Active Structures and their Active Matter Models

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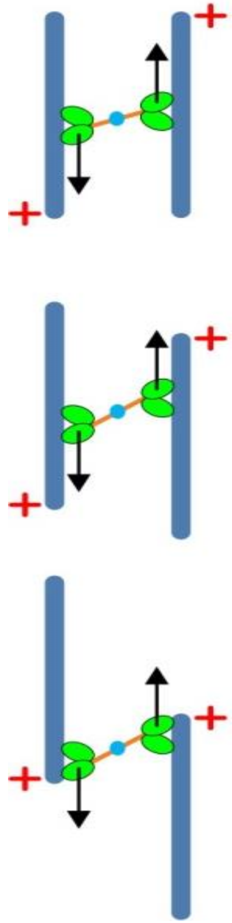

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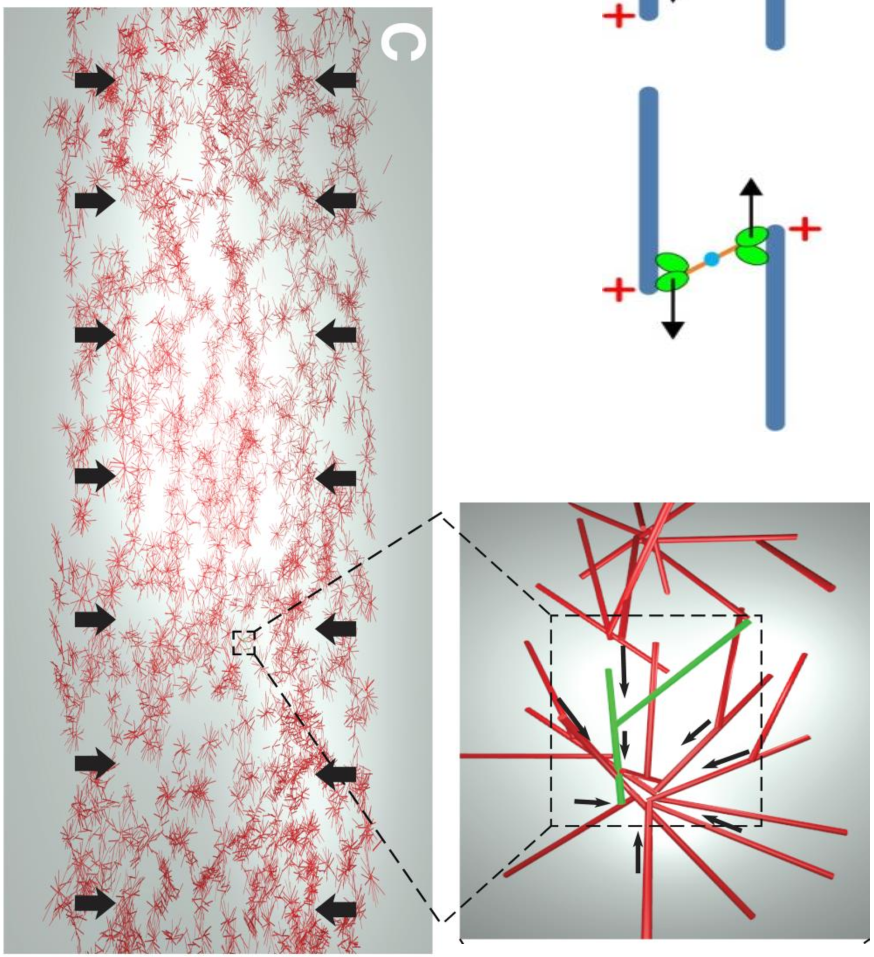
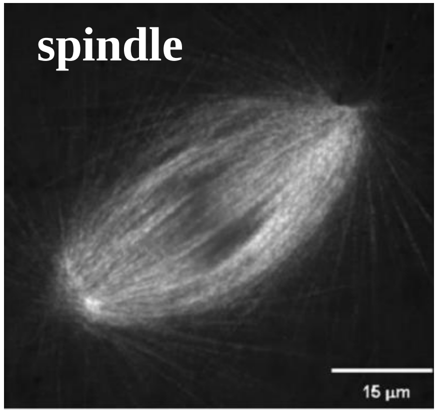


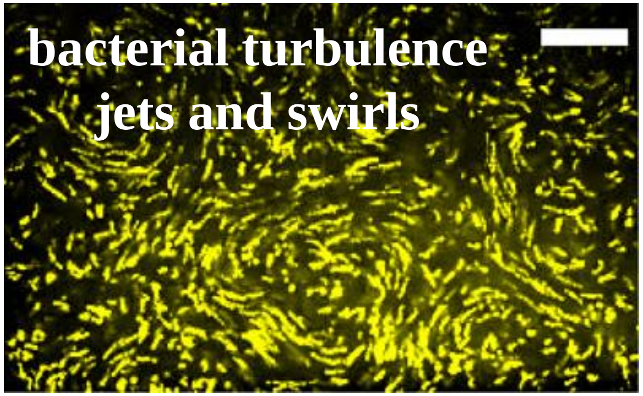
New Directions in Theoretical Physics

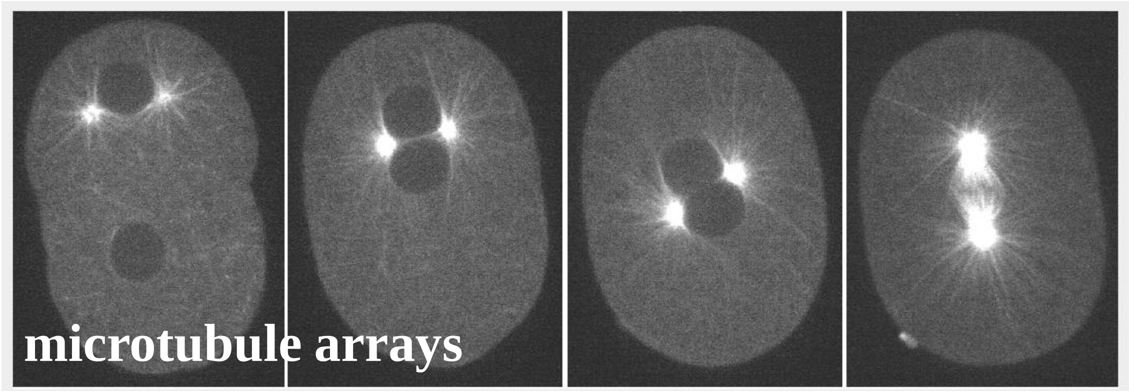
Some **collective structures** of self-propelled or active particles in fluids…

$$\mathbf{Re} >> 1 \Rightarrow \frac{D\omega}{Dt} \approx 0$$

$$\mathbf{Re} = \frac{\rho U L}{\mu}$$





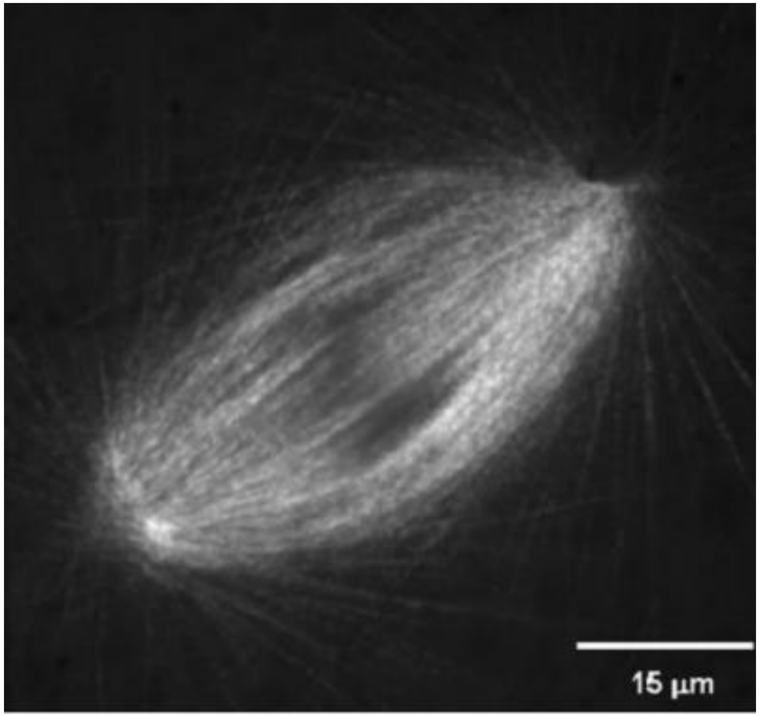


$$\mathbf{Re} << 1 \Rightarrow \Delta\omega \approx 0$$

A common aspect of all of these problems:

flocks, schools, spindles, rotors, motile defects, self-driven flows, …

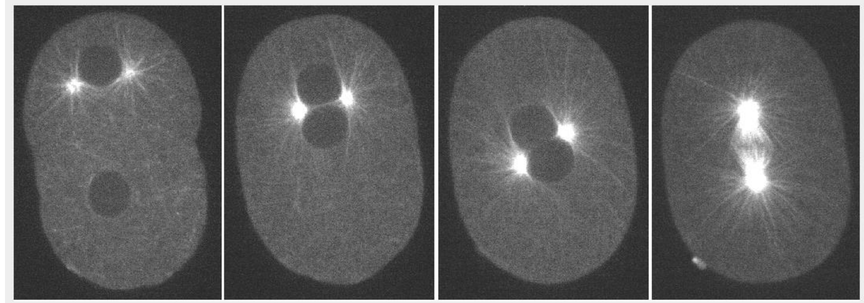
Coherent structures assemble and are maintained by the continuous consumption of energy by its constitutents



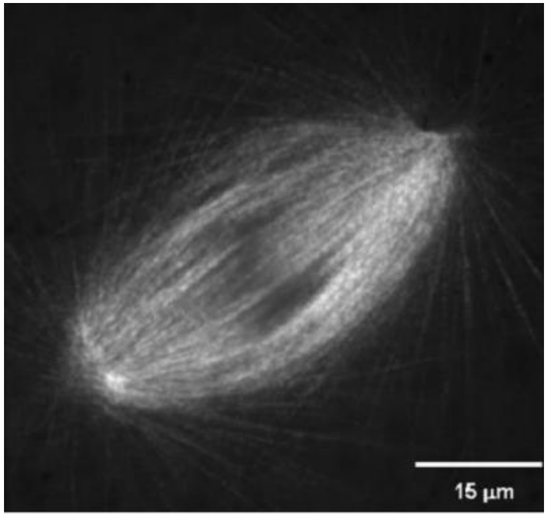
Re << *1*: Active particles, fluids, materials (Active matter)

Fluids with suspended active microstructure:
swimmers, motor proteins, biopolymers

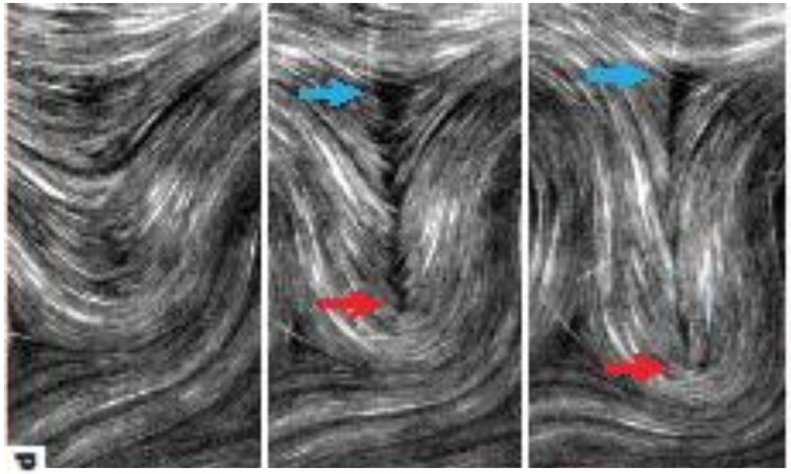
Extreme version of fluid-body interactions at small scales:
Reciprocal coupling between active microstructure
and large-scale flow



Pronuclear positioning Shinar *et al* 2011

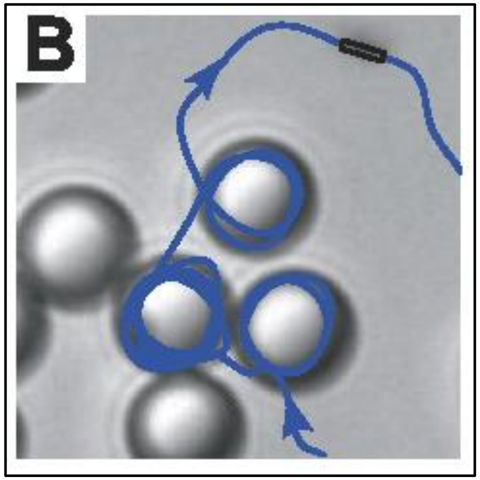


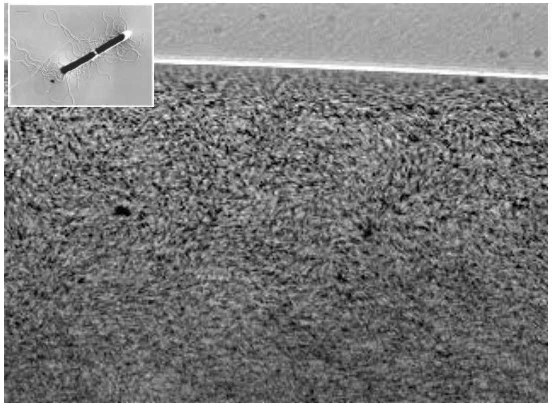
Mitotic spindle
Needleman Lab



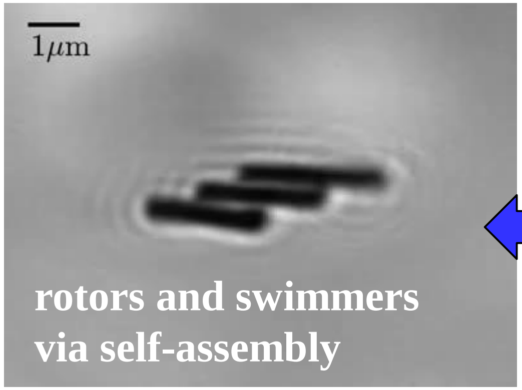
Active nematics & defect dynamics
in MTs/motor-proteins Sanchez *et al* 2012

synthetic swimmers
Paxton *et al JACS* '04
Takagi *et al, PRL* '13, *SM* '14





Goldstein and collaborators
the one and the many

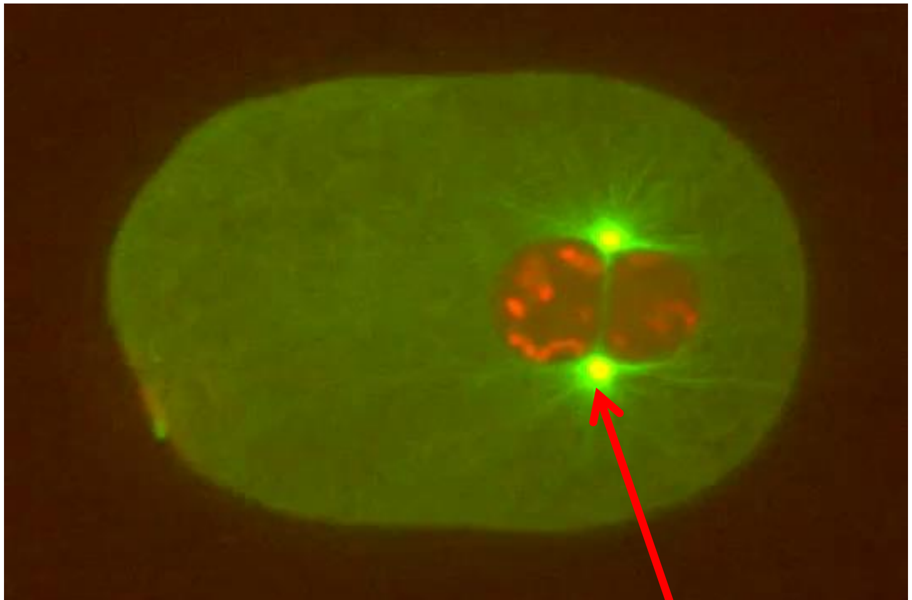


nonmotile but mobile
extensile particles

Davies-Wykes *et al, Soft Matter* 2016

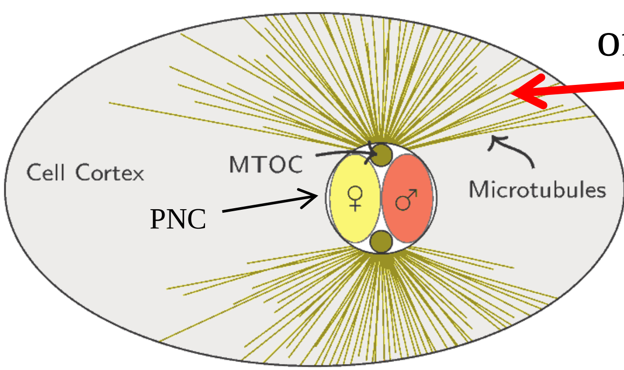
Cellular microtubule/motor-protein assemblies

