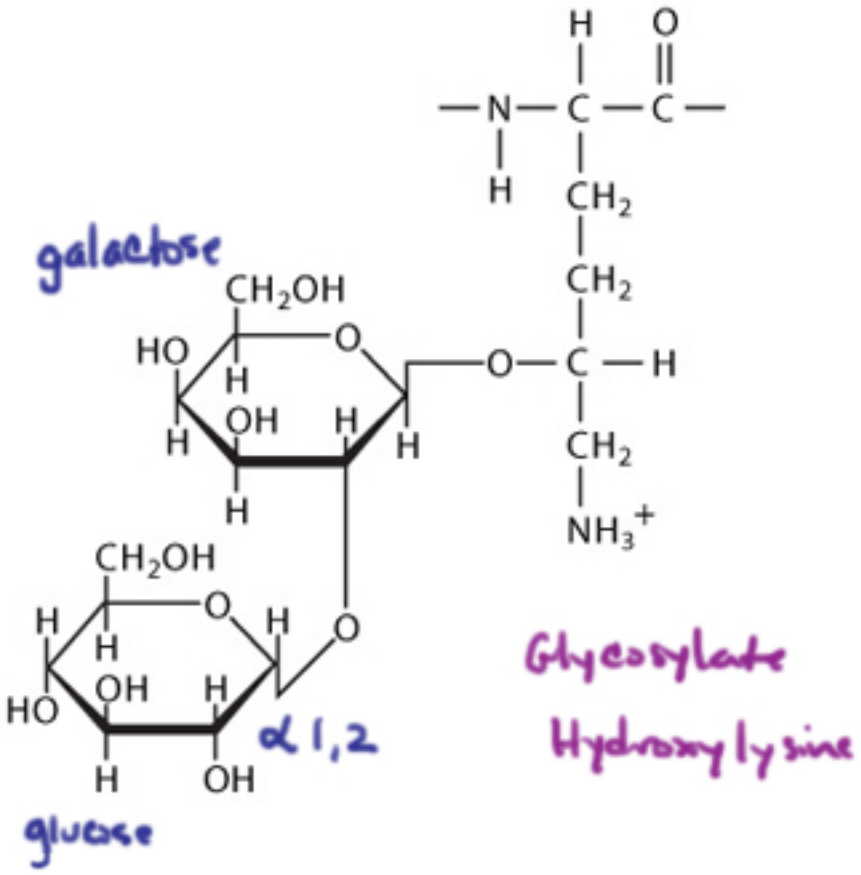


30% glycine

- interior of triple glycine

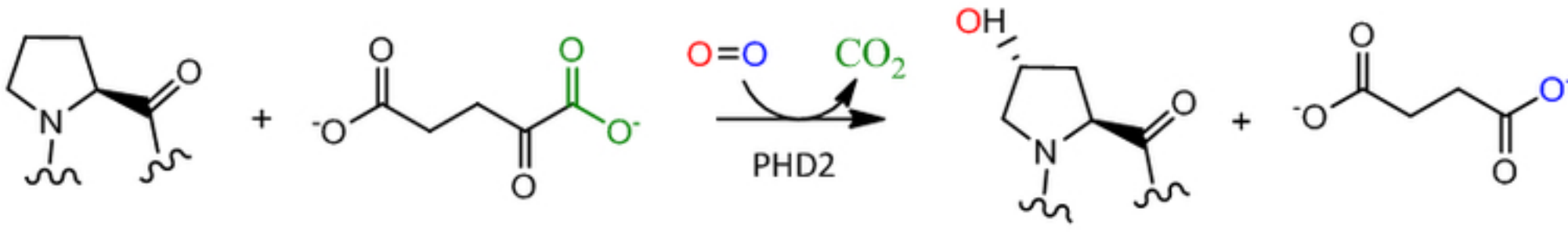


Hydroxy proline



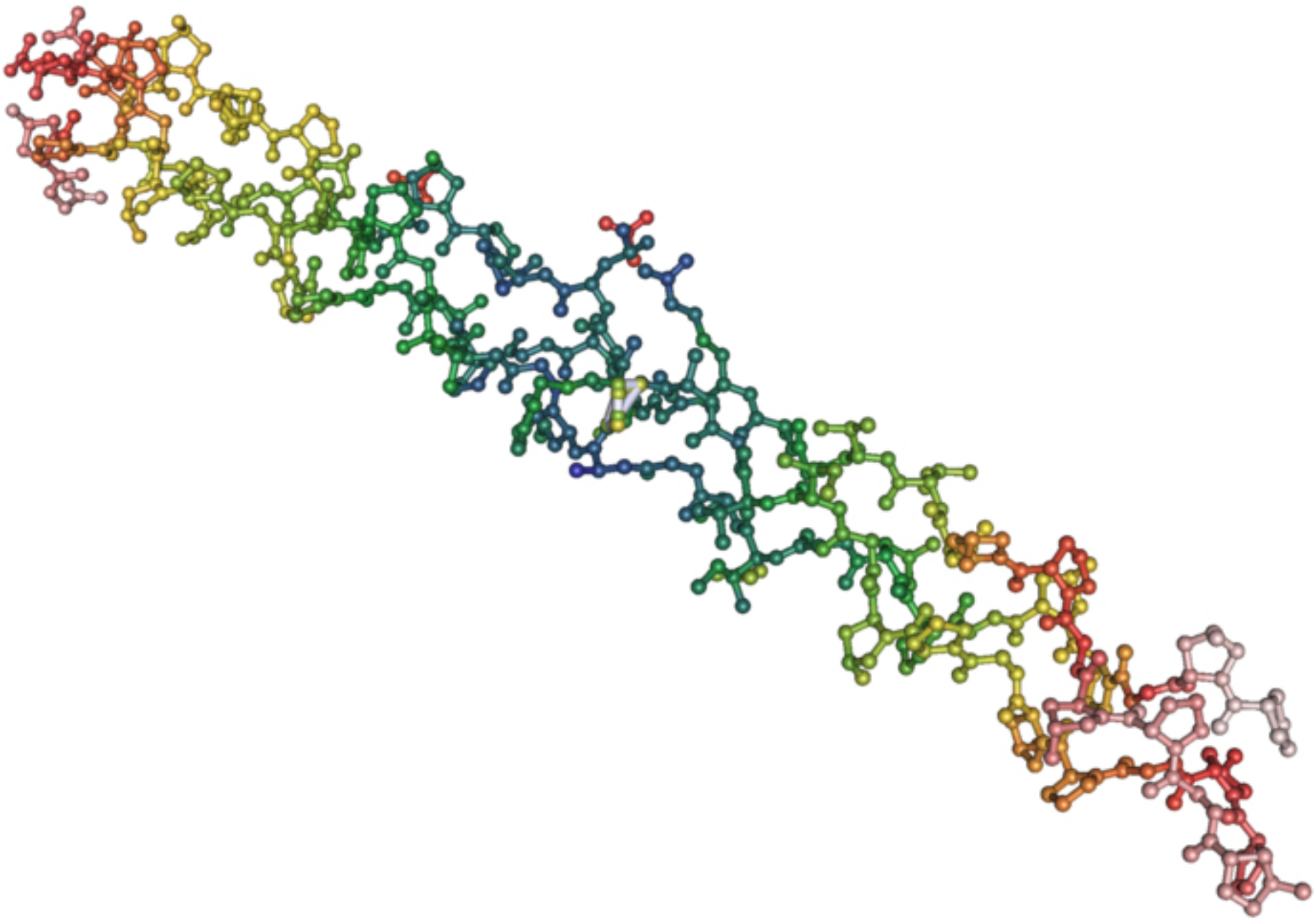
Connective tissue proteins

Synthesis of Hydroxyproline and Hydroxylysine



proline + 2-oxoglutarate → 4-hydroxyproline + succinate

- requires ascorbate (vitamin C)
- returns ferric ⟶ ferrous



procollagen ⟶ tropocollagen
(procollagen peptidase)

