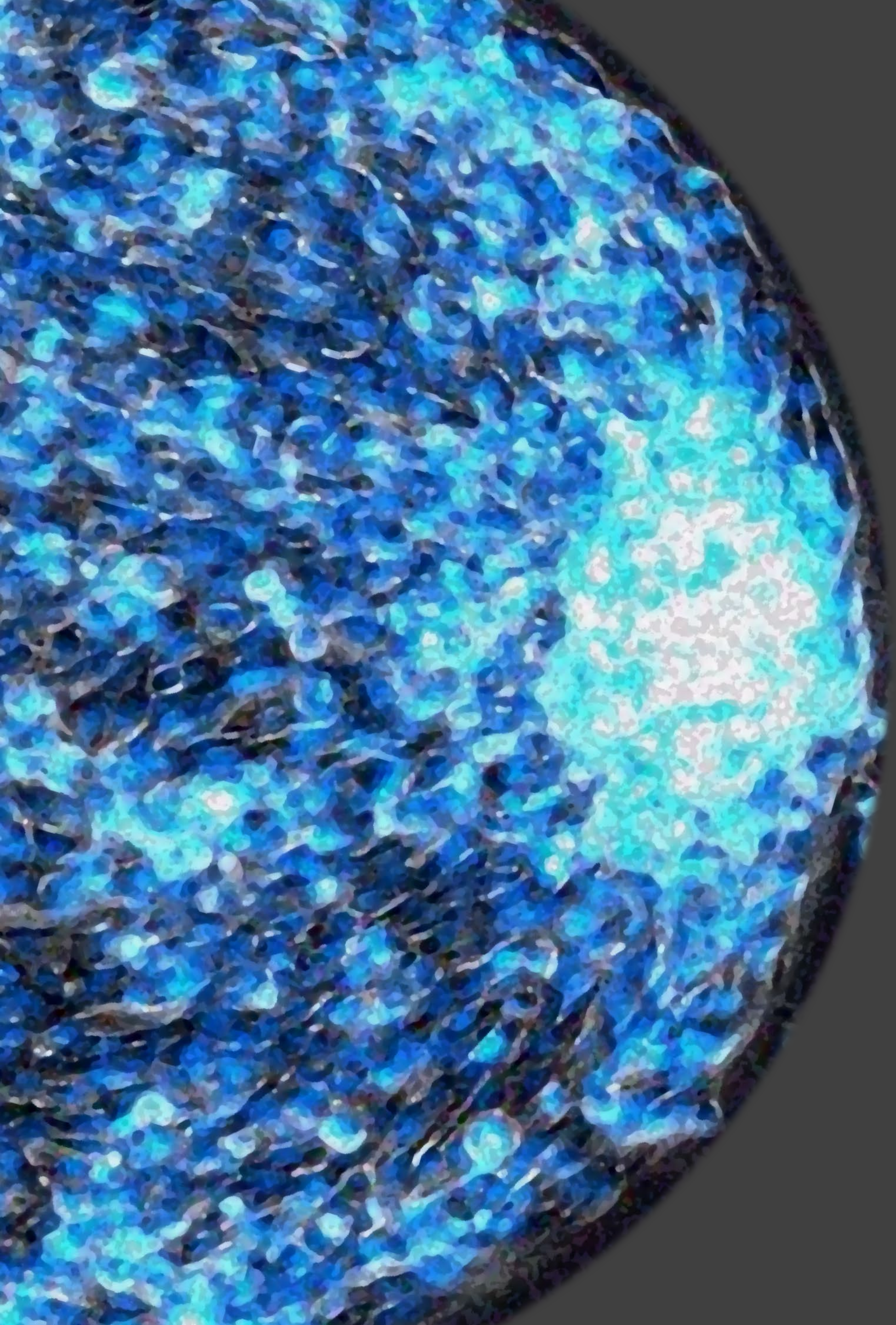


細胞集団運動とトポロジー

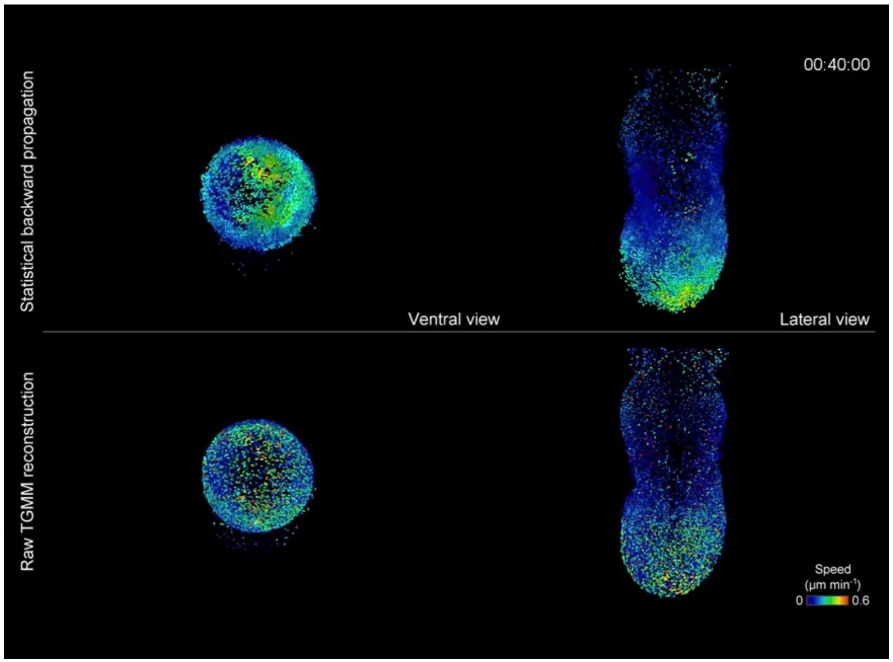
Kyogo Kawaguchi

Nonequilibrium Physics of Living Matter

RIKEN Hakubi Research Team

RIKEN CPR/BDR

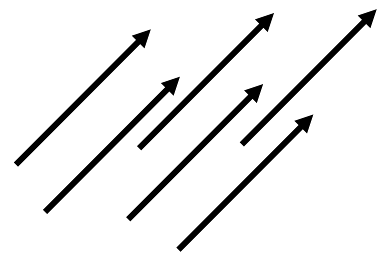
“Equation of motion” in multicellular dynamics



Mouse early embryogenesis
McDole, K. et al. Cell **175**, 859-876.e33 (2018).

Cell interactions, patterning, growth…

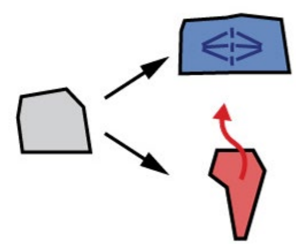
- Migrating cells



“Active matter”

Cultured neural progenitors

- Gain and loss of agents

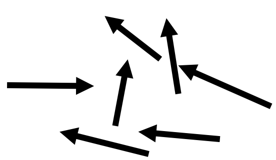


“Interacting particle system”

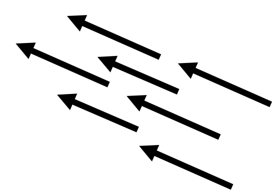
Tissue homeostasis of mouse skin

‘Ordering’ in biology

Disordered



Ordered



Ancel et al., Nature (1997), Animal Behavior (2015)

Vicsek model: long range order of self-propelled particles

Positions of particles:

$$\mathbf{x}_i(t+1) = \mathbf{x}_i(t) + \mathbf{v}_i(t)\Delta t\,. \qquad (1)$$

Direction of velocity:

↓ noise strength η

$$\theta(t+1) = \langle \theta(t) \rangle_r + \Delta\theta\,, \qquad (2)$$

Violation of Mermin-Wagner-Hohenberg:

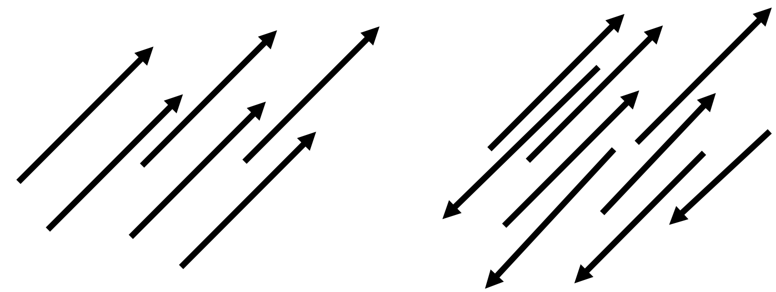
→ ‘New phases’ in collective dynamics of self-propelled (=active) particles

T Vicsek, A Czirók, E Ben-Jacob, I Cohen, & O Shochet, Phys. Rev. Lett. (1995)

J. Toner and Y. Tu, Phys. Rev. Lett. (1995)

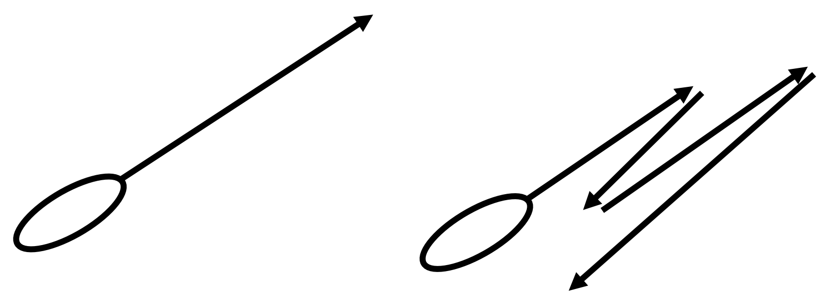
Generalizing Vicsek model

- Polar interaction -> nematic



Polar Nematic

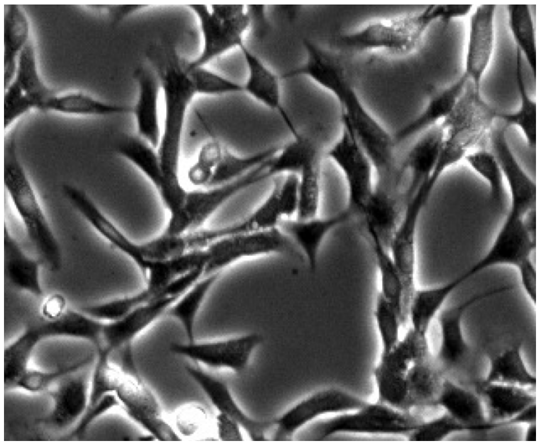
- Unidirectional -> bidirectional



“Flipping” time scale τ

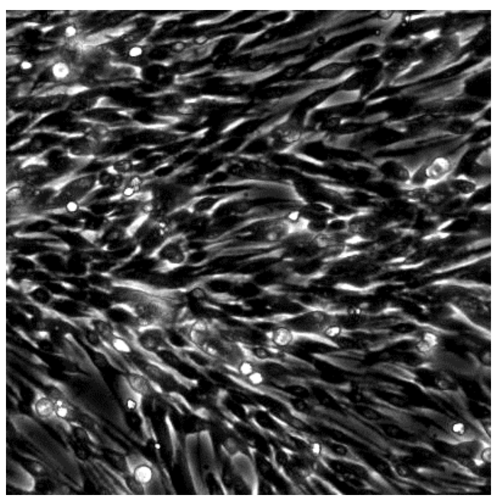
Ordering of neural stem cells

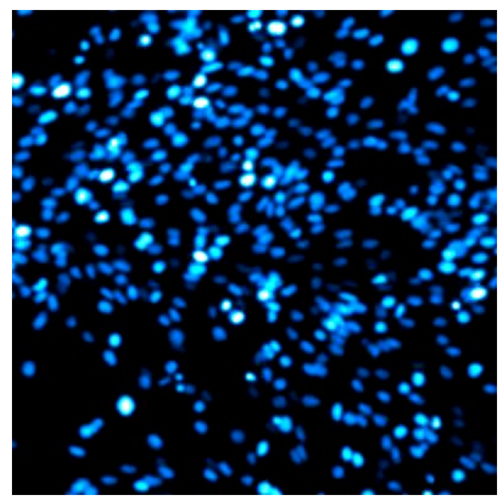
20 um



Growth

Phase contrast image

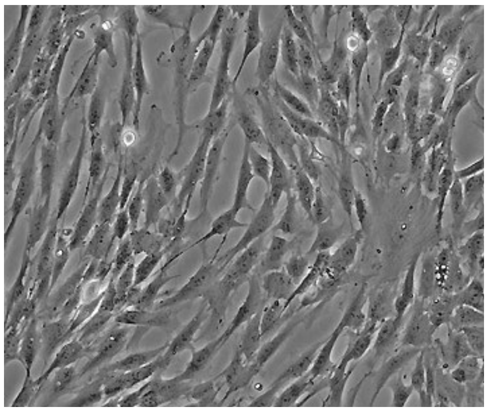




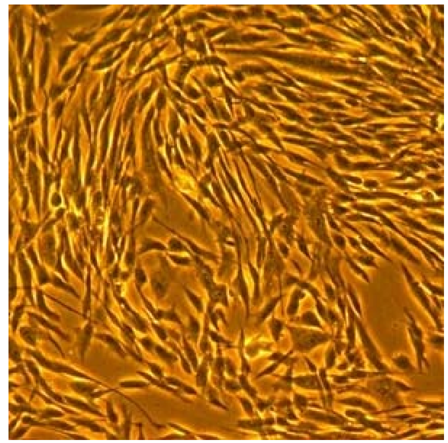
Cell nuclei
(H2B-mCh)