Spindle positioning



Sugimoto Lab

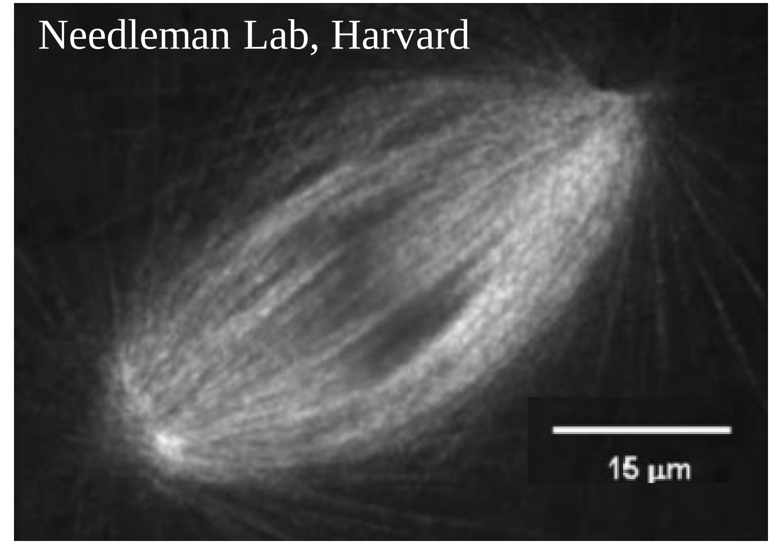
Centrosome (MTOC) and centrosomal array of microtubules (MTs)

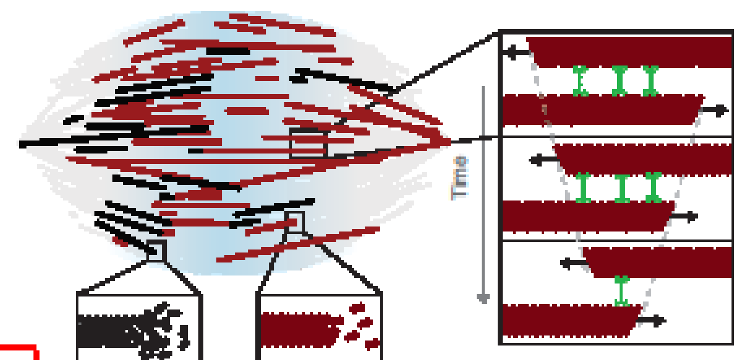


Centrosomal array of MTs maneuvers pronuclear complex (PNC=M+F) to the “proper position”

Shinar, Mano, Piano, Sh., *PNAS* 2011
Shelley, *Ann. Rev. Fluid Mech*, 2016

Mitotic spindle & chromosome segregation





Spindle is self-assembled from overturning MTs, motor proteins, and many other things…

Performs chromosome segregation

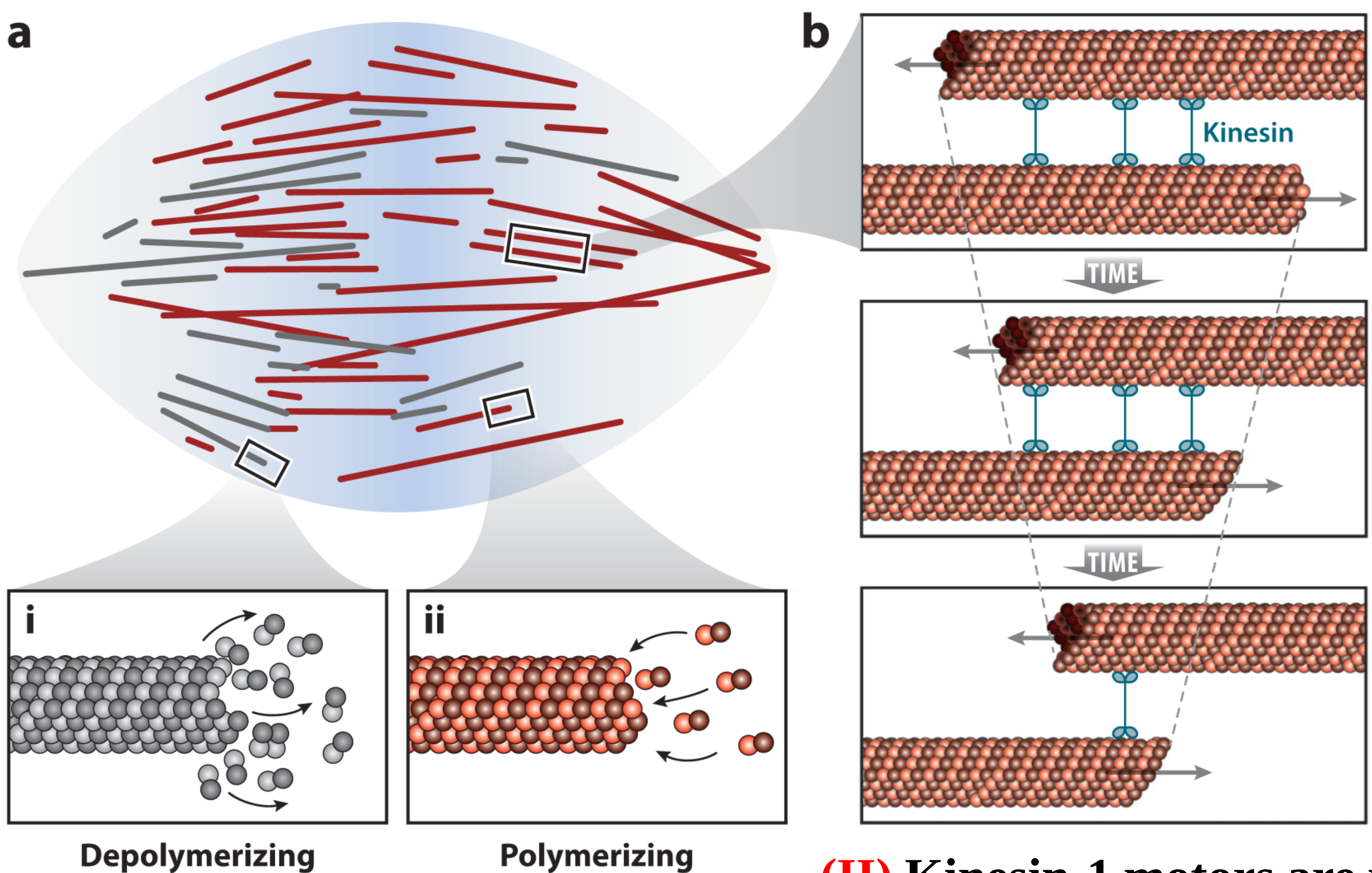
MTs and two of their motor-proteins

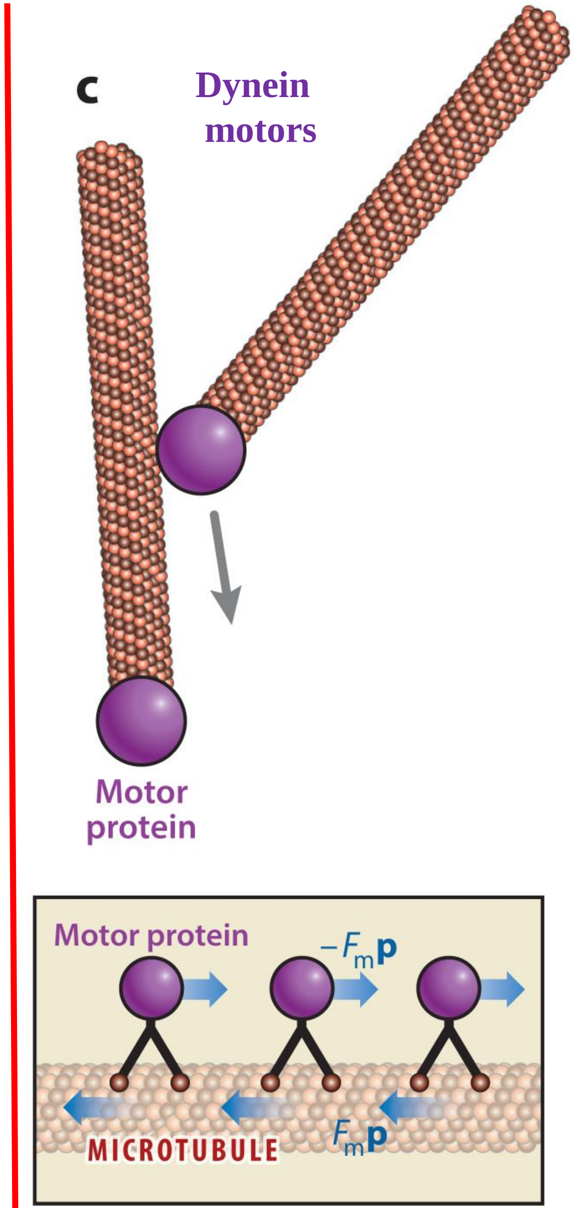
MTs: very thin – 20nm – but microns in length

(I) MTs are highly dynamic (lifetime ~ 1 min)

(II) MTs are polar and the motor-proteins know it.

Kinesin motors



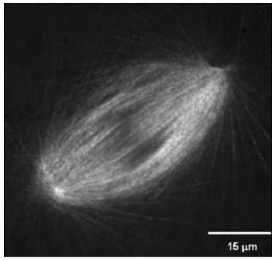


(I) MTs are constantly assembling and disassembling (dynamic instability)

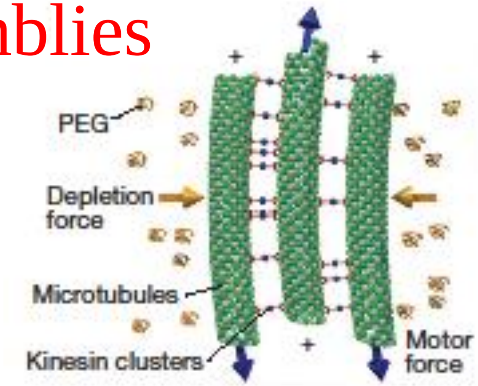
(II) Kinesin-1 motors are plus-end directed and can "polarity-sort" MTs;

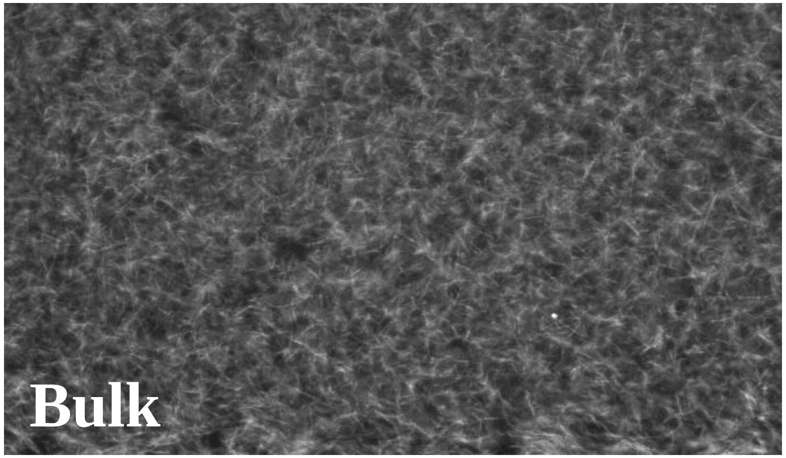
(III) Dyneins are minus-end directed and are thought to cluster MT minus-ends, carry payloads

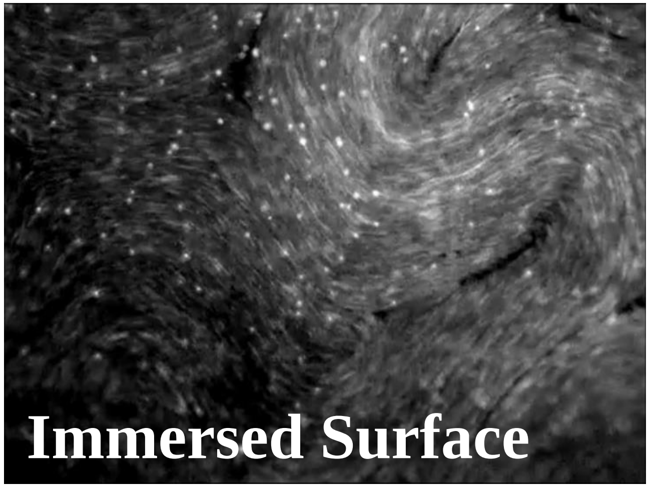
Biosynthetic MT/motor-protein assemblies

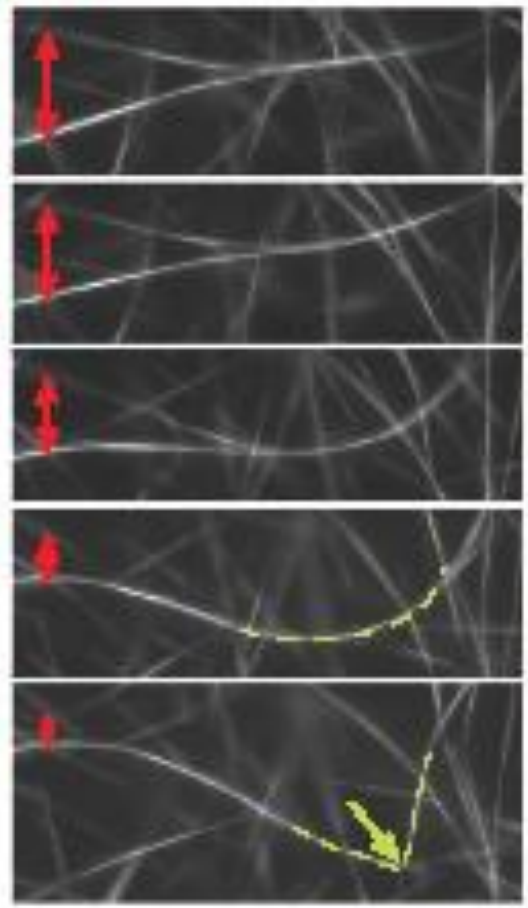


Dogic Lab @ Brandeis: synthetic fluids assembled from MTs, kinesin motor complexes, and ATP

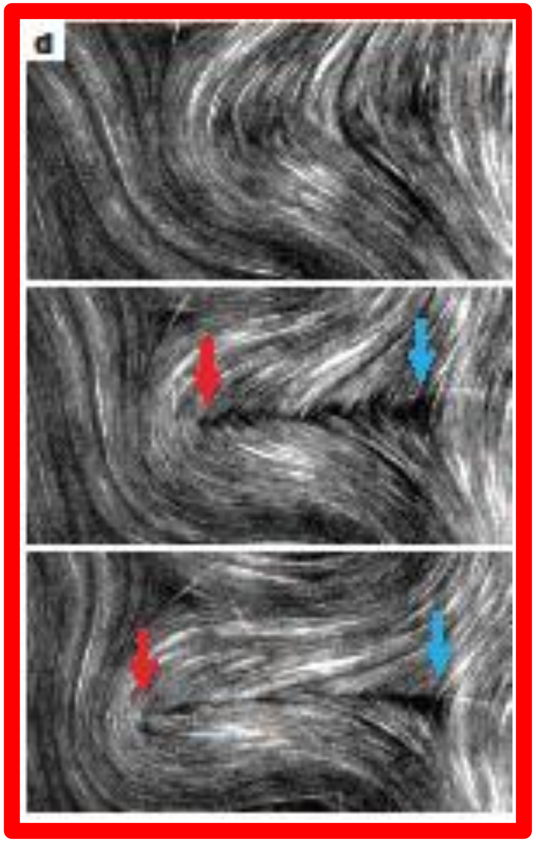








Self-assembly of bundles in bulk; merging, sorting, fracturing, …
Independence of **v-v** correlation length upon ATP concentration

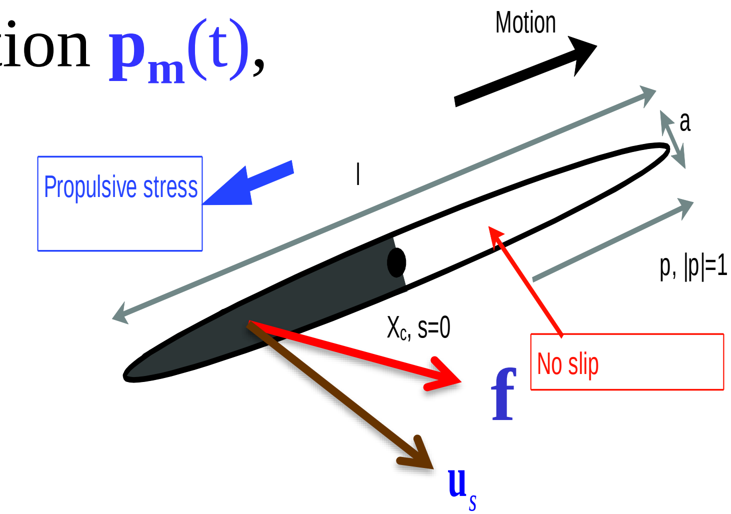


High concentration on surface: active nematic “turbulence”, defect production, annihilation.

