Space dependent adhesion forces mediated by transient elastic linkages : new convergence and global existence results

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Abstract

In the first part of this work we show the convergence with respect to an asymptotic parameter ε of a delayed heat equation. It represents a mathematical extension of works considered previously by the authors [14, 15, 16]. Namely, this is the first result involving delay operators approximating protein linkages coupled with a spatial elliptic second order operator. For the sake of simplicity we choose the Laplace operator, although more general results could be derived. The main arguments are (i) new energy estimates and (ii) a stability result extended from the previous work to this more involved context. They allow to prove convergence of the delay operator to a friction term together with the Laplace operator in the same asymptotic regime considered without the space dependence in [14]. In a second part we extend fixed-point results for the fully non-linear model introduced in [16] and prove global existence in time. This shows that the blow-up scenario observed previously does not occur. Since the latter result was interpreted as a rupture of adhesion forces, we discuss the possibility of bond breaking both from the analytic and numerical point of view.

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1. Introduction

1.1. Biological and mathematical settings

Cell migration is an ubiquitous process underlying morphogenesis, wound healing and cancer, among other biological phenomena [3]. Leading-edge protrusion on flat surfaces - the first step in cell crawling - relies on continuous remodeling of a cytoskeletal structure called the lamellipodium [22], a broad and flat network of actin filaments.

Comprehensive modeling efforts were initiated in 1996 and fall into two groups. The first group includes continuum models for the mechanical behaviour of cytoplasm [1, 24]. The second group makes assumptions about the microscopic organization of the actin network [18, 21]. In an attempt to create a framework that addresses the interplay of macroscopic features of cell migration and the meshwork structure, the Filament Based Lamellipodium Model has been developed. It is a two-dimensional, two-phase, anisotropic continuum model for the dynamics of the lamellipodium network which retains key directional information on the filamentous substructure of this meshwork [20, 12, 13].

The model has been derived from a microscopic description based on the dynamics and interaction of individual filaments [19], and it has by recent extensions [13] reached a certain state of maturity. The main unknowns of the model are the positions of the actin filaments in two locally parallel families. The filaments are submitted to various forces: bending, twisting, in-extensibility, pressure, stretching and adhesion. These two latter mechanisms, that stabilize the whole filament network, are at the heart of our project. In [19], a formal derivation leaded to the expression of these forces as operators depending on friction terms in the equations denoted instantaneous cross-link/adhesion turnover. The dimensionless parameter ε is the ratio between the reference value for the age of adhesions and the maximal life time of a monomer as part of a filament. This parameter is assumed to be small and the fact that the elasticity is $O(\varepsilon^{-1})$, is a scaling assumption required for a non-vanishing effect of adhesions in the limit $\varepsilon \to 0$. Our works construct various tools in order to handle rigorously this asymptotic [14, 15, 16, 17]. In addition, concerning adhesion forces, a similar Ansatz was performed formally in a somehow different mechanical setting in [23, 8].

In previous works we handled a single point adhesion with respect to the space variable. Indeed our unknown was the position of a unique point in time $z_{\varepsilon}(t)$. In [14] we gave the first result of convergence based on a special Lyapunov functional for the linkages population and a comparison principle generalizing Gronwall's Lemma in the case of integral positive operators. In a second step [15] we found a new formulation of the problem, weakened some of the hypotheses of the first paper and gave a fixed point theorem for a fully non-linear version of our new model. Here we

give a comprehensive extension of convergence results in the weakly coupled setting (see below for a precise explanation) in the case of space dependent adhesion forces coupled with a second order elliptic operator. For the sake of simplicity it is chosen to be the Laplacian, but results presented hereafter could be extended to a broad class of linear div-grad operators with Dirichlet boundary conditions. To our knowledge, this is the first extension made in this direction starting from the initial single point model in [14].

In [16] we considered a fully non-linear coupling for which the death rate of bonds depends on the positions of adhesions. There, we have shown that there could be a blow-up in finite time for well-prepared data. Biologically this could be interpreted as tear-off of bonds, a detachment observed in experiences (cf. [23] and references therein). Here the presence of another term in the force balance prevents the blow-up, global existence in time is obtained without restrictions on the data. If moreover β_{ε} , the birth rate of the bond population admits a strictly positive lower bound $\beta_{\varepsilon} \geq \beta_m > 0$, then one shows that this population actually never becomes extinct and an asymptotic profile is computed. We underline that this latter hypothesis is crucial in many of our theoretical results. In a last step we confront these results with a numerical simulation contradicting this latter hypothesis and show that detachment can occur on compact sets inside the domain.

1.2. A detailed mathematical framework

 Ω denotes an open bounded connected set of \mathbb{R}^n , whose boundary $\partial\Omega$ is $C^{1,1}$ (see for instance Definition 1.2.1.1. [9]). For any fixed time T, the parabolic cylinder is denoted $Q_T := \Omega \times (0,T)$. The position of the moving binding site, $z_{\varepsilon}(\boldsymbol{x},t)$, minimizes at each time $t \geq 0$ an energy functional:

$$z_{\varepsilon}(\boldsymbol{x},t) = \underset{w \in H_0^1(\Omega)}{\operatorname{arg\,min}} \, \mathcal{E}(w), \tag{1.1}$$

the energy being defined for every $w \in H_0^1(\Omega)$ as

$$\mathcal{E}_{t}(w(\cdot)) := \frac{1}{2} \int_{\Omega} \left\{ |\nabla w|^{2} + \int_{\mathbb{R}_{+}} \frac{|w(\boldsymbol{x}) - z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a)|^{2}}{\varepsilon} \rho_{\varepsilon}(\boldsymbol{x}, t, a) da \right\} d\boldsymbol{x}, \qquad (1.2)$$

the second term is a delay operator since the minimisation is performed with respect to past positions $z_{\varepsilon}(\boldsymbol{x},t-\varepsilon a)$. When t<0, these are given by the function $z_{\varepsilon}(\boldsymbol{x},t)=z_{p}(\boldsymbol{x},t)$ for t<0. The age distribution $\rho_{\varepsilon}=\rho_{\varepsilon}(\boldsymbol{x},a,t)$ is the solution of the structured model:

$$\begin{cases}
\varepsilon \partial_t \rho_{\varepsilon} + \partial_a \rho_{\varepsilon} + \zeta_{\varepsilon} \rho_{\varepsilon} = 0, & \boldsymbol{x} \in \Omega, a > 0, t > 0, \\
\rho_{\varepsilon}(\boldsymbol{x}, a = 0, t) = \beta_{\varepsilon}(\boldsymbol{x}, t) \left(1 - \mu_{0, \varepsilon}(\boldsymbol{x}, t)\right), & \boldsymbol{x} \in \Omega, a = 0, t > 0, \\
\rho_{\varepsilon}(\boldsymbol{x}, a, t = 0) = \rho_I(\boldsymbol{x}, a), & \boldsymbol{x} \in \Omega, a > 0, t = 0,
\end{cases} \tag{1.3}$$

where $\mu_{0,\varepsilon}(\boldsymbol{x},t) := \int_0^\infty \rho_{\varepsilon}(\boldsymbol{x},\tilde{a},t) d\tilde{a}$ and the on-rate of bonds is a given function β_{ε} times a factor, that takes into account saturation of the moving binding site with linkages. When the off-rate ζ_{ε} is a prescribed function, we say that the problem is weakly coupled: first one solves ρ_{ε} and then ρ_{ε} is the integral term in (1.2) providing z_{ε} . If instead ζ is a function depending on z_{ε} , or which is more biologically sound (cf. [26, 11]), on the elongation $u_{\varepsilon}(\boldsymbol{x}, a, t) := (z_{\varepsilon}(\boldsymbol{x}, t) - z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a))/\varepsilon$ the problem is said to be fully coupled.

Note that the Euler-Lagrange equation associated to the minimization process is a Volterra equation of the first kind [14] given by

$$\begin{cases}
\mathcal{L}_{\varepsilon}(z_{\varepsilon}, \rho_{\varepsilon}) = \Delta_{\boldsymbol{x}} z_{\varepsilon}, & t \geq 0, \, \boldsymbol{x} \in \Omega, \\
z_{\varepsilon}(\boldsymbol{x}, t) = 0, & t \in \mathbb{R}_{+}, \, \boldsymbol{x} \in \partial \Omega, \\
z_{\varepsilon}(\boldsymbol{x}, t) = z_{p}(\boldsymbol{x}, t), & t < 0, \, \boldsymbol{x} \in \Omega,
\end{cases} \tag{1.4}$$

where $\mathcal{L}_{\varepsilon}(z_{\varepsilon}, \rho_{\varepsilon})(\boldsymbol{x}, t) := \frac{1}{\varepsilon} \int_{\mathbb{R}_{+}} (z_{\varepsilon}(\boldsymbol{x}, t) - z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a)) \rho_{\varepsilon}(\boldsymbol{x}, a, t) da$. It is easy to prove that if z_{ε} solves (1.4) in the variational sense for every time $t \geq 0$, then it minimizes (1.2) and vice-versa (cf Appendix A).

In contrast to the previous results reported in [14, 15, 16], we introduce the space dependence through the x variable and through a partial differential operator on the right hand side of (1.4). In a first part, we show rigorously, in the semi-coupled case, that indeed the solutions of (1.3)-(1.4) converge, as ε goes to 0, to the solutions of the limit equations:

$$\begin{cases}
\mu_{1,0}(\boldsymbol{x},t)\partial_t z_0 - \Delta_{\boldsymbol{x}} z_0 = 0, & (\boldsymbol{x},t) \in \Omega \times \mathbb{R}_+, \\
z_0(\boldsymbol{x},t) = 0, & (\boldsymbol{x},t) \in \partial\Omega \times \mathbb{R}_+, \\
z_0(\boldsymbol{x},0) = z_p(\boldsymbol{x},0), & (\boldsymbol{x},t) \in \Omega \times \{0\}.
\end{cases}$$
(1.5)

The first equation above is to be understood in the $L^2(Q_T)$ sense. The function $\mu_{k,0} := \int_{\mathbb{R}_+} a^k \rho_0(\boldsymbol{x}, a, t) da$ represents the moment of order k of $\lim_{\varepsilon \to 0} \rho_{\varepsilon} =: \rho_0$ which solves

$$\begin{cases}
\partial_a \rho_0 + \zeta_0 \rho_0 = 0, & \boldsymbol{x} \in \Omega, \, a > 0, \, t > 0, \\
\rho_0(\boldsymbol{x}, a = 0, t) = \beta_0(\boldsymbol{x}, t) \left(1 - \mu_{0,0}(\boldsymbol{x}, t)\right), & \boldsymbol{x} \in \Omega, \, a = 0, \, t > 0.
\end{cases}$$
(1.6)

These convergence results are essentially due to two new ingredients:

- (i) we prove a new energy estimate (see Theorem 4.1) which states that $\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) \leq \mathcal{E}_0(z_{\varepsilon}(\cdot,0))$ providing a first compactness result. Since delay terms often induce oscillations in time, this key result shows they are controlled by the energy minimized at each step. A similar result is provided when adding a source term \mathcal{E} in section 6.
- (ii) considering the elongation variable introduced in [15], we prove a stability result, which is mathematically more involved than in our previous papers (cf Theorem 4.3 versus estimates (2.6) p.6 in [15]). The main difficulty is caused by the presence of the Laplace operator. Instead in the previous articles a given source term $\mathcal{S}(t)$ (independent on z_{ε}) was prescribed and greatly simplified these stability estimates. This second step provides a stronger control in time on the delay part of the energy \mathcal{E}_t but requires stronger hypotheses on the data as well (see assumptions 2.3 i)b).

In a second step we consider, for a fixed ε , existence and uniqueness of the fully coupled problem where ζ is a Lipschitz function of u_{ε} , the elongation. In [16], this model was considered at a single point. Here the presence of the space variable greatly complexifies the mathematical setting. Nevertheless, we prove that there is global existence with no specific restrictions on the data. This result is to be compared with [16], where a blow-up could be shown under certain conditions on the data. Instead, the presence of the Laplace operator precludes a singular limit of the delay term $\mathcal{L}_{\varepsilon}$ for which $\rho_{\varepsilon} \to 0$ and $z_{\varepsilon}(\boldsymbol{x},t) - z_{\varepsilon}(\boldsymbol{x},t-\varepsilon a)$ explodes when the source term becomes too large. We show, as well, that if $\beta_{\varepsilon} \geq \beta_m > 0$, there is no extinction of the total population $\mu_{0,\varepsilon}$ which demonstrates that however great is the external load \mathcal{S} , no tear-off occurs and new bonds are constantly created at local positions $z_{\varepsilon}(\boldsymbol{x},t)$. We show as well that positivity of the elongation is preserved. As in [16], in the case where $\zeta(u) = 1 + |u|$, an autonomous equation on the total population of bonds is shown:

$$\varepsilon \partial_t \mu_{0,\varepsilon} + (\beta_{\varepsilon} + 1) \mu_{0,\varepsilon} + \Delta z_{\varepsilon} + S = \beta_{\varepsilon}$$
, a.e $(\boldsymbol{x},t) \in \Omega \times (0,T)$,

giving an asymptotic profile for large times. Numerical simulations illustrate these latter comments and show two possible regimes according to whether β_{ε} locally vanishes or not: if for some \boldsymbol{x}_0 and $t > t_0$ $\beta_{\varepsilon}(\boldsymbol{x}_0, t) = 0$, then $\mu_{0,\varepsilon}(\boldsymbol{x}_0, t) \to 0$ when $t \to \infty$ which biologically means detachment, or $\beta_{\varepsilon}(\boldsymbol{x}, t) \to \beta_{\infty}(\boldsymbol{x}) > 0$ and then $\mu_{0,\varepsilon} \to \beta_{\infty}(\boldsymbol{x})/(\beta_{\infty}(\boldsymbol{x}) + 1)$ which represents a steady adhesion.

In section 2, we give notations and hypotheses useful throughout the paper. In section 3, we set up for fixed ε the material necessary to guarantee existence, uniqueness and the correct functional spaces to which our solutions $(\rho_{\varepsilon}, z_{\varepsilon})$ belong, in a way not necessarily uniform with respect to ε . In section 4, we give a new energy inequality, stating that the energy \mathcal{E}_t minimized at each time,

actually decreases. Then, in the same section, we provide a stability result already presented in our previous works but adapted to this more complicated framework. In section 5, we assemble, in Theorem 5.3, previous results and provide a rigorous proof of the convergence of $(\rho_{\varepsilon}, z_{\varepsilon})$ towards the solutions of (1.5)-(1.6). Section 6 extends previous results when a given source term is added to (1.4). In section 7, we show global existence, uniqueness and positivity, for the fully coupled model. Numerical simulations illustrate these results in the same section.

2. Notations and hypotheses

In the rest of the article the subscripts \boldsymbol{x} , a or t denote the functional spaces associated with the corresponding variables. For instance $L_{\boldsymbol{x},a,t}^{\infty} := L^{\infty}(\Omega \times \mathbb{R}_{+} \times (0,T))$ whereas $W_{t}^{1,\infty}L_{\boldsymbol{x}}^{2} := W^{1,\infty}([0,T];L^{2}(\Omega))$.

Assumptions 2.1 The dimensionless parameter $\varepsilon > 0$ is assumed to induce two families of chemical rate functions $\zeta_{\varepsilon} \in L^{\infty}_{x,a,t}$ and $\beta_{\varepsilon} \in L^{\infty}_{x,t}$ that satisfy:

(i) For limit functions $\beta_0 \in W^{1,\infty}(Q_T)$ and $\zeta_0 \in W^{1,\infty}(\Omega \times \mathbb{R}_+ \times [0,T])$ it holds that

$$\|\zeta_{\varepsilon} - \zeta_{0}\|_{L_{x,q}^{\infty}} \to 0 \quad and \quad \|\beta_{\varepsilon} - \beta_{0}\|_{L_{x,t}^{\infty}} \to 0$$

as $\varepsilon \to 0$.

