On the Periodic Gain of the Ribosome Flow Model

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1 Introduction

The Ribosome Flow Model (RFM) model is a deterministic model of translation with n sites [1, 2], It is a mean-field approximation of a standard model for translation elogation Totally Asymmetric Simple Exclusion Process (TASEP) [3, 4]. The model can be written as follows:

$$\begin{aligned}
\dot{x}_1 &= \lambda_0(1-x_1(t)) - \lambda_1 x_1(t)(1-x_2(t)) \\
\dot{x}_k &= \lambda_{i-1}x_{k-1}(t)(1-x_k(t)) - \lambda_1 x_k(t)(1-x_{k+1}(t)), \qquad 1<k<n \\
\dot{x}_n &= \lambda_{n-1}x_{n-1}(t)(1-x_n(t)) - \lambda_n x_n(t)
\end{aligned} \tag{1}$$

where $x(t)$ is the occupancy vector $x(t) = [x_1(t), x_2(t)), \ldots, x_n(t))]$, and where all the $\lambda_0, \lambda_1, \ldots, \lambda_n \geq 0$ are nonnegative. Notice that the box $[0,1]^n$ is forward-invariant.

The system with constant flow rates was previously studied and analyzed. There exists a unique equilibrium point and every trajectory convereges to it [5]. This work studies an RFM with time-varying periodic functions for the $\lambda_0(t), \lambda_1(t), \ldots, \lambda_n(t) \geq 0$ rates. Our motivation is to optimize the periodic flow rate functions to maximize the RFM flow for a given set of average flow rates.

In the following sections, we write the problem in optimal control format and prove that the optimal rate for Ribosome Flow Model (RFM) with a signle stage is constant, using Pontryagin Maximum Principle (PMP).

2 Problem Formulation

Consider the following differential equation as a model of the 1-stage (scalar) RFM $x(t)$ as the ribosome occupancy, with periodic inflow $\lambda_0(t) = \lambda_0(t+T)$ with period T and constant

outflow λ_1.

$$\dot{x} = \lambda_0(t)(1-x) - \lambda_1 x \tag{2}$$

For the above SISO system, the input is inflow rate $\lambda_0(t)$ and the output is out-flow $y(t) = \lambda_1 x$. It has been shown that $x(t)$ of this system converges to a periodic trajectory [6]. The L_1 DC gain is:

$$G = \frac{\int_0^T |y(t)|dt}{\int_0^T |\lambda_0(t)|dt} \tag{3}$$

Now, the problem is to maximize the gain G. This can also be stated as maximizing $\frac{1}{T}\int_0^T \lambda_1 x(t)dt$ over inputs $\lambda_0(t)$ in the set of periodic signals with a given average $\bar{\lambda}_0$, i.e. $(\lambda_0(t) \in S_{\bar{\lambda}_0})$, where:

$$S_{\bar{\lambda}_0} = \left\{ \lambda_0(t) \left| \frac{1}{T}\int_0^T \lambda_0 dt = \bar{\lambda}_0 \right. \right\} \tag{4}$$

3 Optimal Control and Pontryagin Principle

3.1 Optimal Control Formulation

Cosinder the following single state system:

$$\dot{x} = \lambda_0(t)(1-x(t)) - \lambda_1 x(t). \tag{5}$$

Let $\lambda_0(t) : \mathbb{R}_{\geq 0} \to \mathbb{R}_{>0}$ be a measurable signal with a period $T > 0$, i.e, $\lambda_0(t) = \lambda_0(t+T) > 0$, and let $\lambda_1 > 0$ be a constant.

Let $\varphi(t; x(0), \lambda_0(t))$ be the solution of (5) for a given inflow rate and an initial condition (which exists and is unique by Carathéodory conditions [7]). Since the system is contractive, then the solution of (5) entrains to the periodic input, i.e, it converges to a periodic trajectory with a period T [6]. Let $x(t) := \varphi^*(t; \lambda_0)$ be the limit trajectory.

The problem in the last section can be understood as maximizing the average flow, i.e $y(t) = \lambda_1 x(t)$, over the set of inputs with a given average.

In order to write this as an optimal control probem, we consider optimizing the following cost functional over the compact interval $[0, T]$:

$$J(\lambda_0(t)) = \frac{1}{T}\int_0^T \lambda_1 x(t)dt. \tag{6}$$

In order to enforce the periodicity condition, we impose the constraint $x(0) = x(T)$. The set of admissible controls is the set of measurable signals $\lambda_0(t)$ over the interval $[0, T]$ with a given average $\bar{\lambda}_0$ and which satisfy $\lambda_0(t) \in [0, L]$ for some upper bound $L > 0$. The periodic extention of a signal can be defined as $\lambda_0(t) = \lambda(t - mT)$, where $m = \lfloor \frac{t}{mT} \rfloor$, $t \geq 0$.