Sanchez et. al, “Spontaneous motion in hierarchically assembled active matter”, *Nature*, 2012

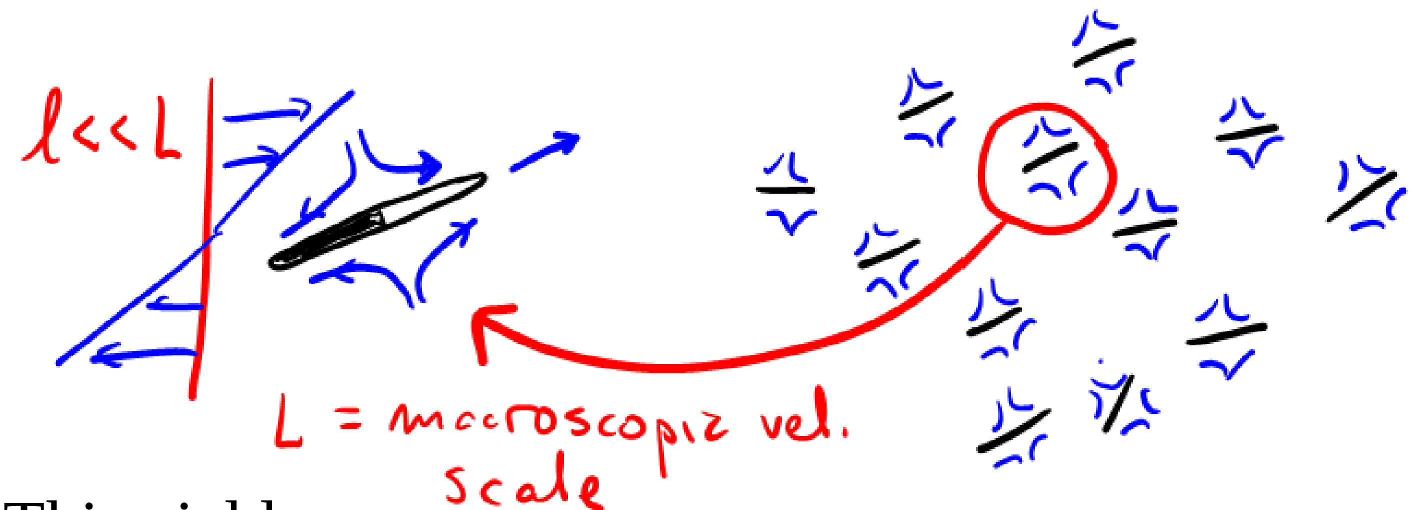
Fluid stresses for swimmers / active particles:

Slender swimmer with position $\mathbf{X}_m(t)$, orientation $\mathbf{p}_m(t)$, exerting force/length $\mathbf{f}_m(s)$ on fluid



Solve the single particle problem using SBT.

Evolve a distribution function $\Psi(\mathbf{x},\mathbf{p},t)$



$\alpha < 0$: Pushers pump energy into system

This yields:

$$\dot{\mathbf{X}}_m = \mathbf{u}(\mathbf{X}_m) + U_0\mathbf{p}_m \;\&\; \dot{\mathbf{p}}_m = (\mathbf{I} - \mathbf{p}_m\mathbf{p}_m)\nabla\mathbf{u}(\mathbf{X}_m)\mathbf{p}_m \;\&\; \mathbf{f}_m = a_m(s)\,\mathbf{p}_m$$

Swimming induced active stress:

$$\mathbf{\Sigma}^a = +\frac{\sigma_0}{V}\sum_{m=1}^{N}\mathbf{p}_m\mathbf{p}_m^T \to \alpha\int dS_p\,\psi(\mathbf{x},\mathbf{p},t)\,\mathbf{p}\mathbf{p}^T = \alpha\mathbf{D}[\psi]$$

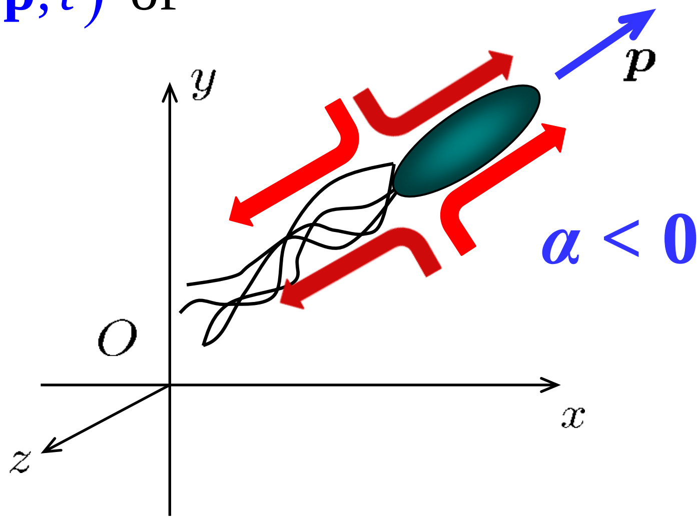
…

Simha & Ramaswamy '04
Saintillan & Sh. '08a&b
Subramanian & Koch, '09
Ezhilan, Sh. Saintillan '13

Most basic kinetic theory for motile suspensions

S&S, *PRL* '08, *PoF* '08, Koch & Subr. *JFM* '09, H&S *PRE* '10, LH Lectures '11, ESS, *PoF* '13

Fokker-Planck equation for distribution function $\Psi(\mathbf{x},\mathbf{p},t)$ of center of mass $\mathbf{x}$ and swimming director $\mathbf{p}$



$$\Psi_t + \nabla_x \cdot (\dot{\mathbf{x}}\Psi) + \nabla_p \cdot (\dot{\mathbf{p}}\Psi) = 0$$

$$\begin{cases} \dot{\mathbf{x}} = \mathbf{p} + \underline{\mathbf{u}}(\mathbf{x},t) - \nabla_x (D \ln \Psi) \\ \dot{\mathbf{p}} = (\mathbf{I} - \mathbf{p}\mathbf{p}^T) \underline{\nabla \mathbf{u}}\, \mathbf{p} - \nabla_p (d \ln \Psi) \end{cases}$$

Stokes Eqs driven by active stress (Kirkwood theory; Batchelor '70):

$$\nabla q - \Delta \mathbf{u} = \nabla \cdot (\boldsymbol{\Sigma}^a + \ldots) \quad \text{and} \quad \nabla \cdot \mathbf{u} = 0$$

$\boldsymbol{\Sigma}^a(\mathbf{x},t) = \alpha \mathbf{D}[\psi](\mathbf{x},t)$ where *Pushers*: $\alpha < 0$, *Pullers*: $\alpha > 0$

w. $\mathbf{D}[\psi] = \int dp\, \psi\, \mathbf{p}\mathbf{p}^T$ the tensor order parameter

Nondimensionalization: $u_c = U_s \to 1,\ l_c = l/\nu,\ t_c = l_c / u_c;\quad \nu = n(l/2)^3$

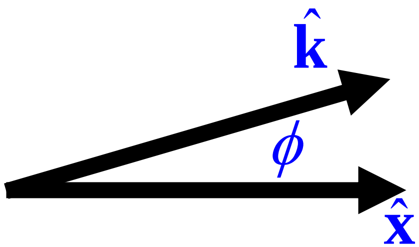
$$\sigma_0 \to \alpha = \sigma_0 / \mu U_0 l^2 = \kappa_1 / \kappa_2 = O(1)$$

Some Results:

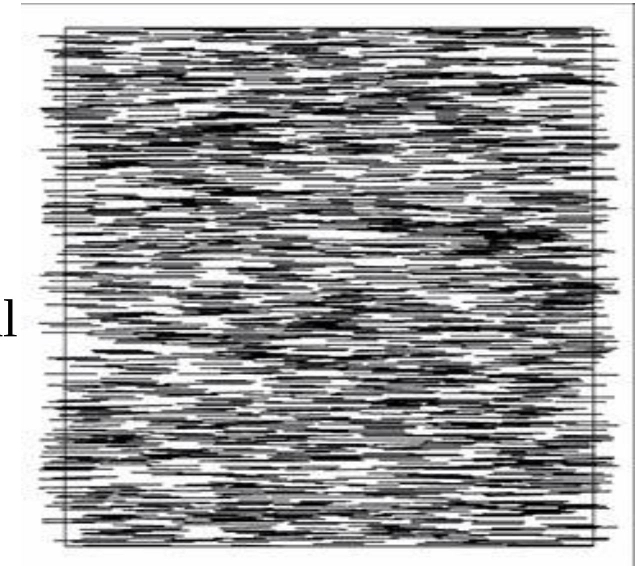
Reviewed by **Saintillan & Shelley, *Comptes Rendes Physique* 2013**

(i) Instability of globally aligned states (no flocks) *

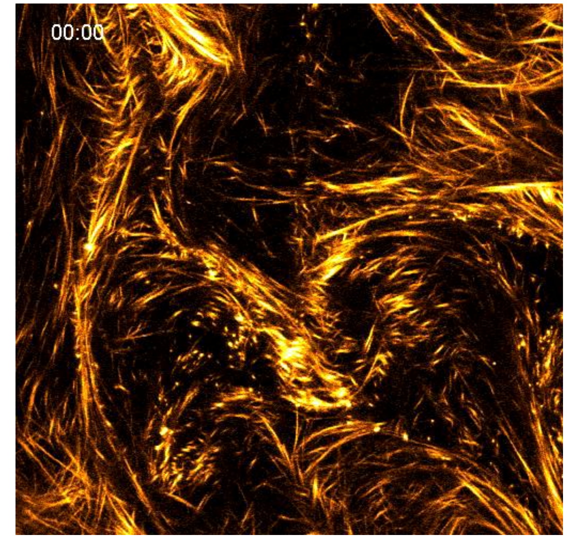
Simha & Ramaswamy '02, Saintillan & Shelley '07, '08, Gao *et al* '15



Wave vector $\hat{\mathbf{k}}(\phi)$ of maximal growth is aligned with the suspension, i.e. $\phi = 0$



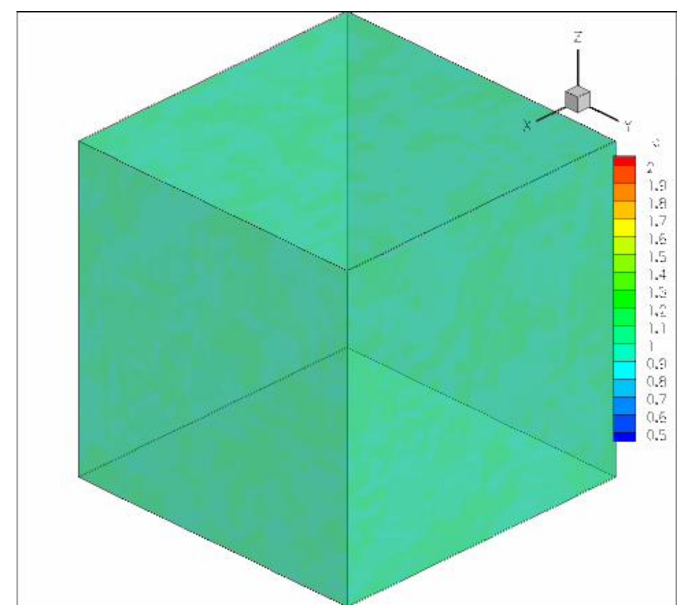
Dogic Lab '16



(ii) Stability criterion for isotropic Puller suspensions: $(L/l)\,\nu > C$ *

Hohenegger & Shelley '10, Saintillan & Shelley '12

Consistent with expts Sokolov et al '07,….



(iii) Simulations show formation of persistent and unsteady coherent structures, concentration fluctuations; strongly mixing flows.

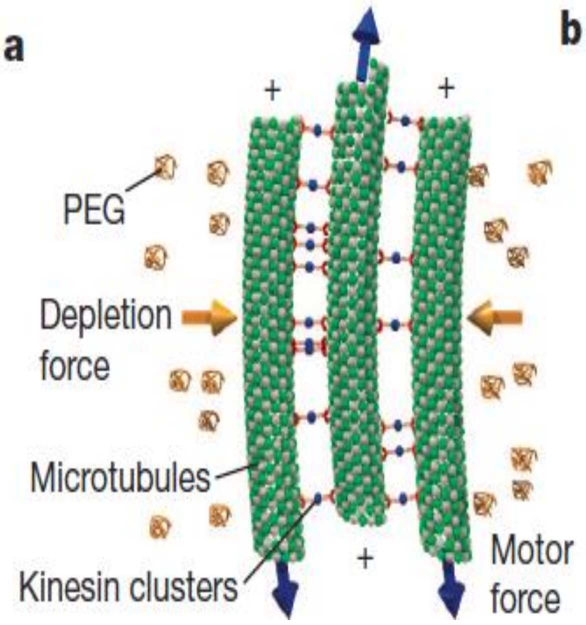
(iv) Active stresses drive instabilities, not self-propulsion.

