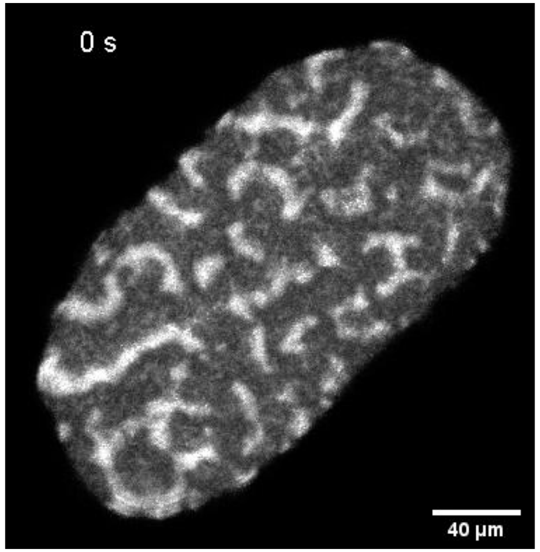
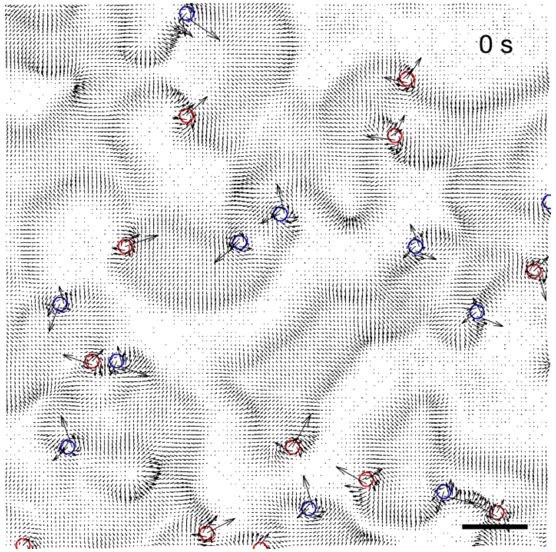
Topological dynamics in the membrane of a living cell





Pearson Miller, Tzer Han Tan, Jinghui Liu, Melis Tekant, Jörn Dunkel, Nikta Fakhri

Massachusetts Institute of Technology

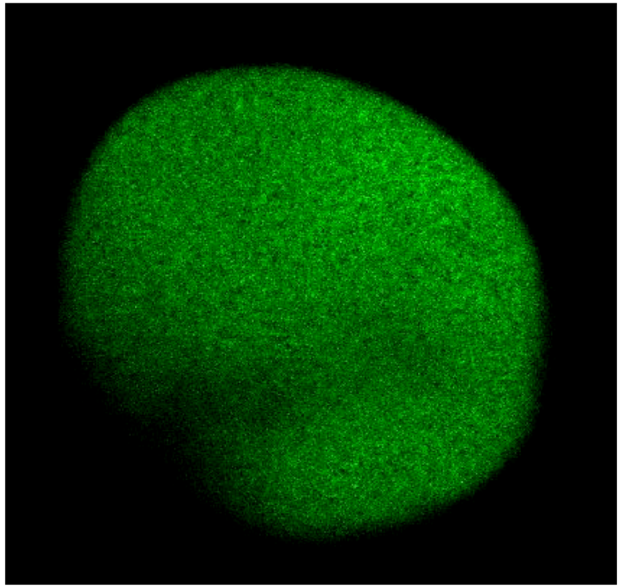
The Chemical Basis of Morphogenesis

How do organisms know how to form complex spatial structures?

Reaction-Diffusion

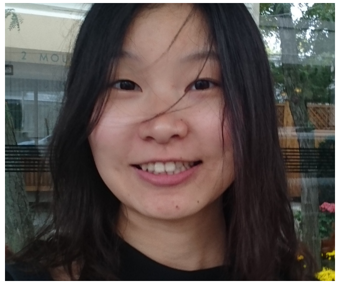
$$\partial_t \boldsymbol{q} = \boldsymbol{D}\,\nabla^2 \boldsymbol{q} + \boldsymbol{R}(\boldsymbol{q})$$

Chemical pattern formation coordinates mechanical growth



(Image from Center for Genomic Regulation)

Reaction-diffusion waves in starfish oocytes



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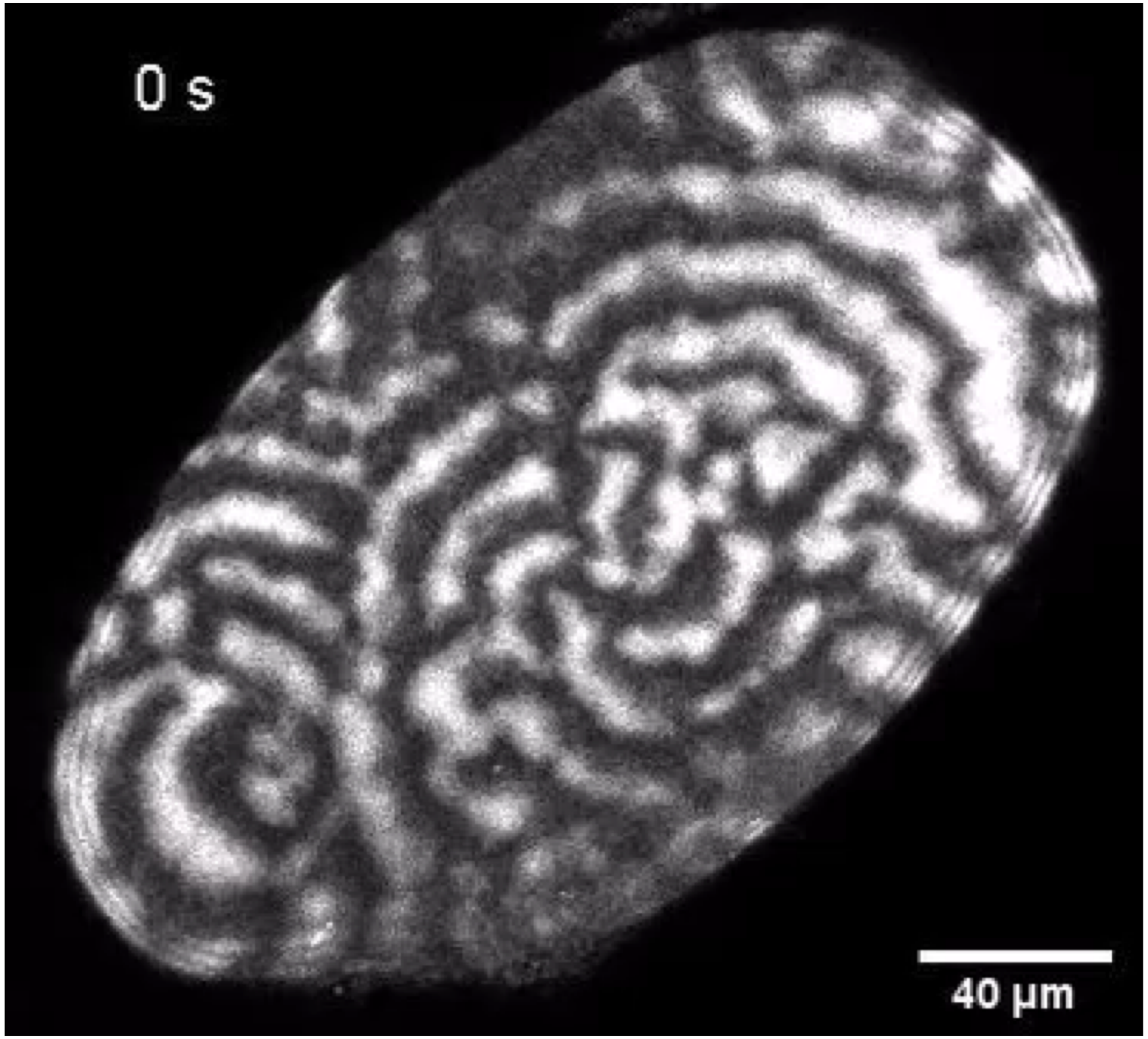
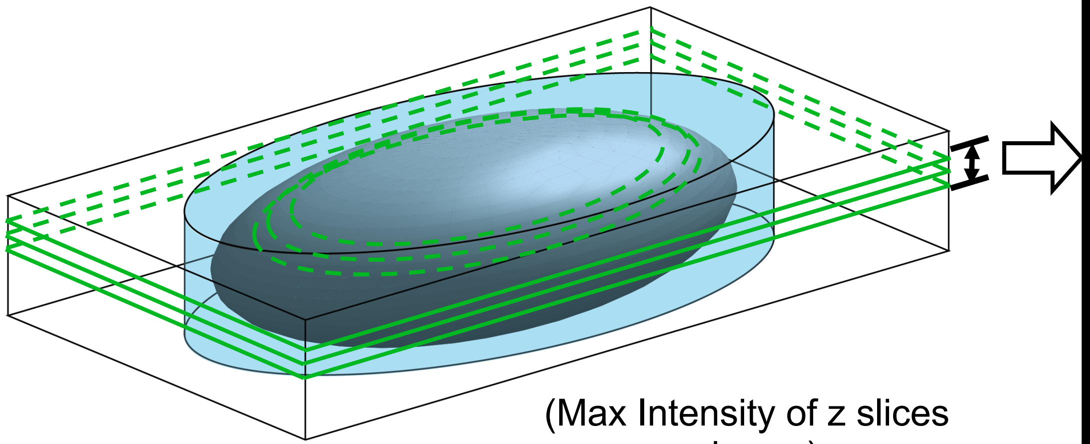


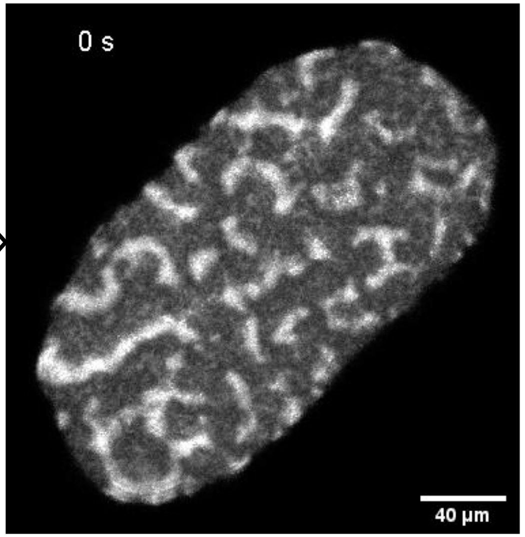
Experiments: *In vivo* self-sustained biochemical wave
Rho-GTP patterns on oocyte membrane

Highly conserved pathway, but poorly understood!

