Mathematical analysis of an adhesive point submitted to an external force of bounded variation

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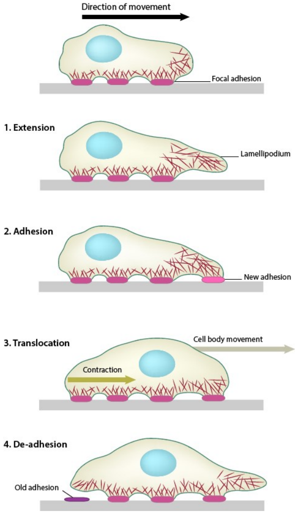
OUTLINE

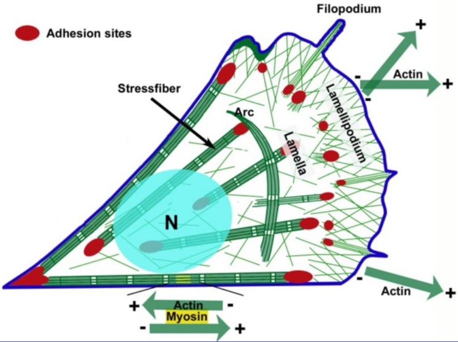
✔ **GENERAL INTRODUCTION :**
- Cell motility
- Adhesion modeling

✔ **MATHEMATICAL RESULTS :**
- Regular source term
- BV source term : Weakly method
- BV source term : Comparison principle

The context



1. Cell motility : ability of cells to move spontaneously.
2. Lamellipodium : main engine of this motion.
3. adhesion mechanism : one of the key features



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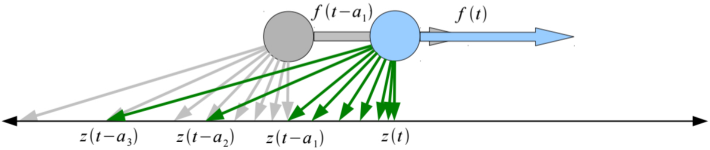
Adhesion modelling

- $z_\varepsilon(t)$ is the position of a single binding site at time t.
- given exterior force $f(t) \in \mathbb{R}$, $z_\varepsilon(t)$ minimizes

$$z_\varepsilon(t) = \underset{w \in \mathbb{R}}{\text{argmin}} \left\{ \frac{1}{2\varepsilon} \int_{\mathbb{R}+} |w - z_\varepsilon(t - \varepsilon a)|^2 \rho_\varepsilon(a,t) da - f(t) w \right\} dt$$



- $a \geq 0$ age of the linkage
- $\epsilon > 0$ speed of linkage turnover.

A mathematical model of adhesion by linkaging

A Volterra integral equation

$$\begin{cases} \frac{1}{\epsilon}\int_0^\infty \left(z_\varepsilon(t) - z_\varepsilon(t-\epsilon a)\right) \rho_\epsilon(a,t)\mathrm{d}a = f(t), & t \geq 0 \\ z_\varepsilon(t) = z_p(t), & t < 0 \end{cases}$$

where

- $\rho_\epsilon = \rho_\epsilon(a,t)$ density of existing linkages to the substrate

ρ_ϵ solves a specific renewal model

$$\begin{cases} \epsilon\partial_t\rho_\epsilon + \partial_a\rho_\epsilon + \zeta_\epsilon(a,t)\rho_\epsilon = 0, & t > 0, a > 0 \\ \rho_\epsilon(a=0,t) = \beta_\epsilon(t)\left(1 - \int_0^\infty \rho_\epsilon(t,\tilde{a})\,\mathrm{d}\tilde{a}\right), & t > 0 \\ \rho_\epsilon(a,t=0) = \rho_{I,\epsilon}(a), & a \geq 0 \end{cases}$$

with the kinetic rate functions

- $\beta_\epsilon(t) \in \mathbb{R}_+$ growth factor and $\zeta_\epsilon(a,t) \in \mathbb{R}_+$ death rate.

