

## A NONLINEAR PARABOLIC–HYPERBOLIC SYSTEM FOR CONTACT INHIBITION OF CELL–GROWTH

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*Dedicated to Professor Jesús Ildefonso Díaz  
on the occasion of his 60th birthday*

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*Abstract.* We consider a tumor growth model involving a nonlinear system of partial differential equations which describes the growth of two types of cell population densities with contact inhibition. In one space dimension, it is known that global solutions exist and that they satisfy the so-called *segregation property*: if the two populations are initially segregated - in mathematical terms this translates into disjoint supports of their densities - this property remains true at all later times. We apply recent results on transport equations and regular Lagrangian flows to obtain similar results in the case of arbitrary space dimension.

### 1. Introduction

In the natural process of cell growth, one can observe cases where cells closely approach and come into contact with each other. This phenomenon is referred to as contact inhibition of growth between cells (cf. [1]). A number of mathematical models (see for instance [9]) have been proposed for the theoretical understanding of the mechanism of contact inhibition. In [5], we have studied a simple partial differential equation model, which describes contact inhibition between normal and abnormal cells (for example cells which potentially become tumor cells at a later stage). It includes the effect of pushing cells away from overcrowded regions so that each cell moves in the direction of lower cell density. The resulting model is given by

$$(P) \begin{cases} u_t = \operatorname{div}(u\nabla(u+v)) + u(1-u-\alpha v) & \text{in } \mathbb{R}^N \times (0, \infty), \\ v_t = \operatorname{div}(v\nabla(u+v)) + \gamma v(1-\beta u - v/k) & \text{in } \mathbb{R}^N \times (0, \infty), \\ u(\cdot, 0) = u_0 \text{ and } v(\cdot, 0) = v_0 & \text{in } \mathbb{R}^N. \end{cases}$$

In ecology, the growth terms are regarded as of Lotka-Volterra competition type. For an introduction to the biological context we refer to [9] and the references therein (see also [5] for a more detailed biological interpretation of Problem (P)).

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Throughout the paper we assume the following hypotheses on the data:

- (H<sub>1</sub>)  $\alpha, \beta, \gamma$  and  $k$  are positive constants;
- (H<sub>2</sub>) the initial functions are bounded and nonnegative:  $u_0, v_0 \in L^\infty(\mathbb{R}^N)$  and  $u_0, v_0 \geq 0$  a.e. in  $\mathbb{R}^N$ ;
- (H<sub>3</sub>)  $0 < B_0 \leq u_0 + v_0 \leq B_0^{-1}$  a.e. in  $\mathbb{R}^N$  for some constant  $B_0$ ,  $u_0 + v_0 \in C^3_{\text{loc}}(\mathbb{R}^N)$  and  $u_0 + v_0$  is uniformly Lipschitz continuous in  $\mathbb{R}^N$ .

We shall refer collectively to these assumptions as *hypothesis H*.

In Section 3, we formulate the main results of this paper: if hypothesis *H* is satisfied, problem (P) has a solution in the sense of distributions, and solutions which are initially segregated, remain segregated:

$$u_0 v_0 = 0 \text{ a.e. in } \mathbb{R}^N \Rightarrow u(\cdot, t)v(\cdot, t) = 0 \text{ a.e. in } \mathbb{R}^N \text{ for } t > 0. \tag{1}$$

This *segregation property* reflects the contact inhibition mechanism for the growth of the cells.

In [5] similar results have been obtained in the one-dimensional case,  $N = 1$  (for a bounded interval with no-flux boundary conditions). The global existence result in [5] is primarily based on *BV*-estimates, which seem to be difficult to obtain if  $N > 1$ . In [5] the existence result of segregated solutions also covers the case that the divergence term in the second equation is multiplied by a constant  $d \neq 1$ , but we are not able to generalize this to the case that  $N \geq 2$ . Another generalization in [5] concerns the gradient  $\nabla(u + v)$ , which is replaced by  $\nabla\chi(u + v)$  for a smooth function  $\chi$  with positive derivative. Our results can be easily extended to this case.

The system without reaction terms was considered in a series of papers in the 80's (see [6, 7, 8]). The absence of reaction terms reduces the problem to a system of conservation laws, which makes its analysis considerably simpler.

The approach in the present paper is based on recent results for transport equations. Setting

$$w = u + v, \quad r = u/(u + v) \text{ (and, similarly, } w_0 = u_0 + v_0, \quad r_0 = u_0/(u_0 + v_0)),$$

the parabolic-hyperbolic nature of the system becomes clear: formally the system can be rewritten as a parabolic equation for  $w$  coupled to a hyperbolic one for  $r$ :

$$\begin{cases} w_t = \operatorname{div}(w\nabla w) + wF(r, w) & \text{in } \mathbb{R}^N \times (0, \infty), \\ r_t = \nabla w \cdot \nabla r + r(1 - r)G(r, w) & \text{in } \mathbb{R}^N \times (0, \infty), \\ w(\cdot, 0) = w_0 \text{ and } r(\cdot, 0) = r_0 & \text{a.e. in } \mathbb{R}^N, \end{cases}$$

where

$$\begin{aligned} F(r, w) &:= r(1 - rw - \alpha(1 - r)w) + \gamma(1 - r)(1 - \beta rw - (1 - r)w/k), \\ G(r, w) &:= (1 - rw - \alpha(1 - r)w) - \gamma(1 - \beta rw - (1 - r)w/k). \end{aligned} \tag{2}$$

Initially, at  $t = 0$ ,  $w = w_0$  is bounded away from zero (hypothesis *H*<sub>3</sub>), and we shall see that this also holds for later times  $t > 0$ . Hence the equation for  $w$  is uniformly

parabolic and its solution is rather smooth. This will imply that the velocity field  $-\nabla w$  of the transport equation for  $r$  is Hölder continuous (but not Lipschitz continuous) and has a certain Sobolev regularity which enables us to use the theory of renormalized solutions of transport equations, originally developed by Di Perna and Lions ([11]). More precisely, we shall use the version given by Ambrosio, Bouchut and De Lellis ([4], see also [10]), although these papers are primarily focussed on the more general (and more difficult) case of velocity fields "with  $BV$  regularity" (see [2]). One could say that the renormalization theory compensates the lack of  $BV$ -estimates, the basic ingredient of the existence theory if  $N = 1$ .

Observe that formally the segregation property follows from the equation for  $r$ : if  $r_0(x_0) = 0$ ,  $r = 0$  along the characteristic starting at  $x_0$  (i.e.  $u = 0$  along the characteristic), and if  $r_0(x_0) = 1$ ,  $r = 1$  ( $v = 0$ ) along the characteristic. Again the renormalization theory will make this rigorous.

In Section 2 we prove a result of independent interest: in bounded domains the system, with no-flux conditions at the boundary, has smooth solutions if the initial data are smooth. They will be used to approximate solutions of problem  $(P)$ . Observe that we are particularly interested in the existence of discontinuous solutions: segregated solutions will be discontinuous at the interfaces which separate the disjoint regions where  $u > 0$  and  $v > 0$ .

In Section 3 we state the main result and in Section 4 we give its proof.

### 2. Smooth solutions in bounded domains

In this section, we prove the existence of a global smooth solution in a bounded domain. This result shows that if initial conditions  $u_0$  and  $v_0$  are smooth, then  $u$  and  $v$  are smooth for all times. In other words,  $u$  and  $v$  do not become segregated in finite time.

**THEOREM 2.1.** *Let  $\Omega \subset \mathbb{R}^N$  a bounded domain with smooth boundary  $\partial\Omega$  and  $\alpha, \beta, \gamma$  and  $k$  positive constants. Let  $u_0, v_0 \in C^3(\overline{\Omega})$  such that  $u_0, v_0 \geq 0$  and  $0 < B_0 \leq u_0 + v_0 \leq B_0^{-1}$  in  $\Omega$  for some constant  $B_0$  and*

$$\frac{\partial(u_0 + v_0)}{\partial \nu} = 0 \text{ on } \partial\Omega,$$

where  $\nu(x)$  denotes the outward normal at  $x \in \partial\Omega$ . Then there exists a pair of nonnegative solutions  $(u, v)$ , such that  $u, v \in C^{2,1}(\overline{\Omega} \times [0, \infty))$  and  $u + v \in C^{2+\mu, \frac{2+\mu}{2}}(\overline{\Omega} \times [0, \infty))$  with  $\mu \in (0, 1)$ , of the problem

$$(P_\Omega) \begin{cases} u_t = \operatorname{div}(u\nabla(u+v)) + u(1-u-\alpha v) & \text{in } \Omega \times (0, \infty), \\ v_t = \operatorname{div}(v\nabla(u+v)) + \gamma v(1-\beta u - v/k) & \text{in } \Omega \times (0, \infty), \\ u \frac{\partial(u+v)}{\partial \nu} = v \frac{\partial(u+v)}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0, \infty), \\ u(\cdot, 0) = u_0, v(\cdot, 0) = v_0 & \text{in } \Omega. \end{cases}$$

*Proof.* The proof is based on Schauder’s fixed point theorem. It is sufficient to prove existence of smooth solutions on a bounded time interval  $[0, T]$  ( $T > 0$  fixed but arbitrary). Since we are interested in smooth solutions, it is equivalent to solve the problem for  $w := u + v$  and  $r := u/(u + v)$ :

$$(\tilde{P}_\Omega) \begin{cases} w_t = \operatorname{div}(w\nabla w) + wF(r, w) & \text{in } Q_T := \Omega \times (0, T], \\ r_t = \nabla w \cdot \nabla r + r(1-r)G(r, w) & \text{in } Q_T, \\ w \frac{\partial w}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0, T], \\ w(\cdot, 0) = w_0 := u_0 + v_0, \quad r(\cdot, 0) = r_0 := u_0/v_0 & \text{in } \Omega, \end{cases}$$

where  $F$  and  $G$  are defined by (2).

