# BME 5742 Bio-Systems Modeling and Control

## Lecture 40
## Heart & Blood Circulation
## Auto-Regulation of the Systemic Flow Resistance

# Auto-Regulation Phenomena

- Measured pressure-flow relationships in tissues often exhibit that there is a range of pressures for which the flow is relatively insensitive to the pressure difference.
- At a constant pressure difference, the flow through many tissues depends on the rate of $O_2$ consumption of the tissue.
- A mathematical model, attributed to Huntsman, Attinger and Noordergraaf accounts for both phenomena through a single mechanism.

# Key Hypothesis regarding the Regulation of a Tissue Resistance

- The resistance of a tissue is regulated by the venous $O_2$ concentration at the tissue.
- Now we know that the concentration of $O_2$ in systemic arterial blood is around 1/5 (which coincidentally is the same concentration of $O_2$ in the atmosphere).
- $[O_2]_a$=1/5. Arterial blood $O_2$ concentration is constant for all of the tissues.

# Cases when $[O_2]_a$ is reduced

- High altitude conditions: Hb may fail to be saturated in the lungs.
- Anemia: Concentration of Hb in the blood is lower than normal.
- The above reduced level of oxygen are felt equally by all the tissues of the body.

# Venous $O_2$ Concentration

$$Q[O_2]_a - Q[O_2]_v = M$$

- $[O_2]_v$ varies from tissue to tissue.
- Let M be the <u>metabolic rate</u>: the rate of $O_2$ consumption in a tissue in [liters/minute].
- Let Q be the blood flow to the tissue.

# Arterial and Venous $O_2$ tissue concentrations and their relation to tissue metabolic rate

$$Q[O_2]_a - Q[O_2]_v = M$$

- The rate at which $O_2$ is delivered to the tissue from arterial blood equals $Q[O_2]_a$.
- The rate at which $O_2$ leaves the tissue to the venous blood equals $Q[O_2]_v$.
- At steady-state M the metabolic rate of the tissue accounts for the difference between delivered and leaving $O_2$

# Venous $O_2$ concentration expression

$$[O_2]_v = [O_2]_a - \frac{M}{Q}$$

- $[O_2]_v$ can serve as an indicator to the adequacy of the blood supply, in relation to the metabolic rate of the tissues:
- $[O_2]_v=0$ if $Q=Q^*= M/[O_2]_a$ – here blood supply is barely sufficient to sustain the metabolism.
- As Q rises $[O_2]_v$ rises. For very large Q we have $[O_2]_v \rightarrow [O_2]_a$.

# Discussion of hypothesis regarding the Regulation of a Tissue Resistance

- The resistance of a tissue is regulated by the venous $O_2$ concentration at the tissue.
- Resistance is regulated on the arterial side of the tissue.
- Venous $O_2$ concentration is determined by the tissue $O_2$ concentration.
- The arterioles that run through the tissue may be influenced by the tissue $O_2$ concentration.

# Tissue Resistance Control Model

$$\boxed{R} = \frac{P}{Q} = \frac{P_{sa} - P_{sv}}{Q} = \boxed{R_0 [O_2]_v}$$

- P is the arteriovenous pressure difference in the tissue.
- $R_0$ is a control constant of proportionality.
- Hypothesis: Tissue resistance to flow is proportional to venous $O_2$ concentration.

# Regulated Pressure-Flow relation of a tissue

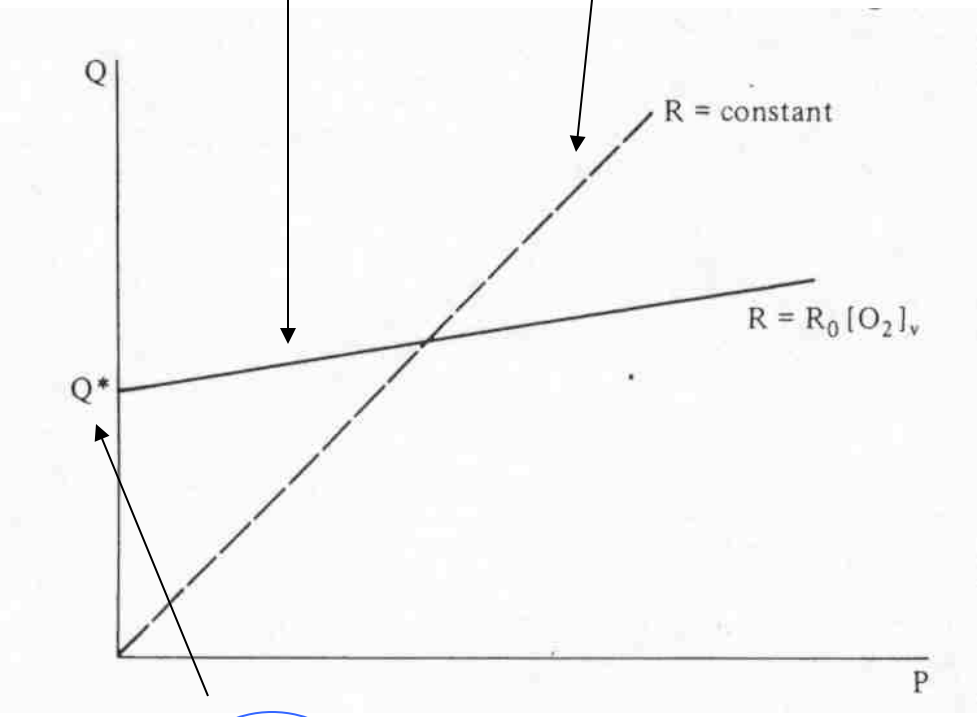
$$R = \frac{P}{Q} = \frac{P_{sa} - P_{sv}}{Q} = R_0[O_2]_v$$

$$Q[O_2]_a - Q[O_2]_v = M$$

$$\Rightarrow Q = \frac{M}{[O_2]_a - [O_2]_v} = \frac{M}{[O_2]_a - \frac{P}{R_0 Q}}$$

