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On the mathematical controllability in a simple growth tumors model by the internal localized action of inhibitors

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Abstract

We study a model of growth of tumors with a free boundary delaying the tumor region. We take into account the presence of inhibitors and its interaction with the nutrients. We study the approximate controllability of the internal distribution of density of cells, that is proportional to concentration of nutrients, injecting inhibitor in a small inner region.

Keywords: Free boundary problem; Controllability; Growth of tumors

1. The model

In this paper, we study the controllability of the growth of tumors by the internal localized action of inhibitors on a simplified mathematical model. The tumor, formed by life cells, is assumed to have a density proportional to the concentrations of a nutrient $\hat{\sigma}(x,t)$, $x=(x_1,x_2,x_3)$, mainly oxygen or glucose. We study the behavior of the tumor after *angiogenesis*, the formation of capillary sprouts from blood vessels, in response to externally supplied chemical stimuli (see, e.g. [5]). Once the angiogenesis occurs, the tumor receives nutrient from the vessels (process named *vasculature*). We assume the tumor is a radially symmetric ball of $\mathbb{R}^3$ of radius $R(t)$, which is unknown (reason why is usually denoted as the free boundary of the problem). Denoting by σ_B the constant nutrient concentration in the vasculature, $\hat{r}_1$ the rate, per unit length, of

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nutrient transferred to the tissue, $\hat{\sigma}$ satisfies the equation

$$\frac{\partial \hat{\sigma}}{\partial t} - d_1 \Delta \hat{\sigma} - \hat{r}_1(\sigma_{\mathrm{B}} - \hat{\sigma}) + \lambda_1 \hat{\sigma} + \lambda \hat{\beta} = 0, \quad |x| < R(t), \ t \in (0, T).$$

Here, d_1 is the diffusion coefficient of the nutrient concentration and $\lambda_1 \hat{\sigma}$, $\lambda \hat{\beta}$ represent the consume rate of nutrient and inhibitor, respectively.

The density of the inhibitor $\hat{\beta}(x,t)$ is assumed to satisfy a similar reaction–diffusion equation,

$$\frac{\partial \hat{\beta}}{\partial t} - d_2 \Delta \hat{\beta} - \hat{r}_2(\beta_{\mathrm{B}} - \hat{\beta}) + \lambda_2 \hat{\beta} = f \chi_{\omega_0}, \quad |x| < R(t), \ t \in (0, T),$$

with d_2 the diffusion coefficient, β_{B} the critical value of the inhibitor concentration for vasculature, $\hat{r}_2$ the rate, per unit length, of inhibitor transferred to the tissue, and $\lambda_2 \beta$ is the inhibitor consumption rate. The permanent supply of inhibitors is assumed to be localized on a small domain ω_0 with a rate given by f (the control of the problem).

According to the mass conservation principle, assuming the cell mass density constant, the tumor mass is proportional to the volume $\frac{4}{3}\pi R(t)^3$. The balance between birth and death cells is determinate by the concentration of nutrient and inhibitor. Denoting by $\hat{S}$ the above balance, after normalizing we obtain the law

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{4}{3}\pi R^3(t)\right) = \int_{\{|x|<R(t)\}} \hat{S}(\hat{\sigma}(x,t), \hat{\beta}(x,t))\,\mathrm{d}x, \quad x \in \mathbb{R}^3.$$

According to the inhibitor nature and the tumor tissue, the function $\hat{S}$ has different representations. In any case we shall assume through the paper that, $\hat{S} \in W^{1,\infty}(\mathbb{R}^2)$.

For the sake of notation we shall assume that the diffusion coefficients are given by a unique positive constants, $d_1 = d_2 = d$. Thus by normalizing the unknown densities

$$\sigma := \hat{\sigma} - \frac{\hat{r}_1 \sigma_{\mathrm{B}}(\hat{r}_2 + \lambda_2) + \lambda \hat{r}_2 \beta_{\mathrm{B}}}{(\hat{r}_1 + \lambda_1)(\hat{r}_2 + \lambda_2)}, \quad \beta := \hat{\beta} - \frac{\hat{r}_2 \beta_{\mathrm{B}}}{\hat{r}_2 + \lambda_2},$$

and denoting by

$$r_1 := \hat{r}_1 + \lambda_1, \quad r_2 := \hat{r}_2 + \lambda_2, \quad S(\sigma, \beta) := \frac{3}{4\pi} \hat{S}(\hat{\sigma}, \hat{\beta}),$$

we arrive to the concrete formulation of the mathematical model under consideration

$$\frac{\partial \sigma}{\partial t} - \mathrm{d}\Delta \sigma + r_1 \sigma + \lambda \beta = 0, \quad |x| < R(t), \ t \in (0, T), \tag{1.1}$$

$$\frac{\partial \beta}{\partial t} - \mathrm{d}\Delta \beta + r_2 \beta = f \chi_{\omega_0}, \quad |x| < R(t), \ t \in (0, T), \tag{1.2}$$

$$R(t)^2 \frac{\mathrm{d}R(t)}{\mathrm{d}t} = \int_{|x|<R(t)} S(\sigma, \beta)\,\mathrm{d}x, \quad R(0) = R_0, \ t \in (0, T), \tag{1.3}$$

$$\sigma(x, 0) = \sigma_0(x), \quad \beta(x, 0) = \beta_0(x), \ |x| < R_0, \tag{1.4}$$

$$\sigma(x, t) = \bar{\bar{\sigma}}, \quad \beta(x, t) = \bar{\bar{\beta}}, \quad |x| = R(t), \ t \in (0, T), \tag{1.5}$$

where $R_0 > 0$, the normalized nutrient and inhibitor densities at the exterior of the tumor $\bar{\bar{\sigma}}$, $\bar{\bar{\beta}}$, the initial densities (σ_0, β_0) are assumed to be given. We shall assume that $(\sigma_0, \beta_0) \in W^{2,\infty}(B(R_0))$. The mathematical treatment of this model has a long history, (see [17,1,4,7,8,15]). A recent reference containing details on the notion of weak solution and existence and uniqueness is the authors work [12]. The main results of this paper shows that this type of action by the inhibitor allows to control (in the usual weak sense typical of parabolic system) the tumor density. This is formulated in the following terms:

Theorem 1.1. *Given $T > 0$, $\omega_0 \subset B(R_0 \exp\{-\|S\|_{L^\infty} T\})$, $\varepsilon > 0$, and $\hat{\sigma}^d \in L^p_{\mathrm{loc}}(\mathbb{R}^3)$, for some $p > 1$, there exists $f \in L^p((0,T) \times \omega_0)$ such that, if (σ, β, R) is the solution of problem* (1.1)–(1.5), *then*

$$\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} \leqslant \varepsilon, \tag{1.6}$$

where $\sigma^d := \hat{\sigma}^d \chi_{B(R(T))}$.

