Self-similarity in a General Aggregation-Fragmentation Problem ; Application to Fitness Analysis

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Abstract

We consider the linear growth and fragmentation equation

$$\frac{\partial}{\partial t}u(x,t) + \frac{\partial}{\partial x}\big(\tau(x)u\big) + \beta(x)u = 2\int_x^\infty \beta(y)\kappa(x,y)\, u(y,t)\, dy,$$

with general coefficients τ, β and κ. Under suitable conditions (see [16]), the first eigenvalue represents the asymptotic growth rate of solutions, also called *fitness* or *Malthus coefficient* in population dynamics ; it is of crucial importance to understand the long-time behaviour of the population. We investigate the dependency of the dominant eigenvalue and the corresponding eigenvector on the transport and fragmentation coefficients. We show how it behaves asymptotically as transport dominates fragmentation or *vice versa*. For this purpose we perform suitable blow-up analysis of the eigenvalue problem in the limit of small/large growth coefficient (resp. fragmentation coefficient). We exhibit possible non-monotonic dependency on the parameters, conversely to what would have been conjectured on the basis of some simple cases.

Keywords: structured populations, fragmentation-drift equation, cell division, long-time asymptotic, eigenproblem, self-similarity.

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Introduction

Growth and division of a population of individuals structured by a quantity supposed to be conserved in the division process may be described by the following growth and fragmentation equation

$$\begin{cases} \dfrac{\partial}{\partial t}u(x,t) + \dfrac{\partial}{\partial x}\big(\tau(x)u(x,t)\big) + \beta(x)u(x,t) = 2\displaystyle\int_x^\infty \beta(y)\kappa(x,y)\,u(y,t)\,dy, \qquad x \geqslant 0, \\ u(x,0) = u_0(x), \\ u(0,t) = 0. \end{cases} \tag{1}$$

This equation is used in many different areas to model a wide range of phenomena: the quantity $u(t,x)$ may represent a density of dusts ([17]), polymers [8, 9], bacteria or cells [4, 5]; the structuring variable x may be size ([31] and references), label ([2, 1]), protein content ([13, 26]), proliferating parasite content ([3]); etc. In the literature, it is refered to as the "size-structured equation", "growth-fragmentation equation', "cell division equation", "fragmentation-drift equation" or yet Sinko-Streifer model.

The growth speed $\tau = \frac{dx}{dt}$ represents the natural growth of the variable x, for instance by nutrient uptake or by polymerization, and the rate β is called the fragmentation or division rate. Notice that if τ is such that $\frac{1}{\tau}$ is non integrable at $x = 0$, then the boundary condition $u(0,t) = 0$ is useless. The so-called fragmentation kernel $\kappa(x,y)$ represents the proportion of individuals of size $x \leq y$ born from a given dividing individual of size y; more rigorously we should write $\kappa(dx,y)$, with $\kappa(dx,y)$ a probability measure with respect to x. The factor "2" in front of the integral term highlights the fact that we consider here binary fragmentation, namely that the fragmentation process breaks an individual into two smaller ones. The method we use in this paper can be extended to more general cases where the mean number of fragments is $n_0 > 1$ (see [16]).

Well-posedness of this problem as well as the existence of eigenelements has been proved in [18, 16]. Here we focus on the first eigenvalue λ associated to the eigenvector $\mathcal{U}$ defined by

$$\begin{cases} \dfrac{\partial}{\partial x}(\tau(x)\mathcal{U}(x)) + (\beta(x)+\lambda)\mathcal{U}(x) = 2\displaystyle\int_x^\infty \beta(y)\kappa(x,y)\mathcal{U}(y)dy, \qquad x \geqslant 0, \\ \tau\mathcal{U}(x=0) = 0, \qquad \mathcal{U}(x) > 0 \text{ for } x > 0, \qquad \int_0^\infty \mathcal{U}(x)dx = 1. \end{cases} \tag{2}$$

The first eigenvalue λ is the asymptotic exponential growth rate of a solution to Problem (1) (see [29, 30]). It is often called the *Malthus* parameter or yet the *fitness* of the population. Hence it is of deep interest to know how it depends on the coefficients: for given parameters, is it favorable or unfavorable to increase fragmentation ? Is it more efficient to modify the transport rate τ or to modify the fragmentation rate β ? Such concerns may have deep impact on therapeutic strategy (see [4, 5, 13, 10]) or on experimental design of devices such as PMCA [1] (see [25] and references therein). Moreover, when modeling polymerization processes, Equation (1) is coupled with the density of monomers $V(t)$, which appears as a multiplier for the polymerization rate (*i.e.,* $\tau(x)$ is replaced by $V(t)\tau(x)$, and $V(t)$ is governed by one or more ODE - see for instance [22, 23, 9]). Asymptotic study of such polymerization processes thus closely depends on such a dependency (see [9, 8], where

[1] *PMCA*, Protein Misfolded Cyclic Amplification, is a protocole designed in order to amplify the quantity of prion protein aggregates thanks to periodic sonication pulses. In this application, u represents protein aggregates density and x their size; the division rate β is modulated by sound waves. See Section 3.3 for more details.

asymptotic results are obtained under the assumption of a monotonic dependency of λ with respect to the polymerization rate τ).

Based on simple cases already studied (see [22, 23, 34, 19]), the first intuition would be that the fitness always increases when polymerization or fragmentation increases. Nevertheless, a closer look reveals that it is not true.

To study the dependency of the eigenproblem on its parameters, we depart from given coefficients τ and β, and study how the problem is modified under the action of a multiplier of either the growth or the fragmentation rate. We thus consider the two following problems: firstly,

$$\begin{cases} \alpha\dfrac{\partial}{\partial x}(\tau(x)\mathcal{U}_\alpha(x)) + (\beta(x)+\lambda_\alpha)\mathcal{U}_\alpha(x) = 2\displaystyle\int_x^\infty \beta(y)\kappa(x,y)\mathcal{U}_\alpha(y)dy, \qquad x \geqslant 0, \\ \tau\mathcal{U}_\alpha(x=0)=0, \qquad \mathcal{U}_\alpha(x)>0 \ \text{ for } x>0, \qquad \int_0^\infty \mathcal{U}_\alpha(x)dx = 1, \end{cases} \tag{3}$$

where $\alpha > 0$ measures the strength of the polymerization (transport) term, as in the Prion problem (see [22]), and secondly

$$\begin{cases} \dfrac{\partial}{\partial x}(\tau(x)\mathcal{V}_\mathfrak{a}(x)) + (\mathfrak{a}\beta(x)+\Lambda_\mathfrak{a})\mathcal{V}_\mathfrak{a}(x) = 2\mathfrak{a}\displaystyle\int_x^\infty \beta(y)\kappa(x,y)\mathcal{V}_\mathfrak{a}(y)dy, \qquad x \geqslant 0, \\ \tau\mathcal{V}_\mathfrak{a}(x=0)=0, \qquad \mathcal{V}_\mathfrak{a}(x)>0 \ \text{ for } x>0, \qquad \int_0^\infty \mathcal{V}_\mathfrak{a}(x)dx = 1, \end{cases} \tag{4}$$

where $\mathfrak{a} > 0$ modulates the fragmentation intensity as for PMCA or therapeutics applied to the cell division cycle (see discussion in Section 3).

To make things clearer, let us give some enlightments on the dependency of $\Lambda_\mathfrak{a}$ and λ_α on their respective multipliers $\mathfrak{a}$ and α. First of all, one suspects that if $\mathfrak{a}$ vanishes or if α explodes, since transport dominates, the respective eigenvectors $\mathcal{U}_\alpha$ and $\mathcal{V}_\mathfrak{a}$ tend to dilute, and on the contrary if $\mathfrak{a}$ explodes or if α vanishes, since fragmentation dominates, they tend to a Dirac mass at zero (see Figure 1 for an illustration). But what happens to the eigenvalues λ_α and $\Lambda_\mathfrak{a}$? Integrating Equation (4), we obtain the relation

$$\Lambda_\mathfrak{a} = \mathfrak{a}\int_0^\infty \beta(x)\mathcal{V}_\mathfrak{a}(x)\,dx$$

which could give the intuition that $\Lambda_\mathfrak{a}$ is an increasing function of $\mathfrak{a}$, what is indeed true if $\beta(x)\equiv\beta$ is a constant since we obtain in this case $\Lambda_\mathfrak{a} = \beta\mathfrak{a}$. However, when β is not a constant, the dependency of the distribution $\mathcal{V}_\mathfrak{a}(x)$ on $\mathfrak{a}$ comes into account and we cannot conclude so easily. A better intuition is given by integration of Equation (4) against the weight x, that gives

$$\Lambda_\mathfrak{a}\int x\mathcal{V}_\mathfrak{a}(x)\,dx = \int \tau(x)\mathcal{V}_\mathfrak{a}(x)\,dx$$

and as a consequence we have that

$$\inf_{x>0}\frac{\tau(x)}{x} \leq \Lambda_\mathfrak{a} \leq \sup_{x>0}\frac{\tau(x)}{x}.$$

This last relation highlights the link between the first eigenvalue $\Lambda_\mathfrak{a}$ and the growth rate $\tau(x)$, or more precisely $\frac{\tau(x)}{x}$. For instance, if $\frac{\tau(x)}{x}$ is bounded, then $\Lambda_\mathfrak{a}$ is bounded too, independently of $\mathfrak{a}$. Notice

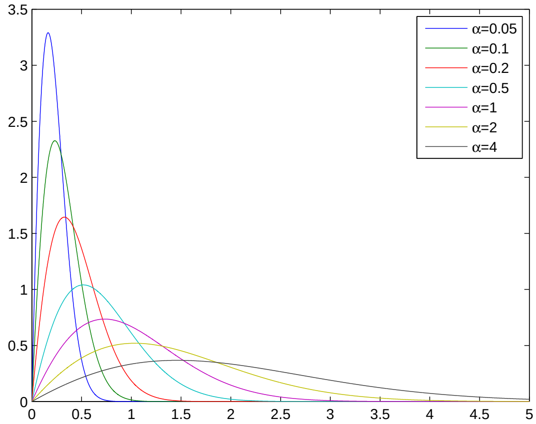


Figure 1: Eigenvectors $\mathcal{U}_\alpha(x)$ for different values of α when $\beta(x) \equiv 1$, $\kappa(x,y) = \frac{1}{y}\mathbb{1}_{0\leq x\leq y}$ and $\tau(x) = x$. In this case we have an explicit expression $\mathcal{U}_\alpha(x) = 2\sqrt{\alpha}\left(\sqrt{\alpha}x + \frac{\alpha x^2}{2}\right)\exp\left(\sqrt{\alpha}x + \frac{\alpha x^2}{2}\right)$. One sees that if α vanishes, $\mathcal{U}_\alpha$ tends to a Dirac mass, whereas it dilutes when $\alpha \to +\infty$.

that in the constant case $\beta(x) \equiv \beta$, there cannot exist a solution to the eigenvalue problem (2) for $\frac{\tau(x)}{x}$ bounded since we have $\Lambda_{\mathfrak{a}} = \beta\mathfrak{a}$ which contradicts the boundedness of $\frac{\tau(x)}{x}$. In fact we check that existence condition (27) in Section 1.2 imposes, for β constant, that $\frac{1}{\tau}$ is integrable at $x = 0$ and so $\frac{\tau(x)}{x}$ cannot be bounded.

Similarly, concerning Equation (3), an integration against the weight x gives

$$\lambda_\alpha = \frac{1}{\alpha}\frac{\int \tau\mathcal{U}_\alpha dx}{\int x\mathcal{U}_\alpha dx},$$

that could lead to the (false) intuition that λ_α decreases with α - what is indeed true in the limiting case $\tau(x) = x$. A simple integration gives more insight: it leads to

$$\lambda_\alpha = \int \beta(x)\mathcal{U}_\alpha(x)\,dx, \qquad \inf_{x>0}\beta(x) \leq \lambda_\alpha \leq \sup_{x>0}\beta(x).$$

This relation makes appear the fragmentation rate β when the parameter α is in front of the transport term. Moreover, we have seen that when the growth parameter α tends to zero for instance, the distribution $\mathcal{U}_\alpha(x)$ is expected to concentrate into a Dirac mass in $x = 0$, so the identity $\lambda_\alpha = \int \beta(x)\mathcal{U}_\alpha(x)\,dx$ indicates that λ_α should tend to $\beta(0)$. Similarly, when α tends to infinity, λ_α should behave as $\beta(+\infty)$.

