

**Authorized documents** : lecture notes and personal notes of this course.

Arguments should be concise and stated carefully, without neglecting partial answers.

**Problem 1 (Ensta and Master students) : Cell growth control**

Consider the state equation

$$\dot{x}(t) = A(x(t)) - au(t)x(t), \quad t \in (0, T); \quad x(0) = x_0 > 0. \quad (1)$$

Here  $x(t) \in \mathbb{R}$  is the number of cells,  $u(t)$  is the drug concentration,  $a > 0$ ,  $x_0 > 0$  and  $T > 0$  are given,  $A : \mathbb{R} \rightarrow \mathbb{R}$  is of class  $C^\infty$ , *increasing and strictly concave*, and  $A(0) = 0$ . The control constraint is that, for some  $u_M > 0$  :

$$u(t) \in [0, u_M], \quad \text{for a.a. } t \in (0, T). \quad (2)$$

We minimize the cost  $x(T)$ , and admit that  $x(t) > 0$  for all  $t \in (0, T)$ .

- 1/ Give the expression of the pre-Hamiltonian and of the costate equation, and show that  $\beta = 1$ .

ANSWER:  $H = p(A(x) - aux)$ . The costate equation is

$$-\dot{p}(t) = (A'(x) - au)p; \quad p(T) = \beta. \quad (3)$$

Necessarily  $\beta = 1$  since there is no final state constraint.

- 2/ Show that  $p(t) > 0$  for all  $t \in (0, T)$ .

ANSWER:

Since  $\beta = 1$ ,  $p(T) = 1$ . If  $p(t_0) = 0$  for some  $t_0$ , then  $p(t) = 0$  for all  $t$  by (3), which is impossible since  $p(T) = 1$ . Since  $p$  is continuous it may therefore have only positive values.

- 3/ Show that the optimal control is  $\bar{u}(t) = u_M$ , for all  $t \in (0, T)$ .

ANSWER: For all  $t \in (0, T)$ , since  $x(t) > 0$  and  $p(t) > 0$ ,  $\bar{H}_u(t) = -ax(t)p(t) < 0$ . By the Hamiltonian inequality, the optimal control is almost always equal to its upper bound.

- 4/ We introduce the additional constraint  $\int_0^T u(t)dt \leq Z_T$  for some given  $Z_T > 0$ . Show that this is equivalent to introduce an additional state variable  $\zeta$  and the additional final state constraint as follows :

$$\dot{\zeta}(t) = u(t), \quad t \in (0, T); \quad \zeta(0) = 0, \quad \zeta(T) \leq Z_T. \quad (4)$$

ANSWER: *Obvious.*

- 5/ Denoting by  $p$ ,  $q$  the costates associated with the states  $x$ ,  $\zeta$ , and by  $\Psi$  the multiplier associated with the final state constraint. Give the expression of the pre-Hamiltonian and costate equations of this problem.

ANSWER:

$$H(\beta, u, x, \zeta, p, q) = p(A(x) - aux) + qu. \quad (5)$$

$$-\dot{p}(t) = (A'(x) - au)p; \text{ for a.a. } t \in (0, T), \quad p(T) = \beta, \quad (6)$$

$$-\dot{q}(t) = 0, \text{ for a.a. } t \in (0, T), \quad q(T) = \Psi. \quad (7)$$

6/ Show that

$$\beta + \Psi > 0; \quad q(t) = \Psi, \quad t \in (0, T); \quad \Psi \geq 0; \quad \Psi(\zeta(T) - Z_T) = 0. \quad (8)$$

ANSWER: *Immediate consequence of the PMP.*

7/ Assuming that  $\Psi = 0$ , give the expression of the optimal control.

ANSWER: *Necessarily  $\beta = 1$  and  $q(t) = 0$  for all  $t$ , so that (by the same arguments as before)  $\bar{H}_u(t) = -ax(t)p(t) < 0$ , and so, again,  $u(t) = u_M$  for a.a.  $t$ .*

8/ Show that  $\beta = 0$  is impossible.

ANSWER: *We would have for all  $t$ ,  $p(t) = 0$  and  $q(t) = \Psi > 0$ , so that  $\bar{H}_u(t) = \Psi > 0$ , so that  $u(t) = 0$  for a.a.  $t$ . But then  $\zeta(T) = 0 < Z_T$ , so that  $\Psi = 0$ , which is a contradiction.*

9/ Deduce from the strict concavity of  $A(x)$  that, for all  $x > 0$ ,  $A(x) > A'(x)x$ .

