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WORKSHOP ON DRIVEN STATES IN SOFT AND BIOLOGICAL MATTER
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Ordered States & Instabilities in Active Polymer Solutions

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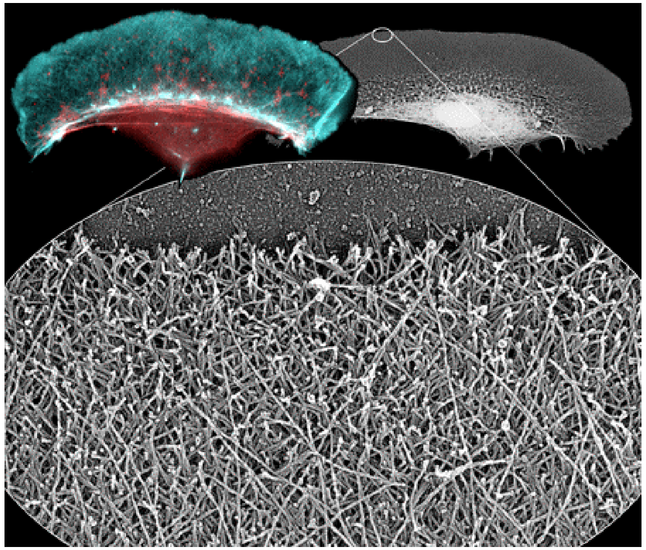
Outline

- The cell cytoskeleton: a novel form of *active* soft matter.
- In vitro filament/motor mixtures as model systems for studying self-organization and rheology
- Theoretical modeling of polar filaments, crosslinkers & motor proteins: from single filaments to hydrodynamics
- Classification of homogeneous bulk phases
- Instabilities and inhomogeneous structures
- Rheology → T. Liverpool on Wed., 4/26

Cell cytoskeleton as active soft material

Dynamical network of long polar filaments (F-actin, MT, intermediate filaments) and a variety of smaller proteins that can crosslink or cap the filaments.

actin
myosin

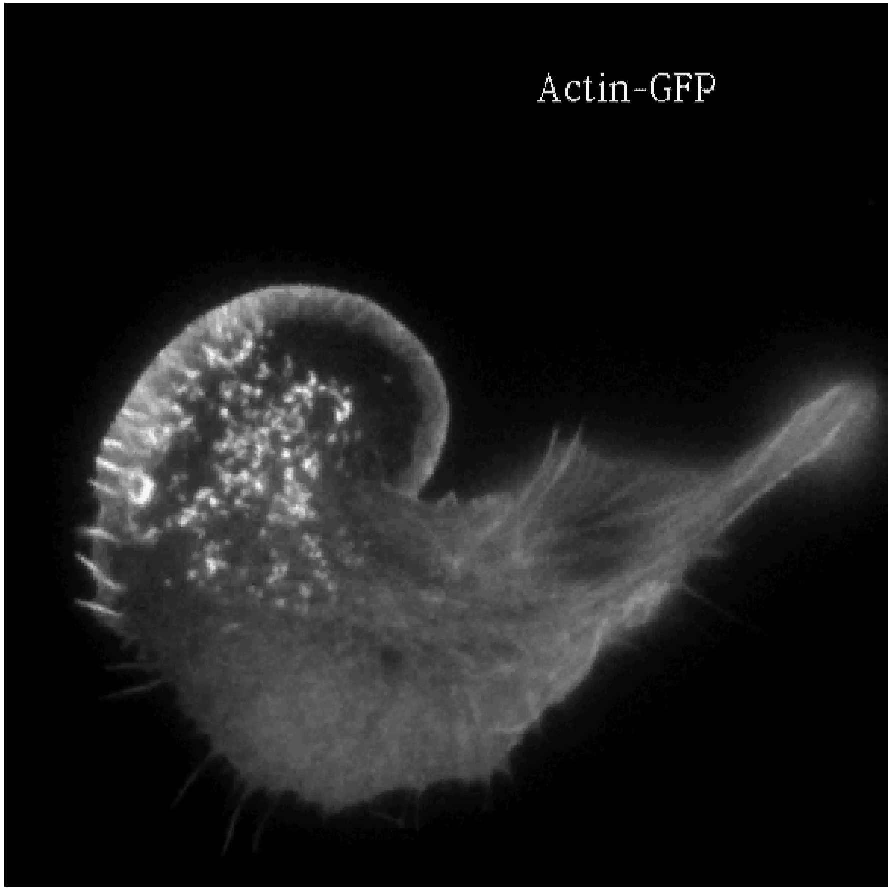


Passive crosslinkers, e.g., α-actinin

Active crosslinkers (myosins, kinesins, dyneins) use chemical energy (ATP) to exchange forces among filaments and remodel the network → active behavior

Svitkina et al. JCB 1997.
Fish epidermal keratocyte cytoskeleton by fluorescence and electron microscopy.

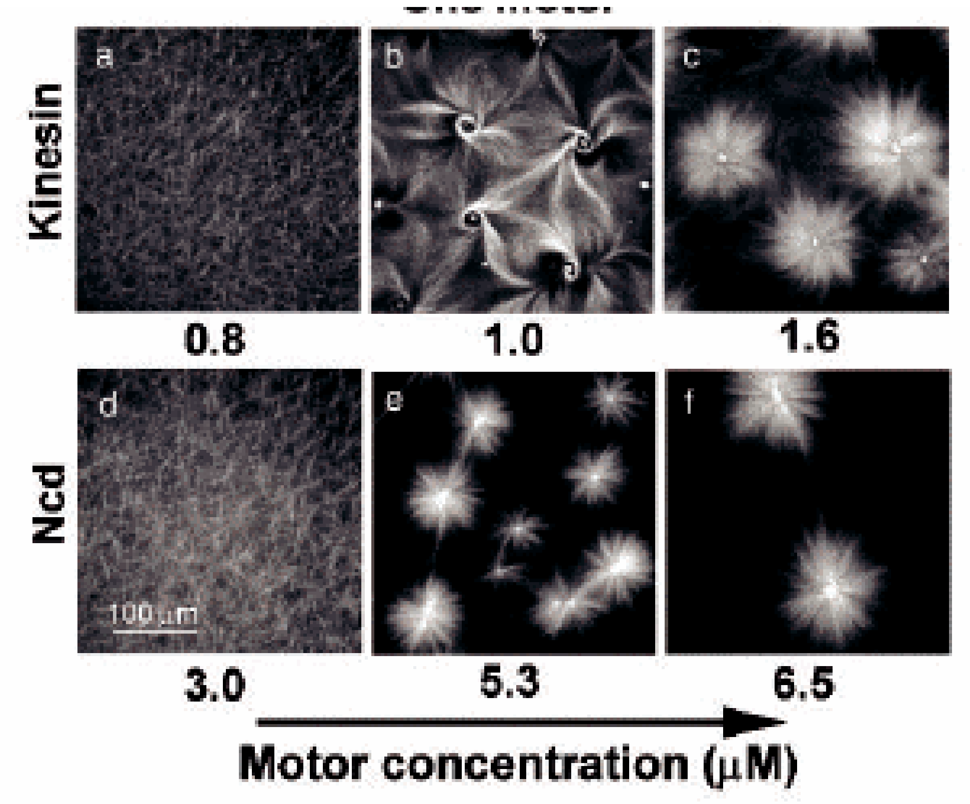
In vivo:



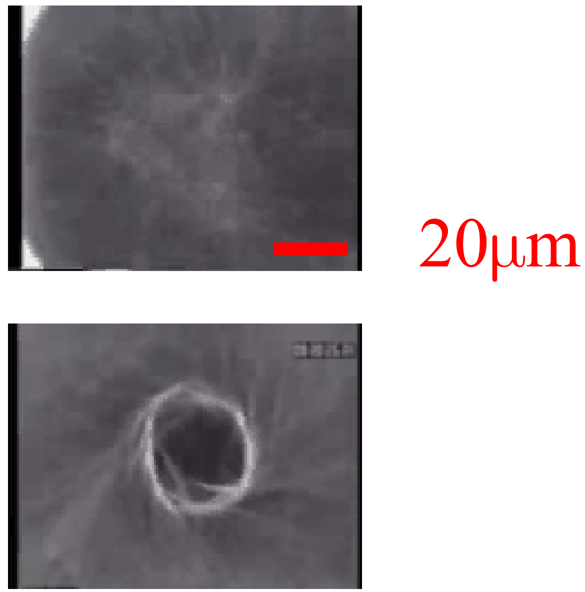
The actin cytoskeleton in a mouse melanoma drives cell migration.
V. Small, IMBA, Vienna.

In vitro: activity drives organization

Cell extracts of *stabilized* microtubules & motors show self-organization on mesoscopic scales.



Surrey et al., Science 2001:
MT & multimeric motors

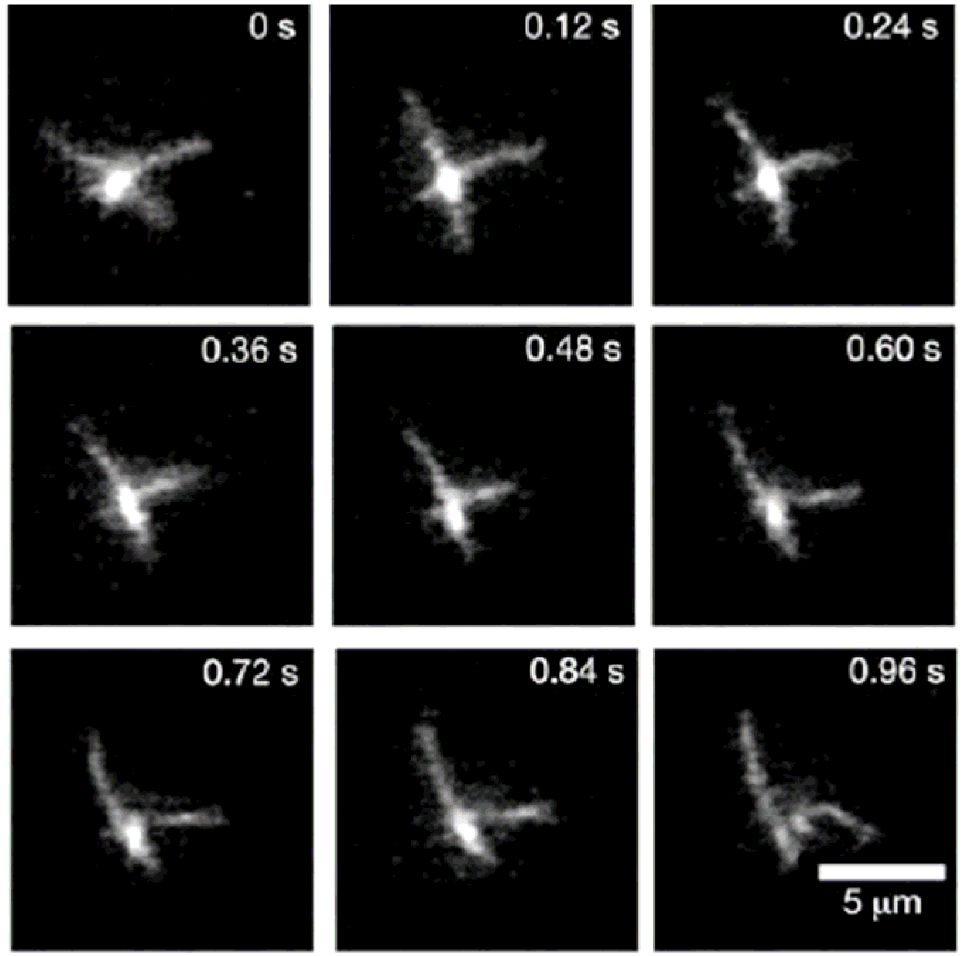


F. Nedelec, Heidelberg
MT & kinesin

Motor-induced filament sliding

D. Humphrey et al.
Nature **416** (2002)

Two labeled actin filament in a dilute solution are made to slide relative to each other by a crosslinking myosin II minifilament (bright spot).



Model systems can be used to address many questions

- How and on which time scale does the structure of the active network change?
- How is the structure related to the mechanical properties?
- How is the structure related to biological function?
- Which behaviors are **specific** and which **generic**?

Theoretical modeling of active polymer solutions

Use methods from soft condensed matter and polymer physics to describe the large scale behavior of active matter.

