Cells crawling and wetting on the surface of a sphere

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Objectives

We build a continuum theory from discrete cell motion equations previously proposed [1]. We investigate the minimal conditions under which cell aggregation occurs on a sphere, considering interaction and self-propulsion forces such as:

1. Cell-cell and cell-substrate adhesion
2. Contact inhibition of locomotion (CIL)
3. Cell-substrate friction
4. Self-propulsive motile force

Theory

Let consider a continuous density of cells $\phi'(\mathbf{x},t) = n(\mathbf{x},t)\frac{V_0}{V}$ such that

$$\phi_0 = \frac{1}{\mathcal{A}}\int d^2x\,\phi'(\mathbf{x},t)$$

with $0 \leqslant \phi_0 \leqslant 1$ the initial cell concentration and $\mathcal{A}$ the total area covered by the cells [2]. A continuum approach is constructed from the cell motion equations [1] without cell-cell friction ($\gamma = 0$) averaged on cell orientations θ_i

$$-F_m e^{-1/4\psi}\hat{n}_i = \gamma_s\dot{\mathbf{x}}_i + \sum_j^{nn} F_{ij}^{cc}\hat{n}_{ij}$$

where γ_s is cell-substrate friction. Including the confinement due to the elastic membranes a Cahn-Hilliard equation is obtained

$$\frac{\partial\phi}{\partial t} = D\nabla^2\left(\frac{\partial f_{CH}}{\partial\phi} - \lambda^2\nabla^2\phi\right) \qquad (1)$$

accounting for the conservation of cell concentration, where $f_{CH} = (c_0^2/2)\phi^2(1-\phi)^2$ is a symmetric double-well free energy that allows phase separation with a given energy cost when ϕ goes from 0 to 1 and vice versa.

Parameter space

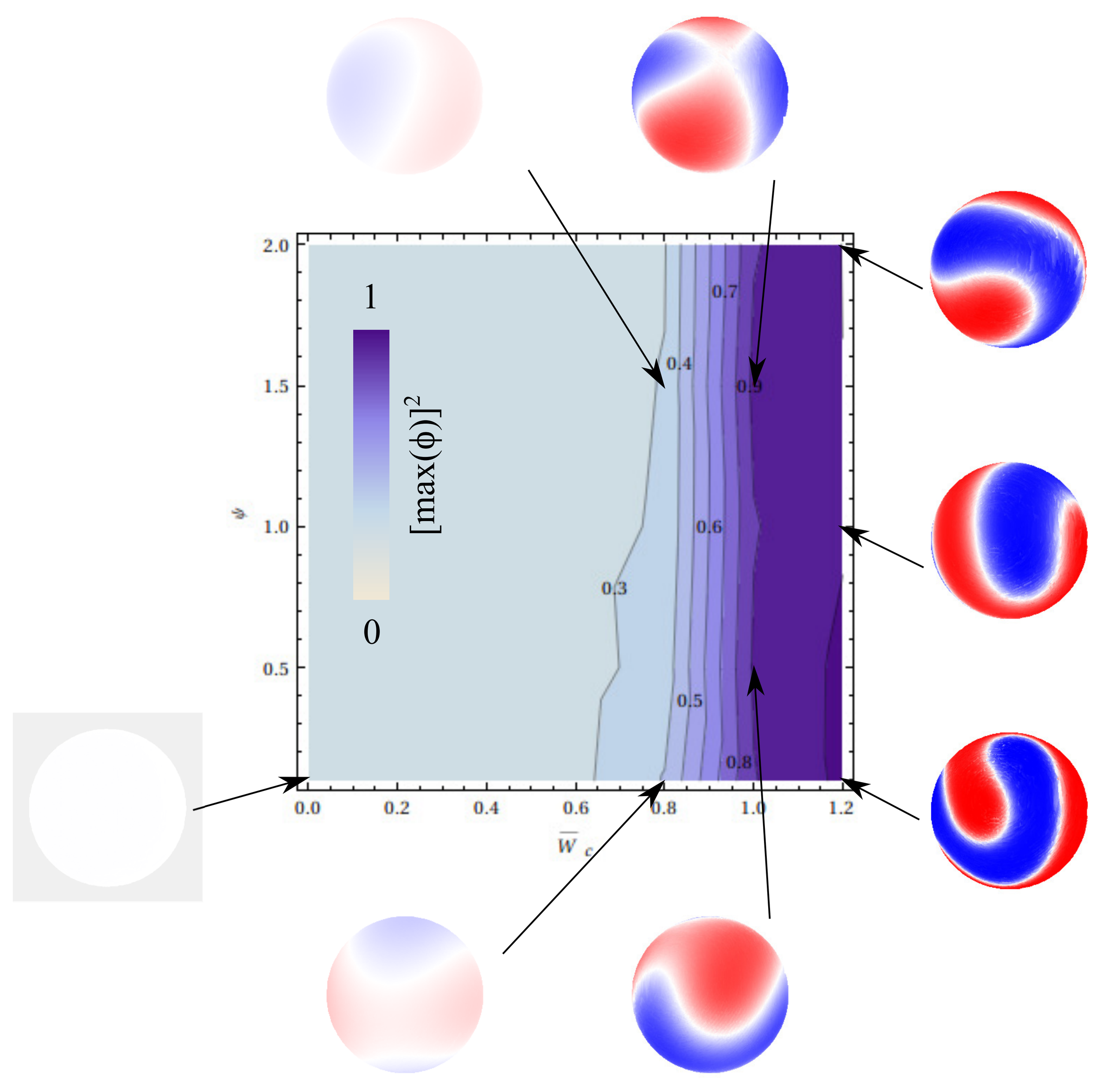

Figure: Parameter space at cell density $\phi_0 = \Omega/2$ within $T_s^* = 2$ [months] time scale. Light (blue) areas indicate homogeneous (non-cohesive) states. Bold (blue) regions indicate heterogeneous (cohesive) phases. Inset: Last phase state at different points in the phase space.