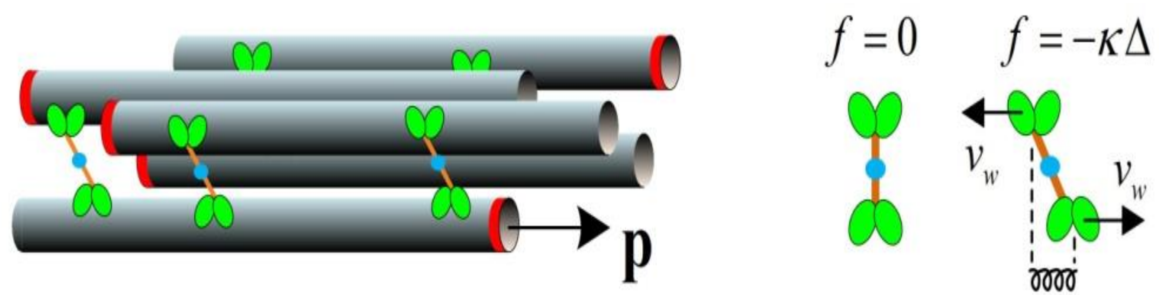
Applications to chemotaxis, confinement, rheology, active nematics, models of MTs/motor protein interactions

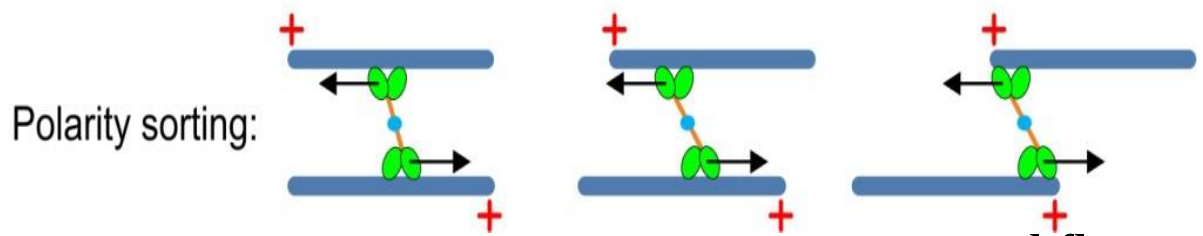
Active stresses for MT assemblies I:

Gao et al, *PRL & PRE* 2015

A basic interaction: polarity sorting of anti-aligned MTs







l ~ 1.5 *um*, v ~ 1.0 *um/s*

extensional flow, like a **pusher**

For bundle of m left-polar MTs, and n right-polar MTs

MT translation: $\dot{x}_j^L = \dfrac{2n}{n+m}v, \quad \dot{x}_k^R = -\dfrac{2m}{n+m}v; \qquad \dot{x}_j^L - \dot{x}_k^R = 2v$

Active stress: $\mathbf{\Sigma}^{active} = -\dfrac{\eta v_w l}{V}\left(\bar{x}_c^L - \bar{x}_c^R\right)\dfrac{mn}{m+n}\mathbf{x}\mathbf{x}^T; \qquad \bar{x}_c^L - \bar{x}_c^R \sim \alpha_1 l$

Crosslinking bias (towards overlap) yields **extensile stress**: $\alpha_1 < 0$

Polar "active nematic" theory for active MT assemblies

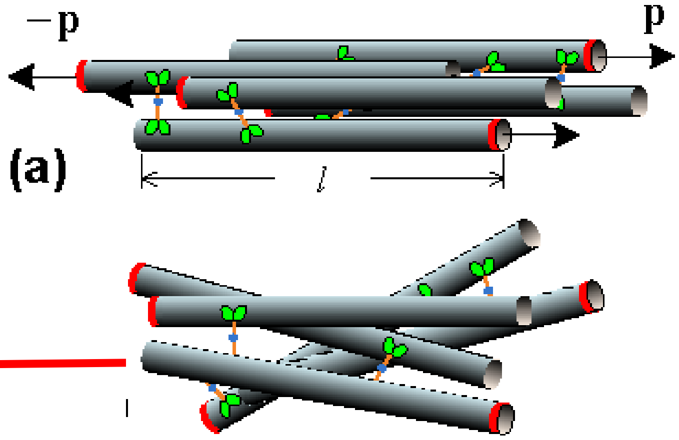
Gao, Blackwell, Betterton, Glaser, Sh., *PRL* '15, *PRE '15;* See Saintillan & Sh *PRL, PoF* '08, Ezhilan, Sa, Sh *PoF* '13

Evolve distribution $\Psi(\mathbf{x},\mathbf{p},t)$ of MT position $\mathbf{x}$ and polar orientation $\mathbf{p}$ ·

$$\phi = \int dp\,\Psi = \text{ local MT concentration}$$

$$\mathbf{q} = \phi^{-1}\int dp\,\mathbf{p}\Psi = \text{ local average MT polarization vector}$$

$$\mathbf{D} = \int dp\ \mathbf{p}\mathbf{p}^T\Psi;\ \ \mathbf{Q}=\phi^{-1}\mathbf{D} = \text{tensor order parameter of MT field}$$



$$\Psi_t + \nabla_x\cdot(\dot{\mathbf{x}}\Psi) + \nabla_p\cdot(\dot{\mathbf{p}}\Psi) = d_x\nabla_x^2\Psi + d_p\nabla_p^2\Psi$$

$$\dot{\mathbf{x}} = \underline{(\mathbf{q}-\mathbf{p})} + \mathbf{u}(\mathbf{x},t),\ \text{ polarity sorting + local background } \mathbf{u}$$

$$\dot{\mathbf{p}} = (\mathbf{I}-\mathbf{p}\mathbf{p}^T)(\nabla\mathbf{u} + \zeta\mathbf{D})\mathbf{p},\ \text{ Jeffery's eqn plus steric alignment torque}$$

$$\nabla q - \Delta\mathbf{u} = \nabla\bullet\boldsymbol{\Sigma}^{extra} \quad \& \quad \nabla\bullet\mathbf{u} = 0 \ \text{ with}$$

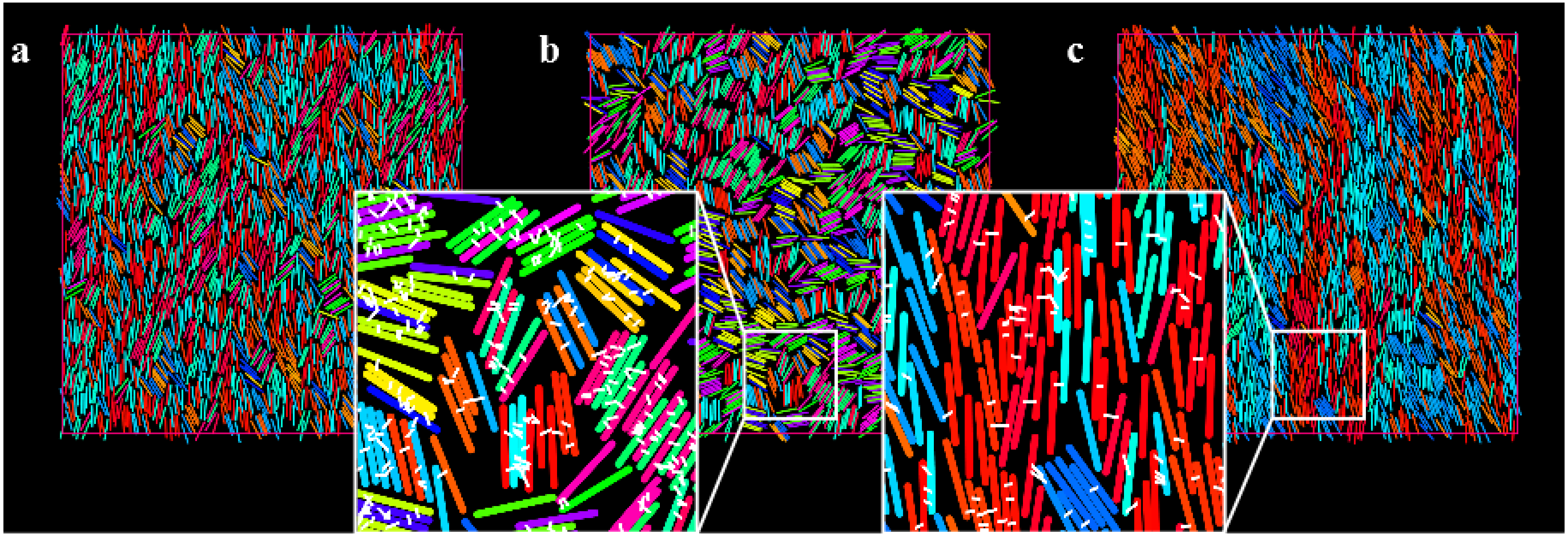
$$\boldsymbol{\Sigma}^{extra} = \boldsymbol{\Sigma}^{active} + \boldsymbol{\Sigma}^{constraint} + \boldsymbol{\Sigma}^{steric}$$

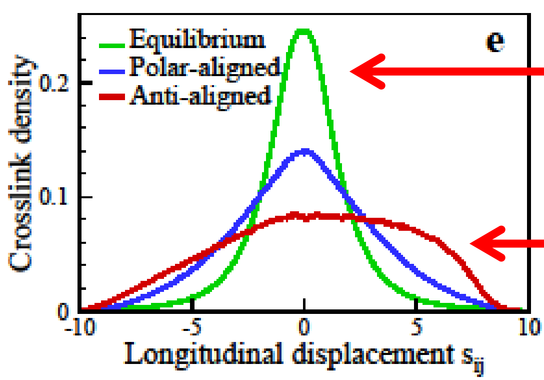
$$\boldsymbol{\Sigma}^{active}(\mathbf{x},t) = \frac{\alpha_1}{2}\left(\underline{\mathbf{D} - \phi\mathbf{q}\mathbf{q}^T}\right) + \frac{\alpha_2}{2}\left(\mathbf{D} + \phi\mathbf{q}\mathbf{q}^T\right)$$

active stresses produced by anti-aligned interactions (polarity sorting)

+ active stresses produced by polar-aligned interactions

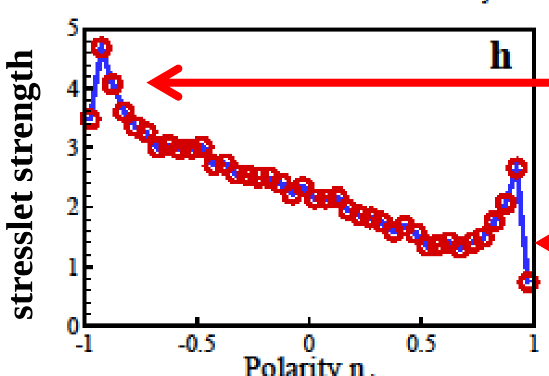
BD-MC simulations estimate parameters (micro to macro)





immobile crosslinks

cross-linked anti-aligned MTs biased towards extension



extensile stress produced by polarity sorting (anti-aligned)

extensile stress produced by polar-aligned MT interactions

BD-MC estimates

$\alpha_1 \approx 2$

$\alpha_2 \approx 0.5$

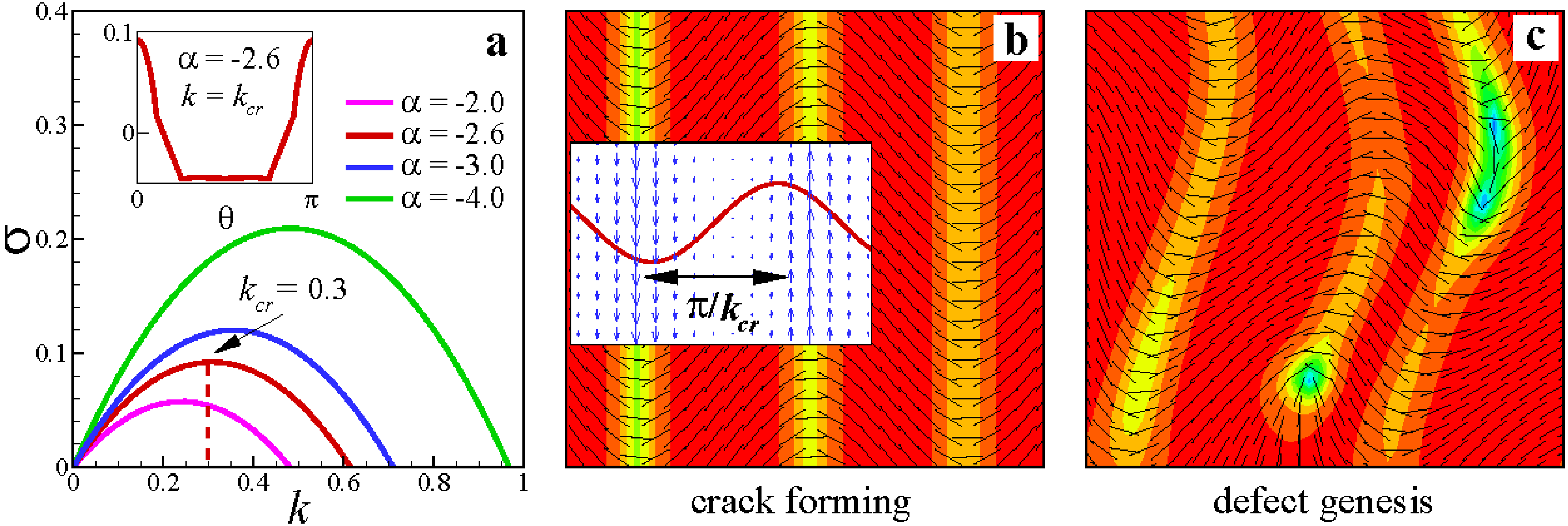
Linear theory of nematic steady state : $\psi = \psi_{\|} + \varepsilon\eta$ with $\hat{\mathbf{m}}_0 = \hat{\mathbf{x}}$

Fastest growing plane-wave vector is aligned

with nematic field: $\hat{\mathbf{k}} = \hat{\mathbf{m}}_0$ (generic)

(as in swimming suspension theory -- RS2004, SS2008)

Activity, diffusion & immersion pick out fastest growth-scale λ_{cr}.



$\theta = 0$, direction of maximal growth

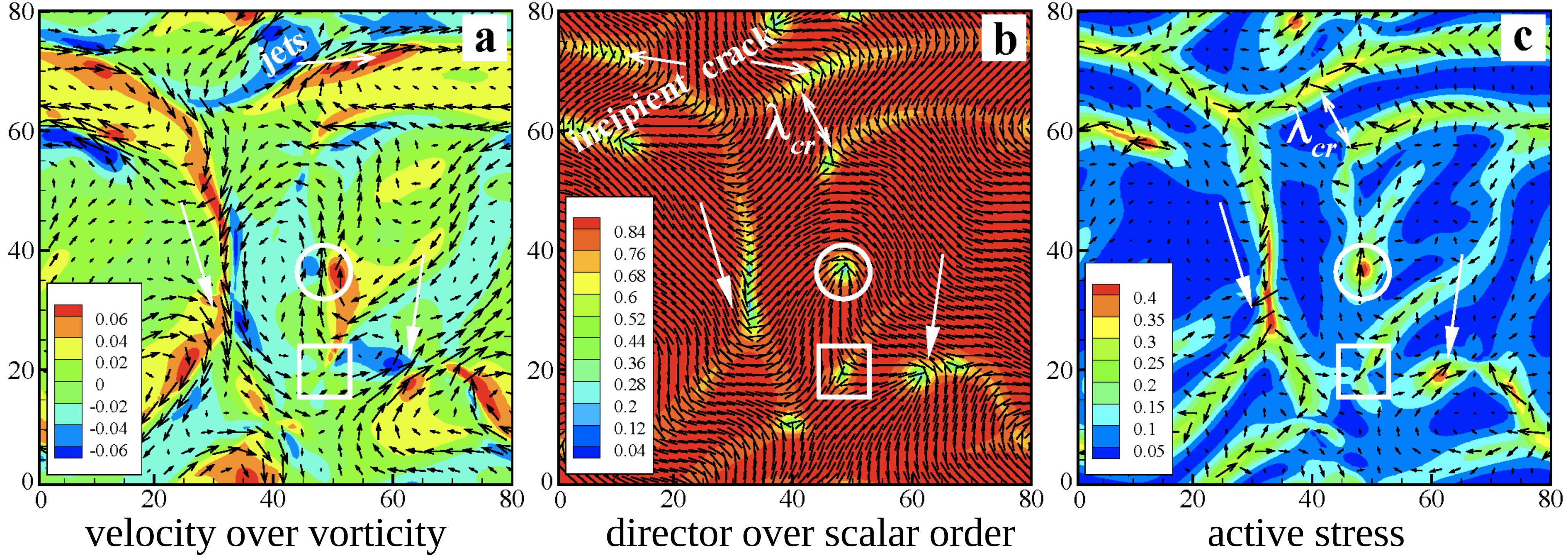
crack forming

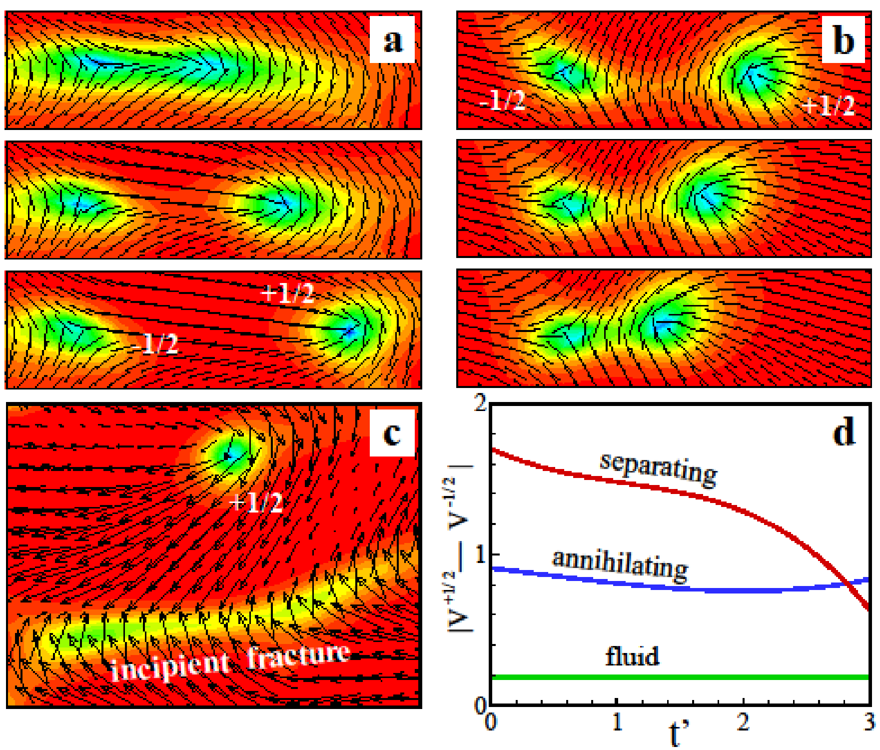
defect genesis

Accounting for outer fluid yields maximal growth-rate at finite k.