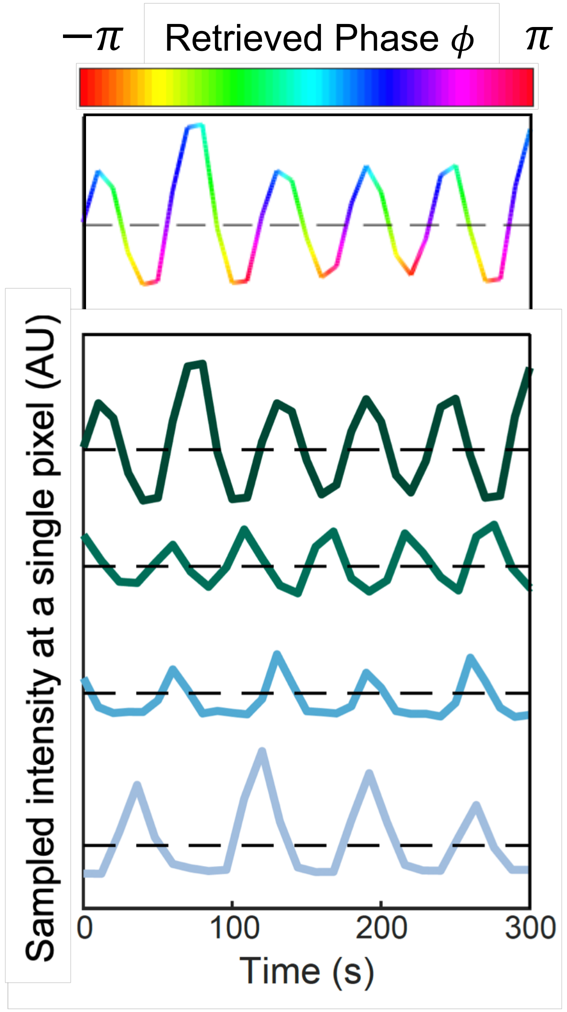
PDMS Chamber (Fused with sea water)

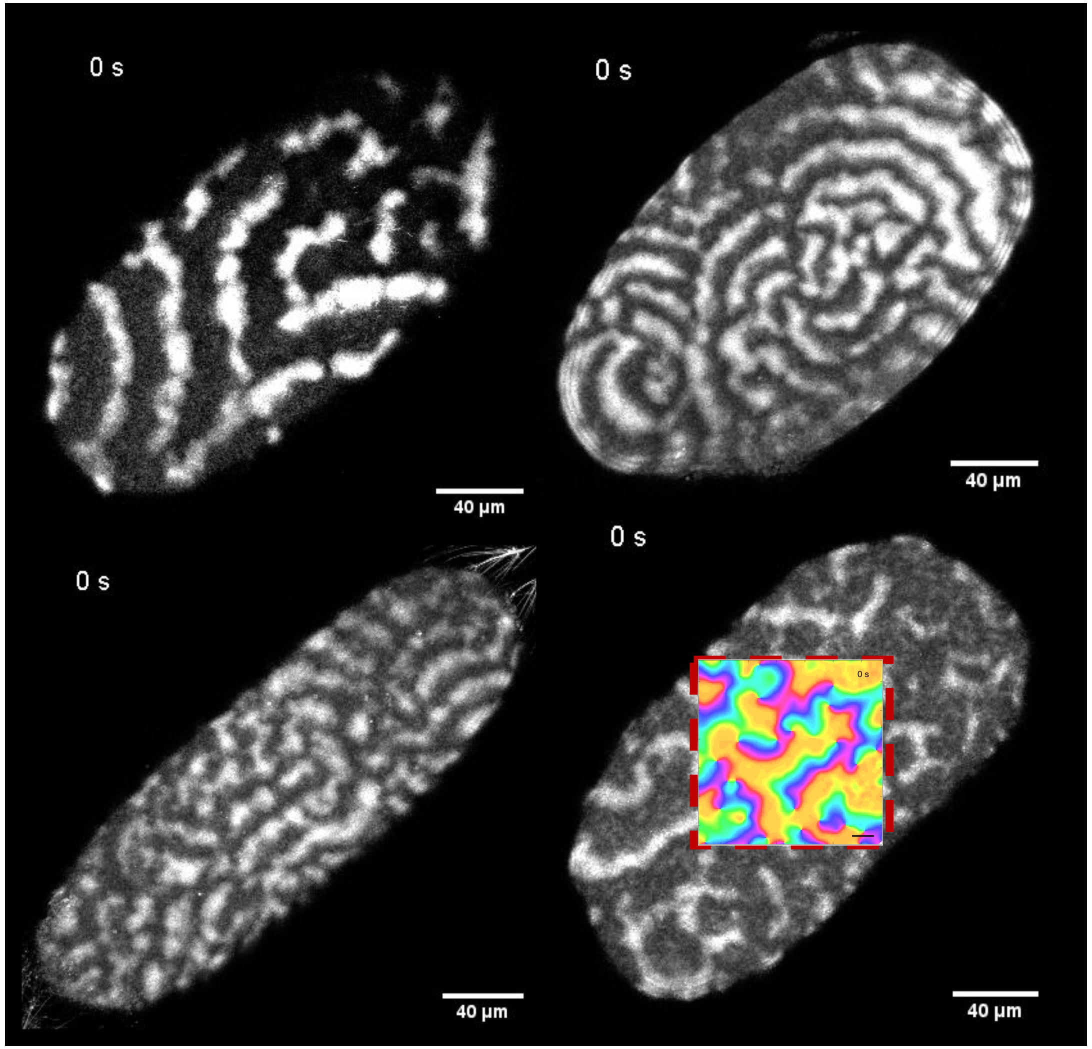


(Max Intensity of z slices near membrane)