We consider numerical simulations on the surface of an elastic sphere, cells motion occurs between two enveloping layers. Membranes deformation is proportional to local cell concentration. The ratio of the employed numerical cell size to the sphere radius is $1/20$. The square of the field maximum is shown at the end of each run.

Phase dynamics

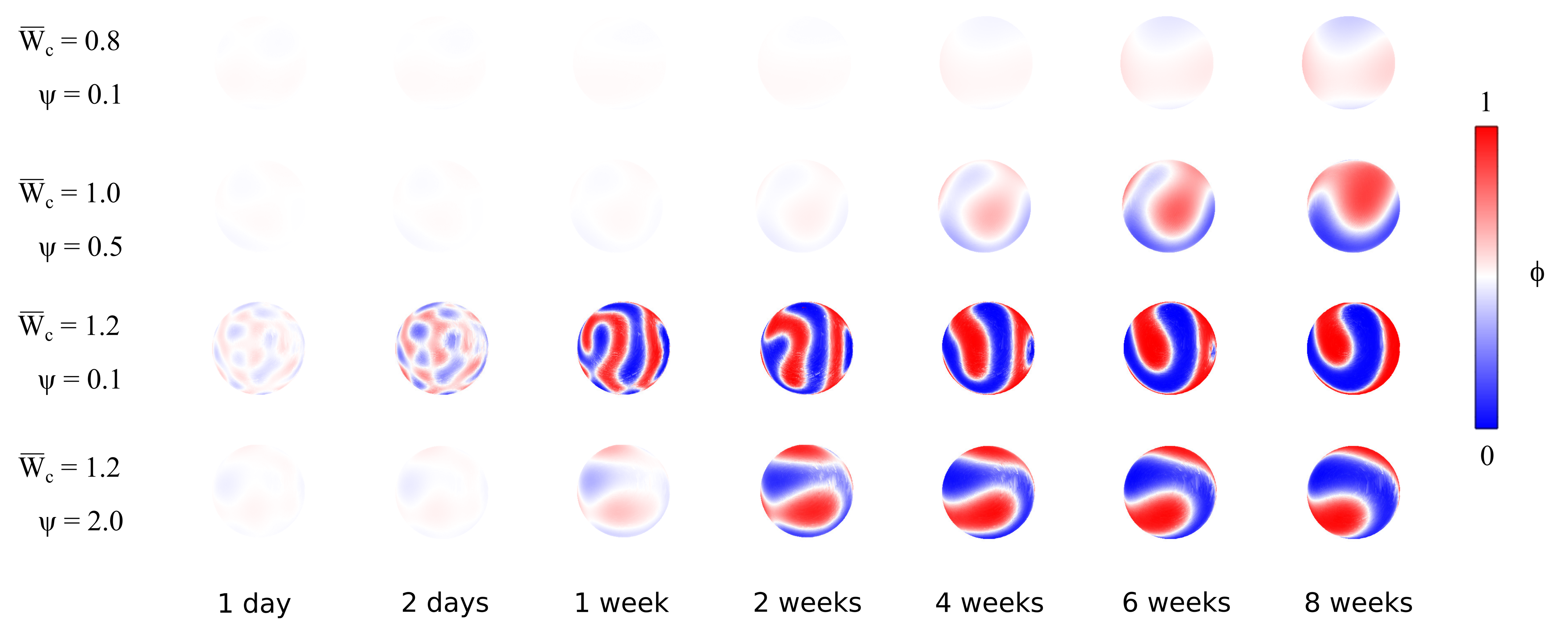

Figure: Phase dynamics at $\phi_0 = \Omega/2$ of 4 points in the parameter space within 2 [months]. Scaled phase fluctuates between 0 (blue) and 1 (red). Cell concentration ranges up to the overlap factor Ω.

The values of (D, λ) in equation (1) are mapped onto the $(\overline{W}_c, \psi)$ space through [2]

$$6D\lambda^2\frac{I\rho g}{h^3 E_f} = \sqrt{2}\frac{R_0}{\gamma_s}\left(\frac{F_m}{R_0^2}e^{-1/4\psi} + 8\frac{W_s}{R_0^3} + 4\frac{k_s}{R_0} - 2k_s\bar{\kappa}\right)$$

with diffusion constant $D = k_s R_0^2/\gamma_s$ and $k_s = 2\frac{W_s+W_c}{R_0^2}$ the stiffness of the virtual springs associated to the elastic force mediating the interaction between two neighboring cells. Cohesive states dominate as increasing $\overline{W}_c$ ratio.

Conclusions

- Different phases are found in agreement with previous results employing self-propelled particle simulations [1], exhibiting gas-like states, polar liquids and 3D structures.

References

[1] B. Smeets et al. Emergent structures and dynamics of cell colonies by contact inhibition of locomotion. *Proc. Nat. Acad. Sci.*, 113(51):14621–14626, 2016.

[2] N. O. Rojas et al. Thermodynamic conditions for biological cell aggregation. *To be submitted to Nat. Phys.*

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