

Tracking nonequilibrium physics in living systems

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LIPhy, Physique Statistique et Modélisation
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Introduction

Biology-Physics collaboration

Biology

Maria Almonacid, Marie-Hélène Verlhac | Collège de France

Biophysics

Wylie W. Ahmed, Matthias Bussonnier, Timo Betz | Curie Institute

Ming Guo, David A. Weitz | University of Harvard

Physics

Nir S. Gov | Weizmann Institute of Science

Introduction

Jean Perrin



Paul Langevin



Tracer dynamics in thermal bath

$$0 = -\nabla V + \text{thermal forces}$$

Introduction

Jean Perrin



Paul Langevin



Tracer dynamics in thermal bath

$$0 = -\nabla V - \gamma \frac{d\mathbf{r}}{dt} + \boldsymbol{\xi}$$

Introduction

Correlation function $C(t) = \langle \mathbf{r}(t)\mathbf{r}(0) \rangle$

External perturbation \mathbf{f}_P

$$0 = -\nabla V - \gamma \frac{d\mathbf{r}}{dt} + \boldsymbol{\xi} + \mathbf{f}_P$$

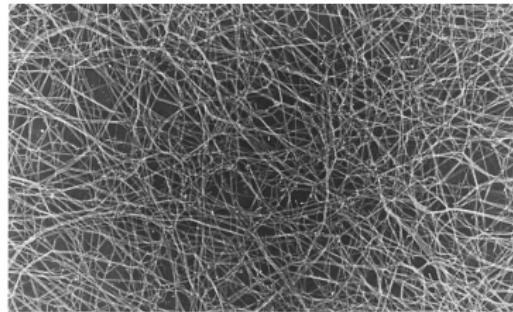
Response function $R(t)$

Fluctuation-dissipation theorem

$$R(t) = -\frac{1}{T} \frac{dC}{dt}$$

Introduction

Passive actin gel

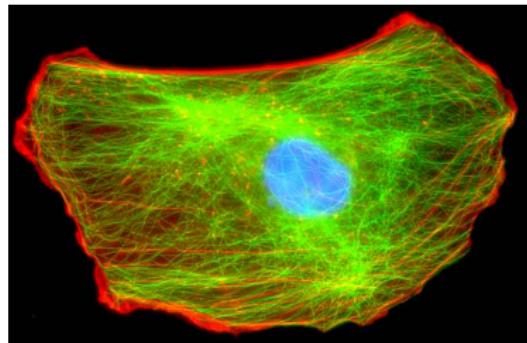


$$0 = -\nabla V - \int dt' \gamma(t-t') \frac{d\mathbf{r}}{dt'} + \xi$$

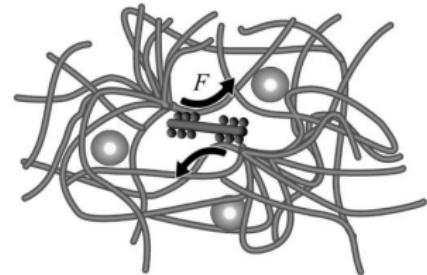
Fluctuation-dissipation theorem

$$R(t) = -\frac{1}{T} \frac{dC}{dt}$$

Introduction



Cytoskeletal network



Molecular motors

Deviation from equilibrium

$$R(t) \neq -\frac{1}{T} \frac{dC}{dt}$$

Outline

1 Microrheology techniques

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- 1 Microrheology techniques
- 2 Phenomenological model

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- 3 Biological system

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- ① Microrheology techniques
- ② Phenomenological model
- ③ Biological system
- ④ Comparison with experiments

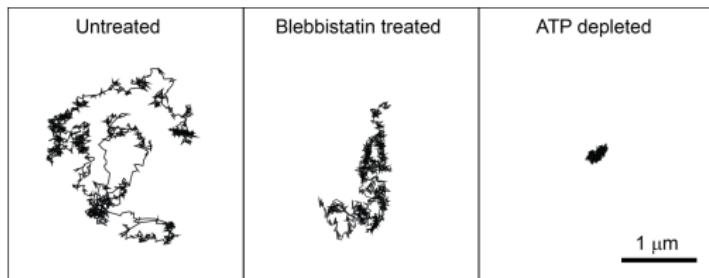
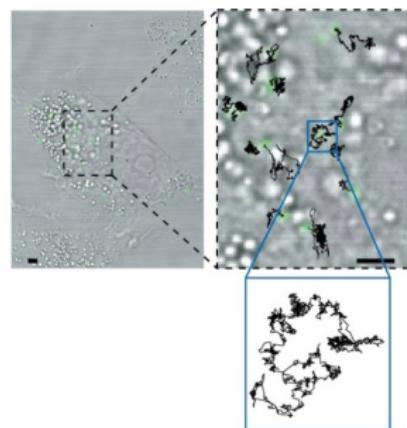
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- ① Microrheology techniques
- ② Phenomenological model
- ③ Biological system
- ④ Comparison with experiments
- ⑤ Energy fluxes using stochastic thermodynamics

