

Chem 452 - Lecture 3

Hemoglobin & Myoglobin

Part 2

Question of the Day: How is hemoglobin, after delivering its cargo, able to return not empty.

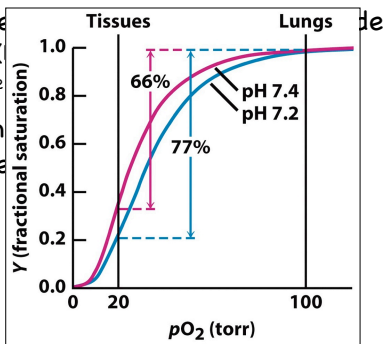
Allosteric Regulation

- Other allosteric regulators include
 - H⁺ (lower pH) - The Bohr Effect
 - CO₂
- Both of these metabolites signal increased metabolic activity

Chem 452, Lecture 3 - Hb and Mb 2

Allosteric Regulation

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Chem 452, Lecture 3 - Hb and Mb 2

Allosteric Regulation

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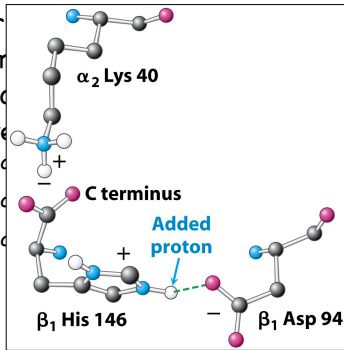
Allosteric Regulation

- Lower pH leads to the formation of salt-bridges (charge/charge interactions), that stabilize the T-state.
- α -chain α -amino group
- β -chain H146
- α -chain H122

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Allosteric Regulation

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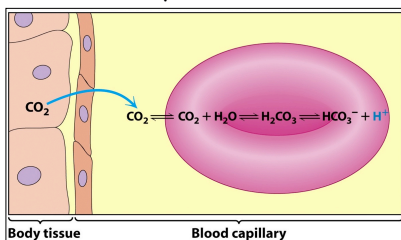
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Allosteric Regulation

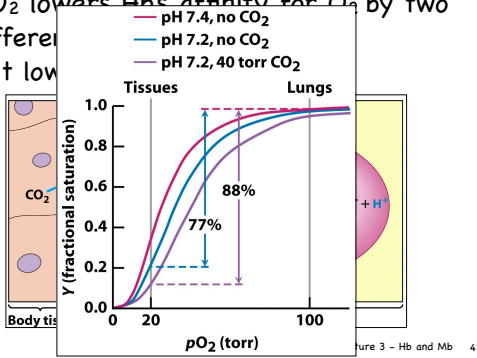
- CO₂ lowers Hb's affinity for O₂ by two different mechanisms.
- It lowers the pH



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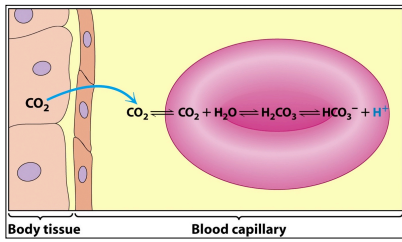
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Allosteric Regulation

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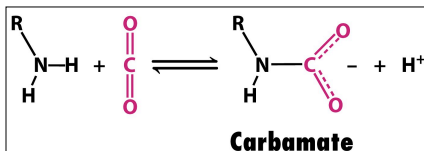
Allosteric Regulation

- CO₂ lowers Hb's affinity for O₂ by two mechanisms.
- It lowers the pH
- It reacts with terminal α-amino groups

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Allosteric Regulation

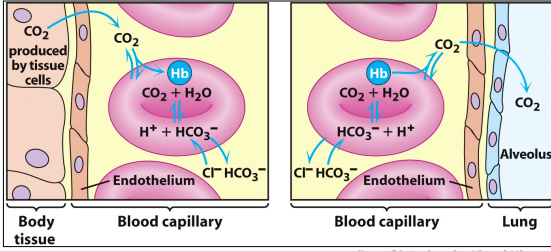
- CO₂ lowers Hb's affinity for O₂ by two mechanisms.
- It lowers the pH
- It reacts with terminal α-amino groups



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Allosteric Regulation

- CO_2 lowers Hb's affinity for O_2 by two mechanisms.
- It lowers the pH

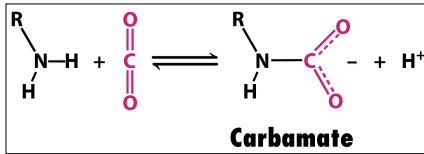


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Allosteric Regulation

- CO_2 lowers Hb's affinity for O_2 by two mechanisms.
- It lowers the pH
- It reacts with terminal α -amino groups

groups



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Genetic Diseases Involving Hb

- Concept of diseases caused by molecular defect was proposed in 1949 by Linus Pauling
- Sickle-cell Hb (Hb-S)



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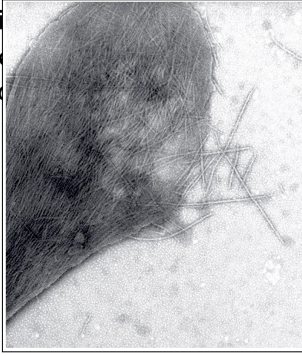
Genetic Diseases Involving Hb

- Sickling of RBC's is caused by the aggregation (polymerization) of Hb molecules.

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Genetic Diseases Involving Hb

- † Sickling of RBCs is caused by the aggregation (polymerization) of Hb molecules.



Chem 452, Lecture 3 - Hb and Mb 7

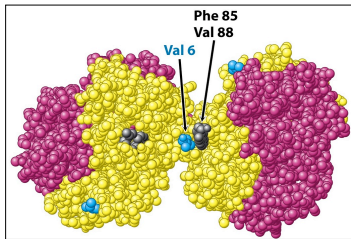
Genetic Diseases Involving Hb

- † Sickling of RBCs is caused by the aggregation (polymerization) of Hb molecules.

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Genetic Diseases Involving Hb

- † Disease is caused by a substitution of a Val for a Glu at position 6 in the β -chain (E6V)



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Genetic Diseases Involving Hb

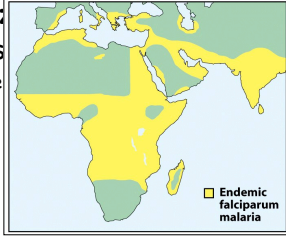
- † Sickle-cell disease is **homozygous recessive**.
- † **Heterozygous** individuals do not express the disease
 - † However, they are more resistant to the malaria parasite (*Plasmodium falciparum*)

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Genetic Diseases Involving Hb

+ Sickle-cell disease is **homozygous recessive**.

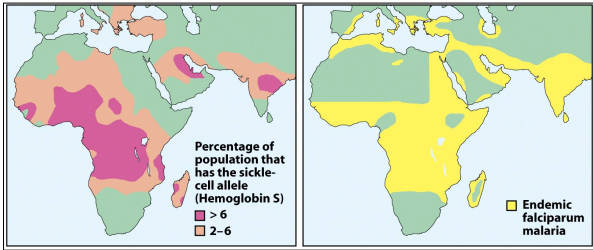
+ **Heterozygotes** do not express the disease (but are carriers).
+ However, malaria is endemic in the same regions.



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Genetic Diseases Involving Hb

+ Sickle-cell disease is **homozygous recessive**.



Chem 452, Lecture 3 - Hb and Mb 9

Next up

+ Enzymes (Chapter 8)

Chem 452, Lecture 3 - Hb and Mb 10