PENALISATION OF LONG TREATMENT TIME AND OPTIMAL CONTROL OF A TUMOUR GROWTH MODEL OF CAHN–HILLIARD TYPE WITH SINGULAR POTENTIAL

ANDREA SIGNORI

Dipartimento di Matematica e Applicazioni, Università di Milano-Bicocca
via Cozzi 55, 20125 Milano, Italy

(Communicated by Irena Lasiecka)

Abstract. A distributed optimal control problem for a diffuse interface model, which physical context is that of tumour growth dynamics, is addressed. The system we deal with comprises a Cahn–Hilliard equation for the tumour fraction coupled with a reaction-diffusion for a nutrient species surrounding the tumourous cells. The cost functional to be minimised possesses some objective terms and it also penalises long treatments time, which may affect harm to the patients, and big aggregations of tumourous cells. Hence, the optimisation problem leads to the optimal strategy which reduces the time exposure of the patient to the medication and at the same time allows the doctors to achieve suitable clinical goals.

1. Introduction. In the last decades, several developments have been obtained by scientists in the field of tumour growth modelling. The key idea behind these models arises from realising that the tumour tissue, as a special material, has to obey physical laws. Hence, the modelling techniques originally developed for engineering purposes can be adapted and exploited to derive mathematical models which better emulate the evolution of tumours (see [10]). The great advantages of mathematics are, among others, that of being able to foresee, make predictions, and capture information that does not interfere with the patient’s health. Moreover, mathematics has the ability to select specific mechanisms we could be interested in. Besides, let us also mention that further understanding from the mathematical point of view can also allow the doctors to tailor a personalised therapeutic pathway.

The diffuse interface model we are going to deal with reads as follows:

\[
\begin{align*}
\alpha \partial_t \mu + \partial_t \varphi - \Delta \mu &= P(\varphi)(\sigma - \mu) & \text{in } Q := \Omega \times (0,T), \\
\mu &= \beta \partial_t \varphi - \Delta \varphi + F'(\varphi) & \text{in } Q, \\
\partial_t \sigma - \Delta \sigma &= -P(\varphi)(\sigma - \mu) + u & \text{in } Q, \\
\partial_n \mu &= \partial_n \varphi = \partial_n \sigma = 0 & \text{on } \Sigma := \partial \Omega \times (0,T), \\
\mu(0) &= \mu_0, \varphi(0) = \varphi_0, \sigma(0) = \sigma_0 & \text{in } \Omega.
\end{align*}
\]

2020 Mathematics Subject Classification. Primary: 35Q92, 49J20, 49K20; Secondary: 35K86, 92C50.

Key words and phrases. Optimal control, free terminal time, phase field, tumour growth, Cahn–Hilliard equation, adjoint system, necessary optimality conditions.
where $\alpha$ and $\beta$ represent two positive relaxation parameters and $\Omega$ and $T > 0$ denote the spatial set in which the evolution takes place and the time horizon, respectively.

This model constitutes a variation of the four-species thermodynamically consistent model proposed by Hawkins–Daruud et al. in [26] (see also [9, 32, 25, 27]), where the velocity contribution and chemotaxis effect are neglected and two relaxation terms $\alpha \partial_t \mu$ and $\beta \partial_t \varphi$ in equation (1.1) and (1.2) are included. Let us notice that equations (1.1)–(1.2) comprise a viscous Cahn–Hilliard system for $(\varphi, \mu)$ (see, e.g., the review article [29] and the references therein for more details) with a non-standard source term $P(\varphi)(\sigma - \mu)$ modelling the growth and death of cells. Since the physical background of the above model has been extensively described in [4, 6, 8, 15], we just sketch the role covered by the occurring symbols. In the above equations, the primary variables of the model are $\varphi$, $\mu$, and $\sigma$ denoting in the order the difference in volume fractions between the tumour and healthy cells, the associated chemical potential, and the nutrient concentration of an unknown nutrient species (e.g., glucose, oxygen). Typically $\varphi$ ranges between $-1$ and $1$, where the two extremes represent the pure phases, i.e., the healthy case and the tumourous case. The function $P$ represents a source/sink term which accounts for biological mechanisms such as proliferation. Besides, as typical for phase field models, the function $F$ denotes a double-well potential whose classical examples are the regular quartic potential and the singular logarithmic potential, which is more relevant for applications. They are defined, in the order, by

$$F_{\text{reg}}(r) := \frac{1}{4} (r^2 - 1)^2 \quad \text{for} \quad r \in \mathbb{R},$$

$$F_{\text{log}}(r) := ((1 - r) \log(1 - r) + (1 + r) \log(1 + r)) - \lambda r^2 \quad \text{for} \quad |r| < 1,$$

where in (1.7) $\lambda$ stands for a positive constant large enough to avoid convexity. The positive constants $\alpha$ and $\beta$ can be seen as relaxation parameters. The first one provides (1.1) with a parabolic structure, whereas the second term in the equation (1.2) is the classical viscous term of the Cahn–Hilliard equation. Let us also refer to [36] and to [4, 6, 8] where these relaxations are incorporated in the model. Lastly, the variable $u$ appearing in (1.3) plays the role of control variable so that the system (1.1)–(1.5) will be referred to as the state system in the sequel.

The well-posedness and long-time behavior of the above model (with $u = 0$), in terms of the omega-limit set, have been addressed in [4] for a general class of double-well potentials, in the case $\alpha = \beta > 0$. Next, in [6] and [8] Colli et al. discuss in which sense the parameters $\alpha$ and $\beta$ can be sent to zero both separately and jointly providing to specify the functional framework under which this can be done depending on the asymptotic study under consideration. Furthermore, we mention [15], where the above system (with $u = 0$) without any relaxation terms, i.e., the system (1.1)–(1.5) with $\alpha = \beta = 0$, is studied. There, despite they restricted the analysis on regular potentials with suitable polynomial growth, they keep the assumptions on the nonlinearity $P$ very general postulating for it a controlled polynomial growth. Then, we refer to [30], where the authors investigate the existence of the global attractor for the dynamical system generated by (1.1)–(1.5) in the case $\alpha = \beta = 0$ (see, e.g., [31] for further details on global attractors). Furthermore, let us point out [16], where a non-local model is taken into account for the challenging case of singular potentials and degenerate mobilities. As for the diffuse interface models including the velocity field effects by assuming a Darcy’s law or a Stokes–Brinkman’s law, we refer to [11, 12, 17, 18, 19, 20, 21, 22, 24, 40], where also further biological mechanisms such as chemotaxis and active transport.
are incorporated in the model. Lastly, we refer to [1, 41] and to the reference therein for some numerical applications.

Before introducing the optimal control problem we are going to address, let us spend some words explaining how the cancer treatments are usually scheduled which motivate some of the modelling considerations made below. A typical medical treatment include surgery, chemotherapy, radiotherapy, and immunotherapy and especially the last three therapies are particularly sensitive to the time exposition of the patient. Moreover, the therapy is divided into cycles consisting of a “short” period of treatment followed by a longer period of rest. The goal of these therapies is usually to reduce the tumour mass to achieve a reasonable stage which is compatible with surgery. Besides, as time passes by the dispensed drug starts to accumulate in the body bringing additional waste items to be purified by kidneys and liver, and in the worst-case scenario, it may happen that after a long-time exposure the tumour cells became resistant to the medicament. This is the reason which leads us to incorporate a long treatment time penalisation in our optimisation problem.

Up to our knowledge, the first contribution concerning an optimal control problem governed by the system (1.1)–(1.5) is [7], where (1.1)–(1.5) was considered without any relaxation terms, i.e., with the choice $\alpha = \beta = 0$. There, the authors proved the existence of a minimiser for the optimisation problem and provide first-order necessary conditions for optimality in the framework of regular potentials exhibiting polynomial growth. Then, we mention [36], where a similar optimisation problem is addressed for the system (1.1)–(1.5) with $\alpha, \beta > 0$ as the state system in the case of singular, while regular, potentials allowing the logarithmic potential to be included in the investigation. In this direction, the artificial relaxation terms $\alpha \partial_t \mu$ and $\beta \partial_t \varphi$ play a crucial role since, owing to their regularizing effect, they allow proving a uniform separation principle for the phase variable which is a key property to handle singular potentials. Next, the same author extends in [35] the optimisation problem to the case of the double-obstacle potential by following the asymptotic scheme known in the literature as to deep quench limit. Then, in [33] and [34] the author proves, by employing proper asymptotic strategies, how the optimal control problem for the case $\alpha, \beta > 0$ can be useful to solve the optimal control problems related to the state system above in which $\alpha = 0, \beta > 0$ and $\alpha > 0, \beta = 0$ by letting the parameters $\alpha$ and $\beta$ go to zero, respectively. Besides, we are also aware of the recent work [3], where, after discussing the long-time behavior of solutions, the authors show that the optimal control problem [7] can be extended to the case in which the cost functional also depends on time. Referring to different models, we mention the contribution [23], where an optimal treatment time has been performed for a slightly different state system of Cahn–Hilliard type, where the control appears in the first equation. Moreover, we refer to [38], where an optimal control problem for the two-dimensional Cahn–Hilliard–Darcy system with mass sources is addressed. Lastly, we point out [13, 14], where optimal control problems for the more involved Cahn–Hilliard–Brinkman model, previously investigated by [12], are addressed. For the interested reader, we also mention [5], where a different type of control problem, known as sliding mode control, is performed for a similar system.

In the spirit of [23] (and [3]), we aim at generalizing the results established in [36] by introducing in the functional to be minimised a time penalisation. The optimisation problem considered in [36] consists in minimising the following cost
for some non-negative constants \( b_0, \ldots, b_4 \) and some given target functions \( \varphi_Q, \sigma_Q, \varphi_\Omega, \sigma_\Omega \) defined in proper functional spaces, under the constrained that the control \( u \) belongs to the set of \textit{admissible controls} \( U_{ad} \) which is defined by

\[
U_{ad} := \{ u \in L^\infty(Q) : u_* \leq u \leq u^* \text{ a.e. in } Q \},
\]

where \( u_* \) and \( u^* \) denote some prescribed functions in \( L^\infty(Q) \), and such that the variables \( \varphi \) and \( \sigma \) are solutions to the state system (1.1)–(1.5). Thus, we aim at extending the above minimisation problem to a time-dependent cost functional by adding a free terminal time, which penalises long treatments time, as well as an objective time to be approached. Moreover, we also introduce in the cost functional an additional penalisation term for large aggregation of tumour cells. Namely, the time-dependent objective cost functional we are going to minimise reads as

\[
J(\varphi, \sigma, u, \tau) := \frac{b_1}{2} \int_{Q_*} |\varphi - \varphi_Q|^2 + \frac{b_2}{2} \int_{\Omega} |\varphi(\tau) - \varphi_\Omega|^2 + \frac{b_3}{2} \int_{Q_*} |\sigma - \sigma_Q|^2
\]

\[
+ \frac{b_4}{2} \int_{\Omega} |\sigma(\tau) - \sigma_\Omega|^2 + \frac{b_5}{2} \int_{Q} |u|^2,
\]

where the symbols \( b_0, \ldots, b_5 \) denote non-negative constants, while \( \varphi_Q, \sigma_Q, \varphi_\Omega, \sigma_\Omega, \) and \( \tau_* \) stand for the targets we want to approximate. Here, let us point out the following comments and differences with respect to the problem discussed in [36]:

(i) Despite the last term in (1.10), the time integrals are performed between zero and \( \tau \in [0, T] \), where \( \tau \) models the treatment time of the cycle which the patient undergoes the clinical therapy, while \( T \) may be regarded as the maximum amount of time prescribed by some protocol. Let us claim that only minor changes are in order if one substitutes the term \( b_5 \tau \) in (1.10) with a more general term like \( b_5 f(\tau) \), where \( f : [0, \infty) \rightarrow [0, \infty) \) is an increasing and continuously differentiable function.