- Numerical simulations **(Nedelec et al. 1997; Surrey et al., 2001)**
- Kinetic equations **(Nakazawa & Sekimoto, 1996; Kruse & Julicher, 2000, 2001, 2003; Aranson & Tsimring, 2005; …)**
- Hydrodynamic equations, generally written on the basis of symmetry **(Lee & Kardar, 2001; Bassetti et al. 2000; Sankararaman et al., 2003; Hatwalne et al., 2004, Kruse et al. 2005; Voituriez et al., 2006; …)**

Our work: bridging between microscopic and hydrodynamics by deriving hydrodynamics from kinetic model → estimate of parameters

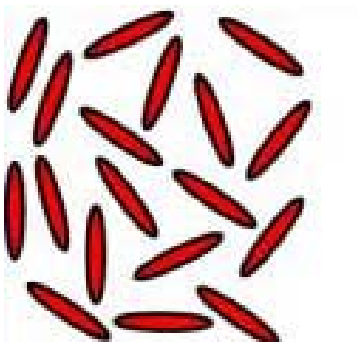
How do active and passive crosslinkers change the behavior of polymer solutions?

- Ordered phases & "phase diagram"
- Instabilities and spatial structures
- Mechanical properties and rheology → 4/26

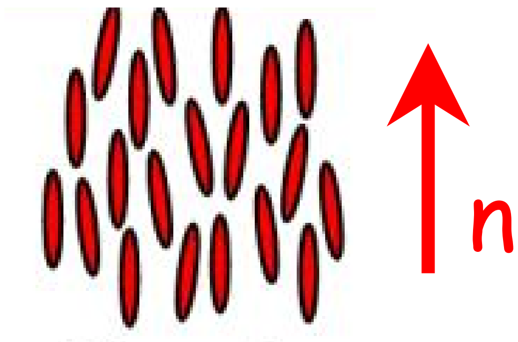
T.B. Liverpool & MCM, PRL **90**, 138102 (2003); **93**, 159802 (2004).
T.B. Liverpool & MCM, EPL **69**, 846 (2005).
A. Ahmadi, T.B. Liverpool & MCM, PRE **72**, 60901R (2005).

Isotropic - nematic transition

A liquid of long, thin (L>>b) hard rods order in a nematic phase at high density ρ (Onsager 1949)



$$\rho_N \sim \frac{1}{\mathrm{v}_{ex}} \sim \frac{1}{L^2 b}$$



isotropic: orientational symmetry

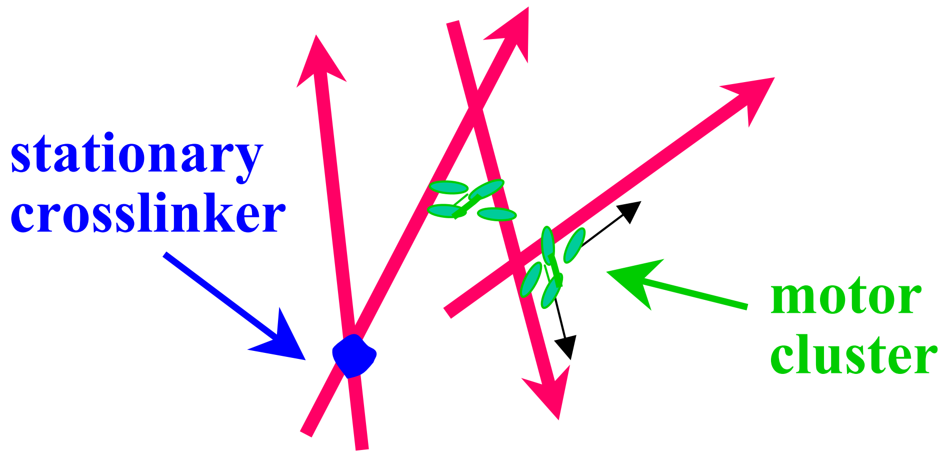
nematic: broken orientational symmetry

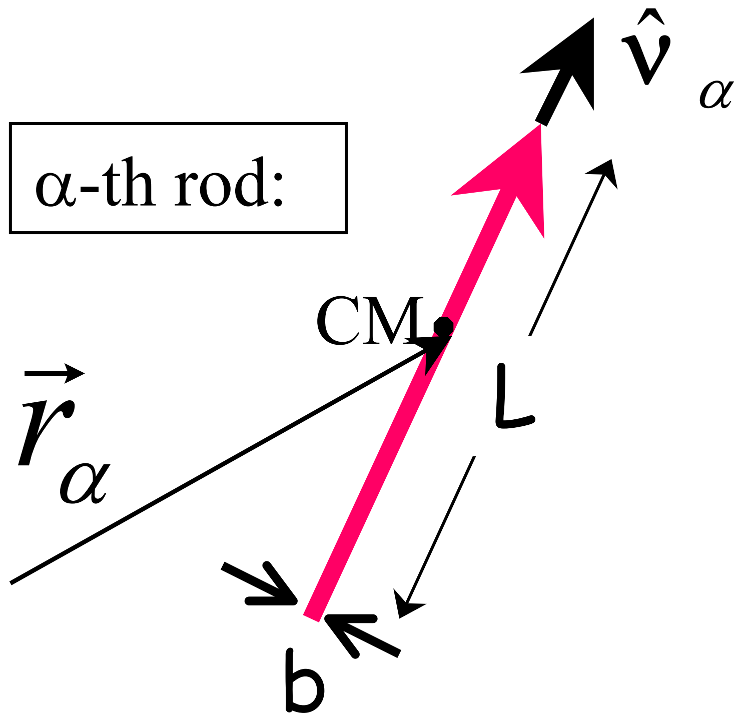
Competition of translational & rotational entropy

Active Polar Rods: model

Rigid polar rods in a quiescent solvent coupled by stationary and mobile crosslinkers

- fixed length L >> b
- excluded volume

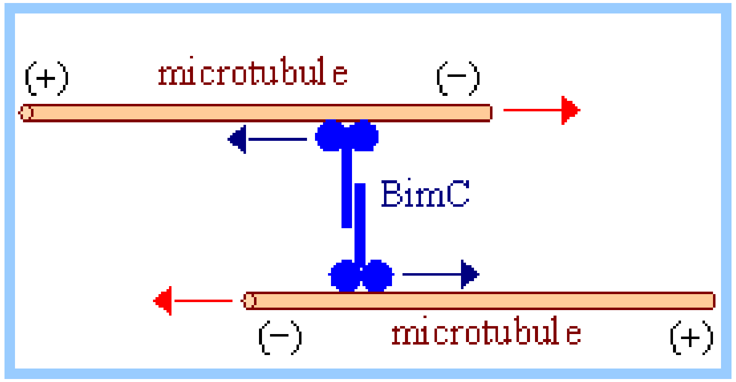




- Lee & Kardar 2001
- Kruse & Julicher, 2000 &2003
- Kruse et al. 2004
- Sankararaman et al. 2004
- …

