Tracking nonequilibrium in living cells

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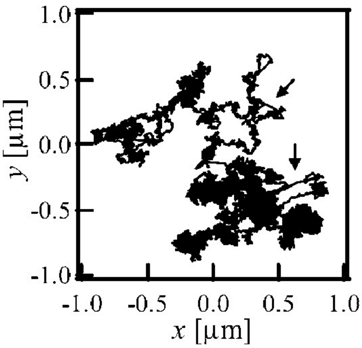
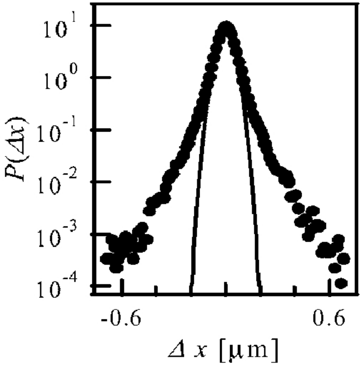
BioLunch Seminar | DAMTP

Introduction

Tracer trajectory



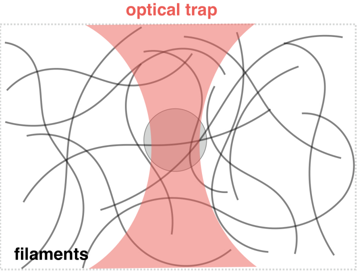
Statistics of tracer displacement

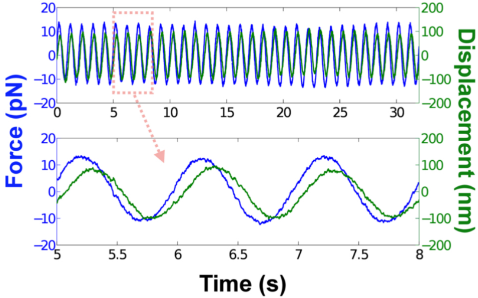


T. Toyota *et al.*, Soft Matter **7**, 3234 (2011)

Introduction

Microrheological properties





$$\langle \delta r(t) \rangle = \int_0^t \underbrace{R(t-s)}_{\text{Response}} F(s) \mathrm{d}s$$

Introduction

Trademark of equilibrium

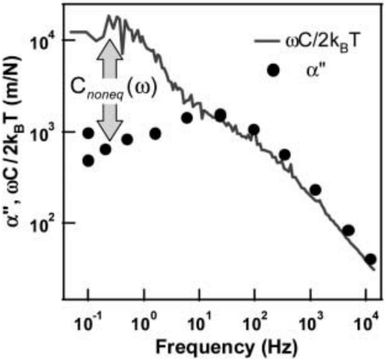
$$R(t) = -\frac{1}{T}\frac{\mathrm{d}}{\mathrm{d}t}\underbrace{\langle x(t)x(0)\rangle}_{C(t)} \quad \rightarrow \quad T = \frac{\omega C(\omega)}{2R''(\omega)}$$

Fluctuation-dissipation theorem

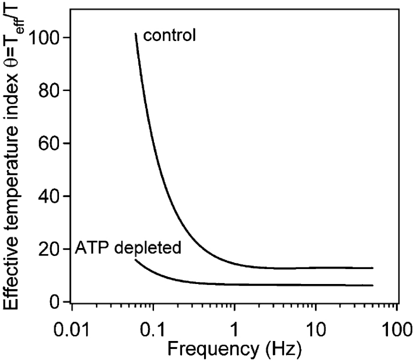
Nonequilibrium dynamics $\qquad T_{\mathrm{eff}}(\omega) = \dfrac{\omega C(\omega)}{2R''(\omega)}$

L. Cugliandolo, J. Phys. A **44**, 483001 (2011)

Introduction



D. Mizuno *et al.*, Science **315**, 370 (2007)



F. Gallet *et al.*, Soft Matter **5**, 2947 (2009)

Outline

1. Tracer dynamics in living cells
   - Can we distinguish thermal vs. active physics?
   - How can we quantify activity?

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2. Energy transfers in living cells
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   - What is the efficiency of energy transfers?

