

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

J.I. Díaz<sup>1,2</sup> and J.I. Tello<sup>1</sup>

## 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  $\omega_0$ .

## 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. Chaplain and Anderson [1996]). Once the angiogenesis occurs, the tumor receives nutrient from the vessels (process named *vasculature*). We assume that the tumor occupies 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  $\sigma_B$  the constant nutrient concentration in the vasculature,  $\hat{r}_1$  the rate, per unit length, of nutrient transferred to the tissue,  $\hat{\sigma}$  satisfies the equation

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

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,

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

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<sup>1</sup>Departamento de Matemática Aplicada, Universidad Complutense de Madrid, 28040 Madrid

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with  $d_2$  the diffusion coefficient,  $\beta_B$  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  $\omega_0$  with a rate given by  $f$  (the control of the problem).

According 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

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

According the inhibitor nature and the tumor tissue, the function  $\hat{S}$  has different representations. In any case we shall assume trough 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

$$\sigma := \hat{\sigma} - \frac{\hat{r}_1\sigma_B(\hat{r}_2 + \lambda_2) + \lambda\hat{r}_2\beta_B}{(\hat{r}_1 + \lambda_1)(\hat{r}_2 + \lambda_2)}, \quad \beta := \hat{\beta} - \frac{\hat{r}_2\beta_B}{\hat{r}_2 + \lambda_2},$$

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

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

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

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

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

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

where  $R_0 > 0$ , the normalized nutrient and inhibitor densities at the exterior of the tumor  $\overline{\overline{\sigma}}, \overline{\overline{\beta}}$ , the initial densities  $(\sigma_0, \beta_0)$  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 See Greenspan [1972], Adams [1986], Byrne – Chaplain [1996], Byrne [1999], Cui – Friedman [1999], Reitich – Friedman [1999], Díaz – Tello [1999]). A recent reference containing details on the notion of weak solution and existence and uniqueness is the authors work (Díaz – Tello [2000]). 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  $T > 0$ ,  $\omega_0 \subset B(R_0 \exp\{-\|S\|_{L^\infty} T\})$ ,  $\epsilon > 0$ , and  $\hat{\sigma}^d \in L^p_{loc}(\mathbb{R}^3)$ , for some  $p > 1$ , there exists  $f \in L^p((0, T) \times \omega_0)$  such that, if  $(\sigma, \beta, R)$  is the solution of the problem (1.1)-(1.5), then*

$$\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} \leq \epsilon, \quad (1.6)$$

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

Due to some technical reasons, we shall prove the theorem firstly for  $p \geq 5$ , (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  $\omega_0$  such that the solution  $(\sigma_n, \beta_n)$  of problem (1.1)-(1.5), satisfies (1.6). Then we obtain  $R_{n+1}$  and  $f_{n+1}$  from  $(\sigma_n, \beta_n)$  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 Lions [1990], [1991], Puel – Fabre – Zuazua [1995], and Díaz – Ramos [1995]). In spite of the large literature on this type of methods, very few seems to be known for the case of systems (see also Díaz-Ramos [1998] for a higher order equation). Some numerical experiences could be developed in the line of the works Glowinski-Lions [1995] and Díaz-Ramos [2000]. 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 Díaz - Tello [2000]), 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 – Tello [2000],

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

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

(Notice since  $R$  is a continuous function and  $\frac{1}{R^2(t)} > 0$ , 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  $B = \{\tilde{x} \in \mathbb{R}^3, \quad |\tilde{x}| < 1\}$ . Problem (1.1)-(1.5) can be equivalently formulated as

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

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

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

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

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

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  $p \geq 5$ , 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 of Díaz and Tello [2000] 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

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

admits a fundamental solution (see Friedman [1964]) 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. Ladyzenkaya, Solonnikov and Uralceva [1991], Theorem 9.1, Chap 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  $q \leq \infty$ . Consequently, we obtain  $R(t) \in W^{2,p}(0, T)$ . □

As a consequence of the lemma we obtain,

**Corollary 2.1** *By using that  $W_0^{1,p}(B \times [0, \tilde{T}]) \subset L^\infty(B \times [0, \tilde{T}])$ , if  $p > 4$ , 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*

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

The uniqueness of solutions is proved in the next proposition.