Mobile crosslinkers: motor proteins

- kinesins and dyneins on MT
- myosin clusters or minifilaments on F-actin



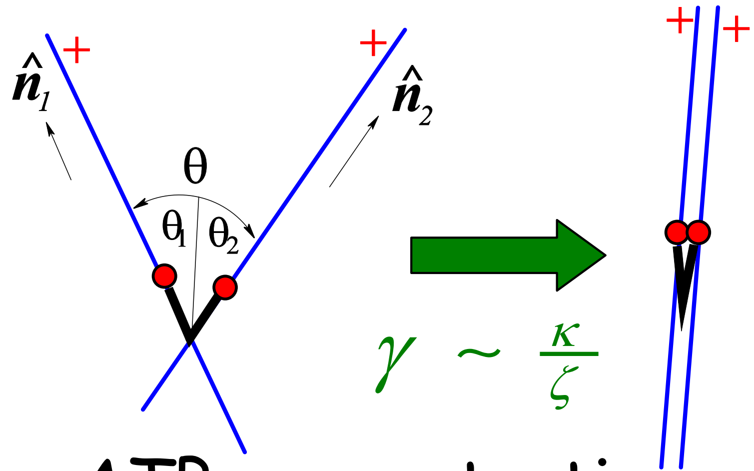
Active crosslinks that use Adenosine TriPhosphate (ATP) to turn chemical energy into mechanical work and can induce relative sliding of the filaments.

Activity influenced by
- ATP concentration
- processivity

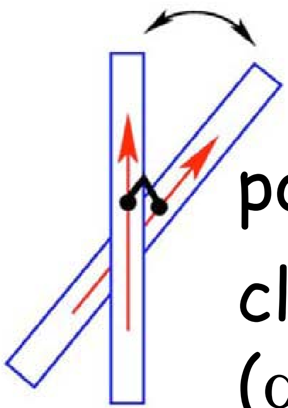
Cartoon from http://www.dentistry.leeds.ac.uk/biochem/

Stationary crosslinkers (e.g., α-actinin)

Can act as torsional springs that induce relative torques at a rate $\gamma \sim \kappa/\zeta$
→ "zipping" of filaments

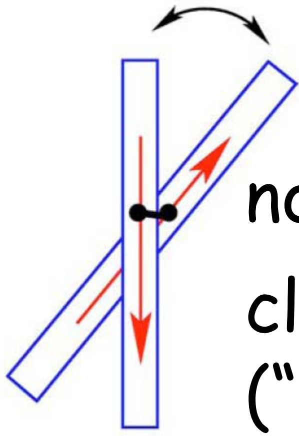


Binding rate may depend weakly on ATP concentration.



polar

clusters: γ_P
(α-actinin)



non-polar

clusters : γ_{NP}
("disordered" myosin clusters)

Smoluchowski equation

Concentration of filaments at $\vec{r}$ along $\hat{\nu}$: $c(\vec{r},\hat{\nu},t)$

$$\boxed{\partial_t c + \nabla \cdot J + \boldsymbol{R} \cdot J^{rot} = 0}$$

$$\boldsymbol{R} = \hat{\nu} \times \partial_{\hat{\nu}}$$

Translational & rotational currents: competition of diffusion (excl. volume, entanglement), crosslinking & and local driving by motors:

$$J = J^{diff} + J^{ex} + J^{act}$$

$$\vec{J}^{diff} = \left[D_{\|} \hat{\nu}\hat{\nu} + D_{\perp} \left(\mathbf{1} - \hat{\nu}\hat{\nu} \right) \right] \cdot \nabla c$$

rods: $D_{\perp} < D_{\|}$

$$\vec{J}^{R,diff} = -D_r \boldsymbol{R} c$$

anisotropic diffusion

Active currents

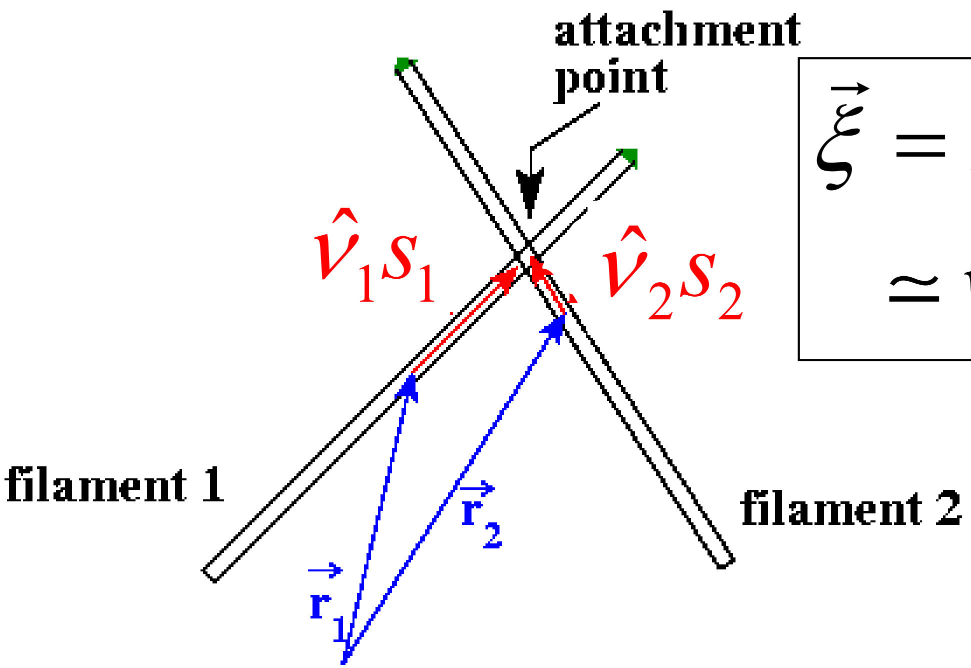
$$\vec{J}^{act}(\vec{r}_1,\hat{v}_1) = \int_{\vec{\xi}} \int_{\Omega_{\text{int}}} m(\vec{r}_1^{\,att})\ \vec{\mathrm{v}}_1(\vec{\xi},\hat{v}_1,\hat{v}_2) c(\vec{r}_1,\hat{v}_1,t) c(\vec{r}_1+\vec{\xi},\hat{v}_2,t)$$