(ii) We also assume that there are upper and lower bounds such that

$$0 < \zeta_m \le \zeta_{\varepsilon}(\boldsymbol{x}, a, t) \le \zeta_M$$
 and $0 < \beta_m \le \beta_{\varepsilon}(\boldsymbol{x}, t) \le \beta_M$

for all $\varepsilon > 0$, $\mathbf{x} \in \Omega$, $a \ge 0$ and t > 0.

The initial data for the density model (1.3) satisfies

Assumptions 2.2 The initial condition $\rho_I \in L^{\infty}(\Omega \times \mathbb{R}_+)$ satisfies

• positivity and boundedness: there exists $M > \beta_M$, s.t.

$$M \ge \rho_I(\boldsymbol{x}, a) \ge 0$$
, a.e. in $\Omega \times \mathbb{R}_+$,

moreover, one has also that the total initial population satisfies

$$0 < \int_{\mathbb{R}} \rho_I(\boldsymbol{x}, a) da < 1$$

for almost every $\mathbf{x} \in \Omega$.

• boundedness of higher moments,

$$0 < \mu_{p,I} := \int_{\mathbb{R}_+} a^p \rho_I(\mathbf{x}, a) \, da \le c_p \,, \quad for \ p \in \{1, 2\} \,,$$

where c_p are positive constants depending only on p.

• initial integrability:

$$\int_{\mathbb{R}_+} \sup_{\boldsymbol{x} \in \Omega} |\rho_I(\boldsymbol{x}, a)| a^p da < \infty, \quad for \ p \in \{0, 1, 2\}.$$

Concerning the integral equation (1.4) we assume

Assumptions 2.3 The past data satisfies:

- i) at time t=0 we assume that
 - a) $z_p(\cdot,0)$ is in $H_0^1(\Omega)$,
 - b) $\Delta z_p(\cdot,0) \in L^1(\Omega)$.
- ii) When $t \le 0$ one assumes furthermore that :

$$z_p \in C(\mathbb{R}_-; L^2(\Omega)), \quad \partial_t z_p \in L^{\infty}(\mathbb{R}_-, L^2(\Omega)).$$

where $C(\mathbb{R}_-; L^2(\Omega))$ denotes continuous L^2 -valued functions endowed with the uniform continuity semi-norms. The latter hypotheses translate into a Lipschitz constant which is L^2 in space :

$$|z_p(\boldsymbol{x},t_2)-z_p(\boldsymbol{x},t_1)| \le C_{z_p}(\boldsymbol{x})|t_2-t_1|, \quad \forall (t_2,t_1) \in (\mathbb{R}_-)^2,$$

where $C_{z_p}(\boldsymbol{x}) \in L^2(\Omega)$.

Remark 2.1 Most of the hypotheses presented here are set for general convenience i.e. in order to give the broader possible sense to mathematical results claimed hereafter. In the biological context, the data are simply measured microscopic constants (see for instance tables given in [13, 19, 20]).

3. Existence and uniqueness results

3.1. Extension of previous results for ρ_{ε}

For the problem solved by ρ_{ε} , \boldsymbol{x} is only a mute parameter and the theory established in [14], holds for a.e. $\boldsymbol{x} \in \Omega$.

Theorem 3.1 Let assumptions 2.1 and 2.2 hold, then for every fixed ε there exists a unique solution $\rho_{\varepsilon} \in C_t(\mathbb{R}_+; L^{\infty}_{\boldsymbol{x}}(\Omega; L^1_a(\mathbb{R}_+))) \cap L^{\infty}(\Omega \times (\mathbb{R}_+)^2)$ of the problem (1.3). It satisfies (1.3) in the sense of characteristics, namely

$$\rho_{\varepsilon}(\boldsymbol{x}, a, t) = \begin{cases}
\beta_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a) \left(1 - \int_{\mathbb{R}_{+}} \rho_{\varepsilon}(\boldsymbol{x}, \tilde{a}, t - \varepsilon a) d\tilde{a}\right) \times \\
\times \exp\left(-\int_{0}^{a} \zeta_{\varepsilon}(\boldsymbol{x}, \tilde{a}, t - \varepsilon (a - \tilde{a})) d\tilde{a}\right), & a < t/\varepsilon, \\
\rho_{I}(\boldsymbol{x}, a - t/\varepsilon) \exp\left(-\frac{1}{\varepsilon} \int_{0}^{t} \zeta_{\varepsilon}(\boldsymbol{x}, (\tilde{t} - t)/\varepsilon + a, \tilde{t}) d\tilde{t}\right), & a \ge t/\varepsilon.
\end{cases}$$
(3.7)

We recall the Lemma 2.1 [14] that we adapt here adding the x contribution:

Lemma 3.2 Let ρ_{ε} be the unique solution of problem (1.3) according to Theorem 3.1, then it satisfies a weak formulation

$$\int_{Q_{T}\times\mathbb{R}_{+}} \rho_{\varepsilon}(\boldsymbol{x},a,t) \left(\varepsilon \partial_{t} \varphi + \partial_{a} \varphi + \zeta_{\varepsilon} \varphi\right) d\boldsymbol{x} dt da - \varepsilon \int_{\Omega\times\mathbb{R}_{+}} \rho_{\varepsilon}(\boldsymbol{x},a,t) \varphi(a,t=T) da d\boldsymbol{x} + \int_{Q_{T}} \rho_{\varepsilon}(\boldsymbol{x},a=0,t) \varphi(\boldsymbol{x},0,t) dt d\boldsymbol{x} + \varepsilon \int_{\Omega\times\mathbb{R}_{+}} \rho_{I}(\boldsymbol{x},a) \varphi(\boldsymbol{x},a,t=0) da = 0, \quad (3.8)$$

for every T > 0 and every test function $\varphi \in C^{\infty}(Q_T \times \mathbb{R}_+) \cap L^{\infty}(Q_T \times \mathbb{R}_+)$.

Lemma 3.3 Let assumptions 2.1 and 2.2 hold, then the unique solution $\rho_{\varepsilon} \in C(\mathbb{R}_+; L^{\infty}(\Omega; L^1(\mathbb{R}_+))) \cap L^{\infty}\left(\Omega \times (\mathbb{R}_+)^2\right)$ of the problem (1.3) from Theorem 3.1 satisfies

$$\rho_{\varepsilon}(\boldsymbol{x}, a, t) \geq 0$$
 a.e. in $\Omega \times \mathbb{R}_{+}^{2}$ and

$$\mu_{0,\min} \le \mu_{0,\varepsilon}(\boldsymbol{x},t) < 1, \quad \forall t \in \mathbb{R}_+ \quad where \quad \mu_{0,\min} := \min\left(\mu_{0,\varepsilon}(0), \frac{\beta_m}{\beta_m + \zeta_M}\right).$$
 (3.9)

Lemma 3.4 Under the hypotheses on ζ_0 and β_0 in assumptions 2.1, one has :

$$\rho_0(\boldsymbol{x}, a, t) \le C \exp(-\zeta_m a), \quad |\partial_t \rho_0(\boldsymbol{x}, a, t)| \le C(1 + a) \exp(-\zeta_m a)$$

where the generic constants depend only on $(\beta_M, \beta_m, |\partial_t \beta_0|_{\infty}, \zeta_M, \zeta_m, |\partial_t \zeta_0|_{\infty})$.

Proof. One solves (1.6)

$$\rho_{0}(\boldsymbol{x}, a, t) \leq \frac{\beta_{M} \zeta_{M}}{\zeta_{M} + \beta_{m}} \exp(-\zeta_{m} a),
|\partial_{t} \rho_{0}(\boldsymbol{x}, a, t)| \leq \left(\frac{|\partial_{t} \beta_{0}|_{\infty} \zeta_{M}}{\zeta_{M} + \beta_{m}} + \frac{\beta_{M} \zeta_{M}^{2}}{(\zeta_{M} + \beta_{m})^{2}} \left(\frac{|\partial_{t} \beta_{0}|_{\infty}}{\zeta_{m}} + \beta_{M} \frac{|\partial_{t} \zeta_{0}|_{\infty}}{\zeta_{m}^{2}}\right)\right) \exp(-\zeta_{m} a) + \frac{\beta_{M} \zeta_{M}}{\zeta_{M} + \beta_{m}} |\partial_{t} \zeta_{0}|_{\infty} a \exp(-\zeta_{m} a)$$

3.2. Characterizing z_{ε} , the solution of (1.4)

We define the space where z_{ε} shall evolve setting $X_T := L^{\infty}((0,T); H_0^1(\Omega))$ for every positive real T.

Definition 3.1 We say that z_{ε} solves (1.4) in the weak sense for ε fixed, if $z_{\varepsilon} \in X_T$ and if it solves the problem:

$$\int_{\Omega} \mathcal{L}_{\varepsilon}(z_{\varepsilon}, \rho_{\varepsilon}) \varphi(\boldsymbol{x}) d\boldsymbol{x} + \int_{\Omega} \nabla z_{\varepsilon}(\boldsymbol{x}, t) \cdot \nabla \varphi(\boldsymbol{x}) d\boldsymbol{x} = 0$$
(3.10)

for almost all $t \ge 0$ and for every $\varphi \in H_0^1(\Omega)$.

We need a preliminary lemma in order to show that our data is well prepared for the existence result.

Lemma 3.5 Under hypotheses 2.2 and 2.3,

$$I(\boldsymbol{x}) := \int_{\mathbb{R}_+} |z_p(\boldsymbol{x}, -\varepsilon a)| \rho_I(\boldsymbol{x}, a) da \in L^2(\Omega).$$

Proof. Using Jensen's inequality, one has

$$\begin{split} &\int_{\Omega} \left\{ \int_{\mathbb{R}_{+}} |z_{p}(\boldsymbol{x}, -\varepsilon a)| \rho_{I}(\boldsymbol{x}, a) da \right\}^{2} d\boldsymbol{x} \leq \int_{\Omega} \mu_{0, I} \int_{\mathbb{R}_{+}} |z_{p}(\boldsymbol{x}, -\varepsilon a)|^{2} \rho_{I}(\boldsymbol{x}, a) da d\boldsymbol{x} \\ &\leq 2 \left(\int_{\Omega} \int_{\mathbb{R}_{+}} |z_{p}(\boldsymbol{x}, 0) - z_{p}(\boldsymbol{x}, -\varepsilon a)|^{2} \rho_{I}(\boldsymbol{x}, a) da d\boldsymbol{x} + \int_{\Omega} \int_{\mathbb{R}_{+}} |z_{p}(\boldsymbol{x}, 0)|^{2} \rho_{I}(\boldsymbol{x}, a) da d\boldsymbol{x} \right) \\ &\leq 2 \left\{ \varepsilon^{2} \left(\int_{\Omega} C_{z_{p}}^{2}(\boldsymbol{x}) d\boldsymbol{x} \right) \left(\sup_{\boldsymbol{x} \in \Omega} \int_{\mathbb{R}_{+}} \rho_{I}(\boldsymbol{x}, a) a^{2} da \right) + \|z_{p}(\cdot, 0)\|_{L^{2}(\Omega)}^{2} \right\} \leq C \end{split}$$

which ends the proof.

Theorem 3.6 Under hypotheses 2.1, 2.2 and 2.3, there exists a unique weak solution $z_{\varepsilon} \in X_T$, T being possibly infinite.

PROOF. We define the map Φ that, given $w \in X_T$, provides z being the weak solution of the problem

$$(\mu_{0,\varepsilon}(\boldsymbol{x},t) - \varepsilon \Delta_{\boldsymbol{x}}) z(\boldsymbol{x},t) = \int_{0}^{t/\varepsilon} w(\boldsymbol{x},t - \varepsilon a) \rho_{\varepsilon}(\boldsymbol{x},a,t) da + \int_{t/\varepsilon}^{\infty} z_{p}(\boldsymbol{x},t - \varepsilon a) \rho_{\varepsilon}(\boldsymbol{x},a,t) da,$$

$$(3.11)$$

for almost every $t \in (0,T)$. We aim at showing that the map admits a unique fixed point using the Banach fixed point theorem.

1. Φ is endomorphic on X_T : by Fubini one has that

$$\begin{split} & \int_{\Omega} \left(\int_{0}^{t/\varepsilon} w(\boldsymbol{x}, t - \varepsilon a) \rho_{\varepsilon}(\boldsymbol{x}, a, t) da \right) v(\boldsymbol{x}) d\boldsymbol{x} \\ & = \int_{0}^{t/\varepsilon} \int_{\Omega} w(\boldsymbol{x}, t - \varepsilon a) \rho_{\varepsilon}(\boldsymbol{x}, a, t) v(\boldsymbol{x}) d\boldsymbol{x} da \\ & \leq M \int_{0}^{t/\varepsilon} \|w(\cdot, t - \varepsilon a)\|_{L^{2}(\Omega)} \|v\|_{L^{2}(\Omega)} da \leq \frac{Mt}{\varepsilon} \|w\|_{X_{T}} \|v\|_{L^{2}(\Omega)}, \end{split}$$

which proves, taking the supremum over all $v \in L^2(\Omega)$ s.t. $||v||_{H^1(\Omega)} \le 1$, that $\int_0^{t/\varepsilon} w(x, t - \varepsilon a) \rho_{\varepsilon}(x, a, t) da$ is indeed an $L^2(\Omega)$ -function.

Setting $J(\boldsymbol{x},t) := \int_{t/\varepsilon}^{\infty} z_p(\boldsymbol{x},t-\varepsilon a) \rho_{\varepsilon}(\boldsymbol{x},a) da$, one has the estimate :

$$\begin{split} |J(\boldsymbol{x},t)| &\leq \int_{t/\varepsilon}^{\infty} |z_p(\boldsymbol{x},t-\varepsilon a)| \rho_{\varepsilon}(\boldsymbol{x},a,t) da \leq \int_{t/\varepsilon}^{\infty} |z_p(\boldsymbol{x},t-\varepsilon a)| \rho_I(\boldsymbol{x},a-t/\varepsilon) da \\ &= \int_{\mathbb{R}_+} |z_p(\boldsymbol{x},-\varepsilon a)| \rho_I(\boldsymbol{x},a) da = I(\boldsymbol{x}) \end{split}$$

By Lemma 3.5, the latter term is bounded in $L^2(\Omega)$ by a constant C_J . The right hand side in (3.11) is thus an $L^2(\Omega)$ function for every time t>0. By the Lax-Milgram theorem, there exists a unique solution $z_{\varepsilon}(\cdot,t) \in H^1_0(\Omega)$ of the problem (3.11) for every fixed time t>0. Moreover one has:

$$\min(\varepsilon,\mu_{0,m})\|z(\cdot,t)\|_{H^1(\Omega)} \leq \frac{Mt}{\varepsilon}\|w\|_{X_T} + \|I\|_{L^2(\Omega)} \leq \frac{Mt}{\varepsilon}\|w\|_{X_T} + C_J\,,$$

and taking the supremum over all times in (0,T), gives:

$$||z||_{X_T} \le \frac{MT}{\varepsilon \min(\varepsilon, \mu_{0,m})} ||w||_{X_T} + C'.$$

This shows that Φ is an endomorphism.

2. Contraction: setting $\hat{z}_{\varepsilon} := z_2 - z_1$ (resp. $\hat{w} := w_2 - w_1$) where $z_i = \Phi(w_i)$ for $i \in \{1, 2\}$ and applying the same arguments as above one has:

$$\|\hat{z}_{\varepsilon}\|_{X_T} \leq \frac{MT}{\varepsilon \min(\varepsilon, \mu_{0,m})} \|\hat{w}\|_{X_T}$$

which proves that Φ contracts as soon as $T < \varepsilon \min(\varepsilon, \mu_{0,m})/M$. These two steps provide local existence of a fixed point $z_{\varepsilon} \in X_T$.