(ii) The term \( \frac{b_5}{2} |\tau - \tau_*|^2 \) forces the optimal time to be as close as possible to \( \tau_* \) which stands for some target time to be reached. Notice that the sum of this latter (which is quadratic in \( \tau \) ) and \( b_5 \tau \) (which is linear) gives still a convex contribution.

(iii) Minimizing the integral \( \int_{Q_*} |\varphi - \varphi_Q|^2 \) leads the phase variable \( \varphi \) to be as close as possible, at the time \( \tau \) and in the sense of the \( L^2 \)-norm, to the prescribed target \( \varphi_Q \). In a similar fashion, it goes for the other variables. Thus, \( \varphi_Q, \sigma_Q, \varphi_\Omega, \sigma_\Omega \) should be chosen as stable configurations of the system or as some desirable configurations which are meaningful for surgery.

(iv) The last term \( \int_{Q} |u|^2 \) penalises the large values of the control variable designing the side-effect that the dispensation of too many drugs to the patient might cause.

(v) The term \( \frac{1 + \varphi(\tau)}{2} \) measures the size of the tumourous mass at the given time \( \tau \). Hence, it penalises the strategies which do not shrink the tumour. Notice that the presence of 1 in the numerator is due to the fact that in the healthy
case we have $\varphi = -1$ so that in that case the corresponding tumour mass is indeed zero. 

(vi) The constants $b_0, \ldots, b_6$ can be chosen accordingly to the therapeutic goal we are interested in.

Compared to [23] and [3], let us underline that we also include in the analysis a target time $\tau_*$. This choice has the advantage to produce a better characterisation of the optimality of the time variable (cf. Theorem 3.9). Notice that the choice $\tau_* = 0$ is allowed. 

To conclude the section, let us introduce some general facts concerning optimal control theory. At first, let us note that since the well-posedness of system (1.1)–(1.5) has already been established in [36], we are in a position to properly define the control-to-state operator which assigns to a given control $u$ the corresponding solution to (1.1)–(1.5). Namely, we have

$$ S : u \mapsto (\mu, \varphi, \sigma), $$

where $(\mu, \varphi, \sigma)$ stands for the unique solution to system (1.1)–(1.5) associated with the control variable $u$. This allows us to suppress the variables $\varphi$ and $\sigma$ in the cost functional $J$ by expressing them as functions of $u$ leading to the corresponding reduced cost functional which is defined as

$$ J_{\text{red}}(u, \tau) := J(S_2(u), S_3(u), u, \tau), $$

where $S_2(u), S_3(u)$ denote the second and third components of $S$, respectively. Although the existence of a minimiser of the above problem can be deduced by following similar reasoning as in [36], the corresponding first-order necessary conditions for optimality present significant differences. However, following classical arguments (see, e.g., [39, 28]), it is clear that that the optimality of $(\pi, \tau) \in U_{\text{ad}} \times [0, T]$ can be characterised by employing the following variational inequalities

$$ \begin{cases} 
D_u J_{\text{red}}(\pi, \tau)(v - \pi, \tau) \geq 0 & \text{for every } v \in U_{\text{ad}}, \\
D_\tau J_{\text{red}}(\pi, \tau)(s - \tau) \geq 0 & \text{for every } s \in [0, T], 
\end{cases} $$

where $D_i J_{\text{red}}, i = \{u, \tau\}$, stand for the derivative of the reduced cost functional $J_{\text{red}}$ with respect to the corresponding variable in a proper functional setting.

To get the necessary conditions for the time optimality, the key argument is to show that the reduced cost functional is Fréchet differentiable so that the abstract conditions (1.13) can be exploited. In particular, the Fréchet differentiability with respect to the time variable requires higher order temporal regularity for the phase variable $\varphi$. In this direction, let us anticipate that the time derivative of the reduced cost functional will produce terms involving $\varphi(\tau)$ and $\partial_\tau \varphi(\tau)$ (cf. Theorem 3.8), where $(\pi, \tau)$ stands for some optimal pair and $(\mu, \varphi, \sigma)$ for the corresponding state. A sufficient condition which gives meaning to the above terms is $\varphi \in H^2(0, T; L^2(\Omega))$ due to the continuous injections of $H^2(0, T; L^2(\Omega))$ in $C^1([0, T]; H^1(\Omega))$ so that the pointwise terms $\varphi(\tau)$ and $\partial_\tau \varphi(\tau)$ are meaningful, at least in $L^2(\Omega)$. In this regards, let us also mention that we can not consider in the cost functional (1.10) any contribution involving $\int_\Omega |\sigma(\tau) - \sigma_\Omega|^2$, where $\sigma_\Omega$ models some target function. The reason is that if such term is present, in the time derivative of $J_{\text{red}}$ it will appear the pointwise term $\partial_\tau \varphi(\tau)$ which, in turn, will require to show $\varphi \in H^2(0, T; L^2(\Omega))$. However, the nutrient equation (1.3) contains the control variable $u$ so that, to get the mentioned regularity for $\sigma$, we would be forced to assume the control variable to be sufficiently regular in time,
say \( u \in H^1(0,T;L^2(\Omega)) \), which is not significant for the applications. For the same reason, we are considering the term \( \int_Q |u|^2 \) in (1.10), instead of \( \int_Q \tau |u|^2 \), to avoid assuming any temporal regularity for \( u \). However, in Section 4, by using the relaxation arguments employed by Garcke et al. in [23], we also show that it is possible to include in the analysis an objective control for the nutrient variable at time \( \tau \).

Hence, introducing the space of admissible states and controls by

\[
A_{ad} := \{(\varphi, \sigma, u, \tau) : (u, \tau) \in U_{ad} \times [0, T], (\varphi, \sigma) = (S_2(u), S_3(u))\},
\]

we can summarise the minimisation problem we are going to address as:

\[
(CP) \quad \inf_{(\varphi, \sigma, u, \tau) \in A_{ad}} J(\varphi, \sigma, u, \tau).
\]

The rest of the paper is outlined as follows: in the next section, we set our conventions, present the assumptions and state our results. The existence of a minimiser for the optimisation problem \((CP)\) and the corresponding first-order necessary conditions for optimality have been addressed in Section 3. Next, in Section 4, we point out some possible generalisations of the work via a relaxation argument.

2. Mathematical setting. Throughout the paper, we assume \( \Omega \subset \mathbb{R}^3 \) to be a smooth bounded domain with boundary \( \Gamma \), and \( T > 0 \) is a fixed final time. For every \( t \in [0,T] \), we employ the classical notation

\[
Q_t := \Omega \times (0,t), \quad \Sigma_t := \Gamma \times (0,t) \quad \text{for every} \quad t \in (0,T],
\]

and

\[
Q := Q_T, \quad \Sigma := \Sigma_T.
\]

For an arbitrary Banach space \( X \), we use \( \|\cdot\|_X \) to denote its norm, \( X^* \) for its topological dual, and \( X^* \langle \cdot, \cdot \rangle_X \) for the duality product between \( X^* \) and \( X \). Meanwhile, for every \( p \in [1, +\infty] \), we simply write \( \|\cdot\|_p \) to indicate the usual norm of the Sobolev spaces \( L^p(\Omega) \). Besides, it turns out to be convenient to set

\[
H := L^2(\Omega), \quad V := H^1(\Omega), \quad W := \{v \in H^2(\Omega) : \partial_n v = 0 \text{ on } \Gamma\},
\]

equipped with their standard norms, where \( \partial_n \) stands for the outward normal derivative of \( \Gamma \). Under these assumptions, it follows that the injections \( V \hookrightarrow H \cong H^* \hookrightarrow V^* \) are both continuous and dense which entails that \( (V, H, V^*) \) forms a Hilbert triple so that we have the following identification

\[
V^* \langle u, v \rangle_V = \int_\Omega uv \quad \text{for every} \quad u \in H, \ v \in V.
\]

As far as the general assumptions are concerned, we postulate that

\[
\begin{align*}
\alpha, \beta & \quad \text{are positive constants.} \quad (2.1) \\
b_0, b_1, b_2, b_3, b_4, b_5, b_6 & \quad \text{are non-negative constants, but not all zero.} \quad (2.2) \\
\varphi_Q, \sigma_Q : Q \to \mathbb{R}, \varphi_\Omega : \Omega \to \mathbb{R} & \quad \text{and } \varphi_Q, \sigma_Q \in L^2(Q), \varphi_\Omega \in L^2(\Omega). \quad (2.3) \\
u_*, u^* & \in L^\infty(Q) \text{ with } u_* \leq u^* \text{ a.e. in } Q. \quad (2.4) \\
\tau_* & \in [0, T]. \quad (2.5)
\end{align*}
\]
\[ P \in C^2(\mathbb{R}) \text{ is non-negative, bounded with bounded derivative.} \quad (2.6) \]
\[ \varphi_0 \in W, \mu_0 \in V \cap L^\infty(\Omega), \sigma_0 \in V. \quad (2.7) \]
\[ F(\varphi_0) \in L^1(\Omega). \quad (2.8) \]

Moreover, let us postulate that the control-box \( U_{ad} \) is defined by (1.9), so that \( U_{ad} \) is a closed and convex subset of \( L^2(Q) \). On the other hand, it will be sometimes necessary to work with an open set. Hence, let us define the open superset \( U_R \) as follows

\[ U_R \subset L^2(Q) \text{ is a non-empty, bounded and open set containing } U_{ad} \text{ such that } \|u\|_2 \leq R \text{ for all } u \in U_R. \]

As for the nonlinear double-well potential \( F \), we require that

\[ F : \mathbb{R} \to [0, +\infty], \text{ with } F := \hat{B} + \hat{\pi}, \quad (2.9) \]

where

\[ \hat{B} : \mathbb{R} \to [0, +\infty] \text{ is convex, and lower semicontinuous, with } \hat{B}(0) = 0. \quad (2.10) \]
\[ \hat{\pi} \in C^3(\mathbb{R}) \text{ and } \pi := \hat{\pi}' \text{ is Lipschitz continuous.} \quad (2.11) \]

Under these assumptions it is well-known that the subdifferential of \( \hat{B} \), \( \partial \hat{B} =: B \), is a maximal and monotone graph \( B \subseteq \mathbb{R} \times \mathbb{R} \) (see, e.g., [2, Ex. 2.3.4, p. 25]) whose domain we indicate by \( D(B) \). Furthermore, we assume that \( F \) is a smooth function when restricted to its domain by assuming that

\[ D(B) = (r_-, r_+), \text{ with } -\infty \leq r_- < 0 < r_+ \leq +\infty. \]
\[ F|_{D(B)} \in C^3(r_-, r_+), \text{ and } \lim_{r \to r_{\pm}} F'(r) = \pm \infty. \quad (2.12) \]

It is worth noting that both the regular potential (1.6) and the logarithmic potential (1.7) do fit the above assumptions. Moreover, we additionally require that the initial datum \( \varphi_0 \) verifies

\[ r_- < \inf \varphi_0 \leq \sup \varphi_0 < r_+, \quad (2.13) \]

which for the logarithmic potential (1.7) has the physical interpretation that \( \varphi_0 \) does not contain any region with pure phases. Notice that the above condition combined with (2.7) entails that

\[ \frac{1}{2}(\mu_0 + \Delta \varphi_0 - B(\varphi_0) - \pi(\varphi_0)) \in H. \quad (2.14) \]

The mathematical assumptions required so far are more or less the same assumed in [36]. However, as already mentioned, the first-order necessary conditions for optimality that we will point out later will demand higher order temporal regularity for the phase variable. To give meaning to all the appearing pointwise terms we replace (2.3) and (2.14) by

\[ \varphi_Q, \sigma_Q \in H^1(0, T; H), \quad (2.15) \]
\[ \frac{1}{2}(\mu_0 + \Delta \varphi_0 - B(\varphi_0) - \pi(\varphi_0)) \in V, \quad (2.16) \]

respectively. Let us also point out that condition (2.16) easily follows once the initial data, in addition to (2.7), fulfils \( \varphi_0 \in H^3(\Omega) \).