c

1. Alpha chain

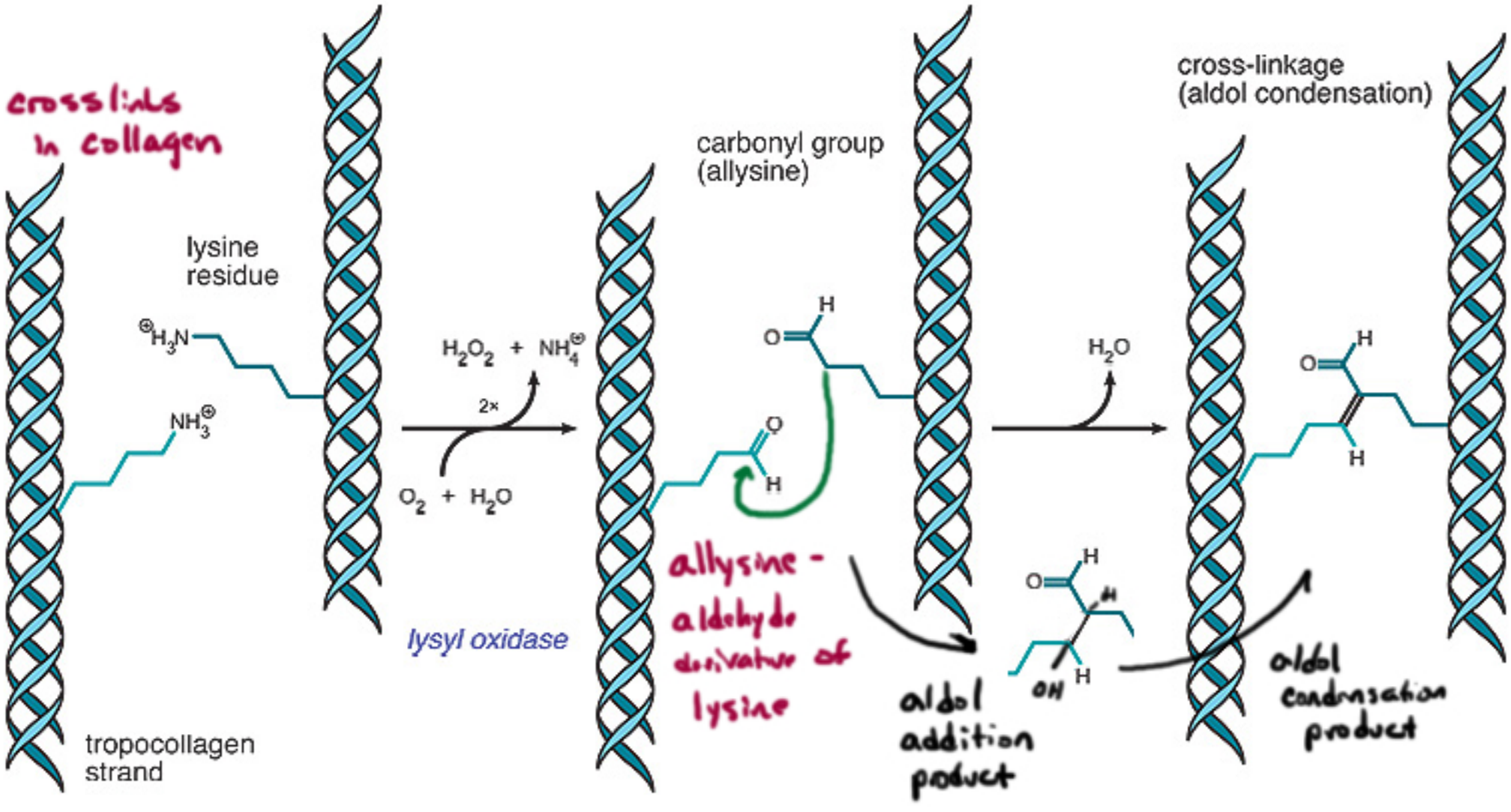
2. Procollagen

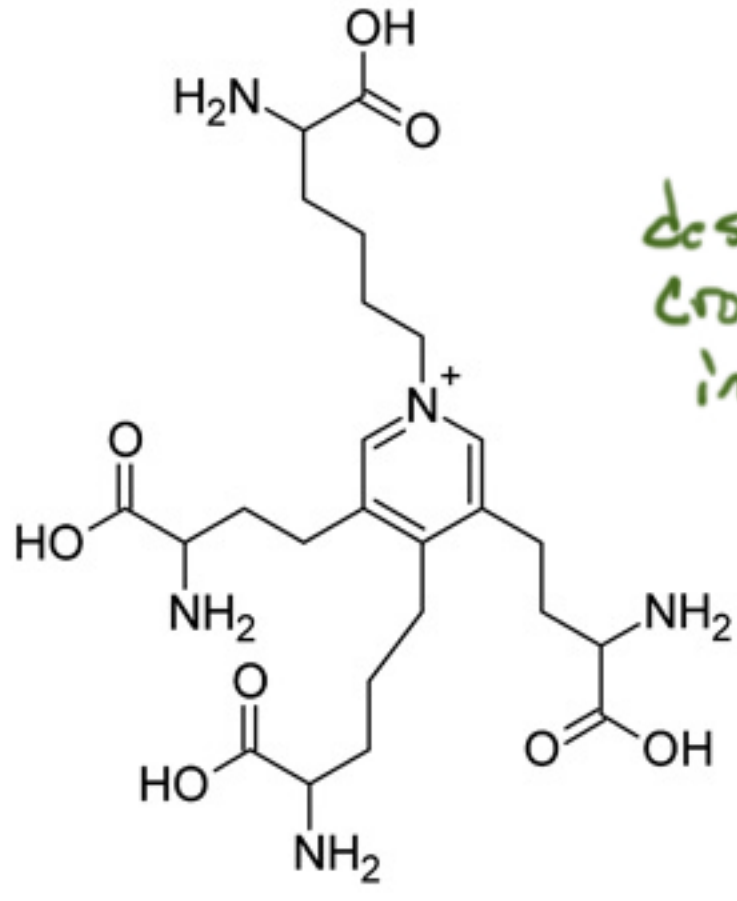
3. Tropocollagen

4. Packing of Tropocollagen molecules into FIBRILS

in bone deposition of hydroxyapatite here

5. Fiber


crosslinks in collagen
lysine residue
tropocollagen strand
lysyl oxidase
2×
carbonyl group (allysine)
allysine - aldehyde derivative of lysine
aldol addition product
cross-linkage (aldol condensation)
aldol condensation product

