Solid-Liquid Transition of Deformable and Overlapping Active Particles

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Experiments and theory have shown that cell monolayers and epithelial tissues exhibit solid-liquid and glass-liquid transitions. These transitions are biologically relevant to our understanding of embryonic development, wound healing, and cancer. Current models typically consider purely two-dimensional monolayers with no overlaps between neighboring cells. In reality, overlaps are important, and they may be precursors of cell extrusion – a key biophysical process to maintain homeostasis in epithelial tissues. Here, we use a multi-phase field model to study the solid-liquid transition in a confluent monolayer of deformable cells which can overlap. When cells overlap rather than deform, we find that the melting transition changes from continuous to discontinuous, and that there is an intermittent regime close to the transition, where solid and liquid states alternate over time. By studying the dynamics of 5- and 7-fold disclinations in the hexagonal lattice formed by the cell centers, we observe that these correlate with spatial fluctuations in the cellular overlap, and that cell extrusion tends to initiate near 5-fold disclinations.

Understanding the dynamics and collective behavior of cells in dense tissues is an important goal of biophysics, with relevance to a number of developmental processes, such as embryogenesis [1], wound healing [2], and cancer [3]. For example, the epithelial-mesenchymal transition can be viewed as a solid-liquid transition occurring in vivo [4–6], where cells become more motile and less adhesive: this transition has been reported to play a role in tissue repair, inflammation, and tumour progression [3, 7, 8]. Experimental studies have also shown that epithelial cells can undergo an unjamming/jamming transition between a glassy phase where their dynamics is slow to a fluid phase with large-scale collective motion both in vitro [9–14] and in vivo [14, 15].

From a theoretical point of view, an appealing model of a dense tissue is provided by a two-dimensional (2D) confluent cell monolayer (i.e., a space-filling cell monolayer with packing fraction equal to unity). This system can be studied by the cellular Potts model [16], the vertex [17, 18] and Voronoi [19] models, and their variants [20, 21]. Such frameworks have recently been used to study the melting transition in monolayers of passive [18, 22, 23] and active/self-motile cells [19, 24–26].

Cell motility and deformability distinguish this problem from the well-studied 2D melting of crystals of hard or soft disks [27–30], which proceeds either via a discontinuous transition [31, 32], or through an intermediate hysteretic phase and the unbinding of topological defects [33–38].

Existing simulation studies of confluent active monolayers suggest that a continuous solid-liquid (or glass-liquid) transition can be observed upon increasing cell motility [19, 26]. While useful in providing quantitative predictions, these models require some strong assumptions. An important one which is relevant to our present work is that of a purely 2D system where neighboring cells cannot overlap. In reality, overlaps may arise in several situations. Most notably, excess cells are routinely extruded from an epithelial monolayer [39], and extrusion requires cellular overlap. Extrusion can be triggered, for instance, by cell overcrowding and is required to maintain tissue homeostasis. Overlap events may also be relevant during early embryogenesis as a single epithelial monolayer is converted into a multi-layered epithelium following a tightly coordinated stratification program [40].

In this context, a model that allows for both particle deformation and overlap is the multi-phase field model [41–44], which describes each cell via a different scalar phase field. This model may also serve as a bridge between particle-based and confluent models. In this work, we use the multi-phase field model to study melting in a confluent system of active deformable particles. In the model, there is a trade-off between deformability and overlap, i.e., the less deformable a particle is, the more it overlaps with its neighbors. As such, by decreasing cell deformability, the system transitions from deformable particles that tessellate their domain without overlap, akin to the vertex model, to a system of almost-circular overlapping disks. We find that melting in the monolayer may proceed in two qualitatively different ways. At high deformability, the system continuously transitions from solid to liquid as motility is increased. Instead, at low deformability the increased overlap affects the nature of the transition, which becomes discontinuous. There is also an intermediate intermittent state, in which the system as a whole alternates between melting and solidification. This intermittent regime implies that layered tissues could exhibit quasi-periodical fluidization. Finally, we observe a strong correlation between unbound structural defects (corresponding to 5- and 7-fold disclinations in the hexagonal lattice formed by the cell centers) generated upon melting and local fluctuations in cell overlap. Specifically, we find that cellular extrusion is favored at the location of 5-fold disclinations.
Our multi-phase field model contains $N$ scalar fields, $\{\phi_i(r)\}_{i=1}^{N}$, each representing a different cell. The equilibrium configuration of the cell layer is determined by the minimization of the following free energy [42, 44]:

$$
F = \sum_{i=1}^{N} \left[ \int d^2r \left( \frac{\alpha}{4} \phi_i^2 \phi_i - \frac{K}{2} \nabla \phi_i \right)^2 \right] + \lambda \left[ 1 - \int d^2r \frac{\phi_i^2}{\pi R^2 \phi_0^2} \right]^2 + \varepsilon \sum_{i<j=1}^{N} \int d^2r \phi_i^2 \phi_j^2.
$$

The first three terms in Eq. (1) determine the shape of the cells. The first term sets $\phi_0$ and zero as the preferred values of the field inside and outside the cell, respectively. The second term penalizes spatial variations of $\phi$. Together, they determine the physical properties of the cell boundary, such as the interfacial thickness, which we define as $\xi = \sqrt{2K/\alpha}$, and surface tension $\sigma = \sqrt{8K\alpha/9}$ [45]. The third term is a soft constraint that sets the preferred area of the cell to that of a circle with target radius $R$. Finally, the fourth term models the steric repulsion between cells by energetically penalizing cell overlap.

