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On the long time behavior of a tumor growth model

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Abstract

We consider the problem of the long time dynamics for a diffuse interface model for tumor growth. The model describes the growth of a tumor surrounded by host tissues in the presence of a nutrient and consists in a Cahn-Hilliard-type equation for the tumor phase coupled with a reaction-diffusion equation for the nutrient concentration. We prove that, under physically motivated assumptions on parameters and data, the corresponding initial-boundary value problem generates a dissipative dynamical system that admits the global attractor in a proper phase space.

MSC: 35D30; 35K57; 35Q92; 35B41; 37L30

Keywords: Tumor growth; Phase field model; Initial-boundary value problem; Well-posedness; Dissipativity; Global attractor

1. Introduction

One of the main examples of complex systems studied nowadays in both the biomedical and the mathematical literature refers to tumor growth processes. In particular, there has been a recent

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surge in the development of phase field models for tumor growth. These models aim to describe the evolution of a tumor mass surrounded by healthy tissues by taking into account biological mechanisms such as proliferation of cells via nutrient consumption, apoptosis, chemotaxis and active transport of specific chemical species. In particular, we will consider here a model that fits into the framework of *diffuse interface* models for tumor growth. In this setting the evolution of the tumor is described by means of an order parameter φ which represents the local concentration of tumor cells; the interface between the tumor and healthy cells, rather than being represented as a surface, is seen as a (narrow) layer separating the regions where $\varphi = \pm 1$, with $\varphi = 1$ denoting the tumor phase and $\varphi = -1$ the healthy phase. Note that in the case of an incipient tumor, i.e., before the development of quiescent cells, the representation of the tumor growth process is often given by a Cahn–Hilliard equation [4] for φ coupled with a reaction-diffusion equation for the nutrient σ (cf., e.g., [9,19–21]). We will consider here this type of situation; we just mention the fact that more sophisticated models may distinguish between different tumor phases (e.g., proliferating and necrotic), or, treating the cells as inertia-less fluids, include the effects of fluid flow into the evolution of the tumor, leading to (possibly multiphase) Cahn-Hilliard-Darcy systems [8,19,30].

In this work, our main purpose is to consider the long time dynamics of a Cahn-Hilliard-reaction-diffusion tumor growth model recently introduced in [19]. On the other hand, in comparison with [19], we have neglected here the effects of chemotaxis and active transport (a more complete model including these effects may be the topic of a future work). Namely, we consider the following PDE system:

$$\varphi_t - \Delta\mu = (P\sigma - A)h(\varphi), \tag{1.1}$$

$$\mu = -\Delta\varphi + \psi'(\varphi), \tag{1.2}$$

$$\sigma_t - \Delta\sigma = -C\sigma h(\varphi) + B(\sigma_s - \sigma), \tag{1.3}$$

settled in $\Omega \times (0, +\infty)$, Ω being a smooth domain of $\mathbb{R}^3$, and complemented with the Cauchy conditions and with no-flux (i.e., homogeneous Neumann) boundary conditions for all unknowns. As already mentioned, φ represents the tumor phase concentration, σ is the concentration of a nutrient for the tumor cells (such as oxygen or glucose), and μ is the chemical potential of the “phase transition” from healthy to tumor cells. The parameters P, A, B, C are assumed to be strictly positive constants and $\sigma_s \in (0, 1)$. Moreover, in order to guarantee dissipativity of the process, some compatibility conditions will be needed. Actually, these conditions will be introduced in Assumption 2.8 below and discussed in more detail in Remark 2.9 and in Subsection 3.4. Here we limit ourselves to outlining the physical meaning of the parameters. Namely, P denotes the tumor proliferation rate, A the apoptosis rate, C the nutrient consumption rate, and B the nutrient supply rate. The function h is assumed to be monotone increasing, nonnegative in the “physical” interval $[-1, 1]$, and normalized so that $h(-1) = 0$ and $h(1) = 1$. The term $P\sigma h(\varphi)$ models the proliferation of tumor cells, which is proportional to the concentration of the nutrient, the term $Ah(\varphi)$ describes the apoptosis (death) of tumor cells, and $C\sigma h(\varphi)$ models the consumption of the nutrient by the tumor cells (owing to the monotonicity of h, it is higher if more tumor cells are present). The constant σ_s acts as a threshold and denotes the nutrient concentration in a pre-existing vasculature, where $B(\sigma_s - \sigma)$ models the supply of nutrient from the blood vessels if $\sigma_s > \sigma$ and the transport of nutrient away from the domain Ω if $\sigma_s < \sigma$. The right-hand side of (1.1) prescribes the local evolution of tumor mass: if $P\sigma - A$ is positive (which may occur for a large nutrient concentration), then the tumor mass increases, and it increases faster when

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the density of tumor cells is high already (because h depends monotonically on φ). On the other hand, when $P\sigma - A$ is negative (which occurs for concentrations σ close to 0), then we have death of tumor cells, and, owing once more to the monotonicity of h, the death rate is higher when φ is larger. Finally, ψ' stands for the derivative of a double-well potential ψ. A typical example of potentials, meaningful in view of applications, has the expression

$$\psi_{reg}(r) = \frac{1}{4}(r^2 - 1)^2, \quad r \in \mathbb{R}, \tag{1.4}$$

but we may observe that in our analysis we can allow for more general regular potentials having at least cubic and at most exponential growth at infinity. Hence, the polynomial potentials normally associated to the Cahn-Hilliard energy are also admissible here. On the other hand, we are not able to consider here the so-called *singular potentials*, e.g. of logarithmic type, which are also popular in connection with Cahn-Hilliard-based models (see, e.g., [25], cf. also [13] for an application of logarithmic potentials to multiphase tumor growth models). It is worth noting that our choice of a "regular" potential like (1.4) implies that we cannot guarantee φ to take values in the "physical" interval $[-1, 1]$. As a consequence, we will need to treat in the analysis also the values $|\varphi| > 1$ and, correspondingly, to extend the function h in order to cover such values. In addition to that, we need to check that the effects we want to describe still occur when $|\varphi| > 1$. In this respect, dissipativity is a very natural property because it somehow prevents φ to go very far from the significance interval $[-1, 1]$ for large times and, in a sense, it provides a "physical" justification of our compatibility conditions on coefficients.

Let us now give, without any claim of completeness, a short overview of the recent mathematical literature on diffuse-interface tumor growth models. Modeling tumor growth dynamics has recently become a major issue in applied mathematics (see, e.g., [1,8,30]). Numerical simulations of diffuse interface models for tumor growth have been carried out in several papers (see, e.g., [8, Ch. 8]); nonetheless, a rigorous mathematical theory of the related systems of PDEs is still at its beginning and many important problems are still open. We may quote [5–7,10–12,15,16] as mathematical references for Cahn-Hilliard-type models and [3,14,22,23] for models also including a transport effect described by Darcy's law.

A further class of diffuse interface models that also include chemotaxis and transport effects has been subsequently introduced (cf. [17,19]); moreover in some cases the sharp interface limits of such models have been investigated generally by using formal asymptotic methods. Rigorous sharp interface limits have been however obtained in some special cases (see, e.g., the two recent works [24,28]).

On the other hand, the problem of characterizing the long time behavior of solutions to tumor growth models is still in its infancy. Up to our knowledge, the only reference available to date for Cahn-Hilliard-reaction-diffusion models is the work [11], where existence of the global attractor is proved in a phase space characterized by an a priori bound on the physical energy. However, the model considered in [11] has some notable differences with respect to the present one (cf. [20] and see also [21,31]). In particular, in [11] the right-hand sides of (1.1) and (1.3) contain the chemical potential μ and this type of coupling implies that a total energy balance can actually be proved.

In this work, we prove the dissipativity of the system and the existence of a global attractor for the dynamical system generated by solutions of the initial-boundary value problem for (1.1)-(1.3) taking values in the natural phase space, which basically consists of the pairs (φ, σ) having finite physical energy (cf. (2.29) below). The main mathematical difficulty in the proof

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stands in establishing the dissipativity of the dynamical process, i.e., existence of a uniformly absorbing set. Indeed, differently from standard Cahn-Hilliard models, here the spatial mean of φ (i.e., the total mass of the tumor) is not conserved in time, but the tumor may grow or shrink in a way that is essentially prescribed by the right-hand side of (1.1) which can be seen as a source of tumor mass. It is then clear that, if this right-hand side remains, say, positive for large values of φ, then the mass of φ may grow indefinitely and there can be no absorbing set. For this reason, dissipativity is only expected to hold under suitable compatibility conditions between the proliferation function h and the various coefficients A, B, C, P, σ_s. Roughly speaking, these conditions (which are thoroughly discussed below, see for instance Remark 2.9) prescribe that, for large positive (negative) values of φ, the right-hand side of (1.1) must become negative (respectively, positive) in such a way that the tumor concentration is forced to remain bounded in the L^∞-norm uniformly for large values of the time variable. For this reason we need to assume in particular that, at least for $\varphi << -1$, $h(\varphi)$ stays *strictly* negative (and not equal to 0 as was generally assumed in former contributions); otherwise we cannot prove a uniform bound from below on φ. We finally observe that, in view of our choice of no-flux boundary conditions, spatially homogeneous solutions exist. Their behavior is analyzed in Subsection 3.4 by means of simple ODE techniques and in particular this gives further evidence of the fact that in absence of compatibility conditions on the coefficients, dissipativity of the process may fail.

The paper is organized as follows: in the next section, we list our assumptions on the coefficients and data, state the problem in a precise form and present our main results. Then, the last section is devoted to the corresponding proofs and to a discussion on the mentioned compatibility conditions and on the behavior of spatially homogeneous solutions.