24 hrs movie

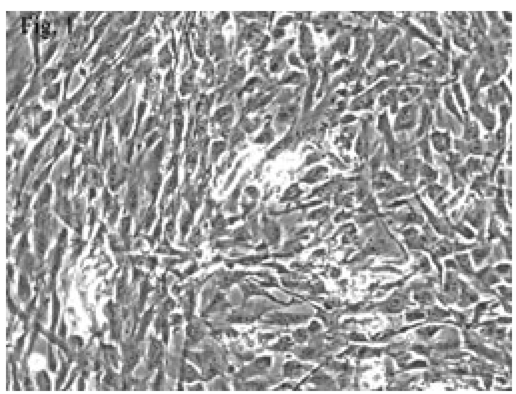
Bipolar cells are typically nematic



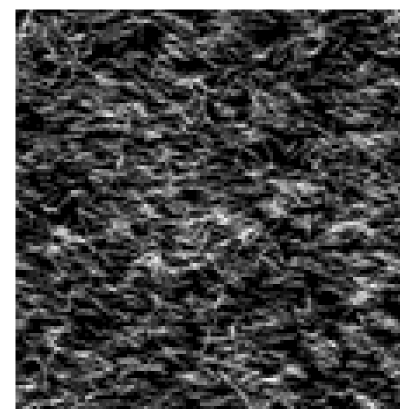
RPE cells (ATCC)



Fibroblasts (ATCC)

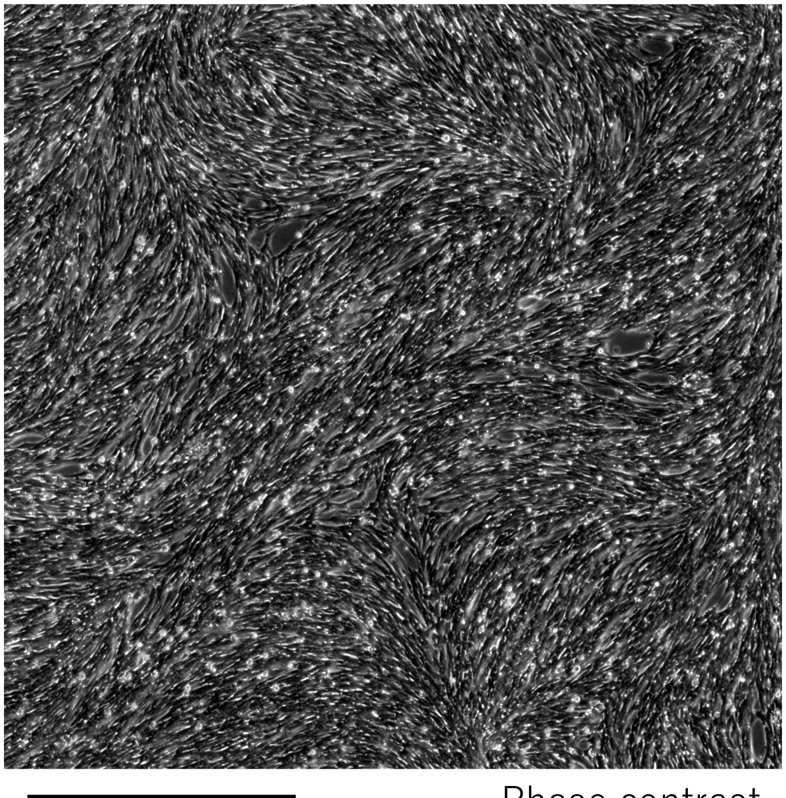


Skeletal muscle cells (CosmoBio)



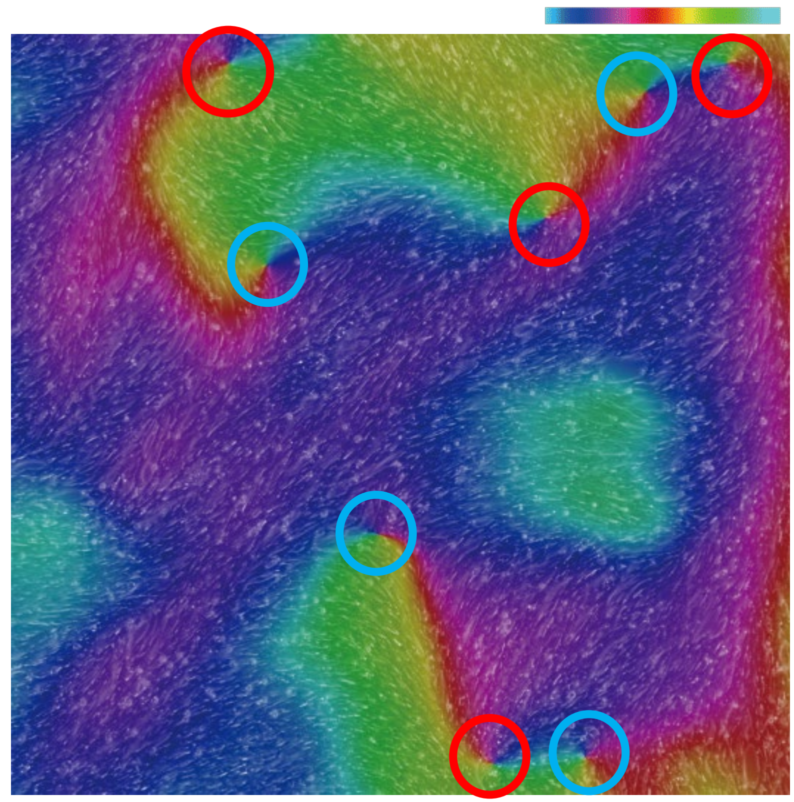
E. coli (bacteria)
D. Nishiguchi et al., Phys. Rev. E (2017)

