2026-4 | 51th congress of the Société de Biomécanique
27-29 October 2026, Montpellier, France

Multidisciplinary Biomechanics Journal

Active Phase Field FrameWork to Model Cell Invasion in ECM

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Received date: 03/04/2026
Accepted date: 25/06/2026
Publication date: 27/10/2026

Keywords: phase-field, mechanobiology, cell invasion, active matter

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1. Introduction

Soft tissue regeneration remains challenging due to the tight coupling between cellular activity and the surrounding extracellular matrix (ECM). In vivo, cells evolve within a dynamic collagen network that both constrains cells and is remodeled by their activity. Cells exert contractile forces to reorganize fibers and degrade the matrix via proteolytic activity, while matrix properties such as density, anisotropy, and stiffness critically regulate migration and growth (Bonnans, 2014). Existing models typically capture either single-cell mechanics or large-scale matrix remodeling, but fail to describe their coupled feedback during tissue growth (Ranamukhaarachchi, 2024; Arellano-Tintó, 2025). This limitation hinders the predictive understanding of scaffold-driven regeneration.

To address this, we propose a two-dimensional multi-species framework combining a fibrous collagen network with an active matter phase-field model, enabling the simultaneous description of cellular expansion and matrix remodeling within a unified mechanobiological framework.

2. Methods

2.1 Active Phase Field framework for cell population

The phase-field method describes the entire simulation domain through a continuous order parameter ϕ that distinguishes two distinct phases: the growing cellular phase ($\phi \approx 1$) and the extracellular space ($\phi \approx 0$). The diffuse interface separating these phases evolves under a free energy functional that drives relaxation toward a stable equilibrium via an Allen-Cahn equation (Monfared, 2026) . To capture active cell behavior and break spatial symmetry, two additional terms are introduced: a logistic growth source term modeling cell proliferation at the interface, and an advection term that propels the cellular phase (eq-1).

$$\frac{\partial \phi}{\partial t} = -M\mu + S(\phi) - \nabla.(\phi \mathbf{V}) \tag{1}$$

With M the mobility, μ the derivative respective to ϕ of the free energy of the system and $S(\phi) = \alpha_p \phi \left(1 - \frac{\phi}{\phi_{max}}\right)$ the logistic growth term.

Concerning the advection term, $\mathbf{V}$ is directly linked to a local polarity direction P, itself governed by a Vicsek-type (Vicsek, 1995) equation coupled with ECM contact guidance (eq-2).

$$\frac{\partial P}{\partial t} = \phi\left[\beta(P - P) + \lambda_{cg}\rho(E.P)E + D_p\text{"}\ P\right] \tag{2}$$

In equation (2), the term $\beta(\langle P \rangle - P)$ drives elements to align with their neighboring ones, $\lambda_{cg}\rho(E.P)E$ promotes alignment of the polarity with the directions defined by the matrix E. Finally, $D_p \Delta P$ acts as a diffusion term that smooths the polarity field.

2.1 Description of the ECM

The extracellular matrix is represented by a scalar density field ρ and a unit orientation vector field $\mathbf{E}$,

To cite this article: Valentin Thieriot, Pamela Camilos, Jean-Louis Milan, Active Phase Field FrameWork to Model Cell Invasion in ECM, *Multidisciplinary Biomechanics Journal*, 2026, vol. 4, p. 175–177, DOI: 10.46298/mbj.19167.

generated stochastically from a Von Mises angular distribution with anisotropy parameter $\varkappa$. Both fields evolve phenomenologically: ρ acts as a local substrate for cell growth and motility, while **E** is progressively reoriented toward the local cell polarity direction P at the migration front, with a diffusive coupling that maintains orientational cohesion along the fiber. This two-way crosstalk of cells and ECM aims to simulate remodelling and contact guidance at the same time.

2.2 Numerical scheme

All simulations were performed in a two-dimensional (2D) computational domain discretized on 256×256 uniform grid using forward Euler scheme (domain size L = 1000 µm, spatial step dx ≈ 3.9 µm, time step dt = 0.04). Spatial derivatives are computed by second-order centered finite differences with reflecting boundary conditions.

