Konuralp Journal of Mathematics, 12 (2) (2024) 106-111

Konuralp Journal of Mathematics

Research Paper

Journal Homepage: www.dergipark.gov.tr/konuralpjournalmath

e-ISSN: 2147-625X

Low-Regret and No-Regret Control of Tumor Development to Fill in Some Limitations of Classical Optimal Control Theory

Cheikh Seck[1*] and Mouhamadou Ngom[2]

[1]*Département de Mathématiques de la FASTEF ex ENS, Université Cheikh Anta Diop de Dakar, Sénégal/Laboratoire d'Analyse Numérique et d'Informatique, UFR SAT, UGB, Saint-Louis, Sénégal.*

[2]*Département de Mathématiques UFR SATIC Université Alioune Diop de Bambey Membre de ER-ANLG, Université Alioune Diop de Bambey, Université Alioune Diop de Bambey, Bp 30 Bambey, Sénégal*

[*]*Corresponding author*

Abstract

This paper is about a Cauchy problem for a parabolic type linear operator. The main system describes the spread and development of a tumor in an organism. From the classical optimal control theory, we show some results of variation calculations. And an optimality system for the considered control problem is established.It is known that the classical techniques of optimal control theory are ineffective for certain evolutionary parabolic systems type with missing data.

Keywords: *Low-regret control, No-regret control, Optimal control, Estimations, Strategic zone control.*

2010 Mathematics Subject Classification: *35Q72; 93B03; 93B07; 93C20; 49A22; 35J99.*

1. Introduction and statement of the problem

Concerning Biosciences, Optimal Control Theory has been applied to the design of optimal therapies, optimal harvest policies and optimal investments in renewable-resources. However, it has not been applied when it comes to elucidating the origins of the observed biological behaviours.

In this work, we propose the use of the Optimal Control Theory to provide a thorouh explanation of the biological phenomenon of the relationships between bio-entities, as well as of the origin of these relationships. The end goal of designing an optimal theory or an optimal harvest or optimal investment is to achieve an objective extreme to the biological entities, that is, to mitigate the downsides of drugs. All this subject to the biological laws describing the existing cross effects see Greenspan [1, 2].

The suitable mathematical approach to study this problem is the Optimal Control Theory. Indeed, in modern biomathematics there is a large body of work developed to study optimal drug therapies and optimal harvest policies.

However, in addition to such well known applications, Optimal Control Theory also constitutes the most appropriate approach to study biological phenomena understood as the result of the behaviour of semi-autonomous bio-entities see Kimmel [3]. The interpretation of biological phenomena as an offshoot of a set of optimal control problems has yet to be established by current biomathematics see Ledzewicz [4]. In this respect, taking economic oligopolistic models as stepping-stone the purpose of this paper is to show how this application of Optimal Control Theory is a promising approach to the analysis of biomedical questions, specially to tumor see Ngom [5, 6], Friedman [7, 8] and Chaplain [9], and references there is for more details.

The optimal control problem of tumor governed by the $p-$Laplacian with homogeneous Dirichlet boundary conditions on an arbitrary domain of the state equation describe the evolution of tumor. We assume that the unknown initial condition belongs to an appropriate space of infinite dimension. We tapped into the no-regret and low-regret control developed by J.L. Lions [10] to characterize the optimal control. We start with the evolution system modeling the evolution of a tumor in an animal organism. Then, we derive the associated optimality system and the functional to be optimized.In the third part, by the low- regrets control technique, the existence of the optimality system solution has been established and approximation provided. Finally, two examples have been provided to support and apply the theoretical results of the work.

Email addresses: **cheikh5.seck@ucad.edu.sn (Cheikh Seck), mouhamadou.ngom@uadb.edu.sn (Mouhamadou Ngom)**

2. Tumor evolution and optimal control

Let $\mathscr{V}$ be a real Hilbert space, $\mathscr{V}'$ its dual and A a parabolic operator modeling a distributed system, $\mathscr{U}_{ad}$ the Hilbert space of control, $B \in \mathscr{L}(\mathscr{U}_{ad}, \mathscr{V}')$, $Q_T =]0,T[\times\Omega$ and $\Gamma_T =]0,T[\times\partial\Omega$ (Ω the spatial domain and t the temporal parameter).

