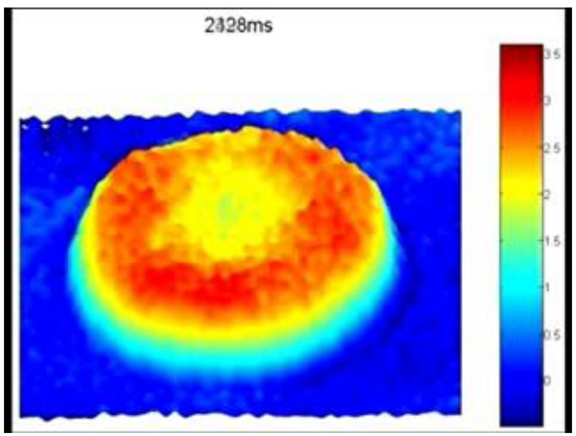
KITP, Santa-Barbara
June 21, 2011

Effective Temperature of Active systems: Red Blood Cell Membrane Fluctuations



Nir Gov

WEIZMANN INSTITUTE OF SCIENCE

FACULTY OF CHEMISTRY
CHEMICAL PHYSICS Department

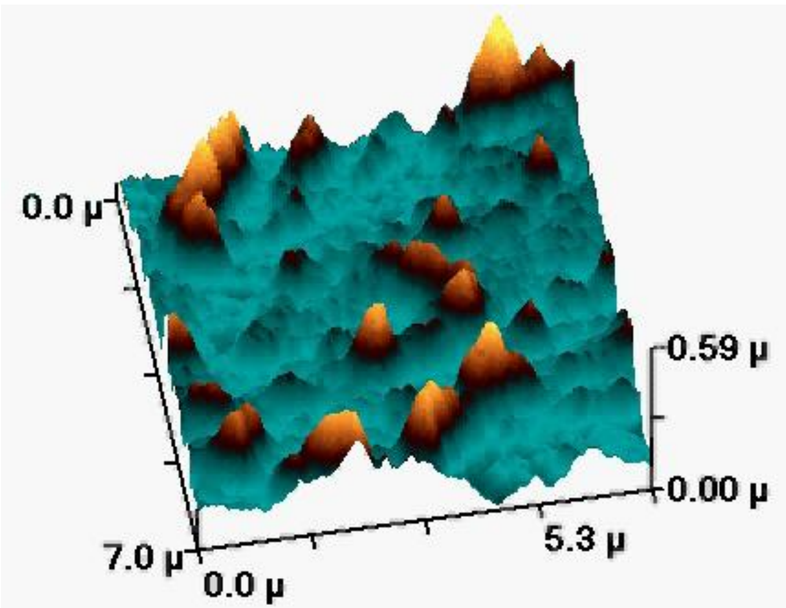
Outline:

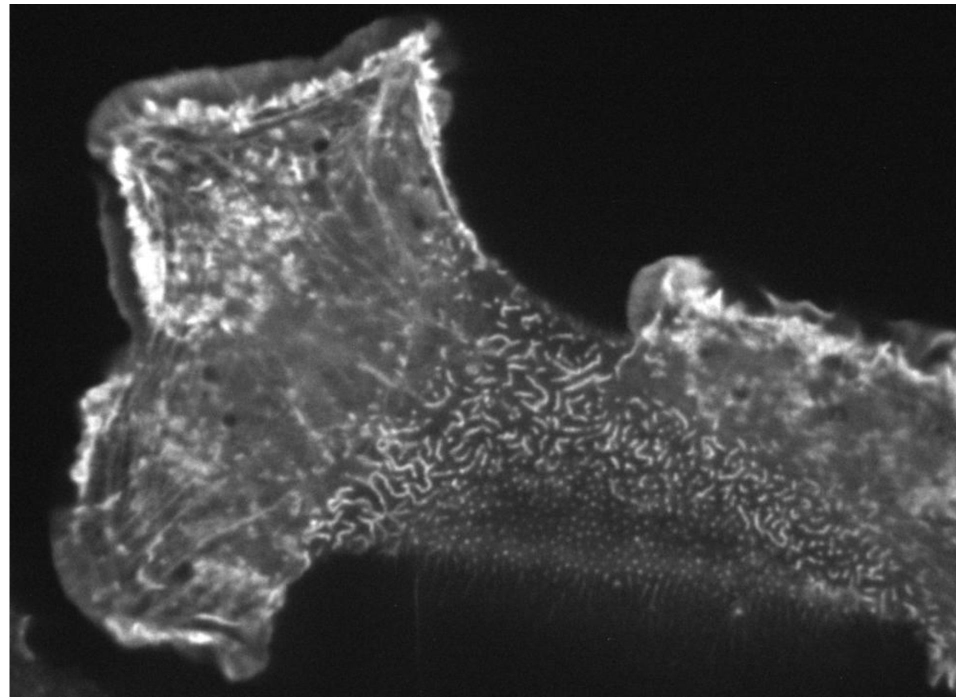
- Motivation: using “effective temperature” in an “active”-thermodynamics scheme to describe patterns in biological systems.

- Red-blood cell: recent experiments showing non-thermal nature of the fluctuations.
- Comparing to a simple quantitative model.

- Actin-driven membrane clusters.

Motivation:





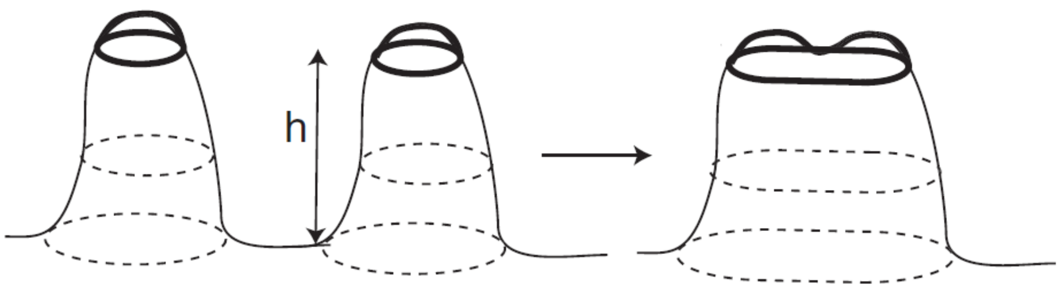
Active Microvilli on the upper surface of cells
(Movie curtsey of Bechara Kachar)

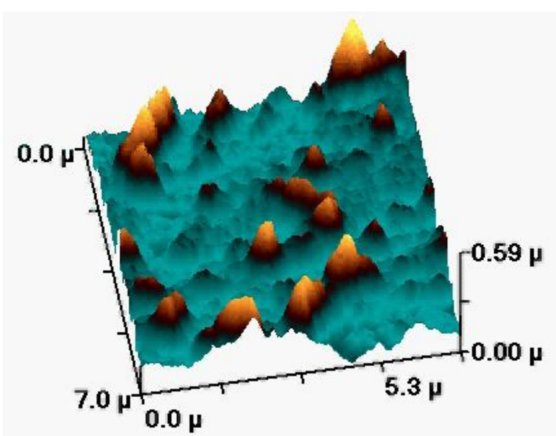
Our treatment of this system in terms of “thermodynamic” phase transitions driven by “effective temperature”:

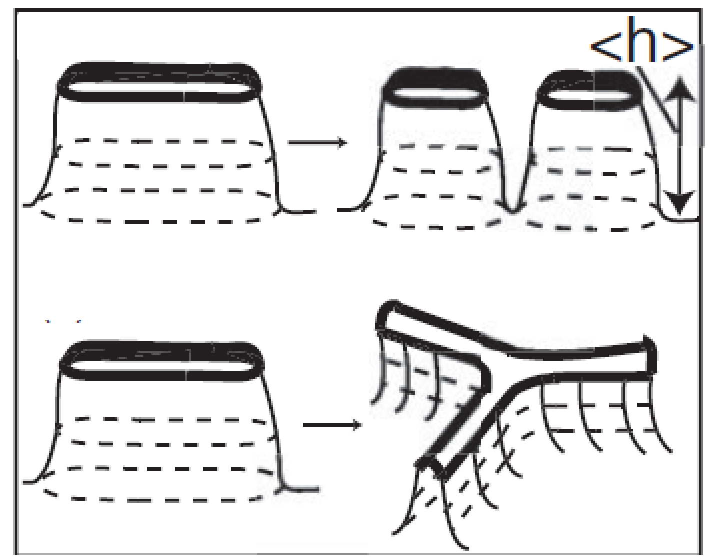
PRL **97,** 018101 (2006) PHYSICAL REVIEW LETTERS week ending 7 JULY 2006

Dynamics and Morphology of Microvilli Driven by Actin Polymerization

Nir S. Gov



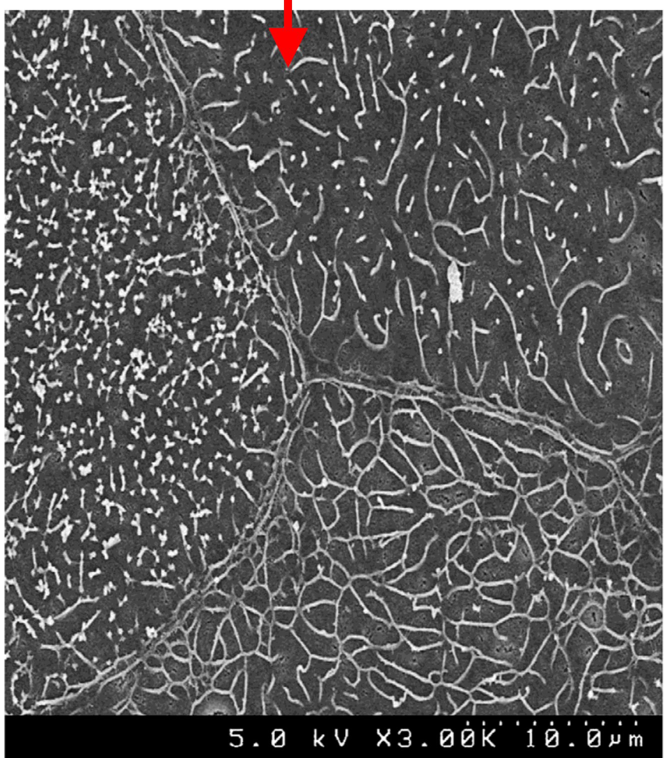


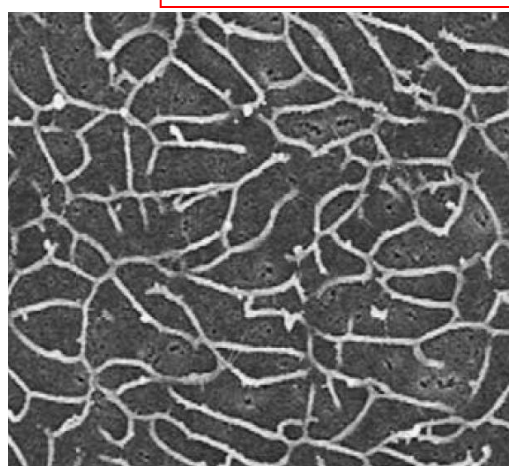


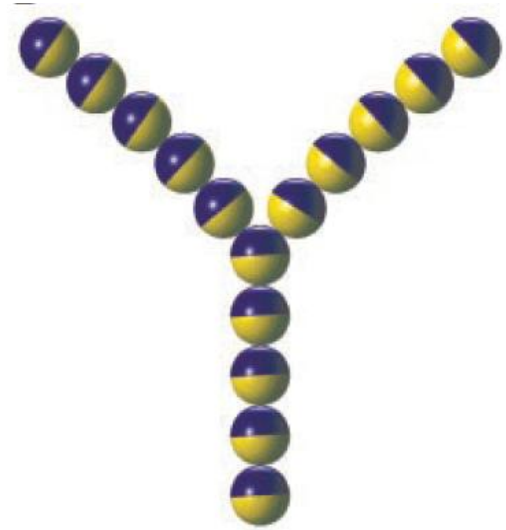
J. Gorelik *et al.*, Proc. Natl. Acad. Sci. U.S.A. **100**, 5819 (2003).
J. Gorelik *et al.*, Molec. Cell. Endocrin. **217**, 101 (2004).

Microvilli: Spatial distribution/patterns

- Linear aggregates due to positive spontaneous curvature of tip complex







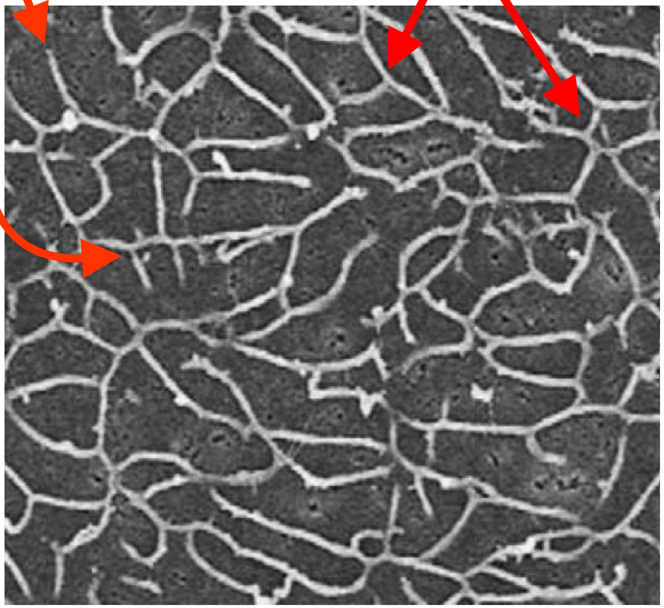
T. Tlusty & S. Safran; Science <u>290</u> (2000) 1328

2D dipolar fluid, network of worm-like micelles etc.

Zilman, A; Safran, S.A.; Sottmann, T.; Strey, R.; *Langmuir,* **20** 2199 (2004).

Microvilli: Spatial distribution/patterns

- Assume single height of MV: <h>
- Excluded volume interactions
- Defects: free ends and 3-fold junctions



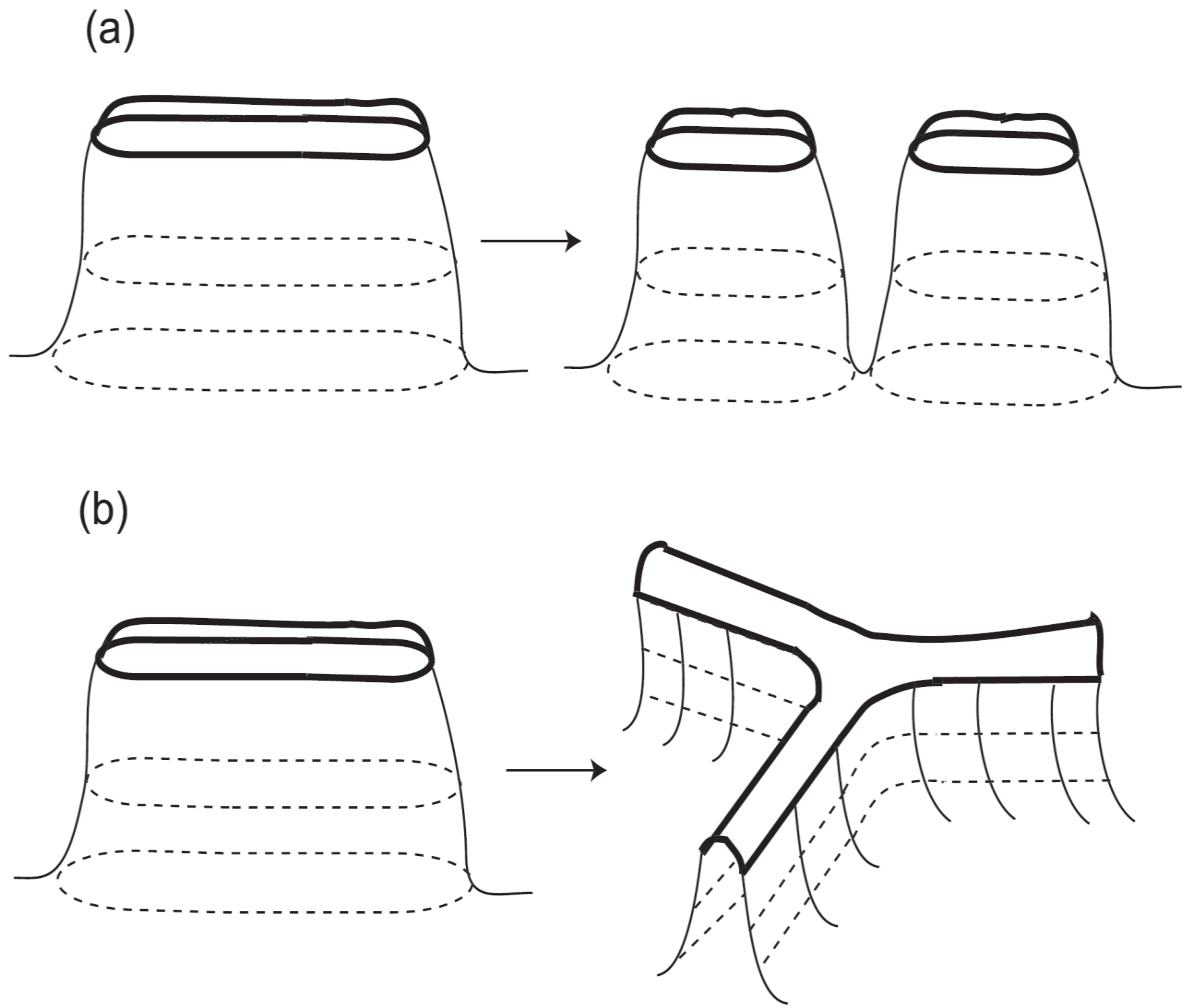
Microvilli: Energy of defects

$$E_{end} \approx \frac{2\pi\kappa h}{R} - \frac{\pi\kappa}{8}$$

Increases with *h*

$$E_{junct} \approx \frac{\pi\kappa h}{6R} + \frac{2\pi\kappa}{15}$$

Increases more slowly with *h*



Free energy of gas of defects

$$F(\phi)/k_B T_{eff} = (1-\phi)\ln(1-\phi) + \phi_e(\ln\phi_e - 1) + \phi_j(\ln\phi_j - 1)$$
$$+ \phi_e\epsilon_e + \phi_j\epsilon_j - \frac{1}{2}\phi_e\ln\phi - \frac{3}{2}\phi_j\ln\phi$$

ϕ is the area fraction of the MV.

