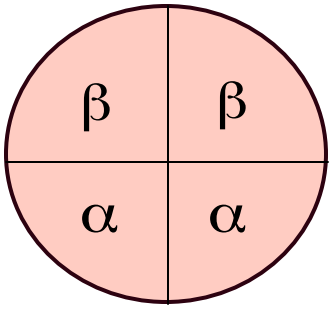
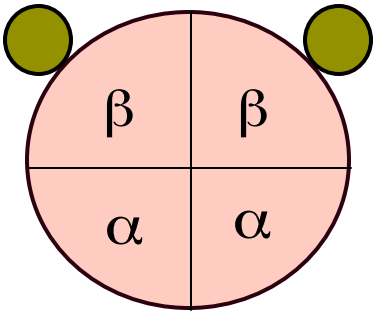
Sickle Cell Mutation

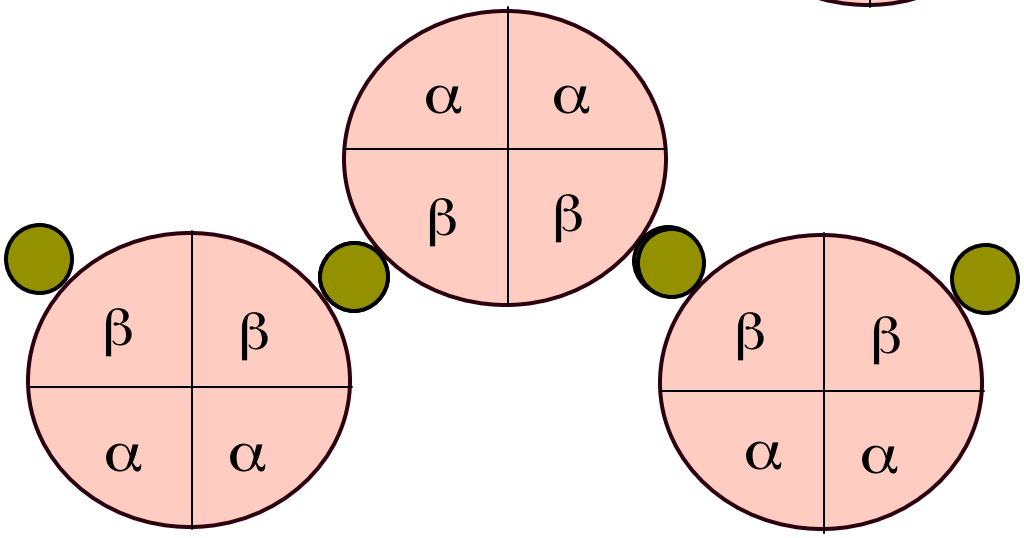
Hemoglobin is usually soluble in red blood cell