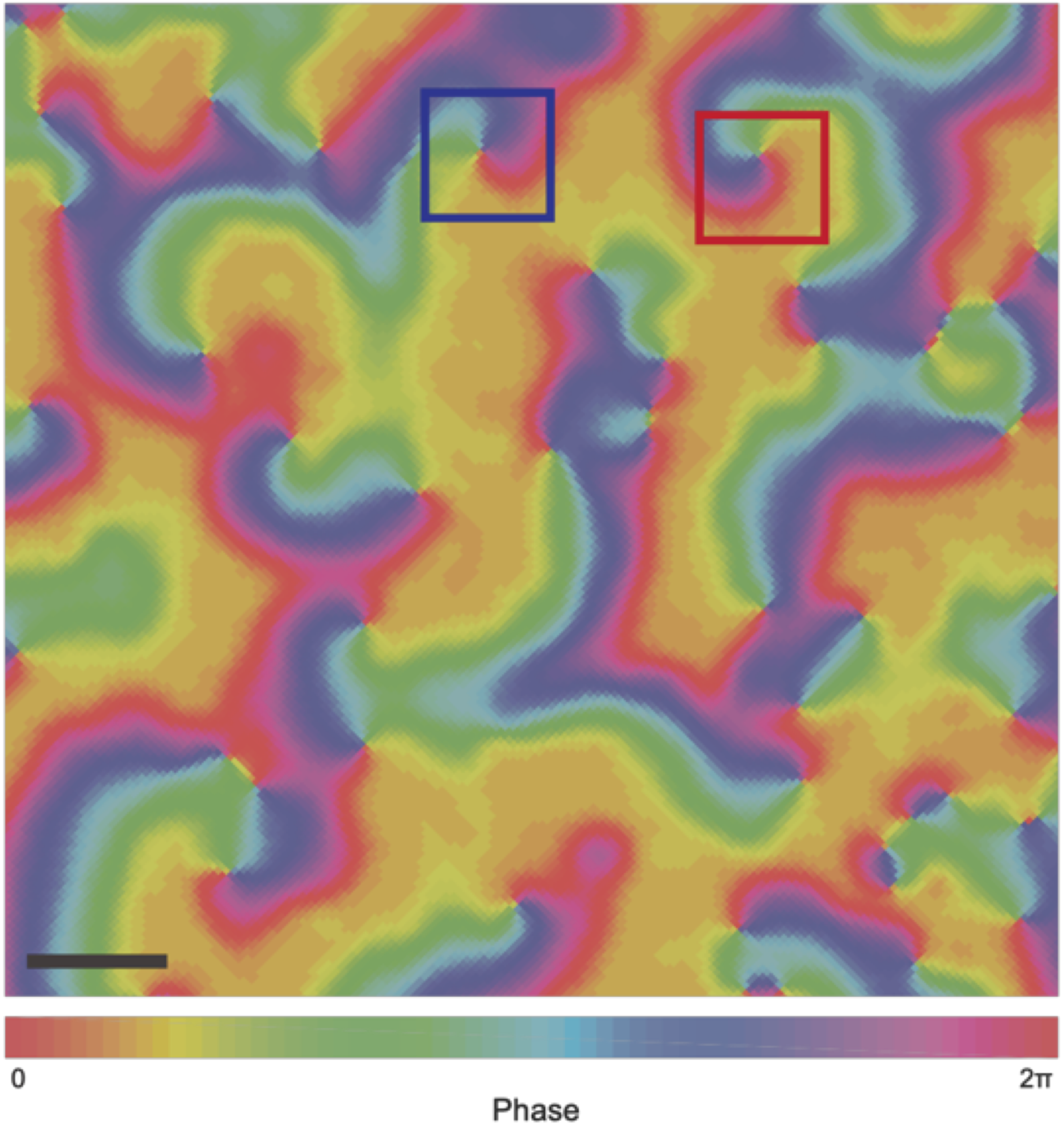


Analyze steady state Rho-GTP waves with reconstructed phase field

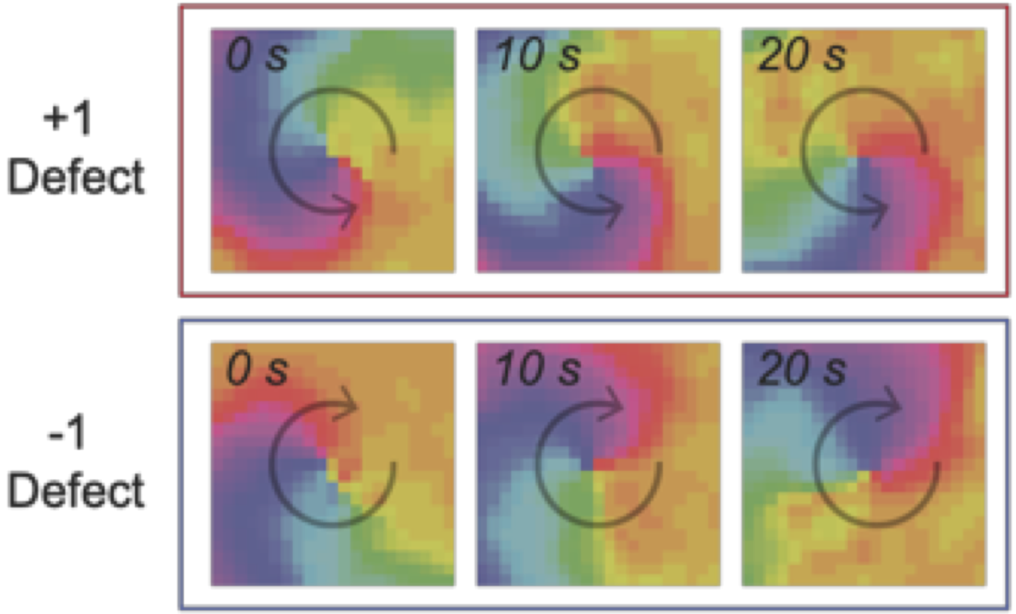




Spiral waves as topological defects

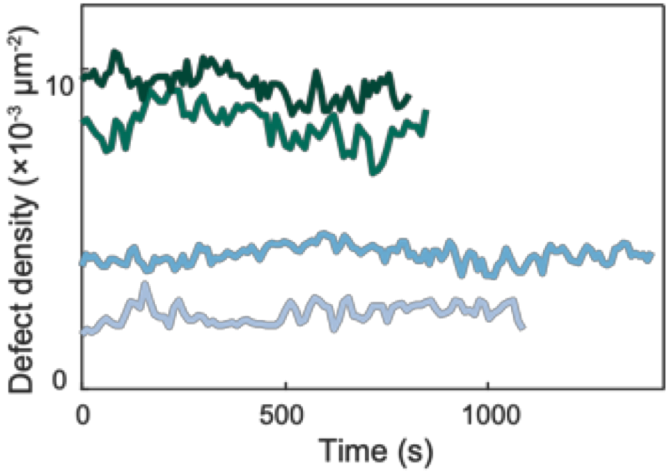


Scale bar: 10 μm



Winding number: $2\pi I = \oint_C \nabla\Phi \cdot d\vec{l}$

Defects created/annihilated in pairs



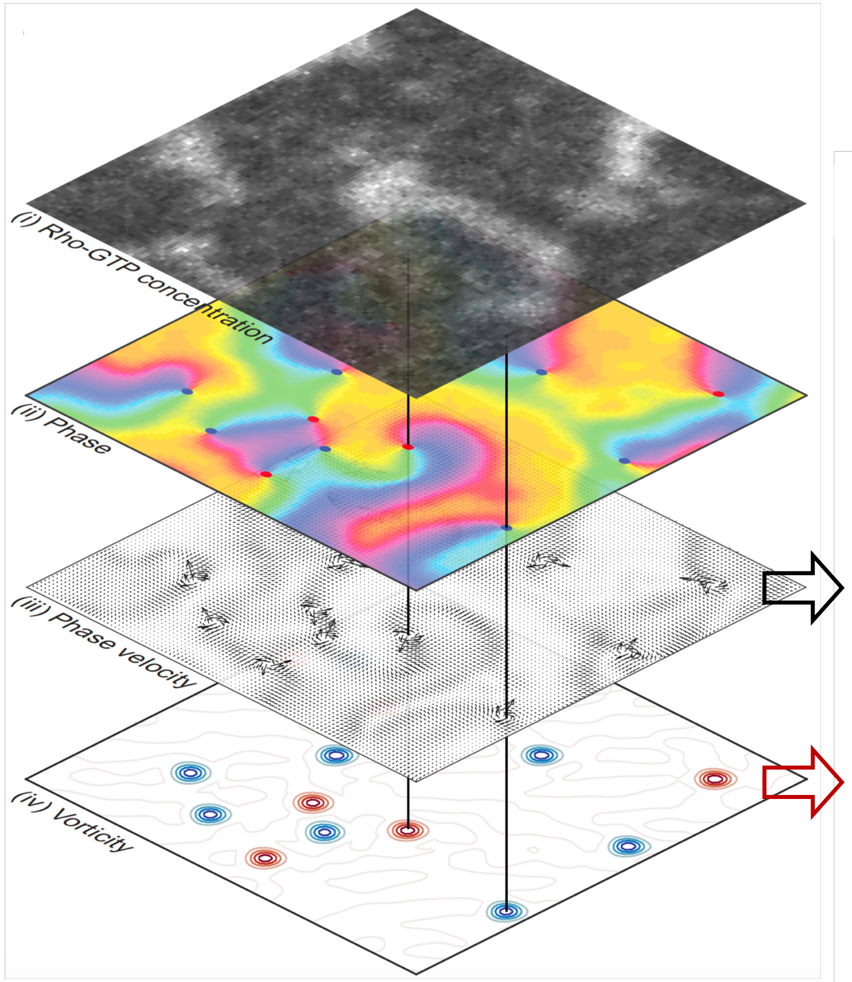
Global analysis: Defects in phase field could be mapped to vortices in phase velocity field

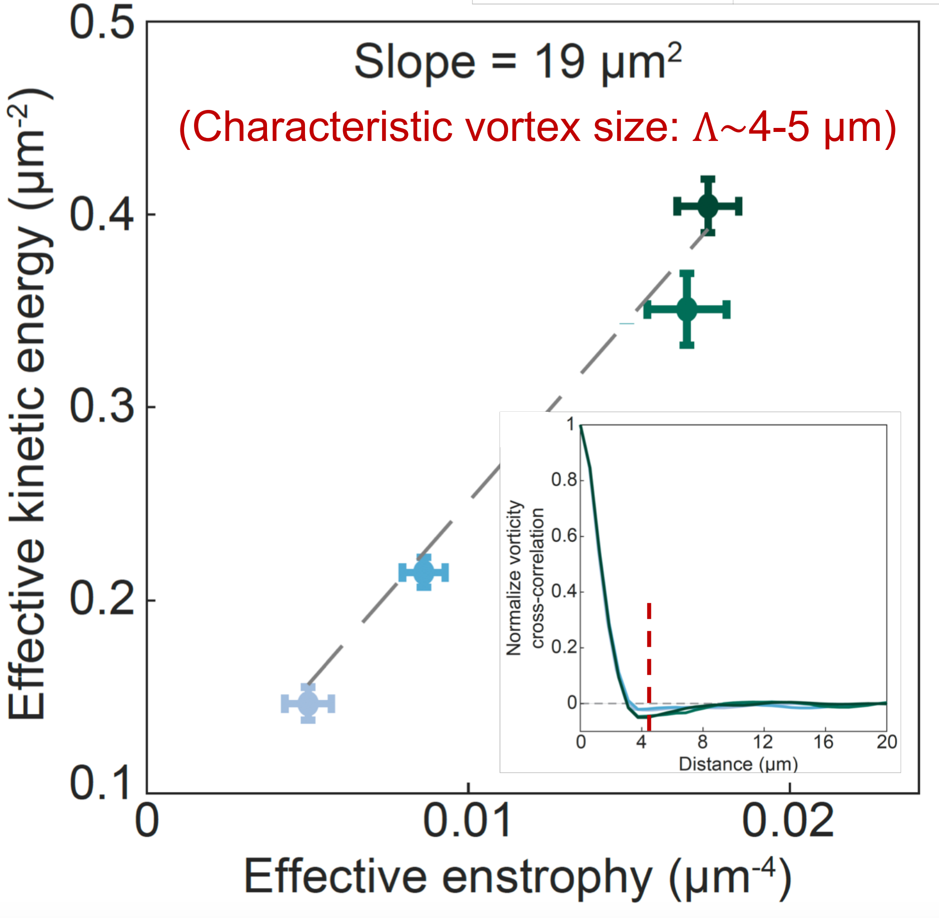
Effective kinetic energy: $\bar{E} = \langle |\vec{V}_\phi|^2 \rangle$

Effective enstrophy: $\bar{\Omega} = \langle \omega^2 \rangle$ $\omega = \nabla \times \vec{V}_\phi$