Due to some technical reasons, we shall prove the theorem firstly for $p \geqslant 5$, (necessary in the proof of Lemma 2.1) and then for all $p > 1$.

We shall prove the result in several steps. For $n \in \mathbb{N}$, we start by assuming $R_n(t)$ prescribed and look for a control f_n in ω_0 such that the solution (σ_n, β_n) of problem (1.1)–(1.5), satisfies (1.6). Then we obtain R_{n+1} and f_{n+1} from (σ_n, β_n) which allow to find $(\sigma_{n+1}, \beta_{n+1})$. The proof of the theorem uses some methods introduced in the study of the approximate controllability (name attributed to conclusions as (1.6)) by different authors (see [19,20,13,9]). In spite of the large literature on this type of methods, very few seems to be known for the case of systems (see also [10] for a higher order equation). Some numerical experiences could be developed in the line of the works [16,11]. Iterating the process we obtain a sequence $(R_n, f_n, \sigma_n, \beta_n)$, we show that there exists a subsequence such that converges to the searched control f and the associate solution of problem (1.1)–(1.5).

2. Regularity and uniqueness of problem (1.1)–(1.5)

Although the existence of weak solutions of problem (1.1)–(1.5), was established by previous authors, (see [12]), we shall need some extra information which is collected in this section.

In order to prove the regularity of the solutions we use the change of variables and unknowns, introduced in Díaz and Tello [12],

$$\tilde{x} := (\tilde{x}_1, \tilde{x}_2, \tilde{x}_3) = \frac{x}{R(t)}, \quad \tilde{t}(t) := \int_0^t R^{-2}(\rho)\,\mathrm{d}\rho, \tag{2.1}$$

$$u(\tilde{x}, \tilde{t}) := \sigma(R(t(\tilde{t}))\tilde{x}, t(\tilde{t})) - \bar{\bar{\sigma}}, \quad v(\tilde{x}, \tilde{t}) := \beta(R(t(\tilde{t}))\tilde{x}, t(\tilde{t})) - \bar{\bar{\beta}}. \tag{2.2}$$

(Notice since R is a continuous function and $1/R^2(t) > 0$, we obtain that $\tilde{t}(t) \in C^1([0,\tilde{T}])$, and by the theorem of implicit function, there exists the inverse function $t(\tilde{t}) \in C^1([0,T])$.

Let $B = \{\tilde{x} \in \mathbb{R}^3, \|\tilde{x}\| < 1\}$. Problem (1.1)–(1.5) can be equivalently formulated as

$$\frac{\partial u}{\partial \tilde{t}} - \mathrm{d}\Delta u - R^2\dot{R}\tilde{x}\cdot\nabla u + R^2 r_1 u = R^2(r_1\bar{\bar{\sigma}} + \lambda(v + \bar{\bar{\beta}})), \quad \tilde{x}\in B,\ \tilde{t}\in(0,\tilde{T}), \tag{2.3}$$

$$\frac{\partial v}{\partial \tilde{t}} - \mathrm{d}\Delta v - R^2\dot{R}\tilde{x}\cdot\nabla v + R^2 r_2 v = R^2 f\chi_{\tilde{\omega}_0} - R^2 r_2\bar{\bar{\beta}}, \quad \tilde{x}\in B,\ \tilde{t}\in(0,\tilde{T}), \tag{2.4}$$

$$R(\tilde{t})\frac{\mathrm{d}}{\mathrm{d}\tilde{t}}R(\tilde{t}) = \int_B S(u(\tilde{x},\tilde{t}) + \bar{\bar{\sigma}}, v(\tilde{x},\tilde{t}) + \bar{\bar{\beta}})\,\mathrm{d}\tilde{x}, \quad R(0) = R_0, \tag{2.5}$$

$$u(\tilde{x},\tilde{t}) = v(\tilde{x},\tilde{t}) = 0, \quad \tilde{x}\in\partial B,\ \tilde{t}\in(0,\tilde{T}), \tag{2.6}$$

$$u(\tilde{x},0) = u_0(\tilde{x}) = \sigma_0(\tilde{x}R_0), \quad v(\tilde{x},0) = v_0(\tilde{x}) = \beta_0(\tilde{x}R_0), \tag{2.7}$$

where $\tilde{T} = \tilde{t}(T)$ and $\tilde{\omega}_0^{\tilde{t}} = \{\tilde{x}\in B \text{ such that } R(t(\tilde{t}))\tilde{x}\in\omega_0\}$, for any $\tilde{t}\in[0,\tilde{T}]$.

Lemma 2.1. *Under the assumptions of Theorem* 1.1, *for* $p \geqslant 5$, *the solution* (u,v,R) *of problem* (2.3)–(2.7), *satisfies*

$$u \in L^q(0,\tilde{T}: W^{2,q}(B)) \cap W^{1,q}(0,\tilde{T}: L^q(B)),$$

for all $1 < q < \infty$ *and*

$$v \in L^p(0,\tilde{T}: W^{2,p}(B)) \cap W^{1,p}(0,\tilde{T}: L^p(B)).$$

Proof. By Theorem 1.1 of Díaz and Tello [12], we know that

$$(u,v,R) \in [L^2(0,\tilde{T}: H^1(B))]^2 \times W^{1,\infty}(0,\tilde{T}).$$

Then the linear parabolic operator

$$\mathscr{L}v := \frac{\partial v}{\partial \tilde{t}} - \mathrm{d}\Delta v - R^2R'\tilde{x}\cdot\nabla v + R^2 r_2 v,$$

admits a fundamental solution (see [14]) and, since $v_0 \in H^2(B)$, $f \in L^p((0,T)\times B)$, we get

$$v \in W^{1,p}((0,\tilde{T})\times B) \cap L^p(0,\tilde{T}: W^{2,p}(B))),$$

(see e.g. [18, Theorem 9.1, Chapter IV]). Since $p > 4$, $W^{1,p}((0,T)\times B) \subset L^\infty([0,\tilde{T}]\times B)$, and then

$$u \in W^{1,q}((0,T)\times B) \cap L^q(0,T: W^{2,q}(B))),$$

for $q < \infty$. Consequently, we obtain $R(t) \in W^{2,p}(0,T)$. □

As a consequence of the lemma, by using that $W_0^{1,p}(B\times[0,\tilde{T}]) \subset L^\infty(B\times[0,\tilde{T}])$, if $p > 4$ we obtain,

Corollary 2.1. *Let* $p>4$. *Then* $u,v\in L^\infty(B\times[0,\tilde T])$.

