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Supplemental Information

Dynamic Migration Modes of Collective Cells

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Supporting Material for "Dynamic Migration Modes of Collective Cells"

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In this Supporting Material, we provide more details for derivation and numerical simulations. Additional data and figures are also included to support the results and conclusions given in the main text.

1. Normalization of the controlling equations

We integrate two typical intercellular social interactions — local alignment (LA) and contact inhibition of locomotion (CIL) into our active vertex model to investigate collective cell dynamics in a coherent cell monolayer. In the main text, we have given the controlling equation for the time evolution of vertices' positions, $\mathbf{r}_i(t)$, as

$$\frac{\mathrm{d}\mathbf{r}_i}{\mathrm{d}t}=\frac{1}{\gamma}\mathbf{f}_i^{\mathrm{U}}+\sum_{J\in C_i}\frac{v_0\mathbf{p}_J}{n_J}+\sum_{J\in C_i}\frac{\varepsilon_{\mathrm{T}}\boldsymbol{\eta}_J^{\mathrm{T}}(t)}{n_J}. \tag{S1}$$

From the potential energy given by Eq. (1) in the main text, the potential force $\mathbf{f}_i^{\mathrm{U}}$ can be derived as

$$\mathbf{f}_i^{\mathrm{U}}=-\sum_{J\in C_i}\frac{1}{2}K_{\mathrm{a}}(A_J-A_0)\big[\mathbf{k}\times(\mathbf{r}_{j_2}-\mathbf{r}_{j_1})\big]-\sum_{J\in C_i}K_{\mathrm{c}}L_J\Big(\frac{\mathbf{r}_i-\mathbf{r}_{j_1}}{|\mathbf{r}_i-\mathbf{r}_{j_1}|}+\frac{\mathbf{r}_i-\mathbf{r}_{j_2}}{|\mathbf{r}_i-\mathbf{r}_{j_2}|}\Big)-\sum_{j\in V_i}\Lambda\frac{\mathbf{r}_i-\mathbf{r}_j}{|\mathbf{r}_i-\mathbf{r}_j|}, \tag{S2}$$

where $\mathbf{k}$ denotes a unit vector normal to the cell monolayer; the summation $\sum_{J\in C_i}$ computes over all cells C_i sharing vertex i, and j_1 and j_2 are the neighboring vertices of vertex i in cell J; the summation $\sum_{j\in V_i}$ is made over all neighboring vertices V_i of vertex i. Substituting (S2) into (S1), we obtain

$$\begin{aligned}\frac{\mathrm{d}\mathbf{r}_i}{\mathrm{d}t}=&-\frac{1}{\gamma}\sum_{J\in C_i}\frac{1}{2}K_{\mathrm{a}}(A_J-A_0)\big[\mathbf{k}\times(\mathbf{r}_{j2}-\mathbf{r}_{j1})\big]-\frac{1}{\gamma}\sum_{J\in C_i}K_{\mathrm{c}}L_J\Big(\frac{\mathbf{r}_i-\mathbf{r}_{j1}}{|\mathbf{r}_i-\mathbf{r}_{j1}|}+\frac{\mathbf{r}_i-\mathbf{r}_{j2}}{|\mathbf{r}_i-\mathbf{r}_{j2}|}\Big)\\&-\frac{1}{\gamma}\sum_{j\in V_i}\Lambda\frac{\mathbf{r}_i-\mathbf{r}_j}{|\mathbf{r}_i-\mathbf{r}_j|}+\sum_{J\in C_i}\frac{v_0\mathbf{p}_J}{n_J}+\sum_{J\in C_i}\frac{\varepsilon_{\mathrm{T}}\boldsymbol{\eta}_J^{\mathrm{T}}(t)}{n_J}.\end{aligned} \tag{S3}$$