$\boldsymbol{v} = \nabla \phi$

$\omega = \nabla \times \boldsymbol{v}$

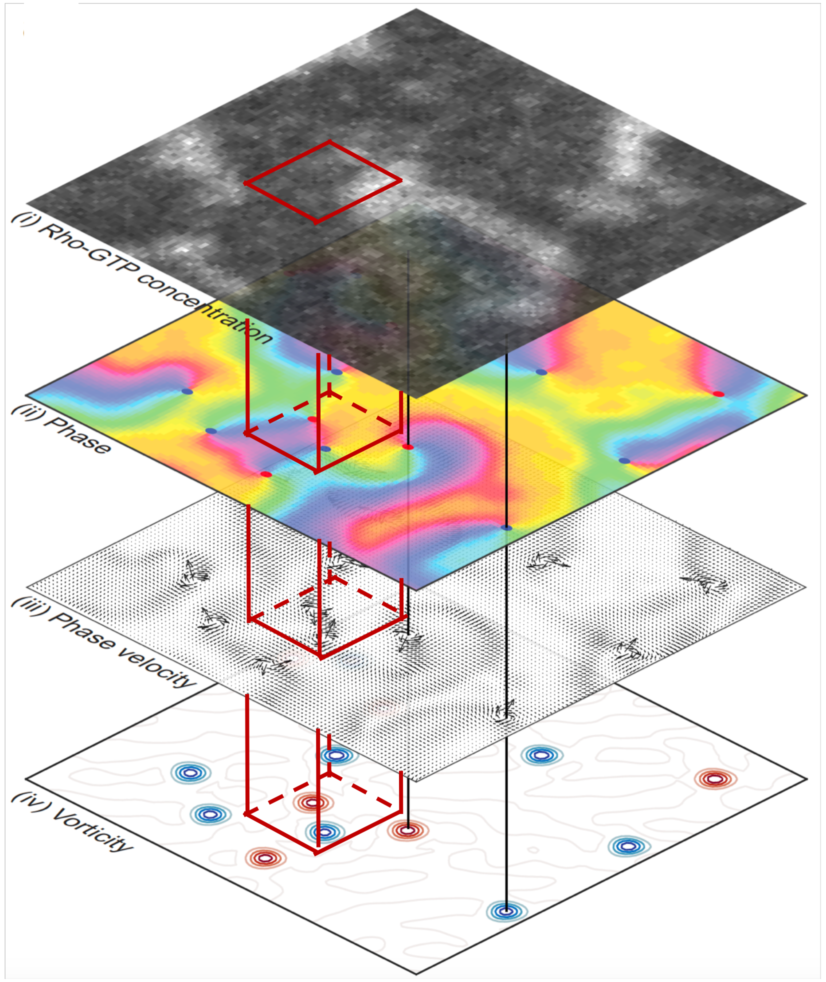


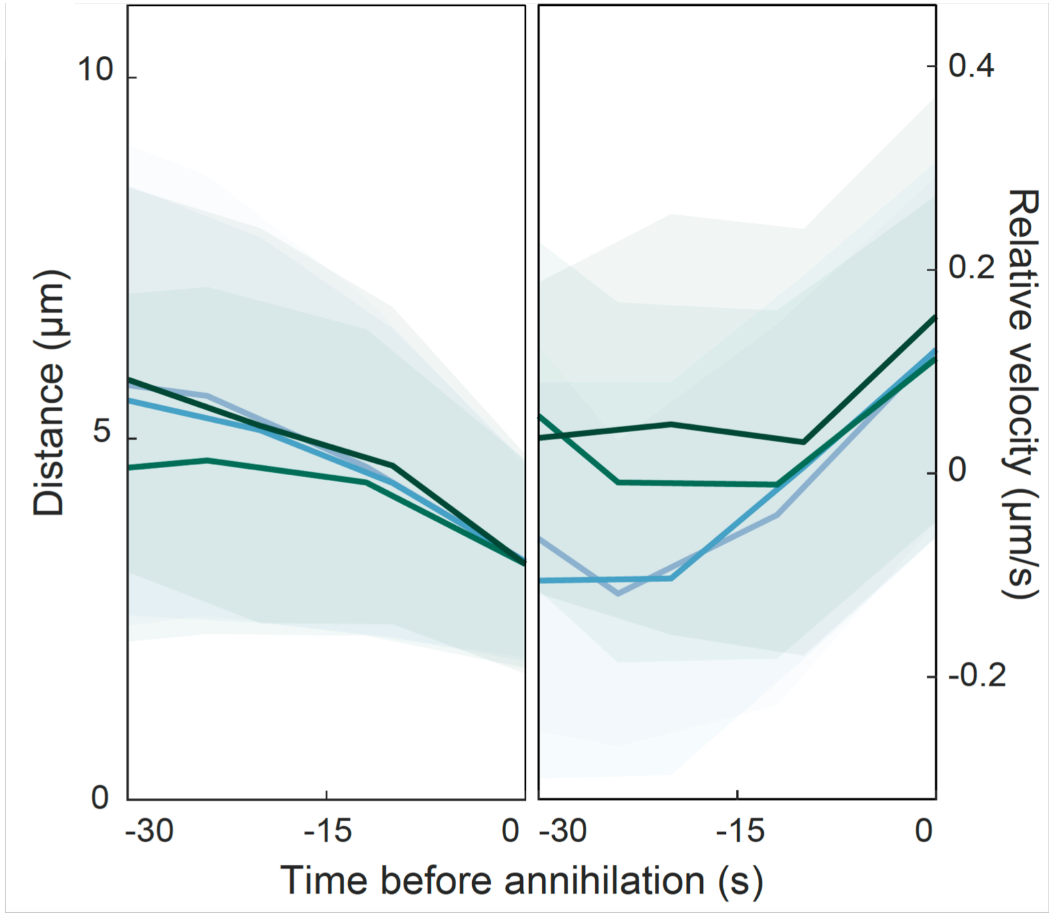


Local analysis: Self-sustained Rho-GTP wave patterns exhibit generic vortex-vortex interaction

$$\boldsymbol{v} = \nabla\phi$$

$$\omega = \nabla\times\boldsymbol{v}$$



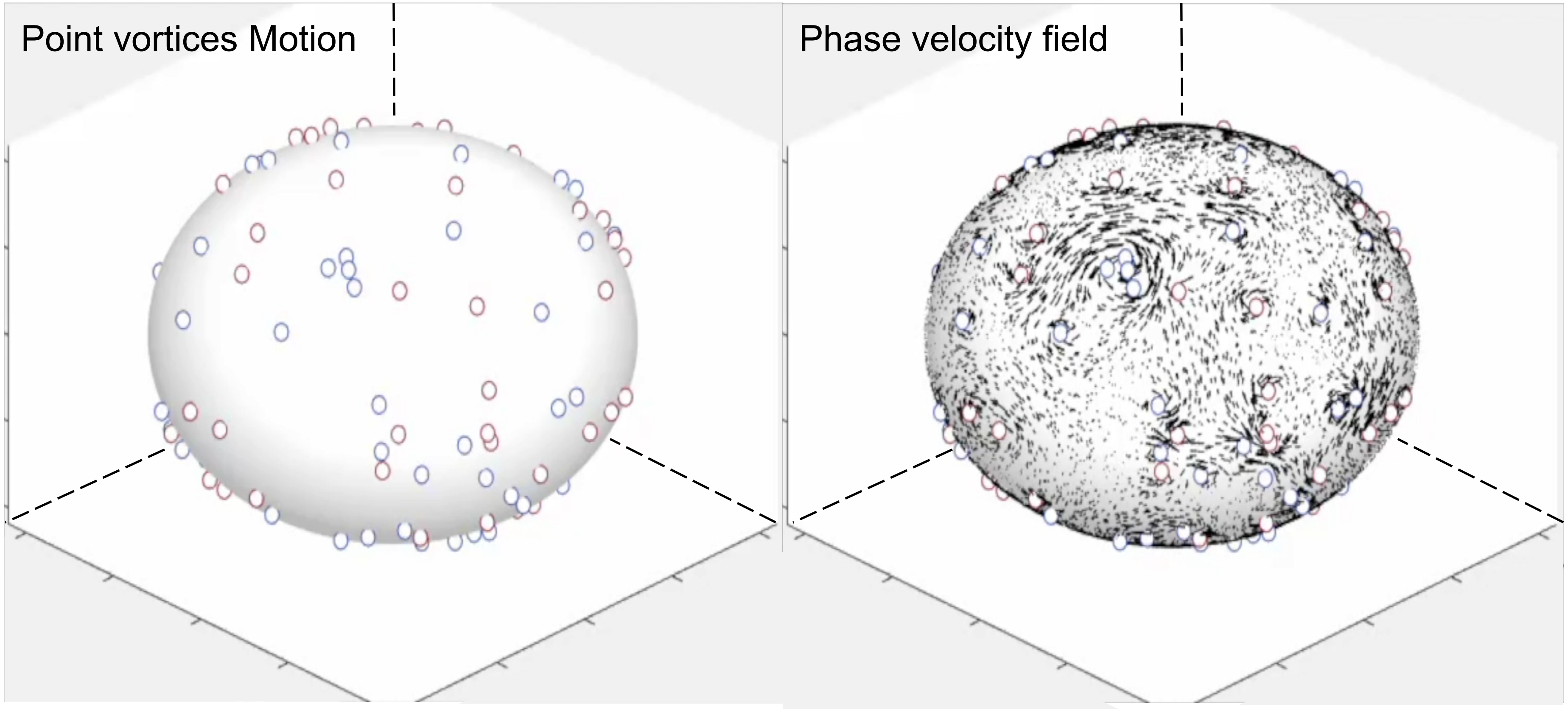


A minimal Helmholtz-Onsager point-vortex model correctly captures Rho-GTP waves vortex statistics

Could statistical laws from passive systems apply for vortex-vortex interaction in Rho-GTP waves?

Point-vortex model: $H = -\frac{1}{2\pi}\sum_{i,j} I_i I_j \ln|\vec{r}_i - \vec{r}_j|$

Blue: $I = +1$, Red: $I = -1$.
(Positive/Negative Circulations)