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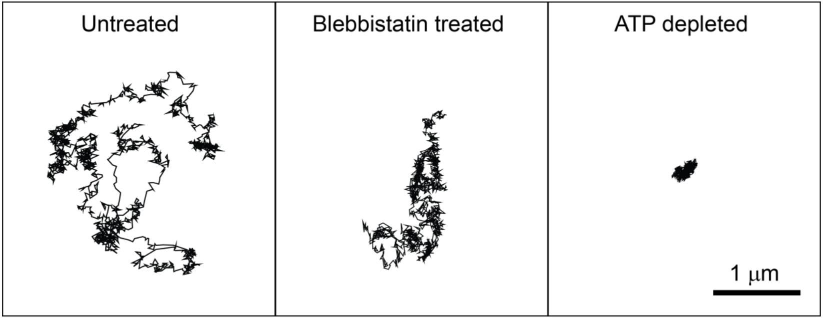
Tracer dynamics in living cells



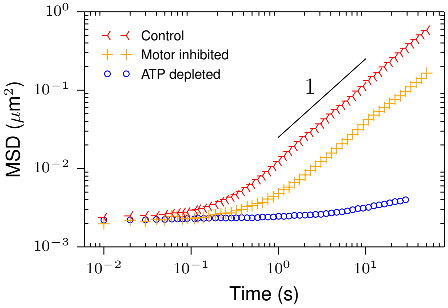
Living melanoma cells

Tracers = Micro-size silica beads

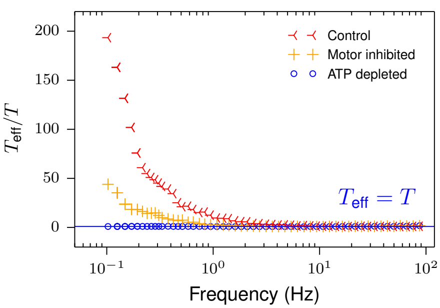
M. Guo, D. A. Weitz (Harvard University)

Tracer dynamics in living cells

Mean square displacement

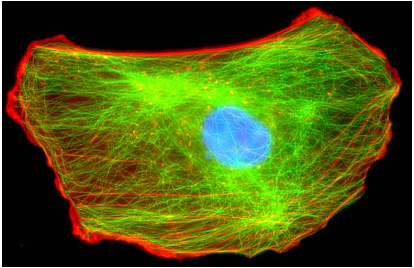


Effective temperature

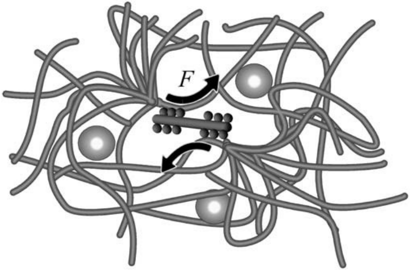


Tracer dynamics in living cells

Cytoskeletal network



Molecular motors

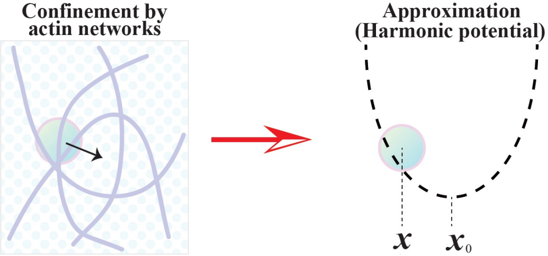


Tracer dynamics in living cells

Tracer dynamics: transitions between local cages

C. P. Brangwynne *et al.*, Trends Cell Biol. **19**, 423 (2009)

Tracer dynamics in living cells



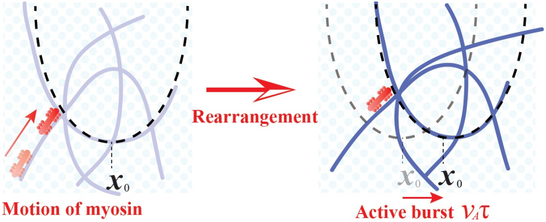
$$0 = -k(x - x_0) - \gamma \frac{\mathrm{d}x}{\mathrm{d}t} + \xi$$

ξ Gaussian white noise

$$\langle \xi(t)\xi(0) \rangle = 2\gamma T \delta(t)$$

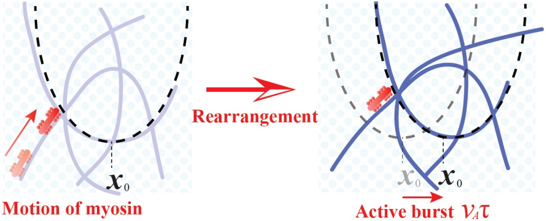
Tracer dynamics in living cells

Active motion of local minimum



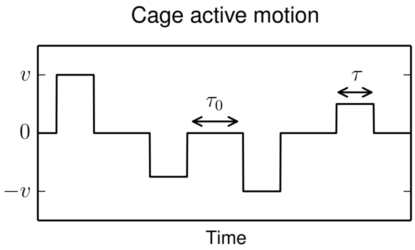
$$\gamma\frac{\mathrm{d}x}{\mathrm{d}t} = -k(x - x_0) + \xi, \quad \gamma\frac{\mathrm{d}x_0}{\mathrm{d}t} = F_{\mathrm{M}}$$

