Review:
"Near the Jamming Transition of Elastic Active Cells: A Sharp-Interface Approach"

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1 Context

This report provides an overview of the work by Bresler, Palmieri and Grant [2]. Jamming is a process whereby individual cells constituting a cellular structure are more or less fixed in place. This is characterized by cells no longer exchanging neighbours and remaining in their relative position within the interface.

The appearance—or on the contrary, the lack—of jamming, has significant implications to biological processes such as: cancer migration, wound healing and bacterial growth.

In the case of cancer cell migration for example, it was found that cancer cells can "defeat" an jammed state by tunneling through channels (i.e. gaps between other cells), a behaviour that is explainable entirely by the difference in elasticity. The softer nature of cancer cells compared to normal cells means that cancer cells can deform more, which allows them to squeeze into gaps where other cells typically cannot fit.

The effect of elastic properties and the influence that various ratios of mixing between hard and soft cells has on jamming is studied in this work. The behaviour of systems in varying degrees of confluence (meaning how tightly packed the cells are) is an additional factor, and will be seen to be the most important.

2 Model

The model used in this work was initially derived from a novel phase-field model developed by the same authors. The phase-field model is defined in terms of the free energy of the cells, which describes each cell individually and includes the interaction terms between them.

The phase-field model is the first of its kind to model a cellular interface of many cells. Previously, jamming was studied using the vertex [3] and self-propelled voronoi methods [1] (among others), and found that cell shape influences jamming behaviour. While these modelling techniques are effective, the sharp interface model used in this work aims to support and then extend those findings.

The original phase-field model is constructed from both bulk and interfacial terms:

$$\mathcal{F} = \mathcal{F}_0 + \mathcal{F}_{\text{int}} \tag{1}$$

Essentially, a cell in free space desires to keep a circular shape of given radius (this minimizes the energy cost of surface tension). A cell which is deformed will regain its shape according to its elasticity parameter. When interacting with other cells, the interfaces must push against each other, which is incorporated by introducing an energy penalty for overlap.

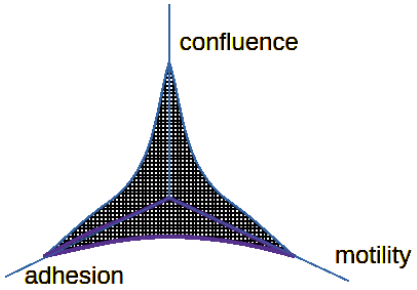


Figure 1: Motility-adhesion-confluence phase diagram for the jamming/unjamming transition, including illustrations of the approach to a jammed state.

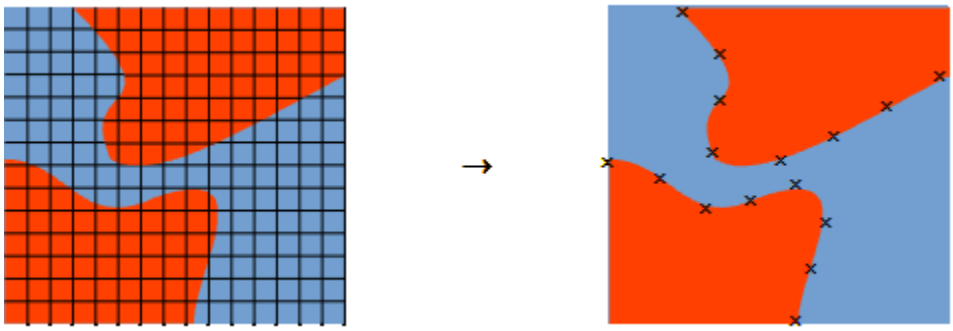


Figure 2: Illustration demonstrating the differential of the computational implementation of the phase-field and sharp-interface models. The phase-field model uses grid elements (a uniform structured grid is shown) for the whole system, whereas the sharp-interface method uses nodes that define the surface of a cell.

The dynamical system of equations of the phase-field model for cells in an interface is then be constructed from:

$$\frac{\partial \phi_n}{\partial t} + \vec{\mathbf{v}} \cdot \nabla \phi_n = -\frac{1}{2} \frac{\delta \mathcal{F}}{\delta \phi_n}, \tag{2}$$

where the right-hand is the functional derivative of the free energy.