2.1. Typical model of tumor growth

Let us consider the following problems:

$$\begin{cases} \varphi_t - \varphi_{xx} + \varphi & = & -\overline{\varphi} \text{ in } Q_T, \\ \varphi & = & 0 \text{ on } \Gamma_T, \\ \varphi(0,x) & = & \varphi_0 \text{ in } \Omega, \end{cases} \tag{2.1}$$

where $\varphi \in L^2(\Omega(t))$ is the nutrient concentration of cells proliferating (for more details see [5]) and ($\overline{\varphi}$ is the defect in nutrient concentration of proliferating cells). We assume like in [7] that in the tumor region $\Omega(t)$ there are tree types of cells : proliferating cells with density p, quiescent cells with density q and necrotic cells with density r.
Nutrient with concentration φ is diffusing in $\Omega(t)$ and affects the transition of cells one type to another :
$p \to q$ at rate $k_Q(\varphi)$, $q \to p$ at rate $k_p(\varphi)$,
$p \to r$ and $q \to r$ at rates $k_A(\varphi)$ and $k_D(\varphi)$ respectively and $p \to p$ at proliferate rate $k_B(\varphi)$. Necrotic cells are removed from the tumor at constant rate k_R. By conservation of mass,

$$\begin{cases} p_t + div(pv) & = & [k_B(\varphi) - k_Q(\varphi) - k_A(\varphi)]p + k_p q \text{ in } Q_T, \\ q_t + div(qv) & = & k_Q(\varphi)p - [k_p(\varphi) + k_D(\varphi)]q \text{ in } Q_T, \\ r_t + div(rv) & = & k_A(\varphi)p + k_D(\varphi)q - k_R r \text{ in } Q_T, \\ p+q+r & = & 1\,, \end{cases} \tag{2.2}$$

where v is the velocity of the cells, caused by motions due to the proliferation and removal of cells.
Making the sum of the three first equations of (2.2) and using the fourth equation of (2.2), we obtain :

$$div(v) = k_B(\varphi)p - k_R r, \tag{2.3}$$

and for more considerations (see [5] or [7]) we take $v = -\nabla\mathscr{P}$ et $k_B(\varphi) = \mu(\varphi - \widetilde{\varphi})$; where $\mathscr{P}$ is the pressure which appears due to cell movements.
Then with these notations, equation (2.3) becomes

$$-\Delta\mathscr{P} = \mu(\varphi - \widetilde{\varphi})p - k_R r. \tag{2.4}$$

2.2. Tumor growth and associated optimality system

In this part, we make an internal control. To avoid confusion in the notations of problem (2.1) and to come back on classical problem, we set $-\overline{\varphi} = f$ and we try to achieve the controllability of the following system:

$$\begin{cases} \varphi_t - \varphi_{xx} + \varphi & = f & \text{in } Q_T, \\ \varphi & = & 0 \text{ on } \Gamma_T, \\ \varphi(0,x) & = & \varphi_0 \text{ in } \Omega \end{cases} \tag{2.5}$$

and let $\varphi_1,...,\varphi_p \in L^2(Q_T)$, $u = (u_1,...,u_n) \in \mathbb{R}^p$ and $\varphi(t,u)$ solution of the control problem

$$\begin{cases} \varphi_t - \varphi_{xx} + \varphi & = & f + \sum_{i=1}^p u_i\varphi_i(t) \text{ in } Q_T \\ \varphi & = & 0 \text{ on } \Gamma_T \\ \varphi(0,x) & = & \varphi_0 \text{ in } \Omega. \end{cases} \tag{2.6}$$

Let $\varphi_d \in L^2(\Omega)$ the desired state and the function

$$J(u) = \frac{1}{2}\int_\Omega (\varphi_u(T,x) - \varphi_d(x))^2 dx + \frac{\alpha}{2}\|u\|^2_{\mathbb{R}^p} \text{ where } \alpha > 0\,. \tag{2.7}$$