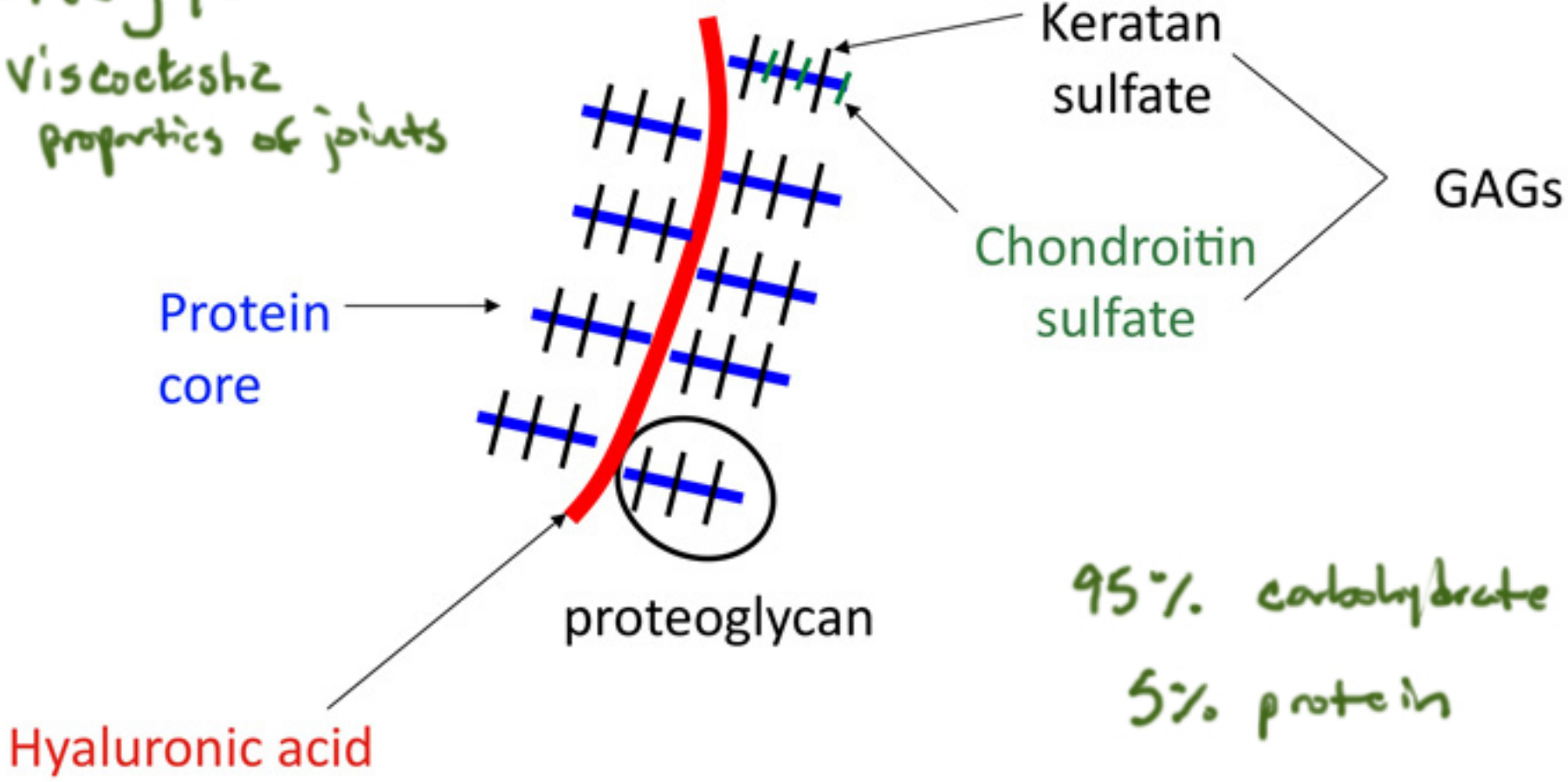


desmosine crosslink in elastin

3 allysines + lysine

Proteoglycan

- viscoelastic properties of joints



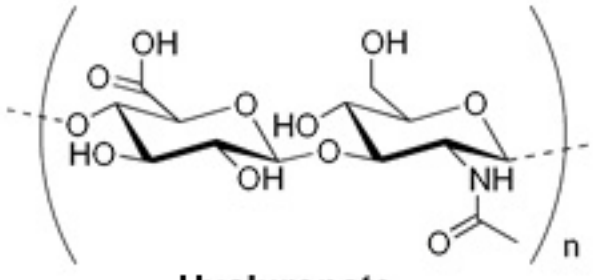
95% carbohydrate

5% protein

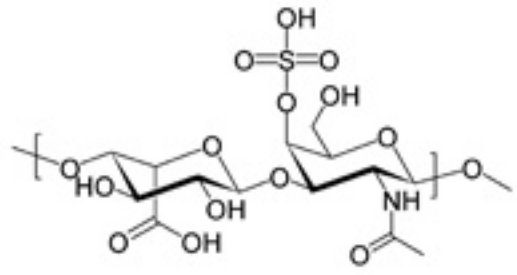
sugar monomers are N-acetyl acidic derivatives of glucosamine