These intuitions on the link between $\frac{\tau(x)}{x}$ and $\Lambda_{\mathfrak{a}}$ on the one hand, β and λ_α on the other hand are expressed in a rigorous way by the following result. The main assumption is that the coefficients $\tau(x)$ and $\beta(x)$ have power-like behaviours in the neighbourhood of $L = 0$ or $L = +\infty$, namely that

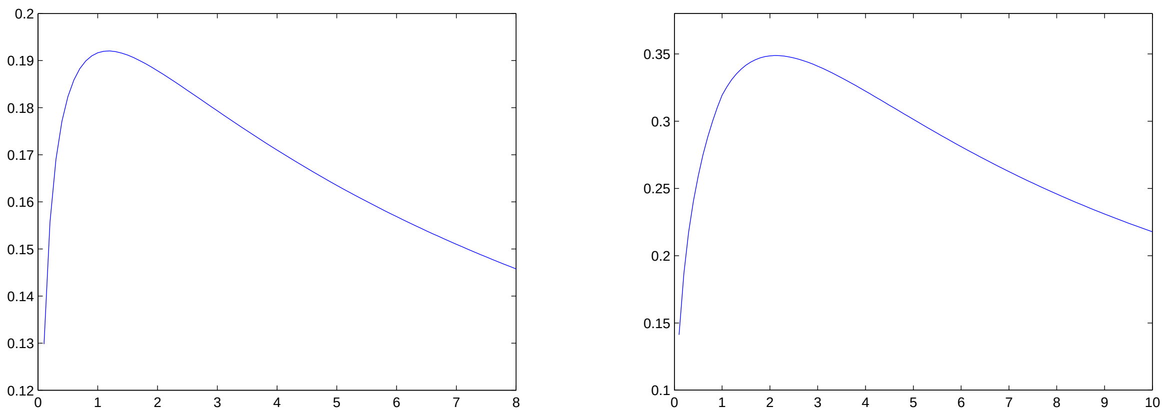
$$\exists\, \nu,\ \gamma \in \mathbb{R} \quad \text{such that} \quad \tau(x) \underset{x\to L}{\sim} \tau x^\nu, \quad \beta(x) \underset{x\to L}{\sim} \beta x^\gamma. \tag{5}$$

Theorem 1. *Under Assumption* (5)*, Assumptions* (12)*-*(13) *on* κ*, and Assumptions* (22)*-*(28) *given in [16] to ensure the existence and uniqueness of solutions to the eigenproblems* (3) *and* (4)*, we have, for* $L = 0$ *or* $L = +\infty$*,*

$$\lim_{\alpha \to L} \lambda_\alpha = \lim_{x \to L} \beta(x) \quad \textit{and} \quad \lim_{\mathfrak{a} \to L} \Lambda_{\mathfrak{a}} = \lim_{x \to \frac{1}{L}} \frac{\tau(x)}{x}.$$

This is an immediate consequence of our main result, stated in Theorem 2 of Section 1.1. As expected by the previous relations, for Problem (3) the eigenvalue behavior is given by a comparison between β and 1 in the neighbourhood of zero if polymerization vanishes ($\alpha \to 0$), and in the neighbourhood of infinity if polymerization explodes ($\alpha \to \infty$). For Problem (4), it is given by a comparison between τ and x (in the neighbourhood of zero when $\mathfrak{a} \to \infty$ or in the neighbourhood of infinity when $\mathfrak{a} \to 0$).
One notices that these behaviors are somewhat symetrical: indeed, the first step of our proof is to use a properly-chosen rescaling, so that both problems (3) and (4) can be reduced to a single one, given by Equation (18). Theorem 2 studies the asymptotic behaviour of this new problem, what allows us to quantify precisely the rates of convergence of the eigenvectors toward self-similar profiles.

A consequence of these results is the possible non-monotonicity of the first eigenvalue as a function of α or $\mathfrak{a}$. Indeed, if $\lim_{x\to 0} \beta(x) = \lim_{x\to\infty} \beta(x) = 0$, then the function $\alpha \mapsto \lambda_\alpha$ satisfies $\lim_{\alpha\to 0} \lambda_\alpha = \lim_{\alpha\to\infty} \lambda_\alpha = 0$ and is positive on $(0, +\infty)$ because $\lambda_\alpha = \int \beta \mathcal{U}_\alpha > 0$ for $\alpha > 0$. If $\lim_{x\to 0} \frac{\tau(x)}{x} = \lim_{x\to\infty} \frac{\tau(x)}{x} = 0$, we have the same conclusion for $\mathfrak{a} \mapsto \Lambda_{\mathfrak{a}}$ (see Figure 2 for examples).



(a) $\alpha \mapsto \lambda_\alpha$ (b) $\mathfrak{a} \mapsto \Lambda_{\mathfrak{a}}$

Figure 2: The dependencies of the first eigenvalue on polymerization and fragmentation parameters for coefficients which satisfy the assumptions of Theorem 1 are plotted. The coefficients are chosen to obtain non monotonic functions. 2(a): $\tau(x) = \frac{8\,x^{0.2}}{1+2\,x^{4.2}}$, $\beta(x) = \frac{x^3}{15+x^{4.5}}$ and $\kappa(x,y) = \frac{1}{y} 1\!\!1_{0\le x\le y}$. We have $\lim_{x\to 0}\beta(x) = \lim_{x\to\infty}\beta(x) = 0$, so $\lim_{\alpha\to 0}\lambda_\alpha = \lim_{\alpha\to\infty}\lambda_\alpha = 0$. 2(b): $\tau(x) = \frac{1.2\,x^{1.8}}{1+2\,x^{2.8}}$, $\beta(x) = \frac{4\,x^2}{10+x^{0.8}}$ and $\kappa(x,y) = \frac{1}{y} 1\!\!1_{0\le x\le y}$. We have $\lim_{x\to 0}\frac{\tau(x)}{x} = \lim_{x\to\infty}\frac{\tau(x)}{x} = 0$, so $\lim_{\mathfrak{a}\to 0}\Lambda_{\mathfrak{a}} = \lim_{\mathfrak{a}\to\infty}\Lambda_{\mathfrak{a}} = 0$.

This article is organised as follows. Section 1 is devoted to state and prove the main result, given in Theorem 2. We first detail the self-similar change of variables that leads to the reformulation of Problems (3) and (4) in Problem (18), as stated in Lemma 1. We then recall the assumptions for the existence and uniqueness result of [16]. We need these assumptions here not only to have well-posed problems but also because the main tool to prove Theorem 2 is given by similar estimates than the ones used in [16] to prove well-posedness.

In Section 2, we give more precise results in the limiting cases, *i.e.* when $\lim_{x\to L}\beta(x)$ or $\lim_{x\to L}\frac{\tau(x)}{x}$ is finite and positive, and conversely more general results under assumptions weaker than Assumption (5).

Finally, Section 3 proposes possible use and interpretation of the results in various fields of application.

1 Self-similarity Result

1.1 Main theorem

The main theorem is a self-similar result, in the spirit of [18]. It declines four times, as Equation (3) or (4) is considered, and as parameter α or $\mathfrak{a}$ goes to zero or to infinity. It gathers the asymptotics of the eigenvalue and possible self-similar behaviors of the eigenvector, when τ and β have power-like behavior in the neighbourhood of 0 or $+\infty$. We first explain in full details how the study of both Equations (3) and (4) reduce to the study of the asymptotic behavior of a unique problem, as Lemma 1 states.

When fragmentation vanishes or polymerization explodes, one expects the eigenvectors $\mathcal{U}_\alpha$ and $\mathcal{V}_\mathfrak{a}$ to disperse more and more. When fragmentation explodes or polymerization vanishes on the contrary, we expect them to concentrate at zero. This leads to the idea of performing an appropriate scaling of the eigenvector ($\mathcal{U}_\alpha$ or $\mathcal{V}_\mathfrak{a}$), so that the rescaled problem converges toward a steady profile instead of a Dirac mass or a more and more spread measure distribution.

For given k and l, we define v_α or $w_\mathfrak{a}$ by the dilation

$$v_\alpha(x) = \alpha^k \mathcal{U}_\alpha(\alpha^k x), \qquad w_\mathfrak{a}(x) = \mathfrak{a}^l \mathcal{V}_\mathfrak{a}(\mathfrak{a}^l x). \tag{6}$$

The function v_α satisfies the following equation

$$\alpha^{1-k}\frac{\partial}{\partial x}\Big(\tau(\alpha^k x)v_\alpha(x)\Big) + \Big(\lambda_\alpha + \beta(\alpha^k x)\Big)v_\alpha(x) = 2\int_x^\infty \beta(\alpha^k y)\kappa(\alpha^k x, \alpha^k y)v_\alpha(y)dy, \tag{7}$$

and similarly the function $w_\mathfrak{a}$ satisfies

$$\mathfrak{a}^{-l}\frac{\partial}{\partial x}\Big(\tau(\mathfrak{a}^l x)w_\mathfrak{a}(x)\Big) + \Big(\Lambda_\mathfrak{a} + \mathfrak{a}\beta(\mathfrak{a}^l x)\Big)w_\mathfrak{a}(x) = 2\mathfrak{a}\int_x^\infty \beta(\mathfrak{a}^l y)\kappa(\mathfrak{a}^l x, \mathfrak{a}^l y)w_\mathfrak{a}(y)dy. \tag{8}$$

A vanishing fragmentation or an increasing polymerization will lead the mass to spread more and more, and thus to consider the behavior of the coefficients τ, β around infinity; on the contrary, a vanishing polymerization or an infinite fragmentation will lead the mass to concentrate near zero, and we then consider the behavior of the coefficients around zero. This consideration drives our main assumption (5) on the power-like behavior of the coefficients $\tau(x)$ and $\beta(x)$ in the neighbourhood of $L=0$ and $L=+\infty$. We recall this assumption here

$$\exists\, \nu_L,\ \gamma_L \in \mathbb{R} \quad \text{such that} \quad \tau(x) \underset{x\to L}{\sim} \tau x^{\nu_L}, \quad \beta(x) \underset{x\to L}{\sim} \beta x^{\gamma_L}.$$

In the class of coefficients satisfying Assumption (5), Assumption (27) of Section 1.2 is equivalent to

$$\gamma_0 + 1 - \nu_0 > 0, \tag{9}$$

Assumption (28) coincides with

$$\gamma_\infty + 1 - \nu_\infty > 0, \tag{10}$$

and in Assumption (26), the condition linking $\bar\gamma$ to $\tau(x)$ becomes

$$\bar\gamma + 1 - \nu_0 > 0. \tag{11}$$

For the sake of simplicity, we omit the indices $_L$ in the sequel.

To preserve the fact that κ is a probability measure, we define

$$\kappa_\alpha(x,y) := \alpha^k \kappa(\alpha^k x, \alpha^k y), \qquad \kappa_{\mathfrak{a}}(x,y) := \mathfrak{a}^l \kappa(\mathfrak{a}^l x, \mathfrak{a}^l y). \tag{12}$$

For our equations to converge, we also make the following assumption concerning the fragmentation kernels κ_α and $\kappa_{\mathfrak{a}}$:

$$\text{For } k>0, \quad \exists\, \kappa_L \quad s.t. \quad \forall \varphi \in \mathcal{C}_c^\infty(\mathbb{R}_+), \quad \int \varphi(x)\kappa_\alpha(x,y)\,dx \underset{\alpha\to L}{\longrightarrow} \int \varphi(x)\kappa_L(x,y)\,dx \quad a.e. \tag{13}$$

It is nothing but the convergence in a distribution sense of $\kappa_\alpha(.,y)$ for almost every y. This is true for instance for fragmentation kernels which can be written in an homogeneous form as $\kappa(x,y) = \frac{1}{y}\tilde\kappa\big(\frac{x}{y}\big)$. In this case κ_α is equal to κ for all α, so $\kappa_L \equiv \kappa$ suits.

Under Assumption (5), in order to obtain steady profiles, we define

$$\tau_\alpha(x) := \alpha^{-k\nu}\tau(\alpha^k x), \qquad \tau_{\mathfrak{a}}(x) := \mathfrak{a}^{-l\nu}\tau(\mathfrak{a}^l x), \qquad \beta_\alpha := \alpha^{-k\gamma}\beta(\alpha^k x), \qquad \beta_{\mathfrak{a}} := \mathfrak{a}^{-l\gamma}\beta(\mathfrak{a}^l x), \tag{14}$$

so that, if $k>0$, there are local uniform convergences on $\mathbb{R}_+^*$ of τ_α and β_α : $\tau_\alpha \underset{\alpha\to L}{\longrightarrow} \tau x^\nu$ and $\beta_\alpha \underset{\alpha\to L}{\longrightarrow} \beta x^\gamma$. Equations (7) and (8) divided respectively by $\alpha^{k\gamma}$ and $\mathfrak{a}^{l(\nu-1)}$ can be written as

$$\alpha^{1+k(\nu-1-\gamma)}\frac{\partial}{\partial x}\Big(\tau_\alpha v_\alpha(x)\Big) + \Big(\alpha^{-k\gamma}\lambda_\alpha + \beta_\alpha\Big)v_\alpha(x) = 2\int_x^\infty \beta_\alpha(y)\kappa_\alpha(x,y)v_\alpha(y)dy, \tag{15}$$

$$\frac{\partial}{\partial x}\Big(\tau_{\mathfrak{a}} w_{\mathfrak{a}}(x)\Big) + \Big(\mathfrak{a}^{l(1-\nu)}\Lambda_{\mathfrak{a}} + \mathfrak{a}^{1-l(\nu-1-\gamma)}\beta_{\mathfrak{a}}\Big)w_{\mathfrak{a}}(x) = 2\mathfrak{a}^{1-l(\nu-1-\gamma)}\int_x^\infty \beta_{\mathfrak{a}}(y)\kappa_{\mathfrak{a}}(x,y)w_{\mathfrak{a}}(y)dy. \tag{16}$$

In order to cancel the multipliers of τ_α and $\beta_{\mathfrak{a}}$, it is natural to define

$$k = \frac{1}{1+\gamma-\nu} > 0, \qquad l = -k = \frac{-1}{1+\gamma-\nu} < 0, \tag{17}$$

which leads to

$$\frac{\partial}{\partial x}(\tau_\alpha(x)v_\alpha(x)) + (\theta_\alpha + \beta_\alpha(x))v_\alpha(x) = 2\int\limits_x^\infty \beta_\alpha(y)\kappa_\alpha(x,y)v_\alpha(y)dy, \tag{18}$$

and

$$\frac{\partial}{\partial x}(\tau_{\mathfrak{a}}(x)w_{\mathfrak{a}}(x)) + (\Theta_{\mathfrak{a}} + \beta_{\mathfrak{a}}(x))w_{\mathfrak{a}}(x) = 2\int\limits_x^\infty \beta_{\mathfrak{a}}(y)\kappa_{\mathfrak{a}}(x,y)w_{\mathfrak{a}}(y)dy, \tag{19}$$

with

$$\theta_\alpha = \alpha^{\frac{-\gamma}{1+\gamma-\nu}}\lambda_\alpha, \qquad \Theta_{\mathfrak{a}} = \mathfrak{a}^{\frac{\nu-1}{1+\gamma-\nu}}\Lambda_{\mathfrak{a}}.$$

The signs of k and l express the fact that for $\alpha > 1$ or $\mathfrak{a} < 1$, v_α and $w_{\mathfrak{a}}$ are contractions of $U_{\alpha,\mathfrak{a}}$, whereas for $\alpha < 1$ or $\mathfrak{a} > 1$ they are dilations - what is in accordance with our intuition of the respective roles of polymerization and fragmentation. Moreover, one notices that if we define $\mathfrak{a} := \frac{1}{\alpha}$, then $\mathfrak{a}^l = \alpha^k$, so Equations (18) and (19) are identical. By uniqueness of a solution to this eigenvalue problem, it implies that $\theta_\alpha = \Theta_{\frac{1}{\alpha}}$ and $v_\alpha = w_{\frac{1}{\alpha}}$. We are ready to state this result in the following lemma.

