Simulating swirling flows in dense microtubule suspensions

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June 9, 2023

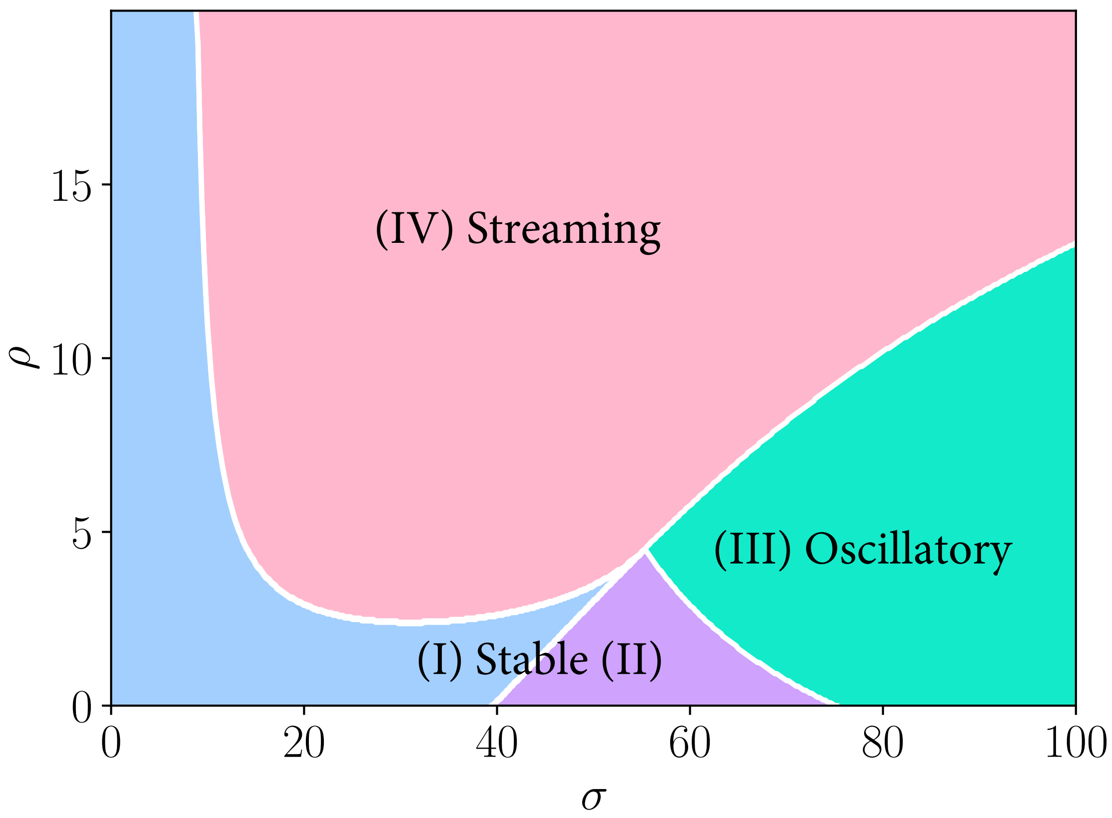
Simulating swirling flows in dense microtubule suspensions

For many fibers interacting in a Stokes fluid,
fiber density is a critical parameter:

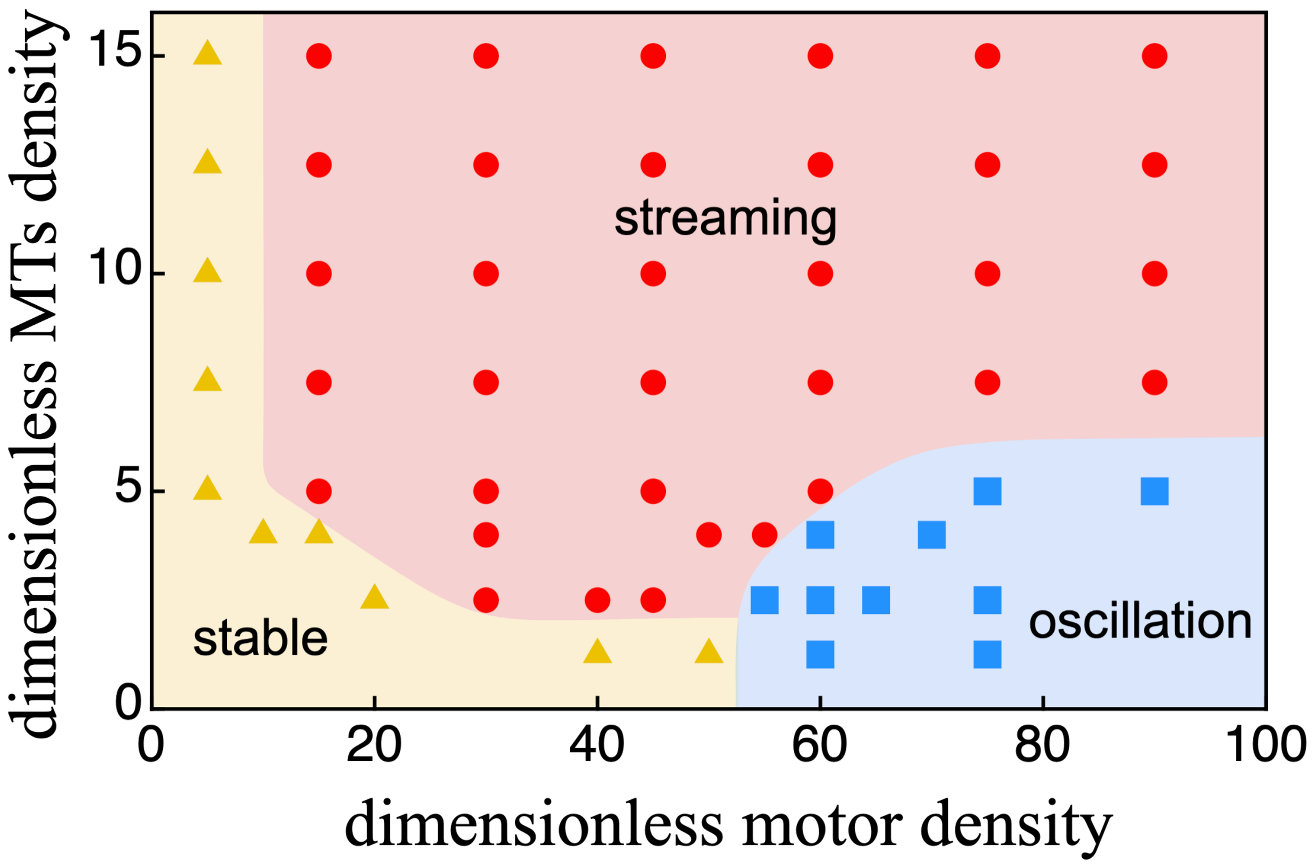
using too few (or too many) fibers leads to simulations that may be *qualitatively wrong*.

Bifurcations in MT # exist

1d coarse-grained linear theory, flat space



3d discrete fiber simulations, in a sphere

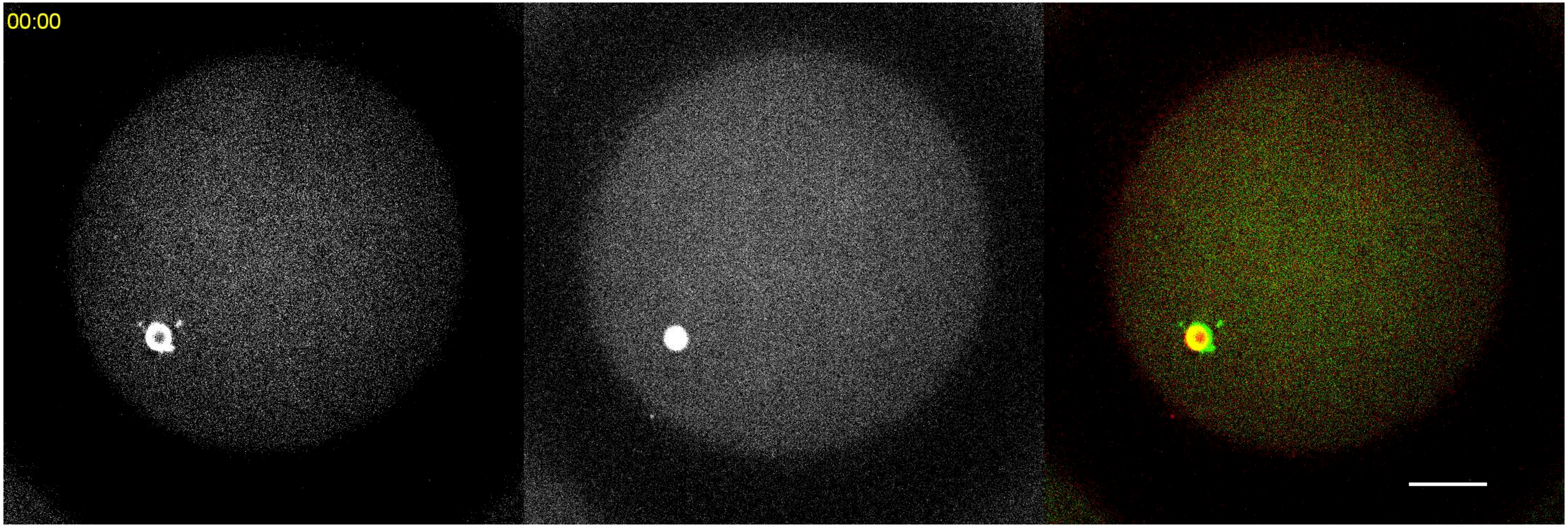


Simulations with too few (or too many) MTs can be *qualitatively* wrong

[David B Stein, Gabriele de Canio, Eric Lauga, Michael J Shelley, Raymond E Goldstein, *Swirling Instability of the Microtubule Cytoskeleton,* Physical Review Letters, 2021.]

[Syantan Dutta, Reza Farhadifar, Wen Lu, Gokberk Kabacaoglu, Robert Blackwell, David Stein, Margot Lakonishok, Vladimir I. Gelfand, Stanislav Y. Shvarstman, Michael J Shelley.]

Rotation of asters in artificial confinement

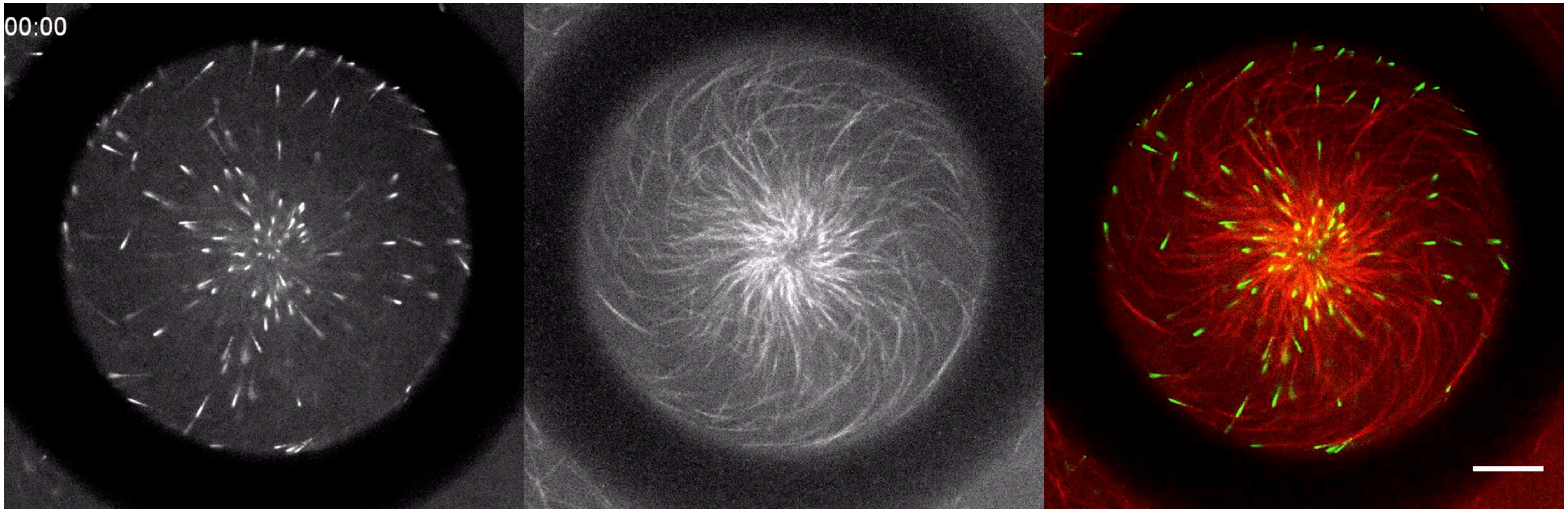


Artificial asters center and rotate in *large scale confinement*

Abdullah Sami, Jay Gatlin
Gökberk Kabacaoğlu, Mike Shelley

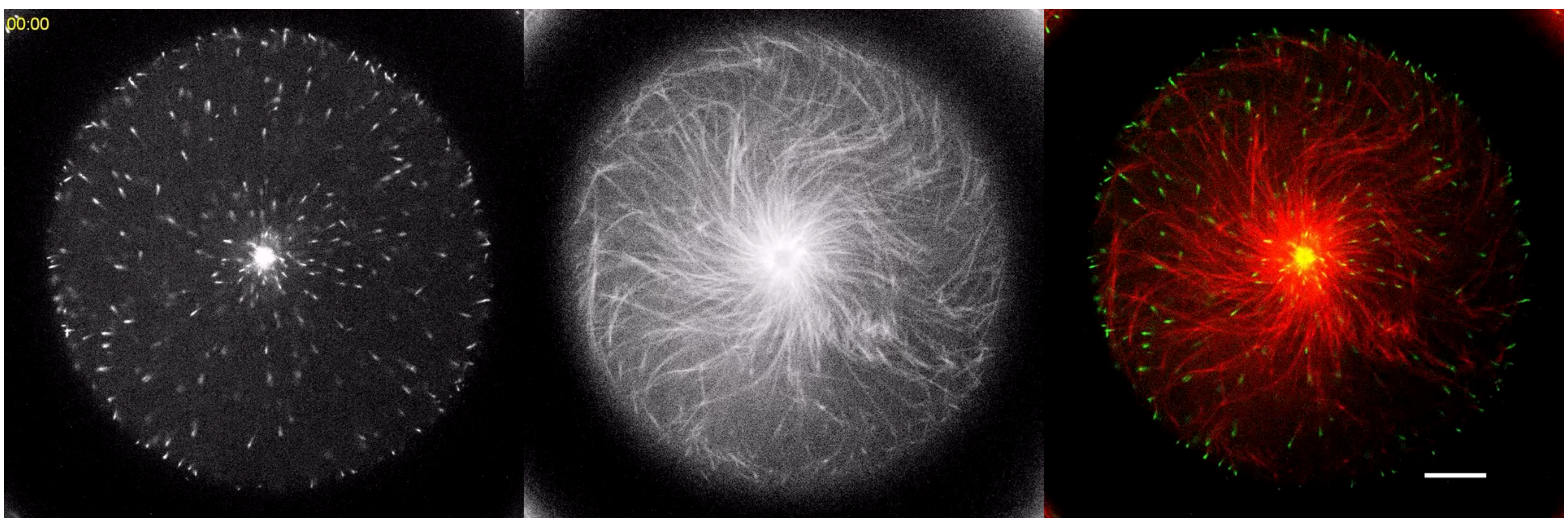
Rotation of asters in artificial confinement