Topological defects in neural stem cell culture

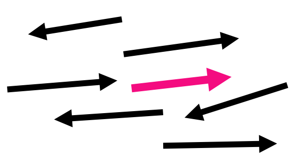


1 mm

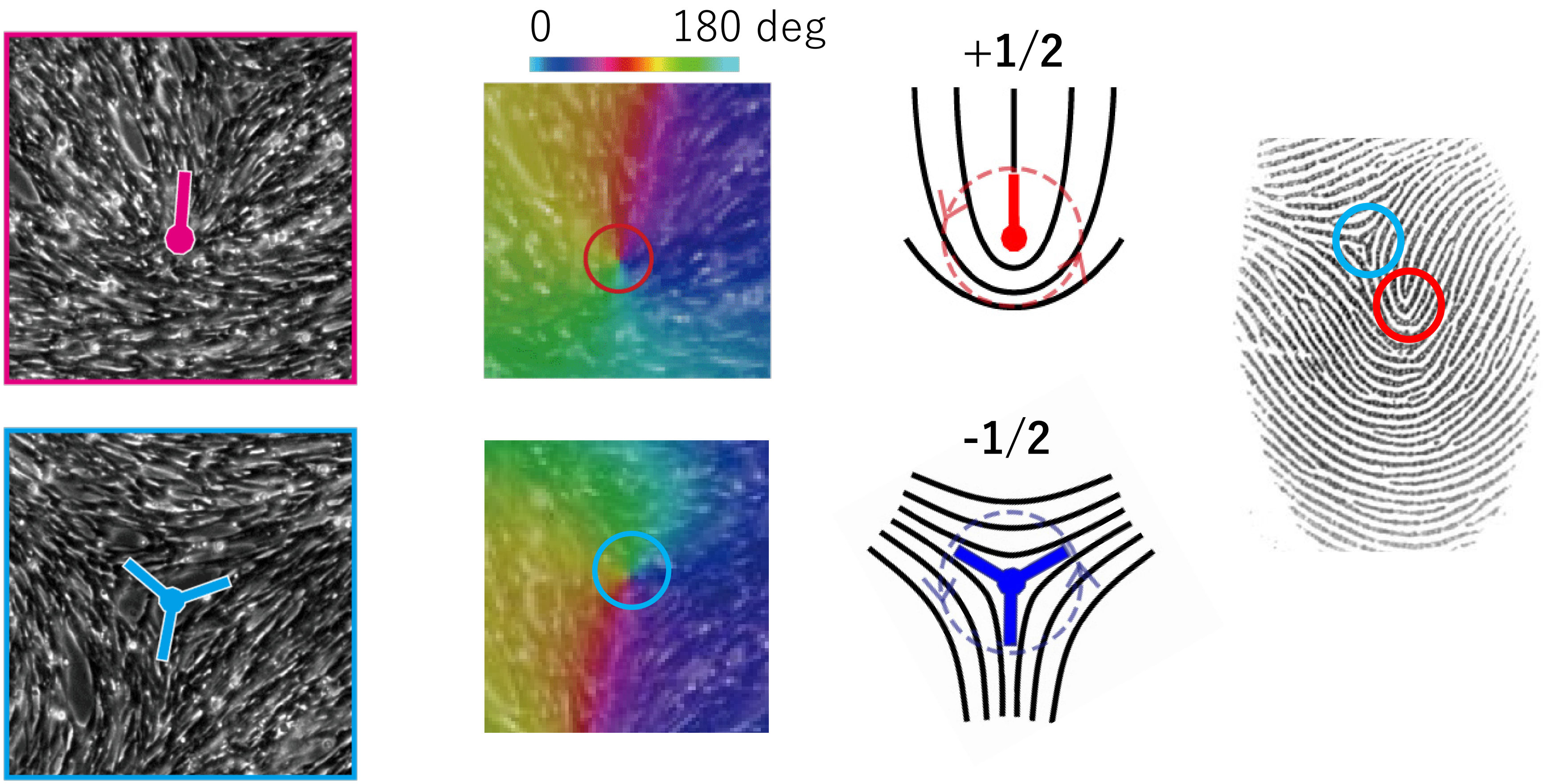
Phase contrast



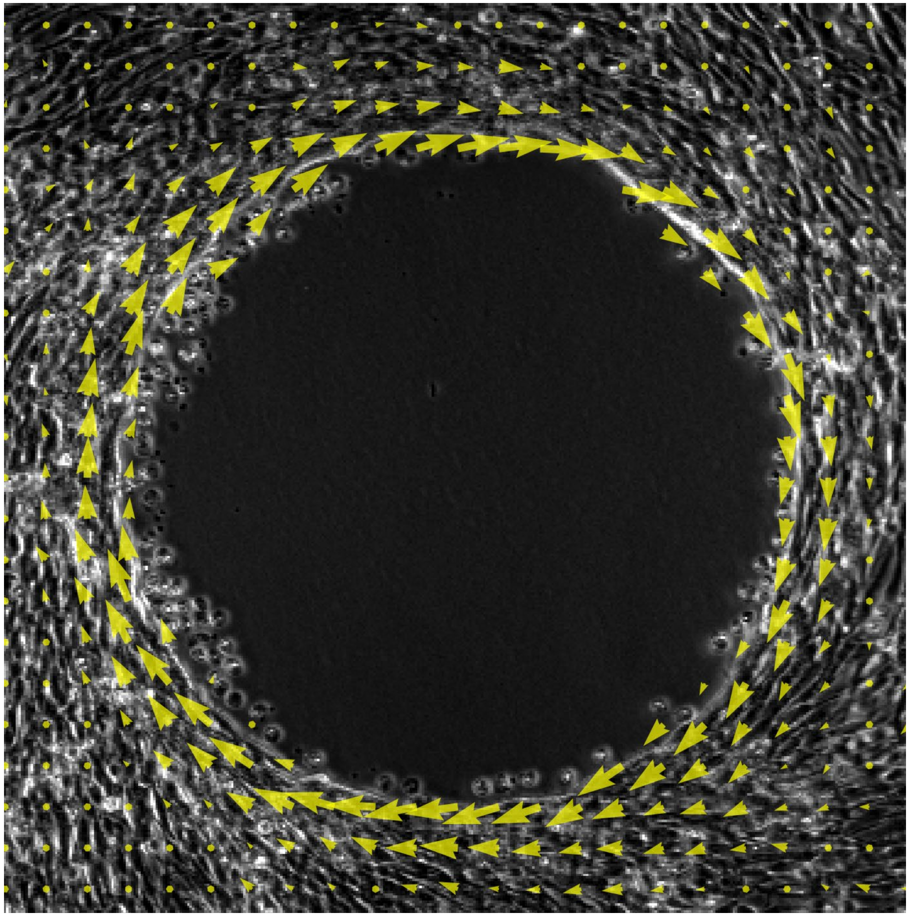
Angle



Two types of topological defects

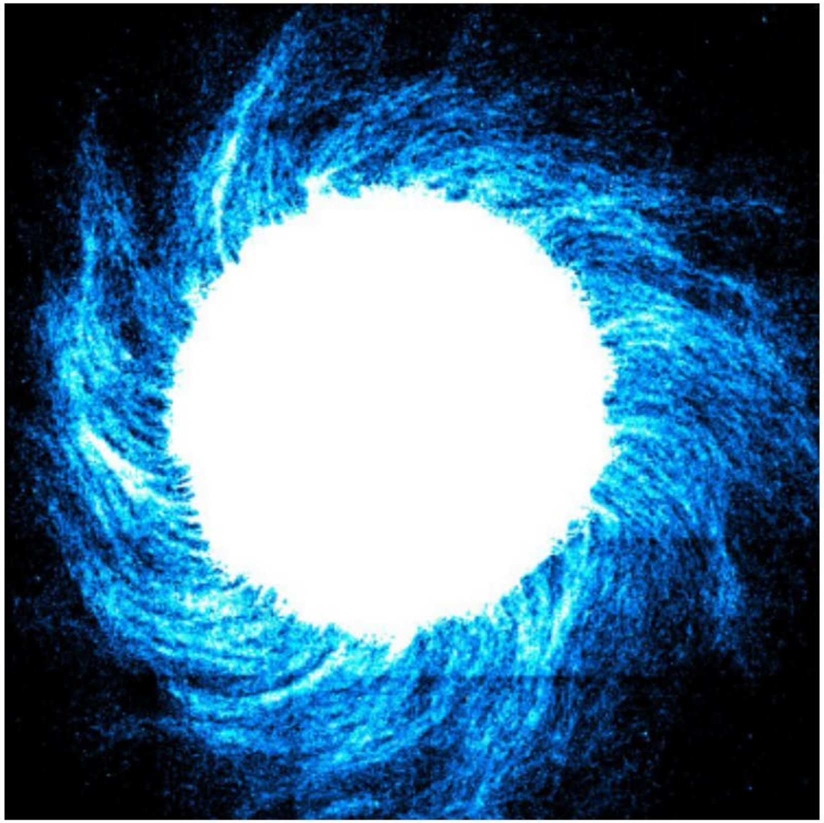


Chiral cell flow is edge localized

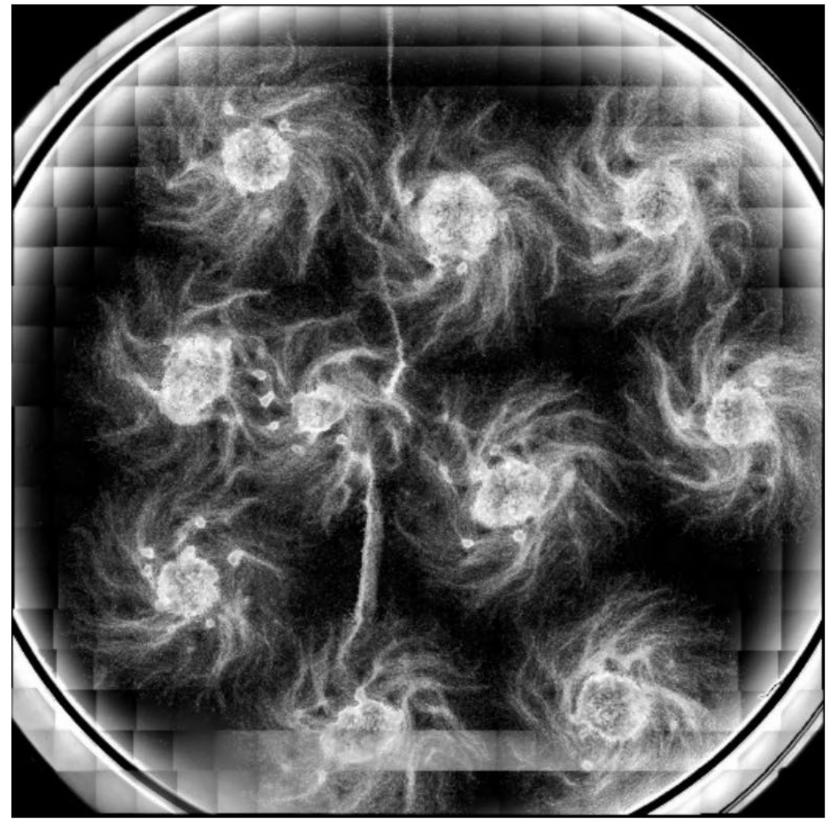


Chirality at macro-scale

Phase contrast



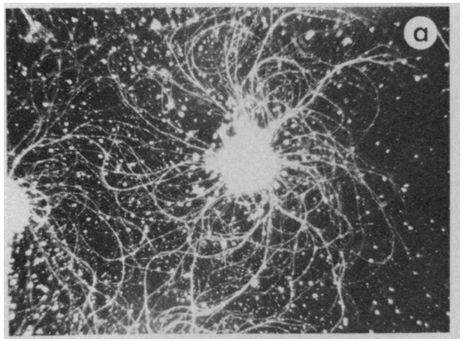
2 mm

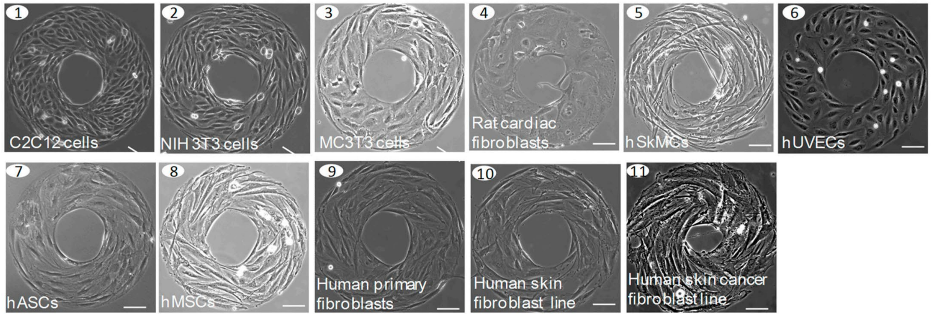


1 cm

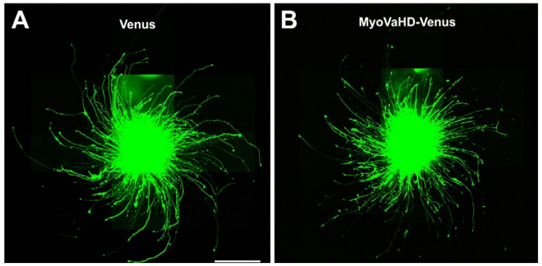
Chirality in cells

Goldfish retinal cells
[Heacock, Agranoff, Science 1977]

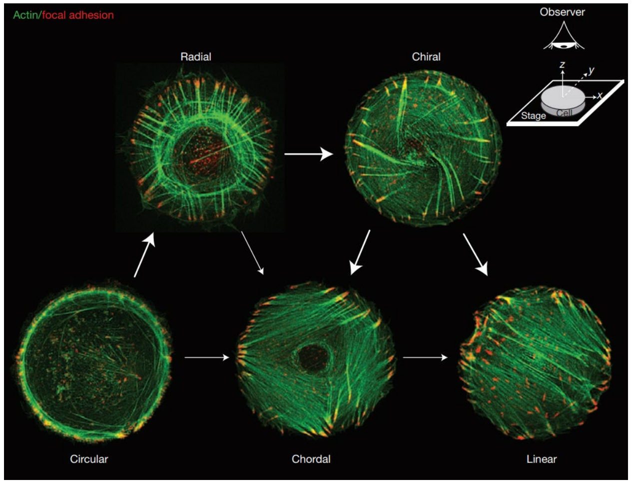




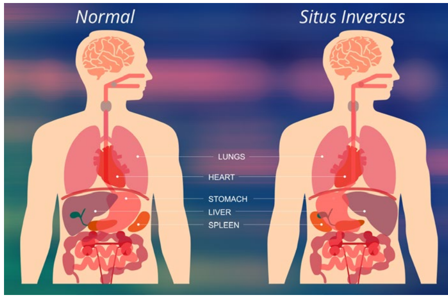
Mammalian cells in stamp culture
[Wan et al., PNAS 2011]



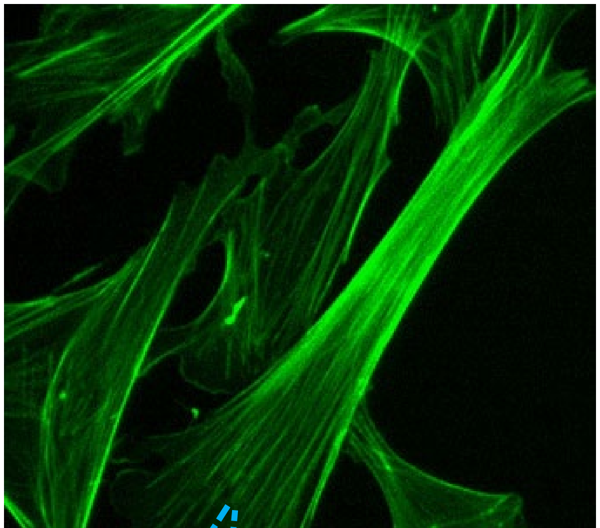
Mouse neuron dendrites
[Tamada et al., JCB 2010]