To model the dynamics of self-motile active cells, we assume simple relaxational and overdamped dynamics,

$$
\frac{\partial \phi_i}{\partial t} + v_i \cdot \nabla \phi_i = -\frac{1}{\gamma} \frac{\delta F}{\delta \phi_i},
$$

where $\gamma$ is a friction and we have included an advection term that propels the cells with velocity $v_i$ (see Supplemental Material (SM)). All cells have the same propulsion speed $v_0$, while their direction of motion $\theta_i$ is controlled by rotational noise with diffusivity $D_r$,

$$
d\theta_i(t) = \sqrt{2D_r} \, dW_i(t),
$$

where $W_i$ is a Wiener process. Cell motility is quantified by the Péclet number $Pe \equiv (v_0/D_r)/R$, which is the ratio between the cells’ persistence length and their target radius. These equations are a generalization of the active Brownian particle model [46, 47] to a system of deformable cells.

Our model allows cells to both deform and overlap. In general, these are competing effects: deformation is energetically penalized by the surface tension, while repulsion penalizes the overlap. We then quantify deformability (i.e., the likeliness of cell deformation) through the dimensionless ratio $d \equiv \varepsilon/\alpha$. When $d \ll 1$, cells tend to acquire a circular shape and overlap with their neighbors (Fig. 1a,c,e). Conversely, when $d \gg 1$, cells change their shape to match with their neighbors and minimize overlap (Fig. 1b,d,f). The squashed cell shape observed in the solid state at $d > 1$ (Fig. 1d) arises from the combined effect of the geometry of the simulation box and noise. The rectangular simulation box slightly compresses the system along the vertical axis (Fig. 1b). Additionally, noise excites soft modes that travel preferentially along this axis, resulting in cell flattening through the interaction between neighboring moving cells.

We first examine the role of deformability and motility on the solid-liquid transition at confluence. To this end, we employ a finite difference method to solve numerically Eqs. (2) and (3) for $N = 36$ and 100 cells in a rectangular box, with periodic boundary conditions, and systematically vary $d$ and $Pe$. We choose $R$ as unit of lengths and $D_r^{-1}$ as unit of times. In these units, we use as our simulation lattice unit and timestep $\delta t = 1/12$ and $\Delta t = 5 \times 10^{-5}$ respectively. To vary deformability, we keep $\varepsilon$ fixed, and vary $\alpha$ and $K$ such that $\xi$ is kept constant. Motility is varied by changing $v_0$. We initiate the cells in a hexagonal lattice and allow the system to achieve confluence by setting the target area $\pi R^2$ of a cell to be larger than the area available to each cell. This renders the force associated with the third term in Eq. (1) qualitatively equivalent to a negative pressure. To ensure near-constant cell area and confluent conditions at all times, we use $\lambda \gtrsim 6000\alpha$. Additional simulation details and the full list of parameters are given in the SM.

FIG. 1. Simulated snapshots of the stationary state for different deformability (quantified by $d$) and motility (quantified by $Pe$). The contours of the cells correspond to the level $\{\phi_i = 1\}_{i=1}^{N}$, while the coloring corresponds to cell-index at $t = 0$ (for visualizing cell rearrangements). (a)-(b) The initial condition of the monolayer at (a) $d = 0.1$ and (b) $d = 2.0$. Note that cells overlap at low $d$, whereas at high $d$ cells deform rather than overlap. (c)-(f) Snapshots of the system at $D_r t = 250$. The system remains in a crystal-like state at low motility ((c) and (d)). At sufficiently high motility, the system melts and cells exchange neighbors ((e) and (f)). See also Suppl. Movies 1-4.
To quantify the melting transition, we compute both dynamical and structural observables. Dynamical arrest is quantified through an effective diffusivity $D_{\text{eff}}$ [19, 24] obtained from the long-time behavior of the mean square displacement MSD($t$) of individual cells as

$$D_{\text{eff}} = \lim_{t \to \infty} \frac{\text{MSD}(t)}{4D_0 t},$$

with $D_0 = v_0^2/(2D_r)$ the diffusivity of an isolated cell. As structural observables, we measure the global bond-orientational order $|\Psi_6|$ and the structure factor $S(q)$ (see SM for details). Choosing $D_{\text{eff}} > 0.0005$ as the threshold for a liquid state, the transition lines obtained from the dynamical and structural measurements coincide. The phase diagram displayed in Fig. 2 shows that both deformability and motility facilitate melting. We also find a region of intermittence at low deformability, discussed further below. The width of the plateau in the MSD at intermediate times (see SM) shrinks with increasing deformability, suggesting that deformability facilitates melting by allowing particles to squeeze more easily through the cages provided by their neighbors.

One of our key results is that the nature of the transition is different at low and high deformability. This can be appreciated by analyzing the standard error of $|\Psi_6|$ across the parameter space ($d, \text{Pe}$), which shows that there is an intermediate Pe range at $d < 1$ for which this quantity is large (see SM). Intriguingly, $d < 1$ is precisely the region in parameter space where the overlap between cells becomes appreciable, implying that the character of monolayer melting depends on whether the rearrangement of particles occurs by cells squeezing past their neighbors or crawling over them.