↑ carboxyl and/or sulfates

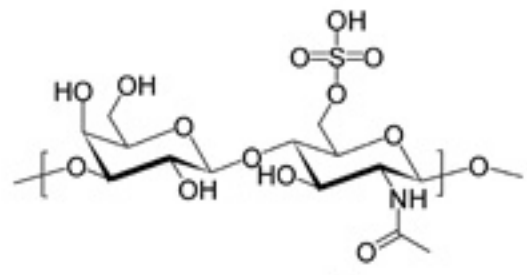
- lots of ⊖ charge
  - very hydrophilic
  - very slippery (repulsion)



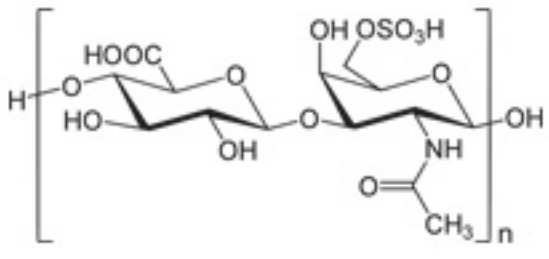
Hyaluronate



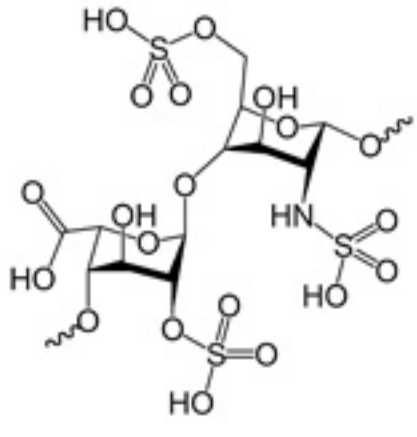
Dermatan sulfate



Keratan sulfate



Chondroitin 6-sulfate



Heparin

Sugar monomers in proteoglycan