2. Main results

We let Ω be a smooth bounded domain of $\mathbb{R}^3$ with boundary Γ. For simplicity, but with no loss of generality, we assume $|\Omega| = 1$. We set $H := L^2(\Omega)$ and $V := H^1(\Omega)$. We will use the same symbols H and V for denoting vector valued functions (we may write, for instance, $\nabla\varphi \in H$). The standard scalar product in H will be noted as $(\cdot, \cdot)$. Since the immersion $V \subset H$ is continuous and dense, identifying H with its topological dual H' through the above scalar product we obtain the *Hilbert triplet* (V, H, V'). The duality pairing between a generic Banach space X and its dual X' will be generally noted as $\langle \cdot, \cdot \rangle_X$. We let R denote a weak form of the Laplace operator with Neumann boundary conditions. Namely, we set

$$R : V \to V', \qquad \langle Rv, z \rangle_V := \int_\Omega \nabla v \cdot \nabla z \, \mathrm{d}x. \tag{2.1}$$

For a generic function (or functional) v defined over Ω, we will note its spatial mean value as

$$v_\Omega := \frac{1}{|\Omega|}(v, 1) = (v, 1), \tag{2.2}$$

the latter equality holding since $|\Omega| = 1$. For, say, $v \in V'$, the above holds replacing scalar products with duality pairings. We also recall the Poincaré-Wirtinger inequality

$$\|v - v_\Omega\| \le c_\Omega \|\nabla v\| \quad \forall\, v \in V. \tag{2.3}$$

Next, for any $\zeta \in V'$ we set

$$V_0' := \{\zeta \in V' : \zeta_\Omega = 0\}, \qquad V_0 := V \cap V_0'. \tag{2.4}$$

The above notation V_0' is suggested just for the sake of convenience; indeed, we mainly see V_0, V_0' as (closed) subspaces of V, V', inheriting their norms, rather than as a pair of spaces in duality.

Clearly, R maps V onto V_0' and its restriction to V_0 is an isomorphism of V_0 onto V_0'. We denote by $\mathcal{N} : V_0' \to V_0$ the inverse of R, so that for any $u \in V$ and $\zeta \in V_0'$ there holds

$$\langle Ru, \mathcal{N}\zeta \rangle_{V_0} = \langle R\mathcal{N}\zeta, u \rangle_V = \langle \zeta, u \rangle_V. \tag{2.5}$$

We can now introduce a set of assumptions on the coefficients and data that will be kept for the rest of the paper, noting that some results will in fact require more specific conditions.

Assumption 2.1. The coefficients are assumed to satisfy

$$P, A, B, C > 0, \qquad \sigma_s \in (0, 1). \tag{2.6}$$

The configuration potential ψ lies in $C^{1,1}_{\mathrm{loc}}(\mathbb{R})$. Moreover its derivative is decomposed as a sum of a monotone part β and a linear perturbation:

$$\psi'(r) = \beta(r) - \lambda r, \quad \lambda \geq 0, \quad r \in \mathbb{R}. \tag{2.7}$$

The monotone part β is normalized so that $\beta(0) = 0$ and further complies with the growth condition

$$\exists\, c_\beta > 0 : \ |\beta(r)| \leq c_\beta(1 + \psi(r)) \ \ \forall\, r \in \mathbb{R}, \tag{2.8}$$

which is more or less equivalent to asking ψ to have at most an exponential growth at infinity. It will also be convenient to indicate by $\widehat{\beta}$ the antiderivative of β such that $\widehat{\beta}(0) = 0$. It then follows that $\widehat{\beta}$ takes only nonnegative values; moreover, from (2.7), it turns out that

$$\psi(r) = \widehat{\beta}(r) - \lambda r^2/2 + K \quad \text{for all } r \in \mathbb{R}, \tag{2.9}$$

where K is an integration constant which, thanks to (2.8), can be chosen in such a way that $\min \psi = 0$. Only for the sake of proving uniqueness, condition (2.8) has to be slightly reinforced: we ask that there exists $c > 0$ such that

$$|\beta(r) - \beta(s)| \leq c|r - s|\big(1 + |\beta(r)| + |\beta(s)|\big) \quad \forall\, r, s \in \mathbb{R}. \tag{2.10}$$

Note that this is still consistent with having at most an exponential growth of β. Next, we assume that h is in $C^1(\mathbb{R})$, increasingly monotone and it satisfies at least $h(-1) = 0$ and $h(r) \equiv 1$ for all $r \geq 1$. Moreover, we ask that there exist $\underline{h} \geq 0$ and $\underline{\varphi} \leq -1$ such that $h(r) \equiv -\underline{h}$ for all $r \leq \underline{\varphi}$. Note that, as a consequence, h is globally Lipschitz continuous. Finally, we assume the initial data to satisfy

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$$\sigma_0 \in L^\infty(\Omega), \qquad 0 \le \sigma_0 \le 1 \text{ a.e. in } \Omega, \tag{2.11}$$

$$\varphi_0 \in V, \qquad \psi(\varphi_0) \in L^1(\Omega). \tag{2.12}$$

We note that the second condition in (2.11) is not strictly necessary for proving existence. On the other hand, it makes sense to assume it in view of the physical interpretation of σ as a nutrient concentration.

Remark 2.2. The simplest situation of a function h satisfying the above assumption is given by the "symmetric" case corresponding to $\underline{h} = 0$ and $\underline{\varphi} = -1$. On the other hand we will see in what follows that dissipativity of trajectories may not hold in such a case. This motivates our choice to consider the possibility of having $\underline{h} > 0$.

Remark 2.3. As mentioned in the introduction, it would also be significant to consider the case when $h(\varphi) = k\varphi + h_0(\varphi)$, where $k > 0$ and h_0 is smooth and uniformly bounded; namely, h is decomposed as a main linear part plus a bounded perturbation. This situation is somehow simpler because, at least as long as we can guarantee that $P\sigma - A < 0$, the linear part of h drives some mass dissipation effect in (1.1).

Remark 2.4. As will be clear in a while when we discuss dissipativity, condition (2.12) corresponds to finiteness of the initial value of the "physical" energy (cf. (2.28) below). In particular, if ψ grows at infinity as a polynomial of (possibly large) degree p, then the latter of (2.12) essentially prescribes that $\varphi_0 \in L^p(\Omega)$.

Remark 2.5. An explicit expression of a potential satisfying our hypotheses and having very slow (linear) growth at infinity is the following:

$$\psi(r) = \begin{cases} \dfrac{1}{2} - r^2 & \text{if } |r| \le \frac{1}{2}, \\ (r-1)^2 & \text{if } r \in \left(\frac{1}{2}, 2\right), \\ (r+1)^2 & \text{if } r \in \left(-2, -\frac{1}{2}\right), \\ 2|r| - 3 & \text{if } |r| \ge 2. \end{cases} \tag{2.13}$$

Then, the conditions in Assumption 2.1 are satisfied with $\lambda = \ell = 2$. On the other hand, we will see below that a potential like that in (2.13) is not suitable for having dissipativity, which seems to require a faster than cubic (but at most exponential) growth rate at infinity. This growth rate is satisfied, for instance, by the standard double-well potential (1.4).

We are now ready to introduce our basic concept of weak solution:

Definition 2.6. We say that a triplet $(\varphi, \mu, \sigma) : (0, \infty) \times \Omega \to \mathbb{R}^3$ is a global weak solution to the tumor-growth model if the following conditions are satisfied:

(a) for every $T > 0$, there hold the regularity properties

$$\varphi \in H^1(0, T; V') \cap C^0([0, T]; V) \cap L^2(0, T; H^2(\Omega)), \tag{2.14}$$

$$\beta(\varphi) \in L^2(0, T; H), \tag{2.15}$$

$$\mu \in L^2(0,T;V), \tag{2.16}$$

$$\sigma \in H^1(0,T;V') \cap C^0([0,T];H) \cap L^2(0,T;V) \cap L^\infty(0,T;L^\infty(\Omega)); \tag{2.17}$$

(b) equations (1.1)-(1.3) are satisfied in the following weak sense:

$$\varphi_t + R\mu = (P\sigma - A)h(\varphi) \quad \text{in } V', \ \text{a.e. in } (0,\infty), \tag{2.18}$$

$$\mu = R\varphi + \psi'(\varphi) \quad \text{in } H, \ \text{a.e. in } (0,\infty), \tag{2.19}$$

$$\sigma_t + R\sigma = -C\sigma h(\varphi) + B(\sigma_s - \sigma), \quad \text{in } V', \ \text{a.e. in } (0,\infty); \tag{2.20}$$

(c) there hold, a.e. in Ω, the initial conditions

$$\varphi|_{t=0} = \varphi_0, \qquad \sigma|_{t=0} = \sigma_0. \tag{2.21}$$

Note that the homogeneous Neumann boundary conditions are now incorporated in the equations by definition of the operator R (cf. (2.1)). Observe also that (2.19) could in fact be interpreted as a pointwise relation (complemented with an explicit boundary condition) thanks to the regularity (2.14).

Our first result is devoted to proving well-posedness in the class of weak solutions:

Theorem 2.7. *Let* Assumption 2.1 *hold. Then the tumor-growth model admits one and only one global in time weak solution in the sense of* Definition 2.6. *Moreover, for any $T > 0$ there exists $\overline{\sigma}_T \ge 1$ such that*

$$0 \le \sigma(t,x) \le \overline{\sigma}_T, \quad \textit{for a.e. } (t,x) \in (0,T) \times \Omega, \tag{2.22}$$

where we can take $\overline{\sigma}_T$ independent of time if $B - C\underline{h} > 0$ and, in particular, $\overline{\sigma}_T = 1$ if $\underline{h} = 0$.

