Q 1. Let γ be a real constant with $\gamma^2 \neq 1$ for the parametric functional

$$S\left[x,y\right] = \int_{0}^{1} \mathrm{d}t \, \left[\sqrt{\dot{x}^{2} + 2\gamma \dot{x}\dot{y} + \dot{y}^{2}} - \lambda \left(x\dot{y} - \dot{x}y\right) \right], \quad \lambda > 0,$$

with the boundary conditions x(0) = y(0) = 0, x(1) = R > 0 and y(1) = 0.

(a) In order to show that the stationary paths of this parametric functional are given by the solutions of the equations

$$\frac{\mathrm{d}x}{\mathrm{d}s} + \gamma \frac{\mathrm{d}y}{\mathrm{d}s} = 2(c - \lambda y)$$
, and

$$\gamma \frac{\mathrm{d}x}{\mathrm{d}s} + \frac{\mathrm{d}y}{\mathrm{d}s} = 2\left(d + \lambda x\right),\,$$

where c and d are constants and

$$s(t) = \int_0^t dt \sqrt{\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2}$$
 (1.1)

consider the following.

From the parametric functional,

$$\Phi = (\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{\frac{1}{2}} - \lambda (x\dot{y} - \dot{x}y), \quad \lambda > 0,$$

$$\frac{\partial \Phi}{\partial \dot{x}} = \frac{1}{2} (\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}} (2\dot{x} + 2\gamma \dot{y}) + \lambda y.$$

$$\frac{\partial \Phi}{\partial x} = -\lambda \dot{y}.$$

The Euler-Lagrange equation is given by

$$\frac{\mathrm{d}}{\mathrm{d}t} \left(\frac{\partial \Phi}{\partial \dot{x}} \right) - \frac{\partial \Phi}{\partial x} = 0.$$

Substituting into the Euler-Lagrange equation for the derivatives obtained above gives,

$$\frac{\mathrm{d}}{\mathrm{d}t} \left(\frac{1}{2!} (\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}} \left(2\dot{x} + 2\gamma \dot{y} \right) + \lambda y \right) + \lambda \dot{y} = 0,$$

$$\frac{\mathrm{d}}{\mathrm{d}t} \left(\left(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2 \right)^{-\frac{1}{2}} \left(\dot{x} + \gamma \dot{y} \right) + \lambda y \right) + \lambda \dot{y} = 0,$$

and integrating the above express with respect to t gives,

$$\left[\left(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2 \right)^{-\frac{1}{2}} \left(\dot{x} + \gamma \dot{y} \right) + \lambda y \right] + \lambda y = 2c,$$

where c is an arbitrary constant.

$$(\dot{x}^2 + 2\gamma\dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}}(\dot{x} + \gamma\dot{y}) + 2\lambda y = 2c,$$

So,

$$(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}}(\dot{x} + \gamma \dot{y}) = 2(c - \lambda y). \tag{1.2}$$

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Now, from (1.1) the definition of s,

$$\frac{\mathrm{d}s}{\mathrm{d}t} = \left(\dot{x}^2 + 2\gamma\dot{x}\dot{y} + \dot{y}^2\right)^{\frac{1}{2}},$$

and

$$\frac{\mathrm{d}t}{\mathrm{d}s} = \left(1/\frac{\mathrm{d}s}{\mathrm{d}t}\right) = \left(\dot{x}^2 + 2\gamma\dot{x}\dot{y} + \dot{y}^2\right)^{-\frac{1}{2}}.$$
 (1.3)

Substituting (1.3) into (1.2) gives,

$$\frac{\mathrm{d}t}{\mathrm{d}s}(\dot{x} + \gamma \dot{y}) = 2(c - \lambda y),$$

and noting that

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \dot{x}$$
 and $\frac{\mathrm{d}y}{\mathrm{d}t} = \dot{y}$,

then

$$\frac{\mathrm{d}t}{\mathrm{d}s} \left(\frac{\mathrm{d}x}{\mathrm{d}t} + \gamma \frac{\mathrm{d}y}{\mathrm{d}t} \right) = 2 \left(c - \lambda y \right)$$

$$\frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}x}{\mathrm{d}t} + \gamma \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}y}{\mathrm{d}t} = 2 \left(c - \lambda y \right),$$

thus, by the chain rule,

$$\frac{\mathrm{d}x}{\mathrm{d}s} + \gamma \frac{\mathrm{d}y}{\mathrm{d}s} = 2(c - \lambda y). \tag{1.4}$$