Rotation is *persistent* in sufficiently small confinement:



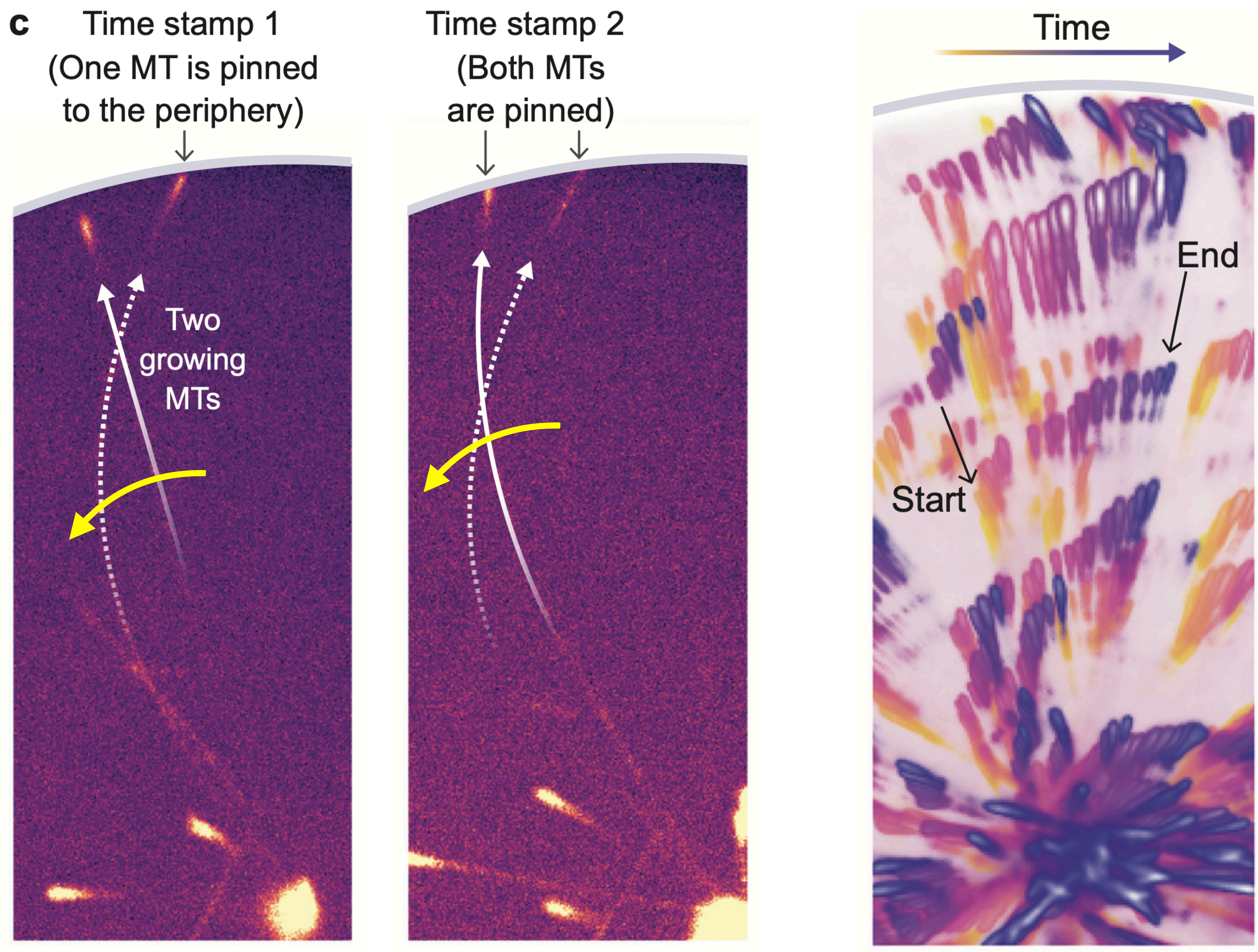
R=30μm

Direction of rotation switches in medium size confinements

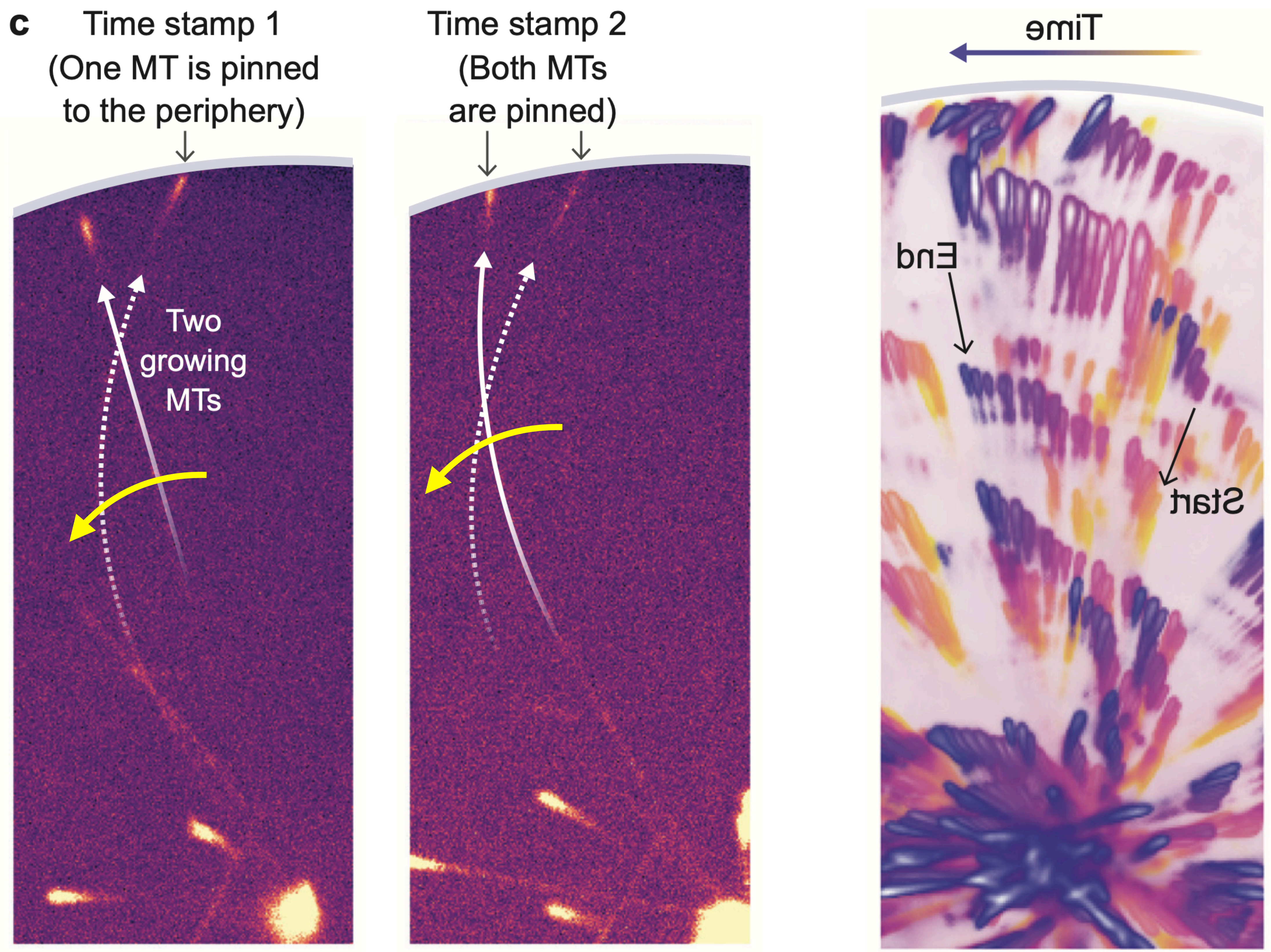


R=35μm

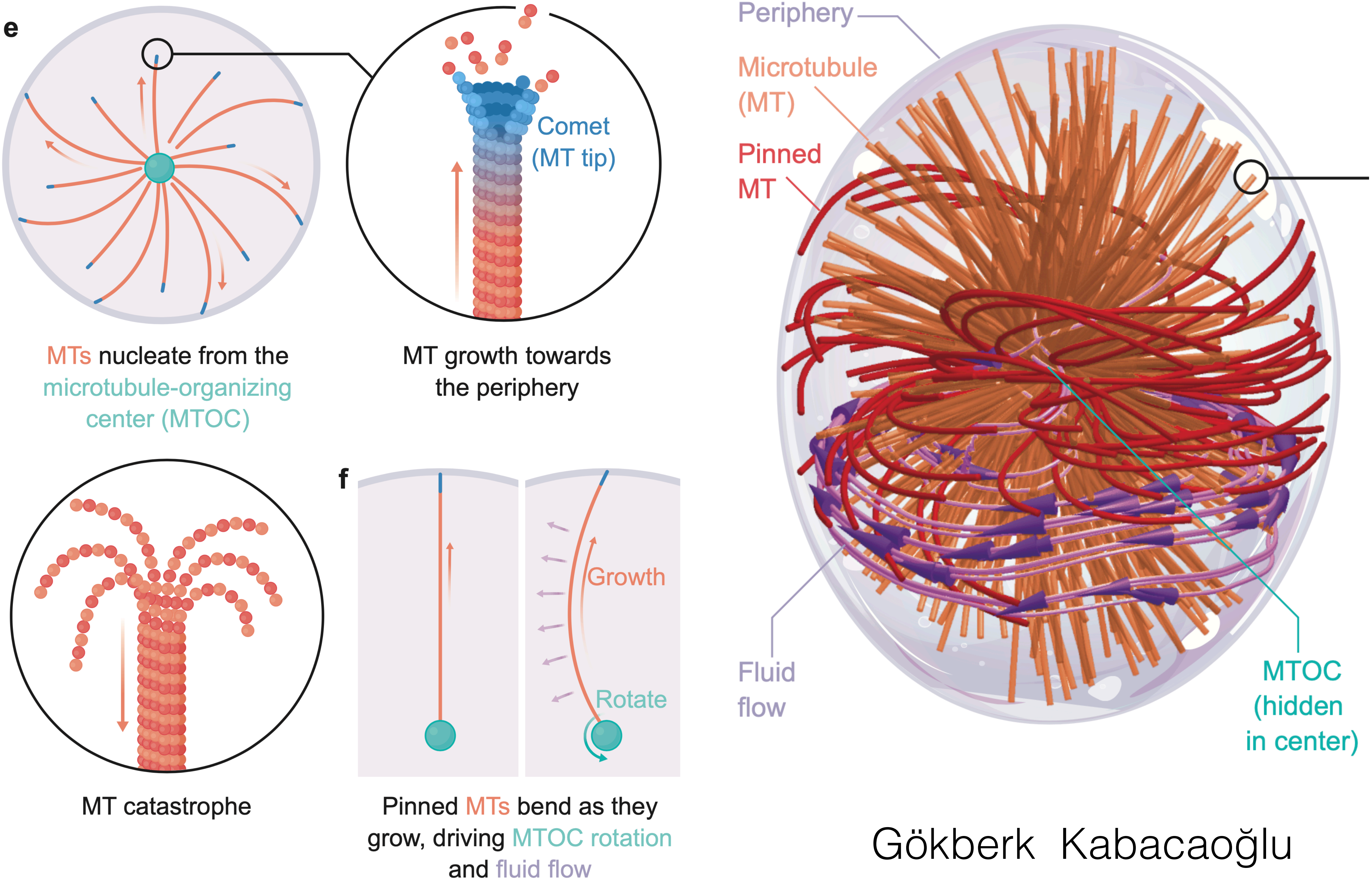
Rotation of asters in artificial confinement