3. Continuation: as the time interval for which Φ is a contraction does not depend on the initial condition, we can extend the solution by continuation. This shows the global existence for any positive time T, possibly infinite, for $\varepsilon > 0$ fixed.

Corollary 3.1 Under the previous hypotheses, $z_{\varepsilon} \in L^{\infty}((0,T); H^{2}(\Omega))$, the bound depending on ε^{-1}

PROOF. The solution of the fixed point solves:

$$-\Delta z_{\varepsilon} = \frac{1}{\varepsilon} \left\{ -\mu_{0,\varepsilon} z_{\varepsilon} + \int_{0}^{t/\varepsilon} z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a) \rho_{\varepsilon}(\boldsymbol{x}, a, t) da + J(\boldsymbol{x}, t) \right\},$$

The right hand side is in $L^2(\Omega)$ for almost any time by the same arguments as above. Because the domain Ω is smooth enough, elliptic regularity holds and the claim follows (cf for instance Theorem 2.4.2.5 p.124 [9]).

For the rest of the article, we need to define $\partial_t z_{\varepsilon}$ and investigate to which function space it belongs.

Theorem 3.7 Under the previous hypotheses, $\partial_t z_{\varepsilon} \in L^{\infty}((0,T); H^2(\Omega) \cap H^1_0(\Omega))$.

PROOF. As we do not know to which space the time derivative belongs, we estimate first a finite difference in time. Namely we set

$$D_t^{\tau}z(\boldsymbol{x},t) := \frac{z(\boldsymbol{x},t+\tau) - z(\boldsymbol{x},t)}{\tau}$$

and compute the problem it solves : for all $v \in H_0^1(\Omega)$

$$(\mu_{0,\varepsilon}D_t^{\tau}z_{\varepsilon},v) + \varepsilon(\nabla D_t^{\tau}z_{\varepsilon}\nabla v) = -\left((D_t^{\tau}\mu_{0,\varepsilon})z_{\varepsilon}(\boldsymbol{x},t) + D_t^{\tau}\int_{\mathbb{R}_+} z_{\varepsilon}(\boldsymbol{x},t-\varepsilon a)\rho_{\varepsilon}(\boldsymbol{x},a,t)da,v\right).$$
(3.12)

The product $p_{\varepsilon}(\boldsymbol{x}, a, t) := z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a) \rho_{\varepsilon}(\boldsymbol{x}, a, t)$ solves the following system :

$$\begin{cases}
(\varepsilon \partial_t + \partial_a + \zeta_{\varepsilon}) p_{\varepsilon} = 0, & (\boldsymbol{x}, a, t) \in \Omega \times (\mathbb{R}_+)^2 \\
p_{\varepsilon}(\boldsymbol{x}, 0, t) = \beta_{\varepsilon}(\boldsymbol{x}, t) (1 - \mu_{0, \varepsilon}(\boldsymbol{x}, t)) z_{\varepsilon}(\boldsymbol{x}, t), & (\boldsymbol{x}, a, t) \in \Omega \times \{0\} \times \mathbb{R}_+ \\
p_{\varepsilon}(\boldsymbol{x}, a, 0) = \rho_I(\boldsymbol{x}, a) z_p(\boldsymbol{x}, -\varepsilon a), & (\boldsymbol{x}, a, t) \in \Omega \times \mathbb{R}_+ \times \{0\}
\end{cases}$$
(3.13)

which is to be understood in the sense of characteristics. One has easily in the sense of distributions,

$$\varepsilon \frac{\mathrm{d}}{\mathrm{d}t} \int_{\mathbb{R}_+} p_{\varepsilon}(\boldsymbol{x}, a, t) da + \int_{\mathbb{R}_+} \zeta_{\varepsilon} p_{\varepsilon}(\boldsymbol{x}, a, t) da = \beta_{\varepsilon}(\boldsymbol{x}, t) (1 - \mu_{0, \varepsilon}(\boldsymbol{x}, t)) z_{\varepsilon}(\boldsymbol{x}, t).$$

We focus on the $L^2(\Omega)$ -bound of $\varepsilon \frac{\mathrm{d}}{\mathrm{d}t} \int_{\mathbb{R}_+} p_\varepsilon da$. Indeed:

$$\left\| \int_{\mathbb{R}_+} \zeta_{\varepsilon} p_{\varepsilon}(\cdot, a, t) da \right\|_{L^2(\Omega)} \leq \frac{M \zeta_M T}{\varepsilon} \|z_{\varepsilon}\|_{X_T} + \zeta_M C_I,$$

whereas

$$\left\|\beta_{\varepsilon}(1-\mu_{0,\varepsilon})z_{\varepsilon}\right\|_{L^{\infty}((0,T);L^{2}(\Omega))}\leq\beta_{M}\left\|z_{\varepsilon}\right\|_{X_{T}}.$$

Using Jensen's inequality and the estimate on the time derivative obtained above, one has:

$$\begin{split} & \left\| D_t^{\tau} \int_{\mathbb{R}_+} p_{\varepsilon}(\cdot, a, t) da \right\|_{L^2(\Omega)}^2 = \left\| \frac{1}{\tau} \int_t^{t+\tau} \frac{\mathrm{d}}{\mathrm{d}t} \int_{\mathbb{R}_+} p_{\varepsilon}(\cdot, a, s) dads \right\|_{L^2(\Omega)}^2 \\ & \leq \left\| \frac{\mathrm{d}}{\mathrm{d}t} \int_{\mathbb{R}_+} p_{\varepsilon}(\cdot, a, \cdot) da \right\|_{L^{\infty}((t, t+\tau); L^2(\Omega))}^2 \leq \left\| \frac{\mathrm{d}}{\mathrm{d}t} \int_{\mathbb{R}_+} p_{\varepsilon}(\cdot, a, \cdot) da \right\|_{L^{\infty}((0, T); L^2(\Omega))}^2 \end{split}$$

for every t>0. The time derivative of $\mu_{0,\varepsilon}$ can be estimated as follows:

$$\varepsilon \partial_t \mu_{0,\varepsilon} = \beta_\varepsilon (1 - \mu_{0,\varepsilon}) - \int_{\mathbb{R}_+} \zeta_\varepsilon \rho_\varepsilon da \leq \beta_M + \zeta_M < \infty$$

and thus $\partial_t \mu_{0,\varepsilon} \in L^{\infty}(\Omega \times \mathbb{R}_+)$. One has then as above : $(D_t^{\tau} \mu_{0,\varepsilon}) z_{\varepsilon} \in L^{\infty}(\mathbb{R}_+; L^2(\Omega))$, which gives by Lax-Milgram applied to (3.12) :

$$\min(\varepsilon, \mu_{0,m}) \| D_t^{\tau} z_{\varepsilon}(\cdot, t) \|_{H^1(\Omega))} < C$$

for every fixed $t \in [0,T]$. Moreover, by standard elliptic regularity and since the right hand side in (3.12) is an $L^2(\Omega)$ function, $\|D_t^T z_{\varepsilon}(\cdot,t)\|_{H^2(\Omega)} < \infty$. Thus, modulo the extraction of a subsequence $(\tau_k)_{k \in \mathbb{N}}$, there exists $L^{\infty}((0,T);H^2(\Omega))$ weak-* limit which is a weak time derivative of z_{ε} (see for instance Theorem 3 Section 5.8.2. [6]), and the derivative satisfies the same $L^{\infty}((0,T);H^2(\Omega))$ bound.

Remark 3.8 Estimates above are not uniform with respect to ε . These computations are performed only in order to give a meaning to the time derivative of z_{ε} , and show that locally with respect to ε it is an $L_t^{\infty} H_x^2$ function.

4. Energy estimates

4.1. The energy \mathcal{E}_t decreases with time

Theorem 4.1 Under hypotheses 2.1, 2.2 and 2.3, for all times $t \ge 0$, the energy \mathcal{E}_t is a decreasing function, i.e.:

$$\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) \leq \mathcal{E}_0(z_n(\cdot,0))$$
.

Moreover, one has as well that

$$\int_0^T \int_{\Omega \times \mathbb{R}_+} \zeta_{\varepsilon}(\boldsymbol{x}, a, t) \rho_{\varepsilon}(\boldsymbol{x}, a, t) \left(\frac{z_{\varepsilon}(\boldsymbol{x}, t) - z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a)}{\varepsilon} \right)^2 da \, d\boldsymbol{x} \, dt < \mathcal{E}_0(z_p(\cdot, 0)).$$

PROOF. We use again the same procedure in order to pass from the position to the elongation as in [15, 16], writing:

$$u_{\varepsilon}(\boldsymbol{x}, a, t) := \begin{cases} \frac{z_{\varepsilon}(\boldsymbol{x}, t) - z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a)}{\varepsilon} & \text{if } t \ge \varepsilon a, \\ \frac{z_{\varepsilon}(\boldsymbol{x}, t) - z_{p}(\boldsymbol{x}, t - \varepsilon a)}{\varepsilon} & \text{otherwise.} \end{cases}$$
(4.14)

Indeed, so defined u_{ε} solves

$$(\varepsilon \partial_t + \partial_a) u_{\varepsilon} = \partial_t z_{\varepsilon} \,, \tag{4.15}$$

this equation has a meaning in the sense of characteristics, while the right hand side is ment as a function in $L^{\infty}((0,T);H^2(\Omega))$ as shown in the previous section.

Considering the equation satisfied by $\rho_{\varepsilon}u_{\varepsilon}^2$ and integrating in age gives :

$$\frac{\varepsilon}{2} \frac{\mathrm{d}}{\mathrm{d}t} \int_{\mathbb{R}_+} \rho_{\varepsilon} u_{\varepsilon}^2 da + \int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^2 da = \left(\int_{\mathbb{R}_+} \rho_{\varepsilon} u_{\varepsilon} da \right) \partial_t z_{\varepsilon} = \Delta z_{\varepsilon} \partial_t z_{\varepsilon} ,$$

which integrated in space gives:

$$\frac{\varepsilon}{2} \frac{\mathrm{d}}{\mathrm{d}t} \int_{\mathbb{R}_{+} \times \Omega} \rho_{\varepsilon} u_{\varepsilon}^{2} dad\boldsymbol{x} + \int_{\mathbb{R}_{+} \times \Omega} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^{2} dad\boldsymbol{x}
= -\int_{\Omega} \nabla z_{\varepsilon} \nabla \partial_{t} z_{\varepsilon} d\boldsymbol{x} = -\frac{1}{2} \frac{\mathrm{d}}{\mathrm{d}t} \int_{\Omega} |\nabla z_{\varepsilon}|^{2} d\boldsymbol{x}.$$
(4.16)

The latter integration by parts is justified as follows. Set $w_{\varepsilon} := \nabla z_{\varepsilon}$, thanks to Corollary 3.1 and Theorem 3.7, one has that $w_{\varepsilon} \in W^{1,\infty}([0,T];L^2(\Omega)) \subset C([0,T];L^2(\Omega))$. The latter space is separable: there exists a $C^{\infty}([0,T] \times \Omega)$ function s.t. $w_{\varepsilon}^{\delta} \to w_{\varepsilon}$ in $C([0,T];L^2(\Omega))$ strong, and $\partial_t w_{\varepsilon}^{\delta} \to \partial_t w_{\varepsilon}$ in $L^{\infty}((0,T);L^2(\Omega))$ weak-* (w_{ε}^{δ} can be obtained by the standard mollification). In this scenario, one is testing against a C^1 function in time, the integration by parts on the regularized functions. Passing to the limit with respect to δ , leads to:

$$\int_{0}^{T} \varphi(t) \int_{\Omega} 2w_{\varepsilon} \partial_{t} w_{\varepsilon} d\boldsymbol{x} dt = \left[\int_{\Omega} |w_{\varepsilon}(\boldsymbol{x}, t)|^{2} d\boldsymbol{x} \varphi(t) \right]_{t=0}^{t=T} - \int_{0}^{T} \int_{\Omega} |w_{\varepsilon}|^{2} d\boldsymbol{x} \partial_{t} \varphi dt$$

for any $\varphi \in C^1([0,T])$. As $\int_{\Omega} |w_{\varepsilon}(\boldsymbol{x},t)|^2 d\boldsymbol{x}$ is an absolutely continuous function of t, the integration by part holds, and thus

$$2\int_{\Omega} w_{\varepsilon} \partial_t w_{\varepsilon} d\boldsymbol{x} = \frac{\mathrm{d}}{\mathrm{d}t} \int_{\Omega} |w_{\varepsilon}|^2 d\boldsymbol{x}, \quad \text{ for } a.e. \quad t \in (0,T).$$

Finally (4.16) gives:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) \leq 0,$$

since $\int_{\mathbb{R}_+ \times \Omega} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^2 da dx$ is positive. But as $z_{\varepsilon}(x,0)$ solves (1.4) at time t = 0, by Lemma A.1, $z_{\varepsilon}(x,0)$ minimizes the energy at time t = 0. This proves that

$$\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) \leq \mathcal{E}_0(z_{\varepsilon}(\cdot,0)) \leq \mathcal{E}_0(z_p(\cdot,0)),$$

giving the first claim provided the last term is bounded. But, by similar arguments as in Lemma 3.5, one has that

$$\mathcal{E}_0(z_p(\cdot,0)) \leq \varepsilon \left(\int_{\Omega} C_{z_p}^2(\boldsymbol{x}) d\boldsymbol{x} \right) \left(\sup_{\boldsymbol{x} \in \Omega} \int_{\mathbb{R}_+} \rho_I(\boldsymbol{x},a) a^2 da \right) + \int_{\Omega} |\nabla z_p(\boldsymbol{x},0)|^2 d\boldsymbol{x} < \infty$$

the last term being bounded since $z_p(\boldsymbol{x},0) \in H_0^1(\Omega)$. Integrating (4.16) in time gives :

$$\int_0^T \int_{\mathbb{R}_+ \times \Omega} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^2 da d\mathbf{x} dt \leq \mathcal{E}_0(z_{\varepsilon}(\cdot, 0)) - \mathcal{E}(z_{\varepsilon}(\cdot, t)) \leq \mathcal{E}(z_{\varepsilon}(\cdot, 0)) \leq \mathcal{E}(z_{\rho}(\cdot, 0)),$$

which ends the proof.

Corollary 4.1 Under the same hypotheses, $z_{\varepsilon} \in X_T$ uniformly with respect to ε .

PROOF. The bound on the gradient is completed by the norm of $z_{\varepsilon}(\cdot,t)$ in $L^2(\Omega)$ by the Poincaré inequality.

Theorem 4.2 Under the same hypotheses as above, $\partial_t z_{\varepsilon}$ in $L^2(Q_T)$ and the bound is uniform in ε .