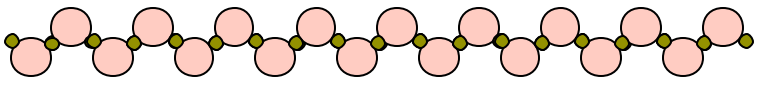
Sickle Cell Anemia

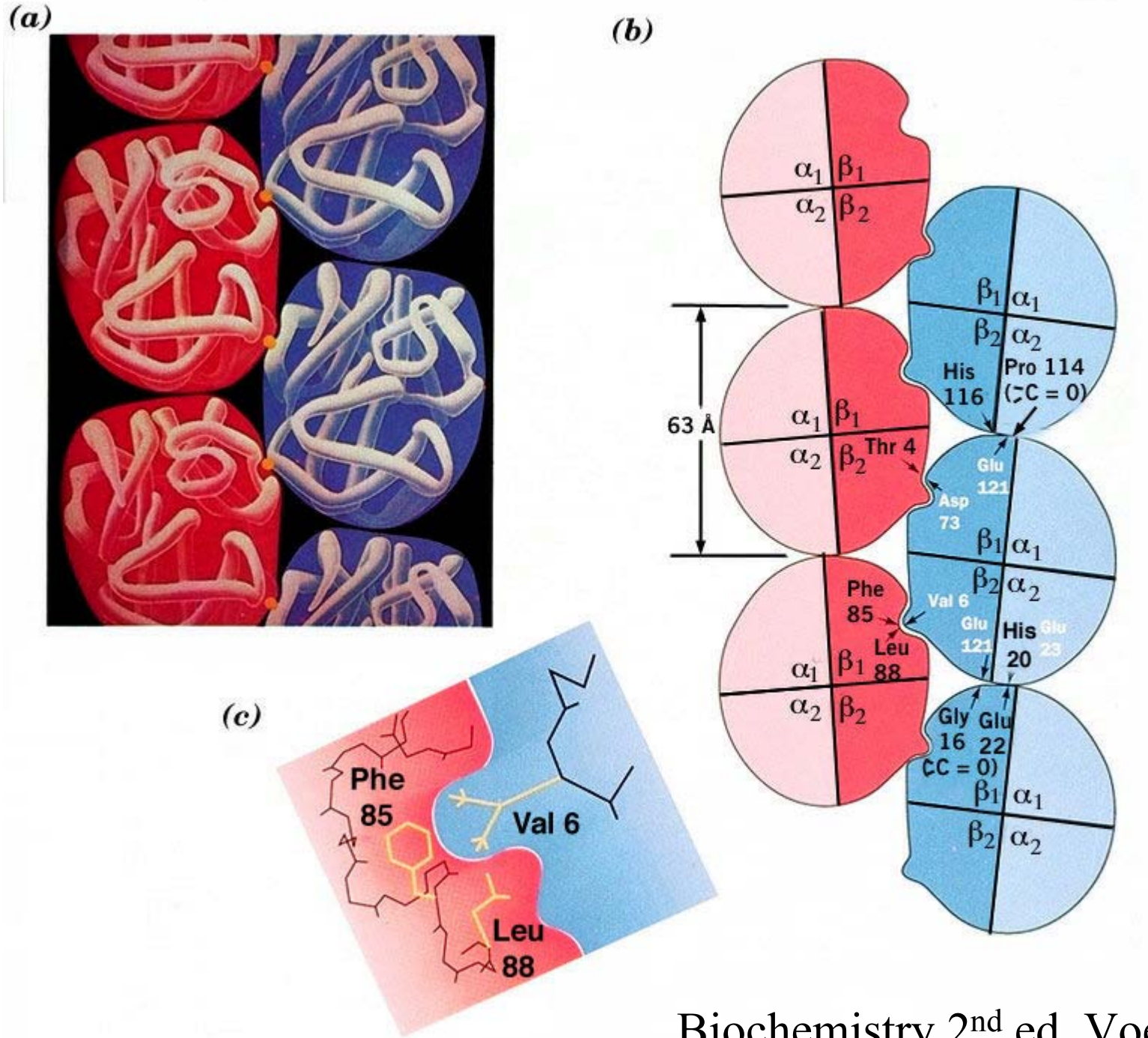
A single amino acid change
- **glu to val on β subunits**
- **change causes non-polar patch**
