

Q 1.

(a)

(b)

(c)

Q 2.

(a)

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Q 3.

(a)

(b)

Q 4.

Q 5.

Q 6.

- (a) The model of tumour growth under radiotherapy from time $t = 0$ to $t = t_1 > 0$ is given as

$$\frac{dC}{dt} = -C \log \left(\frac{C}{C_{max}} \right) - \frac{DC}{1+D}, \quad (6.1)$$

where, at time t , $C(t)$ is the size of the tumour, $C_{max} > 0$ is the maximum size of the tumour, a constant, so that $0 < C(t) \leq C_{max}$, and $D(t) \geq 0$ is the rate at which the drug is administered.

Now, making a change of variable

$$x = \log \left(\frac{C}{C_{max}} \right),$$

then (6.1) becomes

$$\begin{aligned} \frac{dx}{dt} &= \frac{dC}{dt} \cdot \frac{dx}{dC}, \\ \frac{dx}{dt} &= \frac{dC}{dt} \cdot \frac{1}{C}, \\ \frac{dx}{dt} &= \left[-C \log \left(\frac{C}{C_{max}} \right) - \frac{DC}{1+D} \right] \cdot \frac{1}{C}, \\ \frac{dx}{dt} &= -\log \left(\frac{C}{C_{max}} \right) - \frac{D}{1+D}, \\ \text{thus, } \frac{dx}{dt} &= -x - \frac{D}{1+D}, \quad \text{where } -\infty < x \leq 0. \end{aligned}$$

- (b) We are told that:

It is required to reduce the size of the tumour from C_0 at $t = 0$ to C_1 at $t = t_1$. Let $x_0 = \log(C_0/C_{max})$ and $x_1 = \log(C_1/C_{max})$. For the health of the patient, it is desired to minimise the total amount of drug administered, which is given by the functional

$$S[D] = \int_0^{t_1} dt D(t).$$

So, by expressing D in terms of x and $\dot{x} = dx/dt$ it should be possible to show that $S[D]$ may be written as

$$S[x] = - \int_0^{t_1} dt \frac{\dot{x} + x}{1 + \dot{x} + x}.$$

From part (a)

$$\begin{aligned}\dot{x} &= -x - \frac{D}{1+D}, \\ \dot{x} + x &= -\frac{D}{1+D}, \\ (\dot{x} + x)(1+D) &= -D, \\ (\dot{x} + x) + D(\dot{x} + x) &= -D, \\ D(\dot{x} + x) + D &= -(\dot{x} + x), \\ D(\dot{x} + x + 1) &= -\dot{x} - x, \\ D &= \frac{-\dot{x} - x}{\dot{x} + x + 1}.\end{aligned}$$

So

$$S[x] = - \int_0^{t_1} dt \frac{\dot{x} + x}{\dot{x} + x + 1} \quad \text{as required.}$$

(c) To show that the Euler-Lagrange equation for $S[x]$ is given by

$$2\ddot{x} + 3\dot{x} + x = -1, \quad \text{where } \ddot{x} = d^2x/dt^2,$$

consider the following.

The Euler-Lagrange equation is given by

HB p17.

$$\frac{d}{dt} \left(\frac{\partial F}{\partial \dot{x}} \right) - \frac{\partial F}{\partial x} = 0, \quad y(a) = A, \quad y(b) = B.$$

$$\text{Let, } F = \frac{\dot{x} + x}{\dot{x} + x + 1},$$

then using the quotient rule to determine $\partial F/\partial \dot{x}$ and $\partial F/\partial x$

$$\frac{\partial}{\partial \dot{x}} \left(\frac{u}{v} \right) = \left[v \frac{\partial u}{\partial \dot{x}} - u \frac{\partial v}{\partial \dot{x}} \right] / v^2 \quad \text{where, } u = \dot{x} + x \text{ and } v = \dot{x} + x + 1.$$

$$\begin{aligned}\frac{\partial F}{\partial \dot{x}} &= \frac{(\dot{x} + x + 1) \cdot 1 - (\dot{x} + x) \cdot 1}{(\dot{x} + x + 1)^2} = \frac{1}{(\dot{x} + x + 1)^2}, \\ \frac{\partial F}{\partial x} &= \frac{(\dot{x} + x + 1) \cdot 1 - (\dot{x} + x) \cdot 1}{(\dot{x} + x + 1)^2} = \frac{1}{(\dot{x} + x + 1)^2}.\end{aligned}$$

$$\begin{aligned}\frac{d}{dt} \left(\frac{\partial F}{\partial \dot{x}} \right) &= \frac{d}{dt} (\dot{x} + x + 1)^{-2}, \\ &= -2(\dot{x} + x + 1)^{-3} (\ddot{x} + \dot{x}), \\ &= \frac{-2(\ddot{x} + \dot{x})}{(\dot{x} + x + 1)^3}.\end{aligned}$$

