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TEAR-OFF VERSUS GLOBAL EXISTENCE FOR A STRUCTURED MODEL OF ADHESION MEDIATED BY TRANSIENT ELASTIC LINKAGES*

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Abstract. We consider a microscopic non-linear model for friction mediated by transient elastic linkages introduced in our previous works. In the present study, we prove existence and uniqueness of a solution to the coupled system under weaker hypotheses. The theory we present covers the case where the off-rate of linkages is unbounded but increasing at most linearly with respect to the mechanical load.

The time of existence is typically bounded, culminating in tear-off where the moving binding site does not have any bonds with the substrate. However, under additional assumptions on the external force, we prove global in time existence of a solution that consequently stays attached to the substrate.

Key words. Friction coefficient, protein linkages, cell adhesion, renewal equation, effect of chemical bonds, integral equation, Volterra kernel.

AMS subject classifications. 35Q92, 35B40, 45D05.

1. Introduction

Adhesion forces at the cellular and intra-cellular scales play an important role in several phenomenons such as cell motility (see [12] and the references therein) and cancer growth [14]. In [12] the authors derive a complete model for a moving network of actin filaments polymerizing near the boundary of the cell and depolymerizing close to the nucleus, providing biologically plausible steady-state [11] and moving [8] configurations of the cell shape. The main advantage of this method is that the parameters we use are easy to obtain experimentally if not already available in the literature [3, 4, 6, 7, 13]. The adhesion and the stretching between filaments are written as friction terms obtained through a formal limit of a delayed system of equations. Indeed, let ε be a dimensionless parameter denoting the ratio of the typical lifetime of bonds versus the overall timescale of the model, the asymptotic limit is obtained assuming that both, the rate of linkage turnover and the stiffness of the bonds, become large. The rigorous justification of the limit as $\varepsilon \to 0$ is the ultimate goal of our investigations [9, 10]. Nevertheless, the highly non-linear nature of the delayed model leads to consider already the case of a fixed value of ε. In this article we show that the data of the problem determines the well-posedness of the model: the balance between the on-rate of the linkages and the external force is essential. Mathematically this is seen since, depending on this balance, either we can show blow up in finite time or global existence. Physically this means that pulling the binding site too strongly causes a tear-off, and that our model is able to reproduce this feature. Experimentally this is observed and it is used in order to determine the load dependence of detachment rates [1, 2, 5, 16].

More precisely, this study is concerned with a system of equations which describes the evolution of the time-dependent position of a single binding site as it moves on a 1D-substrate. An external force f acts on a moving point-object positioned at $z(t)$,

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which is attached to the substrate through continuously remodeling elastic linkages, i.e. transiently attaching protein bonds. Their age distribution is denoted by $\rho=\rho(t,a)$ where $a\geq 0$ denotes the age of linkages and $t\geq 0$ denotes time.

The position of the moving binding site, $z(t)$, solves a Volterra equation of the first kind [9] reading

$$\begin{cases} \dfrac{1}{\varepsilon}\displaystyle\int_0^\infty (z(t)-z(t-\varepsilon a))\,\rho(t,a)\,da = f(t), & t\geq 0, \\ z(t)=z_p(t), & t<0, \end{cases} \tag{1.1}$$

where the known past positions are given by the Lipschitz function $z_p(t)\in\mathbb{R}$ for $t<0$. The age distribution $\rho=\rho(t,a)$ is the solution of the age-structured model

$$\begin{cases} \varepsilon\partial_t\rho+\partial_a\rho+\zeta\rho=0, & t>0,\, a>0, \\ \rho(t,a=0)=\beta(t)\,(1-\mu_0)\,, & t>0, \\ \rho(t=0,a)=\rho_I(a), & a\geq 0, \end{cases} \tag{1.2}$$

where $\mu_0(t):=\int_0^\infty \rho(t,\tilde a)\,d\tilde a$ and the on-rate of bonds is a given coefficient β times a factor, that takes into account saturation of the moving binding site with linkages. Here we treat ε as a fixed constant, which we keep in our notations in order to maintain consistency with previous studies [9, 10], and to keep track about whether the results we obtain are uniform with respect to ε, having future convergence results in mind.

When the off-rate ζ is a prescribed function, we say that the problem is weakly coupled first one solves ρ and then ρ can be used as a given integration kernel in order to obtain z as the solution of (1.1).

On the other hand, if ζ depends on z as for instance $\zeta=\zeta((z(t)-z(t-\varepsilon a))/\varepsilon)$ (cf. [7, 15]) we speak about strong coupling. In [10] we gave a first result on global existence of weak solutions in this case. These results relied on the change of unknowns

$$u(t,a)=\begin{cases} \frac{z(t)-z(t-\varepsilon a)}{\varepsilon} & \text{if } t\geq\varepsilon a, \\ \frac{z(t)-z_p(t-\varepsilon a)}{\varepsilon} & \text{otherwise.} \end{cases}$$

It was shown in [10] that one could transform the system (1.1)–(1.2) replacing (1.1) by the equation satisfied by u, which is

$$\begin{cases} \varepsilon\partial_t u+\partial_a u=\dfrac{1}{\mu_0}\left(\varepsilon\partial_t f+\displaystyle\int_0^\infty (\zeta(u)u\rho)(t,\tilde a)\,d\tilde a\right), & t>0,\, a>0, \\ u(t,a=0)=0, & t>0, \\ u(t=0,a)=u_I(a), & a\geq 0, \end{cases} \tag{1.3}$$

where the initial condition is related to the past data of (1.1) through $u_I(a):=(z(0)-z_p(-\varepsilon a))/\varepsilon$. The structure of $\zeta=\zeta(u(t,a))$ is then consistent with the new variable and the system (1.3)–(1.2) is closed. In [10] it has turned out to be beneficial to work on the system (1.2)–(1.3), since it allowed to derive powerful *a priori* estimates on u.

The analysis in the older studies [9] and [10] relied on the existence of an upper bound $\zeta_{\max}$ of the function ζ. It is the aim of the present study to relax the hypothesis of boundedness of ζ. This represents a major improvement, because the lower bound on the total mass $\mu_0(t)$ strongly depends on $\zeta_{\max}$ and the analytical arguments in [10] do rely heavily on this control. Furthermore, the upper bound $\zeta_{\max}$ had major importance in the fixed point argument used in [10] to prove the global existence result since we used it to control the non-linear right-hand side in (1.3).

In addition to deepening the analysis, unboundedness of the off-rate is the natural scenario from the application point of view. A typical situation is Bell's law, i.e. an exponential increase of the off-rate as the elastic linker is extended, $\zeta = \zeta_0 \exp(|u|)$ (cf. [7, 15]). However, this strongly non-linear scenario is still out of reach of the rigorous mathematical analysis that we present in this study which relies on ζ being a (globally) Lipschitz continuous function.

The right-hand side of (1.3) for a given function u,

$$g_u(t) := \frac{1}{\mu_{0,u}} \left\{ \varepsilon \partial_t f + \int_{\mathbb{R}_+} \zeta(u(t,a))\, \varrho_u(t,a)\, u(t,a)\, da \right\},$$

where ϱ_u solves (1.2) with $\zeta = \zeta(u)$ and $\mu_{0,u} := \int_{\mathbb{R}_+} \varrho_u(t,a)\, da$, can become infinite if either $\mu_{0,u}$ vanishes or $\int_{\mathbb{R}_+} \zeta(u)\, u\, \varrho_u\, da$ blows up. We define the modified right-hand side

$$\overline{\overline{g}}_u := \frac{1}{\max(\mu_{0,u}, \underline{\mu})} \left\{ \varepsilon \partial_t f + \max\left(-\overline{p}, \min\left(\overline{p}, \int_{\mathbb{R}_+} \zeta(u)\, \varrho_u\, u\, da \right)\right)\right\},$$

where $\underline{\mu}$ and $\overline{p}$ are two strictly positive arbitrary constants. The strategy to prove our existence result is first to establish existence and uniqueness of a solution of this modified problem using a fixed point argument in the space

$$X_T := \left\{ u \in L^\infty_{\mathrm{loc}}((0,T) \times \mathbb{R}_+) \text{ s.t. } \sup_{t \in (0,T)} \| u(t,a)\, \omega(a) \|_{L^\infty_a} < \infty \right\} \tag{1.4}$$

defined for any specific time $T > 0$, with the weight function being

$$\omega(a) := \frac{1}{1+a}. \tag{1.5}$$

To this end we introduce the map $\Phi : v \in X_T \mapsto u \in X_T$ where, given v, we solve (1.2) with $\zeta = \zeta(v)$ and obtain the age distribution ρ_v. Then we look for the solution of the problem:

$$\begin{cases} \varepsilon \partial_t u + \partial_a u = \overline{\overline{g}}_v(t), & t > 0, \quad a > 0, \\ u(t,0) = 0, & t > 0, \\ u(0,a) = u_I(a), & a \geq 0, \end{cases} \tag{1.6}$$

to obtain $u \in X_T$. The right-hand side of (1.6) becomes a bounded function whose bounds depend on the cut-offs $\underline{\mu}$ and $\overline{p}$. This allows to prove contraction of the map Φ on a time interval that is sufficiently small. Due to the uniform bounds this process can be iterated to obtain (ϱ, w), a unique solution which is global in time. Then we establish a uniform bound on $p(t) := \int_{\mathbb{R}_+} \zeta(w) w \rho_w da$, the second integral term in g_w. This shows that for $\overline{p}$ sufficiently large with respect to $1/\underline{\mu}$, $p(t)$ never reaches $\overline{p}$ so that the solution (ρ_w, w) satisfies also a simple-cut-of problem where $\overline{\overline{g}}_u$ can be replaced by $\overline{g}_u$ defined as

$$\overline{g}_u := \frac{1}{\max(\mu_{0,u}, \underline{\mu})} \left\{ \varepsilon \partial_t f + \int_{\mathbb{R}_+} \zeta(u)\, \varrho_u\, u\, da \right\}.$$

In a second step, we prove that if additional assumptions hold, this solution never reaches the cut-off value $\underline{\mu}$. Otherwise, we give a lower bound to the time span during which the cut-off is not reached. In both cases the solution of the modified problem is also the unique solution to the original system (1.2)–(1.3) either globally in time or on the finite interval of time.