Similarly for \dot{y}

$$\Phi = (\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{\frac{1}{2}} - \lambda (x\dot{y} - \dot{x}y), \quad \lambda > 0,$$

$$\frac{\partial \Phi}{\partial \dot{y}} = \frac{1}{2} (\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}} (2\gamma \dot{x} + 2\dot{y}) - \lambda x.$$

$$\frac{\partial \Phi}{\partial y} = \lambda \dot{x}.$$

The Euler-Lagrange equation is given by

$$\frac{\mathrm{d}}{\mathrm{d}t} \left(\frac{\partial \Phi}{\partial \dot{y}} \right) - \frac{\partial \Phi}{\partial y} = 0.$$

Substituting into the Euler-Lagrange equation for the derivatives obtained above gives,

$$\frac{\mathrm{d}}{\mathrm{d}t} \left[\frac{1}{2} \left(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2 \right)^{-\frac{1}{2}} \left(2\gamma \dot{x} + 2\dot{y} \right) - \lambda x \right] - \lambda \dot{x} = 0,$$

$$\frac{\mathrm{d}}{\mathrm{d}t} \left[\left(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2 \right)^{-\frac{1}{2}} (\gamma \dot{x} + \dot{y}) - \lambda x \right] - \lambda \dot{x} = 0,$$

and integrating the above express with respect to t gives,

$$(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}}(\gamma \dot{x} + \dot{y}) - \lambda x - \lambda x = 2d,$$

where d is an arbitrary constant. So,

$$(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}} (\gamma \dot{x} + \dot{y}) - 2\lambda x = 2d,$$

and thus,

$$(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2)^{-\frac{1}{2}} (\gamma \dot{x} + \dot{y}) = 2(d + \lambda x).$$

Recall, (1.3) from above,

$$\frac{\mathrm{d}t}{\mathrm{d}s} = \left(\dot{x}^2 + 2\gamma\dot{x}\dot{y} + \dot{y}^2\right)^{-\frac{1}{2}},$$

and hence,

$$\frac{\mathrm{d}t}{\mathrm{d}s} (\gamma \dot{x} + \dot{y}) = 2 (d + \lambda x),$$

$$\frac{\mathrm{d}t}{\mathrm{d}s} \left(\gamma \frac{\mathrm{d}x}{\mathrm{d}t} + \frac{\mathrm{d}y}{\mathrm{d}t} \right) = 2 (d + \lambda x),$$

$$\gamma \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}x}{\mathrm{d}t} + \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}y}{\mathrm{d}t} = 2 (d + \lambda x),$$

Thus, by the chain rule,

$$\gamma \frac{\mathrm{d}x}{\mathrm{d}s} + \frac{\mathrm{d}y}{\mathrm{d}s} = 2(d + \lambda x).$$
(1.5)

Hence, the stationary paths of the given parametric functional are given by the solutions to equations (1.4) and (1.5).

(b) It can be shown that

$$\left(\frac{\mathrm{d}x}{\mathrm{d}s}\right)^2 + 2\gamma \frac{\mathrm{d}x}{\mathrm{d}s} \cdot \frac{\mathrm{d}y}{\mathrm{d}s} + \left(\frac{\mathrm{d}y}{\mathrm{d}s}\right)^2 = 1,$$

as follows.

From part (a)

$$\frac{\mathrm{d}s}{\mathrm{d}t} = \left(\dot{x}^2 + 2\gamma\dot{x}\dot{y} + \dot{y}^2\right)^{\frac{1}{2}},$$

and squaring both sides of the above expression gives,

$$\frac{\mathrm{d}s}{\mathrm{d}t} \cdot \frac{\mathrm{d}s}{\mathrm{d}t} = \left(\dot{x}^2 + 2\gamma \dot{x}\dot{y} + \dot{y}^2\right),\tag{1.6}$$

Again, recall that

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \dot{x}$$
 and $\frac{\mathrm{d}y}{\mathrm{d}t} = \dot{y}$,

so that (1.6) becomes

$$\frac{\mathrm{d}s}{\mathrm{d}t} \cdot \frac{\mathrm{d}s}{\mathrm{d}t} = \left(\frac{\mathrm{d}x}{\mathrm{d}t} \cdot \frac{\mathrm{d}x}{\mathrm{d}t} + 2\gamma \frac{\mathrm{d}x}{\mathrm{d}t} \cdot \frac{\mathrm{d}y}{\mathrm{d}t} + \frac{\mathrm{d}y}{\mathrm{d}t} \cdot \frac{\mathrm{d}y}{\mathrm{d}t}\right),\tag{1.7}$$