The sharp-interface model is derived from the phase-field model. The two methods can be considered equivalent in principle (actually, they are precisely equivalent in the so-called "sharp-interface limit"), so that the dynamics of a simulation implementing either method will be the roughly equivalent. The advantage of the sharp-interface model is that a simulation using the sharp-interface method is carried out using orders of magnitude fewer nodes than there are grid elements in the phase-field model, and results in significantly shorter runtimes.

The sharp interface method is derived by determining an equation for the dynamics of the interface. As the name suggests, the interface must also be sharp: meaning that the value of function across the interface must change from 0 to 1 very quickly. The function arctan satisfies this requirement. Additionally, the sharp-interface model takes into account that energy is minimized with least curvature. This is also tied to the total area of the cell. The following equation is derived for the points along an interface:

$$\partial_t \mathcal{R}(\theta) = \left[\gamma K(\theta, t) - \frac{1}{R_0} + \mu(A_n - \pi R_0^2) + \beta(\tanh(\alpha d_{n,\theta} - 1)^2) \right] \backslash_\theta + \sqsubseteq_n \tag{3}$$

3 Simulation and Results

The sharp interface model was used to simulate a cellular interface on a grid of 288 cells with periodic boundaries. Three parameters were changed across different simulations: cellular motility ($\mathbf{v}$), confluence of the interface (ρ), and mixing ratio of hard and soft cells.

The authors first examined the effects of different values of motility in varying degrees of confluence between 70% and 95% using only hard cells. Confluence is controlled by fixing the size of the box and tuning ρ according to:

$$\rho = \frac{N_{\text{cell}} \pi R^2}{A_B} \tag{4}$$

where N_{cell} is the number of cells in the system, R is the radius (meaning the numerator actually represents the total area from the cells), and A_B is the total area of the box. Therefore, to get a given ρ, the area of the box is tuned.

Results are computed by first generating a system of 288 cells placed into the system as randomly placed circles, which will typically overlap each other. The system must therefore be equilibrated so that a reasonably low energy state can be achieved, primarily in terms of cell position and shape. Dislocations can and will arise, and cannot be avoided, meaning that potentially a lower energy state can exist but the state with dislocations is still an acceptable starting point. If the simulation starts directly from the initial conditions, too much energy will arise from overlapping and misplaced cells.

Equilibration is reached once time is 80,000, the simulation can be initiated.

From the results, a single-parameter equation for the critical motility for the jamming/unjamming transition is derived, based on only the confluence:

$$v^*(\rho) = \bar{\gamma} \frac{2 \cdot 3^{1/4}}{\pi(R + \lambda/2)} (\sqrt{\rho} - \sqrt{\rho_J}) \tag{5}$$

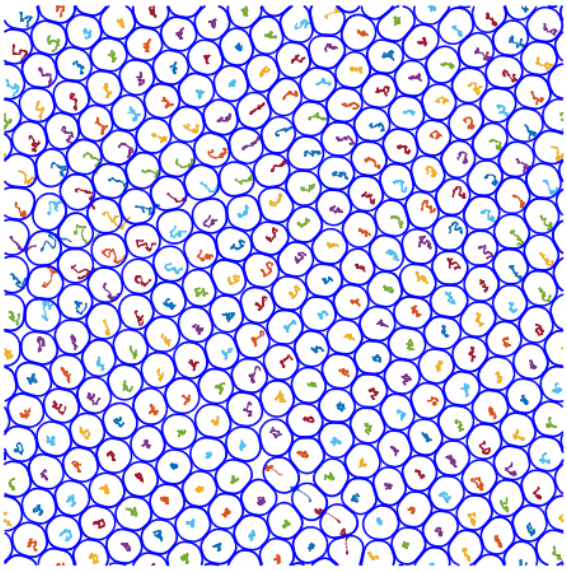


Figure 3: A typical cell interface in a jammed state.