Let  $M > 0$  be a constant and let  $\mu \in (0, 1)$ . Below  $C_M$  will denote a generic constant which for fixed  $\mu$ ,  $w_0$  and  $r_0$ , depends only on  $M$ . Given

$$r \in C^{\mu, \frac{\mu}{2}}(\bar{Q}_T), \quad 0 \leq r \leq 1, \quad \|r\|_{C^{\mu, \frac{\mu}{2}}(\bar{Q}_T)} \leq M,$$

there exists a unique solution  $w \in C^{2+\mu, \frac{2+\mu}{2}}(\bar{Q}_T)$  of the problem

$$(\tilde{P}_{r, \Omega}) \begin{cases} w_t = \operatorname{div}(w\nabla w) + wF(r, w) & \text{in } Q_T, \\ w \frac{\partial w}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0, T], \\ w(\cdot, 0) = w_0 & \text{in } \Omega. \end{cases}$$

Here we have used the a priori estimate  $0 < B_1 \leq w \leq B_2$ , which implies uniformly parabolicity. Indeed,  $0 \leq r \leq 1$  gives us that

$$\begin{aligned} f(rw, (1-r)w) &< 0 & \text{if } w > 1/\min\{1, \alpha\}, \\ f(rw, (1-r)w) &> 0 & \text{if } w < 1/\max\{1, \alpha\}, \end{aligned}$$

and

$$\begin{aligned} g(rw, (1-r)w) &< 0 & \text{if } w > 1/\min\{1/k, \beta\}, \\ g(rw, (1-r)w) &> 0 & \text{if } w < 1/\max\{1/k, \beta\}, \end{aligned}$$

where  $f(u, v) = (1 - u - \alpha v)u$  and  $g(u, v) = \gamma(1 - \beta u - v/k)v$ . Since  $B_0 \leq w_0 \leq B_0^{-1}$ , the maximum principle implies that  $0 < B_1 \leq w \leq B_2$  with

$$\begin{aligned} B_1 &= \min \left\{ B_0, \frac{1}{\max\{1, \alpha\}}, \frac{1}{\max\{1/k, \beta\}} \right\}, \\ B_2 &= \max \left\{ B_0^{-1}, \frac{1}{\min\{1, \alpha\}}, \frac{1}{\min\{1/k, \beta\}} \right\}. \end{aligned}$$

By standard Schauder type estimates ([15], Chapter IV, Theorem 5.3), we have  $\|w\|_{C^{2+\mu, \frac{2+\mu}{2}}(\bar{Q}_T)} \leq C_M$ .

Given the solution  $w$ , we consider for each  $y \in \overline{\Omega}$  the ODE for the characteristic starting at  $y$ :

$$\begin{cases} X_t(y, t) = -\nabla w(X(y, t), t) & \text{for } 0 < t \leq T, \\ X(y, 0) = y & \text{for } y \in \overline{\Omega}. \end{cases}$$

Since the normal derivative of  $w$  at the lateral boundary  $\partial\Omega$  vanishes, we have that  $X(y, t) \in \partial\Omega$  for  $0 < t \leq T$  if  $y \in \partial\Omega$ . In view of the regularity of  $w$ , there exists for each  $y \in \overline{\Omega}$  a unique solution  $t \mapsto X(y, t)$  and the map  $X : \overline{Q}_T \rightarrow \overline{Q}_T$  is one-to-one and onto. The smoothness of  $w$  implies that ([14], Theorem 3.3 p.21)

$$\|X_i\|_{C^{1,1}(\overline{Q}_T)} \leq C_M \quad \text{for all } i = 1, \dots, N.$$

Next we focus on the equation for  $r$ . By a change of variables based on the expression for the characteristics  $x = X(y, t)$ , the transport equation

$$(\tilde{P}_{w,\Omega}) \begin{cases} r_t = \nabla w \cdot \nabla r + r(1-r)G(r, w) & \text{in } Q_T, \\ r(x, 0) = r_0(x) & \text{in } \Omega, \end{cases}$$

reduces to the smooth ODE

$$\begin{cases} R_t = R(1-R)G(R, w(X(y, t))) & \text{for } 0 < t \leq T, \\ R(y, 0) = r_0(y) & \text{for } y \in \Omega, \end{cases} \tag{3}$$

where  $R(y, t) := r(X(y, t), t)$ . So let  $\tilde{R} \in C^{1,1}(\overline{Q}_T)$  be the solution of (3). The regularity of  $w$  and  $X$  implies that  $\|\tilde{R}\|_{C^{1,1}(\overline{Q}_T)} \leq C_M$  ([14], Theorem 3.3). In addition, since  $0 \leq r_0 \leq 1$  in  $\overline{\Omega}$ ,  $0 \leq \tilde{R} \leq 1$  in  $\overline{Q}_T$ .

Before returning to the original  $(x, t)$ -variables, we analyze the regularity of the inverse function  $X^{-1}(x, t)$ . The map  $X$  is invertible in  $Q_T$  and the elements of the Jacobian matrix  $J(y, t)$  of  $X$ , that is  $\{(X_i)_{y_j}(y, t)\}$ , are uniformly bounded in  $Q_T$ . We claim that

the elements of the inverse matrix  $J^{-1}(x, t)$  are uniformly bounded in  $Q_T$ . (4)

By Cramer's Rule, it is sufficient to prove that  $|\det J| \geq a_T$  in  $Q_T$  for some constant  $a_T > 0$ . Below we show that, for all fixed  $y \in \Omega$ ,

$$\frac{d}{dt}(w(X(y, t), t)|\det J|) = w(X(y, t), t)F(r(X(y, t), t), w(X(y, t), t))|\det J|. \tag{5}$$

We multiply the equation for  $w$  by a smooth test function  $\varphi \in C^\infty(\Omega \times [0, T])$  with compact support, and integrate over  $\Omega$ :

$$\frac{d}{dt} \int_{\Omega} w\varphi dx = \int_{\Omega} (w_t\varphi + w\varphi_t) dx = \int_{\Omega} w(\varphi_t - \nabla w \nabla \varphi + F\varphi) dx. \tag{6}$$

Changing variables,  $x = X(y, t)$ , we have that

$$\int_{\Omega} w\varphi dx = \int_{\Omega} w|\det J|\varphi dy$$

and

$$\int_{\Omega} w(\varphi_t - \nabla w \nabla \varphi + F\varphi) dx = \int_{\Omega} w |\det J| ((\varphi(X(y,t),t))_t + F\varphi) dy,$$

and (6) becomes

$$\frac{d}{dt} \int_{\Omega} w |\det J| \varphi dy = \int_{\Omega} w |\det J| (\varphi_t + F\varphi) dy.$$

Hence

$$\int_{\Omega} (w |\det J|)_t \varphi dy = \int_{\Omega} w |\det J| F \varphi dy$$

for all test function  $\varphi \in C^\infty(\Omega \times [0, T])$  with compact support, and we have found (5).