Lemma 1. *Eigenproblems* (3) *and* (4) *are equivalent to the eigenproblem* (18) *with* k *defined by* (17)*,* β_α*,* τ_α *defined by* (14)*,* κ_α *defined by* (12)*,* $\mathfrak{a} = \frac{1}{\alpha}$ *and the following relations linking the different problems:*

$$v_\alpha(x) = \alpha^k \mathcal{U}_\alpha(\alpha^k x) = \alpha^k \mathcal{V}_{\frac{1}{\alpha}}(\alpha^k x), \qquad \theta_\alpha = \alpha^{\frac{-\gamma}{1+\gamma-\nu}}\lambda_\alpha = \alpha^{\frac{1-\nu}{1+\gamma-\nu}}\Lambda_{\frac{1}{\alpha}}. \tag{20}$$

Defining $(v_\infty, \theta_\infty)$ as the unique solution of the following problem

$$\begin{cases} \dfrac{\partial}{\partial x}(\tau x^\nu v_\infty(x)) + (\beta x^\gamma + \theta_\infty)v_\infty(x) = 2\displaystyle\int_x^\infty \beta y^\gamma \kappa_L(x,y)v_\infty(y)dy, & x \geqslant 0, \\ \tau v_\infty(x=0) = 0, \qquad v_\infty(x) > 0 \ \text{ for } x > 0, \qquad \int_0^\infty v_\infty(x)dx = 1, & \theta_\infty > 0, \end{cases} \tag{21}$$

we expect θ_α to converge towards $\theta_\infty > 0$ and v_α towards v_∞ when α tends to L, so the expressions of λ_α, $\Lambda_{\mathfrak{a}}$ given by (20) will provide immediately their asymptotic behavior. It is expressed in the following theorem.

Theorem 2. *Let* τ*,* β *and* κ *verifying Assumptions* (22)-(28)*. Let* $L = 0$ *or* $L = +\infty$*, and* τ *and* β *verifying also Assumption* (5)*. Let* κ_α *defined by* (12) *with* k *defined by* (17) *verifying Assumption* (13)*. Let* $(v_\alpha, \theta_\alpha)$ *be the unique solution to the eigenproblem* (19) *. We have the following asymptotic behaviors*

$$x^r v_\alpha(x) \xrightarrow[\alpha\to L]{} x^r v_\infty(x) \ \textit{strongly in } L^1 \textit{ for all } r \geq 0, \ \textit{and } \theta_\alpha \xrightarrow[\alpha\to L]{} \theta_\infty.$$

Theorem 1 announced in introduction follows immediately from Theorem 2 and the expression of λ_α and $\Lambda_{\mathfrak{a}}$ given by (20).

1.2 Recall of existence results ([27, 16])

We first recall the assumptions of the existence and uniqueness theorem for the eigenequation (2) (see [16] for a complete motivation of these assumptions). This also ensures well-posedness of Problems (3) and (4).

For all $y \geq 0$, $\kappa(.,y)$ is a nonnegative measure with a support included in $[0,y]$. We define κ on $(\mathbb{R}_+)^2$ as follows: $\kappa(x,y) = 0$ for $x > y$. We assume that for all continuous function ψ, the application $f_\psi : y \mapsto \int \psi(x)\kappa(dx,y)$ is Lebesgue measurable.

Mass conservation and physical interpretation lead to suppose

$$\int \kappa(dx,y) = 1, \qquad \int x\kappa(dx,y) = \frac{y}{2}, \tag{22}$$

so $\kappa(y,.)$ is a probability measure and $f_\psi \in L^\infty_{loc}(\mathbb{R}_+)$. We moreover assume that the second moment of κ is uniformly less than the first one

$$\int \frac{x^2}{y^2}\kappa(x,y)dx \leq c < 1/2. \tag{23}$$

For the polymerization and fragmentation rates τ and β, we introduce the set

$$\mathcal{P} := \big\{ f \geq 0 \,:\, \exists \mu \geq 0,\ \limsup_{x\to\infty} x^{-\mu} f(x) < \infty \text{ and } \liminf_{x\to\infty} x^{\mu} f(x) > 0 \big\}.$$

We consider

$$\beta \in L^1_{loc}(\mathbb{R}_+^*) \cap \mathcal{P}, \qquad \exists r_0 \geq 0 \ s.t.\ \tau \in L^\infty_{loc}(\mathbb{R}_+, x^{r_0}dx) \cap \mathcal{P} \tag{24}$$

satisfying

$$\forall K \text{ compact of } (0,\infty),\ \exists m_K > 0 \quad s.t. \quad \tau(x), \beta(x) \geq m_K \text{ for } a.e.\ x \in K \tag{25}$$

$$\exists\, C > 0, \bar\gamma \geq 0 \quad s.t. \qquad \int_0^x \kappa(z,y)\,dz \leq \min\Big(1, C\Big(\frac{x}{y}\Big)^{\bar\gamma}\Big) \qquad \text{and} \qquad \frac{x^{\bar\gamma}}{\tau(x)} \in L^1_0 \tag{26}$$

Notice that if Assumption (26) is satisfied for $\bar\gamma > 0$, then Assumption (23) is automatically fulfilled (see Appendix A in [16]). We assume that growth dominates fragmentation close to $L = 0$ in the following sense:

$$\frac{\beta}{\tau} \in L^1_0 := \big\{ f,\ \exists a > 0,\ f \in L^1(0,a) \big\}. \tag{27}$$

We assume that fragmentation dominates growth close to $L = +\infty$ in the following sense:

$$\lim_{x\to+\infty} \frac{x\beta(x)}{\tau(x)} = +\infty. \tag{28}$$

Under these assumptions, we have existence and uniqueness of a solution to the first eigenvalue problem; let us recall this result (see [27, 16]).

Theorem [16]. *Under Assumptions* (22)-(28)*, for* $0 < \alpha,\ \mathfrak{a} < \infty$, *there exist unique solutions* $(\lambda, \mathcal{U})$, *respectively to the eigenproblems* (2), (3) *and* (4)*, and we have*

$$\lambda > 0,$$

$$x^r \tau \mathcal{U} \in L^p(\mathbb{R}_+), \quad \forall r \geq -\bar\gamma, \quad \forall p \in [1,\infty],$$

$$x^r \tau \mathcal{U} \in W^{1,1}(\mathbb{R}_+), \quad \forall r \geq 0.$$

We also recall the following corollary (first proved in [27]). We shall use it at some step of our blow-up analysis.

Corollary [27, 16]. *Let $\tau > 0$ and $\beta > 0$ two given constants, γ, $\nu \in \mathbb{R}$ such that $1 + \gamma - \nu > 0$, and κ_L verifying Assumptions* (22)*,* (23) *and* (26)*. Then there exists a unique $(\theta_\infty, v_\infty)$ solution to the eigenproblem* (2) *with $\tau(x) = \tau x^\nu$ and $\beta(x) = \beta x^\gamma$:*

Indeed, in this particular case, assumptions of the above existence theorem are immediate, and as already said both assumptions (27) and (28) are verified if and only if $1 + \gamma - \nu > 0$.

1.3 Proof of Theorem 2

It is straightforward to prove that κ_α satisfies Assumptions (22)-(23) and (26) with the same constants c and C as κ, thus independent of α.

We have local uniform convergences in $\mathbb{R}_+^*$ $\tau_\alpha \underset{\alpha\to L}{\longrightarrow} \tau x^\nu$ and $\beta_\alpha \underset{\alpha\to L}{\longrightarrow} \beta x^\gamma$, if Assumption (5) holds, for $L = 0$ as well as $L = \infty$.

For the two cases, the result is based on uniform estimates on v_α and θ_α independent of α, in the same spirit as in the proof of the existence theorem (see [16]). When these estimates lead to compactness in $L^1(\mathbb{R}_+)$, we shall extract a converging subsequence, which will be a weak solution of Equation (21) ; the global convergence result will then be a consequence of the uniqueness of a solution to Equation (21). This type of proofs is classical, and we refer for instance to [31, 16] for more details.

As in [16], the proofs of the estimates that are needed to obtain compactness in L^1 are strongly based on Assumptions (24), (26), (27) and (28). Lemmas 2, 3 and 4 prove respectively that β_α, τ_α and κ_α satisfy Assumption (28), (24) and (26)-(27) *uniformly* for all α.

Here we assume slight generalizations of Assumption (5), as precised in each lemma, in order to make appear more clearly where each part of Assumption (5) is necessary.

Lemma 2. *Suppose that*

$$\exists\, \nu,\ \gamma \in \mathbb{R} \quad s.t. \quad 1 + \gamma - \nu > 0, \quad and \quad \frac{\tau(x)}{\beta(x)} \underset{x\to L}{=} O(x^{\nu-\gamma})\,. \tag{29}$$

Then for all $r > 0$, there exist $A_r > 0$ and $\mathcal{N}_L$ a neighbourhood of L such that

$$\text{for a.e. } x \geq A_r \text{ and for all } \alpha \in \mathcal{N}_L, \quad \frac{x\beta_\alpha(x)}{\tau_\alpha(x)} \geq r. \tag{30}$$

Proof. Let $r > 0$.
For all $\alpha > 0$, we define, thanks to Assumption (28),

$$p_\alpha := \inf\left\{ p\, :\, \frac{x\beta(x)}{\alpha\tau(x)} \geq r, \text{ for } a.e.\ x \geq p \right\}.$$

Observe that p_α is nondecreasing. Let $\varepsilon > 0$, by definition of p_α, there exists a sequence $\{\xi_\alpha\}$ with values in $[1 - \varepsilon, 1]$ such that

$$\frac{\xi_\alpha p_\alpha \beta(\xi_\alpha p_\alpha)}{\alpha\tau(\xi_\alpha p_\alpha)} \leq r. \tag{31}$$

Thanks to Assumptions (24) and (25), we have that $\frac{\tau}{x\beta} \in L^\infty_{loc}(\mathbb{R}_+^*)$ so that $p_\alpha \xrightarrow[\alpha\to+\infty]{} +\infty$ (else, since it is nondecreasing, it would tend to a finite limit, what is absurd by definition of p_α), and also that $\frac{\tau}{x\beta} > 0$ on $\mathbb{R}_+^*$ so that $p_\alpha \xrightarrow[\alpha\to0]{} 0$. Hence, for some constant C :

$$\frac{\tau(\xi_\alpha p_\alpha)}{\beta(\xi_\alpha p_\alpha)} \underset{\alpha\to L}{\leq} C(\xi_\alpha p_\alpha)^{\nu-\gamma}. \tag{32}$$

Then (31)-(32) lead to, for some absolute constant C :

$$(1-\varepsilon)\frac{p_\alpha}{\alpha^k} \leq \frac{\xi_\alpha p_\alpha}{\alpha^k} \leq \left[C\frac{\xi_\alpha p_\alpha \beta(\xi_\alpha p_\alpha)}{\alpha\tau(\xi_\alpha p_\alpha)}\right]^k \leq C^k r^k$$

which implies that $\limsup\limits_{\alpha\to L} \frac{p_\alpha}{\alpha^k} \leq C^k r^k$ is finite. So we can define A_r by

$$A_r := 1 + \limsup_{\alpha\to L} \frac{p_\alpha}{\alpha^k}.$$

Then for any $x > A_r$ we have, when $\alpha \to L$, that $\alpha^k x > p_\alpha$, and so

$$\frac{\alpha^k x\beta(\alpha^k x)}{\alpha\tau(\alpha^k x)} \geq r,$$

and by definition of β_α and τ_α it gives us the desired result. □

Lemma 3. *Suppose that*

$$\exists\, \nu \in \mathbb{R} \quad s.t. \quad \tau(x) \underset{x\to L}{=} O(x^\nu) \quad and \quad \exists\, r_0 > 0 \quad s.t. \quad x^{r_0}\tau(x) \in L^\infty_{loc}(\mathbb{R}_+). \tag{33}$$

Then for all $A > 0$ and $r \geq \max(r_0, -\nu)$, there exist $C > 0$ and $\mathcal{N}_L$ a neighbourhood of L such that

$$for\ a.e.\ x \in [0, A]\ and\ for\ all\ \alpha \in \mathcal{N}_L, \quad x^r\tau_\alpha(x) \leq C.$$

Suppose that

$$\exists\, \nu \in \mathbb{R} \quad s.t. \quad \tau^{-1}(x) \underset{x\to L}{=} O(x^{-\nu}) \quad and \quad \exists\, \mu > 0 \quad s.t. \quad \inf_{x\in[1,+\infty)} x^\mu\tau(x) > 0. \tag{34}$$

for all $\varepsilon > 0$ and $m \geq \max(\mu, -\nu)$, there exist $c > 0$ and $\mathcal{N}_L$ a neighbourhood of L such that

$$for\ a.e.\ x \geq \varepsilon\ and\ for\ all\ \alpha \in \mathcal{N}_L, \quad x^m\tau_\alpha(x) \geq c.$$

Proof. We have to treat separately the case $L = 0$ and $L = +\infty$.

