Beispiele

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Contents

Chapter 1

The Heart and Circulation

1.1 Example 1.8 - Uncontrolled Circulation: Nonzero P_{thorax}

In our model of the uncontrolled circulation, we also needed P_{thorax}. Fix this by changing the equations of the right and left hearts and the pulmonary compliance to the following:

$$Q_r = FC_r(P_{SV} - P_{thorax}) = K_r(P_{SV} - P_{thorax}) \tag{1.1.1}$$

$$Q_l = FC_l(P_{PV} - P_{thorax}) = K_l(P_{PV} - P_{thorax}) \tag{1.1.2}$$

$$V_{Pa} = C_{Pa}(P_{Pa} - P_{thorax}) \tag{1.1.3}$$

$$V_{Pv} = C_{Pv}(P_{Pv} - P_{thorax}) \tag{1.1.4}$$

Here P_{thorax} is a (negative) parameter and the volumes are understood to mean excess volumes.
Solve the equations of the improved model and plot Q and P_{sv} as functions of P_{thorax} for $P_{thorax} \leq 0$.

The notation is: $K\ldots$ pump coefficient, $C\ldots$ compliance, $R\ldots$ resistance, $Q\ldots$ flow, $P\ldots$ pressure, $V\ldots$ volume, $s\ldots$ systemic, $p\ldots$ pulmonary, $a\ldots$ arterial, $v\ldots$ venous, $l\ldots$ left, $r\ldots$ right Mathematical model of the Uncontrolled Circulation:

$$Q_r = K_r P_{sv} \tag{1.1.5}$$

$$Q_l = K_l P_{pv} \tag{1.1.6}$$

$$V_{sa} = C_{sa} P_{sa} \tag{1.1.7}$$

$$V_{sv} = C_{sv} P_{sv} \tag{1.1.8}$$

$$V_{pa} = C_{pa} P_{pa} \tag{1.1.9}$$

$$V_{pv} = C_{pv} P_{pv} \tag{1.1.10}$$

$$Q_s = \frac{1}{R_s}(P_{sa} - P_{sv}) \tag{1.1.11}$$

$$Q_p = \frac{1}{R_p}(P_{pa} - P_{pv}) \tag{1.1.12}$$

$$V_o = V_{sa} + V_{pa} + V_{sv} + V_{pv} \tag{1.1.13}$$

$$Q = Q_r = Q_s = Q_l = Q_p \tag{1.1.14}$$

Now we use the modifications Q_r

$$Q_r = FC_r(P_{SV} - P_{thorax}) = K_r(P_{SV} - P_{thorax}) \tag{1.1.15}$$

$$Q_l = FC_l(P_{PV} - P_{thorax}) = K_l(P_{PV} - P_{thorax}) \tag{1.1.16}$$

$$V_{pa} == C_{Pa}(P_{Pa} - P_{thorax}) \tag{1.1.17}$$

$$V_{Pv} = C_{Pv}(P_{Pp} - P_{thorax}) \tag{1.1.18}$$

and derive a new system:

$$Q_r = K_r(P_{sv} - P_{thorax}) \tag{1.1.19}$$

$$Q_l = K_l(P_{pv} - P_{thorax}) \tag{1.1.20}$$

$$V_{sa} = C_{sa}P_{sa} \tag{1.1.21}$$

$$V_{sv} = C_{sv}P_{sv} \tag{1.1.22}$$

$$V_{pa} = C_{pa}(P_{pa} - P_{thorax}) \tag{1.1.23}$$

$$V_{pv} = C_{pv}(P_{pv} - P_{thorax}) \tag{1.1.24}$$

$$Q_s = \frac{1}{R_s}(P_{sa} - P_{sv}) \tag{1.1.25}$$

$$Q_p = \frac{1}{R_p}(P_{pa} - P_{pv}) \tag{1.1.26}$$

$$V_o = V_{sa} + V_{pa} + V_{sv} + V_{pv} \tag{1.1.27}$$

$$Q = Q_r = Q_s = Q_l = Q_p \tag{1.1.28}$$

To solve this linear system we express the pressures in terms of the flow. We begin with:

$$P_{sv} = \frac{Q}{K_r} + P_{thorax} \tag{1.1.29}$$

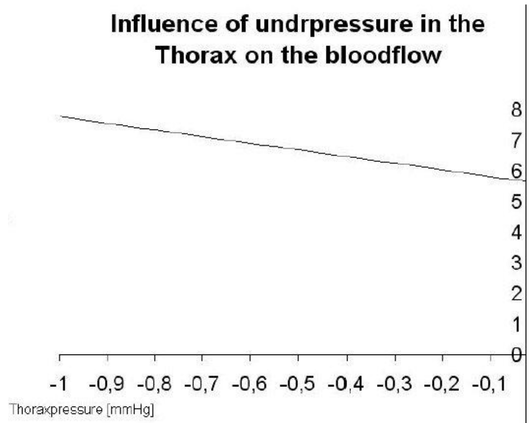
$$P_{pv} = \frac{Q}{K_l} + P_{thorax} \tag{1.1.30}$$

Next, the arterial pressures become

$$P_{sa} = QR_s + \frac{Q}{K_r} + P_{thorax} = Q\left(R_s + \frac{1}{K_r}\right) + P_{thorax} \tag{1.1.31}$$

For the volumes in the different compartments we have the following four equations

$$V_{sa} = C_{sa}(Q(R_s + \frac{1}{K_r}) + P_{thorax}) = (\frac{C_s a}{K_r} + C_{sa}R_s)Q + C_{sa}P_{thorax} \tag{1.1.32}$$



$$V_{sv} = \frac{C_{sv}}{K_r} Q + C_{sv} P_{thorax} \tag{1.1.33}$$

$$V_{pv} = \frac{C_{pv}}{K_l} Q + C_{pv} P_{thorax} \tag{1.1.34}$$

with $\frac{C_{sv}}{K_r} = T_{sv}$ and $\frac{C_{pv}}{K_l} = T_{pv}$. Considering the new equations for the pressures and the volumes we get also a new one for V_0

$$V_0 = (T_{sa} + T_{sv} + T_{pa} + T_{pv}) * Q + (C_{sa} + C_{sv} + C_{pa} + C_{pv}) * P_{thorax}$$

Finally we can express Q and P_{sv} explicit in terms of P_{thorax}

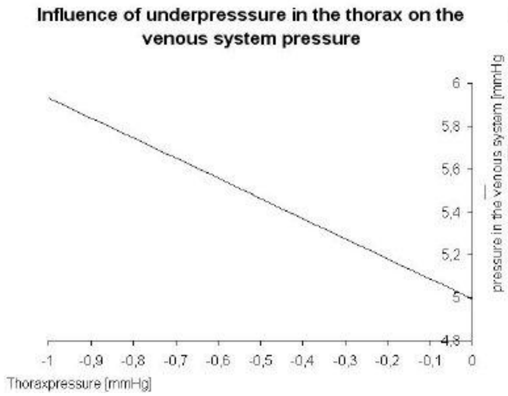
$$Q = \frac{V_0 - (C_{sa} + C_{pv} + C_{sv} + C_{pa}) P_{thorax}}{T_{sa} + T_{sv} + T_{pa} + T_{pv}} \tag{1.1.35}$$

$$P_{sv} = \frac{V_0 - (C_{sa} + C_{pv} + C_{sv} + C_{pa}) P_{thorax}}{K_r (T_{sa} + T_{sv} + T_{pa} + T_{pv})} + P_{thorax} \tag{1.1.36}$$