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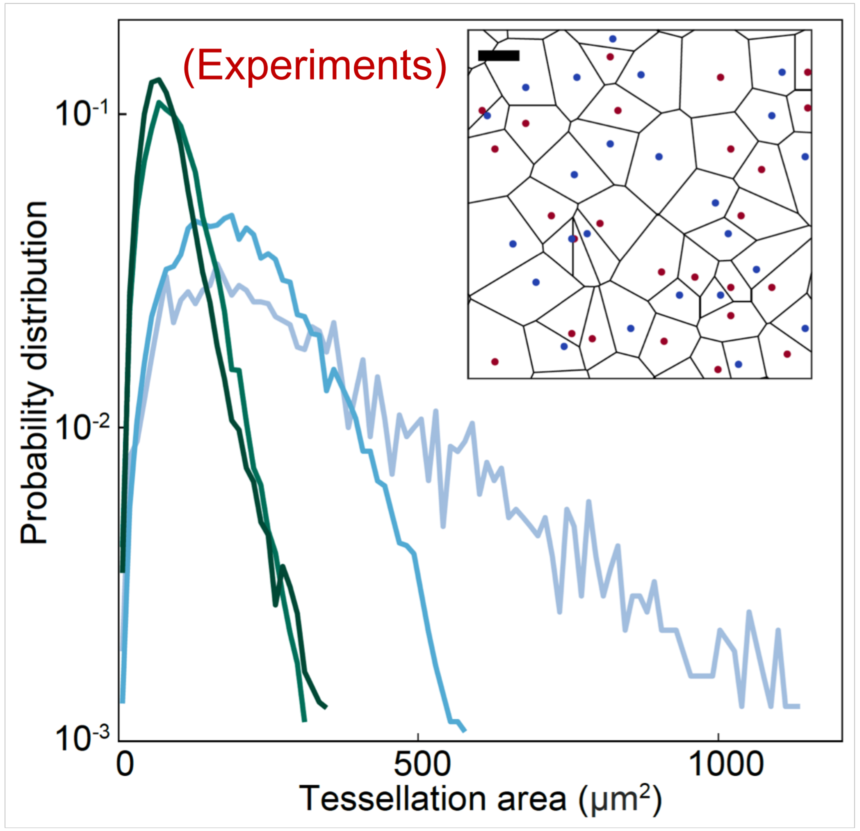
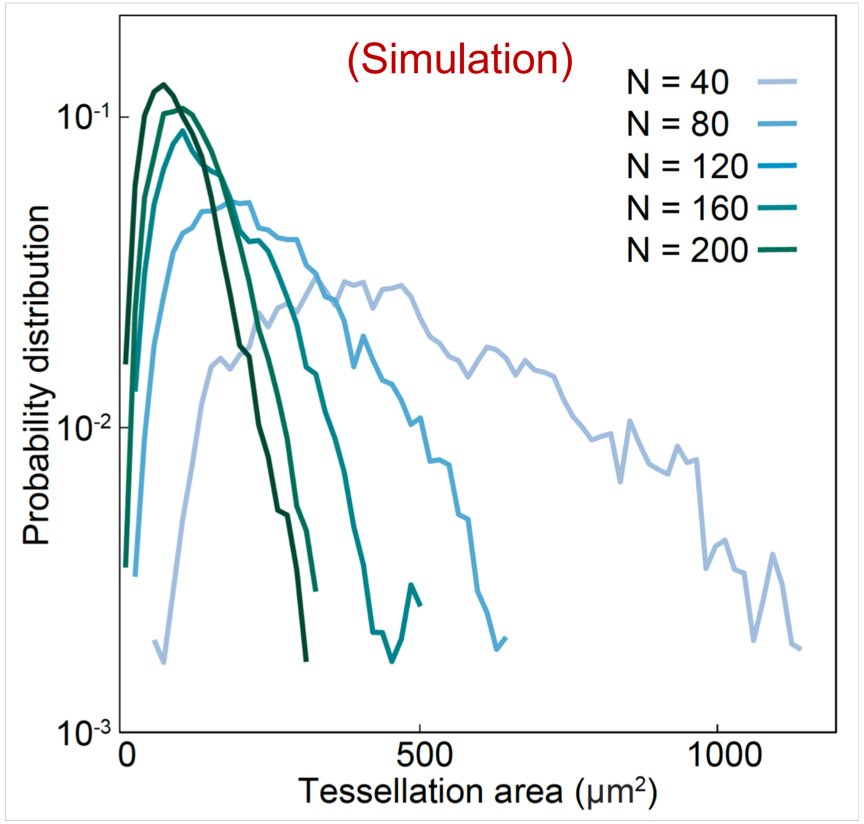
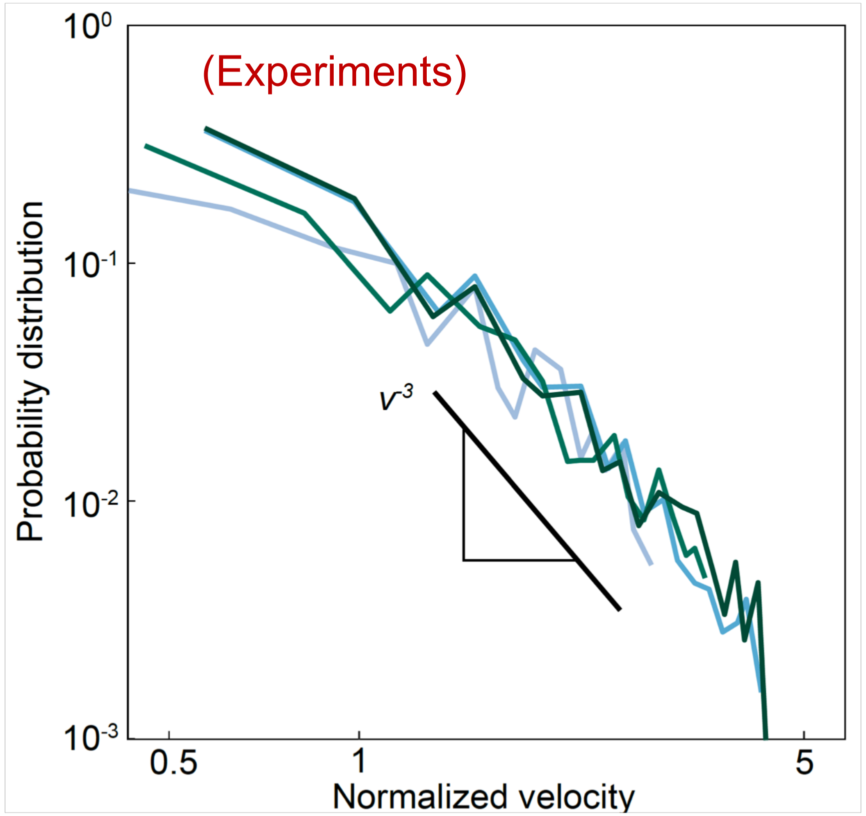
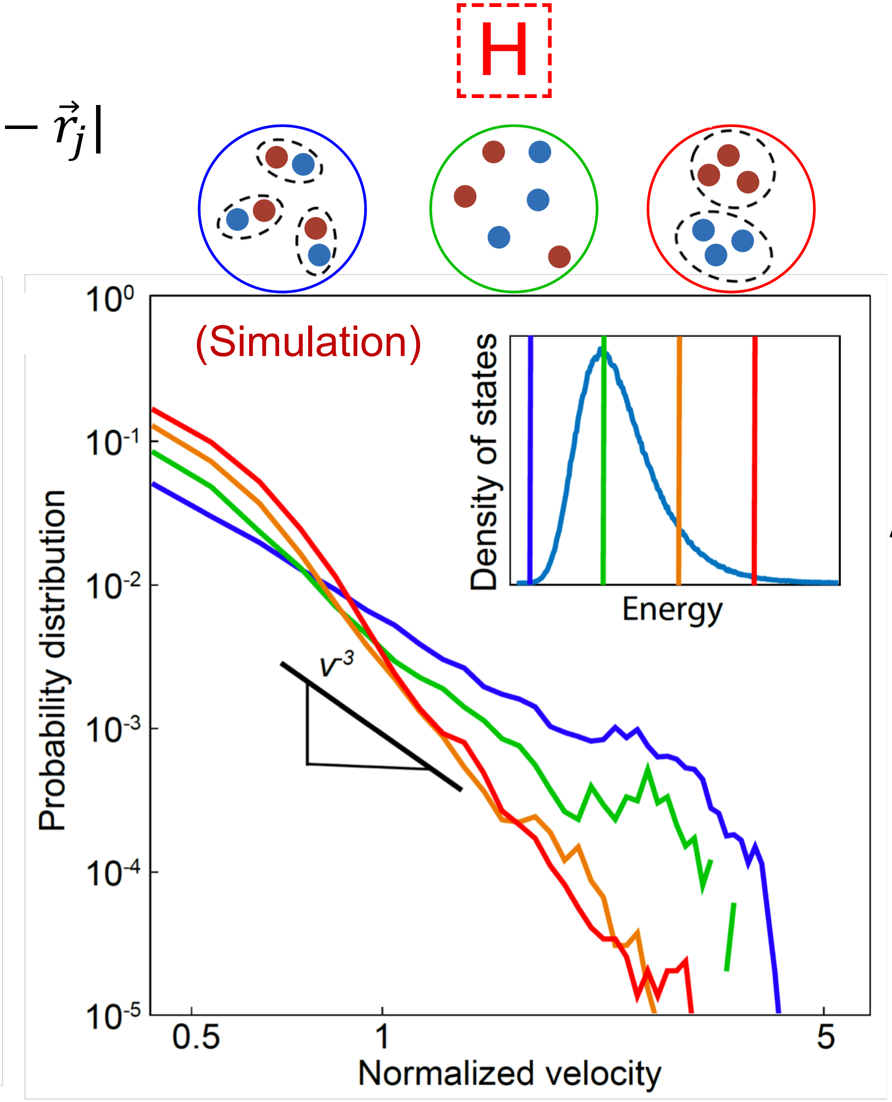




In vivo Rho-GTP waves can be understood in terms of generic 2D vortex-vortex interaction at criticality

Point-vortex model: $H = -\frac{1}{2\pi}\sum_{i,j} I_i I_j \ln|\vec{r}_i - \vec{r}_j|$



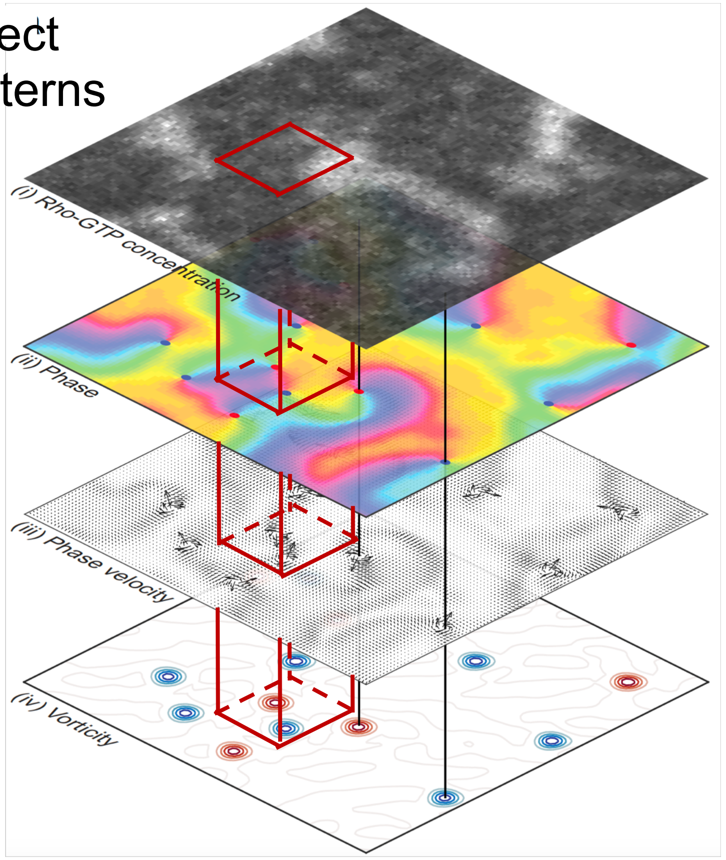


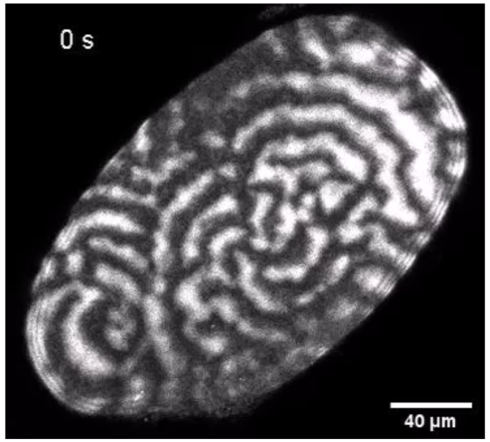
Interpretation:
At criticality, model vortices are randomly distributed over domain.