Before moving on, let us recall some well-known results which we will apply later on. First, we often owe to the standard Sobolev continuous embedding

\[ H^1(\Omega) \hookrightarrow L^q(\Omega), \text{ for every } q \in [1, 6], \quad (2.17) \]
which is also compact for every $q \in [1, 6)$. Moreover, we recall the Young inequality
\[ ab \leq \delta a^2 + \frac{1}{4\delta} b^2, \quad \text{for every } a, b \geq 0 \text{ and } \delta > 0. \quad (2.18) \]
Lastly, we convey to use the symbol small-case $c$ for every constant which only depend on structural data of the problem such as the final time $T$, $\Omega$, $R$, the shape of the nonlinearities, the norms of the involved functions, and possibly $\alpha$ and $\beta$. On the other hand, we devote the capital letters to designate some specific constants.

3. The control problem.

3.1. The state system. To begin with, let us recall the well-posedness result for the system (1.1)–(1.5) obtained in [36].

**Theorem 3.1** ([36, Thms. 2.1, 2.2, and 2.3]). Suppose that (2.1)–(2.14) hold and let $u \in \mathcal{U}_R$. Then, the state system (1.1)–(1.5) admits a unique solution $(\mu, \varphi, \sigma)$ satisfying
\[
\varphi \in W^{1,\infty}(0, T; H) \cap H^1(0, T; V) \cap L^\infty(0, T; W) \subset C^0([0, T]; C^0(\bar{\Omega})), \quad (3.1)
\]
\[
\mu, \sigma \in H^1(0, T; H) \cap L^\infty(0, T; V) \cap L^2(0, T; W) \subset C^0([0, T]; V), \quad (3.2)
\]
\[
\mu \in L^\infty(Q). \quad (3.3)
\]
Moreover, there exists a positive constant $C_1$, which depends on $R$, $\alpha$, $\beta$, and on the data of the system, such that
\[
\|\varphi\|_{W^{1,\infty}(0, T; H) \cap H^1(0, T; V) \cap L^\infty(0, T; W)} + \|\mu\|_{H^1(0, T; H) \cap L^\infty(0, T; V) \cap L^2(0, T; W) \cap L^\infty(Q)} + \|\sigma\|_{H^1(0, T; H) \cap L^\infty(0, T; V) \cap L^2(0, T; W)} \leq C_1. \quad (3.4)
\]
In addition, it holds the so-called uniform separation property. Namely, there exists a compact subset $K \subset (r_-, r_+)$ = $D(B)$ such that
\[
\varphi(x, t) \in K \quad \text{for all } (x, t) \in Q.
\]
Furthermore, the following estimate
\[
\|\varphi\|_{C^0(Q)} + \max_{0 \leq i \leq 3} \|F^{(i)}(\varphi)\|_{L^\infty(Q)} + \max_{0 \leq j \leq 2} \|P^{(j)}(\varphi)\|_{L^\infty(Q)} \leq C_2 \quad (3.5)
\]
is satisfied for a positive constant $C_2$ which depends only on $R$, $\alpha$, $\beta$, $K$ and on the data of the system.

The well-posedness of the state system (1.1)–(1.5) established by the the above theorem allow us to define the control-to-state operator $\mathcal{S}$ as the map which assigns to every control $u$ the corresponding solution $(\mu, \varphi, \sigma)$ to system (1.1)–(1.5).

We are now ready to present the first novelty of the work regarding improved regularity results for the solutions to (1.1)–(1.5) obtained in the above theorem that will be used later on to investigate the optimal control problem (CP).

**Theorem 3.2.** Suppose that (2.1)–(2.13) and (2.16) hold and let $u \in \mathcal{U}_R$. Then, the unique solution $(\mu, \varphi, \sigma)$ to (1.1)–(1.5) obtained from Theorem 3.1, in addition to (3.1)–(3.3), enjoys the following regularity
\[
\varphi \in W^{1,\infty}(0, T; V) \cap H^2(0, T; H) \cap H^1(0, T; H^2(\Omega)) \subset C^1([0, T]; H) \cap C^0([0, T]; H^2(\Omega)). \quad (3.6)
\]
Moreover, there exists a positive constant $C_3$ depending on $R$, $\alpha$, $\beta$, and on the data of the system, such that
\[
\|\varphi\|_{W^{1,\infty}(0, T; V) \cap H^2(0, T; H)} \leq C_3. \quad (3.7)
\]
Proof. For the sake of simplicity, we perform only formal a priori estimates which can be carried out rigorously within an approximation scheme such as the Faedo–Galerkin scheme. We differentiate (1.2) with respect to time, multiply the obtained equation by $\partial_t \varphi$, and integrate over $Q_t$, and by parts to obtain that

$$\frac{1}{2} \int_{Q_t} |\nabla \varphi|^2 + \frac{1}{2} \int_{Q_t} |\nabla \varphi(t)|^2 = \frac{1}{2} \int_{Q_t} (\partial_t \varphi)^2 - \int_{Q_t} P''(\varphi) \partial_t \varphi \partial_t \varphi + \int_{Q_t} \partial_t \mu \partial_t \varphi,$$

where we denote the integrals on the right-hand side by $I_1, I_2$ and $I_3$, respectively. The terms on the left-hand side are non-negative, whereas $I_2$ and $I_3$ can be dealt by means of the Young inequality, along with the estimate (3.5) which is verified by the solution $\varphi$. Namely, we have that

$$|I_2| + |I_3| \leq \frac{\beta}{2} \int_{Q_t} |\partial_t \varphi|^2 + c \int_{Q_t} (|\partial_t \mu|^2 + |\partial_t \varphi|^2).$$

Moreover, by taking $t = 0$ in (1.2) and using the assumption (2.16) we readily infer that

$$|I_1| \leq c.$$

Therefore, owing to the estimate (3.4), we deduce that there exists a positive constant $c$ such that

$$\|\partial_t \varphi\|_{L^2(0,T;H)} + \|\nabla \varphi\|_{L^\infty(0,T;H)} \leq c.$$

Next, let us recall the well-known embedding of $H^1(0,T;H)$ in $C^0([0,T];H)$ which entails also that $\partial_t \varphi \in C^0([0,T];H)$. Lastly, comparison in equation (1.2) produces

$$\Delta \varphi \in H^1(0,T;H) \subset C^0([0,T];H),$$

so that, upon invoking the elliptic regularity theory, the proof is concluded.

**Theorem 3.3.** Suppose that the assumptions of Theorem 3.2 are verified. Moreover, let $\mu_0 \in H^3(\Omega)$. Then, the unique solution $(\mu, \varphi, \sigma)$ to (1.1)–(1.5) obtained from Theorem 3.1, in addition to (3.1)–(3.3) and (3.6) satisfies

$$\mu \in W^{1,\infty}(0,T;V) \cap H^2(0,T;H) \cap H^1(0,T;H^2(\Omega)) \subset C^1([0,T];H) \cap C^0([0,T];H^2(\Omega)).$$

Moreover, there exists a positive constant $C_4$ depending on $R, \alpha, \beta$, and on the data of the system, such that

$$\|\mu\|_{W^{1,\infty}(0,T;V) \cap H^2(0,T;H)} \leq C_4.$$

Proof. As before, we proceed formally and let us claim that the proof can be carried out in a rigorous fashion by employing a Galerkin scheme. We differentiate (1.1) with respect to time, test the obtained equation by $\partial_t \mu$, and integrate over time and by parts to obtain that

$$\alpha \int_{Q_t} |\partial_t \mu|^2 + \frac{1}{2} \int_{Q_t} |\nabla \partial_t \mu|^2 = \frac{1}{2} \int_{Q_t} |\nabla \partial_t \mu(0)|^2 + \int_{Q_t} P'(\varphi) (\sigma - \mu) \partial_t \varphi \partial_t \mu$$

$$+ \int_{Q_t} P(\varphi) (\partial_t \sigma - \partial_t \mu) \partial_t \varphi - \int_{Q_t} \partial_t \varphi \partial_t \mu,$$
where we indicate by $I_1, \ldots, I_4$ the integrals on the right-hand side, in this order. The first term can be bounded by combining the assumption (2.7) with (2.16) and the additional requirement on the initial datum $\mu_0 \in H^3(\Omega)$. In fact, evaluating equation (1.1) at $t = 0$, and then equation (1.2) at $t = 0$ lead us to realise that
\[
\partial_t \mu(0) = \frac{1}{\alpha} \left( \frac{1}{\beta} \left( -\mu_0 - \Delta \varphi_0 + F'(\varphi_0) \right) + \Delta \mu_0 + P(\varphi_0)(\sigma_0 - \mu_0) \right) \in V
\]
so that
\[
|I_1| \leq c.
\]
Then, using the previous estimates (3.4)–(3.5) and (3.7), Hölder’s inequality, the continuous embedding $V \subset L^4(\Omega)$, and the boundedness of $P'$, we have
\[
|I_2| \leq c \int_0^t \left( \|\sigma\|_4 + \|\mu\|_4 \right) \|\partial_t \varphi\|_4 \|\partial_t \mu\|_2
\leq \delta \int_{Q_t} |\partial_t \mu|^2 + c_3 \int_{Q_t} \left( \|\sigma\|_\infty^2 + \|\mu\|_\infty^2 \right) \|\partial_t \varphi\|_V^2
\leq \delta \int_{Q_t} |\partial_t \mu|^2 + c_5,
\]
for a positive $\delta$ yet to be determined, where in the last line we also invoke the fact that, due to (3.1)–(3.3) and to (3.7), we have that $\|\sigma\|_V, \|\mu\|_V$ and $\|\partial_t \varphi\|_V$ belong to $L^\infty(0,T)$. Using the Young inequality, the boundedness of $P$, and (3.5), we infer that
\[
|I_3| + |I_4| \leq \delta \int_{Q_t} |\partial_t \mu|^2 + c_3 \int_{Q_t} (|\partial_t \varphi|^2 + |\partial_t \sigma|^2 + |\partial_t \mu|^2),
\]
for a positive $\delta$ yet to be determined. Hence, adjusting $\delta \in (0,1)$ small enough and accounting for the above estimates, we deduce that
\[
\|\partial_t \mu\|_{L^2(0,T;H)} + \|\nabla \partial_t \mu\|_{L^\infty(0,T;H)} \leq c.
\]
Arguing as above, we easily infer that $\partial_t \mu \in C^0([0,T];H)$ and then, by comparison in equation (1.1) also that
\[
\Delta \mu \in H^1(0,T;H) \subset C^0([0,T];H)
\]
which complete the proof upon invoking the elliptic regularity theory. 