For our calculations we use these values:

$$C_{sa} = 0.01,\ C_{sv} = 1.75,\ C_{pa} = 0.007,\ C_{pv} = 0.08,$$

$$R_s = 17.5,\ R_p = 1.79,\ K_r = 2.8,\ K_l = 1.12$$



1.2 Example 1.9 - Uncontrolled Circulation: Localized Partial Venous Collapse

Our equations to solve are slightly different to the equations in the example before:

$$Q_L = K_L(P_{pv} - P_{thorax}) \tag{1.2.1}$$

$$Q_R = K_R(P_{ra} - P_{thorax}) \tag{1.2.2}$$

$$P_{sv} = 0 \tag{1.2.3}$$

$$Q_s R_c = -P_{ra} \tag{1.2.4}$$

$$V_{pa} = c_{pa}(P_{pa} - P_{thorax}) \tag{1.2.5}$$

$$V_{pv} = c_{pv}(P_{pv} - P_{thorax}) \tag{1.2.6}$$

$$V_{sa} = c_{sa} P_{sa} \tag{1.2.7}$$

$$V_{sv} = c_{sv} P_{sv} \tag{1.2.8}$$

$$Q_p = \frac{P_{pa} - P_{pv}}{R_p} \tag{1.2.9}$$

$$Q_s = \frac{P_{sa}}{R_s}, \tag{1.2.10}$$

because $P_{sv} = 0$ and

$$V_{pa} + V_{pv} + V_{sa} = V_0 \tag{1.2.11}$$

and

$$Q_R = Q_L = Q_s = Q_p = Q. \tag{1.2.12}$$

Making the same steps as in section 1.5, we get

$$P_{pv} = \frac{Q}{K_L} + P_{thorax} \; P_{pa} = QR_p + \frac{Q}{K_L} + P_{thorax} \tag{1.2.13}$$

and

$$P_{sa} = QR_s \tag{1.2.14}$$

Using equation 10. leads us to an equation for Q

$$Q = \frac{V_0}{c_{pa}(R_p + \frac{1}{K_L}) + c_{sa}R_s + c_{pv}\frac{1}{K_L}}$$

which is now independent of P_{thorax}, which had to be shown according to Example 1.9. We've not shown that that R_c increases as P_{thorax} becomes more negative yet. But this is obvious due to

$$P_{ra} = -QR_c$$

in equation 2.

$$(\frac{Q}{R_c} + P_{thorax})(\frac{-1}{Q}) = R_c.$$

Now if P_{thorax} becomes more negative, R_c increases.

1.3 Example 1.10

Using the formula $P_{sa} = R_s Q$ we want to derive the relationship $-\sigma_{QR_s} + \sigma_{P_{sa}R_s} = 1$.

We use following definition of the sensitivity

$$\sigma_{YX} = \frac{ln(\frac{Y'}{Y})}{ln(\frac{X'}{x})}$$

with $X' = X + \Delta X$ and $Y' = Y + \Delta Y$ or for small changes

$$\sigma_{YX} = \frac{dY}{Y} / \frac{dX}{X}.$$

After applying the logarithm and the definition of the sensitivity above and that $P_{sa} = R_s Q$, we get

$$-\frac{lnQ}{lnR_s} + \frac{lnQ}{lnQ} + \frac{lnR_s}{lnQ}$$

which is obviously 1.

Chapter 2

Gas Exchange in the Lungs

2.1 Example 2.4 - An Extreme Mismatch of Ventilation and Perfusion

Gegeben sei eine Lunge mit zwei Teilen. In jedem Teil sei das Ventilations-Perfusions-Verhältnis konstant. Es seien

$$\begin{array}{llll} V_{A,1} = 5.0 & \text{Liter/min}, & Q_1 = 0.0 & \text{Liter/min}, \\ V_{A,2} = 0.0 & \text{Liter/min}, & Q_2 = 5.0 & \text{Liter/min}. \end{array}$$

Berechne f, $\langle P_A \rangle$ und $\langle P_a \rangle$, und drücke sie durch P_I, P_V, σ, und kT aus. Interpretiere die Ergebnisse.