Consistent scaling suggest absence of effective independence of spirals

Conclusion: What are the takeaways?

- Our analysis revealed a class of topological defect dynamics underlying *in vivo* Rho-GTP wave patterns

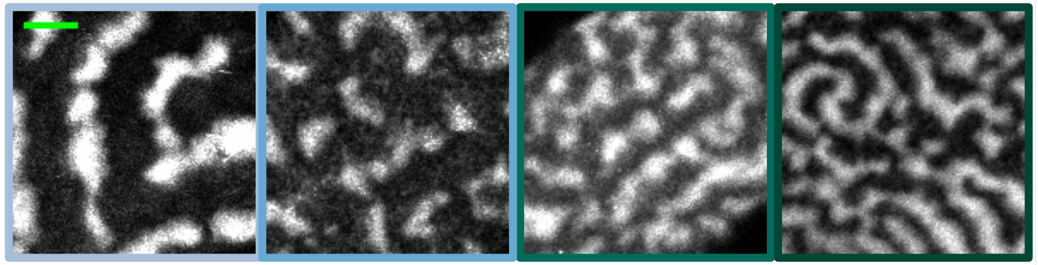


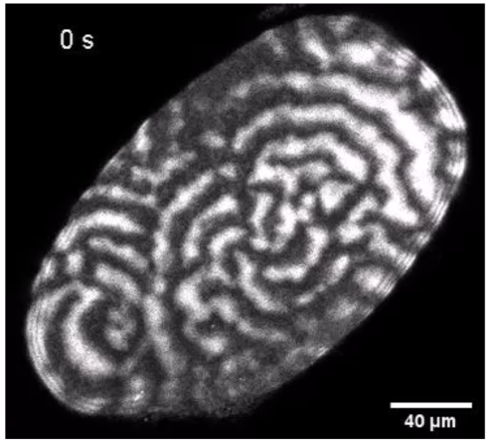


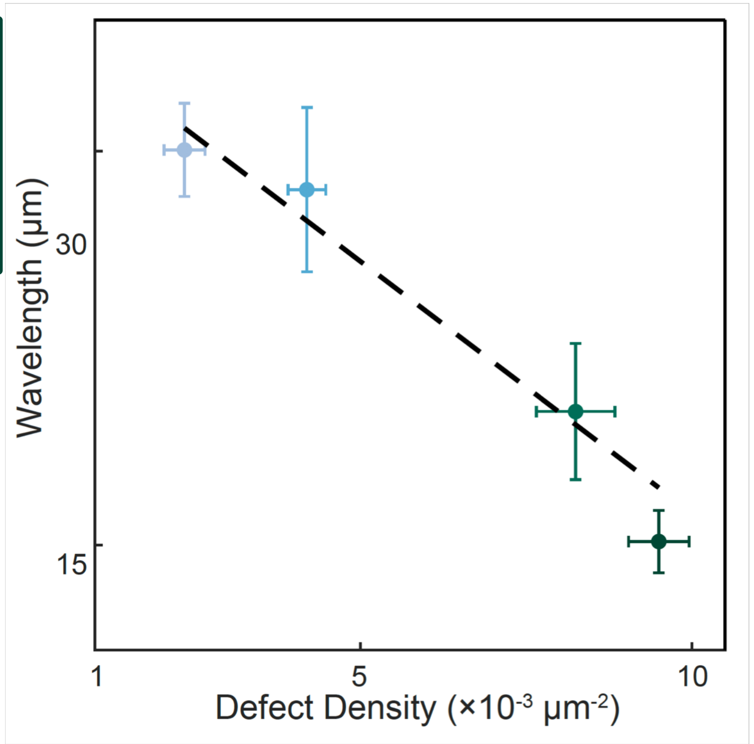
Conclusion: What are the takeaways?

- Our analysis revealed a class of topological turbulence underlying *in vivo* Rho-GTP wave patterns

- Rho-GTP waves are tuned to different "states" in phase space when varying GEF level

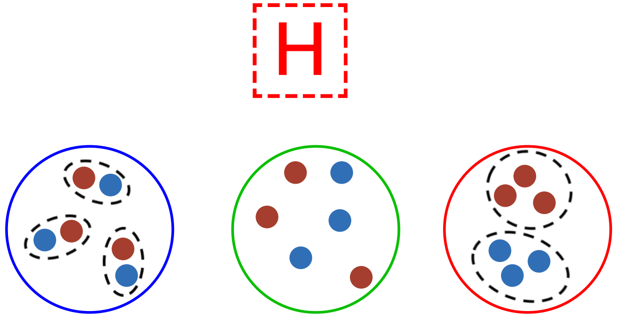


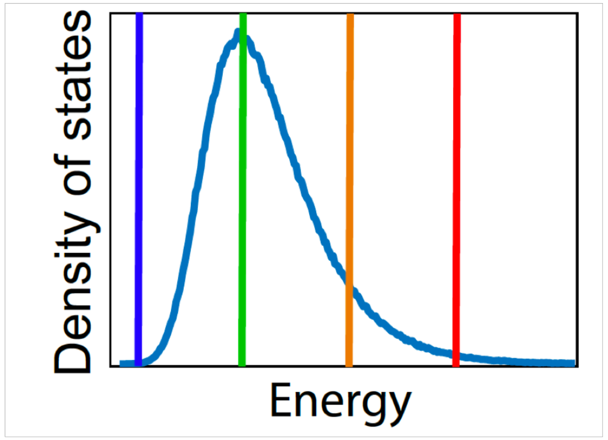




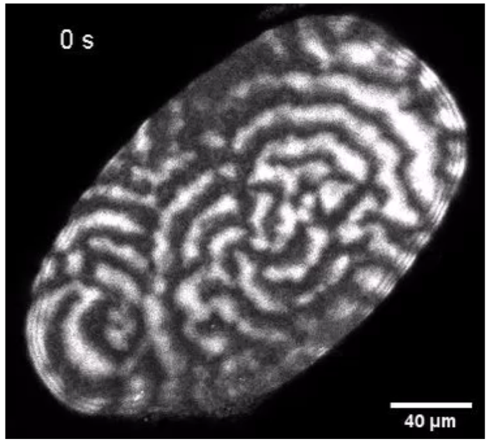
Conclusion: What are the takeaways?

- Our analysis revealed a class of topological turbulence underlying *in vivo* Rho-GTP wave patterns
- Rho-GTP waves are tuned to different “states” in phase space when varying GEF level
- Minimal model suggests a near-critical organization for *in vivo* membrane waves





$$H = -\frac{1}{2\pi}\sum_{i,j} I_i I_j \ln|\vec{r}_i - \vec{r}_j|$$

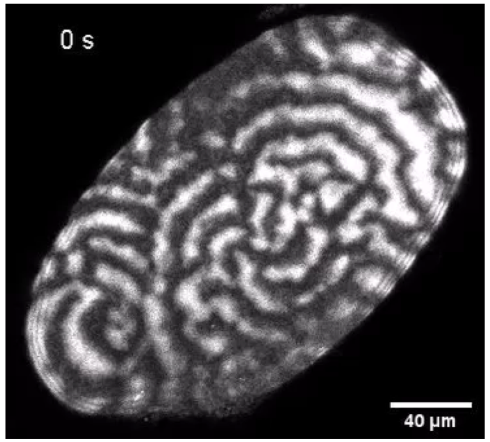


Conclusion: What are the takeaways?

- Our analysis revealed a class of topological turbulence

Future Directions:

- Effects of non-uniform geometry on wave patterns?
- Active deformation: is there chemo-mechanical feedback?
- Continuum models: can we derive observed scaling behavior?



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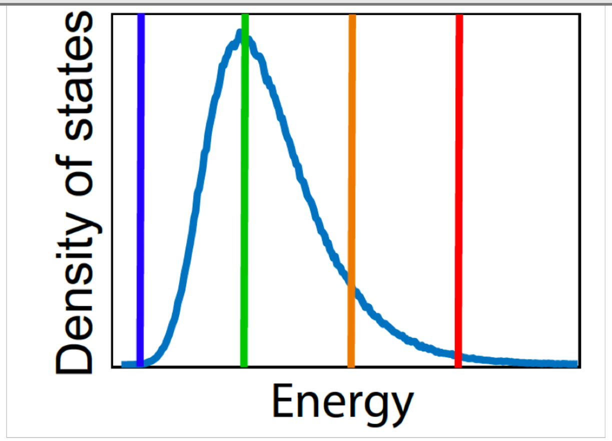
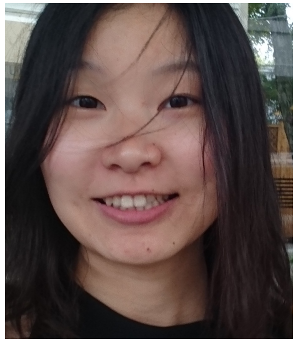