To conclude the section, let us recall the continuous dependence result for (1.1)–(1.5) obtained in [36, Thms. 2.2 and 2.3].

**Theorem 3.4.** Assume that (2.1)–(2.14) are fulfilled. Moreover, for $i = 1, 2$, let $u_i \in U_R$ and $(\mu_i, \varphi_i, \sigma_i)$ be the corresponding solution to (1.1)–(1.5) obtained from Theorem 3.1. Then, there exists a positive constant $C_5$, which depends only on $R$, $\alpha$ and $\beta$, and on the data of the system such that
\[
\begin{align*}
||\alpha (\mu_1 - \mu_2) + (\varphi_1 - \varphi_2) + (\sigma_1 - \sigma_2)||_{L^\infty(0,T;V^*)} + ||\mu_1 - \mu_2||_{L^\infty(0,T;H) \cap L^2(0,T;V)} + ||\varphi_1 - \varphi_2||_{H^1(0,T;H) \cap L^\infty(0,T;V)} + ||\sigma_1 - \sigma_2||_{L^\infty(0,T;H) \cap L^2(0,T;V)} \leq C_5 ||u_1 - u_2||_{L^2(0,T;H)}.
\end{align*}
\]
(3.9)

This latter can be equivalently interpreted as a Lipschitz continuity property for the control-to-state operator $S$ between suitable Banach spaces.
3.2. **Existence of a minimiser.** Here, we prove the existence of a minimiser for the optimisation problem \((CP)\).

**Theorem 3.5.** Assume that \((2.1)–(2.14)\) are fulfilled. Then, the optimal control problem \((CP)\) admits at least a minimiser. Namely, there exists some \((\varphi, \sigma, \pi, \tau) \in \mathcal{A}_{ad}\) such that

\[
\mathcal{J}(\varphi, \sigma, \pi, \tau) = \inf_{(\varphi, \sigma, u, \tau) \in \mathcal{A}_{ad}} \mathcal{J}(\varphi, \sigma, u, \tau).
\]

The control variable \(\pi\) will be referred to as optimal control, whereas \(\tau\) and \((\pi, \varphi, \sigma)\) will be referred to as optimal time and optimal state, respectively.

**Proof.** The proof can be easily carried out by means of the well-known direct method of calculus of variations, e.g., by retracing the proof of [36, Thm. 2.6]. To begin with, let us check that the cost functional \(\mathcal{J}\) is bounded from below. Using the bounds for the phase variable \(\varphi\) expressed by \((3.4)–(3.5)\), we infer that

\[
\mathcal{J}(\varphi, \sigma, u, \tau) \geq \frac{b_1}{2} \int_{\Omega} \varphi(\tau) + \frac{b_4}{2} \|\varphi\|_{C^0(\Omega)}^2 \geq - \frac{b_1}{2} C_2 > -\infty.
\]

Next, we pick a minimizing sequence \(\{u_n, \tau_n\}\) of elements of \(U_{ad} \times (0, T)\) with the sequence of the corresponding solutions \(\{\mu_n, \varphi_n, \sigma_n\}\) to \((1.1)–(1.5)\) obtained from Theorem 3.1. Namely, we have that

\[
\lim_{n \to \infty} \mathcal{J}(\varphi_n, \sigma_n, u_n, \tau_n) = \inf_{(\varphi, \sigma, u, \tau) \in \mathcal{A}_{ad}} \mathcal{J}(\varphi, \sigma, u, \tau) > -\infty.
\]

On the other hand, for every \(n \in \mathbb{N}\), the bounds provided by estimate \((3.4)\) hold independently of \(n\). Therefore, using classical weak and weak-star compactness results we infer that, up to a not relabeled subsequence, there exist some \(\pi \in U_{ad}\) and a triple \((\pi, \varphi, \sigma)\) such that, as \(n \to \infty\),

\[
\begin{align*}
u_n &\to \pi \text{ weakly star in } L^\infty(\Omega), \\
\mu_n &\to \pi \text{ weakly star in } H^1(0, T; H) \cap L^\infty(0, T; V) \cap L^2(0, T; W) \cap L^\infty(Q), \\
\varphi_n &\to \varphi \text{ weakly star in } W^{1, \infty}(0, T; H) \cap H^1(0, T; V) \cap L^\infty(0, T; W), \\
\sigma_n &\to \sigma \text{ weakly star in } H^1(0, T; H) \cap L^\infty(0, T; V) \cap L^2(0, T; W).
\end{align*}
\]

Moreover, standard compactness arguments (see, e.g., [37, Sec. 8, Cor. 4]) yield that, possibly up to a not relabeled subsequence, as \(n \to \infty\),

\[
\varphi_n \to \varphi \text{ strongly in } C^0(\Omega) \quad (3.10)
\]

and also that there exists \(\tau \in [0, T]\) such that, as \(n \to \infty\),

\[
\tau_n \to \tau. \quad (3.11)
\]

Next, by using estimate \((3.5)\), the strong convergence \((3.10)\), and the properties of \(F\) and \(P\), we realise that

\[
F'(\varphi_n) \to F'(\varphi), \quad P(\varphi_n) \to P(\varphi) \quad \text{strongly in } C^0(\Omega).
\]

Thus, it is then a standard matter to pass to the limit, as \(n \to \infty\), in the variational formulation of \((1.1)–(1.5)\) written for \((\mu_n, \varphi_n, \sigma_n)\) and conclude that \((\pi, \varphi, \sigma) = S(\pi)\). Moreover, \((3.11)\) ensures that, as \(n \to \infty\),

\[
\chi_{[0, \tau_n]}(t) \to \chi_{[0, \tau]}(t) \quad \text{for a.a. } t \in (0, T). \quad (3.12)
\]
Hence, we claim that the limit \((\varphi, \sigma, \pi, \tau)\) is indeed the minimiser we are looking for. Before showing how to pass to the limit term by term, let us point out that

\[
\int_{Q_{r_n}} |\cdot|^2 = \int_0^{r_n} \|\cdot\|^2_2 = \int_0^T \|\cdot\|^2_2 \chi_{[0,r_n]}.
\]

As a matter of fact, it follows from the above convergences that \(\varphi_n - \varphi_Q \to \varphi - \varphi_Q\) strongly in \(L^2(0,T; H)\) so that, as \(n \to \infty\),

\[
\int_{Q_{r_n}} |\varphi_n - \varphi_Q|^2 \to \int_{Q_{r_*}} |\varphi - \varphi_Q|^2.
\]

(3.13)

In fact, we have that

\[
\int_0^T \left( \|\varphi_n - \varphi_Q\|^2_2 \chi_{[0,r_n]} - \|\varphi - \varphi_Q\|^2_2 \chi_{[0,r_*]} \right)
\]

\[
\leq \int_0^T \|\varphi_n - \varphi_Q\|^2_2 (\chi_{[0,r_n]} - \chi_{[0,r_*]}) + \chi_{[0,r_*]} \int_0^T \left( \|\varphi_n - \varphi_Q\|^2_2 - \|\varphi - \varphi_Q\|^2_2 \right),
\]

where both the terms on the right-hand side go to zero by combining the Lebesgue convergence theorem with the pointwise convergence (3.12) and the strong convergence of \(\varphi_n - \varphi_Q\). Next, let us claim that the second term of the cost functional verifies that, as \(n \to \infty\),

\[
\int_{\Omega} |\varphi_n(\tau_n) - \varphi_{\Omega}|^2 \to \int_{\Omega} |\varphi(\tau) - \varphi_{\Omega}|^2.
\]

(3.14)

In fact, it holds that

\[
\left| \int_{\Omega} |\varphi_n(\tau_n) - \varphi_{\Omega}|^2 - \int_{\Omega} |\varphi(\tau) - \varphi_{\Omega}|^2 \right| \leq \|\varphi_n(\tau_n) + \varphi(\tau) - 2\varphi_{\Omega}\|_2 \|\varphi_n(\tau_n) - \varphi(\tau)\|_2.
\]

Moreover, the convergences (3.10)–(3.11), along with the triangular inequality and the fundamental theorem of calculus, allow us to handle the last term as

\[
\|\varphi_n(\tau_n) - \varphi(\tau)\|_2 \leq \|\varphi_n(\tau_n) - \varphi_n(\tau)\|_2 + \|\varphi_n(\tau) - \varphi(\tau)\|_2
\]

\[
\leq |\tau_n - \tau|^\frac{1}{2} \left( \int_{\tau}^{\tau_n} \|\partial_t \varphi_n\|^2_2 \right)^{\frac{1}{2}} + \|\varphi_n(\tau) - \varphi(\tau)\|_2
\]

\[
\leq |\tau_n - \tau|^\frac{1}{2} \|\partial_t \varphi_n\|_{L^2(0,T;H)} + \|\varphi_n(\tau) - \varphi(\tau)\|_2.
\]

Notice that the first term on the right-hand side vanishes accounting for the bound (3.4) and for the convergence (3.11). Meanwhile, the second term goes to zero due to the strong convergence (3.10) so that (3.14) follows. Furthermore, owing to (3.11), we easily infer that, as \(n \to \infty\),

\[
|\tau_n - \tau_*|^2 \to |\tau - \tau_*|^2.
\]

The remaining terms can be handled arguing in a similar fashion. Lastly, the weak sequential lower semicontinuity of \(\mathcal{J}\), entails that

\[
\mathcal{J}(\varphi, \sigma, \pi, \tau) \leq \liminf_{n \to \infty} \mathcal{J}(\varphi_n, \sigma_n, u_n, \tau_n) = \inf_{(\varphi, \sigma, u, \tau) \in \mathcal{A}_{ad}} \mathcal{J}(\varphi, \sigma, u, \tau),
\]

so that \((\varphi, \sigma, \pi, \tau)\) is indeed a minimiser for \((CP)\), as we claimed. 

\[\square\]
3.3. The linearised system. Once the existence of minimisers has been obtained, we aim at pointing out some first-order necessary conditions for optimality by exploiting the theoretical conditions (1.13). In this direction, we first show the operator $S$ is Fréchet differentiable between suitable Banach spaces and then use the chain rule and the definition of the reduced cost functional to develop the abstract variational inequalities (1.13).

