On an evolution equation in a cell motility model

Matthew S. Mizuhara^{a,1,*}, Leonid Berlyand^{a,2}, Volodymyr Rybalko^{b,2}, Lei Zhang^{c,3}

^a*Department of Mathematics, The Pennsylvania State University, University Park, PA 16802, USA*

^b*Mathematical Division, B.Verkin Institute for Low Temperature Physics and Engineering of the National Academy of Sciences of Ukraine, 47 Lenin Ave., 61103 Kharkiv, Ukraine*

^c*Institute of Natural Sciences and Department of Mathematics, Shanghai Jiaotong University; Key Laboratory of Scientific and Engineering Computing (Shanghai Jiao Tong University), Ministry of Education, 800 Dongchuan Road, 200240, Shanghai*

Abstract

This paper deals with the evolution equation of a curve obtained as the sharp interface limit of a non-linear system of two reaction-diffusion PDEs. This system was introduced as a phase-field model of (crawling) motion of eukaryotic cells on a substrate. The key issue is the evolution of the cell membrane (interface curve) which involves shape change and net motion. This issue can be addressed both qualitatively and quantitatively by studying the evolution equation of the sharp interface limit for this system. However, this equation is non-linear and non-local and existence of solutions presents a significant analytical challenge. We establish existence of solutions for a wide class of initial data in the so-called subcritical regime. Existence is proved in a two step procedure. First, for smooth (H^2) initial data we use a regularization technique. Second, we consider non-smooth initial data that are more relevant from the application point of view. Here, uniform estimates on the time when solutions exist rely on a maximum principle type argument. We also explore the long time behavior of the model using both analytical and numerical tools. We prove the nonexistence of traveling wave solutions with nonzero velocity. Numerical experiments show that presence of non-linearity and asymmetry of the initial curve results in a net motion which distinguishes it from classical volume preserving curvature motion. This is done by developing an algorithm for efficient numerical resolution of the non-local term in the evolution equation.

*Corresponding author

Email addresses: msm344@psu.edu (Matthew S. Mizuhara), lrb2@psu.edu (Leonid Berlyand), vrybalko@ilt.kharkov.ua (Volodymyr Rybalko), lzhang2012@sjtu.edu.cn (Lei Zhang)

¹This author was supported by the Department of Defense (DoD) through the National Defense Science & Engineering Graduate Fellowship (NDSEG) Program. He also received partial support from NSF grants DMS-1106666 and DMS-1405769.

²This author was supported by NSF grants DMS-1106666 and DMS-1405769.

³The work of this author was supported by NSFC grant 11471214 and 1000 Plan for Young Scientists of China.

Preprint submitted to Elsevier

September 25, 2015

Keywords: sharp interface limit equation, non-linear and non-local evolution equation, eukaryotic cell motility

2010 MSC: 35Q92, 35K55, 65-04, 92B05

1. Introduction

In this work we study a geometric evolution equation arising from a model of crawling cell motility. This equation describes the evolution of a family of curves $\Gamma(t)$:

$$V(s, t) = \kappa(s, t) + \Phi(V(s, t)) - \frac{1}{|\Gamma(t)|} \int_{\Gamma} \kappa(s', t) + \Phi(V(s', t)) ds', \quad (1.1)$$

where s is the arc length parametrization of the curve $\Gamma(t)$, $V(s, t)$ is the normal velocity at location s of the curve $\Gamma(t)$ with respect to the inward normal, $|\Gamma(t)|$ is the length of $\Gamma(t)$, $\kappa(s, t)$ is the signed curvature of $\Gamma(t)$ at location s , and $\Phi(\cdot)$ is a known smooth, non-linear function.

The equation (1.1) is derived in [3] as the sharp interface limit of a phase field model for crawling cell motility. In [3] subcritical and supercritical intervals of a physical parameter β were identified so that the behavior of solutions of (1.1) in these intervals is drastically different. The parameter β represents strength of adhesion of the cell to the substrate and protrusion strength of actin filaments [34]. The main focus of this work is to show that if β (which enters the problem through Φ , see Remarks 1 and 2, and Corollary 1) is subcritical, then there exists a family of evolving curves $\Gamma(t)$ satisfying (1.1) with initial condition $\Gamma(0) = \Gamma_0$.

1.1. Phase field PDE model of cell motility

This work is motivated by a 2D phase field model of crawling cell motility introduced in [34]. This model consists of a system of two PDEs for the phase field function and the orientation vector due to polymerization of actin filaments inside the cell. In addition it obeys a volume preservation constraint. In [3] this system was rewritten in the following simplified form suitable for asymptotic analysis so that all key features of its qualitative behavior are preserved.

Let $\Omega \subset \mathbb{R}^2$ be a smooth bounded domain. Then, consider the following phase field PDE model of cell motility, studied in [3]:

$$\frac{\partial \rho_\varepsilon}{\partial t} = \Delta \rho_\varepsilon - \frac{1}{\varepsilon^2} W'(\rho_\varepsilon) - P_\varepsilon \cdot \nabla \rho_\varepsilon + \lambda_\varepsilon(t) \quad \text{in } \Omega, \quad (1.2)$$

$$\frac{\partial P_\varepsilon}{\partial t} = \varepsilon \Delta P_\varepsilon - \frac{1}{\varepsilon} P_\varepsilon - \beta \nabla \rho_\varepsilon \quad \text{in } \Omega, \quad (1.3)$$

where

$$\lambda_\varepsilon(t) = \frac{1}{|\Omega|} \int_{\Omega} \left(\frac{1}{\varepsilon^2} W'(\rho_\varepsilon) + P_\varepsilon \cdot \nabla \rho_\varepsilon \right) dx$$

is a *Lagrange multiplier* term responsible for total volume preservation of ρ_ε , and

$$W(\rho) = \frac{1}{4}\rho^2(1-\rho)^2 \quad (1.4)$$

is the Allen-Cahn (scalar Ginzburg-Landau) double equal well potential, and $\beta \geq 0$ is a physical parameter that characterizes actin polymerization strength and adhesion strength, introduced in [3].

Figure 1: Sketch of phase-field parameter ρ_ε

In (1.2)-(1.3), $\rho_\varepsilon: \Omega \rightarrow \mathbb{R}$ is the phase-field parameter that, roughly speaking, takes values 1 and 0 inside and outside, respectively, a subdomain $D(t) \subset \Omega$ occupied by the moving cell. These regions are separated by a thin “interface layer” of width $O(\varepsilon)$ around the boundary $\Gamma(t) := \partial D(t)$, where $\rho_\varepsilon(x, t)$ sharply transitions from 1 to 0. The vector valued function $P_\varepsilon: \Omega \rightarrow \mathbb{R}^2$ models the orientation vector due to polymerization of actin filaments inside the cell. On the boundary $\partial\Omega$ Neumann and Dirichlet boundary conditions respectively are imposed: $\partial_\nu \rho_\varepsilon = 0$ and $P_\varepsilon = 0$.

It was shown in [3] that $\rho_\varepsilon(x, t)$ converges to a characteristic function $\chi_{D(t)}$ as $\varepsilon \rightarrow 0$, where $D(t) \subset \mathbb{R}^2$. Namely, the phase-field parameter $0 \leq \rho_\varepsilon(x, t) \leq 1$ is equal to 1 when $x \in D(t)$ and equal to 0 outside of $D(t)$. This is referred to as the sharp interface limit of ρ_ε and we write $\Gamma(t) := \partial D(t)$. More precisely, given a closed, non self-intersecting curve $\Gamma(0) \subset \mathbb{R}^2$, consider the initial profile

$$\rho_\varepsilon(x, 0) = \theta_0 \left(\frac{\text{dist}(x, \Gamma(0))}{\varepsilon} \right)$$

where

$$\theta_0(z) = \frac{1}{2} \left(\tanh \left(\frac{z}{2\sqrt{2}} \right) + 1 \right)$$

is the standing wave solution of the Allen-Cahn equation, and $\text{dist}(x, \Gamma(0))$ is the signed distance from the point x to the curve $\Gamma(0)$. Then, $\rho_\varepsilon(x, t)$ has the asymptotic form

$$\rho_\varepsilon(x, t) = \theta_0 \left(\frac{\text{dist}(x, \Gamma(t))}{\varepsilon} \right) + O(\varepsilon),$$

where $\Gamma(t)$ is a curve which describes the boundary of the cell. It was shown in [3] that the curves $\Gamma(t)$ obey the evolution equation (1.1). That is, (1.1) is the sharp interface limit equation ($\varepsilon \rightarrow 0$) of the system (1.2)-(1.3).

Remark 1. In [3], the equation (1.1) with a specific form of $\Phi(V) = \beta\Phi_0(V)$ was derived from the system (1.2)-(1.3), where

$$\Phi_0(V) := \int_{\mathbb{R}} \psi(z; V) (\theta'_0)^2 dz \quad (1.5)$$

and $\psi(z) = \psi(z; V)$ is the unique solution of

$$\psi''(z) + V\psi'(z) - \psi(z) + \theta'_0 = 0, \quad (1.6)$$

with $\psi(\pm\infty) = 0$.

The case $\beta = 0$ in equations (1.2)-(1.3) leads to $\Phi \equiv 0$ in (1.1), thus reducing to a volume preserving analogue of the Allen-Cahn equation. Properties of this equation were studied in [8, 17], and it was shown that the sharp interface limit as $\varepsilon \rightarrow 0$ recovers volume preserving mean curvature motion: $V = \kappa - \frac{1}{|\Gamma|} \int_{\Gamma} \kappa ds$.

Equations (1.2)-(1.3) are a singularly perturbed parabolic PDE system in two spatial dimensions. Its sharp interface limit given by (1.1) describes evolution of the curve $\Gamma(t)$ (the sharp interface). Since $V(s, t)$ and $\kappa(s, t)$ are expressed via first and second derivatives of $\Gamma(t) (= \Gamma(s, t))$, equation (1.1) can be viewed as the second order PDE for $\Gamma(s, t)$. Since this PDE has spatial dimension one and it does not contain a singular perturbation, qualitative and numerical analysis of (1.1) is much simpler than that of the system (1.2)-(1.3).

Remark 2. It was observed in [3] that both the analysis and the behavior of solutions of system (1.2)-(1.3) crucially depends on the parameter β . Specifically there is critical value β_{cr} such that for $\beta > \beta_{cr}$ complicated phenomena of non-uniqueness and hysteresis arise. This critical value is defined as the maximum β for which $V - \beta\Phi_0(V)$ is a monotone function of V .

While this supercritical regime is a subject of the ongoing investigation, in this work we focus on providing a rigorous analysis of subcritical regime $\beta < \beta_{cr}$. For equation (1.1) the latter regime corresponds to the case of monotone function $V - \Phi(V)$.

1.2. Biological background: cell motility problem

Keratocyte cells are typically harvested from scales of fish (e.g., cichlids [20]) for *in vitro* experiments. Additionally, humans have keratocyte cells in their corneas. These cells are crucial during wound healing, e.g., after corrective laser surgery [27].

The biological mechanisms which give rise to keratocyte cell motion are complicated and they are an ongoing source of research. A review can be found in, e.g., [26] for an overview of the mechanisms governing keratocyte cell motility. Briefly we recall the following key components: assuming that a directional

preference has been established, a keratocyte cell has the ability to maintain self-propagating cell motion via internal forces generated by a protein *actin*. Actin monomers are polarized in such a way that several molecules may join and form filaments. These actin filaments form a dense and rigid network at the leading edge of the cell within the cytoskeleton, known as the lamellipod. The lamellipod forms adhesions to the substrate and by a mechanism known as *actin treadmilling* the cell protrudes via formation of new actin filaments at the leading edge.

We may now explain the heuristic idea behind the model. Roughly speaking, cell motility is determined by two (competing) mechanisms: surface tension and protrusion due to actin polymerization. Note that in the phase field model [34], bending rigidity of the membrane is not present, i.e., membrane elasticity is negligible. Recall that the domain where $\rho_\varepsilon(x) \approx 1$ is occupied by the cell and P_ε is the local averaged orientation of the filament network. Surface tension enters the model (1.2)-(1.3) via the celebrated Allen-Cahn equation with double-well potential (1.4):

$$\frac{\partial \rho_\varepsilon}{\partial t} = \Delta \rho_\varepsilon - \frac{1}{\varepsilon^2} W'(\rho_\varepsilon).$$

In the sharp interface limit ($\varepsilon \rightarrow 0$), surface tension leads to the curvature driven motion of the interface. The actin polymerization enters the system (1.2)-(1.3) through the $-P_\varepsilon \cdot \nabla \rho_\varepsilon$ term. Indeed, recall

$$\frac{D\rho_\varepsilon}{Dt} = \frac{\partial \rho_\varepsilon}{\partial t} + P_\varepsilon \cdot \nabla \rho_\varepsilon$$

is the material derivative of ρ_ε subject to the velocity field P_ε . Thus the term $-P_\varepsilon \cdot \nabla \rho_\varepsilon$ is an advective term generated by actin polymerization. The last term of (1.2), $\lambda_\varepsilon(t)$ is responsible for volume preservation, which is an important physical condition.