Now (4) follows easily. Since

$$-(1 + \alpha + (\beta + 1/k)\gamma)B_2 \leq F(r, w) \leq 1 + \gamma,$$

we deduce from (5) that

$$\frac{d}{dt} (w(X(y,t),t) |\det J|) \begin{cases} \geq -(1 + \alpha + (\beta + 1/k)\gamma)B_2 w(X(y,t),t) |\det J|, \\ \leq (1 + \gamma)w(X(y,t),t) |\det J|. \end{cases}$$

The initial condition  $X(y,0) = y$  implies that  $\det J(y,0) = 1$  for  $y \in \overline{\Omega}$ , which, together with Gronwall's inequality and the uniform bounds on  $w$ , implies that there exists a positive constant  $a_T > 0$  such that

$$0 < a_T \leq |\det J| \leq a_T^{-1} \text{ in } Q_T. \tag{7}$$

Thus we have proved (4). Hence  $X^{-1}(x,t) \in C^{1,1}(\overline{Q}_T)$ , and the Jacobian matrix of  $X^{-1}(x,t)$  is uniformly bounded in  $\overline{Q}_T$ . Differentiating  $X^{-1}(X(y,t),t) = y$  with respect to time yields

$$(X^{-1})_t = -\nabla X^{-1} \cdot X_t = \nabla X^{-1} \cdot \nabla w \text{ for each } i = 1, \dots, N.$$

In particular  $(X^{-1})_t$  is uniformly bounded in  $\overline{Q}_T$ , and

$$\|X_i^{-1}\|_{C^{1,1}(\overline{Q}_T)} \leq C_M \text{ for } i = 1, \dots, N.$$

Next we transform  $\tilde{R}(y,t)$  back to the original variables:

$$\tilde{r}(x,t) := \tilde{R}(X^{-1}(x,t),t) \text{ for } (x,t) \in \overline{Q}_T.$$

We deduce from the regularity of  $X^{-1}$  and  $\tilde{R}$  that  $\|\tilde{r}\|_{C^{1,1}(\overline{Q}_T)} \leq C_M$ ; since  $0 \leq \tilde{R} \leq 1$  in  $\overline{Q}_T$ , also  $0 \leq \tilde{r} \leq 1$  in  $\overline{Q}_T$ .

This leads us to define the map  $r \mapsto w \mapsto \tilde{r} =: \mathcal{F}(r)$  from the convex set

$$\mathcal{U} := \{r \in C^{\mu, \frac{\mu}{2}}(\overline{Q}_T); 0 \leq r \leq 1 \text{ in } Q_T\}$$

into itself.  $\mathcal{F}$  is compact since  $C^{1,1}(\overline{Q}_T)$  is compactly imbedded in  $C^{\mu, \frac{\mu}{2}}(\overline{Q}_T)$ .

We check that  $\mathcal{T}$  is continuous. Let  $\{r_m\}_{m \in \mathbb{N}} \subset \mathcal{U}$  converge to  $r \in \mathcal{U}$  in  $C^{\mu, \frac{\mu}{2}}(\overline{Q}_T)$  as  $m \rightarrow \infty$ . Since  $\{r_m\}_{m \in \mathbb{N}}$  is bounded in  $C^{\mu, \frac{\mu}{2}}(\overline{Q}_T)$ , it follows that the sequence  $\{w_m\}_{m \in \mathbb{N}}$  is bounded in  $C^{2+\mu, \frac{2+\mu}{2}}(\overline{Q}_T)$ , and that it converges to the corresponding solution  $w$  of problem  $(\tilde{P}_{r, \Omega})$  as  $m \rightarrow \infty$ . The sequence  $\{\tilde{r}_m\}_{m \in \mathbb{N}} = \{\mathcal{T}(r_m)\}_{m \in \mathbb{N}}$  is bounded in  $C^{1,1}(\overline{Q}_T)$ . Thus it converges to the solution  $\tilde{r} = \mathcal{T}(r)$  of problem  $(\tilde{P}_{w, \Omega})$  in  $C^{\mu, \frac{\mu}{2}}(\overline{Q}_T)$  for each  $\mu \in (0, 1)$ .

Since  $\mathcal{T}$  is continuous and compact, by Schauder’s fixed point theorem ([12], Theorem 3.2 p.57) it has a fixed point which is a solution of problem  $(\tilde{P}_\Omega)$ . Therefore, the function pair  $(u, v) = (wr, w(1 - r))$  is a solution of problem  $(P_\Omega)$  in  $[0, T]$ . This completes the proof of Theorem 2.1.  $\square$

### 3. Main result

Before stating the main result we specify what we mean by a solution of problem  $(P)$ . We assume that all data satisfy hypothesis  $H$ .

DEFINITION 3.1. A function pair  $(u, v)$  is called a *solution of problem  $(P)$*  if it satisfies the following properties:

- (i)  $u, v \in L^\infty_{\text{loc}}([0, \infty); L^\infty(\mathbb{R}^N))$  and  $u, v \geq 0$  a.e. in  $\mathbb{R}^N \times (0, \infty)$ ;
- (ii)  $\nabla(u + v) \in L^2_{\text{loc}}(\mathbb{R}^N \times (0, \infty))$ ;
- (iii) for any test function  $\varphi \in C^\infty(\mathbb{R}^N \times [0, \infty))$  with bounded support

$$\int_0^\infty \int_{\mathbb{R}^N} (u\varphi_t - u\nabla(u+v) \cdot \nabla\varphi + u(1-u-\alpha v)\varphi) = - \int_{\mathbb{R}^N} u_0\varphi(\cdot, 0), \tag{8}$$

$$\int_0^\infty \int_{\mathbb{R}^N} (v\varphi_t - v\nabla(u+v) \cdot \nabla\varphi + v(1-\beta u - v/k)\varphi) = - \int_{\mathbb{R}^N} v_0\varphi(\cdot, 0). \tag{9}$$

In the rest of the paper we shall prove that problem  $(P)$  has a solution  $(u, v)$  and that the segregation property holds.

THEOREM 3.2. *Let hypotheses  $H$  be satisfied. Then problem  $(P)$  has a solution  $(u, v)$  which satisfies the segregation property (1).*

REMARK 3.3. Initial segregation ( $u_0v_0 = 0$  a.e. in  $\mathbb{R}^N$ ) and the hypothesis  $0 < B_0 \leq u_0 + v_0$  mean that the initial population densities  $u_0$  and  $v_0$  have disjoint supports and that the populations  $u$  and  $v$  already are in contact at time  $t = 0$ .

We shall prove Theorem 3.2 in the next section. The proof is constructive: let  $B_n \subset \mathbb{R}^N$  be the the ball of radius  $n \in \mathbb{N}$  centered at the origin; we use Theorem 2.1, with  $\Omega = B_n$  and smooth initial functions  $(u_{0n}, v_{0n})$  which approximate  $(u_0, v_0)$  locally in  $\mathbb{R}^N$ , to define approximating solutions  $(u_n, v_n)$ ; finally we pass to the limit  $n \rightarrow \infty$ .

More precisely, let  $u_0, v_0 \in C^3(\mathbb{R}^N)$  with  $0 < B_0 \leq u_0 + v_0 \leq B_0^{-1}$  be such that the Lipschitz constant of  $u_0 + v_0$  is uniformly bounded with respect to  $x \in \mathbb{R}^N$ . Then there exist functions  $u_{0n}, v_{0n} \in C^3(\overline{B}_n)$  such that

- (i)  $u_{0n}, v_{0n} \geq 0$  and  $0 < B_0 \leq u_{0n} + v_{0n} \leq B_0^{-1}$  in  $B_n$ ;
- (ii)  $u_{0n} \rightarrow u_0$  and  $v_{0n} \rightarrow v_0$  in  $L^1_{\text{loc}}(\mathbb{R}^N)$  as  $n \rightarrow \infty$ ;
- (iii)  $u_{0n} + v_{0n} \rightarrow u_0 + v_0$  in  $C^3_{\text{loc}}(\mathbb{R}^N)$  and the Lipschitz constant of  $u_{0n} + v_{0n}$  is uniformly bounded with respect to  $x \in \mathbb{R}^N$  and  $n \in \mathbb{N}$ ;
- (iv)  $\frac{\partial(u_{0n} + v_{0n})}{\partial \nu} = 0$  on  $\partial B_n$ .

### 4. Proof of Theorem 3.2

By Theorem 2.1 problem  $(P_{B_n})$ , with initial functions  $u_{0n}$  and  $v_{0n}$  (defined in the previous section), has a solution  $(u_n, v_n)$ . Setting

$$w_n := u_n + v_n \quad \text{and} \quad r_n := \frac{u_n}{u_n + v_n},$$

and

$$\begin{cases} w_{nt} = \text{div}(w_n \nabla w_n) + w_n F(r_n, w_n) & \text{in } B_n \times (0, \infty), \\ w_n \frac{\partial w_n}{\partial \nu} = 0 & \text{on } \partial B_n \times (0, \infty), \\ w_n(\cdot, 0) = w_{0n} := u_{0n} + v_{0n} & \text{in } B_n. \end{cases}$$

Let  $T, \mathcal{R} > 0$  and  $n > \mathcal{R} + 1$ .

