Optimal Control Concepts for Systems

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Systems

Consider

$$
\begin{aligned}
\max_{u} \quad & \int_{t_0}^{t_1} f(t, x_1(t), x_2(t), u_1(t), u_2(t), u_3(t))\, dt \\
\text{subject to} \quad & \\
\frac{dx_1}{dt} &= g_1(t, x_1(t), x_2(t), u_1(t), u_2(t), u_3(t)) \\
\frac{dx_2}{dt} &= g_2(t, x_1(t), x_2(t), u_1(t), u_2(t), u_3(t))
\end{aligned}
$$

$$x_1(t_0) = \alpha, x_2(t_0) = \beta$$

where α and β are fixed.

Notice we have 2 state variables and 3 control variables.

For each state equation, there is one associated adjoint equation.

We consider

$$
\begin{aligned}
H(t, x_1(t), x_2(t), u_1(t), u_2(t), u_3(t), \lambda_1(t), \lambda_2(t)) = \\
f(t, x_1(t), x_2(t), u_1(t), u_2(t), u_3(t)) \\
+\lambda_1(t) g_1(t, x_1(t), x_2(t), u_1(t), u_2(t), u_3(t)) \\
+\lambda_2(t) g_2(t, x_1(t), x_2(t), u_1(t), u_2(t), u_3(t)),
\end{aligned}
$$

then the necessary conditions are

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$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial x_1}, \quad \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial x_2}$$
$$\lambda_1(t_1) = 0, \quad \lambda_2(t_1) = 0$$
$$\frac{\partial H}{du_1} = 0, \quad , \frac{\partial H}{du_2} = 0, \text{ and } \frac{\partial H}{du_3} = 0$$
$$\frac{dx_1}{dt} = \frac{\partial H}{d\lambda_1}, \quad \frac{dx_1}{dt} = \frac{\partial H}{d\lambda_2}$$

REMARK

If each state variable has two conditions (as an initial and a final time condition), then the adjoint variable associated with that state trajectory will have **NO** transversality condition!

Problem 1

$$\begin{aligned}
\min_u J(u) &= \int_0^1 (x_2 + u^2)\, dt \\
\text{subject to } \frac{dx_1}{dt} &= x_2, \frac{dx_2}{dt} = u \\
x_1(0) = x_2(0) &= 0, x_1(1) = 1, x_2(1) \text{ unspecified}
\end{aligned}$$

Here, $H = x_2 + u^2 + \lambda_1 x_2 + \lambda_2 u$. The necessary conditions are as follows:

$$\begin{aligned}
\lambda_1'(t) &= -\frac{\partial H}{\partial x_1} = 0 \\
\lambda_2'(t) &= -\frac{\partial H}{\partial x_2} = -1 - \lambda_1
\end{aligned}$$

with $\lambda_2(1) = 0$ and $\dfrac{\partial H}{\partial u} = 2u + \lambda_2 = 0$. Thus, $u = -\dfrac{\lambda_2}{2}$.

Thus, $\lambda_1(t) = C_1$ where C_1 is a constant.

Also, $\lambda_2(t) = -(1 + C_1)t + C_2$ where $\lambda_2(1) = 0$ gives $C_2 = 1 + C_1$.

Therefore, $\lambda_2(t) = -(1 + C_1)(1 - t)$. Using this and the representation for u in the x_2 differential equation allows us to determine that $x_2(t) = \dfrac{-(1 + C_1)}{2}(t - \dfrac{t^2}{2})$ since $x_2(0) = 0$.

In addition, $x_1(t) = \dfrac{-(1+C_1)}{2}(\dfrac{t^2}{2} - \dfrac{t^3}{6})$ since $x_1(0) = 0$.

Using that $x_1(1) = 1$, we obtain that $C_1 = -7$. Combining all this information, we have the complete representation of the state solution pair, adjoint solution pair, and the optimal control.

$$\begin{aligned} x_1(t) &= \frac{3}{2}t^2 - \frac{1}{2}t^3 \\ x_2(t) &= 3t - \frac{3}{2}t^2 \\ \lambda_1(t) &= -7 \\ \lambda_2(t) &= -6 + 6t \\ u(t) &= 3 - 3t \end{aligned}$$

<u>**Problem for You**</u>

$$\min_u J(u) = \int_0^5 (x_1(t) + \frac{1}{2}u^2(t))\,dt$$

subject to

$$\frac{dx_1}{dt} = x_2(t), \frac{dx_2}{dt} = -x_2(t) + u(t)$$

with $x_1(0) = 2$, and $x_2(0) = 1$.