The diffusion term $\varepsilon \Delta P_\varepsilon$ corresponds to diffusion of actin and does not significantly affect the dynamics of ρ_ε . The term in (1.3), $-\beta \nabla \rho_\varepsilon$, describes the creation of actin by polymerization, which leads to a protrusion force. It gives the rate of growth of polymerization of actin: $\frac{\partial P_\varepsilon}{\partial t} \sim -\beta \nabla \rho_\varepsilon$. The $\frac{1}{\varepsilon} P_\varepsilon$ term provides decay of P_ε away from the interface, for example due to depolymerization.

The system (1.2)-(1.3) is a slightly modified form of the model proposed in [34]. The model presented in [34] can be rewritten in a simplified form suitable for analysis, so as to preserve qualitative behavior. First, in [34] the volume conservation constraint is introduced into the system by adding a non-local term which affects the double-well potential (formulas (2.2), (2.5)-(2.6) in [34]). In (1.2) this constraint is enforced via the Lagrange multiplier $\lambda_\varepsilon(t)$, which is more convenient for analysis. Next for technical simplicity in (1.3) we drop two terms affecting actin depolarization and myosin induced contraction. These two terms still can be incorporated in the equation and simply lead to redefining the function Φ in (1.1). However this does not affect qualitative behavior of this function or the analysis of existence. Moreover, lab experiments confirmed that cells may remain motile upon deactivation of myosin [32], which

justifies dropping the myosin contraction in the second equation. Lastly, we use a diffusive scaling ($t \mapsto \varepsilon^2 t$, $x \mapsto \varepsilon x$) to study the long term behavior of the system, see [3].

We note that ideas proposed in [34], especially the phase field description, have been recently adapted to study problems of cell motility on deformable substrates [33], spontaneous division of cells [16], symmetry breaking and 3D models of cell motility, [19, 31] and hydrodynamic interactions with the cell cytoplasm [23].

1.3. Overview of results and techniques

A main goal of this work is to prove existence of a family of curves which evolve according to the equation (1.1) and to investigate their properties. The problem of mean curvature type motion was extensively studied by mathematicians from both PDE and geometry communities for several decades. A review of results on unconstrained motion by mean curvature can be found in [5, 15, 18]. Furthermore the viscosity solutions techniques have been efficiently applied in the PDE analysis of such problems. These techniques do not apply to mean curvature motion with volume preservation constraints [14, 7, 12], and the analysis becomes especially difficult in dimensions greater than two [13]. Note that existence in two dimensional mean curvature type motions were recently studied (e.g., [4, 7, 12]) and appropriate techniques of regularization were developed. Recently, analogous issues resurfaced in the novel context of biological cell motility problems, after a phase-field model was introduced in [34].

The problem studied in the present work is two dimensional (motion of a curve on the plane). The distinguished feature of this problem is that the velocity enters the evolution equation implicitly via a *non-linear* function $V - \Phi(V)$. Therefore the time derivative in the corresponding PDE that describes the signed distance, $u(\sigma, t)$ of the curve from a given reference curve also enters the PDE implicitly, which leads to challenges in establishing existence.

The following outlines the basic steps of the analysis. First, we consider smooth (H^2) initial data and generalize the regularization idea from [7] (see also [12]) for the implicit dependence described above. Here, the main difficulty is to establish existence on a time interval that does not depend on the regularization parameter ε . To this end, we derive L^2 (in time and space) a priori estimates independent of ε for third order derivatives and uniform in time L^2 estimates for second order derivatives. These estimates allow us to show existence and to pass to the limit as $\varepsilon \rightarrow 0$, and they are derived by considering the equation for $u_\sigma = \frac{\partial u}{\partial \sigma}$. We use “nice” properties of this equation to obtain higher order estimates independent of ε (which are not readily available for the equation for u). In particular, it turns out that the equation for u_σ can be written as a quasi-linear parabolic PDE in divergence form. For such equations quite remarkable classical results establish Hölder continuity of solutions even for discontinuous initial data [21]. This provides a lower bound on the possible blow up time, which does depend on H^2 norm of initial data for u in our problem.

As a result, we establish existence on a time interval that depends on the H^2 norm of initial data.

Second, observe that experiments for cell motility show that the cell shape is not necessarily smooth. For example, in [1] it was observed that keratocytes moving on substrates with high adhesion strengths exhibit traveling waves of protrusion. These traveling waves of protrusion lead to a formation of singularities in the cell membrane which look like corners (see [1], Supplementary Movie 3). Therefore one needs to study if the sharp interface limit (1.1) of the phase-field model (1.2)-(1.3) admits corner-like singularities. To this end we consider initial conditions with generic $W^{1,\infty}$ initial curves. A natural mathematical question is in what regime of physical parameter the equation (1.1) possesses the property of instantaneous parabolic smoothening of initial data, e.g., as in classical mean curvature flow. We show that in the subcritical regime of parameters the equation (1.1) exhibits parabolic type regularization.

For the limiting equations for u and u_σ , we show existence on a time interval that does not depend on the H^2 (and H^1 for u_σ) norms of initial conditions. This is necessary because these norms blow up for non-smooth functions from $W^{1,\infty} \setminus H^2$. The existence is proved by a maximum principle type argument, which is not available for the regularized equations that contain fourth order derivatives. Also it is crucial to establish Hölder continuity results for u_σ , rewriting the equation for u_σ as a quasilinear divergence form parabolic PDE.

After proving short time existence we address the issues of global existence of such curves. The latter is important for the comparison of theoretical and experimental results on cell motility. We will present an exploratory study which combines analytical and numerical results for the long time behavior of the cell motility model. Analytically, we prove that similarly to the classical curvature driven motion with volume preservation, traveling waves with nonzero velocity do not exist. In the context of cell motility, this means that in the subcritical regime of parameters, the membrane tension dominates the actin polymerization and therefore persistent motion of cells does not occur (in fact, our preliminary results in the subsequent work in progress shows that this is not the case in the supercritical regime). However, numerical experiments show that although there is no persistent net motion, a nontrivial (transient) net motion resulting from the non-linearity and asymmetry of the initial shape occurs in the subcritical regime. This observation shows an essential difference between the motion (1.1) in the subcritical regime and the classical volume preserving curvature motion.

Numerically solving (1.1) is a nontrivial task due to the non-linearity and non-locality in the formulation of the normal velocity. Classical methods such as level-set methods cannot be readily used here. We introduce an efficient algorithm which separates the difficulties of non-linearity and non-locality and resolves them independently through an iterative scheme. The accuracy of the algorithm is validated by numerical convergence. Our numerical experiments show that both non-linearity and asymmetry of the initial shape (in the form of non-convexity) can introduce a drift of the center of mass of the cell. Increasing the effects of the non-linearity or increasing the asymmetry results in an increase in the drift distance.

2. Existence of solutions to the evolution equation (1.1)

We study curves propagating via the evolution equation (1.1). The case $\Phi \equiv 0$ corresponds to well-studied volume preserving curvature motion (see, e.g., [7, 12, 13, 14]). We emphasize that the presence of $\Phi(V)$ results in an implicit, non-linear and non-local equation for V , which leads to challenges from an analytical and numerical standpoint.

The goal of this section is to prove the following:

Theorem 1. *Let $\Phi \in L^\infty(\mathbb{R})$ be a Lipschitz function satisfying*

$$\|\Phi'\|_{L^\infty(\mathbb{R})} < 1. \quad (2.1)$$

Then, given $\Gamma_0 \in W^{1,\infty}$, a closed and non self-intersecting curve on $\mathbb{R}^2$, there is a time $T = T(\Gamma_0) > 0$ such that a family of curves $\Gamma(t) \in H^2$ exists for $t \in (0, T]$ which satisfies the evolution equation (1.1) with initial condition $\Gamma(0) = \Gamma_0$.

Remark 3. *The classes $W^{1,\infty}$ and H^2 above refer to curves which are parametrized by mappings from Sobolev spaces $W^{1,\infty}$ and H^2 correspondingly.*

Corollary 1. *Let $\Phi(V) = \beta\Phi_0(V)$ as defined in Remark 1 and let $0 \leq \beta < \beta_{cr}$ as defined in Remark 2 (which is equivalent to (2.1)). Then, given $\Gamma_0 \in W^{1,\infty}$, a closed and non self-intersecting curve on $\mathbb{R}^2$, there is a time $T = T(\Gamma_0) > 0$ such that a family of curves $\Gamma(t) \in H^2$ exists for $t \in (0, T]$ which satisfies the evolution equation (1.1) with initial condition $\Gamma(0) = \Gamma_0$.*

We first prove the existence for smooth (H^2) initial data. The main effort is to pass to non-smooth initial conditions (e.g., initial curves with corners), see the discussion in Section 1.3.

Proof of Theorem 1: The proof of Theorem 1 is split into 4 steps. In Step 1 we present a PDE formulation of the evolution problem (1.1) and introduce its regularization by adding a higher order term with the small parameter $\varepsilon > 0$. In Step 2 we prove a local in time existence result for the regularized problem. In Step 3 we establish a uniform time interval of existence for solutions of the regularized problem via a priori estimates. These estimates allow us to pass to the limit $\varepsilon \rightarrow 0$, which leads to existence for (1.1) for smooth initial data. Finally, Step 4 is devoted to the transition from H^2 -smooth initial data to $W^{1,\infty}$ ones. A crucial role here plays derivation of L^∞ bounds for the solution and its first derivative independent of H^2 norm of the initial data.

Step 1. *Parametrization and PDE forms of (1.1).*

Let $\tilde{\Gamma}_0$ be a C^4 smooth reference curve in a small neighborhood of Γ_0 and let $\tilde{\Gamma}_0$ be parametrized by arc length parameter $\sigma \in I$. Let $\kappa_0(\sigma)$ be the signed curvature of $\tilde{\Gamma}_0$ and $\nu(\sigma)$ be the the inward pointing normal vector to $\tilde{\Gamma}_0$. Consider the tubular neighborhood

$$U_{\delta_0} := \{x \in \mathbb{R}^2 \mid \text{dist}(x, \tilde{\Gamma}_0) < 2\delta_0\}.$$

Figure 2: Visualization of $\mathbb{B}_{\delta_0}$ and the relation between $d(t)$ and $\Gamma(t)$

One can choose $\tilde{\Gamma}_0$ and δ_0 so that the map

$$Y : I \times (-2\delta_0, 2\delta_0) \rightarrow U_{\delta_0}, \quad Y(\sigma, u) := \tilde{\Gamma}_0(\sigma) + u\nu(\sigma)$$

is a C^2 diffeomorphism between $I \times (-2\delta_0, 2\delta_0)$ and its image, and $\Gamma_0 \subset Y(I \times (-2\delta_0, 2\delta_0))$. Then Γ_0 can be parametrized by $\Gamma_0 = \tilde{\Gamma}_0(\sigma) + u_0(\sigma)\nu(\sigma)$, $\sigma \in I$, for some periodic function $u_0(\sigma)$. Finally, we can assume that δ_0 is sufficiently small so that

$$\delta_0 \|\kappa_0\|_{L^\infty} < 1, \quad (2.2)$$

where κ_0 denotes the curvature of $\tilde{\Gamma}_0$.

A continuous function $u : I \times [0, T] \rightarrow [-\delta_0, \delta_0]$, periodic in the σ variable, describes a family of closed curves via the mapping

$$\Gamma(\sigma, t) = \tilde{\Gamma}_0(\sigma) + u(\sigma, t)\nu(\sigma). \quad (2.3)$$

That is, there is a well-defined correspondence between $\Gamma(\sigma, t)$ and $u(\sigma, t)$.