On the other hand, the continuous embeddings

$$W^{1,q}((0,T)\times B)\cap L^q(0,T:W^{2,q}(B)))\subset L^2(0,T:W^{1,\infty}(B)),$$

$$W^{1,p}((0,\tilde T)\times B)\cap L^p(0,\tilde T:W^{2,p}(B)))\subset L^2(0,T:W^{1,\infty}(B))$$

and the reciprocal change of variables and unknown (2.1), (2.2), leads to

Corollary 2.2. *Under the assumptions of Theorem* 1.1, *we have*

$$\int_0^T \|\sigma\|^2_{W^{1,\infty}(R(t))}+\|\beta\|^2_{W^{1,\infty}(R(t))}\,\mathrm{d}t\leqslant k_0.$$

The uniqueness of solutions is proved in the next proposition.

Proposition 2.1. *Let* $f\in L^p(\omega_0\times(0,T))$ *with* $p\geqslant 5$, *and* $(\sigma_0-\bar{\bar\sigma},\beta_0-\bar{\bar\beta})\in W^{2,s}(B(R_0))\cap H^1_0(B(R_0))$, *for* $s>4$. *Then, there exists a unique solution of problem* (1.1)–(1.5).

Proof. We shall show that if we assume that there exist two different solutions, (σ_1,β_1,R_1) and (σ_2,β_2,R_2), we get a contradiction. Let

$$R(t)=\min\{R_1(t),R_2(t)\},\quad \sigma=\sigma_1-\sigma_2,\quad \beta=\beta_1-\beta_2.$$

Then (σ,β,R) satisfies the problem,

$$\frac{\partial\sigma}{\partial t}-\mathrm{d}\Delta\sigma+r_1\sigma+\lambda\beta=0,\quad |x|<R(t),\ t\in(0,T), \tag{2.8}$$

$$\frac{\partial\beta}{\partial t}-\mathrm{d}\Delta\beta+r_2\beta=0,\quad |x|<R(t),\ t\in(0,T), \tag{2.9}$$

$$\sigma(x,0)=0,\quad \beta(x,0)=0,\ |x|<R_0, \tag{2.10}$$

$$\sigma(x,t)=\sigma_1(x,t)-\sigma_2(x,t),\quad |x|=R(t),\ t\in(0,T), \tag{2.11}$$

$$\beta(x,t)=\beta_1(x,t)-\beta_2(x,t),\quad |x|=R(t),\ t\in(0,T). \tag{2.12}$$

We introduce a new unknown defined by

$$z=k_1\sigma-k_2\beta$$

with

$$k_1=1,\quad k_2=\frac{\lambda}{r_1-r_2}\quad \text{if } r_1\neq r_2,$$

$$k_1=\frac{1}{2},\quad k_2=\frac{\lambda}{r_1-2r_2}\quad \text{if } r_1=r_2\neq 0,$$

and by $z=\mathrm{e}^{-\lambda t}\sigma-\beta$ if $r_1=r_2=0$. By construction we have

$$\frac{\partial z}{\partial t}-\mathrm{d}\Delta z+r_1 z=0,\quad |x|<R(t),\ t\in(0,T),$$

$$z(x,0)=0,\quad |x|<R_0,$$

$$z(x,t)=k_1\sigma(x,t)-k_2\beta(x,t),\quad |x|=R(t),\ t\in(0,T).\qquad\square \tag{2.13}$$

Now we prove a preliminary result.

Lemma 2.2. *Let z be the solution of problem* (2.13) *and β the solution of problems* (2.9), (2.12), *then $\mathrm{e}^{r_1 t}z$ and $\mathrm{e}^{r_2 t}\beta$ take their maximum and minimum on $|x|=R(t)$.*

Proof. Multiplying Eq. (2.13) by $\mathrm{e}^{r_1 t}$, we obtain that $\mathrm{e}^{r_1 t}z$ satisfies

$$\frac{\partial}{\partial t}(\mathrm{e}^{r_1 t}z)-\mathrm{d}\Delta(\mathrm{e}^{r_1 t}z)=0,\quad |x|<R(t),\ t\in(0,T),$$

$$z(x,0)=0,\quad |x|<R_0,$$

$$\mathrm{e}^{r_1 t}z(x,t)=\mathrm{e}^{r_1 t}(k_1\sigma(x,t)-k_2\beta(x,t)),\quad |x|=R(t),\ t\in(0,T). \tag{2.14}$$

Repeating the operation, we obtain $\mathrm{e}^{r_2 t}\beta$ which satisfies the equation,

$$\frac{\partial}{\partial t}(\mathrm{e}^{r_2 t}\beta)-\mathrm{d}\Delta(\mathrm{e}^{r_2 t}\beta)=0,\quad |x|<R(t),\ t\in(0,T),$$

$$\beta(x,0)=0,\quad |x|<R_0,$$

$$\mathrm{e}^{r_2 t}\beta(x,t)=\mathrm{e}^{r_2 t}(\beta_1(x,t)-\beta_2(x,t)),\quad |x|=R(t),\ t\in(0,T). \tag{2.15}$$

By Corollary 2.1, we know that

$$|\sigma(x,t)|\leqslant K,\quad |\beta(x,t)|\leqslant K\quad \text{for any } t\in[0,T]\quad\text{and}\quad \text{a.e. } x\in B(R(t)),$$

and then, $\mathrm{e}^{r_1 t}z$ and $\mathrm{e}^{r_2 t}\beta$ are bounded. Let

$$z^{**}=\max\{\mathrm{e}^{r_1 t}z(x,t),\ t\in[0,T],\ x\in\partial B(R(t))\},$$

$$z_{**}=\min\{\mathrm{e}^{r_1 t}z(x,t),\ t\in[0,T],\ x\in\partial B(R(t))\},$$

$$\beta^{**}=\max\{\mathrm{e}^{r_2 t}\beta(x,t),\ t\in[0,T],\ x\in\partial B(R(t))\},$$

$$\beta_{**}=\min\{\mathrm{e}^{r_2 t}\beta(x,t),\ t\in[0,T],\ x\in\partial B(R(t))\}.$$

Let T_k and T^k be defined by

$$T_k(s)=\begin{cases} s & \text{if } s>k,\\ k & \text{if } s\leqslant k\end{cases}$$

and

$$T^k(s) = \begin{cases} k & \text{if } s \geqslant k, \\ s & \text{if } s < k. \end{cases}$$