Unter Verwendung der folgenden Gleichgewichtsannahmen

- $c_E = c_A$ (Alveolarluft wird ausgeatmet)
- $Qc_V + V_A c_I = Qc_a + V_A c_A \Leftrightarrow Q(c_a - c_V) = V_A(c_I - c_A)$
  (die Anzahl der Moleküle, die in den Alveolus gelangen, ist identisch mit der Anzahl von Molekülen, die den Alveolus wieder verlassen)

- $P_A = kTc_A$ (Gas im Alveolus ist ideales Gas)
- $\sigma P_a = c_a$ (Lösung des Gases im Blut ist einfach)
- $P_a = P_A$ (Gleichgewicht bzgl. der Lösung im Blut)

folgt

$$c_{A,j} = \frac{V_{A,j}c_I + Q_j c_V}{V_{A,j} + \sigma kTQ_j} \qquad \text{und} \qquad c_{a,j} = \sigma kTc_{A,j} \qquad j = 1, 2.$$

Weiters sind

$$V_{A,0} = V_{A,1} + V_{A,2} = 5.0 + 0.0 = 5.0$$

und

$$Q_0 = 5.0,$$

wobei r_1 unbestimmt ist (oder ∞) und $r_2 = 0$.
Also folgt insgesamt

$$f_1 = Q_1(c_{a,1} - c_V) = V_{A,2}(c_I - c_{A,2}) = 0 \qquad \Rightarrow \qquad f_0 = 0,$$

und unter Verwendung des idealen Gasgesetzes

$$
\begin{aligned}
\langle P_A \rangle &= kT\langle c_A \rangle \\
&= kT\frac{V_{A,1}c_{A,1} + V_{A,2}c_{A,2}}{V_{A,0}} \\
&= kT\frac{V_{A,1}c_{A,1}}{V_{A,0}} \\
&= kTc_{A,1} \\
&= kT\frac{V_{A,1}c_I + Q_1 c_V}{V_{A,1} + Q_1\sigma kT} \\
&= kT\frac{V_{A,1}c_I}{V_{A,1}} \\
&= kTc_I \\
&= P_I,
\end{aligned}
$$

weiters ist

$$
\begin{aligned}
\langle P_a \rangle &= \frac{\langle c_a \rangle}{\sigma} \\
&= \frac{Q_1 c_{a,1} + Q_2 c_{a,2}}{Q_0\sigma} \\
&= \frac{Q_2 c_{a,2}}{Q_0\sigma} \\
&= \frac{c_{a,2}}{\sigma} \\
&= \frac{1}{\sigma}\sigma kTc_{A,2} \\
&= kTc_{A,2} \\
&= kT\frac{r_2 c_I + c_V}{r_2 + \sigma kT} \\
&= kT\frac{c_V}{\sigma kT} \\
&= \frac{c_V}{\sigma} \\
&= P_V,
\end{aligned}
$$

oder in Worten: Es wird kein Gas transportiert ($f = 0$), die eingeatmete Luft entspricht der Alveolarluft ($\langle P_A \rangle = P_I$) und es erfolgt kein Gasaustausch ($\langle P_a \rangle = P_V$).

Chapter 3

Control of Cell Volume and Electrical Properties of Cell Membranes

3.1 Example 3.5 - Effect of Pump Rate on Cell Volume and Membrane Potential

We use the following data

$$g_{Na} = 3.3 \mu mho/cm^2$$

$$g_K = 240 \mu mho/cm^2$$

$$[Na^+]_o = 145 \mu M/cm^3$$

$$[K^+]_o = 4 \mu M/cm^3$$

$$q = 1.6 \times 10^{-19} coulombs$$

$$\frac{kT}{q} = 25 \times 10^{-3} volts.$$

1. Check the inequality (3.4.34). The inequality (3.4.34) is of the following form

$$\frac{[Na^+]_o}{g_{Na}} > \frac{[K^+]_o}{g_K}.$$

Using the data above we get

$$\frac{145}{3.3} = 43.93 > \frac{4}{240} = 0.0166$$

which is true.