Hence, we write the extended system as:

$$\dot{z} = \begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = f(z) + g(z)\lambda_0(t) = \begin{bmatrix} -\lambda_1 z_1(t) \\ 0 \end{bmatrix} + \begin{bmatrix} 1 - z_1(t) \\ 1 \end{bmatrix} \lambda_0(t), \tag{7}$$

where $z_1(t) := x(t)$, and with the following boundary conditions:

$$z_1(0) = z_1(T),\ z_2(0) = 0,\ z_2(T) = T\bar{\lambda}_0. \tag{8}$$

For a given $L > 0$, the optimal control problem can be stated as follow:

Problem 1. *Find $\lambda_0(t) : [0, T] \to [0, L]$ that maximizes the cost functional* (6) *subject to the ODE* (7) *and the boundary conditions* (8).

Note that Problem 1 is a nonlinear optimal control problem since it has a bilinear term containing the state and control.

The first main result is the following:

Theorem 1. *The signal that solves Problem 1 with $L = 2\bar{\lambda}_0$ is:*

$$\lambda_0(t) \equiv \bar{\lambda}_0, t \in [0, T], \tag{9}$$

and optimal cost is:

$$J(\lambda_0^*(t)) = \frac{\lambda_1 \bar{\lambda}_0}{\lambda_1 + \bar{\lambda}_0}. \tag{10}$$

Hence, the throughput of the system can not be improved by using periodic time-varying inflows. The proof of Theorem 1 will be presented in Section 4.

3.2 Pontryagin's Maximum Principle with periodic inputs

The Pontryagin Maximum Principle (PMP) is a well-known necessary condition for the optimality of control signals [8],[9],[10]. However, Problem 1 has a non-standard boundary condition $z_1(0) = z_2(T)$. Nevertheless, we can use a modified transversality condition to state the PMP. First, we need to define the Hamiltonian associated with the system as:

$$\mathcal{H}(\lambda_0, x, p, p_0) = p(t)^T(f(z(t))+g(z(t))u(t))+p_0\tfrac{\lambda_1}{T}z_1(t) = (-p_1\lambda_1+p_0\tfrac{\lambda_1}{T})z_1+(p_1(1-z_1)+p_2)\lambda_0(t), \tag{11}$$

where $p(t) \in \mathbb{R}^2$ is the costate, and $p_0 \geq 0$ is called the abonormal multiplier.

For Problem 1, the maximum principle can be state as:

Proposition 2 (The Maximum Principle)**.** *Let $\lambda_0^*(t) : [0, T] \to [0, L]$ be an optimal control for Problem 1. Let $z^* : [0, T] \to [0, 1] \times R$ be the corresponding optimal state trajectory. Let $p_0^* = T/\lambda_1$. Then, there exists a function $p^* : [0, T] \to \mathbb{R}^2$ with $p^*(t) \neq 0$ for all $t \in [0, T]$, and satisfying:*

1. *The solution $z^*(t)$ and $p^*(t)$ satisfiy:*

$$\dot{z}^* = \frac{\partial \mathcal{H}}{\partial p}, \tag{12}$$

$$\dot{p}^* = -\frac{\partial \mathcal{H}}{\partial x}, \tag{13}$$

where $\mathcal{H}$ is given by (11) *with the boundary conditions* (8).

2. *The control $\lambda_0^*(t)$ is optimal for all $t \in [0, T]$ while fixing z^*, p^*, i.e,*

$$\mathcal{H}(\lambda, z^*(t), p^*(t)) \leq \mathcal{H}(\lambda_0^*(t), z^*(t), p^*(t)) \tag{14}$$

for all $t \in [0, T]$ and $\lambda \in [0, L]$.

3. *The costate variable statisfies the following transversality condition:*

$$p_1(0) = p_1(T). \tag{15}$$

Proof. We need to prove the transversality condition and that the abnormal multiplier is nonzero.