- **adheres to other hemoglobin**





insoluble fibers of hemoglobin





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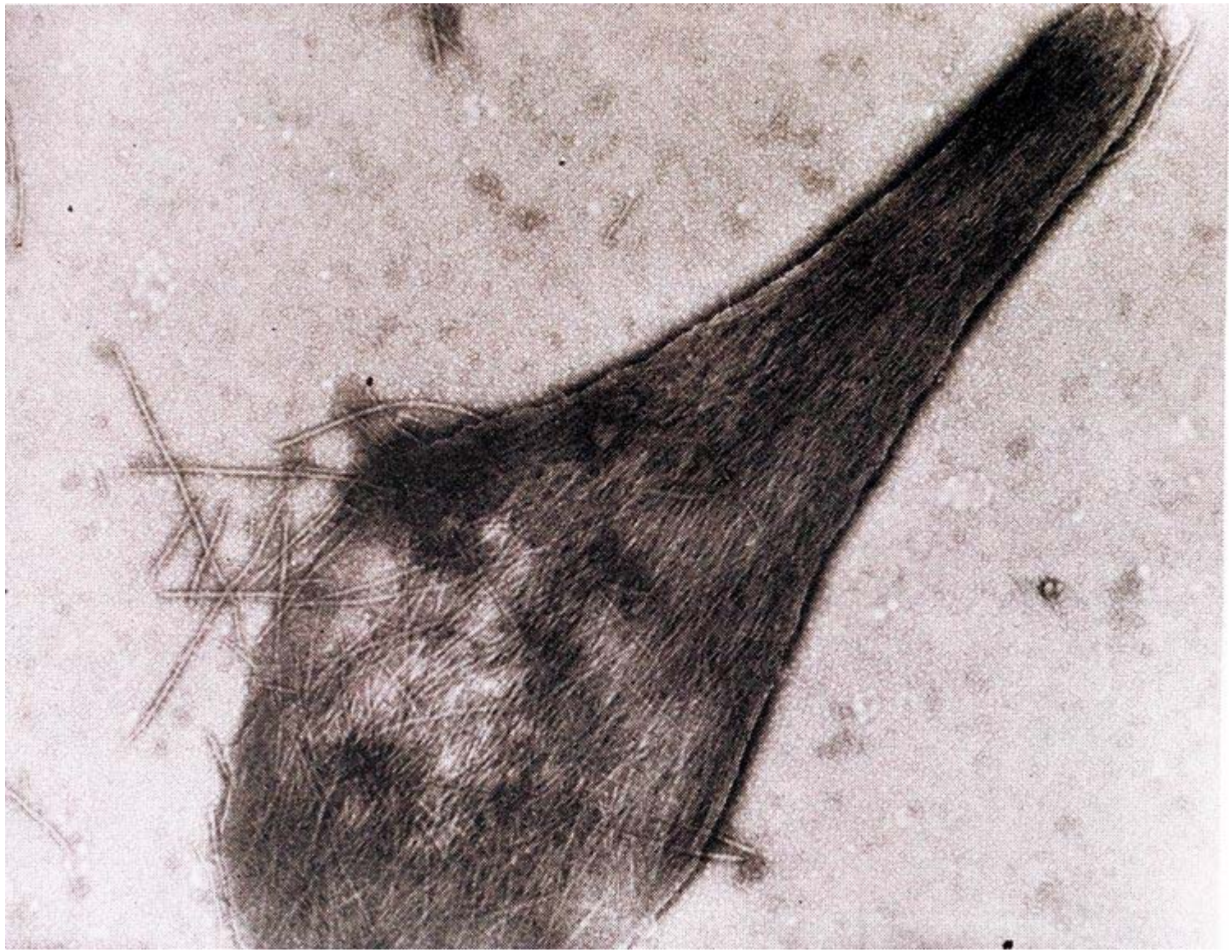