To determine the nature of the intermediate regime found at $d < 1$, we analyze the corresponding time series of $|\Psi_6|$ (Fig. 3a). The time series show clear evidence of an intermittent behavior, where the system jumps between two distinct states with different mean values of $|\Psi_6|$ (see also Suppl. Movie 5). The two states are also apparent from the bimodal character of the $|\Psi_6|$ probability density function (PDF; Fig. 3d). Since $|\Psi_6|$ correlates with the melting transition and our solid state is close to a hexagonal crystal, we can associate $|\Psi_6| \approx 1$ to a solid state, and values of $|\Psi_6|$ close or below $0.5$ to a liquid state. Moreover, the values of $|\Psi_6|$ in the solid and liquid regimes fluctuate around well-defined means, and hence exhibit unimodal PDFs (albeit with different widths), so that bimodality in the PDF signals intermittency. We also identify intermittency by computing the fraction of defects in the system $\langle |\Delta N_{\text{nn}}| \rangle$ (Fig. 3b,c), i.e., the fraction of the total number of cells with a coordination number other than six. The time series for $\langle |\Delta N_{\text{nn}}| \rangle$ shows that defects appear when the monolayer is in the liquid state.

We locate the intermittent region in the phase dia-
gram (Fig. 2) via two separate methods. First, given that there are large fluctuations in $|Ψ_6|$ in this region, we identify states to be intermittent if both the standard error of $|Ψ_6|$ and $\overline{D}_\text{eff}$ are above 0.0005. Second, we binarize the time series of $⟨|ΔN_{mn}|⟩$ and map each time point to either zero (solid) or unity (liquid). For a time series to be intermittent, we require a minimum of two jumps between the states, and a large enough fraction of time spent in either state (see SM for more details). Both methods converge and pinpoint a similar parameter region to be intermittent. Further, this region shrinks with increasing $N$: this suggests that intermittency arises because the solid-liquid transition is first-order-like at low deformability, so that coexistence between the two phases is expected at criticality.

As anticipated, and clear from the phase diagram, the intermittent phase is only present at low deformability, when cells overlap. A possible mechanism through which cell overlap might affect the nature of the transition is the following. When cells are highly deformable and do not overlap with their neighbors, they can escape the local cage in which they are trapped by squeezing through their neighbors. These cage escapes lead to neighbor exchanges, hence to fluidification. On the other hand, if cells are not deformable but can overlap, moving a cell is similar to inserting or moving a coin on a substrate crowded with other coins (as in a “coin-pusher” arcade game). In this case, motion of the coin can either result in simple coin overlap/layering and no motion, or in the collective motion of a raft of coins. The coexistence of different scenarios (overlap or collective motion) may underlie the onset of intermittency in our simulations, and the first-order-like nature of the solid-liquid transition in the low deformability regime.

Finally, we analyze the relation between defects in the bond-orientational order and cell overlap. Experiments with monolayers of progenitor stem cells [48] have shown that these systems can be viewed as active nematics, and that topological defects in the nematic order correlate with the location of cell extrusion and death. Similar behavior has been obtained in MDCK (Madin Darby Canine Kidney) cells [39, 44]. On the other hand, nematic order is often not readily apparent in epithelia, where cells are typically not elongated, and extrusion is presumably associated with high local overlap of a cell with its neighbors [49]. Our work offers an alternative interpretation that correlates cell extrusion not with defects in nematic order, but with cell overlap and associated structural defects in cell packing.

Defects in the hexagonal lattice formed by the cell centers in the ordered solid state are 5-fold and 7-fold disclinations and correspond to pentagonal and heptagonal cells, respectively, in the associated Voronoi tesselation [50]. They are readily identified in the cell packing, as shown in Fig. 4c. We define the local overlap of the $i$th cell as $χ_i(\mathbf{r}) \equiv \sum_{j=1}^{N} H(\phi_i(\mathbf{r}) - 1)H(\phi_j(\mathbf{r}) - 1)$, with $H$ the Heaviside function. We then search for correlations between defects and overlap by recording both overlap and coordination number for each cell, and constructing the PDFs for the local overlap for pentagonal/heptagonal cells, as well as for the entire cell population (Fig. 4).

The PDFs show that pentagons experience, on average, a higher degree of overlap with respect to other cells. This can be understood in terms of the mean cell perimeter. Since changing cell size is energetically very costly, all cells have approximately the same area in our simulations. For fixed area, pentagons have a larger perimeter than both hexagons and heptagons, which provides them with a larger boundary where they can overlap with their neighbors. Our results therefore suggest that extrusion events in cell monolayers, which are likely to occur in the intermittent regime or near the solid-liquid transition, may originate close to the position of pentagonal cells.

In summary, we have used a multi-phase field model to explore the effect of overlap and motility on the solid-liquid transition in confluent monolayers of active deformable cells. This transition can be triggered by increasing motility and/or deformability, which enhances melting by allowing cells to squeeze past their neighbors. We have shown that allowing for cell overlap strongly affects the qualitative nature of the melting transition in the monolayer. Specifically, when cells overlap rather than deform, the solid-liquid transition changes from continuous to first-order-like, and it is accompanied by an intermediate intermittent regime in which the monolayer
alters between solid and liquid states. This intermittent phase could be relevant to morphological processes that require periodic fluidization to restructure the tissue. We have also found a correlation between the location of topological defects in cell packing and fluctuation in local cell overlap, which suggests that cellular extrusion could be linked to the presence of these defects. Extrusion is an important process in epithelial tissues required for proper biological functioning. While it is normally thought that extrusion is determined by biochemical signaling, recent experiments have suggested a correlation between extrusion and topological defects in the orientational order of elongated or spindle-like cells. Here we suggest an alternate, possibly more general, correlation between extrusion and topological defects in the structure of cell packings that applies even when cells are not elongated.