2. Evaluate p_{opt} from equation (3.4.35).

$$p_{opt} = \frac{kT}{q^2}\frac{g_{Na}g_K}{g_{Na}+g_K}\log\frac{g_K[Na^+]_o}{g_{Na}[K^+]_o} = 1.6\ 10^{-20}.$$

V and v have minima at p_{opt} because of the fact that

$$V'(\beta(p_{opt})) = \frac{N}{2[Cl^-]_o}(\frac{1}{2(1-\beta)^{1.5}}) = 0$$

and

$$v'(\beta(p_{opt})) = \frac{kT}{q}\frac{1}{1-\sqrt{1-\beta}}(0.5(1-\beta)^1.5) = 0.$$

3. Assuming that p = p_{opt}, evaluate $[Na^+]_i$, $[K^+]_i$ and $[Cl^-]_i$. Also evaluate v.

At $p = p_{opt}$ the value of β is $\beta(p_{opt}) = 0.0303$.

$$[Na^+]_o + [K^+]_o = [Cl^-]_o = 149$$

Using equation (3.4.16) and (3.4.17) we get for $\beta_{Na} = 6.9\ 10^{-4}$ and $\beta_K = 1.105$. Now we use following equation for γ:

$$\gamma = -\sqrt{1 - \beta(p_{opt})} + 1.$$

This gives us $\gamma = 0.015$.

$$[Na^+]_i = \frac{1}{\gamma}\beta_{Na}[Na^+]_0 = 6.45$$

$$[K^+]_i = \frac{1}{\gamma}\beta_K[K^+]_0 = 289$$

$$[Cl^-]_i = \gamma[Cl^-]_o = 2.235.$$

4. With $p = p_{opt}$ we get

$$E_{Na} = \frac{kT}{q}\log\frac{[Na^+]_o}{[Na^+]_i} = 3.36\ 10^{-2}.$$

$$E_K = \frac{kT}{q}\log\frac{[K^+]_o}{[K^+]_i} = -4.6\ 10^{-2}.$$

$$E_{Cl} = \frac{kT}{-q}\log\frac{[Cl^-]_o}{[Cl^i]_i} = v = -4.5\ 10^{-2}.$$

Using these values in the following equation

$$E_K < E_{Cl} < 0 < E_{Na},$$

we can see that this inequality is true.

Chapter 4

The Renal Countercurrent Mechanism

4.1 Example 4.4

Assume that Assume that $c(0)$ where $1\,mEq = 10^{-3} * 6.0 * 10^{23}$ ions. Using the approximation that $c^*/c(0) \ll 1$, calculate $Q_1(0)$, $Q_1(L)$, $Q_3(0)$, $Q_3(L)$ and $c(L)$. Do this calculation for both the concentrating and diluting modes and use your answers in each case to construct a quantitative diagram of the nephron with flows and Na^+ concentrations labelled at appropriate sites.

$c(x)$ Comparison of the two modes of operation of the model nephron can be summarized as follows: First, the urine is more dilute than blood plasma when ADH is absent and more concentrated when ADH is present. Second, the volume rate of flow is much smaller when ADH is present by a factor of $c^*/ec(0)$. The rate at which Na^+ is excreted is the same in both cases, however. The Diluting mode (ADH Absent):

c^* First we need some physiological assumptions:

* The walls of the descending limb are permeable to water but not to Na^+. (This is only a simplification) Moreover, we assume that the water permeability is so large that the water flux makes the internal ad external Na^+ concentrations equal. So we get $c_1(x) = c(x)$

* Na^+ is pumped out of the ascending limb at a fixed rate f^*_{Na} per unit length and the ascending limb is impermeable to water.

* At the turn of Henle´s loop ($x = L$) all of the salt and water leaving the descending limb enter the ascending limb. This gives the boundary conditions $c_1(L)$

* Finally, we have a relationship between the flux of Na^+ and the flow of water: $f^*_{Na} = c(x) f^{(1)}_{H_2O}(x)$.