Recall the Frenet-Serre formulas applied to $\tilde{\Gamma}_0$:

$$\frac{d\tau}{d\sigma}(\sigma) = \kappa_0(\sigma)\nu(\sigma) \quad (2.4)$$

$$\frac{d\nu}{d\sigma}(\sigma) = -\kappa_0(\sigma)\tau(\sigma) \quad (2.5)$$

where τ is the unit tangent vector. Using (2.3)-(2.5) we express the normal velocity V of Γ as

$$V = \frac{1 - u\kappa_0}{S} u_t \quad (2.6)$$

where $S = S(u) = \sqrt{u_\sigma^2 + (1 - u\kappa_0)^2}$. Also, in terms of u , curvature of Γ is given by

$$\kappa(u) = \frac{1}{S^3} \left((1 - u\kappa_0)u_{\sigma\sigma} + 2\kappa_0 u_\sigma^2 + (\kappa_0)_\sigma u_\sigma u + \kappa_0(1 - u\kappa_0)^2 \right). \quad (2.7)$$

Note that if u is sufficiently smooth [6] one has

$$\int_I \kappa(u) S d\sigma = \int_{\Gamma} \kappa ds = 2\pi,$$

in particular this holds for every $u \in H_{per}^2(I)$ such that $|u| \leq \delta_0$ on I . Hereafter, $H_{per}^k(I)$ denote the Sobolev spaces of periodic functions on I with square-integrable derivatives up to the k -th order and $W_{per}^{1,\infty}(I)$ denotes the space of periodic functions with the first derivative in $L^\infty(I)$.

Combining (2.6) and (2.7), we rewrite (1.1) as the following PDE for u :

$$\begin{aligned} u_t - \frac{S}{1 - u\kappa_0} \Phi \left(\frac{1 - u\kappa_0}{S} u_t \right) &= \frac{S}{1 - u\kappa_0} \kappa(u) \\ &\quad - \frac{S}{(1 - u\kappa_0)L[u]} \left(\int_I \Phi \left(\frac{1 - u\kappa_0}{S} u_t \right) S d\sigma + 2\pi \right), \end{aligned} \quad (2.8)$$

where

$$L[u] = \int_I S(u) d\sigma$$

is the total length of the curve.

The initial condition $u(\sigma, 0) = u_0(\sigma)$ corresponds to the initial profile $\Gamma(0) = \Gamma_0$. Since (2.8) is not resolved with respect to the time derivative u_t , it is natural to resolve (1.1) with respect to V to convert (2.8) into a parabolic type PDE where the time derivative u_t is expressed as a function of u , u_σ , $u_{\sigma\sigma}$. The following lemma shows how to rewrite (2.8) in such a form. This is done by resolving (1.1) with respect to V to get a Lipschitz continuous resolving map, provided that $\Phi \in L^\infty(\mathbb{R})$ and $\|\Phi'\|_{L^\infty(\mathbb{R})} < 1$.

It is convenient to rewrite in the form (1.1)

$$V = \kappa(u) + \Phi(V) - \lambda, \quad \int_I V S(u) d\sigma = 0, \quad (2.9)$$

where both normal velocity V and constant λ are considered as unknowns.

Lemma 1. *Suppose that $\Phi \in L^\infty(\mathbb{R})$ and $\|\Phi'\|_{L^\infty(\mathbb{R})} < 1$. Then for any $u(\sigma) \in H_{per}^2(I)$, such that $|u(\sigma)| \leq \delta_0$, there exists a unique solution $(V(\sigma), \lambda) \in L^2(I) \times \mathbb{R}$ of (2.9). Moreover, the resolving map $\mathcal{F}$ assigning to a given $u \in H_{per}^2(I) \cap \{u; |u| \leq \delta_0\}$ the solution $V = \mathcal{F}(u) \in L^2(I)$ of (2.9) is locally Lipschitz continuous.*

Proof. Let $J := \|\Phi'\|_{L^\infty(\mathbb{R})}$. Fix $\kappa \in C_{per}(I)$, a positive function $S \in C_{per}(I)$ and $\lambda \in \mathbb{R}$, and consider the equation

$$V = \kappa + \Phi(V) - \lambda. \quad (2.10)$$

It is immediate that the unique solution of (2.10) is given by $V = \Psi(\kappa - \lambda)$, where Ψ is the inverse map to $V - \Phi(V)$. Note that $\frac{1}{1+J} \leq \Psi' \leq \frac{1}{1-J}$, therefore Ψ is strictly increasing function and $\Psi(\kappa - \lambda) \rightarrow \pm\infty$ uniformly as $\lambda \rightarrow \mp\infty$. It

follows that there exists a unique $\lambda \in \mathbb{R}$ such that $V = \Psi(\kappa - \lambda)$ is a solution of (2.10) satisfying

$$\int_I V S d\sigma = 0. \quad (2.11)$$

Next we establish the Lipschitz continuity of the resolving map $(\kappa, S) \mapsto V \in L^2(I)$ as a function of $\kappa \in L^2(I)$ and $S \in L_{per}^\infty(I)$, $S \geq 1 - \delta_0 \|\kappa_0\|_{L^\infty(I)} > 0$ (cf. (2.2)), still assuming that $\kappa, S \in C_{per}(I)$. Multiply (2.10) by VS and integrate over I to find with the help of the Cauchy-Schwarz inequality,

$$\begin{aligned} \int_I V^2 S d\sigma &= \int_I \kappa V S d\sigma + \int_I \Phi(V) V S d\sigma \\ &\leq \|S\|_{L^\infty(I)} (\|\kappa\|_{L^2(I)} + (|I| \|\Phi\|_{L^\infty(\mathbb{R})})^{1/2}) \left(\int_I V^2 S d\sigma \right)^{1/2}. \end{aligned}$$

Recalling that $S \geq \omega := 1 - \delta_0 \|\kappa_0\|_{L^\infty(I)} > 0$, we then obtain

$$\|V\|_{L^2(I)} \leq \frac{\|S\|_{L^\infty(I)}}{\omega^{1/2}} (\|\kappa\|_{L^2(I)} + (|I| \|\Phi\|_{L^\infty(\mathbb{R})})^{1/2}). \quad (2.12)$$

To see that $\kappa \mapsto V$ (for fixed S) is Lipschitz continuous, consider solutions V_1, V_2 of (2.10)-(2.11) with $\kappa = \kappa_1$ and $\kappa = \kappa_2$. Subtract the equation for V_2 from that for V_1 multiply by $S(V_1 - V_2)$ and integrate over I ,

$$\int_I ((V_1 - V_2)^2 - (\Phi(V_1) - \Phi(V_2))(V_1 - V_2)) S d\sigma = \int_I (\kappa_1 - \kappa_2)(V_1 - V_2) S d\sigma.$$

Then, since $|\Phi(V_1) - \Phi(V_2)| \leq J|V_1 - V_2|$ we derive that

$$\|V_1 - V_2\|_{L^2(I)} \leq \frac{\|S\|_{L^\infty(I)}}{\omega^{1/2}(1 - J)} \|\kappa_1 - \kappa_2\|_{L^2(I)}.$$

Next consider solutions of (2.10)-(2.11), still denoted V_1 and V_2 , which correspond now $S = S_1$ and $S = S_2$ with the same κ . Subtract the equation for V_2 from that for V_1 multiply by $S_1(V_1 - V_2) + V_2(S_1 - S_2)$ and integrate over I to find

$$\begin{aligned} \int_I ((V_1 - V_2)^2 - (\Phi(V_1) - \Phi(V_2))(V_1 - V_2)) S_1 d\sigma \\ = \int_I V_2 (S_1 - S_2) (\Phi(V_1) - \Phi(V_2) - (V_1 - V_2)) d\sigma. \end{aligned}$$

Then applying the Cauchy-Schwarz inequality we derive

$$\|V_1 - V_2\|_{L^2(I)} \leq \frac{1 + J}{\omega(1 - J)} \|V_2\|_{L^2(I)} \|S_1 - S_2\|_{L^\infty(I)}.$$

Thanks to (2.12) this completes the proof of local Lipschitz continuity of the resolving map on the dense subset (of continuous functions) in

$$\Theta = \left\{ (\kappa, S) \in L^2(I) \times \{S \in L_{per}^\infty(I); S \geq \omega\} \right\}$$

and thus on the whole set Θ . It remains to note that the map $u \mapsto (\kappa(u), S(u))$ is locally Lipschitz on $\{u \in H_{per}^2(I); |u| \leq \delta_0 \text{ on } I\}$, which completes the proof of the Lemma. $\square$

Remark 4. The parameter $\lambda \in \mathbb{R}$ with the property that the solution V of (2.10) satisfies $\int_I VSd\sigma = 0$ is easily seen to be

$$\lambda = \frac{1}{L[u]} \int_I (\kappa(u) + \Phi(V)Sd\sigma) = \frac{\pi}{L[u]} + \frac{1}{L[u]} \int_I \Phi(V)Sd\sigma. \quad (2.13)$$

Remark 5. Under conditions of Lemma 1, if $\kappa(u) \in H_{per}^1(I)$ ($u \in H_{per}^3(I)$) then it holds that $V = \mathcal{F}(u) \in H_{per}^1(I)$.

Equation (1.1) is equivalently rewritten in terms of the resolving operator $\mathcal{F}$ as

$$u_t = \frac{S(u)}{1 - u\kappa_0} \mathcal{F}(u), \text{ or } u_t = \tilde{\mathcal{F}}(u), \quad (2.14)$$

where $\tilde{\mathcal{F}}(u) := S(u)\mathcal{F}(u)/(1 - u\kappa_0)$.

Step 2. Introduction and analysis of regularized PDE.

We now introduce a small parameter regularization term to (2.8) which allows us to apply standard existence results. To this end, let $u^\varepsilon = u^\varepsilon(\sigma, t)$ solve the following regularization of equation (2.14) for $0 < \varepsilon \leq 1$,

$$u_t^\varepsilon + \varepsilon u_{\sigma\sigma\sigma}^\varepsilon = \tilde{\mathcal{F}}(u^\varepsilon), \quad (2.15)$$

with $u^\varepsilon(\sigma, 0) = u_0$. Define

$$V^\varepsilon := \frac{1 - u^\varepsilon \kappa_0}{S^\varepsilon} (u_t^\varepsilon + \varepsilon u_{\sigma\sigma\sigma}^\varepsilon),$$

where $S^\varepsilon = S(u^\varepsilon)$. Since $V^\varepsilon = \mathcal{F}(u^\varepsilon)$, then by definition of the resolving map $\mathcal{F}$ we have that u^ε satisfies the following equation:

$$\begin{aligned} u_t^\varepsilon + \varepsilon u_{\sigma\sigma\sigma}^\varepsilon - \frac{S^\varepsilon}{1 - u^\varepsilon \kappa_0} \Phi(V^\varepsilon) &= \frac{S^\varepsilon}{1 - u^\varepsilon \kappa_0} \kappa(u^\varepsilon) \\ &\quad - \frac{S^\varepsilon}{(1 - u^\varepsilon \kappa_0)L[u^\varepsilon]} \left(\int_I \Phi(V^\varepsilon)S^\varepsilon d\sigma + 2\pi \right). \end{aligned} \quad (2.16)$$

Hereafter we consider $H_{per}^2(I)$ equipped with the norm

$$\|u\|_{H^2(I)}^2 := \|u\|_{L^2(I)}^2 + \|u_{\sigma\sigma}\|_{L^2(I)}^2.$$

Proposition 1. Let Γ_0 and $\Phi(\cdot)$ satisfy the conditions of Theorem 1. Assume that $u_0 \in H_{per}^2$ and $\max |u_0| < \delta_0$. Then there exists a non-empty interval $[0, T^\varepsilon]$ such that a solution u^ε of (2.16) with initial data $u^\varepsilon(\eta, 0) = u_0(\eta)$ exists and

$$\begin{aligned} u^\varepsilon &\in L^2(0, T^\varepsilon; H_{per}^4(I)) \cap H^1(0, T^\varepsilon; L^2(I)) \cap L^\infty(0, T^\varepsilon; H_{per}^2) \\ &\text{and } \sup_{t \in [0, T]} \|u^\varepsilon(t)\|_{L^\infty(I)} \leq \delta_0. \end{aligned} \quad (2.17)$$

Furthermore, this solution can be extended on a bigger time interval $[0, T^\varepsilon + \Delta_t]$ so long as $\delta_0 - \max u(\sigma, T^\varepsilon) \geq \alpha$ and $\|u(T^\varepsilon)\|_{H^2(I)} \leq M$ for some $\alpha > 0$ and $M < \infty$, where Δ_t depends on ε , α and M , $\Delta_t := \Delta_t(\alpha, M, \varepsilon) > 0$.