Rotation of asters in artificial confinement

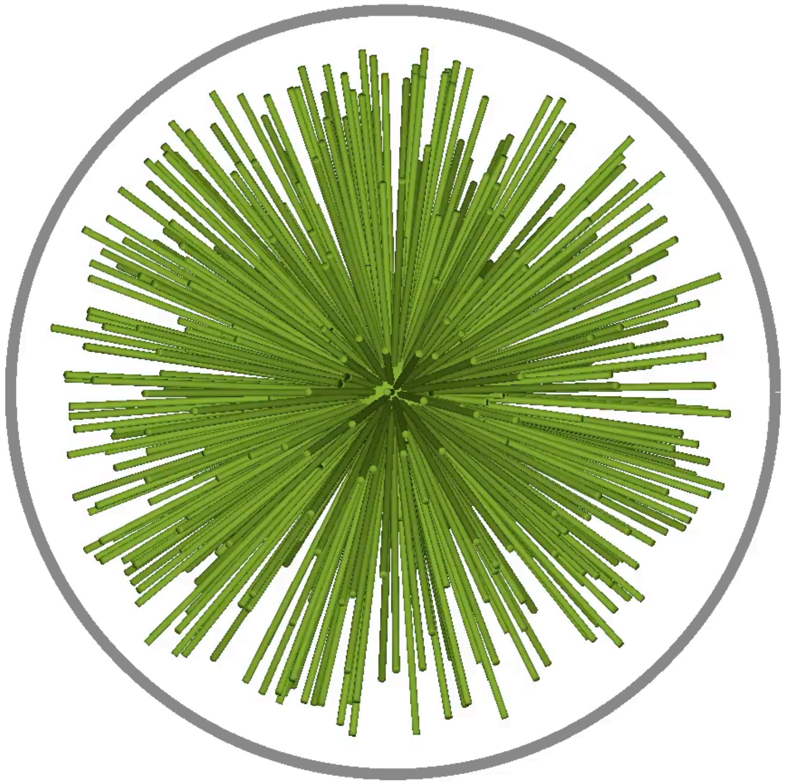


Rotation of asters in artificial confinement

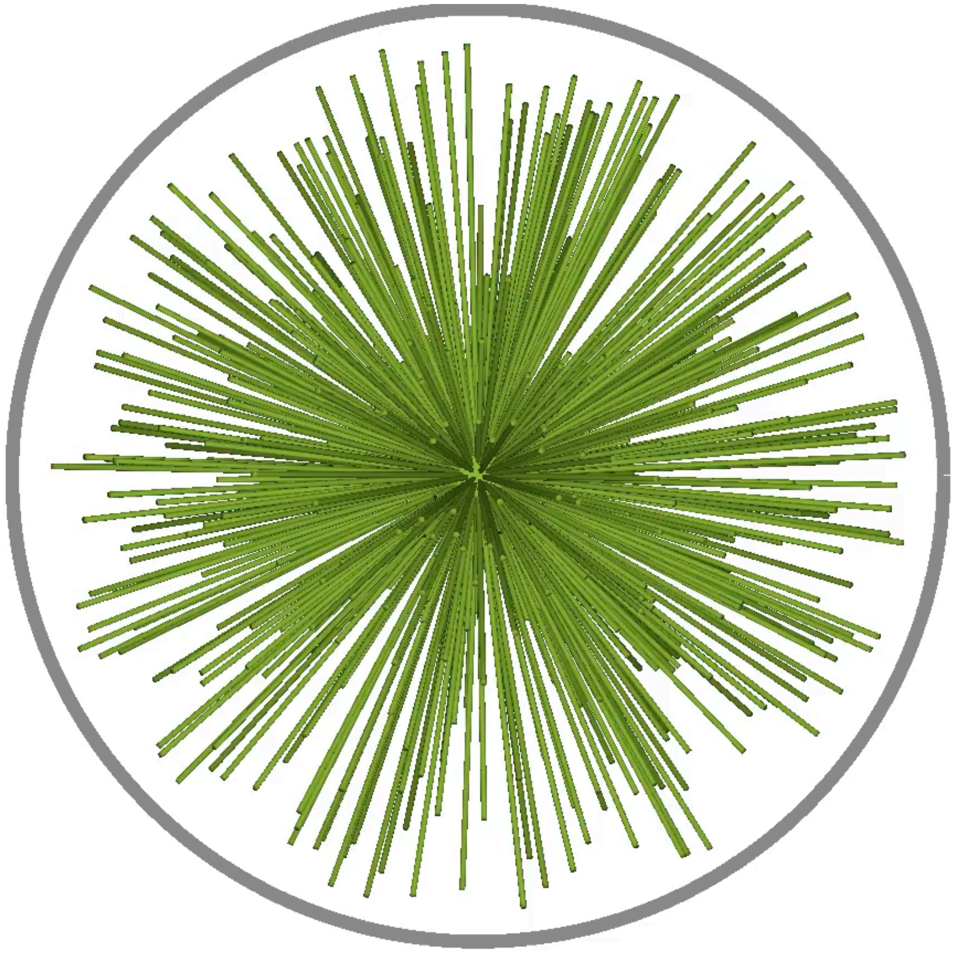


Gökberk Kabacaoğlu

Simulations recapitulate experiments

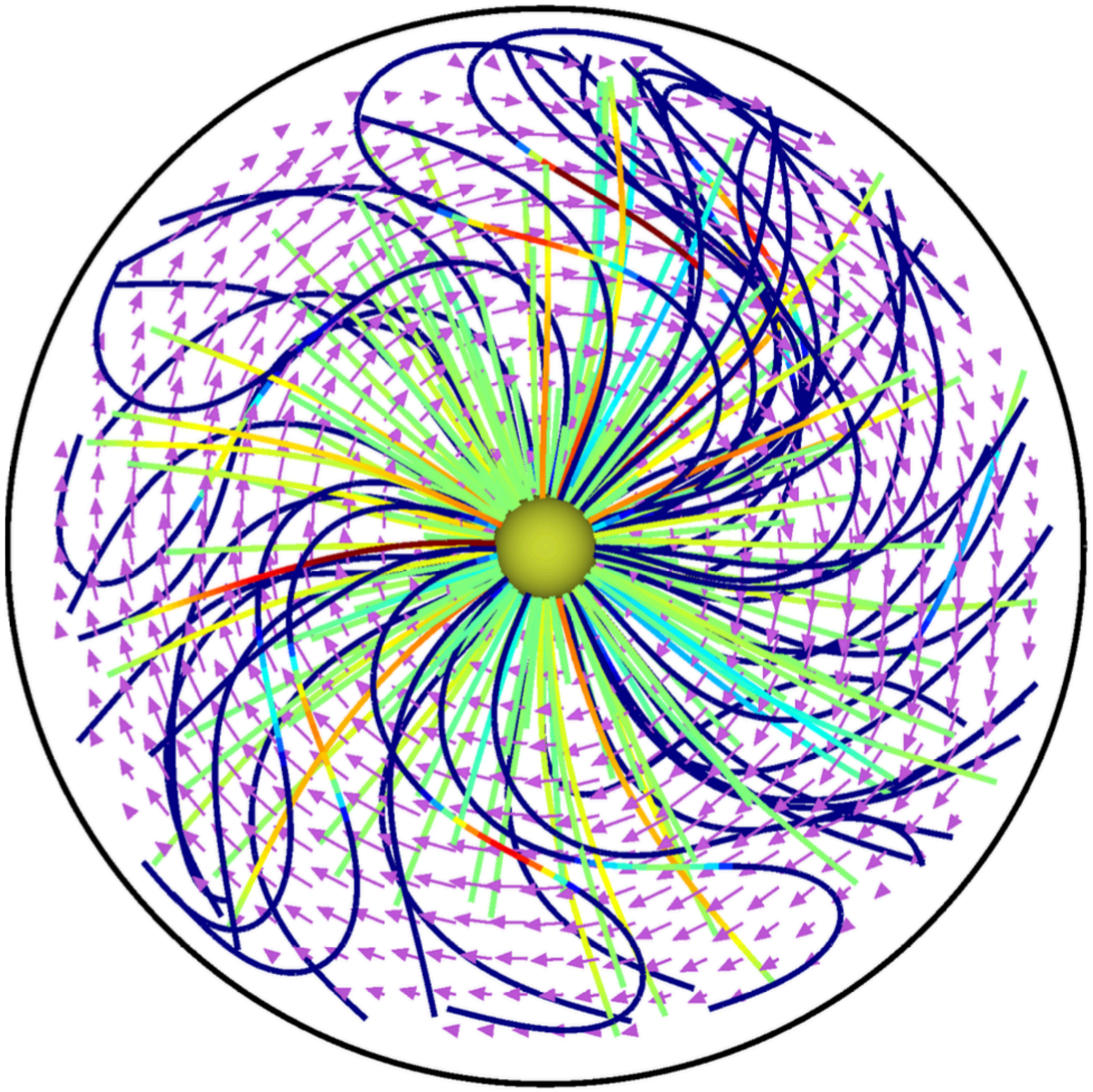


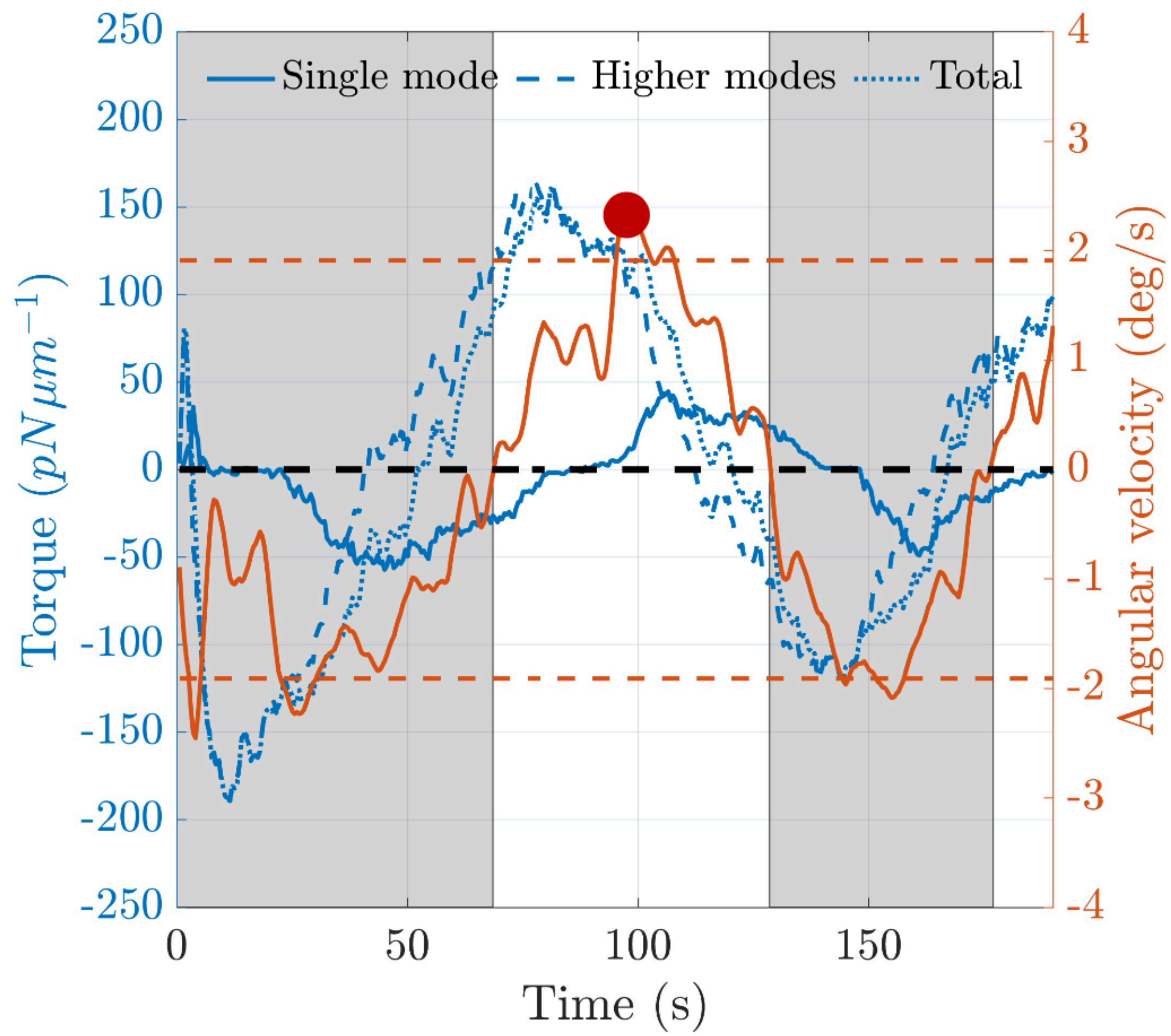
Persistent rotation



Rotation with switches

Why do these things switch?



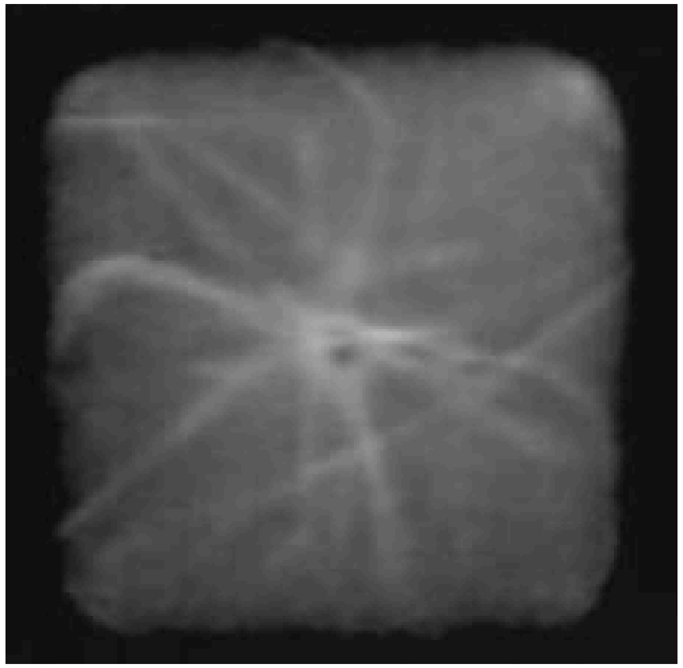


???????

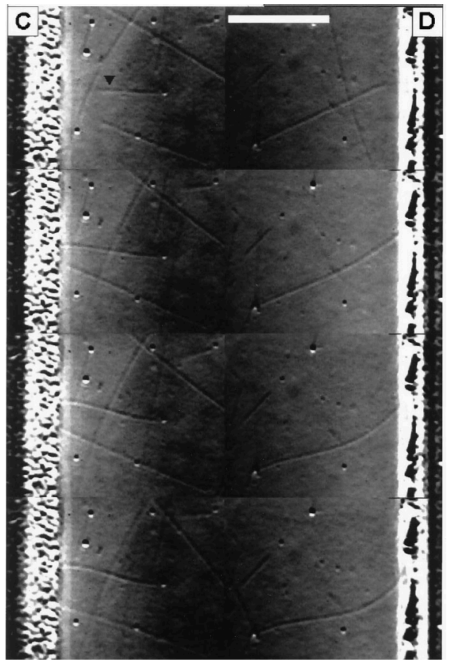
But…

The transitions occur at ~1/2 the length scale as in experiments

“Importantly, MT buckling in these experiments typically occurred at short centrosome-to-barrier distances, on the order of 5-10 μm and under estimated compressive loads of 5 pN, suggesting that MT-based pushing forces can be productive only over relatively short distances.”