For the transversality condition, we utilize a result from [9] that allows for arbitrary initial sets. Let $S \subset \mathbb{R}^4$ be an *initial set*, and have the following constraint:

$$z' := \begin{bmatrix} z(0) \\ z(T) \end{bmatrix} \in S.$$

Then transversality condition for the PMP can be stated as:

$$\begin{bmatrix} p(0) \\ -p(T) \end{bmatrix} \perp \mathcal{T}_{z'} S,$$

where $\mathcal{T}_{z'} S$ is the tanget space of S at z'.
In our case, $S = \{z \in \mathbb{R}^4 | z_1 - z_3 = 0, z_2 = 0, z_4 = T\bar{\lambda}_0\}$. Hence, $T_z S = \text{span}\{[1, 0, 1, 0]^T\}$. Therefore, it is necessary that $p_1^*(0) = p_1^*(T)$.

Next, we show that abnormal multipier can not vanish. For the sake of contradiction, assume $p_0 = 0$. Hence, (13) implies that $\dot{p}_1 = p_1(\lambda_1 + \lambda_0^*(t)) - p_0^*(\lambda_1/T)$. Therefore,:

$$\dot{p}_1 = (\lambda_1 + \lambda_0(t))p_1,$$

which is separable. Hence, integrating we get $\ln(p_1(T)) - \ln(p_1(0)) = \int_0^T (\lambda_1 + \lambda_0(t))dt$. Using the transversality condition derived above this implies that $\int_0^T \lambda_0(t)dt = -\lambda_1 < 0$ which contradicts the fact that $\lambda_0(t) > 0$. Hence, p_0^* can not vanish. Assume now that a pair $(p^*(t), p_0^*) \neq 0$ exists with $p_0^* \neq 0$ that satisfies the PMP. Then, $(p^*(t)/(p_0^*\lambda_1/T), T/\lambda_1)$ also satisfies the PMP. Hence, we can state the PMP with $p_0^* = T/\lambda_1$ without loss of generality. □

4 Optimality of the constant rate

4.1 Charcaterization of the optimal rate

The control input $\lambda_0(t)$ appears linearly in the the Hamiltonian (11), and also $p_2(t) \equiv p_2(0)$ which follows from (13) since $\dot{p}_2 = 0$. Hence, we can define *the switching function* as:

$$\varphi(t) := p^*(t)^T g(z^*(t)) = p_1^*(t)(1 - z_1^*(t)) + p_2^*(0). \tag{16}$$

We have the following lemma:

Lemma 3. *Let $(\lambda_0^*(t), z^*(t), p^*(t))$ be an optimal trajectory, then if $\varphi(t) \neq 0$, then:*

$$\lambda_0^*(t) = \begin{cases} L & : \varphi(t) > 0 \\ 0 & : \varphi(t) < 0 \end{cases}, \tag{17}$$

i.e, $\lambda_0(t)$ is a bang-bang control when the switching function does not vanish.

Proof. Let $\varphi(t) > 0$, and let $\lambda_0^*(t) < L$. However,

$$\mathcal{H}(\lambda_0^*(t), z*(t), p^*(t)) = (-p_1^*(t)+1)z_1^*(t)+\varphi(t)\lambda_0^*(t) < (-p_1^*(t)+1)z_1^*(t)+\varphi(t)L = \mathcal{H}(\lambda, z^*(t), p^*(t)),$$

which violates condition 3 in Proposition 2. Hence, $\lambda_0^*(t) < L$ is not optimal. The same argument can be applied when $\varphi(t) < 0$. □

The switching function can also vanish. In that case the control signal is called *singular*. We provide a characterization of the form of the singular control. First we need some notation. Assume that $\lambda_0^*(t)$ is an optimal control and let φ be the associated switching function. Let $E^+ = \{t \in [0,T] | \varphi(t) > 0\}, E^- = \{t \in [0,T] | \varphi(t) < 0\}$, and $E_0 = \{t \in [0,T] | \varphi(t) = 0\}$. Note that all three sets are measurable. We state the characterization next.

Lemma 4. *Let $\lambda_0^*(t)$ be an optimal control, and let E^+, E^-, E_0 be as defined above such that $\mu(E_0) > 0$, where μ denotes the Lebesgue measure. Then:*

$$\lambda_0^*(t) \equiv c_0 := \frac{T\bar{\lambda}_0 - L\mu(E^+)}{\mu(E_0)}, \text{ for } t \in E_0. \tag{18}$$

and $z_1^*(t) \equiv \frac{\lambda_1}{\lambda_1 + c_0}, t \in E_0$.