**Proposition 2.1** *Let  $f \in L^p(\omega_0 \times (0, T))$  with  $p \geq 5$ , and  $(\sigma_0 - \overline{\sigma}, \beta_0 - \overline{\beta}) \in W^{2,s}(B(R_0)) \cap H_0^1(B(R_0))$ , for  $s > 4$ . Then, there exists a unique solution of the problem (1.1)-(1.5).*

**Proof.** We shall show that if we assume that there exist two different solutions,  $(\sigma_1, \beta_1, R_1)$  and  $(\sigma_2, \beta_2, R_2)$ , 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  $(\sigma, \beta, R)$  satisfies the problem,

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

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

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

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

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

We introduce a new unknown defined by

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

with

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

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

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

$$\begin{cases} \frac{\partial z}{\partial t} - d\Delta z + r_1 z = 0, & |x| < R(t), \quad t \in (0, T), \\ z(x, 0) = 0, & |x| < R_0, \\ z(x, t) = k_1 \sigma(x, t) - k_2 \beta(x, t), & |x| = R(t), \quad t \in (0, T). \end{cases} \quad (2.13)$$

Now we prove a preliminary result:

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

**Proof.** Multiplying the equation (2.13) by  $e^{r_1 t}$  we obtain that  $e^{r_1 t} z$  satisfies

$$\begin{cases} \frac{\partial}{\partial t}(e^{r_1 t} z) - d\Delta(e^{r_1 t} z) = 0, & |x| < R(t), \ t \in (0, T), \\ z(x, 0) = 0, & |x| < R_0, \\ e^{r_1 t} z(x, t) = e^{r_1 t}(k_1 \sigma(x, t) - k_2 \beta(x, t)), & |x| = R(t), \ t \in (0, T). \end{cases} \quad (2.14)$$

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

$$\begin{cases} \frac{\partial}{\partial t}(e^{r_2 t} \beta) - d\Delta(e^{r_2 t} \beta) = 0, & |x| < R(t), \ t \in (0, T), \\ \beta(x, 0) = 0, & |x| < R_0, \\ e^{r_2 t} \beta(x, t) = e^{r_2 t}(\beta_1(x, t) - \beta_2(x, t)), & |x| = R(t), \ t \in (0, T). \end{cases} \quad (2.15)$$

By Corollary 2.1, we know that

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

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

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

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

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

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

Let  $T_k$  and  $T^k$  be defined by

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

and

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

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, after some manipulations, we arrive to

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

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

$$z_{**} \leq e^{r_1 t} z \leq z^{**}. \quad (2.16)$$

The proof of

$$\beta_{**} \leq e^{r_2 t} \beta \leq \beta^{**}, \quad (2.17)$$

is analogous.  $\square$

**End of the proof of Proposition 2.1.** Given  $t \in [0, T]$ , we can suppose, without lost generality,  $R_1(t) \leq R_2(t)$ , 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

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

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

$$\begin{aligned} & \int_0^T \int_{B(R(t))} |S(\sigma_1, \beta_1) - S(\sigma_2, \beta_2)|dxdt \leq \\ & \int_0^T \int_{B(R(t))} |S|_{W^{1,\infty}(\mathbb{R}^2)} (sup|\sigma| + sup|\beta|)dxdt \leq \\ & \int_0^T \int_{B(R(t))} k_0(\frac{1}{k_1}sup|z| + k_2|\beta| + sup|\beta|)dxdt \leq \\ & \int_0^T \int_{B(R(t))} C(sup|z| + sup|\beta|)dxdt \leq \\ & \int_0^T \int_{B(R(t))} C(sup|e^{-r_1 t}e^{r_1 t}z| + sup|e^{-r_2 t}e^{r_2 t}\beta|)dxdt \leq \\ & \int_0^T \int_{B(R(t))} C(e^{|r_1|T}sup|e^{r_1 t}z| + e^{|r_2|T}sup|e^{r_2 t}\beta|)dxdt \leq \\ & \int_0^T \int_{B(R(t))} k_3(sup|e^{r_1 t}z| + sup|e^{r_2 t}\beta|)dx. \end{aligned}$$

From Lemma 2.2, we know

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

By Corollary 2.2, we deduce that

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

and consequently,

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

Since

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

we deduce

$$\begin{aligned}
& e^{r_1 T} \frac{3\pi}{4} R^3(t) \int_0^T \sup_{|x|=R(t)} |z(x, t)| dt \leq \\
& k_4 \int_0^T \|\sigma_2\|_{W^{1,\infty}(B(R_2(t)))} + \|\beta_2\|_{W^{1,\infty}(B(R_2(t)))} |R_1(t) - R_2(t)| dt \leq \\
& k_4 \sup_{0 < t < T} |R_1(t) - R_2(t)| T^{\frac{1}{2}} \int_0^T (\|\sigma_2\|_{W^{1,\infty}(B(R_2(t)))}^2 + \|\sigma_2\|_{W^{1,\infty}(B(R_2(t)))}^2) dt \leq \\
& k \sup_{0 < t < T} |R_1(t) - R_2(t)| T^{\frac{1}{2}}.
\end{aligned}$$