Remark 2.1. *We can make the control at every moment of $[0,T]$ and take $\varphi_u(t,x)$ (by feedback control) and $\varphi_1(t,x)$, but here we make the control by interesting to the final state (at the moment T) that's why we take $\varphi_u(T,x)$ and $\varphi_1(x)$*

Assume the above hypotheses are verified, we have the following fundamental lemma of Seck-Ngom:

Lemma 2.2. (Seck-Ngom) *Let $\mathscr{U}_{ad}$ the set of admissible controls contained in Ω. There exists an optimal control $\overline{u}$ such that*

$$J(\overline{u}) = \min_{u\in\mathscr{U}_{ad}} J(u)$$

where

$$J(u) = \frac{1}{2}\int_\Omega (\varphi_u(T,x) - \varphi_1(x))^2 dx + \frac{\alpha}{2}\|u\|^2_{\mathbb{R}^p} \text{ where } \alpha > 0$$

and an optimality system

$$\begin{cases} \varphi_t - \varphi_{xx} + \varphi & = & f + \sum_{i=1}^{p} u_i \varphi_i(t) \text{ in } Q_T, \\ \varphi & = & 0 \text{ on } \Gamma_T, \\ \varphi(0,x) & = & \varphi_0 \text{ in } \Omega, \\ -p_t - p_{xx} + \overline{p} & = & 0 \text{ in } Q_T, \\ \gamma \overline{p} & = & 0 \text{ on } \Gamma_T, \\ \overline{p}(T) & = & \varphi(T,\overline{u}) - \varphi_1 \text{ in } \Omega, \\ \overline{u}_i & = & -\frac{1}{\alpha} \int_0^T \int_\Omega \overline{p}(t,x) \varphi_i(t,x) dx dt. \end{cases} \tag{2.8}$$

Proof. See Seck et al [?] or Ngom [5] . □

Indeed, once the optimality system has been obtained, the function achieving the optimum is introduced into a new internal and strategic control system.
Next, we deploy the notion of controllability with or without low regret, first introduced by Lions [10].

3. Low-regret and no-regret control of tumor's growth

3.1. Notion of strategic function

Definition 3.1. *A function $\mu : \omega_i \longrightarrow \bar{\mathbb{R}}$ square integrable is said strategic for the following dynamical system if it verify, for all $\varphi_0 \in L^2(\omega_i)$ and $\omega_i \subset \Omega, i \in I, card(I) < \infty$, the solution φ of the following system*

$$\begin{cases} \varphi_t(t,x) - \varphi_{xx}(t,x) + \varphi & = & f(t,x) + \mathscr{B}.u(t,x) + \beta(t)\mu(x) \text{ in } Q_T, \\ \varphi & = & 0 \text{ on } \Gamma_T, \\ \varphi(0,x) & = & \varphi_0(x) \text{ in } \Omega. \end{cases} \tag{3.1}$$

And,

$$\forall\, t > 0, \int_{\omega_i} \mu(x)\varphi(t,x)dx = 0 \qquad \textit{then} \qquad \varphi_0 = 0. \tag{3.2}$$

where $\forall i,\ \omega_i \subset \Omega$ and $\cup_{i\in I}\omega_i = \Omega$, $f \in L^2([0,T];L^2(\Omega))$ and β a time parameter.
Let also $\mu \in \mathscr{G}$ (strategic domain) such that $\mathscr{G}$ a closed vector subspace of $\mathscr{F}$ (the space of uncertainties) and $u := \bar{u}$ which comes from the last line of the optimality system (2.8).