Proof. Choose $T^\varepsilon > 0$ and $M > \|u_0\|_{H^2(I)}$, and introduce the set

$$K := \{u : \|u\|_{H^2} \leq M, |u| \leq \delta_0 \text{ in } I\}.$$

Given $\tilde{u} \in L^\infty(0, T^\varepsilon; K)$, consider the following auxiliary problem

$$u_t + \varepsilon u_{\sigma\sigma\sigma\sigma} = \tilde{\mathcal{F}}(\tilde{u}) \quad (2.18)$$

with $u(\sigma, 0) = u_0(\sigma)$. Classical results (e.g., [22]) yield existence of a unique solution u of (2.18) which possesses the following regularity

$$u \in L^2(0, T^\varepsilon; H_{per}^4(I)) \cap H^1(0, T^\varepsilon; L^2(I)) \cap L^\infty(0, T^\varepsilon; H_{per}^2(I)).$$

That is, a resolving operator

$$\mathcal{T}: L^\infty(0, T^\varepsilon; K) \rightarrow L^\infty(0, T^\varepsilon; H^2(I))$$

which maps $\tilde{u}$ to the solution u is well defined. Next we show that $\mathcal{T}$ is a contraction in K , provided that T^ε is chosen sufficiently small.

Consider $\tilde{u}_1, \tilde{u}_2 \in L^\infty(0, T^\varepsilon; K)$ satisfying the initial condition $\tilde{u}_1(\sigma, 0) = \tilde{u}_2(\sigma, 0) = u_0(\sigma)$ and define $u_1 := \mathcal{T}(\tilde{u}_1)$, $u_2 := \mathcal{T}(\tilde{u}_2)$. Let $\bar{u} := u_1 - u_2$. Then multiply the equality $\bar{u}_t + \varepsilon \bar{u}_{\sigma\sigma\sigma\sigma} = \tilde{\mathcal{F}}(\tilde{u}_1) - \tilde{\mathcal{F}}(\tilde{u}_2)$ by $(\bar{u}_{\sigma\sigma\sigma\sigma} + \bar{u})$ and integrate. Integrating by parts and using the Cauchy-Schwarz inequality yields

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \int_I (\bar{u}_{\sigma\sigma}^2 + \bar{u}^2) d\sigma + \varepsilon \|\bar{u}_{\sigma\sigma\sigma\sigma}\|_{L^2(I)}^2 + \varepsilon \|\bar{u}_{\sigma\sigma}\|_{L^2(I)}^2 \\ \leq \|\tilde{\mathcal{F}}(\tilde{u}_1) - \tilde{\mathcal{F}}(\tilde{u}_2)\|_{L^2(I)} (\|\bar{u}_{\sigma\sigma\sigma\sigma}\|_{L^2(I)} + \|\bar{u}\|_{L^2(I)}). \end{aligned}$$

Note that by Lemma 1 the map $\mathcal{F}(u)$ with values in $L^2(I)$ is Lipschitz on K ; since $\tilde{\mathcal{F}}(u) = S(u)\mathcal{F}(u)/(1 - u\kappa_0)$ it is not hard to see that $\tilde{\mathcal{F}}(u)$ is also Lipschitz. Using this and applying Young's inequality to the right hand side we obtain

$$\frac{1}{2} \frac{d}{dt} \|\bar{u}\|_{H^2(I)}^2 \leq C \|\tilde{u}_1 - \tilde{u}_2\|_{H^2(I)}^2 + \frac{1}{2} \|\bar{u}\|_{H^2(I)}^2 \quad (2.19)$$

with a constant C independent of $\tilde{u}_1$ and $\tilde{u}_2$ and T_ε . Applying the Grönwall inequality on (2.19) we get

$$\sup_{0 \leq t \leq T^\varepsilon} \|\mathcal{T}(\tilde{u}_1) - \mathcal{T}(\tilde{u}_2)\|_{H^2(I)}^2 \leq 2(e^{T^\varepsilon} - 1)C \|\tilde{u}_1 - \tilde{u}_2\|_{L^\infty(0, T^\varepsilon; H^2(I))} \quad (2.20)$$

Similar arguments additionally yield the following bound for $u = \mathcal{T}(\tilde{u})$,

$$\sup_{0 \leq t \leq T^\varepsilon} \|u(t)\|_{H^2(I)}^2 \leq (e^{T^\varepsilon} - 1)C_1 + e^{T^\varepsilon} \|u_0\|_{H^2(I)}^2, \quad (2.21)$$

with C_1 independent of $\tilde{u} \in L^\infty(0, T^\varepsilon; K)$. Choosing T^ε sufficiently small we get that $\|u(t)\|_{H^2(I)} \leq M$ for $0 < t < T^\varepsilon$.

Finally, multiply (2.18) by $(u - u_0)$ and integrate. After integrating by parts and using the fact that $\|u\|_{H^2(I)} \leq M$ we obtain

$$\sup_{0 \leq t \leq T^\varepsilon} \|u(t) - u_0\|_{L^2(I)}^2 \leq C_3(e^{T^\varepsilon} - 1).$$

Then using the interpolation inequality

$$\|u - u_0\|_{C(I)}^2 \leq C \|u - u_0\|_{H^2(I)} \|u - u_0\|_{L^2(I)}$$

we get the bound

$$\sup_{0 \leq t \leq T^\varepsilon} \|u(t) - u_0\|_{C(I)}^4 \leq C_4 \|u(t) - u_0\|_{L^2(I)}^2 \leq C_5(e^{T^\varepsilon} - 1). \quad (2.22)$$

Now by (2.20) and (2.22) we see that, possibly after passing to a smaller T^ε , $\mathcal{T}$ maps K into K and it is a contraction on K . $\square$

Step 3. *Regularized equation: a priori estimates, existence on time interval independent of ε , and limit as $\varepsilon \rightarrow 0$.*

In this step we derive a priori estimates which imply existence of a solution of (2.16) on a time interval independent of ε . These estimates are also used to pass to the $\varepsilon \rightarrow 0$ limit.

Lemma 2. *Assume that $u_0 \in H_{per}^2$ and $\|u_0\|_{L^\infty(I)} < \delta_0$. Let u^ε solve (2.16) on a time interval $[0, T^\varepsilon]$ with initial data $u^\varepsilon(0) = u_0$, and let u^ε satisfy $|u^\varepsilon(\sigma, t)| \leq \delta_0$ on $I \times T^\varepsilon$. Then*

$$\|u_{\sigma\sigma}^\varepsilon\|_{L^2(I)}^2 \leq a(t), \quad (2.23)$$

where $a(t)$ is the solution of

$$\dot{a} = 2Pa^3 + 2Q, \quad a(0) = \|(u_0)_{\sigma\sigma}\|_{L^2}^2 \quad (2.24)$$

(continued by $+\infty$ after the blow up time), and $0 < P < \infty$, $0 < Q < \infty$ are independent of ε and u_0 .

Proof. For brevity we adopt the notation $u := u^\varepsilon$, $V := V^\varepsilon$, $S := S^\varepsilon$. Differentiate equation (2.16) in σ to find that

$$\begin{aligned} u_{\sigma t} + \varepsilon \frac{\partial^5 u}{\partial \sigma^5} - \frac{S}{1 - u\kappa_0} \Phi'(V) V_\sigma &= \frac{S}{1 - u\kappa_0} (\kappa(u))_\sigma \\ &+ \left(\frac{S}{1 - u\kappa_0} \right)_\sigma \left(\kappa(u) - \Phi(V) - \frac{2\pi}{L[u]} - \frac{1}{L[u]} \int_I \Phi(V) S d\sigma \right). \end{aligned} \quad (2.25)$$

Next we rewrite (2.16) in the form $V = \Phi(V) + \kappa - \lambda$ to calculate V_σ ,

$$(1 - \Phi'(V)) V_\sigma = \kappa_\sigma$$

whence

$$V_\sigma = \frac{1}{1 - \Phi'(V)} \kappa_\sigma.$$

Now we substitute this in (2.25) to find that

$$\begin{aligned} u_{\sigma t} + \varepsilon \frac{\partial^5 u}{\partial \sigma^5} &= \frac{u_{\sigma\sigma\sigma}}{S^2(1 - \Phi'(V))} - \frac{\Phi'(V) + 2}{(1 - \Phi'(V))S^4} u_{\sigma} u_{\sigma\sigma}^2 + A(\sigma, V, u, u_{\sigma}) u_{\sigma\sigma} \\ &\quad + B(\sigma, V, u, u_{\sigma}) + \left(\frac{S}{1 - u\kappa_0} \right)_{\sigma} \left(\Phi(V) - \frac{2\pi}{L[u]} - \frac{1}{L[u]} \int_I \Phi(V) S d\sigma \right), \end{aligned} \quad (2.26)$$

where $A(\sigma, V, u, p)$ and $B(\sigma, V, u, p)$ are bounded continuous functions on $I \times \mathbb{R} \times [-\delta_0, \delta_0] \times \mathbb{R}$.

Multiply (2.26) by $u_{\sigma\sigma\sigma}$ and integrate over I , integrating by parts on the left hand side. We find after rearranging terms and setting $\gamma := \sup(1 - \Phi'(V))$ ($0 < \gamma < \infty$),

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \|u_{\sigma\sigma}\|_{L^2(I)}^2 + \varepsilon \|u_{\sigma\sigma\sigma\sigma}\|_{L^2(I)}^2 + \frac{1}{\gamma} \int_I |u_{\sigma\sigma\sigma}|^2 \frac{d\sigma}{S^2} &\leq C \int_I |u_{\sigma\sigma}|^2 |u_{\sigma\sigma\sigma}| \frac{d\sigma}{S^3} \\ &\quad + C_1 (\|u_{\sigma\sigma}\|_{L^2(I)}^3 + 1) \left(\int_I |u_{\sigma\sigma\sigma}|^2 \frac{d\sigma}{S^2} \right)^{1/2}, \end{aligned} \quad (2.27)$$

where we have also used the inequality $\|u_{\sigma}\|_{L^\infty(I)}^2 \leq |I| \|u_{\sigma\sigma}\|_{L^2(I)}^2$ and estimated various terms with the help of the Cauchy-Schwarz inequality. Next we estimate the first term in the right hand side of (2.27) as follows

$$\int_I |u_{\sigma\sigma}|^2 |u_{\sigma\sigma\sigma}| \frac{d\sigma}{S^3} \leq C_{\gamma} \int_I |u_{\sigma\sigma}|^4 \frac{d\sigma}{S^4} + \frac{1}{4C_{\gamma}} \int_I |u_{\sigma\sigma\sigma}|^2 \frac{d\sigma}{S^2} \quad (2.28)$$

and apply the following interpolation type inequality, whose proof is given in Lemma 3: for all $u \in H_{per}^3(I)$ such that $|u| \leq \delta_0$ it holds that

$$\int_I |u_{\sigma\sigma}|^4 \frac{d\sigma}{S^4} \leq \mu \int_I |u_{\sigma\sigma\sigma}|^2 \frac{d\sigma}{S^2} + C_2 \left(\int_I u_{\sigma\sigma}^2 d\sigma \right)^3 + C_3 \quad \forall \mu > 0, \quad (2.29)$$

where C_2 and C_3 depend only on μ . Now we use (2.28) and (2.29) in (2.27), and estimate the last term of (2.27) with the help of Young's inequality to derive that

$$\frac{1}{2} \frac{d}{dt} \|u_{\sigma\sigma}\|_{L^2(I)}^2 + \varepsilon \|u_{\sigma\sigma\sigma\sigma}\|_{L^2(I)}^2 + \frac{1}{4\gamma} \int_I |u_{\sigma\sigma\sigma}|^2 \frac{d\sigma}{S^2} \leq P \|u_{\sigma\sigma}\|_{L^2(I)}^6 + Q. \quad (2.30)$$

Then by a standard comparison argument for ODEs $\|u_{\sigma\sigma}\|_{L^2(I)}^2 \leq a(t)$, where a solves (2.24). The Lemma is proved. $\square$

Lemma 3. Assume that $u \in H_{per}^3(I)$ and $|u| \leq \delta_0$ on I . Then (2.29) holds with C_2 and C_3 depending on μ only.