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multiplying both sides of equation (1.7) by

$$\frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}t}{\mathrm{d}s}$$

gives,

$$\frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}s}{\mathrm{d}t} \cdot \frac{\mathrm{d}s}{\mathrm{d}t} = \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}x}{\mathrm{d}t} \cdot \frac{\mathrm{d}x}{\mathrm{d}t} + 2\gamma \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}x}{\mathrm{d}s} \cdot \frac{\mathrm{d}y}{\mathrm{d}t} + \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}t}{\mathrm{d}s} \cdot \frac{\mathrm{d}y}{\mathrm{d}t} \cdot \frac{\mathrm{d}y}{\mathrm{d}t}, \quad (1.8)$$

then by the chain rule (1.8) becomes

$$1 = \left(\frac{\mathrm{d}x}{\mathrm{d}s}\right)^2 + 2\gamma \frac{\mathrm{d}x}{\mathrm{d}s} \cdot \frac{\mathrm{d}y}{\mathrm{d}s} + \left(\frac{\mathrm{d}y}{\mathrm{d}s}\right)^2,\tag{1.9}$$

as required.

(c) From equation (1.4)

$$\frac{\mathrm{d}x}{\mathrm{d}s} = 2\left(c - \lambda y\right) - \gamma \frac{\mathrm{d}y}{\mathrm{d}s}$$

and from equation (1.5)

$$\frac{\mathrm{d}y}{\mathrm{d}s} = 2\left(d + \lambda y\right) - \gamma \frac{\mathrm{d}x}{\mathrm{d}s}$$

Substituting into equation (1.4) for dy/ds gives,

$$\frac{\mathrm{d}x}{\mathrm{d}s} + \gamma \left(2 \left(d + \lambda x \right) - \gamma \frac{\mathrm{d}x}{\mathrm{d}s} \right) = 2 \left(c - \lambda y \right),$$

$$\frac{\mathrm{d}x}{\mathrm{d}s} + 2\gamma \left(d + \lambda x \right) - \gamma^2 \frac{\mathrm{d}x}{\mathrm{d}s} = 2 \left(c - \lambda y \right),$$

$$\frac{\mathrm{d}x}{\mathrm{d}s} \left(1 - \gamma^2 \right) + 2\gamma \left(d + \lambda x \right) = 2 \left(c - \lambda y \right),$$

$$\frac{\mathrm{d}x}{\mathrm{d}s} \left(1 - \gamma^2 \right) = 2 \left(c - \lambda y \right) - 2\gamma \left(d + \lambda x \right),$$

$$\frac{\mathrm{d}x}{\mathrm{d}s} \left(1 - \gamma^2 \right) = 2c - 2\lambda y - 2\gamma d - 2\gamma \lambda x,$$

$$\frac{\mathrm{d}x}{\mathrm{d}s} \left(1 - \gamma^2 \right) = -2\lambda \left(y + \gamma x \right) + 2 \left(c - \gamma d \right),$$

$$x' \left(1 - \gamma^2 \right) = -X + D = D - X.$$

Therefore,

$$(1 - \gamma^2)x' = D - X,$$

(1.10) Where, $D = 2 (c - \gamma d),$ $X = 2\lambda(x - y) \text{ and}$ $x' = \frac{dy}{ds}.$

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as required.

Equation (1.5) is

$$\gamma \frac{\mathrm{d}x}{\mathrm{d}s} + \frac{\mathrm{d}y}{\mathrm{d}s} = 2 (d + \lambda x).$$

Substituting into equation (1.5) for dx/ds from equation (1.4) gives,

$$\gamma \left(2(c - \lambda y) - \gamma \frac{\mathrm{d}y}{\mathrm{d}s} \right) + \frac{\mathrm{d}y}{\mathrm{d}s} = 2(d + \lambda x),$$

$$2\gamma (c - \lambda y) - \gamma^2 \frac{\mathrm{d}y}{\mathrm{d}s} + \frac{\mathrm{d}y}{\mathrm{d}s} = 2(d + \lambda x),$$

$$\frac{\mathrm{d}y}{\mathrm{d}s} \left(1 - \gamma^2 \right) = 2(d + \lambda x) - 2\gamma (c - \lambda y),$$

$$\frac{\mathrm{d}y}{\mathrm{d}s} \left(1 - \gamma^2 \right) = 2d + 2\lambda x - 2\gamma c + 2\gamma \lambda y,$$

$$\frac{\mathrm{d}y}{\mathrm{d}s} \left(1 - \gamma^2 \right) = 2(d - \gamma c) + 2\lambda (x + \gamma y).$$

$$\therefore \qquad \boxed{\left(1-\gamma^2\right)y'=C+Y}.$$

Where, $C = 2 (d - \gamma c)$, $Y = 2\lambda (x + \gamma y)$ and $y' = \frac{dy}{ds}$

(1.11)

as required.