ϕ_e, ϕ_j *are the area fraction of the ends and 3-fold junctions respectively.*

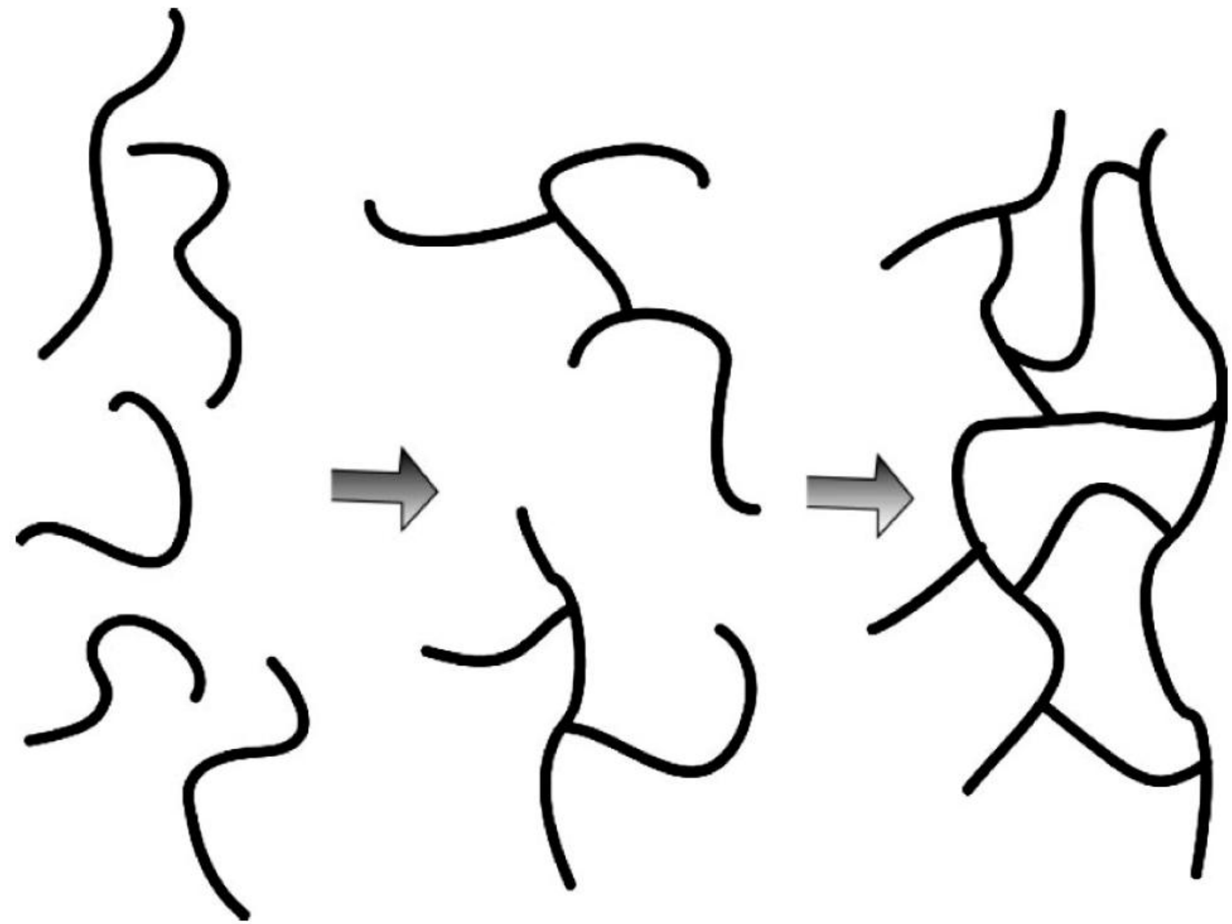
Minimize with respect to independent defects' concentrations:

$$\phi_j = \phi^{3/2} e^{-\epsilon_j}$$

$$\phi_e = \phi^{1/2} e^{-\epsilon_e}$$

Formation of networks

If the MV height increases, junctions multiply over ends:



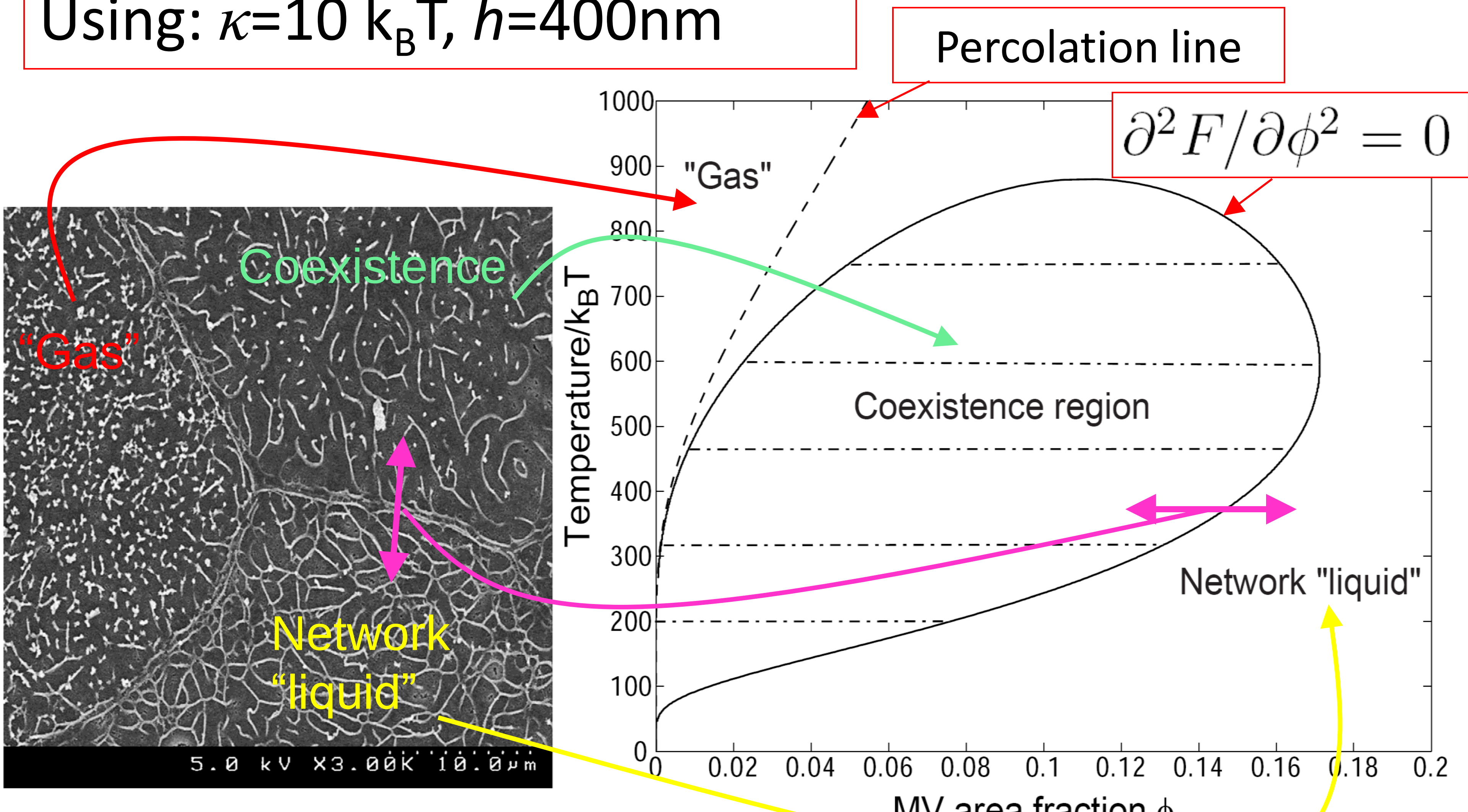
Phase transition to a connected network:

$$\partial^2 F/\partial\phi^2 = 0$$

Spinodal

Microvilli: Spatial distribution/patterns

Using: κ=10 k_BT, h=400nm

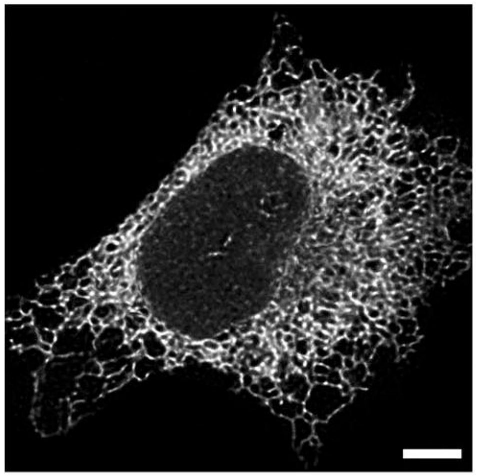


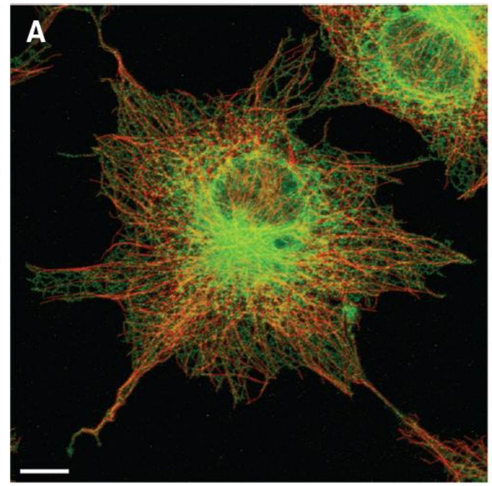
Note the large "effective temperature"

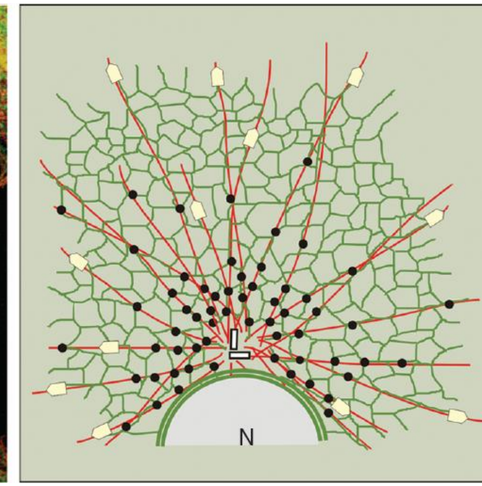
Motivation: Dynamic morphology of motor-driven membrane tubules (ER, golgi)

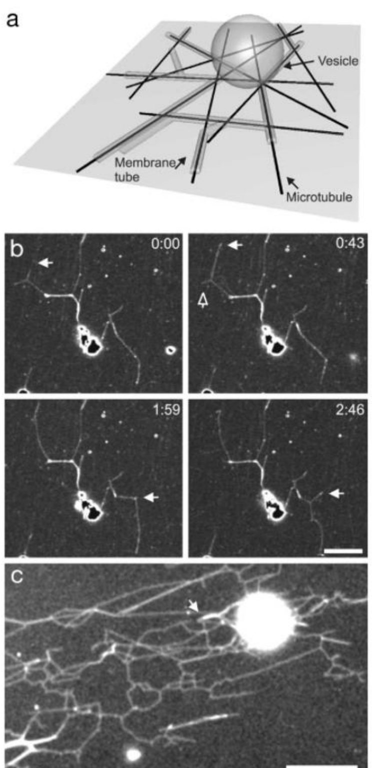
In-vivo:

Vedrenne 2006; Jokitalo 2007



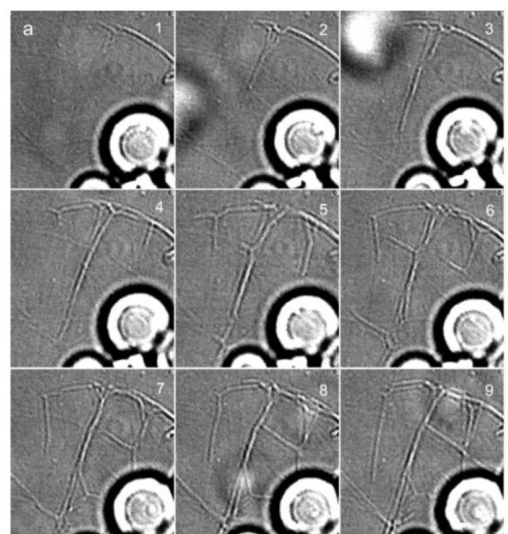


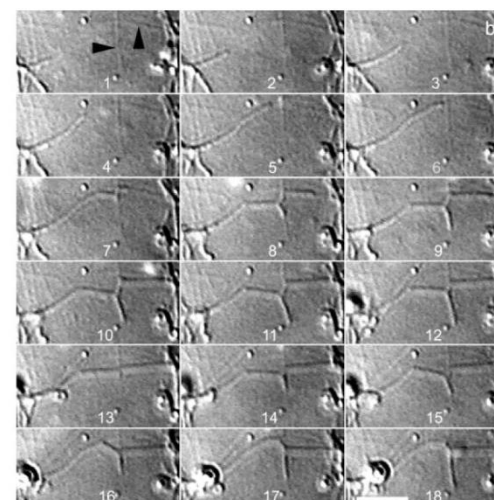




In-vitro:

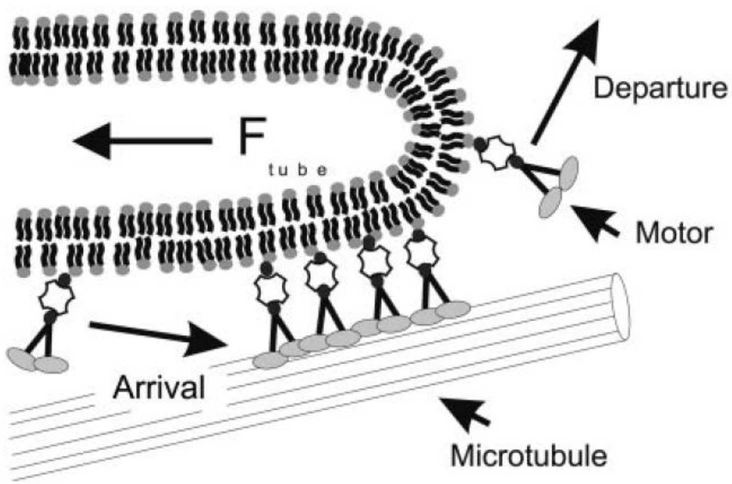
Bassereau 2002,2004; **Dogterom**, 2003

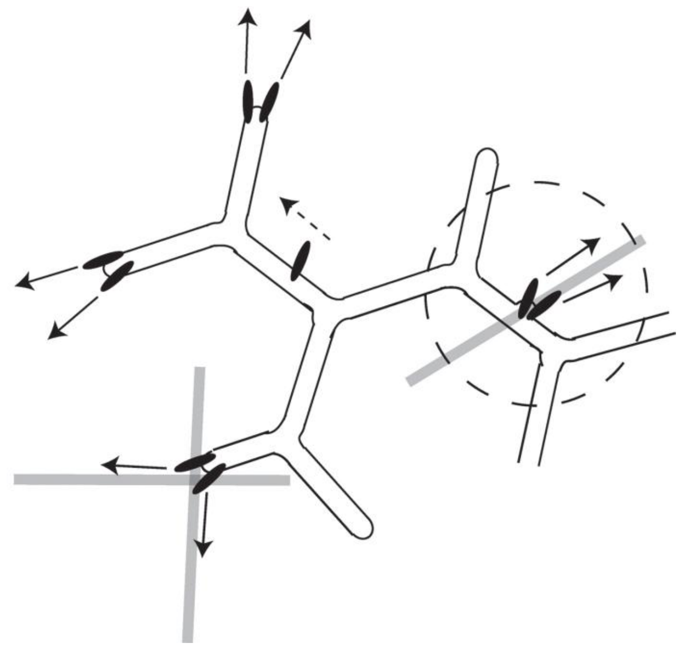




Our model: network phase transitions with “hotter” tips

Motors accumulate at the tubules tips→ Higher effective temperature





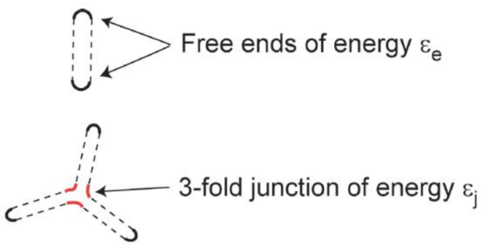
Motors pull the tubules tips→ random motion on the background network of MTs

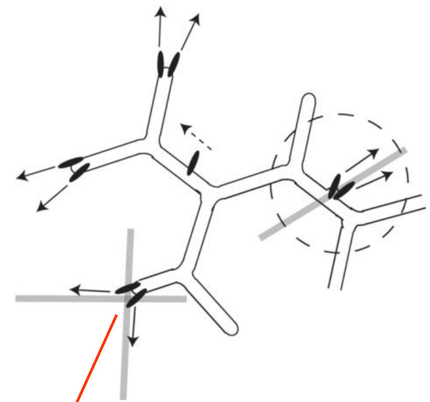
PAPER www.rsc.org/softmatter | Soft Matter