It is worth observing that existence and uniqueness hold without assuming any compatibility conditions on the parameters P, A, B, C, σ_s. On the other hand, as far as one wants to prove dissipativity of the dynamical process associated to weak solutions, it seems necessary to take more restrictive assumptions. Note, for instance, that (2.22) may allow the L^∞-norm of σ to increase in time. Hence, we introduce a new

Assumption 2.8. Let the parameters satisfy

$$\underline{h} > 0, \qquad B - C\underline{h} > 0, \tag{2.23}$$

$$\frac{B\sigma_s}{B - C\underline{h}} < 1, \tag{2.24}$$

$$A - P\frac{B\sigma_s}{B - C\underline{h}} > 0. \tag{2.25}$$

Let also β have a superquadratic behavior at infinity, namely

$$\exists \kappa_\beta > 0, C_\beta \ge 0, p_\beta > 2: \quad \beta(r)\,\mathrm{sign}\, r \ge \kappa_\beta |r|^{p_\beta} - C_\beta \ \ \forall r \in \mathbb{R}. \tag{2.26}$$

Remark 2.9. In order to provide some explanation on the above assumptions, we first observe that (2.23)-(2.24) essentially prescribe $\underline{h}$ to be *strictly positive*, but *small*. Whereas the choice $\underline{h} = 0$ seems natural from the "physical" viewpoint, mathematically, the condition $\underline{h} > 0$ is required for having dissipativity. Indeed, when $\underline{h} = 0$, if $\varphi \leq -1$ at some point (which we cannot exclude under our conditions on ψ), then the right-hand side of (1.1) correspondingly vanishes. In particular, whenever $\varphi(t, x) \leq -1$ for some $t \geq 0$ and a.e. $x \in \Omega$, then integrating (1.1) over Ω we obtain that $(\varphi_\Omega)_t = 0$ at that t, i.e., globally there is no instantaneous tumor mass variation at t. We recall that, when dealing with the "standard" Cahn-Hilliard equation

$$\varphi_t - \Delta\mu = 0, \tag{2.27}$$

which has zero right-hand side, the mass conservation constraint can be "embedded" into the definition of the phase space because it is an *a priori* information holding at any time and for all solutions. Here, however, we cannot do the same because the right-hand side of (1.1) may vanish at some point and have a sign elsewhere. Taking $\underline{h} > 0$ prescribes that, if φ attempts to go below the value -1 (i.e., to assume a somehow "unphysical" value), then, *at least for* $P\sigma - A < 0$, the right-hand side of (1.1) assumes a positive sign forcing φ to somehow "reenter" the physical interval. In this sense, the subsequent conditions (2.24)-(2.25) are finalized to keep the solution in the significance interval, and in particular to ensure that the forcing term (tumor mass source) given by the right-hand side of (1.1) has the appropriate sign at least for large $|\varphi|$. Additional considerations on this fact will be given in Subsection 3.4 below referring to the model case of spatially homogeneous solutions.

Our next result is actually devoted to proving that, if *both* Assumptions 2.1 and 2.8 hold, then weak solutions eventually lie in a *bounded absorbing set* in a proper phase space. To define the latter, we introduce the usual Cahn-Hilliard energy functional

$$\mathcal{E}(\varphi) = \frac{1}{2}\|\nabla\varphi\|^2 + \int_\Omega \psi(\varphi)\,\mathrm{d}x, \tag{2.28}$$

arising as the sum of the interfacial and configurational energy. Then, we can define the "energy space"

$$\mathcal{X} := \left\{(\varphi, \sigma) \in V \times L^\infty(\Omega) : \ \psi(\varphi) \in L^1(\Omega)\right\} \tag{2.29}$$

and correspondingly introduce the "magnitude" of an element $(\varphi, \sigma) \in \mathcal{X}$ as

$$\|(\varphi, \sigma)\|_{\mathcal{X}} := \|\varphi\|_V + \|\sigma\|_{L^\infty(\Omega)} + \|\psi(\varphi)\|_{L^1(\Omega)}. \tag{2.30}$$

Note that, in view of condition (2.22) (which holds with $\overline{\sigma}$ independent of T thanks to (2.23)), we already know that the component σ of any weak solution stays bounded in $L^\infty(\Omega)$ uniformly in time. Observe also that the quantity in (2.30) is not a true norm due to the occurrence of the nonlinear function ψ. On the other hand, convenience justifies the use of the above notation.

We can state our second result about dissipativity of the dynamical process generated by weak solutions:

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Theorem 2.10. *Let* Assumptions 2.1 and 2.8 *hold. Then there exists a positive constant C_0 independent of the initial data and a time T_0 depending only on the $\mathcal{X}$-magnitude of the initial data such that any weak solution satisfies*

$$\|(\varphi(t), \sigma(t))\|_{\mathcal{X}} \leq C_0 \quad \text{for every } t \geq T_0. \tag{2.31}$$

This property states that the dynamical system associated with our problem possesses a bounded absorbing set, i.e., a bounded subset of the phase space in which the images of all bounded sets of initial data enter in finite time; this property is often used as a mathematical definition of dissipation.

The final result of this paper is devoted to the existence of the global attractor. We recall that the global attractor is the unique compact set of the phase space which is invariant by the flow and attracts all bounded sets as time goes to infinity; as it is the smallest closed set satisfying such properties, it appears as a suitable object in view of the study of the asymptotic behavior of the system. Furthermore, once the existence of a bounded absorbing set is known, the existence of the global attractor follows from some compactness argument, e.g., the existence of a relatively compact absorbing set (this is typical of parabolic systems for which the trajectories regularize; one can speak, more generally, of asymptotic compactness of trajectories). We refer the reader to, e.g., [2,27,29] for more details.

Theorem 2.11. *Let* Assumptions 2.1, 2.8 *hold. Then the dynamical system generated by weak trajectories on the phase space $\mathcal{X}$ admits the global attractor $\mathcal{A}$. More precisely, $\mathcal{A}$ is a compact subset of $\mathcal{X}$ which is also bounded in $H^2(\Omega) \times H^1(\Omega)$ and uniformly attracts the trajectories emanating from any bounded set $B \subset \mathcal{X}$.*

Remark 2.12. In view of the fact that system (1.1)-(1.3) has a good parabolic structure, we expect the elements $(\varphi, \sigma) \in \mathcal{A}$ to be in fact smooth functions. More precisely their regularity may only be limited by the smoothness of the nonlinear functions h and ψ. In particular, if h and ψ are C^∞, then the elements of the attractor are expected to be infinitely differentiable as well.

3. Proofs

3.1. Proof of Theorem 2.7: Well-posedness

Approximation and a priori estimates. The main ingredient of the existence proof consists in obtaining a suitable set of a priori estimates. To get them, we proceed here in a formal way by working directly on equations (1.1)-(1.3). The argument, however, may be easily justified within the framework of an appropriate regularization scheme. For the sake of brevity, we prefer not to detail any explicit approximation of the system; indeed, the situation seems to work very similarly with related models (cf. in particular [16]). A possible method will be sketched in Remark 3.2 below.

In what follows, we will denote by $c > 0$ and $\kappa > 0$ some generic positive constants (whose specific value may vary on occurrence) depending only on the given parameters of the system (and neither on the initial data, nor on any hypothetic approximation parameter). The symbol κ will be used in estimates from below. Specific values of the constants will be noted as c_i, κ_i, $i \geq 1$. Constants depending on additional parameters will be noted using subscripts (e.g., c_T if the constant depends on the final time T).

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To start with, we derive the basic boundedness properties for the nutrient. To this aim, we test (1.3) by $-\sigma_-$ (with $\sigma_- \geq 0$ denoting the *negative part* of σ) to deduce

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\sigma_-\|^2 + \|\nabla\sigma_-\|^2 \leq c\|\sigma_-\|^2. \tag{3.1}$$

We used here the uniform boundedness of h and the fact that $B(\sigma_s - \sigma)$ is positive for $\sigma \leq 0$ because $\sigma_s > 0$. Then, by (2.11) and the Gronwall lemma, we obtain that $\sigma(t,x) \geq 0$ for (almost) every $t \geq 0$ and $x \in \Omega$.

To get an upper bound, we test (1.3) by $(\sigma - \overline{\sigma})_+$ with $\overline{\sigma} \geq 1$ to be chosen below. Using the assumptions on h and performing standard manipulations, we deduce

$$\begin{aligned}\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|(\sigma-\overline{\sigma})_+\|^2 + \|\nabla(\sigma-\overline{\sigma})_+\|^2 &\leq -\int_\Omega \big((B - C\underline{h})\sigma - B\sigma_s\big)(\sigma-\overline{\sigma})_+\,\mathrm{d}x\\ &\leq \int_\Omega |B - C\underline{h}|(\sigma-\overline{\sigma})_+^2\,\mathrm{d}x - \int_\Omega \big((B - C\underline{h})\overline{\sigma} - B\sigma_s\big)(\sigma-\overline{\sigma})_+\,\mathrm{d}x\,. \end{aligned}\tag{3.2}$$

We now have two cases. If $B - C\underline{h} > 0$, then we can always choose $\overline{\sigma} \geq 1$ large enough so that $(B - C\underline{h})\overline{\sigma} - B\sigma_s \geq 0$. As a consequence, the latter term on the right-hand side is nonpositive and we can apply Gronwall's lemma to deduce that $\sigma(t,x) \leq \overline{\sigma}$ for a.e. $(t,x) \in (0,\infty)\times\Omega$. Note that, if $\underline{h} = 0$ the above certainly holds with $\overline{\sigma} = 1$ in view of the fact that $\sigma_s < 1$.

On the other hand, if $B - C\underline{h} \leq 0$, then the above procedure fails because we cannot control the last term in (3.2). Nevertheless, an L^∞-estimate on σ *on finite times intervals* can be obtained also in that case. Indeed, one may test (1.3) by σ^{p-1} (recall that we already know that in any case $\sigma \geq 0$) for a generic $p > 2$. Then the boundedness of h and easy computations give

$$\frac{1}{p}\frac{\mathrm{d}}{\mathrm{d}t}\|\sigma\|^p_{L^p(\Omega)} \leq c\big(1 + \|\sigma\|^p_{L^p(\Omega)}\big), \tag{3.3}$$

with $c > 0$ independent of p. Hence, setting $y_p := \|\sigma\|^p_{L^p(\Omega)}$, we obtain the differential inequality

$$(1 + y_p)' \leq cp(1 + y_p), \tag{3.4}$$

whence

$$\|\sigma(t)\|^p_{L^p(\Omega)} \leq 1 + y_p(t) \leq (1 + y_p(0))e^{cpt} \leq 2e^{cpt}. \tag{3.5}$$

Thus, taking the $1/p$-power and then letting $p \nearrow \infty$, we get the desired conclusion. Summarizing, in any case we have obtained

$$\|\sigma\|_{L^\infty(0,T;L^\infty(\Omega))} \leq c_T\,. \tag{3.6}$$

This relation may be intended as an a priori estimate independent of any hypothetic regularization parameter. Note that the constant on the right-hand side is independent of T if $B - C\underline{h} > 0$, and in particular it can be taken as $c_T = 1$ if $\underline{h} = 0$.