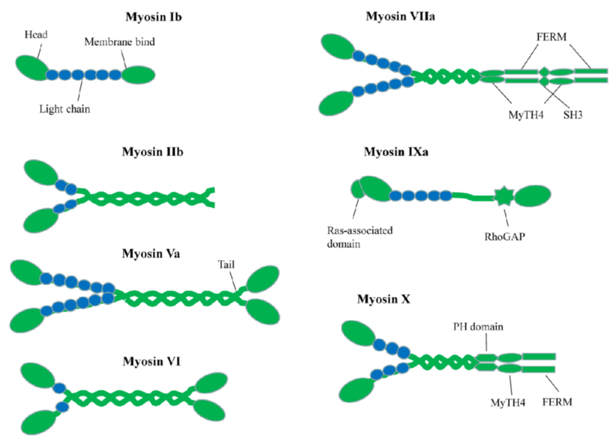
Actin fibers in cells
[Tee et al., Nat Cell Biol 2015]



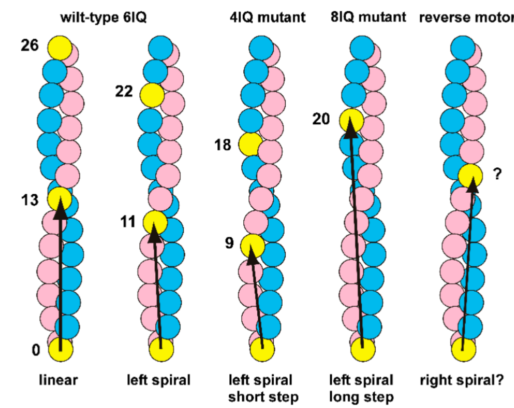
Components of cells are chiral



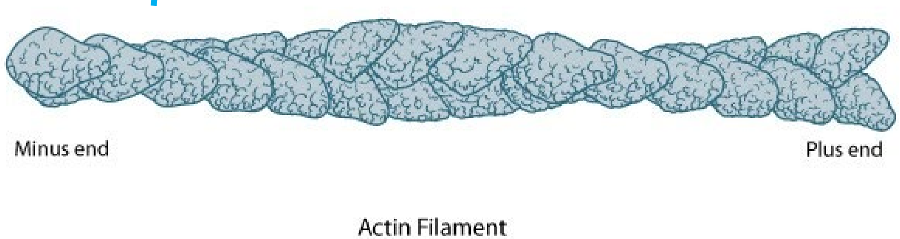
Y tambe (wikipedia)

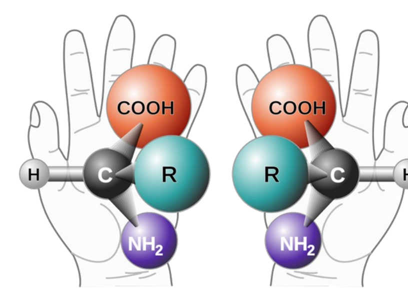


McConnell and Tyska (2010)



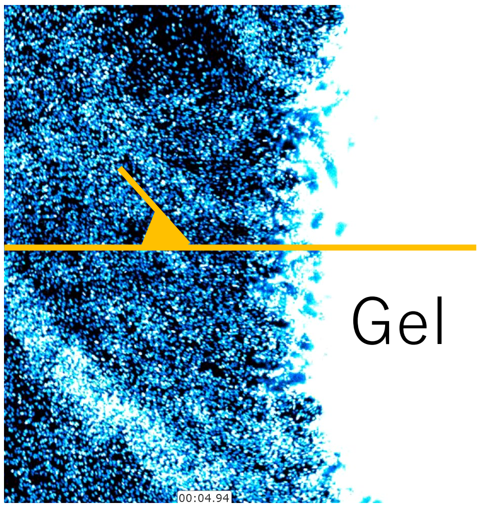
Tamada [Symmetry, 2019]



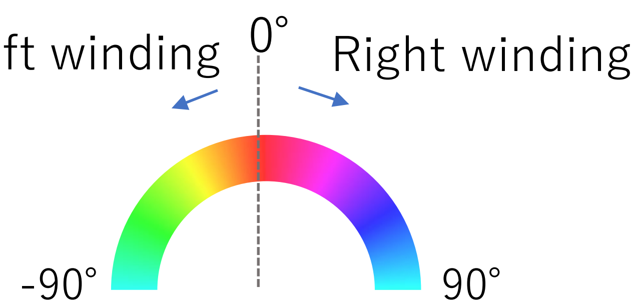


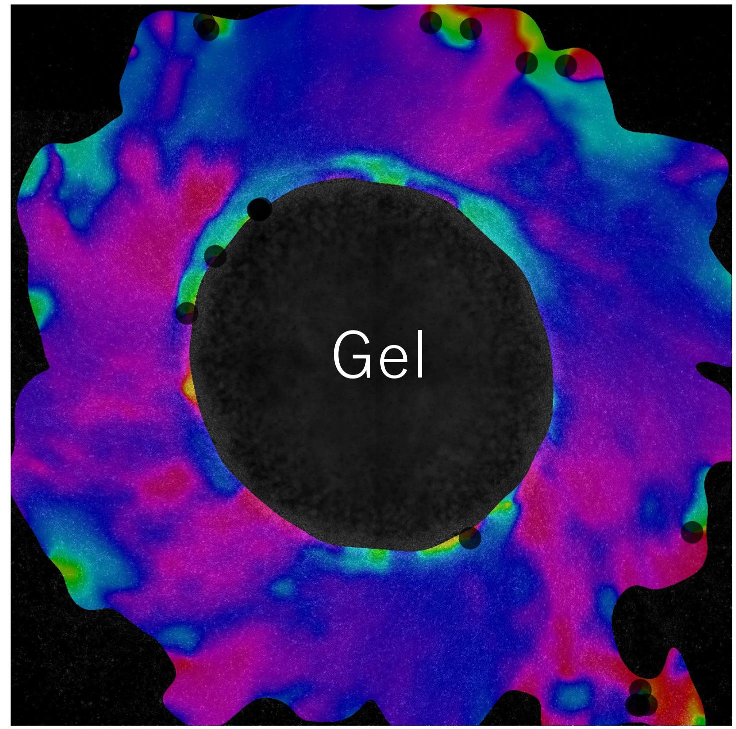
mechanobio.info

Quantification of chirality shows that cells are right winding



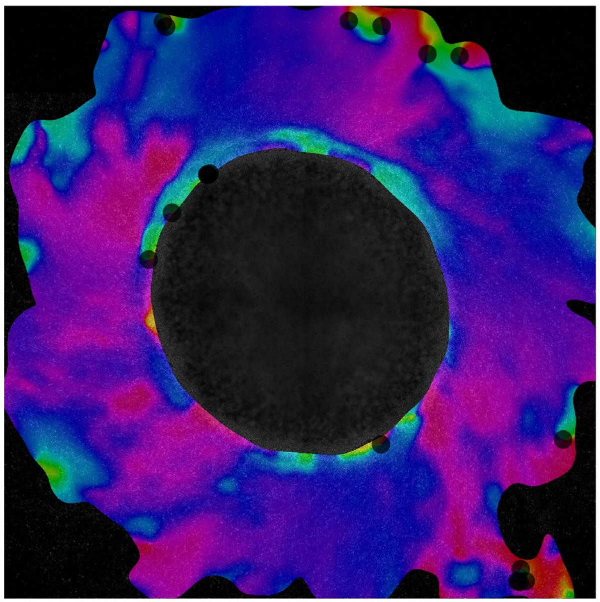
Cell alignment angle with respect to the radial direction:



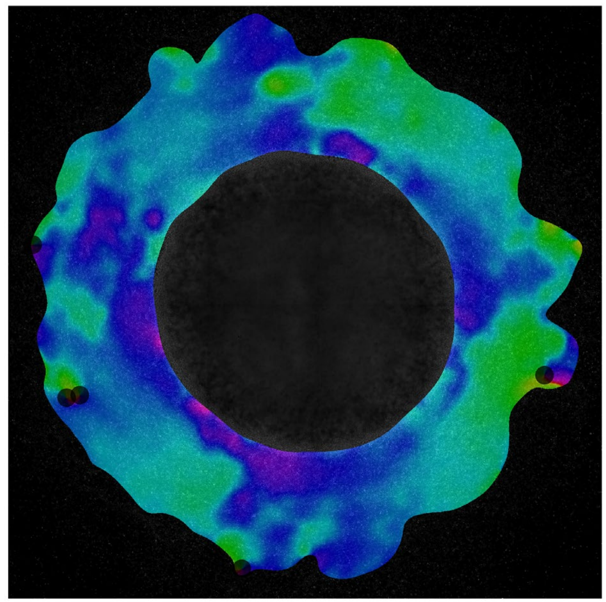


Cytoskeleton inhibitors can change the chirality

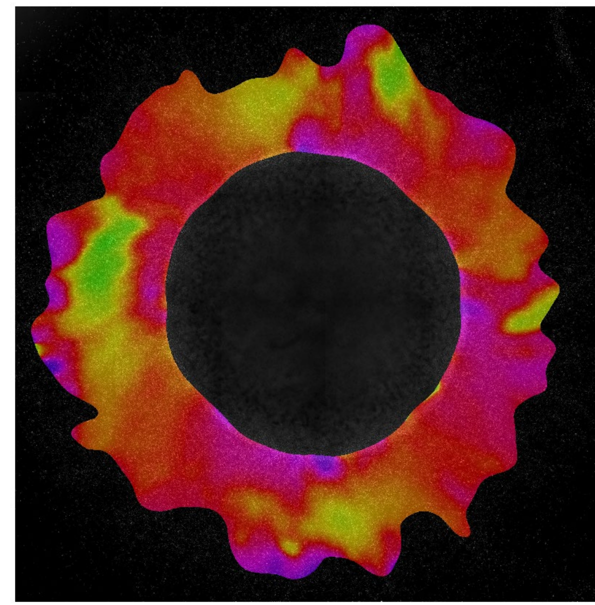
No drug

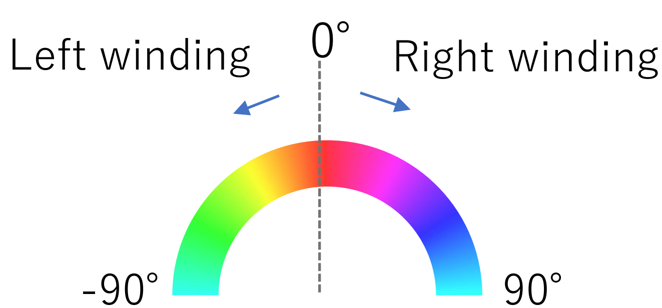


Blebbistatin 2.5 uM
(Myosin II inhibitor)

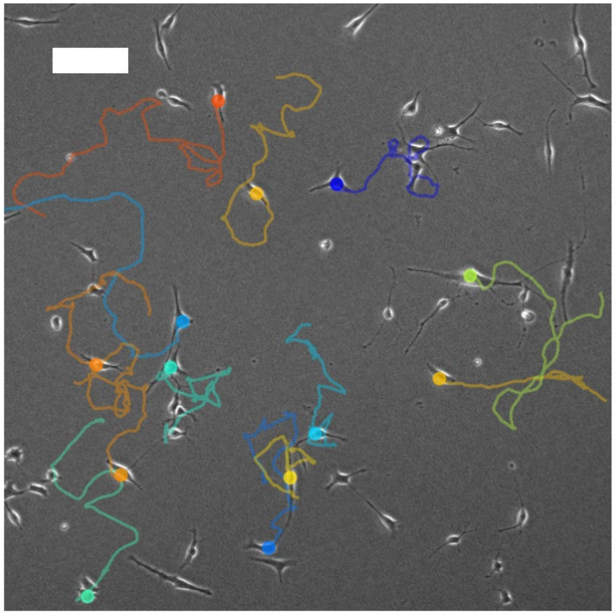


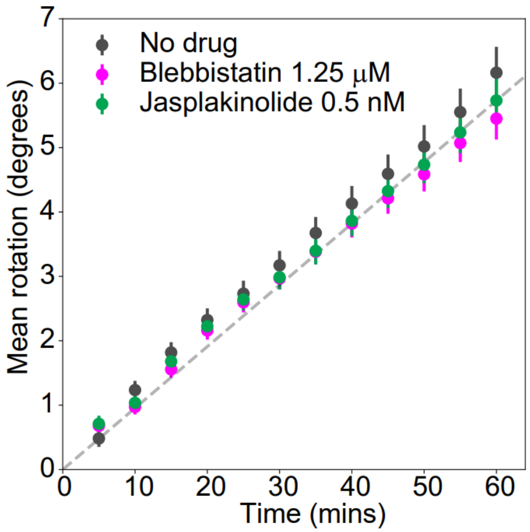
Jasplakinolide 12.5 nM
(Actin depolymerization inhibitor)