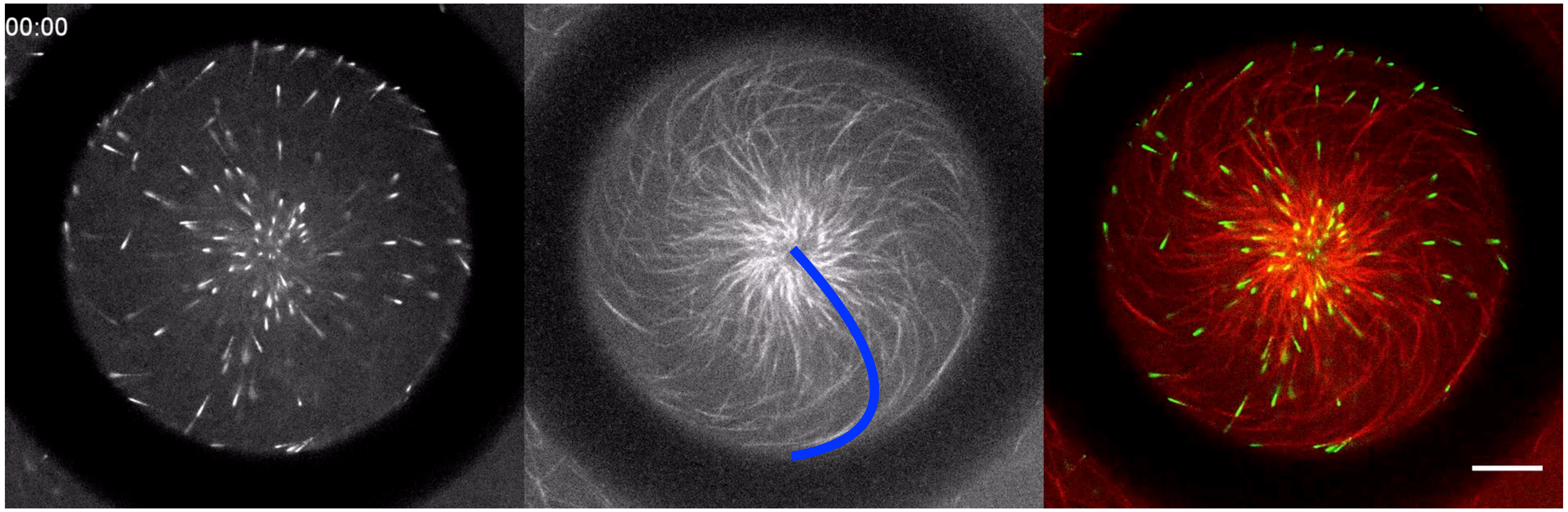


[Holy et al, PNAS, 1997]



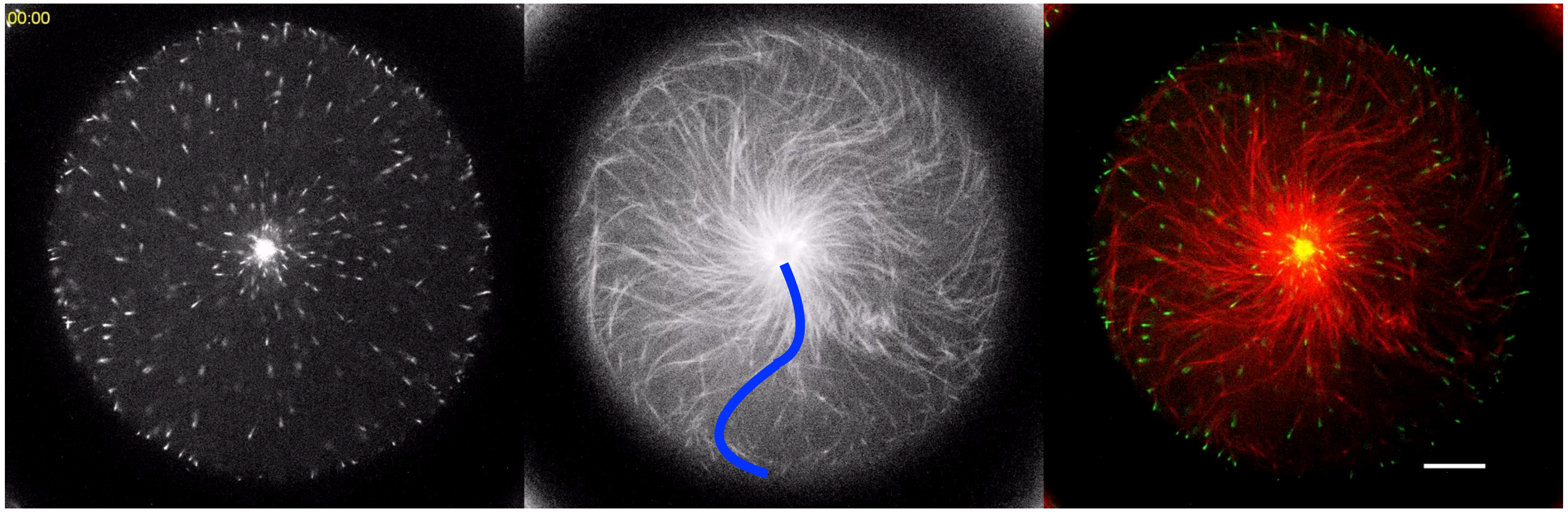
[Dogterum, Yorke Science, 1997]

Actual length scales?



$r_{exp} \sim 20\mu m$
$r_{sim} \sim 10\mu m$

C-modes



$r_{exp} \sim 35\mu m$
$r_{sim} \sim 15\mu m$

S-modes

- How do asters exert pushing forces over such long length scales?
- Why do our simulations produce transitions at half the scale?
- Why do they switch at all?

“Brinkman” filaments

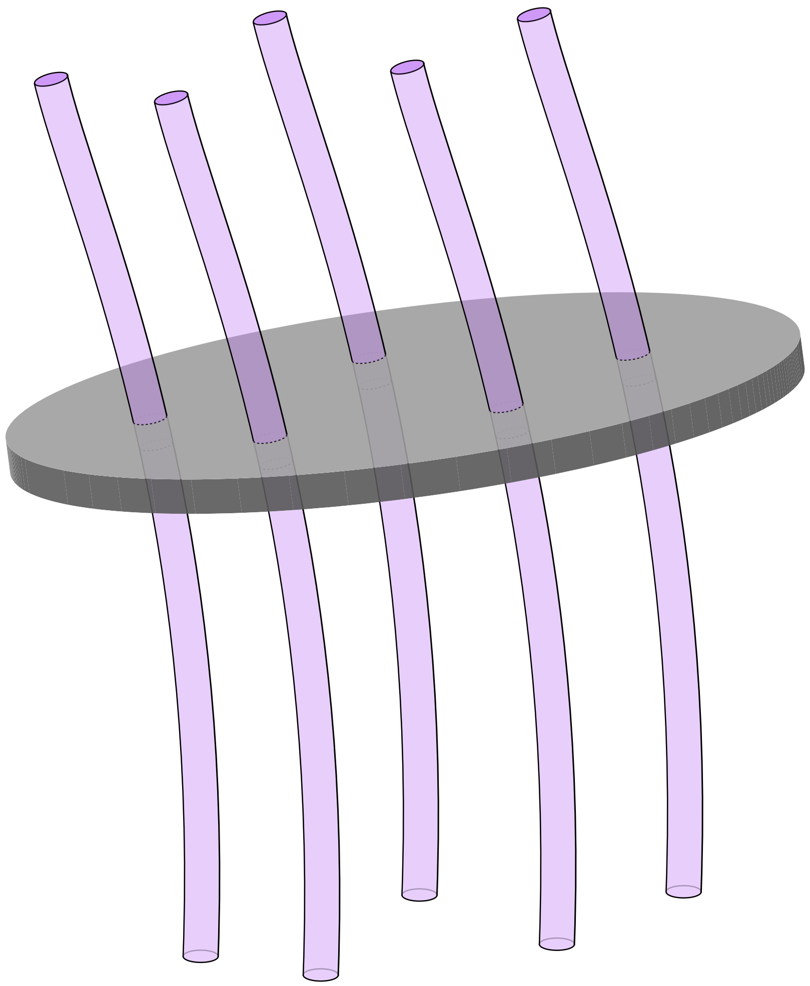
Parameter

$$-\Delta\mathbf{u}(\mathbf{x}) + \nabla p(\mathbf{x}) = [\boxed{\rho_0}\mathcal{J}^{-1}\mathbf{f}](\mathbf{X}^{-1}(\mathbf{x}))$$

$$\nabla\cdot\mathbf{u}(\mathbf{x}) = 0$$

$$\eta(\mathbf{V}(\boldsymbol{\alpha}) - \mathbf{u}(\mathbf{X}(\boldsymbol{\alpha})) = \mathcal{A}(\boldsymbol{\alpha})\mathbf{f}(\boldsymbol{\alpha})$$

$$\mathbf{f}(\alpha) = -E\mathbf{X}_{\alpha\alpha\alpha\alpha} + (T\mathbf{X}_\alpha)_\alpha$$

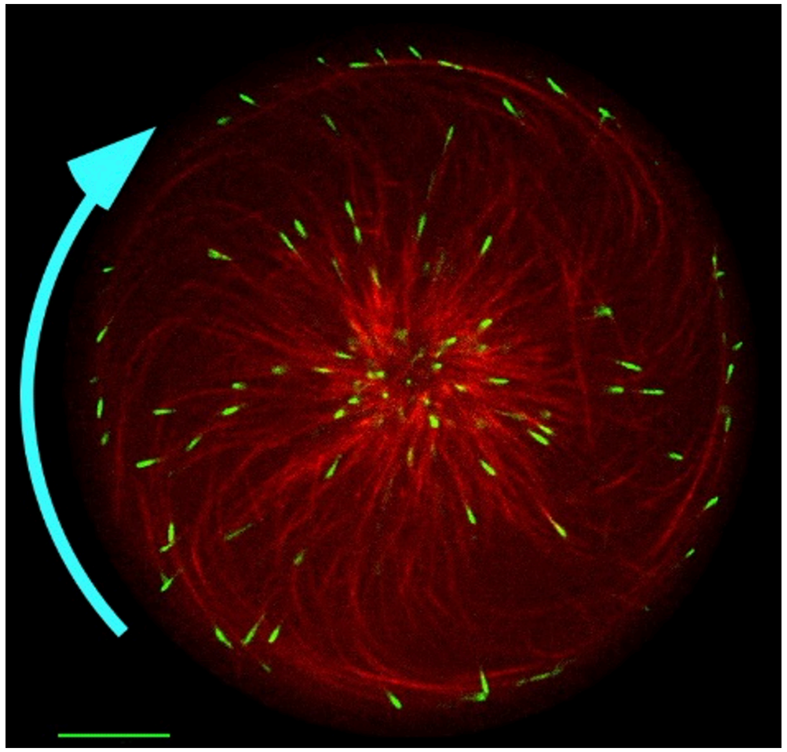


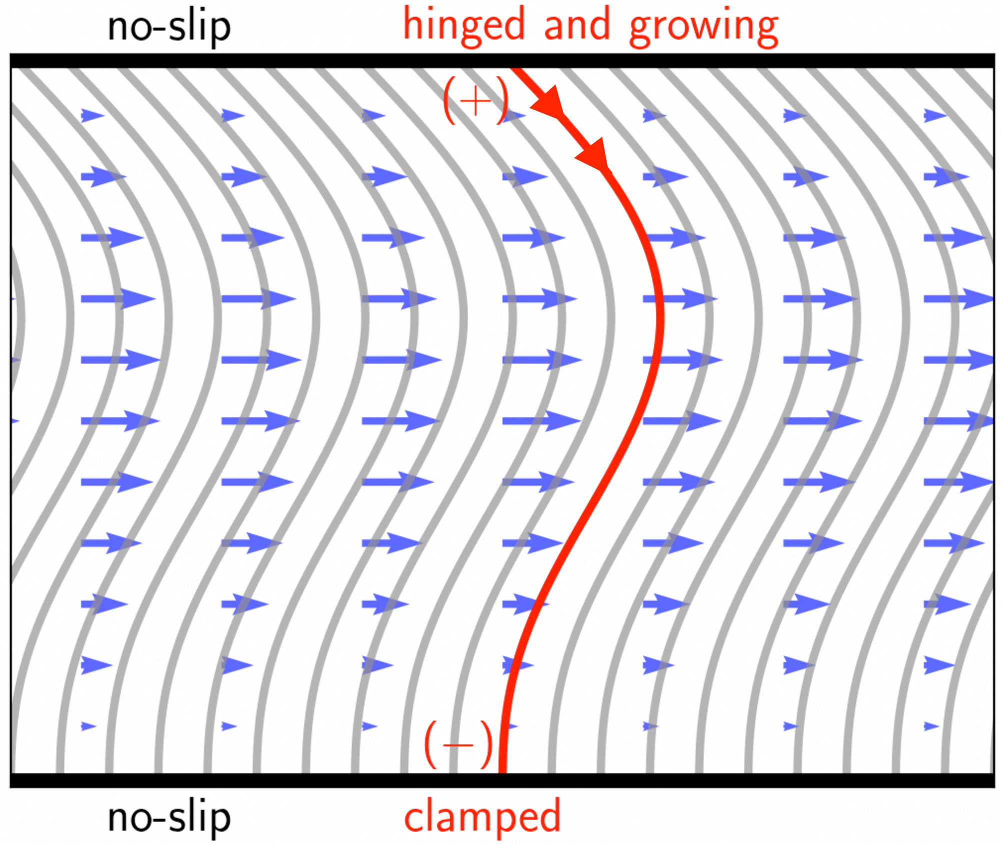
Density as a *parameter*.