Proof. Let $E \subset E_0$ be the set of accumelation points of E_0. Note $\mu(E) = \mu(E_0)$, since $E_0 - E$ is the set of isolated points of E which is countable, and hence has measure zero. Then, $\varphi(t) = 0$ for $t \in E$ implies that $d^n/dt^n(\varphi(t)) = 0, t \in E$ for all positive integers n.
Hence, we calculate $\dot{\varphi}(t)$, $\ddot{\varphi}(t)$ below. Lie brackets are usually utilized for such calculation. Using $\varphi(t) = p_1(1 - z_1) + p_2(0)$, we can write:

$$\dot{\varphi}(t) = \dot{p}_1(1 - z_1) - p_1\dot{z}_1 = p_1\lambda_1 - (1 - z_1) \tag{19}$$

$$\ddot{\varphi}(t) = \lambda_1\dot{p}_1 + \dot{z}_1 = \lambda_0(t)(1 - z_1 + \lambda_1 p_1) - \lambda_1(1 + z_1 - \lambda_1 p_1), \tag{20}$$

In order to find the form of the singular trajectory on E, we find that $\varphi(t) = \dot{\varphi}(t) = 0$ implies that $p_1^*(t)(1 - z_1^*(t)) \equiv -p_2^*(0)$, and $\lambda_1 p_1^*(t) \equiv 1 - z_1^*(t)$. Hence, we find that $p_1^*(t) \equiv 1 - z_1^*(t) \equiv K$, where K is a constant. Since $z(t) \in (0,1)$, then $K \in (0,1)$. Hence, $p_2^*(0) = -K^2/\lambda_1 < 0$.

Substituting $p_1^*(t), z_1^*(t)$ in $\ddot{\varphi}(t) = 0$ we get that:

$$\lambda_0(t) = \frac{\lambda_1 K}{1 - K}, t \in E_0$$

which is a constant. Using the fact that $\int_0^T \lambda_0(t) = T\bar{\lambda}_0$, and noting that $\lambda_0(t) \in \{0, c_0, L\}$ we can write $L\mu(E^+) + c_0\mu(E_0) = T\bar{\lambda}_0$, and hence (18) follows (i.e, $\lambda_0^*(t) = c_0$), and $z_1(t) \equiv 1 - K = \frac{c_0}{\lambda_1 + c_0}$. □

Lemma 1 and 4 above lead to the following charcterization of optimal control signals:

Proposition 5. *Let $\lambda_0^*(t)$ be a control input that solves Problem 1, then $\lambda_0(t) \in \{0, c_0, L\}$, for some $c_0 \in (0, L)$.*

Remark 1. *If $\mu(E_0) = 0$ then the control signal is said to be* fully bang-bang*, while if $\mu(E_0) = T$ then the control signal is* fully singular*. Otherwise, the control signal is said to be a patching of* bang-bang arcs *and* singular arcs*. Hence, Theorem 1 asserts that the control is fully-singular. In that case $\lambda_0^*(t) = \bar{\lambda}_0$ and $z_1^*(t) = \lambda_0/(\lambda_1 + \bar{\lambda}_0)$.*

Remark 2. *The singular control satisfies the necessary conditions such as the Legendre-Clebsch condition [9]. However, we will not include a proof as we will be showing that it is indeed optimal within the class of three-level signals.*

4.2 Any patching of bang-bang with singular arcs is suboptimal

Proposition 5 shows that an optimal control takes up to three values only. Hence, in order to prove Theorem 1 we need to show that the cost functional with a fully singular control achieves better than any other signals in that class. We parametrize, the class of signals for a given average $\bar{\lambda}_0$ as follows:

$$\lambda_0(t) = \bar{\lambda}_0 + \varepsilon\alpha(t), \tag{21}$$

where $\alpha(t)$ is measurable such that $\alpha(t) \in \{-1, c, 1\}$, where $|c| < 1$ and $0 \leq \varepsilon \leq \bar{\lambda}_0$. It also satsfies $\int_0^T \alpha(t)dt = 0$. For every choice of $\lambda_0(t)$ we let $x(t)$ denote the solution of (5) that satisfies $x(0) = x(T)$.

We will show that $J(\lambda_0(t)) \leq \frac{\lambda_1\bar{\lambda}_0}{\bar{\lambda}_0+\lambda_1}$ for any choice ε and $\alpha(t)$ above.

First, we study the case when $\alpha(t)$ has a *finite* number of switchings, which we define next. A set $E \subset [0, T]$ is said to be *elementary* if it can be written as a *finite* union of open, closed, or half-open intervals. Let E^+, E^-, E_0 be defined similar to te previous subsection, i.e, we let $E^+ = \{t|\alpha(t) = 1\}, E^- = \{t|\alpha(t) = -1\}, E_0 = \{t|\alpha(t) = c\}$. Then $\alpha(t)$ is said to have a finite number of switchings if E^+, E^-, E_0 are elementary sets.