PROOF. Multiplying u_{ε} by ρ_{ε} it solves in the sense of characteristics :

$$(\varepsilon \partial_t + \partial_a + \zeta_{\varepsilon}) \rho_{\varepsilon} u_{\varepsilon} = \rho_{\varepsilon} \partial_t z_{\varepsilon}.$$

Integrating with respect to the age variable, and because $u_{\varepsilon}(x,0,t)=0$, one has

$$\varepsilon \partial_t \int_{\mathbb{R}_+} \rho_\varepsilon u_\varepsilon da + \int_{\mathbb{R}_+} \zeta_\varepsilon \rho_\varepsilon u_\varepsilon da = \mu_{0,\varepsilon} \partial_t z_\varepsilon.$$

We recall that z_{ε} solves :

$$\int_{\Omega} \int_{\mathbb{R}_{+}} \rho_{\varepsilon}(\boldsymbol{x}, a, t) u_{\varepsilon}(\boldsymbol{x}, a, t) da \, v(\boldsymbol{x}) d\boldsymbol{x} + (\nabla z_{\varepsilon}, \nabla v) = 0, \quad \forall v \in H_{0}^{1}(\Omega)$$

for almost every fixed $t \in (0,T)$. Due to Theorem 3.7, $(\nabla z_{\varepsilon}, \nabla v)$ is a differentiable function in time for any $v \in H_0^1(\Omega)$ and thus

$$\varepsilon \partial_t \int_{\Omega} \int_{\mathbb{R}_+} \rho_{\varepsilon}(\boldsymbol{x}, a, t) u_{\varepsilon}(\boldsymbol{x}, a, t) da \, v(\boldsymbol{x}) d\boldsymbol{x} + \varepsilon \left(\nabla \partial_t z_{\varepsilon}, \nabla v \right) = 0, \quad \forall v \in H^1_0(\Omega) \, .$$

This shows that $\partial_t z_{\varepsilon}$ solves indeed

$$\int_{\Omega} \mu_{0,\varepsilon} \partial_t z_{\varepsilon}(\boldsymbol{x},t) v(\boldsymbol{x}) d\boldsymbol{x} + \varepsilon \int_{\Omega} \nabla \partial_t z_{\varepsilon} \cdot \nabla v d\boldsymbol{x} = \int_{\Omega} \left(\int_{\mathbb{R}_+} \rho_{\varepsilon} \zeta_{\varepsilon} u_{\varepsilon} da \right) v(\boldsymbol{x}) d\boldsymbol{x}$$

for every fixed t>0 and any $v\in H_0^1(\Omega)$. On the other hand, using Jensen's inequality one has

$$\left(\int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} |u_{\varepsilon}| da\right)^2 \leq \int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} da \int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^2 da,$$

which integrated in space and time gives

$$\left\| \int_{\mathbb{R}_{+}} \rho_{\varepsilon} \zeta_{\varepsilon} u_{\varepsilon} da \right\|_{L^{2}(Q_{T})}^{2} \leq \left(\sup_{(\boldsymbol{x},t) \in Q_{T}} \int_{\mathbb{R}_{+}} \zeta_{\varepsilon} \rho_{\varepsilon} da \right) \int_{0}^{T} \int_{\Omega} \int_{\mathbb{R}_{+}} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^{2} da d\boldsymbol{x} dt$$
$$\leq \zeta_{M} \int_{0}^{T} \int_{\Omega} \int_{\mathbb{R}_{+}} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^{2} da d\boldsymbol{x} dt.$$

By Lax-Milgram, one has the estimates:

$$\|\partial_t z_{\varepsilon}(\cdot,t)\|_{L^2(\Omega)} \leq \frac{1}{\mu_{0,m}} \left\| \int_{\mathbb{R}_+} \rho_{\varepsilon}(\cdot,a,t) \zeta_{\varepsilon}(\cdot,a,t) u_{\varepsilon}(\cdot,a,t) da \right\|_{L^2(\Omega)}$$

for almost every $t \in (0,T)$, which gives after integration in time that $\partial_t z_{\varepsilon} \in L^2(Q_T)$ uniformly with respect to ε .

Corollary 4.2 Under the previous hypotheses, there exists a subsequence $(z_{\varepsilon_k})_{k\in\mathbb{N}}$ converging strongly in $C([0,T];L^2(\Omega))$.

PROOF. The imbedding $H_0^1(\Omega)$ is compact in $L^2(\Omega)$ which gives by the Lions-Aubin-Simon theorem that there exists a subsequence $(z_{\varepsilon_k})_{k\in\mathbb{N}}$ converging strongly in $C([0,T];L^2(\Omega))$ (cf. Theorem II.5.16 p.102 [2]).

4.2. A stability result in the elongation variable

The problem solved by u_{ε} reads formally:

$$\begin{cases}
(\varepsilon \partial_t + \partial_a) u_{\varepsilon} = \partial_t z_{\varepsilon}(\boldsymbol{x}, t), & (\boldsymbol{x}, a, t) \in \Omega \times \mathbb{R}_+ \times (0, T) \\
(\mu_{0,\varepsilon} - \varepsilon \Delta) \partial_t z_{\varepsilon} = \int_{\mathbb{R}_+} (\zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}) (\boldsymbol{x}, a, t) da, & (\boldsymbol{x}, t) \in \Omega \times (0, T), \\
\partial_t z_{\varepsilon}(\boldsymbol{x}, t) = 0 & (\boldsymbol{x}, t) \in \Omega \times (0, T), \\
u_{\varepsilon}(\boldsymbol{x}, 0, t) = 0 & (\boldsymbol{x}, a, t) \in \Omega \times \{a = 0\} \times (0, T) \\
u_{\varepsilon}(\boldsymbol{x}, a, t) = 0 & (\boldsymbol{x}, a, t) \in \partial \Omega \times \mathbb{R}_+ \times (0, T) \\
u_{\varepsilon}(\boldsymbol{x}, a, 0) = u_{\varepsilon, I}(\boldsymbol{x}, a) & (\boldsymbol{x}, a, t) \in \Omega \times \mathbb{R}_+ \times \{t = 0\}
\end{cases} \tag{4.17}$$

where $u_{\varepsilon,I}(\boldsymbol{x},a) := \frac{z_{\varepsilon}(\boldsymbol{x},0) - z_{p}(\boldsymbol{x},-\varepsilon a)}{\varepsilon}$ and $z_{\varepsilon}(\boldsymbol{x},0)$ solves

$$(\mu_{0,I}(\boldsymbol{x}) - \varepsilon \Delta_{\boldsymbol{x}}) z(\boldsymbol{x},0) = \int_0^\infty z_p(\boldsymbol{x}, -\varepsilon a) \rho_I(\boldsymbol{x}, a) da. \tag{4.18}$$

The elliptic problem solved by $\partial_t z_{\varepsilon}$ in (4.17) is to be understood in the variational sense. This system has to be compared with (2.1) p.5 [15], here the inverse of the operator $(\mu_{0,\varepsilon}I - \varepsilon\Delta)$ appears as a space contribution. In what follows we show how to deal with and extend stability estimates (2.6) p.6 [15] in this setting.

Theorem 4.3 Under hypotheses 2.1 and 2.2, and if $\int_{\mathbb{R}_+} \rho_I |u_I| da dx < \infty$, one has:

$$\int_{\Omega\times\mathbb{R}_+} (\rho_\varepsilon|u_\varepsilon|)(\boldsymbol{x},a,t) da d\boldsymbol{x} \leq \int_{\Omega\times\mathbb{R}_+} \rho_I(\boldsymbol{x},a)|u_I(\boldsymbol{x},a)| da \, d\boldsymbol{x} \, .$$

Moreover, if u_I satisfies

$$\sup_{a\in\mathbb{R}_+}\frac{\int_{\Omega}|u_I(\boldsymbol{x},a)|d\boldsymbol{x}}{(1+a)}<\infty,$$

then

$$\int_{\Omega}|u_{\varepsilon}(\boldsymbol{x},a,t)|d\boldsymbol{x}\in Y_{T}:=L^{\infty}\left(\mathbb{R}_{+}\times(0,T),\frac{1}{1+a}\right)$$

and the bound is uniform with respect to ε .

PROOF. A simple use of Theorem 4.1, shows that

$$\int_{\Omega\times\mathbb{R}_+} \zeta_\varepsilon \rho_\varepsilon u_\varepsilon^2 da d\boldsymbol{x} \leq \zeta_M \int_{\Omega\times\mathbb{R}_+} \rho_\varepsilon u_\varepsilon^2 da d\boldsymbol{x} \leq \frac{\zeta_M}{\varepsilon} \mathcal{E}(z_\varepsilon(\cdot,t) \leq \frac{\zeta_M}{\varepsilon} \mathcal{E}(z_p(\cdot,0)),$$

which, using again Jensen's inequality, implies that

$$\int_{\Omega} \left(\int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} |u_{\varepsilon}| da \right)^2 d\boldsymbol{x} \leq \frac{\zeta_M^2}{\varepsilon} \mathcal{E}(z_p(\cdot, 0)).$$

This bound ensures that for fixed ε , $f(\boldsymbol{x},t) := \int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon} da$ belongs to $L^{\infty}((0,T); L^2(\Omega))$. We consider the problem : for a given $f(\boldsymbol{x},t)$ find $g(\boldsymbol{x},t)$ solving

$$\begin{cases} \mu_{0,\varepsilon}g - \varepsilon \Delta g = f, & \text{in } \Omega, \\ g = 0, & \text{on } \partial \Omega. \end{cases}$$

For almost every $t \in (0,T)$, one solves this elliptic problem. Thus there exists a unique $g \in L^{\infty}((0,T);H^2(\Omega) \cap H^1_0(\Omega))$ by Lax-Milgram and standard elliptic regularity. These considerations

allow to fulfill hypotheses of the main theorem in [4], namely for a.e. $t \in (0,T)$, $g(\cdot,t) \in L^1(\Omega)$, $\Delta g(\cdot,t) \in L^1(\Omega)$ and $\partial_{\nu} g(\cdot,t) \in L^1(\partial\Omega)$ which ensures that $g(\cdot,t) \in \mathbb{X}$ where

$$\mathbb{X} := \left\{ u \in W^{1,1}(\Omega) \text{ s.t. } \left| \int \nabla u \cdot \nabla \psi d\boldsymbol{x} \right| < C \|\psi\|_{L^{\infty}(\Omega)} \, \forall \psi \in C^{1}(\overline{\Omega}) \right\}$$

and thus a Green's inequality holds (cf. Theorem 1.3, [4]):

$$\int_{\Omega} \nabla g^{+} \cdot \nabla \psi d\mathbf{x} \leq \int_{\partial \Omega} H \psi - \int_{\Omega} G \psi, \quad \forall \psi \in C^{1}(\overline{\Omega}), \quad \psi \geq 0,$$

where g^+ denotes the positive part of g and $G \in L^1(\Omega)$ and $H \in L^1(\partial \Omega)$ are given by :

$$G := \begin{cases} \Delta g & \text{on } \{g > 0\} \\ 0 & \text{on } \{g \le 0\} \end{cases}, \quad H := \begin{cases} \partial_{\nu} g & \text{on } \{g > 0\} , \\ 0 & \text{on } \{g < 0\} , \\ \min \left(\partial_{\nu} g, 0\right) & \text{on } \{g = 0\} . \end{cases}$$

Applying the latter result to $|g| := g^+ - g^-$, since g vanishes on the boundary, one obtains that

$$\int_{\Omega} \Delta g \operatorname{sgn} g \, d\boldsymbol{x} \leq 0.$$

Returning to (4.17), one has

$$\varepsilon \partial_t u_\varepsilon + \partial_a u_\varepsilon = g \,,$$

where we set $g := \partial_t z_{\varepsilon}$. In the sense of characteristics, one establishes, after integration with respect to age:

$$\varepsilon \partial_t \int_{\mathbb{R}_+} \rho_\varepsilon |u_\varepsilon| da + \int_{\mathbb{R}_+} \zeta_\varepsilon \rho_\varepsilon |u_\varepsilon| da \le \mu_{0,\varepsilon} |g|.$$

Integrating in space, one obtains

$$\varepsilon \frac{\mathrm{d}}{\mathrm{d}t} \int_{\Omega \times \mathbb{R}_{+}} \rho_{\varepsilon} |u_{\varepsilon}| dad\boldsymbol{x} + \int_{\Omega \times \mathbb{R}_{+}} \zeta_{\varepsilon} \rho_{\varepsilon} |u_{\varepsilon}| dad\boldsymbol{x} \leq \int_{\Omega} \mu_{0,\varepsilon} |g| d\boldsymbol{x}.$$

But then

$$\int_{\Omega} \mu_{0,\varepsilon} |g| d\boldsymbol{x} = \int_{\Omega} \left(\int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon} da \right) \operatorname{sgn} g d\boldsymbol{x} + \varepsilon \int_{\Omega} \Delta g \operatorname{sgn} g d\boldsymbol{x} \leq \int_{\Omega \times \mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} |u_{\varepsilon}| da d\boldsymbol{x}.$$

This leads to

$$\varepsilon \frac{\mathrm{d}}{\mathrm{d}t} \int_{\Omega \times \mathbb{R}_+} \rho_{\varepsilon} |u_{\varepsilon}| da dx \leq 0,$$

which, after integration in time, proves the first result. Then, one has that $q(a,t) := \int_{\Omega} |u_{\varepsilon}| dx$ solves

$$\begin{split} \varepsilon \partial_t q + \partial_a q &\leq \frac{1}{\mu_{0,m}} \int_{\Omega} \mu_{0,\varepsilon} |v| d\boldsymbol{x} \leq \frac{1}{\mu_{0,m}} \int_{\Omega \times \mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} |u_{\varepsilon}| \, dad\boldsymbol{x} \\ &\leq \frac{\zeta_M}{\mu_{0,m}} \int_{\mathbb{R}_+} \rho_I |u_I| dad\boldsymbol{x} < C \,. \end{split}$$

Applying then the same results as in Theorem 6.1 [15], one concludes that $q \in Y_T$.

It remains to show that the assumptions of theorem 4.3 are fulfilled. This is the scope of next two lemmas.

Lemma 4.4 Under assumptions 2.3 it holds that :

$$J := \int_{\Omega \times \mathbb{R}_+} \rho_I |u_I| dadx < C,$$

where the generic constant C is finite and independent on ε .

PROOF. A triangle inequality gives:

$$J \leq \int_{\Omega} \frac{|z_{\varepsilon}(\boldsymbol{x},0) - z_{p}(\boldsymbol{x},0)|}{\varepsilon} \mu_{0,I}(\boldsymbol{x}) d\boldsymbol{x} + \int_{\Omega \times \mathbb{R}_{+}} \frac{|z_{p}(\boldsymbol{x},0) - z_{p}(\boldsymbol{x},-\varepsilon a)|}{\varepsilon} \rho_{I}(\boldsymbol{x},a) da d\boldsymbol{x}.$$

By similar arguments as above, one considers the problem solved by $\hat{z}_{\varepsilon}(\boldsymbol{x},0) := z_{\varepsilon}(\boldsymbol{x},0) - z_{p}(\boldsymbol{x},0)$:

$$\mu \hat{z}_{\varepsilon}(\boldsymbol{x},0) - \varepsilon \Delta \hat{z}_{\varepsilon}(\boldsymbol{x},0) = -\int_{\mathbb{R}_{+}} \left(z_{p}(\boldsymbol{x},0) - z_{p}(\boldsymbol{x},-\varepsilon a) \right) \rho_{I}(\boldsymbol{x},a) da + \varepsilon \Delta z_{p}(\boldsymbol{x},0).$$

Since $z_p(\cdot,0)$ is in $H^1_0(\Omega)$, the right hand side is in $H^{-1}(\Omega)$, thus by Lax-Milgram, $\hat{z}_{\varepsilon}(\boldsymbol{x},0) \in H^1_0(\Omega) \subset W^{1,1}_0(\Omega)$. Moreover since the right hand side is in $L^1_{\boldsymbol{x}}$ as well, one fulfills the hypotheses of Proposition 4.2 [4] which shows that $\hat{z}_{\varepsilon}(\boldsymbol{x},0) \in \mathbb{X}$ and $\partial_{\nu}\hat{z}_{\varepsilon}(\cdot,0) \in L^1(\partial\Omega)$. Again Theorem 1.3 [4] applies and one obtains that

$$\|\mu_{0,I}\hat{z}_{\varepsilon}(\cdot,0)\|_{L_{\boldsymbol{x}}^{1}} \leq \left\| \int_{\mathbb{R}_{+}} \left(z_{p}(\boldsymbol{x},0) - z_{p}(\boldsymbol{x},-\varepsilon a) \right) \rho_{I}(\boldsymbol{x},a) da \right\|_{L^{1}} + \varepsilon \|\Delta z_{p}(\cdot,0)\|_{L_{\boldsymbol{x}}^{1}},$$

which together with the Lipschitz-like assumption 2.3 (ii) ends the proof.