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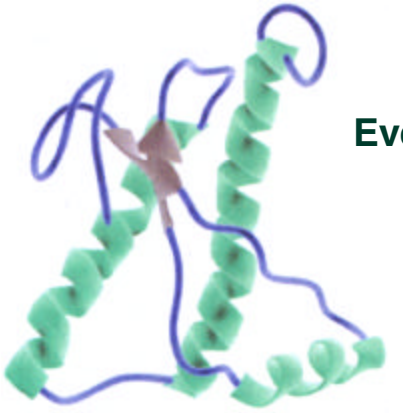
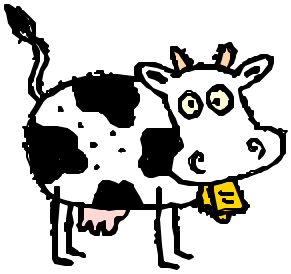
Prions

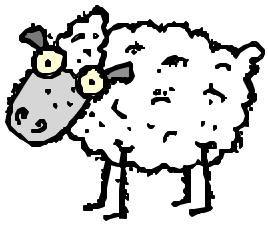
Infectious proteins
- no DNA or RNA present
- causes Creutzfeldt-Jakob Disease
  - loss of memory
  - loss of motor skills
  - dementia
    - scraping and biting off of skin
  - invariably fatal



Everyone has normal protein in brain
- Prp
- mostly α-helical, soluble

In patients with disease
- have Prpsc
  - -same protein, different conformation
  - -mostly β-sheet, insoluble
  - altered protein converts the normal protein to the altered conformation