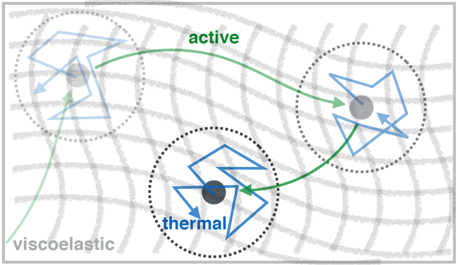
Active motion of local minimum



$$\gamma\frac{\mathrm{d}x}{\mathrm{d}t} = -kx + \underbrace{F_{\mathrm{A}}}_{kx_0} + \xi, \quad \gamma\frac{\mathrm{d}x_0}{\mathrm{d}t} = F_{\mathrm{M}}$$

Tracer dynamics in living cells





$$\color{red}{\langle F_{\mathrm{M}}(t) F_{\mathrm{M}}(0) \rangle} \sim D_{\mathrm{A}} \frac{\mathrm{e}^{-|t|/\tau}}{\tau}$$

Active diffusion coefficient $D_{\mathrm{A}} = \dfrac{(v\tau)^2}{3(\tau + \tau_0)}$

Tracer dynamics in living cells

Spectrum of stochastic forces

$$S_{\text{tot}}(\omega) = \mathcal{F}\left\langle \left(\xi + F_{\text{A}}\right)(t)\left(\xi + F_{\text{A}}\right)(0)\right\rangle$$

Combining response and fluctuations

Active and thermal contributions

$$S_{\text{tot}}(\omega) \;=\; S_{\text{th}}(\omega) \;+\; S_{\text{A}}(\omega)$$

Tracer dynamics in living cells

Spectrum of stochastic forces

$$S_{\text{tot}}(\omega) = \mathcal{F} \left\langle \left(\xi + F_{\text{A}}\right)(t) \left(\xi + F_{\text{A}}\right)(0) \right\rangle$$

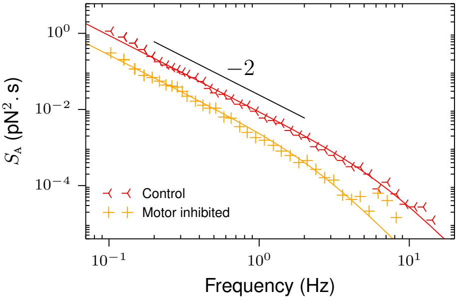
Combining response and fluctuations

Active and thermal contributions

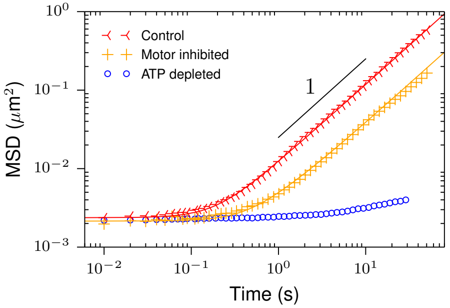
$$\underbrace{S_{\text{tot}}(\omega) \;=\; S_{\text{th}}(\omega)}_{\text{ATP depleted}} + \cancel{S_{\text{A}}(\omega)}$$

Tracer dynamics in living cells

Active force spectrum



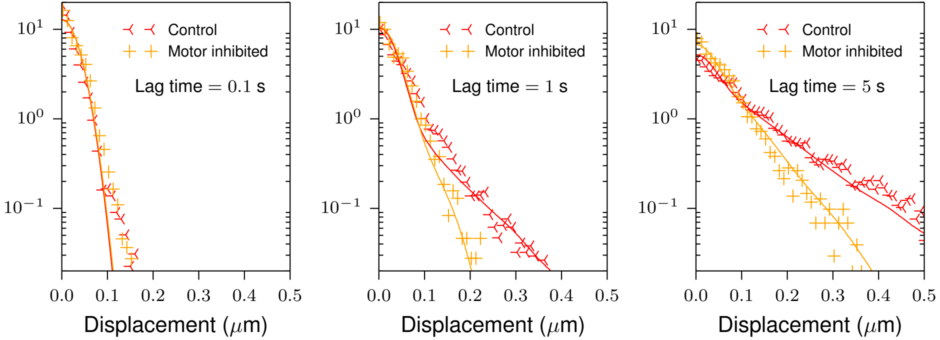
Mean square displacement



Control	$\tau \sim 0.16\,\mathrm{s}$	$D_A \sim 2.8 \cdot 10^{-3} D_T$
Motor inhibited	$\tau \sim 0.39\,\mathrm{s}$	$D_A \sim 0.9 \cdot 10^{-3} D_T$