Taking $T_0(e^{r_1 t}z - z^{**})$ as test function in (2.14), integrating by parts in $B(R(t))$, and by Leibnitz Theorem's, after some manipulations, we arrive at

$$\frac{d}{dt}\int_{B(R(t))} [T_0(e^{r_1 t}z - z^{**})]^2\, dx \leqslant 0,$$

and we deduce that $e^{r_1 t}z$ takes its maximum in $|x| = R(t)$. In the same way, taking $T^0(e^{r_1 t}z - z_{**})$ as test function we obtain

$$z_{**} \leqslant e^{r_1 t}z \leqslant z^{**}. \tag{2.16}$$

The proof of

$$\beta_{**} \leqslant e^{r_2 t}\beta \leqslant \beta^{**}, \tag{2.17}$$

is analogous. □

End of the proof of Proposition 2.1. Given $t \in [0, T]$, we can suppose, without lost generality, $R_1(t) \leqslant R_2(t)$, otherwise the argument is similar by changing R_1 for R_2. Using that

$$R_1^2(t)\dot{R}_1(t) - R_2^2(t)\dot{R}_2(t) = \int_{B(R(t))} (S(\sigma_1, \beta_1) - S(\sigma_2, \beta_2))\, dx - \int_{R_1(t)<|x|<R_2(t)} S(\sigma_2, \beta_2)\, dx.$$

Since S is bounded, then

$$\left| \int_{R_1(t)<|x|<R_2(t)} S(\sigma_2, \beta_2)\, dx \right| \leqslant N|R_1^3(t) - R_2^3(t)| \leqslant M|R_1(t) - R_2(t)|,$$

where M depends only of $|S|_{L^\infty}$. Since S is Lipschitz continuous, integrating in time, it results

$$\begin{aligned} &\int_0^T \int_{B(R(t))} |S(\sigma_1, \beta_1) - S(\sigma_2, \beta_2)|\, dx\, dt \\ &\leqslant \int_0^T \int_{B(R(t))} |S|_{W^{1,\infty}(\mathbb{R}^2)}(\sup|\sigma| + \sup|\beta|)\, dx\, dt \\ &\leqslant \int_0^T \int_{B(R(t))} k_0 \left(\frac{1}{k_1} \sup|z + k_2\beta| + \sup|\beta| \right) dx\, dt \\ &\leqslant \int_0^T \int_{B(R(t))} C(\sup|z| + \sup|\beta|)\, dx\, dt \end{aligned}$$

$$\leqslant \int_0^T \int_{B(R(t))} C(\sup|e^{-r_1 t}e^{r_1 t}z| + \sup|e^{-r_2 t}e^{r_2 t}\beta|)\,dx\,dt$$

$$\leqslant \int_0^T \int_{B(R(t))} C(e^{|r_1|T}\sup|e^{r_1 t}z| + e^{|r_2|T}\sup|e^{r_2 t}\beta|)\,dx\,dt$$

$$\leqslant \int_0^T \int_{B(R(t))} k_3(\sup|e^{r_1 t}z| + \sup|e^{r_2 t}\beta|)\,dx.$$

From Lemma 2.2, we know

$$\int_0^T \int_{B(R(t))} \sup|e^{r_1 t}z(x,t)|\,dx\,dt \leqslant e^{r_1 T}\,\frac{3\pi}{4}\,R^3(t)\int_0^T \sup_{|x|=R(t)}|z(x,t)|\,dt.$$

By Corollary 2.2, we deduce that

$$\int_0^T (\|\sigma_2\|^2_{W^{1,\infty}(B(R(t))} + \|\beta_2\|^2_{W^{1,\infty}(B(R(t))})\,dt \leqslant K_0,$$

and consequently,

$$\int_0^T \|z\|^2_{W^{1,\infty}(B(R(t)))}\,dt \leqslant K.$$

Since

$$e^{r_1 t}z(x,t) = e^{r_1 t}(k_1(\sigma_2(x,t) - \bar{\bar{\sigma}}) - k_2(\beta_2(x,t) - \bar{\bar{\beta}})), \quad \text{on } |x| = R(t),$$

we deduce

$$e^{r_1 T}\,\frac{3\pi}{4}\,R^3(t)\int_0^T \sup_{|x|=R(t)}|z(x,t)|\,dt$$

$$\leqslant k_4 \int_0^T \|\sigma_2\|_{W^{1,\infty}(B(R_2(t)))} + \|\beta_2\|_{W^{1,\infty}(B(R_2(t)))}|R_1(t) - R_2(t)|\,dt$$

$$\leqslant k_4 \sup_{0<t<T}|R_1(t) - R_2(t)|T^{1/2}\int_0^T (\|\sigma_2\|^2_{W^{1,\infty}(B(R_2(t)))} + \|\sigma_2\|^2_{W^{1,\infty}(B(R_2(t)))})\,dt$$

$$\leqslant k \sup_{0<t<T}|R_1(t) - R_2(t)|T^{1/2}.$$

In the same way,

$$\int_0^t \int_{B(R(t))} k_3 \sup|\beta| \leqslant k \sup_{0<t<T}|R_1(t) - R_2(t)|T^{1/2}.$$

Then

$$\int_0^t |R_1^2(t)\dot{R}_1(t) - R_2^2(t)\dot{R}_2(t)|\,dt \leqslant C_0 \sup_{0<t<T}|R_1(t) - R_2(t)|(T + T^{1/2}). \tag{2.18}$$

Denoting by $\delta = \max_{t\in[0,T]}\{R_1(t) - R_2(t)\}$, we obtain

$$|R_1^3(t) - R_2^3(t)| \leqslant 3C_0\delta(T + T^{1/2}),$$

and since $|R_1^3(t) - R_2^3(t)| \geqslant 3R_0^2|R_1(t) - R_2(t)|$, we conclude, $\delta \leqslant k_0\delta(T + T^{1/2})$. Then, if $T < T_1 = \min\{1/4k_0^2, 1\}$, necessarily $R_1(t) = R_2(t)$. Since $e^{r_1 t}z$ and $e^{r_2 t}\beta$ take his maximum and minimum on $R(t) = R_1(t) = R_2(t)$ and it is zero, then $\beta = 0$ and $z = 0$, and we deduce $\beta = 0$ and $\sigma = 0$.

Repeating the same argument, now from T_1 we conclude the uniqueness of solutions for a $T > 0$ arbitrary. □

3. Approximate controllability: proof of Theorem 1.1

The next result shows the conclusion of Theorem 1.1 (the so-called approximate controllability in L^p) under some particular assumptions (mainly when $R(t)$ is a priori prescribed).

Proposition 3.1. *Let* $\omega_0 \subset B(R_0 \exp\{-\|S\|_{L^\infty} T\}$, *and* $\sigma_0 = \beta_0 = \bar{\bar{\sigma}} = \bar{\bar{\beta}} = 0$. *Let* $R \in W^{1,\infty}(0,T)$ *a given function such that* $R(0) = R_0$, $|\dot{R}| \leqslant \|S\|_{L^\infty} R_0 \exp\{|S|_{L^\infty} T\}$. *Then, given* $\hat{\sigma}^d \in L^2_{\text{loc}}(\mathbb{R}^3)$, *there exists* $f \in L^p(\omega_0 \times (0,T))$, *with* $p \geqslant 5$, *such that, if* (σ, β) *is the solution of problem* (1.1), (1.2), (1.4) *and* (1.5), *with* $R(t)$ *prescribed, then*

$$\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} \leqslant \varepsilon,$$

where $\sigma^d = \hat{\sigma}^d|_{B(R(T))}$.