Proof. The following straightforward bounds will be used throughout the proof,

$$\frac{1}{\sqrt{2}} (|u_{\sigma}| + (1 - \delta_0 \|\kappa_0\|_{L^\infty(I)})) \leq S(u) \leq |u_{\sigma}| + 1, \quad (2.31)$$

$$|(S(u))_\sigma| \leq \frac{1}{S}(|u_\sigma||u_{\sigma\sigma}| + C|u_\sigma| + C_1). \quad (2.32)$$

Note that

$$\int_I u_{\sigma\sigma}^4 \frac{d\sigma}{S^4} \leq C \|u_{\sigma\sigma}^2/S\|_{L^\infty(I)} \int_I u_{\sigma\sigma}^2 d\sigma, \quad (2.33)$$

where $C > 0$ is independent of u . Since $\int_I u_{\sigma\sigma} d\sigma = 0$ we have

$$\|u_{\sigma\sigma}^2/S\|_{L^\infty(I)} \leq \int_I |(u_{\sigma\sigma}^2/S)_\sigma| d\sigma. \quad (2.34)$$

Next we use (2.31), (2.32) to estimate the right hand side of (2.34) with the help of the Cauchy-Schwarz inequality,

$$\begin{aligned} \int_I |(u_{\sigma\sigma}^2/S)_\sigma| d\sigma &\leq 2 \int_I |u_{\sigma\sigma\sigma} u_{\sigma\sigma}| \frac{d\sigma}{S} + C \left(\int_I |u_{\sigma\sigma}|^3 \frac{d\sigma}{S^2} + \int_I u_{\sigma\sigma}^2 d\sigma \right) \\ &\leq 2 \left(\int_I u_{\sigma\sigma\sigma}^2 \frac{d\sigma}{S^2} \right)^{1/2} \left(\int_I u_{\sigma\sigma}^2 d\sigma \right)^{1/2} \\ &\quad + C \left(\int_I u_{\sigma\sigma}^4 \frac{d\sigma}{S^4} \right)^{1/2} \left(\int_I u_{\sigma\sigma}^2 d\sigma \right)^{1/2} + C \int_I u_{\sigma\sigma}^2 d\sigma. \end{aligned} \quad (2.35)$$

Plugging (2.34)-(2.35) into (2.33) and using Young's inequality yields

$$\begin{aligned} \int_I u_{\sigma\sigma}^4 \frac{d\sigma}{S^4} &\leq 2 \left(\int_I u_{\sigma\sigma\sigma}^2 \frac{d\sigma}{S^2} \right)^{1/2} \left(\int_I u_{\sigma\sigma}^2 d\sigma \right)^{3/2} \\ &\quad + \frac{1}{2} \int_I u_{\sigma\sigma}^4 \frac{d\sigma}{S^4} + C \left(\int_I u_{\sigma\sigma}^2 d\sigma \right)^3 + C. \end{aligned}$$

Finally, using here Young's inequality once more time we deduce (2.29). $\square$

Consider a time interval $[0, T^*]$ with $T^* > 0$ slightly smaller than the blow up time T^{bu} of (2.24). As a byproduct of Lemma 2 (cf. (2.30)) we then have for any $0 < T \leq \min\{T^\varepsilon, T^*\}$

$$\sup_{t \in [0, T]} \|u_{\sigma\sigma}\|_{L^2(I)}^2 + \varepsilon \int_0^T \|u_{\sigma\sigma\sigma}\|_{L^2(I)}^2 dt + \int_0^T \int_I \|u_{\sigma\sigma\sigma}\|_{L^2(I)}^2 dt \leq C \quad (2.36)$$

where $u := u^\varepsilon(\sigma, t)$ is the solution of (2.16) described in Proposition 1, and C is independent of ε and T . In order to show that the solution of (2.16) exists on a time interval independent of ε , it remains to obtain a uniform in ε estimate on the growth of $\|u^\varepsilon - u_0\|_{C(I)}$ in time. Arguing as in the end of the proof of Proposition 1 and using (2.36) one can prove

Lemma 4. *Assume that $u_0 \in H_{per}^2(I)$, $\|u_0\|_{L^\infty(I)} < \delta_0$ and assume that the solution u^ε of (2.16) satisfies $|u^\varepsilon(\sigma, t)| \leq \delta_0$ on $I \times [0, T^\varepsilon]$. Then for all $0 < t \leq \min\{T^\varepsilon, T^*\}$,*

$$\|u^\varepsilon - u_0\|_{C(I)}^4 \leq C(e^t - 1) \quad (2.37)$$

where C is independent of ε . In particular, there exists $0 < T^{**} \leq T^*$, independent of ε , such that $\sup\{\|u^\varepsilon(t)\|_{L^\infty(I)}; 0 \leq t \leq \min\{T^\varepsilon, T^{**}\}\} < \delta_0$.

Combining Proposition 1 with Lemma 2 and Lemma 4 we see that the solution u^ε of (2.16) exists on the time interval $[0, T^{**}]$ and (2.36) holds with $T = T^{**}$. Now, it is not hard to pass to the limit $\varepsilon \rightarrow 0$ in (2.16). Indeed, exploiting (2.36) we see that, up to extracting a subsequence, $u^\varepsilon \rightharpoonup u$ weak star in $L^\infty(0, T^{**}; H_{per}^2(I))$ as $\varepsilon \rightarrow 0$. Using (2.36) in (2.15) we also conclude that the family $\{u_t^\varepsilon\}_{0 < \varepsilon \leq 1}$ is bounded in $L^2(I \times [0, T^{**}])$. Combining uniform estimates on $\|u_{\sigma\sigma\sigma}^\varepsilon\|_{L^2(I \times [0, T])}$ (from (2.36)) and $\|u_t^\varepsilon\|_{L^2(I \times [0, T^{**}])}$ we deduce $u^\varepsilon \rightarrow u$ strongly in $L^2(0, T^{**}; H_{per}^2(I)) \cap C(0, T^{**}; H_{per}^1(I))$. Moreover, $u_t^\varepsilon + \varepsilon u_{\sigma\sigma\sigma}^\varepsilon \rightharpoonup u_t$ weak star in $L^\infty(0, T^{**}; L^2(I))$ and $u_t^\varepsilon + \varepsilon u_{\sigma\sigma\sigma}^\varepsilon \rightarrow u_t$ strongly in $L^2(0, T^{**}; H_{per}^2(I))$. Thus, in the limit we obtain a solution u of (2.8). That is we have proved

Theorem 2. *(Existence for smooth initial data) For any $u_0 \in H_{per}^2(I)$ such that $\|u_0\|_{L^\infty(I)} < \delta_0$ there exists a solution u of (2.8) on a time interval $[0, T]$, with $T > 0$ depending on u_0 .*

Remark 6. *Note that the time interval in Theorem 2 can be chosen universally for all u_0 such that $\|u_0\|_{L^\infty(I)} \leq \alpha < \delta_0$ and $\|u_0\|_{H^2(I)} \leq M < \infty$, that is $T = T(M, \alpha) > 0$.*

Step 4. *Passing to $W^{1,\infty}$ initial data*

In this step we consider a solution u of (2.8) granted by Theorem 2 and show that the requirement on H^2 smoothness of the initial data can be weakened to $W^{1,\infty}$. To this end we pass to the limit in (2.8) with an approximating sequence of smooth initial data.

The following result establishes a bound on $\|u\|_{L^\infty(I)}$ independent of the H^2 -norm of initial data (unlike in Lemma 4) and provides also an estimate for $\|u\|_{W^{1,\infty}(I)}$.

Lemma 5. *Let u be a solution of (2.8) (with initial value u_0) on the interval $[0, T]$ satisfying $\|u(t)\|_{L^\infty(I)} \leq \delta_0$ for all $t < T$. Then*

$$\|u(t)\|_{L^\infty(I)} \leq \|u_0\|_{L^\infty(I)} + Rt \quad (2.38)$$

where $R \geq 0$ is a constant independent of u_0 . Furthermore, the following inequality holds

$$\|u_\sigma(t)\|_{L^\infty(I)} \leq a_1(t), \quad (2.39)$$

where $a_1(t)$ is the solution of

$$\frac{da_1}{dt} = P_1 a_1^2 + Q_1 a_1 + R_1, \quad a(0) = \|(u_0)_\sigma\|_{L^\infty(I)} \quad (2.40)$$

(continued by $+\infty$ after the blow up time) and P_1, Q_1, R_1 are positive constants independent of u_0 .

Proof. Both bounds (2.38) and (2.39) are established by using the maximum principle.

Consider $g(\sigma, t) = g(t) := \|u_0\|_{L^\infty(I)} + Rt$, where $R > 0$ is to be specified. Since Φ is bounded it holds that $g_t - \Phi(g_t) \geq R - \sup \Phi$. Assuming that

$u - g$ attains its maximum on $(0, t] \times I$, say at (σ_0, t_0) , we have $u_\sigma(\sigma_0, t_0) = 0$, $u_{\sigma\sigma}(\sigma_0, t_0) \leq 0$, $g_t(\sigma_0, t_0) \leq u_t(\sigma_0, t_0)$ and $S/(1 - u\kappa_0) = 1$. Using (2.8) and monotonicity of the function $V - \Phi(V)$ we also get for $t = t_0$, $\sigma = \sigma_0$

$$\begin{aligned} R - \sup \Phi &\leq g_t - \Phi(g_t) \leq u_t - \frac{S}{1 - u\kappa_0} \Phi\left(\frac{1 - u\kappa_0}{S} u_t\right) \\ &\leq \frac{\kappa_0}{1 - u\kappa_0} - \frac{1}{L[u]} \left(\int_I \Phi\left(\frac{1 - u\kappa_0}{S} u_t\right) S d\sigma + 2\pi \right). \end{aligned}$$

The last term in this inequality is uniformly bounded for all functions u satisfying $|u| \leq \delta_0$, and therefore $u - g$ cannot attain its maximum on $(0, t] \times I$ when R is sufficiently large, hence $u(\sigma, t) \leq \|u_0\|_{L^\infty(I)} + Rt$. Similarly one proves that $u(\sigma, t) \geq -\|u_0\|_{L^\infty(I)} - Rt$.

To prove (2.39) we write down the equation obtained by differentiating (2.8) in σ (cf. (2.26)),

$$\begin{aligned} u_{\sigma t} - \frac{u_{\sigma\sigma\sigma}}{S^2(1 - \Phi'(V))} + \frac{\Phi'(V) + 2}{(1 - \Phi'(V))S^4} u_\sigma u_{\sigma\sigma}^2 &= A u_{\sigma\sigma} \\ &+ B + \left(\frac{S}{1 - u\kappa_0} \right)_\sigma \left(\Phi(V) - \frac{2\pi}{L[u]} - \frac{1}{L[u]} \int_I \Phi(V) S d\sigma \right), \end{aligned} \quad (2.41)$$

where we recall that $A(\sigma, V, u, p)$ and $B(\sigma, V, u, p)$ are bounded continuous functions on $I \times \mathbb{R} \times [-\delta_0, \delta_0] \times \mathbb{R}$. Consider the function $u_\sigma(\sigma, t) - a_1(t)$, with $a_1(t)$ satisfying $a_1(0) = \|u_\sigma(0)\|_{L^\infty(I)}$. If this function attains its maximum over $I \times (0, t]$ at a point (σ_0, t_0) with $t_0 > 0$, we have at this point

$$\begin{aligned} \frac{da_1}{dt} \leq u_{\sigma t} &\leq B + \left(\frac{S}{1 - u\kappa_0} \right)_\sigma \left(\Phi(V) - \frac{2\pi}{L[u]} - \frac{1}{L[u]} \int_I \Phi(V) S d\sigma \right) \\ &< C_1 + C_2 u_\sigma^2 + C_3 u_\sigma, \end{aligned} \quad (2.42)$$

where C_1, C_2, C_3 are some positive constants independent of u . We see now that for $P_1 \geq C_2$, $Q_1 \geq C_3$ and $R_1 \geq C_1$, either $u_\sigma(\sigma_0, t_0) \leq a_1(t_0)$ or inequality (2.42) contradicts (2.40). This yields that for all $\sigma \in I$ and all $t < \sup\{\tau; a_1(\tau) \text{ is finite}\}$,

$$u_\sigma(\sigma, t) - a_1(t) \leq \max\{0, \max_{\sigma \in I} u_\sigma(\sigma, 0) - a_1(0)\} = 0.$$

The lower bound for $u_\sigma(\sigma, t)$ is proved similarly. $\square$

Lemma 5 shows that for some $T_1 > 0$ the solution u of (2.8) satisfies

$$\|u\|_{L^\infty(I)} < \delta_0 \text{ and } \|u_\sigma\|_{L^\infty(I)} \leq M_1, \quad (2.43)$$

when $0 < t \leq \min\{T, T_1\}$, where T is the maximal time of existence of u . Moreover, T_1 and constant M_1 in (2.43) depend only on the choice of constants $0 < \alpha < 1$ and $M > 0$ in the bounds for the initial data $|u_0| \leq \alpha$ and $\|(u_0)_\sigma\|_{L^\infty(I)} \leq M$. We prove next that actually $T \geq T_1$.