Nonlinear crack solns unstable to transverse modes.
See Giomi *et al*. 2011

Giomi, Marchetti, *et al*, 2013,…
Thampi *et al* 2013, …





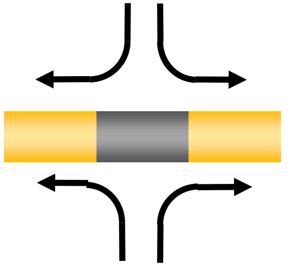
- Disclination singularities emerge from "cracks", or lines of low order. +1/2-order defects are highly mobile
- Cracks associated with surface jets, vortex pairs, and nematic bending
- Active force concentrated at +1/2-order defects; Defects leave behind polarity-sorted material.
- Defects separate on the motor-protein speed.

Gao et al, *PRL*, *PRE* '15

Active nematic flows in confinement

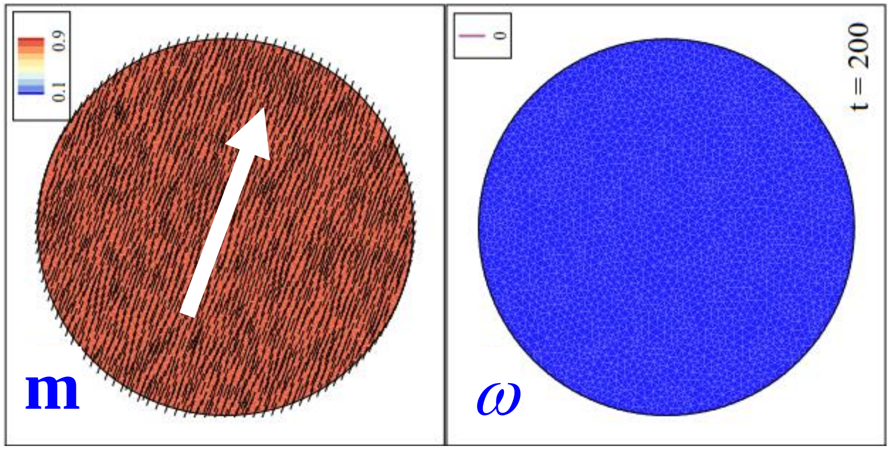
Gao, Betterton, Shelley ’16

Woodhouse & Goldstein ’12, Saintillan *et al* ’16 (w.o. steric interactions), Dogic *et al*



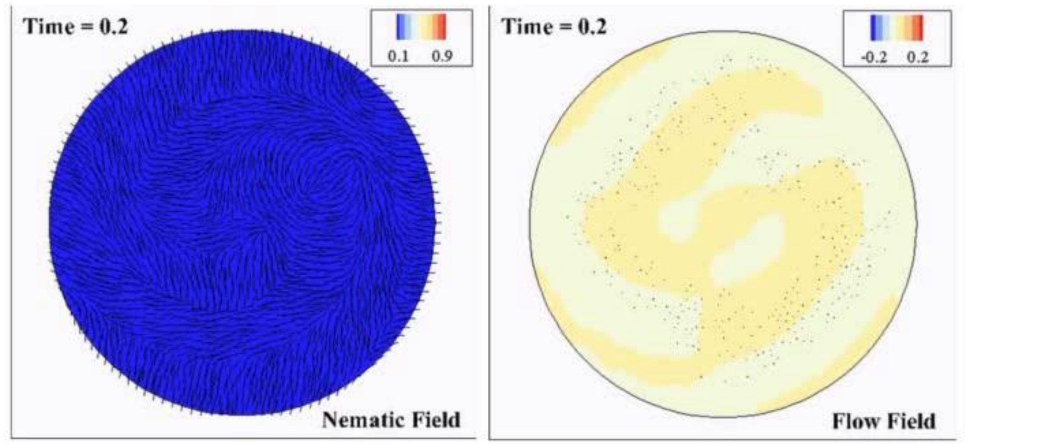
BCs: $\mathbf{u} = 0$ and $D_x\left(\partial\psi / \partial n\right) = 0$

relaxation to nematic alignment



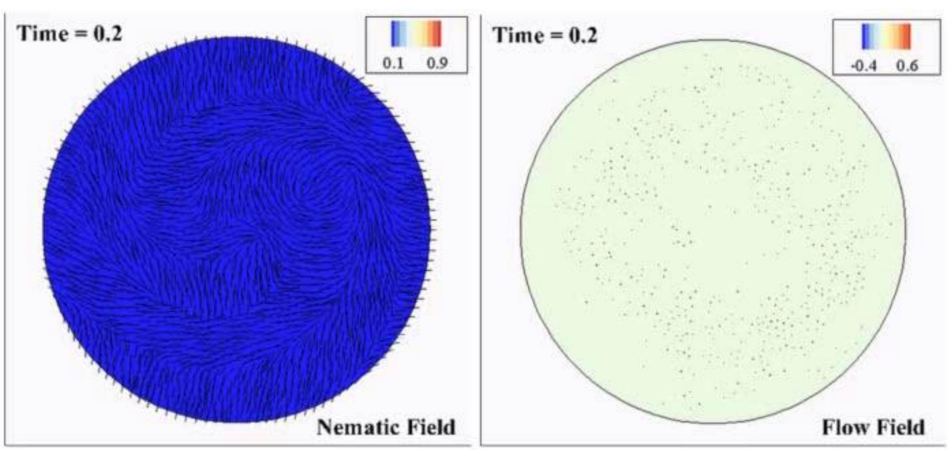
$\alpha = -0.3$

symmetry breaking to time-periodic flows by defects



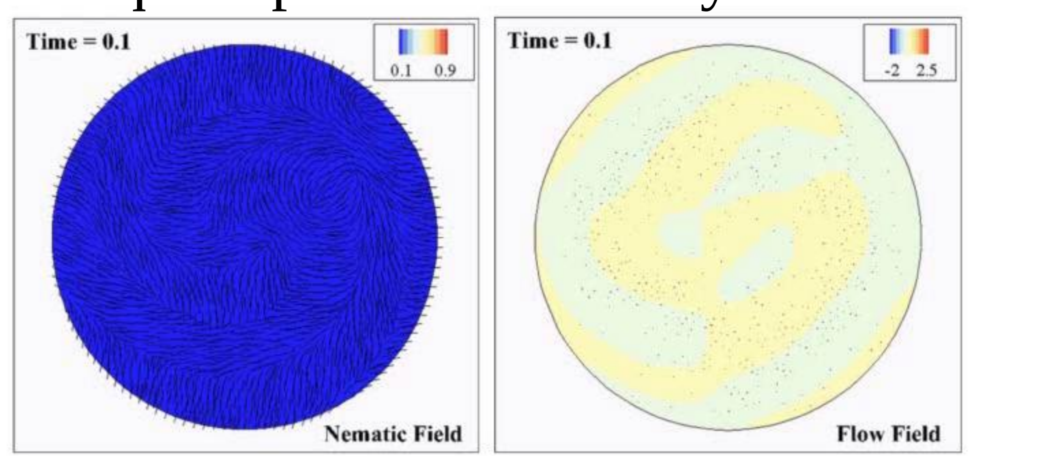
$\alpha = -2.5$

boundary annihilation of defects



$\alpha = -3$

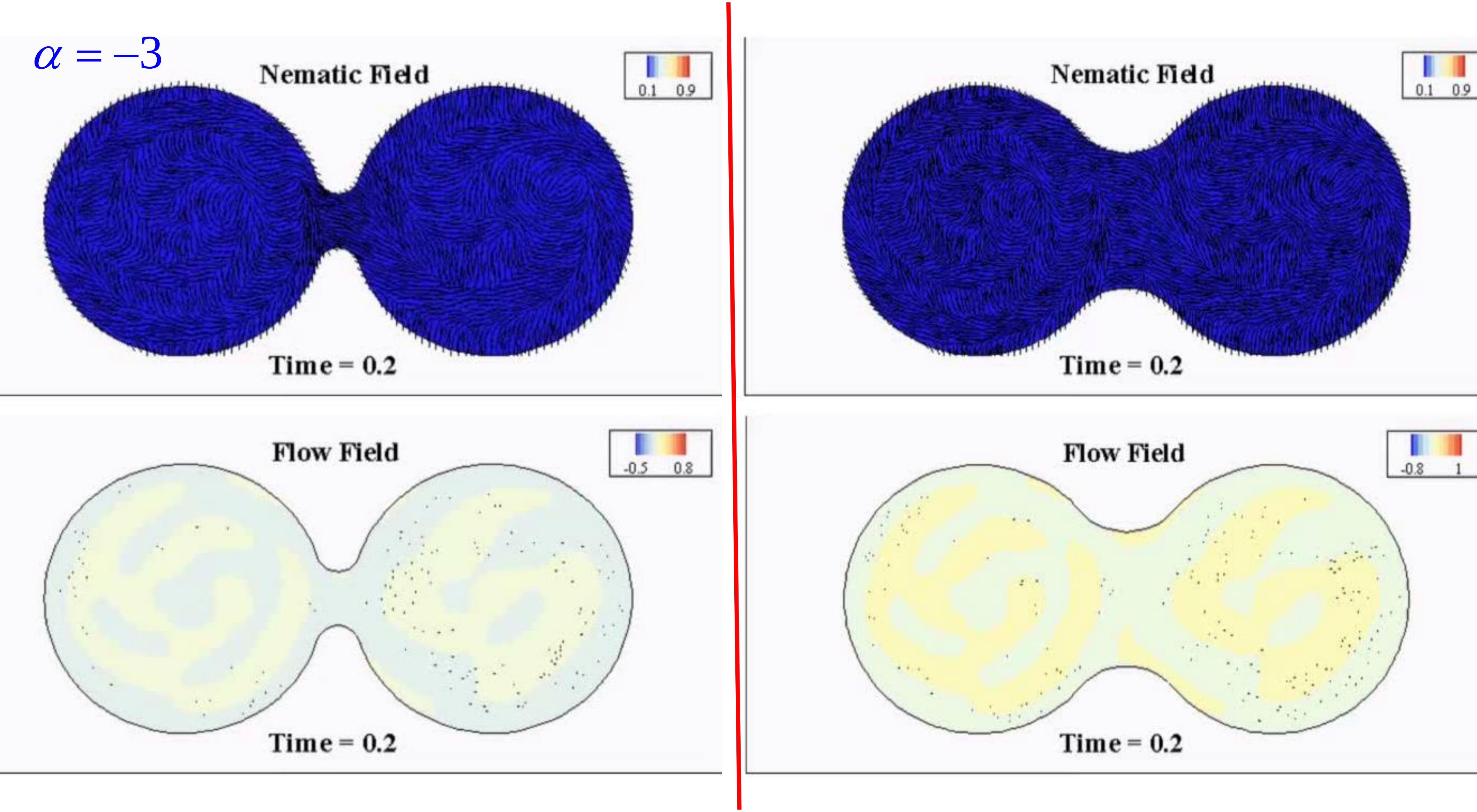
quasi-periodic defect dynamics



$\alpha = -4$

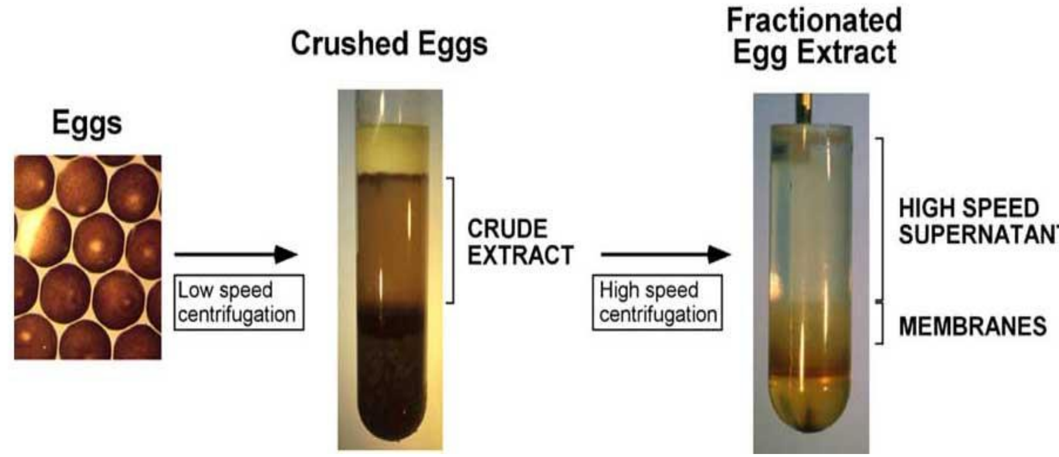
Biconvex domains (w a Fredericks transition)

$\alpha = -3$

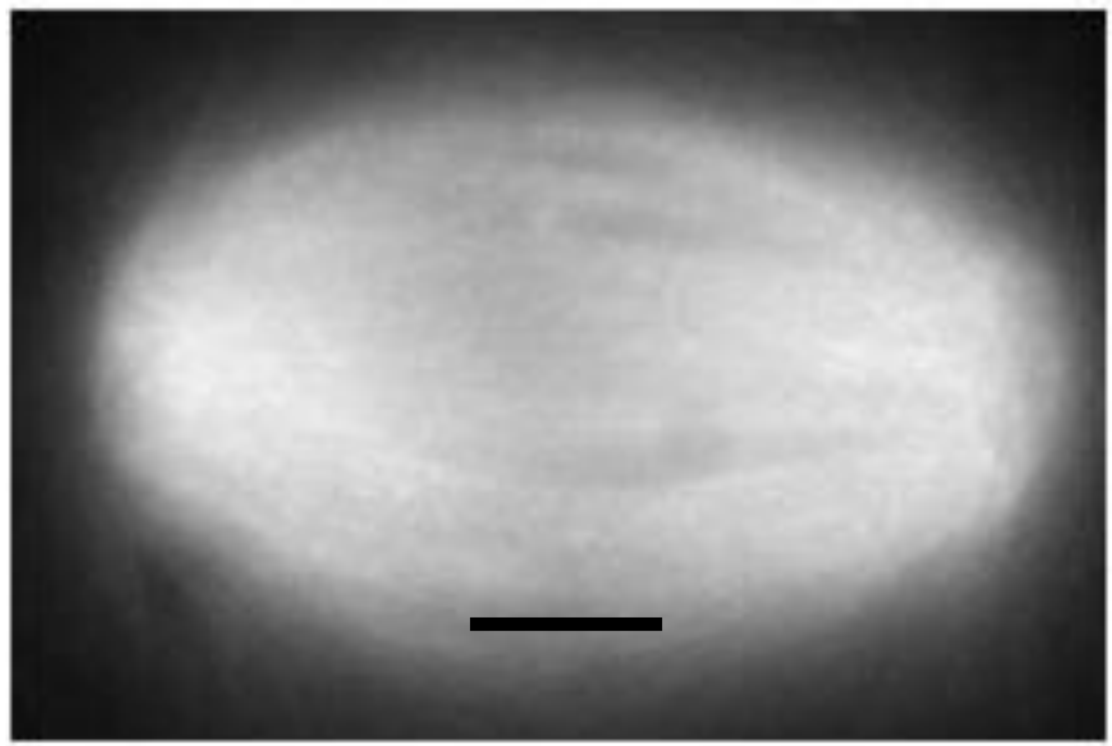


Active stresses for MT assemblies II:

Contractions in *Xenopus Laevis* egg extract

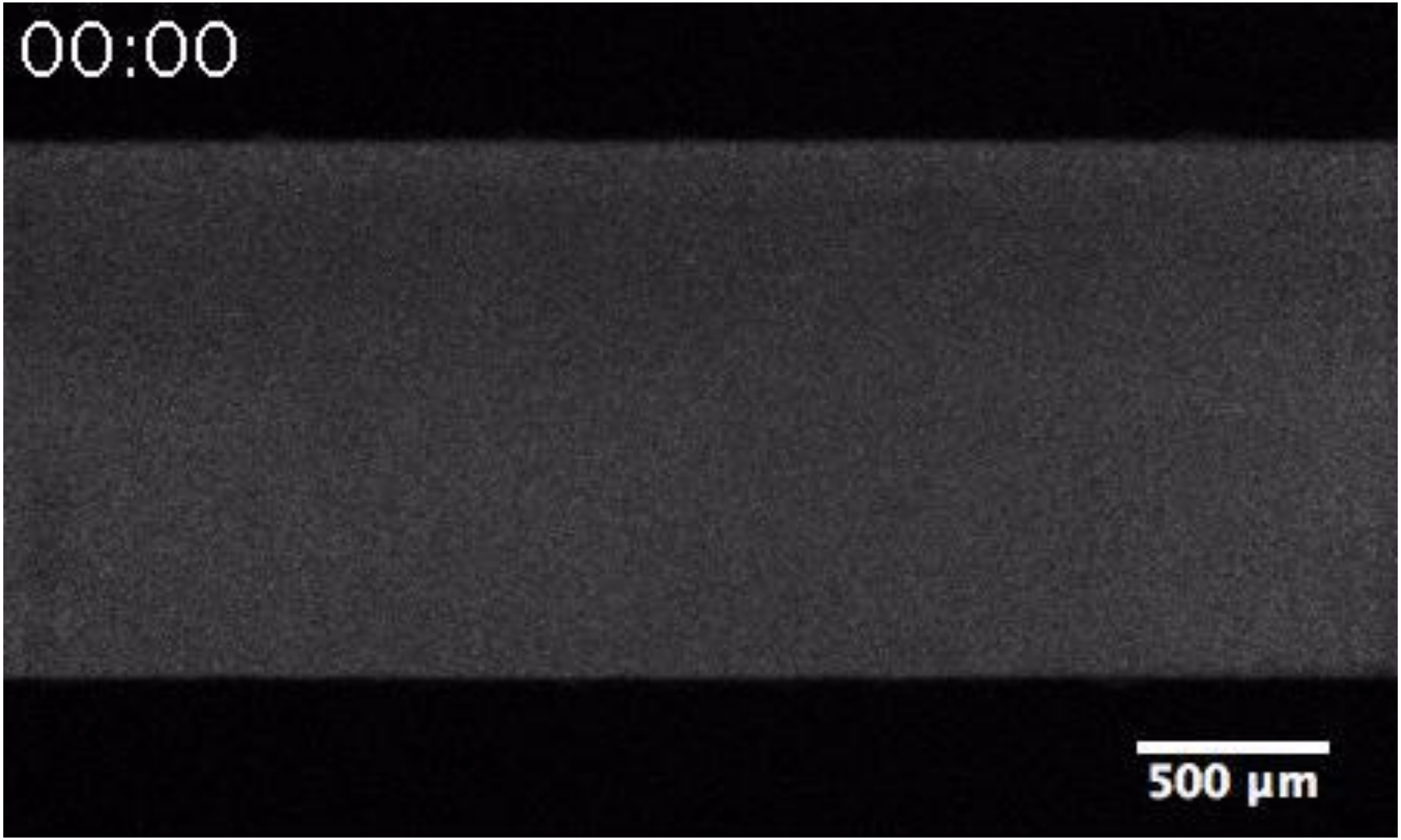


+ DNA



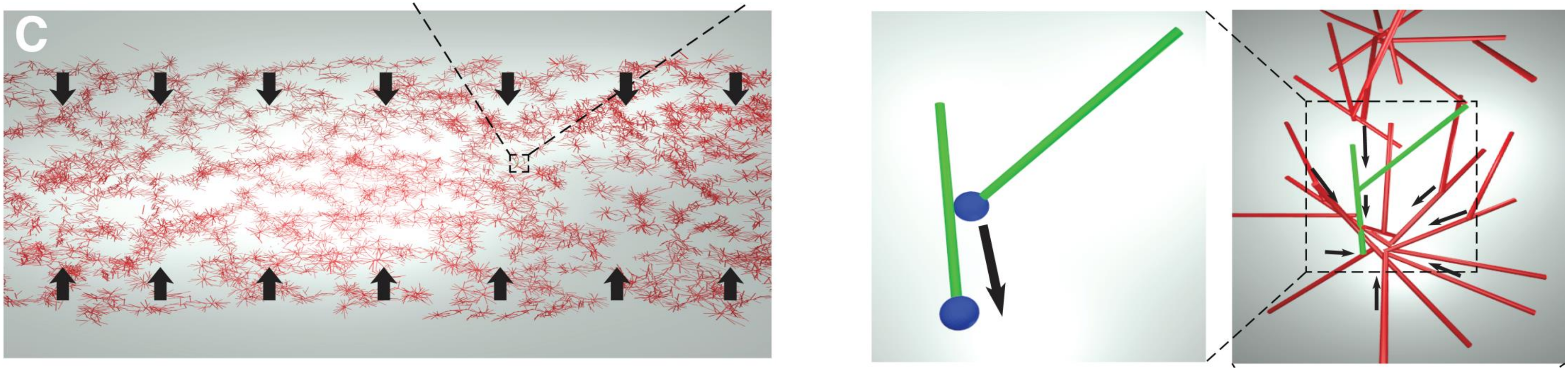
X. Laevis extract spindle (Needleman Lab)

Instead of DNA, add taxol (an anti-cancer drug) which both nucleates and stabilizes MTs



Contraction, not extension

A simple active material model



Dyneins pull MT minus ends together $\Rightarrow$ $\boldsymbol{\sigma}_1 \sim -s\rho\mathbf{I}$

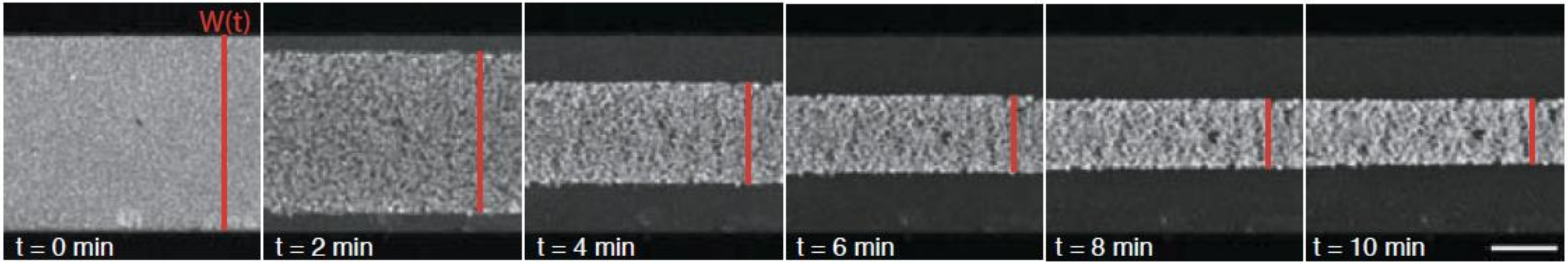
Steric interactions push MTs apart $\Rightarrow$ $\boldsymbol{\sigma}_2 \sim s\rho^2\mathbf{I}$

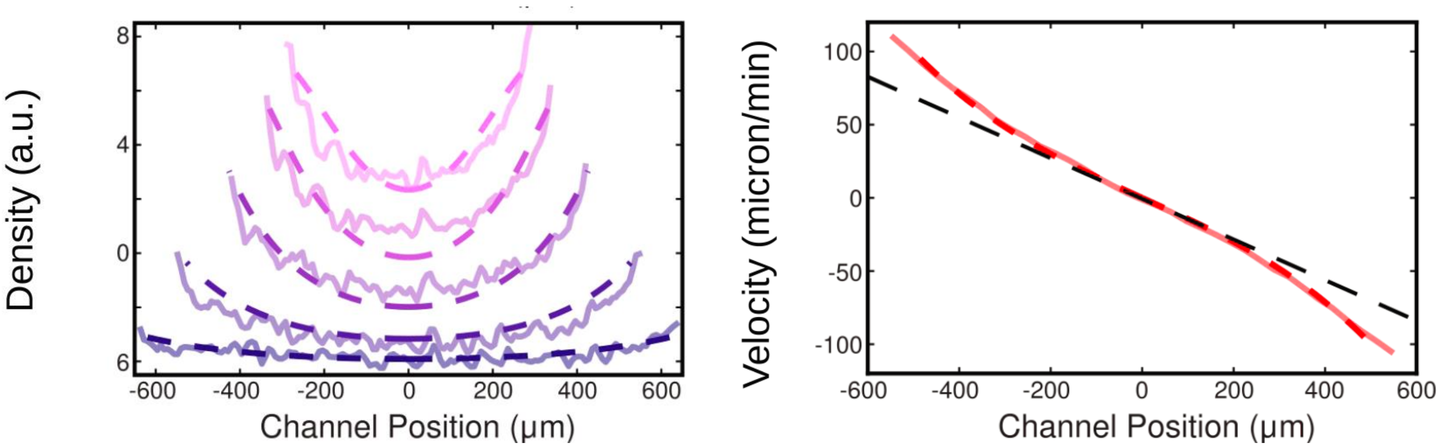
Gives active stress of form: $\boldsymbol{\sigma}_a \sim s\rho\left(\rho-\rho_0\right)\mathbf{I}$

For a viscously damped material dragging itself through the fluid:

$$\eta\Delta\mathbf{v}-\gamma\mathbf{v}=\nabla\bullet\boldsymbol{\sigma}_a \quad \text{and} \quad \rho_t+\nabla\bullet\left(\rho\mathbf{v}\right)=0$$

plus BCs: $\left(\eta\nabla\mathbf{v}-\boldsymbol{\sigma}_a\right)\bullet\mathbf{n}\,|_\Gamma=\mathbf{0}$ and $\mathbf{V}_\Gamma=\mathbf{v}\,|_\Gamma$



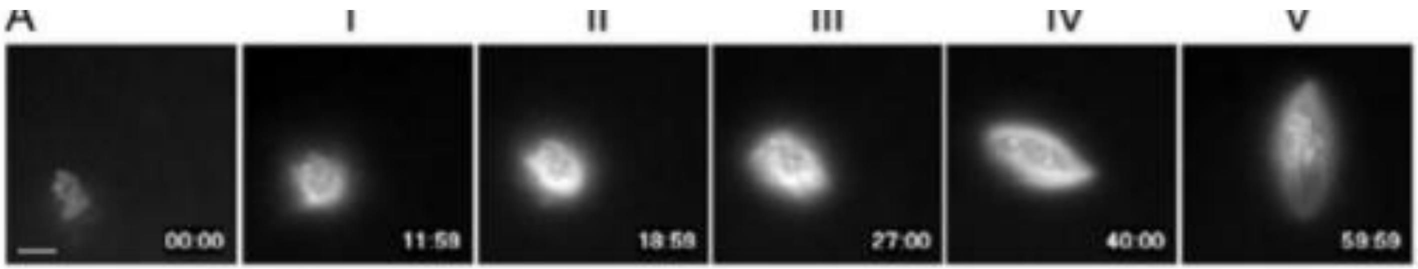


1D version gives a quantitative match to the film's contraction and velocity dynamics with reasonable parameter choices.

Suggests that contractile dynein-driven stresses could be operative in spindle…

Foster, Furthauer, Shelley, Needlemen, *e*Life 2015

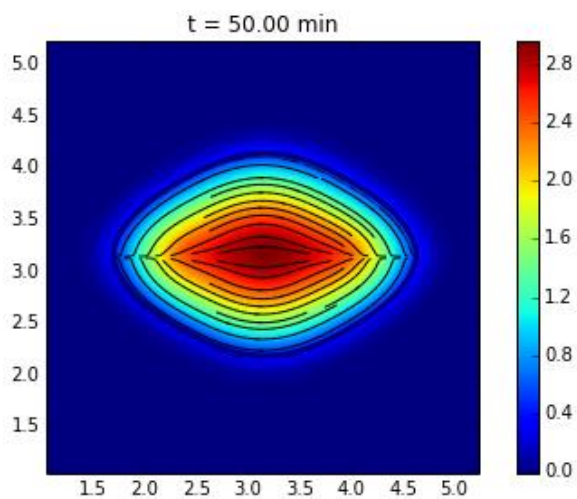
Ongoing:

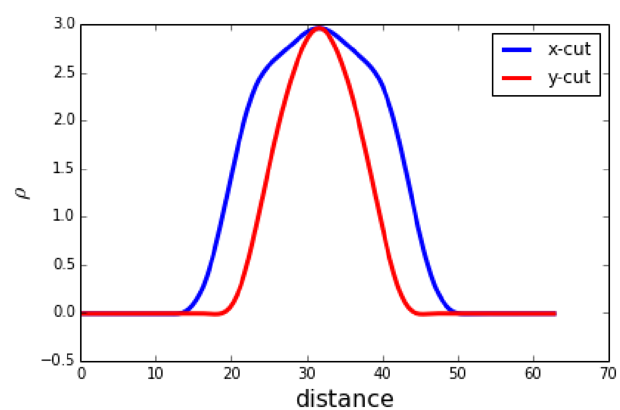


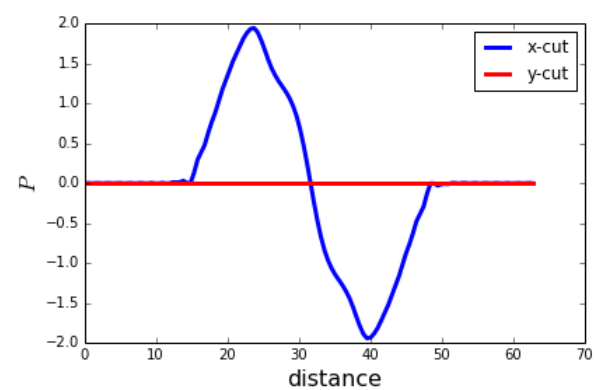
Spontaneous formation of spindle in Xenopus extract
A.C. Groen et al, MCB ‘09

Polar active nematic model of spindle formation via microtubule nucleation, polarity sorting, active contractile stresses

Furthauer, Needleman, Sh, 2016







$30 \times 20\ \mu m$

Agrees well with measurements of Brugues & Needleman *PNAS* 2014

Discrete structure methods for MT dynamics (BIM)

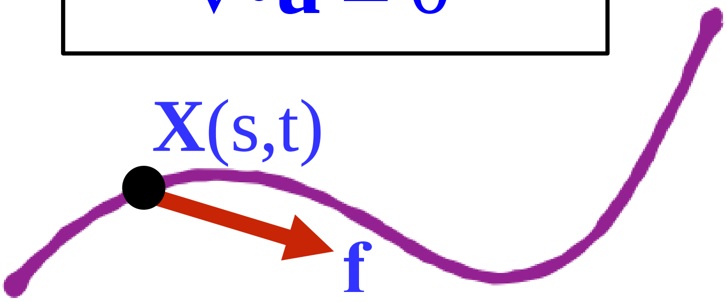
$$\mathbf{u}(\mathbf{x}) = \Sigma_i \mathbf{u}_i^{mt}(\mathbf{x}) + \mathbf{u}^{pnc}(\mathbf{x}) + \mathbf{u}^{cor}(\mathbf{x})$$

$$-\nabla p + \mu \Delta \mathbf{u} = \mathbf{0}$$
$$\nabla \bullet \mathbf{u} = 0$$