Phases of membrane tubules pulled by molecular motors†

N. S. Gov* ***Soft Matter***, (2009) **5**, 2431-2437

Our model: network phase transitions with “hotter” tips





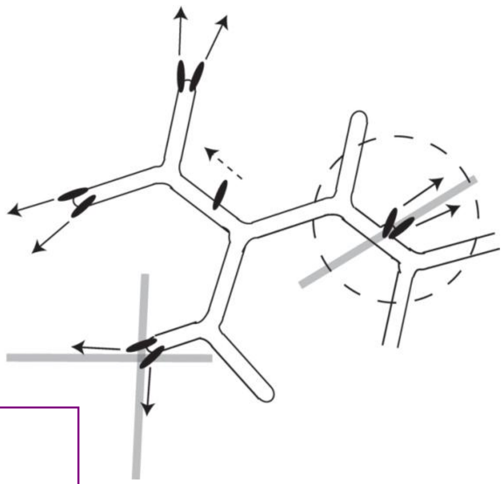
$$\tilde{F}(\phi)/k_BT = (1-\phi)\ln(1-\phi) + T_e\phi_e(\ln\phi_e - 1) + \phi_j(\ln\phi_j - 1) + \phi_e\varepsilon_e + \phi_j\varepsilon_j - \tfrac{1}{2}\phi_e\ln\phi - \tfrac{3}{2}\,\phi_j\ln\phi$$

- **Activity is limited to just one specie (structure).**
- **Different “effective temperatures” in different parts of the network.**
- **Do not equilibrate.**

The “effective temperature” depends on the number of motors:

$$T_e \propto \langle v^2 \rangle \propto \left(1 - \frac{F_0}{F_m}\right)^2$$

$$F_m = F_s n_b$$

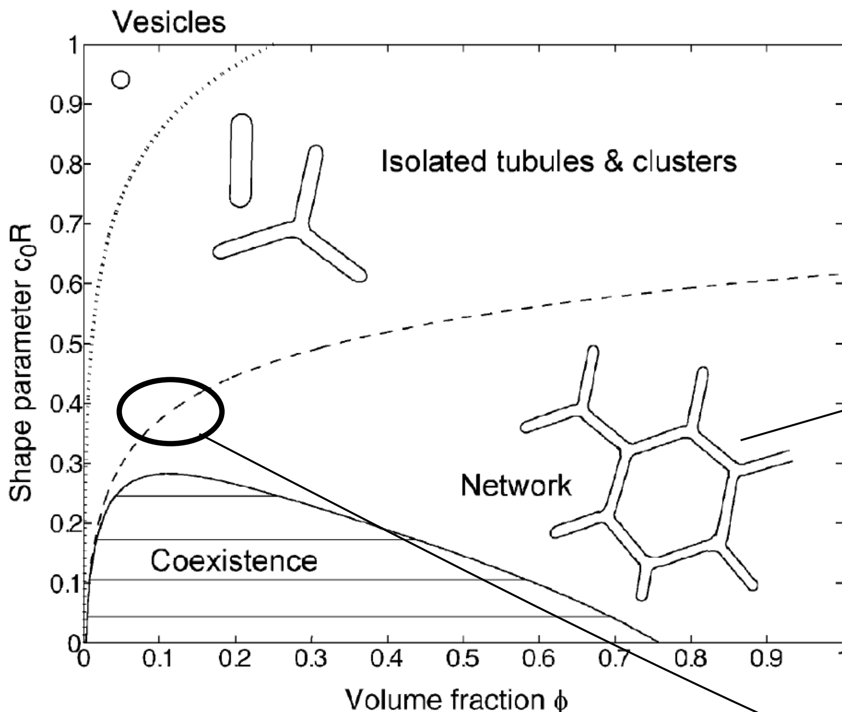


F_s is the stall force of each motor
n_b is the average number of motors at the tips

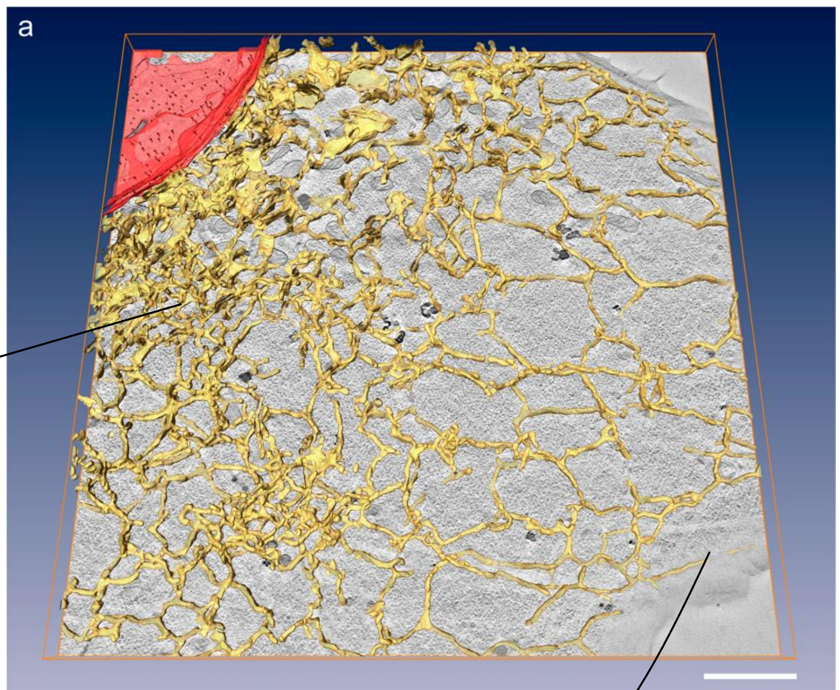
We can treat two cases:

- Constant n_b and T_e (saturation of motors).
- Average number of motors gets diluted as a function of the density of ends.

Our model: network phase transitions with “hotter” tips

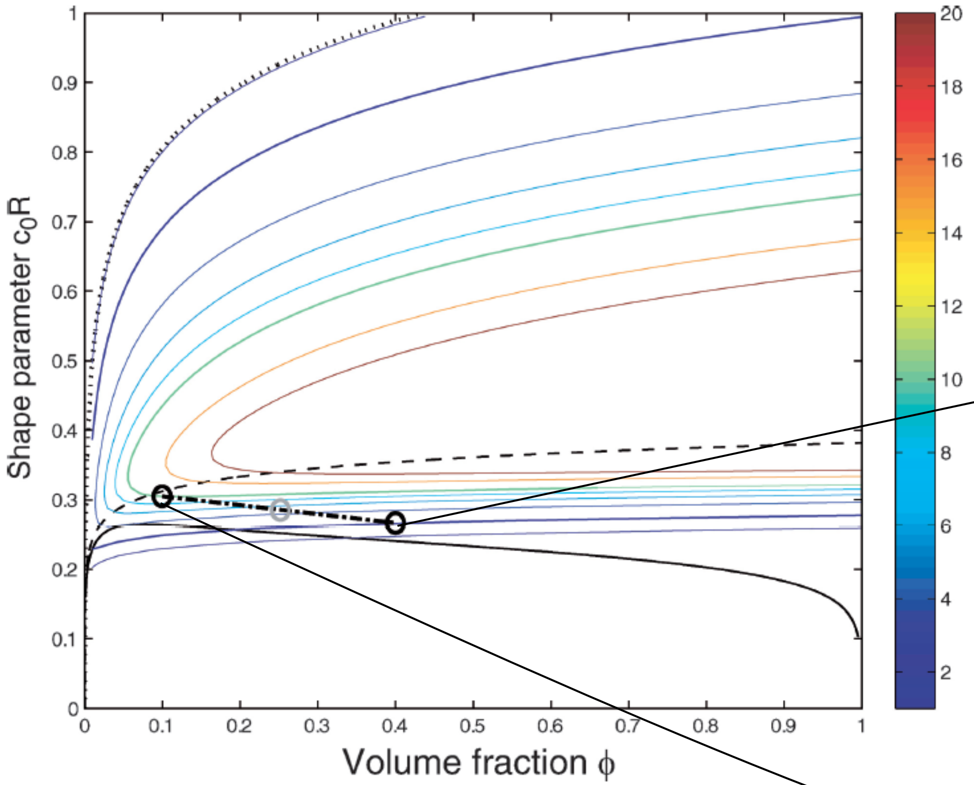


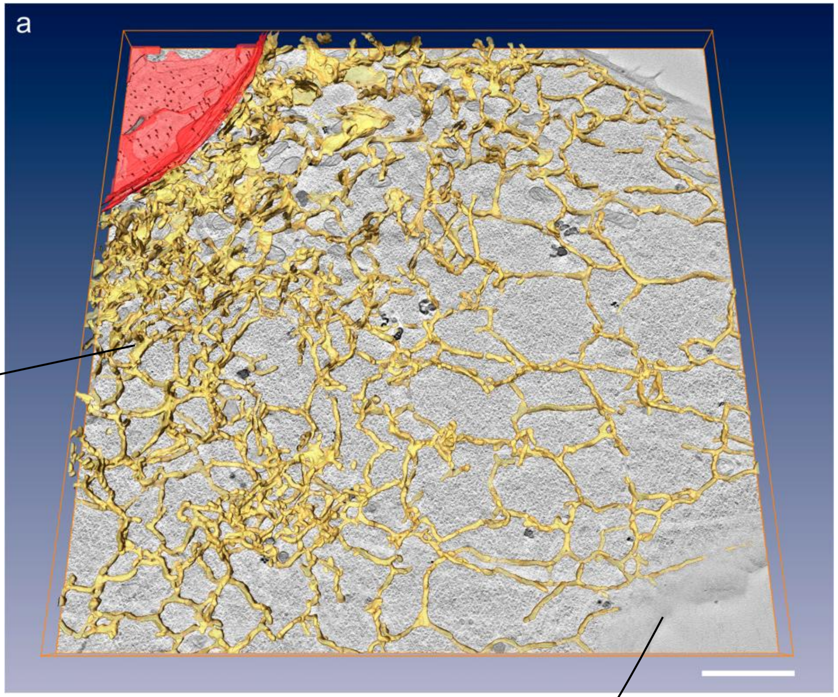
M. Puhka, H. Vihinen, M. Joensuu and E. Jokitalo, *J. Cell Biol.*, 2007, **179**, 895.



Comparing to observations:

Mean segment length: $\frac{\bar{L}}{R} = \frac{\phi}{\frac{1}{2}(\phi_e + 3\phi_j)}$ $R \approx 50\ \text{nm}$





$T_{eff} \sim 3k_BT$

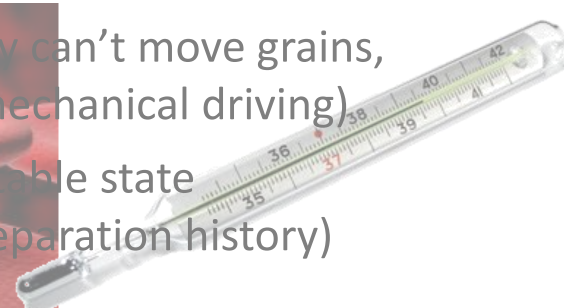
Can effective temperature describe non-equilibrium steady state ?

Live matter:

Molecular motors consume ATP and generate fluctuations that can be much larger than thermal fluctuations

→ far from thermodynamic equilibrium

Dead non-equilibrium systems:

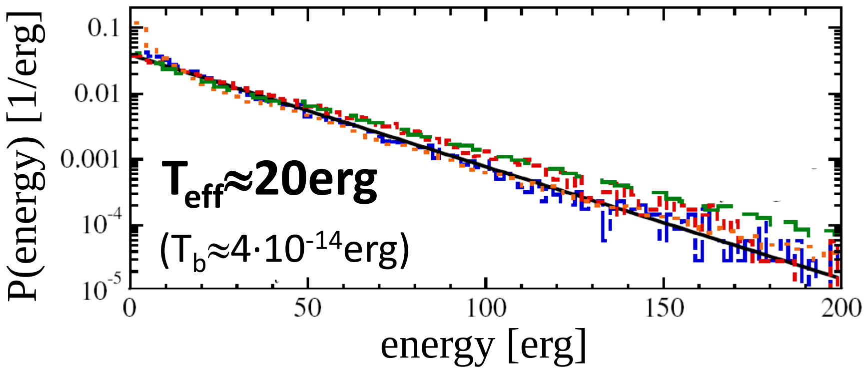


- Granular (thermal energy can't move grains, usually have mechanical driving)
- Glass (jammed in metastable state reminiscent of preparation history)
- And many more…

Fluctuations are **not thermal**, but are there situations in which they are **thermal-like**? (=equivalent to those of some elevated effective temperature)

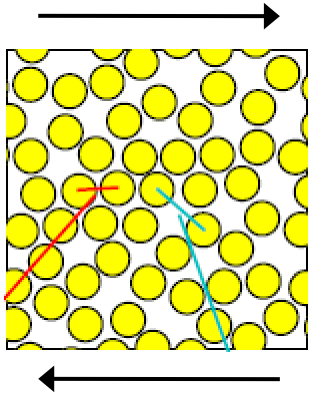
Thermal-Like (1): $P(E) \approx \exp(-E/T_{eff})$

Air fluidized ping-pong balls
(model for granular matter)

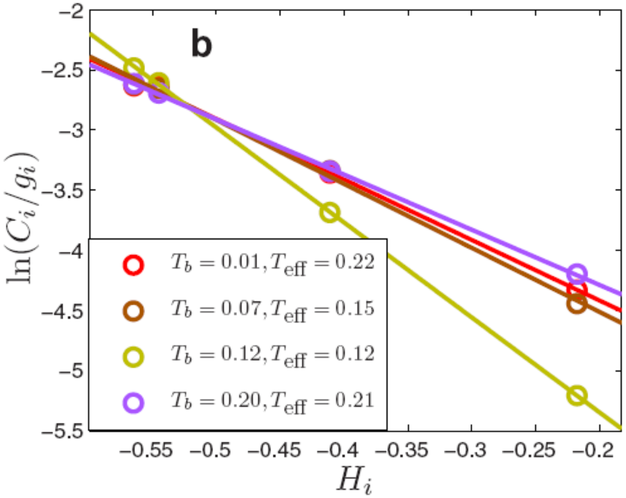


Abate & Durian (2008)

Sheared amorphous solid



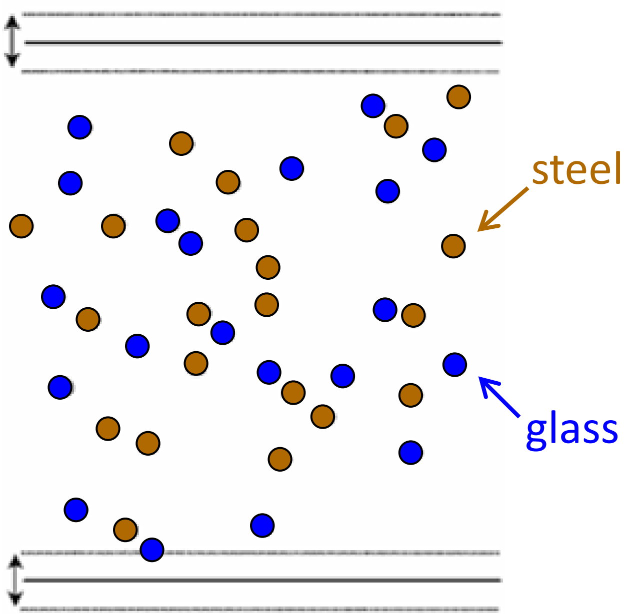
concentration of quasispecies:



Boue, Hentschel, Procaccia, Regev, Zylberg (2010)

Thermal-Like (2): T_{eff} equilibrates at contact ?