In the same way,

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

Then

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

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

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

and since  $|R_1^3(t) - R_2^3(t)| \geq 3R_0^2 |R_1(t) - R_2(t)|$ , we conclude,  $\delta \leq k_0 \delta (T + T^{\frac{1}{2}})$ . Then, if  $T < T_1 = \min\{\frac{1}{4k_0^2}, 1\}$ , 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.  $\square$

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

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

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



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

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

for  $\varphi_0 \in L^{p'}(B(R(T)))$ , where  $\psi$  is the component of the solution  $(\varphi, \psi)$  of the “dual” problem

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

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

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

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

We point out that the existence of a weak solutions of (3.1)-(3.4),  $(\varphi, \psi)$  can be obtained as in section 2, by making the change of variable (2.1), (2.2), (see Tello [2001]).

In order to prove the uniqueness of solutions, we suppose there exists two solutions,  $(\varphi_1, \psi_1)$ ,  $(\varphi_2, \psi_2)$ , 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,

$$-\frac{d}{dt} \int_{B(R(t))} |\varphi|^{p'} dx \leq r_1 \int_{B(R(t))} |\varphi|^{p'} dx,$$

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  $\liminf J \rightarrow \infty$  if  $\|\varphi^0\|_{L^{p'}(B(R_0))} \rightarrow \infty$ ). Then  $J$  takes a minimum  $\varphi_0$  (see, e.g., Brezis [1983], Corollary III.20). Moreover if  $(\xi, \zeta)$  is the solution of the problem (3.1)–(3.4) with initial datum  $(\xi_0, 0)$ . We have

$$\begin{aligned} & \int_0^T \int_{\omega_0} |\psi|^{p'-2} \psi \zeta dx dt - \int_{B(R(T))} \sigma^d \xi_0 dx + \\ & \epsilon \|\varphi^0\|_{L^{p'}(B(R(T)))}^{1-p'} \int_{B(R(T))} |\varphi^0|^{p'-2} \varphi^0 \xi^0 dx = 0. \end{aligned} \quad (3.5)$$

Multiplying (1.1), (1.2) by  $(\xi, \zeta)$ , integrating by parts and applying Leibnitz Theorem, we arrive to

$$\begin{aligned} & - \int_0^T \langle \sigma, \frac{\partial \xi}{\partial t} \rangle dt - d \int_0^T \langle \sigma, \Delta \xi \rangle dt + \int_0^T \int_{B(R(t))} r_1 \sigma \xi dx dt + \\ & \int_0^T \int_{B(R(t))} \lambda \beta \xi dx dt - \int_0^T \langle \beta, \frac{\partial \zeta}{\partial t} \rangle dt - d \int_0^T \langle \beta, \Delta \zeta \rangle dt + \\ & \int_0^T \int_{B(R(t))} r_2 \beta \zeta dx dt - \int_0^T \int_{\omega_0} f \zeta dx dt + \int_{B(R(t))} \sigma \xi dx \Big|_0^T + \int_{B(R(t))} \beta \zeta dx \Big|_0^T = 0, \end{aligned}$$

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

$$-\int_0^T \int_{\omega_0} f \zeta dx dt + \int_{B(R(T))} \sigma(T) \xi^0 dx = 0. \quad (3.6)$$

Now, let us take  $f$ ,

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

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

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

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

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

since  $p = 1 + \frac{1}{p'-1}$ , we obtain

$$\begin{aligned} & \|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))}^p = \\ & \epsilon \|\varphi^0\|_{L^{p'}(B(R(T)))}^{1-p'} \int_{B(R(T))} |\varphi^0|^{p'-2} \varphi^0 |\sigma(T) - \sigma^d|^{\frac{1}{p'-1}-1} (\sigma(T) - \sigma^d) dx. \end{aligned}$$

Applying Hölder inequality, we obtain that

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

which leads to

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

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,

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

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

First we shall see that  $J_3$  is convex. Let  $\varphi_1^0, \varphi_2^0 \in L^p(B(R(T)))$  and  $(\varphi_1, \psi_1)$  and  $(\varphi_2, \psi_2)$  be the respective solutions of problem (3.1)–(3.4), and let  $\alpha \in (0, 1)$ . Then, since the system is linear we get

