

# Transport Phenomena in Biomedical Engineering (196 C)

**DATES:** January 28 to May 20, 2008

**TIMES:** 6:00-8:45 PM

**ROOM:** 333

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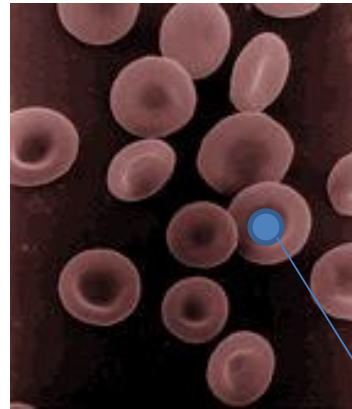
# OUTLINE

- Review of Oxygen Transport
- Review Assignment
- Pop Quiz
- Mini-Presentations
- Introduction to Pharmacokinetics

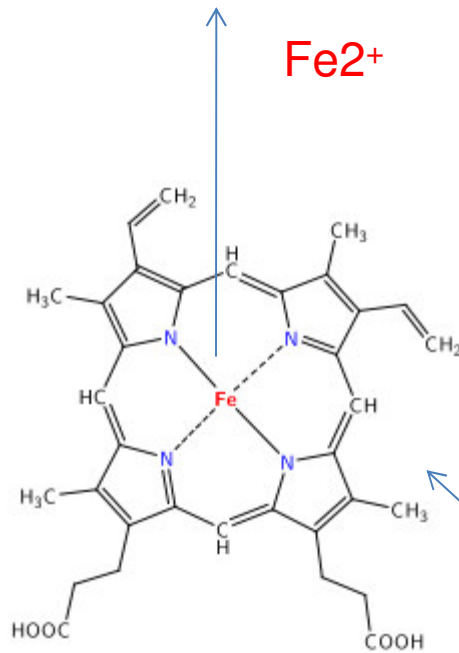
# USEFUL REFERENCES

- *Basic Transport Phenomena in Biomedical Engineering* by R.L. Fournier
- [\*Blood Substitutes Review\*](#) *for the Artificial Blood Section*
- *Elementary Differential Equations and Boundary Value Problems* by Boyce and DiPrima or any other Differential Equations Book.
- *Pharmacokinetic Analysis, a Practical Approach*, by I-Der Lee, Gordon L.

# RED BLOOD CELLS (REVIEW)

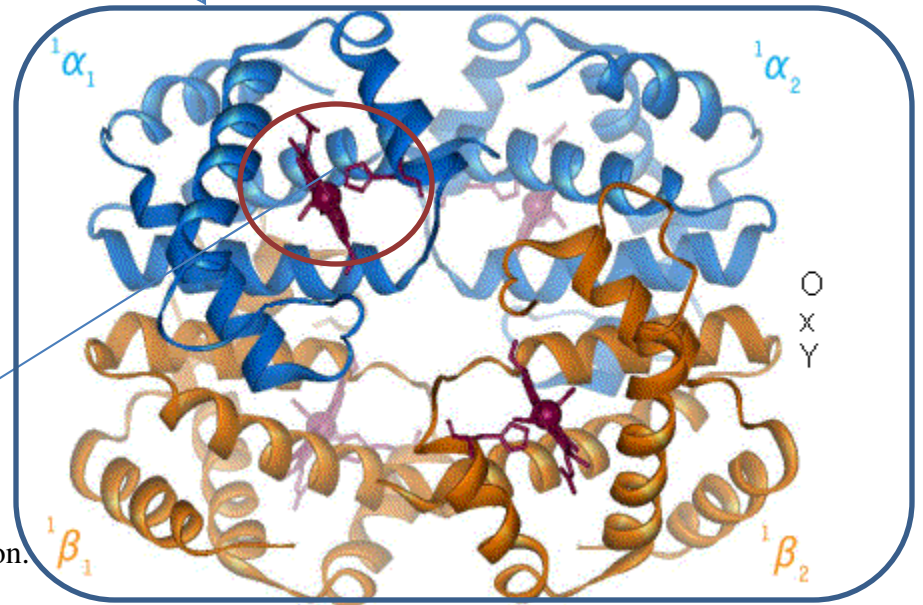


**Hemoglobin (68 K)** is the **allosteric** protein molecule in red blood cells that carries **oxygen** from the lungs to the body's tissues and returns carbon dioxide from the tissues to the lungs. The iron contained in hemoglobin is responsible for the red color of blood.