Let us start with $L = 0$. Notice that in this case, if $\tau(x) = O(x^\nu)$ then thanks to Assumption (24) $r_0 = -\nu$ suits to have (33). Considering $r \geq -\nu$, we have for some constant $C > 0$:

$$\begin{aligned} \operatorname*{sup\,ess}_{x\in[0,A]} (x^r\tau_\alpha(x)) &= \operatorname*{sup\,ess}_{y\in[0,\alpha^k A]} (\alpha^{-k(r+\nu)} y^r \tau(y)) \\ &\underset{\alpha\to0}{\leq} C \sup_{[0,\alpha^k A]} (\alpha^{-k(r+\nu)} y^{r+\nu}) = CA^{r+\nu}. \end{aligned}$$

For $m \geq \max(\mu, -\nu)$ and using Assumption (34) we have for some constants $c_1, c_2 > 0$:

$$\begin{aligned}
\inf_{x\in[\varepsilon,\infty)} \text{ess}\,(x^m \tau_\alpha(x)) &= \inf_{y\in[\alpha^k\varepsilon,\infty)} \text{ess}\,(\alpha^{-k(m+\nu)} y^m \tau(y)) \\
&\geq \min\left(\inf_{[\alpha^k\varepsilon,1]} \text{ess}\,(\alpha^{-k(m+\nu)} y^m \tau(y)), \inf_{[1,\infty)} \text{ess}\,(\alpha^{-k(m+\nu)} y^\mu \tau(y))\right) \\
&\underset{\alpha\to 0}{\geq} \min\left(c_1 \inf_{[\alpha^k\varepsilon,1]} (\alpha^{-k(m+\nu)} y^{m+\nu}), c_2 \alpha^{-k(m+\nu)}\right) = \min\left(c_1 \varepsilon^{m+\nu}, c_2 \alpha^{-k(m+\nu)}\right)
\end{aligned}$$

Now we consider $L = +\infty$ and $r \geq \max(r_0, -\nu)$. Thanks to Assumption (33) we have for some constants $C_1, C_2 > 0$:

$$\begin{aligned}
\sup_{x\in[0,A]} \text{ess}\,(x^r \tau_\alpha(x)) &= \sup_{y\in[0,\alpha^k A]} \text{ess}\,(\alpha^{-k(r+\nu)} y^r \tau(y)) \\
&\leq \sup_{[0,1]} \text{ess}\,(\alpha^{-k(r+\nu)} y^{r_0} \tau(y)) + \sup_{[1,\alpha^k A]} \text{ess}\,(\alpha^{-k(r+\nu)} y^r \tau(y)) \\
&\underset{\alpha\to\infty}{\leq} C_1 \alpha^{-k(r+\nu)} + C_2 A^{r+\nu}.
\end{aligned}$$

For $m \geq -\nu$ and using Assumption (34), we have for some $c > 0$:

$$\begin{aligned}
\inf_{x\in[\varepsilon,\infty)} \text{ess}\,(x^m \tau_\alpha(x)) &= \inf_{y\in[\alpha^k\varepsilon,\infty)} \text{ess}\,(\alpha^{-k(m+\nu)} y^m \tau(y)) \\
&\underset{\alpha\to\infty}{\geq} c \inf_{[\alpha^k\varepsilon,\infty)} (\alpha^{-k(m+\nu)} y^{m+\nu}) = c\varepsilon^{m+\nu}.
\end{aligned}$$

□

Lemma 4. *Suppose that*

$$\exists\, \nu,\ \gamma \in \mathbb{R} \quad \textit{s.t.} \quad \gamma + 1 - \nu > 0, \quad \textit{and} \quad \frac{\beta(x)}{\tau(x)} \underset{x\to L}{=} O(x^{\gamma-\nu}). \tag{35}$$

Then for all $\rho > 0$, there exist $\varepsilon > 0$ and $\mathcal{N}_L$ a neighbourhood of L such that

$$\forall \alpha \in \mathcal{N}_L, \qquad \int_0^\varepsilon \frac{\beta_\alpha(x)}{\tau_\alpha(x)}\, dx \leq \rho.$$

Proof. Thanks to Assumption 35 we have for some constant $C > 0$:

$$\int_0^\varepsilon \frac{\beta_\alpha(x)}{\tau_\alpha(x)}\, dx = \frac{1}{\alpha} \int_0^{\varepsilon\alpha^k} \frac{\beta(x)}{\tau(x)}\, dx \underset{\alpha\to L}{\leq} C\frac{1}{\alpha} \int_0^{\varepsilon\alpha^k} x^{\gamma-\nu} dx = Ck\varepsilon^{\frac{1}{k}}.$$

The result follows for ε small enough. □

Thanks to these preliminary lemmas, we can prove Theorem 2.

Proof of Theorem 2. We prove estimates on $\{v_\alpha\}$ and $\{\theta_\alpha\}$, uniform in $\alpha \to L$, in order to have compactness. Then the convergence of the sequences is a consequence of the uniqueness of $(\theta_\infty, v_\infty)$.

First estimate: L^1bound for $x^r v_\alpha$, $r \geq 0$. For $r \geq 2$, we have by definition and thanks to Assumption (23)

$$\begin{aligned}\int_0^y \frac{x^r}{y^r}\kappa_\alpha(x,y)\,dx &\leq \int_0^y \frac{x^2}{y^2}\kappa_\alpha(x,y)\,dx\\ &= \int_0^{\alpha^k y} \frac{x^2}{(\alpha^k y)^2}\kappa(x,\alpha^k y)\,dx \leq c.\end{aligned}$$

So, multiplying the equation (18) on v_α by x^r and then integrating on $[0,\infty)$, we find

$$\begin{aligned}\int (1-2c)x^r\beta_\alpha(x)v_\alpha(x)\,dx &\leq r\int x^{r-1}\tau_\alpha(x)v_\alpha(x)\,dx\\ &= r\int_{x\leq A} x^{r-1}\tau_\alpha(x)v_\alpha(x)\,dx + r\int_{x\geq A} x^{r-1}\tau_\alpha(x)v_\alpha(x)\,dx.\end{aligned} \tag{36}$$

Thanks to Lemma 2, and choosing $A = A_{\frac{r}{\omega}}$ in (36) with $\omega < 1-2c$, we obtain

$$\int x^r\beta_\alpha(x)v_\alpha(x)\,dx \leq \frac{r\sup_{(0,A_{\frac{r}{\omega}})}\{x^{r-1}\tau_\alpha\}}{1-2c-\omega},$$

and the right hand side is uniformly bounded for $r-1 \geq \max(r_0,-\nu)$ when $\alpha \to L$, thanks to Lemma 3. Finally

$$\forall r \geq \max(2, 1+r_0, 1-\nu), \quad \exists C_r, \quad \int x^r\beta_\alpha(x)v_\alpha(x)\,dx \leq C_r. \tag{37}$$

Moreover for all α we have $\int v_\alpha dx = 1$. So, using Lemma 3 with $\beta^{-1}(x) = O(x^{-\gamma})$ instead of $\tau^{-1}(x) = O(x^{-\nu})$, we conclude that uniformly in $\alpha \to L$

$$x^r v_\alpha \in L^1(\mathbb{R}_+), \ \forall r \geq 0. \tag{38}$$

Second estimate: θ_α upper bound. The next step is to prove the same estimate as (37) for $0 \leq r < \max(2, 1+r_0, 1-\nu)$ and for this we first give a bound on $\tau_\alpha v_\alpha$. Let $m = \max(2, 1+r_0, 1-\nu)$, then, using ε and $\rho < \frac{1}{2}$ defined in Lemma 4 and integrating (18) between 0 and $x \leq \varepsilon$, we find (noticing that the quantity $\tau_\alpha(x)v_\alpha(x)$ is well defined because Theorem [16] ensures that $\tau_\alpha v_\alpha$ is continuous)

$$\begin{aligned}\tau_\alpha(x)v_\alpha(x) &\leq 2\int_0^x\int \beta_\alpha(y)v_\alpha(y)\kappa_\alpha(z,y)\,dy\,dz\\ &\leq 2\int \beta_\alpha(y)v_\alpha(y)\,dy\\ &= 2\int_0^\varepsilon \beta_\alpha(y)v_\alpha(y)\,dy + 2\int_\varepsilon^\infty \beta_\alpha(y)v_\alpha(y)\,dy\\ &\leq 2\sup_{(0,\varepsilon)}\{\tau_\alpha v_\alpha\}\int_0^\varepsilon \frac{\beta_\alpha(y)}{\tau_\alpha(y)}\,dy + 2\varepsilon^{-m}\int_0^\infty y^m\beta_\alpha(y)v_\alpha(y)\,dy\\ &\leq 2\rho\sup_{(0,\varepsilon)}\{\tau_\alpha v_\alpha\} + 2\varepsilon^{-m}C_m.\end{aligned}$$

Consequently, we obtain

$$\sup_{x\in(0,\varepsilon)} \tau_\alpha(x)v_\alpha(x) \leq \frac{1+2C_m\varepsilon^{-m}}{1-2\rho} := C. \tag{39}$$

Then we can write for any $0 \le r < m$

$$\begin{aligned}
\int x^r \beta_\alpha(x) v_\alpha(x)\,dx &= \int_0^\varepsilon x^r \beta_\alpha(x) v_\alpha(x)\,dx + \int_\varepsilon^\infty x^r \beta_\alpha(x) v_\alpha(x)\,dx \\
&\le \varepsilon^r \sup_{(0,\varepsilon)}\{\tau_\alpha v_\alpha\} \int_0^\varepsilon \frac{\beta_\alpha(x)}{\tau_\alpha(x)}\,dx + \varepsilon^{r-m} \int_\varepsilon^\infty x^m \beta_\alpha(x) v_\alpha(x)\,dx \\
&\le C\rho\varepsilon^r + C_m \varepsilon^{r-m} := C_r.
\end{aligned}$$

Finally we have that

$$\forall r \ge 0, \quad \exists C_r, \quad \int x^r \beta_\alpha(x) v_\alpha(x)\,dx \le C_r \tag{40}$$

and so

$$\theta_\alpha = \int \beta_\alpha v_\alpha \le C_0. \tag{41}$$

Third estimate: L^∞bound for $x^{-\bar\gamma}\tau_\alpha v_\alpha$. First, integrating equation (18) between 0 and x we find

$$\tau_\alpha(x) v_\alpha(x) \le 2 \int \beta_\alpha(y) v_\alpha(y)\,dy = 2\theta_\alpha \le 2C_0, \quad \forall x > 0. \tag{42}$$

It remains to prove that $x^{-\bar\gamma}\tau_\alpha v_\alpha$ is bounded in a neighborhood of zero.
Let us define $f_\alpha : x \mapsto \sup_{(0,x)} \tau_\alpha v_\alpha$. If we integrate (2) between 0 and $x' < x$, we find

$$\tau_\alpha(x') v_\alpha(x') \le 2 \int_0^{x'} \int \beta_\alpha(y) v_\alpha(y) \kappa_\alpha(z,y)\,dy\,dz \le 2 \int_0^x \int \beta_\alpha(y) v_\alpha(y) \kappa_\alpha(z,y)\,dy\,dz$$

and so for all x

$$f_\alpha(x) \le 2 \int_0^x \int \beta_\alpha(y) v_\alpha(y) \kappa_\alpha(z,y)\,dy\,dz.$$

Considering ε and ρ from Lemma 4 and using (26), we have for all $x < \varepsilon$

$$\begin{aligned}
f_\alpha(x) &\le 2 \int_0^x \int \beta_\alpha(y) v_\alpha(y) \kappa_\alpha(z,y)\,dy\,dz \\
&= 2 \int \beta_\alpha(y) v_\alpha(y) \int_0^x \kappa_\alpha(z,y)\,dz\,dy \\
&\le 2 \int_0^\infty \beta_\alpha(y) v_\alpha(y) \min\Big(1, C\Big(\frac{x}{y}\Big)^{\bar\gamma}\Big)\,dy \\
&= 2 \int_0^x \beta_\alpha(y) v_\alpha(y)\,dy + 2C \int_x^\varepsilon \beta_\alpha(y) v_\alpha(y) \Big(\frac{x}{y}\Big)^{\bar\gamma} dy + 2C \int_\varepsilon^\infty \beta_\alpha(y) v_\alpha(y) \Big(\frac{x}{y}\Big)^{\bar\gamma} dy \\
&= 2 \int_0^x \frac{\beta_\alpha(y)}{\tau_\alpha(y)} \tau_\alpha(y) v_\alpha(y)\,dy + 2Cx^{\bar\gamma} \int_x^\varepsilon \frac{\beta_\alpha(y)}{\tau_\alpha(y)} \frac{\tau_\alpha(y) v_\alpha(y)}{y^{\bar\gamma}}\,dy + 2C \int_\varepsilon^\infty \beta_\alpha(y) v_\alpha(y) \Big(\frac{x}{y}\Big)^{\bar\gamma} dy \\
&\le 2f_\alpha(x) \int_0^\varepsilon \frac{\beta_\alpha(y)}{\tau_\alpha(y)}\,dy + 2Cx^{\bar\gamma} \int_x^\varepsilon \frac{\beta_\alpha(y)}{\tau_\alpha(y)} \frac{f_\alpha(y)}{y^{\bar\gamma}}\,dy + 2C\varepsilon^{-\bar\gamma} \|\beta_\alpha v_\alpha\|_{L^1} x^{\bar\gamma}.
\end{aligned}$$

If we set $\mathcal{V}_\alpha(x) = x^{-\bar\gamma} f_\alpha(x)$, we obtain when $\alpha \to L$

$$(1-2\rho)\mathcal{V}_\alpha(x) \le K_\varepsilon + 2C \int_x^\varepsilon \frac{\beta_\alpha(y)}{\tau_\alpha(y)} \mathcal{V}_\alpha(y)\,dy$$

and, thanks to the Grönwall's lemma, we find that $\mathcal{V}_\alpha(x) \le \dfrac{K_\varepsilon e^{\frac{2C\rho}{1-2\rho}}}{1-2\rho}$. Finally

$$\sup_{(0,\varepsilon)}\{x^{-\bar{\gamma}}\tau_\alpha(x)v_\alpha(x)\} \le \frac{K_\varepsilon e^{\frac{2C\rho}{1-2\rho}}}{1-2\rho}. \tag{43}$$

The bound (42) with Assumption (25) and the bound (43) with Lemma 4 (in which we replace $\beta_\alpha(x)$ by $x^{\bar{\gamma}}$) ensure that the family $\{v_\alpha\}$ is uniformly integrable. This result, associated to the first estimate, gives that $\{v_\alpha\}$ belongs to a compact set in L^1-weak thanks to the Dunford-Pettis theorem. The sequence $\{\theta_\alpha\}$ belongs also to a compact interval of $\mathbb{R}_+$, so there is a subsequence of $\{(v_\alpha, \theta_\alpha)\}$ which converges in L^1-weak $\times\, \mathbb{R}$. The limit is a solution to (21), but such a solution is unique so the sequence converges entirely. To have convergence in L^1-strong, we need one more estimate.

