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)

(d)