Substituting for x' and y' from equations (1.10) and (1.11), respectively, $y' = \frac{dy}{ds}$ into equation (1.9)

$$\frac{(D-X)^2}{(1-\gamma^2)^2} + 2\gamma \frac{(D-X)}{(1-\gamma^2)} \frac{(C+Y)}{(1-\gamma^2)} + \frac{(C+Y)^2}{(1-\gamma^2)^2} = 1$$

Expanding the above and cross multiplying by $(1 - \gamma^2)^2$ gives,

$$D^{2} - 2DX + X^{2} + 2\gamma (D - X) (C + Y) + C^{2} + 2CY + Y^{2} = (1 - \gamma^{2})^{2},$$

$$D^{2} - 2DX + X^{2} + (2\gamma D - 2\gamma X) (C + Y) + C^{2} + 2CY + Y^{2} = (1 - \gamma^{2})^{2},$$

$$D^{2} - 2DX + X^{2} + 2\gamma CD + 2\gamma DY - 2\gamma CX - 2\gamma XY + C^{2} + 2CY + Y^{2} = (1 - \gamma^{2})^{2},$$

$$X^{2} + Y^{2} - 2\gamma XY + C^{2} + D^{2} + 2\gamma CD - 2DX + 2\gamma DY - 2\gamma CX + 2CY = (1 - \gamma^{2})^{2},$$

Collecting terms in just X and just Y gives,

$$X^{2}+Y^{2}-2\gamma XY+C^{2}+D^{2}+2\gamma CD-2X\left(D+\gamma C\right)+2Y\left(C+\gamma D\right)=\left(1-\gamma^{2}\right)^{2}. \tag{1.12}$$

Now, from above (see margin notes)

$$(D + \gamma C) = 2(c - \gamma d) + \gamma (2(d - \gamma c)),$$

= $2c - 2\gamma d + 2\gamma d - 2\gamma^2 c,$
= $2c(1 - \gamma^2).$

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$$\begin{split} (C+\gamma D) =& 2\left(d-\gamma c\right) + \gamma \left(2\left(c-\gamma d\right)\right), \\ =& 2d-2\gamma c + 2\gamma c - 2\gamma^2 d, \\ =& 2d\left(1-\gamma^2\right). \end{split}$$

So,

$$D + \gamma C = 2c (1 - \gamma^2)$$
 and $C + \gamma D = 2d (1 - \gamma^2)$.

Substituting these expressions into equation (1.12) gives,

$$X^{2}+Y^{2}-2\gamma XY+C^{2}+D^{2}+2\gamma CD-4c\left(1-\gamma^{2}\right)X+4d\left(1-\gamma^{2}\right)Y=\left(1-\gamma^{2}\right)^{2}$$
, as required.

The boundary conditions are

$$x(0) = y(0) = 0$$
, $x(1) = R > 0$, $y(1) = 0$.

Now, applying these boundary conditions to equation (1.12) and from the margin notes above we have:

$$X(t) = 2\lambda \left(\gamma x(t) + y(t)\right).$$

$$Y(t) = 2\lambda (x(t) + \gamma y(t)).$$

At t=0,

$$X(0) = 2\lambda (\gamma x(0) + y(0)) = 0.$$

$$Y(0) = 2\lambda (x(0) + \gamma y(0)) = 0.$$

Thus, equation (1.12) at t = 0 reduces to

$$C^2 + D^2 + 2\gamma CD = (1 - \gamma^2)^2$$
.