Besides, the cell polarity $\mathbf{p}_J=(\cos\theta_J,\sin\theta_J)$ is mediated by LA and CIL, and evolves as

$$\frac{\mathrm{d}\theta_J}{\mathrm{d}t}=\frac{\mu_{\mathrm{a}}}{n_J}\sum_{K\in C_J}\sin(\theta_K^{(\mathrm{vel})}-\theta_J)+\frac{\mu_{\mathrm{c}}}{n_J}\sum_{K\in C_J}\sin(\alpha_{J,K}-\theta_J)+\varepsilon_{\mathrm{R}}\eta_J^{\mathrm{R}}(t). \tag{S4}$$

We normalize the governing equations for the vertices' positions (i.e. (S3)) and the polarity directions of cells (i.e. (S4)) through the length scale $l=\sqrt{A_0}$ and the time scale $\tau=\gamma/(K_{\mathrm{a}}A_0)$. The normalized equations can be written as

$$\begin{aligned}\frac{\mathrm{d}\tilde{\mathbf{r}}_i}{\mathrm{d}\tilde{t}}=&-\sum_{J\in C_i}\frac{1}{2}(\tilde{A}_J-1)\big[\mathbf{k}\times(\tilde{\mathbf{r}}_{j2}-\tilde{\mathbf{r}}_{j1})\big]-\sum_{J\in C_i}\tilde{K}_{\mathrm{c}}\tilde{L}_J\Big(\frac{\tilde{\mathbf{r}}_i-\tilde{\mathbf{r}}_{j1}}{|\tilde{\mathbf{r}}_i-\tilde{\mathbf{r}}_{j1}|}+\frac{\tilde{\mathbf{r}}_i-\tilde{\mathbf{r}}_{j2}}{|\tilde{\mathbf{r}}_i-\tilde{\mathbf{r}}_{j2}|}\Big)\\&-\sum_{j\in V_i}\tilde{\Lambda}\frac{\tilde{\mathbf{r}}_i-\tilde{\mathbf{r}}_j}{|\tilde{\mathbf{r}}_i-\tilde{\mathbf{r}}_j|}+\sum_{J\in C_i}\frac{\tilde{v}_0\mathbf{p}_J}{n_J}+\sum_{J\in C_i}\frac{\tilde{\varepsilon}_{\mathrm{T}}\tilde{\boldsymbol{\eta}}_J^{\mathrm{T}}(\tilde{t})}{n_J}\end{aligned} \tag{S5}$$

and

$$\frac{\mathrm{d}\theta_J}{\mathrm{d}\tilde{t}}=\frac{\tilde{\mu}_{\mathrm{a}}}{n_J}\sum_{K\in C_J}\sin(\theta_K^{(\mathrm{vel})}-\theta_J)+\frac{\tilde{\mu}_{\mathrm{c}}}{n_J}\sum_{K\in C_J}\sin(\alpha_{J,K}-\theta_J)+\tilde{\varepsilon}_{\mathrm{R}}\tilde{\eta}_J^{\mathrm{R}}(\tilde{t}), \tag{S6}$$

where the dimensionless parameters are defined as

$$\begin{aligned}
&\tilde{\mathbf{r}}_i = \frac{\mathbf{r}_i}{\sqrt{A_0}}, \quad \tilde{t} = \frac{t}{\tau}, \quad \tilde{A}_J = \frac{A_J}{A_0}, \quad \tilde{L}_J = \frac{L_J}{\sqrt{A_0}}, \\
&\tilde{K}_{\mathrm{c}} = \frac{K_{\mathrm{c}}}{K_{\mathrm{a}} A_0}, \quad \tilde{\Lambda} = \frac{\Lambda}{K_{\mathrm{a}} A_0^{3/2}}, \quad \tilde{v}_0 = \frac{v_0 \tau}{\sqrt{A_0}}, \quad \tilde{\mu}_{\mathrm{a}} = \mu_{\mathrm{a}} \tau, \quad \tilde{\mu}_{\mathrm{c}} = \mu_{\mathrm{c}} \tau, \\
&\tilde{\varepsilon}_{\mathrm{T}} = \frac{\varepsilon_{\mathrm{T}} \sqrt{\tau}}{\sqrt{A_0}}, \quad \tilde{\boldsymbol{\eta}}_J^{\mathrm{T}} = \boldsymbol{\eta}_J^{\mathrm{T}} \sqrt{\tau}, \quad \tilde{\varepsilon}_{\mathrm{R}} = \varepsilon_{\mathrm{R}} \sqrt{\tau}, \quad \tilde{\eta}_J^{\mathrm{R}} = \eta_J^{\mathrm{R}} \sqrt{\tau}.
\end{aligned} \tag{S7}$$