More precisely, in Section 4, we analyze the dependence of the lower bound of $\mu_{0,u}$ with respect to the $L^\infty(0,T)$ norm of $\overline{g}_u$. This naturally leads to local existence results for the original problem (1.2)–(1.3) in Section 5 by providing a minimal time for which the solution (ρ_w, w) does not reach the cut-off value $\underline{\mu}$.

Even stronger results are rigorously obtained in sections 6 and 7 generalizing a straightforward computation in the special case where $\zeta(u) = 1 + |u|$ and assuming that u remains strictly positive. In this case, integrating (1.2) in age, and using the fact that (1.1) transforms into $\int_{\mathbb{R}_+} \rho(t,a) u(t,a) da = f(t)$, we obtain that

$$\varepsilon \partial_t \mu_0 - \beta(1-\mu_0) + \mu_0 + f = 0,$$

which can be solved directly. This provides immediately the bounds

$$\min\left(\mu_0(0), \frac{\beta_{\min} - f_{\max}}{\beta_{\max}+1}\right) \le \mu_0(t) \le \mu_0(0)\left(1 - \frac{t}{t_0}\right),$$

where

$$t_0 := \frac{\varepsilon}{\beta_{\min}+1} \ln\left(1 + \frac{\mu_0(0)(\beta_{\min}+1)}{f_{\min} - \beta_{\max}}\right)$$

and leads to 3 possible scenarios:

i) a strictly positive lower bound of μ_0 when $\beta_{\min} > f_{\max}$, in which case one has global existence,

ii) if $f_{\min} > \beta_{\max}$, the time t_0 is well defined and the binding site tears off, i.e. $\mu_0(t)$ becomes zero, at $t = t_0$, this leads to a blow up,

iii) intermediate cases for which we do not know if μ_0 becomes zero in finite time, so both previous possibilities could occur according to the balance between β and f.

These basic ideas provide global existence results (Section 6) versus tear-off results (Section 7) under more general assumptions on ζ.

2. Technical assumptions, preliminary results and a priori estimates

2.1. Hypotheses.

ASSUMPTIONS 2.1.

a) There exists a minimal value $\zeta_{\min}$ *such that* $\zeta(w) \ge \zeta_{\min} > 0$, $\forall w \in \mathbb{R}$.

b) The derivative of ζ *is bounded i.e.* $|\zeta'(w)| \le \zeta_{\text{Lip}}$, $\forall w \in \mathbb{R}$.

c) The function f *is Lipschitz continuous on* $[0,T]$ *for any positive fixed* T*. If* $T = \infty$ *then* f *is supposed to be globally Lipschitz i.e.* $f \in W^{1,\infty}(\mathbb{R}_+)$ *in this case.*

REMARK 2.1. Note that this definition does not allow more than a linear growth for ζ. But in contrast to [9,10], one does not have a hypothesis concerning boundedness on ζ from above.

REMARK 2.2. In the literature [7, 8, 12, 15], ζ is a smooth function of $|u|$, which motivates choice of the Lipschitz property above.

As in [10] we assume also some hypotheses on the initial and boundary data of (1.2)

ASSUMPTIONS 2.2. *The initial condition* $\rho_I \in L^\infty_a(\mathbb{R}_+)$ *is* *(i) non-negative, i.e.* $\rho_I(a) \geq 0$, *a.e. in* $\mathbb{R}_+$,

(ii) moreover, the total initial population satisfies

$$0 < \int_0^\infty \rho_I(a) da < 1,$$

(iii) and higher moments are bounded,

$$0 < \int_0^\infty a^p \rho_I(a)\, da \leq c_p, \quad \textit{for } p = 1,2.$$

ASSUMPTIONS 2.3. *For* β *we assume that*

a) $\beta = \beta(t)$ *is a continuous function,*

b) $0 < \beta_{\min} \leq \beta(t) \leq \beta_{\max}$ *for all positive times* t.

We detail hereafter results from [9] still valid under the weaker set of assumptions 2.1, 2.2, and 2.3.

THEOREM 2.1. *We suppose that* u *is a given function in* X_T. *Let assumptions 2.1, 2.2 and 2.3 hold, then for every fixed* ε *there exists a unique solution* $\varrho \in C^0(\mathbb{R}_+; L^1(\mathbb{R}_+)) \cap L^\infty(\mathbb{R}_+^2)$ *of the problem* (1.2)*, with the off-rate* $\zeta := \zeta(u(t,a))$. *It satisfies* (1.2) *in the sense of characteristics, namely*

$$\varrho(t,a) = \begin{cases} \beta(t-\varepsilon a)\left(1 - \int_0^\infty \varrho(\tilde{a}, t-\varepsilon a)\, d\tilde{a}\right) & \\ \qquad \times \exp\left(-\int_0^a \zeta(\tilde{a}, t-\varepsilon(a-\tilde{a}))\, d\tilde{a}\right), & \textit{when } a < t/\varepsilon, \\ \rho_I(a - t/\varepsilon)\exp\left(-\frac{1}{\varepsilon}\int_0^t \zeta((\tilde{t}-t)/\varepsilon + a, \tilde{t})\, d\tilde{t}\right), & \textit{if } a \geq t/\varepsilon, \end{cases} \tag{2.1}$$

where, in an abuse of notation, we wrote $\zeta = \zeta(u(t,a)) = \zeta(t,a)$.

LEMMA 2.2. *Under the same assumptions as in Theorem 2.1, let* ϱ *be the unique solution of problem* (1.2)*, then it satisfies a weak formulation of this problem, namely*

$$\int_0^\infty \int_0^T \varrho(t,a)\,(\varepsilon \partial_t \varphi + \partial_a \varphi - \zeta \varphi)\, dt\, da - \varepsilon \int_0^\infty \varrho(t,a) \varphi(t=T, a)\, da \\ + \int_0^T \varrho(t, a=0)\, \varphi(t,0)\, dt + \varepsilon \int_0^\infty \rho_I(a) \varphi(t=0,a)\, da = 0, \tag{2.2}$$

for every $T > 0$ *and every test function* $\varphi \in \mathcal{D}([0,T] \times \mathbb{R}_+)$.

Following the same argumentation as Lemma 2.2 in [9], one has

LEMMA 2.3. *Under the same assumptions as in Theorem 2.1, it holds that* $\mu_0(t) < 1$ *for any time. This in turn implies that* $\varrho(t,a) \geq 0$ *for almost every* (t,a) *in* $\mathbb{R}_+^2$.

For $p \in \mathbb{N}$ we define the pth moment of the solution ρ of (1.2)

$$\mu_p(t) := \int_0^\infty a^p \varrho(t,a)\, da.$$

Then, following the same argumentation as Lemma 2.2 in [9], one has

LEMMA 2.4. *Under the same assumptions as in Theorem 2.1,*

$$\mu_p(t) \leq \mu_{p,\max} \quad \textit{for} \quad p = 1,2,$$

where the generic constants $\mu_{p,\max}$ read:

$$\mu_{p,\max} := \sum_{\ell=0}^{p} \frac{p!}{\ell! \zeta_{\min}^{p-\ell}} \mu_\ell(0) + \frac{p!}{\zeta_{\min}^{p}} \frac{\beta_{\max}}{\beta_{\min}+\zeta_{\min}}.$$

Proof. When $p=0$ we simply integrate (1.2) with respect to age

$$\varepsilon \partial_t \mu_0 + \beta \mu_0 + \int_{\mathbb{R}_+} \zeta \rho da = \beta,$$

as ζ is bounded from below and using Gronwall's Lemma one has

$$\mu_0(t) \leq \mu_0(0) + \frac{\beta_{\max}}{\beta_{\min}+\zeta_{\min}}.$$

For any integer p we then write

$$\varepsilon \partial_t \mu_p + \zeta_{\min} \mu_p - p \mu_{p-1} \leq 0,$$

which, using Gronwall's Lemma again, gives

$$\|\mu_p\|_{L^\infty(0,T)} \leq \mu_p(0) + \frac{p}{\zeta_{\min}} \|\mu_{p-1}\|_{L^\infty(0,T)}.$$

By induction, one proves the claim. ∎

We define the entropy introduced in [9] that compares solutions of (1.2)

$$\mathcal{H}_0[\rho](t) := \int_{\mathbb{R}_+} |\rho(t,a)|\, da + \left| \int_{\mathbb{R}_+} \rho(t,a)\, da \right|.$$

PROPOSITION 2.5. *Under assumptions 2.1, 2.2, and 2.3, setting $\hat{\rho} := \varrho_2 - \varrho_1$ where ϱ_2 and ϱ_1 solve* (1.2) *with off-rates $\zeta(w_2)$ (resp. $\zeta(w_1)$) where w_2 (resp. w_1) is a function in X_T, we find that*

$$\mathcal{H}_0[\hat{\rho}](t) \leq c_0 (1 - \exp(\zeta_{\min} t/\varepsilon)) \|\hat{w}\|_{X_t}, \quad \forall t \in (0,T),$$

where $\hat{w} := w_2 - w_1$, $c_0 := \frac{2}{\zeta_{\min}} \zeta_{\mathrm{Lip}} \mu_{1,\max}$, $\mu_{1,\max}$ being the bound on the first moment of ϱ_1.