Lemma 6. *Let u solve (2.8) and let (2.43) hold on $0 \leq t \leq T_2$, where $0 < T_2 \leq T_1$. Then for any $\delta > 0$*

$$|u_\sigma(\sigma', t) - u_\sigma(\sigma'', t)| \leq C_\delta |\sigma' - \sigma''|^\vartheta \text{ when } \delta \leq t \leq T_2, \quad (2.44)$$

where $0 < \vartheta < 1$ and C_δ depend only on δ and constant M_1 in (2.43).

Proof. Recall from Lemma 1 that Ψ denotes the inverse function of $V - \Phi(V)$, and that

$$\lambda(t) := \frac{1}{L[u]} \left(2\pi + \int_I \Phi(V) S d\sigma \right),$$

so that the solution V of the equation $V = \Phi(V) + \kappa - \lambda$ is given by $\Psi(\kappa - \lambda)$. This allows us to write the equation (2.41) for $v := u_\sigma$ in the form of a quasilinear parabolic equation,

$$v_t = \left(a(v_\sigma, \sigma, t) \right)_\sigma - \frac{\lambda(t) u_\sigma}{S(u)(1 - u\kappa_0)} v_\sigma - \lambda(t) (u\kappa_0)_\sigma \frac{u_\sigma^2}{S(u)(1 - u\kappa_0)^2}, \quad (2.45)$$

where

$$a(p, \sigma, t) = \frac{S(u)}{1 - u\kappa_0} \left(\Phi(\Psi[\bar{\kappa}(p, \sigma, t) - \lambda(t)]) + \bar{\kappa}(p, \sigma, t) \right)$$

with

$$\bar{\kappa}(p, \sigma, t) = \frac{1}{S^3(u)} \left((1 - u\kappa_0)p + 2\kappa_0 u_\sigma^2 + (\kappa_0)_\sigma u_\sigma u + \kappa_0(1 - u\kappa_0)^2 \right).$$

Note that setting $V := \Psi[\bar{\kappa}(p, \sigma, t) - \lambda(t)]$ we have

$$\frac{\partial a}{\partial p}(p, \sigma, t) = \frac{S(u)}{1 - u\kappa_0} \left(\frac{\Phi'(V)}{1 - \Phi'(V)} + 1 \right) \frac{\partial \bar{\kappa}}{\partial p}(p, \sigma, t) = \frac{1}{S^2(u)(1 - \Phi'(V))}.$$

It follows that if (2.43) holds then the quasilinear divergence form parabolic equation (2.45) satisfies all necessary conditions to apply classical results on Hölder continuity of bounded solutions, see e.g. [21] [Chapter V, Theorem 1.1]; this completes the proof. $\square$

The property of Hölder continuity established in Lemma 6 allows us to prove the following important result

Lemma 7. *Let u solve (2.8) and assume that (2.43) holds then for any $\tau \geq \delta > 0$*

$$\|u_{\sigma\sigma}(t)\|_{L^2(I)}^2 \leq (\|u_{\sigma\sigma}(\tau)\|_{L^2(I)}^2 + 1) e^{P_2(t-\tau)} \text{ when } t \geq \tau, \quad (2.46)$$

where P_2 depends only on δ and constant M_1 in (2.43) (the latter constant depend not on the H^2 norm of u_0 but on its norm in the space $W^{1,\infty}(I)$).

Proof. Introduce smooth cutoff functions $\phi_n(\sigma)$ satisfying

$$\begin{cases} \phi_n(\sigma) = 1 \text{ on } [1/n, 2/n] \\ 0 \leq \phi_n(\sigma) \leq 1 \text{ on } [0, 1/n] \cup [2/n, 3/n] \\ \phi_n(\sigma) = 0 \text{ otherwise,} \end{cases} \quad \text{and} \quad |(\phi_n)_\sigma| \leq Cn. \quad (2.47)$$

Consider $t \geq \delta$. Multiply (2.41) by $-(\phi_n^2 u_{\sigma\sigma})_\sigma$ and integrate in σ , integrating by parts in the first term. We obtain

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \int_I \phi_n^2 u_{\sigma\sigma}^2 d\sigma + \frac{1}{\gamma'} \int_I \phi_n^2 u_{\sigma\sigma\sigma}^2 d\sigma &\leq C \int_I \phi_n^2 (u_{\sigma\sigma}^2 + |u_{\sigma\sigma}|) |u_{\sigma\sigma\sigma}| d\sigma \\ &\quad + Cn \int_I \phi_n (|u_{\sigma\sigma\sigma}| |u_{\sigma\sigma}| + |u_{\sigma\sigma}|^2 + |u_{\sigma\sigma}|^3) d\sigma, \end{aligned} \quad (2.48)$$

where $\gamma' > 0$ and C are independent of u and n . Applying the Cauchy-Schwarz and Young's inequalities to various terms in the right hand side of (2.48) leads to

$$\frac{1}{2} \frac{d}{dt} \int_I \phi_n^2 u_{\sigma\sigma}^2 d\sigma + \frac{1}{2\gamma'} \int_I \phi_n^2 u_{\sigma\sigma\sigma}^2 d\sigma \leq C_1 \int_I \phi_n^2 u_{\sigma\sigma}^4 d\sigma + C_2 n^2 \int_{s(\phi_n)} (|u_{\sigma\sigma}|^2 + 1) d\sigma, \quad (2.49)$$

where C_1, C_2 are independent of u and n and $s(\phi_n)$ denotes the support of ϕ_n . Next we apply the following interpolation type inequality (see, e.g., [21], Chapter II, Lemma 5.4) to the first term in the right hand side of (2.49):

$$\begin{aligned} \int_I \phi_n^2 u_{\sigma\sigma}^4 d\sigma &\leq C_3 \left(\sup\{|u_\sigma(\sigma') - u_\sigma(\sigma'')|; \sigma', \sigma'' \in s(\phi_n)\} \right)^2 \\ &\quad \times \left(\int_I \phi_n^2 u_{\sigma\sigma\sigma}^2 d\sigma + \int_{s(\phi_n)} |u_{\sigma\sigma}|^2 |(\phi_n)_\sigma|^2 d\sigma \right). \end{aligned} \quad (2.50)$$

Now we use (2.44) in (2.50) to bound $\sup\{|u_\sigma(\sigma') - u_\sigma(\sigma'')|; \sigma', \sigma'' \in s(\phi_n)\}$ by $C_\delta(1/n)^\vartheta$ and choose n so large that $C_2 C_3 C_\delta^2 (1/n)^{2\vartheta} \leq 1/4\gamma'$, then (2.49) becomes

$$\frac{1}{2} \frac{d}{dt} \int_I \phi_n^2 u_{\sigma\sigma}^2 d\sigma + \frac{1}{4\gamma'} \int_I \phi_n^2 u_{\sigma\sigma\sigma}^2 d\sigma \leq C_4 n^2 \int_{s(\phi_n)} (|u_{\sigma\sigma}|^2 + 1) d\sigma. \quad (2.51)$$

It is clear that we can replace $\phi_n(\sigma)$ in (2.51) by its translations $\phi_n(\sigma + k/n)$, $k \in \mathbb{Z}$, then taking the sum of obtained inequalities we derive

$$\frac{1}{2} \frac{d}{dt} \int_I \bar{\phi}_n u_{\sigma\sigma}^2 d\sigma + \frac{1}{4\gamma'} \int_I \bar{\phi}_n u_{\sigma\sigma\sigma}^2 d\sigma \leq C_5 \left(\int_I |u_{\sigma\sigma}|^2 d\sigma + 1 \right), \quad (2.52)$$

where C_5 is independent of u , and $\bar{\phi}_n = \sum_k \phi_n^2(\sigma + k/n)$. Note that $1 \leq \bar{\phi}_n \leq 3$, therefore applying Grönwall's inequality to (2.52) we obtain (2.46). $\square$

Corollary 2. *Assume that a solution u of (2.8) exists on $[0, T]$ for some $T > 0$, and (2.43) holds. Then, given an arbitrary positive $\delta < T$, we have*

$$\int_{\tau}^T \int_I |u_{\sigma\sigma}|^2 d\sigma dt \leq \tilde{C}_{\delta} \|u_{\sigma\sigma}(\tau)\|_{L^2(I)}^2, \quad (2.53)$$

for all $\delta \leq \tau \leq T$, where $\tilde{C}_{\delta}$ depends only on δ .

Proof. The bound follows by integrating (2.52) in time and using (2.46). $\square$

Using Lemma 7 and Lemma 5, taking into account also Remark 6, we see that solutions in Theorem 2 exist on a common interval $T = T(\alpha, M)$, provided that $\|u_0\| \leq \alpha < 1$ and $\|(u_0)_{\sigma}\|_{L^{\infty}(I)} \leq M$.

In the following Lemma we establish an integral bound for $\|u_{\sigma\sigma}\|_{L^2(I)}$.

Lemma 8. *Let u be a solution (2.8) on $[0, T]$ satisfying (2.43). Then*

$$\|u_{\sigma\sigma}\|_{L^2(I \times [0, T])}^2 \leq C, \quad (2.54)$$

where C depends only on the constants in (2.43).

Proof. To obtain (2.54) one multiplies (2.8) by $u_{\sigma\sigma}$ integrates in σ , integrating by parts in the first term. Then applying the Cauchy-Schwarz and Young's inequalities and integrating in t one derives (2.54), details are left to the reader. $\square$

Various estimates obtained in Lemmas 5, 7, and Corollary 2 as well as Lemma 8 make it possible to pass to general initial data $u_0 \in W_{per}^{1, \infty}(I)$. Indeed, assume $\alpha := \|u_0\|_{L^{\infty}(I)} < 1$ and let $M := \|(u_0)_{\sigma}\|_{L^{\infty}(I)}$. Construct a sequence $u_0^k \rightharpoonup u_0$ converging weak star in $W_{per}^{1, \infty}(I)$ as $k \rightarrow \infty$, where $u_0^k \in H_{per}^2(I)$. This can be done in a standard way by taking convolutions with mollifiers so that $\|u_0^k\|_{L^{\infty}(I)} \leq \alpha$ and $\|(u_0^k)_{\sigma}\|_{L^{\infty}(I)} \leq M$. Let $u^k(\sigma, t)$ be solutions of (2.8) corresponding to the initial data $u_0^k(\sigma)$. We know that all these solutions exist on a common time interval $[0, T]$ and that we can choose $T > 0$ such that (2.43) holds with a constant M_1 independent of k . By Lemma 8 the sequence $u^k(\sigma, t)$ is bounded in $L^2(0, T; H^2(I))$. Therefore, up to a subsequence, $u^k(\sigma, t)$ weakly converges to some function $u(\sigma, t) \in L^2(0, T; H^2(I))$. Using (2.8) we conclude that $u_t^k(\sigma, t)$ converge to $u_t(\sigma, t)$ weakly in $L^2(0, T; L^2(I))$. It follows, in particular, that $u(\sigma, 0) = u_0(\sigma)$. Next, let $\delta > 0$ be sufficiently small. It follows from Lemma 8 that there exists $\tau \in [\delta, 2\delta]$ such that $\|u_{\sigma\sigma}^k(\tau)\| \leq C/\delta$. Then by Lemma 7 and Corollary 2 norms of u^k in $L^{\infty}(2\delta, T; H_{per}^2(I))$ and $L^2(2\delta, T; H_{per}^3(I))$ are uniformly bounded. Thus $u^k(\sigma, t)$ converge to $u(\sigma, t)$ strongly in $L^2(2\delta, T; H_{per}^2(I))$. This in turn implies that $u_t^k(\sigma, t)$ converge to $u_t(\sigma, t)$ strongly in $L^2(0, T; L^2(I))$. Therefore the function $u(\sigma, t)$ solves (2.8) on $[2\delta, T]$. Since $\delta > 0$ can be chosen arbitrarily small, Theorem 1 is completely proved.

3. Non-existence of traveling wave solutions

The following result proves that smooth (H^2) non-trivial traveling wave solutions of (1.1) do not exist in the subcritical regime (i.e., when conditions of Theorem 1 are satisfied). We interpret this result physically as a regime where persistent cell motion is inhibited. For example, if $\beta < \beta_{cr}$ in (1.3) (see Remark 2), then the sharp interface limit equation satisfies the conditions of Theorem 1. Physically β incorporates strength of actin polymerization as well as strength of adhesive bonds. The non-existence of traveling wave solutions implies that membrane tension (curvature) is sufficiently strong to prevent the locomotion mechanisms from effectively functioning. This result parallels simulations in [33], which show that a minimal driving force exists which is necessary to initiate persistent motion of cells.