Vertically shaken box of grains



$\langle E_{steel} \rangle > \langle E_{glass} \rangle$

<E> not useful as effective temperature

Feitosa & Menon (2002)

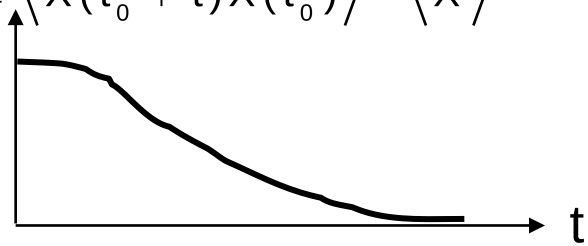
But sometimes can identify operational temperature that controls direction of energy flow and eventually equilibrates

Shokef, Shulkind, Levine (2007)

Thermal-Like (3): Fluctuation-Dissipation Relations

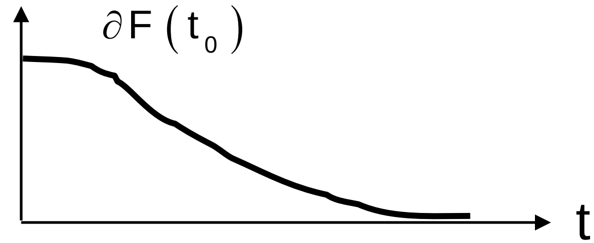
Correlation (fluctuation):

$$C(t) \equiv \langle X(t_0 + t) X(t_0) \rangle - \langle X \rangle^2$$



Response (dissipation):

$$R(t) \equiv \frac{\partial \langle X(t_0 + t) \rangle}{\partial F(t_0)}$$



- Equilibrium: Correlation = Temperature x Response

Callen & Welton (1951)

- Far from equilibrium:

  - Define $\mathbf{T}_{\mathbf{eff}} = \dfrac{\text{Correlation}}{\text{Response}}$

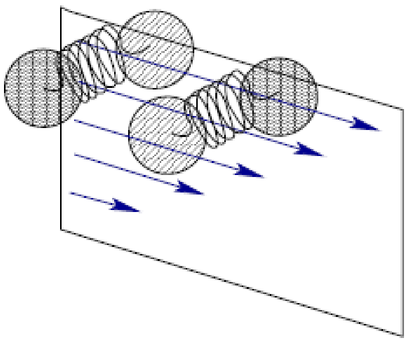
  - Does $\mathbf{T}_{\mathbf{eff}}$ depend on: observable **?** waiting time (measurement frequency) **?**

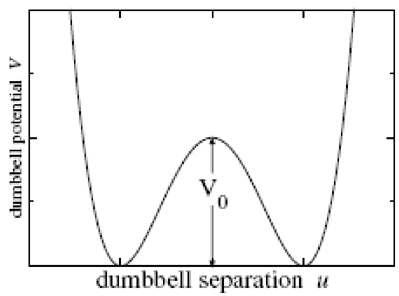
  - Is $\mathbf{T}_{\mathbf{eff}}$ related to other effective “temperatures” **?**

Cugliandolo, Kurchan, Peliti (1997)

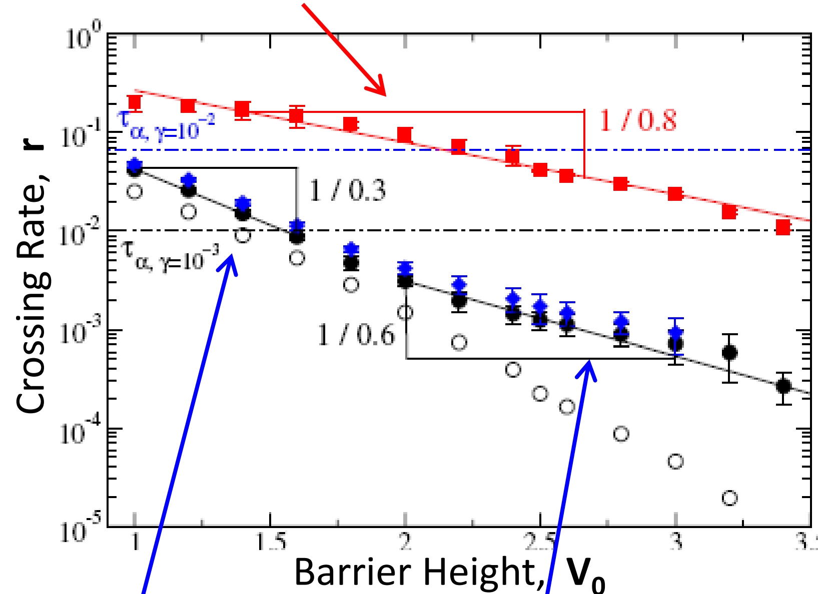
Thermal-Like (4): T_{eff} Determines Reaction Rates

Double-well dumbbell in sheared glassy fluid





T_B=0.8 Thermal: **r ∝ exp(-V_0/T_B)**



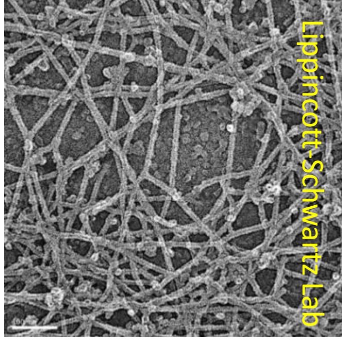
T_B=0.3 Glassy:

small V_0:
bath dominates:
r ∝ exp(-V_0/T_B)

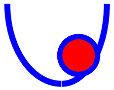
high V_0:
driving dominates:
r ∝ exp(-V_0/T_{eff}) , T_{eff}=0.6

(FD gives T_{eff}=0.65 ≈0.6)

Ilg & Barrat (2007)



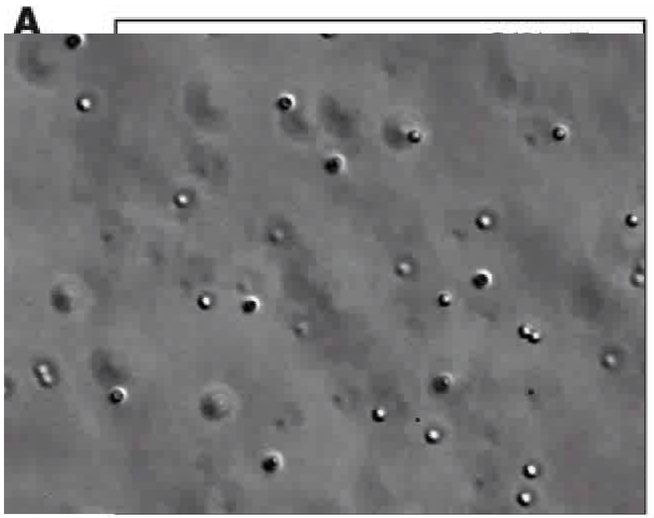
In Vitro Acto-Myosin Network

Micro-rheology (μm bead + optical tweezers): 

Passive: measure spontaneous fluctuations → power spectrum $C(\omega)$

Active: apply periodic force, measure resulting displacement → response function $\alpha(\omega)$

Only actin (thermal)



Beads hardly move

Fluctuation-dissipation theorem works: $\omega C(\omega) = 2k_B T\alpha''(\omega)$

6.8hr after introduction of myosin ("live")

Beads move much more

Enhanced fluctuations at low frequency: $C_{non\text{-}eq}(\omega) > 10x\ C_{eq}(\omega)$

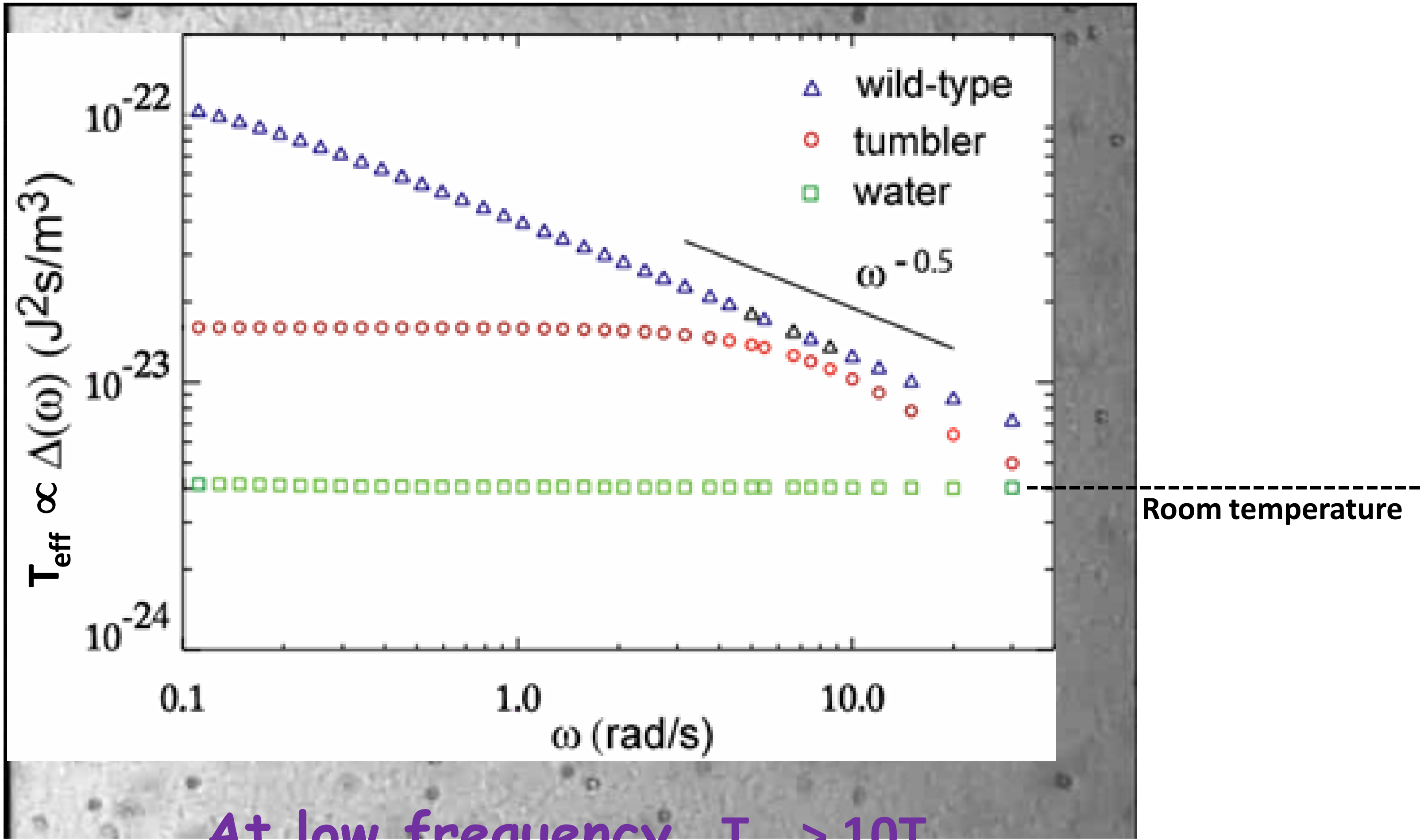
Response hardly effected:

$$\alpha_{non\text{-}eq}(\omega) \approx \alpha_{eq}(\omega)$$

Mizuno, Tardin, Schmidt, MacKintosh (2005)

Bacterial Bath

Two-point microrheology (~1μm beads) in solution with E. Coli (~3μm)



At low frequency, $T_{eff} > 10T_B$

Chen, Lau, Hough, Islam, Goulian, Lubensky, Yodh (2007)

Even Genes do it....

84 Biophysical Journal Volume 91 July 2006 84–94

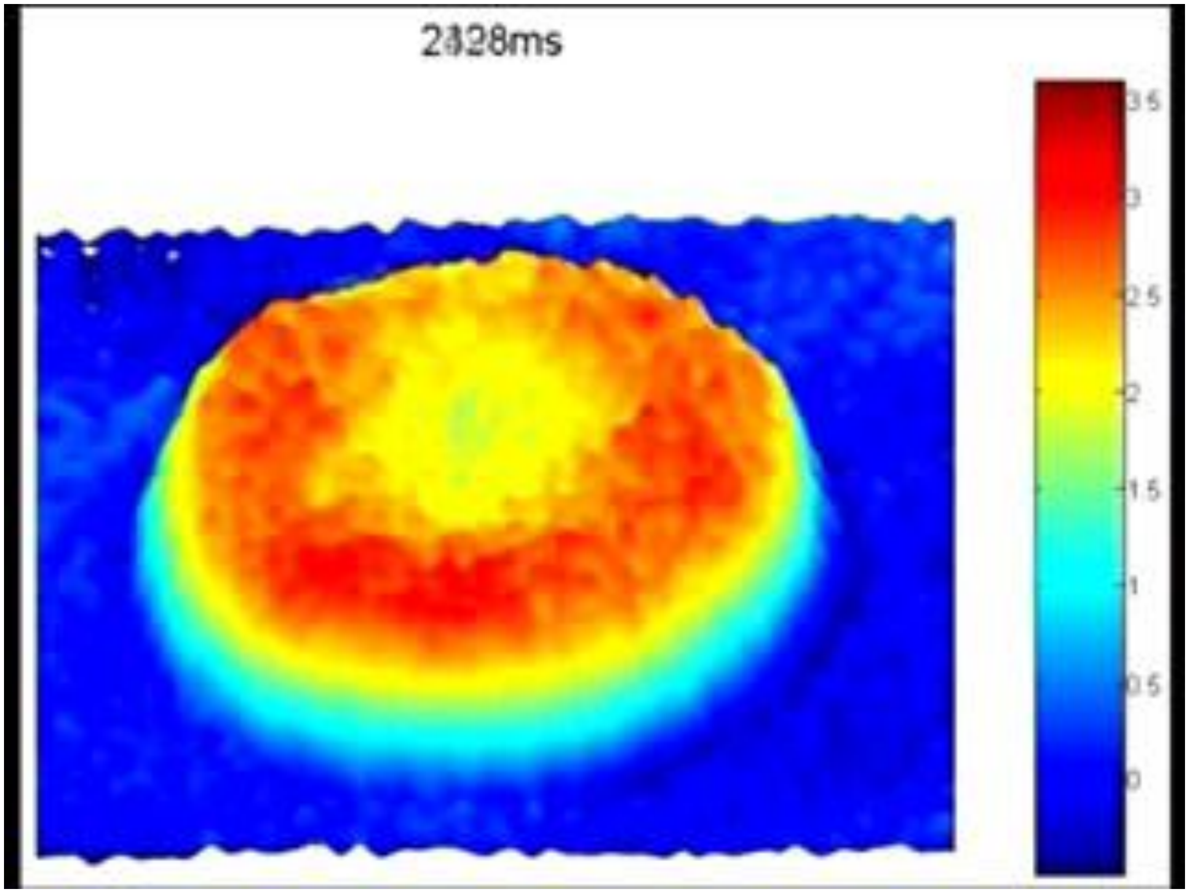
Effective Temperature in Stochastic Kinetics and Gene Networks

Ting Lu,[*§] Jeff Hasty,[†] and Peter G. Wolynes[*‡§]

...But lets get back to biological matter

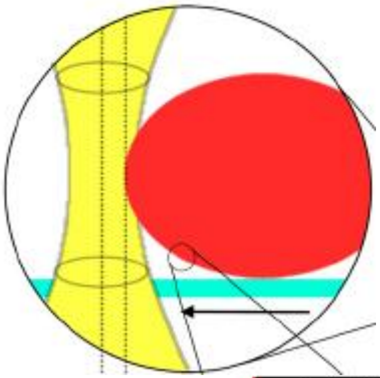
Red Blood Cell Membrane Fluctuations

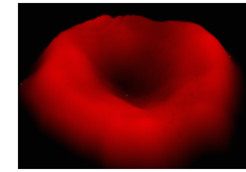
Cell Waltz:



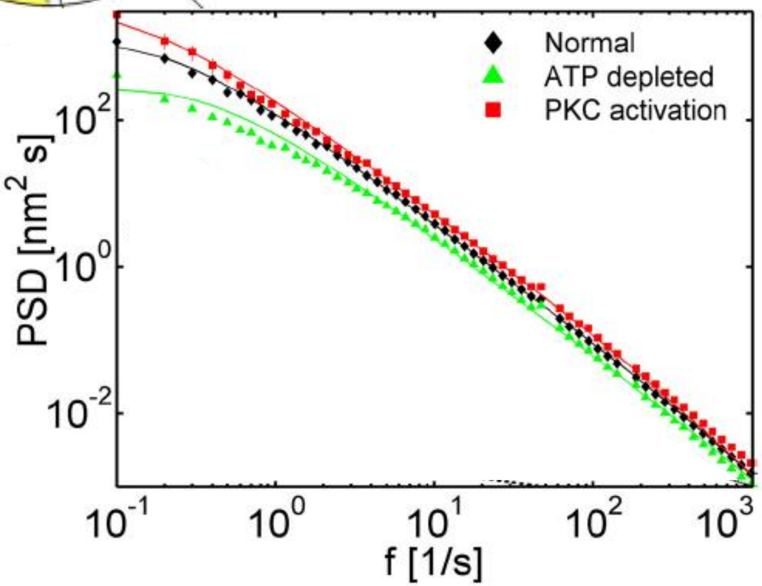
Gabriel Popescu
Quantitative Light Imaging Laboratory
University of Illinois at Urbana-Champaign
Department of Electrical and Computer Engineering
http://light.ece.illinois.edu/

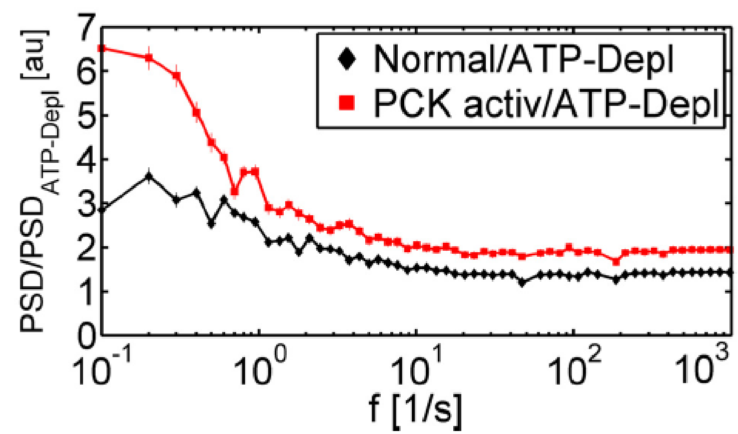
Red Blood Cell Edge Fluctuations: Recent experiments





Position: y(t) → Power spectrum: $PSD(\omega) = \int \langle y(t)y(0)\rangle e^{i\omega t}dt$

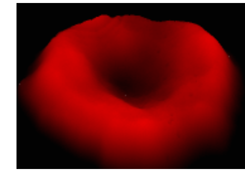




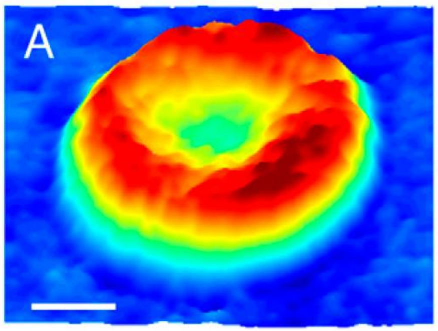
Fluctuations larger than thermal by 3(normal)-6(PKC activated), but cannot infer T_{eff} without response measurement…