Proof. The proof follows the same lines as for Lemma 3.2 and Lemma 3.3 in [9] based on the system satisfied by $\hat{\rho}$,

$$\begin{cases} \varepsilon \partial_t \hat{\rho} + \partial_a \hat{\rho} + \zeta_2 \hat{\rho} = -\hat{\zeta} \varrho_1 & t>0, a>0, \\ \hat{\rho}(t,0) = -\beta(t) \displaystyle\int_{\mathbb{R}_+} \hat{\rho}(t,\tilde{a})\, d\tilde{a}, & t>0, \\ \hat{\rho}(0,a) = 0, & a>0, \end{cases}$$

where $\hat{\zeta} := \zeta(w_2) - \zeta(w_1)$. ∎

For $k \geq 1$ we define

$$\mathcal{H}_k[\rho] := \int_{\mathbb{R}_+} (1+a)^k \rho(t,a) da.$$

For these functionals one has

PROPOSITION 2.6. *Under the same hypotheses as in the previous proposition, and if moreover*

$$\int_{\mathbb{R}_+} (1+a)^\ell \rho_I(a)\,da < \infty, \quad \forall \ell \in \{0,k+1\},$$

then

$$\mathcal{H}_k[\hat{\rho}](t) \leq h_k(1-\exp(-\zeta_{\min} t/\varepsilon))\|\hat{w}\|_{X_t}, \quad \forall t \in (0,T),$$

where the constants h_k depend only on $\zeta_{\min}$, ζ_{Lip}, and on the constants $(\mu_{\ell,\max})_{\ell\in\{0,k+1\}}$ related to the bound on the ℓth moment of ϱ_2.

Proof. We apply a recursion argument. The case $k=0$ is proved by Proposition 2.5. We suppose that the claim is true for $\ell \leq k-1$. We have formally that

$$\varepsilon\partial_t(1+a)^k|\hat{\rho}| + \partial_a(1+a)^k|\hat{\rho}| - k(1+a)^{k-1}|\hat{\rho}| + \zeta_{\min}(1+a)^k|\hat{\rho}| \leq |\hat{\zeta}|(1+a)^k\varrho_2.$$

Integrating in age, one gets that

$$\varepsilon\partial_t\mathcal{H}_k[\hat{\rho}] - \beta|\hat{\mu}| + \zeta_{\min}\mathcal{H}_k[\hat{\rho}] \leq k\mathcal{H}_{k-1}[\hat{\rho}] + \zeta_{\mathrm{Lip}}\|\hat{w}\|_{X_t}\int_{\mathbb{R}_+}(1+a)^{k+1}\varrho_2(t,a)da,$$

which is then estimated giving

$$\varepsilon\partial_t\mathcal{H}_k[\hat{\rho}] + \zeta_{\min}\mathcal{H}_k[\hat{\rho}] \leq k\mathcal{H}_{k-1}[\hat{\rho}] + \zeta_{\mathrm{Lip}}C_{k+1}\|\hat{w}\|_{X_t} + \beta_{\max}\mathcal{H}_0[\hat{\rho}].$$

Using Gronwall's Lemma gives

$$\mathcal{H}_k[\hat{\rho}](t) \leq \frac{1-\exp(-\zeta_{\min}t/\varepsilon)}{\zeta_{\min}} \sup_{s\in(0,t)} \left(k\mathcal{H}_{k-1}[\hat{\rho}](s) + \beta_{\max}\mathcal{H}_0[\hat{\rho}](s) + \zeta_{\mathrm{Lip}}C_{k+1}\|\hat{w}\|_{X_s}\right),$$

where we used, in the last estimates, the recursion hypothesis and Proposition 2.5. □

We give ourselves $T>0$ and a function $g \in L^\infty(0,T)$ and we compute w as the solution in the sense of characteristics of

$$\begin{cases} \varepsilon\partial_t w + \partial_a w = g(t), & t>0,\, a>0, \\ w(t,0) = 0, & t>0, \\ w(0,a) = u_I(a), & a \geq 0. \end{cases} \tag{2.3}$$

And all along the paper we will assume that the initial condition u_I belongs to $L^\infty(\mathbb{R}_+,\omega)$. For this simple transport problem it holds that

THEOREM 2.7. *For any fixed $T>0$, any $g\in L^\infty(0,T)$, and for any fixed ε, there exists a unique $w \in X_T$ solving problem* (2.3)*. Moreover one has the* a priori *estimates*

$$\|w\|_{X_T} \leq \left(\frac{T}{T+\varepsilon}\right)\|g\|_{L^\infty(0,T)} + \|u_I\|_{L^\infty_a(\mathbb{R}_+,\omega)}$$

Moreover the maximal time of existence is infinite if $g \in L^\infty(\mathbb{R}_+)$.

For sake of clarity we repeat and detail here the proof given in [10, Theorem 6.1, p. 2116].

Proof. Since $g \in L^\infty(0,T)$, w is a mild solution (in the sense of characteristics). We use the Duhamel's principle: w can be computed explicitly and reads

$$w(t,a) = \begin{cases} \int_{-a}^0 g\left(t+\frac{s}{\varepsilon}\right) ds & \text{if } t \geq \varepsilon a, \\ u_I(a-t/\varepsilon) + \int_{-t}^0 g\left(t+\frac{s}{\varepsilon}\right) ds & \text{otherwise,} \end{cases}$$

and then, using Hölder's inequality, we write for all (t,a) such that $\varepsilon a \leq t \leq T$,

$$\left|\frac{w(t,a)}{1+a}\right| \leq \frac{a}{1+a}\|g\|_{L^\infty(0,T)} \leq \frac{T}{T+\varepsilon}\|g\|_{L^\infty(0,T)},$$

the latter inequality being true since $a/(1+a)$ is an increasing function on $\mathbb{R}_+$. On the contrary, if $t \leq \varepsilon a$ then

$$\left|\frac{w(t,a)}{1+a}\right| \leq \frac{|u_I(a-t/\varepsilon)|}{1+a} + \frac{\int_{-t}^0 \left|g\left(t+\frac{s}{\varepsilon}\right)\right| ds}{1+a} \leq \frac{|u_I(a-t/\varepsilon)|}{1+a-t/\varepsilon} + \frac{t}{1+a}\|g\|_{L^\infty(0,T)},$$

thus one concludes that if $t \leq \varepsilon a$

$$\left|\frac{w(t,a)}{1+a}\right| \leq \|u_I\|_{L^\infty(\mathbb{R}_+,\omega)} + \frac{T}{T+\varepsilon}\|g\|_{L^\infty(0,T)}.$$

Gathering both cases, one recovers

$$\|w(t,\cdot)\|_{L^\infty(\mathbb{R}_+,\omega)} \leq \|u_I\|_{L^\infty(\mathbb{R}_+,\omega)} + \frac{T}{T+\varepsilon}\|g\|_{L^\infty(0,T)}.$$

Taking then the supremum over all $t \in (0,T)$ gives the bound in X_T as claimed. We underline that this estimate is uniform with respect to T and ε, in particular if the maximal time of definition of g is infinite then w is in $L^\infty(\mathbb{R}_+;L^\infty(\mathbb{R}_+,\omega))$. ☐

3. Global existence results for cut-off problems

We solve the coupled problem: find (ϱ, w) satisfying

$$\begin{cases} \varepsilon\partial_t \varrho + \partial_a \varrho + \zeta(w)\varrho = 0, & t>0,\, a>0, \\ \varrho(t,0) = \beta(t)\left(1 - \int_{\mathbb{R}_+} \varrho(t,a)da\right), & t>0, \\ \varrho(0,a) = \rho_I(a), & a \geq 0, \end{cases} \tag{3.1}$$

and

$$\begin{cases} \varepsilon\partial_t w + \partial_a w = \overline{\overline{g}}_w(t), & t>0, \quad a>0, \\ w(t,0) = 0, & t>0, \\ w(0,a) = u_I(a) & a \geq 0, \end{cases} \tag{3.2}$$

where we set

$$\overline{\overline{g}}_w(t) := \frac{1}{\max(\mu_0(t), \underline{\mu})}\left(\varepsilon\partial_t f + \max\left(-\overline{p}, \min\left(\int_{\mathbb{R}_+} (\zeta(w)\varrho w)(t,a)\,da, \overline{p}\right)\right)\right), \tag{3.3}$$

where $\mu_0(t) = \int_{\mathbb{R}_+} \varrho(t,a)\,da$. The two constants $\underline{\mu}$ and $\overline{p}$ are positive.

THEOREM 3.1. *We suppose that assumptions 2.1, 2.2, and 2.3 hold. Moreover we assume that* $u_I \in L^\infty(\mathbb{R}_+,\omega)$ *and* $\|\partial_t f\|_{L^\infty(\mathbb{R}_+)}$ *is finite and that the constants* $\underline{\mu}$ *and* $\overline{p}$ *are fixed. For any fixed time T possibly infinite, there exists a unique pair of solutions* $(\varrho,w)\in C([0,T];L^1(\mathbb{R}_+))\times X_T$ *solving the coupled problems* (3.1), (3.2), *and* (3.3).