The idea of the proof is to write equations of motion of the front and back parts of a curve, which is supposed to be a traveling wave solution, using a Cartesian parametrization. Next we show that it is not possible to form a closed, H^2 -smooth curve from these two parts (see Figure 3). We note that every traveling wave curve is always H^2 smooth since it is the same profile for all times up to translations.

Theorem 3. *Let Φ satisfy the conditions of Theorem 1. If $\Gamma(\sigma, t)$ is a family of closed curves which are a traveling wave solution of (1.1), that is $\Gamma(\sigma, t) = \Gamma(\sigma, 0) + vt$, then $v = 0$ and $\Gamma(\sigma, 0)$ is a circle.*

Proof. It is clear that if $v = 0$ then a circle is the unique solution of (1.1). Let $\Gamma(\sigma, t)$ be a traveling wave solution of (1.1) with non-zero velocity v . By Theorem 1, $\Gamma(\cdot, t)$ is smooth (H^2) for all $t > 0$. By rotation and translation, we may assume without loss of generality that $v_x = 0$, $v_y = c$ with $c > 0$ and that $\Gamma(\sigma, t)$ is contained in the upper half plane for all $t \geq 0$. Let $\Gamma(\sigma_0, 0)$ be a point of $\Gamma(\sigma, 0)$ which is closest to the x -axis. Without loss of generality we assume that $\Gamma(\sigma_0, 0) = 0$. Locally, we can represent $\Gamma(\sigma, t)$ as a graph over the x -axis, $y = y(x) + ct$. Observe that the normal velocity is given by

$$V = \frac{c}{\sqrt{1 + (y'(x))^2}} \quad (3.1)$$

and the curvature κ is expressed as

$$\kappa(x) = \frac{y''(x)}{(1 + (y'(x))^2)^{3/2}}. \quad (3.2)$$

Adopting the notation

$$f_\lambda^c(z) := \left(\frac{c}{\sqrt{1 + z^2}} - \Phi \left(\frac{c}{\sqrt{1 + z^2}} \right) + \lambda \right) (1 + z^2)^{3/2}, \quad (3.3)$$

it follows that y solves the equation

$$y'' = f_\lambda^c(y') \quad (3.4)$$

where, by construction,

$$y(0) = y'(0) = 0. \quad (3.5)$$

Observe that (3.4) is a second order equation for y which depends only on y' . Thus, we may equivalently study $w := y'$ which solves

$$w' = f_\lambda^c(w), \quad w(0) = 0. \quad (3.6)$$

Note that (3.6) is uniquely solvable on its interval of existence by Lipschitz continuity of f_λ^c . Further, the definition of f_λ^c guarantees that w has reflectional symmetry over the y -axis.

If (3.6) has a global solution, w , then it is immediate that $y(x) := \int_0^x w(s)ds$ cannot describe part of a closed curve. As such we restrict to the case where w has finite blow-up.

Assume the solution w_B of (3.6) has finite blow-up, $w_B(x) \rightarrow +\infty$ as $x \rightarrow x_B^*$ for some $0 < x_B^* < \infty$. Then $y_B(x) := \int_0^x w_B(s)ds$ has a vertical tangent vector at $\pm x_B^*$. To extend the solution beyond the point x_B^* , we consider w_F , the solution of (3.6) with right hand side f_λ^{-c} . As above we assume that w_F has a finite blow-up at $x_F^* > 0$. Defining $y_F(x) := \int_0^x w_F(s)ds$, we have the following natural transformation,

$$\hat{y}_F(x) := -y_F(x - (x_B^* - x_F^*)) + y_B(x_B^*) + y_B(x_F^*). \quad (3.7)$$

Note that gluing $\hat{y}_F$ to y_B forms an H^2 smooth curve at the point $(x_B^*, y_B(x_B^*))$ if and only if $w_F(x) \rightarrow +\infty$ as $x \rightarrow x_F^*$. We claim that this is the unique, smooth extension of y_B at x_B^* . To that end, consider the rotated coordinate system $(x, y) \mapsto (y, -x)$. In this frame, the traveling wave moves with velocity $v_x = c$, $v_y = 0$, and can be locally represented as the graph $x = x(y) + ct$, $x(y)$ solving

$$x'' = g_\lambda^c(x') \quad (3.8)$$

with

$$g_\lambda^c(z) := \left(\frac{-cz}{\sqrt{1+z^2}} - \Phi\left(\frac{-cz}{\sqrt{1+z^2}}\right) + \lambda \right) (1+z^2)^{3/2}. \quad (3.9)$$

As before, g_λ^c is Lipschitz and so solutions of (3.8) are unique, establishing the claim.

To complete the proof, we prove that $x_F^* > x_B^*$, which guarantees that the graphs of $y_B(x)$ and $\hat{y}_F(x)$ can not smoothly meet at $-x_B^*$. Due to the monotonicity of $V - \Phi(V)$ we have that for any w , $f_\lambda^c(w) > f_\lambda^{-c}(w)$. Thus $w_B' > w_F'$ for any fixed w . Since $w_B(0) = w_F(0)$, we deduce that $w_B(x) > w_F(x)$ for all $x > 0$. It follows that $x_F^* \geq x_B^*$. Let $x_2 \in (0, x_B^*)$ and observe by continuity of w_B that there exists $x_1 \in (0, x_2)$ such that $w_B(x_1) = w_F(x_2)$. Consider the solution $\tilde{w}$ of

$$\tilde{w}' = f_\lambda^c(\tilde{w}) \quad \tilde{w}(x_2) = w_F(x_2). \quad (3.10)$$

Note that $\tilde{w}(x) = w_B(x - (x_2 - x_1))$ and so the blow-up of $\tilde{w}(x)$ occurs at $x_B^* + x_2 - x_1$. Since $\tilde{w}(x) \geq w_F(x)$ for all $x \in (x_2, x_B^* + x_2 - x_1)$ it follows that $x_F^* \geq x_B^* + x_2 - x_1 > x_B^*$. $\square$

Figure 3: A closed curve cannot be a traveling wave solution

4. Numerical simulation; comparison with volume preserving curvature motion

The preceding Section 2 proves short time existence of curves propagating via (1.1), and Section 3 shows the nonexistence of traveling wave solution. In this section we will numerically solve (1.1) and for that purpose we will introduce a new splitting algorithm. Using this algorithm, we will be able to study the long time behavior of the cell motion by numerical experiments, in particular, we find that both non-linearity and asymmetry of the initial shape will result in a net motion of the cell.

Specifically we numerically solve the equation (1.1) written so that the dependence on β is explicit ($\beta\Phi_0(V) = \Phi(V)$, see remark 1):

$$V(s, t) = \kappa(s, t) + \beta\Phi_0(V(s, t)) - \frac{1}{|\Gamma(t)|} \int (\kappa(s', t) + \beta\Phi_0(V(s', t))) ds', \quad (4.1)$$

We propose an algorithm and use it to compare curves evolving by (4.1) with $0 < \beta < \beta_{cr}$, with curves evolving by volume preserving curvature motion ($\beta = 0$). For simplicity, we assume that $\Phi_0(V)$ defined via (1.5) has a Gaussian shape $\Phi_1(V) := Ae^{-B|V|^2}$. Then Φ_0 and Φ_1 share qualitative features such as even symmetry and exponential decay (see Figure 4) but use of Φ_1 significantly decreases computational time in numerical simulations. Moreover, comparison of simulations for functions Φ_0 and Φ_1 show similar qualitative and quantitative results.

4.1. Algorithm to solve (4.1)

In the case $\beta = 0$ (corresponding to volume preserving curvature motion), efficient techniques such as level-set methods [28, 30] and diffusion generated motion methods [24, 29] can be used to accurately simulate the evolution of curves by (4.1). Furthermore, other modern numerical schemes (e.g., [2, 9, 10, 25]) are

Figure 4: Graph of Φ_0 (computed via (1.5)-(1.6) using the software package Chebfun [11]) and Φ_1 (with $A = 0.012$, $B = 0.011$; least squares fitting of $\log(\Phi_0)$ with $\log(\Phi_1)$)

well suited to solve more general geometric flow problems. However, there is no straightforward way to implement these methods when $\beta > 0$ since V enters equation (4.1) non-linearly, and thus solving (4.1) requires special treatment. Our method is simple to implement and shows numerical convergence in the subcritical regime, $\beta < \beta_{cr}$. Furthermore, since steady state curve profiles are observed in this regime, we believe that simulations are not sensitive to the specific numerical method (unlike in the study of moving states). In the supercritical regime $\beta > \beta_{cr}$ more sophisticated numerical techniques need to be developed due to non-uniqueness and instabilities [3]. Here we expect that more accurate and reliable discretizations and non-linear solvers will be needed. This case is currently under investigation by the authors and will be addressed in future papers.

Moreover, due to the non-local term, a naive discrete approximation of (4.1) leads to a system of non-linear equations. Instead of using a non-linear root solver, we introduce a *splitting scheme* which resolves the two main computational difficulties (non-linearity and volume preservation) separately.

In particular, we decouple the system by solving the N local equations

$$V_i = \kappa_i + \beta \Phi_1(V_i) - C, \quad (4.2)$$

where C is a constant representing the volume preservation constraint which must be determined. For $\beta < \beta_{cr}$, (4.2) can be solved using an iterative method which (experimentally) converges quickly. The volume constraint can be enforced by properly changing the value of C .

We recall the following standard notations. Let $p_i = (x_i, y_i)$, $i = 1, \dots, N$

be a discretization of a curve. Then $h := 1/N$ is the grid spacing and

$$Dp_i := \frac{p_{i+1} - p_{i-1}}{2h} \text{ and } D^2p_i := \frac{p_{i+1} - 2p_i + p_{i-1}}{h^2} \quad (h = 1/N) \quad (4.3)$$

are the second-order centered approximations of the first and second derivatives, respectively. Additionally, $(a, b)^\perp = (-b, a)$.

We introduce the following algorithm for a numerical solution of (4.1).

Algorithm 1. *To solve (4.1) up to time $T > 0$ given the initial shape $\Gamma(0)$.*

Step 1: *(Initialization) Given a closed curve $\Gamma(0)$, discretize it by N points $p_i^0 = (x_i^0, y_i^0)$.*

Use the shoelace formula to calculate the area of $\Gamma(0)$:

$$A^o = \frac{1}{2} \left| \sum_{i=1}^{n-1} x_i^0 y_{i+1}^0 + x_n^0 y_1^0 - \sum_{i=1}^{n-1} x_{i+1}^0 y_i^0 - x_1^0 y_n^0 \right|. \quad (4.4)$$

Set time $t := 0$, time step $\Delta t > 0$, and the auxiliary parameter $C := 0$.

Step 2: *(time evolution) If $t < T$, calculate the curvature at each point, κ_i using the formula*

$$\kappa_i = \frac{\det(Dp_i^t, D^2p_i^t)}{\|Dp_i^t\|^3}, \quad (4.5)$$

where $\|\cdot\|$ is the standard Euclidean norm. Use an iteration method to solve

$$V_i^t = \kappa_i + \beta \Phi_1(V_i^t) - C \quad (4.6)$$

to within a fixed tolerance $\varepsilon > 0$.

Define the temporary curve

$$p_i^{temp} := p_i^t + V_i^t \nu_i \Delta t,$$

where $\nu_i = (Dp_i^0)^\perp / \|Dp_i^0\|$ is the inward pointing normal vector.

Calculate the area of the temporary curve A^{temp} using the shoelace formula (4.4) and compute the discrepancy

$$\Delta A := (A^{temp} - A^o) \cdot (A^o)^{-1},$$

If $|\Delta A|$ is larger than a fixed tolerance ε , adjust $C \mapsto C + \Delta A$ and return to solve (4.6) with updated C . Otherwise define $p_i^{t+\Delta t} := p_i^{temp}$ and

$$\Gamma(t + \Delta t) := \{p_i^{t+\Delta t}\},$$

Let $t = t + \Delta t$, if $t < T$ iterate Step 2; else, stop.

In practice, we additionally reparametrize the curve by arc length after a fixed number of time steps in order to prevent regions with high density of points p_i which could lead to potential numerical instability and blow-up.

Remark 7. In Step 2, for $\beta \leq 1$, the right hand side of (4.6) is contractive and thus we may guarantee convergence of the iterative solver to the solution of (4.6).