Then  $w_n$  is a smooth solution of the equation for  $w$  in  $B_{\mathcal{R}+1} \times (0, T)$  and satisfies the gradient estimate ([15], Theorem 3.1, p. 417)

$$\max_{B_n \times [0, T]} |\nabla w_n| \leq C \tag{10}$$

for some constant  $C$  which does not depend on  $n$ . Let  $p \geq 2$ . By Agmon-Douglis-Nirenberg type interior  $L^p$  estimates ([16], p. 175)

$$\|D^2 w_n\|_{L^p(B_{\mathcal{R}} \times (0, T))} + \|w_{nt}\|_{L^p(B_{\mathcal{R}} \times (0, T))} \leq C \tag{11}$$

for some constant  $C = C(\mathcal{R}, T, p)$  which does not depend on  $n$ . By (10), (11) and the uniform bound on  $w_n$  in  $Q_T$ ,

$$\|w_n\|_{W^{2,1}_p(B_{\mathcal{R}} \times (0, T))} \leq C \quad \text{if } n > \mathcal{R} + 1 \tag{12}$$

for some constant  $C = C(\mathcal{R}, T, p)$  which does not depend on  $n$ . If  $p > N + 2$ , then

$$W^{2,1}_p(B_{\mathcal{R}} \times (0, T)) \text{ is compactly imbedded into } C^{1+\mu, \frac{1+\mu}{2}}(\overline{B_{\mathcal{R}}} \times [0, T])$$

with  $\mu \in (0, 1 - (N + 2)/p)$  ([15], Chapter II, Lemma 3.3). Hence

$$\|w_n\|_{C^{1+\mu, \frac{1+\mu}{2}}(\overline{B_{\mathcal{R}}} \times [0, T])} \leq C. \tag{13}$$



By a standard diagonal procedure, there exist a subsequence  $\{w_{n_k}\}$  and a function  $w \in W_{p,\text{loc}}^{2,1}(\mathbb{R}^N \times [0, \infty)) \cap L_{\text{loc}}^\infty([0, \infty); W^{1,\infty}(\mathbb{R}^N))$  such that

$$w_{n_k} \rightarrow w \text{ in } C_{\text{loc}}^{1+\mu,(1+\mu)/2}(\mathbb{R}^N \times [0, \infty)) \text{ as } k \rightarrow \infty \tag{14}$$

(we have used (10) to conclude that  $w \in L_{\text{loc}}^\infty([0, \infty); W^{1,\infty}(\mathbb{R}^N))$ ).

The next step is the construction of  $r(x, t)$ . We shall use the characteristics induced by the velocity fields  $b_n$  and  $b$  defined by

$$\begin{aligned} b_n(x, t) &:= -\nabla w_n(x, t) \text{ in } B_n \times [0, \infty), \\ b(x, t) &:= -\nabla w(x, t) \text{ a.e. in } \mathbb{R}^N \times [0, \infty), \end{aligned}$$

respectively. Since  $b = -\nabla w(x, t)$  is not Lipschitz continuous with respect to  $x$ , the ODE's for its characteristics

$$\begin{cases} X_t(y, t) = -\nabla w(X(y, t), t) & \text{for } t > 0, \\ X(y, 0) = y & \text{for } y \in \mathbb{R}^N, \end{cases} \tag{15}$$

are not well defined in the classical sense. Di Perna and Lions ([11]) have generalized the concept of characteristics if the velocity field possesses only Sobolev regularity:

$$b \in L^\infty(\mathbb{R}^N \times [0, \infty)) \cap L_{\text{loc}}^1([0, \infty); W_{\text{loc}}^{1,1}(\mathbb{R}^N)).$$

Below we construct  $r(x, t)$  according to their theory.

### 4.1. Regular Lagrangian flow

Regular Lagrangian flows generalize the concept of characteristics.

**DEFINITION 4.1.** (Definition 3.1 in [10]) Let  $b \in L^\infty(\mathbb{R}^N \times [0, \infty); \mathbb{R}^N)$ . A map  $\Phi : \mathbb{R}^N \times [0, \infty) \rightarrow \mathbb{R}^N$  is a *regular Lagrangian flow induced by  $b$*  if

- (i) for a.e.  $t > 0$  we have that  $|\{y \in \mathbb{R}^N; \Phi(y, t) \in A\}| = 0$  for any Borel set  $A \subset \mathbb{R}^N$  with  $|A| = 0$ ;
- (ii) the ODE's for the characteristics,

$$\begin{cases} \Phi_t(y, t) = b(\Phi(y, t), t) & \text{for } t > 0, \\ \Phi(y, 0) = y & \text{for } y \in \mathbb{R}^N, \end{cases}$$

hold in the sense of distributions: for any  $\varphi \in C^\infty(\mathbb{R}^N \times [0, \infty); \mathbb{R}^N)$  with bounded support,

$$\iint_{\mathbb{R}^N \times \mathbb{R}^+} (\Phi(y, t) \cdot \varphi_t(y, t) + b(\Phi(y, t), t) \cdot \varphi(y, t)) dy dt = - \int_{\mathbb{R}^N} y \cdot \varphi(y, 0) dy.$$

REMARK 4.2. Condition (i) implies that, given  $f \in L_{\text{loc}}^\infty(\mathbb{R}^N \times [0, \infty))$ , the function  $f(\Phi(y, t), t)$  is well-defined for a.e.  $(y, t) \in \mathbb{R}^N \times [0, \infty)$ . By time invertibility of the flow (replace  $b$  by  $-b$ ), the inverse map  $\Psi(x, t) = \Phi^{-1}(x, t)$  and  $f(\Psi(x, t), t)$  (with  $f \in L_{\text{loc}}^\infty(\mathbb{R}^N \times [0, \infty))$ ) are also defined for a.e.  $(x, t)$ .

The organization of the proof is as follows: let  $x = X_n(y, t)$  denote the smooth characteristics induced by  $b_n(x, t) = -\nabla w_n(x, t)$ . After introducing some more basic concepts of transport equations, in section 4.4 we show the convergence of  $\{X_n\}$ , up to subsequences, to a regular Lagrangian flow  $X$  induced by  $b = -\nabla w$ :

$$X_{n_k} \rightarrow X \text{ in } L_{\text{loc}}^1(\mathbb{R}^N \times [0, \infty); \mathbb{R}^N) \text{ as } k \rightarrow \infty. \quad (16)$$

We set  $R_n(y, t) := r_n(X_n(y, t), t)$  for  $y \in \mathbb{R}^N$  and  $t \geq 0$ . In section 4.5 we use the ODE for  $R_n(y, \cdot)$  for each  $y \in \mathbb{R}^N$  to construct a limiting function  $R \in L_{\text{loc}}^1(\mathbb{R}^N \times [0, \infty))$ :

$$R_{n_k} \rightarrow R \text{ in } L_{\text{loc}}^1(\mathbb{R}^N \times [0, \infty)) \text{ as } k \rightarrow \infty. \quad (17)$$

Hence we can use the inverse maps  $Y_n = X_n^{-1}$  and  $Y = X^{-1}$  (see Remark 4.2) to define the corresponding function in the original variables:

$$\begin{aligned} r_n(x, t) &:= R_n(Y_n(x, t), t) \quad \text{for } (x, t) \in B_n \times [0, \infty), \\ r(x, t) &:= R(Y(x, t), t) \quad \text{for a.e. } (x, t) \in \mathbb{R}^N \times [0, \infty). \end{aligned}$$

In section 4.6 we prove our key result, the strong convergence of  $r_{n_k}$ :

$$r_{n_k} \rightarrow r \text{ in } L_{\text{loc}}^2(\mathbb{R}^N \times [0, \infty)) \text{ as } k \rightarrow \infty. \quad (18)$$

This implies the strong convergence of the sequences

$$u_{n_k} = r_{n_k} w_{n_k} \quad \text{and} \quad v_{n_k} = (1 - r_{n_k}) w_{n_k}$$

to their limits and allows us to pass to the limit in the equations for  $u_n$  and  $v_n$ . Hence the limit function  $(u, v)$  is a solution of problem (P) and in section 4.7 we show that it satisfies the segregation property (1).

## 4.2. Nearly incompressible velocity field

We need some more concepts from the theory of transport equations. Details can be found in the review paper [10] by De Lellis.

DEFINITION 4.3. (Definition 3.6 in [10]) We say that a bounded velocity field  $b$  is *nearly incompressible* if there exists a function  $\eta \in L^\infty(\mathbb{R}^N \times [0, \infty))$  and a positive constant  $C$  such that  $C \leq \eta \leq C^{-1}$  and

$$\eta_t + \text{div}(\eta b) = 0$$

in the sense of distributions.

Let  $w_n$  be defined as above, let  $X_n(y, t)$  be the smooth characteristics induced by the velocity field  $b_n = -\nabla w_n$ , and let  $J_n(y, t)$  be the Jacobian matrix  $\{(X_{ni})_{y_j}\}$ . Let  $T > 0$  be arbitrary. We set

$$\rho_n(x, t) = |\det(J_n^{-1}(x, t))| \quad \text{for } (x, t) \in \bar{B}_n \times [0, T].$$

Arguing as in (7),

$$0 < a_T \leq |\det J_n(y, t)| \leq a_T^{-1} \quad \text{in } B_n \times (0, T)$$

for some constant  $a_T$  which does not depend on  $n$ . Since

$$J_n^{-1}(x, t) = (J_n(y, t))^{-1} \quad \text{and} \quad \det J_n(y, t) \cdot \det((J_n(y, t))^{-1}) = 1,$$

it follows that for all  $n \in \mathbb{N}$

$$0 < a_T \leq \rho_n \leq a_T^{-1} \quad \text{in } B_n \times (0, T). \tag{19}$$

It is well-known that  $\rho_n(x, t)$  satisfies the continuity equation:

$$\begin{cases} (\rho_n)_t = \operatorname{div}(\rho_n \nabla w_n) & \text{in } B_n \times [0, \infty), \\ \rho_n(x, 0) = 1 & \text{in } B_n, \end{cases} \tag{20}$$

(see for example [3], Proposition 2.1; it is enough to use the weak formulation of the continuity equation and to change variables,  $y = X_n^{-1}$ , in the integrals).