Proof. We apply the Banach fixed point Theorem to Φ mapping $w\in X_T \mapsto u\in X_T$ such that

$$\begin{cases} \varepsilon\partial_t u+\partial_a u=\overline{\overline{g}}_w(t), & t>0,a>0,\\ w(t,0)=0, & t>0,\\ w(0,a)=u_I(a), & a>0. \end{cases}$$

We prove that Φ is actually contractive in X_T for a time T small enough.

a) The map Φ is endomorphic. For any given $w\in X_T$ one has invariably

$$|\overline{\overline{g}}_w|\le \frac{1}{\underline{\mu}}\left(\varepsilon\|\partial_t f\|_{L^\infty(0,T)}+\overline{p}\right), \tag{3.4}$$

which by the same method as in Theorem 2.7 provides a bound independent on T in X_T on u

$$\|u\|_{X_T}\le \left\|\overline{\overline{g}}_w\right\|_{L^\infty(0,T)}+\|u_I\|_{L^\infty_\omega(\mathbb{R}_+)}.$$

b) The map Φ is a contraction. We set $\hat{g}_w := \overline{\overline{g}}_{w_2}-\overline{\overline{g}}_{w_1}$ and $\hat{\rho} := \varrho_{w_2}-\varrho_{w_1}$ and so on. As $\overline{\overline{g}}_w$ is Lipschitz with respect to $\mu_0(t)$ and $\int_{\mathbb{R}_+}\zeta\varrho w\, da$

$$|\hat{g}_w(t)|\le \frac{|\hat{\mu}|}{\underline{\mu}^2}\left\{\varepsilon\|\partial_t f\|_{L^\infty(0,T)}+\overline{p}\right\}+\frac{1}{\underline{\mu}}\left|\widehat{\left(\int_{\mathbb{R}_+}\zeta\varrho w da\right)}\right| =: I_1+I_2.$$

I_1 is immediately estimated thanks to Proposition 2.5, and one has

$$I_1\le \frac{1}{\underline{\mu}^2}\left\{\varepsilon\|\partial_t f\|_{L^\infty(0,T)}+\overline{p}\right\}\mathcal{H}_0[\hat{\rho}](t)\le \frac{1}{\underline{\mu}^2}\left\{\varepsilon\|\partial_t f\|_{L^\infty(0,T)}+\overline{p}\right\}c_0\|\hat{w}\|_{X_t},$$

while we decompose the difference of triple products in I_2 as

$$\begin{aligned} I_2 \le& \frac{1}{\underline{\mu}}\left|\int_{\mathbb{R}_+}\hat{\zeta}\varrho_{w_2}w_2+\zeta_1\hat{\rho}w_2+\zeta_1\varrho_{w_1}\hat{w}da\right|\\ \le& \frac{1}{\underline{\mu}}\Bigg(\int_{\mathbb{R}_+}\zeta_{\mathrm{Lip}}|\hat{w}|\varrho_{w_2}|w_2|da\\ &+\left(\zeta_{\mathrm{Lip}}\|w_1\|_{X_t}+\zeta_0\right)\left\{\int_{\mathbb{R}_+}(1+a)^2|\hat{\rho}|da\|w_2\|_{X_t}+\int_{\mathbb{R}_+}(1+a)^2\varrho_{w_1}da\|\hat{w}\|_{X_t}\right\}\Bigg)\\ \le& c\left\{\|\hat{w}\|_{X_t}+\mathcal{H}_2[\hat{\rho}](t)\right\}\le \overline{c}\|\hat{w}\|_{X_t}, \end{aligned}$$

where the constant $\overline{c}$ depends on ζ_{Lip}, ζ_0, $(\|w_i\|_{X_t})_{i\in\{1,2\}}$, $\underline{\mu}$, and $\int_{\mathbb{R}_+}a^k\rho_I(a)da$ for $k\in\{0,1,2\}$. Using again Theorem 2.7, one has

$$\|\hat{u}\|_{X_t}\le \frac{t}{t+\varepsilon}\|\hat{g}_w\|_{L^\infty(0,t)}\le \frac{t}{\varepsilon}\|\hat{g}_w\|_{L^\infty(0,t)}\le \frac{t\overline{c}}{\varepsilon}\|\hat{w}\|_{X_t}.$$

If $T_0<\varepsilon/\overline{c}$ then there exists a unique fixed point $w\in X_{T_0}$ of the mapping Φ.

c) Global existence for any time. We suppose that existence and uniqueness are established for the tuple (ϱ, w) solving (3.1)–(3.2), on the time interval $[0, T_{n-1}]$ for $n \geq 1$. We construct a fixed point for the next interval $[T_{n-1}, T_n := T_{n-1} + \Delta T_n]$ on the map $u = \Phi(v)$

$$\begin{cases} \varepsilon \partial_t u + \partial_a u = \overline{\overline{g}}_v(t), & t \in (T_{n-1}, T_n), a > 0, \\ u(t,0) = 0, & t \in (T_{n-1}, T_n), \\ u(T_{n-1}, a) = w(T_{n-1}, a) & a > 0, \end{cases}$$

and

$$\begin{cases} \varepsilon \partial_t \rho + \partial_a \rho + \zeta(v) \rho = 0, & t \in (T_{n-1}, T_n), a > 0, \\ \rho(t,0) = \beta(t) \left(1 - \int_{\mathbb{R}_+} \rho(t,a) da \right), & t \in (T_{n-1}, T_n), \\ \rho(T_{n-1}, a) = \varrho(T_{n-1}, a), & a > 0. \end{cases}$$

If we denote the extensions to $[0, T_n]$ of (ρ, u) as

$$\rho_e(t,a) := \begin{cases} \rho(t,a) & \text{if } t \in [T_{n-1}, T_n) \\ \varrho(t,a) & t \in (0, T_{n-1}] \end{cases}, \quad w_e := \begin{cases} u(t,a) & \text{if } t \in [T_{n-1}, T_n) \\ w(t,a) & t \in (0, T_{n-1}]. \end{cases},$$

The continuity of ρ_e allows to apply Lemma 2.4. Similarly for w_e one has

$$\begin{aligned} \|w_e\|_{X_{T_n}} &\leq \left\| \overline{\overline{g}}_v(t) \chi_{[T_{n-1}, T_n)} + \overline{\overline{g}}_w \chi_{[0, T_{n-1}]} \right\|_{X_{T_n}} + \|u_I\|_{L^\infty_\omega(\mathbb{R})} \\ &\leq \frac{(\varepsilon \|\partial_t f\|_{L^\infty(0,T_n)} + \overline{p})}{\underline{\mu}} + \|u_I\|_{L^\infty_\omega(\mathbb{R})}, \end{aligned}$$

where χ_A is the characteristic function of the set A, and we used the uniform estimate on $\overline{\overline{g}}_w$ provided by (3.4). These estimates prove that the constant $\overline{c}$ in the contraction in b) is not changing as time evolves. Thus we can fix-point again choosing ΔT_n as in the previous paragraph and prove contraction in $[T_{n-1}, T_n]$. At this step the recursion is complete. The theorem is proven for any positive time.

□

COROLLARY 3.2. *Under the same hypotheses as above, for any pair of positive definite reals $(\underline{\mu}, \overline{p})$, the solution-pair (ϱ, w) solving* (3.1)–(3.3) *satisfies the* a priori *estimates*

$$\int_{\mathbb{R}_+} \varrho(t,a) |w(t,a)| da \leq \int_{\mathbb{R}_+} \rho_I(a) |u_I(a)| da + \int_0^t |\partial_t f(\tilde{t})| d\tilde{t} =: 1/\gamma_0. \tag{3.5}$$

Proof. We use that

$$\begin{aligned} &|\overline{\overline{g}}_w(t)| \leq \frac{1}{\mu_0(t)} \left\{ \varepsilon |\partial_t f| + \min \left(\overline{p}, \left| \min \left(\int_{\mathbb{R}_+} \zeta(w) w \varrho da, \overline{p} \right) \right| \right) \right\} \\ &\leq \frac{1}{\mu_0(t)} \left\{ \varepsilon |\partial_t f| + \min \left(\overline{p}, \int_{\mathbb{R}_+} \zeta(w) \varrho |w| da \right) \right\} \leq \frac{1}{\mu_0(t)} \left\{ \varepsilon |\partial_t f| + \int_{\mathbb{R}_+} \zeta(w) \varrho |w| da \right\}. \end{aligned}$$

Then same arguments as in the proof of Lemma 5.1 in [10] provide *a priori* estimates. Indeed, in the sense of characteristics $|w|$ satisfies

$$\varepsilon\partial_t|w|+\partial_a|w|\leq|\overline{\overline{g}}_w|\leq\frac{1}{\mu_0(t)}\left\{\varepsilon|\partial_t f|+\int_{\mathbb{R}_+}\zeta(w)\varrho|w|da\right\}.$$

Then multiplying the later inequality by ϱ and integrating with respect to age, one gets

$$\varepsilon\partial_t\int_{\mathbb{R}_+}\varrho|w|da+\int_{\mathbb{R}_+}\zeta(w)|w|\varrho da\leq\varepsilon|\partial_t f|+\int_{\mathbb{R}_+}\zeta(w)|w|\varrho da.$$