2. Estimation of the dimensionless parameters

According to experimental measurements (1), the viscosity of biological tissues is in the order of $10^4 - 10^5\ \mathrm{N \cdot s \cdot m^{-2}}$, leading to an estimation of the friction coefficient $\gamma \sim 0.01 - 0.1\ \mathrm{N \cdot s \cdot m^{-1}}$. Taking the cell areal stiffness $K_{\mathrm{a}} \sim 10^5 - 10^7\ \mathrm{N \cdot m^{-3}}$ for epithelial tissues (2, 3), and the reference area $A_0 = 900\ \mu\mathrm{m}^2$, we have the estimation of the length scale and the time scale used for normalization as $l = \sqrt{A_0} \sim 30 \mu\mathrm{m}$ and $\tau = \gamma/(K_{\mathrm{a}} A_0) \sim 100\ \mathrm{s}$, respectively. The cell contraction force is in the range of $1 - 10\ \mathrm{nN}$ for epithelial cell sheets (4), corresponding to the cell contraction modulus $K_{\mathrm{c}} \sim 10^{-5} - 10^{-4}\ \mathrm{N \cdot m^{-1}}$. The intercellular tension is of the order $\Lambda \sim 10^{-9} - 10^{-8}\ \mathrm{N}$, as estimated from experimental measurements on biological tissues (1). Therefore, we have the estimation of dimensionless cell contractile modulus $\tilde{K}_{\mathrm{c}} = K_{\mathrm{c}}/(K_{\mathrm{a}} A_0) \sim 0.01 - 0.1$ and the dimensionless intercellular tension $\tilde{\Lambda} = \Lambda/(K_{\mathrm{a}} A_0^{3/2}) \sim 0.01 - 0.1$. Besides, the cell protrusive force is of the order $1\ \mathrm{nN}$ (5), resulting in a self-propelled velocity $v_0 \sim 10^{-8} - 10^{-7}\ \mathrm{m \cdot s^{-1}}$, with its dimensionless form of the order $\tilde{v}_0 = v_0 \tau/\sqrt{A_0} \sim 0.01 - 0.1$. Consequently, we use the following values for the dimensionless parameters in our study: $\tilde{K}_{\mathrm{c}} = 0.02$, $\tilde{\Lambda} = 0.1$, $\tilde{v}_0 = 0.1$. Besides, the intensities of LA and CIL (in their dimensionless forms) are assumed to be of the order $\tilde{\mu}_{\mathrm{a}} = 0.1$ and $\tilde{\mu}_{\mathrm{c}} = 1.0$, respectively. Moreover, to focus on the roles of LA and CIL in regulating collective cell dynamics in a confluent cell monolayer, we set the noises $\varepsilon_{\mathrm{T}} = 0$ and $\varepsilon_{\mathrm{R}} = 0$ for simplicity.