$$\vec{J}^{act}_{rot}(\vec{r}_1,\hat{v}_1) = \int_{\vec{\xi}} \int_{\Omega_{\text{int}}} m(\vec{r}_1^{\,att})\ \vec{\omega}_1(\vec{\xi},\hat{v}_1,\hat{v}_2) c(\vec{r}_1,\hat{v}_1,t) c(\vec{r}_1+\vec{\xi},\hat{v}_2,t)$$

motor density m at attachment point

$$\vec{r}_1^{\,att} = \vec{r}_1 + \hat{v}_1 s_1$$

below m=constant



$$\boxed{\begin{aligned}\vec{\xi} &= \vec{r}_2 - \vec{r}_1 \\ &\simeq \hat{v}_1 s_1 - \hat{v}_2 s_2\end{aligned}}$$

Kinematics of filament pair

- overdamped dynamics → net force/torque on filaments balanced by fluid friction
- third law: no net force/torque by motor on filament pair

$\vec{\mathrm{v}}_1, \vec{\mathrm{v}}_2$ cm velocities

$\vec{\omega}_1, \vec{\omega}_2$ angular velocities

$$\begin{cases} \varsigma_r \vec{\omega}_1 = \vec{N} \\ \varsigma_r \vec{\omega}_2 = -\vec{N} \end{cases} \quad \boxed{\rightarrow \ \vec{\omega}_1 = -\vec{\omega}_2}$$

$$\begin{cases} \zeta_{ij}(\hat{v}_1)\mathrm{v}_{1\mathrm{j}} = F_i \\ \zeta_{ij}(\hat{v}_2)\mathrm{v}_{2\mathrm{j}} = -F_i \end{cases} \quad \boxed{\rightarrow \ \vec{\mathrm{v}}_1 \neq -\vec{\mathrm{v}}_2}$$

Anisotropy of rod diffusion allows for a net velocity of the pair

Motor cluster dynamics

Each cluster is modeled as a rigid object made up of two heads attached at $\vec{r}_\alpha^{\,m} = \vec{r}_\alpha + \hat{\nu}_\alpha s_\alpha$. Each head:

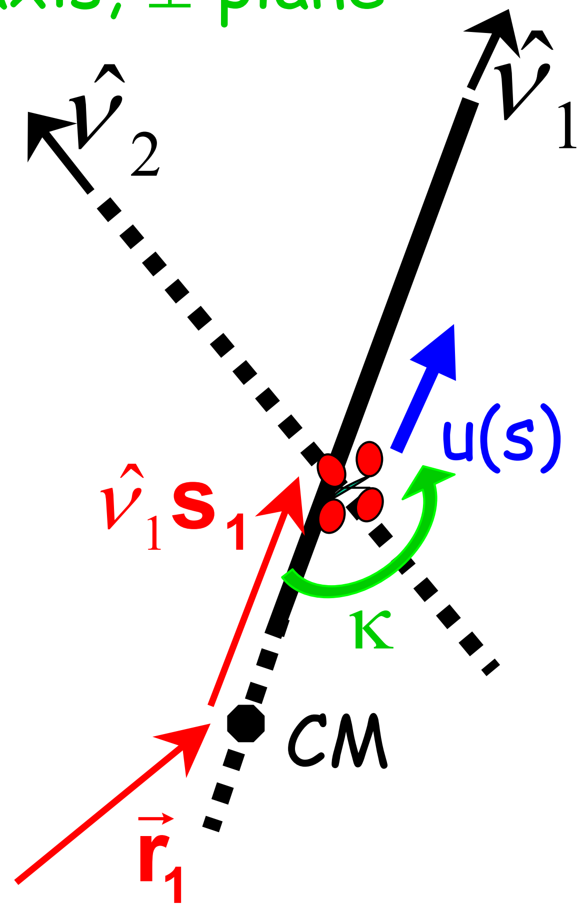
- steps at a inhomogeneous rate u(s) along the fil.
- rotates at rate ~ κ about the motor axis, ⊥ plane of the filaments: $\zeta\dot{\theta} = \kappa \sin\theta \simeq \kappa\theta$

$$\vec{\mathrm{v}}_\alpha^{\,m} = \frac{d\vec{r}_\alpha^{\,m}}{dt} = \vec{\mathrm{v}}_\alpha + \hat{\nu}_\alpha u(s_\alpha) + s_\alpha \vec{\omega}_\alpha \times \hat{\nu}_\alpha$$

$$\vec{\omega}_\alpha^{\,m} = \vec{\omega}_\alpha + (-1)^\alpha \dot{\theta}(\hat{\nu}_1 \times \hat{\nu}_2)$$

Motors in cluster rigidly connected:

$$\vec{\mathrm{v}}_1^{\,m} = \vec{\mathrm{v}}_2^{\,m} \qquad \vec{\omega}_1^{\,m} = \vec{\omega}_2^{\,m}$$



⇒ Active velocities

$$\vec{\mathrm{v}}_1 - \vec{\mathrm{v}}_2 = \beta(\hat{\nu}_2 - \hat{\nu}_1) + \alpha\vec{\xi}$$

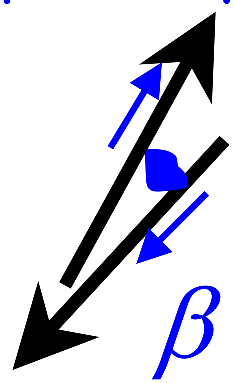
$$\vec{\mathrm{v}}_1 + \vec{\mathrm{v}}_2 = \frac{\zeta_\perp - \zeta_\parallel}{\zeta_\perp + \zeta_\parallel}\left[-\beta(\hat{\nu}_2 + \hat{\nu}_1) + \alpha(\hat{\nu}_1 s_1 + \hat{\nu}_2 s_2)\right]$$

$$\vec{\omega}_1 - \vec{\omega}_2 = \left[\gamma_{\mathrm{P}} + \gamma_{\mathrm{NP}}(\hat{\nu}_1 \bullet \hat{\nu}_2)\right](\hat{\nu}_1 \times \hat{\nu}_2)$$