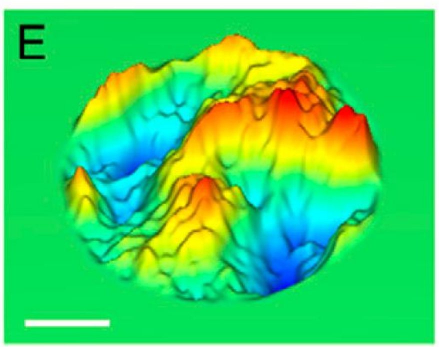
Betz, Lenz, Joanny, Sykes (2009)

Red Blood Cell Edge Fluctuations: Recent experiments

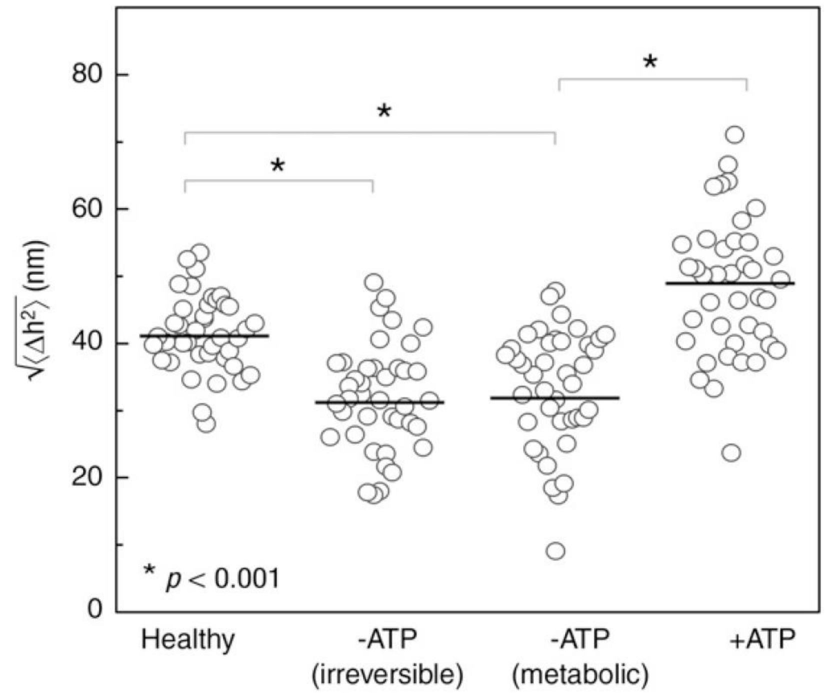


High resolution optical measurements of the membrane displacement field:





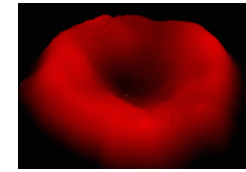
Amplitude of the displacement field depends on the ATP content:



But how do we know that they are non-thermal ?
(i.e. not due to changes to the elastic constants)

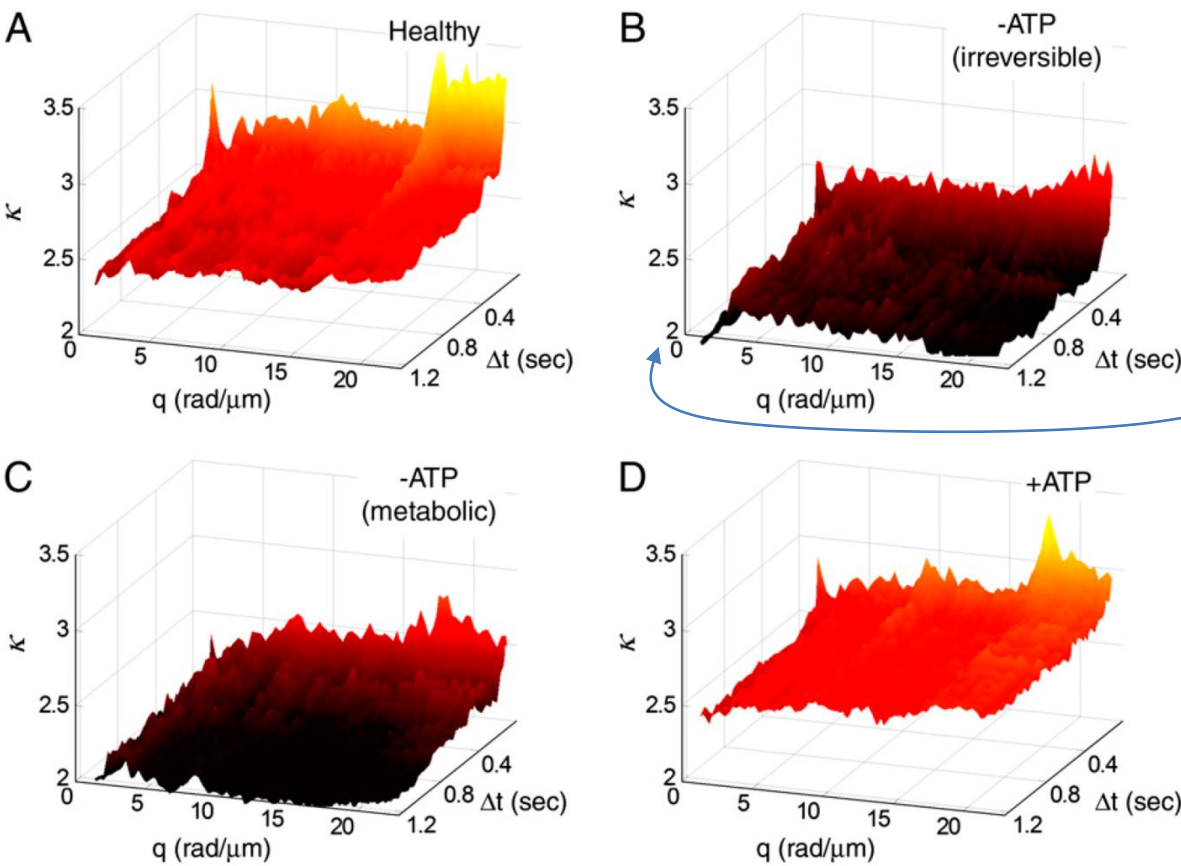
Park, Popescu et. al. (2010)

Red Blood Cell Edge Fluctuations: Recent experiments



Measure the Kurtosis, non-Gaussianity of the fluctuation distribution:

$$\kappa = \langle |h(q,\Delta t) - h(q,0)|^4 \rangle / \langle |h(q,\Delta t) - h(q,0)|^2 \rangle^2$$



For a (thermal) Gaussian: $\kappa=2$

But what is the elusive motor in the RBC ?

Park, Popescu et. al. (2010)

Can we explain these observations using a simple theoretical model ?

Yes, and its just out:

PRL **106,** 238103 (2011) PHYSICAL REVIEW LETTERS week ending 10 JUNE 2011

Effective Temperature of Red-Blood-Cell Membrane Fluctuations

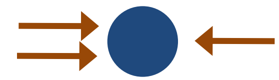
Eyal Ben-Isaac,[1] YongKeun Park,[2] Gabriel Popescu,[3] Frank L. H. Brown,[4] Nir S. Gov,[1,*] and Yair Shokef[5,†]

Minimal Model for Active Fluctuations

(of Red Blood Cell Membranes)

"Particle" (= Degree of freedom, spatial mode, …)

N_m "Motors" (= Elements that occasionally apply force)



(one dimension)

Thermal bath (at temperature T_B): viscous drag, random force (Gaussian, white)

Langevin dynamics: $\dot{v} = -\lambda v + f_T + f_A + f_R$

(v = velocity)

Small periodic force for response measurement

Sum of forces exerted by motors

<u>Each motor</u>:

- turns on as Poisson process with average waiting time τ
- exerts constant force f_0 in random direction
- turns off after time $\Delta\tau$ (typically constant)
- uncorrelated from other motors (in direction and timing)

Minimal Model for Active Fluctuations

(of Red Blood Cell Membranes)

#1: **Linear** differential equation: $\dot{v} = -\lambda v + f_T + f_A + f_R$

$\Downarrow$

Solution is **superposition**: $v(t) = v_T(t) + v_A(t) + v_R(t)$ of solutions to:

$$\dot{v_T} = -\lambda v_T + f_T$$
$$\dot{v_A} = -\lambda v_A + f_A$$
$$\dot{v_R} = -\lambda v_R + f_R$$

<u>Consequences for FD measurement</u>:

i) Response independent of bath & motors: $f_R = F_0 e^{i\omega t} \longrightarrow \langle \delta x(t) \rangle = \chi_{xx}(\omega) F_0 e^{i\omega t}$

with: $\chi_{xx}(\omega) = \dfrac{1}{\omega(i\lambda - \omega)}$

ii) v_T & v_A uncorrelated → $\langle v(t)v(0) \rangle = \langle v_T(t)v_T(0) \rangle + \langle v_A(t)v_A(0) \rangle$

$= \langle v_T^2 \rangle e^{-\lambda t}$

(f_T Gaussian&white)

We're left with calculating active part of fluctuations

#2: Direction of force uncorrelated (different motors & different pulses of same motor)

$$\langle v_A(t)v_A(0) \rangle = \frac{N_m \Delta\tau}{\tau + \Delta\tau} \langle v_p(t)v_p(0) \rangle$$

$\dfrac{N_m \Delta\tau}{\tau + \Delta\tau}$: **Average number of pulses per unit time**

$v_p(t) =$ **velocity change following single pulse**

And after not that much algebra…

$$T_{eff}(\omega) = T_B + \frac{N_m v_0^2 \lambda \left[1 - \cos(\omega \Delta\tau)\right]}{(\tau + \Delta\tau)\omega^2}$$

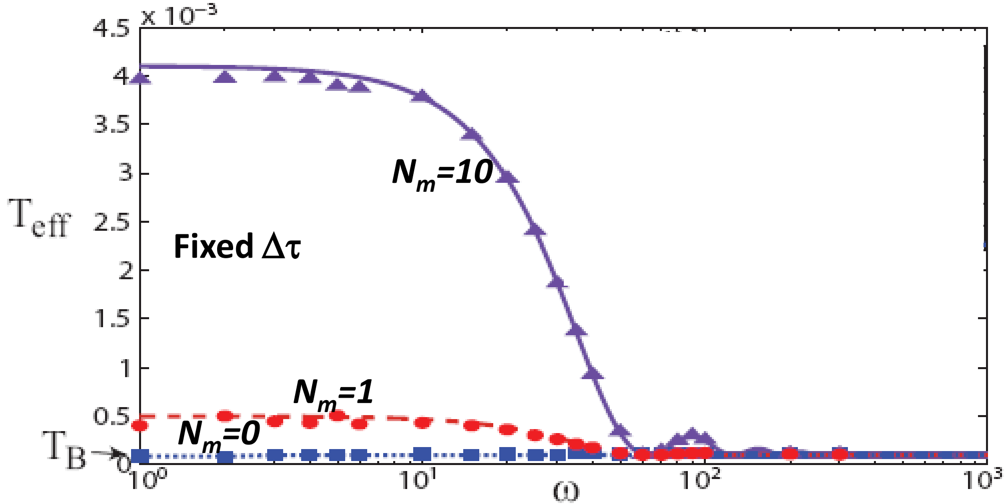
$(v_0 \equiv f_0/\lambda)$

Effective Temperature

$$T_{eff}(\omega) = T_B + \frac{N_m v_0^2 \lambda \left[1 - \cos(\omega \Delta\tau)\right]}{(\tau + \Delta\tau)\omega^2}$$

Straightforward to generalize to variable pulse length $T_{eff}(\omega) = T_B + \frac{N_m v_0^2 \lambda \langle 1 - \cos(\omega \Delta\tau) \rangle}{(\tau + \langle \Delta\tau \rangle)\omega^2}$

P(Δτ)=Poisson → $f_A(t)$=shot noise [Gov 2004] and: $T_{eff}(\omega) = T_B + \frac{N_m v_0^2 \lambda}{(\tau + \langle \Delta\tau \rangle)\left(\omega^2 + \frac{1}{\langle \Delta\tau \rangle^2}\right)}$



$\lambda = 50,\ \Delta\tau = 0.1,\ \tau = 0.15,\ T_B = 10^{-4},\ v_0 = 0.02$

Are Active Fluctuations Thermal-Like?

Velocity fluctuations
- **amplitude** > thermal $\langle v^2\rangle = \langle v_T^2\rangle + \langle v_A^2\rangle = T_B + \frac{N_m v_0^2\left(\lambda\Delta\tau - 1 + e^{-\lambda\Delta\tau}\right)}{\lambda(\tau+\Delta\tau)}$
- is their **nature** thermal-like? **(is the system effectively in equilibrium at T_{eff}=<v^2>?)**

1) Fluctuation-dissipation ratio:

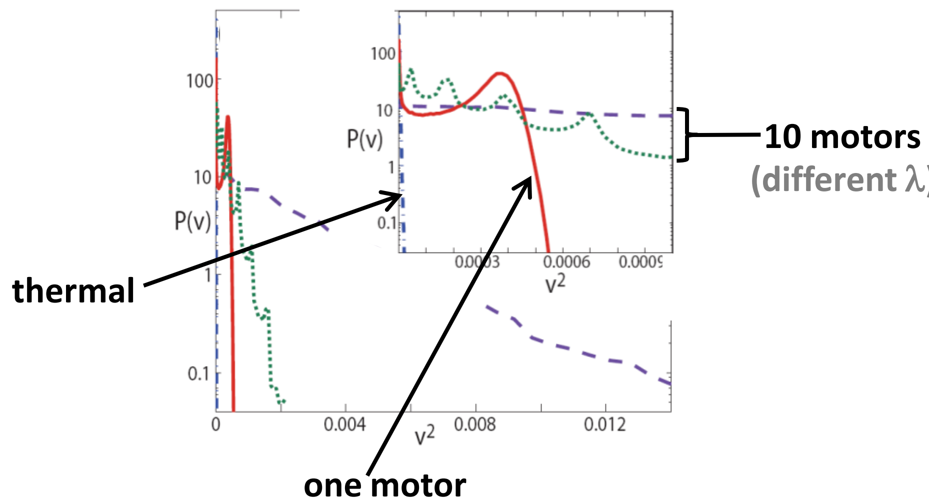
depends on frequency: $T_{eff}(\omega)$

$T_{eff}(\omega)$=*const.* only in thermal limit

but:

$T_{eff}(\omega) \rightarrow$ *const.* for small ω

2) Velocity distribution, $P(v) \approx exp(-v^2/T_{eff})$?



Quantify deviation from Gaussian by Kurtosis $\kappa \equiv \frac{\langle v^4\rangle}{\langle v^2\rangle^2}$

($\kappa_{Gaussian}$=3)

Kurtosis ($\kappa \equiv \frac{<v^4>}{<v^2>^2}$)

2nd moment: $v(t) = v_T(t) + v_A(t)$, v_T & v_A uncorrelated → $<v_T v_A>=0$ → $<v^2> = <v_T^2> + <v_A^2>$

$v_A(t) = \Sigma \sigma_i v_p(t-t_i)$, directions uncorreloated ($\sigma_i \sigma_j = \delta_{ij}$) → $<v_A^2> \propto <v_p^2>$

sum over pulses

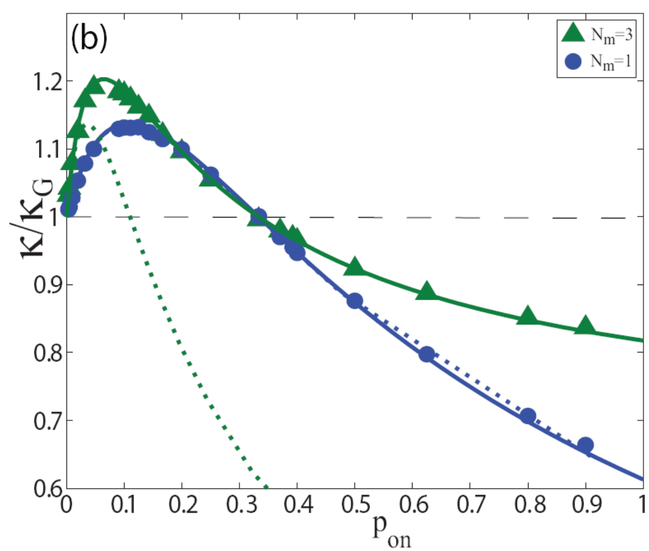
direction of pulse i

time pulse i started

4th moment: $<v^4> = <v_T^4> + 6<v_T^2><v_A^2> + <v_A^4>$, but now $<v_A^4> \propto <v_p^4> + <v_p^2(t-t_i) v_p^2(t-t_j)>$

Solution: Assume $v_p \approx 0$ by the time next pulse starts (→ neglect cross term)

Valid only for $N_m=1$ & $\lambda\tau >> 1$:



Kurtosis ($\kappa \equiv \frac{\langle v^4 \rangle}{\langle v^2 \rangle}$)

For multiple motors, we use another description:

Assume each motor immediately generates $v_0 = f_0/\lambda$ ($\rightarrow \lambda\Delta\tau >> 1$)