ANSWER: *By the mean value theorem, since  $A(0) = 0$ ,  $A(x) = A'(y)x$  with  $y \in (0, x)$ . Since  $A$  is strictly concave,  $A'(y) > A'(x)$ . The conclusion follows.*

10/ In the sequel we assume that  $\Psi > 0$ . Show that  $\bar{H}_u(t)$  is monotone, i.e., either nondecreasing or nonincreasing [HINT : COMPUTE ITS TIME DERIVATIVE]. Deduce the expression of the optimal control.

ANSWER: *Since  $\beta = 1$ , by the same arguments as before,  $p(t) > 0$  for all  $t$ . Since  $\bar{H}_u(t) = q(t) - ax(t)p(t) = \Psi - ax(t)p(t)$ , we have that, skipping time arguments :*

$$\frac{1}{a} \dot{\bar{H}}_u = -\frac{d}{dt}(xp) = -p(A(x) - aux) + xp(A'(x) - au) = -p(A(x) - A'(x)x) < 0. \quad (9)$$

*So,  $\bar{H}_u(t)$  is decreasing. If its sign is constant, since  $\Psi > 0$ , the final state constraint is active so that  $\bar{H}_u(t) < 0$  for all  $t \in (0, T)$  and the control has always its maximal value; this can happen only if  $Z_T = Tu_M$ . Otherwise,  $Z_T < Tu_M$  (since the final state constraint is active), and  $\bar{H}_u(t)$  has at most one change of sign at some time  $\tau \in (0, T)$ . Then  $\bar{u}(t) = 0$  if  $t < \tau$ , and  $\bar{u}(t) = u_M$  if  $t > \tau$ . Observe that  $\tau$  is determined by the relation  $(T - \tau)u_M = Z_T$ .*

## Problem 2 (Master students) : Cell growth control with state constraints

The model is the same as before, with an additional state constraint : minimize  $x(T)$  subject to

$$\dot{x}(t) = A(x(t)) - au(t)x(t), \quad t \in (0, T); \quad x(0) = x_0 > 0, \quad (10)$$

$$\dot{\zeta}(t) = u(t) \in [0, u_M], \quad t \in (0, T); \quad \zeta(0) = 0, \quad (11)$$

with the running and final constraint

$$x(t) \leq x_M; \quad t \in (0, T); \quad \zeta(T) \leq Z_M. \quad (12)$$

We assume that  $x_0 < x_M$  and  $Z_M > 0$ .

1/ Give the expression of the pre-Hamiltonian and costate equation.

ANSWER: As before,  $H = p(A(x) - aux) + qu$ . The costate equation is

$$-dp(t) = H_x dt + d\mu(t) = (A'(x(t)) - au(t))p(t)dt + d\mu(t); \quad p(T) = \beta, \quad (13)$$

$$-\dot{q}(t) = H_\zeta = 0; \quad q(T) = \Psi. \quad (14)$$

2/ Check that  $p(t) \geq 0$ , for all  $t \in [0, T)$ , with strict inequality if  $\beta = 1$ . [HINT : CHECK THAT  $dp(t) \leq c|p(t)|dt$ , FOR SOME  $c > 0$ ].

ANSWER: Observe that

$$dp(t) = -(A'(x(t)) - au(t))p(t)dt - d\mu(t) \leq -(A'(x(t)) - au(t))p(t)dt \leq c|p(t)|dt, \quad (15)$$

for some  $c > 0$ . Now assume that  $p(t_0) < 0$ , with  $t_0 \in [0, T)$ . Let

$$t_1 := \sup\{t' \geq t_0; p(t) \leq 0 \text{ over } (t_0, t')\}. \quad (16)$$

Since the jumps of  $p$  are nonpositive,  $p(t_1^+) \leq 0$ , and as long as  $p(t) \leq 0$ , we have that  $dp(t) \leq -cp(t)dt$ , so that necessarily  $t_1 = T$  and  $p(T) \leq e^{c(t_0-T)}p(t_0) < 0$ . This contradicts the final condition on  $p$ . If  $\beta > 0$  we obtain a contradiction by the same arguments when assuming that  $p(t_0) \leq 0$ , with  $t_0 \in [0, T)$ .

3/ Compute the optimal control in the case when  $\Psi = 0$ .

ANSWER: By the above results, for a.a.  $t$ ,  $\bar{H}_u(t) < 0$  and so,  $u(t) = u_M$ . This is feasible, and optimal, iff  $Z_M \geq Tu_M$ .