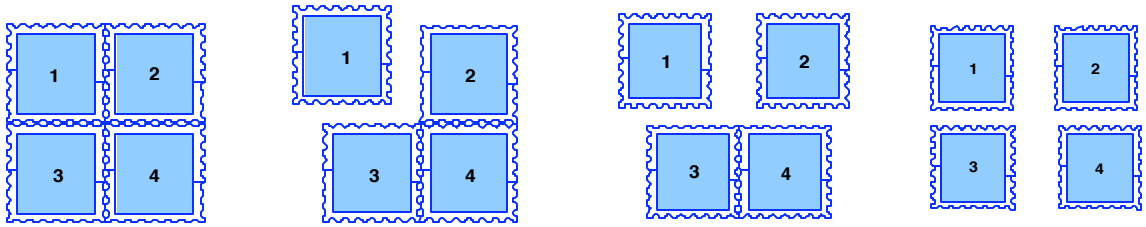


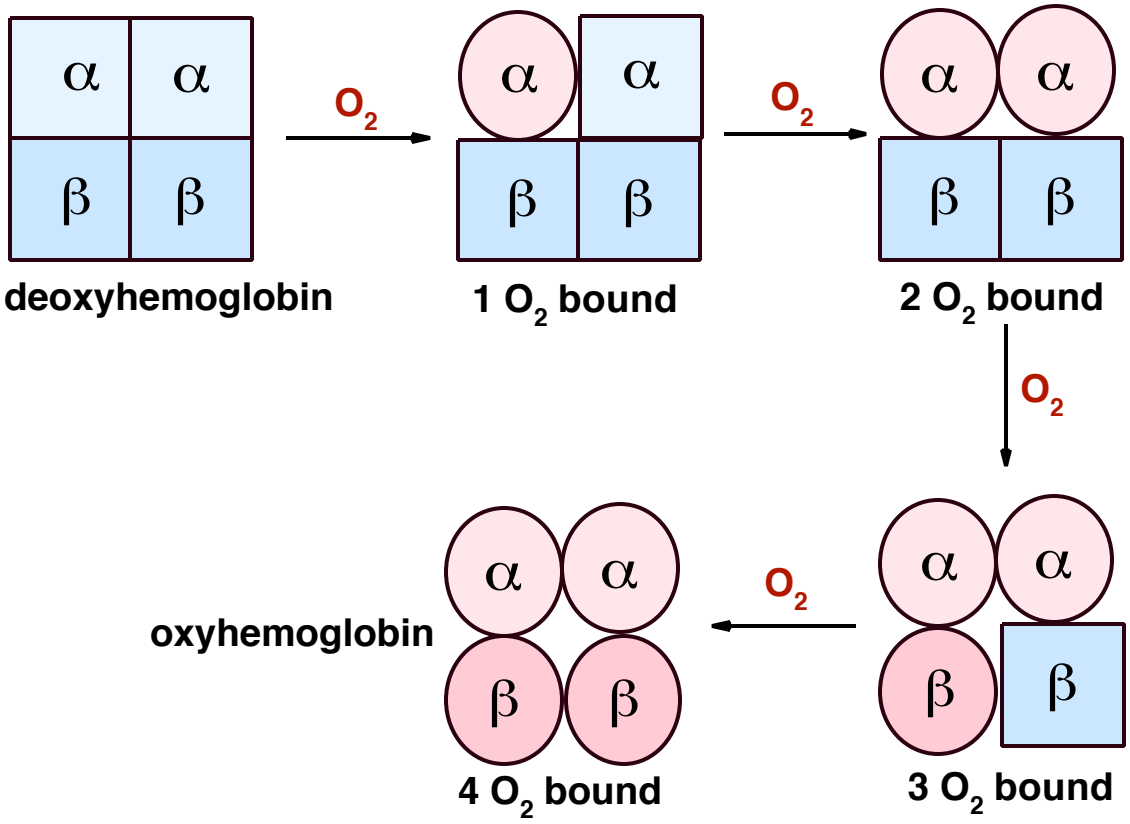


Catch this disease....
- hereditary
- sporatic
- eating infected meat (human or cow)

Hemoglobin (cooperativity)

Each hemoglobin has 4 subunits, 2 α and 2 β
Each hemoglobin can bind 4 molecules of O_2
Binding of each O_2 makes binding the rest easier
Called Cooperativity

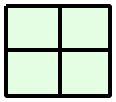




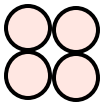
Hemoglobin Conformational Change

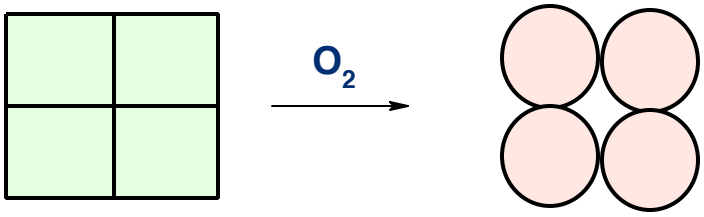
Change in 3° and 4° structure upon O_2 binding.

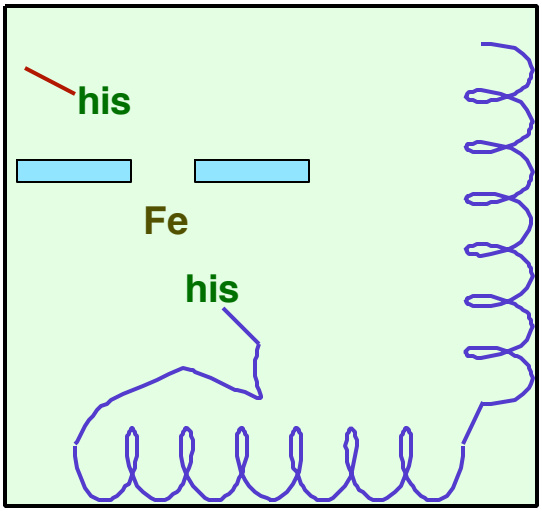
deoxyhemoglobin → T form (tense)



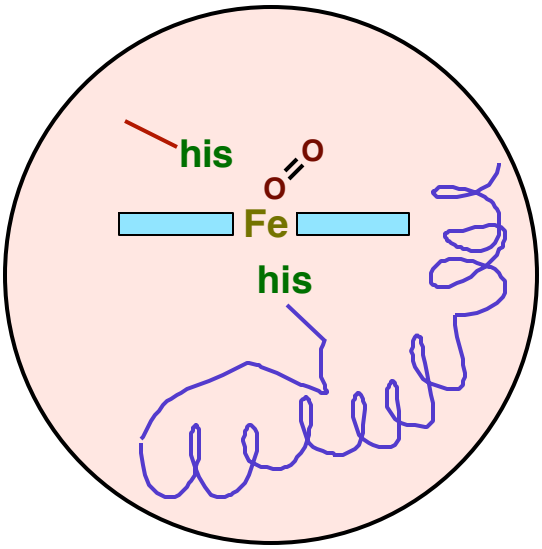
oxyhemoglobin → R form (relaxed)