CM separation:

$$\vec{\xi} = \vec{r}_2 - \vec{r}_1$$
$$\simeq \hat{\nu}_1 s_1 - \hat{\nu}_2 s_2$$

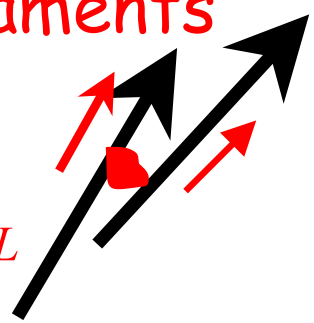
sorting of opposite-polarity filaments



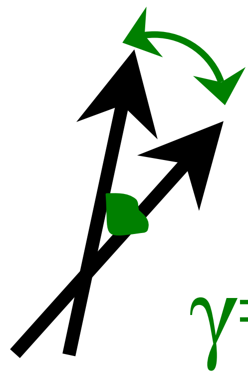
$$\beta = \langle u \rangle_L$$

bundling of same-polarity filaments

$$\alpha = L\left\langle \frac{du}{ds} \right\rangle_L$$



rotation



$$\gamma = \kappa/\zeta$$

From Smoluchowski to Hydrodynamics

Hydrodynamics: description of phases and dynamics of systems of many interacting degrees of freedom in terms of a few coarse-grained fields:

- Conserved densities
- Broken symmetry variables in states with spatial order

Two routes:

Phenomenology:

Write free energy or hydrodynamics on the basis of symmetry → unknown parameters

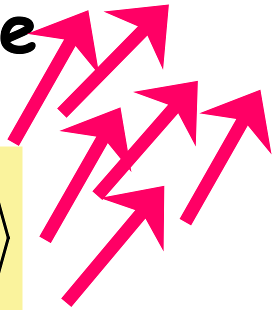
Microscopic approach:

Derive hydrodynamics by coarse-graining microscopic dynamics

Order parameters & broken symmetry variables

Polarized state

polarization:



$$\vec{P} = \left\langle \sum_{\alpha} \hat{v}_{\alpha} \, \delta(\vec{r} - \vec{r}_{\alpha}) \right\rangle$$

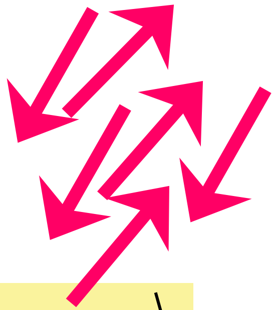
$$\vec{P} = \rho \, \mathbf{P_0} \hat{p}$$

$$P_0 \neq 0 \rightarrow S \neq 0$$

$$\mathbf{p} \neq -\mathbf{p}$$

Nematic state

alignment tensor:



$$Q_{ij} = \left\langle \sum_{\alpha} \left(\hat{v}_{\alpha i} \hat{v}_{\alpha j} - \tfrac{1}{d} \delta_{ij} \right) \delta(\vec{r} - \vec{r}_{\alpha}) \right\rangle$$

$$Q_{ij} = \rho \, \mathbf{S} \left(n_i n_j - \tfrac{1}{d} \delta_{ij} \right)$$

$$S \neq 0 \quad P_0 = 0$$

$$\mathbf{n} \leftrightarrow -\mathbf{n}$$

Hydrodynamic fields:

- Filament density ρ
- Director **p**

- Filament density ρ
- Director **n**

Coarse-graining the Smoluchowski eqn.

Dynamics on length scales >> L → gradient expansion:

$$c(\vec{r}_1+\vec{\xi},\hat{v}_2)=c(\vec{r}_1,\hat{v}_2)+\xi_i\partial_i c+\tfrac{1}{2}\xi_i\xi_j\partial_i\partial_j c+\ldots \qquad \vec{\xi}=\vec{r}_2-\vec{r}_1$$

Moment expansion of concentration + truncation:

$$\rho(\vec{r},t)=\int_{\hat{v}} c(\hat{v},\vec{r},t) \qquad \text{density - conserved density}$$

$$\left.\begin{array}{ll} \vec{P}(\vec{r},t)=\int_{\hat{v}}\hat{v}\; c(\hat{v},\vec{r},t) & \text{polarization} \\ Q_{ij}(\vec{r},t)=\int_{\hat{v}}(\hat{v}_i\hat{v}_i - \tfrac{1}{d}\delta_{ij})\; c(\hat{v},\vec{r},t) & \text{alignment tensor} \end{array}\right\} \text{possible broken symmetries}$$

Homogeneous states

$m =$ bound x-link density

$$\partial_t \rho = 0$$

$$\partial_t P_i = -[D_r - \gamma_P m \rho] P_i + [D_r \tfrac{1}{\rho_N} - \gamma m] Q_{ij} P_j$$

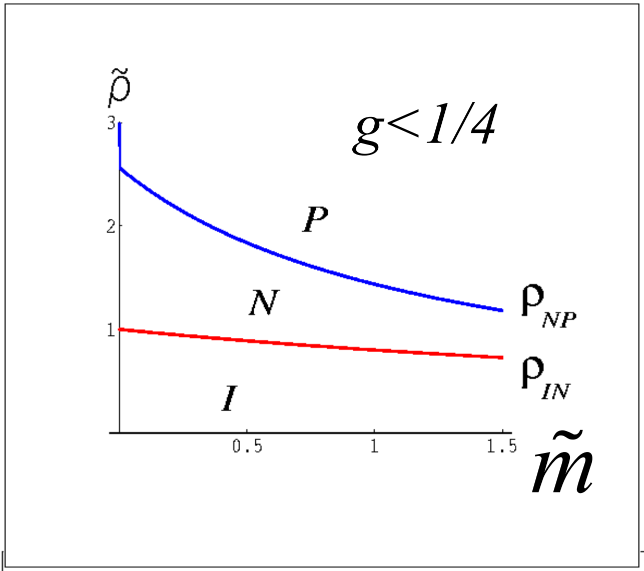
$$\partial_t Q_{ij} = -[D_r (1 - \tfrac{\rho}{\rho_N}) - \gamma_{NP} m \rho] Q_{ij} + 2 \gamma_P m (P_i P_j - \tfrac{1}{2} \delta_{ij} P^2)$$