Proof. Let $p' = p/(p-1)$, we consider the functional $J : L^{p'}(B(R(T))) \to \mathbb{R}$ defined by

$$J(\varphi^0) = \frac{1}{p'} \int_0^T \int_{\omega_0} |\psi(x,t)|^{p'}\, \mathrm{d}x\, \mathrm{d}t + \varepsilon \|\varphi^0\|_{L^{p'}(B(R(T)))} - \int_{B(R(T))} \sigma^d \varphi^0\, \mathrm{d}x,$$

for $\varphi_0 \in L^{p'}(B(R(T)))$, where ψ is the component of the solution (φ, ψ) of the "dual" problem

$$-\frac{\partial \varphi}{\partial t} - \mathrm{d}\Delta\varphi - r_1\varphi = 0, \quad |x| < R(t), \ t \in (0,T), \tag{3.1}$$

$$-\frac{\partial \psi}{\partial t} - \mathrm{d}\Delta\psi - r_2\psi + \lambda\varphi = 0, \quad |x| < R(t), \ t \in (0,T), \tag{3.2}$$

$$\varphi(x,T) = \varphi_0(x), \ \psi(x,T) = 0, \quad |x| < R(T), \tag{3.3}$$

$$\varphi(x,t) = 0, \quad \psi(x,t) = 0, \quad |x| = R(t), \ t \in (0,T). \tag{3.4}$$

We point out that the existence of a weak solutions of (3.1)–(3.4), (φ, ψ) can be obtained as in Section 2, by making the change of variable (2.1), (2.2), (see [21]).

In order to prove the uniqueness of solutions, we suppose there exists two solutions, (φ_1, ψ_1), (φ_2, ψ_2), then $\varphi := \varphi_1 - \varphi_2$, satisfies the equation (3.1), taking $|\varphi|^{p'-2}\varphi$ as test function, and integrating by parts, it results,

$$-\frac{\mathrm{d}}{\mathrm{d}t} \int_{B(R(t))} |\varphi|^{p'}\, \mathrm{d}x \leqslant r_1 \int_{B(R(t))} |\varphi|^{p'}\, \mathrm{d}x,$$

by Gronwall's Lemma, since $\varphi(T)=0$, we obtain $\varphi=\varphi_1-\varphi_2=0$. Once proved $\varphi\equiv 0$, in the same way, $\psi:=\psi_1-\psi_2$ satisfies (3.2), taking $|\psi|^{p'-2}\psi$ as test function, we obtain $\psi\equiv 0$, and consequently, the uniqueness is proved.

Let us assume that J is convex, continuous and coercive (in the sense that lim inf $J\to\infty$ if $\|\varphi^0\|_{L^{p'}(B(R_0))}\to\infty$). Then J takes a minimum φ_0 (see, e.g., [3, Corollary III, p. 20]). Moreover if (ξ,ζ) is the solution of the problem (3.1)–(3.4) with initial datum $(\xi_0,0)$. We have

$$\int_0^T\int_{\omega_0}|\psi|^{p'-2}\psi\zeta\,\mathrm{d}x\,\mathrm{d}t-\int_{B(R(T))}\sigma^d\xi_0\,\mathrm{d}x$$
$$+\varepsilon\|\varphi^0\|^{1-p'}_{L^{p'}(B(R(T)))}\int_{B(R(T))}|\varphi^0|^{p'-2}\varphi^0\xi^0\,\mathrm{d}x=0. \tag{3.5}$$

Multiplying (1.1), (1.2) by (ξ,ζ), integrating by parts and applying Leibnitz Theorem, we arrive at

$$-\int_0^T\left\langle\sigma,\frac{\partial\xi}{\partial t}\right\rangle\mathrm{d}t-\mathrm{d}\int_0^T\langle\sigma,\Delta\xi\rangle\,\mathrm{d}t+\int_0^T\int_{B(R(t))}r_1\sigma\xi\,\mathrm{d}x\,\mathrm{d}t$$
$$+\int_0^T\int_{B(R(t))}\lambda\beta\xi\,\mathrm{d}x\,\mathrm{d}t-\int_0^T\left\langle\beta,\frac{\partial\zeta}{\partial t}\right\rangle\mathrm{d}t-\mathrm{d}\int_0^T\langle\beta,\Delta\zeta\rangle\,\mathrm{d}t$$
$$+\int_0^T\int_{B(R(t))}r_2\beta\zeta\,\mathrm{d}x\,\mathrm{d}t-\int_0^T\int_{\omega_0}f\zeta\,\mathrm{d}x\,\mathrm{d}t+\int_{B(R(t))}\sigma\xi\,\mathrm{d}x]_0^T+\int_{B(R(t))}\beta\zeta\,\mathrm{d}x]_0^T=0,$$

where $\langle,\rangle$ represents the duality $W_0^{1,p'}(B(R(t))\times W_0^{-1,p'}(B(R(t))$. From the choice of (ξ,ζ) and since $\sigma(0,x)=\beta(0,x)=0$, we obtain

$$-\int_0^T\int_{\omega_0}f\zeta\,\mathrm{d}x\,\mathrm{d}t+\int_{B(R(T))}\sigma(T)\xi^0\,\mathrm{d}x=0. \tag{3.6}$$

Now, let us take f,

$$f:=|\psi|^{p'-2}\psi.$$

Substituting it in (3.6) and using (3.5) it results

$$\int_{B(R(T))}(\sigma(T)-\sigma^d)\xi^0\,\mathrm{d}x+\varepsilon\|\varphi^0\|^{1-p'}_{L^{p'}(B(R(T)))}\int_{B(R(T))}|\varphi^0|^{p'-2}\varphi^0\xi_0\,\mathrm{d}x=0$$

for all $\xi^0\in L^{p'}(B(R(T)))$. Taking

$$\xi^0=(\sigma(T)-\sigma^d)^{1/(p'-1)}\in L^{p'}(B(R(T)))$$

since $p=1+1/(p'-1)$, we obtain

$$\|\sigma(T)-\sigma^d\|^p_{L^p(B(R(T)))}$$
$$=\varepsilon\|\varphi^0\|^{1-p'}_{L^{p'}(B(R(T)))}\int_{B(R(T))}|\varphi^0|^{p'-2}\varphi^0|\sigma(T)-\sigma^d|^{1/(p'-1)-1}(\sigma(T)-\sigma^d)\,\mathrm{d}x.$$

Applying Hölder inequality, we obtain that

$$\|\varphi^0\|^{1-p'}_{L^{p'}(B(R(T)))}\int_{B(R(T))}|\varphi^0|^{p'-2}\varphi^0|\sigma(T)-\sigma^d|^{1/(p'-1)-1}(\sigma(T)-\sigma^d)\,\mathrm{d}x$$

$$\leqslant \|\sigma(T)-\sigma^d\|^{p-1}_{L^p(B(R(T)))},$$

which leads to

$$\|\sigma(T)-\sigma^d\|_{L^p(B(R(T)))}\leqslant \varepsilon$$

and the conclusion holds.

