Q 1.

(a)

(b)

(c)

Q 2.

(a)

(b)

(c)

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

$$\frac{\mathrm{d}C}{\mathrm{d}t} = -C \log\left(\frac{C}{C_{max}}\right) - \frac{DC}{1+D}, \tag{6.1}$$

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

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

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

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

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

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

$$S[x] = -\int_0^{t_1} \mathrm{d}t \ \frac{\dot{x}+x}{\dot{x}+x+1} \qquad \text{as required.}$$

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

$$2\ddot{x} + 3\dot{x} + x = -1, \qquad \text{where } \ddot{x} = \mathrm{d}^2x/\,\mathrm{d}t^2,$$

consider the following.

The Euler-Lagrange equation is given by HB p17.

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

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

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

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

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

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

Therefore, the Euler-Lagrange equation is

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

(d)