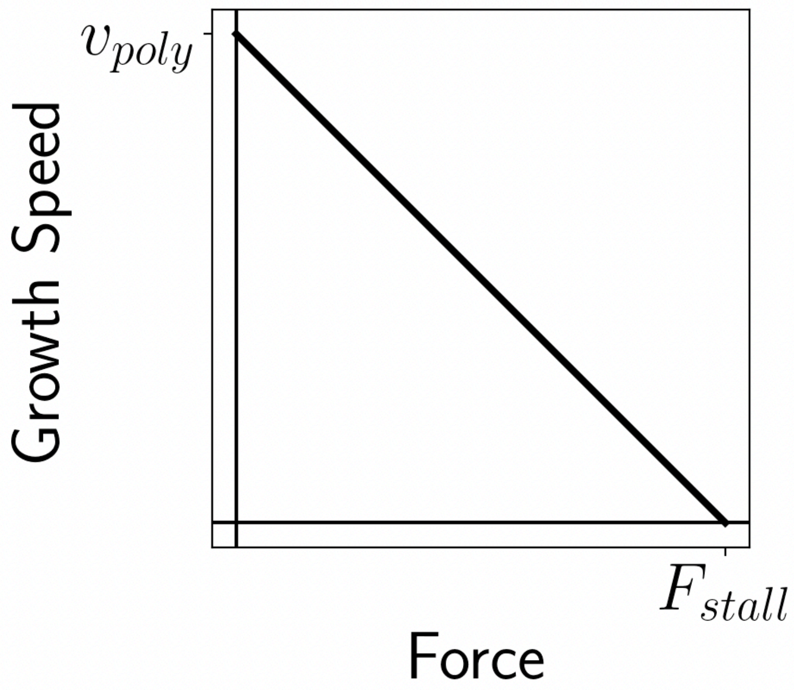
[David B Stein, Michael J Shelley, Coarse-graining the dynamics of immersed and driven fiber assemblies, Physical Review Fluids, 2019.]

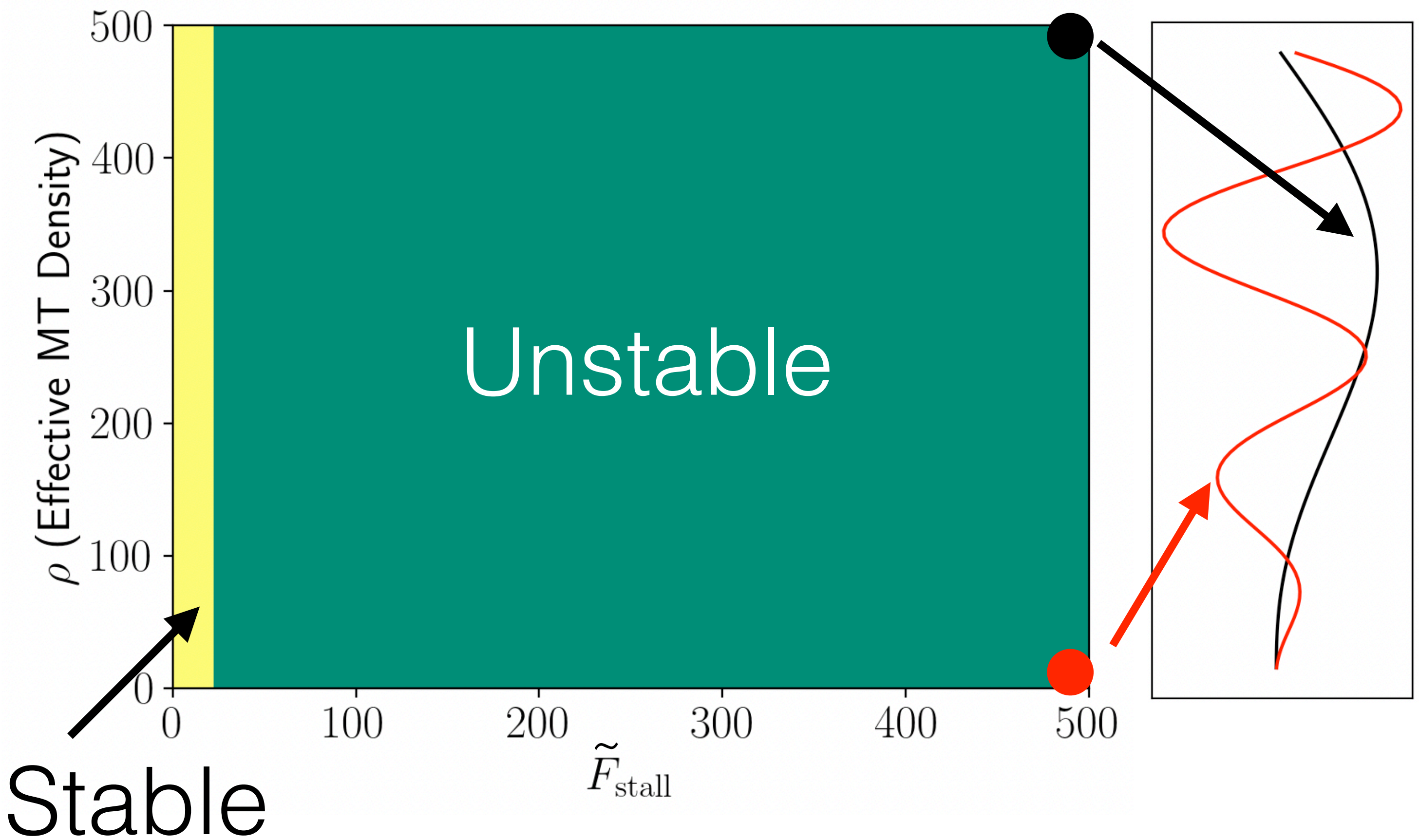
[David B Stein, Gabriele de Canio, Eric Lauga, Michael J Shelley, Raymond E Goldstein, *Swirling Instability of the Microtubule Cytoskeleton,* Physical Review Letters, 2021.]

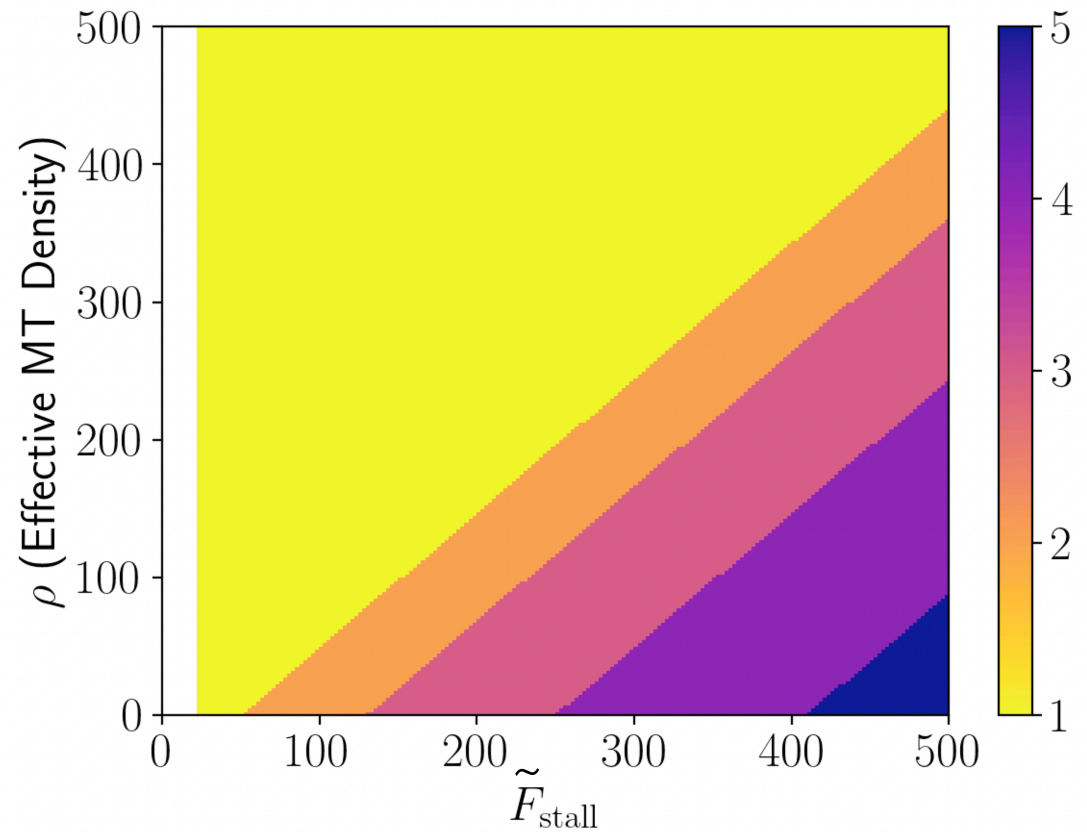
Theory provides clues



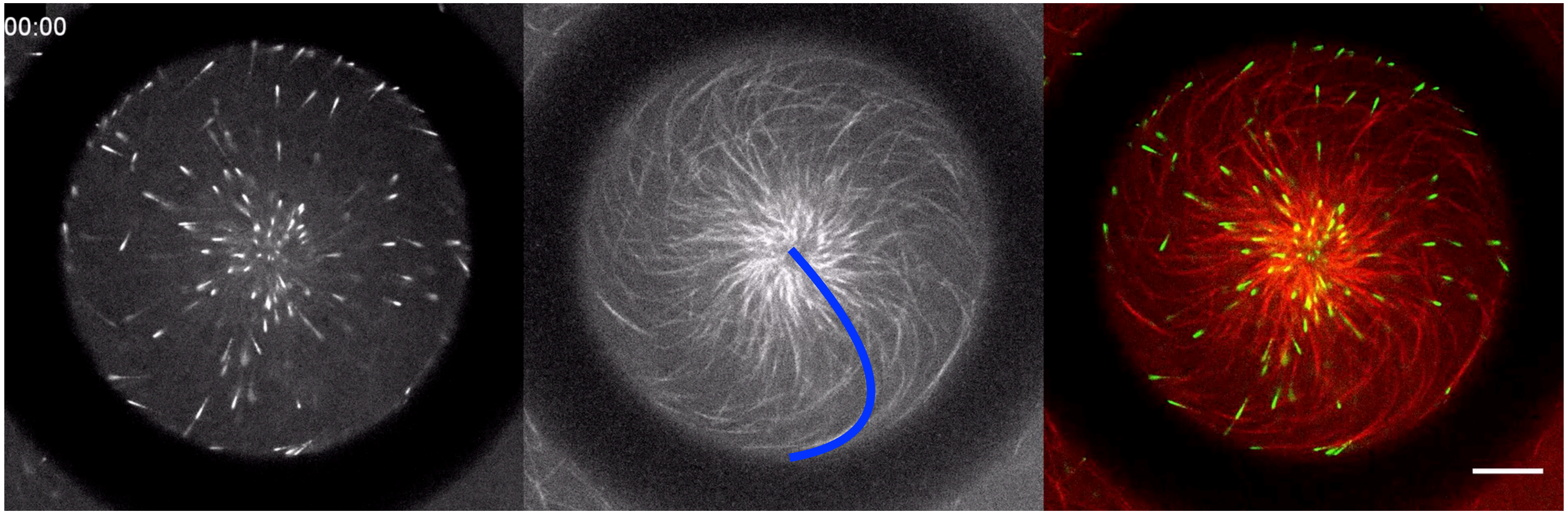




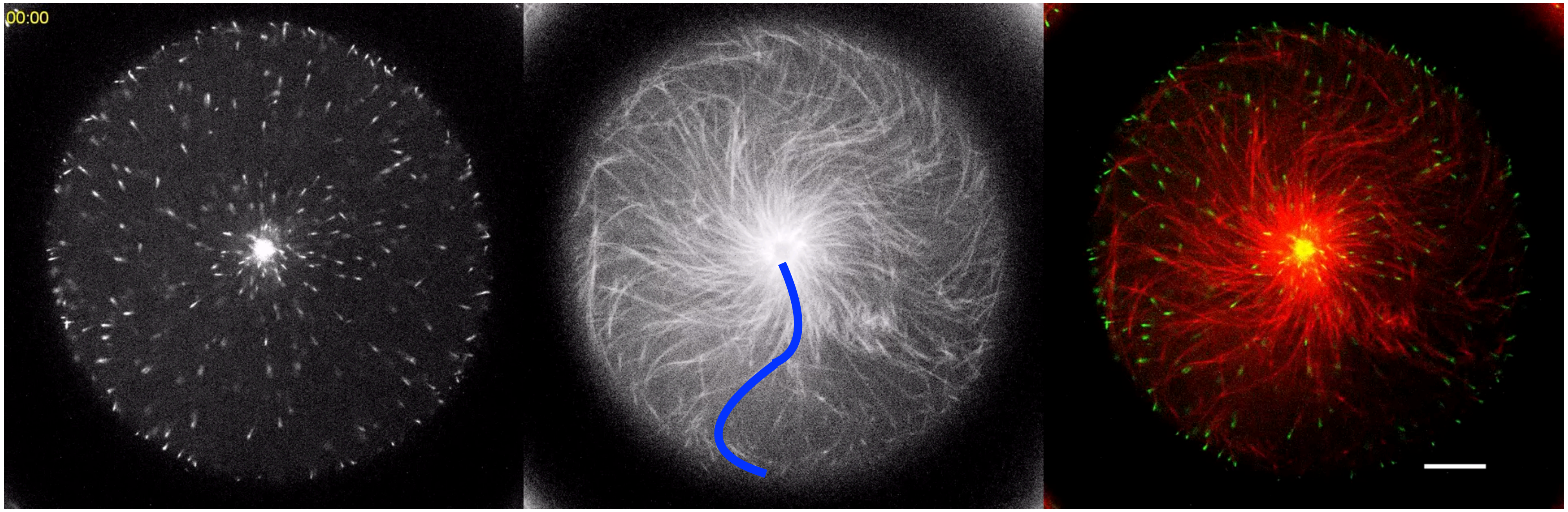




Experimental conformations?