Tracer dynamics in living cells

Distribution of displacement



Control	$\tau_0 \sim 2.5$ s
Motor inhibited	$\tau_0 \sim 2.8$ s

Outline

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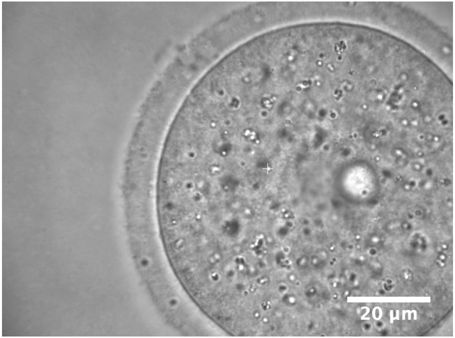
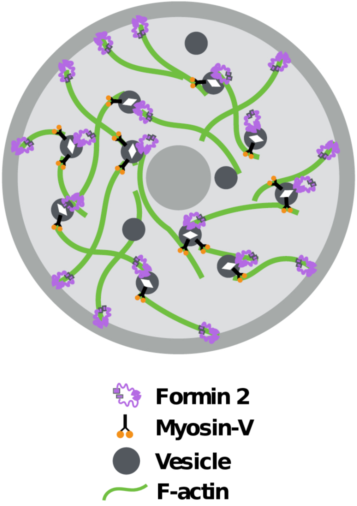
Energy transfers in living cells



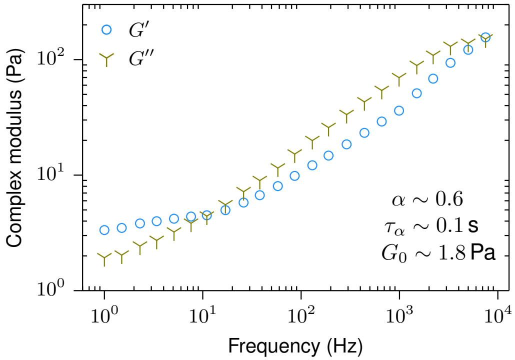
Living mouse oocytes

Tracers = Vesicles

W. W. Ahmed, T. Betz (Curie Institute)



Visco-elastic mechanics



$$G^*(\omega) \sim 1/R(\omega)$$

$$G^* = \underbrace{G'}_{\text{Elastic mod.}} + \underbrace{\mathrm{i}G''}_{\text{Viscous mod.}}$$

$$G^*(\omega) = G_0\left[1 + (\mathrm{i}\omega\tau_\alpha)^\alpha\right]$$

Energy transfers in living cells

Tracer dynamics

$$\gamma * \frac{\mathrm{d}x}{\mathrm{d}t} = -kx + F_{\mathrm{A}} + \xi, \quad \gamma * \frac{\mathrm{d}x_0}{\mathrm{d}t} = F_{\mathrm{M}}$$

ξ Gaussian colored noise

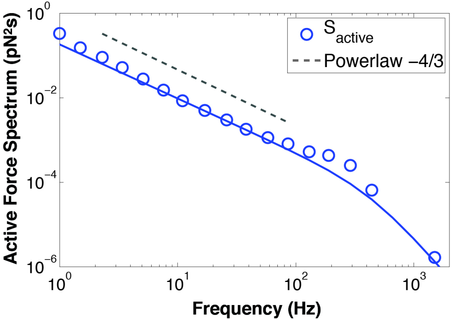
$$\langle \xi(t)\xi(0) \rangle = T\gamma(|t|)$$

Non-markovian dynamics

Energy transfers in living cells

Spectrum of stochastic forces

$$S_{\rm tot}(\omega) = \underbrace{S_{\rm th}(\omega)}_{\text{mechanics (FDT)}} + S_{\rm A}(\omega)$$



$D_{\rm A} \sim 5 D_{\rm T}$ $\tau \sim 0.3\,{\rm ms}$

Myosin-V power stroke $\sim 0.5\,{\rm ms}$

G. Cappello *et al.*, PNAS **104**, 15328 (2007)

Energy transfers in living cells

Power injected into tracer

$$J_{\text{TRAC}} = \left\langle F_{\text{A}} \frac{\mathrm{d}x}{\mathrm{d}t} \right\rangle$$

How is it related to dissipated power?

$$J_{\text{TRAC}} = \left\langle \left(\gamma * \frac{\mathrm{d}x}{\mathrm{d}t} - \xi \right) \frac{\mathrm{d}x}{\mathrm{d}t} \right\rangle + \left\langle kx \frac{\mathrm{d}x}{\mathrm{d}t} \right\rangle$$