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

and then

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

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

Since  $p' > 1$  we obtain

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

and integrating we obtain,

$$\frac{1}{p'} \int_0^T \int_{B(R(t))} (|\alpha\psi_1 + (1-\alpha)\psi_2|^{p'} - \alpha|\psi_1|^{p'} - (1-\alpha)|\psi_2|^{p'}) dx dt \leq 0,$$

which proves the convexity of  $J_3$ . Finally  $J_1$  is linear and so convex and since  $\|\cdot\|_{L^{p'}(B(R(T)))}$  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  $\varphi_n^0 \rightarrow \varphi^0$  and let  $(\varphi_n, \psi_n), (\varphi, \psi)$  be the solutions of the problem (3.1)-(3.4) with initial data  $\varphi_n^0$  and  $\varphi^0$ , 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. Alt and Luckhaus [1983]) and Young inequality, we arrive to

$$\begin{aligned} & -\frac{\partial}{\partial t} \int_{B(R(t))} [(\varphi - \varphi_n)^{p'} + (\psi - \psi_n)^{p'}] dx + \\ & \int_{B(R(t))} (r_1 p' - |\lambda|) |\varphi - \varphi_n|^{p'} dx + \int_{B(R(t))} (r_2 p' - |\lambda|) |\psi - \psi_n|^{p'} dx \leq 0. \end{aligned}$$

Denoting by

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

we obtain the differential inequality

$$-X'_n(t) \leq C X_n(t), \quad t \in (0, T),$$

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

where

$$C = \max\{-r_1 p' + |\lambda|, -r_2 p' + |\lambda|\}.$$

Thus we obtain

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

But

$$0 \leq \int_{\omega_0} |\psi - \psi_n|^{p'} dx \leq X_n(t),$$

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

$$\int_0^T \int_{\omega_0} |\psi - \psi_n|^{p'} dx dt \leq \int_0^T X_n(t) dt \rightarrow 0,$$

which shows the continuity of  $J_3$ .

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

$$\liminf_{n \rightarrow \infty} \frac{J(\varphi_n^0)}{\|\varphi_n^0\|_{L^{p'}(B(R(T)))}} \geq \epsilon.$$

Let

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

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

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

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

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

Now, it is clear that if

$$\liminf_{n \rightarrow \infty} \int_0^T \int_{\omega_0} \bar{\psi}_n^{p'} dx \geq \alpha_0, \quad (3.7)$$

for some  $\alpha_0$  then

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

as  $n \rightarrow \infty$ , 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

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

therefore  $\bar{\psi}_{n_i} \rightarrow 0$  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

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

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

$$\int_0^T \int_{\omega_0} \bar{\varphi}_{n_i} \zeta dx dt \rightarrow 0, \quad (3.8)$$

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

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

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

$$\begin{cases} -\frac{\partial \bar{u}_{n_i}}{\partial \tilde{t}} - D \Delta \bar{u}_{n_i} - R^2 R' \tilde{x} \cdot \nabla \bar{u}_{n_i} + R^2 r_1 \bar{u}_{n_i} = 0, & |\tilde{x}| < 1, \quad \tilde{t} \in (0, \tilde{T}), \\ \bar{u}_{n_i}(\tilde{x}, \tilde{t}) = 0, & |\tilde{x}| = 1, \quad \tilde{t} \in (0, \tilde{T}), \\ \bar{u}_{n_i}(\tilde{x}, 0) = u_0(\tilde{x}) = \bar{\varphi}_{n_i}^0(\tilde{x} R_0), & |\tilde{x}| < 1, \end{cases} \quad (3.10)$$

such that  $\bar{u}_{n_i}^0 \rightharpoonup \bar{u}_0$  in  $L^{p'}(B)$ , and furthermore  $\bar{u}_{n_i} \rightharpoonup \bar{u}$  solution of (3.10), with initial data  $\bar{u}_0 = \bar{\varphi}_{n_i}^0$ . By (3.8),  $\bar{u}_{n_i} \rightarrow 0$ , 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  $0 \leq \tilde{t} \leq \tilde{T}$ . By the unique continuation for the equation (3.10) (see Chi-Cheung Poon [1996], Theorem 1.1') we deduce that  $\bar{u} = 0$  in  $B \times (0, \tilde{T})$ , and by the uniqueness of problem (3.10), it result  $\bar{u}_0 \equiv 0$  and  $\bar{\varphi}^0 \equiv 0$ . Furthermore