At t = 1,

$$X(1) = 2\lambda \left(\gamma x(1) + y(1)\right) = 2\lambda \gamma R.$$

$$Y(1) = 2\lambda \left(x(1) + \gamma y(1)\right) = 2\lambda R.$$

Thus, when applied to equation (1.12),

$$4\lambda^{2}\gamma^{2}R^{2} + 4\lambda^{2}R^{2} - 2\gamma (2\lambda\gamma R) (2\lambda R) - 4c (1 - \gamma^{2}) (2\lambda\gamma R) +4d (1 - \gamma^{2}) (2\lambda R) + C^{2} + D^{2} + 2\gamma CD = (1 - \gamma^{2})^{2}.$$

$$4\lambda^{2}\gamma^{2}R^{2} + 4\lambda^{2}R^{2} - 8\lambda^{2}\gamma^{2}R^{2} - 8c(1 - \gamma^{2})\lambda\gamma R + 8d(1 - \gamma^{2})\lambda R + C^{2} + D^{2} + 2\gamma CD = (1 - \gamma^{2})^{2}.$$

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Note from above that $C^2 + D^2 + 2\gamma CD = (1 - \gamma^2)^2$, thus

$$4\lambda^2\gamma^2R^2 + 4\lambda^2R^2 - 8\lambda^2\gamma^2R^2 - 8c\left(1 - \gamma^2\right)\lambda\gamma R + 8d\left(1 - \gamma^2\right)\lambda R = 0,$$

which, after dividing through by $4\lambda R$, gives

$$\lambda \gamma^2 R + \lambda R - 2\lambda \gamma^2 R - 2c \left(1 - \gamma^2\right) \gamma + 2d \left(1 - \gamma^2\right) = 0, \qquad \lambda, R \neq 0 \text{ and } \gamma^2 \neq 1$$
$$\lambda R - \lambda \gamma^2 R - 2c \left(1 - \gamma^2\right) \gamma + 2d \left(1 - \gamma^2\right) = 0,$$
$$\lambda R \left(1 - \gamma^2\right) - 2c \left(1 - \gamma^2\right) \gamma + 2d \left(1 - \gamma^2\right) = 0,$$

and dividing through by $(1 - \gamma^2)$, gives

$$\lambda R - 2c\gamma + 2d = 0.$$

Simplifying,

$$\lambda R - 2\left(c\gamma + d\right) = 0,$$

and noting that the quantity $2(c\gamma + d)$ is equal to C, then

$$\lambda R + C = 0.$$

Finally,

$$C = -\lambda R, \quad R > 0, \tag{1.13}$$

as required.

Recall that $C^2 + D^2 + 2\gamma CD = (1 - \gamma^2)^2$ and $C = -\lambda R$, R > 0.

Thus,

$$\lambda^{2}R^{2} + D^{2} + 2\gamma (-\lambda R) D = (1 - \gamma^{2})^{2},$$

$$D^{2} - 2\lambda \gamma RD + \lambda^{2}R^{2} - (1 - \gamma^{2})^{2} = 0.$$

Solving for D in the above quadratic,

$$D = \frac{2\lambda\gamma R \pm \sqrt{4\lambda^2 \gamma^2 R^2 - 4\left(\lambda^2 R^2 - (1 - \gamma^2)^2\right)}}{2},$$

$$D = \lambda\gamma R \pm \sqrt{\lambda^2 \gamma^2 R^2 - \lambda^2 R^2 + (1 - \gamma^2)^2},$$

$$D = \lambda\gamma R \pm \sqrt{\lambda^2 R^2 (\gamma^2 - 1) + (1 - \gamma^2)^2},$$

$$D = \lambda\gamma R \pm \sqrt{-\lambda^2 R^2 (1 - \gamma^2) + (1 - \gamma^2)^2}$$

It is seen that D will always have two real roots if $\gamma^2 > 1$, as in the expression below

$$D = \lambda \gamma R \pm \sqrt{-\lambda^2 R^2 (1 - \gamma^2) + (1 - \gamma^2)^2}$$

 $(1-\gamma^2)^2 > 0$ and $(1-\gamma^2) < 0$ and consequently $-\lambda^2 R^2(1-\gamma^2) > 0$ making the entire quantity inside the radical positive.

Also, if $\gamma^2 < 1$ the $(1 - \gamma^2) > 0$ with $-\lambda^2 R^2 (1 - \gamma^2) < 0$ and the quantity $(1 - \gamma^2)^2 - \lambda^2 R^2 (1 - \gamma^2) > 0$ provided that $\lambda^2 R^2 (1 - \gamma^2) < (1 - \gamma^2)^2$, that is if $\lambda R < \sqrt{(1 - \gamma^2)}$, there will be two real roots of D.

Conversely, if $(1-\gamma^2)^2 - \lambda^2 R^2 (1-\gamma^2) < 0$ then $\lambda^2 R^2 (1-\gamma^2) > (1-\gamma^2)^2$, that is $\lambda R > \sqrt{(1-\gamma^2)}$, there will not be any real solutions of D.