Fourth estimate: $W^{1,1}$ bound for $x^r\tau_\alpha v_\alpha,\ r \ge 0$. First, the estimates (38) and (43) ensure that $x^r\tau_\alpha v_\alpha$ is uniformly bounded in L^1 for any $r > -1$. Then, equation (18) gives immediately that

$$\int \Big|\frac{\partial}{\partial x}(x^r\tau_\alpha(x)v_\alpha(x))\Big|\, dx \le r\int x^{r-1}\tau_\alpha(x)v_\alpha(x)\, dx + \theta_\alpha + 3\int \beta_\alpha(x)v_\alpha(x) \tag{44}$$

is also uniformly bounded. For $r = 0$, the same computation works and finally $x^r\tau_\alpha v_\alpha$ is bounded in $W^{1,1}(\mathbb{R}_+)$ for any $r \ge 0$.

The consequence is, thanks to the Rellich-Kondrachov theorem, that $\{x^r\tau_\alpha v_\alpha\}$ is compact in L^1-strong and so converges strongly to $\tau x^{r+\nu}v_\infty(x)$. Then, using Lemma 3 and estimate (43), we can write

$$\begin{aligned}\int x^r|v_\alpha(x) - v_\infty(x)|\, dx &\le \int_0^\varepsilon x^r|v_\alpha(x) - v_\infty(x)|\, dx + \int_\varepsilon^\infty x^r|v_\alpha(x) - v_\infty(x)|\, dx \\ &\le C\int_0^\varepsilon \frac{x^{r+\bar{\gamma}}}{\tau_\alpha(x)}dx + C\int_\varepsilon^\infty x^r|\tau_\alpha(x)v_\alpha(x) - \tau x^\nu v_\infty(x)|\, dx.\end{aligned}$$

The first term is small for ε small thanks to Lemma 4 and the second term is small for α close to L due to the strong L^1 convergence of $\{x^r\tau_\alpha(x)v_\alpha(x)\}$. This proves the strong convergence of $\{x^r v_\alpha(x)\}$ and ends the proof of Theorem 2.

$\square$

2 Further Results

2.1 Critical case

In the case when $\lim_{x\to 0}\beta(x)$ or $\lim_{x\to 0}\frac{\tau(x)}{x}$ is a positive constant, we can enhance the result of Theorem 1 if we know the higher order term in the series expansion. Assumptions (45) and (47) of Corollary 1 are stronger than Assumption (5), but provide a more precise result on the asymptotic behavior of $\lambda_\alpha,\ \Lambda_{\mathfrak{a}}$.

Corollary 1. *If β admits an expansion of the form*

$$\beta(x) = \beta_0 + \beta_1 x^{\gamma_1} + \underset{x\to 0}{o}(x^{\gamma_1}), \quad \gamma_1 > 0 \tag{45}$$

with $\beta_0 > 0$ and $\beta_1 \neq 0$, then we have the following expansion for λ

$$\lambda_\alpha = \beta_0 + \left(\beta_1 \int x^{\gamma_1} v_\infty(x)\, dx\right) \alpha^{k\gamma_1} + \underset{\alpha\to 0}{o}(\alpha^{k\gamma_1}). \tag{46}$$

In the same way, if τ admits an expansion of the form

$$\tau(x) = \tau_0 x + \tau_1 x^{\nu_1} + \underset{x\to 0}{o}(x^{\nu_1}), \quad \nu_1 > 1 \tag{47}$$

with $\tau_0 > 0$ and $\tau_1 \neq 0$, then we have

$$\Lambda_{\mathfrak{a}} = \tau_0 + \left(\tau_1 \frac{\int x^{\nu_1} v_\infty(x)\, dx}{\int x v_\infty(x)\, dx}\right) \mathfrak{a}^{l(\nu_1 - 1)} + \underset{\mathfrak{a}\to \infty}{o}(\mathfrak{a}^{l(\nu_1-1)}). \tag{48}$$

Proof. First we assume that β admits an expansion of the form (45) and we want to prove (46). By integrating Equation (18) we know that $\lambda_\alpha \int v_\alpha dx = \int \beta_\alpha(x) v_\alpha(x)\, dx$ and so multiplying by $\alpha^{-k\gamma_1}$ gives

$$\alpha^{-k\gamma_1}(\lambda_\alpha - \beta_0) = \int \alpha^{-k\gamma_1}(\beta_\alpha(x) - \beta_0) v_\alpha(x)\, dx.$$

Now the proof is complete if we prove the convergence

$$\int \alpha^{-k\gamma_1}(\beta_\alpha(x) - \beta_0) v_\alpha(x)\, dx \xrightarrow[\alpha\to 0]{} \int \beta_1 x^{\gamma_1} v_\infty(x)\, dx. \tag{49}$$

For this we use the expansion (45) which provides, for all $x \geq 0$, the following one

$$\beta_\alpha(x) \underset{\alpha\to 0}{=} \beta_0 + \beta_1 x^{\gamma_1} \alpha^{k\gamma_1} + o(\alpha^{k\gamma_1}). \tag{50}$$

Let $m \geq \gamma_1$ such that $\limsup\limits_{x\to\infty} x^{-m}\beta(x) < \infty$ (see Assumption (24)) and define

$$f_\alpha : x \mapsto \frac{\alpha^{-k\gamma_1}(\beta_\alpha(x) - \beta_0)}{x^{\gamma_1} + x^m}.$$

We know thanks to (50) that $f_\alpha(x) \xrightarrow[\alpha\to 0]{} \dfrac{\beta_1 x^{\gamma_1}}{x^{\gamma_1} + x^m}$ for all x. Moreover we have thanks to Theorem 2 that $(x^{\gamma_1} + x^m) v_\alpha(x) \xrightarrow[\alpha\to 0]{} (x^{\gamma_1} + x^m) v_\infty(x)$ in L^1. So we simply have to prove that f_α is uniformly bounded to get (49) (see Section 5.2 in [21]). Thanks to (45) and the fact that $\limsup\limits_{x\to\infty} x^{-m}\beta(x) < \infty$ with $m \geq \gamma_1 > 0$, we know that there exists a constant C such that

$$|\beta(y) - \beta_0| \leq C(y^{\gamma_1} + y^m), \quad \forall y \geq 0,$$

and so, because $\alpha \to 0$

$$\alpha^{-k\gamma_1}|\beta(y) - \beta_0| \leq C(\alpha^{-k\gamma_1} y^{\gamma_1} + \alpha^{-km} y^m),$$

what gives, for $x = \alpha^k y$

$$\alpha^{-k\gamma_1}|\beta(\alpha^k x) - \beta_0| \leq C(x^{\gamma_1} + x^m)$$

and we have proved that $f_\alpha(x) \le C$.

The same method allows to prove the result on $\Lambda_{\mathfrak{a}}$, starting from the identity

$$(\Lambda_{\mathfrak{a}} - \tau_0) \int x w_{\mathfrak{a}}(x)\, dx = \int (\tau_{\mathfrak{a}}(x) - \tau_0 x) w_{\mathfrak{a}}(x)\, dx$$

and using the fact that (47) provides the expansion

$$\tau_{\mathfrak{a}}(x) \underset{\mathfrak{a}\to\infty}{=} \tau_0 x + \tau_1 x^{\nu_1} \mathfrak{a}^{l(\nu_1-1)} + o(\mathfrak{a}^{l(\nu_1-1)}).$$

$\square$

2.2 Relaxed case

Here we relax Assumption (5) and look if the asymptotic behavior of λ_α and $\Lambda_{\mathfrak{a}}$ obtained in Theorem 1 remain true. The case we are the most interested in is the case when the limits are zero (see the applications at Section 3): is the condition $\lim\limits_{x\to L} \beta(x) = 0$ (resp. $\lim\limits_{x\to \frac{1}{L}} \dfrac{\tau(x)}{x} = 0$) necessary and sufficient to have $\lim\limits_{\alpha\to L} \lambda_\alpha = 0$ (resp. $\lim\limits_{\mathfrak{a}\to L} \Lambda_{\mathfrak{a}} = 0$)? The following theorem gives partial results in the direction of a positive answer to this question. The assumptions required are weaker, but the results also are less strong: we obtain asymptotic behavior for the eigenvalue but cannot say anything yet on the eigenvector behavior.

Theorem 3. *Let us suppose that all assumptions of Theorem 2 are verified except Assumption* (5)*.*

1. *If $\tau(x) \underset{x\to 0}{=} o(x^\nu)$, $\beta \underset{x\to 0}{=} O(x^\gamma)$ and $\beta(x)^{-1} \underset{x\to 0}{=} O(x^{-\gamma})$ with $\gamma + 1 - \nu > 0$, we have that*

$$\text{if } \gamma > 0, \text{ then } \lim_{\alpha\to 0} \lambda_\alpha = 0, \text{ and more precisely } \quad \lambda_\alpha \underset{\alpha\to 0}{=} o(\alpha^{\frac{\gamma}{1+\gamma-\nu}}),$$

$$\text{if } \nu \ge 1, \text{ then } \lim_{\mathfrak{a}\to\infty} \Lambda_{\mathfrak{a}} = 0, \text{ and more precisely } \quad \Lambda_{\mathfrak{a}} \underset{\mathfrak{a}\to\infty}{=} o(\mathfrak{a}^{\frac{1-\nu}{1+\gamma-\nu}}).$$

2. *If $\beta(x) \underset{x\to\infty}{=} o(x^\gamma)$ and $\tau(x)^{-1} \underset{x\to\infty}{=} O(x^{-\nu})$ with $\gamma + 1 - \nu > 0$ and $\gamma \le 0$ (so that $\nu < 1$), we have that*

$$\lim_{\alpha\to\infty} \lambda_\alpha = \lim_{\mathfrak{a}\to 0} \Lambda_{\mathfrak{a}} = 0, \text{ and more precisely } \quad \lambda_\alpha \underset{\alpha\to+\infty}{=} o(\alpha^{\frac{\gamma}{1+\gamma-\nu}}),\ \Lambda_{\mathfrak{a}} \underset{\mathfrak{a}\to 0}{=} o(\mathfrak{a}^{\frac{1-\nu}{1+\gamma-\nu}}).$$

Remark. In the second assertion of this theorem, we notice that Assumption (28) means $\frac{\tau(x)}{x} \underset{x\to\infty}{=} o(\beta(x))$, so the condition $\beta(x) = o(x^\gamma)$ with $\gamma \le 0$ imposes $\lim_{x\to\infty} \frac{\tau(x)}{x} = 0$.

Proof of Theorem 3.1. We perform the dilation defined by (6): $v_\alpha(x) = \alpha^k \mathcal{U}_\alpha(\alpha^k x)$ with $k = \frac{1}{1+\gamma-\nu}$. Thanks to the assumption $\beta(x)^{-1} \underset{x\to 0}{=} O(x^{-\gamma})$ and $\tau = O(x^\nu)$, the conclusions of Lemma 2 and Lemma 3 still hold true. Hence we have the following bound (see the first estimate in the proof of Theorem 2)

$$\int x^r \beta_\alpha(x) v_\alpha(x)\, dx \le \frac{r \sup_{(0,A_{\frac{r}{\omega}})} (x^{r-1}\tau_\alpha)}{1 - 2c - \omega}$$

where $\tau_\alpha(x)$ and β_α are defined by (14), and the right hand side is bounded uniformly in α for $r \geq \max(2, 1+r_0, 1-\nu)$. Let $\varepsilon > 0$ and write

$$\begin{aligned}
\alpha^{-\frac{\gamma}{1+\gamma-\nu}}\lambda_\alpha = \theta_\alpha = \int \beta_\alpha v_\alpha \quad &\leq \quad \int_0^\varepsilon \beta_\alpha(x) v_\alpha(x)\,dx + \varepsilon^{-r}\int_0^\infty x^r \beta_\alpha(x) v_\alpha(x)\,dx \\
&\leq \quad \sup_{(0,\varepsilon)} \beta_\alpha + \varepsilon^{-r} \frac{r \sup_{(0,A_{\frac{r}{\omega}})}(x^{r-1}\tau_\alpha)}{1-2c-\omega}
\end{aligned}$$

Thus, since $\sup\limits_{(0,A_{\frac{r}{\omega}})} x^{r_0}\tau_\alpha \underset{\alpha\to 0}{\longrightarrow} 0$, we obtain

$$\limsup_{\alpha\to 0} \theta_\alpha \leq \limsup_{\alpha\to 0} \sup_{(0,\varepsilon)} \beta_\alpha \leq C\varepsilon^\gamma.$$

This is true for all $\varepsilon > 0$ so the assertion 1 of Theorem 3 is proved (the same proof works with the fragmentation parameter $\mathfrak{a}$).

□

Proof of Theorem 3.2. We perform the dilation defined by (6) $v_\alpha(x) = \alpha^k \mathcal{U}_\alpha(\alpha^k x)$ with $k = \frac{1}{1+\gamma-\nu}$. Thanks to Assumption (35) for $L = +\infty$, we still have the conclusion of Lemma 4 and it is sufficient to bound $\tau_\alpha v_\alpha$ on $(0,\varepsilon)$ for $\varepsilon > 0$. We refer to the proof of Theorem 2 in Section 1.3, second estimate, and write:

$$\begin{aligned}
\tau_\alpha(x) v_\alpha(x) \quad &\leq \quad 2\sup_{(0,\varepsilon)}\{\tau_\alpha v_\alpha\} \int_0^\varepsilon \frac{\beta_\alpha(y)}{\tau_\alpha(y)}\,dy + 2\int_\varepsilon^\infty \beta_\alpha(y) v_\alpha(y)\,dy \\
&\leq \quad 2\rho \sup_{(0,\varepsilon)}\{\tau_\alpha v_\alpha\} + 2\sup_{(\varepsilon,+\infty)} \beta_\alpha.
\end{aligned}$$

Taking for instance ε small enough so that $\rho \leq \frac{1}{4}$ in this estimate, and α large enough so that $\sup_{(\varepsilon,+\infty)} \beta_\alpha \leq C$, we obtain the boundedness of $\tau_\alpha v_\alpha$ on $(0,\varepsilon_0)$. Then we write for $\varepsilon > 0$,

$$\begin{aligned}
\alpha^{-\frac{\gamma}{1+\gamma-\nu}}\lambda_\alpha = \theta_\alpha \quad &= \quad \int \beta_\alpha v_\alpha \\
&\leq \quad \underbrace{\sup_{(0,\varepsilon)} \tau_\alpha v_\alpha}_{\leq C} \underbrace{\int_0^\varepsilon \frac{\beta_\alpha}{\tau_\alpha}}_{\underset{\varepsilon\to 0}{\longrightarrow} 0} + \underbrace{\sup_{(\varepsilon,\infty)} \beta_\alpha}_{\underset{\alpha\to\infty}{\longrightarrow} 0}.
\end{aligned}$$

The latter estimate is a consequence of the assumption $\beta(x) \underset{x\to\infty}{=} o(x^\gamma)$.