Let  $w$  be the limit of  $w_{n_k}$  defined by (14). Along a subsequence  $\rho_{n_k}$  converges weakly\* to some  $\rho \in L^\infty(\mathbb{R}^N \times (0, T))$ , and, by (14),

$$\begin{cases} \rho_t = \operatorname{div}(\rho \nabla w) & \text{in } \mathbb{R}^N \times (0, \infty), \\ \rho(x, 0) = 1 & \text{in } x \in \mathbb{R}^N \end{cases}$$

in the sense of distributions. We will see below that  $\rho$  is uniquely defined so that the whole sequence  $\rho_{n_k}$  converges. Since also

$$a_T \leq \rho \leq a_T^{-1} \quad \text{a.e. in } \mathbb{R}^N \times [0, T], \tag{21}$$

$\rho$  satisfies Definition 4.3 with  $b = -\nabla w$ , whence  $b$  is a nearly incompressible velocity field. The function  $\rho$  is called the *density induced by  $b$* .

### 4.3. Renormalization property

The  $r_n$  is a smooth solution of the transport equation

$$\begin{cases} r_{nt} = \nabla r_n \cdot \nabla w_n + r_n(1 - r_n)G(r_n, w_n) & \text{in } B_n \times (0, T), \\ r_n(x, 0) = r_{0n} & \text{in } B_n, \end{cases}$$

or, equivalently (by (20)),

$$\begin{cases} (r_n \rho_n)_t = \operatorname{div}(r_n \rho_n \nabla w_n) + \rho_n r_n (1 - r_n) G(r_n, w_n) & \text{in } B_n \times (0, T), \\ [r_n \rho_n](x, 0) = r_{0n} & \text{in } B_n. \end{cases}$$

By the chain rule, the solution  $r_n$  also satisfies

$$\begin{cases} \beta(r_n)_t = \nabla \beta(r_n) \cdot \nabla w_n + \beta'(r_n) r_n (1 - r_n) G(r_n, w_n) & \text{in } B_n \times (0, T), \\ r_n(x, 0) = r_{0n} & \text{in } B_n, \end{cases}$$

or, equivalently,

$$\begin{cases} (\beta(r_n) \rho_n)_t = \operatorname{div}(\beta(r_n) \rho_n \nabla w_n) + \beta'(r_n) \rho_n r_n (1 - r_n) G(r_n, w_n) & \text{in } B_n \times (0, T), \\ [\beta(r_n) \rho_n](x, 0) = r_{0n} & \text{in } B_n. \end{cases}$$

If the transport equation is satisfied in the sense of distributions, we cannot use the chain rule and we need the concept of renormalization property.

DEFINITION 4.4. (Extended version of Definition 3.9 in [10]) We say that the bounded nearly incompressible velocity field  $b$  with density  $\eta$  has the *renormalization property* if for all  $c \in L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$  and  $q \in L^\infty_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$  such that

$$(q\eta)_t + \operatorname{div}(b\eta q) = c\eta$$

in the sense of distributions,  $\beta(q)$  satisfies

$$(\beta(q)\eta)_t + \operatorname{div}(b\eta\beta(q)) = c\eta\beta'(q)$$

in the sense of distributions for all  $\beta \in C^1(\mathbb{R})$ .

It follows essentially from the results by Di Perna and Lions ([11]) that "the Sobolev regularity" of  $b$ , implies that  $b$  has the renormalization property. A more precise reference can be found in [4]: Remark 4.5 on page 1646 explains how to use the absolute continuity of  $\operatorname{div} b$  with respect to the Lebesgue measure to obtain the version of the renormalization property which we use in this paper (Remark 4.5 treats the case  $c = 0$ , but it can be easily extended to the case  $c \neq 0$ ).

#### 4.4. Strong convergence of regular Lagrangian flows

The fact that  $b(x, t) = -\nabla w(x, t)$  is a nearly incompressible velocity field with the renormalization property makes it possible to apply several results proved in [10].

PROPOSITION 4.5. (Theorem 3.22 in [10]) *Let  $b$  a bounded nearly incompressible velocity field with the renormalization property. Then there exists a unique regular Lagrangian flow  $\Phi$  for  $b$ . Moreover, let  $b_n$  be a sequence of bounded nearly incompressible velocity fields with renormalization property such that*

- (i)  $\{b_n\}$  is uniformly bounded in  $L^\infty(\mathbb{R}^N \times (0, \infty); \mathbb{R}^N)$  and  $b_n \rightarrow b$  strongly in  $L^1_{\text{loc}}(\mathbb{R}^N \times (0, \infty); \mathbb{R}^N)$ ;
- (ii) the densities  $\eta_n$  generated by  $b_n$  satisfy  $\limsup_n (\|\eta_n\|_\infty + \|\eta_n^{-1}\|_\infty) < \infty$ .

Then the regular Lagrangian flows  $\Phi_n$  generated by  $b_n$  converge to  $\Phi$  in  $L^1_{\text{loc}}(\mathbb{R}^N \times (0, \infty); \mathbb{R}^N)$ .

**COROLLARY 4.6.** (Corollary 3.15 in [10]) *Let  $\bar{\zeta} \in L^\infty(\mathbb{R}^N)$ . If  $b$  is a bounded nearly incompressible velocity field with the renormalization property, then there exists a unique bounded distributional solution  $\zeta$  of*

$$\begin{cases} \zeta_t + \text{div}(\zeta b) = 0, \\ \zeta(\cdot, 0) = \bar{\zeta}. \end{cases}$$

Moreover, if  $\bar{\zeta}$  is bounded away from zero, so is  $\zeta$ .

By Proposition 4.5  $b = -\nabla w$  induces a unique regular Lagrangian flow  $X(y, t)$  and

$$X_{n_k} \rightarrow X \text{ in } L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty)) \text{ as } k \rightarrow \infty \tag{22}$$

(due to the local character of the convergence it is not a problem that  $b_n$  is not defined in all of  $\mathbb{R}^N$ ).

By Corollary 4.6 the density  $\rho$  induced by  $b$  is uniquely determined. Therefore, the convergence of  $\rho_{n_k}$  does not depend on subsequences, as was announced before.

**4.5. Strong convergence in  $(y, t)$ -variables: proof of (17)**

In this subsection, we prove (17), that is,

$$R_{n_k} \rightarrow R \text{ in } L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty)) \text{ as } k \rightarrow \infty.$$

The key ingredient is (22), the convergence of the regular Lagrangian flow.

We set

$$W_{n_k}(y, t) := w_{n_k}(X_{n_k}(y, t), t) \text{ for } (y, t) \in \bar{B}_{n_k} \times \mathbb{R}^+,$$

$$W(y, t) := w(X(y, t), t) \text{ for a.e } (y, t) \in \mathbb{R}^N \times \mathbb{R}^+.$$

First we prove that

$$W_{n_k} \rightarrow W \text{ in } L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty)) \text{ as } n_k \rightarrow \infty. \tag{23}$$

Let  $T, \mathcal{R} > 0$  and let  $k$  be so large that  $n_k > \mathcal{R} > 0$ . Then

$$\iint_{B_{\mathcal{R}} \times (0, T)} |W_{n_k}(y, t) - W(y, t)| dy dt \leq I_{1k} + I_{2k},$$

where

$$I_{1k} := \iint_{B_{\mathcal{R}} \times (0, T)} |w_{n_k}(X_{n_k}(y, t), t) - w(X_{n_k}(y, t), t)| dy dt$$

$$I_{2k} := \iint_{B_{\mathcal{R}} \times (0, T)} |w(X_{n_k}(y, t), t) - w(X(y, t), t)| dy dt.$$

Since, by (19), the densities  $\rho_{n_k}$  are uniformly bounded in  $B_{n_k} \times (0, T)$  and  $w_{n_k}$  and  $w$  are uniformly bounded in  $Q_T$ , we have that

$$\begin{aligned} I_{1k} &\leq \iint_{B_{\mathcal{B}+TC_T} \times (0, T)} |w_{n_k}(x, t) - w(x, t)| \rho_{n_k}(x, t) dx dt \\ &\leq a_T^{-1} \iint_{B_{\mathcal{B}+TC_T} \times (0, T)} |w_{n_k}(x, t) - w(x, t)| dx dt. \end{aligned}$$

Hence, by (14),  $I_{1k} \rightarrow 0$  as  $k \rightarrow \infty$ . Since  $w$  is Lipschitz continuous in  $x$  on  $B_{\mathcal{B}}$ , it follows from (22) that  $I_{2k} \rightarrow 0$  as  $k \rightarrow \infty$ . So we have proved (23).