Energy transfers in living cells

Power injected into tracer

$$J_{\text{TRAC}} = \left\langle F_{\text{A}} \frac{\mathrm{d}x}{\mathrm{d}t} \right\rangle$$

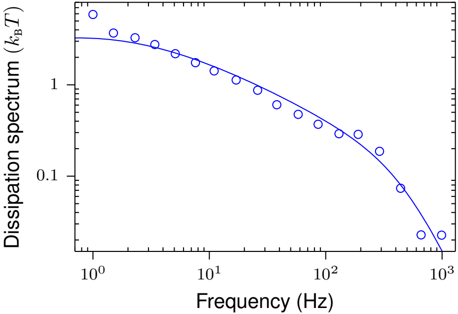
How is it related to dissipated power?

$$J_{\text{TRAC}} = \underbrace{\left\langle \left(\gamma * \frac{\mathrm{d}x}{\mathrm{d}t} - \xi \right) \frac{\mathrm{d}x}{\mathrm{d}t} \right\rangle}_{\text{Dissipated power}} + \cancel{\left\langle kx \frac{\mathrm{d}x}{\mathrm{d}t} \right\rangle}$$

Energy transfers in living cells

Spectral decomposition

$$J_{\text{TRAC}} = \int I(\omega)\frac{\mathrm{d}\omega}{2\pi}$$



$$I(\omega) = \frac{2\left[T_{\text{eff}}(\omega) - T\right]}{1 - \left[R''(\omega)/R'(\omega)\right]^2}$$

$$J_{\text{TRAC}} \sim 360\ k_B T/\ \text{s}$$

Energy transfers in living cells

Tracer dynamics

$$\gamma * \frac{\mathrm{d}x}{\mathrm{d}t} = -kx + F_{\mathrm{A}} + \xi, \quad \gamma * \frac{\mathrm{d}x_0}{\mathrm{d}t} = F_{\mathrm{M}}$$

Power injected into cage

$$J_{\mathrm{CAGE}} = \left\langle F_{\mathrm{M}} \frac{\mathrm{d}x_0}{\mathrm{d}t} \right\rangle \sim 2 \cdot 10^5 \, k_{\mathrm{B}} T / s$$

Power injected by one myosin-V $\sim 10^4 \, k_{\mathrm{B}} T/\mathrm{s}$

K. Fujita *et al.*, Nat. Com. **3**, 956 (2012)

Energy transfers in living cells

Efficiency of power transfer

$$\mathcal{E} = \frac{\text{Cage} \to \text{Tracer}}{\text{Motors} \to \text{Cage}} = \frac{J_{\text{TRAC}}}{J_{\text{CAGE}}} \sim 1.8 \times 10^{-3}$$

Energy injection $\Rightarrow$ Network remodelling $\rightarrow$ Tracer motion

Conclusion

Nonequilibrium physics in living cells

- Kinetics of fluctuations

  Active diffusion coefficient, persistence time

  $\rightarrow$ Motor kinetics

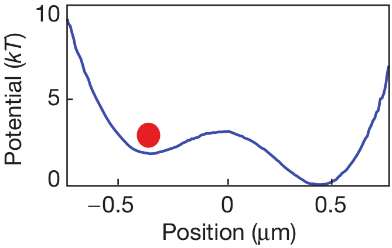
- Separating dissipation from injection

  Dissipated power from fluctuation and response

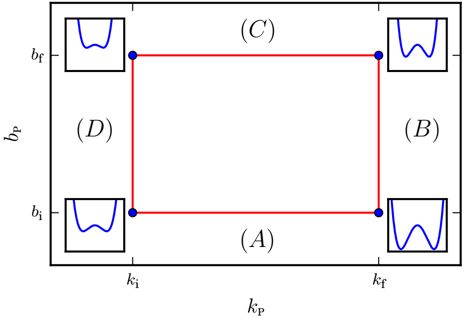
  $\rightarrow$ Low transfer from motors to tracers

Conclusion

Extract work from cyclic protocol



A. Bérut *et al.*, Nature **483**, 187 (2012)



ÉF *et al.*, Phys. Rev. E **90**, 042724 (2014)

Conclusion

Collaborators

- N. S. Gov (Weizmann Institute of Science)
- M. Guo, D. A. Weitz (Harvard University)
- W. W. Ahmed, T. Betz (Curie Institute)
- M. Almonacid, M.-H. Verlhac (Collège de France)

EPL **110**, 48005 (2015) | `arXiv:1510.08299` | EPL **116**, 30008 (2016)

Living mouse oocytes

Distribution of displacement