Therefore, the Euler-Lagrange equation is

$$\begin{aligned}
 -\frac{2(\ddot{x} + \dot{x})}{(\dot{x} + x + 1)^3} - \frac{1}{(\dot{x} + x + 1)^2} &= 0, \\
 \frac{2(\ddot{x} + \dot{x})}{(\dot{x} + x + 1)^3} &= -\frac{1}{(\dot{x} + x + 1)^2}, \\
 \frac{2(\ddot{x} + \dot{x})}{(\dot{x} + x + 1)} &= -1, \\
 2(\ddot{x} + \dot{x}) &= -(\dot{x} + x + 1), \\
 2(\ddot{x} + \dot{x}) + (\dot{x} + x) &= -1, \\
 2\ddot{x} + 3\dot{x} + x &= -1, \quad \text{as required.}
 \end{aligned} \tag{6.2} \quad \ddot{x} = d^2x/dt^2.$$

- (d) Now solving the second-order linear ordinary differential equation (6.2) with the boundary conditions $x(0) = x_0$ and $x(t_1) = x_1$ as follows.

The auxiliary equation is

$$2\lambda^2 + 3\lambda + 1 = 0.$$

This has roots $\lambda_1 = -1$ and $\lambda_2 = -\frac{1}{2}$. These roots are real and different so the complementary function is given by

$$y_c = c_1 e^{-t} + c_2 e^{-\frac{1}{2}t}, \quad \text{where } c_1 \text{ and } c_2 \text{ are arbitrary constants.}$$

Using the method of undetermined coefficients to determine the particular solution to (6.2) as follows.

The particular solution to

$$2\frac{d^2x(t)}{dt^2} + 3\frac{dx(t)}{dt} + x(t) = -1,$$

is of the form

$$x_p(t) = a_1,$$

where a_1 is an unknown constant to be determined as follows:

$$\frac{dx(t)}{dt} = \frac{d}{dt}(a_1) = 0,$$

and therefore

$$\frac{d^2x(t)}{dt^2} = 0.$$

Substituting the particular solution $x_p(t)$ in to (6.2) gives

$$2 \times 0 + 3 \times 0 + a_1 = -1.$$

Therefore, $a_1 = -1$ and the general solution is

$$x(t) = c_1 e^{-t} + c_2 e^{-\frac{1}{2}t} - 1. \tag{6.3}$$

Now using the boundary conditions to solve for the unknown constants c_1 and c_2 as follows.

At $t = 0$, $x(0) = x_0$ and substituting this condition into (6.3) gives,

$$c_1 + c_2 - 1 = x_0. \quad (6.4)$$

At $t = t_1$, $x(t_1) = x_1$ and substituting this condition into (6.3) gives,

$$c_1 e^{-t_1} + c_2 e^{-\frac{1}{2}t_1} - 1 = x_1 \quad (6.5)$$

From (6.4)

$$c_1 = (x_0 + 1) - c_2 \quad (6.6)$$

Substituting into (6.5) for c_1 from (6.6) and rearranging in terms of c_2

$$\begin{aligned} (x_0 + 1) e^{-t_1} - c_2 e^{-t_1} + c_2 e^{-\frac{1}{2}t_1} &= x_1 + 1, \\ (x_0 + 1) e^{-t_1} + c_2 \left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right) &= (x_1 + 1), \\ c_2 \left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right) &= (x_1 + 1) - (x_0 + 1) e^{-t_1}, \\ c_2 &= \frac{(x_1 + 1) - (x_0 + 1) e^{-t_1}}{\left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right)}. \end{aligned} \quad (6.7)$$

Substituting for c_2 in (6.6) from (6.7)

$$\begin{aligned} c_1 &= (x_0 + 1) - \left[\frac{(x_1 + 1) - (x_0 + 1) e^{-t_1}}{\left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right)} \right], \\ c_1 &= \frac{(x_0 + 1) \left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right) - (x_1 + 1) + (x_0 + 1) e^{-t_1}}{\left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right)} \\ c_1 &= \frac{(x_0 + 1) e^{-\frac{1}{2}t_1} - (x_0 + 1) e^{-t_1} - (x_1 + 1) + (x_0 + 1) e^{-t_1}}{\left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right)} \\ c_1 &= \frac{(x_0 + 1) e^{-\frac{1}{2}t_1} - (x_1 + 1)}{\left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right)} = \alpha. \end{aligned} \quad (6.8)$$

Therefore, from (6.4)

$$c_2 = (x_0 + 1) - \alpha. \quad (6.9)$$

Substituting into (6.3) for c_1 and c_2 from (6.8) and (6.9) respectively gives,

$$x(t) = \alpha e^{-t} + (x_0 + 1 - \alpha) e^{-\frac{1}{2}t} - 1 \quad (\alpha \text{ given in (6.8)}),$$

as required.