We recall (see (3)) that  $R_n(y, t) := r_n(X_n(y, t), t)$  satisfies

$$\begin{cases} R_{nt} = R_n(1 - R_n)G(R_n, W_n) & \text{in } B_n \times \mathbb{R}^+, \\ R_n(y, 0) = r_{0n}(y) & \text{for } y \in B_n. \end{cases}$$

We must prove that  $R_{n_k}$  converges in  $L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$  to the solution  $R$  of

$$\begin{cases} R_t = R(1 - R)G(R, W) & \text{in } \mathbb{R}^N \times \mathbb{R}^+, \\ R(y, 0) = r_0(y) & \text{for } y \in \mathbb{R}^N. \end{cases}$$

Setting

$$h(s, y, t) = s(1 - s)G(s, W(y, t)), \quad h_k(s, y, t) = s(1 - s)G(s, W_{n_k}(y, t)),$$

we have that

$$(R_{n_k} - R)_t = h_k(R_{n_k}, y, t) - h(R_{n_k}, y, t) + h(R_{n_k}, y, t) - h(R, y, t).$$

Observe that

$$\begin{aligned} |h_{n_k}(R_{n_k}, y, t) - h(R_{n_k}, y, t)| &= \tilde{h}(R_{n_k}) |W_{n_k}(y, t) - W(y, t)| \\ &\leq C_1 |W_{n_k}(y, t) - W(y, t)|, \end{aligned}$$

where  $\tilde{h}(R) = |(\gamma\beta - 1)R + (\gamma/k - \alpha)(1 - R)|$ , and

$$|h(R_{n_k}, y, t) - h(R, y, t)| \leq C_2 |R_{n_k} - R|.$$

Therefore

$$(e^{-C_2 t} |R_{n_k} - R|)_t \leq C_1 e^{-C_2 t} |W_{n_k} - W| \leq C_1 |W_{n_k} - W|$$

and

$$|R_{n_k}(y, t) - R(y, t)| \leq e^{C_2 t} |r_{0n_k}(y) - r_0(y)| + C_1 e^{C_2 t} \int_0^t |W_{n_k}(y, \tau) - W(y, \tau)| d\tau.$$

Since  $r_{0n} \rightarrow r_0$  in  $L^1_{\text{loc}}(\mathbb{R}^N)$ , (23) implies the convergence of  $R_{n_k}$  to  $R$  in  $L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$  and we have proved (17).

#### 4.6. Strong convergence in $(x, t)$ -variables: proof of (18)

In this subsection we use the strong convergence of  $R_{n_k}(y, t)$  to prove the strong convergence of  $r_{n_k}(x, t)$ .

Let  $Y_n(x, t)$  be the inverse of  $X_n(y, t)$ , that is  $Y_n(X_n(y, t), t) = y$  in  $\bar{B}_n \times [0, T]$ . Since  $Y_n$  is constant along the characteristics  $X_n$ , each of its components satisfies the transport equation

$$\begin{cases} ((Y_n)_i)_t = \nabla(Y_n)_i \cdot \nabla w_n & \text{in } B_n \times (0, T), \\ (Y_n)_i(x, 0) = x_i & \text{in } x \in B_n, \end{cases}$$

or, equivalently,

$$\begin{cases} (\rho_n(Y_n)_i)_t = \operatorname{div}((Y_n)_i \rho_n \nabla w_n) & \text{in } B_n \times (0, T), \\ [(Y_n)_i \rho_n](x, 0) = x_i & \text{in } x \in B_n, \end{cases}$$

where  $\rho_n$  are the densities induced by  $b_n$ .

Similarly, we define  $Y(x, t)$  as the inverse of  $X(y, t)$  in  $\mathbb{R}^N \times (0, T)$ . We will show that it satisfies the problem

$$\begin{cases} (\rho Y)_t = \operatorname{div}(Y \rho \nabla w) & \text{in } \mathbb{R}^N \times (0, T), \\ [Y \rho](x, 0) = x_i & \text{in } x \in \mathbb{R}^N, \end{cases} \quad (24)$$

where  $\rho$  is the density of the regular Lagrangian flow  $X(y, t)$  induced by  $-\nabla w$ . The existence of a solution of (24) follows from the following result.

**PROPOSITION 4.7.** (Proposition 3.13 in [10]) *Assume that  $b$  is a bounded nearly incompressible velocity field and  $\eta \geq 0$  be the density induced by  $b$ . Then for every bounded  $\bar{u}$  and  $\bar{\eta}$  there exists a unique solution of*

$$\begin{cases} (\eta u)_t + \operatorname{div}(u \eta b) = 0, \\ [u \eta](0, \cdot) = \bar{u} \bar{\eta}. \end{cases}$$

It follows from Proposition 4.7 that the limit equation has a solution  $Y$ , i.e. for all  $i = 1, \dots, N$  there exists a solution  $Y_i$  satisfying the transport equation (24). The following result gives us the convergence of  $Y_n$  to  $Y$ .

**PROPOSITION 4.8.** (Corollary 3.20 in [10]) *Let  $\{b_n\}$ ,  $b \in L^\infty(\mathbb{R}^N \times [0, \infty); \mathbb{R}^N)$ ,  $\{\zeta_n\}$ ,  $\zeta$ ,  $\{u_n\}$ ,  $u \in L^\infty(\mathbb{R}^N \times [0, \infty))$  and  $\{\bar{u}_n\}$ ,  $\bar{u} \in L^\infty(\mathbb{R}^N)$  be such that*

- (i)  $\zeta, \zeta_n > 0$ ,  $\zeta^{-1}, \zeta_n^{-1} \in L^\infty$  and  $\|\zeta_n\|_\infty + \|\zeta_n^{-1}\|_\infty + \|\bar{u}_n\|_\infty$  is uniformly bounded;
- (ii)  $\{b_n\}$  and  $b$  have the renormalization property and  $b_n \rightarrow b$  in  $L^1_{\text{loc}}$ ;
- (iii)  $\zeta_t + \operatorname{div}(\zeta b) = \zeta_{n_t} + \operatorname{div}(\zeta_n b_n) = 0$ ;
- (iv)  $u_n$  and  $u$  are the unique solutions of

$$\begin{cases} (\zeta_n u_n)_t + \operatorname{div}(\zeta_n u_n b_n) = 0, & \begin{cases} (\zeta u)_t + \operatorname{div}(\zeta u b) = 0, \\ [\zeta u](\cdot, 0) = \zeta(\cdot, 0) \bar{u}. \end{cases} \\ [\zeta_n u_n](\cdot, 0) = \zeta_n(\cdot, 0) \bar{u}_n, & \end{cases}$$

If  $\zeta_n(\cdot, 0) \rightharpoonup^* \zeta(\cdot, 0)$  in  $L^\infty$  and  $\bar{u}_n \rightarrow \bar{u}$  in  $L^1_{\text{loc}}$ , then  $u_n \rightarrow u$  in  $L^1_{\text{loc}}$ .

By this stability result for transport equations,  $Y_n$  converges strongly to  $Y$  in  $L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$  as  $n \rightarrow \infty$ .

As we observed in Remark 4.2,  $Y$  can be regarded as a backward Lagrangian flow: starting from  $(x, t)$  we follow the flow back to arrive at  $y$  at time  $t = 0$ . Also the backward Lagrangian flow is regular, in particular the function  $(x, t) \mapsto f(Y(x, t), t)$  belongs to  $L^\infty_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$  for all  $f \in L^\infty_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$ .