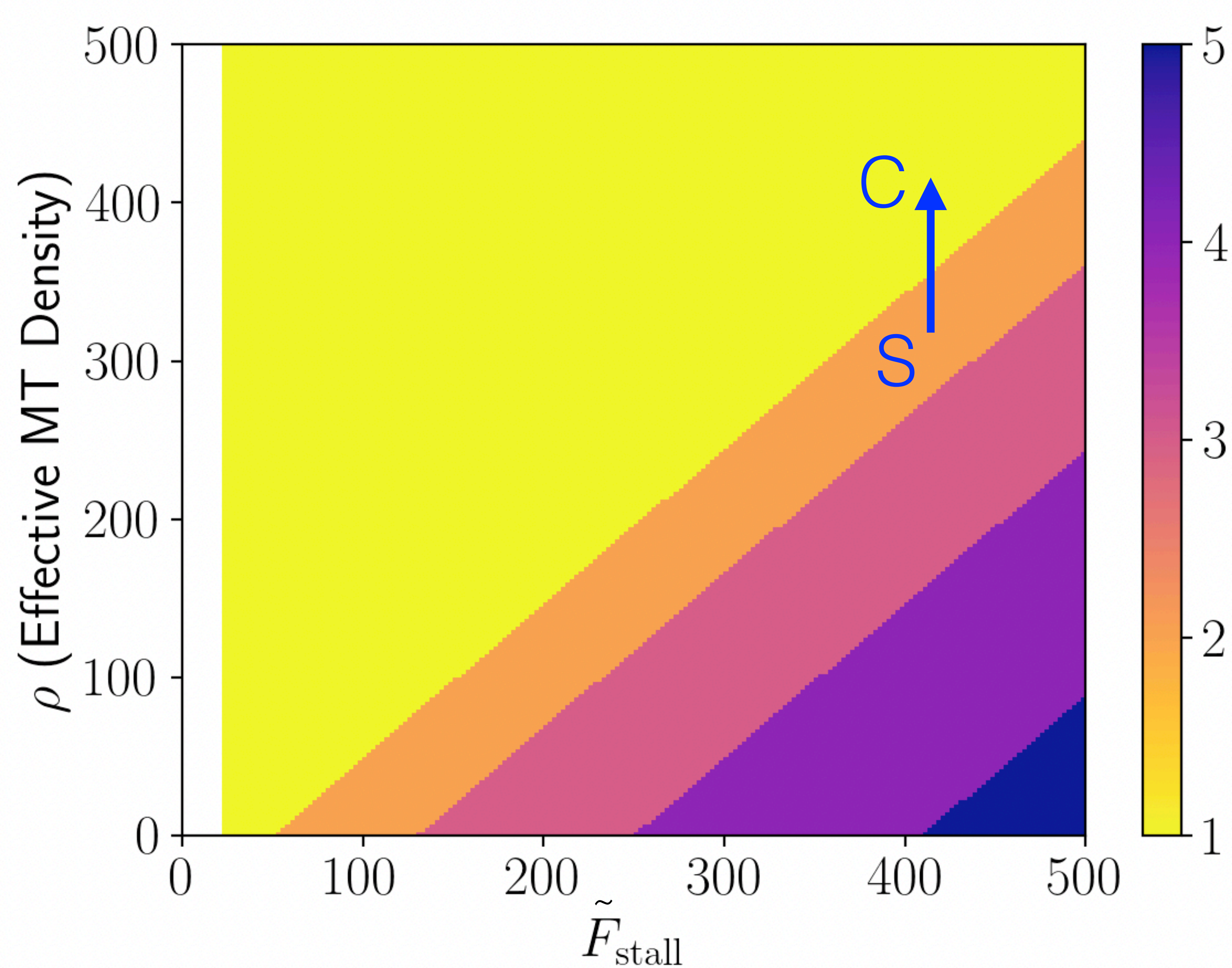


C-modes

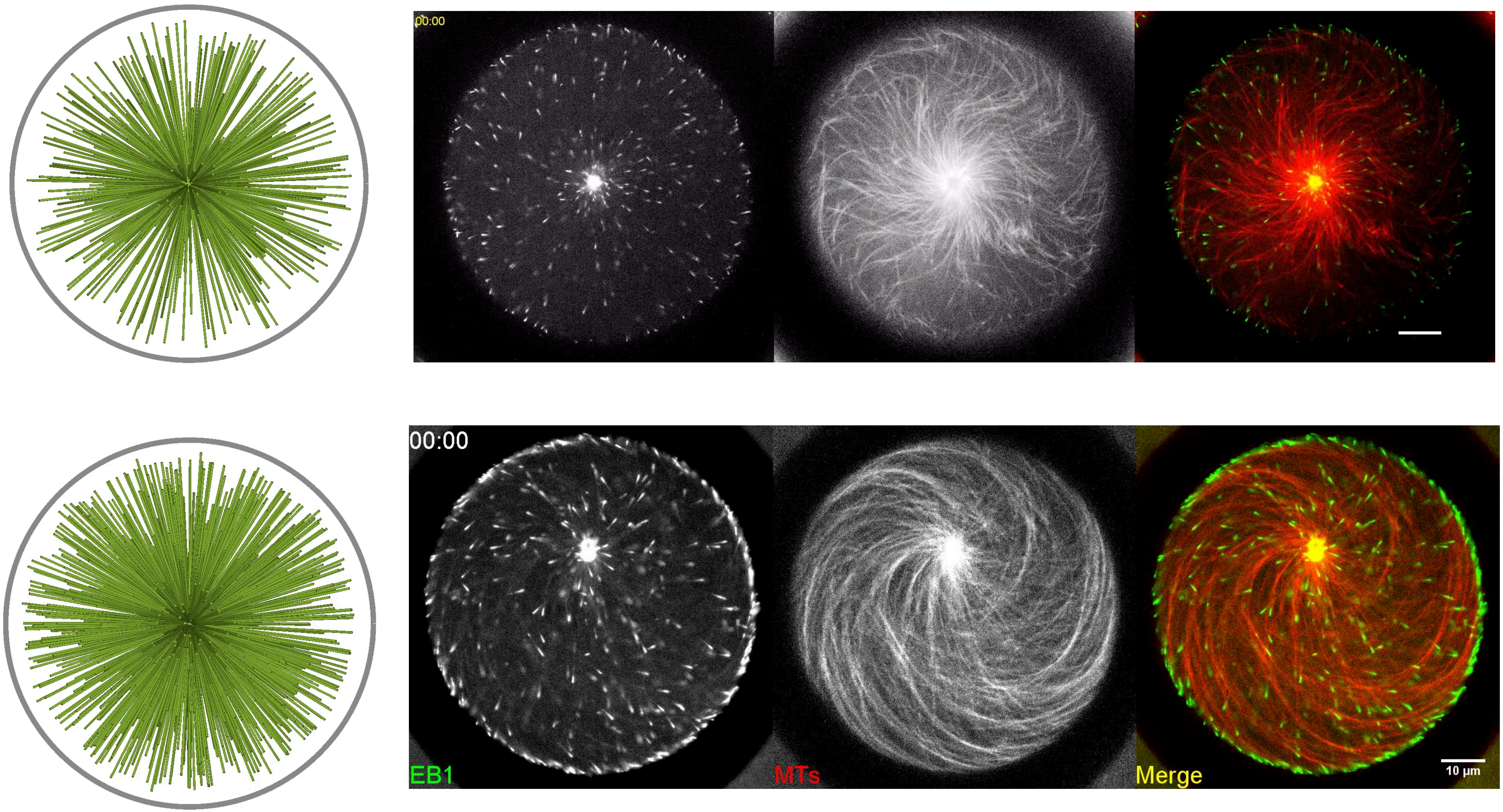


S-modes

Can we just supress S modes to kill switching?



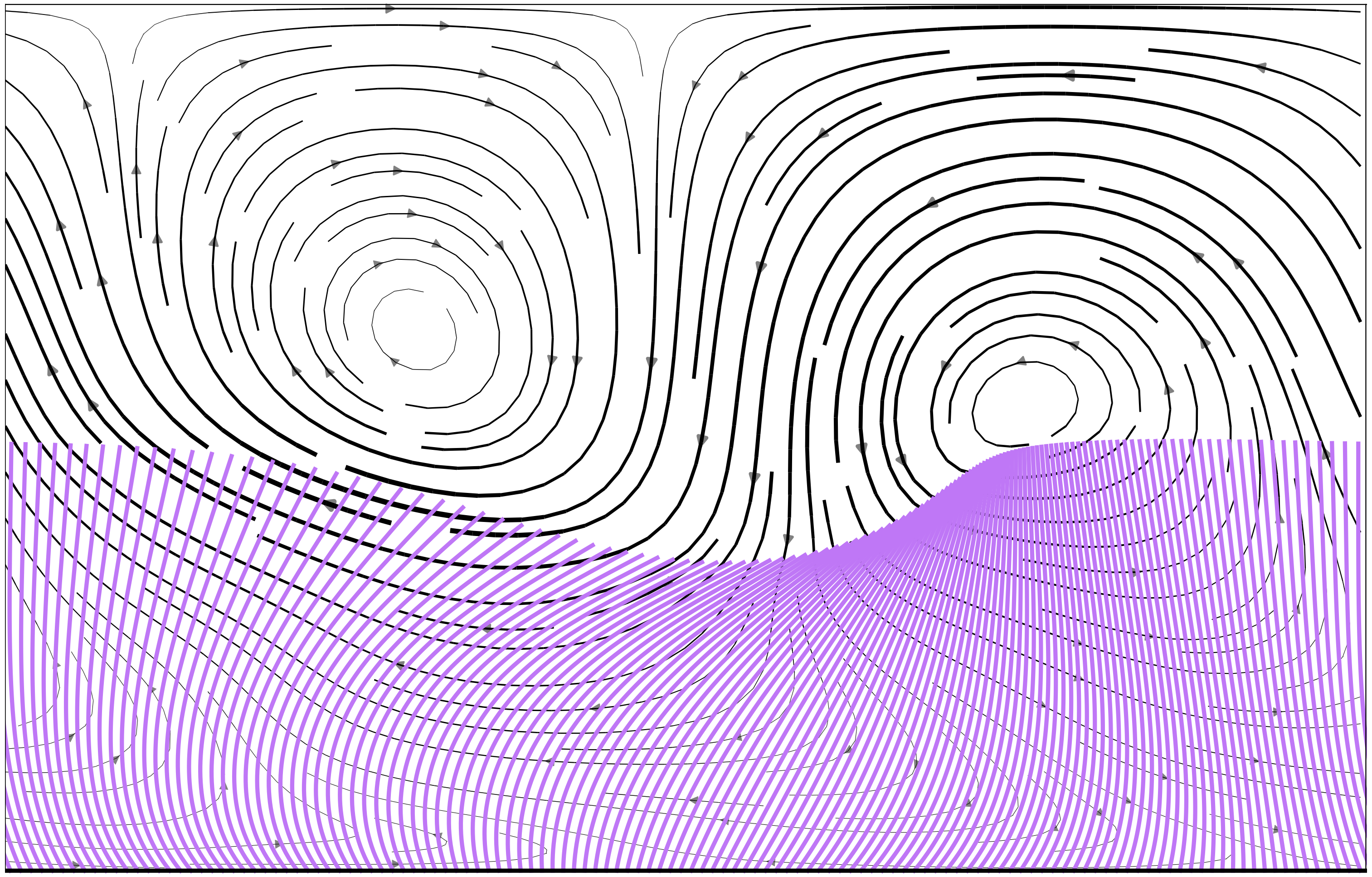
Yet another case where MT density is crucial



Coarse-graining this system

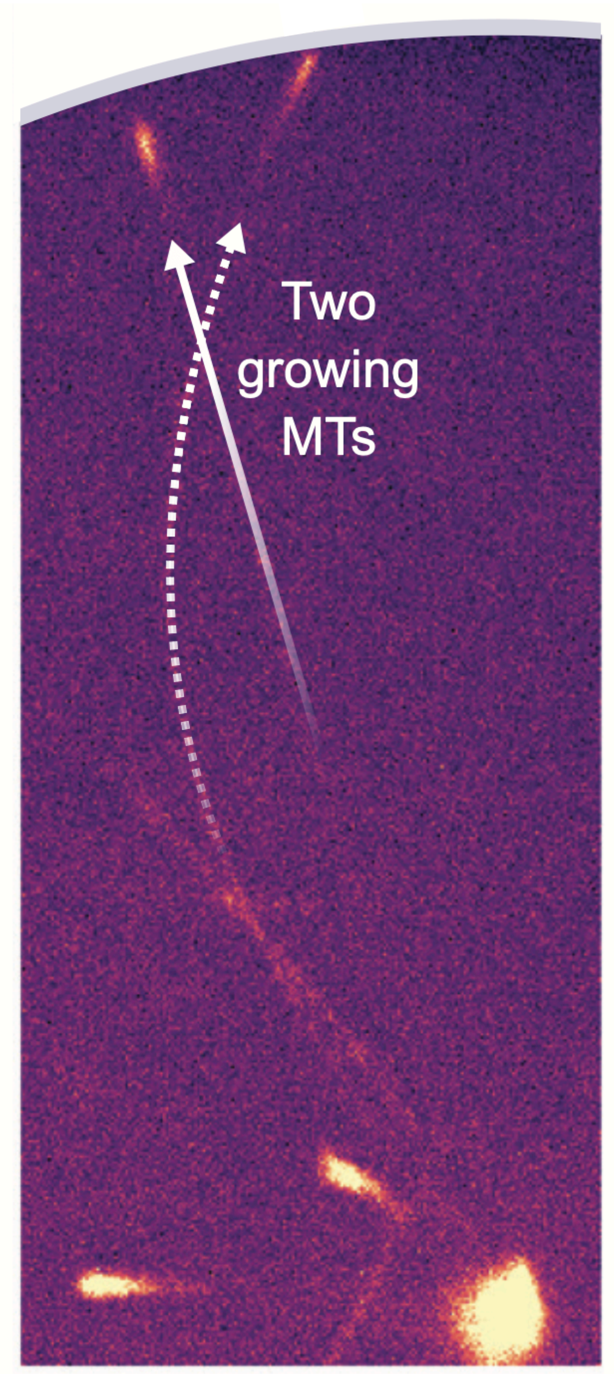
$$-\Delta \mathbf{u}(\mathbf{x}) + \nabla p(\mathbf{x}) = [\rho_0 \mathcal{J}^{-1}\mathbf{f}](\mathbf{X}^{-1}(\mathbf{x}))$$
$$\nabla \cdot \mathbf{u}(\mathbf{x}) = 0$$
$$\eta(\mathbf{V}(\boldsymbol{\alpha}) - \mathbf{u}(\mathbf{X}(\boldsymbol{\alpha}))) = \mathcal{A}(\boldsymbol{\alpha})\mathbf{f}(\boldsymbol{\alpha})$$