Lemma 4.5 Under assumptions 2.3, one has also that the second requirement on u_I holds:

$$\sup_{a \in \mathbb{R}_+} \frac{\int_{\Omega} |u_I(\boldsymbol{x}, a)| d\boldsymbol{x}}{(1+a)} < C,$$

where the generic constant is independent on ε .

PROOF. The same triangle inequality holds but we do not integrate in age:

$$\begin{split} & \int_{\Omega} |u_I| d\boldsymbol{x} \leq \int_{\Omega} \frac{|z_{\varepsilon}(\boldsymbol{x},0) - z_p(\boldsymbol{x},0)|}{\varepsilon} d\boldsymbol{x} + \int_{\Omega} \frac{|z_p(\boldsymbol{x},0) - z_p(\boldsymbol{x},-\varepsilon a)|}{\varepsilon} d\boldsymbol{x} \\ & \leq \int_{\Omega} \mu_{0,I} \frac{|z_{\varepsilon}(\boldsymbol{x},0) - z_p(\boldsymbol{x},0)|}{\varepsilon \mu_{0,m}} d\boldsymbol{x} + a \int_{\Omega} C_{z_p}(\boldsymbol{x}) d\boldsymbol{x} \leq C + a \sqrt{|\Omega|} \|C_{z_p}\|_{L^2(\Omega)} \,. \end{split}$$

Dividing by (1+a) and taking the supremum on \mathbb{R}_+ ends the proof.

Lemma 4.6 Under hypotheses above, one has also that $\|\partial_t z_{\varepsilon}\|_{L^{\infty}_{+}L^{1}_{2}} < \infty$ uniformly in ε .

PROOF. By Theorem 4.3 and the hypotheses on ζ_{ε} one has that $\int_{\Omega \times \mathbb{R}_+} \rho_{\varepsilon} \zeta_{\varepsilon} u_{\varepsilon} da dx \in C([0,T])$. Since $\Delta \partial_t z_{\varepsilon}$ belongs for almost every $t \in (0,T)$ to $L^2(\Omega)$ by Theorem 3.7, we satisfy the hypotheses of Theorem 1.3, [4] and we conclude that

$$\int_{\Omega} \mu_{0,\varepsilon}(\boldsymbol{x},t) |\partial_t z_{\varepsilon}(\boldsymbol{x},t)| d\boldsymbol{x} \leq \int_{\Omega} \left| \int_{\mathbb{R}_+} (\rho_{\varepsilon} \zeta_{\varepsilon} u_{\varepsilon})(\boldsymbol{x},a,t) da \right| d\boldsymbol{x}.$$

Finally, taking the ess-sup in time, one concludes the proof.

5. Convergence when ε goes to zero

Since the system (1.3)-(1.4) is weakly coupled, and the space variable x is a mute parameter for the density of linkages ρ_{ε} , the convergence results from the previous articles are adapted and attention is paid only on the order of functional spaces with respect to x, a and t in section 5.1. Then in section 5.2, we present the main result of the first part of the paper.

5.1. Convergence of ρ_{ε}

Concerning the convergence of ρ_{ε} , we recall the Lyapunov functional, [14]:

$$\mathcal{H}[u(\boldsymbol{x},\cdot)] := \left| \int_0^\infty u(\boldsymbol{x},a) \, da \right| + \int_0^\infty |u(\boldsymbol{x},a)| \, da \,, \tag{5.19}$$

for every a-measurable function $u(\mathbf{x},\cdot)$. Consider the difference $\hat{\rho}_{\varepsilon} := \rho_{\varepsilon} - \rho_{0}$. A formal computation using (1.3) and (1.6) implies that it satisfies

$$\begin{cases} \varepsilon \partial_t \hat{\rho}_{\varepsilon} + \partial_a \hat{\rho}_{\varepsilon} + \zeta_{\varepsilon}(\boldsymbol{x}, a, t) \hat{\rho}_{\varepsilon} = \mathcal{R}_{\varepsilon, \boldsymbol{x}}, & a > 0, t > 0, \\ \hat{\rho}_{\varepsilon}(\boldsymbol{x}, a = 0, t) = -\beta_{\varepsilon}(\boldsymbol{x}, t) \int_0^{\infty} \hat{\rho}_{\varepsilon}(\boldsymbol{x}, \tilde{a}, t) d\tilde{a} + \mathcal{M}_{\varepsilon, \boldsymbol{x}}, & t > 0, \\ \hat{\rho}_{\varepsilon}(\boldsymbol{x}, a, t = 0) = \rho_{\varepsilon, I}(\boldsymbol{x}, a) - \rho_0(\boldsymbol{x}, a, 0), & a \ge 0, \end{cases}$$

$$(5.20)$$

with $\mathcal{R}_{\varepsilon}(\boldsymbol{x},a,t) := -\varepsilon \partial_{t} \rho_{0}(\boldsymbol{x},a,t) - \rho_{0}(\boldsymbol{x},a,t) (\zeta_{\varepsilon}(\boldsymbol{x},a,t) - \zeta_{0}(\boldsymbol{x},a,t))$ and $\mathcal{M}_{\varepsilon}(\boldsymbol{x},t) := (\beta_{\varepsilon}(\boldsymbol{x},t) - \beta_{0}(\boldsymbol{x},t)) (1 - \int_{0}^{\infty} \rho_{0}(\boldsymbol{x},a,t) da)$.

Lemma 5.1 According to assumptions 2.1, one has:

$$\mathcal{H}[\hat{\rho}_{\varepsilon}(\boldsymbol{x},\cdot,t)] \leq \mathcal{H}[\rho_{\varepsilon,I}(\boldsymbol{x},\cdot) - \rho_{0}(\boldsymbol{x},\cdot,0)]e^{\frac{-\zeta_{m}t}{\varepsilon}} + \frac{2}{\zeta_{m}} \left\{ \|\mathcal{R}_{\varepsilon}\|_{L_{\boldsymbol{x},a,t}^{\infty}} + \|\mathcal{M}_{\varepsilon}\|_{L_{\boldsymbol{x},t}^{\infty}} \right\}$$

for all $t \ge 0$ and a.e. $x \in \Omega$.

Using the method of characteristics one can also write pointwise estimates :

Lemma 5.2 One can estimate the difference $\hat{\rho}_{\varepsilon}$ locally with respect to (\boldsymbol{x}, a, t) :

$$|\hat{\rho}_{\varepsilon}(\boldsymbol{x}, a, t)| \lesssim \begin{cases} \beta_{M} \exp\left(-\frac{\zeta_{m} t}{\varepsilon}\right) \|\hat{\rho}_{\varepsilon, I}(\boldsymbol{x}, \cdot)\|_{L_{a}^{1}} + (1 + a)^{2} \exp(-\zeta_{m} a) & \text{if } t \geq \varepsilon a \\ |\hat{\rho}_{\varepsilon, I}\left(\boldsymbol{x}, a - \frac{t}{\varepsilon}\right)| \exp\left(-\frac{\zeta_{m} t}{\varepsilon}\right) + (1 + a)^{2} \exp(-a\zeta_{m}) & \text{otherwise} \end{cases}$$

for almost every $\mathbf{x} \in \Omega$ and $L_a^1 := L^1(\mathbb{R}_+)$.

PROOF. We use Duhamel's formula and write:

• if $t \ge \varepsilon a$,

$$\begin{aligned} |\hat{\rho}_{\varepsilon}(\boldsymbol{x}, a, t)| &\leq |\hat{\rho}_{\varepsilon}(\boldsymbol{x}, 0, t - \varepsilon a)| \exp(-\zeta_{m} a) \\ &+ \int_{0}^{a} \exp(-\zeta_{m} (a - s)) |\mathcal{R}_{\varepsilon, \boldsymbol{x}}(\boldsymbol{x}, s, t + \varepsilon (s - a))| ds \\ &\leq |\hat{\rho}_{\varepsilon}(\boldsymbol{x}, 0, t - \varepsilon a)| \exp(-\zeta_{m} a) \\ &+ o(1) \int_{0}^{a} \exp(-\zeta_{m} (a - s)) (1 + s) \exp(-\zeta_{m} s) ds \\ &\leq \left\{ |\hat{\rho}_{\varepsilon}(\boldsymbol{x}, 0, t - \varepsilon a)| + o(1) (1 + a)^{2} \right\} \exp(-\zeta_{m} a) \end{aligned}$$

where we used Lemma 3.4 in the integral part of the right hand side. Then, thanks to Lemma 5.1, the first term can be estimated as

$$|\hat{\rho}_{\varepsilon}(\boldsymbol{x},0,t-\varepsilon a)|\exp(-\zeta_{m}a) \leq (\beta_{M}|\hat{\mu}(\boldsymbol{x},t-\varepsilon a)| + |\mathcal{M}_{\varepsilon,\boldsymbol{x}}|)\exp(-\zeta_{m}a)$$
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which using again Lemma 5.1 gives:

$$|\hat{\rho}_{\varepsilon}(\boldsymbol{x},0,t-\varepsilon a)| \exp(-\zeta_{m}a) \leq$$

$$\leq \left(\beta_{M} \|\hat{\rho}_{\varepsilon,I}\|_{L_{\infty}^{\infty}L_{t}^{1}} \exp\left(-\frac{\zeta_{m}(t-\varepsilon a)}{\varepsilon}\right) + o(1) + |\mathcal{M}_{\varepsilon,\boldsymbol{x}}|\right) \exp(-\zeta_{m}a)$$

$$\leq C_{1} \exp\left(-\frac{\zeta_{m}t}{\varepsilon}\right) + o(1)(1+a) \exp(-\zeta_{m}a)$$

where $L_{\boldsymbol{x}}^{\infty}L_t^1 := L^{\infty}(\Omega; L^1(\mathbb{R}_+)).$

• if $t \le \varepsilon a$, the claim follows from Duhamel formula and Lemma 3.4 directly.

Corollary 5.1 Under hypotheses 2.1 and 2.2, one has that

$$\int_{\mathbb{R}_+} \sup_{\boldsymbol{x} \in \Omega} |\rho_{\varepsilon}(\boldsymbol{x}, a, t) - \rho_0(\boldsymbol{x}, a, t)| da \leq C \left(1 + \frac{t}{\varepsilon}\right) \exp\left(-\frac{\zeta_m t}{\varepsilon}\right) + o(1) \,,$$

which means that $\sup_{\boldsymbol{x}} |\rho_{\varepsilon}(\boldsymbol{x}, a, t) - \rho_0(\boldsymbol{x}, a, t)|$ converges strongly in $L^1((0, T) \times \mathbb{R}_+)$.

PROOF. The proof follows by integrating in age the previous Lemma.

Corollary 5.2 Under the same hypotheses, $\sup_{\boldsymbol{x}\in\Omega} |\rho_{\varepsilon}(\boldsymbol{x},a,t) - \rho_0(\boldsymbol{x},a,t)|$ converges strongly in $L^1((0,T)\times\mathbb{R}_+,(1+a))$.

5.2. Convergence of z_{ε}

Theorem 5.3 Under hypotheses 2.1, 2.2 and 2.3, the weak solution z_{ε} (cf Definition 3.1) tends to $z_0 \in L^{\infty}([0,T]; H_0^1(\Omega))$ with $\partial_t z_0 \in L^2(Q_T)$, the weak solution of (1.5), i.e.

$$\int_{Q_T} \mu_{1,0} \partial_t z_0 \varphi(\boldsymbol{x}, t) d\boldsymbol{x} dt + \int_{Q_T} \nabla z_0 \cdot \nabla \varphi d\boldsymbol{x} dt = 0.$$
 (5.21)

for every test function $\varphi \in \dot{H}^1(Q_T) := \{ u \in H^1(Q_T) \text{ s.t. } u = 0 \text{ a.e. in } \partial\Omega \times (0,T) \}$

PROOF. We test the weak formulation in Definition 3.1 by a function $v \in H_0^1(\Omega) \cap L^{\infty}(\Omega)$ and we integrate in time after testing by $w \in L^{\infty}((0,T))$. Rewriting in terms of the elongation variable we obtain:

$$\int_{Q_T} \int_{\mathbb{R}_+} \rho_{\varepsilon}(\boldsymbol{x}, a, t) u_{\varepsilon}(\boldsymbol{x}, a, t) da v(\boldsymbol{x}) d\boldsymbol{x} w(t) dt + \int_{Q_T} \nabla z_{\varepsilon}(\boldsymbol{x}, t) \cdot \nabla v(\boldsymbol{x}) w(t) d\boldsymbol{x} dt = 0.$$
 (5.22)

We denote $\varphi(\mathbf{x},t) := v(\mathbf{x})w(t)$ and start with the convergence of the first term above

$$\begin{split} & \int_{\Omega} \int_{0}^{T} \int_{\mathbb{R}_{+}} \rho_{\varepsilon}(\boldsymbol{x}, a, t) u_{\varepsilon}(\boldsymbol{x}, a, t) \varphi(\boldsymbol{x}, t) da dt d\boldsymbol{x} \\ & = \int_{\Omega} \int_{0}^{T} \int_{\mathbb{R}_{+}} (\rho_{\varepsilon}(\boldsymbol{x}, a, t) - \rho_{0}(\boldsymbol{x}, a, t)) u_{\varepsilon}(\boldsymbol{x}, a, t) \varphi(\boldsymbol{x}, t) da dt d\boldsymbol{x} \\ & + \int_{\Omega} \int_{0}^{T} \int_{\mathbb{R}_{+}} \rho_{0}(\boldsymbol{x}, a, t) u_{\varepsilon}(\boldsymbol{x}, a, t) \varphi(\boldsymbol{x}, t) da dt d\boldsymbol{x} =: I_{1} + I_{2}. \end{split}$$

Due to Corollary 5.2 and Theorem 4.3, I_1 can be estimated :

$$|I_1| \leq \|\hat{\rho}_{\varepsilon}(1+a)\|_{L^1((0,T)\times\mathbb{R}_+;L^{\infty}(\Omega))} \left\| \frac{u_{\varepsilon}}{1+a} \right\|_{L^{\infty}((0,T)\times\mathbb{R}_+;L^1(\Omega))} \|\varphi\|_{L^{\infty}(Q_T)} \sim o_{\varepsilon}(1).$$

For the second term one has:

$$\begin{split} &\int_{Q_T} \int_0^\infty \rho_0(\boldsymbol{x}, a, t) u_\varepsilon(\boldsymbol{x}, a, t) \varphi(\boldsymbol{x}, t) \, da \, d\boldsymbol{x} \, dt \\ &= \int_0^{T/\varepsilon} \left(\int_{\varepsilon a}^T \int_{\Omega} \rho_0 \frac{u_\varepsilon}{a} \varphi d\boldsymbol{x} dt \right) a da + \int_0^T \int_{t/\varepsilon}^\infty \int_{\Omega} \rho_0(\boldsymbol{x}, a, t) u_\varepsilon(\boldsymbol{x}, a, t) \varphi(\boldsymbol{x}, t) \, d\boldsymbol{x} \, da \, dt \\ &= I_{2.1} + I_{2.2} \, . \end{split}$$

The first part of this expression can be rewritten as:

$$I_{2,1} = \int_0^{T/\varepsilon} \left(\int_{\varepsilon a}^T \int_{\Omega} \rho_0 \frac{(z_{\varepsilon}(\boldsymbol{x},t) - z_{\varepsilon}(\boldsymbol{x},t - \varepsilon a))}{\varepsilon a} \varphi(\boldsymbol{x},t) d\boldsymbol{x} dt \right) a da.$$

For almost every fixed $a \in \mathbb{R}_+$, one has convergence of the term

$$\int_{\varepsilon a}^{T} \int_{\Omega} \rho_{0} \frac{(z_{\varepsilon}(\boldsymbol{x},t) - z_{\varepsilon}(\boldsymbol{x},t - \varepsilon a))}{\varepsilon a} \varphi(\boldsymbol{x},t) d\boldsymbol{x} dt \rightarrow \int_{0}^{T} \int_{\Omega} \rho_{0}(\boldsymbol{x},a,t) \partial_{t} z_{0}(\boldsymbol{x},t) \varphi(\boldsymbol{x},t) d\boldsymbol{x} dt$$

because of the weak convergence in $L^2(Q_T)$ of the sequence $\frac{(z_{\varepsilon}(\boldsymbol{x},t)-z_{\varepsilon}(\boldsymbol{x},t-\varepsilon a))}{\varepsilon a}$. Moreover, thanks to the estimates on ρ_0 , one has that

$$\begin{split} f_{\varepsilon}(a) &:= a \int_{\varepsilon a}^{T} \int_{\Omega} \rho_{0} \frac{\left(z_{\varepsilon}(\boldsymbol{x}, t) - z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a)\right)}{\varepsilon a} \varphi \, d\boldsymbol{x} \, dt \\ &\leq C \, a \exp\left(-\zeta_{m} a\right) \left\|\chi_{(\varepsilon a, T)} D_{t}^{-\varepsilon a} z_{\varepsilon}\right\|_{L^{2}(Q_{T})} \left\|\varphi\right\|_{L^{2}(Q_{T})} \\ &\lesssim a \exp\left(-\zeta_{m} a\right) \sup_{\tau \in (0, T)} \left\|\chi_{(\tau, T)} D_{t}^{-\tau} z_{\varepsilon}\right\|_{L^{2}(Q_{T})} \lesssim a \exp\left(-\zeta_{m} a\right) \left\|\partial_{t} z_{\varepsilon}\right\|_{L^{2}(Q_{T})}. \end{split}$$

Due to Theorem 4.2 the norm $\partial_t z_{\varepsilon}$ is bounded uniformly in ε , and thus the majorizing function is a L^1 function in age. Applying Lebesgue's Theorem gives the commutation of the limit and the integral in age of f_{ε} .