Formal limit when $\varepsilon \to 0$

The formal limit is given by

$$\begin{cases} \mu_{1,0}\, \partial_t z_0 = f(t) \quad \text{with} \quad \mu_{1,0}(t) := \int_0^\infty a\rho_0(a,t)da \ \ t > 0, \\ z_0(t=0) := z_p(0), \end{cases}$$

where the limit distribution ρ_0 is the solution of

$$\begin{cases} \partial_a \rho_0 + \zeta_0(a,t)\rho_0 = 0, & t > 0, a > 0, \\ \rho_0(a=0,t) = \beta_0(t)\left(1 - \int_0^\infty \rho_0(\tilde{a},t)\, d\tilde{a}\right), & t > 0, \end{cases}$$

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On the asymptotic regime of a model for friction mediated by transient elastic linkages
J. Math. Pures Appl. 96 (2011).

- Rigorous proof of convergence when $\varepsilon \to 0$ for a lipshitz function f :

$$\|z_\varepsilon - z_0\|_{C^0([0,T])} + \|\rho_\varepsilon - \rho_0\|_{C^0([0,T];L^1(\mathbb{R}_+))} \to 0.$$

- Ingredients :
  - ➢ First, convergence of density ρ_ε by using a Liapunov functional,
  - ➢ Then, convergence of z_ε by using a comparison principle.

V. M. and D. Oelz,
On the asymptotic regime of a model framework for friction mediated by transient elastic linkages
SIAM SIMA (2015).

- new unknown : Elongation

$$u_\varepsilon(a,t) = \frac{z_\varepsilon(t) - z_\varepsilon(t-\varepsilon a)}{\varepsilon}$$

- Transport problem with a non- local source term

$$\begin{cases} \varepsilon\partial_t u_\varepsilon + \partial_a u_\varepsilon = \dfrac{1}{\mu_{0,\varepsilon}}\left(\varepsilon\partial_t f + \displaystyle\int_0^\infty \zeta_\varepsilon(\tilde{a},t)\, u_\epsilon\ \rho_\varepsilon(\tilde{a},t)\,\mathrm{d}\tilde{a}\right), & t>0, a>0, \\ u_\varepsilon(a=0,t) = 0, & t>0 \\ u_\varepsilon(a,t=0) = u_{I,\varepsilon}(a), & a \geq 0, \end{cases}$$

where $\mu_{0,\varepsilon}(t) := \int_0^\infty \rho_\varepsilon(a,t)da$,

- Weak convergence of u_ε implies strong convergence of z_ε.

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Mathematical results

- Main assumption : $f \in BV((0,T)) \cap L^\infty((0,T))$ where

$$BV(0,T) = \left\{ f \in L^1(0,T) \text{ s.t } \sup \int_0^T f \partial_t \psi \mathrm{d}t < \infty, \ \psi \in \mathcal{C}_c((0,T)), |\psi| < 1 \right\}$$

- Main results :
  - **Case when** $\rho := \rho(a,t)$ **:** Convergence result

$$z_\epsilon \to z_0 \textit{ strongly in } L^\infty(0,T) \textit{ as } \epsilon \to 0,$$

  - **Case when** $\rho := \rho(a)$ **:** Convergence result

$$z_\epsilon \to z_0 \textit{ strongly in } L^1(0,T) \textit{ as } \epsilon \to 0,$$

Tools needed for the proof of the convergence result :

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SIAM SIMA (2015).