From a theoretical point of view, it would be of interest to ask whether our active monolayers of deformable cells also exhibit a hexatic phase, which has been recently found in high-density suspensions of active Brownian particles [30, 51]. Addressing this question will require simulations of much larger systems.

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Solid-Liquid Transition of Deformable and Overlapping Active Particles: Supplemental Material

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PHASE FIELD DYNAMICS

In our study we consider a dry system of deformable particles, described as interacting phase fields with the solvent only providing friction. The particles are self-propelled and interact with each other via a repulsive interaction. Our particles are essentially deformable active Brownian particles (ABP) capable of overlap. The dynamics of the \( i \)th phase field is governed by the equation

\[
\partial_t \phi_i + v_i^n \cdot \nabla \phi_i = -\frac{1}{\gamma} \frac{\delta F}{\delta \phi_i},
\]

where \( F \) is the cells’ equilibrium free energy

\[
F = \sum_{i=1}^{N} \left[ \int d^2 r \left( \frac{\alpha}{4} \phi_i^2 (\phi_i - \phi_0)^2 + \frac{K}{2} (\nabla \phi_i)^2 \right) + \lambda \delta V[\phi_i] + \varepsilon \sum_{i<j=1}^{N} \int d^2 r \phi_i^2 \phi_j^2 \right],
\]

with

\[
\delta V[\phi_i] = 1 - \int d^2 r \frac{\phi_i^2}{\pi R_i^2 \phi_0^2}.
\]

Here, we discuss the physical origin of the advective velocity \( v_i^n \), where an additional superscript \( a \) has been introduced for clarity (but it is dropped in the main paper). In particular, we would like to contrast \( v_i^n \) to the center of mass velocity of the cell, defined as

\[
v_i^{cm} = \frac{d}{dt} R_i^{cm},
\]

where

\[
R_i^{cm} = \frac{1}{M_i} \int d^2 r \phi_i
\]

and \( M_i \) is the cell’s total “mass”,

\[
M_i = \int d^2 r \phi_i.
\]

Single Cell

For a single isolated cell in the absence of external driving forces, it is easy to show that \( v_i^{cm} = v_i^n \), as all forces acting on the cell are internal and cancel out. This is seen explicitly by taking the time derivative of Eq. (5)

\[
v_i^{cm} = \frac{1}{M_i} \int d^2 r (\partial_t \phi_i) - R_i^{cm} \frac{1}{M_i} \int d^2 r (\partial_t \phi_i),
\]

which, using Eq. (1), can be rewritten as

\[
M_i v_i^{cm} = - \int d^2 r (v_i^n \cdot \nabla \phi_i) + R_i^{cm} \int d^2 r v_i^n \cdot \nabla \phi_i - \frac{1}{\gamma} \int d^2 r (r - R_i^{cm}) \frac{\delta F}{\delta \phi_i}.
\]

Integrating the first two terms by parts, replacing the explicit form of the free energy, Eq. (2), but without interactions, and changing variables to coordinates relative to the particle’s center of mass, \( u = r - R_i^{cm} \), we obtain

\[
v_i^{cm} = v_i^n - \frac{1}{\gamma M_i} \int d^2 u \left[ \alpha \left( \phi_i^3 - \frac{3}{2} \phi_0 \phi_i^2 + \frac{1}{2} \phi_0^2 \phi_i \right) - K \nabla^2 \phi_i - \frac{4 \lambda \phi_i}{\pi R_i^2 \phi_0^2} \delta V[\phi_i] \right].
\]

Assuming that the field \( \phi_i \) is approximately uniform in the interior of the cell, we can write

\[
\int d^2 u \phi_i^3 \approx \int d^2 u \phi_i^2 \approx \int d^2 u \phi_i = 0,
\]

thus allowing us to neglect the first term in the integral in Eq. (9). The third term also vanishes by the same reasoning. Similarly, given that \( \phi_i \) is localized, we have

\[
\int d^2 u \nabla^2 \phi_i = 0,
\]

and the second term also vanishes. Hence, for a single isolated cell we find

\[
v_i^n = v_i^{cm}.
\]

In other words, for an isolated cell the advective velocity in Eq. (1) coincides with the center of mass velocity of the cell. If no externally applied nor internally generated (such as motility) forces act on the cell, then \( v_i^n = v_i^{cm} = 0 \). In contrast, if the cell is active and self-motile, then \( v_i^n = v_i^{cm} = v_i^{SP} \), where \( v_i^{SP} = v_0 \hat{e} \) is the cell motility, modeled as a propulsive velocity of constant speed \( v_0 \) and direction \( \hat{e} \), randomly rotated by noise, as described in the main paper.
Interacting Cells