We use that $Q_1 c = const$ and get an expression for $Q_1(x)$ in terms of c(x) : $Q_1(x) = Q_1(0)c(0)/c(x)$. With $c(L) = c(0)\exp\left(\frac{f^*_{Na}L}{Q_1(0)c(0)}\right)$ we get an equation for $Q_1(L)Q_1(L) = Q_1(0)c(0)/c(L)$. Note that $f^*_{Na}L$ is the total rate at which Na^+ is actively pumped out trough the walls of the ascending limb of Henle´s loop, while $Q_1(0)c(0)$ is the rate at which Na^+ enters the loop from the proximal tube. Thus, the ratio of these fluxes $\alpha = \frac{f^*_{\mathrm{Na}}L}{Q_1(0)c(0)} < 1$ determines the maximum concentrating ability of the model nephron for Na^+ through the equation $c(L) = c(0)e^{\alpha}$.

Next we consider the ascending limb of Henle´s loop. Since this tubule is impermeable to water we have $Q_2(x) = Q_2(L) = -Q_1(L)$.

We assume that the inflow $Q_1(0)$ to the loop of Henle takes on whatever value is needed to satisfy the equation $c_2(0) = c^*$, where $c^* < c(0)$ is the target concentration sought by the juxtaglomerular apparatus. Further, we get $a = \exp(\alpha)(1-\alpha)$, where

$$a = c^*/c(0) < 1. \tag{4.1.1}$$

Because we know a (4.1.1) is an equation for α and hence for $Q_1(0)$. Moreover we can see directly >from (4.1.1) that as a $\rightarrow 0$, $\alpha \rightarrow 1$. Thus for small values of a , α.

We can now rewrite the previous results under the assumption that $c^* \ll c(0)$. $Q_1(0)$

Now there is just one thing missing. The influence of the antidiuretic hormone (ADH). This is the hormone which determines whether to excrete a large volume of dilute urine or a small volume of concentrated urine. When ADH is absent, we assume that the distal tubule and the collecting ducts are simple conduits, impermeable to both salt and water. In these circumstances the fluid that leaves the top of the ascending limb becomes urine without further modification. Thus, the flow leaving and entering the collecting duct are the same: $Q_3(0) = Q_3(L) = -Q_2$.

The Concentrating mode (ADH Present):

e$c(0)$ When ADH is present, the situation in the distal tubule and the collecting ducts is more complicated. The effect of ADH is to make the distal tubule and the collecting duct permeable to water. Because of this we get a new equation for the flow leaving the collecting duct: $Q_3(L) = -Q_2c^*/c(L) = f^*_{Na}Lc^*/(\mathrm{e}c(0))^2$.

Summarized:

| calculation for: | concentrating mode | diluting mode |

$Q_1(0)$	0.000000125	0.000000125
$Q_1(L)$	0.000000046	0.000000046
$Q_3(0)$	0.000000046	0.000000046
$Q_3(L)$	0.000000007	0.000000046
c(L)	380.559456	380.559456

Repeat part 1, but without making the approximation that $c^*/c(0) \ll 1$. (Hint: Start from the value of α that was determined in Exercise 4.3)

According to the instructions we use $a = 0.42857$ and $\alpha = 0.87718$. From $[eq : alpha]$ we derive $Q_1(0) = \frac{f^*_{\mathrm{Na}} L}{\alpha c(0)}$. Summarized:

calculation for:	concentrating mode	diluting mode
$Q_1(0)$	0.000000143	0.000000143
$Q_1(L)$	0.000000059	0.000000059
$Q_3(0)$	0.000000059	0.000000059
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Now there is just one thing missing. The influence of the antidiuretic hormone (ADH). This is the hormone which determines whether to excrete a large volume of dilute urine or a small volume of concentrated urine. When ADH is absent, we assume that the distal tubule and the collecting ducts are simple conduits, impermeable to both salt and water. In these circumstances the fluid that leaves the top of the ascending limb becomes urine without further modification. Thus, the flow leaving and entering the collecting duct are the same: $Q_3(0) = Q_3(L) = -Q_2$.