Acknowledgements

Tzer Han Tan



Jinghui Liu

Melis Tekant

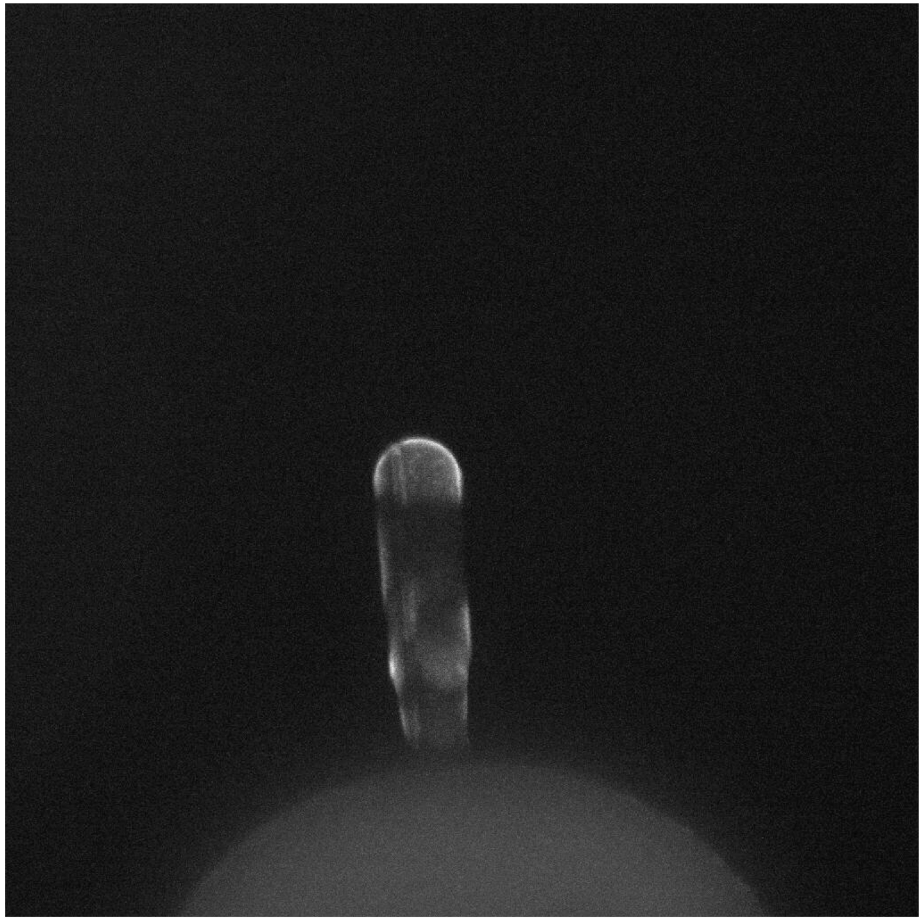
Prof. Jörn Dunkel

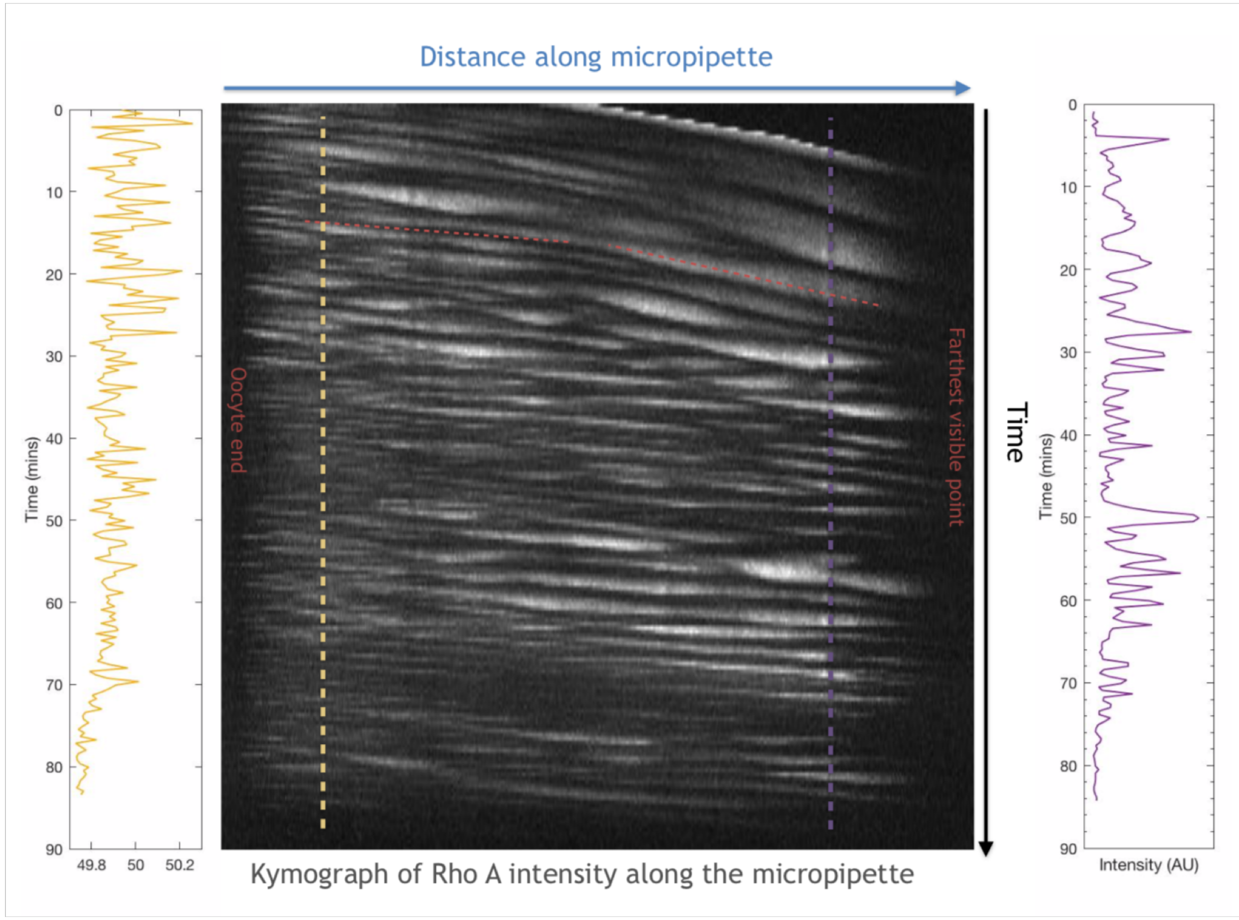
Prof. Nikta Fakhri

Please send us feedback!

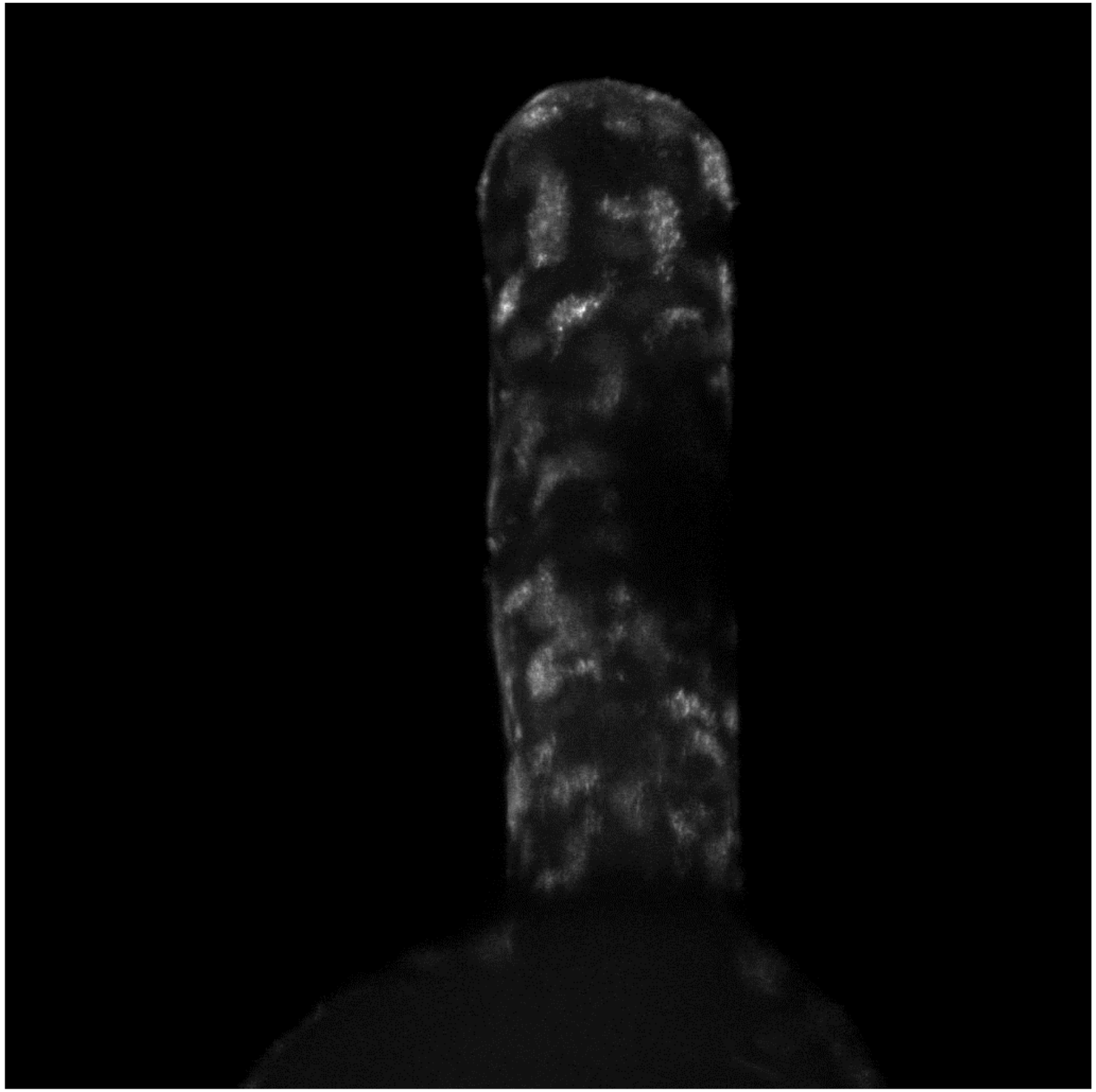
TH Tan[1], J Liu[1], PW Miller[1], M Tekant, J Dunkel[*], N Fakhri[*] 2019. (Submitted)