- MTs: Use slender body theory, local or nonlocal

$$\mathbf{u}_i^{mt}(\mathbf{x}) = \int_0^{L_i} ds\, \mathbf{G}(\mathbf{x} - \mathbf{X}_i(s))\mathbf{f}_i(s)$$

(distribution of Stokeslets)



$$8\pi\mu\left(\frac{\partial \mathbf{X}_i}{\partial t} - \overline{\mathbf{u}_i^{mt}}(\mathbf{X}_i)\right) = -\mathbf{\Lambda}[\mathbf{f}_i](s) - \mathbf{K}[\mathbf{f}_i](s)$$

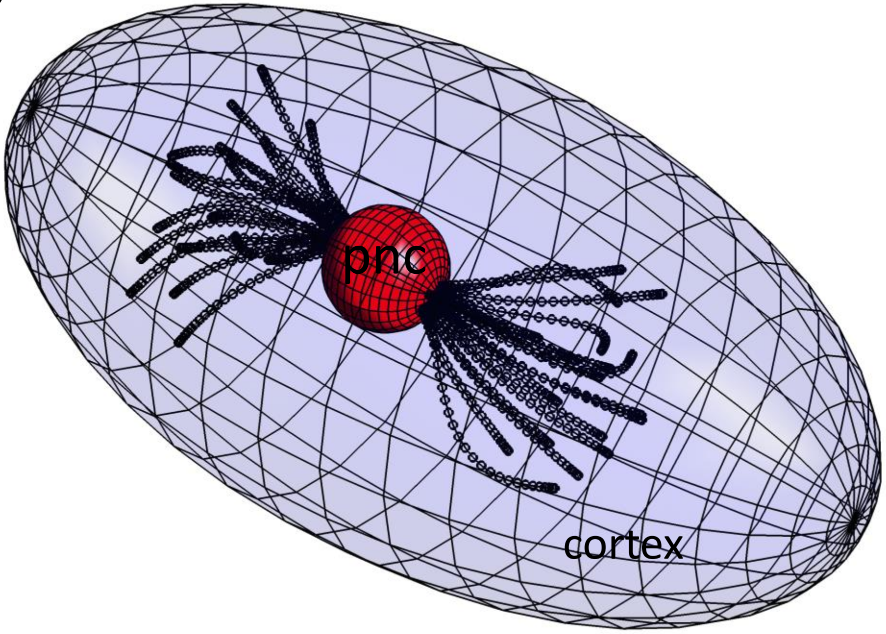
with $\mathbf{f}_i = -(T\mathbf{X}_{i,s})_s + E\mathbf{X}_{i,ssss}$ inextensible, elastic beam

Keller & Rubinow *JFM* '76
Johnson *JFM* '80, Gotz '00
Tornberg & Shelley *JCP* '04
Nazockdast *et al*, *JCP* '16

- Immersed surfaces (pnc) and boundaries (cor)

use *stresslet distribution* Power & Miranda '87

(yields well-conditioned 2nd-kind boundary integral equations)

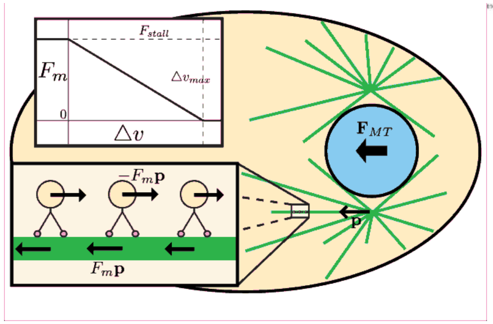


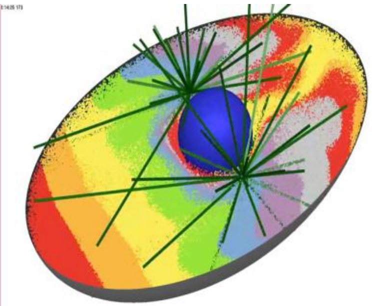
$$\mathbf{u}^{pnc}(\mathbf{x}) = \int_{pnc} dS_{x'} \mathbf{n}(\mathbf{x}')\mathbf{T}(\mathbf{x}-\mathbf{x}')\mathbf{q}_{pnc}(\mathbf{x}')$$
$$+ \mathbf{G}(\mathbf{x} - \mathbf{X}_0)\mathbf{F}_{pnc}^{ext} + \mathbf{R}(\mathbf{x} - \mathbf{X}_0)\mathbf{L}_{pnc}^{ext}$$

Positioning: Our "early" work using IBM, with ~50 rigid MTs, and w. no transverse MT drag.

Shinar *et al*, *PNAS* 2011

Underestimates motor-protein forces by an order of magnitude, but does the right thing...





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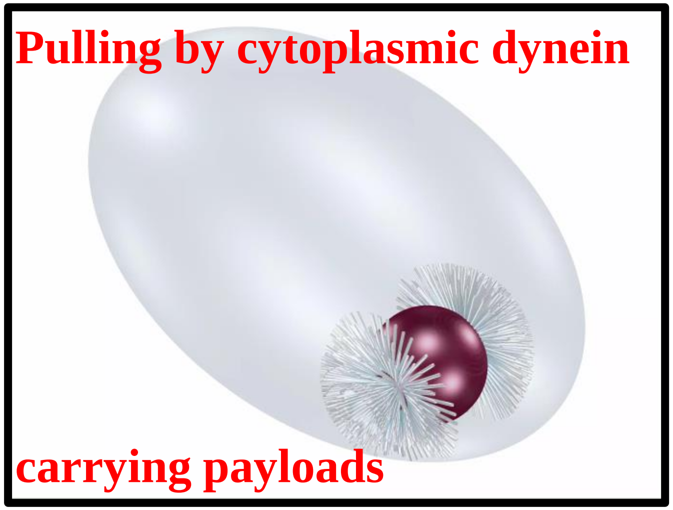
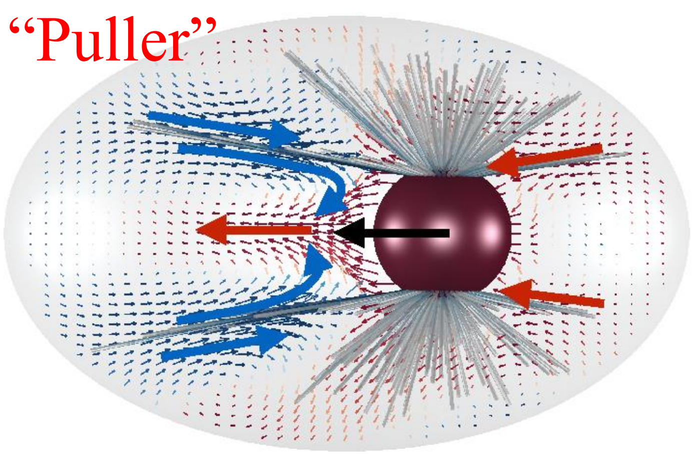
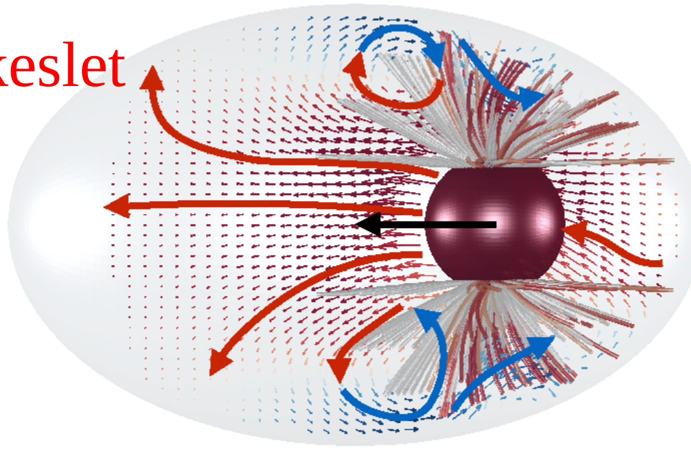
3 different models of pronuclear positioning, ~1000 MTs





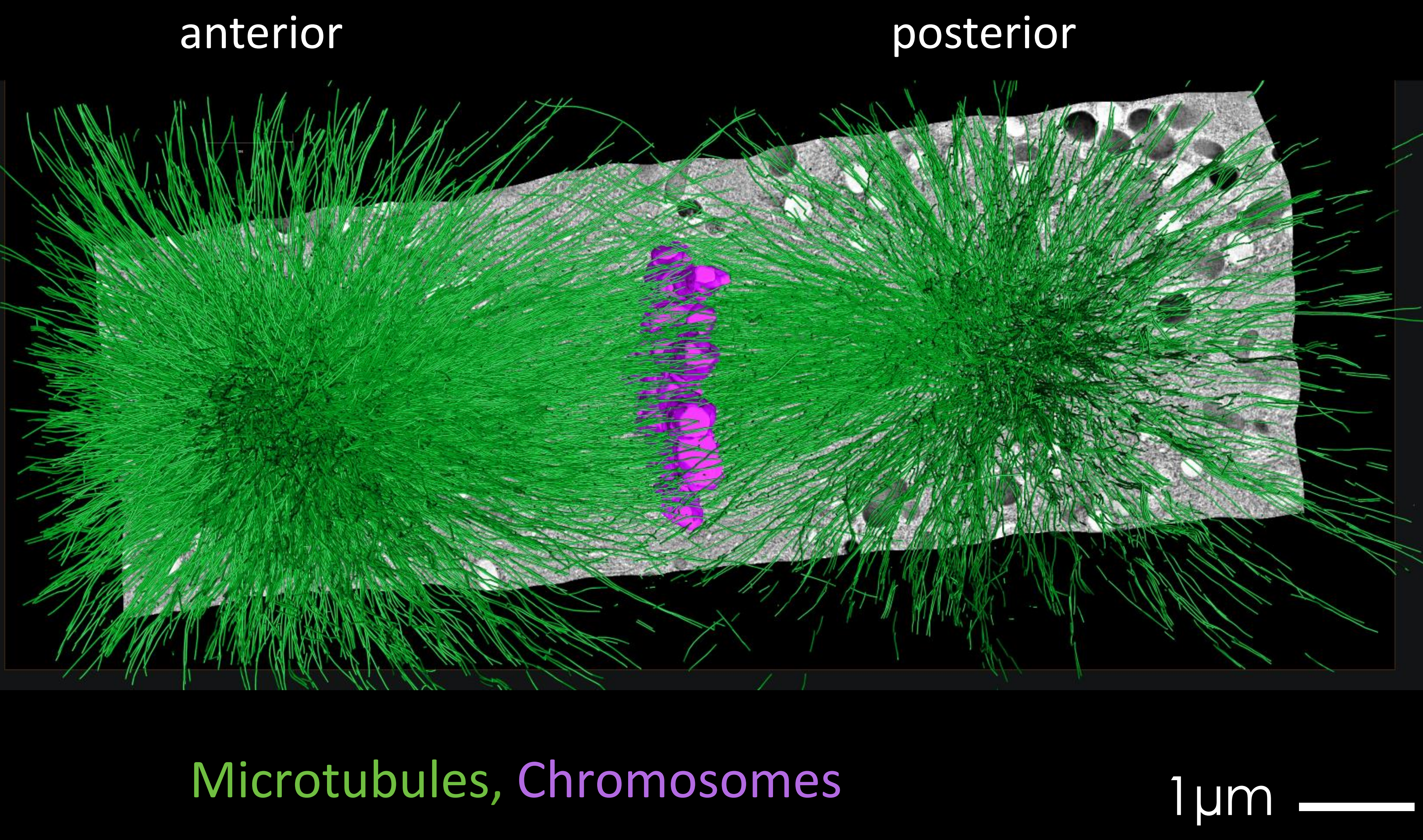
Different mechanisms leave different signatures in cytoplasmic flow and MT conformation



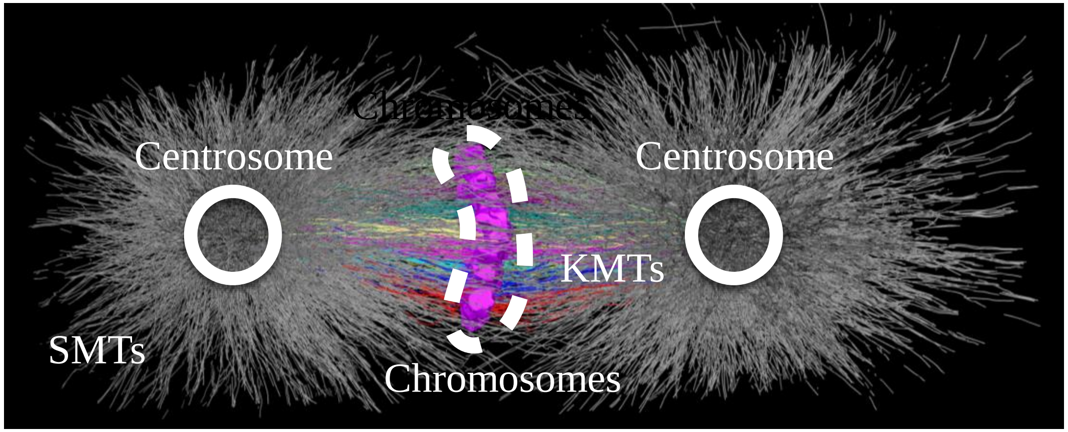
Zia *et al* '16, Nazockdast, Rahimian, Needleman, Shelley, to appear, *MBOC* '16

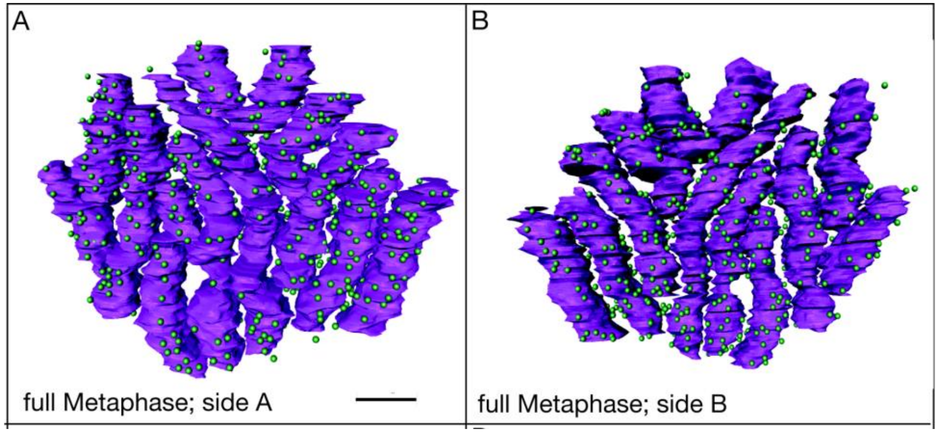
3D ET reconstruction of *C. elegans* metaphase spindle

Redemann, …, SF, EN, …, MS, Muller-Reichert, submitted 2016



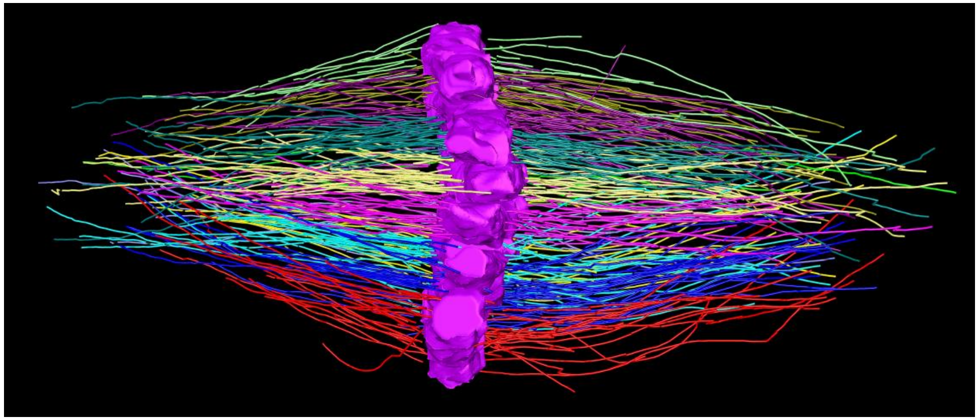
Main Structural Elements of Mitotic Spindle