Chirality at single cell level (sparse condition)

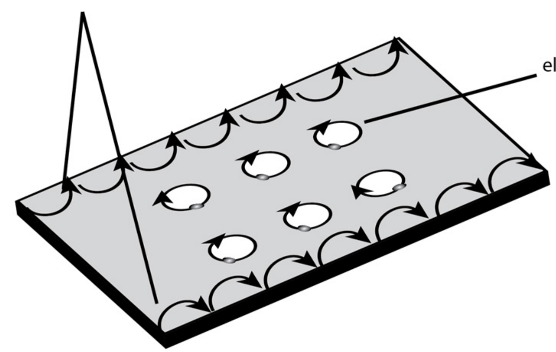


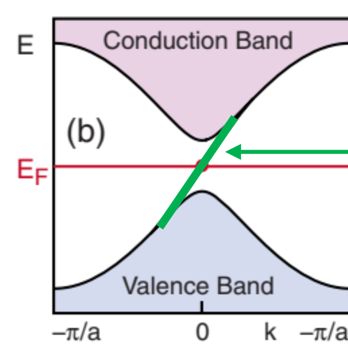


Collective cell dynamics and topological edge mode?

- Quantum Hall effect, topological insulators

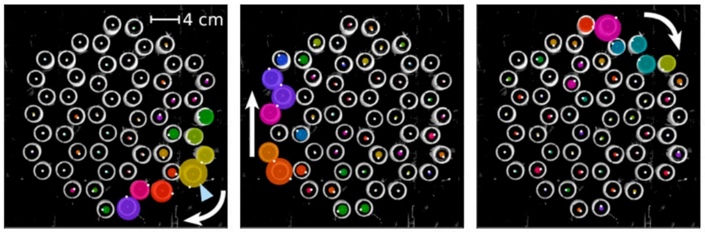
Cells ⇔ Electrons





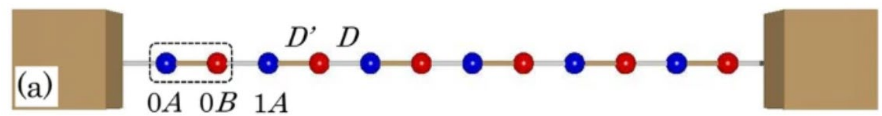
Hasan, Kane, Rev Mod Phys (2010)

Topological edge modes in classical systems



t = 0.0 s t = 3.2 s t = 6.4 s

Gyroscope metamaterial:
Nash et al. [PNAS, 2015]

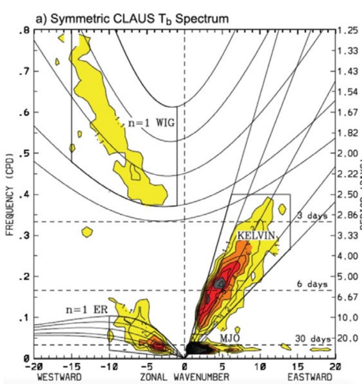


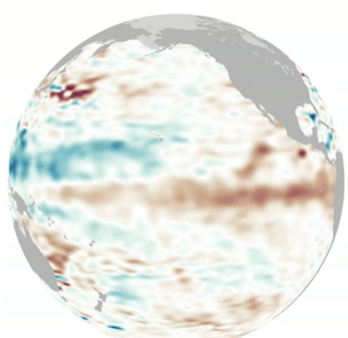
Diffusion, heat conduction:
Yoshida, Kudo, Hatsugai [Sci Rep, 2021]

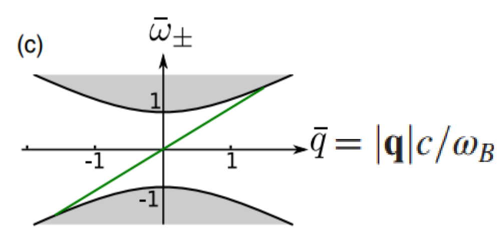
Fluid mechanics with Coriolis force

Chirality

$$i\omega \begin{bmatrix} \rho/\rho_0 \\ u_x/c \\ u_y/c \end{bmatrix} = i \begin{bmatrix} 0 & q_x & q_y \\ q_x & 0 & -i(\omega_B - \eta_o q^2) \\ q_y & i(\omega_B - \eta_o q^2) & 0 \end{bmatrix} \begin{bmatrix} \rho/\rho_0 \\ u_x/c \\ u_y/c \end{bmatrix}$$





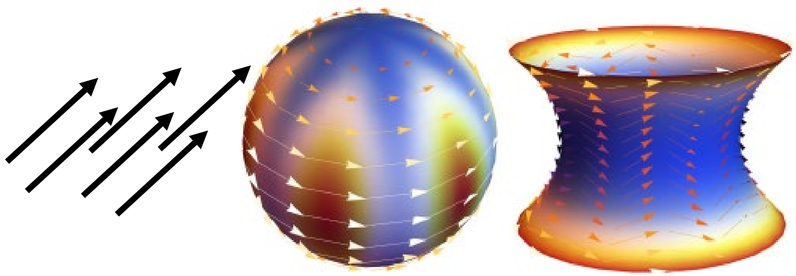


Equatorial wave (causing El Niño): Delplace et al. [Science, 2017]

In active systems (1)

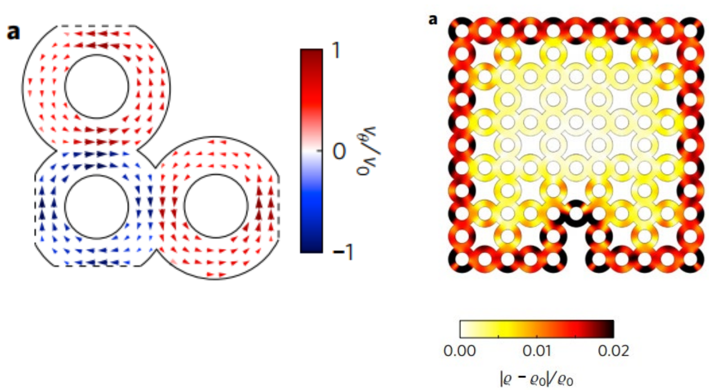
Review: Shankar et al. [arXiv:2010.00364]

Polar active fluid…

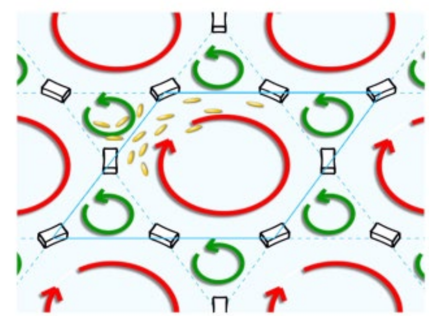


on curved geometry:
Shankar et al. [Phys Rev X 2017]

in Lieb lattice rings:
Souslov et al. [Nat Phys 2017]

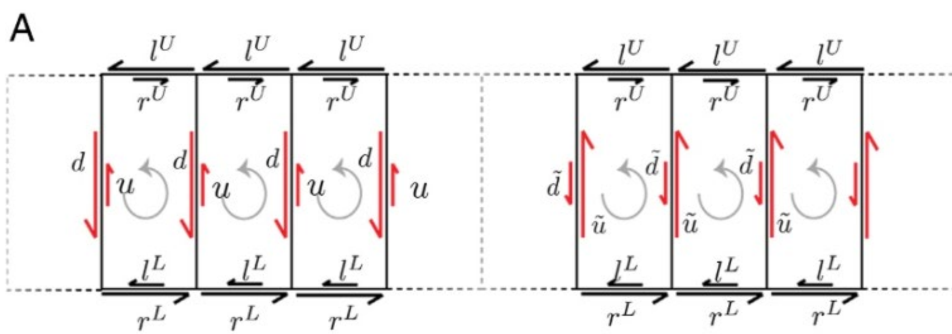


without time-reversal symmetry breaking:
Sone, Ashida [Phys Rev Lett 2019]

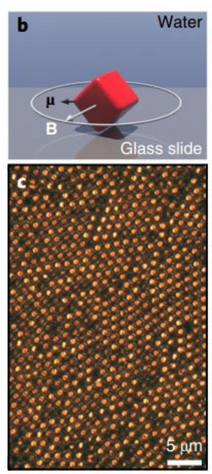


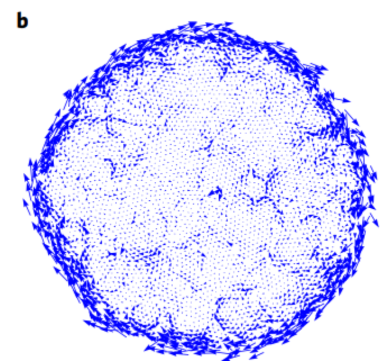
In active systems (2)

Non-Hermitian skin effect: Dasbiswas et al. [PNAS 2018]



Chiral active fluid: Soni et al. [Nat Phys 2019] etc.





Eq of motion of chiral active nematic gas

Time evolution equation of cell density (position $\mathbf{r}$, angle ϕ)

$$\partial_t f(\mathbf{r},\phi,t) + v_0 \mathbf{e}_\phi \cdot \nabla f(\mathbf{r},\phi,t) - \theta \partial_\phi f(\mathbf{r},\phi,t) = \frac{1}{\tau}\left[f(\mathbf{r},\phi+\pi,t) - f(\mathbf{r},\phi,t)\right] + D_\phi \frac{\partial^2}{\partial \phi^2} f(\mathbf{r},\phi,t) + I_{\mathrm{col}},$$

Fourier modes: $f(\mathbf{r},\phi,t) = \frac{1}{2\pi}\sum_{k=0}^{\infty} f_k(\mathbf{r},t) e^{-ik\phi}$

Chirality

$$\partial_t f_0 = -v_0 \partial_x \mathrm{Re} f_1 - v_0 \partial_y \mathrm{Im} f_1,$$

$$\partial_t f_1 = -\frac{2}{\tau} f_1 - D_\phi f_1 - i(\theta + \nu_1 \Delta) f_1 - \frac{v_0}{2}\partial_x f_0 - i\frac{v_0}{2}\partial_y f_0 - \frac{v_0}{2}\partial_x f_2 + i\frac{v_0}{2}\partial_y f_2$$

$$\partial_t f_2 = -4D_\phi f_2 - 2i(\theta + \nu_2 \Delta) f_2 - \frac{v_0}{2}\partial_x f_1 - i\frac{v_0}{2}\partial_y f_1 + \nu \Delta f_2 + \left(\mu[\rho] - \xi |f_2|^2\right) f_2,$$