- New unknown : Elongation

$$u_\varepsilon(a,t) = \frac{z_\varepsilon(t) - z_\varepsilon(t-\varepsilon a)}{\varepsilon}$$

- Regularisation of system on u :

$$\begin{cases} \varepsilon\partial_t u_\varepsilon^\delta + \partial_a u_\varepsilon^\delta = \dfrac{1}{\mu_{0,\varepsilon}}\left(\varepsilon f_\delta' + \displaystyle\int_0^\infty \zeta_\varepsilon(\tilde{a},t)\, u_\epsilon^\delta\ \rho_\varepsilon(\tilde{a},t)\, \mathrm{d}\tilde{a}\right), & t>0, a>0, \\ u_\varepsilon^\delta(a=0,t) = 0, & t>0 \\ u_\varepsilon^\delta(a,t=0) = u_{I,\varepsilon}^\delta(a), & a \geq 0, \end{cases}$$

- Existence and uniqueness of solution u_ε^δ in X_T, where

$$X_T := \{g \in L^\infty_{loc}((0,T)\times\mathbb{R}_+) \textit{ such that } \sup_{t\in(0,T)} \|g(t,a)/(1+a)\|_{L^\infty_a} < \infty\}$$

by Banach fixed point Theorem.

- The uniform a priori estimates :

$$\int_0^\infty \rho_\varepsilon(a,t)|u_\varepsilon^\delta(a,t)|\,da \le C\left(\|f\|_{BV(0,T)}, \|(1+a)\rho_I\|_{L^1(\mathbb{R}_+)}, \left\|z_p'\right\|_{L^\infty(\mathbb{R}_-)}\right)$$

where C is uniform on ε and on δ.

- We have

$$\|u_\varepsilon^\delta\|_{X_T} \le \|w\|_{X_T} + \frac{\|f_\delta\|_{L^\infty(\Omega)}}{\mu_{0,min}} < +\infty$$

Mathematical results

$\rho := \rho(a,t)$

WEAK FORMULATION :

$$-\int_0^T\int_0^\infty u_\varepsilon^\delta(\varepsilon\partial_t\varphi+\partial_a\varphi)\;da\;dt+\left[\int_0^\infty u_\varepsilon^\delta(s,a)\varphi(s,a)\;da\right]_{s=0}^{s=T}$$
$$=\int_0^T\frac{1}{\mu_{0,\varepsilon}}\left(\varepsilon f_\delta'+\int_0^\infty\zeta_\varepsilon u_\varepsilon^\delta\rho_\varepsilon\;da\right)\left(\int_0^\infty\varphi(t,\tilde a)\;d\tilde a\right)\;dt$$

Lemma

Let $f\in BV(0,T)$. *Then there exists* $g\in \mathrm{BPV}([0,T])$ *s.t*

$$[f\varphi]_{t=0^+}^{t=T^-}-\int_0^T f\varphi' dx=\int_0^T\varphi dg,\quad \forall\varphi\in C^1([0,T])$$

s.t. $f(t)=g(t),\quad \text{a.e. } t\in(0,T).$

Convergence as $\delta \to 0$:

- $u_\varepsilon^\delta \rightharpoonup u_\varepsilon$ **weakly-* in** X_T **as** $\delta \to 0$**, where** u_ε **is also a solution of weak problem**

$$-\int_0^T \int_0^\infty u_\varepsilon(\varepsilon\partial_t + \partial_a)\varphi \, da \, dt + \varepsilon \left[\int_0^\infty u_\varepsilon(a,s)\varphi(a,s) \, da \right]_{s=0}^{s=T}$$
$$= \varepsilon \int_0^T \frac{\int_0^\infty \varphi(\tilde{a},t) d\tilde{a}}{\mu_{0,\varepsilon}} dg + \int_0^T \frac{\int_0^\infty \zeta_\varepsilon \rho_\varepsilon u_\varepsilon \, da}{\mu_{0,\varepsilon}} \left(\int_0^\infty \varphi(\tilde{a},t) \, d\tilde{a} \right)$$

where

$$[f\varphi]_{t=0^+}^{t=T^-} - \int_0^T f\varphi' dx = \int_0^T \varphi dg,$$

for any $\varphi \in C_c^1([0,T] \times \mathbb{R}_+)$**.**

Mathematical results

$\rho := \rho(a,t)$

- $z_\varepsilon^\delta \rightarrow z_\varepsilon$ strongly in $L^\infty(0,T)$ where z_ε is given by