- 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

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

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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 $0 < C(t) \le C_{max}$, and $D(t) \ge 0$ 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

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

(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 $\dot{x} = dx/dt$ 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)

$$\dot{x} = -x - \frac{D}{1+D},$$

$$\dot{x} + x = -\frac{D}{1+D},$$

$$(\dot{x} + x)(1+D) = -D,$$

$$(\dot{x} + x) + D(\dot{x} + x) = -D,$$

$$D(\dot{x} + x) + D = -(\dot{x} + x),$$

$$D(\dot{x} + x + 1) = -\dot{x} - x,$$

$$D = \frac{-\dot{x} - x}{\dot{x} + x + 1}.$$

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

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

consider the following.

The Euler-Lagrange equation is given by

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

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

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

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t} \left(\frac{\partial F}{\partial \dot{x}} \right) = \frac{\mathrm{d}}{\mathrm{d}t} \left(\dot{x} + x + 1 \right)^{-2},$$

$$= -2 \left(\dot{x} + x + 1 \right)^{-3} \left(\ddot{x} + \dot{x} \right),$$

$$= \frac{-2 \left(\ddot{x} + \dot{x} \right)}{\left(\dot{x} + x + 1 \right)^{3}}.$$

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Therefore, the Euler-Lagrange equation is

$$-\frac{2(\ddot{x}+\dot{x})}{(\dot{x}+x+1)^3} - \frac{1}{(\dot{x}+x+1)^2} = 0,$$

$$\frac{2(\ddot{x}+\dot{x})}{(\dot{x}+x+1)^3} = -\frac{1}{(\dot{x}+x+1)^2},$$

$$\frac{2(\ddot{x}+\dot{x})}{(\dot{x}+x+1)} = -1,$$

$$2(\ddot{x}+\dot{x}) = -(\dot{x}+x+1),$$

$$2(\ddot{x}+\dot{x}) + (\dot{x}+x) = -1,$$

$$2\ddot{x}+3\dot{x}+x=-1, \text{ as required.}$$

$$(6.2) \quad \ddot{x} = d^2x/dt^2.$$

(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

$$y_c = c_1 e^{-t} + c_2 e^{-\frac{1}{2}t}$$
, where c_1 and c_2 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:

$$\frac{\mathrm{d}x(t)}{\mathrm{d}t} = \frac{\mathrm{d}}{\mathrm{d}t}(a_1) = 0,$$

and therefore

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

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

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

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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,

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

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

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

From (6.4)

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

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

$$(x_0 + 1) e^{-t_1} - c_2 e^{-t_1} + c_2 e^{-\frac{1}{2}t_1} = x_1 + 1,$$

$$(x_0 + 1) e^{-t_1} + c_2 \left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right) = (x_1 + 1),$$

$$c_2 \left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right) = (x_1 + 1) - (x_0 + 1) e^{-t_1},$$

$$c_2 = \frac{(x_1 + 1) - (x_0 + 1) e^{-t_1}}{\left(e^{-\frac{1}{2}t_1} - e^{-t_1} \right)}.$$

$$(6.7)$$

Substituting for c_2 in (6.6) from (6.7)

$$c_{1} = (x_{0} + 1) - \left[\frac{(x_{1} + 1) - (x_{0} + 1) e^{-t_{1}}}{(e^{-\frac{1}{2}t_{1}} - e^{-t_{1}})} \right],$$

$$c_{1} = \frac{(x_{0} + 1) \left(e^{-\frac{1}{2}t_{1}} - e^{-t_{1}} \right) - (x_{1} + 1) + (x_{0} + 1) e^{-t_{1}}}{(e^{-\frac{1}{2}t_{1}} - e^{-t_{1}})}$$

$$c_{1} = \frac{(x_{0} + 1) e^{-\frac{1}{2}t_{1}} - (x_{0} + 1) e^{-t_{1}} - (x_{1} + 1) + (x_{0} + 1) e^{-t_{1}}}{(e^{-\frac{1}{2}t_{1}} - e^{-t_{1}})}$$

$$c_{1} = \frac{(x_{0} + 1) e^{-\frac{1}{2}t_{1}} - (x_{1} + 1)}{(e^{-\frac{1}{2}t_{1}} - e^{-t_{1}})} = \alpha.$$
(6.8)

Therefore, from (6.4)

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

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

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

as required.