Optimal Control Related To Immunotherapy

The goal is to maximize the functional below over a class of piecewise continuous controls ,$u(t)$, subject to three ordinary differential equations that describe the interaction of the

- **effector (activated immune system) cells - x(t)**,
- **tumor cells - y(t)**,
- and the **interleukin-2 (IL-2) cells in the single tumor site - z(t)**.

The differential equations(state system) are

$$\frac{dx}{dt} = cy - \mu_2 x + \frac{p_1 x z}{g_1 + z} + u(t) s_1 \quad (1)$$

$$\frac{dy}{dt} = r_2 y(1 - by) - \frac{axy}{g_2 + y} \quad (2)$$

$$\frac{dz}{dt} = \frac{p_2 x y}{g_3 + y} - \mu_3 z \quad (3)$$

with initial conditions
$x(0) = 1$, $y(0) = 1$, and $z(0) = 1$.

Table 1. Parameter values

Eq.(2)	$0 \leq c \leq 0.05$	$\mu_2 = 0.03$	$p_1 = 0.1245$	$g_1 = 2x10^7$
Eq.(3)	$g_2 = 1x10^5$	$r_2 = 0.18$	$b = 1x10^{-9}$	a=1
Eq.(4)	$\mu_3 = 10$	$p_2 = 5$	$g_3 = 1x10^3$	0

$$U = \{u(t) \text{ piecewise continuous} | 0 \leq u(t) \leq 1, \forall t \in [0, T]\} \quad (4)$$

$$J(u) = \int_0^T [x(t) - y(t) + z(t) - \frac{B}{2}(u(t))^2] dt \quad (5)$$

The basic framework of this problem is to prove the following:

- the existence of the optimal control and uniqueness of the optimality system (state system coupled with the adjoint system)
- and the characterization of the optimal control.

Existence

Theorem 1 *Given the objective functional,* $J(u) = \int_0^T [x(t) - y(t) + z(t) - \frac{1}{2}B(u(t))^2]dt$, *where* $U = \{u(t)$ *piecewise continuous* $\mid 0 \leq u(t) \leq 1\ \forall t \in [0,T]\}$ *subject to Eq. (1) , (2), (3) with* $x(0) = 1$, $y(0) = 1$, *and* $z(0) = 1$, *then there exists an optimal control* u^* *such that* $\max_{0 \leq u \leq 1} J(u) = J(u*)$ *if the following conditions are met.*

1. *The class of all initial conditions with a control u in the admissible control set along with each state equation being satisfied is not empty.*
2. *The admissible control set U is closed and convex.*
3. *Each right hand side of Eq. (1), (2), (3) is continuous, is bounded above by a sum of the bounded control and the state, and can be written as a linear function of u with coefficients depending on time and the state.*
4. *The integrand of J(u) is concave on U and is bounded above by* $c_2 - c_1 u^2$ *with* $c_1 > 0$.

Proof. For the third condition,the system is bilinear in the control and can be rewritten as

$$\overrightarrow{f}(t, \overrightarrow{X}, u) = \overrightarrow{\alpha}(t, \overrightarrow{X}) + s_1 u \qquad (6)$$

where $\overrightarrow{X} = (x, y, z)$ and $\overrightarrow{\alpha}$ is a vector valued function of $\overrightarrow{X}$.

Using that the solutions are bounded, we see that

$$\left[\left|\vec{f}(t, \vec{X}, u)\right| \leq \left| \begin{pmatrix} p_1 & c & 0 \\ 0 & r_2 & 0 \\ p_2 & 0 & 0 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \end{pmatrix} \right| + \left| \begin{pmatrix} s_1 u \\ 0 \\ 0 \end{pmatrix} \right| \leq C_1 \left|\vec{X}\right| + s_1 \left|u\right| \right]$$

where C_1 depends on the coefficients on the system.

For the last condition, J is concave on U and

$$\begin{aligned} x(t) - y(t) + z(t) - \frac{B}{2}\ [u(t)]^2 &\leq x(t) + z(t) - \frac{B}{2}[u(t)]^2 \\ &\leq \quad C_2 - C_1 \mid u(t) \mid^2 . \end{aligned}$$

Characterization

Here, we discuss the theorem that relates to the characterization of the optimal control. This technique relates to the concept of Lagrange multipliers studied in calculus.

$$\begin{aligned} L(x, \quad y &, z, u, \lambda_1, \lambda_2, \lambda_3, w_1, w_2) \\ &= x(t) - y(t) + z(t) - \frac{B}{2}(u(t))^2 + \lambda_1 \left(cy - \mu_2 x + \frac{p_1 x z}{g_1 + z} + u(t) s_1 \right) \\ &+ \lambda_2 \left(r_2 y(1 - by) - \frac{axy}{g_2 + y} \right) + \lambda_3 \left(\frac{p_2 x y}{g_3 + y} - \mu_3 z \right) \\ &+ w_1(t) u(t) + w_2(t) \left(1 - u(t)\right) \end{aligned}$$

where $w_1(t) \geq 0$, $w_2(t) \geq 0$ are penalty multipliers satisfying

$$w_1(t) u(t) = 0, \qquad w_2(t) \left(1 - u(t)\right) = 0$$

at the optimal u^*.