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As a next step, we derive the *Energy estimate* for the Cahn-Hilliard system. This is the basic a priori information that any hypothetic weak solution is expected to satisfy. To obtain it, we test (1.1) by μ, (1.2) by φ_t and sum up to obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\nabla\varphi\|^2 + \int_\Omega \psi(\varphi)\,\mathrm{d}x\Big) + \|\nabla\mu\|^2 = \int_\Omega (P\sigma - A)h(\varphi)\mu\,\mathrm{d}x. \tag{3.7}$$

Then let us replace the expression for μ as given by (1.2):

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\nabla\varphi\|^2 + \int_\Omega \psi(\varphi)\,\mathrm{d}x\Big) + \|\nabla\mu\|^2 &= \int_\Omega (P\sigma - A)\big(h'(\varphi)|\nabla\varphi|^2 + h(\varphi)\beta(\varphi)\big)\,\mathrm{d}x \\ &+ \int_\Omega \lambda(A - P\sigma)h(\varphi)\varphi\,\mathrm{d}x + P\int_\Omega h(\varphi)\nabla\sigma\cdot\nabla\varphi\,\mathrm{d}x,\end{aligned} \tag{3.8}$$

where $\psi'(\varphi)$ has been decomposed according to (2.7). Let us now control the terms on the right-hand side. First, as a consequence of Assumption 2.1, $|h(r)| + |h'(r)| \le c$ for every $r \in \mathbb{R}$. Hence, using also (3.6),

$$\int_\Omega (P\sigma - A)h'(\varphi)|\nabla\varphi|^2\,\mathrm{d}x \le c\big(1 + \|\sigma\|_{L^\infty(\Omega)}\big)\|\nabla\varphi\|^2 \le c_T\|\nabla\varphi\|^2. \tag{3.9}$$

Next, thanks to (2.8),

$$\int_\Omega (P\sigma - A)h(\varphi)\beta(\varphi)\,\mathrm{d}x \le c\big(1 + \|\sigma\|_{L^\infty(\Omega)}\big)\Big(1 + \int_\Omega \psi(\varphi)\,\mathrm{d}x\Big) \le c_T + c_T\int_\Omega \psi(\varphi)\,\mathrm{d}x. \tag{3.10}$$

Finally, using also Young's inequality it is not difficult to deduce

$$\begin{aligned}&\int_\Omega \lambda(A - P\sigma)h(\varphi)\varphi\,\mathrm{d}x + P\int_\Omega h(\varphi)\nabla\sigma\cdot\nabla\varphi\,\mathrm{d}x \\ &\qquad\le \frac{1}{2}\|\nabla\sigma\|^2 + c_T\big(1 + \|\varphi\|_{L^1(\Omega)} + \|\nabla\varphi\|^2\big).\end{aligned} \tag{3.11}$$

Note that the above constants c_T depend on T only through the L^∞-norm of σ (cf. (3.6)). In order to control the first term on the right-hand side of (3.11), we test (1.3) by σ. Then, straightforward calculations yield

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\sigma\|^2 + \|\nabla\sigma\|^2 \le c\big(1 + \|\sigma\|^2\big). \tag{3.12}$$

Summing (3.8) to (3.12) and using (3.9)-(3.11), we arrive at

$$\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\nabla\varphi\|^2+\int_\Omega \psi(\varphi)\,\mathrm{d}x+\frac{1}{2}\|\sigma\|^2\Big)+\|\nabla\mu\|^2+\frac{1}{2}\|\nabla\sigma\|^2$$
$$\le c_T\bigg(1+\|\varphi\|_{L^1(\Omega)}+\|\nabla\varphi\|^2+\|\sigma\|^2+\int_\Omega \psi(\varphi)\,\mathrm{d}x\bigg). \tag{3.13}$$

Now, testing (1.1) by φ, using the uniform boundedness of σ and of the function h, and performing standard manipulations, we deduce

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\varphi\|^2\le\frac{1}{2}\|\nabla\mu\|^2+\frac{1}{2}\|\nabla\varphi\|^2+c\big(1+\|\varphi\|^2\big). \tag{3.14}$$

Summing the above to (3.13) and recalling (2.9), we infer

$$\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\varphi\|_V^2+\int_\Omega \psi(\varphi)\,\mathrm{d}x+\frac{1}{2}\|\sigma\|^2\Big)+\frac{1}{2}\|\nabla\mu\|^2+\frac{1}{2}\|\nabla\sigma\|^2$$
$$\le c_T\bigg(1+\|\varphi\|_V^2+\|\sigma\|^2+\int_\Omega \psi(\varphi)\,\mathrm{d}x\bigg). \tag{3.15}$$

Hence, by Gronwall's lemma, (3.15) provides the following set of a priori estimates:

$$\|\varphi\|_{L^\infty(0,T;V)}\le c_T, \tag{3.16}$$
$$\|\nabla\mu\|_{L^2(0,T;H)}\le c_T, \tag{3.17}$$
$$\|\psi(\varphi)\|_{L^\infty(0,T;L^1(\Omega))}\le c_T, \tag{3.18}$$
$$\|\sigma\|_{L^2(0,T;V)\cap L^\infty(0,T;H)}\le c_T, \tag{3.19}$$

with c_T as in (3.6).

Next, integrating (1.2) over Ω and using once more (2.8), we deduce

$$|\mu_\Omega|=\bigg|\int_\Omega \mu\,\mathrm{d}x\bigg|=\bigg|\int_\Omega (\beta(\varphi)-\lambda\varphi)\,\mathrm{d}x\bigg|\le c_T\bigg(1+\int_\Omega \psi(\varphi)\,\mathrm{d}x\bigg), \tag{3.20}$$

where we have used (3.16) to control the λ-term. Recalling (3.18) we then infer

$$\|\mu_\Omega\|_{L^\infty(0,T)}\le c_T, \tag{3.21}$$

which, combined with (3.17), gives in turn

$$\|\mu\|_{L^2(0,T;V)}\le c_T. \tag{3.22}$$

Now, testing (1.2) by $\beta(\varphi)$ and using (3.16), (3.22) and the monotonicity of β, it is a standard matter to deduce

$$\|\beta(\varphi)\|_{L^2(0,T;H)}\le c_T. \tag{3.23}$$

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Then, a comparison of terms in (1.2) and elliptic regularity results give

$$\|\varphi\|_{L^2(0,T;H^2(\Omega))} \leq c_T. \tag{3.24}$$

Finally, we derive some estimates on the time derivatives of φ and σ. Multiplying (1.1) by a generic nonzero test function $v \in V$ and using the previous estimates, we actually get

$$\langle \varphi_t, v\rangle_V = (\nabla\mu, \nabla v) + \int_\Omega (P\sigma - A)h(\varphi)v\,\mathrm{d}x, \tag{3.25}$$

whence estimates (3.16), (3.22) and standard manipulations yield

$$\|\varphi_t\|_{L^2(0,T;V')} \leq c_T. \tag{3.26}$$

Operating in an analogue way with equation (1.3) we similarly obtain

$$\|\sigma_t\|_{L^2(0,T;V')} \leq c_T. \tag{3.27}$$

Remark 3.1. Using a more refined regularity argument in (1.2) and 3D Sobolev embeddings (see, e.g., [26]) one could improve (3.23)-(3.24) up to

$$\|\beta(\varphi)\|_{L^2(0,T;L^6(\Omega))} + \|\varphi\|_{L^2(0,T;W^{2,6}(\Omega))} \leq c_T. \tag{3.28}$$

Weak sequential stability. We assume here to have a sequence of weak solutions $(\varphi_n, \mu_n, \sigma_n)$ satisfying the a priori estimates obtained above uniformly with respect to the approximation parameter n. In other words, the constants c or c_T on the right-hand sides of the bounds are assumed independent of n. We then prove that, up to the extraction of subsequences, $(\varphi_n, \mu_n, \sigma_n)$ tends in a suitable way to a triplet (φ, μ, σ) solving the tumor growth model in the sense of Definition 2.6 on the assigned but otherwise arbitrary time interval $(0, T)$. This argument, generally noted as a "weak stability property", may be seen as an abbreviated procedure for passing to the limit in some approximation, for instance a Faedo-Galerkin scheme, that may also involve the regularization of some terms (see Remark 3.2 below for more details).

Actually, using the bounds (3.6), (3.16)-(3.19), (3.22)-(3.24), (3.26)-(3.27) and standard weak compactness argument, we are able to take a (nonrelabelled) subsequence of n such that $(\varphi_n, \mu_n, \sigma_n) \to (\varphi, \mu, \sigma)$ in the sense of weak or weak star convergence in proper Sobolev spaces. Moreover, using (3.26), (3.27), and the Aubin-Lions lemma, we obtain that (φ_n, σ_n) tends to (φ, σ) strongly in some L^p-space, hence pointwise. This allows us to pass to the limit in the nonlinear terms thanks to continuity of h and β. In particular, we may observe that, combining (3.23) with the pointwise convergence of φ_n and using a generalized version of Lebesgue's dominated convergence theorem, there follows

$$\beta(\varphi_n) \to \beta(\varphi) \quad \text{weakly in } L^2(0, T; H). \tag{3.29}$$

Actually, even if in the approximation β is replaced by some regularization β_n the above property still works (with $\beta_n(\varphi_n)$ in place of $\beta(\varphi_n)$ on the left-hand side) up to adaptations, provided that one assumes that β_n tends to β uniformly on compact subsets of $\mathbb{R}$.

