

# On the asymptotic regime of a model for friction mediated by transient elastic linkages

Vuk Milišić<sup>a,b,\*</sup>, Dietmar Oelz<sup>c</sup>

<sup>a</sup> *Laboratoire Analyse, Géométrie & Applications, Université Paris 13, France*

<sup>b</sup> *Wolfgang Pauli Institute (WPI), UMI CNRS 2841, Vienna, Austria*

<sup>c</sup> *Mathematical Biology Group, Johann Radon Institute for Computational and Applied Mathematics (RICAM), Vienna, Austria*

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## Abstract

In this work we study a system of an integral equation of Volterra type coupled with an original renewal equation. This model arises in the context of cell motility (Oelz et al., 2008 [6]): the integral equation describes the trajectory of a binding site which is connected via transiently remodelling linkages to the substrate and which evolves driven by a given force. The renewal model accounts for the remodelling process of linkages which attach and break with given probabilities.

In the present paper we analyze existence and uniqueness issues for the coupled system of interest and provide a rigorous justification of the asymptotic limit of infinitesimally rapid turnover of linkages.

The renewal model for the age distribution of linkages differs from more classical ones in that it describes competition between population size and birth and because it admits a new and specific Lyapunov functional. On the other side, using a comparison principle which applies to non-convolution linear Volterra kernels and the peculiar transport properties of the linkages, one establishes a convergence result when the turnover parameter  $\varepsilon$  tends to zero.

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## Résumé

Dans cet article, on étudie un système d'une équation intégrale de Volterra couplée avec une équation de renouvellement d'un type particulier. Ce modèle apparaît dans le contexte de la motilité cellulaire (Oelz et al., 2008 [6]) : l'équation intégrale décrit la trajectoire d'un site d'adhésion connecté au substrat par des liaisons protéiques éphémères et soumis à une force extérieure. Le processus de remodelage des liaisons qui se détruisent ou se créent sur ce site avec une certaine probabilité est décrit par une équation de renouveau.

Ici, on analyse les questions d'existence et d'unicité des solutions de ce système couplé et on donne une justification rigoureuse de la limite asymptotique instantanée du taux de renouvellement des liaisons (noté  $\varepsilon$ ).

Le modèle de renouvellement pour la distribution de l'âge des liaisons diffère des modèles classiques en ce qu'il décrit la compétition entre la taille totale de la population et le taux de naissance. Pour tenir compte de cette dernière difficulté, on a exhibé une nouvelle fonctionnelle de Liapounov. Par ailleurs, en utilisant un principe de comparaison propre aux équations de Volterra à noyau non-convolutif, on établit un résultat de convergence lorsque le paramètre  $\varepsilon$  tend vers zéro.

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\* Corresponding author at: Laboratoire Analyse, Géométrie & Applications, Université Paris 13, France.  
E-mail address: [milisc@math.univ-paris13.fr](mailto:milisc@math.univ-paris13.fr) (V. Milišić).

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### 1. Introduction

We consider the integral equation:

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

where  $z_\varepsilon = z_\varepsilon(t) \in \mathbb{R}$  represents the time dependent position of a linkage binding site and the function  $f(t) \in \text{Lip}(\mathbb{R}_+, \mathbb{R})$  represents a given exterior force. The kernel  $\rho_\varepsilon = \rho_\varepsilon(a, t)$  is interpreted as the density of existing linkages to the substrate with respect to the age  $a \geq 0$  and is defined by the renewal model,

$$\begin{cases} \varepsilon \partial_t \rho_\varepsilon + \partial_a \rho_\varepsilon + \zeta_\varepsilon(a, t) \rho_\varepsilon = 0, & t > 0, a > 0, \\ \rho_\varepsilon(a = 0, t) = \beta_\varepsilon(t) \left( 1 - \int_0^\infty \rho_\varepsilon(\tilde{a}, t) d\tilde{a} \right), & t > 0, \\ \rho_\varepsilon(a, t = 0) = \rho_{I, \varepsilon}(a), & a \geq 0, \end{cases} \tag{2}$$

with the kinetic rate functions  $\beta_\varepsilon = \beta_\varepsilon(t) \in \mathbb{R}_+$  and  $\zeta_\varepsilon = \zeta_\varepsilon(a, t) \in \mathbb{R}_+$ , both possibly depending on the dimensionless parameter  $\varepsilon > 0$  which represents the speed of linkage turnover. The two submodels are finally complemented by their respective past and initial data  $z_p \in \text{Lip}((-\infty, 0])$  and  $\rho_I \in L^1(\mathbb{R}_+) \cap L^\infty(\mathbb{R}_+)$ .

The system (1)–(2) is a model describing the mechanical effect of a set of chemical linkages dynamically remodelled in time. For instance the cross-linking proteins attaching to actin filaments in the lamellipodia of living cells can be modelled in this way. The complete model was introduced and developed in [6]. A reverse coupling between both submodels was established through the possible dependence of  $\beta_\varepsilon$ , the on-rate and  $\zeta_\varepsilon$ , the off-rates on the geometrical configuration of the mechanical structures where the binding sites are located. In the present study, however, we do not take into account a functional dependence of these rates on the function  $z_\varepsilon$ .

The integral equation (1) models a force balance between the time dependent exterior force  $f(t)$  and elastic forces exerted by a population of linkages which connect the moving binding site to binding sites on the substrate. The competing force contributions are visualized in Fig. 1 by arrows.

Linkages are originally established between the moving binding site positioned at  $z_\varepsilon(t)$  and the substrate at the very same position. As a consequence linkages with a given age  $a$  connect the moving binding site to the substrate at position  $z_\varepsilon(t - \varepsilon a)$  where the dimensionless scaling parameter  $\varepsilon$  represents the ratio of the age scale in the  $\rho_\varepsilon$ -model and the time scale in the  $z_\varepsilon$ -model, i.e. small  $\varepsilon$  reflects rapid lifecycle of the linkage proteins.

The model (2) for the age distribution of linkages states that chemical bonds break, respectively detach with a given rate  $\zeta_\varepsilon = \zeta_\varepsilon(a, t) \geq 0$ . Moreover, creation of new chemical bonds with a given rate  $\beta_\varepsilon = \beta_\varepsilon(t) \geq 0$  is proportional to the abundance of empty binding sites which itself is given by the difference of the constant total number of binding sites, in this study scaled to 1, and the number of occupied ones.

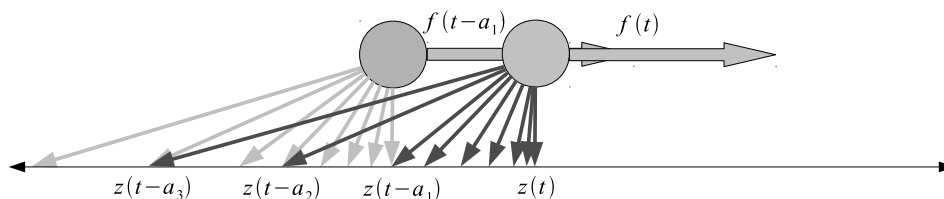


Fig. 1. The position of the moving binding site at time  $t$  and time  $t - a_1$  with some of the respective linkages. The scaling parameter is set to  $\varepsilon = 1$ .

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