The first step consists in investigating the linearised system of (1.1)–(1.5). For a fixed control $\pi \in U_R$ with the corresponding state $(\bar{\eta}, \bar{\varphi}, \bar{\rho})$, and for an arbitrary $h \in L^2(Q)$ the linearised system to (1.1)–(1.5) reads as

\begin{align}
\alpha \partial_t \eta + \partial_t \vartheta - \Delta \eta &= P'(\varphi)(\varphi - \bar{\varphi})\vartheta + P(\varphi)(\rho - \eta) \quad \text{in } Q, \\
\eta &= \beta \partial_t \vartheta - \Delta \vartheta + F''(\varphi)\vartheta \quad \text{in } Q, \\
\partial_t \rho - \Delta \rho &= -P'\varphi(\varphi - \bar{\varphi})\vartheta - P(\varphi)(\rho - \eta) + h \quad \text{in } Q, \\
\partial_n \rho &= \partial_n \varphi = \partial_n \eta = 0 \quad \text{on } \Sigma, \\
\rho(0) = \vartheta(0) = \eta(0) &= 0 \quad \text{in } \Omega.
\end{align}

The expectation is as follows: for every $h \in L^2(Q)$, provided to find the proper Banach space $Y$, the operator $S$ is Fréchet differentiable in $Y$ and its directional derivative along $h$ is given by the corresponding solution to the linearised system above, i.e., $DS(\pi)h = (\eta, \vartheta, \rho)$. Since the linearised system is independent of the choice of the cost functional, but only depends on the state system (1.1)–(1.5), the well-posedness for the above system directly follows from [36].

**Theorem 3.6 ([36, Thm. 2.4]).** Assume that (2.1)–(2.14) are fulfilled. Then, for every $h \in L^2(Q)$, the linearised system (3.15)–(3.19) admits a unique solution $(\eta, \vartheta, \rho)$ satisfying

\begin{equation}
\eta, \vartheta, \rho \in H^1(0,T; H) \cap L^\infty(0,T; V) \cap L^2(0,T; W) \subset C^0([0,T]; V). \tag{3.20}
\end{equation}

In addition, there exists a positive constant $C_6$, which depends on the data of the system, and possibly on $\alpha$ and $\beta$, such that

\begin{align*}
|||\eta|||_{H^1(0,T; H) \cap L^\infty(0,T; V) \cap L^2(0,T; W)} + |||\vartheta|||_{H^1(0,T; H) \cap L^\infty(0,T; V) \cap L^2(0,T; W)} \\
+ |||\rho|||_{H^1(0,T; H) \cap L^\infty(0,T; V) \cap L^2(0,T; W)} \leq C_6.
\end{align*}

Now, we can rigorously formulate our expectation concerning the Fréchet differentiability of the map $S$.

**Theorem 3.7 ([36, Thm. 2.5]).** Assume that (2.1)–(2.14) are satisfied and let $\pi$ and $(\bar{\eta}, \bar{\varphi}, \bar{\rho})$ be an optimal control for (CP) with the corresponding state. Then, the control-to-state operator $S$ is Fréchet differentiable at $\pi$ as a mapping from $U_R$ into the space $Y$, where

\begin{equation}
Y := \left(H^1(0,T; H) \cap L^\infty(0,T; V) \cap L^2(0,T; W)\right)^3. \tag{3.21}
\end{equation}

Moreover, for any $\pi \in U_R$, the Fréchet derivative $DS(\pi)$ is a linear and continuous operator from $L^2(Q)$ to $Y$ such that

\begin{equation}
DS(\pi)h = (\eta, \vartheta, \rho) \quad \text{for every } h \in L^2(Q),
\end{equation}

where $(\eta, \vartheta, \rho)$ is the unique solution to system (3.15)–(3.19) corresponding to $h$ obtained from Theorem 3.6.

To derive an explicit representation from (1.13) we are left with the task of proving the Fréchet differentiability of the reduced cost functional $J_{\text{red}}$ with respect
to the treatment time $\tau$. This can be performed rigorously by virtue of the improved regularity results obtained from Theorem 3.2.

**Theorem 3.8.** Suppose that (2.1)–(2.13) and (2.16) hold, and in addition to (2.3), we assume (2.15). Moreover, let $(u, \tau)$ be an admissible control pair with the corresponding state $(\mu, \varphi, \sigma)$. Then, the reduced cost functional $J_{\text{red}}$ is Fréchet differentiable with respect to time and

$$D_\tau J_{\text{red}}(u, \tau) = \frac{b_1}{2} \int_\Omega |\varphi(\tau) - \varphi_Q(\tau)|^2 + b_2 \int_\Omega (\varphi(\tau) - \varphi_\Omega) \partial_t \varphi(\tau)$$

$$+ \frac{b_3}{2} \int_\Omega |\varphi(\tau) - \varphi_Q(\tau)|^2 + \frac{b_4}{2} \int_\Omega \partial_t \varphi(\tau) + b_5$$

$$+ b_6(\tau - \tau_*). \quad (3.22)$$

**Proof.** It readily follows from computing the derivative. Moreover, let us notice that the terms $b_2 \int_\Omega (\varphi(\tau) - \varphi_\Omega) \partial_t \varphi(\tau)$ and $\frac{b_3}{2} \int_\Omega \partial_t \varphi(\tau)$ are meaningful by virtue of the refined result Theorem 3.1. For more details we refer to [23], where the authors showed how the time derivative for time-dependent cost functionals can be performed in a general setting. \qed

**Theorem 3.9.** Assume that (2.1)–(2.13) and (2.16) are fulfilled. Furthermore, in addition to (2.3) we assume (2.15), and let $(\bar{\pi}, \bar{\tau})$ be an optimal control for $(CP)$ with the corresponding optimal state $(\bar{\mu}, \bar{\varphi}, \bar{\sigma})$ obtained from Theorems 3.1, and 3.2. Then, $(\bar{\pi}, \bar{\tau})$ necessarily fulfills the following variational inequality

$$b_1 \int_{Q_\tau} (\bar{v} - \varphi_Q) \bar{\theta} + b_2 \int_{Q_\tau} (\varphi(\tau) - \varphi_\Omega) \bar{\varphi}(\tau) + b_3 \int_{Q_\tau} (\bar{v} - \sigma_Q) \bar{\rho} + \frac{b_4}{2} \int_\Omega \bar{\rho}$$

$$+ b_6 \int_{Q_\tau} \bar{\pi}(v - \bar{\pi}) \geq 0 \quad \text{for every } v \in \mathcal{U}_{\text{ad}}, \quad (3.23)$$

where $(\eta, \bar{\theta}, \bar{\rho})$ is the unique solutions to the linearised system (3.15)–(3.19) corresponding to $h = v - \bar{\pi}$ obtained from Theorem 3.6. Moreover, we have that

$$D_\tau J_{\text{red}}(\bar{\pi}, \bar{\tau}) \begin{cases} 
\geq 0 & \text{if } \bar{\tau} = 0, \\
= 0 & \text{if } \bar{\tau} \in (0, T), \\
\leq 0 & \text{if } \bar{\tau} = T, \quad (3.24)
\end{cases}$$

where $D_\tau J_{\text{red}}(\bar{\pi}, \bar{\tau})$ is given by (3.22) evaluated at the optimum pair $(\bar{\pi}, \bar{\tau})$. In addition, setting

$$\Lambda(\bar{\pi}, \bar{\tau}) := \frac{b_1}{2} \int_\Omega |\varphi(\tau) - \varphi_Q(\tau)|^2 + b_2 \int_\Omega (\varphi(\tau) - \varphi_\Omega) \partial_t \varphi(\tau)$$

$$+ \frac{b_3}{2} \int_\Omega |\varphi(\tau) - \varphi_Q(\tau)|^2 + \frac{b_4}{2} \int_\Omega \partial_t \varphi(\tau) + b_5.$$ 

it follows that $D_\tau J_{\text{red}}(\bar{\pi}, \bar{\tau}) = \Lambda(\bar{\pi}, \bar{\tau}) + b_6(\bar{\tau} - \tau_*).$ Hence, if $b_6 \neq 0$, the condition (3.24) can be implicitly characterised as

$$\begin{cases} 
\Lambda(\bar{\pi}, 0) \geq b_6 \tau_* & \text{if } \bar{\tau} = 0, \\
\bar{\tau} = \tau_* - b_6^{-1} \Lambda(\bar{\pi}, \bar{\tau}) & \text{if } \bar{\tau} \in (0, T), \\
\Lambda(\bar{\pi}, T) \leq b_6 (\tau_* - T) & \text{if } \bar{\tau} = T. \quad (3.25)
\end{cases}$$

**Proof.** As already mentioned, the variational inequalities (3.23) and (3.24) directly follow by exploiting the abstract conditions (1.13). As (3.23) is concerned, let us
notice that, loosely speaking, \( J_{\text{red}} \) is the composition of \( J \) with \( S \) so that it suffices to combine the Fréchet differentiability of the two operators with the chain rule to get (3.23). In this direction, let us introduce the auxiliary operator \( \tilde{S} : \mathcal{U}_R \to X \times \mathcal{U}_R \), where

\[
  X := (H^1(0, T; H) \cap L^\infty(0, T; V) \cap L^2(0, T; W))^2,
\]

defined by \( \tilde{S}(u) := (S_2(u), S_3(u), u) \) so that \( J_{\text{red}}(u, \tau) = J(\tilde{S}(u), \tau) \). Then, from Theorem 3.7 we infer that

\[
  D\tilde{S}(u) : h \mapsto (\vartheta, \rho, h) \quad \text{for every } h \in \mathcal{U}_R,
\]

where \((\eta, \vartheta, \rho)\) is the unique solution to the linearised system (3.15)–(3.19) corresponding to \( h \) obtained from Theorem 3.6. Moreover, it is straightforward to realise that \( J \) is Fréchet differentiable with respect to \( u \) and that, for every \( \tau \in [0, T] \), it holds that

\[
  [D_u J(\varphi, \sigma, u, \tau)](\Phi, \Psi, h, \tau) = b_1 \int_{Q_\tau} (\varphi - \varphi_Q) \Phi + b_2 \int_\Omega (\varphi(\tau) - \varphi_\Omega) \Phi(\tau)
  + b_3 \int_{Q_\tau} (\sigma - \sigma_Q) \rho + b_4 \int_\Omega \Phi(\tau) + b_0 \int_Q uh
  \quad \text{for every } (\Phi, \Psi, h) \in X \times \mathcal{U}_R.
\]

Thus, we invoke the chain rule to obtain that

\[
  [D_u J_{\text{red}}(\varphi, \sigma, u, \tau)](h, \tau) = [D_u J(\tilde{S}(\pi), \tau)]([D\tilde{S}(\pi)](h, \tau)
  = [D_u J(\varphi, \sigma, \pi, \tau)](\vartheta, \rho, h, \tau)
  = b_1 \int_{Q_{\tau^*}} (\varphi - \varphi_Q) \vartheta + b_2 \int_\Omega (\varphi(\tau) - \varphi_\Omega) \vartheta(\tau)
  + b_3 \int_{Q_{\tau^*}} (\sigma - \sigma_Q) \rho + b_4 \int_\Omega \vartheta(\tau) + b_0 \int_Q \pi h,
\]

which leads to (3.23).

As for the second inequality (3.24), it readily follows from the second of (1.13) along with the characterisation given by (3.22). Lastly, the first and the last conditions of (3.24) are consequences of the fact that we cannot exclude the cases \( s = 0 \) and \( s = T \), while the middle one follows from the fact that, whenever \( \tau \in (0, T) \), we can simply take \( s = \tau \pm \zeta \), with \( \zeta > 0 \), to argue that \( D_\tau J_{\text{red}}(\pi, \tau) = 0 \).