Fe<sup>2+</sup>

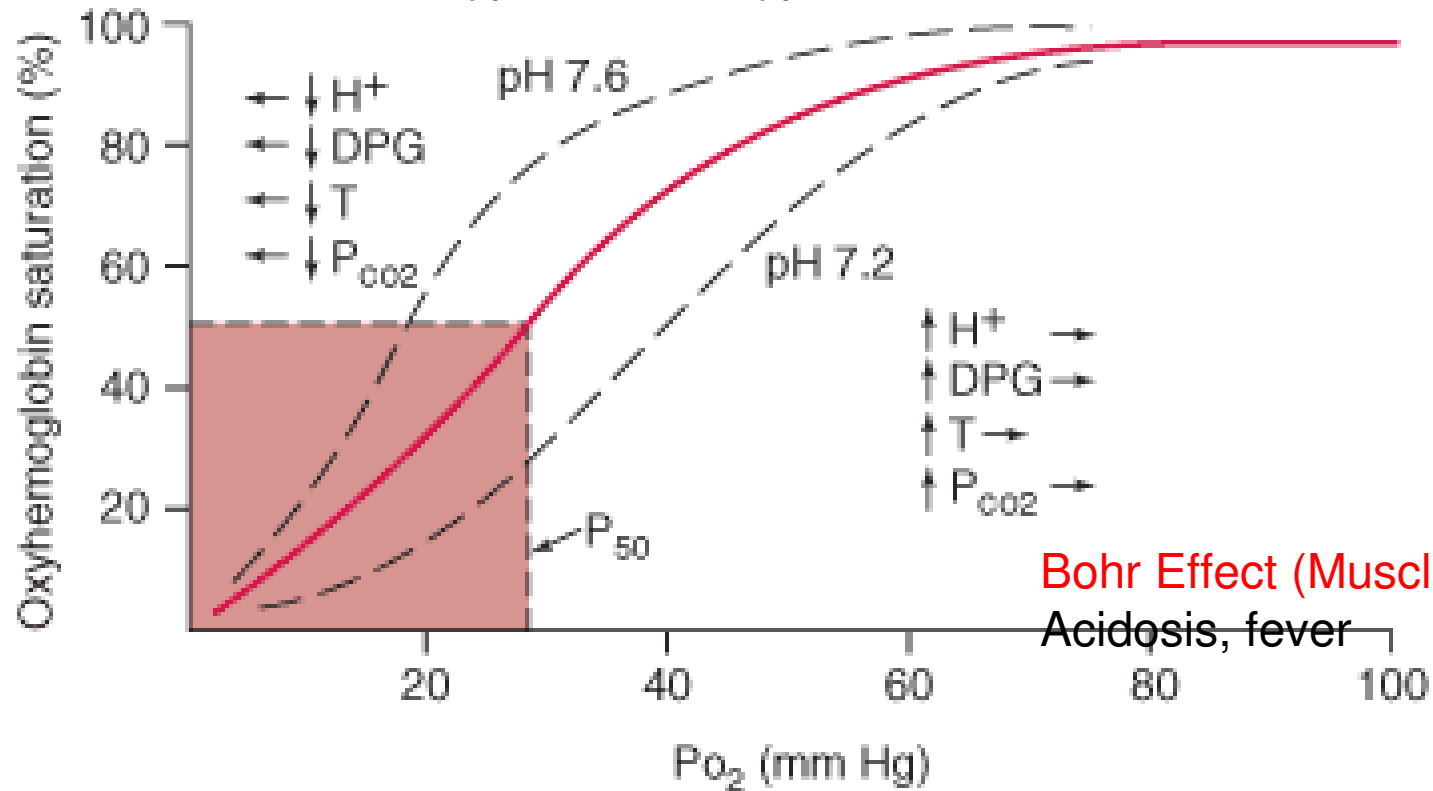
The blood Gases bind to the **Heme** Molecule in a **cooperative** fashion.