We are ready to state the next proposition:

Proposition 6. *Let $\lambda_0(t)$ be given as in* (21) *such that $\alpha(t)$ has a finite number of switchings. Then,*

$$J(\lambda_0(t)) < \frac{\lambda_1\bar{\lambda}_0}{\bar{\lambda}_0 + \lambda_1}$$

for $\varepsilon > 0, \mu(E_0) < T$.

The proof will be presented after some preliminaries.

First, we derive few relations with respect to the scalar linear system $\dot{x} = a - bx$, where $a, b > 0$ are constants. This linear system has a unique steady state at $x_{ss} = \frac{a}{b}$ which is globally stable. We state the following lemma:

Lemma 7. *Let $t_0, t_1 > 0$ be the initial and final time. Consider the initial value problem $\dot{x}(t) = a - bx$ with $x(t_0) = x_0$. Let $x(t)$ be solution of the problem, and let $x_1 = x(t_1)$. Then:*

$$\int_{t_0}^{t_1} x(t)dt = \frac{a}{b}(t_1 - t_0) - \frac{1}{b}(x_1 - x_0) \tag{22}$$

Proof. Since the scalar linear system is separable, we can write: $\int_{t_0}^{t_1} dt = \int_{x_0}^{x_1} dx/(a - bx)$. Hence,

$$(t_1 - t_0) = \frac{1}{b} \ln \left| \frac{a - bx_0}{a - bx_1} \right|, \tag{23}$$

which implies

$$x_1 = x_0 e^{-b(t-t_0)} + \frac{a}{b}\Big(1 - e^{-b(t-t_0)}\Big) \tag{24}$$

Next, we show that the integral of $x(t)$ over time can transform to integration over occupancy:

$$\int_{t_0}^{t_1} x dt = \int_{x_0}^{x_1} \frac{x}{a - bx} dx = \frac{a}{b}\left(\frac{1}{b} \ln \left| \frac{a - bx_0}{a - bx_1} \right|\right) - \left(\frac{x_1 - x_0}{b}\right) \tag{25}$$

Using (23) we get the required formula (22).

□

Going back to our problem, note that the system (5) with an input (21) is a *switched linear system* which switches between three linear systems. Fig. 1 illustrates this switched system with two lines in $(\dot{x}, x)$ coordinates, where:

$$a_1 = \bar{\lambda}_0 + \varepsilon, a_2 = \bar{\lambda}_0 - \varepsilon, a_c = \bar{\lambda}_0 + c\varepsilon, \tag{26}$$

$$b_1 = \bar{\lambda}_0 + \varepsilon + \lambda_1, b_2 = \bar{\lambda}_0 - \varepsilon + \lambda_1, b_c = \bar{\lambda}_0 + c\varepsilon + \lambda_1 \tag{27}$$

The upper line is when $\alpha(t) = 1$, and the lower line is when $\alpha(t) = -1$. Note that there is no line for the case $\alpha(t) = c$ since the characterization in Lemma 4 implies that $x(t)$ is constant on a singular arc, and hence $\dot{x}(t) = 0$. Hence, when the control is singular, the system $\dot{x} = a_c - b_c x$ is at steady-state, and the trajectory stays at a single point in $(x, \dot{x})$-coordinates.

We need the following lemma to charcterize the behaviour of the system for a given $\alpha(t)$ with finite switchings:

Lemma 8. *Let $\lambda_0(t)$ given with a finite number of switchings, and let $x(t)$ the solution of (5) with $x(0) = x(T)$. Let $t^c = \mu(E_0)$. Then there exists a positive integer n, and $x_0^-, x_0^+, x_1^-, x_1^+, ..., x_n^-, x_n^+ > 0$ such that:*

$$\int_0^T x(t)dt = \sum_{i=0}^{n} \left(\int_{x_i^-}^{x_i^+} \frac{xdx}{a_1 - b_1 x} + \int_{x_i^+}^{x_i^-} \frac{xdx}{a_2 - b_2 x} dt \right) + t^c \frac{a_c}{b_c} \tag{28}$$

Proof. The trajectory starts from $x(0)$ and returns to $x(0)$ at $t = T$, which forms a grand loop. (note that the time spent when $\alpha(t) = c$ is part of the loop). Since $\alpha(t)$ can have multiple swtichings, it can have multiple loops. We observe the following: if the trajectory transverses from x_i^- to x_i^+ on the upper line, then it must transverse back from x_i^+ to x_i^- on the lower line. Hence any trajectory can be partitioned into a finite number of trajectories. The ith trajectory consists of two segments: a segment on the upper line (from x_i^- to x_i^+)

