Mechanisms of control in Cardiovascular circulation

Math 392 - Mathematical Models in Biology

January, 2014
Analysis of equations

\[ Q = K_L P_{pv} \]
\[ Q = K_R P_{sv} \]

\[ V_{sa} = C_{sa} P_{sa} \]
\[ V_{sv} = C_{sv} P_{sv} \]
\[ V_{pa} = C_{pa} P_{pa} \]
\[ V_{pv} = C_{pv} P_{pv} \]

\[ Q = \frac{1}{R_s} (P_{sa} - P_{sv}) \]
\[ Q = \frac{1}{R_p} (P_{pa} - P_{pv}) \]

\[ V_{sa} + V_{sv} + V_{pa} + V_{pv} = V_0. \]
Cardiac output equilibrium

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$$Q \approx 5.6 \text{ L/m}$$

$$V_s \approx 4.5 \text{ L, } V_p \approx 0.5 \text{ L.}$$
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If $K_R$ is reduced, then the following happens:

- $Q_R < Q_L$
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$$\frac{V_p}{V_s} = \frac{T_{pv} + T_{pa}}{T_{sa} + T_{sv}} = \frac{C_{pa}/K_L + C_{pa}R_p + C_{pv}/K_L}{C_{sa}/K_R + C_{sa}R_s + C_{sv}/K_R}$$
Dependence of flow on pressure

The previous regulatory mechanism relies on the dependence of $Q$ on $P$. Suppose $Q$ does not depend on $P$, and is thus, a parameter in the equations. The two pump equations are eliminated, leaving 8 unknowns, $(V_i, P_i)$ and 6 equations (4 compliance, 2 resistance). Introduce new parameters, $V_s, V_p$:

$$V_s a + V_s v = V_s, \quad V_p a + V_p v = V_p.$$ 

This leads to 8 equations with 8 unknowns, but no mechanism guaranteeing a reasonable relationship between $V_s$ and $V_p$. So the relationship of $Q$ and $P$ is crucial for a controlled partitioning of blood into the pulmonary and systemic circulations.
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Need for an external control

During an exercise, the following is observed:

Arterioles dialate $\rightarrow R_s$ falls $\rightarrow Q_L$ rises $\rightarrow P_{sa}$ is maintained

Here the increase in $Q_L$ comes from an increase in the heart rate with stroke volume = const.
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$$Q = \frac{V_0}{T_{sa} + T_{sv} + T_{pa} + T_{pv}}, \quad P_{sa} = \frac{V_0}{C_{sa}} \frac{T_{sa}}{T_{sa} + T_{sv} + T_{pa} + T_{pv}}$$
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\]

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>(R_s \rightarrow R_s/2)</th>
<th>Change</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Q)</td>
<td>5.6 L/m</td>
<td>6.2 L/m</td>
<td>+0.6 L/m</td>
<td>+11%</td>
</tr>
<tr>
<td>(P_{sa})</td>
<td>100 mmHg</td>
<td>57 mmHg</td>
<td>-43 mmHg</td>
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This is inadequate to sustain exercise of any length.
Sensitivity

Q: How sensitive are $Q$ and $P_{sa}$ to changes in $R_s$?

Let $Y = Y(X)$, define the sensitivity of $Y$ to changes in $X$ as

$$\sigma_{YX} = \frac{\log Y(X + \Delta X) - \log Y(X)}{\log (X + \Delta X) - \log X} \approx \frac{\Delta Y}{Y} / \frac{\Delta X}{X}.$$ 

$\sigma_{YX}$ measures roughly the rate of relative changes. For example, $Y = aX^n = \Rightarrow \sigma_{YX} = \log a(X + \Delta X)^n - \log aX^n \log (X + \Delta X) - \log X^n = n$, so in particular $Y \sim X \Rightarrow \sigma_{YX} = 1$, and if $Y \sim 1/X \Rightarrow \sigma_{YX} = -1$.

From the changes in $Q$ and $P_{sa}$, while $R_s \rightarrow R_s/2$, $\sigma_{QR} = \log 6/2 - \log 5/6 \log (1/2) \approx -0.15$, $\sigma_{P_{sa}R} = \log 100 - \log 57 \log (1/2) \approx +0.81$.

Observe that $-\sigma_{QR} + \sigma_{P_{sa}R} \approx 1$, which follows from $P_{sa} \approx QR$. 


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Observe that $-\sigma_{QR_s} + \sigma_{P_{sa}R_s} \approx 1$, which follows from $P_{sa} \approx QR_s$. 
Neural control: Baroreceptor loop

Need a mechanism to hold $P_{sa}$ constant and to guarantee blood flow to nonexercising tissue, i.e.

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The loop adjusts the heart rate $F$ to keep $P_{sa} = P^*$ constant.
Effect of the baroreceptor loop
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To solve, ignore $P_{sv}$ in the systemic resistance equation (2% error),

$$Q R_s = P^*$$

ignore the volume of pulmonary blood in the total volume equation (10% error)

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Q = \frac{P^*}{R_s}.
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F = \frac{Q}{C_R P_{sv}} = \frac{P^* C_{sv}}{R_s C_R(V_0 - C_{sa} P^*)}.
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Blood loss leads to increased heart rate \((F)\), which compensates for decrease in the stroke volume. \(F\) breaks down when \(V_0 = C_{sa} P^*\), i.e. when \(V_0 = V_{sa}\), and \(V_{sv} = 0\).
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Autoregulation

Q: What controls $R_s$ on the local level?

There is a range of pressures, for which $Q$ is insensitive to $\Delta P$.

When $\Delta P = \text{const}$, $Q$ depends on the rate of $O_2$ consumption.

Define:

$[O_2]_a$ - arterial oxygen concentration, in (liters of $O_2$)/(liters of blood)

$[O_2]_v$ - venous oxygen concentration, in (liters of $O_2$)/(liters of blood)

$M$ - metabolic rate of the tissue ($O_2$ consumption rate), in liters/minute

Fick's principle:

$Q [O_2]_a - Q [O_2]_v = M \Rightarrow [O_2]_v = [O_2]_a - M / Q$

When $[O_2]_v = 0$, then $Q = Q^* = M / [O_2]_a$, which is the minimum blood flow to sustain the metabolic rate $M$. 
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combining equations we have

$$M = Q([O_2]_a - [O_2]_v) = Q[O_2]_a - \frac{\Delta P}{R_0},$$

hence

$$Q = \frac{M}{[O_2]_a} + \frac{\Delta P}{R_0[O_2]_a} = Q^* + \frac{\Delta P}{R_0[O_2]_a}.$$
Model for $R_s$

- $\sigma_{QP}$ is less in the new model
- $Q \geq Q^*$, min flow guaranteed
- When $\Delta P = \text{const}$, $\Delta Q = \Delta M/[O_2]_a = \Delta Q^*$.
- When $\Delta P = \text{const}$, an increase in $M$ results in a decrease in $R$.
- When $[O_2]_a$ changes, $Q$ adjusts, so that $Q[O_2]_a = \text{const}$. 