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Uniqueness. We give here a proof of uniqueness. A different (and somehow simpler) proof is given in [18] (cf. also [15]) in the case where ψ has polynomial (of degree four) growth. On the other hand, the argument given here works also for exponential ψ (cf. (2.10)). Assume to have two solutions $(\varphi_1, \mu_1, \sigma_1)$ and $(\varphi_2, \mu_2, \sigma_2)$ corresponding to two sets of initial data $(\varphi_{1,0}, \sigma_{1,0})$ and $(\varphi_{2,0}, \sigma_{2,0})$. Then the differences $(\varphi, \mu, \sigma) := (\varphi_1 - \varphi_2, \mu_1 - \mu_2, \sigma_1 - \sigma_2)$ satisfy the following equations:

$$\varphi_t + R\mu = P\sigma h(\varphi_1) + (P\sigma_2 - A)(h(\varphi_1) - h(\varphi_2)) \quad \text{in } V', \quad \text{a.e. in } (0,\infty), \tag{3.30}$$

$$\mu = R\varphi + \psi'(\varphi_1) - \psi'(\varphi_2) \quad \text{in } H, \quad \text{a.e. in } (0,\infty), \tag{3.31}$$

$$\sigma_t + R\sigma = -C\sigma h(\varphi_1) - C\sigma_2(h(\varphi_1) - h(\varphi_2)) - B\sigma, \quad \text{in } V', \quad \text{a.e. in } (0,\infty); \tag{3.32}$$

with the initial conditions

$$\varphi|_{t=0} = \varphi_0, \qquad \sigma|_{t=0} = \sigma_0, \tag{3.33}$$

where $\varphi_0 := \varphi_{1,0} - \varphi_{2,0}$, $\sigma_0 := \sigma_{1,0} - \sigma_{2,0}$. In particular, integrating (3.30) over Ω, we obtain

$$(\varphi_\Omega)_t = \int_\Omega P\sigma h(\varphi_1)\,\mathrm{d}x + \int_\Omega (P\sigma_2 - A)(h(\varphi_1) - h(\varphi_2))\,\mathrm{d}x. \tag{3.34}$$

Testing the above by φ_Ω and using the boundedness of h and of σ_2 with the Lipschitz continuity of h, we obtain

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}|\varphi_\Omega|^2 \le c\big(|\varphi_\Omega|^2 + \|\sigma\|^2 + \|\varphi\|^2\big). \tag{3.35}$$

Next, let us take the difference of (3.30) and (3.34) and test it by $\mathcal{N}(\varphi - \varphi_\Omega)$. Simple calculations yield

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\varphi - \varphi_\Omega\|_{V'}^2 + \int_\Omega \mu(\varphi - \varphi_\Omega)\,\mathrm{d}x \le c\big(\|\varphi - \varphi_\Omega\|_{V'}^2 + \|\sigma\|^2 + \|\varphi\|^2\big). \tag{3.36}$$

Now, testing (3.31) by $\varphi - \varphi_\Omega$, we infer

$$\begin{aligned} \|\nabla\varphi\|^2 &= \int_\Omega \mu(\varphi - \varphi_\Omega)\,\mathrm{d}x - \int_\Omega (\psi'(\varphi_1) - \psi'(\varphi_2))(\varphi - \varphi_\Omega)\,\mathrm{d}x \\ &\le \int_\Omega \mu(\varphi - \varphi_\Omega)\,\mathrm{d}x + \varphi_\Omega \int_\Omega (\beta(\varphi_1) - \beta(\varphi_2))\,\mathrm{d}x + \lambda\|\varphi - \varphi_\Omega\|^2, \end{aligned} \tag{3.37}$$

where we also used the decomposition (2.7) and the monotonicity of β.

Next, testing (3.32) by σ, using the Lipschitz continuity of h and performing standard manipulations, we deduce

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\sigma\|^2 + \|\nabla\sigma\|^2 \le c\big(\|\sigma\|^2 + \|\varphi\|^2\big). \tag{3.38}$$

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Combining (3.35)-(3.38), we obtain

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\big(|\varphi_\Omega|^2 + \|\varphi-\varphi_\Omega\|^2_{V'} + \|\sigma\|^2\big) + \|\nabla\varphi\|^2 + \|\nabla\sigma\|^2$$
$$\le \varphi_\Omega \int_\Omega (\beta(\varphi_1)-\beta(\varphi_2))\,\mathrm{d}x + c\big(\|\varphi-\varphi_\Omega\|^2 + \|\sigma\|^2 + |\varphi_\Omega|^2\big). \tag{3.39}$$

In order to control the terms on the right-hand side we first observe that, thanks to the Poincaré-Wirtinger inequality and to Ehrling's lemma,

$$c\|\varphi-\varphi_\Omega\|^2 \le \frac{1}{4}\|\nabla\varphi\|^2 + c\|\varphi-\varphi_\Omega\|^2_{V'}. \tag{3.40}$$

To control the remaining term, we need to use assumption (2.10) and then we derive

$$\varphi_\Omega \int_\Omega (\beta(\varphi_1)-\beta(\varphi_2))\,\mathrm{d}x \le c|\varphi_\Omega| \int_\Omega |\varphi|\big(1+|\beta(\varphi_1)|+|\beta(\varphi_2)|\big)\,\mathrm{d}x$$
$$\le c|\varphi_\Omega|\|\varphi\|\big(1+\|\beta(\varphi_1)\|+\|\beta(\varphi_2)\|\big)$$
$$\le c|\varphi_\Omega|^2\big(1+\|\beta(\varphi_1)\|^2+\|\beta(\varphi_2)\|^2\big) + c\|\varphi-\varphi_\Omega\|^2 + c|\varphi_\Omega|^2$$
$$\le c|\varphi_\Omega|^2\big(1+\|\beta(\varphi_1)\|^2+\|\beta(\varphi_2)\|^2\big) + c\|\varphi-\varphi_\Omega\|^2_{V'} + \frac{1}{4}\|\nabla\varphi\|^2. \tag{3.41}$$

Thanks to (3.40) and (3.41), (3.39) gives

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\big(|\varphi_\Omega|^2 + \|\varphi-\varphi_\Omega\|^2_{V'} + \|\sigma\|^2\big) + \frac{1}{2}\|\nabla\varphi\|^2 + \|\nabla\sigma\|^2$$
$$\le c|\varphi_\Omega|^2\big(1+\|\beta(\varphi_1)\|^2+\|\beta(\varphi_2)\|^2\big) + c\big(\|\varphi-\varphi_\Omega\|^2_{V'} + \|\sigma\|^2\big). \tag{3.42}$$

Then, using the regularity property (2.15) both for φ_1 and for φ_2 and applying Gronwall's lemma, we get uniqueness whenever $(\varphi_{0,1},\sigma_{0,1}) = (\varphi_{0,2},\sigma_{0,2})$. In the general case, we obtain the continuous dependence estimate

$$|(\varphi_1)_\Omega(t) - (\varphi_2)_\Omega(t)|^2 + \big\|\big(\varphi_1(t)-(\varphi_1)_\Omega(t)\big) - \big(\varphi_2(t)-(\varphi_2)_\Omega(t)\big)\big\|^2_{V'} + \|\sigma_1(t)-\sigma_2(t)\|^2$$
$$\le C_T\Big(|(\varphi_{0,1})_\Omega - (\varphi_{0,2})_\Omega|^2 + \big\|\big(\varphi_{0,1}-(\varphi_{0,1})_\Omega\big) - \big(\varphi_{0,2}-(\varphi_{0,2})_\Omega\big)\big\|^2_{V'} + \|\sigma_{0,1}-\sigma_{0,2}\|^2\Big), \tag{3.43}$$

for every $T > 0$ and every $t \in (0,T]$, the constant $C_T > 0$ depending on the $\mathcal{X}$-magnitude of the initial data and on T.

Remark 3.2. As mentioned above, the procedure given to prove existence should in fact be performed on a suitable approximation of the system. We now sketch one of the many possible ways to construct a discretization scheme. Actually, in view of the facts that the system (1.1)-(1.3) has a good semilinear parabolic structure and that the unknowns φ, μ, σ satisfy identical no-flux boundary conditions, it appears very natural to obtain existence of a weak solution by using the

Faedo-Galerkin method. Note that the variable μ can be easily eliminated by replacing (1.2) into (1.1). Then, one can use as a "special" basis for the discretization the set of eigenfunctions of the Neumann Laplacian, properly normalized, e.g., with respect to the H-norm. In this way, (1.1)-(1.3) is converted into a system of two ODE's for the discretized variables φ and σ. Moreover, these ODE's are *in normal form* and only involve locally Lipschitz nonlinearities (indeed, both the nonlinear functions h and ψ' are assumed to have such a regularity, cf. Assumption 2.1). As a consequence, Cauchy's theorem provides existence of one and only one *local in time* solution to the Faedo-Galerkin discretized system. This solution is sufficiently smooth both with respect to space (because as a function of time it takes values in finite-dimensional subspaces consisting of regular functions) and to time variables (indeed it is at least C^1 as a consequence of Cauchy's theorem). For this reason, the a priori estimates reported above can be performed rigorously when one works on the discretized solution, with the only exception being given by the maximum principle used in order to prove uniform boundedness of σ. Indeed, that argument cannot be reproduced at the discretized level because it uses powers, or truncations, of σ as test functions, which is not allowed once the equations are projected onto finite-dimensional subspaces. To overcome such a difficulty one may replace the function σ in (1.1) with a suitable truncation of it. In this way, the boundedness of σ required for the energy estimate (cf. in particular (3.10)-(3.11)) is "forced" and the argument still works. The resulting information is sufficient to take the limit in the Faedo-Galerkin scheme. After this is achieved, one can operate the maximum principle argument for σ at a second stage (i.e., on the limit version of (1.3)). The resulting L^∞-bound on σ automatically eliminates the truncation operator from (1.1). We finally observe that all the estimates proved above are uniform over the assigned reference interval $(0, T)$. Hence, standard extension arguments imply that, after taking the limit with respect to the approximation parameter, we obtain in fact a *global in time* solution.