Remark 3.2. *The system (3.1) comes from the system (2.8) to which is added a term called zone strategic operator see Seck [11] and Jai [12].*

Let Ω be an open bounded set in $\mathbb{R}^n (n = 2,3)$ with smooth boundary $\partial\Omega$.
We introduce the cost function

$$J(u) := \frac{1}{2}\int_\Omega \rho(x)\left(\varphi(t,u(x)) - \varphi_d(x)\right)^2 dx + \frac{\alpha}{2}||S(u-u_0)||^2_{L^2(\Omega)}, \tag{3.3}$$

where $\alpha > 0, \rho \geq 0, \rho \in L^2(\Omega)$, S a given linear operator and where φ_d is the optimal state we wish to get close to, taking into account the cost of the control expressed by the term

$$\frac{\alpha}{2}||S(u-u_0)||^2_{L^2(\Omega)} = \frac{\alpha}{2}\sum_{i\in I}\int_{\omega_i} S(u-u_0)^2 dx. \tag{3.4}$$

Let $\mathscr{V}$ be a Hilbert space on $\mathbb{R}$ with dual $\mathscr{V}'$ and $\mathscr{A}$ an elliptical differential operator modelling the distributed system (1).
Consider $\mathscr{U}_{ad}$: the Hilbert space of control and $\mathscr{B} \in \mathscr{L}(\mathscr{U};\mathscr{V}')$, F a Hilbert space will be the space of uncertainties, $\beta \in \mathscr{L}(F;\mathscr{V}')$ and finally $\mathscr{G}$ a closed Hilbert subspace of F.
The first equation of system (3.1) can be formally rewritten in the following standard form

$$\mathscr{A}\dot{\varphi} = f + \mathscr{B}u + \beta\mu. \tag{3.5}$$

Lemma 3.3. *(Lions [10]) For $f \in \mathscr{V}'$, we call the equation of state relating to the control $u \in \mathscr{U}_{ad}$ and the strategic uncertainties function $\mu \in \mathscr{G}$. If $\mathscr{A}$ is an isomorphism of $\mathscr{V}$ on $\mathscr{V}'$, the equation (3.5) admits a unique solution noted $\varphi(u,\mu)$*

For each fixed μ, we thus have a possible state attached (3.5) a cost given by

$$J(u,\mu) = ||C\varphi_{\mu(t,u)} - \varphi_d||^2_{\mathscr{H}} + N||u||^2{}_{\mathscr{U}_{ad}} \tag{3.6}$$

where $C \in \mathscr{L}(\mathscr{V},\mathscr{H})$, $\mathscr{H}$ a Hilbert space, $\varphi_d \in \mathscr{H}$ fixed, $N > 0$ and $||\dots||_X$ designates the norm in Hilbert space X.

Remark 3.4. *1. If $\mathscr{G} = \{0\}$ then we have a standard problem of optimal control. So, the optimal control problem is:*

$$\inf_{u\in\mathscr{U}_{ad}} J(u,0) \tag{3.7}$$

2. if $\mathscr{G} \neq \{0\}$, the optimal control problem (3.7) has no sense.

Definition 3.5. *One calls control with no-regret relating to u_0, the element u realizing:*

$$\inf_{u\in\mathscr{U}_{ad}} \sup_{\mu\in\mathscr{G}} \{J(u,\mu) - J(u_0,\mu)\}. \tag{3.8}$$

Remark 3.6. *i. If $u_0 = 0$, then we find the definition of control without regret of Lions* [10].
ii. For fixed $u_0 \in \mathscr{U}_{ad}$ and $\forall u \in \mathscr{U}_{ad}$, we have

$$J(u,\mu) - J(u_0,\mu) = J(u,0) - J(u_0,0) + 2\langle S(u-u_0),\mu\rangle_{\mathscr{G}',\mathscr{G}} \ \forall\mu \in \mathscr{G} \tag{3.9}$$

there exist a regular function ζ defined on $\mathscr{U}_{ad}$ such that

$$\mathscr{A}^*\zeta(u) = C^*C\,(y(u,0) - y(0,0)) \tag{3.10}$$

So $S(u) = \beta^*\zeta(u)$; In other words $\langle S(u),\mu\rangle = \langle\zeta(u),\beta\mu\rangle$, $\forall\mu \in \mathscr{G}$

Remark 3.7. *Obviously the problem (3.8) is only defined for the controls $u \in \mathscr{U}_{ad}$ such that*

$$\sup_{\mu\in\mathscr{G}} \{J(u,\mu) - J(u_0,\mu)\} < +\infty. \tag{3.11}$$

For (3.9), the controllability is achieved if and only if $u \in \mathscr{K} + u_0$ where the set $\mathscr{K}$ is defined by

$$\mathscr{K} = \{w \in \mathscr{U}_{ad}, \langle S(w),\mu\rangle = 0, \forall\mu \in \mathscr{G}\}. \tag{3.12}$$