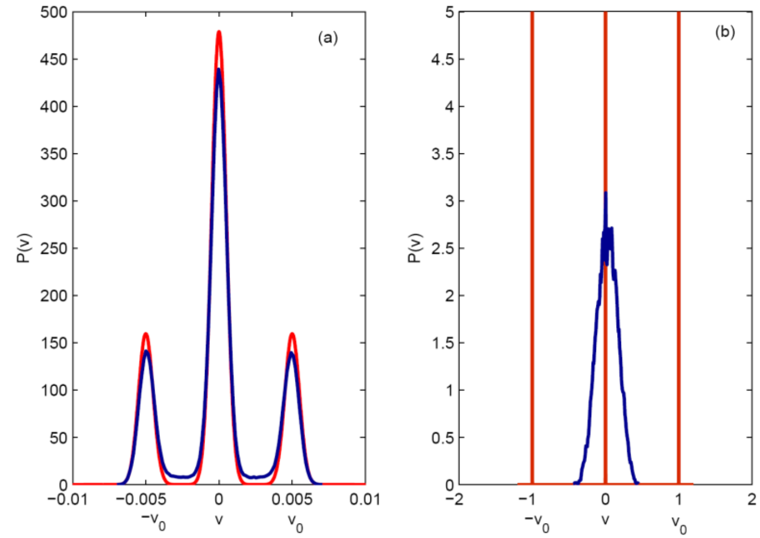
⇩

P(v) is sum of shifted thermal Gaussians (weighted according to combinatoric probability that a given number of motors are simultaneously on)

Probability of each motor to be on: $p_{on} = \frac{\Delta\tau}{\tau + \Delta\tau}$

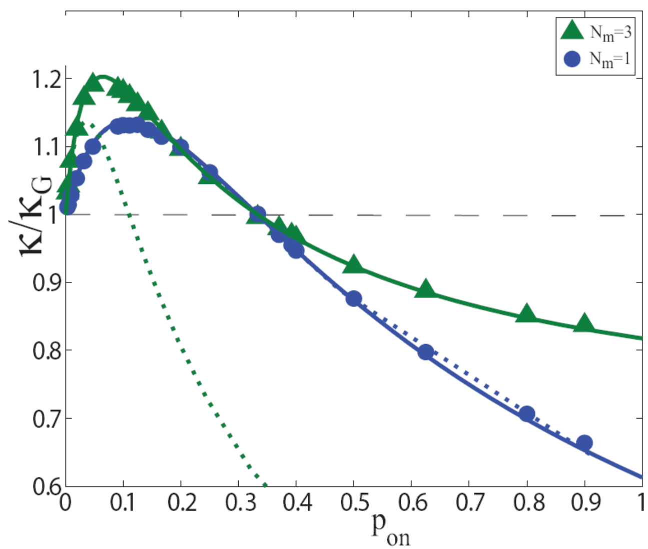
$N_m=1$

$\lambda\Delta\tau >> 1$ $\lambda\Delta\tau < 1$

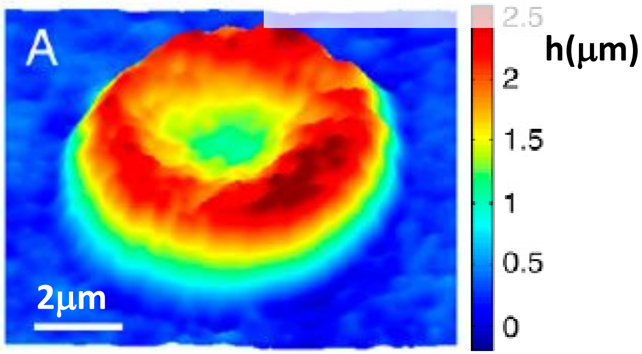


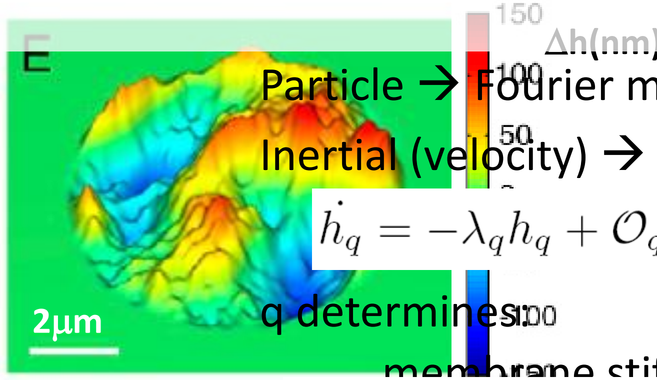
- **Perfect agreement with simulations**
- **Non-monotonic dependence of κ on activity (p_{on})**
- **Can retain $\kappa_{Gaussian}$ even when far from equilibrium**

$\lambda\Delta\tau >> 1$



Minimal Model for **Active Fluctuations** of Red Blood Cell Membranes





Park, Best, Auth, Gov, Safran, Popescu, Suresh, Feld (2010)

Particle → Fourier mode q

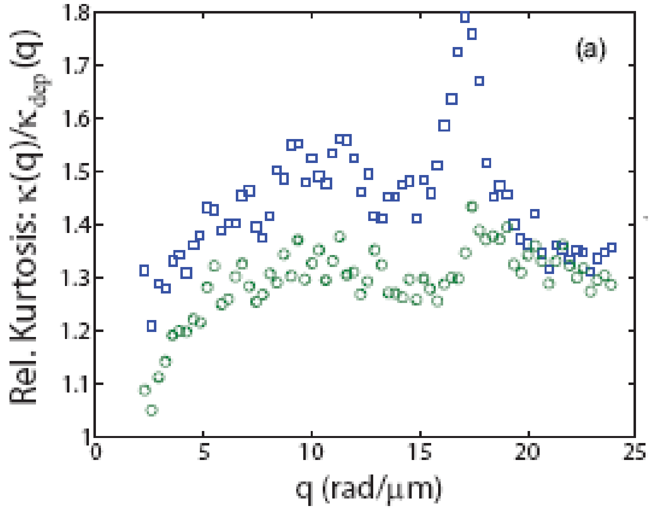
Inertial (velocity) → Overdamped (position)

$$\dot{h}_q = -\lambda_q h_q + \mathcal{O}_q \left[F_T(q,t) + F_A(q,t) \right]$$

q determines:

membrane stiffness $\lambda_q = \mathcal{O}_q \left(\bar{\kappa} q^4 + \sigma q^2 \right)$

New experimental measurements of kurtosis with vs without ATP



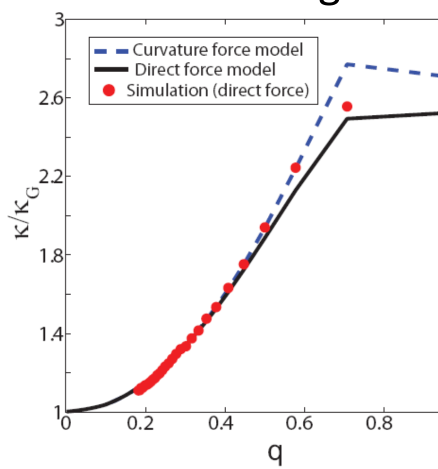
κ(w/ATP) **>** κ(w/o ATP)

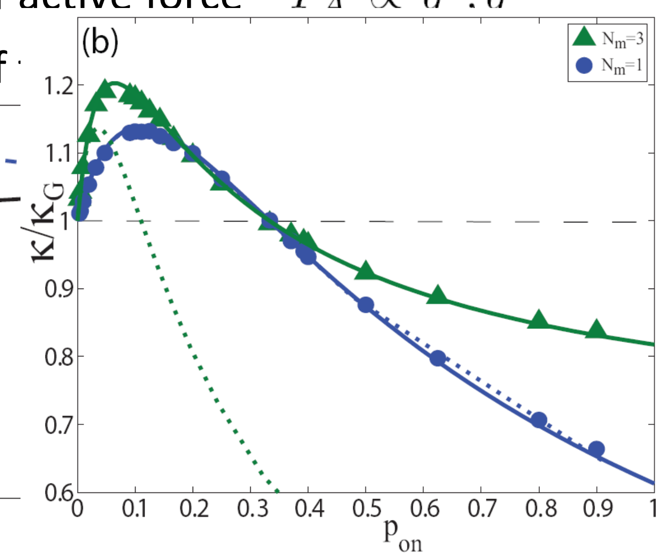
→ *κ grows with activity*

→ *we're in the low* $\mathbf{p_{on}}$ *region*

strength of active force $F_A \propto q^0, q^2$

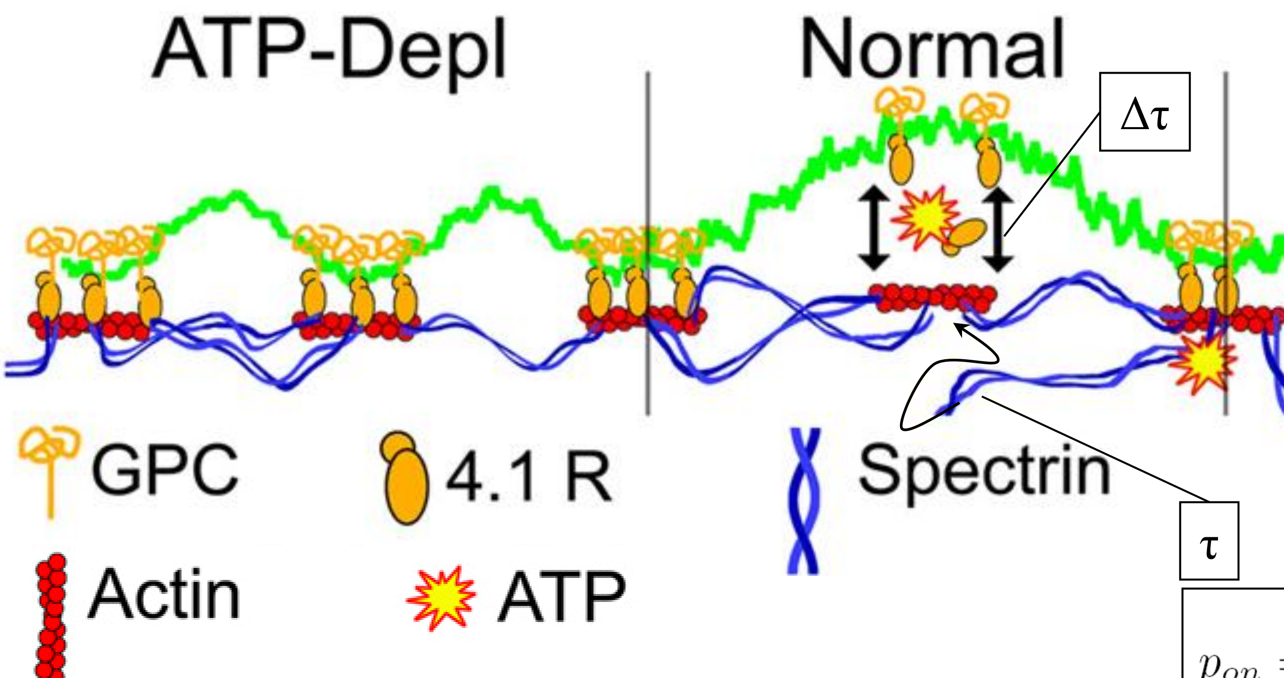
strength of





The analysis can teach us about the physical properties of the elusive motor:

• Low p_{on} → the RBC membrane motor has a long recovery time
• Supports a model of the ATP-driven activity through filament dissociations

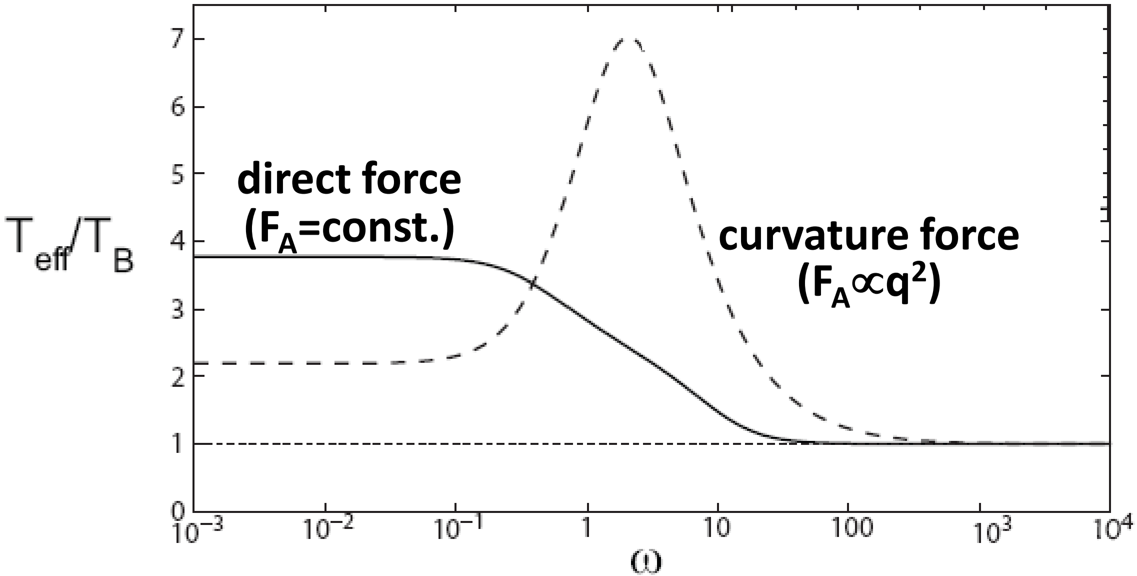


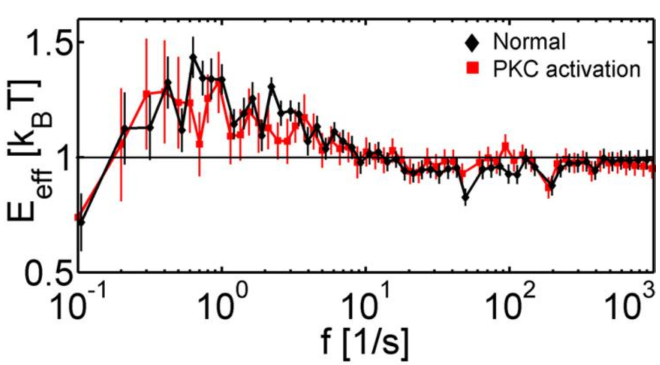
$$p_{on} = \frac{\Delta\tau}{\tau + \Delta\tau}$$

Minimal Model for Active Fluctuations of Red Blood Cell Membranes

(Local) fluctuation-dissipation measurement → integrate over q

(here $P(\Delta\tau)$=Poisson)





Betz, Lenz, Joanny, Sykes (2009)

- Calls for experiments that would measure also response and not only fluctuations in RBC
- Would be interesting to see if indeed $\mathbf{T_{eff}(\omega)}$ is non-monotonic ? (preliminary data indicate monotonic behavior).

Take-Home Messages on the Non-Equilibrium Nature of Active Fluctuations

1. When using fluctuations to quantify deviation from equilibrium, need to compare to appropriate response (via the fluctuation-dissipation formalism)

2. Kurtosis may be misleading in characterizing deviation from equilibrium: Gaussian values may result from large $\mathbf{N_m}$ effects; in such cases $\mathbf{T_{eff}(\omega)}$ still shows strong frequency dependence

3. **Kurtosis** vs. **activity** is non-monotonic

4. $\mathbf{T_{eff}(\omega)}$ vs. **activity** and **frequency** may be **non-monotonic**

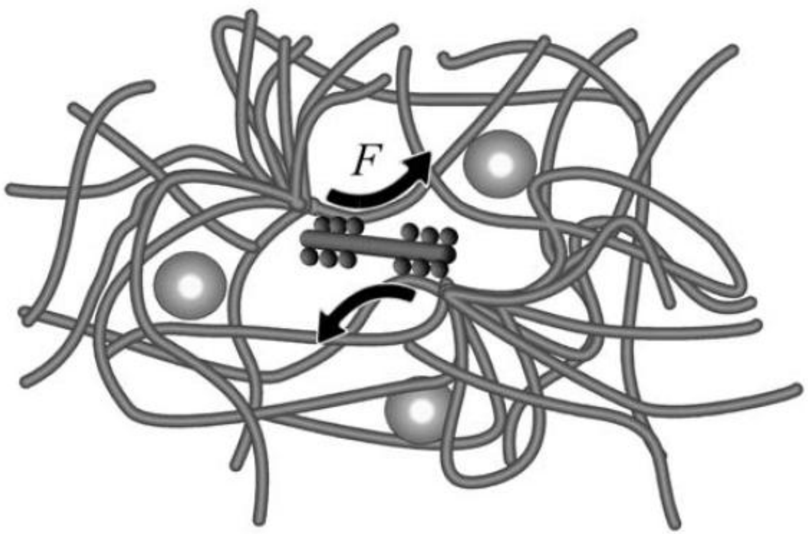
Suggestions for our experimental collaborators…

Timo Betz (Curie): Measure response of red blood cell membrane to deduce $T_{eff}(\omega)$ and see if it's non-monotonic

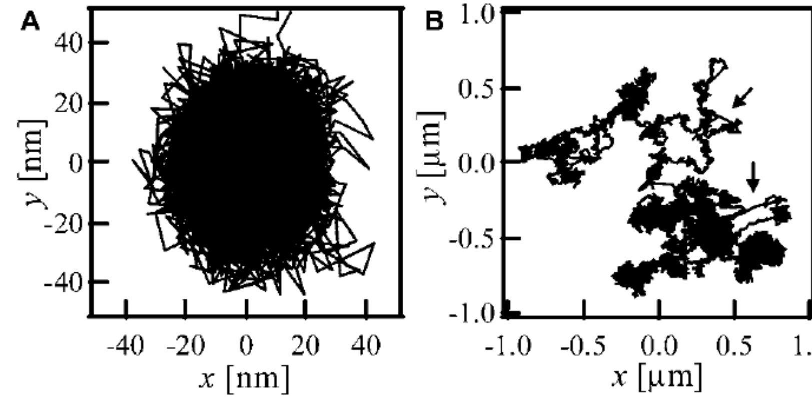
Paul Park (KAIST): Increase activity or decrease wavevector to identify situations in which kurtosis decreases with activity