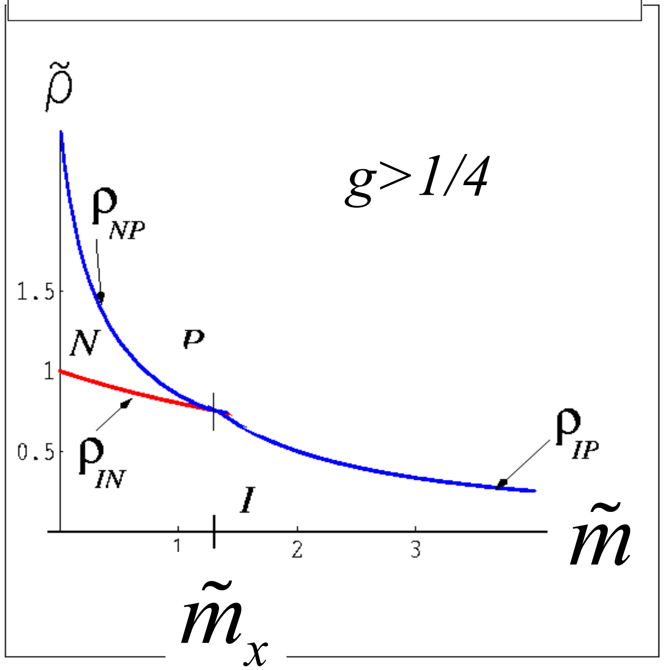
m=0: Isotropic→Nematic at $\rho > \rho_N = 3\pi/2L^2$

$\gamma_P, \gamma_{NP} \sim \kappa / \zeta$ rates of rotation from Polar & NonPolar crosslinks

Competition of diffusion, excluded volume & "zipping"

“Phase Diagrams” of bulk states





$$g = \gamma_P / \gamma_{NP}$$

$$\tilde{m} = \frac{\rho_N m \gamma_{NP}}{D_r}$$

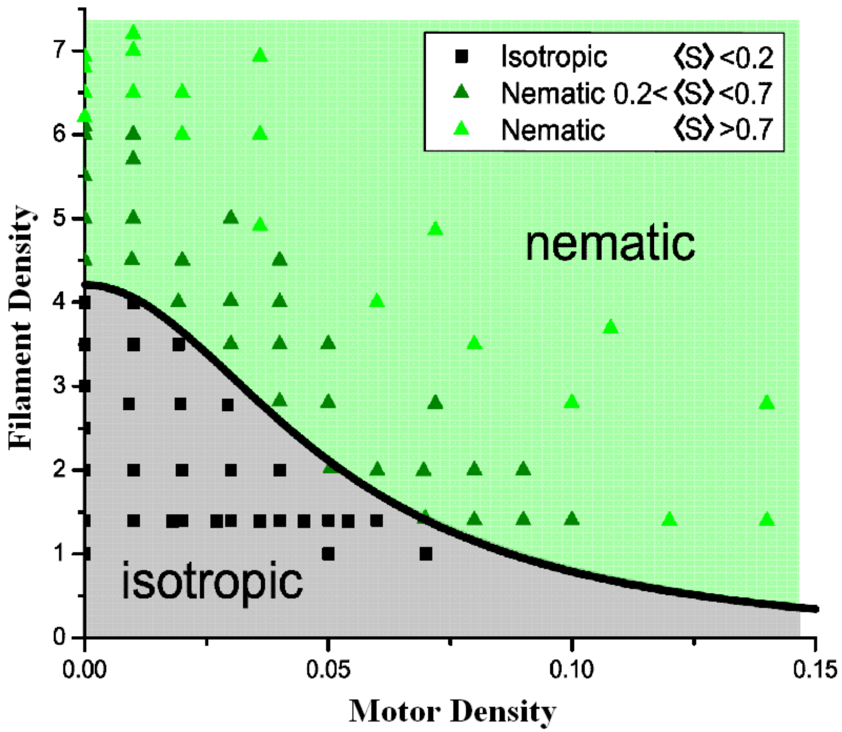
$$\rho_{IN}(\tilde{m}) = \frac{\rho_N}{1+\tilde{m}/4}$$

$$\rho_{NP}(\tilde{m}) = \frac{\rho_N}{\tilde{m}}$$

critical density $\tilde{m}_x = \dfrac{1}{g-1/4}$

$$\text{using}\left.\begin{array}{l} D_r \sim \gamma_P \\ L \sim 10\mu \\ b \sim 10nm \end{array}\right\} \tilde{m}_x \sim 1 \rightarrow \quad m_x \sim 0.5\mu M$$

Numerical simulation of 2d rigid filaments interacting with motors grafted to a substrate



Pavel Kraikivski, PhD Dissertation (2005).

Hydrodynamics of polarized phase

u(s)→stepsize x R_{ATP}
μ ~ m x R_{ATP}

$$\vec{P} = \rho p_0 \hat{p}$$
$$p_0 = \text{const.}, \quad |\hat{p}| = 1$$
$$\rho = \rho_0 + \delta\rho$$

$$\left(\partial_t - \boxed{\beta\mu\hat{p}\cdot\vec{\nabla}}\right)\delta\rho = \boxed{\beta'\mu\vec{\nabla}\cdot\hat{p}} + (D - \alpha\mu\rho)\nabla^2\delta\rho$$

$$\left(\partial_t + \boxed{\tilde{\beta}\mu\hat{p}\cdot\vec{\nabla}}\right)\hat{p} = \boxed{\tilde{\beta}'\mu\vec{\nabla}\delta\rho} + (K + \gamma_P\mu\rho - \alpha\mu\rho)\nabla^2\hat{p} + (K' - \alpha'\mu)\vec{\nabla}\left(\vec{\nabla}\cdot\hat{p}\right)$$