References

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Supplemental figures

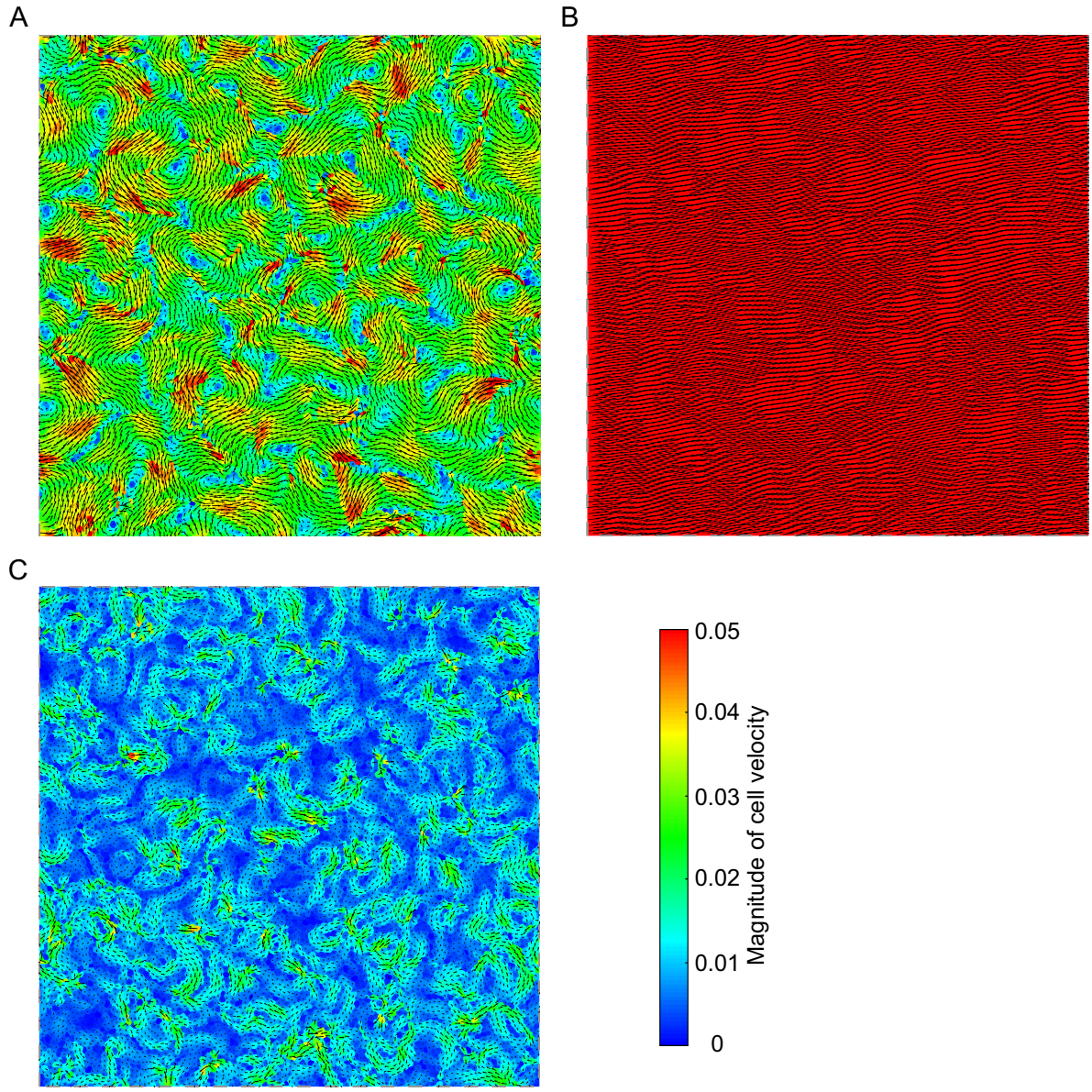

Fig. S1. Typical velocity fields of collective cell migration obtained from our active vertex model. The arrows denote velocity vectors of cells and the color code indicates magnitude of cell velocity. Parameters values: (*A*) $\mu_{\mathrm{a}} = 0.05$ and $\mu_{\mathrm{c}} = 1.0$; (*B*) $\mu_{\mathrm{a}} = 0.1$ and $\mu_{\mathrm{c}} = 0$; and (*C*) $\mu_{\mathrm{a}} = 0.0$ and $\mu_{\mathrm{c}} = 1.0$.