Because on the right- and on the left-hand sides the same integral terms cancel, the claim follows. ∎

Proposition 3.3. *Under assumptions 2.1, 2.2, and 2.3, let* (ϱ,w) *be the solution of the fully coupled and stabilized problem* (3.1)–(3.3)*, there exists a positive finite constant* γ_1 *such that*

$$\int_{\mathbb{R}_+}\zeta(w(t,a))|w(t,a)|\varrho(t,a)da\leq\frac{\gamma_1}{\underline{\mu}},\quad\forall t\geq 0,$$

where the constant γ_1 *depends on*

- *the* a priori *bound only on* $\int_{\mathbb{R}_+}\varrho|w|da$ *(obtained in Corollary 3.2) ,*
- $\|\partial_t f\|_{L^\infty(0,T)}$*,*
- ζ_{Lip}*, and* $\zeta(0)$*.*

Proof. Using equations (3.1), (3.2), and hypotheses 2.1, one has

$$\varepsilon\partial_t(\varrho|w|\zeta)+\partial_a(\varrho|w|\zeta)+\zeta^2|w|\varrho\leq\varrho|w|(\varepsilon\partial_t\zeta+\partial_a\zeta)+\zeta\varrho|\overline{\overline{g}}_w|.$$

Integrating in age and setting $p(t):=\int_{\mathbb{R}_+}\varrho(t,a)|w(t,a)|\zeta(w(t,a))\,da$ gives

$$\begin{aligned}\varepsilon\partial_t p+\int_{\mathbb{R}_+}\zeta^2|w(t,a)|\varrho(t,a)da&\leq|\overline{\overline{g}}_w|\left(\zeta_{\mathrm{Lip}}\int_{\mathbb{R}_+}\varrho|w|\,da+\int_{\mathbb{R}_+}\zeta(w)\varrho(t,a)da\right)\\&\leq|\overline{\overline{g}}_w|\left(2\zeta_{\mathrm{Lip}}\int_{\mathbb{R}_+}\varrho|w|\,da+\zeta(0)\right)\\&\leq\frac{1}{\underline{\mu}}(\varepsilon|\partial_t f|+p)(2\zeta_{\mathrm{Lip}}/\gamma_0+\zeta(0)),\end{aligned}$$

where $\int_{\mathbb{R}_+}\varrho|w|da\leq 1/\gamma_0$. Now, we consider the second term in the left-hand side above: using Jensen's inequality one writes

$$\left(\frac{\int_{\mathbb{R}_+}\zeta(w)|w(t,a)|\varrho(t,a)da}{\int_{\mathbb{R}_+}|w|\varrho da}\right)^2\leq\frac{\int_{\mathbb{R}_+}(\zeta(w))^2|w(t,a)|\varrho(t,a)da}{\int_{\mathbb{R}_+}|w|\varrho da},$$

since $|w|\varrho/\int_{\mathbb{R}_+}|w|\varrho da$ is a unit measure. This implies that

$$\int_{\mathbb{R}_+}(\zeta(w))^2|w(t,a)|\varrho(t,a)\,da\geq\frac{\left(\int_{\mathbb{R}_+}\zeta(w)|w(t,a)|\varrho(t,a)da\right)^2}{\int_{\mathbb{R}_+}|w|\varrho da}\geq\gamma_0 p^2.$$

We obtain a Riccati inequality

$$\varepsilon\partial_t p+\gamma_0 p^2 \le h/\underline{\mu}+p/\underline{\mu}, \quad p(0)=\int_{\mathbb{R}_+}\zeta(u_I(a))|u_I(a)|\rho_I(a)\,da,$$

where $h:=\varepsilon\|\partial_t f\|_\infty(2\zeta_{\mathrm{Lip}}/\gamma_0+\zeta(0))$ is a constant. We denote by $P_\pm$ the solutions of the steady state equation associated to the last inequality, *i.e.* P solves $\gamma_0 P^2-P/\underline{\mu}-h/\underline{\mu}=0$. The solutions are given by

$$P_\pm=\frac{1}{\underline{\mu}}\left(1\pm\sqrt{1+4h\underline{\mu}\gamma_0}\right)/(2\gamma_0)\le\frac{1}{\underline{\mu}}\max\left(p(0),\left(1\pm\sqrt{1+4h\gamma_0}\right)/(2\gamma_0)\right)=:\frac{\gamma_1}{\underline{\mu}}.$$

Applying Lemma A.1, we conclude that $p(t)\le\max\{p(0),P_+\}\le\gamma_1/\underline{\mu}$, which ends the proof. ∎

THEOREM 3.4. *Suppose that assumptions 2.1, 2.2, and 2.3 hold, moreover, suppose that* $u_I\in L^\infty(\mathbb{R}_+,\omega)$ *and that* $\|\partial_t f\|_{L^\infty(0,T)}$ *is finite, if* (ϱ,w) *is the unique solution of the stabilized problem* (3.1)–(3.3), *it is also the unique solution of* (3.1)–(3.2) *together with the modified right-hand side*

$$\overline{g}_w=\frac{1}{\max(\mu_{0,w},\underline{\mu})}\left(\varepsilon\partial_t f+\int_{\mathbb{R}_+}\zeta(w)w\varrho\,da\right). \tag{3.6}$$

Proof. The proof is a simple application of Proposition 3.3 above and taking $\overline{p}>\gamma_1/\underline{\mu}$ when solving (3.1)–(3.3). Indeed, in this case, the truncated right-hand side from (3.3) becomes (3.6), since $p(t):=\int_{\mathbb{R}_+}\zeta(w)w\varrho da$ never reaches $\pm\overline{p}$. ∎

4. Impact of the cut-off value on the mean bonds' population

In the previous section, (3.2) was solved with a bounded source term (either $\overline{\overline{g}}_w$ or $\overline{g}_w$) that we denote in this section as a generic bounded function $g\in L^\infty(0,T)$, so that hereafter w solves (3.2) with g as a source term. In what follows we are interested in computing a sharp lower bound on the total population $\mu_{0,w}(t):=\int_{\mathbb{R}_+}\varrho(t,\tilde a)d\tilde a$ where ϱ solves (3.1) with $\zeta(w)$.

LEMMA 4.1. *Let assumptions 2.1 and 2.3 hold. Let* $w\in X_T$ *be given arbitrarily. Let* ϱ *be the solution of* (3.1) *with* $\zeta(w)$. *We suppose that* $\mu_{0,w}(0)<1$. *Let us fix a positive constant* γ_2 *such that*

$$\gamma_2<\min\left(1-\mu_{0,w}(0),\frac{\zeta_{\min}}{\zeta_{\min}+\beta_{\max}}\right).$$

Under assumptions 2.1, 2.2, and 2.3, $\mu_{0,w}(t)<1-\gamma_2$ *holds for every positive time* t.

Proof. We proceed similarly as in Lemma 2.2 in [9]. The computations are thus only formal although they can be made rigorous exactly as therein. By hypothesis, the data satisfies $1-\gamma_2-\mu_{0,w}(0)>0$. By continuity this also holds on a time interval $[0,t_0)$ small enough. We proceed by contradiction and suppose that at time t_0 the mass $\mu_{0,w}(t_0)$ reaches $1-\gamma_2$. The equation on $\mu_{0,w}$ reads

$$\varepsilon\partial_t\mu_{0,w}-\beta(1-\mu_{0,w})+\int_{\mathbb{R}_+}\varrho(t,a)\zeta(w(t,a))da=0.$$

Multiplying by -1 and using the upper bound of β, one deduces that

$$\varepsilon\partial_t(1-\gamma_2-\mu_{0,w})+\beta_{\max}(1-\gamma_2-\mu_{0,w})+\gamma_2\beta_{\max}-\int_{\mathbb{R}_+}\varrho(t,a)\zeta(w(t,a))da\geq 0,$$

then the lower bound on ζ implies

$$\varepsilon\partial_t(1-\gamma_2-\mu_{0,w})+\beta_{\max}(1-\gamma_2-\mu_{0,w})+\gamma_2\beta_{\max}\geq\zeta_{\min}\mu_{0,w}.$$

We transform the latter right-hand side writing

$$\zeta_{\min}\mu_{0,w}=-\zeta_{\min}(1-\gamma_2-\mu_{0,w})+\zeta_{\min}(1-\gamma_2).$$

Setting $q(t):=(1-\gamma_2-\mu_{0,w}(t))$, one then has

$$\varepsilon\partial_t q+(\zeta_{\min}+\beta_{\max})q\geq\zeta_{\min}-(\zeta_{\min}+\beta_{\max})\gamma_2>0,$$

the latter estimate being true under the hypothesis that $\gamma_2<\zeta_{\min}/(\zeta_{\min}+\beta_{\max})$. The conclusion then follows integrating the latter inequality in time

$$q(t_0)>\exp\left(-\frac{(\beta_{\max}+\zeta_{\min})t_0}{\varepsilon}\right)q(0)>0,$$

under the hypothesis that $\gamma_2<(1-\mu_{0,w}(0))$. But this contradicts the assumption that $q(t_0)=0$, which ends the proof. ∎

PROPOSITION 4.2. *Let $g\in L^\infty(0,T)$ be given, and let (ϱ,w) be the solutions of* (3.1)–(3.2) *with g as a source term. Under assumptions 2.1, 2.2, and 2.3 and if $\mu_{0,w}(0)\leq 1-\gamma_2$, there exists a constant $\bar\zeta$ independent of ε such that it holds that for any $\delta>0$,*

$$\int_{\mathbb{R}_+}\zeta(w(t,a))\frac{\varrho(t,a)}{\mu_{0,w}+\delta}da\leq\bar\zeta+\zeta_{\mathrm{Lip}}\|g\|_{L^\infty(0,T)}\min\left(\frac{2}{\gamma_2\beta_{\min}},\frac{T}{\varepsilon}\right),\quad\forall t\geq 0,$$

where $\bar\zeta:=\zeta(0)+\int_{\mathbb{R}_+}\zeta(u_I(a))\tilde\rho_{\varepsilon,I}(a)da$.