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Chapter 5

Muscle Mechanics

5.1 Example 5.3 - Superisometric Force

When a force greater than the isometric force is applied to a muscle, the muscle stretches at a velocity that depends on the applied force. Calculate the force - velocity curve for stretch, making the same assumptions that were made in this chapter.

Remarks: Treat stretch as a negative velocity of shortening ($v < 0$). Crossbridges still format $x = A$, but now they are carried into the region $x > A$ by the sliding process. Thus $u = 0$ for $x < A$, and the equation that replaces (5.2.4) is

$$\alpha(1 - U) = \beta \int_A^{x_0} u(x)dx - vu(x_0). \tag{1}$$

Starting from this equation, repeat the derivation that led to the force - velocity curve and see what you get.

To get the differential equation we differentiate (1) with respect to x_0. The result is

$$0 = \beta u(x_0) - v\frac{du}{dx}(x_0).$$

Since x_0 can be of any value of x, we get

$$v\frac{du}{dx} = \beta u.$$

The solutions of this equation are of the form

$$u(x) = u(A)\exp\frac{\beta(x-A)}{v}. \tag{2}$$

To derive any situation for $u(A)$, we go back to (1) and set $x = A$. Having made this, we get

$$\alpha(1-U) = -vu(A). \tag{3}$$

But this still does not determine $u(A)$. Now we integrate (2) and we find that

$$U = \int_{-\infty}^{A} u(x)dx = \frac{vu(A)}{\beta}. \tag{4}$$

Now we can solve (3) using (4)

$$\alpha(1-U) = -v\beta \Rightarrow U = \frac{\alpha}{\beta-\alpha}.$$

From this we get the following equation

$$u(A) = -\frac{\alpha(1-\frac{\alpha}{\beta-\alpha})}{v}.$$

Hence

$$u(x) = \frac{\beta\alpha}{v(\beta-\alpha)}\exp\frac{\beta(x-A)}{v}. \tag{5}$$

Now we want to calculate the force velocity curve. From (5.2.3), we have that

$$P = \eta_0 \int_{-\infty}^{\infty} p(x)u(x)dx$$

$$\Rightarrow P = \frac{\alpha\beta}{v(\beta-\alpha)} \int_{-\infty}^{A} \eta_0 p(x) e^{\frac{\beta(x-A)}{v}} dx.$$

We assume that $p(x) = p_1(e^{\gamma x} - 1)$. Then we have

$$P = \frac{\alpha\beta\eta_0 p_1}{v(\beta-\alpha)} \int_{-\infty}^{A} e^{\frac{\beta(x-A)}{v}+\gamma v} - e^{\frac{\beta(x-A)}{v}} dx.$$

Solving this we get

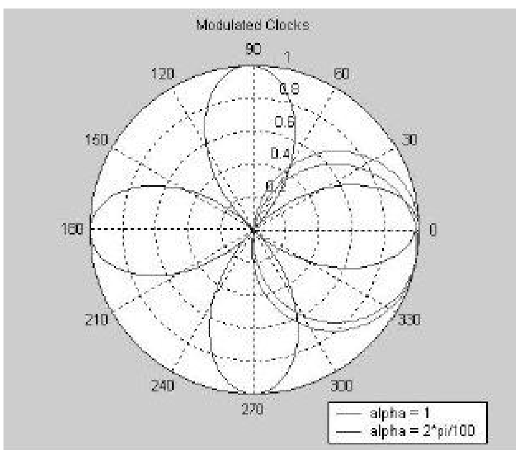
$$P = \frac{\alpha\eta_0 p_1}{\beta-\alpha}(e^{A\gamma}\frac{\beta}{v\gamma} - 1).$$

Chapter 6

Neural Systems

6.1 Example 6.4

Plot the values of $v(t) = \cos(\alpha t + \phi(t))$, where $\frac{d\phi}{dt} = \cos(2\pi t/100)$, for each of the values $\alpha = 1.0$ and $\alpha = 2\pi/100$.



Modulated Clocks
90
120
60
150
30
180
0
210
330
240
300
270
1
0.8
0.6
0.4
alpha = 1
alpha = 2*pi/100