3.2. *Proof of Theorem 2.10: Dissipativity*

As a first step, we consider some auxiliary ODE's. Namely, we define S_+ and S_- as the solutions to the following Cauchy problems:

$$S_+' = -(B - C\underline{h})S_+ + B\sigma_s, \tag{3.44}$$

$$S_+(0) = 1, \tag{3.45}$$

and

$$S_-' = (-B - C)S_- + B\sigma_s, \tag{3.46}$$

$$S_-(0) = 0. \tag{3.47}$$

Then we can readily compute

$$S_+(t) = e^{-(B - C\underline{h})t} + \frac{B\sigma_s}{B - C\underline{h}}\big(1 - e^{-(B - C\underline{h})t}\big), \tag{3.48}$$

$$S_-(t) = \frac{B\sigma_s}{B + C}\big(1 - e^{-(B+C)t}\big). \tag{3.49}$$

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Lemma 3.3. *Let the assumptions of* Theorem 2.10 *hold. Let* (φ, σ) *be any weak solution to* (1.1)-(1.3). *Then we have*

$$S_-(t) \leq \sigma(t, x) \leq S_+(t) \quad \textit{for every } t \geq 0 \textit{ and } x \in \Omega. \tag{3.50}$$

Proof. We first recall that $\sigma(t, x) \geq 0$ for a.e. $t \geq 0$, $x \in \Omega$ thanks to the minimum principle argument in the proof of Theorem 2.7 (cf. (3.1)). Then, we can prove that S_- is a subsolution, namely the first inequality in (3.50) holds. Taking the difference between (1.3) and (3.46) we actually obtain

$$(\sigma - S_-)' - \Delta(\sigma - S_-) = -B(\sigma - S_-) - C(\sigma h(\varphi) - S_-), \tag{3.51}$$

whence testing by $-(\sigma - S_-)_-$ and using the fact that $h \leq 1$ we readily get the assert. Indeed, since $\sigma \geq 0$, we notice that

$$C(\sigma h(\varphi) - S_-)(\sigma - S_-)_- \leq C(\sigma - S_-)(\sigma - S_-)_- \leq 0. \tag{3.52}$$

Analogously, the difference between (1.3) and (3.44) gives

$$(\sigma - S_+)' - \Delta(\sigma - S_+) = -B(\sigma - S_+) - C(\sigma h(\varphi) + S_+\underline{h}). \tag{3.53}$$

Testing by $(\sigma - S_+)_+$, noting that

$$-C(\sigma h(\varphi) + S_+\underline{h})(\sigma - S_+)_+ \leq -C(-\sigma\underline{h} + S_+\underline{h})(\sigma - S_+)_+ \leq C\underline{h}(\sigma - S_+)_+^2, \tag{3.54}$$

and recalling (2.23), we easily obtain the second assertion. □

Recalling (2.24) and (2.25), we can take $\epsilon > 0$ to be a small number satisfying

$$2\epsilon < A - P\frac{B\sigma_s}{B - C\underline{h}} \quad \text{and} \quad \frac{B\sigma_s}{B - C\underline{h}} + \frac{\epsilon}{P} < 1. \tag{3.55}$$

We can then prove the following.

Lemma 3.4. *Let the assumptions of* Theorem 2.10 *hold. Let* (φ, σ) *be any weak solution in the sense of* Definition 2.6. *Then there exist* $T_1 > 0$ *and* $C_1 > 0$ *independent of the initial data such that*

$$\frac{B\sigma_s}{C + B} - \frac{\epsilon}{P} \leq \sigma(t, x) \leq \frac{B\sigma_s}{B - C\underline{h}} + \frac{\epsilon}{P} \quad \textit{for all } t \geq T_1, \ \textit{a.e. } x \in \Omega, \tag{3.56}$$

$$\|(\varphi(T_1), \sigma(T_1))\|_{\mathcal{X}} \leq C_1\big(1 + \|(\varphi_0, \sigma_0)\|_{\mathcal{X}}\big). \tag{3.57}$$

Proof. Thanks to (3.50) the component σ evolves between the subsolution S_- and the supersolution S_+. Then, a simple computation based on (3.48)-(3.49) shows that (3.56) holds provided that we choose

$$T_1 := \max\left\{\frac{1}{B + C}\log\left(\frac{B\sigma_s P}{\epsilon(B + C)}\right), \frac{1}{B - C\underline{h}}\log\left(\frac{P(B - C\underline{h} - B\sigma_s)}{\epsilon(B - C\underline{h})}\right)\right\}. \tag{3.58}$$

Notice in particular that the argument of the second logarithm is strictly positive thanks to assumption (2.24). Next, to prove (3.57), it suffices to repeat the a priori estimates of Subsec. 3.1. We may incidentally notice that the constant c_T in (3.13) can now be taken independent of T thanks to Lemma 3.3. Anyway, integrating (3.13) over the time interval $(0, T_1)$ and applying once more the Gronwall lemma, we readily obtain the assertion. □

Proof of Theorem 2.10. We start again from relation (3.8), which we will now consider for $t \geq T_1$. Hence, in particular we can take advantage of the second inequality in (3.56). As a consequence, we can observe that, thanks to (3.55),

$$\sigma \leq \frac{B\sigma_s}{B - C\underline{h}} + \frac{\epsilon}{P} \Rightarrow P\sigma - A \leq P\frac{B\sigma_s}{B - C\underline{h}} + \epsilon - A \leq -\epsilon. \tag{3.59}$$

Consequently, for $t \geq T_1$ (3.8) implies the following inequality:

$$\begin{aligned} &\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\nabla\varphi\|^2 + \int_\Omega \psi(\varphi)\,\mathrm{d}x\Big) + \|\nabla\mu\|^2 + \epsilon\int_\Omega h'(\varphi)|\nabla\varphi|^2\,\mathrm{d}x \\ &\quad + \int_\Omega (A - P\sigma)h(\varphi)\beta(\varphi)\,\mathrm{d}x \leq \int_\Omega \lambda(A - P\sigma)h(\varphi)\varphi\,\mathrm{d}x + P\int_\Omega h(\varphi)\nabla\sigma\cdot\nabla\varphi\,\mathrm{d}x. \end{aligned} \tag{3.60}$$

Now, the terms on the right-hand side can be controlled as in (3.11). On the other hand, using Assumptions 2.1 and 2.8 (and in particular the facts that $\underline{h}$ is strictly positive and that $\beta(\varphi)$ has the same sign as φ), it is not difficult to check that

$$h(\varphi)\beta(\varphi) \geq \kappa|\beta(\varphi)| - c, \tag{3.61}$$

whence the latter term on the left-hand side of (3.60) gives

$$\int_\Omega (A - P\sigma)h(\varphi)\beta(\varphi)\,\mathrm{d}x \geq \kappa\epsilon\|\beta(\varphi)\|_{L^1(\Omega)} - c, \tag{3.62}$$

so that (3.60) implies the differential inequality

$$\begin{aligned} &\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\nabla\varphi\|^2 + \int_\Omega \psi(\varphi)\,\mathrm{d}x\Big) + \|\nabla\mu\|^2 + \kappa\epsilon\|\beta(\varphi)\|_{L^1(\Omega)} \\ &\quad \leq \frac{1}{2}\|\nabla\sigma\|^2 + c\big(1 + \|\varphi\|_{L^1(\Omega)} + \|\nabla\varphi\|^2\big). \end{aligned} \tag{3.63}$$

Adding (3.12) to the above relation, we arrive at

$$\begin{aligned} &\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\nabla\varphi\|^2 + \int_\Omega \psi(\varphi)\,\mathrm{d}x + \frac{1}{2}\|\sigma\|^2\Big) + \frac{1}{2}\|\nabla\sigma\|^2 + \|\nabla\mu\|^2 \\ &\quad + \kappa\epsilon\|\beta(\varphi)\|_{L^1(\Omega)} \leq c\big(1 + \|\varphi\|_{L^1(\Omega)} + \|\nabla\varphi\|^2\big), \end{aligned} \tag{3.64}$$

where the norm of σ on the right-hand side of (3.12) has disappeared because we now know that $0 \le \sigma \le 1$ almost everywhere.

Next, let us multiply (1.2) by $-\Delta\varphi$. We deduce

$$\|\Delta\varphi\|^2+\int_\Omega \beta'(\varphi)|\nabla\varphi|^2\,\mathrm{d}x \le (\nabla\varphi,\nabla\mu)-\lambda(\varphi,\Delta\varphi) \le (\nabla\varphi,\nabla\mu)+\frac{1}{2}\|\Delta\varphi\|^2+\frac{\lambda^2}{2}\|\varphi\|^2. \quad (3.65)$$

Correspondingly, testing (1.1) by φ we obtain

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\varphi\|^2+(\nabla\varphi,\nabla\mu)+\int_\Omega (A-P\sigma)h(\varphi)\varphi\,\mathrm{d}x=0, \quad (3.66)$$

whence in particular

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\varphi\|^2+(\nabla\varphi,\nabla\mu)\le c\big(1+\|\varphi\|^2\big). \quad (3.67)$$

Adding (3.65) and (3.67) to (3.64) and adding also the inequality $\frac{1}{2}\|\sigma\|^2 \le c$, neglecting some positive term on the left-hand side, we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\varphi\|_V^2+\int_\Omega \psi(\varphi)\,\mathrm{d}x+\frac{1}{2}\|\sigma\|^2\Big)+\frac{1}{2}\|\Delta\varphi\|^2+\|\nabla\mu\|^2$$
$$+\kappa\epsilon\|\beta(\varphi)\|_{L^1(\Omega)}+\frac{1}{2}\|\sigma\|_V^2\le c\big(1+\|\varphi\|^2+\|\nabla\varphi\|^2\big). \quad (3.68)$$

Now, to control the right-hand side, we first observe that

$$c\|\nabla\varphi\|^2=c(-\Delta\varphi,\varphi)\le\frac{1}{4}\|\Delta\varphi\|^2+c\|\varphi\|^2. \quad (3.69)$$