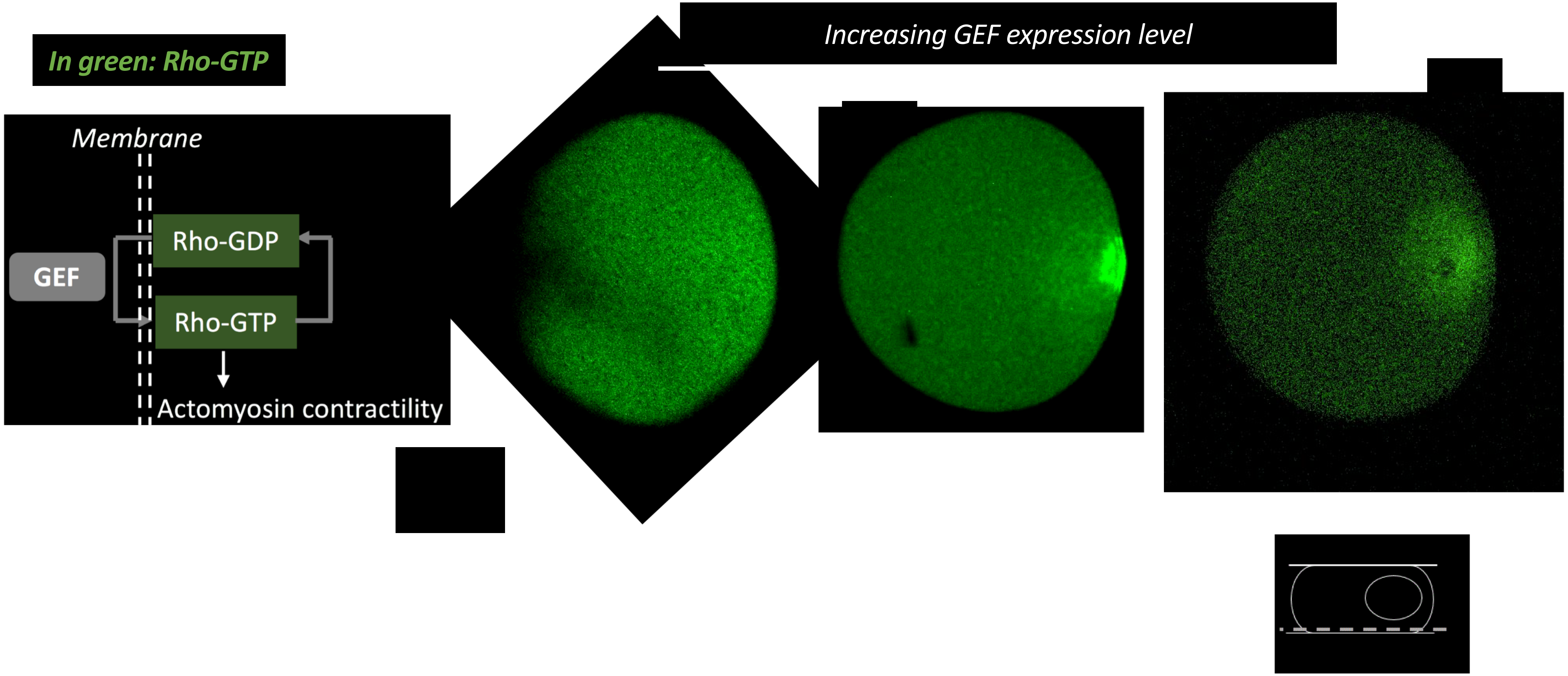
Spiral Waves on a Changing Domain

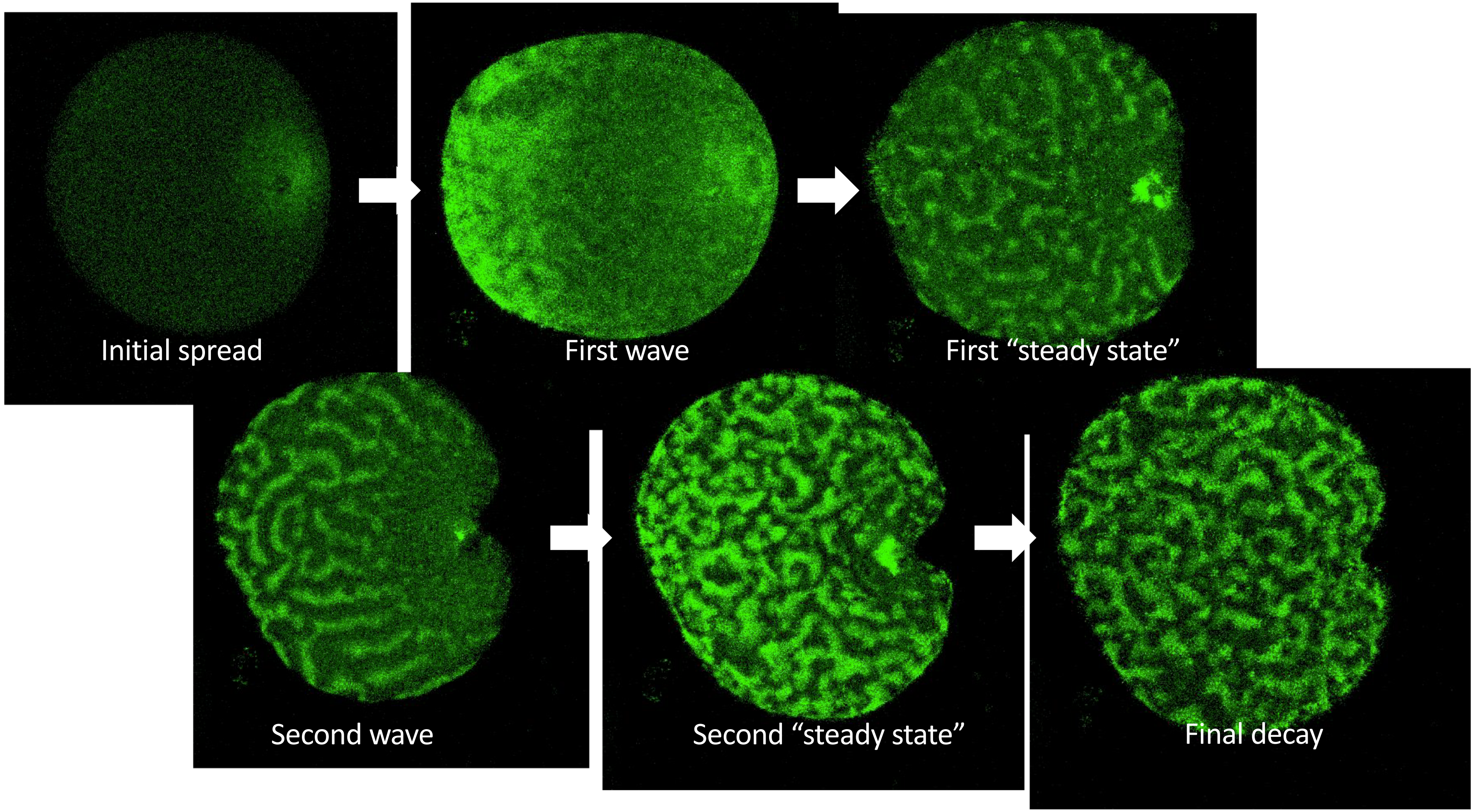


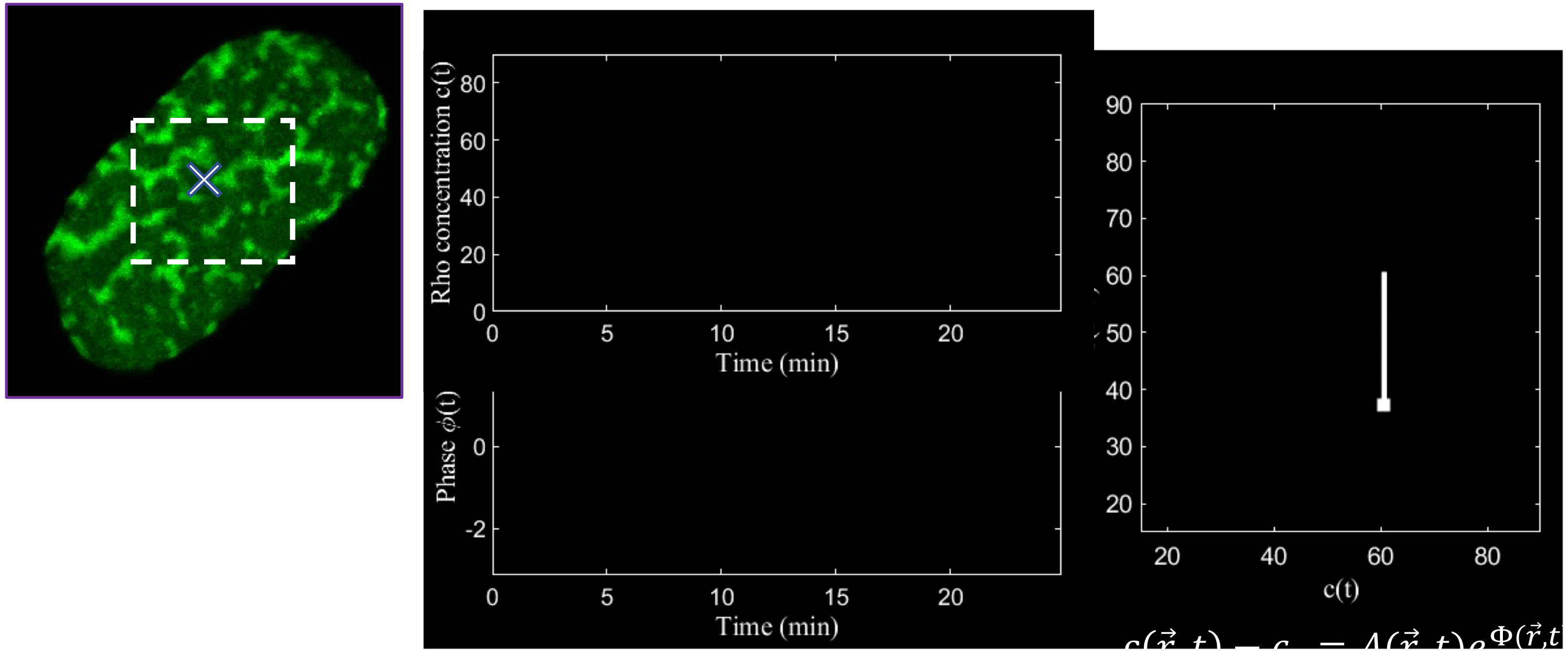


Spiral Waves on a Changing Domain




In green: Rho-GTP
Membrane
GEF
Rho-GDP
Rho-GTP
Actomyosin contractility
Increasing GEF expression level


Initial spread
First wave
First "steady state"
Second wave
Second "steady state"
Final decay



Rho concentration c(t)
Time (min)
Phase $\phi(t)$
Time (min)
c(t)