With regard to the rest, we set $I_{2,2} =: \int_0^T h_{\varepsilon}(t)dt$ and infer that

$$h_{\varepsilon}(t) \leq \int_{t/\varepsilon}^{\infty} C \exp(-\zeta_m a) (1+a) \sup_{a \in \mathbb{R}_+} \frac{\int_{\Omega} |u_{\varepsilon}| d\boldsymbol{x}}{(1+a)} \|\varphi\|_{L^{\infty}(Q_T)} da$$
$$\leq C \left(1 + \frac{t}{\varepsilon}\right) \exp\left(-\frac{\zeta_m t}{\varepsilon}\right),$$

which integrated in time gives $|I_{2,2}| \sim O(\varepsilon)$. On the other hand, by standard arguments of weak convergence, one easily proves thanks to the energy estimates that

$$\int_{Q_T} \nabla z_{\varepsilon} \cdot \nabla \varphi \, d\boldsymbol{x} \, dt \to \int_{Q_T} \nabla z_0 \cdot \nabla \varphi \, d\boldsymbol{x} \, dt.$$

The weak formulation (5.22) tends, as ε goes to zero, to

$$\int_{Q_T} \mu_{1,0} \partial_t z_0 v(\boldsymbol{x}) w(t) d\boldsymbol{x} dt + \int_{Q_T} \nabla z_0 \cdot \nabla v(\boldsymbol{x}) w(t) d\boldsymbol{x} dt = 0$$

for every $v \in H_0^1(\Omega) \cap L^{\infty}(\Omega)$ and every $w \in L^{\infty}((0,T))$. Thanks to Corollary 4.2 and Theorem 4.2, $z_0 \in C([0,T]; H_0^1(\Omega))$ and $\partial_t z_0 \in L^2(Q_T)$. For the consistency with the initial condition it follows from Lemma 4.4 in $L^1(\Omega)$. Using the variational form (3.10) at t=0, one obtains as well that

$$||z_{\varepsilon}(\cdot,0) - z_p(\cdot,0)||_{L^2(\Omega)} \lesssim o_{\varepsilon}(1)$$

thanks to the fact that $z_p \in H_0^1(\Omega)$. We consider a test function $\varphi \in \mathcal{D}(Q_T)$. By Theorem III p.108 [25], the subspace of functions $\varphi(\boldsymbol{x},t)$ of the form $\varphi := \sum_j v_j(\boldsymbol{x}) w_j(t)$ is dense in $\mathcal{D}(Q_T)$. Thus, the previous expression becomes : for all $\varphi \in \mathcal{D}(Q_T)$,

$$<\mu_{1,0}\partial_t z_0, \varphi>_{\mathfrak{D}'(Q_T),\mathfrak{D}(Q_T)} = <\Delta z_0, \varphi>_{\mathfrak{D}'(Q_T),\mathfrak{D}(Q_T)}$$

which means that (i) the equality holds a.e. in Q_T and (ii) as $\mu_{1,0}\partial_t z_0 \in L^2(Q_T)$, so does Δz_0 . Using a test function $\varphi \in C^{\infty}([0,T] \times \Omega)$ vanishing on $[0,T] \times \partial \Omega$, for every fixed $t \in [0,T]$, one

can test the weak form (3.10) and integrate in time, which implies that z_{ε} solves:

$$\int_{Q_T} \int_{\mathbb{R}_+} \rho_\varepsilon u_\varepsilon da \varphi(\boldsymbol{x},t) d\boldsymbol{x} dt + \int_{Q_T} \nabla z_\varepsilon \cdot \nabla \varphi d\boldsymbol{x} dt = 0.$$

This converges in the same way as above to the limit weak form (5.21) for every test function $\varphi \in C^{\infty}([0,T] \times \Omega)$ vanishing on $[0,T] \times \partial \Omega$. Now thanks to Lemma B.1 this set is dense in $\dot{H}^1(Q_T)$. The integration by parts in time is well defined and gives:

$$(z_0(\cdot,T)\mu_{1,0}(\cdot,T),\varphi(\cdot,T)) + \int_0^T (z_0(\cdot,t),\partial_t\mu_{1,0}\varphi + \mu_{1,0}\partial_t\varphi)dt - \int_0^T (\nabla z_0,\nabla\varphi)dt$$
$$= (\mu_{1,0}(\cdot,0)z_p(\cdot,0),\varphi(\cdot,0))$$

for any φ in $\dot{H}^1(Q_T)$. Thus z_0 is a weak solution in the sense of [10] p.136.

6. Adding a source term

If one adds a source term to (1.4), it becomes

$$\begin{cases}
\mathcal{L}_{\varepsilon}(z_{\varepsilon}, \rho_{\varepsilon}) = \Delta_{\boldsymbol{x}} z_{\varepsilon} + \mathcal{S}(\boldsymbol{x}, t), & t \geq 0, \, \boldsymbol{x} \in \Omega, \\
z_{\varepsilon}(\boldsymbol{x}, t) = 0, & t \in \mathbb{R}_{+}, \, \boldsymbol{x} \in \partial \Omega, \\
z_{\varepsilon}(\boldsymbol{x}, t) = z_{p}(\boldsymbol{x}, t), & t < 0, \, \boldsymbol{x} \in \Omega,
\end{cases}$$
(6.23)

where we choose $\mathcal{S} \in W^{1,\infty}((0,T);L^2(\Omega))$ for instance. We give some hints in order to extend the previous results. Existence and uniqueness for ε fixed work the same, we detail those of Section 4. The extension of Theorem 4.1 reads:

Theorem 6.1 If $S \in W^{1,\infty}((0,T);L^2(\Omega))$ and under hypotheses 2.1, 2.2 and 2.3, one has that

$$\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) \leq C_1 \exp(C_2 t) \mathcal{E}_0(z_{\varepsilon}(\cdot,0)) + C_3$$

and $\int_{(0,T)\times\mathbb{R}_+\times\Omega}\zeta_{\varepsilon}\rho_{\varepsilon}u_{\varepsilon}^2dadxdt < C_4$ as well. The constants $(C_i)_{i\in\{1,\dots,4\}}$ are independent on ε .

PROOF. By similar arguments as in Theorem 4.1 we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) + \int_{\Omega \times \mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon}^2 da d\boldsymbol{x} = \int_{\Omega} \partial_t z_{\varepsilon} \mathcal{S} d\boldsymbol{x}$$

Thanks to Theorem 3.7, we can integrate by parts in time the latter expression which gives:

$$\mathcal{E}_{t}(z_{\varepsilon}(\cdot,t)) \leq \mathcal{E}_{0}(z_{\varepsilon}(\cdot,0)) + (z_{\varepsilon}(\cdot,t),\mathcal{S}(\cdot,t)) - (z_{\varepsilon}(\cdot,0),\mathcal{S}(\cdot,0)) + \int_{0}^{t} (z_{\varepsilon}(\cdot,s),\partial_{t}\mathcal{S}(\cdot,s))ds$$

where the parentheses denote the scalar product in $L^2(\Omega)$. Then using Poincaré-Wirtinger in order to estimate $||z_{\varepsilon}(\cdot,t)||_{L^2(\Omega)} \lesssim \mathcal{E}_t(z_{\varepsilon}(\cdot,t))$ and Young's inequality twice (for a given positive δ), one obtains:

$$\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) \lesssim \delta \mathcal{E}_t(z_{\varepsilon}(\cdot,t)) + \delta \int_0^t \mathcal{E}_t(z_{\varepsilon}(\cdot,t)) + C$$

where C depends on $\mathcal{E}_0(z_{\varepsilon}(\cdot,0))$ and on S. By Gronwall, one concludes.

Of course since z_{ε} now solves (6.23) the corresponding energy functional is to be redefined as

$$\tilde{\mathcal{E}}_t(w(\cdot)) := \frac{1}{2} \int_{\Omega} \left\{ |\nabla w|^2 + \int_{\mathbb{R}_+} \frac{|w(\boldsymbol{x}) - z_{\varepsilon}(\boldsymbol{x}, t - \varepsilon a)|^2}{\varepsilon} \rho_{\varepsilon}(\boldsymbol{x}, t, a) da - \mathcal{S}(\boldsymbol{x}, t) w(\boldsymbol{x}) \right\} d\boldsymbol{x}$$

Lemma 6.2 Under the same hypotheses as above, one has $\mathcal{E}_t(z_{\varepsilon}(\cdot,0)) < C$.

The rest follows the same lines as in the homogeneous case since the source term \mathcal{S} belongs to the appropriate functional space.

7. The fully coupled problem

For sake of simplicity we restrict ourselves in this section to the one-dimensional case in the space variable, and set $\Omega := (0,1)$. We consider here the case where ζ_{ε} depends on the elongation. The density of bonds ρ_{ε} solves

$$\begin{cases}
\varepsilon \partial_{t} \rho_{\varepsilon} + \partial_{a} \rho_{\varepsilon} + \zeta(u_{\varepsilon}) \rho_{\varepsilon} = 0, & (\boldsymbol{x}, a, t) \in \Omega \times \mathbb{R}_{+} \times (0, T), \\
\rho_{\varepsilon}(\boldsymbol{x}, a, t) = \beta_{\varepsilon}(\boldsymbol{x}, t)(1 - \mu_{0, \varepsilon}(\boldsymbol{x}, t)), & (\boldsymbol{x}, a, t) \in \Omega \times \{0\} \times (0, T), \\
\rho_{\varepsilon}(\boldsymbol{x}, a, 0) = \rho_{I}(\boldsymbol{x}, a), & (\boldsymbol{x}, a) \in \Omega \times \mathbb{R}_{+},
\end{cases}$$
(7.24)

coupled with the system

$$\begin{cases}
\varepsilon \partial_t u_{\varepsilon} + \partial_a u_{\varepsilon} = g(\boldsymbol{x}, t), & (\boldsymbol{x}, a, t) \in \Omega \times \mathbb{R}_+ \times (0, T), \\
u_{\varepsilon}(\boldsymbol{x}, 0, t) = 0, & (\boldsymbol{x}, a, t) \in \Omega \times \{0\} \times (0, T), \\
u_{\varepsilon}(\boldsymbol{x}, a, t) = 0, & (\boldsymbol{x}, a, t) \in \partial\Omega \times \mathbb{R}_+ \times (0, T), \\
u_{\varepsilon}(\boldsymbol{x}, a, 0), = u_I(\boldsymbol{x}, a) & (\boldsymbol{x}, a) \in \Omega \times \mathbb{R}_+,
\end{cases}$$
(7.25)

where g solves in the variational sense in $H_0^1(\Omega)$:

$$(\mu_{0,\varepsilon} - \varepsilon \Delta)g = \int_{\mathbb{R}_+} \zeta_{\varepsilon} \rho_{\varepsilon} u_{\varepsilon} da + \varepsilon \partial_t \mathcal{S}, \quad \text{a.e } \boldsymbol{x} \in \Omega$$
 (7.26)

and we assume

Assumptions 7.1 Hypotheses 2.2 hold, moreover we add,

- i) ζ is a Lipschitz function s.t. $|\zeta'(u)| \leq \zeta_{Lip}$ for all $u \in \mathbb{R}$ and $\zeta(u) \geq \zeta_m > 0$ but there is not necessarily an upper bound
- ii) β_{ε} is a given bounded function in space and time, moreover

$$0 < \beta_{\varepsilon}(\boldsymbol{x}, t) < \beta_{M}$$
 a.e $(\boldsymbol{x}, t) \in \Omega \times (0, T)$.

- iii) for sake of simplicity we assume that $\mathcal{S} \in W^{1,\infty}((0,T);L^2(\Omega))$,
- iv) for z_p the Lipschitz constant $C_{z_p} \in L^{\infty}_{\boldsymbol{x}}$. This implies that u_{ε} defined as in (4.17) satisfies $u_I/(1+a) \in L^{\infty}_{\boldsymbol{x},a}$.
- v) $z_{\varepsilon}(\boldsymbol{x},0)$ satisfies the variational problem : find $z \in H_0^1(\Omega)$ s.t.

$$(\mu_{0,I} - \varepsilon \Delta)z = \int_{\mathbb{R}_{+}} z_{p}(\boldsymbol{x}, -\varepsilon a)\rho_{I}(\boldsymbol{x}, a)da + \mathcal{S}(\boldsymbol{x}, 0)$$
(7.27)

We define the Banach space Y_T

$$Y_T := \left\{ u \in \mathcal{D}'(\Omega \times \mathbb{R}_+ \times (0,T)) \text{ s.t. } \frac{u}{1+a} \in L^{\infty}_{\boldsymbol{x},a,t} \right\}.$$

endowed with its natural norm $\|u\|_{Y_T} := \|u/(1+a)\|_{L^\infty_{x,a,t}}.$ 20

7.1. Existence and uniqueness for a truncated problem

Theorem 7.1 Under assumptions 7.1, there is a unique solution $(\rho, w) \in L_t^{\infty} L_a^1 L_x^{\infty} \times Y_T$ solving (7.24-7.25) where in the latter equation the right hand side is replaced by $T_k(g_w)$, $T_k(g)$ being the usual truncation operator defined as $T_k(g) := \max((-k), \min(g, k))$ for a fixed positive integer k and g_w solves (7.26).