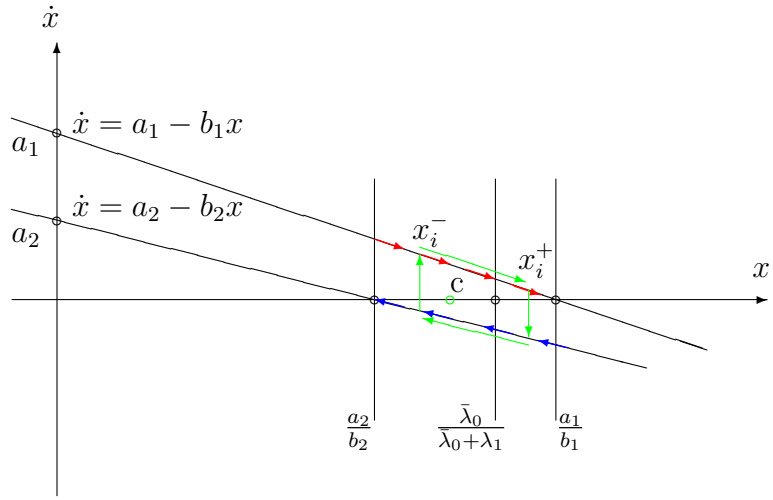

Figure 1: A trajectory of the switched system in the $(\dot{x}, x)$-coordinates.

matched with a segment on the lower line (from x_i^+ to x_i^-). Note that the two segments are not necessarily consecutive in time, and the paritioning is not necessarily unique. Using the same transformation used in (25) and accounting for the total time spent in the singular arc, we can write the integral as in (28).

□

Before completing the proof of Proposition 6, we state following lemma:

Lemma 9. *The following inequality holds:*

$$\forall a, b > 0 : \qquad \frac{(1-e^{-a})(1-e^{-b})}{1-e^{-(a+b)}} < \frac{ab}{a+b} \tag{29}$$

Proof. Let $f(a,b) = \frac{1-e^{-(a+b)}}{(1-e^{-a})(1-e^{-b})} - \frac{1}{a} - \frac{1}{b}$. The inequality is proved if we show that $f(a,b) > 0$ for $a, b > 0$. Note that $\lim_{(a,b)\to(0,0),a,b>0} f(a,b) = 0$.

Differentiating with respect to a:

$$\frac{\partial f}{\partial a} = \frac{1}{a^2} + \frac{1}{2 - 2\cosh(a)}.$$

Using the Taylor series of $\cosh(a)$ we can find that $2\cosh(a) - 2 > a^2$ for $a > 0$. Hence $\partial f/\partial a > 0$. Similarly, $\partial f/\partial b > 0$. Hence, f increases in all directions in the positive quartar which proves the lemma. □

We complete the proof of Proposition 6 below

Proof of Proposition 6. Let $t^c = \mu(E_0), t^+ = \mu(E^+), t^- = \mu(E^-)$. Using the fact that total time is T, and that $\int_0^T \alpha(t)dt = 0$. Then t^+ and t^- can be written as a function of t^c and T (30):

$$\begin{array}{c} t^+ + t^- + t^c = T \\ t^+ - t^- + ct^c = 0 \end{array} \Rightarrow \left\{ \begin{array}{ll} t^+ & = \frac{1}{2}(T - t^c(1+c)) \\ t^- & = \frac{1}{2}(T - t^c(1-c)) \end{array} \right. \tag{30}$$

Now consider the decomposition stipulated in Lemma 8, with $\{x_i^-, x_i^+\}_{i=0}^n$. Let t_i^+ be the time spent on the upper segment from x_i^- to x_i^+, and let t_i^- be the time spent on the lower segment from x_i^+ to x_i^-.