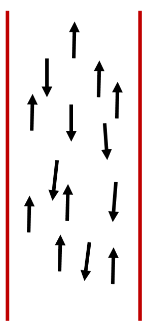
→ Density ρ

→ Flow field P

→ Nematic order Q

Linearize (first-order deviation from perfect nematic order at small chirality)

$$\partial_t \begin{pmatrix} \delta\rho/\rho_0 \\ \delta P_x \\ \delta P_y \\ \delta Q_{xx} \\ \delta Q_{xy} \end{pmatrix} = \begin{pmatrix} 0 & -v_0\partial_x & -v_0\partial_y & 0 & 0 \\ -\frac{v_0}{2}(1-r)\partial_x & -\frac{2}{\tau} - D_\phi & \theta + \nu_1\Delta & -\frac{v_0}{2}\partial_x & -\frac{v_0}{2}\partial_y \\ -\frac{v_0}{2}(1+r)\partial_y & -(\theta+\nu_1\Delta) & -\frac{2}{\tau} - D_\phi & \frac{v_0}{2}\partial_y & -\frac{v_0}{2}\partial_x \\ \left(\mu[\rho_0] - 8D_\phi - \nu\Delta\right) r & -\frac{v_0}{2}(1+2r)\partial_x & \frac{v_0}{2}(1-2r)\partial_y & -2(\mu[\rho_0] - 4D_\phi) + \nu\Delta & 2(\theta + \nu_2\Delta) \\ 0 & -\frac{v_0}{2}\partial_y & -\frac{v_0}{2}\partial_x & -2(\theta+\nu_2\Delta) & \nu\Delta \end{pmatrix} \begin{pmatrix} \delta\rho/\rho_0 \\ \delta P_x \\ \delta P_y \\ \delta Q_{xx} \\ \delta Q_{xy} \end{pmatrix} + \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 2\theta r \end{pmatrix}.$$



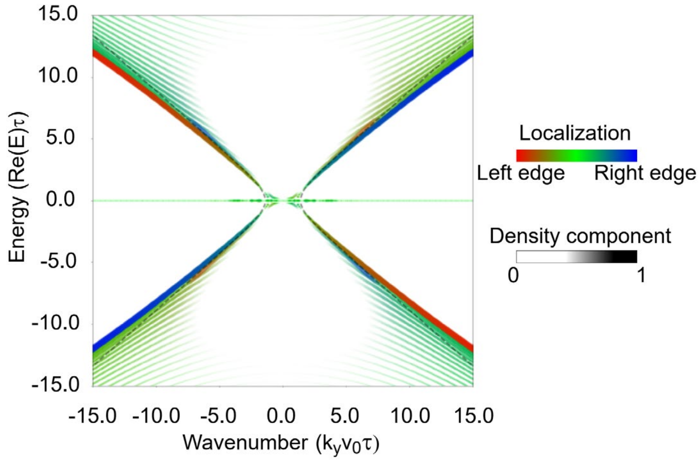
$$\longrightarrow \quad i\partial_t \Psi = \boxed{\mathcal{H}}\Psi + s$$

Peshkov et al. [Euro. Phys. J 2014], Patelli et al. [Phys. Rev. Lett. 2019],
Yamauchi, Hayata et al. [arXiv:2008.10852 (2020)]

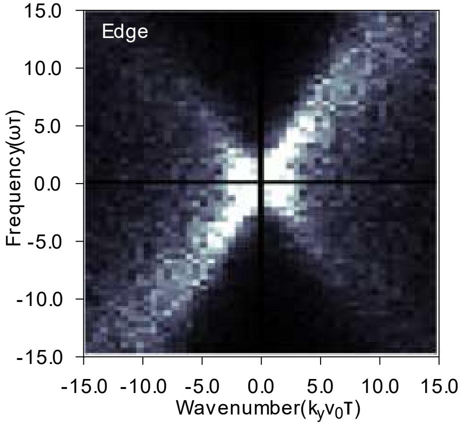
Tomoki Ozawa
Tohoku Univ.

Real part of the eigenvalues and the localization

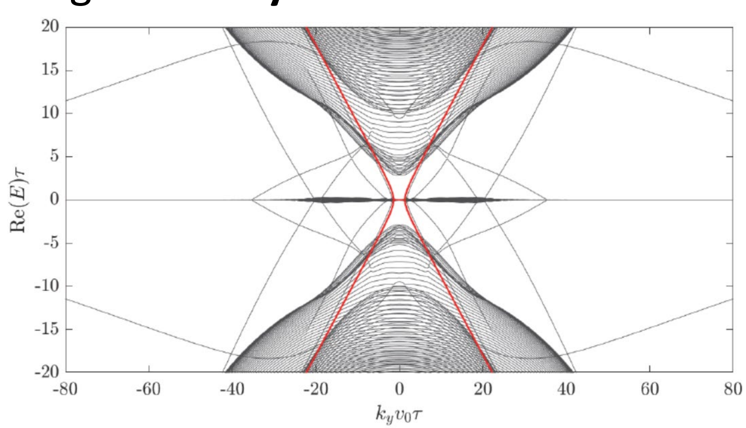
$$i\partial_t \Psi = \boxed{\mathcal{H}}\Psi + s$$



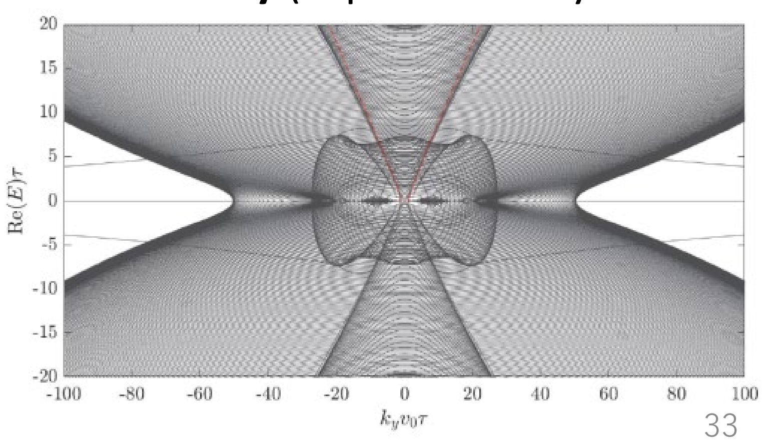
Spectrum (fluctuation) of cell density



Large **chirality**:

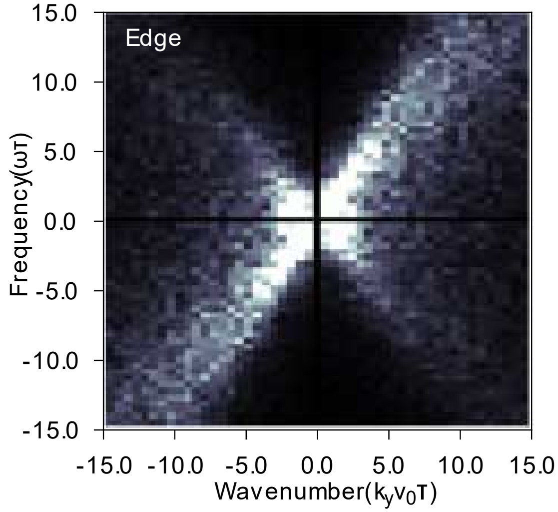


Smaller **chirality** (experimentally relevant):

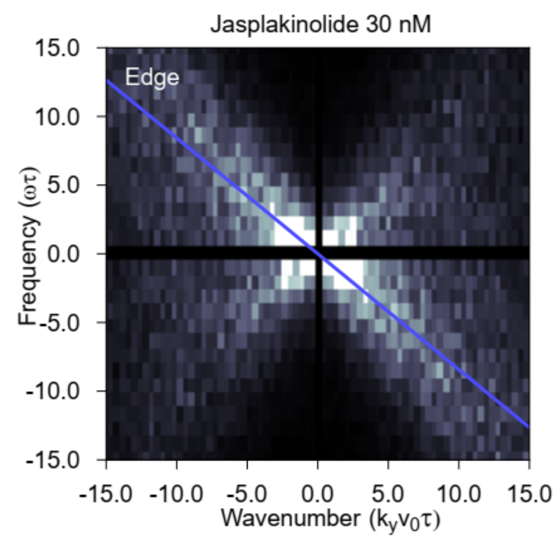


Spectrum changes by drug

Control



Perturbation in chirality



Active matter in the broader context?

- Topological insulators and polar/nematic active matter

Shankar et al. [Phys Rev X 2017]
Dasbiswas et al. [PNAS 2018]
Sone, Ashida [Phys Rev Lett 2019]
Yamauchi, Hayata et al., [arXiv:2008.10852 (2020)]
Shankar et al. [arXiv:2010.00364]...

- Correspondence between quantum models and active matter equations

Toner, Tu [Phys Rev E (1998)]
Alicea et al. [Phys Rev B 71, 2353222 (2005)]
Mitra et al. [Phys Rev Lett 97, 236808 (2006)]
Loewe et al. [New J Phys 20, 013020 (2018)]

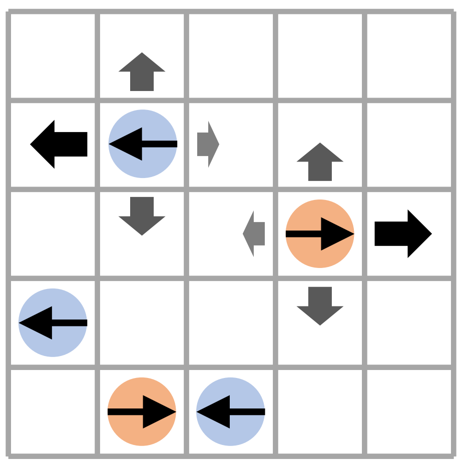
- Non-reciprocal phase transitions and active matter

Fruchart, Hanai, Littlewood, Vitelli [Nature 2021]

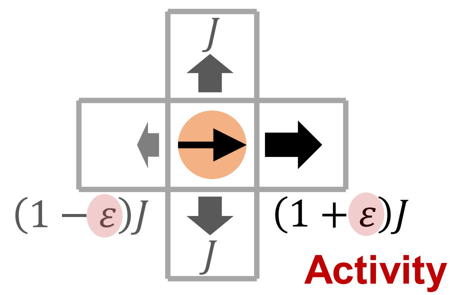
What is special about non-eq (non-Hermitian) quantum systems?
Relation with activity-induced phenomena in classical models?
→ Addressing through a specific quantum model that 'includes' the classical regime

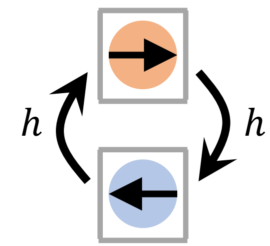
Starting point:
lattice model undergoing MIPS

Classical exclusive process in 1D or 2D:



Spin-dependent hopping rate





Flipping of spin

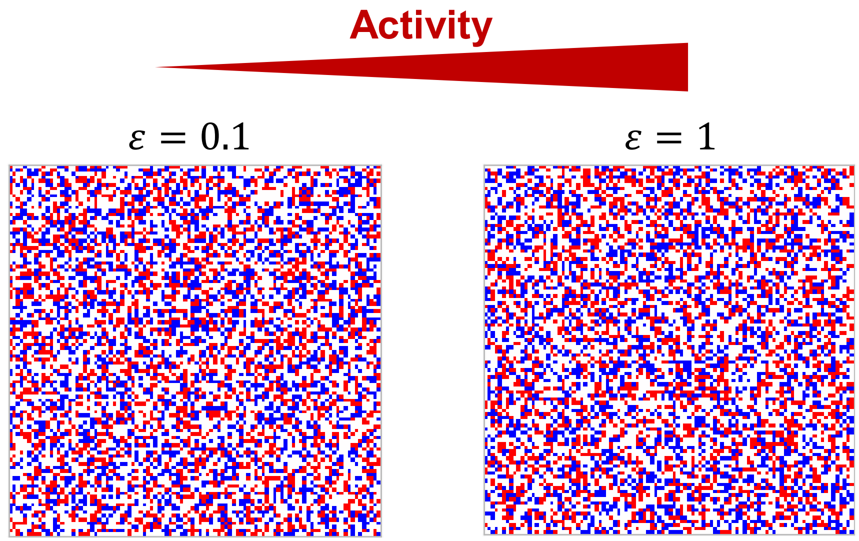
3 parameters: $\varepsilon, h, \rho \quad (J = 1)$

$\varepsilon = 0 \Rightarrow$ Detailed balance (equilibrium)

Adachi, K., Takasan, K. & Kawaguchi, K. *arXiv:2008.00996* (2020).