3.2. Low-regrets disturbances and approximate optimality systems

Here, we are interested in the existence and the characterization of the control without regrets relating to u_0.
For that, one introduces by relaxation a series of approximate problems. It is the method of disturbance with low-regrets of Lions [10] see also Nakoulima [13].
Indeed, we relax the problem (3.8) by introducing for $\gamma > 0$ fixed,

$$inf_{u\in\mathscr{U}_{ad}} sup_{\mu\in\mathscr{G}} \left\{J(u,\mu) - J(u_0,\mu) - \gamma||u||^2_{\mathscr{G}}\right\}. \tag{3.13}$$

Using the relation (3.9), the problem (3.13) is rewritten

$$\inf_{u\in\mathscr{U}_{ad}} \left\{J(u,0) - J(u_0,0) + \sup_{\mu\in\mathscr{G}} \left(\langle 2S(u-u_0),\mu\rangle - \gamma||u||^2_{\mathscr{G}}\right)\right\}. \tag{3.14}$$

Remark 3.8. *The perturbation in* (3.13) *makes it possible to better explain the term*

$$\sup_{\mu\in\mathscr{G}} \left(\langle 2S(u-u_0),\mu\rangle - \gamma||u||^2_{\mathscr{G}}\right). \tag{3.15}$$

By simple calculations, we find that:

$$\sup_{\mu\in\mathscr{G}} \left(\langle 2S(u-u_0),\mu\rangle - \gamma||u||^2_{\mathscr{G}}\right) = \frac{1}{\gamma}||S(u-u_0)||^2_{\mathscr{G}'} \tag{3.16}$$

By identifying $\mathscr{G}$ and its dual $\mathscr{G}^{'}$, the problem (3.13) become

$$\inf_{u\in\mathscr{U}_{ad}} J_\gamma(u) \tag{3.17}$$

where

$$J_\gamma(u) = J(u,0) - J(u_0,0) + \frac{1}{\gamma}||S(u-u_0)||^2_{\mathscr{G}'}. \tag{3.18}$$

Proposition 3.9. *(Swan [14]) The problem* (3.17) *admits an unique solution u, called low-regret control.*

The main result of low-regret control is the following:

Theorem 3.10 (LRC)**.** *The solution u_γ of problem* (3.17) *converges weakly in the set of admissible controls towards the optimal control without regret relating to u_0.*

Proof. Under the above assumptions, let u the solution of (3.17); so we have

$$J(u_\gamma,0) - J(u_0,0) + \frac{1}{\gamma}||S(u_\gamma - u_0)||^2_{\mathscr{G}'} \leq J(v,0) - J(u_0,0) + \frac{1}{\gamma}||S(v-u_0)||^2_{\mathscr{G}'} \ \forall v \in \mathscr{U}_{ad} \tag{3.19}$$

In particular for $v = u_0$, we have:

$$J(u_\gamma,0) - J(u_0,0) + \frac{1}{\gamma}||S(u_\gamma - u_0)||^2_{\mathscr{G}'} \leq 0. \tag{3.20}$$

And the predefined structure in (3.14), gives us

$$||\rho(x)(\varphi(t,x),u(x),\mu)-\varphi_d(t,x)||_H^2+N||u_\gamma||^2_{\mathscr{U}_{ad}}+\frac{1}{\gamma}||S(u_\gamma-u_0)||^2_{\mathscr{G}'}\leq J(u_0,0). \tag{3.21}$$

We can deduce that the sequence $(u_\gamma)_{\gamma>0}$ is bounded in $\mathscr{U}_{ad}$: therefore we can extract a subsequence denoted $(u_\gamma)_{\gamma>0}$ which weakly converges to an element u of $\mathscr{U}_{ad}$ solution of the equation (3.17).
On the other hand,

$$\forall v\in\mathscr{U}_{ad},J(u,\mu)-J(u_0,\mu)-\gamma||\mu||^2\leq J(v,\mu)-J(u_0,\mu)\forall\mu\in\mathscr{G}, \tag{3.22}$$