# FACTORS AFFECTING THE OXYGENATION CURVE (REVIEW)

## Haldane Effect (Lungs)

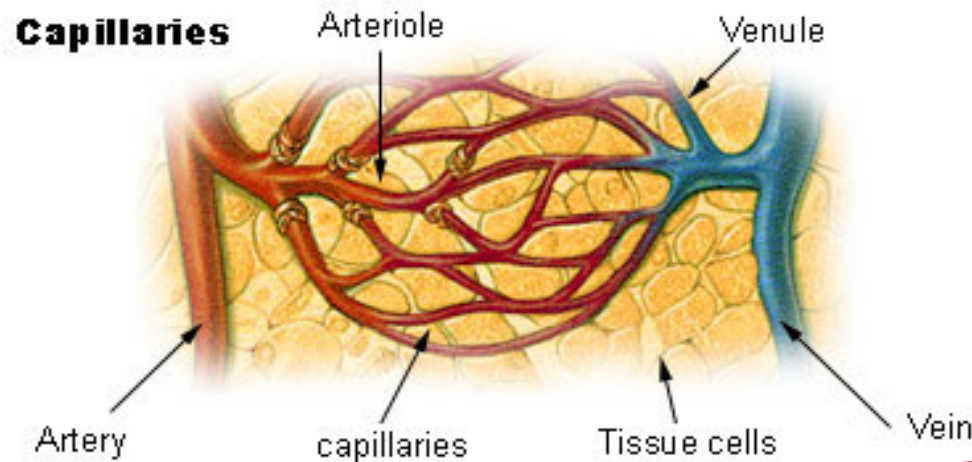
Alkalosis, hypothermia, hypoxia



## Bohr Effect (Muscles)

Acidosis, fever

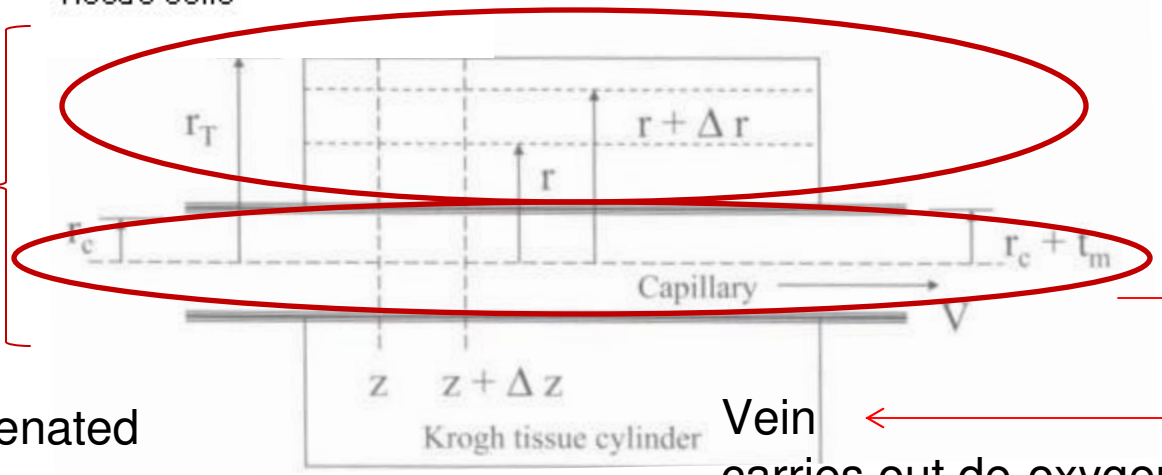
# TISSUE OXYGENATION SIMPLIFIED (REVIEW)