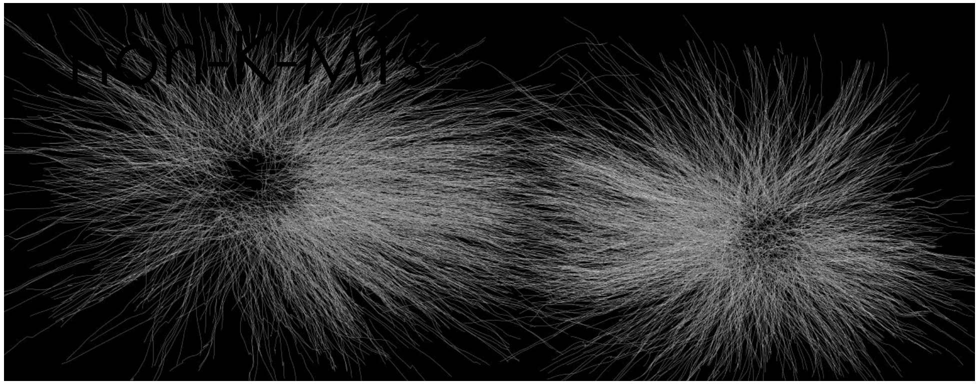
Kinetochore Microtubules (KMTs):

- Connected to chromosomes
- Mechanical agents for chromosome segregation
- About 500 KMTs (250 each half spindle)



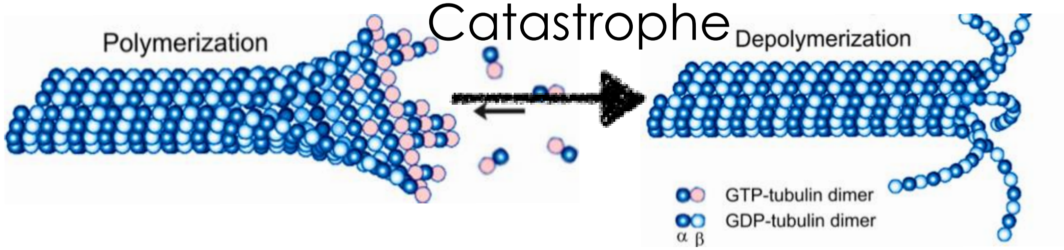
Non-Kinetochore MTs (nKMTs)

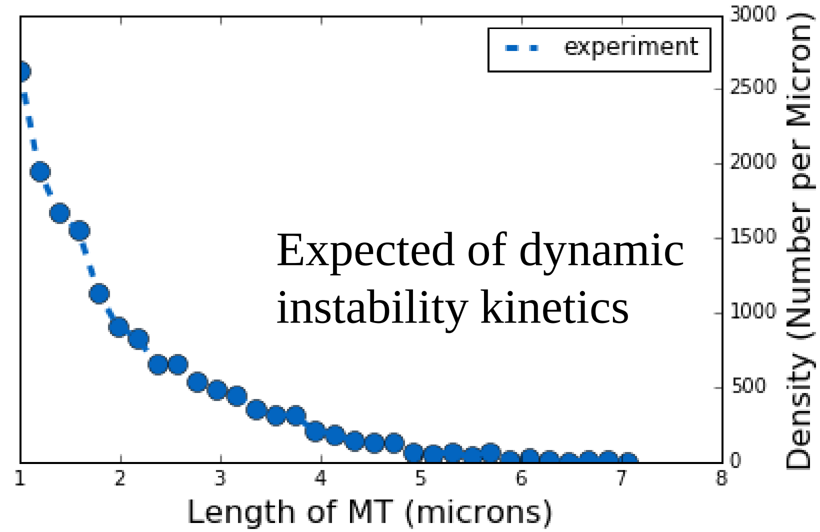
- One end is mainly located near centrosomes
- About 15000 nKMTs (>> 250 KTs) in each half-spindle
- Large number of short nKMTs and very few longer than the half-spindle



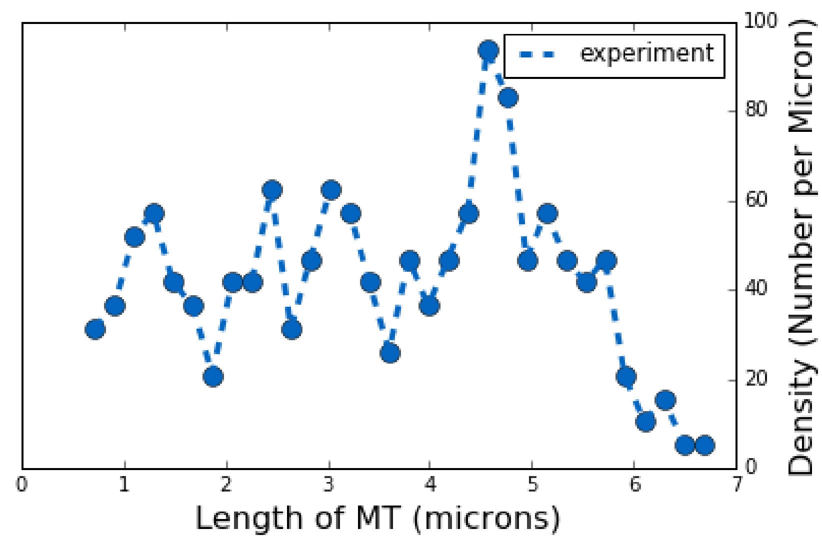
Length Distribution of KMTs and SMTs

nKMTs: Exponential



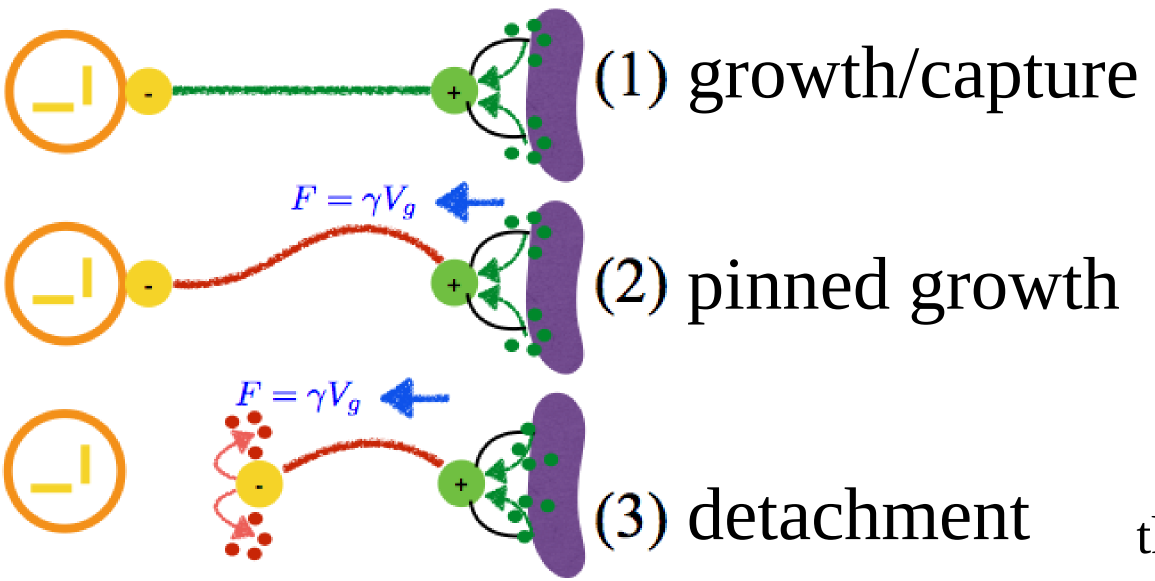


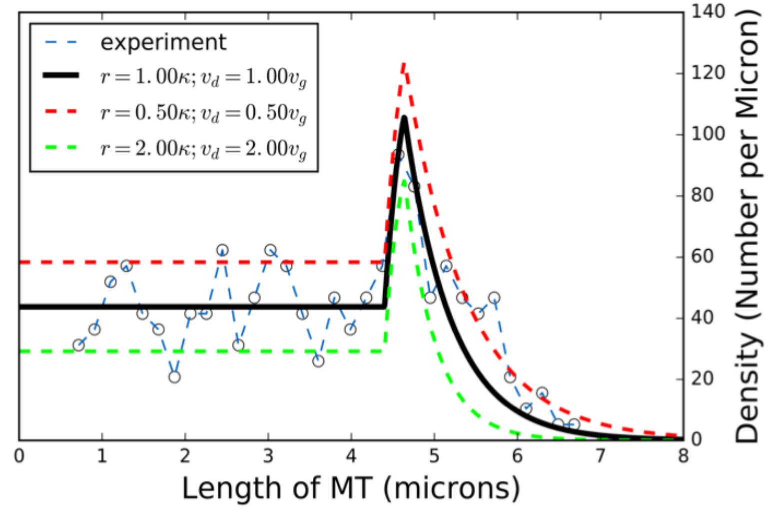
- K-MTs: Uniform with a maximum around the length of half-spindle
- There are very few K-MTs that are directly connected to the centrosomes.
- K-MTs cannot directly pull the chromosomes apart



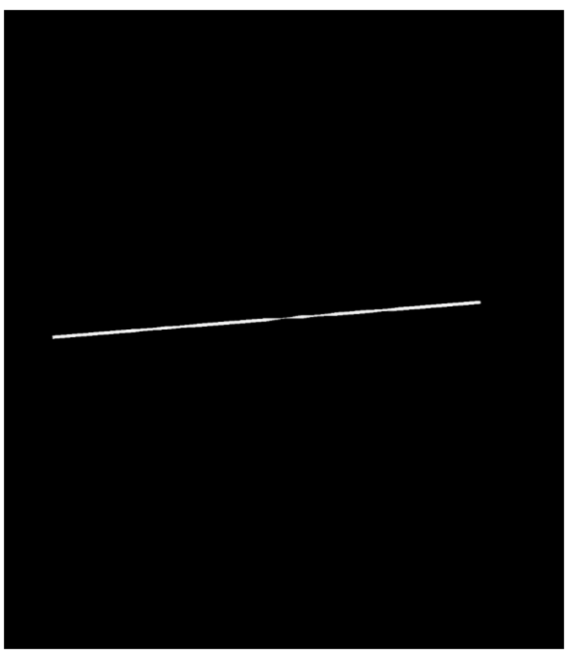
Simple model of KMT origin gives qualitative agreement with experiments

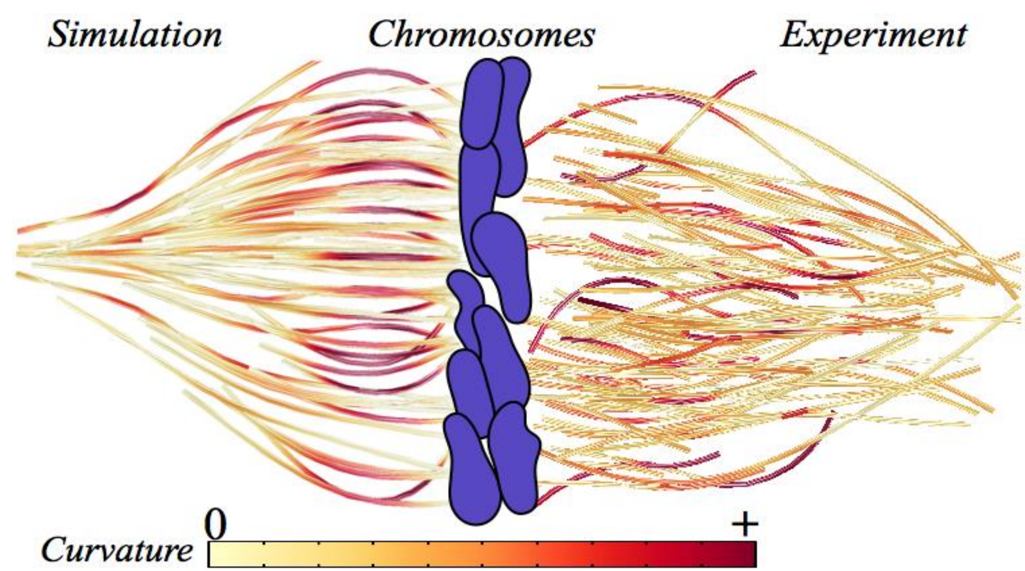
Redemann *et al*, '16





there is evidence for KMT-SMT linkage





Nazockdast *et al*, '16

Viscosity is the only unknown parameter $\eta \approx 10\,\mathrm{Pa.s}$

Ongoing:

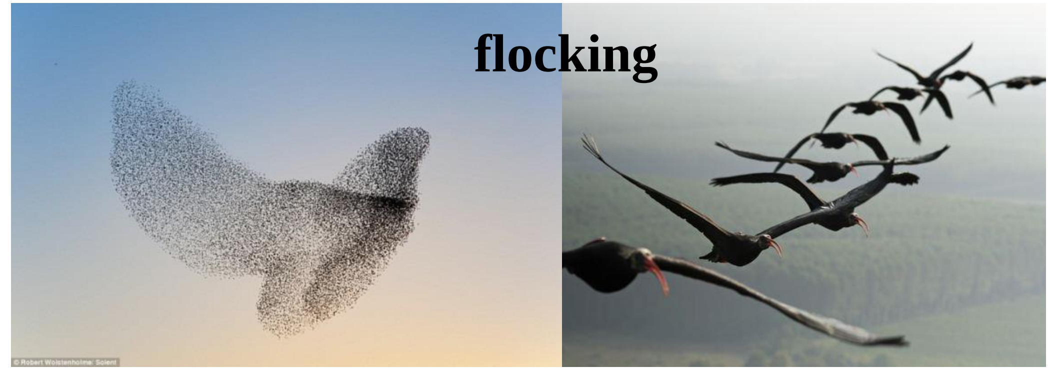
Working w the Needleman lab on understanding their laser ablation experiments.

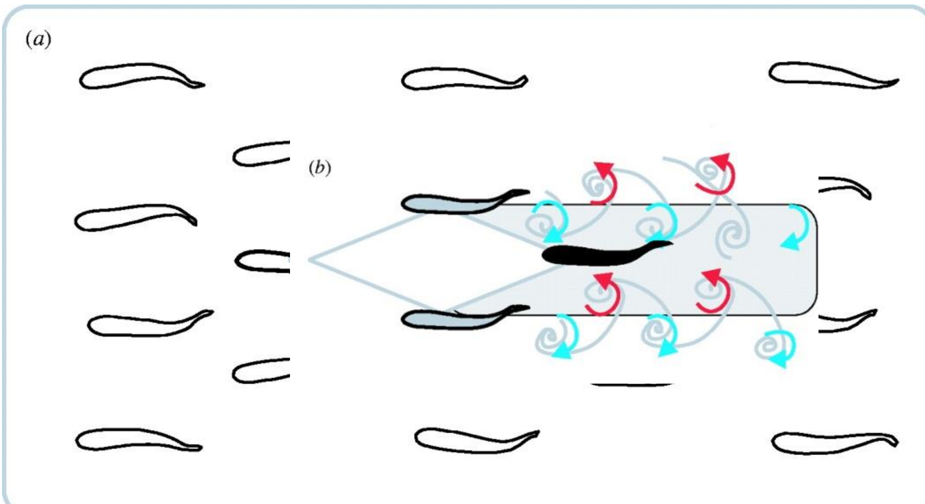
→ a comprehensive model of spindle positioning & segregation

thanks

Some **collective behaviors/self-organized structures** moving in fluids…

laning up





Weihs ’73, Liao et al ’03, 06, … and many others

***Re >> 1*:** the fluid can store information in the fluid as shed vortices – introduces delay

Becker *et al*, *Nature Comm.* 2015