μ is strategic function in $\mathscr{G}$, therefore $\mu\neq 0$ as long as $u_0\neq 0$.
From

$$J(u_\gamma,\mu)-J(u_0,\mu)-\gamma||\mu||^2\leq sup_{\mu\in\mathscr{G}}\left(J(v,\mu)-J(u_0,\mu)\right),\forall v\in\mathscr{G}. \tag{3.23}$$

And by going to the limit at γ, we get:

$$J(u,\mu)-J(u_0,\mu)\leq sup_{\mu\in\mathscr{G}}\left(J(v,\mu)-J(u_0,\mu)\right),\forall v\in\mathscr{G} \tag{3.24}$$

From Definition 3.1 relating to strategic area functions and relation (3.24), we deduce that u is a control without regret relating to u_0. □ □

Example 3.11. Neumann type boundary uncertainty and boundary cost *Let ω be a subdomain of a non-empty open set Ω of $\mathbb{R}^n$,with regular boundary $\partial\omega\subset\partial\Omega$. Consider the following distributed system*

$$\begin{cases}\psi_t-\psi_{tt} &= (f+v)\chi_\omega \text{ in } \Omega,\\ \frac{\partial\psi}{\partial n} &= g \text{ on } \partial\Omega,\end{cases} \tag{3.25}$$

where $v\in\mathscr{U}_{ad}=L^2(\omega)$, $g\in\mathscr{G}\subset\mathscr{F}=L^2(\partial\Omega)$. $\mathscr{G}$ a closed vector subspace of $\mathscr{F}$ endowed with the scalar product induced by $\mathscr{F}$. If $f\in L^2(\omega)$, there exist $\psi(v,g)\in H^{\frac{3}{2}}(\omega)$ solution of (3.25).
We associate to the state $\psi(v;g)$ the following cost function:

$$J(v,g)=|\psi(v,g)-y_d|^2_{L^2(\partial\Omega)}+N||v||^2_{L^2(\omega)}. \tag{3.26}$$

For u_0 fixed in $\mathscr{U}$, there exists a unique no-regrets control u relative to u_0 solution of the system (3.25) and (3.27).The problem consists in explaining the optimality system characterizing it. To put it simply, we take $u_0=0$.
Therefore the low-regrets disturbance associated with (3.25), (3.27) is defined by

$$J^\gamma(v)=J(v,0)-J(0,0)+\frac{1}{\gamma}||S(v)||_{\mathscr{G}}, \tag{3.27}$$

where $S(v)=\zeta(v)$ is the solution of:$\{AS(v)=0$ in ω, $\frac{\partial S}{\partial vA}=\psi(v,0)-\psi(0,0)$ on $\partial\Omega\}$, with the operator $A=-\Delta+I$.
The $\inf_{v\in\mathscr{U}}J^\gamma(v)$ problem admits a unique solution u_γ.

Example 3.12. Neumann-type partitioned boundary uncertainty and boundary cost
Let ω be a subdomain of a non-empty open set Ω of $\mathbb{R}^n$,with regular boundary $\partial\omega\subset\partial\Omega=\partial\omega_1\cup\partial\omega_2$ where $\partial\omega_1$ and $\partial\omega_2$ being two regular boundaries and empty intersection.
Consider the following distributed system

$$\begin{cases}\psi-\Delta\psi &= 0 \text{ in } \omega,\\ \frac{\partial\psi}{\partial n} &= v \text{ on } \partial\omega_1,\\ \frac{\partial\psi}{\partial n} &= g \text{ on } \partial\omega_2\end{cases} \tag{3.28}$$

where $v\in\mathscr{U}_{ad}=L^2(\omega_1)$, $g\in\mathscr{G}\subset\mathscr{F}=L^2(\partial\omega_2)$. $\mathscr{G}$ a closed vector subspace of $\mathscr{F}$ endowed with the scalar product induced by $\mathscr{F}$. If $f\in L^2(\omega)$, there exist $\psi(v,g)\in H^{\frac{3}{2}}(\omega)$ solution of (3.28).
We associate to the state $\psi(v,g)$ the cost function:

$$J(v,g)=|\psi(v,g)-y_d|^2_{L^2(\partial\Omega)}+N_1||v||^2_{L^2(\omega_1)} \tag{3.29}$$

where y_d the desired state of system.
For u_0 fixed in $\mathscr{U}_{ad}$, there exists a unique no-regrets control u relative to u_0 solution of the system (3.28) and (3.29).The problem consists in explaining the optimality system characterizing it. To put it simply again, we take $u_0=0$.
Therefore the least regrets disturbance associated with (3.28), (3.29) is defined by

$$J^\gamma(v)=J(v,0)-J(0,0)+\frac{1}{\gamma}||S(v)||^2_{L^2(\partial\omega_1)}, \tag{3.30}$$

where $S(v)=\zeta(v)$ is the solution of: $\{AS(v)=0$ in ω_1, $\frac{\partial S}{\partial v_A}=\psi(v,0)-\psi(0,0)$ on $\partial\omega_2\}$, with the operator $A=-\Delta+I$.
The $\inf_{v\in\mathscr{U}J^\gamma(v)}$ problem admits a unique solution u_γ.

Remark 3.13. *The least regrets perturbation method allows, as we have just seen, to transform systematically a problem with uncertainty into a standard control problem.*
This point of view will be reinforced in where we deal with the case of evolution and in where we will find other developments and other examples.

Remark 3.14. *The method, LRC resulting from the optimality system, presented in the paper is a bit special because of the parabolic character of the operator associated with the system see [21]. It can be generalized without great difficulty; and, it covers a large class of systems, therefore, we could generalize the situation with more control systems (regional, punctual, ...) and of different natures with missing data (source term, boundary conditions, etc.)*

Conclusion and Perspectives of this work

In this work, we are interested in an internal optimal control that resolves the concentration rate of a substance emitted or injected at the target domain (internal control) or a surface treatment for example the application of an ointment on the skin (boundary control). After the injection, controls are performed to examine the propagation of a tumor in an organism. To do this investigation project, we set out to reduce calculations and these certain complexities but without harming the general scope of controllability with or without regret, the domain Q_T is a prescribed cylinder see also Cui [20], Chaplain [9] and Seck [16]. Indeed, once the optimality system has been obtained, we unroll the controllability technique of distributed systems with fewer or no Lions regrets. This technique makes it possible to solve non-classical or missing-data optimality problems.
So, in the near future, we plan to resume calculations for non-convex domains with cracks or corners. These kinds of domains are more suitable (biomedical applications) for the proliferation of tumor cells and their constituencies for their treatments Cui [20] and Friedman [7], Cui[17], Bazaly [19]. The notion of scalability for the regional controllability analysis will be adapted for this technique. Thus, one can make conjectures on the scalabilty, stability and spread of tumors for its possible local control.
The same work is being repeated for distributed systems with border and mixed control. This work could also be extended to non-convex, cracked and wedge domains.
Another work is planned to do the numerical simulations with FreeFem ++/FreeFem 3D on the functional to consolidate the results that we obtained on this work.

Article Information

Acknowledgements: The authors would like to express their sincere thanks to the editor and the anonymous reviewers for their helpful comments and suggestions.

Author's contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflict of Interest Disclosure: No potential conflict of interest was declared by the author.

Supporting/Supporting Organizations: No grants were received from any public, private or non-profit organizations for this research.

Ethical Approval and Participant Consent: It is declared that during the preparation process of this study, scientific and ethical principles were followed and all the studies benefited from are stated in the bibliography.

Plagiarism Statement: This article was scanned by the plagiarism program. No plagiarism detected.