Using (28) and (23), we can write:

$$\begin{aligned}\tilde{J}(\lambda_0(t)) &:= \frac{1}{T}\int_0^T x(t).dt - \frac{\bar{\lambda}_0}{\bar{\lambda}_0+\lambda_1} \\ &= \frac{1}{T}\Big(\sum_i \Big[\int_{x_i^-}^{x_i^+} \frac{dx}{a_1-b_1x} + \int_{x_i^+}^{x_i^-} \frac{dx}{a_2-b_2x}\Big] + t^c\frac{a_c}{b_c}\Big) - \frac{\bar{\lambda}_0}{\bar{\lambda}_0+\lambda_1} \\ &= \frac{1}{T}\sum_i \Big[t_i^+\frac{a_1}{b_1} + t_i^-\frac{a_2}{b_2} + (x_i^+ - x_i^-)\Big(\frac{-1}{b_1}+\frac{1}{b_2}\Big)\Big] + \frac{t^c}{T}\frac{a_c}{b_c} - \frac{\bar{\lambda}_0}{\bar{\lambda}_0+\lambda_1} \qquad (31)\end{aligned}$$

We proceed to rewrite $x_i^+ - x_i^-$ using equation (24) as follows:

$$\begin{cases} x_i^+ = x_i^- e^{-b_1 t_i^+} + \frac{a_1}{b_1}\Big(1-e^{-b_1 t_i^+}\Big) = \Big(x_i^+ e^{-b_2 t^-} + \frac{a_2}{b_2}\Big(1-e^{-b_2 t^-}\Big)\Big)e^{-b_1 t^+} + \frac{a_1}{b_1}\Big(1-e^{-b_1 t^+}\Big) \\ x_i^- = x_i^+ e^{-b_2 t_i^-} + \frac{a_2}{b_2}\Big(1-e^{-b_2 t_i^-}\Big) = \Big(x_i^- e^{-b_1 t^+} + \frac{a_1}{b_1}\Big(1-e^{-b_1 t^+}\Big)\Big)e^{-b_2 t^-} + \frac{a_2}{b_2}\Big(1-e^{-b_2 t^-}\Big) \end{cases} \qquad (32)$$

Hence,

$$(x_i^+ - x_i^-) = \Big(\frac{a_1}{b_1} - \frac{a_2}{b_2}\Big)\frac{\big(1-e^{-b_1 t_i^+}\big)\big(1-e^{-b_2 t_i^-}\big)}{1-e^{-b_1 t_i^+ - b_2 t_i^-}} \qquad (33)$$

Using Lemma (9) and (33) we get the following upper bound:

$$x_i^+ - x_i^- < \Big(\frac{a_1}{b_1} - \frac{a_2}{b_2}\Big)\frac{(b_1 t_i^+)(b_2 t_i^-)}{b_1 t_i^+ + b_2 t_i^-} \qquad (34)$$

Rewriting the equation (31):

$$\tilde{J}(\lambda_0(t)) = \frac{1}{T}\Big(t^+\frac{a_1}{b_1} + t^-\frac{a_2}{b_2} + t^c\frac{a_c}{b_c}\sum_i\Big[(x_i^+ - x_i^-)(\frac{-1}{b_1}+\frac{1}{b_2})\Big]\Big) - \frac{\bar{\lambda}_0}{\bar{\lambda}_0+\lambda_1} \qquad (35)$$

$$< \frac{1}{T}\Big(t^+\frac{a_1}{b_1} + t^-\frac{a_2}{b_2} + t^c\frac{a_c}{b_c} + \sum_i\Big[\Big(\frac{a_1}{b_1} - \frac{a_2}{b_2}\Big)\frac{(b_1 t_i^+)(b_2 t_i^-)}{b_1 t_i^+ + b_2 t_i^-}(\frac{-1}{b_1}+\frac{1}{b_2})\Big]\Big) - \frac{\bar{\lambda}_0}{\bar{\lambda}_0+\lambda_1} \qquad (36)$$

Let $\delta_i := t_i^+ - t_i^-$. Note that it can be either positive or negative. Note that $\sum_i \delta_i = -ct^c$. Define $t_i := t_i^+ + t_i^-$, and hence $\sum_i [t_i] = t^+ + t^- = T - t^c$. Using the definitions, we get:

$$t_i^+ = \frac{t_i + \delta_i}{2}, t_i^- = \frac{t_i - \delta_i}{2} \qquad (37)$$

Hence, we can write (36) as follows:

$$
\begin{aligned}
&\sum_i \Big[\Big(\frac{a_1}{b_1}-\frac{a_2}{b_2}\Big)\frac{(b_1t_i^+)(b_2t_i^-)}{b_1t_i^++b_2t_i^-}\Big(\frac{-1}{b_1}+\frac{1}{b_2}\Big)\Big] \\
&\quad= \frac{4\lambda_1\varepsilon^2}{\Big((\bar\lambda_0+\lambda_1)^2-\varepsilon^2\Big)}\sum_i\Big[\frac{t_i^+t_i^-}{\Big((t_i^++t_i^-)(\bar\lambda_0+\lambda_1)+(t_i^+-t_i^-)\varepsilon\Big)}\Big] \\
&\quad= \frac{\lambda_1\varepsilon^2}{\Big((\bar\lambda_0+\lambda_1)^2-\varepsilon^2\Big)(\bar\lambda_0+\lambda_1)}\sum_i\Big[\frac{t_i^2-\delta_i^2}{t_i+\frac{\delta_i\varepsilon}{\bar\lambda_0+\lambda_1}}\Big] \\
&\quad= \frac{\lambda_1\varepsilon^2}{\Big((\bar\lambda_0+\lambda_1)^2-\varepsilon^2\Big)(\bar\lambda_0+\lambda_1)}\sum_i\Big[\frac{t_i^2-\delta_i^2}{t_i^2-\big(\frac{\varepsilon}{\bar\lambda_0+\lambda_1}\big)^2\delta_i^2}\times\Big(t_i-\frac{\delta_i\varepsilon}{\bar\lambda_0+\lambda_1}\Big)\Big] \\
&\quad\le \frac{\lambda_1\varepsilon^2}{\Big((\bar\lambda_0+\lambda_1)^2-\varepsilon^2\Big)(\bar\lambda_0+\lambda_1)}\sum_i\Big[t_i-\frac{\delta_i\varepsilon}{\bar\lambda_0+\lambda_1}\Big] \\
&\quad\le \frac{\lambda_1\varepsilon^2(T-t^c+t^c\frac{c\varepsilon}{\bar\lambda_0+\lambda_1})}{\Big((\bar\lambda_0+\lambda_1)^2-\varepsilon^2\Big)(\bar\lambda_0+\lambda_1)}
\end{aligned}
\tag{38}
$$

Substituting (38) in the inequality (31) and substituting the values of all the variables, we get that (39) simplifies to:

$$
\tilde J(\lambda_0(t)) < -\frac{c^2\varepsilon^2\lambda_1t^c}{T(\bar\lambda_0+\lambda_1)^2(c\varepsilon+\bar\lambda_0+\lambda_1)} < 0. \tag{39}
$$

□

In order to prove Theorem 1, we need to cosnider an arbitrary measurable signal $\alpha(t)$. For that purpose, use the following charcterization of measurable sets:

Lemma 10. *[11] Let $E\subset[0,T]$. Then E is measurable if and only if for every $\varepsilon>0$ there exists an elementary set $B_\varepsilon\subset[0,T]$ such that $\mu(E\Delta B_\varepsilon)<\varepsilon$, where Δ is the symmetric difference of sets.*

We improve on the lemma above, by the following:

Lemma 11. *Let $E\subset[0,T]$. Then E is measurable if and only if for every $\varepsilon>0$ there exists an elementary set $B_\varepsilon\subset[0,T]$ with $\mu(B_\varepsilon)=\mu(E)$ such that $\mu(E\Delta B_\varepsilon)<\varepsilon$, where Δ is the symmetric difference of sets.*

Proof. Suffciency is clear. For necessity, let $B_{\varepsilon/2}$ be the elementary set given by Lemma 10. We can modifiy the intervals contained in $B_{\varepsilon/2}$ by up to $\varepsilon/2$ to get B_ε with $\mu(B_\varepsilon)=\mu(E)$. □

We generalize Proposition 6 as follows:

Proposition 12. *Let $\lambda_0(t)$ be given as in (21) such that $\alpha(t)$ is measurable. Then,*

$$
J(\lambda_0(t)) \le \frac{\lambda_1\bar\lambda_0}{\bar\lambda_0+\lambda_1}
$$

.

Proof. Let E^0, E^+, E^- be defined as before. Using Lemma 11, let E_i^0, E_i^+, E_i^- be elementary sets such that $\mu(E_i^0) = \mu(E^0)$ and $\mu(E^0 \Delta E_i^0) < 1/2^i$, and similarly for E_i^+, E_i^-. We have also $\mu(E_i^0) + \mu(E_i^+) + \mu(E_i^-) = T$.
Let $\alpha_i(t)$ be defined as follows:

$$\alpha_i(t) = \begin{cases} 1 & : t \in E_i^+ \\ c & : t \in E_i^0 \\ -1 & : t \in E_i^- \end{cases}$$

Then $\alpha_i(t)$ are elemenary simple functions, and we have $\alpha_i(t) \to \alpha(t)$ for all t. The proposition follows using Proposition 6 and Lebesgue's bounded convergence theorem [11]. □

Theorem 1 follows from Propositions 5 and 12.

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