Then, by virtue of assumption (2.26), for κ,ϵ as in (3.68), we have

$$c\|\varphi\|^2\le\frac{\kappa\epsilon}{2}\|\beta(\varphi)\|_{L^1(\Omega)}+c_{\kappa,\epsilon}. \quad (3.70)$$

Taking (3.69) and (3.70) into account, (3.68) gives

$$\frac{\mathrm{d}}{\mathrm{d}t}\Big(\frac{1}{2}\|\varphi\|_V^2+\int_\Omega \psi(\varphi)\,\mathrm{d}x+\frac{1}{2}\|\sigma\|^2\Big)+\frac{1}{4}\|\Delta\varphi\|^2+\frac{\kappa\epsilon}{2}\|\beta(\varphi)\|_{L^1(\Omega)}$$
$$+\|\nabla\mu\|^2+\frac{1}{2}\|\sigma\|_V^2\le c. \quad (3.71)$$

Now, using (2.26) again together with the continuous embedding $H^2(\Omega)\subset L^\infty(\Omega)$, we notice that

$$\frac{1}{4}\|\Delta\varphi\|^2+\frac{\kappa\epsilon}{2}\|\beta(\varphi)\|_{L^1(\Omega)}\ge\kappa\|\varphi\|_{H^2(\Omega)}-c\ge\kappa_1\|\varphi\|_{L^\infty(\Omega)}-c. \quad (3.72)$$

Let us then define

$$Z(r) := \widehat{\beta}(r) + \widehat{\beta}(-r), \quad \forall r \geq 0, \tag{3.73}$$

where $\widehat{\beta}$ is the antiderivative of β satisfying $\widehat{\beta}(0) = 0$ (hence in particular $\widehat{\beta}$ is convex and nonnegative due to Assumption 2.1). Noting that Z is monotone over $[0, \infty)$ with $Z(0) = 0$, we have

$$\int_\Omega \widehat{\beta}(\varphi)\,\mathrm{d}x \leq \int_\Omega Z(|\varphi|)\,\mathrm{d}x \leq \int_\Omega Z\big(\|\varphi\|_{L^\infty(\Omega)}\big)\,\mathrm{d}x = Z\big(\|\varphi\|_{L^\infty(\Omega)}\big). \tag{3.74}$$

As a consequence,

$$\|\varphi\|_{L^\infty(\Omega)} \geq Z^{-1}\bigg(\int_\Omega \widehat{\beta}(\varphi)\,\mathrm{d}x\bigg). \tag{3.75}$$

Hence, recalling also (3.72), relabelling some constants, and rearranging some terms, (3.71) implies

$$\begin{aligned} &\frac{\mathrm{d}}{\mathrm{d}t}\bigg[\frac{1}{2}\|\varphi\|_V^2 + \frac{1}{2}\|\sigma\|^2 + \int_\Omega \psi(\varphi)\,\mathrm{d}x\bigg] + \frac{\kappa_3}{2}\big(\|\varphi\|_V^2 + \|\sigma\|^2\big) \\ &\quad + \kappa_1 Z^{-1}\bigg(\int_\Omega \widehat{\beta}(\varphi)\,\mathrm{d}x\bigg) + \kappa_2\big(\|\Delta\varphi\|^2 + \|\nabla\mu\|^2 + \|\nabla\sigma\|^2\big) \leq c, \end{aligned} \tag{3.76}$$

where the term $\frac{\kappa_3}{2}\|\varphi\|_V^2$ has been added to both hands sides. Then its occurrence on the right-hand side has been controlled essentially by repeating the procedure in (3.69)-(3.70). Now, for $K > 0$ as in Assumption 2.1, there holds

$$\widehat{\beta}(r) = \psi(r) + \frac{\lambda}{2}r^2 - K \geq \psi(r) \quad \forall |r| \geq \Big(\frac{2K}{\lambda}\Big)^{1/2}. \tag{3.77}$$

As a consequence, for some $c > 0$ we have

$$\kappa_1 Z^{-1}\bigg(\int_\Omega \widehat{\beta}(\varphi)\,\mathrm{d}x\bigg) \geq \kappa_1 Z^{-1}\bigg(\int_\Omega \psi(\varphi)\,\mathrm{d}x\bigg) - c. \tag{3.78}$$

Actually, to prove this relation it suffices to split the integration domain Ω into the sets where $|\varphi|$ is smaller and respectively larger than $\big(\frac{2K}{\lambda}\big)^{1/2}$ and to use (3.77).

Thanks to the above relations, (3.76) takes now the form

$$\frac{\mathrm{d}}{\mathrm{d}t}\big(\mathcal{E}_1 + \mathcal{E}_2\big) + \kappa_3\mathcal{E}_1 + \kappa_1 Z^{-1}(\mathcal{E}_2) + \kappa_2\mathcal{D} \leq c_1, \tag{3.79}$$

where we have set

$$\mathcal{E}_1 := \frac{1}{2}\big(\|\varphi\|_V^2 + \|\sigma\|^2\big), \qquad \mathcal{E}_2 := \int_\Omega \psi(\varphi)\,\mathrm{d}x, \tag{3.80}$$

$$\mathcal{D} := \|\Delta\varphi\|^2 + \|\nabla\mu\|^2 + \|\nabla\sigma\|^2 \tag{3.81}$$

and we can notice that the above quantities are nonnegative. In order to prove that the above differential inequality is dissipative, we first observe that, as a consequence of (2.8),

$$\frac{|\beta(r)|}{\widehat{\beta}(r)} \le c \quad \text{for sufficiently large } |r|, \tag{3.82}$$

whence, recalling (3.73), it is easy to deduce, for some $c \ge 0$,

$$Z(r) \le c + e^{cr} \quad \forall r \ge 0 \tag{3.83}$$

and, in turn, passing to inverse functions,

$$Z^{-1}(r) \ge \kappa \ln(y - c) \quad \forall r \ge \bar{r}, \tag{3.84}$$

where $\bar{r}$ is some computable positive number. The above implies

$$\kappa_1 Z^{-1}(r) \ge \kappa_4 \ln(y + 1) - c \quad \forall r \ge 0, \tag{3.85}$$

so that inequality (3.79) takes the form

$$\frac{\mathrm{d}}{\mathrm{d}t}\big(\mathcal{E}_1 + \mathcal{E}_2\big) + \kappa_3 \mathcal{E}_1 + \kappa_4 \ln(\mathcal{E}_2 + 1) \le c_2. \tag{3.86}$$

Then, setting $\phi(r) = \ln(1 + r)$ for $r \ge 0$ and using the elementary inequalities $r \ge \phi(r)$ and $\phi(r + s) \le \phi(r) + \phi(s)$ holding for every $r, s \ge 0$, we readily obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\big(\mathcal{E}_1 + \mathcal{E}_2\big) + \kappa_5 \ln(\mathcal{E}_1 + \mathcal{E}_2 + 1) \le c_3, \tag{3.87}$$

which is a dissipative differential inequality and implies the desired condition (2.31). Actually, it can be easily checked that there exists a finite and computable time $T_0 \ge T_1$ depending only on the "energy" (in the sense of (2.30)) of the initial data such that for every $t \ge T_0$ there holds

$$\kappa_5 \ln(\mathcal{E}_1 + \mathcal{E}_2 + 1) \le 2c_3, \quad \text{i.e. } \mathcal{E}_1 + \mathcal{E}_2 \le e^{\frac{2c_3}{\kappa_5}} - 1. \tag{3.88}$$

Indeed, if condition (3.88) is violated, then the time derivative of $\mathcal{E}_1 + \mathcal{E}_2$ is less than $-c_3$, implying that $\mathcal{E}_1 + \mathcal{E}_2$ decreases at least linearly with time until (3.88) starts holding after some computable time T_0. Relation (2.31) is then an immediate consequence of (3.88). □

Remark 3.5. We point out that it may be possible to allow $p_\beta = 2$ in (2.26) at least in the case when κ_β is large enough. We leave the details to the reader.

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3.3. Proof of Theorem 2.11: Attractor

Thanks to the dissipativity property of Theorem 2.10, we only need to show asymptotic compactness of solutions. To this aim, we prove a further regularity estimate. As above, we will directly work on system (1.1)-(1.3), being intended that this formal procedure may be justified within some approximation scheme. In what follows the various constants c will be allowed to depend on the $\mathcal{X}$-radius C_0 (cf. (2.31)) of the absorbing set.

That said, we first test (1.1) by μ_t. Then, integrating by parts in time the term on the right-hand side, we get

$$
\begin{aligned}
(\mu_t,\varphi_t) + \frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\|\nabla\mu\|^2 + \frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega (A-P\sigma)h(\varphi)\mu\,\mathrm{d}x &= \int_\Omega \mu\big((A-P\sigma)h(\varphi)\big)_t\mathrm{d}x \\
&= \int_\Omega (A-P\sigma)h'(\varphi)\varphi_t\mu\,\mathrm{d}x - \int_\Omega P\sigma_t h(\varphi)\mu\,\mathrm{d}x \\
&\le c\big(\|\varphi_t\|+\|\sigma_t\|\big)\|\mu\| \le \frac{1}{2}\|\varphi_t\|^2 + \frac{1}{2}\|\sigma_t\|^2 + c\|\mu\|^2. \qquad (3.89)
\end{aligned}
$$

We used here the boundedness of h and h', and the fact that $0\le\sigma\le 1$. These conditions will be repeatedly used again below without further mentioning them. Next, we differentiate (1.2) in time and test the result by φ_t to obtain

$$
(\mu_t,\varphi_t) = \|\nabla\varphi_t\|^2 + \int_\Omega \beta'(\varphi)\varphi_t^2\,\mathrm{d}x - \lambda\|\varphi_t\|^2. \qquad (3.90)
$$

Multiplying now (1.1) by $(1+2\lambda)\varphi_t$ we obtain

$$
\begin{aligned}
(1+2\lambda)\|\varphi_t\|^2 &= -(1+2\lambda)(\nabla\mu,\nabla\varphi_t) + (1+2\lambda)\int_\Omega \big(P\sigma - A)h(\varphi)\varphi_t\,\mathrm{d}x \\
&\le \frac{1}{2}\|\nabla\varphi_t\|^2 + c_\lambda\|\nabla\mu\|^2 + \lambda\|\varphi_t\|^2 + c_\lambda. \qquad (3.91)
\end{aligned}
$$