We do the same computations for the parameter $\mathfrak{a}$.

□

2.3 Generalized case

In this section, we completely free ourselves of Assumption (5) and give some results about the asymptotic behavior of the first eigenvalues for general coefficients. The technics used are completely different than the self-similar ones. But the results still give comparisons between λ_α and $\beta(x)$, and between $\Lambda_{\mathfrak{a}}$ and $\frac{\tau(x)}{x}$.

Theorem 4. *1.* **Polymerization dependency.**

$$\text{If } \beta \in L^\infty_{loc}(\mathbb{R}_+^*) \text{ and } \limsup_{x\to\infty} \frac{\tau(x)}{x} < \infty, \quad \text{then } \limsup_{\alpha\to 0}\lambda_\alpha \le \limsup_{x\to 0}\beta(x). \tag{51}$$

$$\text{If } \frac{1}{\tau} \in L^1_0 := \{f,\ \exists a>0,\ f\in L^1(0,a)\}, \quad \text{then } \liminf_{\alpha\to\infty}\lambda_\alpha \ge \liminf_{x\to\infty}\beta(x). \tag{52}$$

2. **Fragmentation dependency.**

$$\text{If } \beta \in L^\infty_{loc}(\mathbb{R}_+), \text{ then there exists } r>0 \quad \text{such that} \quad \limsup_{\mathfrak{a}\to 0}\Lambda_{\mathfrak{a}} \le r \limsup_{x\to\infty}\frac{\tau(x)}{x}. \tag{53}$$

$$\text{If } \liminf_{x\to\infty}\beta(x) > 0, \text{ and if } \frac{1}{\tau}\in L^1_0, \qquad \text{then} \qquad \lim_{\mathfrak{a}\to\infty}\Lambda_{\mathfrak{a}} = +\infty. \tag{54}$$

We first state a lemma which links the moments of the eigenvector, the eigenvalue and the polymerization rate.

Lemma 5. *Let $(\mathcal{U},\lambda)$ solution to the eigenproblem* (2)*. For any $r\ge 0$ we have*

$$\int x^r\mathcal{U}(x)\,dx \le \frac{r}{\lambda}\int x^{r-1}\tau(x)\mathcal{U}(x)\,dx. \tag{55}$$

Proof. Integrating Equation (2) against x^r we find

$$\begin{aligned}
-\int rx^{r-1}\tau(x)\mathcal{U}(x)\,dx &+ \lambda\int x^r\mathcal{U}(x)\,dx + \int x^r\beta(x)\mathcal{U}(x)\,dx \\
&= 2\int x^r\int_0^x \beta(y)\kappa(x,y)\mathcal{U}(y)\,dydx \\
&= 2\int \beta(y)\mathcal{U}(y)\int_0^y x^r\kappa(x,y)\,dxdy \\
&\le 2\int \beta(y)\mathcal{U}(y)y^{r-1}\int_0^y x\kappa(x,y)\,dxdy \\
&= \int y^r\beta(y)\mathcal{U}(y)\,dy.
\end{aligned}$$

□

Proof of Theorem 4.1.(51). We only have to consider the case $\limsup_{x\to 0}\beta(x) < \infty$. In this case, $\beta\in L^\infty_{loc}(\mathbb{R}_+)$ since it is assumed that $\beta\in L^\infty_{loc}(\mathbb{R}_+^*)$. So for $\varepsilon>0$, we can define $\overline{\beta_\varepsilon} := \sup_{(0,\varepsilon)}\beta(x) < \infty$ and, thanks to Assumption (24), there exist positive constants C_ε and r such that $\beta(x)\le Cx^r$ for almost every $x\ge\varepsilon$. As a consequence, we have by integration of Equation (3)

$$\lambda_\alpha = \int \beta(x)\mathcal{U}_\alpha(x)\,dx \le \overline{\beta_\varepsilon} + C\int x^r\mathcal{U}_\alpha(x)\,dx.$$

We can consider that $r\ge r_0+1$, with r_0 defined in Assumption (24), and thus Lemma 5 and Assumption $\limsup_{x\to\infty}\frac{\tau(x)}{x} < \infty$ give

$$\int x^r\mathcal{U}_\alpha(x)\,dx \le \frac{\alpha r}{\lambda_\alpha}\int x^{r-1}\tau(x)\mathcal{U}_\alpha(x)\,dx \le \frac{\alpha}{\lambda_\alpha}C\left(1+\int x^r\mathcal{U}_\alpha(x)\,dx\right)$$

for a new constant C. Combining these two inequalities we obtain

$$\lambda_\alpha \le \alpha C \left(1 + \frac{1}{\int x^r \mathcal{U}_\alpha(x)\,dx}\right) \le \alpha C \left(1 + \frac{1}{\lambda_\alpha - \overline{\beta_\varepsilon}}\right).$$

Then, either $\lambda_\alpha \le \overline{\beta_\varepsilon}$, or we obtain by multiplication by $\lambda_\alpha - \overline{\beta_\varepsilon} > 0$ that

$$\lambda_\alpha^2 - (\overline{\beta_\varepsilon} + \alpha C)\lambda_\alpha - (1 - \overline{\beta_\varepsilon})\alpha C \le 0,$$

and so

$$\lambda_\alpha \le \frac{1}{2}\left(\overline{\beta_\varepsilon} + \alpha C + \sqrt{\overline{\beta_\varepsilon}^2 + 4\alpha C + \alpha^2 C^2}\right).$$

Finally we have

$$\limsup_{\alpha\to 0} \lambda_\alpha \le \overline{\beta_\varepsilon}$$

and this is true for any $\varepsilon > 0$, so

$$\limsup_{\alpha\to 0} \lambda_\alpha \le \limsup_{x\to 0} \beta(x).$$

□

Proof of Theorem 4.1.(52). Let $A > 0$ and define $\underline{\beta_A} := \inf_{(A,\infty)} \beta$. Since $\frac{1}{\tau} \in L^1_0$ and thanks to Assumption (25) we can define $I_A := \int_0^A \frac{dx}{\tau(x)} < \infty$. Then we have by integration of Equation (3)

$$\begin{aligned}
\lambda_\alpha &= \int \beta(y)\mathcal{U}_\alpha(y)\,dy \\
&\ge \underline{\beta_A} \int_A^\infty \mathcal{U}_\alpha(y)\,dy \\
&= \underline{\beta_A}\Big(1 - \int_0^A \mathcal{U}_\alpha(y)\,dy\Big).
\end{aligned}$$

We know, by integration of Equation (3) between 0 and x, that for all $x > 0$, $\alpha\tau(x)\mathcal{U}_\alpha(x) \le 2\lambda_\alpha$. Thus we obtain

$$\lambda_\alpha \ge \underline{\beta_A}\Big(1 - \int_0^A 2\lambda_\alpha \frac{dy}{\alpha\tau(y)}\Big)$$

which gives

$$\lambda_\alpha \ge \frac{\underline{\beta_A}}{1 + \frac{2}{\alpha}\underline{\beta_A} I}$$

and

$$\liminf_{\alpha\to\infty} \lambda_\alpha \ge \underline{\beta_A}.$$

Finally, since the previous inequality is true for all $A > 0$, we find

$$\liminf_{\alpha\to\infty} \lambda_\alpha \ge \liminf_{x\to+\infty} \beta(x).$$

□

Proof of Theorem 4.2.(53). The fact that $\beta \in L^\infty_{loc}(\mathbb{R}_+)$ associated to Assumption (24) ensures the existence of two positive constants C and r such that for almost every $x \geq 0$, $\beta(x) \leq C(1+x^r)$. So, integrating Equation (4), we have

$$\Lambda_\mathfrak{a} = \mathfrak{a}\int \beta(x)\mathcal{V}_\mathfrak{a}(x)\,dx \leq \mathfrak{a}C\left(1+\int_0^\infty x^r\mathcal{V}_\mathfrak{a}(x)\,dx\right).$$

To prove (53), we only have to consider the case $\limsup_{x\to\infty}\frac{\tau(x)}{x} < \infty$. So, for any $A>0$, we can define $\overline{\tau_A} := \sup_{x>A}\frac{\tau(x)}{x} < \infty$ and we have, thanks to Lemma 5 and considering $r \geq r_0+1$ where r_0 is defined in Assumption (24),

$$\int x^r\mathcal{V}_\mathfrak{a}(x)\,dx \leq \frac{r}{\Lambda_\mathfrak{a}}\int x^{r-1}\tau(x)\mathcal{V}_\mathfrak{a}(x)\,dx \leq \frac{r}{\Lambda_\mathfrak{a}}\left(C+\overline{\tau_A}\int x^r\mathcal{V}_\mathfrak{a}(x)\,dx\right).$$

Combining the two inequalities we obtain

$$\Lambda_\mathfrak{a} \leq r\left(\overline{\tau_A}+\frac{C}{\int x^r\mathcal{V}_\mathfrak{a}(x)\,dx}\right) \leq r\left(\overline{\tau_A}+\frac{\mathfrak{a}C}{\Lambda_\mathfrak{a}-\mathfrak{a}C}\right).$$

Then, either $\Lambda_\mathfrak{a} \leq \mathfrak{a}C$, or we obtain by multiplication by $\Lambda_\mathfrak{a}-\mathfrak{a}C>0$ that

$$\Lambda_\mathfrak{a}^2-(r\overline{\tau_A}+\mathfrak{a}C)\Lambda_\mathfrak{a}-r(1-\overline{\tau_A})\mathfrak{a}C \leq 0,$$

and so

$$\Lambda_\mathfrak{a} \leq \frac{1}{2}\left(r\overline{\tau_A}+\mathfrak{a}C+\sqrt{(r\overline{\tau_A})^2+4r\mathfrak{a}C+\mathfrak{a}^2C^2}\right).$$

In the two cases we obtain that

$$\limsup_{\mathfrak{a}\to 0}\Lambda_\mathfrak{a} \leq r\overline{\tau_A},$$

and, doing $A\to\infty$, we conclude

$$\limsup_{\mathfrak{a}\to 0}\Lambda_\mathfrak{a} \leq r\limsup_{x\to\infty}\frac{\tau(x)}{x}.$$

□

Proof of Theorem 4.(54). Let $\varepsilon>0$. Since $\liminf_{x\to\infty}\beta(x)>0$, we have thanks to Assumption (25) that $\underline{\beta_\varepsilon} := \inf_{(\varepsilon,\infty)}\beta > 0$. Since $\frac{1}{\tau}\in L^1_0$, we have thanks to Assumption (25) that $I_\varepsilon := \int_0^\varepsilon\frac{dx}{\tau(x)} < \infty$ and that $\lim_{\varepsilon\to 0} I_\varepsilon = 0$.
By integration of equation (4), we find

$$\begin{aligned}\Lambda_\mathfrak{a} &= \mathfrak{a}\int\beta(y)\mathcal{V}_\mathfrak{a}(y)\,dy\\ &\geq \mathfrak{a}\underline{\beta_\varepsilon}\int_\varepsilon^\infty\mathcal{V}_\mathfrak{a}(y)\,dy\\ &= \mathfrak{a}\underline{\beta_\varepsilon}\Big(1-\int_0^\varepsilon\mathcal{V}_\mathfrak{a}(y)\,dy\Big).\end{aligned}$$

We know, as previously by integration between 0 and x, that for all $x>0$, $\tau(x)\mathcal{V}_\mathfrak{a}(x) \leq 2\Lambda_\mathfrak{a}$. Thus we obtain

$$\Lambda_\mathfrak{a} \geq \mathfrak{a}\underline{\beta_\varepsilon}\Big(1-\int_0^\varepsilon 2\Lambda_\mathfrak{a}\frac{dy}{\tau(y)}\Big)$$

which gives

$$\Lambda_{\mathfrak{a}} \geq \frac{\mathfrak{a}\underline{\beta_\varepsilon}}{1+2\mathfrak{a}\underline{\beta_\varepsilon} I_\varepsilon}.$$

Finally we have

$$\liminf_{\mathfrak{a}\to\infty} \Lambda_{\mathfrak{a}} \geq \frac{1}{2I_\varepsilon} \xrightarrow[\varepsilon\to 0]{} +\infty$$

and it ends the proof of Theorem 4.(54). □

3 Applications

Before giving applications, we remind a regularity result whose proof can be found in [28].

Lemma 6. *Under the assumptions of Section 1.2, the functions* $\alpha \mapsto \lambda_\alpha$ *and* $\mathfrak{a} \mapsto \Lambda_{\mathfrak{a}}$ *are well defined and differentiable on* $(0,\infty)$.

3.1 Numerical scheme based on Theorem 2

Let us first present the method we use to compute numerically the principal eigenvector λ without considering any dependency on parameters. Then we explain how the self-similar change of variable (6) and the convergence result of Theorem 2 can be used to compute the dependencies $\alpha \mapsto \lambda_\alpha$ and $\mathfrak{a} \mapsto \Lambda_{\mathfrak{a}}$, when parameters α and $\mathfrak{a}$ are very large or very small.