Recent observation of non-monotonous kurtosis:

In-vitro actin-myosin gel:

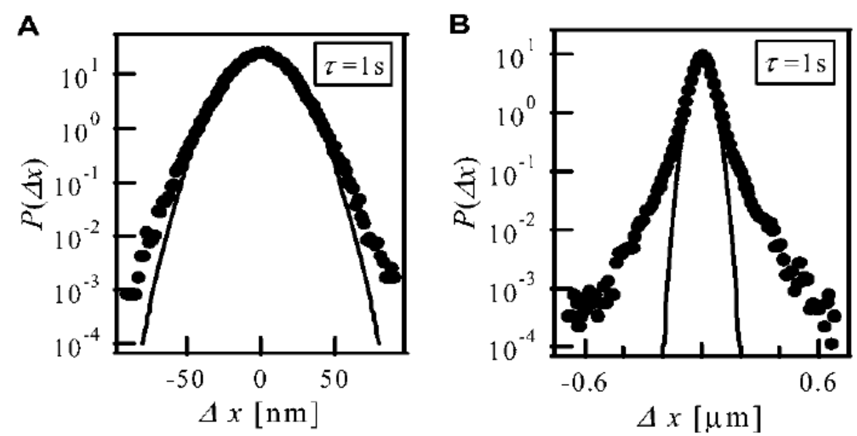


“Dead”: “Alive”:



Van-Hove correlations:

$$P(\Delta x(\tau)),\ \Delta x(\tau) = x(t+\tau) - x(t)$$



Cite this: *Soft Matter*, 2011, **7**, 3234

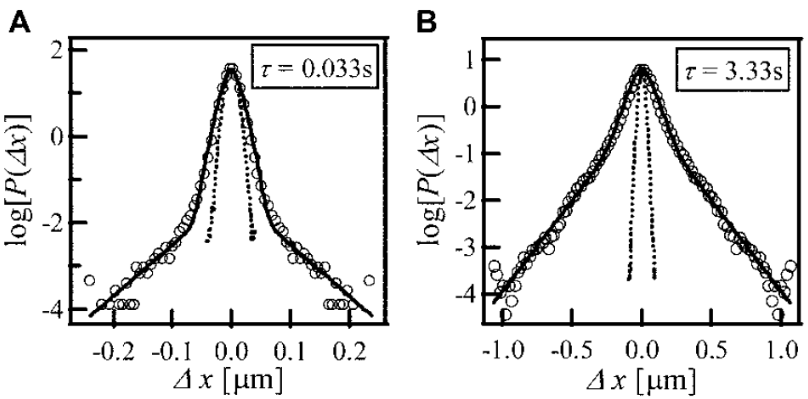
www.rsc.org/softmatter

Non-Gaussian athermal fluctuations in active gels†

Toshihiro Toyota,[a] David A. Head,[b] Christoph F. Schmidt[c] and Daisuke Mizuno*[a]

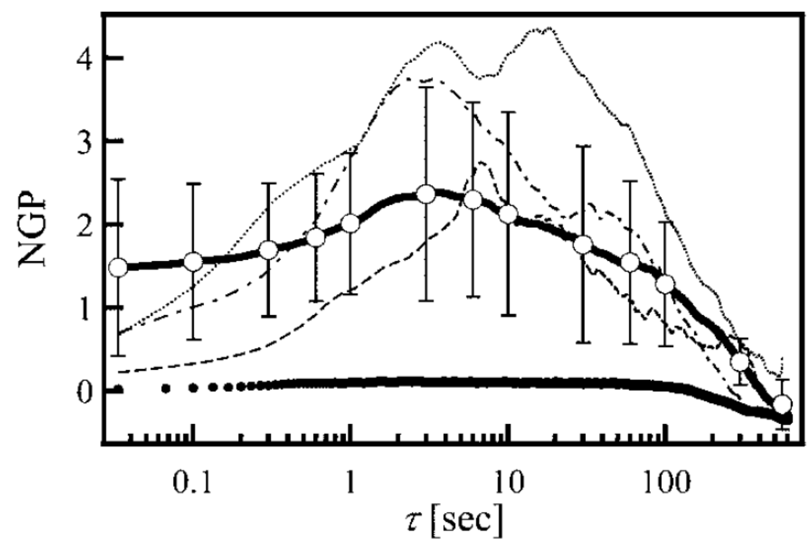
Recent observation of non-monotonous kurtosis:

Distribution of velocity increment depend on the lag-time:



Non-Gaussianity Parameter:

$$\mathrm{NGP} = \frac{\left\langle \Delta x(\tau)^4 \right\rangle}{3\left\langle \Delta x(\tau)^2 \right\rangle^2} - 1,$$



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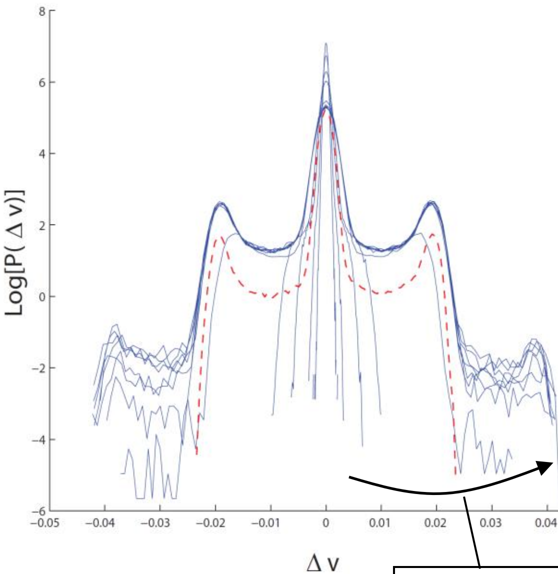
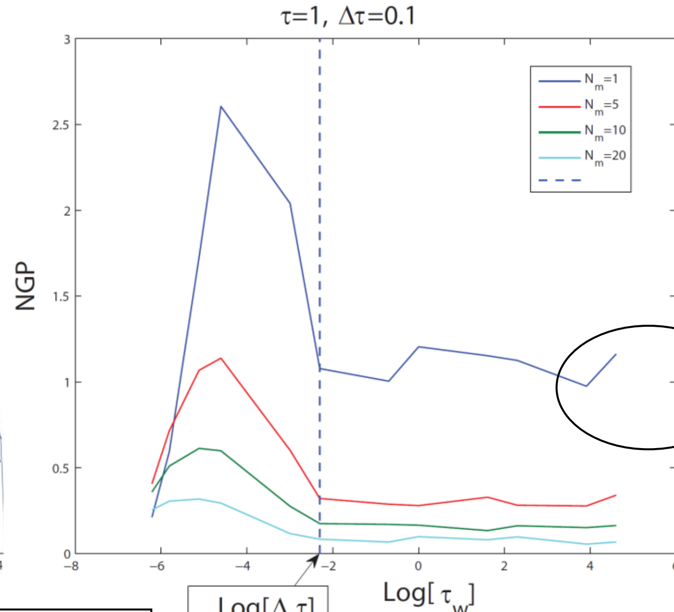
Non-Gaussian athermal fluctuations in active gels†

Toshihiro Toyota,[a] David A. Head,[b] Christoph F. Schmidt[c] and Daisuke Mizuno*[a]

Comparing to our simple model:

Single motor, p_{on}~0.1:





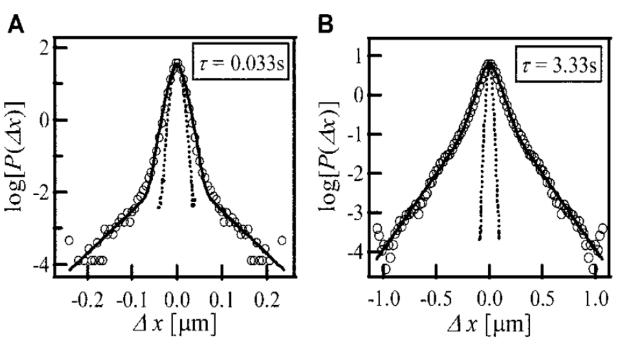
Increasing τ_w

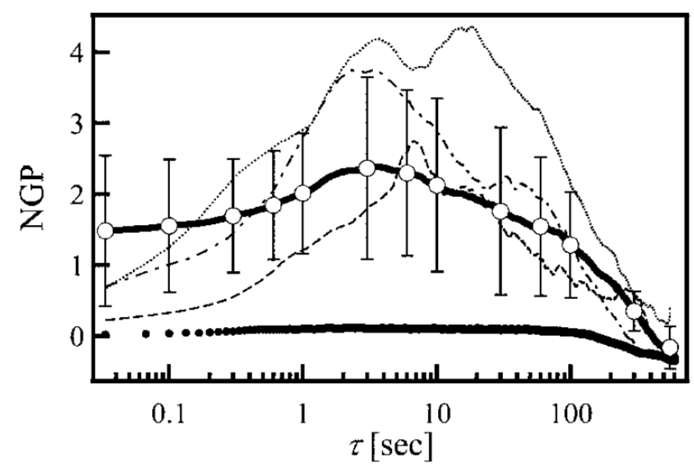
Log[Δ τ]

The limit of $\tau_w \rightarrow \infty$ we have:

$$P(\Delta v(\tau_w)) \rightarrow \int_{-\infty}^{\infty} P(v) P(v + \Delta v) dv$$

which is not necessarily a Gaussian !

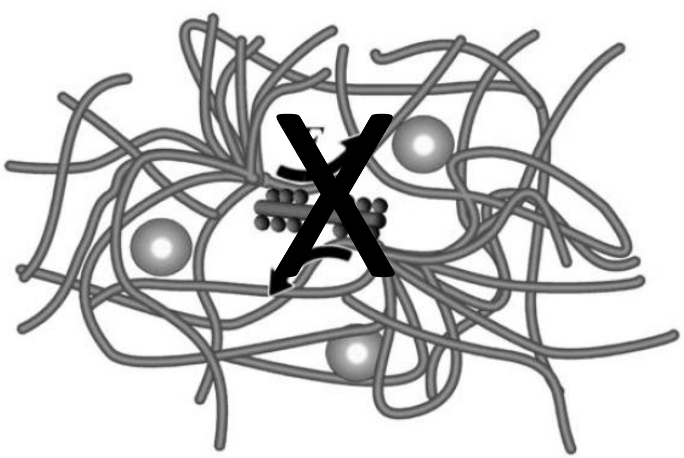


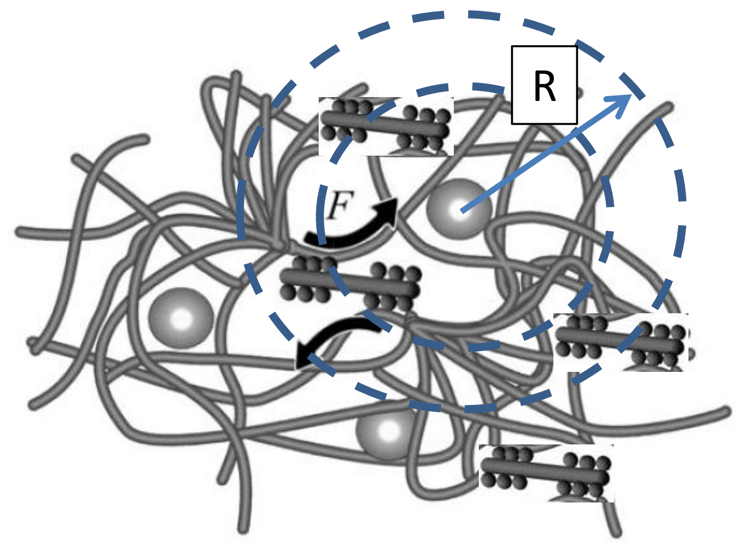


Comparing to our simple model:

$\Rightarrow$

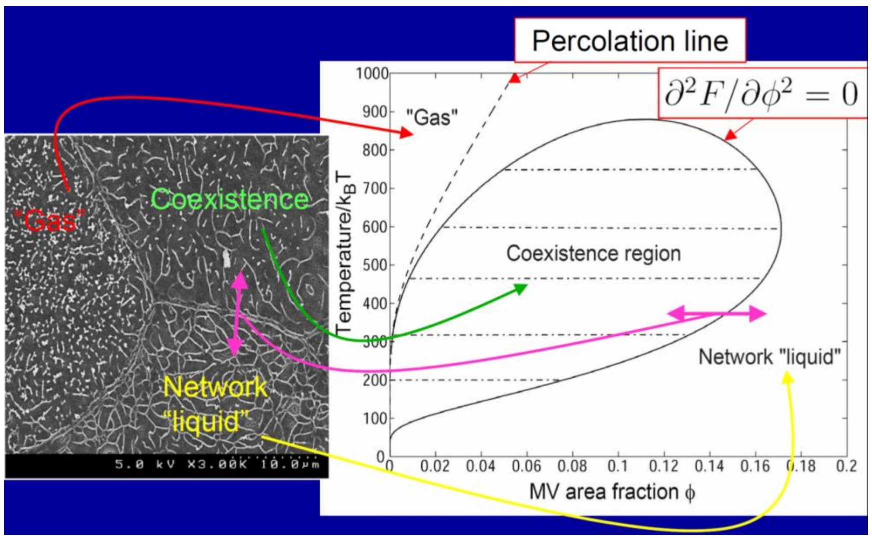
- The bead is NOT affected by only one proximal motor, but by the whole spatial distribution of motors:
- Numerous motors: $N_m \sim R^2$
- But weaker: $f_0 \sim 1/R^2$

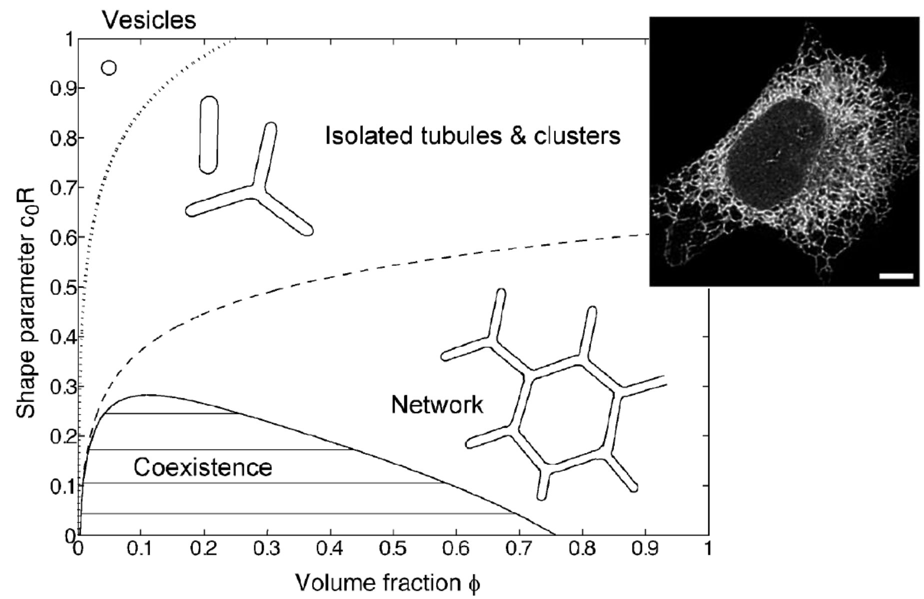




We're now calculating this spatially-extended problem

The future: how to describe phase transitions with active fluctuations ?

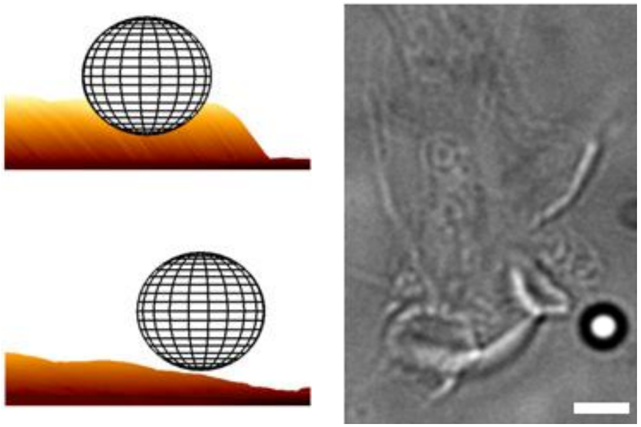


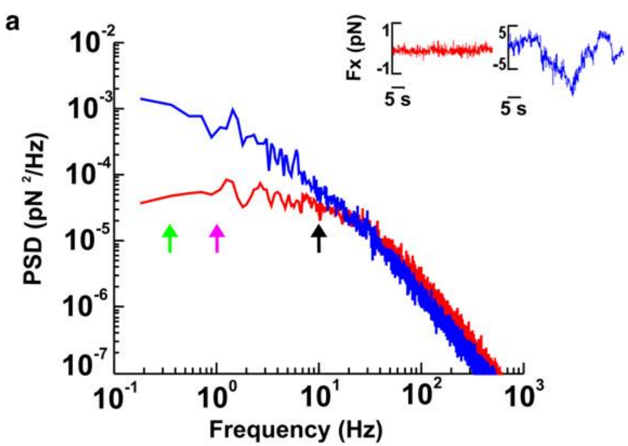


- Is there a critical effective temperature for a phase transition, especially when the components have different effective temperatures?

- What are the critical exponents near such a transition (active-RG) ?