In the presence of interactions, the procedure described above yields

$$v_{cm}^i = v_i^a - \frac{2 \varepsilon}{\gamma M_i} \sum_{j \neq i} \int d^2 u \, u \phi_i \phi_j^2. \quad (13)$$

The second term on the right hand side of Eq. (13) arises from the forces acting on cell $i$ due to all other cells. Eq. (13) is a statement of force balance and can be rewritten as

$$\gamma v_{cm}^i = F_i^a + F_i^{\text{int}}, \quad (14)$$

where the friction coefficient is assumed equal to the one in Eq. (1) and

$$F_i^a = \gamma v_i^a, \quad (15)$$

$$F_i^{\text{int}} = -\frac{2 \varepsilon}{M_i} \sum_{j \neq i} \int d^2 u \, u \phi_i \phi_j^2. \quad (16)$$

It is evident that the center of mass velocity is indeed determined by both self-propulsion $v_i^a = v_i^{\text{SP}}$ and interactions. Incorporating interactions in the advective velocity $v_i^a$ as done in much of the literature would lead to double counting for our dry system.

The situation changes, however, if we assume the tissue to be surrounded by a solvent at low Reynolds number. In this case, the cell is not only advected by its self-propulsion but also by the velocity field of the solvent. Assuming that the solvent is in mechanical equilibrium with the cells, then the solvent velocity field must be equal to the gradient of the cell’s stress tensor. In this case, fluid-mediated interactions do lead to advection and $v_i^a$ must include this contribution, as discussed in the literature [1, 2].

MODEL IMPLEMENTATIONS

Here we describe the details of our numerical solution of Eq. (1). The full list of parameter values used in the simulations is provided in Table SI. Evaluating the functional derivative of $F$, Eq. (1) can be written as

$$\partial_t \phi_i = -v_i^a \cdot \nabla \phi_i - \frac{1}{\gamma} \left[ \alpha \left( \phi_i^3 - \frac{3}{2} \phi_i^2 \phi_0 + \frac{1}{2} \phi_i \phi_0^2 \right) - K \nabla^2 \phi_i - \frac{4 \lambda \phi_i}{\pi R^2 \phi_0^2} \delta V[\phi_i] + 2 \varepsilon \phi_i \left( h(\mathbf{r}) - \phi_i^2 \right) \right], \quad (17)$$

where we have introduced an auxiliary field $h(\mathbf{r}) = \sum_{i=1}^N \phi_i^2(\mathbf{r})$. This auxiliary field enables one to decouple and parallelize the computation of individual phase fields [3]. More precisely, we first calculate $h(\mathbf{r})$ using the phase fields at the current timestep, and then perform the update of individual phase fields in parallel with the knowledge of $h(\mathbf{r})$.

We simulate Eq. (17) using a finite difference method. Length is expressed in terms of the lattice spacing $\delta x$, and time in simulation time unit $\delta t$. For numerical stability, we set each timestep $\Delta t$ to 0.5$\delta t$. The simulation code is written in a mixture of C and C++ and is parallelized using OpenMP. In line with previous work [2, 3], we use domain decomposition to improve computational efficiency. Each field is discretized as a square lattice with linear dimension $\ell_s = 41$ (which is much larger than the target radius of each cell, $R = 12$, but much smaller than the whole lattice), and we solve Eq. (17) using fixed boundary conditions (i.e., $\phi_i = 0$) in these subdomains. Note that the boundary conditions for the full lattice are still periodic. During the simulations, we keep the cell near the center of its subdomain by performing a shifting algorithm which moves the cell back to the center of the subdomain when it has moved more than two lattice units in any direction. At the same time, we store reference coordinates of each cell relative to the full lattice, and these are updated accordingly when a shift has been performed.

We consider both a system of $N = 36$ and 100 cells [4]. We initialize the cells in a hexagonal arrangement, which is achieved by placing a circular droplet of radius $r = 7$ (with $\phi = 2$ within the droplet) on every point of a triangular lattice with spacing $\ell_s = 8$. We set the number of cells in each row to be $\sqrt{N}$. Thus, the dimensions of the full lattice are $160 \times 138$ ($96 \times 83$) for $N = 100$ ($N = 36$). We then allow these cells to relax and grow (with $Pe = 0$) for $10^4$ timesteps such that the system becomes confluent. Next, we switch on motility and evolve the cells for $10^4$ timesteps. In the main production runs, we sample the system every $10^3$ timesteps for $2 \times 10^7$ timesteps (or $D_t t = 1000$). We explore the parameter space $d = 0.1$–4.0 and $Pe = 0.0$–3.0 to locate the solid and liquid regimes of the system.

| Parameter | Dimensions | Value         |
|-----------|------------|---------------|
| $\alpha$  | $E/L^2$   | 0.025–1.0     |
| $K$       | $E$       | 0.05–2.0      |
| $\lambda$ | $E$       | 6000          |
| $\varepsilon$ | $E/L^2$ | 0.1           |
| $\phi_0$  | -         | 2             |
| $\xi$     | $L$       | 2             |
| $R$       | $L$       | 12            |
| $\gamma$  | $ET$      | 10            |
| $D_r$     | $T^{-1}$  | 0.0001        |
| $v_0$     | $L/T$     | 0.0–0.0036    |

TABLE. SI. Parameter dimensions and values used in the simulation model. These values are in simulation units of length $\delta x$, time $\delta t$, and energy $\delta E$. Notice that the actual scale of energy is irrelevant as it scales out of Eq. (1).
DYNAMICAL OBSERVABLES