Separate Well-Mixed Regions

Artery brings in oxygenated blood

Vein carries out de-oxygenate blood



# MASS BALANCE EQUATIONS FOR OXYGEN TRANSPORT IN VASCULAR BEDS (REVIEW)

*Assume zero accumulation under metabolic Steady State conditions :*

$$qV_T(C + C')_A - qV_T(C + C')_V - P_c S_c (C_v - C_T) = 0 \quad \text{Blood} \quad (6)$$

$$P_c S_c (C_v - C_T) - V_T \Gamma_{\text{metabolic}} = 0 \quad \text{Tissue} \quad (7)$$

$q$  *tissue perfusion rate ( ml of blood / cm<sup>3</sup> tissue / min)*

$V_T$  *volume of tissue space ( including capillaries ) in cm<sup>3</sup>*

$C$  *Dissolved oxygen concentration (  $\mu\text{M}$  )*

$C'$  *Bound oxygen concentration (  $\mu\text{M}$  )*

$C_T$  *Concentration of oxygen dissolved within the interstitial tissue space (  $\mu\text{M}$  )*

$C_v$  *Concentration of oxygen dissolved in the capillary (  $\mu\text{M}$  )*

$P_c$  *Oxygen permeability through capillary wall ( cm / s )*

$S_c$  *Capillary Surface area ( cm<sup>2</sup> )*

$\Gamma_{\text{metabolic}}$  *The tissue metabolic volumetric tissue consumption (  $\mu\text{M} / \text{s}$  )*

$$(6) + (7) \Leftrightarrow \Gamma_{\text{metabolic}} = q[(C + C')_A - (C + C')_V] \quad (8)$$

## Example 6.2

# KINETICS OF OXYGEN VOLUMETRIC METABOLIC CONSUMPTION RATE

(Review)  $\Gamma_{metabolic} = \frac{V_{max} pO_2}{K_m + pO_2} \quad (9)$

*In most cases  $K_m \ll 0$  (zero order reaction)*

$$\Gamma_{metabolic} = V_{max} \quad (10)$$

*Eq (10) invalid at very low  $pO_2$*

$$Y \equiv \frac{(pO_2)^n}{P_{50}^n + (pO_2)^n} \quad (4)$$

$$C' = \frac{C'_{sat} (HC)^n}{P_{50}^n + (HC)^n} \quad (11)$$

*Substitute in equation (8)*

$$\left[ C + \frac{C'_{sat} (HC)^n}{P_{50}^n + (HC)^n} \right] = (C + C')_A - \frac{\Gamma_{metabolic}}{q} = (C + C')_V \quad (12)$$

## EXAMPLE 6.3

# OXYGEN TRANSPORT IN BIOARTIFICIAL ORGANS (Artificial Pancreas)

Steady State Shell Balance over a thickness  $\Delta x$  of the cell layer

$$-AD_e \left. \frac{dC}{dx} \right|_x + AD_e \left. \frac{dC}{dx} \right|_{x+\Delta x} - \Gamma_{\text{metabolic}} A \Delta x (1 - \varepsilon) = 0 \quad (13)$$

Divide by  $\Delta x$  and taking the limit as  $\Delta x \rightarrow 0$  and applying Henry's Law:

$$D_e \frac{d^2 pO_2}{dx^2} = \Gamma_{\text{metabolic}} H (1 - \varepsilon) \quad (14)$$

$$BC1: \quad x=0, pO_2 = pO_2^{x=0}$$

$$BC2: \quad x=\delta, \frac{d pO_2}{dx} = 0$$

$$pO_2(x) = pO_2^{x=0} + \left[ \frac{\Gamma_{\text{metabolic}} (1 - \varepsilon) \delta^2}{2D_e} \right] \left[ \left( \frac{x^2}{\delta} \right) - 2 \left( \frac{x}{\delta} \right) \right] \quad (15)$$