We set

$$\begin{aligned} r(x, t) &:= R(Y(x, t), t) \quad \text{for a.e. } (x, t) \in \mathbb{R}^N \times [0, T), \\ r_n(x, t) &:= R_n(Y_n(x, t), t) \quad \text{for } (x, t) \in B_n \times [0, T). \end{aligned}$$

**PROPOSITION 4.9.** (Extended version of Proposition 3.5 in [10]) *Let  $\Phi$  be a regular Lagrangian flow for the velocity field  $b$  with density  $\eta \in L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$ : for all  $\psi \in L^\infty(\mathbb{R}^N \times \mathbb{R}^+)$  with bounded support*

$$\iint_{\mathbb{R}^N \times \mathbb{R}^+} \psi(\Phi(y, t), t) dy dt = \iint_{\mathbb{R}^N \times \mathbb{R}^+} \psi(x, t) \eta(x, t) dx dt.$$

(i) *Let  $\bar{\zeta} \in L^\infty(\mathbb{R}^N)$  and  $c \in L^\infty(\mathbb{R}^N \times [0, \infty))$ , and let the measure  $\mu$  on  $\mathbb{R}^N \times \mathbb{R}^+$  be such that for all  $\varphi \in L^\infty(\mathbb{R}^N \times \mathbb{R}^+)$  with bounded support*

$$\iint \varphi(x, t) d\mu(x, t) = \iint_{\mathbb{R}^N \times \mathbb{R}^+} \varphi(\Phi(y, t), t) \left( \bar{\zeta}(y) + \int_0^t c(\Phi(y, \tau), \tau) d\tau \right) dy dt.$$

*Then there exists  $\zeta \in L^1_{\text{loc}}(\mathbb{R}^N \times [0, \infty))$  such that  $\mu = \zeta \mathcal{L}^{n+1}$  and  $\zeta$  satisfies the following equation in the sense of distributions:*

$$\begin{cases} \zeta_t + \text{div}(\zeta b) = \eta c & \text{in } \mathbb{R}^N \times \mathbb{R}^+, \\ \zeta(\cdot, 0) = \bar{\zeta} & \text{in } \mathbb{R}^N. \end{cases}$$

(ii) *If  $u \in L^\infty(\mathbb{R}^N \times \mathbb{R}^+)$ ,  $\bar{u} \in L^\infty(\mathbb{R}^N)$  and  $c \in L^\infty(\mathbb{R}^N \times [0, \infty))$  satisfy*

$$u(\Phi(y, t), t) = \bar{u}(y) + \int_0^t c(\Phi(y, \tau), \tau) d\tau \quad \text{for a.e. } (y, t),$$

*then the following equation holds in the sense of distributions:*

$$\begin{cases} (\eta u)_t + \text{div}(u \eta b) = \eta c & \text{in } \mathbb{R}^N \times \mathbb{R}^+, \\ [u \eta](\cdot, 0) = \bar{u} & \text{in } \mathbb{R}^N. \end{cases}$$

This result generalizes Proposition 3.5 in [10] to the case  $c \neq 0$ . For the sake of completeness we give the proof in the appendix.

Applying Proposition 4.9 to

$$\begin{aligned} u(x, t) &:= r(x, t), \quad b := -\nabla w, \quad \eta := \rho \quad \text{and} \\ c(x, t) &:= r(x, t)(1 - r(x, t))G(r(x, t), w(x, t)), \end{aligned}$$



we deduce that  $r$  is a distributional solution of the transport equation

$$\begin{cases} (\rho r)_t = \operatorname{div}(r\rho\nabla w) + \rho r(1-r)G(r,w) & \text{in } \mathbb{R}^N \times (0, \infty), \\ [r\rho](\cdot, 0) = r_0 & \text{in } \mathbb{R}^N. \end{cases} \quad (25)$$

Finally, we prove the strong convergence (18) of  $r_{n_k}$  to  $r$ . Recalling that

$$\begin{cases} (\rho_n r_n)_t = \operatorname{div}(r_n \rho_n \nabla w_n) + \rho_n r_n (1 - r_n) G(r_n, w_n) & \text{in } B_n \times (0, \infty), \\ [r_n \rho_n](\cdot, 0) = r_{0n} & \text{in } B_n, \end{cases}$$

we first prove that

$$r_{n_k} \rho_{n_k} \text{ converges weakly to } r\rho \text{ as } k \rightarrow \infty$$

and

$$\rho_{n_k} c_{n_k} \text{ converges weakly to } \rho c \text{ as } k \rightarrow \infty,$$

where  $c_n := r_n(1 - r_n)G(r_n, w_n)$  and  $c := r(1 - r)G(r, w)$ .

Let  $\varphi(x, t)$  be a smooth test function with bounded support. Then, by the strong convergence of  $R_{n_k}$  and  $X_{n_k}$  as  $k \rightarrow \infty$ ,

$$\begin{aligned} \iint_{\mathbb{R}^N \times \mathbb{R}^+} R_{n_k}(y, t) \varphi(X_{n_k}(y, t), t) dy dt &\rightarrow \iint_{\mathbb{R}^N \times \mathbb{R}^+} R(y, t) \varphi(X(y, t), t) dy dt \\ &= \iint_{\mathbb{R}^N \times \mathbb{R}^+} r(x, t) \varphi(x, t) \rho(x, t) dx dt. \end{aligned}$$

On the other hand, let  $\xi$  be the weak limit of  $r_{n_k} \rho_{n_k}$  (up to subsequences). Then

$$\begin{aligned} \iint_{\mathbb{R}^N \times \mathbb{R}^+} R_{n_k}(y, t) \varphi(X_{n_k}(y, t), t) dy dt &= \iint_{\mathbb{R}^N \times \mathbb{R}^+} r_{n_k}(x, t) \varphi(x, t) \rho_{n_k}(x, t) dx dt \\ &\rightarrow \iint_{\mathbb{R}^N \times \mathbb{R}^+} \xi(x, t) \varphi(x, t) dx dt \end{aligned}$$

and hence  $\xi = r\rho$ .

Next, let  $\chi$  be the weak limit of  $\rho_{n_k} c_{n_k}$ . Taking the limit in

$$(\rho_{n_k} r_{n_k})_t = \operatorname{div}(r_{n_k} \rho_{n_k} \nabla w_{n_k}) + \rho_{n_k} c_{n_k} \text{ (in the sense of distributions),}$$

we find that

$$(\rho r)_t = \operatorname{div}(r\rho\nabla w) + \chi \text{ (in the sense of distributions).}$$

But we already know that

$$(\rho r)_t = \operatorname{div}(r\rho\nabla w) + \rho c \text{ (in the sense of distributions),}$$

so that  $\chi = \rho c$ .

We repeat this procedure, replacing  $r_{n_k}$  by  $r_{n_k}^2$ . Since the strong convergence of  $R_{n_k}$  implies the strong convergence of  $R_{n_k}^2$ ,

$$\begin{aligned} \iint_{\mathbb{R}^N \times \mathbb{R}^+} R_{n_k}^2(y, t) \varphi(X_{n_k}(y, t), t) dy dt &\rightarrow \iint_{\mathbb{R}^N \times \mathbb{R}^+} R^2(y, t) \varphi(X(y, t), t) dy dt \\ &= \iint_{\mathbb{R}^N \times \mathbb{R}^+} r^2(x, t) \varphi(x, t) \rho(x, t) dx dt. \end{aligned}$$

On the other hand, let  $\tilde{\xi}$  be the weak limit of  $r_{n_k}^2 \rho_{n_k}$ . Then,

$$\begin{aligned} \iint_{\mathbb{R}^N \times \mathbb{R}^+} R_{n_k}^2(y, t) \varphi(X_{n_k}(y, t), t) dy dt &= \iint_{\mathbb{R}^N \times \mathbb{R}^+} r_{n_k}^2(x, t) \varphi(x, t) \rho_{n_k}(x, t) dx dt \\ &\rightarrow \iint_{\mathbb{R}^N \times \mathbb{R}^+} \tilde{\xi}(x, t) \varphi(x, t) dx dt. \end{aligned}$$

Therefore,  $\tilde{\xi} = r^2 \rho$  and

$$r_{n_k}^2 \rho_{n_k} \text{ converges weakly to } r^2 \rho \text{ as } n_k \rightarrow \infty.$$

Finally we consider

$$\rho_{n_k}(r_{n_k} - r)^2 = \rho_{n_k} r_{n_k}^2 + \rho_{n_k} r^2 - 2\rho_{n_k} r_{n_k} r.$$

We deduce from the weak convergences above that, for any test function  $\varphi \in C^\infty(\mathbb{R}^N \times \mathbb{R}^+)$  with bounded support,

$$\begin{aligned} \iint_{\mathbb{R}^N \times \mathbb{R}^+} \rho_{n_k}(r_{n_k} - r)^2 \varphi &= \iint_{\mathbb{R}^N \times \mathbb{R}^+} (\rho_{n_k} r_{n_k}^2 + \rho_{n_k} r^2 - 2\rho_{n_k} r_{n_k} r) \varphi \\ &\rightarrow \iint_{\mathbb{R}^N \times \mathbb{R}^+} (\rho r^2 + \rho r^2 - 2\rho r^2) \varphi = 0 \end{aligned}$$

as  $k \rightarrow \infty$ . Since  $\rho_{n_k} \geq a_T > 0$ , this implies that  $r_{n_k}$  strongly converges to  $r$  in  $L^2_{\text{loc}}(\mathbb{R}^N \times (0, \infty))$ .

#### 4.7. Solution of problem (P); segregation property

In the previous subsection we have proved that  $r_{n_k} \rightarrow r$  in  $L^2_{\text{loc}}(\mathbb{R}^N \times (0, \infty))$ . Since also  $w_{n_k} \rightarrow w$  in  $L^2_{\text{loc}}(\mathbb{R}^N \times (0, \infty))$ , we have that

$$u_{n_k} := r_{n_k} w_{n_k} \rightarrow u := r w \quad \text{in } L^1_{\text{loc}}(\mathbb{R}^N \times (0, \infty)) \quad \text{as } k \rightarrow \infty$$

and

$$v_{n_k} := (1 - r_{n_k}) w_{n_k} \rightarrow u := (1 - r) w \quad \text{in } L^1_{\text{loc}}(\mathbb{R}^N \times (0, \infty)) \quad \text{as } k \rightarrow \infty.$$

Since  $(u_{n_k}, v_{n_k})$  is a solution of problem  $(P_{B_{n_k}})$ , we may pass to the limit in the equations for  $u_{n_k}$  and  $v_{n_k}$  to conclude that  $(u, v)$  is a solution of problem (P) in the sense of Definition 3.1.