3. Results and discussion

For each simulation, 300 fibers were initialized across the domain and a single cell cluster of radius 60 µm was placed at its center. Simulations were run for two values of the anisotropy parameter: κ = 0 (isotropic), and 5 (highly anisotropic), over 40 000 time steps. For the anisotropic case, the fiber orientation bias was set to θ = 45°, directing the principal fiber axis along the diagonal of the simulation domain.

3.1 Morphogenesis output

In the isotropic case, the cluster expands radially and develops a roughly circular morphology, with cell polarity vectors P oriented in all directions with no preferential axis. In the anisotropic case, the cluster progressively elongates along the 45° fiber axis, developing asymmetric protrusions at the invasion front that align with the local orientation ECM.

3.2 ECM remodeling

As the cluster expands, cells at the migration front progressively reorient the local ECM orientation field E toward their polarity direction P. This remodeling is locally coherent: each cell exerts a traction that aligns neighboring fibers along its own migration axis, producing well-ordered fiber orientations in the immediate invasion front.

However, at the scale of the full domain, the cumulative effect of many cells migrating in slightly different directions results in a loss of global orientational coherence. The remodeled ECM exhibits fragmented and heterogeneous orientation patterns, with no single dominant direction emerging outside the invasion front.

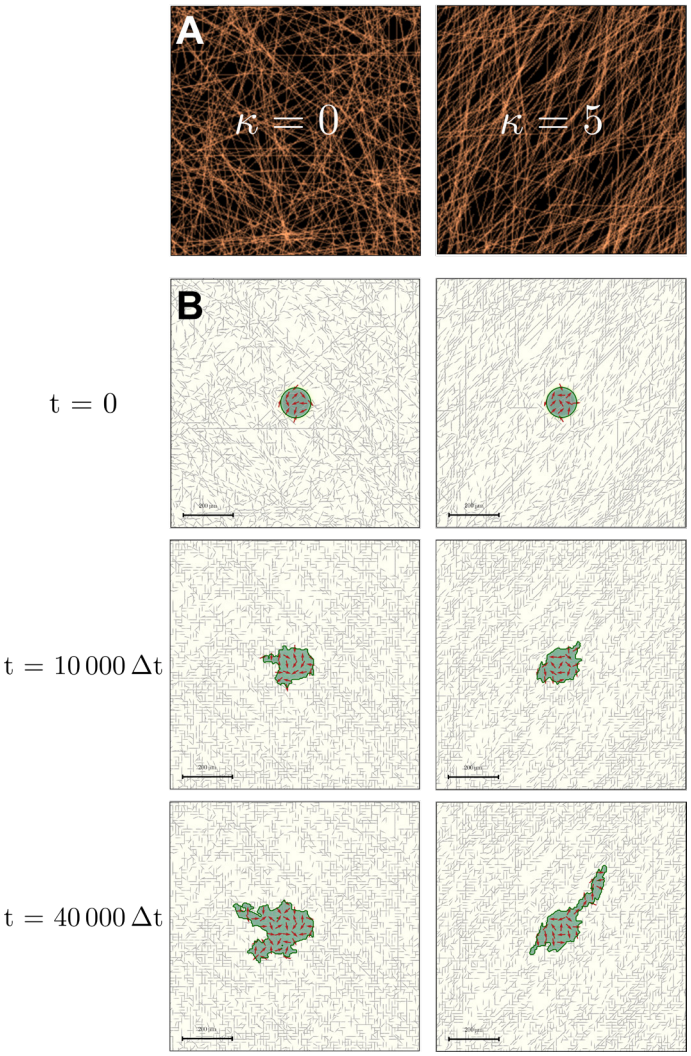

Figure 1. (a) Initial ECM density field. (b) Snapshots of cluster morphology at three successive time steps. Green: cell density **ϕ** ; red arrows: local cell polarity P; grey arrows: ECM orientation field E.

4. Conclusions

By coupling phase-field dynamics, active matter, and ECM remodeling, this framework successfully reproduces key features of cell invasion, such as symmetry breaking and front fingering. However, the lack of an explicit mechanical description of fiber deformation remains a limitation. Integrating a physically grounded mechanical model of cell-matrix force transmission represents the natural next step for this study.

Conflict of Interest Statement

The authors declare that there is no conflict or interest regarding the publication of this work.

Contributor Roles

VT: Conceptualization, Methodology, Writing original draft; PC: Methodology, Writing- review & editing; JlM: Conceptualization, Supervision, Writing – review & editing.

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