4/ In the sequel we assume that the state constraint becomes active for the first time at time  $t_1 \in (0, T)$ , that  $\beta = 1$ , and that

$$A(x_M) - au_M x_M < 0, \quad (17)$$

meaning that the state constraint cannot remain active when the control is maximal. Show that, over  $(0, t_1)$ ,  $\bar{H}_u(t)$  is monotonic, with positive values, and that the control is a.e. equal to 0.

ANSWER: By the same arguments as for problem 1 (without state constraints),  $\bar{H}_u(t)$  is decreasing over  $(0, t_1)$ , and if it has negative values over a non negligible subset of  $(0, t_1)$ , then the control is maximal over  $(t_1 - \varepsilon, t_1)$  for some  $\varepsilon > 0$ . Then, by (17), the state constraint cannot be active near  $t_1$ , which gives a contradiction.

5/ Let  $t_2$  be the minimal time for which  $x(t) < x_M$ , for all  $t \in (t_2, T]$ . Show that  $u(t) = u_M$  over  $(t_2, T)$ .

ANSWER: Same type of argument : over  $(t_2, T)$ ,  $\bar{H}_u(t)$  is decreasing since the state constraint is not active. If it had positive values over  $(t_2, t_2 + \varepsilon)$  for some  $\varepsilon > 0$ , then over  $(t_2, t_2 + \varepsilon)$  the control would have zero value, and therefore the state constraint would be violated. So, over  $(t_2, T)$ ,  $\bar{H}_u(t)$  has negative values and the conclusion follows with the Hamiltonian inequality.

6/ Show that the state constraint is active over  $[t_1, t_2]$ . [HINT : ASSUME THE CONTRARY AND DEDUCE A CONTRADICTION BASED ON THE ANALYSIS OF PROBLEM 1.]

ANSWER: If the state constraint is not active at  $t_0 \in (t_1, t_2)$ , it is not active over a maximal interval  $(t', t'')$  such that  $t_1 \leq t' < t_0 < t'' \leq t_2$ . By the analysis of problem 1, over  $(t', t'')$ ,

the control is first minimal then maximal with possibly one of these two phases empty. But since necessarily the state constraint is active at times  $t'$  and  $t''$ , a firstly minimal control would violate the state constraint for some  $t > t'$  since  $A(x) > 0$  when  $x > 0$ , and a maximal control for  $t < t''$  close to  $t''$  would contradict  $x(t'') = x_M$  in view of (17). The conclusion follows.

7/ Explain how to compute  $t_1$  and  $t_2$ , and the control over  $(t_1, t_2)$ .

ANSWER: The time  $t_1$  is the unique one for which the solution of the ODE  $\dot{x}(t) = A(x(t))$ , with initial condition  $x(0) = x_0$  takes value  $x_M$ . Over  $(t_1, t_2)$ , we have that  $0 = \dot{x}(t) = A(x_M) - aux_M$  so that the control has the constant value  $u_c := A(x_M)/(ax_M)$ . Then, by the final state constraint

$$u_c(t_2 - t_1) + u_M(T - t_2) = Z_M, \quad (18)$$

which gives  $t_2$  as function of  $t_1$  (well defined since, by our hypotheses,  $u_c < u_M$ ).

8/ Show that, over  $(t_1, t_2)$ ,  $p$  is constant, and  $\mu$  is affine.

ANSWER: Over  $(t_1, t_2)$  we must have  $0 = \bar{H}_u(t) = \Psi - ax_M p(t)$ , so that  $p(t) = p_c := \Psi/(ax_M)$ . Then by the costate equation

$$0 = dp(t) = (A'(x_M) - au_c)p_c dt + d\mu(t). \quad (19)$$

The conclusion follows.

9/ Do  $p$  and  $\mu$  have jumps at time  $t_1$  and  $t_2$ ?

ANSWER: Since  $\mu$  is nondecreasing, and  $p$  and  $\mu$  have jumps of opposite value, the jumps of  $p$  are negative. If  $p$  had a jump at time  $t_1$ , we would have

$$[H_u(t_1)] = -ax(t_1)[p(t_1)] > 0. \quad (20)$$

Since  $H_u(t) = 0$  over  $(t_1, t_2)$ , this would imply, for  $t < t_1$  close to  $t_1$ ,  $H_u(t) < 0$  and therefore  $u(t) = u_M$  which gives a contradiction with the previous results. By a similar argument at time  $t_2$  we show that  $\mu$  and  $p$  have no jump.

NOTA : it easily follows that  $\mu$  and  $p$  have essentially bounded derivatives.