$$z_\varepsilon(t) = z_\varepsilon(0^+) + \int_0^t \frac{\varepsilon}{\mu_{0,\varepsilon}}\, dg + \int_0^t \frac{1}{\mu_{0,\varepsilon}} \int_0^\infty \zeta_\varepsilon u_\varepsilon \rho_\varepsilon \, da \, d\tilde{t}$$

and satisfies

$$\begin{cases} \dfrac{1}{\epsilon}\displaystyle\int_0^\infty \left(z_\varepsilon(t) - z_\varepsilon(t-\epsilon a)\right) \rho_\epsilon(a,t) \mathrm{d}a = f(t), & t \geq 0 \\ z_\varepsilon(t) = z_p(t), & t < 0 \end{cases}$$

Convergence as $\varepsilon \to 0$:

Theorem

Suppose that $\zeta_{min} \leq \zeta_\varepsilon \leq \zeta_{max}$*, then*

$$u_\varepsilon \rightharpoonup u_0 \text{ weakly-* in } X_T$$

as $\varepsilon \to 0$*, where* u_0 *satisfies*

$$\int_0^\infty u_0(a, t)\, \rho_0(a, t)\, da = f(t) \text{ a.e } t \in (0, T).$$

Furthermore, it also holds that

$$z_\varepsilon \to z_0 \text{ strongly in } L^\infty(0, T) \text{ as } \varepsilon \to 0.$$

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Comparison principle in a particular case

$\varrho := \varrho(a)$

- $\varrho := \varrho(a)$ satisfies

$$\begin{cases} \partial_a \varrho + \zeta(a)\varrho = 0, & a > 0, \\ \varrho(0) = \beta \left(1 - \int_0^\infty \varrho(\tilde{a})\, d\tilde{a}\right), \end{cases}$$

- Error estimates between z_ε and z_0 : $\hat{z}_\varepsilon := z_\varepsilon(t) - z_0(t)$ satisfies

$$\hat{z}_\varepsilon(t) = \frac{1}{\mu_0} \int_0^{\frac{t}{\varepsilon}} \hat{z}_\varepsilon(t - \varepsilon a)\varrho(a) da + \tilde{h}_\varepsilon(t)$$

- New unknown

$$\hat{Z}_\varepsilon(t) = \int_0^t |\hat{z}_\varepsilon(\tau)|\, d\tau$$

- $\hat{Z}_\varepsilon(t)$ solves :

$$\hat{Z}_\varepsilon(t) \leq \frac{1}{\mu_0} \int_0^{\frac{t}{\varepsilon}} \hat{Z}_\varepsilon(t - \varepsilon a)\, \varrho(a)\, da + \int_0^t \tilde{h}_\varepsilon(\tau)\, d\tau$$

Comparison principle in a particular case

$\varrho := \varrho(a)$

Theorem

z_ε tends to z_0 strongly in $L^1(0,T)$ as ε goes to zero. Moreover, there exists a generic constant C depending only on the data of the problem but not on ε, such that :

$$\|z_\varepsilon - z_0\|_{L^1(0,T)} \leq \varepsilon C.$$

- Comparison principle : construction of a super-solution $U_\varepsilon(t) := \varepsilon(K_0 + K_1 t)$ s.t $U_\varepsilon \geq |\hat{Z}_\varepsilon|$ and $U_\varepsilon \to 0$ as $\varepsilon \to 0$. for specific constants K_0 and K_1.

Perspective

Studying the existence and convergence of the solution in the case when

- $f \in L^1(0, T)$,
- f is a Radon measure.

Related papers

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On the asymptotic regime of a model framework for friction mediated by transient elastic linkages
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V. Milišić and S.Allouch
Mathematical analysis of an adhesive point submitted to an external force of bounded variation
Preprint (2021).

THANK YOU