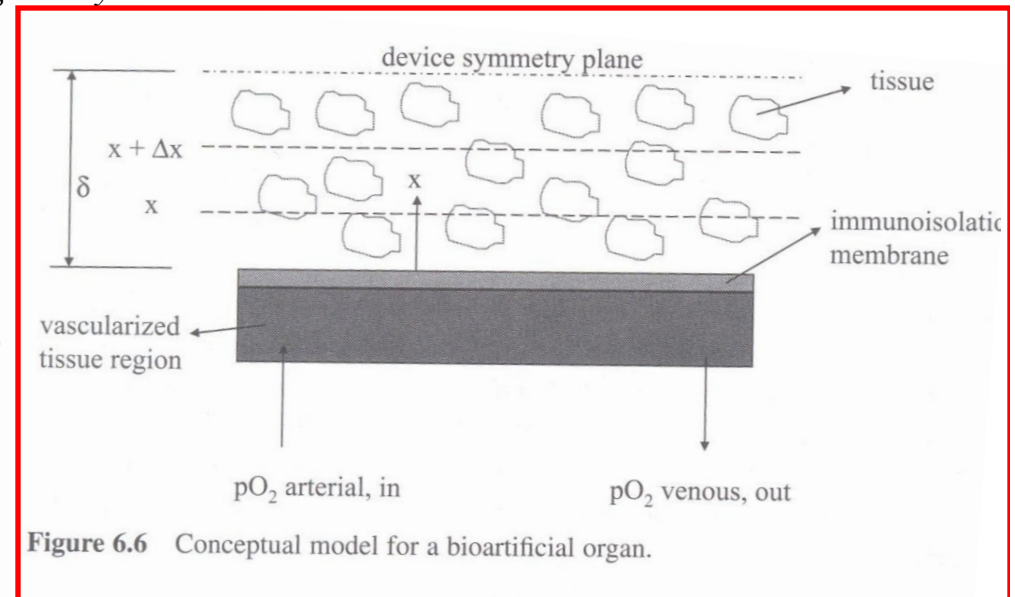
Need to solve for  $pO_2^{x=0}$

$$\frac{AP_m}{H} (pO_2^B - pO_2^{x=0}) = A \delta \Gamma_{\text{metabolic}} (1 - \varepsilon) \quad (16)$$

$P_m$  Permeability of the immuno-isolation membrane

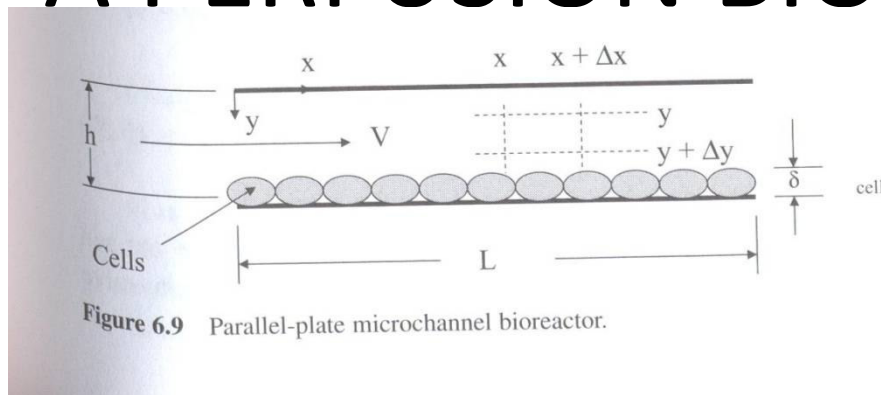
$pO_2^B$  Average partial pressure of oxygen in the vascular bed

$$pO_2^{x=0} = pO_2^B - \left[ \frac{\delta \Gamma_{\text{metabolic}} (1 - \varepsilon) H}{P_m} \right] \quad (17)$$



EXAMPLES 6.4 and 6.5

# STEADY STATE OXYGEN TRANSPORT IN A PERFUSION BIOREACTOR (REVIEW)



Tilles et al (2001);  
Allen and Bhatia (2003)

EXAMPLES 6.4 and 6.5

The oxygen concentration can be controlled within the bioreactor by adjusting the flowrate of media through the device. ([Artificial Liver](#)).