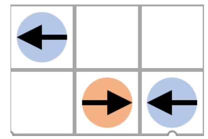
cf. Thompson et al., J. Stat. Mech. (2011) P02029
Kourbane-Houssene et al., PRL 120, 268003 (2018)

Simulation



Transition rate matrix vs quantum Hamiltonian

Configuration:



…

$$\frac{\partial}{\partial t} P_C(t) = \sum\nolimits_{C'} W_{CC'} P_{C'}(t)$$

$$\frac{\partial}{\partial t} |\psi_{\mathrm{t}}\rangle = -iH|\psi_{\mathrm{t}}\rangle$$

$$-W_{CC'} = \langle C|H|C'\rangle$$

Fock basis of hard-core boson $|C\rangle$

Steady state distribution
in the classical model: $P_C(t \to \infty)$

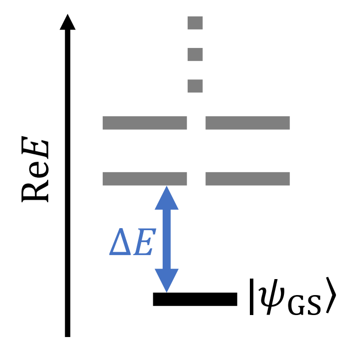
Non-Hermitian Hamiltonian H

$\langle C|H|C'\rangle = -W_{CC'}$

Ground state of a quantum model

$$|\psi_{\mathrm{GS}}\rangle = \sum\nolimits_C P_C(t \to \infty)|C\rangle$$

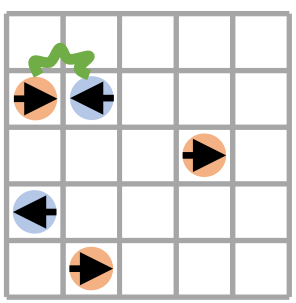
$$(E_0 =)\mathrm{Re}E_0 < \mathrm{Re}E_1 \leq \mathrm{Re}E_2 \leq \cdots$$



Components of the quantum Hamiltonian

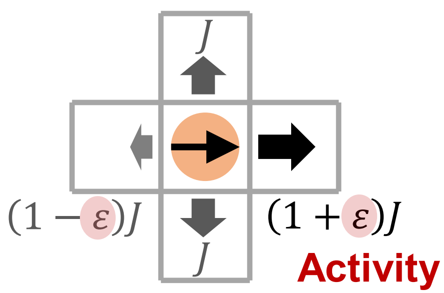
$$H = \underbrace{H_{\mathrm{hop}} + H_{\mathrm{flip}} + H_{\mathrm{int}}}_{\text{Hermitian}} \underbrace{- \varepsilon J \sum_{i,s} s\left(a_{i,s}^{\dagger} a_{i-\hat{x},s} - a_{i,s}^{\dagger} a_{i+\hat{x},s}\right)}_{\text{Anti-Hermitian}}$$

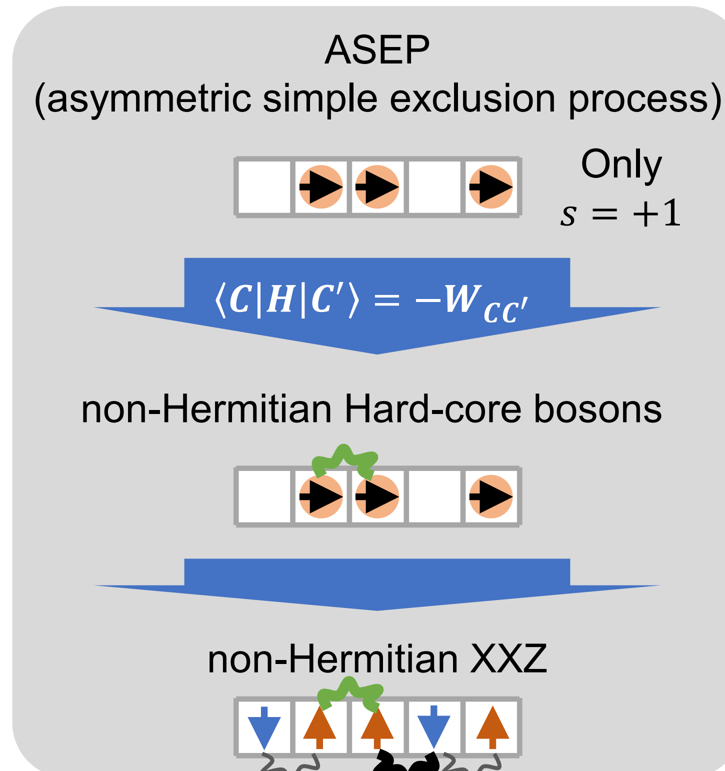
Hard-core bosons



spin

$s = \pm 1$





Extending to the quantum regime: parameter in the diagonal terms

$$H_{\mathrm{hop}} + H_{\mathrm{flip}} = -J\sum_{\langle i,j\rangle,s}\left(a_{i,s}^{\dagger}a_{j,s} + a_{j,s}^{\dagger}a_{i,s}\right) - h\sum_{i}\left(a_{i,+}^{\dagger}a_{i,-} + a_{i,-}^{\dagger}a_{i,+}\right)$$

$$H = H_{\mathrm{hop}} + H_{\mathrm{flip}} + H_{\mathrm{int}} - \varepsilon J\sum_{i,s} s\left(a_{i,s}^{\dagger}a_{i-\hat{x},s} - a_{i,s}^{\dagger}a_{i+\hat{x},s}\right)$$

$$H_{\mathrm{int}} = -2J\sum_{\langle i,j\rangle} n_i n_j - \varepsilon J\sum_i m_i\left(n_{i+\hat{x}} - n_{i-\hat{x}}\right)$$

Prob. conservation $\sum_i W_{ij} = 0$

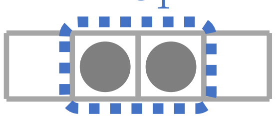
$\langle \boldsymbol{C}|\boldsymbol{H}|\boldsymbol{C}'\rangle = -\boldsymbol{W}_{\boldsymbol{CC}'}$

$$\langle C|H|C\rangle = -\sum_{C'(\neq C)}\langle C'|H|C\rangle$$

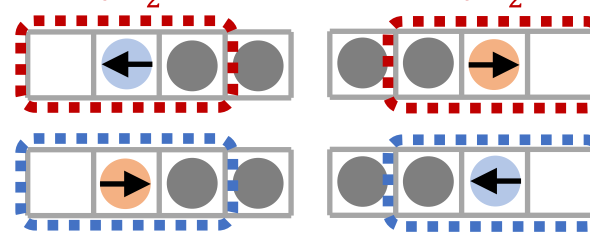
Generalization to purely quantum model

$n_i = n_{i,+} + n_{i,-}$

$m_i = n_{i,+} - n_{i,-}$



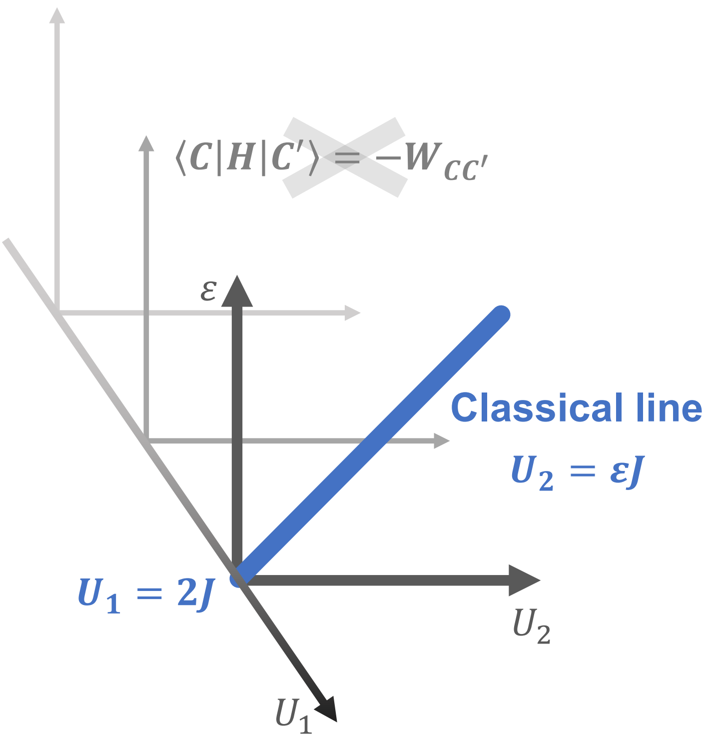
$$H_{\mathrm{int}} = -U_1\sum_{\langle i,j\rangle} n_i n_j - U_2\sum_i m_i\left(n_{i+\hat{x}} - n_{i-\hat{x}}\right)$$



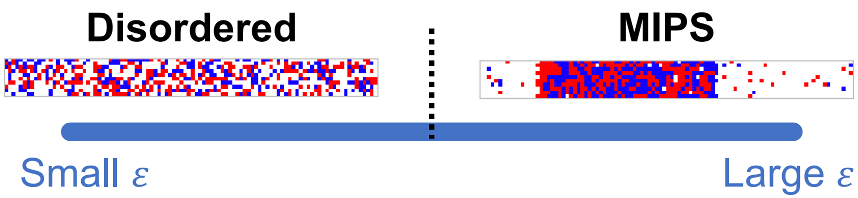
5 parameters: $\varepsilon, h, U_1, U_2, \rho \quad (J = 1)$

$\boldsymbol{U_1 = 2J, U_2 = \varepsilon J} \Rightarrow \langle \boldsymbol{C}|\boldsymbol{H}|\boldsymbol{C}'\rangle = -\boldsymbol{W}_{\boldsymbol{CC}'}$ **&** $|\boldsymbol{\psi}_{\mathbf{GS}}\rangle = \sum_{\boldsymbol{C}} \boldsymbol{P}_{\boldsymbol{C}}(\boldsymbol{t} \to \infty)|\boldsymbol{C}\rangle$

MIPS on the classical line



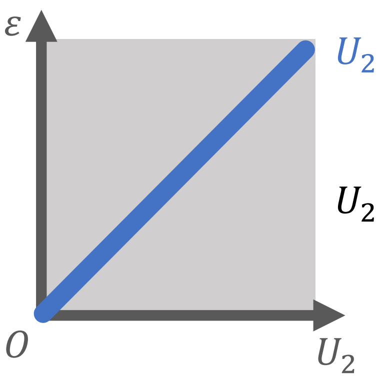
$\langle \boldsymbol{C}|\boldsymbol{H}|\boldsymbol{C}'\rangle = -\boldsymbol{W}_{\boldsymbol{CC}'}$ **&** $|\boldsymbol{\psi}_{\mathbf{GS}}\rangle = \sum_{\boldsymbol{C}} \boldsymbol{P}_{\boldsymbol{C}}(\boldsymbol{t} \rightarrow \infty)|\boldsymbol{C}\rangle$



In the following, $\boldsymbol{U_1} = \mathbf{2}$, $h = 0.025$ & $\rho = 0.5$ $(J = 1)$

Numerical simulation in the quantum regime

e.g., Giardinà et al., PRL 96, 120603 (2006)