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

and  $I = \epsilon$ , from where we deduce that  $J$  is coercive.  $\square$

### Proof of the Theorem 1.1.

We construct the sequence  $\{R_n(t)\}$ , such that  $R_n$  verifies

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

for  $n > 1$ , where  $(\sigma_{n-1}^s, \beta_{n-1}^s)$  is the solution of the problem (1.1), (1.2), (1.4) and (1.5), with  $f \equiv 0$ , and initial data  $\sigma_{n-1}^s(x, 0) = \sigma_0(x)$ ,  $\beta_{n-1}^s(x, 0) = \beta_0(x)$ , 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  $\varphi_n^0$ . We shall show that the sequence  $\|\varphi_n^0\|_{L^{p'}(B(R_n(T)))}$  is uniformly bounded. We consider

$$J_n(\varphi_n^0) := \int_0^T \int_{\omega_0} |\psi_n|^{p'} dx dt + \epsilon \|\varphi_n^0\|_{L^{p'}(B(R_n(T)))} - \int_{B(R_n(T))} \sigma_n^d \varphi_n^0 dx,$$

where  $\sigma_n^d = \hat{\sigma}^d \chi_{B(R_n(T))}$ . Supposing  $\|\varphi_n^0\|_{L^{p'}(B(R_n(T)))} \rightarrow \infty$ , since  $J_n(0) = 0$  and (by definition of  $\varphi_n^0$ ),  $J_n(\varphi_n^0) \leq 0$ ,

$$\frac{J_n(\varphi_n^0)}{\|\varphi_n^0\|_{L^{p'}}} = \|\varphi_n^0\|_{L^{p'}(B(R_n(T)))}^{p'-1} \int_0^T \int_{\omega_0} \bar{\psi}_n^p dx dt + \epsilon - \int_{B(R_n(T))} \sigma_n^d \bar{\varphi}_n^0 dx \leq 0, \quad (3.11)$$

since

$$\int_{B(R_n(T))} \sigma_n^d \frac{\varphi_n^0}{\|\varphi_n^0\|_{L^{p'}(B(R_n(T)))}} dx \leq \|\sigma_n^d\|_{L^p(B(R_n(T)))} \leq \|\hat{\sigma}^d\|_{L^p(B(R_0 \exp\{\|S\|_{L^\infty} T\}))},$$

it results, by (3.11),

$$\int_0^T \int_{\omega_0} \bar{\psi}_n^p dx dt \rightarrow 0 \quad \text{when } n \rightarrow \infty.$$

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

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

and

$$\liminf_{n \rightarrow \infty} \frac{J_n(\varphi_n^0)}{\|\varphi_n^0\|} \geq \epsilon,$$

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

$$\|f_n\|_{L^p(0,T;L^p(\omega_0))} \leq C, \quad (3.12)$$

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 transformed 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

$$\begin{cases} \frac{\partial u_{ni}}{\partial t} - \frac{d}{R_{ni}^2} \Delta u_{ni} - \frac{R'_{ni}}{R_{ni}} \tilde{x} \cdot \nabla u_{ni} + r_1 u_{ni} + \lambda v_{ni} = 0, & |\tilde{x}| < 1, \ t \in (0, T), \\ \frac{\partial v_{ni}}{\partial t} - \frac{d}{R_{ni}^2} \Delta v_{ni} - \frac{R'_{ni}}{R_{ni}} \tilde{x} \cdot \nabla v_{ni} + r_2 v_{ni} = f_n \chi_{\tilde{\omega}_0}, & |\tilde{x}| < 1, \ t \in (0, T), \\ u_{ni}(\tilde{x}, t) = v_{ni}(\tilde{x}, t) = 0, & |\tilde{x}| = 1, \ t \in (0, T), \\ u_{ni}(\tilde{x}, 0) = u_{ni}^0(\tilde{x}), \ v_{ni}(\tilde{x}, 0) = v_{ni}^0(\tilde{x}), & |\tilde{x}| < 1, \end{cases} \quad (3.13)$$

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

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

Moreover

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

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

where

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

Making the change of variable (2.1), and since

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

we obtain

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

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

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

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

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

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

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

$$\|\sigma(T) - \sigma^d\|_{L^p(B(R(T)))} \leq \frac{3\pi}{4} B(R(T)) \|\sigma(T) - \sigma^d\|_{L^5(B(R(T)))} \leq \frac{3\pi}{4} \exp\{T \|S\|_{L^\infty}\} \epsilon,$$

taking  $\epsilon = \epsilon'(\frac{3\pi}{4} \exp\{T \|S\|_{L^\infty}\})^{-1}$  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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