Mean Square Displacement (MSD)

To pinpoint the solid-liquid transition, we first examine dynamical observables. We compute the mean square displacement (MSD) of the cells as

$$\text{MSD}(t) = \left\langle \frac{1}{N} \sum_{i=1}^{N} (\mathbf{R}^\text{cm}_i(t + \tau) - \mathbf{R}^\text{cm}_i(\tau))^2 \right\rangle_{\tau},$$  \hspace{1cm} (18)

where $\mathbf{R}^\text{cm}_i$ is the center of mass of the $i$th cell in the rest frame of the full monolayer. Fig. S1 shows the MSD curves for several values of deformability. They suggest that increasing deformability $d$ facilitates melting, with lower motility required. Further, the region in which the MSD curve plateaus shrinks with increasing $d$, indicating that cells can squeeze pass each other more easily as cells become more deformable.

Effective Diffusivity

From the MSD data, we determine the dynamical arrest of the system by calculating a normalized effective diffusivity

$$\overline{D}_{\text{eff}} = \lim_{t \to \infty} \frac{\text{MSD}(t)}{4D_0 t},$$  \hspace{1cm} (19)

where $D_0 = \frac{v_0^2}{2D_r}$ is the diffusivity of an isolated active Brownian particle undergoing rotational diffusion. In practice, we measure $\overline{D}_{\text{eff}}$ by performing linear fits of the MSD curves at late times ($5 \times 10^6$ to $1.5 \times 10^7$ timesteps, or $D_r t = 250$ to 750) and using the slope of the fit to estimate the diffusivity. Fig. S2 reports the measured $\overline{D}_{\text{eff}}$ for a range of deformability values as a function of motility. The plot suggests that the system fluidizes (i.e., $\overline{D}_{\text{eff}} > 0$) at lower motility as they become more deformable.

We identify the system as a liquid if $\overline{D}_{\text{eff}} > 0.0005$ and a solid otherwise. This threshold is chosen to match the results from structural observables (see below). Fig. S3 displays a phase diagram constructed based on this criterion (and also the structural observables) for $N = 36$ and 100. The transition boundary is similar in both system sizes for $d > 1$, but it occurs at a slightly lower motility value as $N$ increases for $d \ll 1$. 

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**FIG. S1.** Mean square displacement (MSD) for (a) $d = 0.1$, (b) 1.0, and (c) 2.0. In each plot, we show MSD curves for Pe values ranging from 0.8 to 3.0 in increments of 0.2. Each curve is averaged over three simulation runs.

**FIG. S2.** Normalized effective diffusivity $\overline{D}_{\text{eff}}$ as a function of motility for a range of deformability values. Each point is sampled from three simulation runs.
FIG. S3. Quantifying the solid-liquid transition based on the system’s effective diffusivity $D_{\text{eff}}$ and its global bond-orientational order $|\Psi_6|$, for (a) $N = 36$ and (b) $N = 100$. The points on these plots indicate the locations that we have explored in the parameter space. The results are averaged over three simulation runs. At these points, the system is labeled as a liquid (orange) if $D_{\text{eff}} > 0.0005$ or a solid (blue) otherwise. The heat maps in the background are constructed from interpolating the measured $|\Psi_6|$ values at these points.

**STRUCTURAL OBSERVABLES**

**Bond-Orientational Order Parameter**

We measure structural observables as an alternative way to quantify the melting transition. Since we initialize the cells in a regular hexagonal arrangement, these cells have near perfect 6-fold coordination if the system remains a solid. On the other hand, when the system melts, cells exchange positions with one another, and their nearest neighbors are not, in general, arranged as a hexagonal lattice. A suitable observable which captures the change in orientational order is the local bond-orientational order parameter $\Psi_{6,j}$, which is defined for each cell (say cell $j$) as

$$\Psi_{6,j}(t) = \frac{1}{N_{\text{nn},j}} \sum_{k \in \text{nn}} \exp[i 6 \theta_{jk}(t)],$$  \hspace{1cm} (20)

where the sum is over the nearest neighbors of the cell, $N_{\text{nn},j}$ is its number of nearest neighbors, and $\theta_{jk}$ is the angle between the line connecting the center of mass of cell $j$ and $k$ and a reference axis (taken to be the $x$ axis here). We use Delaunay triangulation to determine the nearest neighbors of each cell when computing this observable. The global bond-orientational order parameter $\Psi_6(t)$ is defined as the average of $\Psi_{6,j}(t)$ over all cells. Note that $|\Psi_6| \simeq 1$ when cells have nearest neighbors close to perfect hexagonal arrangement (i.e., in the solid state), whereas $|\Psi_6| \simeq 0$ when local orientational order is lost (i.e., in the liquid state). In Fig. S3, we also display the heat maps of $|\Psi_6|$ underneath the phase diagram constructed based on the dynamical criterion $D_{\text{eff}}$. Notably, the region where $|\Psi_6| \simeq 1$ is in agreement with the points classified as a solid, whereas $|\Psi_6| \simeq 0$ maps to the points labeled as a liquid.