So, it only remains to check the mentioned properties of J:

J is convex: We express J as addition of the functionals,

$$J_1(\varphi^0):=-\int_{B(R(T))}\sigma^d\varphi^0\,\mathrm{d}x,\quad J_2(\varphi^0):=\varepsilon\|\varphi^0\|_{L^{p'}(B(R(T)))},$$

$$J_3(\varphi^0):=\frac{1}{p'}\int_0^T\int_{B(R(t))}|\psi|^{p'}\,\mathrm{d}x\,\mathrm{d}t.$$

First, we shall see that J_3 is convex. Let φ_1^0, $\varphi_2^0\in L^p(B(R(T)))$ and (φ_1,ψ_1) and (φ_2,ψ_2) be the respective solutions of problem (3.1)–(3.4), and let $\alpha\in(0,1)$. Then, since the system is linear we get

$$J_3(\alpha\varphi_1^0+(1-\alpha)\varphi_2^0)=\frac{1}{p'}\int_0^T\int_{B(R(t))}(|\alpha\psi_1+(1-\alpha)\psi_2|^{p'}\,\mathrm{d}x\,\mathrm{d}t,$$

and then

$$J_3(\alpha\varphi_1^0+(1-\alpha)\varphi_2^0)-\alpha J_3(\varphi_1^0)-(1-\alpha)J_3(\varphi_2^0)$$

$$=\frac{1}{p'}\int_0^T\int_{B(R(t))}(|\alpha\psi_1+(1-\alpha)\psi_2|^{p'}-\alpha|\psi_1|^{p'}-(1-\alpha)|\psi_2|^{p'})\,\mathrm{d}x\,\mathrm{d}t.$$

Since $p'>1$ we obtain

$$|\alpha\psi_1+(1-\alpha)\psi_2|^{p'}-\alpha|\psi_1|^{p'}-(1-\alpha)|\psi_2|^{p'}\leqslant 0,$$

and integrating we obtain,

$$\frac{1}{p'}\int_0^T\int_{B(R(t))}(|\alpha\,\psi_1+(1-\alpha)\psi_2|^{p'}-\alpha|\psi_1|^{p'}-(1-\alpha)|\psi_2|^{p'})\,\mathrm{d}x\,\mathrm{d}t\leqslant 0,$$

which proves the convexity of J_3. Finally, J_1 is linear and so convex and since the norm $\|\cdot\|_{L^{p'}(B(R(T))}$ is convex, J_2 is also convex.

J is continuous: By construction, J_1 and J_2 are continuous. Now, we shall prove that J_3 is continuous too. Let $\varphi_n^0\in L^{p'}(B(R(T)))$ such that $\varphi_n^0\to\varphi^0$ and let (φ_n,ψ_n), (φ,ψ) be the solutions of the problem (3.1)–(3.4) with initial data φ_n^0 and φ^0, respectively. Subtracting both systems and taking

$$(p'|\varphi-\varphi_n|^{p'-2}(\varphi-\varphi_n),\,p'|\psi-\psi_n|^{p'-2}(\psi-\psi_n)),$$

as test function and using the integration by parts formula (see e.g. [2]) and Young inequality, we arrive to

$$-\frac{\partial}{\partial t}\int_{B(R(t))}[(\varphi-\varphi_n)^{p'}+(\psi-\psi_n)^{p'}]\,\mathrm{d}x$$
$$+\int_{B(R(t))}(r_1p'-|\lambda|)|\varphi-\varphi_n|^{p'}\,\mathrm{d}x+\int_{B(R(t))}(r_2p'-|\lambda|)|\psi-\psi_n|^{p'}\,\mathrm{d}x\leqslant 0.$$

Denoting by

$$X_n(t)=\|\varphi-\varphi_n\|^{p'}_{L^{p'}(B(R(t)))}+\|\psi-\psi_n\|^{p'}_{L^{p'}(B(R(t)))},$$

we obtain the differential inequality

$$-X_n'(t)\leqslant CX_n(t),\quad t\in(0,T),$$
$$X_n(T)=\|\varphi_n^0-\varphi^0\|^{p'}_{L^{p'}(B(R(T)))},$$

where

$$C=\max\{-r_1p'+|\lambda|,-r_2p'+|\lambda|\}.$$

Thus, we obtain

$$0\leqslant X_n(t)\leqslant|X_n(T)|\mathrm{e}^{-C(t-T)}.$$

But

$$0\leqslant\int_{\omega_0}|\psi-\psi_n|^{p'}\,\mathrm{d}x\leqslant X_n(t),$$

integrating on $[0,T]$ and taking limits as $n\to\infty$ we conclude that

$$\int_0^T\int_{\omega_0}|\psi-\psi_n|^{p'}\,\mathrm{d}x\,\mathrm{d}t\leqslant\int_0^T X_n(t)\,\mathrm{d}t\to 0,$$

which shows the continuity of J_3.

J is coercive: Let $\varphi_n^0\in L^{p'}(B(R(T)))$ such that $\|\varphi_n^0\|_{L^{p'}(B(R(T)))}\to\infty$, when $n\to\infty$. Now, we shall see

$$\liminf_{n\to\infty}\frac{J(\varphi_n^0)}{\|\varphi_n^0\|_{L^{p'}(B(R(T)))}}\geqslant\varepsilon.$$

Let

$$I:=\liminf_{n\to\infty}\frac{J(\varphi_n^0)}{\|\varphi_n^0\|_{L^{p'}(B(R(T)))}}\geqslant-\|\sigma^d\|_{L^p(B(R(T)))}.$$

Then there exists a minimizing subsequence, (which we denote again by φ_n^0) such that

$$\lim_{n\to\infty}\frac{J(\varphi_n^0)}{\|\varphi_n^0\|_{L^{p'}(B(R(T)))}}=I.$$

We define

$$\bar{\varphi}_n^0:=\frac{\varphi_n^0}{\|\varphi_n^0\|_{L^{p'}(B(R(T)))}},$$

and denote by $(\bar{\varphi}_n, \bar{\psi}_n)$ the solution of problem (3.1)–(3.4) with initial data $(\bar{\varphi}_n^0, 0)$. Since the system is linear we have

$$(\bar{\varphi}_n, \bar{\psi}_n) = \frac{1}{\|\varphi_n^0\|_{L^{p'}}}(\varphi_n, \psi_n).$$