Theorem 2 *Given an optimal control u^* and solutions of the corresponding state system, there exist adjoint variables λ_i for $i = 1, 2, 3$ satisfying the following:*

$$
\begin{aligned}
\frac{d\lambda_1}{dt} = -\frac{\partial L}{\partial x} &= -[1 + \lambda_1(-\mu_2 + \frac{p_1 x z}{g_1 + z}) \\
&- \lambda_2 \frac{ay}{g_2 + y} + \lambda_3 \frac{p_2 y}{g_3 + y}] \\
\frac{d\lambda_2}{dt} = -\frac{\partial L}{\partial y} &= -[-1 + \lambda_1 c - \lambda_2(r_2 - 2r_2 b y) \\
&- \lambda_2 \frac{g_2 a x}{(g_2 + y)^2} + \lambda_3 \frac{g_3 p_2 x}{(g_3 + y)^2}] \\
\frac{d\lambda_3}{dt} = -\frac{\partial L}{\partial z} &= -[1 + \lambda_1 \frac{g_1 p_1 x}{(g_1 + z)^2} - \lambda_3 \mu_3]
\end{aligned}
$$

where $\lambda_i(T) = 0$ for i=1, 2, 3. Further, u^* can be represented by

$$
u^* = \min\left(1, \left(\frac{\lambda_1 s_1}{B}\right)^+\right).
$$

Sketch of the proof

As in calculus, to determine the interior maximum for our Lagrangian, we take the partial derivative of L with respect to u and set it equal to zero.

$$\frac{\partial L}{\partial u} = 0$$

Upon simplification we have

$$u^*(t) = \frac{\lambda_1 s_1 + w_1(t) - w_2(t)}{B} \tag{7}$$

(i) On the set $\{t|0 < u^*(t) < 1\}$, $w_1(t) = 0 = w_2(t)$. From equation (7),
$u^*(t) = \dfrac{\lambda_1 s_1}{B}$.

(ii) On the set $\{t|u^*(t) = 1\}$, $w_1(t) = 0$. Consequently,

$$1 = u^*(t) = \frac{\lambda_1 s_1 - w_2(t)}{B}$$

or $1 + \dfrac{w_2(t)}{B} = \dfrac{\lambda_1 s_1}{B}$.

Since $w_2(t) \geq 0$, then $1 + \dfrac{w_2(t)}{B} \geq 1$. Thus, $1 = u^* \leq \dfrac{\lambda_1 s_1}{B}$.

(iii) On the set $\{t|u^*(t) = 0\}$, $w_2(t) = 0$. From equation 7, we have

$$0 = u^*(t) = \frac{\lambda_1 s_1 + w_1(t)}{b}.$$

Since $w_1(t) \geq 0$, then $\lambda_1 s_1 \leq 0$.

Notice $\left(\frac{\lambda_1 s_1}{B}\right)^+ = 0 = u^*(t)$ in this case.

Combining all three cases in a compact form gives

$$u^*(t) = \min\left(1, \left(\frac{\lambda_1 s_1}{B}\right)^+\right) \tag{8}$$

Optimality System

Incorporating the representation of the optimal treatment control, we have the state system coupled with the adjoint system below.

$$
\begin{aligned}
\frac{dx}{dt} &= cy - \mu_2 x + \frac{p_1 x z}{g_1 + z} + (\min\left(1, \left(\frac{\lambda_1 s_1}{B}\right)^{+}\right)) s_1 \\
\frac{dy}{dt} &= r_2 y(1 - by) - \frac{axy}{g_2 + y} \\
\frac{dz}{dt} &= \frac{p_2 xy}{g_3 + y} - \mu_3 z \\
\frac{d\lambda_1}{dt} &= -[1 + \lambda_1(-\mu_2 + \frac{p_1 x z}{g_1 + z}) \\
&- \lambda_2 \frac{ay}{g_2 + y} + \lambda_3 \frac{p_2 y}{g_3 + y}] \\
\frac{d\lambda_2}{dt} &= -[-1 + \lambda_1 c - \lambda_2(r_2 - 2r_2 by) \\
&- \lambda_2 \frac{g_2 a x}{(g_2 + y)^2} + \lambda_3 \frac{g_3 p_2 x}{(g_3 + y)^2}] \\
\frac{d\lambda_3}{dt} &= -[1 + \lambda_1 \frac{g_1 p_1 x}{(g_1 + z)^2} - \lambda_3 \mu_3]
\end{aligned}
$$

with $x(0) = 1$, $y(0) = 1$, $z(0) = 1$, $\lambda_i(T) = 0$ for

$i = 1, 2, 3.$

Uniqueness

Since the state system moves forward in time and the adjoint system moves backward in time, we have a small challenge with uniqueness.