**Structure Factor**

In addition to $\Psi_6$, we analyze the structure factor $S(q)$ of the system, which is given by

$$S(q) = \left\langle \frac{1}{N} \sum_{i=1}^{N} \sum_{j=1}^{N} e^{i q \cdot (R_i - R_j)} \right\rangle.$$  \hspace{1cm} (21)

In the ideal crystalline state, cells are arranged in a regular triangular lattice with spacing $\ell_t$ between lattice points. The real space lattice can be defined by two lattice vectors forming a unit cell:

$$a_1 = (\ell_t, 0) \quad a_2 = \frac{\ell_t}{2} \left(-1, \sqrt{3}\right).$$  \hspace{1cm} (22)

The corresponding reciprocal lattice vectors are

$$b_1 = \frac{2\pi}{\ell_t} \left(1, \frac{1}{\sqrt{3}}\right) \quad b_2 = \frac{2\pi}{\ell_t} \left(0, \frac{2}{\sqrt{3}}\right).$$  \hspace{1cm} (23)

Fig. S4 shows $S(q)$ at several points near the transition boundary for both low and high deformability values. The data are consistent with those from other observables. In particular, for points that are labeled as a solid, $S(q)$ has maxima at the reciprocal lattice points, indicating that the system exhibits translational order. On the other hand, for points in the fluid regime, these maxima fade away and $S(q)$ becomes isotropic (as demonstrated by the formation of a ring).
FIG. S4. Structure factor $S(q)$ for (a) $d = 0.1$ and (b) $d = 2.0$ at three different Pe values across the solid-liquid transition boundary. Each plot shows data from a single simulation. The white arrows indicate the reciprocal lattice vectors, $b_1$ and $b_2$.

INTERMITTENT STATE

At low deformability ($d < 1$) there is an intermittent region near the transition boundary in which the system experiences episodes of fluidization and freezing events. This is demonstrated in the time series of the bond-orientational order $|\Psi_6|$ (Fig. 3). We employ two different methods to locate this region.

First, we examine the standard error of $|\Psi_6|$, which measures the fluctuations between solid and liquid states. We calculate this quantity using the time series data from three simulation runs for each point sampled in the parameter space. Fig. S5 reports heat maps of this standard error. One can see that the region with large error shrinks as deformability increases. We associate a state to be within the intermittent regime if both the standard error of $|\Psi_6|$ and the value of the diffusivity $D_{\text{eff}}$ are above 0.0005. The resulting phase diagrams are displayed in Fig. S6a,b.

Second, we note that intermittence is not only associated with large fluctuations, but also requires that such fluctuations be correlated over finite times, hence the system spends a finite fraction of time in each state. To quantify time-correlations, we examine the time persistence in fluctuations of the number of disclinations. We define a “topological charge” for each cell (say cell $i$) as its deviation from a 6-fold coordination,

$$\Delta N_{nn,i}(t) = N_{nn,i}(t) - 6,$$

where $N_{nn,i}$ is the number of nearest neighbors of the cell. We associate cells with $\Delta N_{nn,i} < 0$ as negative defects, whereas those with $\Delta N_{nn,i} > 0$ as positive defects. We estimate the fraction of cells with defects as

$$\langle |\Delta N_{nn}| \rangle(t) = \frac{1}{N} \sum_{i=1}^{N} |\Delta N_{nn,i}(t)| .$$

Since there are few defects in the solid regime, we can identify the system as solid-like when the time series of $\langle |\Delta N_{nn}| \rangle$ is below 5%, and liquid-like when it goes above this threshold. This allows us to binarize the defect time series, with zero for solid and unity for liquid. To ensure that the solid and liquid states are persistent in time, we smooth the data by removing any jumps in the signal that lasts less than $5D_{\text{eff}}^{-1}$. We label states as intermittent if there are at least two jumps in the binarized signal, and if additionally the system’s effective diffusivity $D_{\text{eff}}$ is above 0.0005. The latter condition ensures that the system is actually fluidized when there are many defects present. Fig. S7 reports examples of the time series of $\langle |\Delta N_{nn}| \rangle$ and
FIG. S5. Heat maps showing the standard error of $|\Psi_6|$ within the explored parameter space for (a) $N = 36$ and (b) $N = 100$.

FIG. S6. Phase diagram constructed from analyzing (a,b) the standard error of $|\Psi_6|$ and (c,d) the binarized signal for the fraction of cells with defects $\langle |\Delta N_{\text{avg}}| \rangle$, for both $N = 36$ and 100. The liquid (orange points) and solid phases (blue points) are identified using the dynamical criterion $D_{\text{eff}} > 0.0005$. In (a,b), the intermittent region (labeled as SL; gray points) is located where the standard error of $|\Psi_6|$ and the value of $D_{\text{eff}}$ are above 0.0005. In (c,d), this region is identified as where the binarized defect signal shows more than two jumps and that $D_{\text{eff}} > 0.0005$. The cyan (magenta) line indicates the lower (upper) bound of the intermittent region and is computed from interpolating the boundaries separating the three regimes. The phase diagram shown in Fig. 2 in the main paper is based on the boundaries drawn in (b).
FIG. S7. Time series for the fraction of cells with defects $\langle |\Delta N_{nn}| \rangle$ in the system for $d = 0.1$ when it is in the (a) solid ($Pe = 1.6$), (b) intermittent ($Pe = 2.2$), and (c) liquid ($Pe = 3.0$) regime (from a single simulation run). The orange curves show the measured $\langle |\Delta N_{nn}| \rangle$ over time, whereas the blue curves are the binarized version of the signal with zero for solid and unity for liquid.