*At Steady State*

$$V \frac{\partial C}{\partial x} = D \frac{\partial^2 C}{\partial y^2} \quad (18)$$

$$BC1: \quad x=0, \quad C(0, y) = C_{in}$$

$$BC2: \quad y=h, \quad D \frac{\partial C}{\partial y} \Big|_{y=0} = \Gamma_{metabolic} \delta_{cell} (1 - \epsilon)$$

$$BC3: \quad y=0, \quad \frac{\partial C}{\partial y} \Big|_{y=h} = 0$$

Let  $\alpha = L/h$ ,  $\hat{x} = x/L$ ,  $\hat{y} = y/h$ ,  $\hat{C} = C/C_{in}$

$$V \frac{\partial \hat{C}}{\partial \hat{x}} = \frac{\alpha}{Pe} \frac{\partial^2 \hat{C}}{\partial \hat{y}^2} \quad (19)$$

$$BC1: \quad \hat{x} = 0, \quad \hat{C} = 1$$

$$BC2: \quad \hat{y} = 1, \quad \left. \frac{\partial \hat{C}}{\partial \hat{y}} \right|_{\hat{y}=0} = Da = \frac{\Gamma_{metabolic} (1 - \varepsilon) h \delta_{cell}}{DC_{in}}$$

$$BC3: \quad \hat{y} = 0, \quad \left. \frac{\partial \hat{C}}{\partial \hat{y}} \right|_{\hat{y}=h} = 0$$

$Pe$  Peclet number (convection/diffusion)

$Da$  Damkohler number (dimensionless oxygen flux)

The dimensionless oxygen profile in the bioreactor is given by :

$$\hat{C}(\hat{x}, \hat{y}) = 1 + Da \left[ \frac{1 - 3\hat{y}^2}{6} - \frac{\alpha}{Pe} \hat{x} + \frac{2}{\pi^2} \sum_{n=1}^{\infty} \frac{(-1)^n}{n^2} \exp\left(-\frac{\alpha n^2 \pi^2 \hat{x}}{Pe}\right) \cos(n\pi \hat{y}) \right] \quad (20)$$

Integration of eq.( 20 ) from  $\hat{y} = 0$  to  $\hat{y} = 1$  yields to the oxygen concentration at any  $\hat{x}$ .

For large  $Pe$  numbers ( at the entrance )

$$\hat{C}(\hat{x}, \hat{y}) = 1 + Da \left( \frac{1 - 3\hat{y}^2}{6} - \frac{\alpha}{Pe} \hat{x} \right) \quad (21); \quad \text{At the surface } \hat{y} = 1, \hat{x}_{critical} = \left( \frac{\alpha}{Pe} \right)^{-1} \left( \frac{1}{Da} - \frac{1}{3} \right) \quad (22)$$

# OXYGEN TRANSPORT IN KROGH'S TISSUE CYLINDER (REVIEW)

- In reality Tissue and Blood are not well-mixed regions.
- KROGH'S approach takes into account the oxygen diffusion and consumption WITHIN the tissue space.
- Sections 6.10 and 6.11 of the textbook.
- Example 6.8

# ARTIFICIAL BLOOD (REVIEW)

*Pioneered by TMS CHANG at McGill University*

## FUNCTION

- Transport and release of oxygen under normal physiological conditions.
- Avoid blood-type cross-matching.
- Disease-free either through sterilization methods or through animal-free production methods such as recombinant protein production in E. coli or yeast.
- Storage at RT.

## TYPES

- Modified Hb (cross-linked, micro-encapsulated)
- Synthetic Hemes
- Perfluorocarbons
- Transgenic hemoglobin

# INTRODUCTION TO PHARMACOKINETICS

*[Premier Pharmacokinetics Software from SummitPK.com](http://SummitPK.com)*

# ASSIGNMENT

- Presentations on 5/5/08.