Proof. We do not have a positive definite lower bound on $\mu_{0,w}$ yet: at this stage we only know that $\mu_{0,w}(t)\geq 0$. For this reason we define $\tilde\varrho^\delta(t,a):=\varrho(t,a)/(\mu_{0,w}(t)+\delta)$ and we observe that this new function is in $L^\infty_{\mathrm{loc}}((0,T)\times\mathbb{R}_+)\cap C([0,T];L^1(\mathbb{R}_+))$. It solves, in the sense of characteristics, the equation

$$\begin{cases}\varepsilon\partial_t\tilde\varrho^\delta+\partial_a\tilde\varrho^\delta+\left(\zeta-\int_{\mathbb{R}_+}\zeta\tilde\varrho^\delta\right)\tilde\varrho^\delta \\ \qquad\qquad+\beta\left(\frac{1}{\mu_{0,w}+\delta}-\frac{\mu_{0,w}}{\mu_{0,w}+\delta}\right)\tilde\varrho^\delta=0, & t>0,\,a>0,\\ \tilde\varrho^\delta(t,a=0)=\beta(t)\left(\frac{1}{\mu_{0,w}+\delta}-\frac{\mu_{0,w}}{\mu_{0,w}+\delta}\right), & t>0,\\ \tilde\varrho^\delta(t=0,a)=\rho_I(a)/(\mu_{0,w}+\delta), & a\geq 0.\end{cases}\tag{4.1}$$

The product $\pi(t,a):=\zeta(w(t,a))\tilde\varrho^\delta(t,a)$ satisfies

$$\varepsilon\partial_t\pi+\partial_a\pi+\left(\zeta^2-\zeta\int_{\mathbb{R}_+}\zeta\tilde\varrho^\delta\right)\tilde\varrho^\delta+\tilde\varrho^\delta(t,0)\pi=\zeta'(w)g(t)\tilde\varrho^\delta.$$

Indeed, using arguments as in Lemma 2.1 (p. 489) and Lemma 3.1 (p. 493) [9], one proves that if w solves (2.3) and ζ is uniformly Lipschitz on $\mathbb{R}$, then $\zeta(w)$ solves $(\varepsilon\partial_t+\partial_a)\zeta(w)=\zeta'(w)g$ in the sense of characteristics (as in Theorem 2.1) with the corresponding boundary conditions. Then the latter equation on π is understood in the same manner.

Integrating in age and setting $q(t):=\int_{\mathbb{R}_+}\pi(t,a)da$, we conclude that

$$\varepsilon\partial_t q-\zeta(t,0)\tilde{\varrho}^\delta(t,0)+\int_{\mathbb{R}_+}\zeta^2\tilde{\varrho}^\delta da-\left(\int_{\mathbb{R}_+}\zeta\tilde{\varrho}^\delta\right)^2+q\tilde{\varrho}^\delta(t,0)\le\zeta_{\mathrm{Lip}}\|g\|_\infty. \tag{4.2}$$

To find a lower bound for $\tilde{\varrho}^\delta(0,t)$ we choose $\delta<\gamma_2/2$ and use the upper bound on $\mu_{0,w}(t)$ established in Lemma 4.1 in order to obtain

$$\tilde{\varrho}^\delta(t,0)\ge\beta_{\min}\left(\frac{1}{1-\gamma_2+\delta}-1\right)\ge\beta_{\min}\frac{\gamma_2}{2}. \tag{4.3}$$

Assuming $\mu_{0,w}(t)>0$ we also find, using Jensen's inequality, that

$$\begin{aligned}\left(\int_{\mathbb{R}_+}\zeta(w(t,a))\tilde{\varrho}^\delta(t,a)da\right)^2&\le\int_{\mathbb{R}_+}(\zeta(w(t,a)))^2\tilde{\varrho}^\delta da\frac{\mu_{0,w}}{(\mu_{0,w}+\delta)}\\&\le\int_{\mathbb{R}_+}(\zeta(w(t,a)))^2\tilde{\varrho}^\delta da.\end{aligned}$$

If $\mu_{0,w}(t)=0$ the same inequality holds true since then $\varrho(t,a)=0$ for almost every a. These considerations allow then to rewrite (4.2) as

$$\varepsilon\partial_t q+\tilde{\varrho}^\delta(t,0)(q-\zeta(0))\le\zeta_{\mathrm{Lip}}\|g\|_\infty.$$

Setting $\tilde{q}:=q-\zeta(0)$ and using Gronwall's Lemma gives

$$\tilde{q}(t)\le\exp\left(-\frac{1}{\varepsilon}\int_0^t\tilde{\varrho}^\delta(s,0)ds\right)\tilde{q}(0)+\frac{\zeta_{\mathrm{Lip}}\|g\|_\infty}{\varepsilon}\int_0^t\exp\left(-\frac{1}{\varepsilon}\int_\tau^t\tilde{\varrho}^\delta(s,0)ds\right)d\tau.$$

Thanks to the uniform lower bound (4.3), we conclude

$$\tilde{q}(t)\le\exp\left(-\frac{\beta_{\min}\gamma_2 t}{2\varepsilon}\right)\tilde{q}(0)+\frac{2\zeta_{\mathrm{Lip}}\|g\|_\infty}{\gamma_2\beta_{\min}}\left(1-\exp\left(-\frac{\beta_{\min}\gamma_2 t}{2\varepsilon}\right)\right),$$

which then gives, turning to the variable q, that

$$q(t)\le\zeta(0)+\int_{\mathbb{R}_+}\zeta(u_I(a))\tilde{\rho}_{\varepsilon,I}(a)da+\frac{2\zeta_{\mathrm{Lip}}\|g\|_\infty}{\gamma_2\beta_{\min}}\left(1-\exp\left(-\frac{\beta_{\min}\gamma_2 t}{2\varepsilon}\right)\right). \tag{4.4}$$

This bound is uniform in δ. □

PROPOSITION 4.3. *Let $g\in L^\infty(0,T)$ be given, and let (ϱ,w) be the solutions of (3.1)–(3.2) with g as a source term. Under assumptions 2.1, 2.2, and 2.3 and if $\mu_{0,w}(0)\le 1-\gamma_2$, and choosing $\mu_{0,\min}$ such that*

$$\mu_{0,\min}<\min\left(\mu_{0,w}(0),\frac{\beta_{\min}}{\beta_{\min}+\bar{\zeta}+\zeta_{\mathrm{Lip}}\|g\|_{L^\infty(0,T)}\min\left(\frac{2}{\gamma_2\beta_{\min}},\frac{T}{\varepsilon}\right)}\right),$$

one has a lower bound on $\mu_{0,w}$

$$\mu_{0,w}(t) \geq \mu_{0,\min}, \quad \forall t \geq 0.$$

Proof. We integrate (1.2) with respect to age

$$\begin{cases} \varepsilon \partial_t \mu_{0,w} - \beta(1-\mu_{0,w}) + \int_{\mathbb{R}_+} \varrho(t,a)\zeta(w(t,a))da = 0, & t>0, \\ \mu_{0,w}(0) = \int_{\mathbb{R}_+} \rho_I(a)da, & t=0. \end{cases}$$

In a weak form this means for any $\varphi \in W^{1,\infty}(0,T)$ and any $t_0 \leq T$,

$$-\int_0^{t_0} \mu_{0,w} \frac{\mathrm{d}\varphi}{\mathrm{d}t} d\tau + [\mu_{0,w}\varphi]_{\tau=0}^{\tau=t_0} + \int_0^{t_0} \beta \mu_{0,w} \varphi d\tau \\ + \int_0^{t_0} \frac{\int_{\mathbb{R}_+} \zeta(w(\tau,a))\varrho(\tau,a)da}{\mu_{0,w}(\tau)+\delta} (\mu_{0,w}(\tau)+\delta)\varphi d\tau = \int_0^{t_0} \beta \varphi d\tau.$$

Now if we denote $L_\delta(t) := \int_{\mathbb{R}_+} \zeta(w(\tau,a))\varrho(\tau,a)da/(\mu_{0,w}(\tau)+\delta)$. By Proposition 4.2, $L_\delta \in L^\infty(0,t_0)$ uniformly with respect to δ: there exists a weak-* limit $L \in L^\infty(0,t_0)$ when δ goes to zero, satisfying the same bound. On the other hand $\mu_{0,w}(\tau)+\delta$ converges strongly in $L^1(0,t_0)$ to $\mu_{0,w}(\tau)$ which means, passing to the limit when $\delta \to 0$ in the weak formulation above, that

$$-\int_0^{t_0} \mu_{0,w} \frac{\mathrm{d}\varphi}{\mathrm{d}t} d\tau + [\mu_{0,w}\varphi]_{\tau=0}^{\tau=t_0} + \int_0^{t_0} (\beta+L)\mu_{0,w}\varphi d\tau = \int_0^{t_0} \beta\varphi d\tau.$$