Availability of data and materials: Not applicable

References

[1] H.P. Greenspan. *On the growth on cell culture and solid tumors,* Theoretical Biology 56 (1976), 229-242.
[2] H.P. Greenspan. *Models for the growth of a solid tumor by diffusion,* Studies Appl. Math. 52 (1972), 317-340.
[3] M. Kimmel and A. Swierniak. *Control Theory Approach to Cancer Chemotherapy: Benefiting from Phase Dependence and Overcoming Drug Resistance*, Lect. Notes Math. Vol. 1872, 2006 pp. 185-221.
[4] U. Ledzewicz and H. Sachattlerl. *Drug resistance in cancer chemotherapy as an optimal control problem,* Discrete and continuous dynamical systems-series-B Volume 6, Number 1, January 2006,pp. 129-150.
[5] M.Ngom, I.Ly and D.Seck. *Chemotherapy of a tumor by optimal control approach.* Mathematica Aeterna, Vol. 2, 2012, no. 9, 779 - 803.
[6] M.Ngom, I.Ly and D.Seck. *Study of a tumor by shape and topological optimization.* Applied Mathematical Sciences, Vol. 5, 2011, no. 1, 1-21.
[7] A.Friedman. *Free boundary problems arising in tumor models* Mat. Acc. Lincei (2004) s.9, v.15 : 161-168
[8] A.Friedman and F.Reitich *Analysis of a mathematical model for the growth of tumors* J. Math. Biol. (1999) 38: 262-284.
[9] M.A. J. Chaplain. *The development of a spatial pattern in a model for cancer growth,* Experimental and Theoretical Advances in Biological Pattern Formation (H. G. Othmer, P. K. Maini, and J. D. Murray, eds.), Plenum Press, 1993, pp. 45-60.
[10] J. L. Lions. *Controle a moindres regrets des systemes distribues*. C.R.Acad. Sci. Paris, Ser. I Math.315, (1992), 125312.
[11] M. L. L. Ane, C. Seck and A. Sène *Boundary Exact Controllability of the Heat Equation in 1D by Strategic Actuators and a Linear Surjective Compact Operator* Applied Mathematics,(2020), 991-999.
[12] E. A. Jai. *Quelques problemes de controle propres aux systemes distribues.* Annals of University of Craiova. Math. Comp. Sci. Ser. 2003;30:137-153.
[13] O. Nakoulima, A. Omrane, J. Velin. *Perturbations a moindres regrets dans les systemes distribues a donnees manquantes.* C. R. Acad. Sci. Ser. I Math. (Paris), (2000);330:801 806.
[14] G. W. Swan, B. Dumitru, J. Claire M. Gisele. *Low-regret control for a fractional wave equation with incomplete data,* Baleanu et al. Advances in Difference Equations, 2016, DOI 10.1186/s13662-016-0970-8.
[15] S. Cui, A. Friedman. *Analysis of a mathematical of the effect inhibitors on the growth of tumors*. Mathematical Biosciences 164 (2000), 103-137.
[16] C. Seck, M. L. L. Ane and A. Sene *Boundary Exact Controllability of the Heat Equation in 1D by Strategic Actuators and a Linear Surjective Compact Operator* Applied Mathematics, 2020, 11, 991-999: Applied Mathematics , 11, 991-999, https://doi.org/10.4236/am.2020.1110065.
[17] S.Cui and A.Friedman. *Analysis of a mathematical model of the growth of necrotic tumors* Journal of Mathematical Analysis and Applications 255, 636-677 (2001).
[18] J. D. Djida, G. Mophou and I. Area. *Optimal Control of Diffusion Equation with Fractional Time Derivative with Nonlocal and Nonsingular Mittag-Leffler Kernel* Springer, 2018.
[19] B.V. Bazaly and A.Friedman *A Free Boundary Probleme for an Elliptic-Parabolic System : Application to a Model of Tumor Growth* Communication in Partial Differential Equations Vol. 28 Nos 3 and 4 text(2003), pp. 517-560.
[20] C. Seck, M. Ngom, L. Ndiaye *A study on non-classical optimal control and dymamic regional controllability by scalability of tumor evolution* .International Journal of Numerical Methods and Applications © Pushpa Publishing House, Prayagraj, India, http://www.pphmj.com http://dx.doi.org/10.17654/0975045223004 Volume 23, Number 1, (2023), Pages 67-85 P-ISSN: 0975-0452.