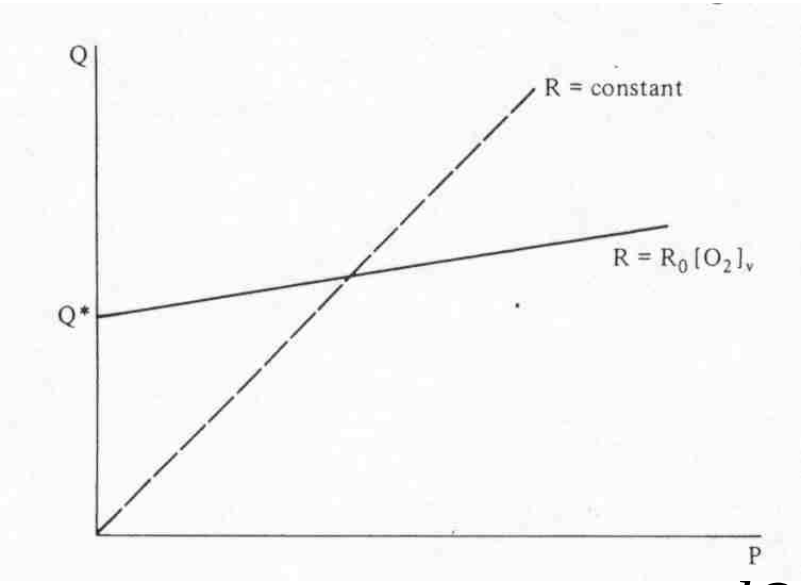
$$\Rightarrow \boxed{Q = \frac{M}{[O_2]_a} + \frac{P}{R_0[O_2]_a}}$$

# Regulated vs unregulated Pressure-Flow relation in a tissue




$$Q = \frac{M}{[O_2]_a} + \frac{P}{R_0[O_2]_a}$$

# Sensitivity of Flow to Pressure




Sensitivity of Q to P is reduced if R varies according to $[O_2]_v$, compared with R=constant

$$Q = \frac{M}{[O_2]_a} + \frac{P}{R_0[O_2]_a} \Rightarrow \sigma_{QP} \approx \frac{(\frac{dQ}{Q})}{(\frac{dP}{P})} = \frac{P}{R_0 M + P} < 1$$

$$Q = \frac{P}{R} \Rightarrow \sigma_{QP} = 1$$

If $R_0$ is large, sensitivity (for compensated case) can become very small

# With compensation, tissue always receives at least the minimum flow required to sustain its metabolic rate

$$Uncompensated: _P = QR \Leftrightarrow P = 0 \Rightarrow Q = 0 \Rightarrow M = 0$$

$$Compensated: _P = QR_0[O_2]_v \Leftrightarrow \{P = 0, M \neq 0\} \Rightarrow Q \neq 0 \Leftrightarrow$$

$$\Leftrightarrow R \to 0, [O_2]_v \to 0 \Rightarrow Q \to \frac{M}{[O_2]_a}$$

- For an uncompensated tissue, if for some reason P=0, flow stops, and so does the metabolism.
- A compensation allows flow to go on, at a minimum level, even if P=0 (zero pressure difference)

# If P=const, what happens if tissue metabolic rate M changes?

$$Uncompensated: _R = \frac{P}{Q} \Rightarrow \{P = const, R = const\} \leftrightarrow Q = const$$

$$Q[O_2]_a - Q[O_2]_v = M, [O_2]_a = const, M \rightarrow M + \Delta M \Rightarrow$$

$$\Rightarrow [O_2]_v \rightarrow [O_2]_v - \Delta[O_2]_v$$

ΔM must not be too large!

---

$$Compensated: _Q = \frac{M}{[O_2]_a} + \frac{P}{R_0[O_2]_a} \Rightarrow$$

$$\Rightarrow \{M \rightarrow M + \Delta M, P = const\} \Rightarrow Q \rightarrow Q + \frac{\Delta M}{[O_2]_a}$$

ΔQ follows ΔM to support the extra $O_2$ consumption!

# R dependence on M, for P=const

$$R = \frac{P}{Q} = \frac{P}{\frac{M}{[O_2]_a} + \frac{P}{R_0[O_2]_a}} = \frac{PR_0[O_2]_a}{MR_0 + P}$$

- Under the control $R=R_0[O_2]_v$, the tissue resistance becomes a function of the tissue metabolic rate M.
- If P=const and M increases, R automatically decreases.

# Q dependence on $[O_2]_a$

$$Q = \frac{M}{[O_2]_a} + \frac{P}{R_0[O_2]_a} \Rightarrow Q[O_2]_a = M + \frac{P}{R_0}$$

- If M=const and P=const, then changes in $[O_2]_a$ cause Q to change, keeping the product $Q[O_2]_a$ constant.
- Under compensation, the rate of $O_2$ supply to the tissue becomes insensitive to changes in the arterial oxygen concentration.

# In summary:

- Part of the body “homeostasis” is that blood supply to the tissues is (a) not so sensitive to blood pressure changes, and (b) very responsive to the needs of the tissues.
- All this can be accounted for by the simple compensation model, in which tissue flow resistance is proportional to its venous oxygen concentration.