The method used to compute λ solution to Equation (2) is first to compute a numerical approximation of the first eigenvector $\mathcal{U}$, and then use the identity

$$\lambda = \int_0^\infty \beta(x)\mathcal{U}(x)\,dx.$$

The General Relative Entropy (GRE) introduced by [29, 30, 31] provides the long time asymptotic behavior of any solution to the fragmentation-drift equation (1). At sufficiently large times, these solutions look like $\mathcal{U}(x)e^{\lambda t}$ where $\mathcal{U}$ and λ are the eigenelements defined at (2). More precisely we have

$$\int_0^\infty |u(x,t)e^{-\lambda t} - \langle u(\cdot,t=0),\phi\rangle \mathcal{U}(x)|\phi(x)\,dx \xrightarrow[t\to\infty]{} 0,$$

where ϕ is the dual eigenvector of Equation (2) (see [16, 30] for more details) and $\langle u,\phi\rangle = \int_0^\infty u(x)\phi(x)\,dx$. It is even proved in [24, 6], under some assumptions on the coefficients, that this convergence occurs exponentially fast. We use this convergence to compute numerically the eigenvector $\mathcal{U}$. We consider, for $u_0 \in L^1(\mathbb{R}_+)$ an initial function satisfying $\int_0^\infty u_0(x)\,dx = 1$, the solution $u(x,t)$ to the fragmentation-drift equation (1). Since we do not know yet the value of λ, we define the normalized function

$$\tilde{u}(x,t) := \frac{u(x,t)}{\int_0^\infty u(x,t)\,dx}.$$

We can easily check that $\tilde{u}$ satisfies the equation

$$\partial_t \tilde{u}(x,t) + \partial_x\left(\tau(x)\tilde{u}(x,t)\right) + \left(\int_0^\infty \beta(y)\tilde{u}(y,t)\,dy\right)\tilde{u}(x,t) + \beta(x)\tilde{u}(x,t) = 2\int_x^\infty \beta(y)\kappa(x,y)\tilde{u}(y,t)\,dy, \tag{56}$$

with the boundary condition $\tau(0)\tilde{u}(0,t) = 0$, and that the convergence occurs

$$\int_0^\infty |\tilde{u}(x,t) - \mathcal{U}(x)|\phi(x)\,dx \xrightarrow[t\to\infty]{} 0. \tag{57}$$

The scheme used to compute $\mathcal{U}$ is based on the resolution of Equation (56) for large times and the use of (57) for the stop condition.

Numerically, Equation (56) is solved on a truncated domain $[0,R]$ so the integration bounds have to be changed and we obtain, for $x \in [0,R]$,

$$\partial_t\tilde{u}(x,t) + \partial_x\left(\tau(x)\tilde{u}(x,t)\right) + \left(\int_0^R \beta(y)\tilde{u}(y,t)\,dy\right)\tilde{u}(x,t) + \beta(x)\tilde{u}(x,t) = 2\int_x^R \beta(y)\kappa(x,y)\tilde{u}(y,t)\,dy. \tag{58}$$

What we loose when we solve this truncated equation are the integral terms $\int_R^\infty \beta(x)\tilde{u}(x,t)\,dx$ and $\int_R^\infty \beta(y)\kappa(x,y)\tilde{u}(y,t)\,dy$, and the outgoing flux $\tau(R)\tilde{u}(R,t)$ at the boundary $x = R$. To be as close as possible to the non-truncated solution, we have to choose R large enough so that these quantities are small enough. It is proved in [16] that $\beta(x)\mathcal{U}(x)$ and $\tau(x)\mathcal{U}(x)$ are fast decreasing when $x \to +\infty$. The value of R has to be adapted to have, when $\tilde{u}$ is close to the equilibrium $\mathcal{U}$, values of $\tau(x)\tilde{u}(x,t)$ and $\beta(x)\tilde{u}(x,t)$ smaller than a fixed parameter ϵ for x close to R. Parameter ϵ is expected to be very small, it is also used for the stop condition (60).

We assume that $[0,R]$ is divided into N uniform cells and we denote $x_i = i\Delta x$ for $0 \le i \le N$ with $\Delta x = \frac{R}{N}$. The time is discretized with the time step Δt and we denote $t^n = n\Delta t$ for $n \in \mathbb{N}$. We adopt the finite difference point of view, namely we compute an approximation $\tilde{u}_i^n$ of $\tilde{u}(x_i, t^n)$. It remains to explain how we go from the time t^n to the time t^{n+1}. To enforce that $\sum_{i=1}^N \tilde{u}_i^n = 1$ at each time step, we split the evolution into two steps. First we compute, from $(\tilde{u}_i^n)_{1\le i\le N}$, a vector $(u_i^{n+1})_{1\le i\le N}$ which is obtain with the formula

$$\frac{u_i^{n+1} - \tilde{u}_i^n}{\Delta t} = -\frac{\tau_i\tilde{u}_i^{n+1} - \tau_{i-1}\tilde{u}_{i-1}^n}{\Delta x} - \beta_i^{n+1} + 2\Delta x\sum_{j=1}^N \beta_j\kappa_{i,j}\tilde{u}_j^n, \tag{59}$$

where $\beta_i = \beta(x_i)$, $\tau_i = \tau(x_i)$ and $\kappa_{i,j} = \kappa(x_i,x_j)$. This is a semi-implicit Euler discretization of the growth-fragmentation equation (1). We choose this scheme to ensure the stability without any CFL condition, since the scheme is positive. Then we set

$$\tilde{u}_i^{n+1} := \frac{u_i^{n+1}}{\Delta x\sum_{j=1}^N u_j^{n+1}}$$

and we have that the discrete integral of $(\tilde{u}_i^{n+1})_{1\le i\le N}$ satisfies $\Delta x\sum_{i=1}^N \tilde{u}_i^{n+1} = \Delta x\sum_{i=1}^N \tilde{u}_i^n = 1$. Inspired from the L^1 convergence (57), we end the algorithm when

$$\frac{\Delta x}{\Delta t}\sum_{i=1}^N |\tilde{u}_i^n - \tilde{u}_i^{n-1}| < \epsilon \tag{60}$$

where $\epsilon \ll \Delta x$. Then we have

$$\lambda \simeq \Delta x\sum_{i=1}^N \beta_i\tilde{u}_i^n.$$

The semi-implicit scheme (59) is efficient to avoid oscillations on the numerical solution but it is not conservative. It has to be avoided if we want to solve Equation (1) for any time. Here we are only interested in the steady state of Equation (56), so the non conservativity does not matter because the steady state is the same for an implicit or an explicit scheme.

Now we want to compute λ_α and $\Lambda_{\mathfrak{a}}$ for a large range of α and $\mathfrak{a}$. According to the discussion in introduction, the eigenvectors $\mathcal{U}_\alpha$ and $\mathcal{V}_{\mathfrak{a}}$ are concentrated at the origin for α small or $\mathfrak{a}$ large and, conversely, it is spread for α large or $\mathfrak{a}$ small. Then, to avoid an adaptation of the truncature parameter R or an adaptation of the discretization size step Δx when α and $\mathfrak{a}$ vary, we compute θ_α defined in Equation (18). To this end, we have to compute the dilated eigenvector v_α defined in (6) which converges to a fixed profile v_∞ when $\alpha \to L$, as stated in Theorem 2. This convergence ensures that the vector v_α does neither disperse nor concentrate too much when α varies, and so we can find a truncature and a size step which suit for any $\alpha \to L$. It remains to distinguish $L = 0$ from $L = +\infty$ by dividing $(0, +\infty)$ into two sets: for instance $(0, 1]$ and $(1, +\infty)$. For $0 < \alpha < 1$, we use the dilation coefficient k associated to ν and γ such that $\tau(x) \underset{x\to 0}{\sim} x^\nu$ and $\beta(x) \underset{x\to 0}{\sim} x^\gamma$. For $\alpha > 1$ we do the dilation associated to ν and γ such that $\tau(x) \underset{x\to\infty}{\sim} x^\nu$ and $\beta(x) \underset{x\to\infty}{\sim} x^\gamma$. Finally, we use Equation (20) in Lemma 1 to recover λ_α or $\Lambda_{\mathfrak{a}}$ from the numerical value of θ_α.

All the figures of the paper are obtained with this numerical scheme.

3.2 Steady States of the Prion Equation

To model polymerization processes, Equation (1) can be coupled to an ODE which leads the evolution of the quantity of monomers. It is the case in the so-called "prion equation" (see [22, 34])

$$\begin{cases} \dfrac{dV(t)}{dt} &= \xi - V(t)\left[\delta + \displaystyle\int_0^\infty \tau(x)u(x,t)\,dx\right], \\ \dfrac{\partial}{\partial t}u(x,t) &= -V(t)\dfrac{\partial}{\partial x}\big(\tau(x)u(x,t)\big) - [\beta(x) + \mu(x)]u(x,t) + 2\displaystyle\int_x^\infty \beta(y)\kappa(x,y)\,u(y,t)\,dy, \\ u(0,t) &= 0, \end{cases} \tag{61}$$

where the quantity of monomers is denoted by $V(t)$. In this model, the monomers are prion proteins, produced and degraded by the cells with rates ξ and δ, and attached to polymers of size x with respect to the rate $\tau(x)$. The polymers are fibrils of misfolded pathogenic proteins, which have the ability to transconform normal proteins (monomers) into abnormal ones by a polymerization process not yet very well understood. The size distribution of polymers $u(x, t)$ is solution to the growth-fragmentation equation (1) in which $V(t)$ is added as a multiplier for the polymerization rate. A degradation rate $\mu(x)$ is also considered for the polymers. For the sake of simplicity, this rate is assumed to be size-independent in the following study ($\mu(x) \equiv \mu_0$).

Equation (61) models the proliferation of prion disease. An individual is said to be infected by prion disease when polymers of misfolded proteins are present, namely when $u(\cdot, t) \not\equiv 0$ at the present time t.

The coupling between $V(t)$ and $u(t, x)$ appears in the equation for u as a modulation of the polymerization rate. One sees immediately the link with the eigenproblem (3) satisfied by $\mathcal{U}_\alpha$. Indeed, $\mathcal{U}_\alpha$ is the principal eigenvector linked to the linearization of the prion equation around a given monomer quantity $V = \alpha$. Investigating the dependency of the fitness λ_V with respect to the polymerization and fragmentation coefficients is a first step towards a better understanding of the disease propagation. Indeed it has been reported that the course of prion infection in the brain follows heterogeneous patterns. It has been postulated that the neuropathology of prion infection could be related to different kinetics in different compartments of the brain [12].

Modelling the propagation of prion in the brain requires a good understanding of possible dynamics (*e.g.* monostable, bistable etc). Such a study can be done through the dependency of the first eigenvalue on parameters. In [9, 8], it is shown that, under some conditions, the coexistence of two stable steady states can happen (one endemic and one disease-free). A steady state $(V_\infty, u_\infty(x))$ is a solution to

$$\begin{cases} 0 &= \xi - V_\infty \left[\delta + \int_0^\infty \tau(x) u_\infty(x)\, dx \right], \\ \mu_0 u_\infty(x) &= -V_\infty \dfrac{\partial}{\partial x}\big(\tau(x) u_\infty(x)\big) - \beta(x) u_\infty(x) + 2 \displaystyle\int_x^\infty \beta(y)\kappa(x,y)\, u_\infty(y)\, dy, \\ u_\infty(0) &= 0. \end{cases} \tag{62}$$

The disease-free steady state corresponds to the solution without any polymer $\left(\overline{V} = \frac{\xi}{\delta}, \overline{u} \equiv 0\right)$.

Other steady states can exist and are called endemic or disease steady states. They are solution to System (62) with $V_\infty > 0$ and $u_\infty \not\equiv 0$ nonnegative. To know if such disease steady states exist, we recall briefly here the method of [8, 9]. A positive steady state u_∞ can be seen as an eigenvector solution of (3) with $\alpha = V_\infty$ such that

$$\lambda_\alpha = \lambda_{V_\infty} = \mu_0. \tag{63}$$

It shows the crucial importance of a study of the map $V \mapsto \lambda_V$. Any value V_∞ solution to (63) provides a size distribution of polymers

$$u_\infty(x) = \varrho_\infty \mathcal{U}_{V_\infty}(x).$$

The quantity of polymers ϱ_∞ is then prescribed by the equation on monomers and has to satisfy the relation

$$\varrho_\infty = \frac{\xi V_\infty^{-1} - \delta}{V_\infty \int \tau(x) \mathcal{U}_{V_\infty}(x)\, dx}.$$

The quantity of polymers has to be positive, what is equivalent to the condition

$$V_\infty < \frac{\xi}{\delta} = \overline{V}.$$

Finally, the disease steady states correspond exactly to the zeros of the map $V \mapsto \lambda_V - \mu_0$ in the interval $(0, \overline{V})$. Thanks to the different results of Sections 1 and 2, we know that this map is not necessarily monotonic, as assumed in [9]. Thus, by continuity of the dependency of λ on V (see Lemma 6), there can exist several disease steady states for μ_0 well chosen and $\overline{V} = \frac{\xi}{\delta}$ large enough. This point is illustrated on the example below, for which there exist two disease steady states.

We can investigate the stability of the disease-free steady state through the results obtained in [8, 9]. For this, we introduce the dual eigenvector $\overline{\varphi}$ of the growth-fragmentation operator with transport term $\overline{V}$

$$\begin{cases} -\overline{V}\tau(x)\dfrac{\partial}{\partial x}(\overline{\varphi}(x)) + (\beta(x) + \lambda)\overline{\varphi}(x) = 2\beta(x) \displaystyle\int_0^x \kappa(y,x)\overline{\varphi}(y) dy, \qquad x \geqslant 0, \\ \overline{\varphi}(x) \geq 0, \qquad \int_0^\infty \overline{\varphi}(x) \mathcal{U}_{\overline{V}}(x) dx = 1. \end{cases} \tag{64}$$

We assume that we are in a case when there exist two constants K_1 and K_2 such that

$$\left|\tau(x)\frac{\partial}{\partial x}\overline{\varphi}(x)\right| \leq K_1\overline{\varphi}(x), \quad \text{and} \quad \tau(x) \leq K_2\overline{\varphi}(x). \tag{65}$$

This assumption generally holds true when $\frac{\tau(x)}{x}$ is bounded because $\overline{\varphi}$ grows linearly at infinity according to general properties proved in [16, 27, 31, 32]. Then we can reformulate the theorems of [8, 9].