Finally, multiplying (1.3) by $2\sigma_t$ and standardly controlling the right-hand side, it is not difficult to deduce

$$
\|\sigma_t\|^2 + \frac{\mathrm{d}}{\mathrm{d}t}\|\nabla\sigma\|^2 \le c. \qquad (3.92)
$$

Taking the sum of relations (3.89), (3.91) and (3.92), and using (3.90), we arrive at

$$
\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t}\left[\frac{1}{2}\|\nabla\mu\|^2 + \|\nabla\sigma\|^2 + \int_\Omega (A-P\sigma)h(\varphi)\mu\,\mathrm{d}x\right] + \frac{1}{2}\|\nabla\varphi_t\|^2 + \int_\Omega \beta'(\varphi)\varphi_t^2\,\mathrm{d}x \\
&\quad + \frac{1}{2}\|\sigma_t\|^2 + \frac{1}{2}\|\varphi_t\|^2 \le c + c\|\nabla\mu\|^2 + c\|\mu\|^2. \qquad (3.93)
\end{aligned}
$$

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Now, using the Poincaré-Wirtinger inequality (2.3) we have

$$c\|\mu\|^2 = c\|\mu-\mu_\Omega\|^2 + c\|\mu_\Omega\|^2 \le c\|\nabla\mu\|^2 + c\left|\int_\Omega \psi'(\varphi)\,\mathrm{d}x\right|^2$$
$$\le c\|\nabla\mu\|^2 + c + c\left|\int_\Omega \psi(\varphi)\,\mathrm{d}x\right|^2 \le c + c\|\nabla\mu\|^2, \tag{3.94}$$

where we have also used condition (2.8) and the uniform bound on the L^1-norm of $\psi(\varphi)$.

Then, noting as $\mathcal{E}_3$ the sum of the terms in square brackets on the left-hand side of (3.93), we can observe that

$$\mathcal{E}_3 \ge \frac{1}{2}\|\nabla\mu\|^2 + \|\nabla\sigma\|^2 - c\|\mu\|_{L^1(\Omega)}$$
$$\ge \frac{1}{2}\|\nabla\mu\|^2 + \|\nabla\sigma\|^2 - c\|\mu-\mu_\Omega\|_{L^1(\Omega)} - c|\mu_\Omega|$$
$$\ge \frac{1}{2}\|\nabla\mu\|^2 + \|\nabla\sigma\|^2 - c\|\nabla\mu\| - c - c\left|\int_\Omega \psi(\varphi)\,\mathrm{d}x\right|$$
$$\ge \frac{1}{4}\|\nabla\mu\|^2 + \|\nabla\sigma\|^2 - c_0, \tag{3.95}$$

where c_0 depends only on the uniform bound on the $\mathcal{X}$-magnitude of the solution (cf. (2.31)) holding for $t \ge T_0$.

Thanks to (3.94) and (3.95), (3.93) gives rise to the following inequality:

$$\frac{\mathrm{d}}{\mathrm{d}t}(\mathcal{E}_3 + c_0) + \frac{1}{2}\|\nabla\varphi_t\|^2 + \int_\Omega \beta'(\varphi)\varphi_t^2\,\mathrm{d}x$$
$$+ \frac{1}{2}\|\sigma_t\|^2 + \frac{1}{2}\|\varphi_t\|^2 \le c + c\|\nabla\mu\|^2. \tag{3.96}$$

Now, coming back to (3.79), integrating it over the generic time interval $(t, t+1)$, $t \ge T_1$, and recalling (3.81), we obtain

$$\int_t^{t+1} \left(\|\nabla\mu\|^2 + \|\nabla\sigma\|^2\right)\mathrm{d}s \le c. \tag{3.97}$$

Consequently, we can apply the uniform Gronwall lemma (see, e.g., [29]) to (3.96) to obtain

$$\|\mu(t)\|_V + \|\sigma(t)\|_V \le C_1 \quad \forall t \ge T_0 + 1, \tag{3.98}$$

where $C_1 > 0$ is independent of the initial data. To get additional regularity on φ it is then sufficient to go back to (1.2) and apply standard elliptic regularity results to obtain

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$$\|\varphi(t)\|_{H^2(\Omega)} \leq C_2 \quad \forall t \geq T_0 + 1, \tag{3.99}$$

where $C_2 > 0$ is independent of the initial data. Properties (3.98) and (3.99), combined with the dissipativity proved in Theorem 2.10, provide existence of the global attractor $\mathcal{A}$ as well as its boundedness in $H^2(\Omega) \times H^1(\Omega)$, which concludes the proof.

3.4. Spatially homogeneous case

We give here some evidence of the fact that, if conditions (2.23)-(2.25) do not hold, then dissipativity of the process may fail. To this aim, we analyze the behavior of spatially homogeneous solutions. Indeed, in view of the no-flux boundary conditions, these are particular solutions to system (1.1)-(1.3) starting from spatially homogeneous initial data. Let us denote by $X = X(t)$ and by $S = S(t)$ the spatially homogeneous versions of φ and σ, respectively. Then, our problem reduces to the following ODE system for the vector variable (X, S):

$$X' + (A - PS)h(X) = 0, \tag{3.100}$$

$$S' + CSh(X) + B(S - \sigma_s) = 0. \tag{3.101}$$

We can first observe that, if $\underline{h} = 0$ and $X(t) \leq -1$ at some time t (for instance, at $t = 0$), then X remains ≤ -1 ever after; indeed, because $h(X) = 0$, equation (3.100) prescribes $X(t)$ to be constant and hence there is no hope to prove dissipativity. We actually recall that, when choosing a "smooth" potential ψ defined on the whole real line, as in our case, the values of φ lying outside the reference interval $[-1, 1]$ are likely to be attained by the solution, even when this is not the case at the initial time; hence such an eventuality has to be taken into account in the long-time analysis of solutions.

Now, let us move to the case when $\underline{h} > 0$. Then, we may observe that

$$B\sigma_s - (C + B)S \leq S' \leq B\sigma_s - (B - C\underline{h})S. \tag{3.102}$$

The first inequality implies that

$$S < \frac{B\sigma_s}{C + B} \Rightarrow S' > 0. \tag{3.103}$$

For what concerns the second inequality, we have two cases. Let us first consider the situation when $C\underline{h} \geq B$, i.e. (2.23) does not hold. Let also the initial data be chosen in such a way that $X(0) \leq -1$ and $S(0)$ is large enough so that $PS(0) - A > 0$. Note that, at least for $P > A$, we have $P\sigma > A$ when σ is lower than but sufficiently close to 1. Actually, even if it is not necessary for the mathematical analysis, the choice $P > A$ is natural because otherwise the apoptosis effect would always prevail over the proliferation effect, even for high nutrient concentrations. Under such conditions, we have

$$X' = -(PS - A)\underline{h} < 0, \tag{3.104}$$

$$S' = B\sigma_s + (C\underline{h} - B)S > 0, \tag{3.105}$$

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a priori at $t = 0$, but actually ever after. As a consequence, both $|X|$ and S grow forever. Hence, not only we do not have dissipativity, but both the nutrient concentration and the tumor phase exit their physically significant intervals.

In view of the above discussion, it looks reasonable to assume $\underline{h} > 0$ and (2.23). Under these conditions, the second inequality in (3.102) implies

$$S > \frac{B\sigma_s}{B - C\underline{h}} \Rightarrow S' < 0. \tag{3.106}$$

We can then define the region

$$\mathcal{S} := \left\{ (X, S) \in \mathbb{R}^2 : \frac{B\sigma_s}{C + B} \le S \le \frac{B\sigma_s}{B - C\underline{h}} \right\} \tag{3.107}$$

and it follows from (3.103) and (3.106) that $\mathcal{S}$ is positively invariant for the dynamical process generated by (3.100)-(3.101). Now, if we want to keep the physical constraint $S(t) \in [0, 1]$, we need to assume $\frac{B\sigma_s}{B-C\underline{h}} < 1$, i.e. (2.24) (otherwise basically our results still hold provided that we allow S to take also values larger than 1). In such a situation, we need to emphasize the role of (2.25). To this purpose, let us assume that $X \ge 1$ at some time, so that $h(X) = 1$. Then, (3.100) reduces to

$$X' = (PS - A) \tag{3.108}$$

and in this sense condition (2.25) (which can be rewritten as $\frac{A}{P} > \frac{B\sigma_s}{B-C\underline{h}}$) prescribes that (if we reason in the (X, S)-plane with X represented in the horizontal axis), in the intersection between $\mathcal{S}$ and the semiplane $\{X \ge 1\}$, X' stays negative (hence arbitrary growth of X is prevented, because trajectories tend to eventually enter the region $\mathcal{S}$).

On the other hand, we can see that, when $\frac{A}{P} \le \frac{B\sigma_s}{B+C}$, dissipativity cannot hold. Indeed if $S(0) \in \left[\frac{B\sigma_s}{C+B}, \frac{B\sigma_s}{B-C\underline{h}}\right]$ and $X(0) \ge 1$, then $X(t)$ is forced to increase forever, because (X, S) can never leave the positively invariant region $\mathcal{S}$ where, now, $X' > 0$. On the other hand, the situation when $\frac{A}{P} \in \left(\frac{B\sigma_s}{C+B}, \frac{B\sigma_s}{B-C\underline{h}}\right]$ is unclear, in the sense that, when $X \ge 1$, in the "upper" part of the strip $\mathcal{S}$, X' is positive, whereas X' is negative in the "lower" part of $\mathcal{S}$, so the evolution of (X, S) may be more difficult to capture. Of course, the behavior may be even more complicated once one considers general (i.e., not necessarily spatially homogeneous) solutions to (1.1)-(1.3), because in that case also equation (1.2) plays an important role (whereas (1.2) "disappears" in the spatially homogeneous setting).

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