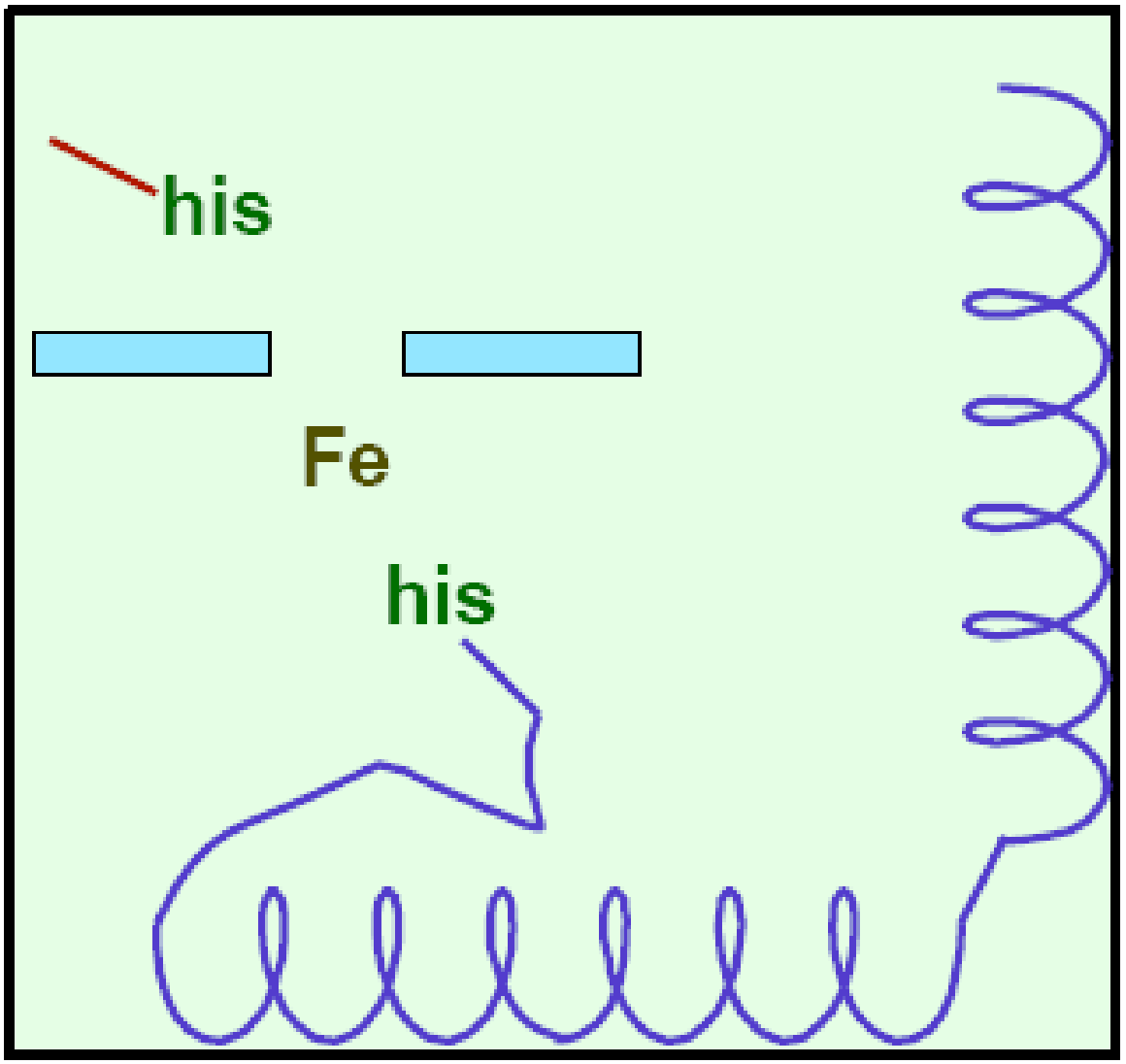




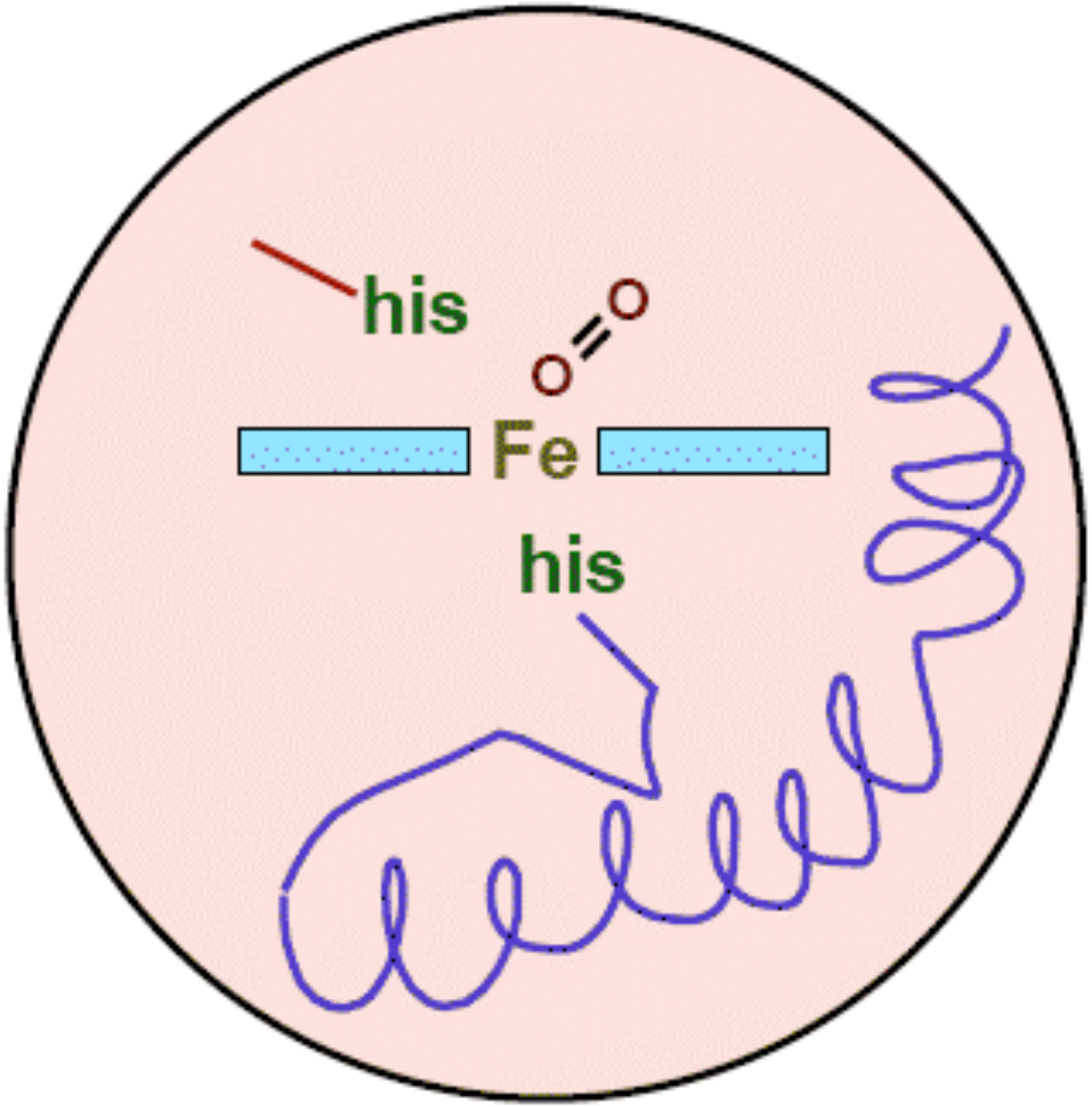
deoxyhemoglobin



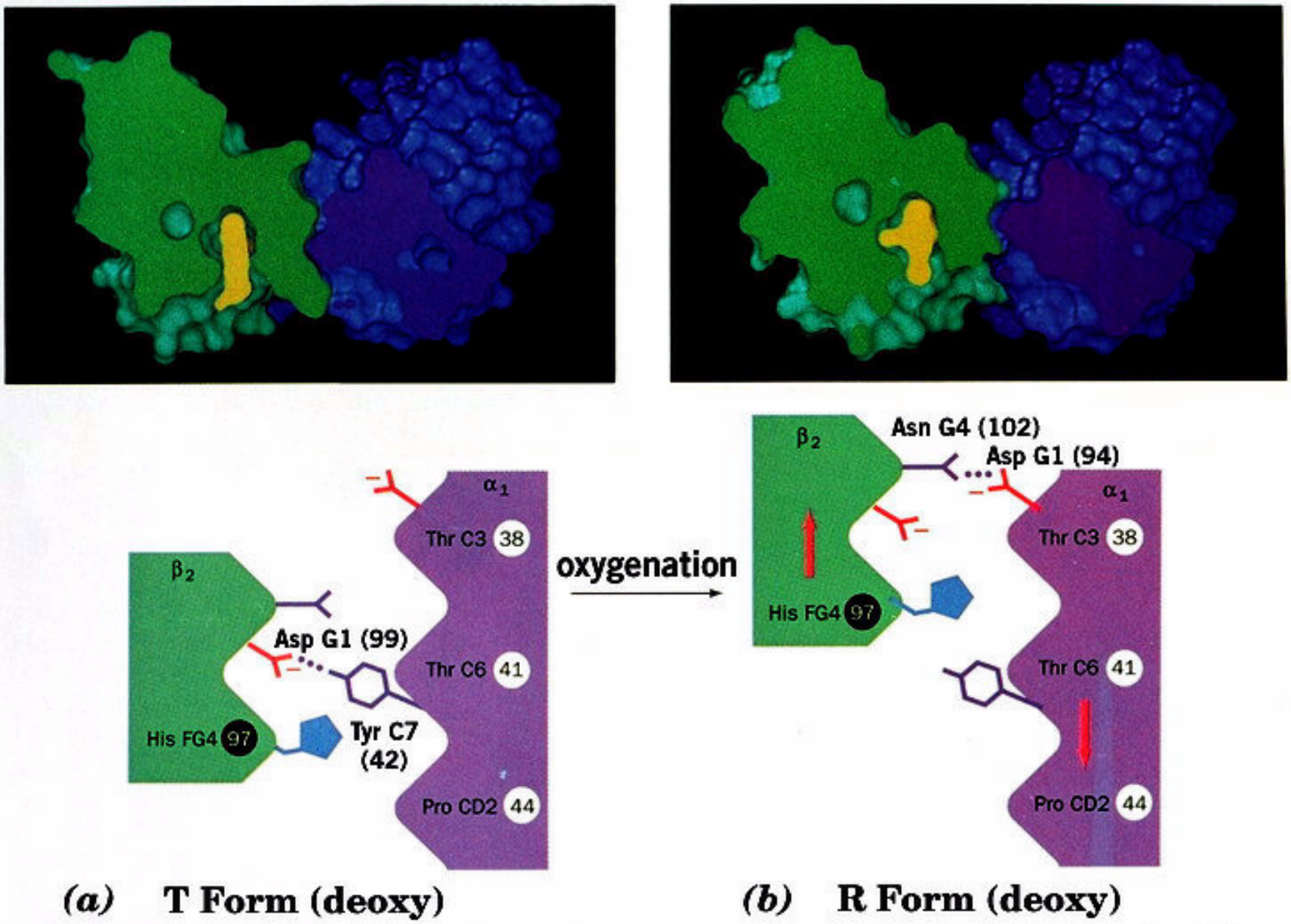
oxyhemoglobin



deoxyhemoglobin



oxyhemoglobin



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Mechanism of Phosphoglycerate Mutase