Actin-myosin-driven cellular shape fluctuations

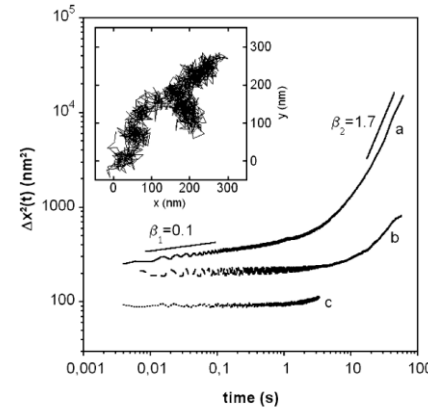


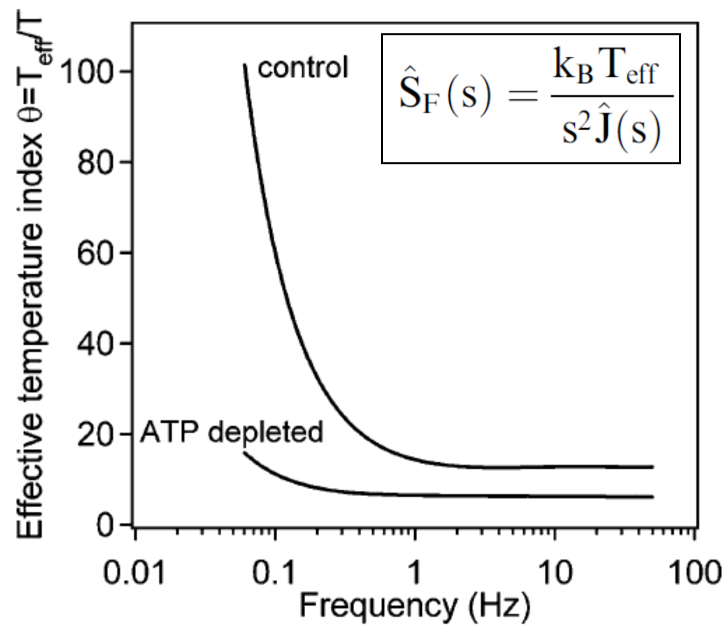


Biophysical Journal Volume 98 March 2010 979–988

Force Generation in Lamellipodia Is a Probabilistic Process with Fast Growth and Retraction Events

Rajesh Shahapure,† Francesco Difato,†‡ Alessandro Laio,† Giacomo Bisson,† Erika Ercolini,†§ Ladan Amin,† Enrico Ferrari,¶ and Vincent Torre†‡*





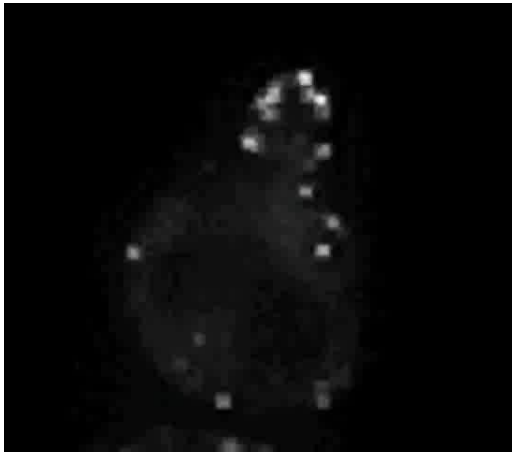
Power spectrum of out-of-equilibrium forces in living cells: amplitude and frequency dependence

François Gallet,* Delphine Arcizet,† Pierre Bohec and Alain Richert

Soft Matter, 2009, **5**, 2947–2953

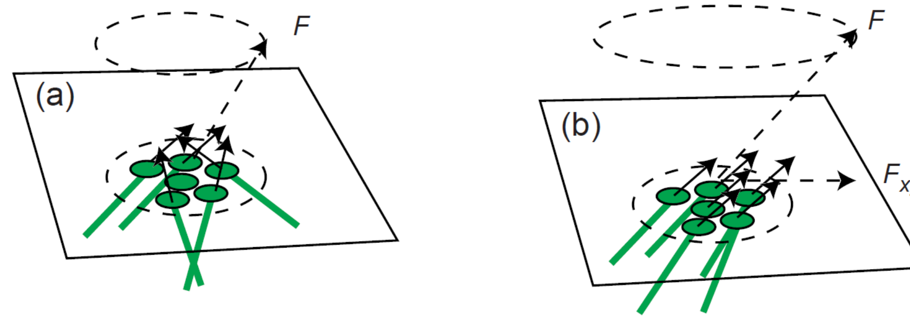
Detailed model of the Active Fluctuations of actin-driven membrane patches and protrusions

Motion of actin patches in yeast cell



Smith, Swamy, Pon (2001)

Model: random and bundled actin



• Each patch has different number of pushing actin filaments, i.e. number of motors **N**

C.M. mean-square velocity for patch of mass M (shot-noise force correlations, τ):

$$\langle F'(t)F'(t')\rangle = \frac{Ncf^2}{M^2} e^{-|t-t'|/\tau}$$

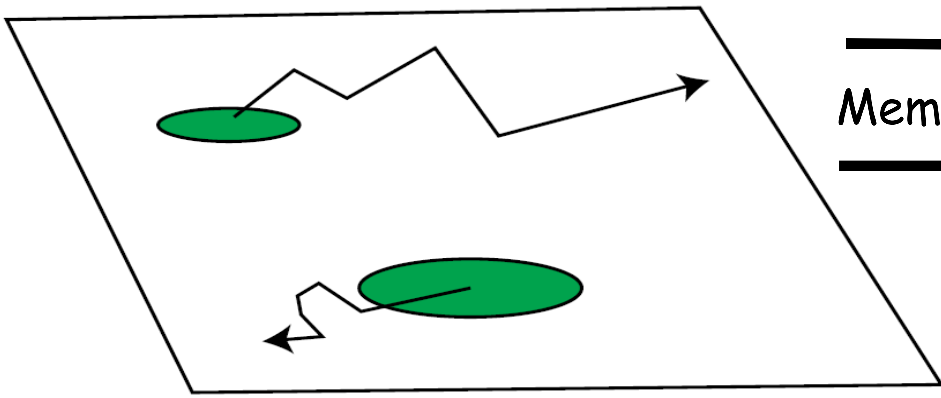
$$\langle v_{cm}^2 \rangle_{t\to\infty} = \frac{cf^2\tau}{2M\lambda(1+\lambda\tau/M)}$$

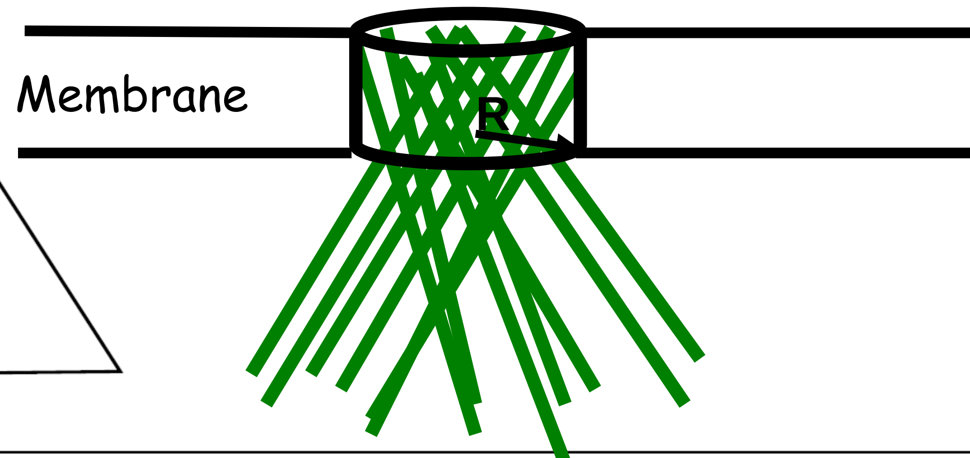
$$\langle F'(t)F'(t')\rangle_{thermal} = \frac{4k_B T\lambda}{M^2}\delta(t-t')$$

Thermal forces depend on the friction

Effective temperature of actin-driven membrane patches

Different forms of patch friction give different forms of effective temperature:





- Hydrosynamics in 2D (Saffman-Delbruck) → Const.
- Stokes-like behavior (D~1/R) → $\propto \sqrt{N}$
- Stick-slip with underlying cytoskeleton → $\propto N$

Friction λ	δ-correlations or Shot-Noise $\tau << 1$	Shot-Noise correlations $\tau >> 1$
Const.	$< v^2 > \propto N^{-1}$	$< v^2 > \propto Const.$
$\propto \sqrt{N}$	$< v^2 > \propto N^{-3/2}$	$< v^2 > \propto N^{-1}$
$\propto N$	$< v^2 > \propto N^{-2}$	$< v^2 > \propto N^{-2}$

Very different behaviors:

$$k_B T_{eff,N} = M \langle v_{cm}^2 \rangle / 2.$$

$T_{eff}(N) \sim N$

$T_{eff}(N) \sim 1/N$

Size-distribution of actin-driven membrane patches (active thermodynamics)

Interacting patches of different effective temperatures:

$$F = \sum_N \rho_N \left[k_B T_{eff}(N) \ln(\rho_N) - \mu N + \gamma\sqrt{N} \right]$$

Minimizing this free energy with respect to the cluster size distribution:

$$\rho_N = A e^{-\left[\frac{-\mu N + \gamma\sqrt{N}}{k_B T_{eff}(N)}\right]}$$

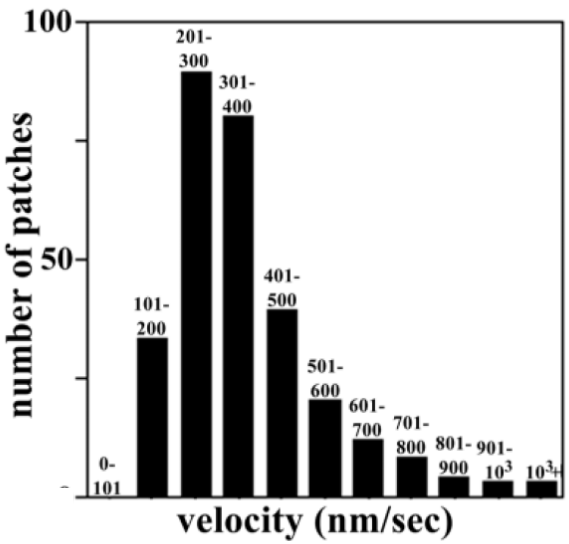
for dilute systems such that $\mu \ll 0$ and the system is far from phase separation (phase transition).

But is this a "kosher" procedure ? Doe this actually happen ?

Work in progress…

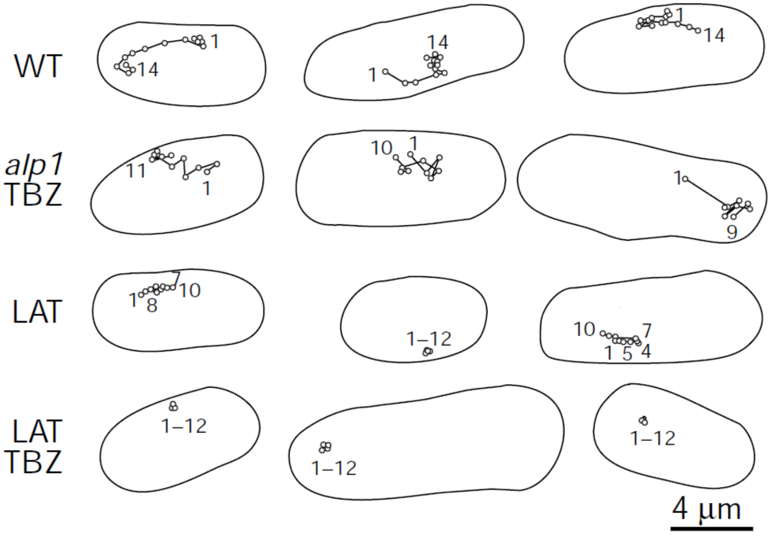
Comparison to observations:

Velocity distribution of patches:



Smith, Swamy, Pon (2001)

Actin drives the random motion:



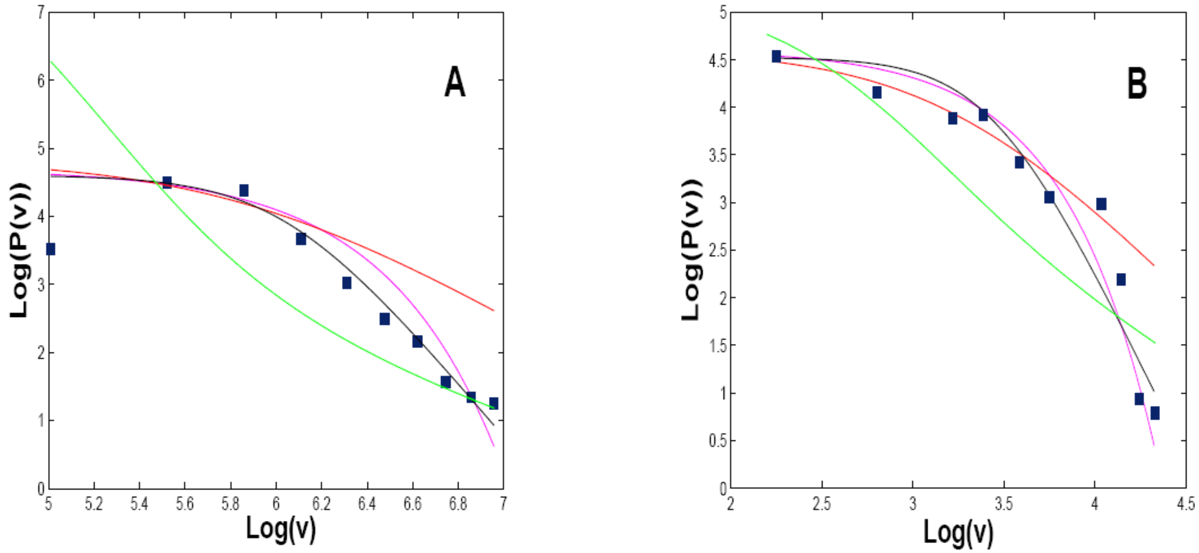
Chang (1999)

Comparison to observations:

Thermal case: $P(v) \propto (a + v^2)^{-1}$ (red)

Active cases: $T_{eff}(N) \propto N, N^2$ we get $P(v) \propto \exp(-v^2)$ (purple)

$T_{eff}(N) \propto \sqrt{N}$ we get $P(v) \propto (a + v^2)^{-2}$ (black)



$\Rightarrow$

- An indication that the clusters are active
- May furthermore indicate what is the dominant friction mechanism

Conclusion:

• Active motion in living systems, driven by a variety of molecular motors, affects pattern formation

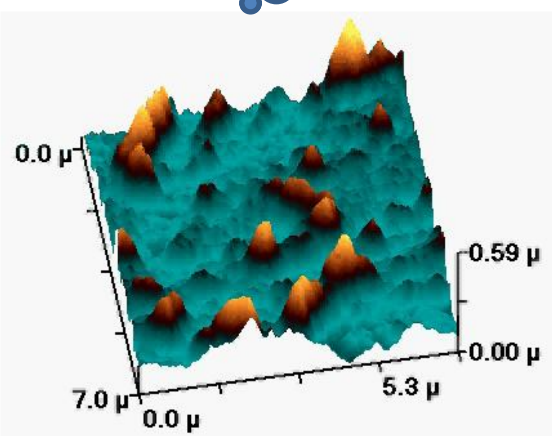
• The random motion may be treated as “effective temperature” ?

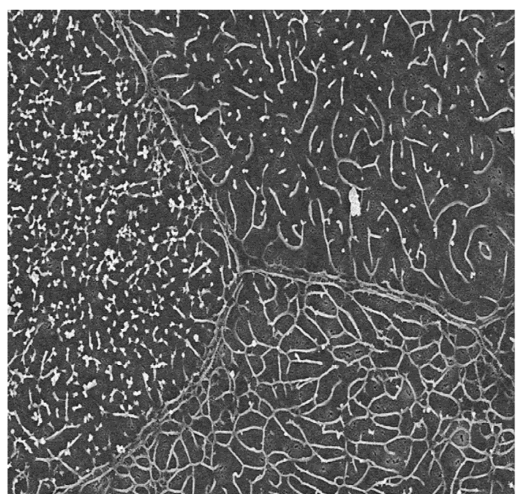
• Example where Biological Physics motivates research into new non-equilibrium systems.

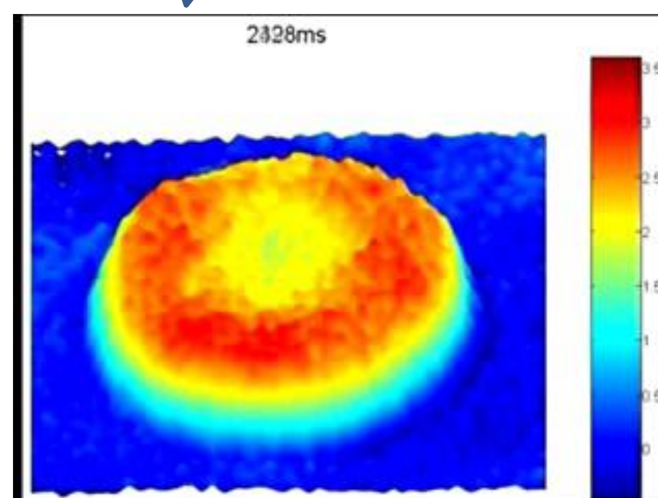
• We are just beginning to quantify and ask the questions regarding these active phase-transitions.

Its moving…

Its alive !







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