Then

$$\frac{J(\varphi_n^0)}{\|\varphi_n^0\|_{L^{p'}(B(R(T)))}} = \|\varphi_n^0\|^{p'-1}\int_0^T\int_{\omega_0}\bar{\psi}_n^{p'}\,dx\,dt - \int_{B(R(T)}\sigma^d\bar{\varphi}_n^0\,dx + \varepsilon.$$

Now, it is clear that if

$$\liminf_{n\to\infty}\int_0^T\int_{\omega_0}\bar{\psi}_n^{p'}\,dx \geqslant \alpha_0, \tag{3.7}$$

for some α_0 then

$$\frac{J(\varphi_n^0)}{\|\varphi_n^0\|_{L^{p'}(B(R(T)))}} \geqslant \alpha_0\|\varphi_n^0\|_{L^{p'}(B(R(T)))}^{p'-1} + \varepsilon - \|\sigma^d\|_{L^p(B(R((T)))} \to \infty$$

as $n\to\infty$, which proves the property. Let us assume now that $\liminf\int_0^T\int_{\omega_0}\bar{\psi}_n^{p'}\,dx=0$. Then there exists a subsequence $\bar{\psi}_{n_i}$ such that

$$\int_0^T\int_{\omega_0}|\bar{\psi}_{n_i}|^{p'}\,dx\,dt \to 0,$$

therefore $\bar{\psi}_{n_i}\to 0$ in $L^{p'}(\omega_0\times[0,T])$. Taking $(0,\zeta)$ as test function in (3.2), where $\zeta\in C_c^2((0,T)\times\omega_0)$, we obtain

$$\int_0^T\int_{\omega_0}\bar{\psi}_{n_i}\frac{\partial\zeta}{\partial t}\,dx\,dt - \int_0^T\int_{\omega_0}\bar{\psi}_{n_i}\Delta\zeta\,dx\,dt$$
$$-r_2\int_0^T\int_{\omega_0}\bar{\psi}_{n_i}\zeta\,dx\,dt + \lambda\int_0^T\int_{\omega_0}\bar{\varphi}_{n_i}\zeta\,dx\,dt = 0.$$

Now, passing to the limit then $n_i\to\infty$ it results

$$\int_0^T\int_{\omega_0}\bar{\varphi}_{n_i}\zeta\,dx\,dt \to 0, \tag{3.8}$$

where $\bar{\varphi}_{n_i}$ is the solution of the problem

$$-\frac{\partial\bar{\varphi}_{n_i}}{\partial t} - D_1\Delta\bar{\varphi}_{n_i} - r_1\bar{\varphi}_{n_i} = 0, \quad |x|<R(t),\ t\in(0,T),$$
$$\bar{\varphi}_{n_i}(0,x) = \bar{\varphi}^0. \tag{3.9}$$

Making the change of variable (2.1), and

$$\bar{u}_{n_i}(\tilde{x},\tilde{t}) := \bar{\varphi}_{n_i}(R(t(\tilde{t}))\tilde{x}, t(\tilde{t})),$$

we obtain

$$-\frac{\partial \bar{u}_{n_i}}{\partial \tilde{t}} - D\Delta \bar{u}_{n_i} - R^2 R' \tilde{x} \cdot \nabla \bar{u}_{n_i} + R^2 r_1 \bar{u}_{n_i} = 0, \quad |\tilde{x}| < 1, \ \tilde{t} \in (0, \tilde{T}),$$

$$\bar{u}_{n_i}(\tilde{x}, \tilde{t}) = 0, \quad |\tilde{x}| = 1, \ \tilde{t} \in (0, \tilde{T}),$$

$$\bar{u}_{n_i}(\tilde{x}, 0) = u_0(\tilde{x}) = \bar{\varphi}^0_{n_i}(\tilde{x} R_0), \quad |\tilde{x}| < 1, \tag{3.10}$$

such that $\bar{u}^0_{n_i} \rightharpoonup \bar{u}_0$ in $L^{p'}(B)$, and furthermore $\bar{u}_{n_i} \rightharpoonup \bar{u}$ solution of (3.10), with initial data $\bar{u}_0 = \bar{\varphi}^0_{n_i}$. By (3.8), $\bar{u}_{n_i} \to 0$, weakly in $L^{p'}(B(\hat{\omega}_0))$, where $\hat{\omega}_0$ is an open subset of B, such that $\hat{\omega}_0 \subset \tilde{\omega}_0$. Consequently, $\bar{u} \equiv 0$ on $\tilde{\omega}_0$ for all $0 \leqslant \tilde{t} \leqslant \tilde{T}$. By the unique continuation for the equation (3.10) (see [6, Theorem 1.1]) we deduce that $\bar{u} = 0$ in $B \times (0, \tilde{T})$, and by the uniqueness of problem (3.10), it results in $\bar{u}_0 \equiv 0$ and $\bar{\varphi}^0 \equiv 0$. Furthermore,

$$-\int_{B(R(T))} \sigma^d \bar{\varphi}^0 \, dx = 0,$$

and $I = \varepsilon$, from where we deduce that J is coercive. □

Proof of the Theorem 1.1. We construct the sequence $\{R_n(t)\}$, such that R_n verifies

$$R_n^2(t)\dot{R}_n(t) = \int_{B(R_{n-1}(t))} S(\sigma_{n-1} + \sigma^s_{n-1}, \beta_{n-1} + \beta^s_{n-1})\, dx, \quad R_n(0) = R_0$$

for $n > 1$, where $(\sigma^s_{n-1}, \beta^s_{n-1})$ is the solution of the problem (1.1), (1.2), (1.4) and (1.5), with $f \equiv 0$, and initial data $\sigma^s_{n-1}(x,0) = \sigma_0(x)$, $\beta^s_{n-1}(x,0) = \beta_0(x)$, and $R(t) = R_{n-1}(t)$, and $(\sigma_{n-1}, \beta_{n-1})$ is the solution mentioned in Proposition 3.1. We start the process by taking, e.g. $R_1(t) = R_0$. Since S is bounded, $R_n \in W^{1,\infty}(0,T)$ and we deduce there exists a subsequence of functions R_{n_i} such that converges weakly to $R(t)$ in $W^{1,q}(0,T)$, for all $q \in (1, \infty)$. By Proposition 3.1, for each R_n there exists a minimum function φ^0_n. We shall show that the sequence $\|\varphi^0_n\|_{L^{p'}(B(R(T)))}$ is uniformly bounded. We consider