PROOF. We proceed as in Theorem 3.2 [16]. Indeed, for a given w, ϱ_w solves (7.24) with $\zeta(w)$ as the death rate. The density ϱ_w exists in the sense of characteristics and is unique in $L_t^\infty L_a^1 L_x^\infty$ as showed above. One then computes (7.26) with at the right hand side $\int_{\mathbb{R}_+} \zeta(w) \varrho_w w da$ as a first term. Then u_w solves (7.25) with the truncated right hand side $T_k(g)$. Since $|T_k(g)| \leq k$, if $w \in Y_T$ so is u_w invariably, since

$$||u_w||_{Y_T} \le k + ||u_I/(1+a)||_{L_{\infty}^{\infty}}.$$

At this stage the map $\overline{\Phi}$ is complete $u_w = \overline{\Phi}(w)$ and $\overline{\Phi}$ is endomorphic. Next we prove it is a contraction.

$$|\hat{g}(\boldsymbol{x},t)| \leq \|\hat{g}\|_{L_{x}^{\infty}} \leq \omega \|\hat{g}\|_{H_{0}^{1}(\Omega)} \lesssim \left\| \int_{\mathbb{R}_{+}} \widehat{\zeta(w)\varrho_{w}} w da + \hat{\mu}g_{1} \right\|_{L_{x}^{1}} \leq C \|\hat{w}\|_{Y_{T}}$$

where $\hat{g} := g_{w_2} - g_{w_1}$ and so on. The second estimate is due to the Sobolev embedding $H_0^1(\Omega) \subset C(\Omega)$ holding when n = 1, while the third one is the consequence of the Lax-Milgram Theorem. In order to obtain the last estimate above, we follow the steps in part b) of the proof of Theorem 3.2 [16], the construction follows up to a time T small enough. Then it is possible to show (see part c) in the proof of Theorem 3.1 [16]) that the contraction time does not depend on the initial data but on k, one concludes the global existence result.

Theorem 4.3 holds as well for (ϱ_w, w) , the solution of the truncated problem.

7.2. A stability result

Here the scope is to prove that the truncation constant k can be chosen s.t. g solving (7.26) actually never reaches truncation bounds $\{-k\} \cup \{k\}$.

Proposition 7.2 Under assumptions 7.1, let (ϱ_w, w) be the solution of the fully coupled and stabilized problem (7.24)-(7.25)-(7.26), with the modified source term $T_k(g)$ in (7.25), there exists a positive finite constant γ_2 s.t.

$$p(t) := \int_{\mathbb{R}_+ \times \Omega} \zeta_{\varepsilon}(w(t, a)) |w(t, a)| \varrho_w(t, a) d\mathbf{x} da \le \gamma_2, \quad \forall t \ge 0,$$

where the constant γ_2 depends on the a priori bound on $\int_{\mathbb{R}_+} \varrho_w |w| da$ (obtained in Theorem 4.3), $\|\partial_t f\|_{L^\infty_t,L^2_x}$, ζ_{Lip} , and $\zeta(0)$, but not on k.

PROOF. Using equations (7.24), (7.25) and hypotheses on ζ , one has

$$\varepsilon \partial_t (\varrho_w | w | \zeta_\varepsilon) + \partial_a (\varrho_w | w | \zeta_\varepsilon) + \zeta_\varepsilon^2 | w | \varrho_w \le \varrho_w | w | (\varepsilon \partial_t \zeta_\varepsilon + \partial_a \zeta_\varepsilon) + \zeta_\varepsilon \varrho_w | T_k(g) |.$$

Integrating in age and space gives

$$\varepsilon \partial_{t} p + \int_{\mathbb{R}_{+} \times \Omega} \zeta_{\varepsilon}^{2} |w(t, a)| \varrho_{w}(t, a) d\boldsymbol{x} da \leq \|T_{k}(g)\|_{L_{\boldsymbol{x}}^{\infty}} \int_{\mathbb{R}_{+} \times \Omega} (\zeta_{\operatorname{Lip}} \varrho_{w} |w| + \zeta(w) \varrho_{w}(t, a)) d\boldsymbol{x} da \\
\leq \|T_{k}(g)\|_{L_{\boldsymbol{x}}^{\infty}} \left(2\zeta_{\operatorname{Lip}} \int_{\mathbb{R}_{+}} \varrho_{w} |w| da + \zeta(0) \right) \leq (2\zeta_{\operatorname{Lip}} / \gamma_{1} + \zeta(0)) \|T_{k}(g)\|_{L_{\boldsymbol{x}}^{\infty}}, \tag{7.28}$$

where we use Theorem 4.3 to bound the braquets on right hand side, and we denote

$$\int_{\mathbb{R}_+\times\Omega}\varrho_w|w|dxda\leq\gamma_1^{-1}.$$

As the domain is one-dimensional, one has the embedding $H_0^1(\Omega) \subset C(\Omega)$ and thus there exists a constant ω independent of g s.t.

$$\begin{split} \|T_k(g(\cdot,t))\|_{L^\infty_x} &\leq \|g(\cdot,t)\|_{L^\infty_x} \leq \omega \|g(\cdot,t)\|_{H^1_0(\Omega)} \leq \frac{\omega}{\varepsilon} \left\| \int_{\mathbb{R}_+} \zeta(w) \varrho_w w da + \varepsilon \partial_t \mathcal{S} \right\|_{H^{-1}_x(\Omega)} \\ &\leq \frac{\omega}{\varepsilon} \left\| \int_{\mathbb{R}_+} \zeta(w) \varrho_w w da \right\|_{L^1_x} + \omega \|\partial_t \mathcal{S}\|_{H^{-1}_x} \leq \frac{\omega}{\varepsilon} p + \omega \|\partial_t \mathcal{S}\|_{H^{-1}_x} \end{split}$$

Now we consider the second term in the left hand of (7.28): using Jensen's inequality one writes

$$\left(\frac{\int_{\mathbb{R}_{+}\times\Omega}\zeta(w)|w(\boldsymbol{x},a,t)|\varrho_{w}(\boldsymbol{x},a,t)d\boldsymbol{x}da}{\int_{\mathbb{R}_{+}\times\Omega}|w|\varrho_{w}d\boldsymbol{x}da}\right)^{2}\leq\frac{\int_{\mathbb{R}_{+}\times\Omega}(\zeta_{\varepsilon}(w))^{2}|w(\boldsymbol{x},a,t)|\varrho_{w}(\boldsymbol{x},a,t)d\boldsymbol{x}da}{\int_{\mathbb{R}_{+}\times\Omega}|w|\varrho_{w}d\boldsymbol{x}da}\,,$$

since $|w|\varrho_w/\int_{\mathbb{R}_+\times\Omega}|w|\varrho_w\,dxda$ is a unit measure on $\Omega\times\mathbb{R}_+$. This implies that

$$\int_{\Omega \times \mathbb{R}_+} (\zeta_{\varepsilon}(w))^2 |w(\boldsymbol{x}, a, t)| \varrho_w(t, a) \, dad\boldsymbol{x} \geq \frac{\left(\int_{\Omega \times \mathbb{R}_+} \zeta(w) |w(\boldsymbol{x}, a, t)| \varrho_w(\boldsymbol{x}, a, t) dad\boldsymbol{x}\right)^2}{\int_{\Omega \times \mathbb{R}_+} |w| \varrho_w dad\boldsymbol{x}} \geq \gamma_1 p^2.$$

We obtain a Riccati inequality

$$\varepsilon \partial_t p + \gamma_1 p^2 \le h + \omega p/\varepsilon$$
, $p(0) = \int_{\mathbb{R}_+} \zeta_\varepsilon(u_I(a)) |u_I(a)| \rho_I(a) da$,

where $h := \omega \|\partial_t \mathcal{S}\|_{L^\infty_t H^{-1}_x} (2\zeta_{\text{Lip}}/\gamma_1 + \zeta(0))$ is a constant. We denote by P_\pm the solutions of the steady state equation associated to the last inequality, *i.e.* P solves $\gamma_1 P^2 - P/\varepsilon - h = 0$. The solutions are given by

$$P_{\pm} = \left(\frac{\omega}{\varepsilon} \pm \sqrt{\frac{\omega^2}{\varepsilon^2} + 4h\gamma_1}\right) / (2\gamma_1) \le \max\left(p(0), \left(\omega + \sqrt{\omega^2 + 4h\gamma_1\varepsilon^2}\right) / (2\varepsilon\gamma_1)\right) =: \gamma_2.$$

Applying A.1 in the appendix [16], we conclude that $p(t) \le \max\{p(0), P_+\} \le \gamma_2$, which ends the proof.

Corollary 7.1 Under hypotheses 7.1, there exists a unique global solution of (7.24-7.25-7.26).

PROOF. It suffices to take $k > \gamma_2/\varepsilon + \|\partial_t \mathcal{S}\|_{L^\infty_t H^{-1}_x}$, and it is clear from above that g never reaches k a.e. x,t. Thus the solution (ϱ_w,w) is also the solution of (7.24-7.25-7.26) without truncating g. Thus existence is proved. Since the truncated solution pair is unique so is the latter one.

7.3. If $\beta_m > 0$, the total bonds' population never vanishes

Once a global $L_{x,a,t}^{\infty}$ bound is proved for g solving (7.26), one should use again arguments of Lemma 4.1, Proposition 4.2 and 4.3 [16] and prove exactly in the same way:

Theorem 7.3 Under assumptions 7.1, if $\beta_{\varepsilon} \geq \beta_m > 0$ and $\|\mu_{0,I}\|_{L_{x}^{\infty}} \leq \gamma_0 < 1$, then the solution $(\rho_{\varepsilon}, u_{\varepsilon})$ of (7.24-7.25-7.26) satisfies

i) defining $\gamma_1 > 0$ as $\gamma_1 < \min(1 - \gamma_0, \zeta_m/(\zeta_m + \beta_M))$

$$\|\mu_{0,\varepsilon}\|_{L_x^{\infty}} \le 1 - \gamma_1, \quad \forall t > 0,$$

ii) this in turn implies that

$$\frac{\int_{\mathbb{R}_{+}} \zeta(u_{\varepsilon}(\boldsymbol{x},a,t)) \rho_{\varepsilon}(\boldsymbol{x},a,t) da}{\int_{\mathbb{R}_{+}} \rho_{\varepsilon}(\boldsymbol{x},a,t) da} \leq \zeta(0) + C \left(1 + \left\|\frac{u_{I}}{1+a}\right\|_{L_{\boldsymbol{x},a}^{\infty}}\right) \frac{2}{\gamma_{1}\beta_{m}} \|g\|_{L_{\boldsymbol{x},t}^{\infty}} =: \gamma_{2}$$

for almost every x in Ω .

iii) choosing $\mu_{0,m} > 0$ s.t.

$$\mu_{0,m} < \min \left(\inf_{\boldsymbol{x} \in \Omega} \mu_{0,I}(\boldsymbol{x}), \frac{\beta_m}{\beta_m + \gamma_2} \right)$$

one guarantees that

$$\mu_{0,\varepsilon}(\boldsymbol{x},t) \ge \mu_{0,m}$$
, a.e $\boldsymbol{x} \in \Omega$, $\forall t > 0$.

This result proves that it is not possible to have extinction of bonds at the contrary to the situation observed in [16].

 $7.4. \ Equivalence \ with \ the \ initial \ formulation$

Lemma 7.4 Under hypotheses 7.1, if $(\rho_{\varepsilon}, u_{\varepsilon})$ solves (7.24-7.25-7.26), then defining $z_{\varepsilon}(\boldsymbol{x}, t) := \int_0^t g(\boldsymbol{x}, s) ds + z_{\varepsilon}(\boldsymbol{x}, 0)$ where $z_{\varepsilon}(\boldsymbol{x}, 0)$ is the solution of (7.27), one has (4.14) and $(\rho_{\varepsilon}, z_{\varepsilon}) \in C_t L_a^1 L_{\boldsymbol{x}}^{\infty} \times C_t^1 L_{\boldsymbol{x}}^{\infty}$ solves (7.24) coupled with (1.4).

PROOF. Using the method of characteristics, starting from (7.25), one recovers by definition of z_{ε} (4.14). Using (7.25) and integrating against ρ_{ε} , one has

$$\begin{split} &\left(\varepsilon\partial_t\int_{\mathbb{R}_+}\rho_\varepsilon u_\varepsilon da + \int_{\mathbb{R}_+}\zeta\rho_\varepsilon u_\varepsilon da,v\right) = \\ &= \left(\mu_{0,\varepsilon}g,v\right) = -\varepsilon(\nabla g,\nabla v) + \left(\int_{\mathbb{R}_+}\zeta\rho_\varepsilon u_\varepsilon da + \varepsilon\partial_t\mathcal{S},v\right), \quad \forall v\in H^1_0(\Omega), \end{split}$$

where the exterior barquets denote the scalar product in L_x^2 . After a simplification and integration in time, the latter expression becomes:

$$\left(\int_{\mathbb{R}_+} \rho_{\varepsilon} u_{\varepsilon} da, v\right) = -\left(\nabla \int_0^t g(\boldsymbol{x}, s) ds, \nabla v\right) + \left(\mathcal{S}(\boldsymbol{x}, t) - \mathcal{S}(\boldsymbol{x}, 0) + \int_{\mathbb{R}_+} \rho_I u_I da, v\right),$$

but because of the definition of u_I and $z_{\varepsilon}(\boldsymbol{x},0)$ one recovers that

$$\left(\int_{\mathbb{R}_{+}} \rho_{\varepsilon} u_{\varepsilon} da, v\right) = -\left(\nabla\left(\int_{0}^{t} g(\boldsymbol{x}, s) ds + z_{\varepsilon}(\boldsymbol{x}, 0)\right), \nabla v\right) + (\mathcal{S}(\boldsymbol{x}, t), v)$$

$$= -(\nabla z_{\varepsilon}(\boldsymbol{x}, t), \nabla v) + (\mathcal{S}(\boldsymbol{x}, t), v),$$

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which ends the proof.

7.5. Positivity and concluding remarks

Theorem 7.5 Under assumptions 7.1, if moreover $u_I(a) \ge 0$ for a.e. $(\boldsymbol{x}, a) \in \mathbb{R}_+$ and $\partial_t \mathcal{S}(\boldsymbol{x}, t) \ge 0$ for a.e. $(\boldsymbol{x}, t) \in \Omega \times (0, T)$, then $u_{\varepsilon}(\boldsymbol{x}, a, t)$ is non-negative for a.e. $(\boldsymbol{x}, a, t) \in \Omega \times (\mathbb{R}_+)^2$.