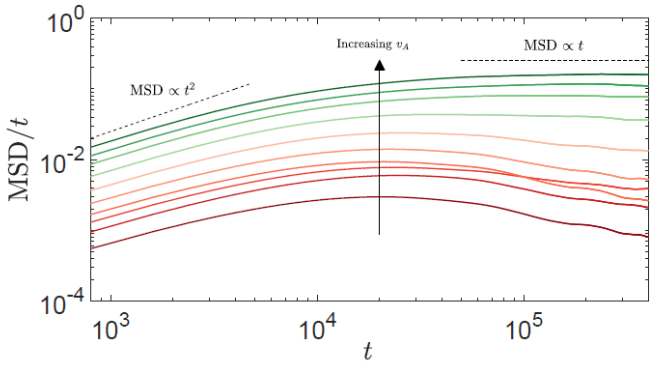


Figure 4: The mean square displacement over time for different values of motility across the same system configuration.

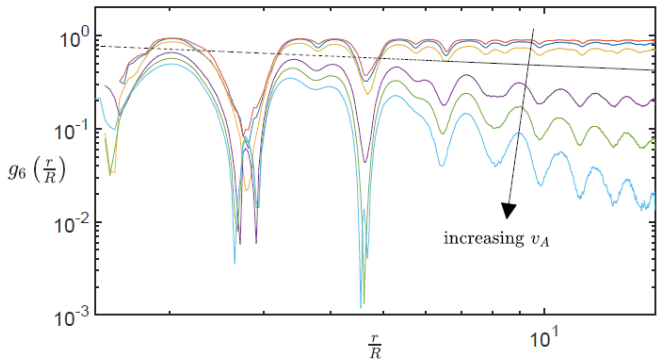
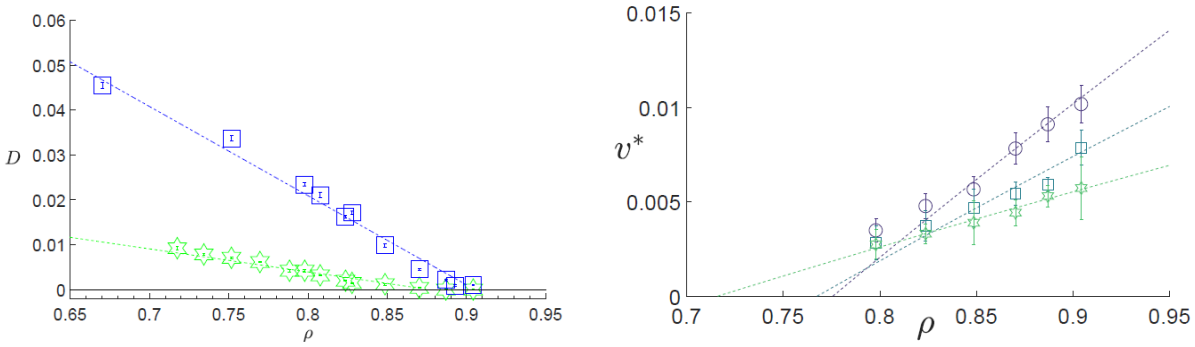


Figure 5: Plot demonstrating hexagonal arrangement of the system. This is calculated from the six-fold bond correlation function, which essentially describes how closely each of the cells can be found in a configuration where their neighbours are precisely 60 degrees from each other (i.e. a triangular arrangement).



(a) (b)

Figure 6: Two figures are shown: a Diffusion with a fixed motility with two different parameter sets, and; b the jamming/unjamming transition point as a function of confluence.

References

[1] Dapeng Bi, Xingbo Yang, M. Cristina Marchetti, and M. Lisa Manning. Motility-Driven Glass and Jamming Transitions in Biological Tissues. *Phys. Rev. X*, 6(2):021011, April 2016.

[2] Yony Bresler, Benoit Palmieri, and Martin Grant. Near the jamming transition of elastic active cells: A sharp-interface approach, 2018.

[3] Ugo Lopez, Jacques Gautrais, Iain D. Couzin, and Guy Theraulaz. From behavioural analyses to models of collective motion in fish schools. *Interface Focus*, 2(6):693–707, October 2012.