Let us emphasise that the above characterisation (3.25) is new with respect to the previous contributions [3] and [23], where just the condition (3.24) was obtained. In fact, the more explicit condition (3.25) can be now obtained by virtue of the additional tracking-type term \( b_6 \frac{1}{2} |\tau - \tau_\ast|^2 \) that we have added in the cost functional.

3.4. Adjoint system and first-order optimality condition. This section is devoted to the introduction and discussion of the adjoint system to (1.1)–(1.5) which is a key argument in simplifying the variational inequality (3.23). Only straightforward modifications are in order with respect to [36] and it can be easily
shown that the (formal) adjoint system to (1.1)–(1.5) reads as

\[- \beta \partial_t q - \partial_t p - \Delta q + F''(\tau)q + P'(\tau)(\tau - \bar{\tau})(r - p)\]

\[= b_1(\tau - \varphi_Q) \quad \text{in } Q_{\tau}, \quad (3.26)\]

\[- \alpha \partial_t p - \Delta p - q + P(\tau)(p - r) = 0 \quad \text{in } Q_{\tau}, \quad (3.27)\]

\[- \partial_t r - \Delta r + P'(\tau)(r - p) = b_3(\tau - \sigma_Q) \quad \text{in } Q_{\tau}, \quad (3.28)\]

\[\partial_n q = \partial_n p = \partial_n r = 0 \quad \text{on } \Sigma_{\tau}, \quad (3.29)\]

\[\beta q(\tau) = b_2(\tau - \varphi_Q) + \frac{b_4}{\tau^2}, \quad p(\tau) = 0, \quad r(\tau) = 0 \quad \text{in } \Omega. \quad (3.30)\]

The main differences with respect to [36] are:

(i) The system (3.26)–(3.30) has to be considered for a.a. \( t \in (0, \tau) \) instead of a.a. \( t \in (0, T) \).

(ii) In the final condition of \( \beta q(\tau) \) there appears a new term \( \frac{b_4}{\tau^2} \) which is due to the presence of \( \frac{b_2}{\tau} \int_{\Omega} (1 + \varphi(\tau)) \) in the cost functional.

(iii) The final condition for \( r \) is zero since we are not considering any term involving the contribution \( \int_{\Omega} |\sigma(\tau) - \sigma_{\Omega}|^2 \) in the cost functional.

It is worth noting that the above system is a backward-in-time problem with terminal data for \( q \) only belonging to \( L^2(\Omega) \) (see assumption (2.3)). Therefore, the first equation (3.26) has to be considered in a weak sense, i.e., we require that

\[- \langle \nu(t), \partial_t(p + \beta q)(t) \rangle_{\nu} + \int_\Omega \nabla q(t) \cdot \nabla v + \int_\Omega F''(\tau(t))q(t) v \]

\[+ \int_\Omega P'(\tau(t))(\tau(t) - \varphi(t))(r(t) - p(t)) v \]

\[= \int_\Omega b_1(\tau(t) - \varphi_Q(t)) v \quad \text{for every } v \in V \text{ and, a.a. } t \in (0, \tau).\]

**Theorem 3.10.** Assume that the assumptions (2.1)–(2.14) are verified. Then, the adjoint system (3.26)–(3.30) admits a unique solution \((q, p, r)\) such that

\[q \in H^1(0, \tau; V) \cap L^\infty(0, \tau; H) \cap L^2(0, \tau; V) \subset C^0([0, \tau]; H), \quad (3.31)\]

\[p, r \in H^1(0, \tau; H) \cap L^\infty(0, \tau; V) \cap L^2(0, \tau; W) \subset C^0([0, \tau]; V). \quad (3.32)\]

**Proof.** As before, we proceed formally since the approach is standard and the system is linear.

**First estimate.** First, we add to both sides of (3.27) and (3.28) the terms \( p \) and \( r \), respectively. Then, we multiply (3.26) by \( q \), the new (3.27) by \( \partial_t p \), the new (3.28) by \( \partial_t r \), add the resulting equalities, integrate over \( Q_{\tau} \) and by parts. After some rearrangements and a cancellation, we obtain that

\[\frac{\beta}{2} \int_\Omega |q(t)|^2 + \int_{Q_{\tau}} |\nabla q|^2 + \alpha \int_{Q_{\tau}} |\partial_t p|^2 + \frac{1}{2} \|p(t)\|_V^2 + \int_{Q_{\tau}} |\partial_t r|^2 + \frac{1}{2} \|r(t)\|_V^2\]

\[= \frac{\beta}{2} \int_\Omega |q(\tau)|^2 + \int_{Q_{\tau}} b_1(\tau - \varphi_Q) q - \int_{Q_{\tau}} b_3(\tau - \sigma_Q) \partial_t r\]

\[- \int_{Q_{\tau}} F''(\tau)|q|^2 - \int_{Q_{\tau}} P'(\tau)(\tau - \varphi)(r - p) q + \int_{Q_{\tau}} P(\tau)(r - p) \partial_t p\]

\[- \int_{Q_{\tau}} p \partial_t p + \int_{Q_{\tau}} P(\tau)(r - p) \partial_t r - \int_{Q_{\tau}} r \partial_t r,\]
Lastly, by comparison in (3.26) we immediately realise that 
\[ |I_5| + |I_6| + |I_7| + |I_8| \leq \delta \int_{Q^-} (|\partial_t p|^2 + |\partial_t r|^2) + c_\delta \int_{Q^-} (|q|^2 + |p|^2 + |r|^2) + c, \]
for a positive \( \delta \) yet to be determined and for a positive constant \( c_\delta \) which only depends on \( \delta \). Furthermore, using the Hölder and Young inequalities we infer that, for every \( \delta > 0 \),

\[
|I_5| + |I_6| + |I_8| \leq c \int_0^\tau (||p||_4 + ||p||_4)(||r||_4 + ||p||_4)||q||_2 \\
+ c \int_{Q^-} (|p| + |r|)(|\partial_t p| + |\partial_t r|) \\
\leq c \int_0^\tau (||p||_V + ||p||_V)(||r||_V + ||p||_V)||q||_H \\
+ \delta \int_{Q^-} (|\partial_t p|^2 + |\partial_t r|^2) + c_\delta \int_{Q^-} (|p|^2 + |r|^2) \\
\leq c \int_0^\tau (||p||_V^2 + ||p||_V^2)(||r||_V^2 + ||p||_V^2) + c \int_{Q^-} |q|^2 \\
+ \delta \int_{Q^-} (|\partial_t p|^2 + |\partial_t r|^2) + c_\delta \int_{Q^-} (|p|^2 + |r|^2),
\]

where we also used the continuous embedding \( V \subset L^4(\Omega) \) and that \( \overline{\pi} \) and \( \overline{\sigma} \), as solutions to (1.1)–(1.5), satisfy (3.4) so that \((||p||_V^6 + ||p||_V^6) \in L^\infty(0,T) \). Lastly, adjusting \( \delta \in (0,1) \) small enough, a Gronwall argument yields that 
\[
||q||_{L^\infty(0,T;H)} + ||p||_{H^1(0,T;H) \cap L^\infty(0,T;V)} + ||r||_{H^1(0,T;H) \cap L^\infty(0,T;V)} \leq c.
\]

**Second estimate.** Next, comparison in (3.27) and then in (3.28), along with the above estimate, and the elliptic regularity theory allow us to deduce that 
\[
||p||_{L^2(0,T;W)} + ||r||_{L^2(0,T;W)} \leq c.
\]

**Third estimate.** Lastly, by comparison in (3.26) we immediately realise that 
\[
||\partial_t q||_{L^2(0,T;V')} \leq c,
\]
which conclude the proof since the uniqueness directly follows from the above a priori estimates by classical arguments since the adjoint system (3.26)–(3.30) is linear in \((q,p,r)\). \( \square \)

Here, let us point out that the terminal condition of the adjoint variable \( q \) given by (3.30) allows us to rewrite the sum of the second and fourth terms of (3.22), i.e.,
\[
b_2 \int_{\Omega} (\varphi (\tau) - \varphi_\Omega) \partial_\tau \varphi (\tau) + \frac{b_2}{2} \int_{\Omega} \partial_\tau \varphi (\tau) + \beta \int_{\Omega} \partial_\tau \varphi (\tau) q(\tau).
\]
This latter can be characterised also in different ways. In fact, upon multiplying by \( \beta \) the weak formulation of (1.1) and the weak formulation of (1.2) by \( q \), we infer that, for all \( t \in [0,T] \),
\[
\beta \int_{\Omega} \partial_\tau \varphi (t)q(t) = \int_{\Omega} \Delta \varphi (t)q(t) - \int_{\Omega} F'(\varphi (t))q(t) + \int_{\Omega} \mu (t)q(t),
\]
as well as
\[
\beta \int_\Omega \partial_t \varphi(t) q(t) = \beta \int_\Omega P(\varphi(t))(\sigma(t) - \mu(t)) q(t) \\
- \alpha \beta \int_\Omega \partial_t \mu(t) q(t) + \beta \int_\Omega \nabla \mu(t) q(t).
\]
These are completely meaningful in a pointwise sense if we can guarantee that
\[
\sigma, q \in C^0([0, T]; H), \quad \partial_t \mu, \partial_t \varphi \in C^0([0, T]; H), \quad \text{and} \quad \mu, \varphi \in C^0([0, T]; H^2(\Omega)).
\]
Indeed these requirements are fulfilled under the framework of the refined regularity results expressed by Theorem 3.2 and Theorem 3.3.

Next, by using the adjoint variables \((q, p, r)\) we can eliminate the linearised variables from the variational inequality (3.23) producing a simpler formulation for the first-order necessary conditions for optimality.

**Theorem 3.11.** Suppose that (2.1)–(2.13) and (2.16) are satisfied. Let \((\varpi, \tau)\), \((\varpi, \bar{r}, \bar{p})\) and \((q, p, r)\) be an optimal control pair with the corresponding state and adjoint variables obtained from Theorems 3.1, 3.2, and 3.10, respectively. Then, \((\varpi, \tau)\) necessarily satisfies
\[
\int_Q r(v - \varpi) + b_0 \int_Q p(v - \varpi) \geq 0 \quad \text{for every } v \in U_{\text{ad}}. \tag{3.33}
\]

**Corollary 1.** Let the assumptions of Theorem 3.11 be satisfied. Moreover, let us set \(\bar{r}\) as the zero extension of \(r\) in \([0, T]\). Then, the optimal pair \((\varpi, \tau)\) necessarily satisfies
\[
\int_Q (\bar{r} + b_0 \varpi)(v - \varpi) \geq 0 \quad \text{for every } v \in U_{\text{ad}}. \tag{3.34}
\]
Moreover, if \(b_0 \neq 0\), the optimal control \(\varpi\) is nothing but the \(L^2(0, T; H)\)-orthogonal projection of \(-b_0^{-1} \bar{r}\) onto the closed subspace \(U_{\text{ad}}\).

**Remark 1.** Note that the case \(\bar{r} = 0\) covers a special and trivial role. In fact, in this case the above variational inequality (3.33) reduces to
\[
b_0 \int_Q \varpi(v - \varpi) \geq 0 \quad \text{for every } v \in U_{\text{ad}},
\]
which, whenever \(b_0 > 0\), yields that \(\varpi\) is the orthogonal projection of 0 onto the closed subspace \(U_{\text{ad}}\). The same consequence can be drawn from evaluating the variational inequality (3.23) at \(\varpi = 0\) and using that \(\vartheta(0) = 0\).