We implement the above algorithm in C++ and visualize the data using Scilab. We choose the time step Δt and spatial discretization step $h = \frac{1}{N}$ so that

$$\frac{\Delta t}{h^2} \leq \frac{1}{2}, \quad (4.7)$$

in order to ensure stability. Further, we take an error tolerance

$$\varepsilon = .0001$$

in Step 2 for both iteration in (4.6) and iteration in C .

4.2. Convergence of numerical algorithm

To validate results, we check convergence of the numerical scheme in the following way: taking a fixed initial curve $\Gamma(0)$, we discretize it with varying numbers of points: $N = 2^m$ for $m = 5, \dots, 8$, and fix a final time step sufficiently large so that $\Gamma(k\Delta t)$ reaches a steady state circle. Since there is no analytic solution to (1.1), there is no absolute measure of the error. Rather, we define the error between successive approximations N and $2N$. To this end, we calculate the center location, $C_N = (C_N^1, C_N^2)$, of each steady state circle as the arithmetic mean of the data points. Define the error between circles as

$$err_N = \|C_N - C_{2N}\|_{\ell^2}.$$

Then, the convergence rate can be expressed as

$$\rho := \lim_{N \rightarrow \infty} \rho_N = \lim_{N \rightarrow \infty} \log_2 \frac{err_N}{err_{2N}}.$$

We record our results in Table 1, as well as in Figure 5. Note that $\rho \approx 1$, namely our numerical method is first-order.

N	err_N	ρ_N
32	.2381754	.9141615
64	.1263883	.9776830
128	.0641793	1.0019052
256	.0320473	-

Table 1: Table for stability of numerical simulations

Figure 5: Convergence of numerical simulation for decreasing mesh size $h = 1/N$ (zoomed in)

4.3. Numerical experiments for the long time behavior of cell motion

We next present two numerical observations for the subcritical case $\beta < \beta_{cr}$.

1. *If a curve globally exists in time, then it tends to a circle.*

That is, in the subcritical β regime, curvature motion dominates non-linearity due to $\Phi(V)$. This is natural, since for small β the equation (4.1) can be viewed as a perturbation of volume preserving curvature motion, and it has been proved (under certain hypotheses) that curves evolving via volume preserving curvature motion converge to circles [13].

In contrast, the second observation distinguishes the evolution of (4.1) from volume preserving curvature motion.

2. *There exist curves whose centers of mass exhibit net motion on a finite time interval (transient motion).*

The key issue in cell motility is (persistent) net motion of the cell. Although Theorem 3 implies that no non-trivial traveling wave solution of (1.1) exists, observation 2 implies that curves propagating via (4.1) may still experience a transient net motion compared to the evolution of curves propagating via volume preserving curvature motion. We investigate this transient motion quantitatively with respect to the non-linear parameter β and the initial geometry of the curve.

4.3.1. Quantitative investigation of observation 2

Given an initial curve $\Gamma(0)$ discretized into N points p_i^0 and given $0 \leq \beta < \beta_{cr}$, we let $\Gamma_\beta(k\Delta t) := \{p_i^k\}$ be the curve at time $k\Delta t$, propagating by (4.1). In particular, $\Gamma_0(k\Delta t)$ corresponds to the evolution of the curve by volume preserving curvature motion.

Our prototypical initial curve $\Gamma(0)$ is parametrized by four ellipses and is sketched in Figure 6.

Figure 6: Initial curve

$$(4 \cos(\theta), 3 \sin(\theta)) \text{ for } -\frac{\pi}{2} \leq \theta \leq \frac{\pi}{2} \quad (4.8)$$

$$(2 \cos(\theta), \frac{3}{4} \sin(\theta) + \frac{9}{4}) \text{ for } \frac{\pi}{2} \leq \theta \leq \frac{3\pi}{2} \quad (4.9)$$

$$(\zeta \cos(\theta), \frac{3}{2} \sin(\theta)) \text{ for } -\frac{\pi}{2} \leq \theta \leq \frac{\pi}{2} \quad (4.10)$$

$$(2 \cos(\theta), \frac{3}{4} \sin(\theta) - \frac{9}{4}) \text{ for } \frac{\pi}{2} \leq \theta \leq \frac{3\pi}{2}. \quad (4.11)$$

The parameter ζ determines the depth of the non-convex well and is used as our measure of initial asymmetry of the curve.

To study the effect of β and asymmetry on the overall motion of the curve, we measure the total transient motion by the following notion of the *drift* of Γ_β . First fix $\Gamma(0)$. Note that observation 1 implies that for sufficiently large time $k\Delta t$, $\Gamma_\beta(k\Delta t)$ and $\Gamma_0(k\Delta t)$ will both be steady state circles. Define the *drift* of Γ_β to be the distance between the centers of these two circles.

Remark 8. *Note that this definition is used in order to account for numerical errors which may accumulate over time. Numerical drift of the center of mass of the curve caused by errors/approximations is offset by “calibrating” to the $\beta = 0$ case.*

We consider the following two numerical tests:

1. *Dependence of drift on β :* Starting with the initial profile (4.8)-(4.11) with $\zeta = 1$, compute the drift of Γ_β for various values of β .

Figure 7: Overall drift of curve with $\beta = 1$ (blue, solid) compared to $\beta = 0$ (green, dashed), starting from initial data (4.8)-(4.11) with $\zeta = 2$

2. *Dependence of drift on initial asymmetry:* Starting with the initial curve (4.8)-(4.11) with $\beta = 1$, compute the drift of Γ_β for various values of ζ .

Taking $T = 20$ is sufficient for simulations to reach circular steady state. We observe that drift increases with respect to ζ and increases linearly with respect to β . These data are recorded in Figure 8.

Figure 8: Dependence of drift on the parameters β and ζ

Acknowledgments. The authors would like to extend their gratitude to the referees for their careful reading of the manuscript and insightful comments.

- [1] E. L. BARNHART, K. LEE, K. KEREN, A. MOGILNER, AND J. A. THE-RIOT, *An adhesion-dependent switch between mechanisms that determine*

motile cell shape, PLoS Biol, 9 (2011), p. e1001059.

- [2] J. W. BARRETT, H. GARCKE, AND R. NÜRNBERG, *The approximation of planar curve evolutions by stable fully implicit finite element schemes that equidistribute*, Numer. Methods Partial Differential Equations, 27 (2011), pp. 1–30.
- [3] L. BERLYAND, M. POTOMKIN, AND V. RYBALKO, *Non-uniqueness in a nonlinear sharp interface model of cell motility*, arXiv:1409.5925v1, (2014).
- [4] A. BONAMI, D. HILHORST, AND E. LOGAK, *Modified motion by mean curvature: local existence and uniqueness and qualitative properties*, Differential Integral Equations, 13 (2000), pp. 1371–1392.
- [5] K. A. BRAKKE, *The motion of a surface by its mean curvature*, Princeton University Press and University of Tokyo Press, 1978.
- [6] M. P. D. CARMO, *Differential geometry of curves and surfaces*, Pearson, 1976.
- [7] X. CHEN, *The Hele-Shaw problem and area-preserving curve-shortening motions*, Arch. Rational Mech. Anal., 123 (1993), pp. 117–151.
- [8] X. CHEN, D. HILHORST, AND E. LOGAK, *Mass conserving Allen-Cahn equation and volume preserving mean curvature flow*, Interfaces Free Bound., 12 (2010), pp. 527–549.
- [9] K. DECKELNICK AND G. DZIUK, *On the approximation of the curve shortening flow*, in Calculus of variations, applications and computations (Pont-à-Mousson, 1994), Longman Sci. Tech., 1995.
- [10] K. DECKELNICK, G. DZIUK, AND C. M. ELLIOTT, *Computation of geometric partial differential equations and mean curvature flow*, Acta Numerica, 14 (2005), pp. 139–232.
- [11] T. A. DRISCOLL, N. HALE, AND L. N. TREFETHEN, *Chebfun Guide*, Pafnuty Publications, 2014.
- [12] C. M. ELLIOTT AND H. GARCKE, *Existence results for diffusive surface motion laws*, Adv. Math. Sci. Appl., 7 (1997), pp. 467–490.
- [13] J. ESCHER AND G. SIMONETT, *The volume preserving mean curvature flow near spheres*, Proc. Amer. Math. Soc., 126 (1998), pp. 2789–2796.
- [14] M. GAGE, *On an area-preserving evolution equation for plane curves*, Contemp. Math., 51 (1986), pp. 51–62.
- [15] M. GAGE AND R. S. HAMILTON, *The heat equation shrinking convex plane curves*, J. Differential Geom., 23 (1986), pp. 69–96.

- [16] L. GIOMI AND A. DESIMONE, *Spontaneous division and motility in active nematic droplets*, Physical review letters, 112 (2014), p. 147802.
- [17] D. GOLOVATY, *The volume-preserving motion by mean curvature as an asymptotic limit of reaction-diffusion equations*, Quart. Appl. Math, 55 (1997), pp. 243–298.
- [18] M. A. GRAYSON, *The heat equation shrinks embedded plane curves to round points*, J. Differential Geom., 26 (1987), pp. 285–314.
- [19] R. J. HAWKINS, R. POINCLOUX, O. BÉNICHOU, M. PIEL, P. CHAVRIER, AND R. VOITURIEZ, *Spontaneous contractility-mediated cortical flow generates cell migration in three-dimensional environments*, Biophysical journal, 101 (2011), pp. 1041–1045.
- [20] K. KEREN, Z. PINCUS, G. M. ALLEN, E. L. BARNHART, G. MARRIOTT, A. MOGILNER, AND J. A. THERIOT, *Mechanism of shape determination in motile cells*, Nature, 453 (2008), pp. 475–480.
- [21] O. A. LADYZENSKAJA, V. A. SOLONNIKOV, AND N. N. URAL’CEVA, *Linear and quasi-linear equations of parabolic type*, The American Mathematical Society, 1968.
- [22] J. L. LIONS AND E. MAGENES, *Non-homogeneous boundary value problems and applications*, Springer-Verlag, 1972.
- [23] W. MARTH, S. PRAETORIUS, AND A. VOIGT, *A mechanism for cell motility by active polar gels*, Journal of The Royal Society Interface, 12 (2015), p. 20150161.
- [24] B. MERRIMAN, J. BENCE, AND S. OSHER, *Diffusion generated motion by mean curvature motion*, in AMS Select Lectures in Mathematics: The Computational Crystal Grower’s Workshop, J. Taylor, ed., Am. Math. Soc., 1993.
- [25] K. MIKULA AND D. SEVČOVIČ, *Computational and qualitative aspects of evolution of curves driven by curvature and external force*, Comput. Visual Sci., 6 (2004), pp. 211–225.
- [26] A. MOGILNER, *Mathematics of cell motility: have we got its number?*, J. Math. Biol., 58 (2009), pp. 105–134.
- [27] R. R. MOHAN, A. E. K. HUTCHEON, R. CHOI, J. HONG, J. LEE, R. R. MOHAN, R. A. JR., J. D. ZIESKE, AND S. E. WILSON, *Apoptosis, necrosis, proliferation, and myofibroblast generation in the stroma following LASIK and PRK*, Exp. Eye. Res., 76 (2003), pp. 71–87.
- [28] S. OSHER AND J. A. SETHIAN, *Fronts propagating with curvature dependent speed: algorithms based on Hamilton-Jacobi formulations*, J. Comput. Phys., 79 (1988), pp. 12–49.

- [29] S. J. RUUTH AND B. T. R. WETTON, *A simple scheme for volume-preserving motion by mean curvature*, J. Sci. Comput., 19 (2003), pp. 373–284.
- [30] P. SMEREKA, *Semi-implicit level set methods for curvature and surface diffusion motion*, J. Sci. Comput., 19 (2003), pp. 439–456.
- [31] E. TJHUNG, A. TIRIBOCCHI, D. MARENDUZZO, AND M. E. CATES, *A minimal physical model captures the shapes of crawling cells*, Nature communications, 6 (2015).
- [32] D. WESSELS, D. R. SOLL, D. KNECHT, W. F. LOOMIS, A. D. LOZANNE, AND J. SPUDICH, *Cell motility and chemotaxis in dictyostelium amebae lacking myosin heavy chain*, Developmental biology, 128 (1988), pp. 164–177.
- [33] F. ZIEBERT AND I. S. ARANSON, *Effects of adhesion dynamics and substrate compliance on the shape and motility of crawling cells*, PLoS ONE, 8 (2013), p. e64511.
- [34] F. ZIEBERT, S. SWAMINATHAN, AND I. S. ARANSON, *Model for self-polarization and motility of keratocyte fragments*, J. R. Soc. Interface, 9 (2012), pp. 1084–1092.