Theorem 3 *For T sufficiently small, the solution to the optimality system is unique.*

Sketch. We suppose that (x,y,z,λ_1,λ_2,λ_3) and ($\bar{x}$,$\bar{y}$,$\bar{z}$,$\bar{\lambda}_1$,$\bar{\lambda}_2$,$\bar{\lambda}_3$) are two distinct solutions to the optimality system.

Let $m > 0$ be chosen such that $x = e^{mt}h$, $y = e^{mt}q$, $z = e^{mt}f$, $\lambda_1 = e^{-mt}w$, $\lambda_2 = e^{-mt}v$, $\lambda_3 = e^{-mt}j$, $\bar{x} = e^{mt}\bar{h}$, $\bar{y} = e^{mt}\bar{q}$, $\bar{z} = e^{mt}\bar{f}$, $\bar{\lambda}_1 = e^{-mt}\bar{w}$, $\bar{\lambda}_2 = e^{-mt}\bar{v}$, and $\bar{\lambda}_3 = e^{-mt}\bar{j}$. In addition,

$$u = \min\left(1, \left(\frac{e^{-mt}ws_1}{B}\right)^+\right) \tag{9}$$

and

$$\bar{u} = \min\left(1, \left(\frac{e^{-mt}\bar{w}s_1}{B}\right)^+\right). \tag{10}$$

Substitution of $z = e^{mt}f$ and $\lambda_3 = e^{-mt}j$ into the third and the sixth differential equation of the optimality system yields the following where $\cdot = \frac{d}{.dt}$

$$\begin{aligned}\dot{f} + mf &= \frac{p_2 hqe^{mt}}{g_3 + qe^{mt}} - \mu_3 f \\ \dot{j} - mj &= -e^{mt} - \frac{wp_1 hg_1 e^{mt}}{(g_1 + fe^{mt})^2} - j\mu_3\end{aligned}$$

Example of an estimate...

$$\begin{aligned}\int_0^T (j - \bar{j})(\; \bar{f}^2 \; wh - f^2 \bar{w}\bar{h})dt \leq \int_0^T \bar{f}^2(wh - \bar{w}\bar{h})(j - \bar{j})dt \\ &+ \int_0^T \bar{w}\bar{h}(f^2 - \bar{f}^2)(j - \bar{j})dt \\ &\leq M_1^2 \int_0^T (j - \bar{j})(wh - \bar{w}\bar{h})dt \\ &+ 2M_7 M_2 M_1 \int_0^T (j - \bar{j})(f - \bar{f})dt \\ &\leq \frac{M_1^2 M_7}{2} \int_0^T (h - \bar{h})^2 dt + \frac{M_1^2 M_2}{2} \int_0^T (w - \bar{w})^2 dt \\ &+ \frac{M_1^2 M_7 + M_1^2 M_2 + 2M_7 M_2 M_1}{2} \int_0^T (j - \bar{j})^2 dt \\ &+ M_7 M_2 M_1 \int_0^T (f - \bar{f})^2 dt\end{aligned}$$

where M_1, M_7, M_2 are the upper bounds for $\bar{f}, \bar{w}, \bar{h}$ respectively.

Using the nonnegativity of the variable expressions evaluated at the initial and the final time and simplifying, the inequality is reduced to the following:

$$(m - D_1 - \tilde{C}e^{3mT})\int_0^T[(h-\bar{h})^2 + (q-\bar{q})^2 dt$$
$$+ \int_0^T (f-\bar{f})^2 + (w-\bar{w})^2 + (v-\bar{v})^2 + (j-\bar{j})^2]dt \leq 0$$

where $D_1, \tilde{C}$ depend on all coefficients and bounds on all solution variables.

We choose m such that $m - D_1 - \tilde{C}e^{3mT} > 0$. Since the natural logarithm is an increasing function, then

$$ln\left(\frac{m-D_1}{\tilde{C}}\right) > 3mT \tag{11}$$

if $m > \tilde{C} + D_1$. Thus, this gives that $T < \frac{1}{3m} ln\left(\frac{m-D_1}{\tilde{C}}\right)$.

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