Inserting a constant $\mu_{0,\min}$ in the previous expression and rearranging the different terms, one has

$$-\int_0^{t_0} (\mu_{0,w} - \mu_{0,\min}) \left(\frac{\mathrm{d}\varphi}{\mathrm{d}t} - (\beta+L)\varphi \right) d\tau + [(\mu_{0,w} - \mu_{0,\min})\varphi]_{\tau=0}^{\tau=t_0} \\ = \int_0^{t_0} (\beta(1-\mu_{0,\min}) - L\mu_{0,\min})\varphi d\tau.$$

We choose $\varphi(t) := \exp\left(-\int_{t_0-t}^{t_0} (\beta+L)d\tau\right)$ as a test function. This gives

$$[(\mu_{0,w} - \mu_{0,\min})\varphi]_{\tau=0}^{\tau=t_0} = \int_0^{t_0} (\beta(1-\mu_{0,\min}) - L\mu_{0,\min})\varphi d\tau.$$

Setting $\overline{L} := \bar{\zeta} + \zeta_{\mathrm{Lip}} \|g\|_{L^\infty(0,t_0)} \min\left(\frac{2}{\gamma_2 \beta_{\min}}, \frac{t_0}{\varepsilon}\right)$ and using the definition of $\mu_{0,\min}$ one has that

$$(\mu_{0,w}(t_0) - \mu_{0,\min}) \geq (\mu_{0,w}(0) - \mu_{0,\min}) \exp\left(-\int_0^{t_0} (\beta+L)d\tau \right) > 0.$$

Now suppose that there exists a time small enough such that $\mu_{0,w}(t) > \mu_{0,\min}$ for all $t \in [0,t_0)$ and that $\mu_{0,w}(t_0) = \mu_{0,\min}$. Then the previous estimate contradicts the fact that $\mu_{0,w}(t_0) = \mu_{0,\min}$. This ends the proof. $\square$

5. Local existence of the fully coupled problem

THEOREM 5.1. *Let f be a Lipschitz function on $(0,T)$ and $u_I \in L^\infty(\mathbb{R}_+,\omega)$. We suppose that assumptions 2.1, 2.2, and 2.3 hold. Let (ϱ,w) be the solution of* (3.1)–(3.2) *together with $\overline{g}_w$, the simple cut-off defined by* (3.6). *Then for any fixed $\underline{\mu} < \mu_{0,w}(0)$ there exists a time*

$$T = \frac{\varepsilon}{\gamma_3}\left(\beta_{\min}\underline{\mu} - (\beta_{\min}+\bar{\zeta})\underline{\mu}^2\right)$$

for which $\mu_{0,w}(t) > \underline{\mu}$ for any $t \in (0,T)$. So the solution (ϱ,w) of (3.1)–(3.6) *is also the unique local solution of the fully coupled system* (1.2)–(1.3).

Proof. Gathering results above, one has

$$\|\overline{g}_w\|_{L^\infty(0,T)} \le \frac{1}{\underline{\mu}}(\varepsilon|\partial_t f| + p(t)) \le \frac{1}{\underline{\mu}}\left(\varepsilon\|\partial_t f\|_{L^\infty(0,T)} + \frac{\gamma_1}{\underline{\mu}}\right) \le \frac{\gamma_3}{\underline{\mu}^2},$$

since we suppose that $\underline{\mu} < 1$ and we set $\gamma_3 := \varepsilon\|\partial_t f\|_{L^\infty(0,T)} + \gamma_1$. Thanks to Proposition 4.3, the lower bound on $\mu_{0,w}$ then becomes

$$\mu_{0,w}(t) > \min\left(\mu_{0,w}(0), \frac{\beta_{\min}\underline{\mu}^2}{(\beta_{\min}+\bar{\zeta})\underline{\mu}^2 + \frac{\gamma_3 T}{\varepsilon}}\right).$$

Choosing $\underline{\mu} < \mu_{0,w}(0)$ we define T such that

$$\frac{\beta_{\min}\underline{\mu}^2}{(\beta_{\min}+\bar{\zeta})\underline{\mu}^2 + \frac{\gamma_3 T}{\varepsilon}} > \underline{\mu},$$

so that $\max(\mu_{0,w}(t), \underline{\mu}) = \mu_{0,w}(t)$ on $[0,T]$ and thus $\overline{g}_w(t) = g_w(t)$ on that same time interval. ∎

6. Global existence for specific data

Under hypotheses of Theorem 3.1, whatever be the time of existence T for (ϱ,w), the solutions of the stabilized model, then thanks to Corollary 3.2 one has that

$$\begin{aligned}\int_{\mathbb{R}_+} \zeta(w(t,a))\varrho(t,a)da &\le \int_{\mathbb{R}_+} (\zeta(0) + \zeta_{\text{Lip}}|w|)\varrho da \\ &\le \zeta(0) + \zeta_{\text{Lip}}\left(\int_{\mathbb{R}_+} |u_I|\rho_I da + \int_0^T |\partial_t f| ds\right) =: \breve{\zeta}, \quad \forall t \in (0,T).\end{aligned}$$

PROPOSITION 6.1. *Under assumptions 2.1, 2.2, and 2.3, if $\beta_{\min} > \breve{\zeta}$ and if we set*

$$0 < \mu_{0,\min} < \min\left(1 - \frac{\breve{\zeta}}{\beta_{\min}}, \mu_{0,w}(0)\right),$$

one has that $\mu_{0,w}(t) \ge \mu_{0,\min}$, $\forall t \in (0,T)$.

Proof. We set $\hat{\mu} := \mu_{0,w}(t) - \mu_{0,\min}$ and write the equation that it satisfies

$$\varepsilon\partial_t\hat{\mu} + \beta\hat{\mu} = -\int_{\mathbb{R}_+} \zeta\varrho da + \beta(1-\mu_{0,\min}) \ge -\breve{\zeta} + \beta_{\min}(1-\mu_{0,\min}).$$

The lower bound is positive definite provided that $\beta_{\min} > \breve{\zeta}$ and that $\mu_{0,\min} < 1 - \breve{\zeta}/\beta_{\min}$. Using Gronwall's Lemma, one has

$$\hat{\mu}(t) \geq \exp(-\beta_{\max} t/\varepsilon)\hat{\mu}(0) > 0$$

if $\mu_{0,\min} < \mu_{0,w}(0)$, which ends the proof. ∎

THEOREM 6.2. *If we fix a finite time $T>0$, under assumptions 2.1 and 2.2, and assuming that*

i) f is Lipschitz on $(0,T)$,

ii) β satisfies Assumptions 2.3 together with $\beta_{\min} > \breve{\zeta}$

there exists a unique solution $(\rho,u) \in C(0,T;L^1(\mathbb{R}_+)) \times X_T$ solving system (1.2)–(1.3).

Proof. By Theorem 3.4, there exists a unique couple $(\varrho,w) \in C(0,\infty;L^1(\mathbb{R}_+)) \times X_\infty$ solving (3.1)–(3.6) for any given constant $\underline{\mu}$. We choose $T>0$ and provided that β satisfies hypothesis required by Proposition 6.1, we set the constants $0 < \underline{\mu} < \mu_{0,\min}$ according to Proposition 6.1. Then $\mu_{0,w}$ does not reach the threshold value $\underline{\mu}$ so that

$$\begin{aligned}\overline{g}_w(t) &= \frac{1}{\max(\mu_{0,w}(t),\underline{\mu})}\left(\varepsilon\partial_t f + \int_{\mathbb{R}_+} (\zeta(w)\varrho w)(t,a)da\right)\\ &= \frac{1}{\mu_{0,w}(t)}\left(\varepsilon\partial_t f + \int_{\mathbb{R}_+} (\zeta(w)\varrho w)(t,a)da\right) = g_w(t), \quad a.e.\, t \in (0,T).\end{aligned}$$

The pair (ϱ,w) is in fact also solving (1.2)–(1.3) on this time interval. This provides existence of a solution $(\rho,u) = (\varrho,w)$ on $[0,T]$. Since by Theorem 3.4 (ϱ,w) is unique, so is (ρ,u) in this time period. ∎

7. Blow up for positive solutions

THEOREM 7.1. *Under Assumption 2.2 and if T_0 is the time of existence of (ρ,u) solving (1.2)–(1.3), and if*

i) $u_I(a) \geq 0$ for a.e. $a \in \mathbb{R}_+$,

ii) $\partial_t f(t) > 0$ for a.e. $t \in (0,T_0)$,

then the product $\rho(t,a)u(t,a)$ is non-negative for a.e. $(t,a) \in (0,T_0) \times \mathbb{R}_+$.