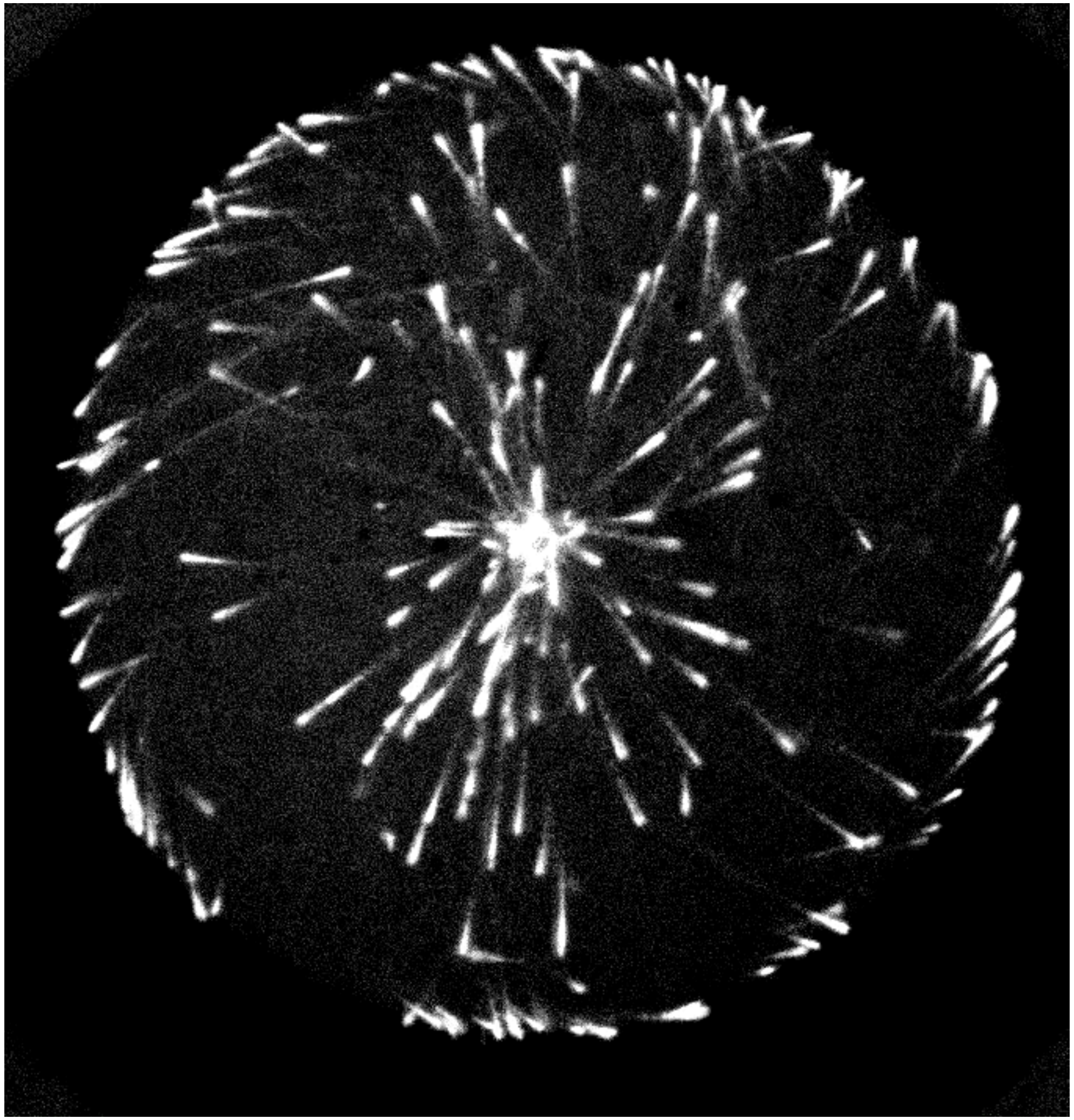
$$\mathbf{f}(\alpha) = -E\mathbf{X}_{\alpha\alpha\alpha\alpha} + (T\mathbf{X}_\alpha)_\alpha$$



Fundamentally for describing a single "bed" of fibers, which are all locally the same.

This is not what we have here.





A one family model

$$\eta(\mathbf{V} - \mathbf{u}) = \mathcal{A}\mathbf{f}$$ ← Slender-body theory

$$\mathbf{f} = -E\mathbf{X}_{\alpha\alpha\alpha\alpha} + (T\mathbf{X}_\alpha)_\alpha$$ ← Fiber forces

$$-\Delta\mathbf{u} + \nabla p = \rho_0 \mathcal{J}^{-1}\mathbf{f}$$
$$\nabla \cdot \mathbf{u} = 0$$
← Coarse-grained velocity driven by averaged forces

A two family model

$$\eta(\mathbf{V} - \mathbf{u}) = \mathcal{A}\mathbf{f}$$ ← Slender-body theory

$$\mathbf{f} = -E\mathbf{X}_{\alpha\alpha\alpha\alpha} + (T\mathbf{X}_\alpha)_\alpha$$ ← Fiber forces

$$\eta(\mathbf{V} - \mathbf{u}) = \mathcal{A}\mathbf{f}$$ ← Slender-body theory

$$\mathbf{f} = -E\mathbf{X}_{\alpha\alpha\alpha\alpha} + (T\mathbf{X}_\alpha)_\alpha$$ ← Fiber forces

$$-\Delta\mathbf{u} + \nabla p = \rho_0 \mathcal{J}^{-1}\mathbf{f} + \rho_0 \mathcal{J}^{-1}\mathbf{f}$$
$$\nabla \cdot \mathbf{u} = 0$$
← Coarse-grained velocity driven by sum of averaged forces

An N-family model

Fiber dynamics

$$\eta(\mathbf{V}_i - \mathbf{u}) = \mathcal{A}^i \mathbf{f}_i$$

$$\mathbf{f}_i = -E\mathbf{X}^i_{\alpha\alpha\alpha\alpha} + (T_i \mathbf{X}^i_\alpha)_\alpha$$

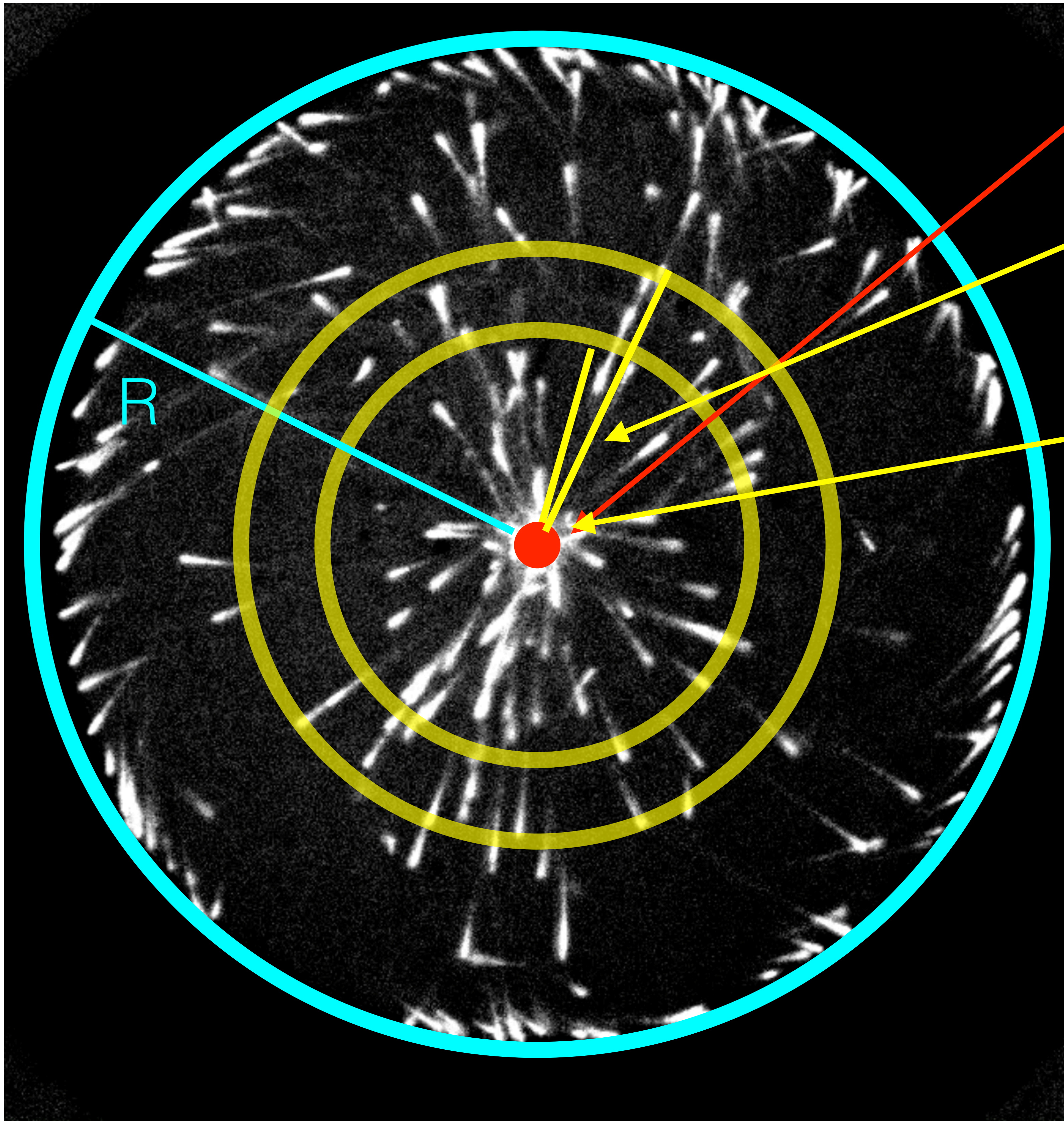
Fluid equations

$$-\Delta \mathbf{u} + \nabla p = \sum_{i=1}^{N} \rho^i(t) \mathcal{J}_i^{-1} \mathbf{f}_i$$

$$\nabla \cdot \mathbf{u} = 0$$

Each MT beds can have different densities, different lengths, different conformations, different boundary conditions.

Coarse-grained aster

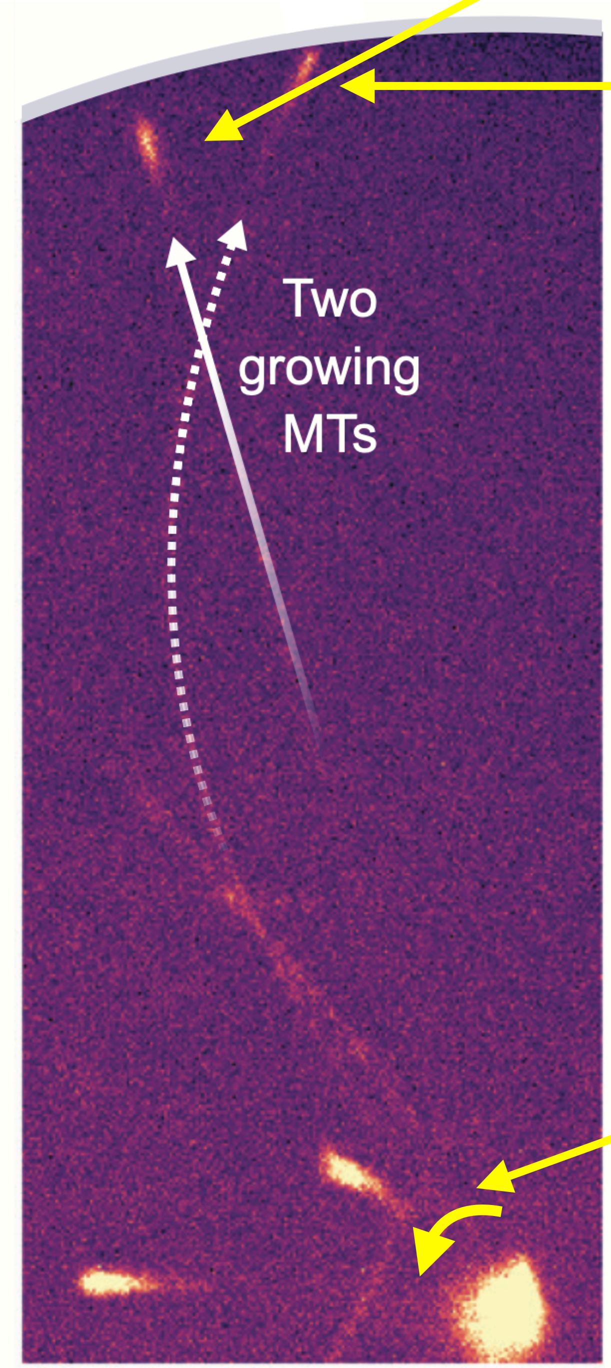


Single aMTOC with radius r = 0.6μm

Growing beds of MTs

MT lower BCs:
all MT beds are clamped normally to aMTOC

Coarse-grained aster



Beds of MTs that have yet to grow into the wall obey force & torque-free BCs

Beds of MTs that have contacted the wall obey “pinned” BCs — location fixed and torque free