**Remark 2.** As a consequence of (3.34), we can identify, via Riesz’s representation theorem, the gradient of the reduced cost functional as
\[
\nabla J_{\text{red}}(\varpi, \tau) = \bar{r} + b_0 \varpi.
\]
This fact is extremely important from the numerical viewpoint since it implies the possibility to analyse the optimal control problem \((CP)\) as a constrained minimisation problem via standard techniques (e.g., by applying the conjugate gradient method).
Proof of Theorem 3.11. Comparing the two variational inequalities (3.23) and (3.33), we realise that it suffices to check that
\[ \int_{Q_\tau} h = b_1 \int_{Q_\tau} (\tau - \varphi_Q) \vartheta + b_2 \int_{\Omega} (\tau - \varphi_{\Omega}) \vartheta + b_3 \int_{Q_\tau} (\tau - \sigma_{\Omega}) \rho + b_4 \int_{\Omega} \vartheta, \]
where \( h \) is taken as \( h = v - \pi \) and \((\eta, \vartheta, \rho)\) is the unique solution to (3.15)–(3.19) associated to \( h \) obtained from Theorem 3.6. In this direction, we multiply (3.15) by \( p \), (3.16) by \( q \), (3.17) by \( r \), and integrate over \( Q_\tau \) to get
\[ 0 = \int_{Q_\tau} p [\alpha \partial_t \eta + \Delta \eta - P'(\tau)(\sigma - \pi) \vartheta - P(\tau)(\rho - \eta)] \]
\[ + \int_{Q_\tau} q [\beta \partial_t \vartheta - \Delta \vartheta + F''(\tau) \vartheta - \eta] \]
\[ + \int_{Q_\tau} r [\partial_t \rho - \Delta \rho + P'(\tau)(\sigma - \pi) \vartheta + P(\tau)(\rho - \eta) - h]. \]
Then, we move the last term to the left-hand side and integrate by parts to obtain that
\[ \int_{Q_\tau} h = \int_{Q_\tau} \eta [\alpha \partial_t p - \Delta p - q + P(\tau)(p - r)] \]
\[ + \int_{Q_\tau} \vartheta [\beta \partial_t q - \partial_t \vartheta - \Delta q + F''(\tau)q + P'(\tau)(\sigma - \pi)(r - p)] \]
\[ + \int_{Q_\tau} \rho [\partial_t r - \Delta \rho + P(\tau)(r - p)] \]
\[ + \int_{\Omega} [\alpha \eta(\tau)p(\tau) + \vartheta(\tau)p(\tau) + \beta \vartheta(\tau)q(\tau) + \rho(\tau)r(\tau)], \]
where we also owe to the homogeneous Neumann boundary conditions for the linearised and adjoint variables, and to the initial conditions for the linearised variables. Finally, accounting for the adjoint system (3.26)–(3.30), we conclude that the above equation reduces to (3.35).

4. Some possible generalisations. In the remainder of the paper, we aim at providing some indications concerning some further generalisations. First, we will show how to possibly overcome the issue already mentioned regarding the control of the nutrient variable \( \sigma \) at the given time \( \tau \). Next, we will spend some words concerning a similar minimisation problem in which the role of the control variable slightly differs from our choice.

4.1. A relaxation argument. From the mathematical viewpoint, a natural term to be considered in the cost functional is \( \int_{\Omega} |\sigma(\tau) - \sigma_{\Omega}|^2 \). However, as already emphasised, to give meaning to the necessary conditions that will eventually appear, further temporal regularity for \( \sigma \) has to be established. This will force us to demand the control \( u \) to be more regular in time, say \( H^1(0, T; H) \), which is unrealistic in the application. Anyhow, a possible way to overcome this issue could be to follow the relaxation strategy employed in [23]. To this aim, let us fix a positive constant
\( \varepsilon \) and define the relaxed cost functional \( J_\varepsilon \) as follows
\[
J_\varepsilon(\varphi, \sigma, u, \tau) := J(\varphi, \sigma, u, \tau) + \frac{\gamma}{2\varepsilon} \int_{\tau-\varepsilon}^{\tau} \int_{\Omega} |\sigma - \sigma_{\Omega}|^2,
\]
for a non-negative constant \( \gamma \) and for a given target function \( \sigma_{\Omega} \). Note that the factor \( \frac{1}{\varepsilon} \) is due to normalisation since \( \frac{1}{\varepsilon} \int_{\tau-\varepsilon}^{\tau} = 1 \). With this adjustment on the cost functional, we can control the final configuration of the nutrient without demanding any additional regularity for the nutrient variable \( \sigma \). Hence, instead of considering \((CP)\) we consider
\[
(CP)_\varepsilon \inf_{(\varphi, \sigma, u, \tau) \in \mathcal{A}_{\text{ad}}} J_\varepsilon(\varphi, \sigma, u, \tau).
\]
The most part of the results follow in the same way. Hence, we proceed schematically just mentioning the main differences.

**Existence.** The first arrangement to be done concerns the existence of a minimiser (cf. Section 3.2). The proof can be reproduced using the direct method of calculus of variations provided to explain how the new term of the cost functional can be handled. In this direction, let us point out that, along with (3.12), we also have, as \( n \to \infty \),
\[
\chi_{[\tau_n-\varepsilon, \tau_n]}(\cdot) \to \chi_{[\tau-\varepsilon, \tau]}(\cdot) \quad \text{for a.a. } t \in (0, T).
\]
Hence, by similar reasoning, we also conclude that, as \( n \to \infty \),
\[
\frac{\gamma}{2\varepsilon} \int_{\tau_n-\varepsilon}^{\tau_n} \int_{\Omega} |\sigma_n - \sigma_{\Omega}|^2 \to \frac{\gamma}{2\varepsilon} \int_{\tau-\varepsilon}^{\tau} \int_{\Omega} \left| \sigma(\tau) - \sigma_{\Omega} \right|^2,
\]
while the rest of the proof is exactly the same as in the proof of Theorem 3.5.

**Fréchet differentiability of the reduced cost functional.** As expected, the main differences are related to the Fréchet differentiability of the corresponding reduced cost functional. In fact, the corresponding of (3.23) becomes
\[
\begin{align*}
&b_1 \int_0^\tau \int_{\Omega} (\varphi - \varphi_Q) \vartheta + b_2 \int_{\Omega} (\varphi(\tau) - \varphi_{\Omega}) \vartheta(\tau) + b_3 \int_{\Omega} (\sigma - \sigma_{\Omega}) \rho \\
&+ \frac{\gamma}{\varepsilon} \int_{\tau-\varepsilon}^{\tau} \int_{\Omega} (\varphi - \varphi_{\Omega}) \partial_t \varphi + \frac{b_4}{2} \int_{\Omega} \vartheta(\tau) + b_0 \int_Q \pi(v - \bar{\pi}) \geq 0 \quad \text{for every } v \in \mathcal{U}_{\text{ad}}.
\end{align*}
\]
As the time derivative is concerned, we have to adjust a little the framework by assuming that \( \sigma_{\Omega} \in H^1(-\varepsilon,T; H) \) and that the variable \( \sigma \) is meaningful for negative time. Hence, we simply postulate that \( \sigma(t) := \sigma_0 \) if \( t < 0 \). Thus, the corresponding Fréchet derivative with respect to time reads as
\[
D_\tau J_{\text{red}}(u, \tau) = \frac{b_1}{2} \int_{\Omega} |\varphi(\tau) - \varphi_Q(\tau)|^2 + b_2 \int_{\Omega} (\varphi(\tau) - \varphi_{\Omega}) \partial_t \varphi(\tau) \\
+ \frac{b_3}{2} \int_{\Omega} |\sigma(\tau) - \sigma_{\Omega}(\tau)|^2 \\
+ \frac{\gamma}{2\varepsilon} \int_{\Omega} \left| (\sigma - \sigma_{\Omega})(\tau - \varepsilon) \right|^2 \\
+ \frac{b_4}{2} \int_{\Omega} \partial_t \varphi(\tau) + b_5 + b_6 (\tau - \tau_*)
\]
The adjoint system. Lastly, the adjoint system slightly differs and becomes

\[
- \beta \partial_t q - \partial_t p - \Delta q + F'(\tau)q + P'(\tau)(\sigma - \tau)(r - p) = b_1(\tau - \varphi_Q) \quad \text{in } Q_r,
\]

\[
- \alpha \partial_t p - \Delta p - q + P(\tau)(p - r) = 0 \quad \text{in } Q_r,
\]

\[
- \partial_t r - \Delta r + P(\tau)(r - p) = b_3(\tau - \sigma_Q) + \frac{\gamma}{2} \chi_{(\tau - \varepsilon, \tau)}(\cdot)(\tau - \sigma_{\Omega}) \quad \text{in } Q_r,
\]

\[
\partial_n q = \partial_n p = \partial_n r = 0 \quad \text{on } \Sigma_r,
\]

\[
p(\tau) + \beta q(\tau) = b_2(\tau(\tau) - \varphi_{\Omega}) + \frac{b}{2}, \quad \alpha p(\tau) = 0, \quad r(\tau) = 0 \quad \text{in } \Omega.
\]

Notice that the only difference is the right-hand side of the third equation which, however, still belongs to \(L^2(0, T; H)\) and therefore the well-posedness of the above system easily follows adapting the lines of argument of Theorem 3.10.

4.2. A different control variable. Let us conclude the paper by pointing out that another popular choice for the control variable \(u\) is the one employed in [23, 14, 13]. There, the control variable \(u\) is placed in equation (1.1) and it models the elimination of tumour cells by the effect of a cytotoxic drug. Namely, we can consider the following state system

\[
\alpha \partial_t \mu + \partial_t \varphi - \Delta \mu = P(\varphi)(\sigma - \mu) - \kappa h(\varphi) \quad \text{in } Q,
\]

\[
\mu = \beta \partial_t \varphi - \Delta \varphi + F'(\varphi) \quad \text{in } Q,
\]

\[
\partial_t \sigma - \Delta \sigma = -P(\varphi)(\sigma - \mu) \quad \text{in } Q,
\]

\[
\partial_n \mu = \partial_n \varphi = \partial_n \sigma = 0 \quad \text{on } \Sigma,
\]

\[
\mu(0) = \mu_0, \quad \varphi(0) = \varphi_0, \quad \sigma(0) = \sigma_0 \quad \text{in } \Omega,
\]

where \(\kappa\) is a positive constant, whereas the symbol \(h\) stands for an interpolation function which vanishes at \(-1\) and attains value 1 at 1. Moreover, the control \(u\) ranges between 0 and 1 in order to model no dosage and full dosage of the drug, respectively. So, when \(\varphi = -1\) no drug is dispensed, when \(\varphi = 1\) there is a full dosage of the drug, and in between there is an intermediate supply.