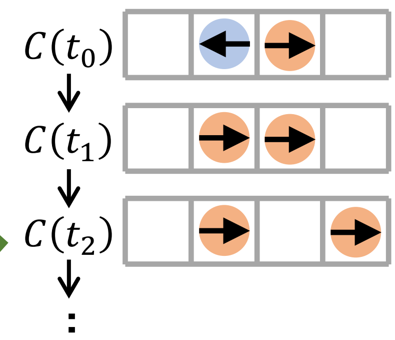
$U_2 = \varepsilon$ → Classical MC

$$|\psi_{GS}\rangle = \sum_C P_C(t \to \infty)|C\rangle$$

$U_2 \neq \varepsilon$ → Classical MC

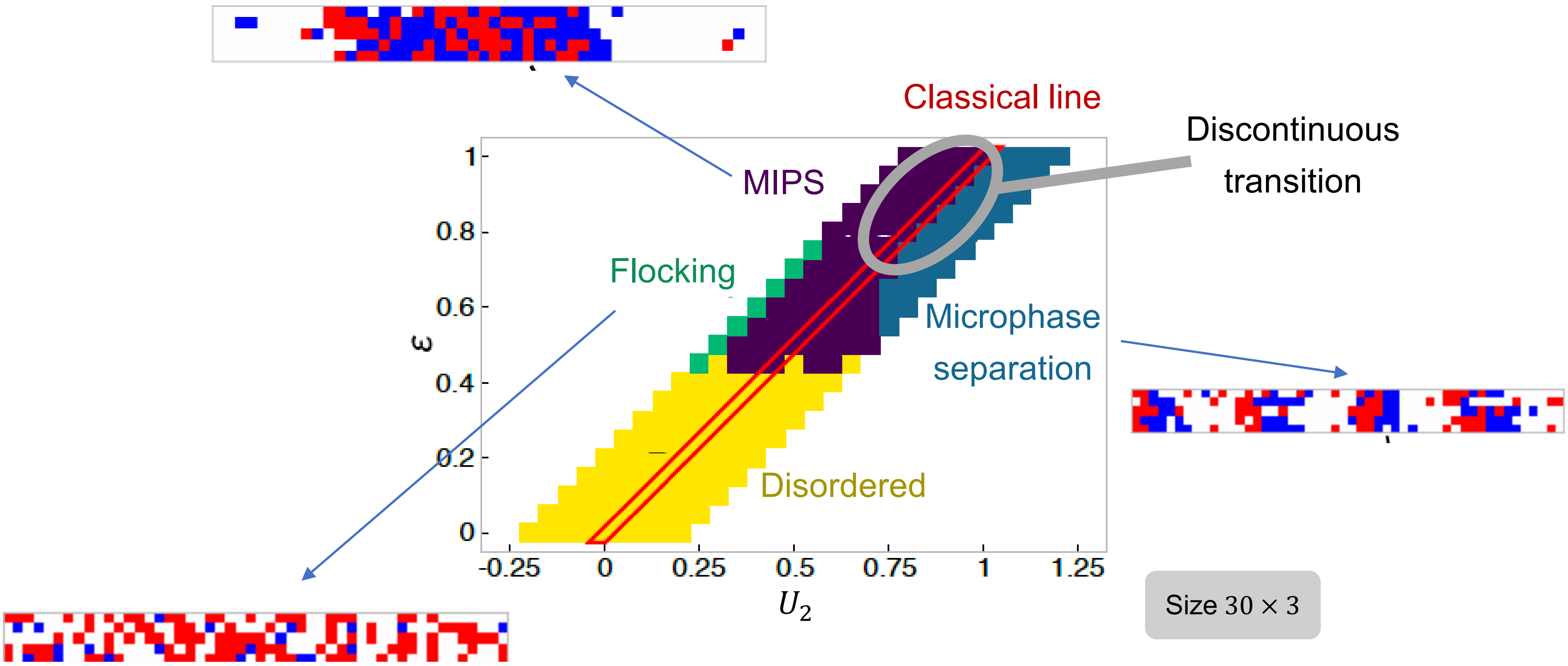
Classical MC **with trajectory bias**

$$B = B[C(t_0) \to C(t_1) \to C(t_2) \to \cdots \to C(t)]$$



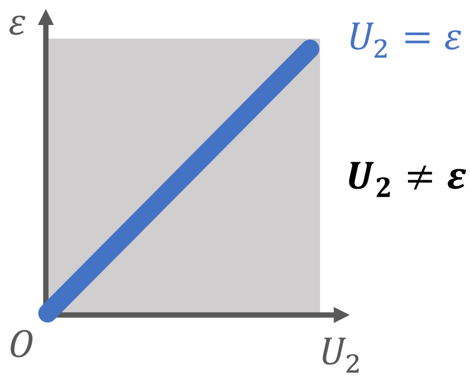
Quantum Monte Carlo
a.k.a. Population dynamics (classical)

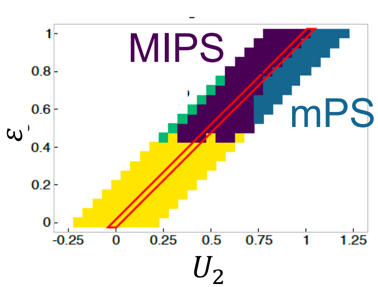
Additional phases in the quantum model



Quantum regime and the dynamical phase transition (1)

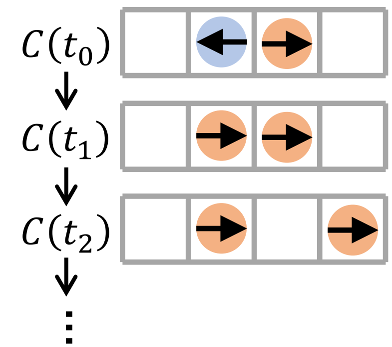
cf. Jack & Sollich., PTPS 184, 304 (2010)





$\langle\cdots\rangle_{\mathrm{tr}}^{\mathrm{cl}}$: **Classical average over trajectory**

$\boldsymbol{U_2 \neq \varepsilon}$ $\Rightarrow$ $\langle A\rangle = \lim_{t\to\infty} \langle A \exp(B)\rangle_{\mathrm{tr}}^{\mathrm{cl}} / \langle \exp(B)\rangle_{\mathrm{tr}}^{\mathrm{cl}}$



Bias (~weight) to trajectory

$$B = B[C(t_0) \to C(t_1) \to C(t_2) \to \cdots \to C(t)]$$

$$= \boldsymbol{(U_2 - \varepsilon)} \int \boldsymbol{dt} \sum_i \boldsymbol{m_i (n_{i+\hat{x}} - n_{i-\hat{x}})} \big|_{C(t)}$$

Deviation from classical line

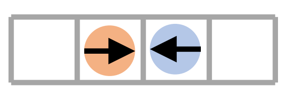
$\sim\Phi_{\mathrm{mPS}}$

Bias-induced transition of typical classical trajectory:

Dynamical phase transition

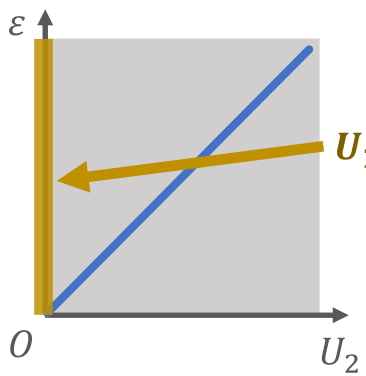
Garrahan et al., PRL 98, 195702 (2007)

$\boldsymbol{U_2 > \varepsilon}$ $\Rightarrow$ **Trajectory with large Φ_{mPS} is favored.**



Quantum regime and the dynamical phase transition (2)

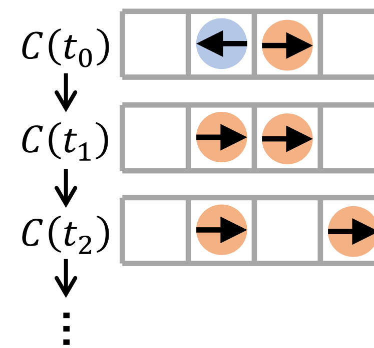
cf. Nemoto et al., PRE 99, 022605 (2019) Tociu et al., PRX 9, 041026 (2019) Fodor et al., NJP 22, 013052 (2020)



$\boldsymbol{U_2 = 0}$

$\langle \cdots \rangle_{\mathrm{tr}}^{\mathrm{cl}}$: Classical average over trajectory

$$\langle A \rangle = \lim_{t\to\infty} \langle A \exp(B) \rangle_{\mathrm{tr}}^{\mathrm{cl}} / \langle \exp(B) \rangle_{\mathrm{tr}}^{\mathrm{cl}}$$

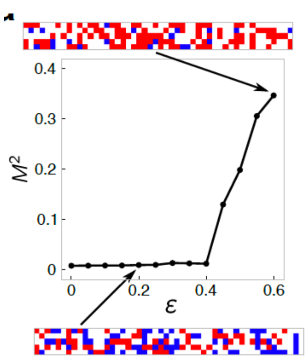


Bias to trajectory

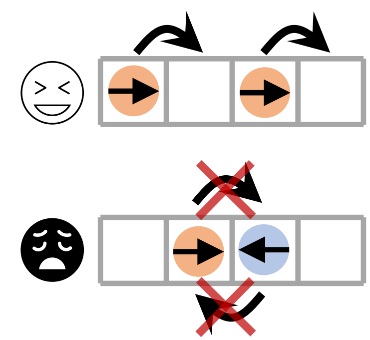
Dissipation

$B =$ $\ln(1+\varepsilon)$ × (# of hopping in **spin** direction)

$+ \ln(1-\varepsilon)$ × (# of hopping in **anti-spin** direction)



For $\varepsilon > 0$, trajectory with many hopping events in spin direction is favored.



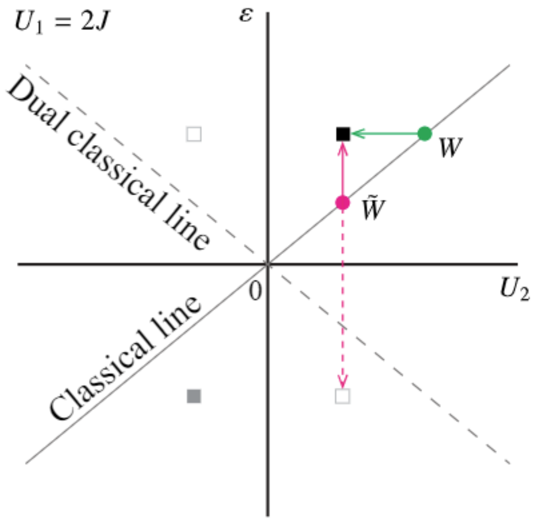
Quantum regime and the dynamical phase transition (3)

Bias = deviation from classical line

Symmetry of Hamiltonian →

$$H(J,\varepsilon,U_1,U_2,h) = \hat{U}^\dagger H(J,-\varepsilon,U_1,-U_2,h)\hat{U}$$

$$H(J,-\varepsilon,U_1,U_2,h)^\dagger = H(J,\varepsilon,U_1,U_2,h)$$



Summary:

- Activity-induced MIPS & flocking
- Discontinuous transition b/w MIPS & microphase separation at the classical line
- Useful correspondence to classical stochastic process with trajectory bias

Adachi, Takasan, Kawaguchi Arxiv:2008.00996 (2020)

Overview

Migrating cells

- Geometry and collective active force can induce flow
  → cell accumulation at topological defects

Kawaguchi, Kageyama, Sano, Nature (2017)

- Cell chirality, activity, and edge wave

Yamauchi, Hayata, Uwamichi, Ozawa, and Kawaguchi Arxiv: 2008.10852 (2020)

- Active matter & statmech/quantum models

Adachi, Kawaguchi Arxiv:2012.02517 (2020)
Adachi, Takasan, Kawaguchi Arxiv:2008.00996 (2020)

Gain and loss of cells

- Tissue homeostasis and the voter model Mesa, Kawaguchi, Cockburn et al. Cell Stem Cell (2018)
- Skin homeostasis and cell-interaction rule inference using GNN

Yamamoto, Cockburn, Greco, Kawaguchi bioRxiv
10.1101/2021.06.23.449559 (2021)

Intracellular many-body physics

- Protein motif grammar for biological condensates
- Chromatin dynamics