$$J_n(\varphi^0_n) := \int_0^T \int_{\omega_0} |\psi_n|^{p'} \, dx \, dt + \varepsilon \|\varphi^0_n\|_{L^{p'}(B(R_n(T)))} - \int_{B(R_n(T))} \sigma^d_n \varphi^n_0 \, dx,$$

where $\sigma^d_n = \hat{\sigma}^d \chi_{B(R_n(T))}$. Supposing $\|\varphi^0_n\|_{L^{p'}(B(R_n(T)))} \to \infty$, since $J_n(0) = 0$ and (by definition of φ^0_n), $J_n(\varphi^0_n) \leqslant 0$,

$$\frac{J_n(\varphi^0_n)}{\|\varphi^0_n\|_{L^{p'}}} = \|\varphi^0_n\|^{p'-1}_{L^{\prime}(B(R_n(T)))} \int_0^T \int_{\omega_0} \bar{\psi}^p_n \, dx \, dt + \varepsilon - \int_{B(R_n(T))} \sigma^d_n \bar{\varphi}^0_n \, dx \leqslant 0, \tag{3.11}$$

since

$$\int_{B(R_n(T))} \sigma^d_n \frac{\varphi^0_n}{\|\varphi^0_n\|_{L^{p'}(B(R(T)))}} \, dx \leqslant \|\sigma^d_n\|_{L^p(B(R_n(T)))} \leqslant \|\hat{\sigma}^d\|_{L^p(B(R_0 \exp\{\|S\|_{L^\infty} T\}))},$$

it results, by (3.11),

$$\int_0^T \int_{\omega_0} \bar{\psi}_n^{p'} \, dx \, dt \to 0 \quad \text{when } n \to \infty.$$

Repeating the argument used in the proof that J is coercive, we obtain

$$\bar{\varphi}_0^n \rightharpoonup 0 \quad \text{in } L^{p'}(B(R(T)))$$

and

$$\liminf_{n\to\infty} \frac{J_n(\varphi_n^0)}{\|\varphi_n^0\|} \geqslant \varepsilon,$$

which is a contradiction with (3.11). Consequently $\|\varphi_n^0\|_{L^{p'}(B(R_n(T)))}$ is uniformly bounded and so $\|\varphi_n\|_{L^{p'}(B(R_n(T)))}$ is also uniformly bounded, and furthermore,

$$\|f_n\|_{L^p(0,T:L^p(\omega_0))} \leqslant C, \tag{3.12}$$

for some C independent of n.

Making the change of variable (2.1), (2.2), by Lemma 2.1, we obtain that if (u_n, v_n, R_n) is the transformation of $(\sigma_n + \sigma_n^s, \beta_n + \beta_n^s, R_n)$ then it is uniformly bounded in $(W^{1,p}(B\times(0,\tilde{T}))^2, H^2(0,T))$, and by compact embedding, there exists a subsequence (u_{ni}, v_{ni}, R_{ni}) such that converges strongly in $(C^\alpha((0,T]\times B)^2, C^1([0,T]))$, to (u,v,R) for $\alpha = \frac{1}{6}$, where (u_{ni}, v_{ni}) satisfies

$$\begin{aligned}
&\frac{\partial u_{ni}}{\partial t} - \frac{d}{R_{ni}^2}\Delta u_{ni} - \frac{R'_{ni}}{R_{ni}}\tilde{x}\cdot\nabla u_{ni} + r_1 u_{ni} + \lambda v_{ni} = 0 \quad \text{in } B\times(0,T),\\
&\frac{\partial v_{ni}}{\partial t} - \frac{d}{R_{ni}^2}\Delta v_{ni} - \frac{R'_{ni}}{R_{ni}}\tilde{x}\cdot\nabla v_{ni} + r_2 v_{ni} = f_n\chi_{\tilde{\omega}_0} \quad \text{in } B\times(0,T),\\
&u_{ni}(\tilde{x},t) = v_{ni}(\tilde{x},t) = 0 \quad \text{on } \partial B\times(0,T),\\
&u_{ni}(\tilde{x},0) = u_{ni}^0(\tilde{x}), \quad v_{ni}(\tilde{x},0) = v_{ni}^0(\tilde{x}) \quad \text{in } B
\end{aligned} \tag{3.13}$$

and (u,v,R) is solution of (2.3)–(2.7). In particular,

$$\|u(T) - u_n(T)\|_{L^p(B)}^p \to 0, \quad \text{as } n_i \to +\infty. \tag{3.14}$$

Moreover,

$$\begin{aligned}
\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} &= \|\sigma(T) - \sigma_n(T)\|_{L^p(B(\min\{R(T),R_n(T)\}))}\\
&\quad + \|\sigma_n(T) - \sigma^d\|_{L^p(B(\min\{R(T),R_n(T)\}))} + \|\sigma - \sigma^d\|_{L^p(B_n^*(T))},
\end{aligned}$$

where

$$B_n^*(T) = \begin{cases} B(R(T)) \cap B^c(B(R_n(T))) & \text{if } R(T) > R_n(T),\\ \emptyset & \text{if } R(T) \leqslant R_n(T). \end{cases}$$

Making the change of variable (2.1), and since

$$\|\sigma_n(T) - \sigma^d\|_{L^p(B(\min\{R(T),R_n(T)\}))} \leqslant \varepsilon,$$

we obtain

$$\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} \leqslant \|u(T) - u_n(T)\|_{L^p(B)} + \|\sigma - \sigma^d\|_{L^p(B_n^*(T))} + \varepsilon.$$

Since $|\sigma - \sigma^d|^p \chi_{B_n^*(T)} \leqslant |\sigma - \sigma^d|^p$ and $\mu(B_n^*(T)) \to 0$, by the Lebesgue dominated convergence theorem we obtain that

$$\lim_{n\to\infty} \|\sigma - \sigma^d\|_{L^p(B_n^*(T))} = 0.$$

Taking limits when $n \to \infty$ it results

$$\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} \leqslant \varepsilon,$$

and the theorem is thereby proved in the case $p \geqslant 5$.

In the case $p < 5$, we consider the control f for $p = 5$, then

$$\begin{aligned}\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} &\leqslant \frac{3\pi}{4} B(R(T))\|\sigma(T) - \sigma^d\|_{L^5(B(R(T)))}\\ &\leqslant \frac{3\pi}{4} \exp\{T\|S\|_{L^\infty}\}\varepsilon,\end{aligned}$$

taking $\varepsilon = \varepsilon'(\frac{3\pi}{4}\exp\{T\|S\|_{L^\infty}\})^{-1}$ we conclude the Theorem. $\square$

Remark 3.1. Notice that the final observation is made on the density $\sigma(T,\cdot)$ and that once we chose the control in order to have (1.6) the free boundary, $R(t)$, and the inhibitor density $\beta(T,\cdot)$ are univocally determined.

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