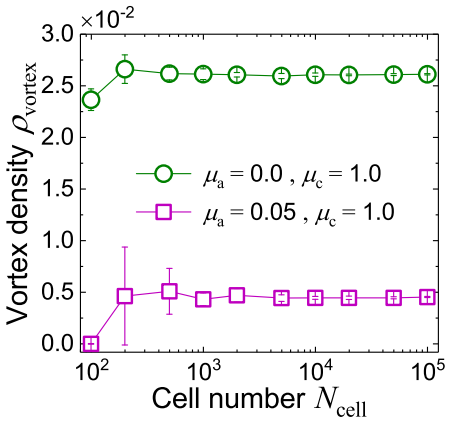

Fig. S2. Intrinsic vortex density in confluent cell monolayers. The vortex density ρ_{vortex} approaches a constant for large enough system ($N_{\mathrm{cell}} \to +\infty$). Data are mean $\pm$ SD.

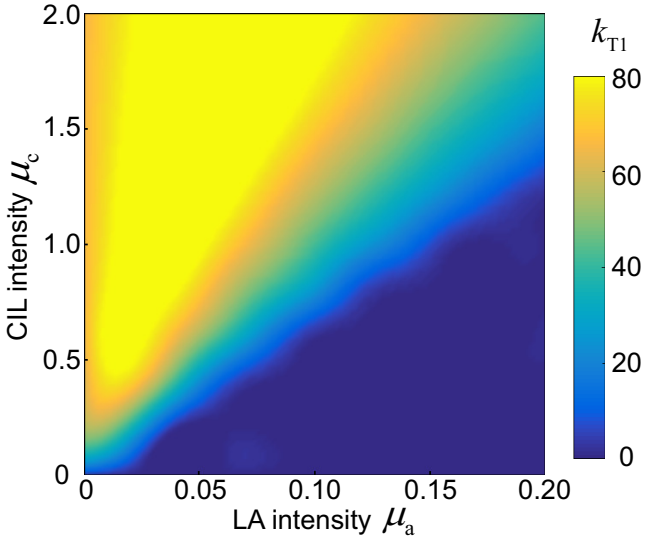

Fig. S3. The frequency of cell neighbor exchange regulated by intercellular social interactions. Phase diagrams of the frequency of cell neighbor exchange k_{T1} under the regulation of LA (μ_{a}) and CIL (μ_{c}).

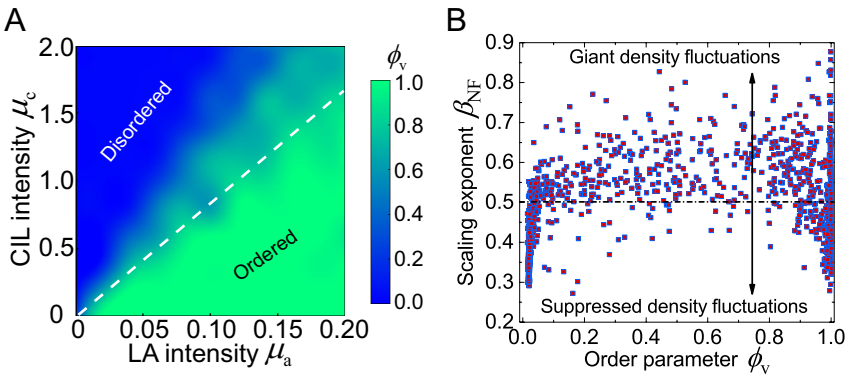

Fig. S4. Giant density fluctuations in confluent cell monolayers are not restricted to emerge in the highly ordered state of collective motions, but take place in a state with the motion order in a rather broad range. (*A*) Phase diagrams of the order parameter $\phi_{\rm v}$ regulated by LA ($\mu_{\rm a}$) and CIL ($\mu_{\rm c}$). Here, the order parameter is defined as $\phi_{\rm v} = \left\langle \left| (1/N_{\rm cell}) \sum_J \mathbf{v}_J / |\mathbf{v}_J| \right| \right\rangle_t$. The ordered phase and disordered phase are distinguished at $\phi_{\rm v} = 0.8$. (*B*) Scatter diagram of the scaling exponent for number fluctuations $\beta_{\rm NF}$ versus the motion order $\phi_{\rm v}$.