LOCAL OVERLAP

To analyze the correlation between defects and cell overlap, we define a local overlap field $\chi_i(r)$ for each cell (say cell $i$) as

$$\chi_i(r) = \sum_{j=1}^{N} H(\phi_i(r) - 1)H(\phi_j(r) - 1),$$

where $H(x)$ is the Heaviside step function (i.e., we only consider the region within a cell where $\phi > 1$). More precisely, the field is one when the cell overlaps with another cell and zero otherwise (it can exceed one at sites where there are multiple pairwise overlaps). With this field, we estimate the area fraction of a cell overlapped by other cells as

$$\chi_i = \frac{1}{A_i} \int_{\Omega_i} d^2r \chi_i(r),$$

where $A_i$ is the area of the cell and $\Omega_i$ is the region where $\phi_i > 1$. Fig. S8 presents simulation snapshots of the system highlighting the degree of local overlap $\chi_i$ and the local bond-orientational order $\Psi_{6i}$ of each cell and the location of the defects. Not surprisingly, cells with defects are those with a lower orientational order, as they do not have a 6-fold coordination. More important, a careful inspection reveals these defects correlate with the degree of overlap, with negative defects showing more overlap than positive defects. To quantify this observation, we study time frames in which defects exist when the system is in the intermittent or liquid regime, and we construct distributions of the local overlap $\chi$ for cells with defects and for all cells (Fig. S9). These distributions reinforce the visual impression that negative defects indeed have a higher degree of overlap than the average population, whereas positive defects have a lower degree of overlap. The deviation between these distributions is also significant as quantified by performing the non-parametric Kolmogorov-Smirnov (KS) two-sample test (Table SII).

SIMULATION MOVIES

Here we provide captions for the supplemental movies:

- **Supplemental Movies 1-4**: Example simulation runs showing the dynamics of the system both in the overlapping and non-overlapping regime and both at low and high motility. The movie begins at the point when motility has just been switched on in the monolayer. The parameters are (Movie 1) $(d, Pe) = (0.1, 1.0)$, (Movie 2) $(0.1, 3.0)$, (Movie 3) $(2.0, 0.6)$, and (Movie 4) $(2.0, 2.0)$. Same as Fig. 1 in the main paper, the coloring corresponds to the cell-index at $t = 0$.

- **Supplemental Movie 5**: A simulation run showing the intermittent behavior of the system at low deformability, where it experiences episodes of freezing and melting events. The parameters are $(d, Pe) = (0.1, 2.2)$, and the coloring scheme is the same as above. Time series of the global orientational order $|\Psi_6|$ and the fraction of cells with defects $\langle |\Delta N_{nn}| \rangle$ for this simulation run are shown at the bottom.

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[2] R. Mueller, J. M. Yeomans, and A. Doostmohammadi, Phys. Rev. Lett. 122, 048004 (2019).

[3] M. Nonomura, PLoS One 7, e33501 (2012).

[4] Unless otherwise stated, the figures shown in this document are for the system size $N = 100$. 

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FIG. S8. Simulated snapshots of the system for (a) \((d, Pe) = (0.1, 2.2)\) and (b) \((0.1, 3.0)\), showing the correlation between (i) the degree of local overlap \(\chi_i\), (ii) the topological charge \(\Delta N_{nn,i}\), and (iii) the local bond-orientational order \(|\Psi_{6,i}|\). In (ii) and (iii), we plot a Voronoi deconstruction of the system to aid visualization. Black arrows highlight a positive (a cell with 7-fold disclination) and a negative defect (a cell with 5-fold disclination). The negative defect has a higher degree of overlap than the positive defect.

FIG. S9. Probability density of the local overlap \(\chi\) for negative defects, positive defects, and all cells at four different parameter sets: (a) \((d, Pe) = (0.1, 2.2)\), (b) \((0.1, 3.0)\), (c) \((0.3, 1.8)\), and (d) \((0.3, 2.6)\). In each case, the distribution is constructed from sampling time frames from two separate simulation runs in which defects exist. Note that negative defects tend to have a higher degree of overlap than positive defects.
TABLE. SII. Kolmogorov-Smirnov (KS) two-sample test results for determining the significance in the deviation between the distributions of the local overlap values for negative defects, positive defects, and all cells. A higher $D$ value suggests that the two populations are more deviated from one another.

| $(d, Pe)$ | All vs. Positive Defects | All vs. Negative Defects | Positive vs. Negative Defects |
|----------|--------------------------|--------------------------|------------------------------|
| (0.1, 2.2) | $D = 0.31, p < 10^{-4}$ | $D = 0.52, p < 10^{-4}$ | $D = 0.72, p < 10^{-4}$ |
| (0.1, 3.0) | $D = 0.27, p < 10^{-4}$ | $D = 0.38, p < 10^{-4}$ | $D = 0.61, p < 10^{-4}$ |
| (0.3, 1.8) | $D = 0.023, p = 2.1 \times 10^{-3}$ | $D = 0.18, p < 10^{-4}$ | $D = 0.19, p < 10^{-4}$ |
| (0.3, 2.6) | $D = 0.086, p < 10^{-4}$ | $D = 0.097, p < 10^{-4}$ | $D = 0.18, p < 10^{-4}$ |