The proof of the segregation property (1) follows at once for the ODE for  $R(y, t)$ . Initial segregation,  $u_0 v_0 = 0$  a.e. in  $\mathbb{R}^N$  is equivalent to  $r_0(1 - r_0) = 0$  a.e. in  $\mathbb{R}^N$ . By the equation for  $R$  (see (3)),  $R(1 - R)$  satisfies

$$\begin{cases} (R(1 - R))_t = R(1 - R)(1 - 2R)G(R, W) & \text{in } \mathbb{R}^N \times (0, \infty), \\ (R(1 - R))(y, 0) = 0 & \text{in } \mathbb{R}^N. \end{cases}$$

Since  $R$  and  $W$  are uniformly bounded, it follows from Gronwall's inequality that  $R(y, t)(1 - R(y, t)) = 0$  for all  $t > 0$  and a.e.  $y \in \mathbb{R}^N$ , whence  $u(x, t)v(x, t) = 0$  for all  $t > 0$  and a.e.  $x \in \mathbb{R}^N$ .

### 5. Appendix: Proof of Proposition 4.9

We proceed as in [10]. For any Borel set  $A \subset \Omega \times (0, T)$ , with characteristic function  $\chi_A$ ,

$$\begin{aligned} |\mu(A)| &= \left| \iint_{\mathbb{R}^N \times \mathbb{R}^+} \left( \bar{\zeta}(y) + \int_0^t c(\Phi(y, \tau), \tau) d\tau \right) \chi_A(\Phi(y, t), t) dy dt \right| \\ &\leq (\|\bar{\zeta}\|_\infty + \|c\|_\infty T) \iint_A \eta(x, t) dx dt, \end{aligned}$$

and, since  $\eta \in L^1$ ,  $\mu$  is absolutely continuous with respect to the Lebesgue measure and there exists  $\zeta$  such that  $\mu = \zeta L^{n+1}$ .

Let  $\psi \in C^\infty(\mathbb{R}^N \times [0, \infty))$  be a test function with bounded support. We must show that

$$\begin{aligned} \iint_{\mathbb{R}^N \times \mathbb{R}^+} (\psi_t(x, t) + b(x, t) \cdot \nabla \psi(x, t)) \zeta(x, t) dx dt \\ = - \iint_{\mathbb{R}^N \times \mathbb{R}^+} c \eta \psi dx dt - \int_{\mathbb{R}^N} \bar{\zeta}(x) \psi(x, 0) dx. \end{aligned}$$

By hypothesis, the left hand side is equal to

$$\iint_{\mathbb{R}^N \times \mathbb{R}^+} \left( \bar{\zeta}(y) + \int_0^t c(\Phi(y, \tau), \tau) d\tau \right) [\psi_t + b \cdot \nabla \psi](\Phi(y, t), t) dy dt.$$

For any  $y$  for which Lemma 3.2 in [10] holds

$$\psi_t(\Phi(y, t), t) + b(\Phi(y, t), t) \cdot \nabla \psi(\Phi(y, t), t) = \frac{d}{dt}(\psi(\Phi(y, t), t))$$

and integrating by parts we obtain that

$$\begin{aligned} \iint_{\mathbb{R}^N \times \mathbb{R}^+} \left( \bar{\zeta}(y) + \int_0^t c(\Phi(y, \tau), \tau) d\tau \right) [\psi_t + b \cdot \nabla \psi](\Phi(y, t), t) dy dt \\ = \iint_{\mathbb{R}^N \times \mathbb{R}^+} \left( \bar{\zeta}(y) + \int_0^t c(\Phi(y, \tau), \tau) d\tau \right) \frac{d}{dt}(\psi(\Phi(y, t), t)) dy dt \\ = - \int_{\mathbb{R}^N} \bar{\zeta}(y) \psi(\Phi(y, 0), 0) dy - \iint_{\mathbb{R}^N \times \mathbb{R}^+} c(\Phi(y, t), t) \psi(\Phi(y, t), t) dy dt \\ = - \int_{\mathbb{R}^N} \bar{\zeta}(x) \psi(x, 0) dx - \iint_{\mathbb{R}^N \times \mathbb{R}^+} c(x, t) \psi(x, t) \eta(x, t) dx dt. \end{aligned}$$

This completes the proof (i).

Let  $u$  and  $\bar{u}$  be as in (ii). Set  $\bar{\zeta} := \bar{u}$  and  $\zeta := u\eta$ . For every  $L^\infty$  function  $\varphi$  with bounded support we have that

$$\begin{aligned} & \iint_{\mathbb{R}^N \times \mathbb{R}^+} u(x,t)\eta(x,t)\varphi(x,t)dxdt \\ &= \iint_{\mathbb{R}^N \times \mathbb{R}^+} u(\Phi(y,t),t)\varphi(\Phi(y,t),t)dydt \\ &= \iint_{\mathbb{R}^N \times \mathbb{R}^+} \left( \bar{u}(y) + \int_0^t c(\Phi(y,t),\tau)d\tau \right) \varphi(\Phi(y,t),t)dydt, \end{aligned}$$

and the proof follows immediately from (i).

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## REFERENCES

- [1] M. ABERCROMBIE, *Contact inhibition in tissue culture, In Vitro*, **6** (1970), 128–142.
- [2] L. AMBROSIO, *Transport equations and Cauchy problem for BV vector fields*, *Invent. Math.*, **158** (2004), 227–260.
- [3] L. AMBROSIO, *Transport equation and Cauchy problem for non-smooth vector fields*, in: *Calculus of Variations and Non-Linear Partial Differential Equations*, eds. B. Dacorogna, P. Marcellini, *Lect. Notes Math.*, 1927 (2008), Springer, Berlin-Heidelberg.
- [4] L. AMBROSIO, F. BOUCHUT AND C. DE LELLIS, *Well-posedness for a class of hyperbolic systems of conservation laws in several space dimensions*, *Comm. Partial Diff. Equ.*, **29** (2004), 1635–1651.
- [5] M. BERTSCH, R. DAL PASSO AND M. MIMURA, *A free boundary problem arising in a simplified tumour growth model of contact inhibition*, *Interfaces Free Boundaries*, **12** (2010), 235–250.
- [6] M. BERTSCH, M. E. GURTIN AND D. HILHORST, *On a degenerate diffusion equation of the form  $c(z)_t = \varphi(z_x)_x$  with application to population dynamics*, *Journal Differential Equations*, **30** (1987), 56–89.
- [7] M. BERTSCH, M. E. GURTIN AND D. HILHORST, *On interacting populations that disperse to avoid crowding: the case of equal dispersal velocities*, *Nonlinear Analysis TMA*, **11** (1987), 493–499.
- [8] M. BERTSCH, M. E. GURTIN, D. HILHORST AND L. A. PELETIER, *On interacting populations that disperse to avoid crowding: preservation of segregation*, *Journal Mathematical Biology*, **23** (1985), 1–13.
- [9] M. CHAPLAIN, L. GRAZIANO AND L. PREZIOSI, *Mathematical modelling of the loss of tissue compression responsiveness and its role in solid tumour development*, *Math. Med. Biol.*, **23** (2006), 197–229.
- [10] C. DE LELLIS, *Notes on hyperbolic systems of conservation laws and transport equations*, *Handbook of Differential Equations: Evolutionary Differential Equations*, (2006), 277–383.
- [11] R. DI PERNA AND P.-L. LIONS, *Ordinary differential equations, transport theory and Sobolev spaces*, *Invent. Math.*, **98** (1989), 511–517.

- [12] J. DUGUNDJI AND A. GRANAS, *Fixed Point Theory Volume I*, PWN-Polish scientific publishers, 1982.
- [13] M. E. GURTIN, R. C. MACCAMY AND E. A. SOCOLOVSKY, *A coordinate transformation for the porous media equation that renders the free-boundary stationary*, Quart. Appl. Math., **42** (1984), 345–357.
- [14] J. HALE, *Ordinary Differential Equations*, Krieger publishing company, 1980.
- [15] O. A. LADYZHENSKAYA, V. A. SOLONNIKOV AND N. N. URAL'CEVA, *Linear and quasilinear equations of parabolic type*, Transl. Math. Monographs, **23**, Amer. Math. Soc., Providence, R.I., 1968.
- [16] G. M. LIEBERMAN, *Second order parabolic differential equations*, World Scientific Publishing Co., 1996.

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