Proof. Since $f(0) = \int_{\mathbb{R}_+} \rho_I(a)u_I(a)\,da$ and $f(t) = \int_{\mathbb{R}_+} \rho(t,a)u(t,a)\,da$, by Corollary 3.2, it holds that

$$\begin{aligned}\int_{\mathbb{R}_+} \rho(t,a)|u(t,a)|da &\leq \int_{\mathbb{R}_+} \rho_I(a)|u_I(a)|da + \int_0^t |\partial_t f(\tilde{t})|d\tilde{t}\\ &= \int_{\mathbb{R}_+} \rho_I(a)u_I(a)da + \int_0^t \partial_t f(\tilde{t})\,d\tilde{t} = f(t) = \int_{\mathbb{R}_+} \rho(t,a)u(t,a)\,da,\end{aligned}$$

which implies the result. ∎

PROPOSITION 7.2. *Under assumptions 2.2 and 2.3 and if*

i) ζ satisfies Assumption 2.1 and admits a locally differentiable lower convex envelop ζ_c such that $\zeta_c(u) \leq \zeta(u)$ for all $u \in \mathbb{R}_+$ with $\zeta_c'(0) > 0$,

ii) let f be a Lipschitz function such that $\partial_t f(t) > 0$ for a.e. $t \in (0,T)$,

iii) f and β are such that $\beta_{\max} < \zeta_c'(0) f_{\min}$,
iv) $u_I(a) \geq 0$ for a.e. $a \in \mathbb{R}_+$,
then if the solution (ρ,u) solving (1.2)–(1.3) exists until a finite time T_0, this time cannot be greater than

$$t_0 := \frac{\varepsilon}{\beta_{\min} + \zeta_c(0)} \ln\left(1 + \frac{\mu_0(0)(\beta_{\min} + \zeta_c(0))}{\zeta_c'(0) f_{\min} - \beta_{\max}}\right),$$

for which

$$\mu_0(T_0) \leq 0.$$

Moreover, on $(0,t_0)\times\mathbb{R}_+$, one has a lower bound on the profile of u namely

$$u(t,a) \geq \varepsilon\gamma_5 \ln\left(1 + \frac{\min(t,\varepsilon a)}{(t_0 - t)}\right),$$

where $\gamma_5 := t_0 \inf_{t\in(0,t_0)} \partial_t f / \mu_0(0)$.

Proof. By Theorem 7.1, $u(t,a) \geq 0$ a.e. $(t,a) \in (0,T_0)\times\mathbb{R}_+$. The equation for μ_0 reads

$$\varepsilon \partial_t \mu_0 - \beta(1-\mu_0) + \int_{\mathbb{R}_+} \zeta(u(t,a))\rho(t,a)da = 0.$$

Since ζ admits ζ_c, a lower convex envelope, it follows that

$$\varepsilon \partial_t \mu_0 - \beta(1-\mu_0) + \zeta_c'(0)\int_{\mathbb{R}_+} u(t,a)\rho(t,a)da + \zeta_c(0)\mu_0 \leq 0$$

which becomes simply

$$\varepsilon \partial_t \mu_0 - \beta(1-\mu_0) + \zeta_c'(0) f + \zeta_c(0)\mu_0 \leq 0. \tag{7.1}$$

We can deduce from this inequality that

$$\varepsilon \partial_t \mu_0 + (\beta_{\min} + \zeta_c(0))\mu_0 \leq \beta_{\max} - \zeta_c'(0) f_{\min},$$

which gives using Gronwall's Lemma that $\mu_0(t) \leq \overline{\overline{\mu}}(t)$, where

$$\overline{\overline{\mu}}(t) := \mu_0(0)\exp\left(-\frac{(\beta_{\min}+\zeta_c(0))}{\varepsilon} t\right) - \frac{\zeta_c'(0) f_{\min} - \beta_{\max}}{(\beta_{\min}+\zeta_c(0))}\left(1 - \exp\left(-\frac{(\beta_{\min}+\zeta_c(0))}{\varepsilon} t\right)\right).$$

Looking for the time t_0 such that $\overline{\overline{\mu}}(t_0) = 0$ provides the explicit form of t_0 in the claim. Thus $T_0 < t_0$. Moreover, as $\overline{\overline{\mu}}(t)$ is a convex function in time, one has that

$$\mu_0(t) \leq \left(1 - \frac{t}{t_0}\right)\overline{\overline{\mu}}(0) + \frac{t}{t_0}\overline{\overline{\mu}}(t_0) \equiv \left(1 - \frac{t}{t_0}\right)\overline{\overline{\mu}}(0),$$

and because, by Theorem 7.1, $\zeta(u)u\rho$ is positive almost everywhere on $(0,t_0)\times\mathbb{R}_+$,

$$\varepsilon \partial_t u + \partial_a u \geq \frac{\varepsilon \partial_t f}{\mu_0(t)} \geq \frac{\varepsilon\gamma_5}{t_0 - t}, \qquad \text{a.e. in } (0,t_0)\times\mathbb{R}_+.$$

Using Duhamel's formula provides

$$u(t,a) \geq \begin{cases} \varepsilon\gamma_5 \int_{-a}^{0} \frac{ds}{t_0-(t+\varepsilon s)} ds, & \text{if } t \geq \varepsilon a, \\ u_I(a-t/\varepsilon) + \varepsilon\gamma_5 \int_{-t/\varepsilon}^{0} \frac{ds}{t_0-(t+\varepsilon s)} ds & \text{otherwise,} \end{cases}$$

which then gives the lower estimate on u. ∎

Appendix A. Riccati inequalities.

LEMMA A.1. *Let $\varepsilon > 0$ and real, let y be a positive differentiable function of $t \in \mathbb{R}_+$, satisfying*

$$\begin{cases} \varepsilon \partial_t y + A y^2 \leq B y + C, & t > 0, \\ y(0) = y_0, & t = 0, \end{cases}$$

where $y_0 > 0$ and $(A,B,C) \in (\mathbb{R}_+)^3$. Setting $y_+ := (B + \sqrt{B^2 + 4AC})/(2A)$, one has that

$$y(t) \leq \max(y_0, y_+), \quad \forall t \in \mathbb{R}_+.$$

Proof. We set $m := \max(y_0, y_+)$, it satisfies $-Am^2 + Bm + C \leq 0$. Then we define $\tilde{y} := y - m$ which then solves the differential inequality

$$\varepsilon \partial_t \tilde{y} + A\tilde{y}^2 + (2mA - B)\tilde{y} \leq 0. \tag{A.1}$$

Since the quadratic term is positive we neglect it and apply Gronwall's Lemma

$$\tilde{y}(t) \leq \exp\left(-\frac{(2Am-B)t}{\varepsilon}\right)\tilde{y}(0) = \exp\left(-\frac{(2Am-B)t}{\varepsilon}\right)(y_0 - m) \leq 0,$$

which ends the proof. ∎

REFERENCES

[1] W. Baumgartner, P. Hinterdorfer, W. Ness, A. Raab, D. Vestweber, H. Schindler, and D. Drenckhahn, *Cadherin interaction probed by atomic force microscopy*, Proceedings of the National Academy of Sciences, 97(8), 4005–4010, 2000.

[2] E. Canetta, A. Duperray, A. Leyrat, and C. Verdier, *Measuring cell viscoelastic properties using a force-spectrometer: influence of protein-cytoplasm interactions*, Biorheology, 42(5), 321–333, 2005.

[3] F. Gittes, B. Mickey, J. Nettleton, and J. Howard, *Flexural rigidity of microtubules and actin filaments measured from thermal fluctuations in shape*, J. Cell Biol., 120(4), 923–934, Feb. 1993.

[4] W.H. Goldmann and G. Isenberg, *Analysis of filamin and alpha-actinin binding to actin by the stopped flow method*, FEBS Lett., 336(3), 408–410, Dec. 1993.

[5] W. Hanley, O. McCarty, S. Jadhav, Y. Tseng, D. Wirtz, and K. Konstantopoulos, *Single molecule characterization of p-selectin/ligand binding*, Journal of Biological Chemistry, 278(12), 10556–10561, 2003.

[6] S.A. Koestler, S. Auinger, M. Vinzenz, K. Rottner, and J.V. Small, *Differentially oriented populations of actin filaments generated in lamellipodia collaborate in pushing and pausing at the cell front*, Nat. Cell Biol., 10(3), 306–313, Mar 2008.

[7] F. Li, S.D. Redick, H.P. Erickson, and V.T. Moy, *Force measurements of the alpha5beta1 integrin-fibronectin interaction*, Biophys. J., 84(2), 1252–1262, 2003.

[8] 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.

[9] V. Milišić and D. Oelz, *On the asymptotic regime of a model for friction mediated by transient elastic linkages*, J. Math. Pures Appl., 96(5), 484–501, 2011.

[10] 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.

[11] D. Oelz and C. Schmeiser, *Derivation of a model for symmetric lamellipodia with instantaneous cross-link turnover*, Arch. Rat. Mech. Anal., 198(3), 963–980, 2010.

[12] D. Oelz, C. Schmeiser, and V. Small, *Modelling of the actin-cytoskeleton in symmetric lamellipodial fragments*, Cell Adhesion and Migration, 2, 117–126, 2008.

[13] Y. Osterg, S.V. Noorden, and A.G. Pearse, *Cytochemical, immunofluorescence, and ultrastructural investigations on polypeptide hormone localization in the islet parenchyma and bile duct mucosa of a cyclostome, Myxine glutinosa*, Gen. Comp. Endocrinol., 25(3), 274–291, Mar 1975.

[14] L. Preziosi and G. Vitale, *A multiphase model of tumor and tissue growth including cell adhesion and plastic reorganization*, Math. Models Meth. Appl. Sci., 21(9), 1901–1932, 2011.

[15] H. Suda, *Origin of friction derived from rupture dynamics*, Langmuir, 17(20), 6045–6047, 2001.

[16] M. Sun, J.S. Graham, B. Hegedus, F. Marga, Y. Zhang, G. Forgacs, and M. Grandbois, *Multiple membrane tethers probed by atomic force microscopy*, Biophys. J., 89(6), 4320–4329, Dec 2005.