It is worth noting that \(\kappa h(\varphi)u \in L^\infty(Q)\) so that the same arguments employed in [36] can be reproduced in the same manner to obtain the corresponding of Theorem 3.1. However, notice that Theorem 3.2 cannot directly be reproduced. In fact, since the control variable is now placed in the phase equation, it will be necessary to require that \(u \in H^1(0, T; H)\). Therefore, in the spirit of the above section one is reduced to consider a relaxed cost functional

\[
J_\varepsilon(\varphi, \sigma, u, \tau) := \frac{a_1}{2} \int_{Q_r} |\varphi - \varphi_Q|^2 + \frac{a_2}{2\varepsilon} \int_{\tau - \varepsilon}^\tau \int_{Q_r} |\varphi - \varphi_Q|^2 + \frac{a_3}{2} \int_{Q_r} |\sigma - \sigma_Q|^2
\]

\[
+ \frac{a_4}{2} \int_{Q_r} |\sigma - \sigma_Q|^2 + \frac{a_5}{2\varepsilon} \int_{\tau - \varepsilon}^\tau \int_{Q} (1 + \varphi) + a_6 \tau + \frac{a_7}{2} |\tau - \tau_1|^2
\]

\[
+ \frac{a_8}{2} \int_{Q} |u|^2,
\]

for some non-negative constants \(a_0, \ldots, a_7\). Let us claim that, providing to require some natural assumptions, the variable \(\sigma\) may enjoy higher temporal regularity so that the third term in the cost functional above can be considered without any relaxation arguments. Let us claim that, after proving higher temporal regularity for the variable \(\sigma\), the expected optimality conditions read as

\[
a_7 \int_{Q} \overline{u}(v - \overline{u}) - \kappa \int_{Q_r} h(\tau)p(v - \overline{u}) \geq 0 \quad \text{for every } v \in U_{ad},
\]
where $p$ stands for the associated adjoint variable and

$$
\begin{align*}
\frac{a_1}{2} & \int_\Omega |\phi(\tau) - \phi(0)|^2 + \frac{a_2}{2\varepsilon} \int_\Omega \left[ \left( (\phi - \phi_{Q})(\tau) \right)^2 - \left( (\phi - \phi_{Q})(\tau - \varepsilon) \right)^2 \right] \\
& + \frac{a_3}{2} \int_\Omega |\phi(\tau) - \phi_{Q}(\tau)|^2 + a_4 \int_\Omega (\phi(\tau) - \phi_{Q}) \partial_\tau \phi(\tau) \\
& + \frac{a_5}{2\varepsilon} \int_\Omega (\phi(\tau) - \phi(\tau - \varepsilon)) + a_6 + a_7 (\tau - \tau_*) \begin{cases} 
\geq 0 & \text{if } \tau = 0, \\
= 0 & \text{if } \tau \in (0, T), \\
\leq 0 & \text{if } \tau = T.
\end{cases}
\end{align*}
$$

The details are left to the reader.

**Acknowledgments.** The author wishes to express his gratitude to Professor Pierluigi Colli for several useful discussions and suggestions which have improved the manuscript. Moreover, the author would like to thank Professor Elisabetta Rocca whose useful comments have helped to clarify some technical points.

**REFERENCES**

[1] A. Agosti, P. F. Antonietti, P. Ciarletta, M. Grasselli and M. Verani, *A Cahn–Hilliard-type equation with application to tumor growth dynamics*, Math. Methods Appl. Sci., 40 (2017), 7598–7626.

[2] H. Brézis, *Opérateurs Maximaux Monotones et Semi-groupes de Contractions dans les Espace de Hilbert*, North-Holland Publishing Co., Amsterdam-London; American Elsevier Publishing Co., Inc., New York, 1973.

[3] C. Cavaterra, E. Rocca and H. Wu, *Long-time dynamics and optimal control of a diffuse interface model for tumor growth*, Appl. Math. Optim., (2019), 1–49.

[4] P. Colli, G. Gilardi and D. Hilhorst, *On a Cahn–Hilliard type phase field system related to tumor growth*, Discrete Contin. Dyn. Syst., 35 (2015), 2423–2442.

[5] P. Colli, G. Gilardi, G. Marinoschi and E. Rocca, *Sliding mode control for a phase field system related to tumor growth*, Appl. Math. Optim., 79 (2019), 647–670.

[6] P. Colli, G. Gilardi, E. Rocca and J. Sprekels, *Vanishing viscosities and error estimate for a Cahn–Hilliard type phase field system related to tumor growth*, Nonlinear Anal. Real World Appl., 26 (2015), 93–108.

[7] P. Colli, G. Gilardi, E. Rocca and J. Sprekels, *Optimal distributed control of a diffuse interface model of tumor growth*, Nonlinearity, 30 (2017), 2518–2546.

[8] P. Colli, G. Gilardi, E. Rocca and J. Sprekels, *Asymptotic analyses and error estimates for a Cahn–Hilliard type phase field system modeling tumor growth*, Discrete Contin. Dyn. Syst. Ser. S, 10 (2017), 37–54.

[9] V. Cristini, X. Li, J. S. Lowengrub and S. M. Wise, *Nonlinear simulations of solid tumor growth using a mixture model: Invasion and branching*, J. Math. Biol., 58 (2009), 723–763.

[10] V. Cristini and J. Lowengrub, *Multiscale Modeling of Cancer: An Integrated Experimental and Mathematical Modeling Approach*, Cambridge University Press, Leiden, 2010.

[11] M. Dai, E. Feireisl, E. Rocca, G. Schimperna and M. E. Schonbek, *Analysis of a diffuse interface model of multispecies tumor growth*, Nonlinearity, 30 (2017), 1639–1658.

[12] M. Ebenbeck and H. Garcke, *Analysis of a Cahn–Hilliard–Brinkman model for tumour growth with chemotaxis*, J. Differential Equations, 266 (2019), 5998–6036.

[13] M. Ebenbeck and P. Knopf, *Optimal control theory and advanced optimality conditions for a diffuse interface model of tumor growth*, ESAIM Control Optim. Calc. Var., 26 (2020), Paper No. 71, 38 pp.

[14] M. Ebenbeck and P. Knopf, *Optimal medication for tumors modeled by a Cahn–Hilliard–Brinkman equation*, Calc. Var. Partial Differential Equations, 58 (2019), no. 4, Paper No. 131, 31 pp.

[15] S. Frigeri, M. Grasselli and E. Rocca, *On a diffuse interface model of tumor growth*, European J. Appl. Math., 26 (2015), 215–243.
S. Frigeri, K. F. Lam and E. Rocca, On a diffuse interface model for tumour growth with non-local interactions and degenerate mobilities, In Solvability, Regularity, and Optimal Control of Boundary Value Problems for PDEs, P. Colli, A. Favini, E. Rocca, G. Schimperna, J. Sprekels (ed.), Springer INdAM Series, Springer, Cham, 22 (2017), 217–254.

S. Frigeri, K. F. Lam, E. Rocca and G. Schimperna, On a multi-species Cahn–Hilliard–Darcy tumour growth model with singular potentials, Comm. Math. Sci., 16 (2018), 821–856.

H. Garcke and K. F. Lam, Well-posedness of a Cahn–Hilliard system modelling tumour growth with chemotaxis and active transport, European J. Appl. Math., 28 (2017), 284–316.

H. Garcke and K. F. Lam, Analysis of a Cahn–Hilliard system with non-zero Dirichlet conditions modeling tumor growth with chemotaxis, Discrete Contin. Dyn. Syst., 37 (2017), 4277–4308.

H. Garcke and K. F. Lam, Global weak solutions and asymptotic limits of a Cahn–Hilliard–Darcy system modelling tumour growth, AIMS Mathematics, 1 (2016), 318–360.

H. Garcke and K. F. Lam, On a Cahn–Hilliard–Darcy system for tumour growth with solution dependent source terms, in Trends on Applications of Mathematics to Mechanics, E. Rocca, U. Stefanelli, L. Truskinovski, A. Visintin (ed.), Springer INdAM Series, Springer, Cham, 27 (2018), 243–264.

H. Garcke, K. F. Lam, R. Nürnberg and E. Sitka, A multiphase Cahn–Hilliard–Darcy model for tumour growth with necrosis, Math. Models Methods Appl. Sci., 28 (2018), 525–577.

H. Garcke, K. F. Lam and E. Rocca, Optimal control of treatment time in a diffuse interface model of tumor growth, Appl. Math. Optim., 78 (2018), 495–544.

H. Garcke, K. F. Lam, R. Nürnberg, E. Rocca and V. Styles, A Cahn–Hilliard–Darcy model for tumour growth with chemotaxis and active transport, Math. Models Methods Appl. Sci., 26 (2016), 1095–1148.

A. Hawkins-Daruud, S. Prudhomme, K. G. van der Zee and J. T. Oden, Bayesian calibration, validation, and uncertainty quantification of diffuse interface models of tumor growth, J. Math. Biol., 67 (2013), 1457–1485.

A. Hawkins-Daruud, K. G. van der Zee and J. T. Oden, Numerical simulation of a thermodynamically consistent four-species tumor growth model, Int. J. Numer. Meth. Biomed. Engng., 28 (2012), 3–24.

D. Hilhorst, J. Kampmann, T. N. Nguyen and K. G. van der Zee, Formal asymptotic limit of a diffuse-interface tumor-growth model, Math. Models Methods Appl. Sci., 25 (2015), 1011–1043.

J.-L. Lions, Contrôle Optimal de Systèmes Gouvernés par des Équations aux Dérivées Partielles, Dunod, Paris, 1968.

A. Miranville, The Cahn–Hilliard equation and some of its variants, AIMS Mathematics, 2 (2017), 479–544.

A. Miranville, E. Rocca and G. Schimperna, On the long time behavior of a tumor growth model, J. Differential Equations, 267 (2019), 2616–2642.

A. Miranville and S. Zelik, Attractors for dissipative partial differential equations in bounded and unbounded domains, in Handbook of Differential Equations: Evolutionary Equations, Vol. IV (eds. C.M. Dafermos and M. Pokorný), Elsevier/North-Holland, (2008), 103–200.

J. T. Oden, A. Hawkins and S. Prudhomme, General diffuse-interface theories and an approach to predictive tumor growth modeling, Math. Models Methods Appl. Sci., 20 (2010), 477–517.

A. Signori, Vanishing parameter for an optimal control problem modeling tumor growth, Asymptot. Anal., 117 (2020), 43–66.

A. Signori, Optimal treatment for a phase field system of Cahn–Hilliard type modeling tumor growth by asymptotic scheme, Math. Control Related. Fields, 10 (2020), 305–331.

A. Signori, Optimality conditions for a phase field system of Cahn–Hilliard type modeling tumor growth by asymptotic scheme, Math. Control Relat. Fields, 10 (2020), 305–331.

F. Tröltzsch, Optimal Control of Partial Differential Equations. Theory, Methods and Applications, Grad. Stud. in Math., 112, AMS, Providence, RI, 2010.
[40] S. M. Wise, J. S. Lowengrub, H. B. Frieboes and V. Cristini, Three-dimensional multispecies nonlinear tumor growth–I: Model and numerical method. J. Theor. Biol., 253 (2008), 524–543.

[41] X. Wu, G. J. van Zwieten and K. G. van der Zee, Stabilized second-order splitting schemes for Cahn–Hilliard models with applications to diffuse-interface tumor-growth models, Int. J. Numer. Meth. Biomed. Engng., 30 (2014), 180–203.

Received May 2020; revised September 2020.

E-mail address: andrea.signori02@universitadipavia.it