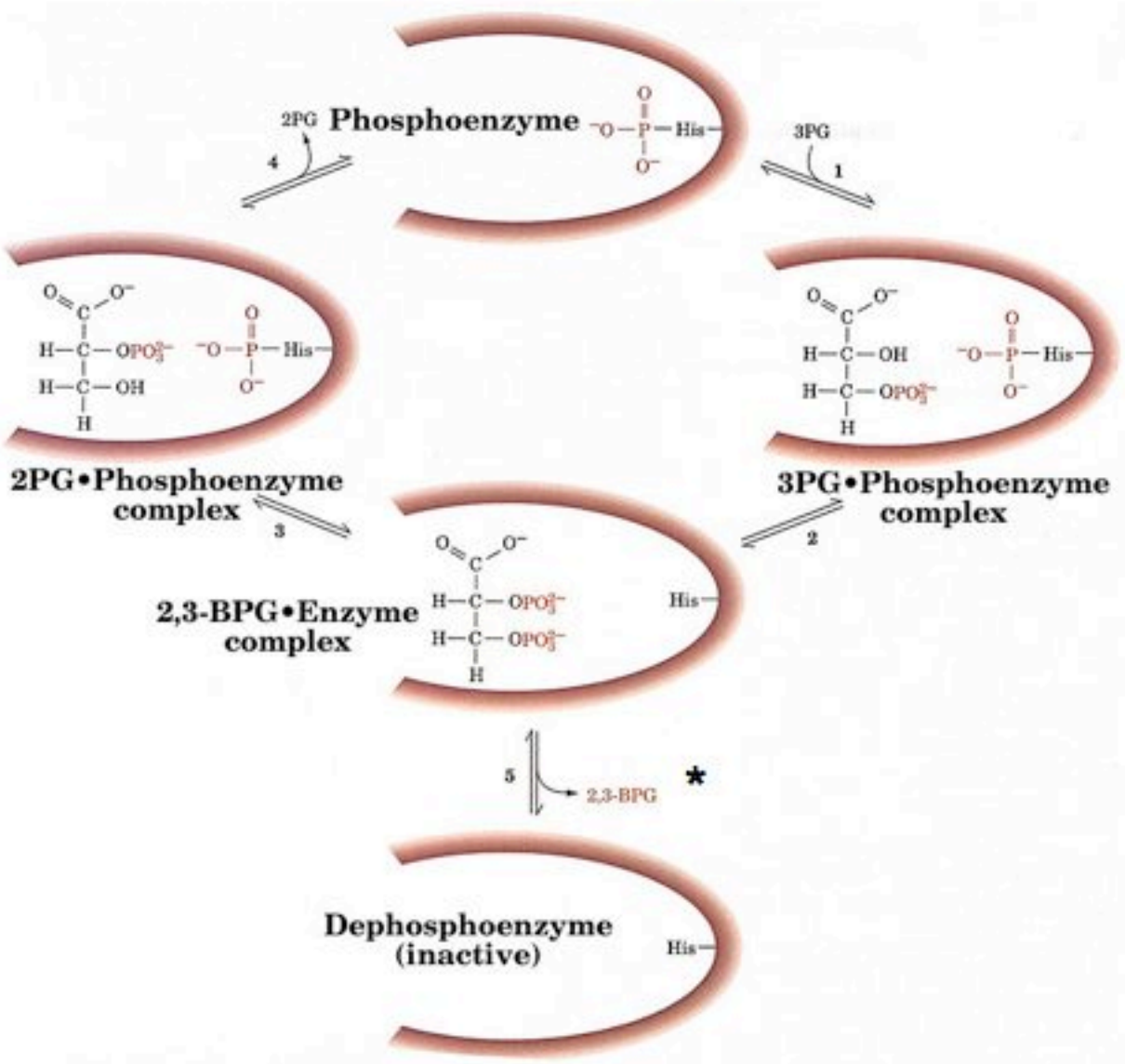

Fig 16.8

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BPG Modulates O_2 Binding to Hb

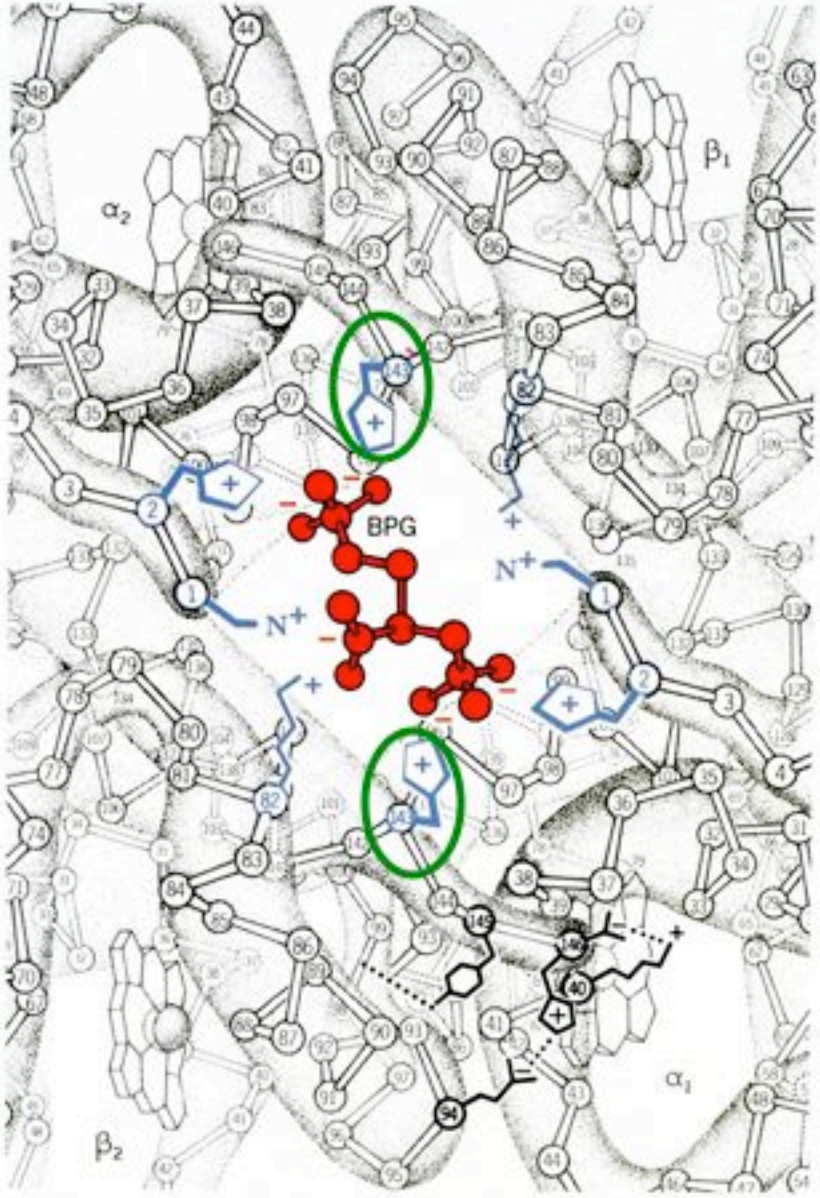

Fig 9.22

BPG decreases Hb affinity for O_2

BPG bound in T form (stabilizes)

BPG released in T to R conversion

Without BPG, O_2 not released

*BPG increases in altitude adaptation

*Fetal Hb has reduced affinity for BPG

His changed to Ser

Higher affinity for O_2

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