PROOF. We define $[u]_-$ (resp. $[u]_+$) the negative (resp. positive) part of u i.e. $[u]_- := \min(0, u)$, (resp. $[u]_+ := \max(0, u)$). We set $H_-(u) := -\operatorname{sgn}_-(u)$ with sgn_- being the negative part of the sign function. We look for $(\rho_{\varepsilon}, u_{\varepsilon}^+)$ solving the coupled system :

$$\begin{cases}
\varepsilon \partial_{t} u_{\varepsilon}^{+} + \partial_{a} u_{\varepsilon}^{+} = g_{+} & \boldsymbol{x} \in \Omega, a > 0, t > 0, \\
(\mu_{0,\varepsilon} - \varepsilon \Delta) g_{+} = \left(\varepsilon \partial_{t} \mathcal{S} + \int_{0}^{\infty} \left(\zeta_{\varepsilon} [u_{\varepsilon}^{+}]_{+} \rho_{\varepsilon} \right) (t, \tilde{a}) d\tilde{a} \right), & (\boldsymbol{x}, t) \in \Omega \times (0, T), \\
u_{\varepsilon}^{+} (\boldsymbol{x}, 0, t) = 0, & t > 0, \\
u_{\varepsilon}^{+} (\boldsymbol{x}, a, t) = 0, & \boldsymbol{x} \in \partial \Omega, t > 0, \\
u_{\varepsilon}^{+} (\boldsymbol{x}, a, 0) = u_{I} (\boldsymbol{x}, a), & \boldsymbol{x} \in \Omega, a > 0,
\end{cases}$$
(7.29)

together with $\rho_{\varepsilon}(u_{\varepsilon}^{+})$ being the solution of (7.24) with the death rate $\zeta(u_{\varepsilon}^{+})$. The results of Corollary 7.1 can be repeated and provide global existence and uniqueness. Multiplying (7.29) by $H_{-}(u_{\varepsilon}^{+})$, (cf the rigorous explanation in Lemma 3.1 [14] that holds here for a. e. $x \in \Omega$), one gets

$$\varepsilon \partial_t [u_\varepsilon^+]_- + \partial_a [u_\varepsilon^+]_- = H_-(u_\varepsilon^+) g_+.$$

Because of the weak maximum principle (Theorem 8.1, p.179 [7]), $g_+ \ge 0$. As H_- is positive, one concludes that:

$$\varepsilon \partial_t [u_\varepsilon^+]_- + \partial_a [u_\varepsilon^+]_- \ge 0$$

which using the Duhamel formula provides that

$$0 \ge [u_{\varepsilon}^+(\boldsymbol{x},a,t)]_- \ge \begin{cases} [u_{\varepsilon}^+(\boldsymbol{x},0,t-\varepsilon a)]_- = 0 & \text{if } t \ge \varepsilon a, \\ [u_I(\boldsymbol{x},a-t/\varepsilon)]_- = 0 & \text{if } t \le \varepsilon a. \end{cases}$$

for almost every $\boldsymbol{x} \in \Omega$. But as u_{ε}^+ is then almost everywhere positive $(\rho_{\varepsilon}, u_{\varepsilon}^+)$ satisfies as well system (7.24)-(7.25), which by uniqueness proves that actually $(\rho_{\varepsilon}(u_{\varepsilon}), u_{\varepsilon}) = (\rho_{\varepsilon}(u_{\varepsilon}^+), u_{\varepsilon}^+)$, which implies the claim.

Under hypotheses above u_{ε} is positive and thus the equation satisfied by $\mu_{0,\varepsilon}$ can be made explicit if we suppose that $\zeta(u) := 1 + |u|$ for instance. Indeed,

$$\begin{split} \varepsilon \partial_t \mu_{0,\varepsilon} - \beta_\varepsilon (1 - \mu_{0,\varepsilon}) + \int_{\mathbb{R}_+} \zeta(u_\varepsilon) \rho_\varepsilon da &= \varepsilon \partial_t \mu_{0,\varepsilon} - \beta_\varepsilon (1 - \mu_{0,\varepsilon}) + \mu_{0,\varepsilon} + \int_{\mathbb{R}_+} \rho_\varepsilon u_\varepsilon da = \\ &= \varepsilon \partial_t \mu_{0,\varepsilon} - \beta_\varepsilon (1 - \mu_{0,\varepsilon}) + \mu_{0,\varepsilon} + \mathcal{S} + \Delta z_\varepsilon = 0. \end{split}$$

According to that, one sees that there is a new balance of terms when compared to the case without the Laplace operator considered in [16].

$$(\varepsilon \partial_t + (\beta_\varepsilon + 1))\mu_{0,\varepsilon} + \Delta z_\varepsilon + S = \beta_\varepsilon \tag{7.30}$$

Indeed without the Laplace operator, there could be a sufficient tear-off (\mathcal{S} large enough) so that the birth source term becomes too small and $\mu_{0,\varepsilon}$ is shown to go to zero in finite time (see Proposition 7.3 [16]). It suffices to take $\mathcal{S}_{\min} > \beta_M$ for example. Here instead, the presence of the Laplace operator stabilizes the exterior force and provides global existence. One observes that if \mathcal{S} and β_{ε} converge as time grows to some functions of \boldsymbol{x} , the asymptotic profile (for large times) $(\rho_{\infty}, z_{\infty})$ is s.t.

$$S_{\infty} = -\Delta z_{\infty}, \quad \mu_{\infty}(\boldsymbol{x}) = \frac{\beta_{\infty}}{\beta_{\infty} + 1}.$$

Indeed $\mathcal{L}_{\varepsilon}z_{\infty} = 0$ so that the first equation is the asymptotic limit in time of (1.4), while the second comes from (7.30) with $\partial_t \mu_{\infty} = 0$.

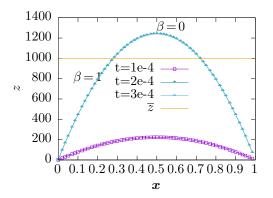
7.6. A numerical simulation

We discretize (7.24) using an explicit upwind method with the CFL constant being equal to 1. We use a trapezoidal rule to compute the non-local boundary condition $\rho_{\varepsilon}(\boldsymbol{x},0,t) = \beta_{\varepsilon}(\boldsymbol{x},t)(1-\mu_{0,\varepsilon})$. We solve (1.4) using a P2 Discontinuous Galerkin method for the Laplace operator in space [5] and a trapezoidal rule to discretize $\mathcal{L}_{\varepsilon}$.

The constants are defined as: $\mathcal{S} = 1e4$, $z_p(\boldsymbol{x},t) = \sin(\pi \boldsymbol{x})/\pi$, the initial condition for $\rho_I = \exp(-a)$ is uniform with respect \boldsymbol{x} , $\zeta(u) = 1 + |u|$ and the maximal age is $a_{\text{max}} = 10$ with a discretisation step $\Delta a = 10^4$ and $\varepsilon = 1e - 3$. The on-rate β in (7.24) is defined s.t. it is z_{ε} dependent

$$\beta(\boldsymbol{x},t) = \begin{cases} 1 & \text{if } z_{\varepsilon} \in (0,\overline{z}) \\ 0 & \text{otherwise} \end{cases}$$

with $\overline{z} = 1000$, then we observe at least locally in space that total extinction of bonds' population occurs.



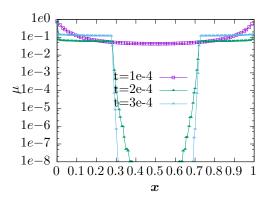


Figure 1: $z_{\varepsilon}(x,t)$ at given times, when t>2e-4 the curves are superposed

Figure 2: $\mu_{0,\varepsilon}(\boldsymbol{x},t)$ at given times, in logscale

The non-local boundary condition does not exactly fit in the framework presented in this section, since β_{ε} depends on z_{ε} which is not in assumptions (7.1), but conditionally β_{ε} vanishes. Nevertheless the previous results could be extended in this case. The fact that β_{ε} vanishes contradicts the hypothesis of Theorem 7.3. We display in figure 1 the displacement z_{ε} as a function of \boldsymbol{x} for different times and in figure 2, $\mu_{0,\varepsilon}$ is displayed as well. Since the convergence towards the steady state is exponential we focus on small times. One observes that asymptotically in time two regimes occur: either $z_{\infty} > \overline{z}$ and then $\mu_{\infty} = 0$, or $z_{\infty} < \overline{z}$ and $\mu_{\infty} = \frac{1}{2}$. One should note that in this case, there is an elliptic-parabolic transition inside the domain since $\mathcal{L}_{\varepsilon}$ may vanish on some compact sub-interval.

In order to conclude, this simulation show that in order to have detachments of an adhesion site, it seems that a necessary condition is that the adhesion on-rate should vanish, at the contrary to what was shown in the single point adhesion model [16] where the explosion of the non-linear death-rate was enough.

A. Euler-Lagrange equation versus minimization

Lemma A.1 The function $z_{\varepsilon} \in X_T$ is the weak solution of system (1.4) if and only if it satisfies (1.1)-(1.2).

PROOF. As the square function is convex, one has for all $v \in H_0^1(\Omega)$ that :

$$\begin{aligned} &\frac{1}{2} \left\{ (z_{\varepsilon}(\boldsymbol{x},t) - z_{\varepsilon}(\boldsymbol{x},t - \varepsilon a))^{2} - (v(\boldsymbol{x}) - z_{\varepsilon}(\boldsymbol{x},t - \varepsilon a))^{2} \right\} \\ &\leq &(z_{\varepsilon}(\boldsymbol{x},t) - z_{\varepsilon}(\boldsymbol{x},t - \varepsilon a))(z_{\varepsilon}(\boldsymbol{x},t) - v(\boldsymbol{x})) \\ &\qquad \qquad 25 \end{aligned}$$

multiplying by $\rho_{\varepsilon} \geq 0$, integrating in age and then in space, one gets that

$$\begin{split} &\frac{1}{2\varepsilon}\left\{\int_{\Omega}\int_{\mathbb{R}_{+}}(z_{\varepsilon}(\boldsymbol{x},t)-z_{\varepsilon}(\boldsymbol{x},t-\varepsilon a))^{2}\rho_{\varepsilon}(\boldsymbol{x},a,t)dad\boldsymbol{x}\right.\\ &\left.-\int_{\Omega}\int_{\mathbb{R}_{+}}(v(\boldsymbol{x})-z_{\varepsilon}(\boldsymbol{x},t-\varepsilon a))^{2}\rho_{\varepsilon}(\boldsymbol{x},a,t)dad\boldsymbol{x}\right\}\leq\left(\mathcal{L}_{\varepsilon}(z_{\varepsilon},\rho_{\varepsilon}),z_{\varepsilon}-v\right). \end{split}$$

As z_{ε} is a weak solution in the sense of Definition 3.1, and $z_{\varepsilon} - v$ is in the test space, one can write that

$$(\mathcal{L}_{\varepsilon}(z_{\varepsilon}, \rho_{\varepsilon}), z_{\varepsilon} - v) + (\nabla z_{\varepsilon}, \nabla(z_{\varepsilon} - v)) = 0$$

and using the previous convexity argument, one concludes that

$$\mathcal{E}_t(z_{\varepsilon}(\cdot,t)) \leq \mathcal{E}_t(v), \quad \forall v \in H_0^1(\Omega).$$

Conversely, set $i(\tau) := \mathcal{E}_t(z_{\varepsilon} + \tau v)$ for any $v \in H_0^1(\Omega)$, then since z_{ε} satisfies (1.1), one has i'(0) = 0. As the expression is explicit with respect to τ the claim follows by simple computations.

B. A density result

Lemma B.1 Ω is a Lipschitz bounded domain, the set $\{u \in C^{\infty}(\Omega \times [0,T]) \text{ s.t. } u=0 \text{ on } \partial\Omega \times [0,T]\}$, is dense in $\dot{H}^1(Q_T) := \{u \in H^1(\Omega \times [0,T]) \text{ s.t. } u=0 \text{ on } \partial\Omega \times [0,T]\}$ endowed with the $H^1(\Omega \times [0,T])$ norm.

PROOF. According to [10], p.89, Lemma 4.12, the set of functions of the form $\sum_{k=1}^{N} d_k(t) \psi_k(x)$ is dense in $\dot{H}^1(Q_T)$, where $d_k(t) \in C^{\infty}([0,T])$ and $(\psi_k)_{k \in \mathbb{N}}$ is a fundamental system of functions in $H_0^1(\Omega)$. Then, approximating each $\psi_k \in H_0^1(\Omega)$ by a $\mathcal{D}(\Omega)$ function completes the proof, since the number N is finite.

References

- [1] W. Alt and M. Dembo. Cytoplasm dynamics and cell motion: two-phase flow models. *Math Biosci*, 156(1-2):207–228, Mar 1999.
- [2] F. Boyer and P. Fabrie. Mathematical tools for the study of the incompressible Navier-Stokes equations and related models, volume 183 of Applied Mathematical Sciences. Springer, New York, 2013.
- [3] D. Bray. Cell Movements: From Molecules to Motility. Garland Pub., 2001
- [4] H. Brezis and A. C. Ponce. Kato's inequality up to the boundary. Commun. Contemp. Math., 10(6):1217-1241, 2008.
- [5] A. Ern and J.-L. Guermond. Theory and Practice of Finite Elements, volume 159 of Applied Mathematical Series. Springer-Verlag, New York, 2004.
- [6] L. C. Evans. Partial differential equations, volume 19 of Graduate Studies in Mathematics. American Mathematical Society, Providence, RI, 1998.
- [7] D. Gilbarg and N. S. Trudinger. Elliptic partial differential equations of second order. Classics in Mathematics. Springer-Verlag, Berlin, 2001. Reprint of the 1998 edition.
- [8] Bérénice Grec, Bertrand Maury, Nicolas Meunier, and Laurent Navoret. A 1D model of leukocyte adhesion coupling bond dynamics with blood velocity. working paper or preprint, July 2017.
- [9] P. Grisvard. Elliptic problems in nonsmooth domains, volume 24 of Monographs and Studies in Mathematics. Pitman (Advanced Publishing Program), Boston, MA, 1985.
- [10] O. A. Ladyzhenskaya, V. A. Solonnikov, and N. N. Uraltseva. Linear and quasilinear equations of parabolic type. Izdat. "Nauka", Moscow, 1967.
- [11] F. Li, S. D. Redick, H. P. Erickson, and V. T. Moy. Force measurements of the α5β1 integrinfibronectin interaction. Biophysical Journal, 84(2):1252 – 1262, 2003.
- [12] A. Manhart, D. Oelz, C. Schmeiser, and N. Sfakianakis. An extended Filament Based Lamellipodium Model produces various moving cell shapes in the presence of chemotactic signals. J. Theoret. Biol., 382:244–258, 2015.
- [13] A. Manhart, D. Oelz, C. Schmeiser, and N. Sfakianakis. Numerical treatment of the filament-based lamellipodium model (FBLM). In *Modeling cellular systems*, volume 11 of *Contrib. Math. Comput. Sci.*, pages 141–159. Springer, Cham, 2017.
- [14] V. Milišić and D. Oelz. On the asymptotic regime of a model for friction mediated by transient elastic linkages. J. Math. Pures Appl. (9), 96(5):484–501, 2011.

- [15] V. Milišić and D. Oelz. On a structured model for the load dependent reaction kinetics of transient elastic linkages. SIAM J. Math. Anal., 47(3):2104–2121, 2015.
- [16] V. Milišić and D. Oelz. Tear-off versus global existence for a structured model of adhesion mediated by transient elastic linkages. *Commun. Math. Sci.*, 14(5):1353–1372, 2016.
- [17] V. Milišić. Initial layer analysis for a linkage density in cell adhesion mechanisms. preprint, submitted.
- [18] A. Mogilner and G. Oster. Cell motility driven by actin polymerization. Biophys. J., 71(6):3030–3045, Dec 1996.
- [19] D. Oelz and C. Schmeiser. Derivation of a model for symmetric lamellipodia with instantaneous cross-link turnover. Archive for Rational Mechanics and Analysis, 198(3):963–980, 2010.
- [20] D. Oelz, C. Schmeiser, and V. Small. Modelling of the actin-cytoskeleton in symmetric lamellipodial fragments. Cell Adhesion and Migration, 2:117–126, 2008.
- [21] T. D. Pollard. Regulation of actin filament assembly by Arp2/3 complex and formins. Annu Rev Biophys Biomol Struct, 36:451–477, 2007.
- [22] T. D. Pollard and G. G. Borisy. Cellular motility driven by assembly and disassembly of actin filaments. Cell, 112(4):453–465, Feb 2003.
- [23] L. Preziosi and G. Vitale. A multiphase model of tumor and tissue growth including cell adhesion and plastic reorganization. Math. Models Methods Appl. Sci., 21(9):1901–1932, 2011.
- [24] Boris R., K. Jacobson, and A. Mogilner. Multiscale two-dimensional modeling of a motile simple-shaped cell. Multiscale Modeling and Simulation, 3(2):413–439, 2005.
- [25] L. Schwartz. *Théorie des distributions*. Publications de l'Institut de Mathématique de l'Université de Strasbourg, No. IX-X. Nouvelle édition, entiérement corrigée, refondue et augmentée. Hermann, Paris, 1966.
- [26] H. Suda. Origin of friction derived from rupture dynamics. Langmuir, 17(20):6045-6047, 2001.