Theorem [9] (Local stability)**.** *Suppose that assumption* (65) *holds true and that* $\lambda_{\overline{V}} < \mu_0$. *Then the steady state* $(\overline{V}, 0)$ *is locally non-linearly stable.*

Theorem [8] (Persistence)**.** *Suppose that assumption* (65) *holds true,* $V(0) \leq \overline{V}$, $\int_0^\infty (1+x)u(t,x)\,dx$ *is uniformly bounded, and that* $\lambda_{\overline{V}} > \mu_0$. *Then the system remains away from the steady state* $(\overline{V}, 0)$. *More precisely we have:*

$$\liminf_{t\to\infty} \int_0^\infty \overline{\varphi}(x)u(x,t)\,dx > 0.$$

Example. Let us consider the same coefficients as in Figure 2(a). We can choose μ_0 small enough to ensure the existence of two values $V_1 < V_2$ such that $\lambda_{V_1} = \lambda_{V_2} = \mu_0$. As a consequence, we know thanks to the previous study that there exists no disease steady state if $\overline{V} < V_1$, one if $V_1 < \overline{V} < V_2$, and two if $\overline{V} > V_2$. Concerning the stability of the disease-free steady state, we first notice that the fragmentation rate $\beta(x)$ satisfies the assumption $\beta(x) \leq A + Bx$ which is sufficient to have that $\int_0^\infty (1+x)u(t,x)\,dx$ is uniformly bounded (see [8] Theorem 2.1). Thus we can apply the previous theorems and we have that $(\overline{V}, 0)$ is stable if $\overline{V} < V_1$, unstable if $V_1 < \overline{V} < V_2$, and recovers its (local) stability if $\overline{V} > V_2$. In Figure 3, the graph of the negative fitness $V \mapsto \mu_0 - \lambda_V$ is plotted (because the quantity of polymers influences the evolution of $V(t)$ with a negative contribution) and the zones of stability and unstability for $\overline{V}$ are pointed out. The non intuitive conclusion is that an increase of the production rate ξ or a decrease of the death rate δ can stabilize the disease-free steady state. What happens in this situation is that the largest polymers are the most stable since $\lim_{x\to\infty}\beta(x) = 0$ (this situation is biologically relevant, see for instance [35]). When the quantity of polymers is large, the polymerization is strong and it forms such long stable polymers. Because they do not break easily, their number does not increase very fast, *i.e.* the fitness of the polymerization-fragmentation equation is small. But the degradation term is assumed to be size-independent, and then the fitness λ_V becomes smaller than μ_0 for V large enough. This phenomenon stabilizes the disease-free steady state because, when polymers are injected in a cell, they tend to disappear immediately since $\lambda_{\overline{V}} < \mu_0$.

Concerning the stability of the disease steady states, the study is much more complicated. Nevertheless, we can imagine that V_1 is stable and V_2 unstable. This postulate is based on Figure 3 and on the results obtained in [22, 23] in a case when System (61) can be reduced to a system of ODEs.

3.3 Optimization of the PMCA protocole

Prion diseases, briefly described in Section 3.2 (see [25] for more details), are fatal, infectious and neurodegenerative diseases with a long incubation time. They include bovine spongiform encephalopathies in cattle, scrapie in sheep and Creutzfeldt-Jakob disease in human. It is then of importance to be able to diagnose infected individuals to avoid propagation of the disease in a population. But the dynamics of proliferation is slow and the amount of prion proteins is low at the begining of the disease. Moreover, these proteins are concentrated in vital organs like brain, and are present in minute quantities in

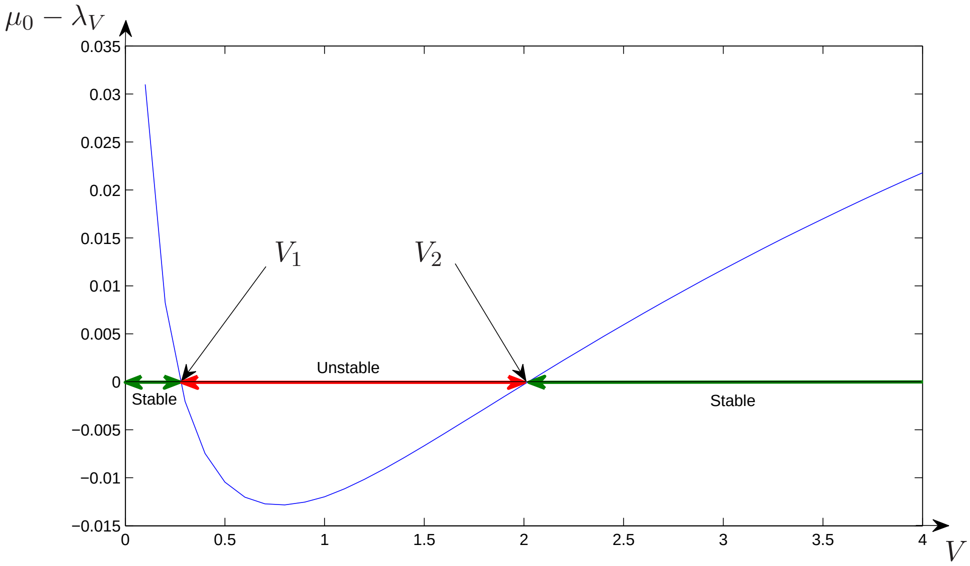


Figure 3: The negative fitness $V \mapsto \mu_0 - \lambda_V$ is plotted for the same coefficients as in Figure 2(a). The zeros V_1 and V_2 correspond to disease steady states and separate the areas of stability or unstability of the disease-free steady state.

tissues like blood. To be able to detect prions in these tissues, a solution is to amplify their quantity. A promising recent technique of amplification is the PMCA (Protein Misfolded Cyclic Amplification). Nevertheless, this protocole is not able to amplify prions for all the prion diseases from tissues with low infectivity. It remains to be improved and mathematical modelling and analysis can help to do so.

PMCA is an *in vitro* cyclic process that quickly amplifies very small quantities of prion proteins present in a sample. In this sample, the pathogenic proteins (polymers) are put in presence of a large quantity of normal proteins (monomers). Then the protocole consists in the alternance of two phases:

- a phase of incubation during which the sample is left to rest and the polymers can attach the monomers (increase of the size of polymers),

- a phase of sonication during which waves are sent on the sample in order to break the polymers into numerous smaller ones (increase of the number of polymers).

To model this process, we can use the growth-fragmentation equation (1) as in (61). The main difference is that the PMCA takes place *in vitro*, then there is no production of monomers. The monomers are in large excess to improve the polymerization, so we can assume that their concentration is constant during the PMCA. It remains to introduce the "sonication" in the equation. Because the sonication phase increases the fragmentation of polymers, a first modelling can be to add a time-dependent parameter $\mathfrak{a}(t)$ in front of the fragmentation parameter $\beta(x)$. Then the alternance incubation-sonication corresponds to a rectangular function $\mathfrak{a}(t)$ which is equal to 1 during the incubation time (since the sample is left to rest), and $\mathfrak{a}_{max}$ during the sonication pulse (where $\mathfrak{a}_{max}$ represents the maximal power of the sonicator). We obtain the model

$$\frac{\partial}{\partial t}u(x,t) = -V_0\frac{\partial}{\partial x}\big(\tau(x)u(x,t)\big) - \mathfrak{a}(t)\beta(x)u(x,t) + 2\mathfrak{a}(t)\int_x^\infty \beta(y)\kappa(x,y)\,u(y,t)\,dy, \tag{66}$$

where $u(x,t)$ still denotes the quantity of polymers of size x at time t.

With this model, the problem of PMCA improvement becomes an optimization mathematical problem: find a control $\mathfrak{a}(t)$ which maximizes the quantity $\int xu(T,x)\,dx$ (total mass of pathogenic proteins) at a given final time T. The answer to this problem is difficult. First we can wonder if the rectangular strategie used in the PMCA (alternance incubation-sonication) is the best one or if there exists a constant control which is better. This last question leads naturally to the problem of the fitness optimization for Equation (66) when $\mathfrak{a}(t) \equiv \mathfrak{a}$ is a time-independent parameter. Is $\mathfrak{a}_{max}$ the best constant to maximize $\Lambda_{\mathfrak{a}}$? Is there a compromise $\mathfrak{a}_{opt} \in (1, \mathfrak{a}_{max})$ to find? The answer depends on the coefficients τ and β as indicated by the different theorems of this paper. More precisely, Theorem 2 ensures that the situation when an optimum $\mathfrak{a}_{opt}$ exists between 1 and $\mathfrak{a}_{max}$ can happen, and an example is given below.

Example Let consider the same coefficients as in Figure 2(b) and suppose that the sonicator can multiply by 4 the fragmentation at its maximal power. Then in our model $\mathfrak{a}_{max} = 4$ and we can see on Figure 4 that the best strategy to maximize the fitness with a constant coefficient is not the maximal power but an intermediate $\mathfrak{a}_{opt}$ between 1 and $\mathfrak{a}_{max}$.

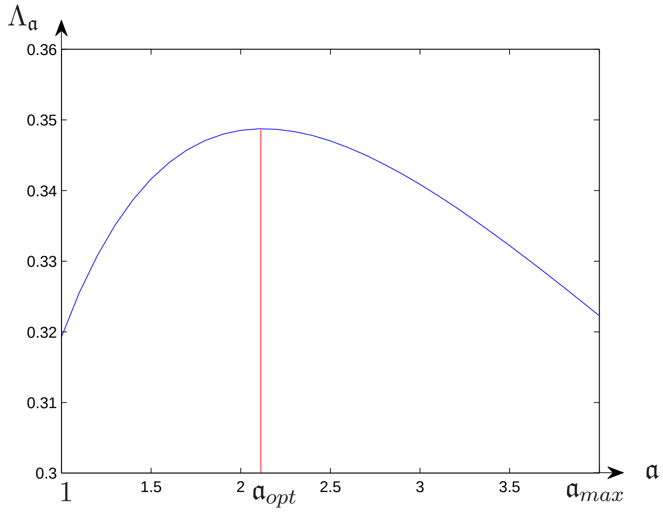


Figure 4: The fitness is plotted as a function of $\mathfrak{a}$ for the coefficients of Figure 2(b). There is a sonication value $\mathfrak{a}_{opt}$ in the interior of the window $[1, \mathfrak{a}_{max}]$ which maximizes this fitness.

In [7], the time dependent optimization problem is investigated on a discrete model. The study highlights the link between the optimal control $\mathfrak{a}(t)$ and the constant $\mathfrak{a}_{opt}$ which optimizes the fitness of the system.

3.4 Therapeutic optimization for a cell population

In the case when Problem (1) models the evolution of a size (or protein, or label, or parasite...)-structured cell population, τ represents the growth rate of the cells and β their division rate. It is of deep interest to know how a change on these rates can affect the Malthus parameter of the total population, see for instance [11, 10]. It is possible to act on the growth rate by changing the nutrient properties - the richer the environment, the faster the growth rate of the cells. We can model such an influence by Equation (3), and the question is then: how to make λ_α as large (if we want to speed up the population growth, for instance for tissue regeneration) or as small (in the case of cancerous cells) as possible ?

Plausible assumptions (see [14] for instance for the case of a size-structured population of E. Coli) for the growth of individual cells is that it is exponential up to a certain threshold, meaning that $\tau(x) = \tau x$ in a neighbourhood of zero, and tending to a constant (or possibly vanishing) around infinity, meaning that the cells reach some maximal size or protein-content, leading to $\tau \underset{x\to\infty}{\to} \tau_\infty < +\infty$.

Concerning the division rate β, it is most generally vanishing around zero, either of the form $\beta(x) \sim \beta x^\gamma$ with $\gamma > 1$ or with support $[b, \infty]$ with $b > 0$. It presents a maximum, and then decreases for large x - probably vanishing. Note that for τ as for β, very little is known about their precise behaviour for large sizes x, since such values are very rarely reached by cells in the real world.

These assumptions allow us to apply our results. Theorem 1 and Corollary 1 lead to vanishing Malthus parameter λ_α either for $\alpha \to 0$ or for $\alpha \to +\infty$. It means that against cancer, stressing the cells by diminishing nutrients can reveal efficient - this is very intuitive and it is known and used for tumors (by preventing them from vascularization for instance). What is less intuitive is that forcing them to grow too rapidly in size could also reveal an efficient strategy, as soon as it is established that the division rate decreases for large sizes (this last point could be studied by inverse problem techniques, see [33, 15, 14]). It rejoins the same ideas as for Prions, as said in Section 3.2.

On the opposite, in order to optimize tissue regeneration for instance, these results tend to prove that there exists an optimal value for α such that the Malthus parameter is maximum. This value can be established numerically (see Section 3.1 and [20]) as soon as the shape of the division rate is known, for instance by the use of the previously-quoted inverse problem techniques.

Conclusion

The first motivation of our research was to investigate the dependency of the dominant eigenvalue of Problem (1) upon the coefficients β and τ, since a first wrong intuition, based on simple cases, was that it should be monotonic (see [9, 8]). By the use of a self-similar change of variables, we have explored the asymptotic behaviour of the first eigenvalue when fragmentation dominates the transport term or *vice versa*. This lead us to counter-examples where the eigenvalue depends on the coefficients in a non-monotonic way ; moreover, these counter-examples are far from being exotic and seem perfectly plausible in many applications, as shown in Section 3. A still open problem is thus to find what would be necessary and sufficient assumptions on τ and β, or still better on the ratio $\frac{x\beta}{\tau}$, so that λ_α or $\Lambda_{\mathfrak{a}}$ be indeed monotonic with respect to α or $\mathfrak{a}$.

Concerning our assumptions, a first sight at the statement of Theorem 1 gives the feeling that only the behaviour of the fragmentation rate β plays a role in the asymptotic behaviour of λ_α, and only the ratio $\frac{\tau}{x}$ in the one of $\Lambda_{\mathfrak{a}}$. This seems puzzling and counter-intuitive. In reality, things are not that simple: to ensure well-posedness of the eigenvalue problems (3) and (4), Assumptions (27) and (28) strongly link τ with β, so that a dependency on β hides a dependency on τ and *vice versa.*

Moreover, the mathematical techniques used here (moment estimates, multiplication by polynomial weights) force us to restrict ourselves to the space $\mathcal{P}$ of functions of polynomial growth or decay. The questions of how relaxing these (already almost optimal, as shown in [16]) assumptions and how, if possible, express them in terms of pure comparison between τ, κ and β like in Assumptions (27) and (28) are still open.

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