Fibers beds grow —

$$\frac{dL^i}{dt} = \gamma_0 \mathcal{G}(F^i(t, s = L))$$

Fibers beds decay —

$$\rho^i(t) = \rho_0 e^{-\kappa t_i}$$

aMTOC rotates —

$$\zeta\omega - \int \tau_H dS - \sum_i \tau_i = 0.$$

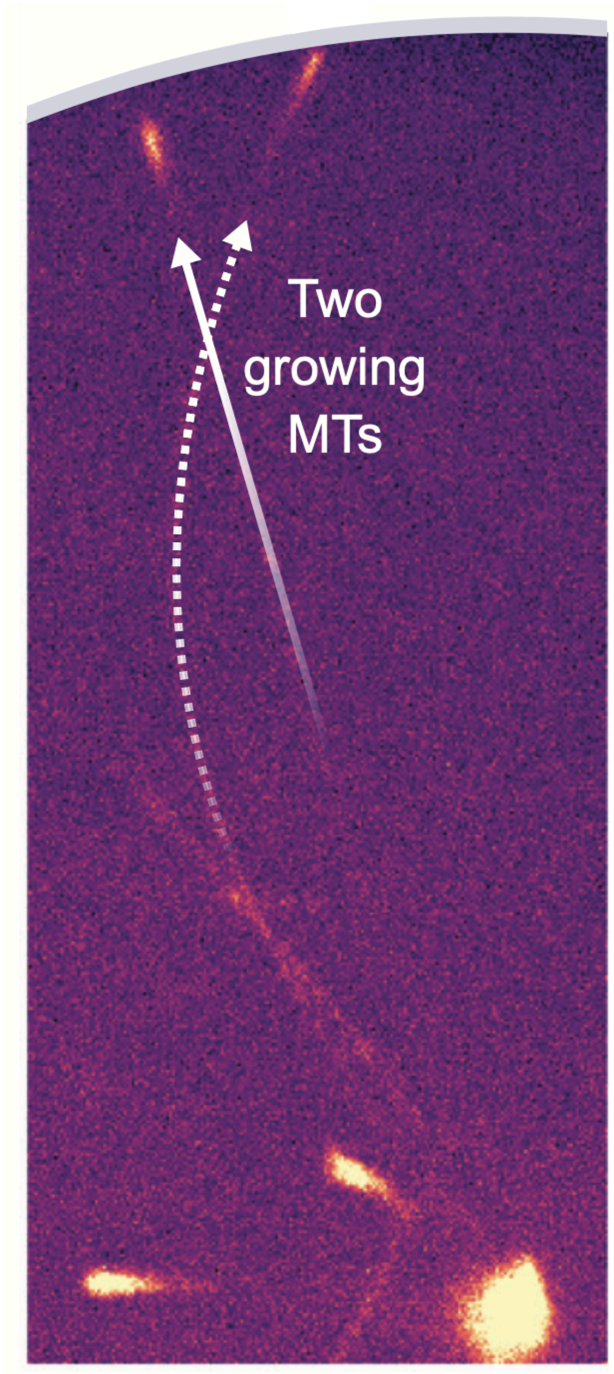
This gives:

N fourth-order nonlinear PDE with a strict inextensibility constraint, coupled by:

$$-\Delta \mathbf{u} + \nabla p = \sum_{i=1}^{N} \rho^i(t) \mathcal{J}_i^{-1} \mathbf{f}_i$$

$$\nabla \cdot \mathbf{u} = 0$$

$$\zeta \omega - \int \tau_H dS - \sum_i \tau_i = 0.$$

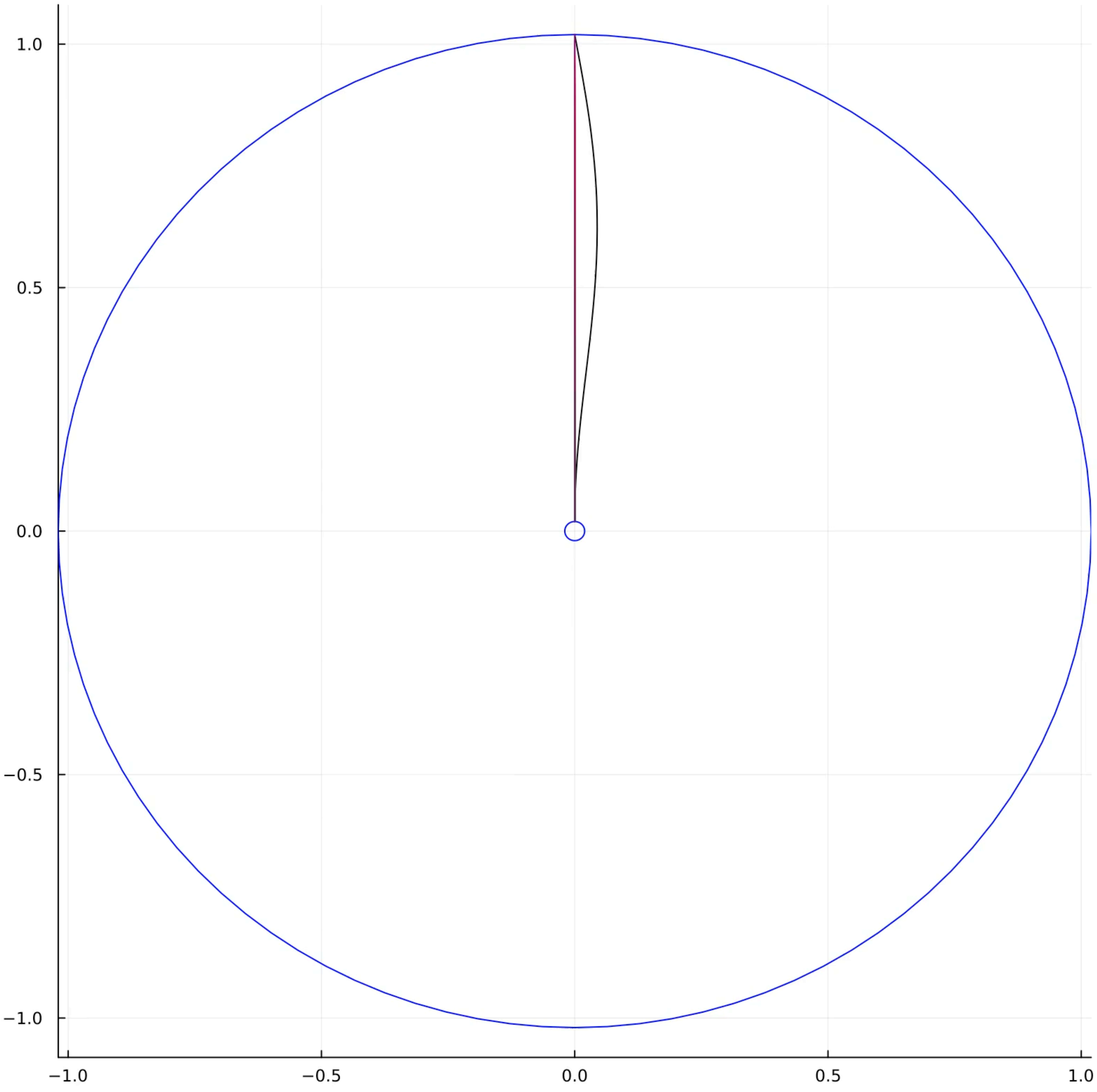


Assume axisymmetry to make everything viable

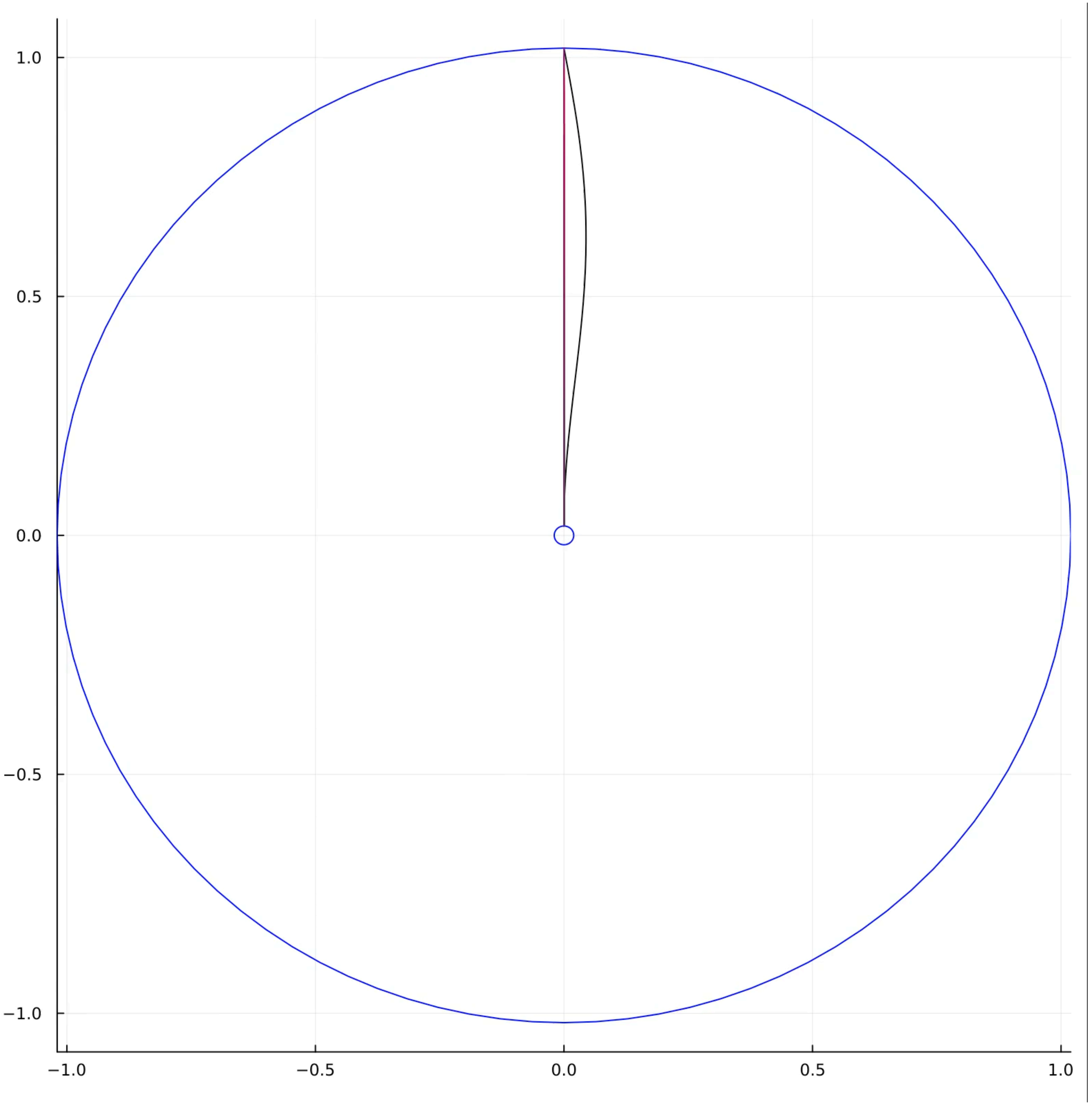
Newton-Krylov method; block-diagonal Jacobian preconditioner

Timestep reduction at near-singular points to solve system with high accuracy

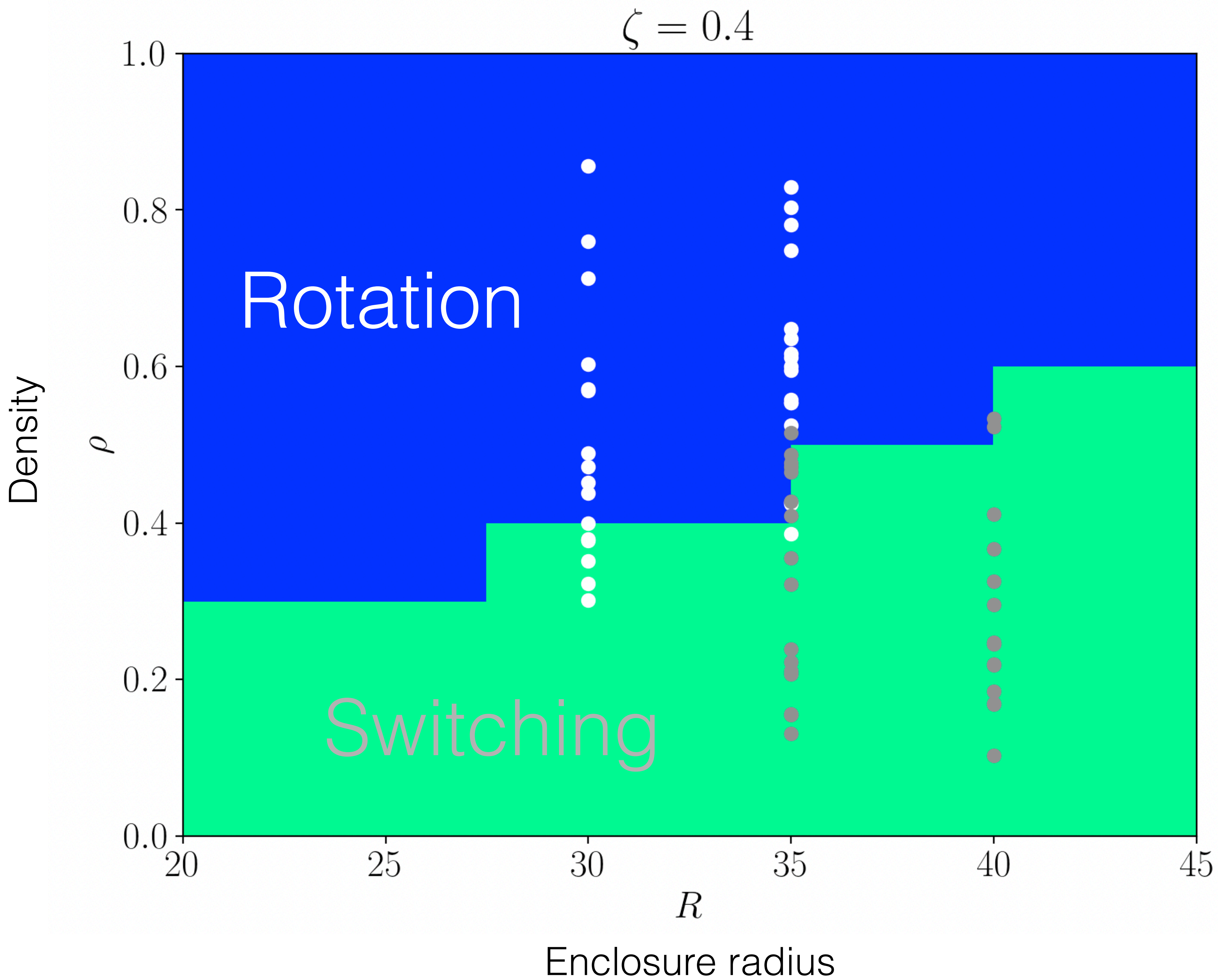
In action — persistent rotation



In action — switching



Parameter sweep — R, ρ, ζ



Takeaways

- Fiber density should be treated as a critical parameter which drives both quantitative and *qualitative dynamics*
- Be skeptical of discrete fiber simulations
- Coarse-grained models can be usefully extended to complex systems