filament advection along $\hat{p}$

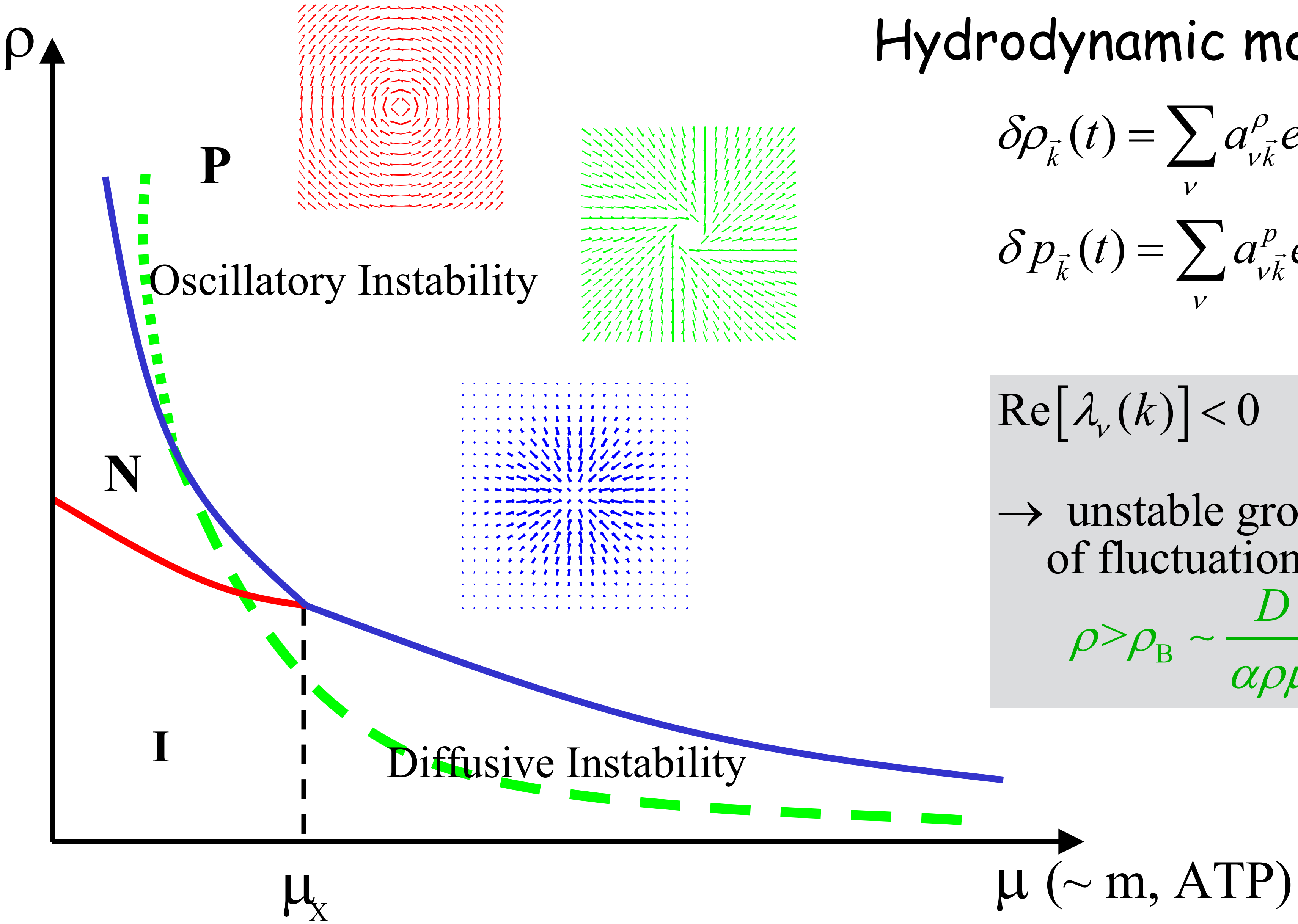
Simha & Ramaswamy, PRL 2002

coupling between splay and density fluctuations allowed in a polar fluid

Kruse et al., 2004; Voituriez et al. 2006; Kung et al. 2006

Filament bundling α renormalizes diffusion, bend and splay →instability

Inhomogeneous Structures



Hydrodynamic modes:

$$\delta\rho_{\vec{k}}(t) = \sum_{\nu} a^{\rho}_{\nu\vec{k}} e^{-\lambda_\nu(k)t}$$

$$\delta p_{\vec{k}}(t) = \sum_{\nu} a^{p}_{\nu\vec{k}} e^{-\lambda_\nu(k)t}$$

$\mathrm{Re}\left[\lambda_\nu(k)\right] < 0$

$\rightarrow$ unstable growth of fluctuations for

$$\rho > \rho_B \sim \frac{D}{\alpha\rho\mu}$$

Active mechanisms & parameters

Activity $\mu \sim$ motor density x R_{ATP}: driving force that maintains the system out of equilibrium

Rotations → Polar and NP "zipping" rates $\gamma_P, \gamma_{NP} \sim \kappa/\zeta$: control homogeneous states and build up polarization & nematic order (may be independent of R_{ATP})

Uniform stepping of motors → polarization sorting rate $\beta \sim$ mean motor speed $\langle u(s) \rangle_L$: yields filament drift & vortices

Inhomogeneities in motor speed → bundling rate α: softens all elastic constants and is the main pattern-forming mechanism

Numerical estimates

$$\gamma \sim \frac{\kappa}{\zeta} = \frac{\kappa D_r}{k_B T}$$

$$\kappa_{\text{kinesin}} \sim 10^{-22}\, nm/rad$$

$$\beta \sim u_0 \sim {}^{nm}/_{msec}$$

$$\alpha = L\left\langle \frac{du}{ds} \right\rangle_L \sim u_0 \frac{b}{L}$$

Competition of:

diffusion	driving by motors
$D_r \sim 10^{-2}/s$	$\gamma \sim 10^{-1}/s$
$D/L^2 \sim 10^{-2}/s$	$\alpha/L \sim 10^{-4}/s$
	$\beta \sim 10^{-6}\, m/s$

instability:

$$m\rho\alpha/L \sim D/L^2$$

$$\left.\begin{array}{l} m_{\text{kinesin}} = 1.2\mu M \\ \rho_{\text{tubulin}} = 26\mu M \\ L = 10\mu m \\ b = 10nm \\ \text{sample thickness} = 1\mu m \end{array}\right\} \to m\rho\, \alpha/L \sim 10^{-2} f$$

Conclusions

- Active filament solutions are significantly different from passive ones
- Non-equilibrium analogues of bulk phase transitions driven by crosslink-induced rotations
- Inhomogeneous states with mesoscopic structures driven by motor activity. Type of defect structures depend on homogeneous states.
- Bundling – the main pattern-forming mechanism - is due to spatial inhomogeneities in the motor velocity
- Next: include flow of solvent.