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- 2 Phenomenological model
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- 5 Energy fluxes using stochastic thermodynamics

Microrheology techniques

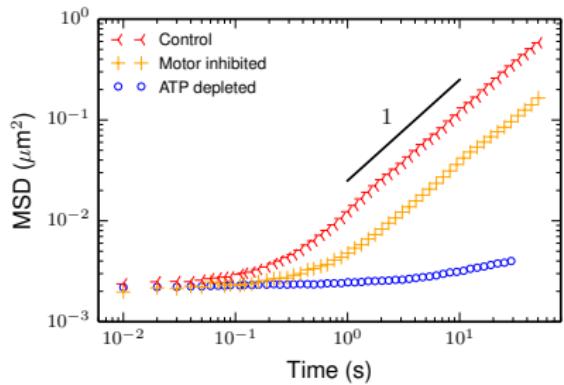


Living A7 cells
Tracers = Micro-size silica beads

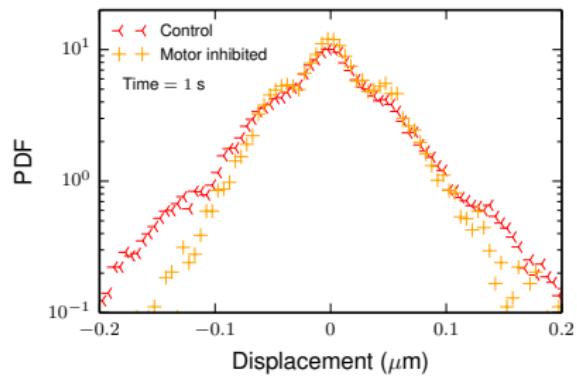
M. Guo, A. Ehrlicher, M. Jensen, M. Renz, J. Moore, R. Goldman,
J. Lippincott-Schwartz, F. MacKintosh, D. A. Weitz, *Cell* **158**, 822 (2014)

Microrheology techniques

Mean square displacement

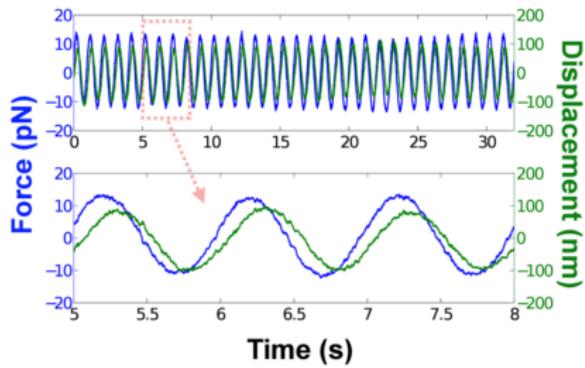
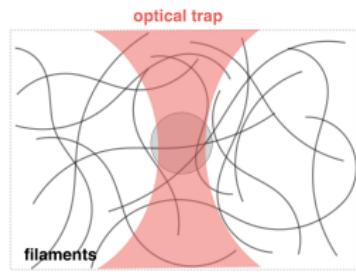


Distribution of displacement



É.F., M. Guo, N. S. Gov, P. Visco, D. A. Weitz,
F. van Wijland, EPL 110, 48005 (2015)

Microrheology techniques

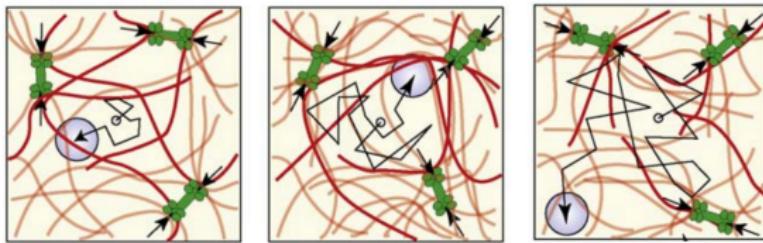


$$\langle \mathbf{r}(t) \rangle = \int dt' \underbrace{R(t-t')}_{\text{Response}} \mathbf{f}_P(t')$$

Outline

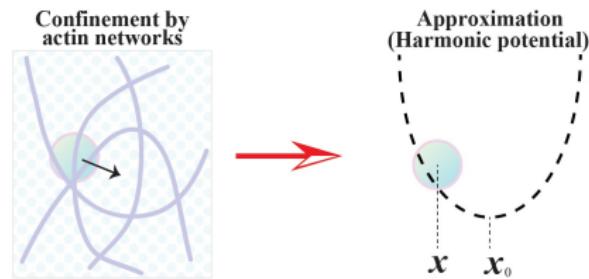
- 1 Microrheology techniques
- 2 Phenomenological model
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- 4 Comparison with experiments
- 5 Energy fluxes using stochastic thermodynamics

Phenomenological model



C. P. Brangwynne, G. H. Koenderink, F. C. MacKintosh,
D. A. Weitz, Trends Cell Biol. **19**, 423 (2009)

Phenomenological model

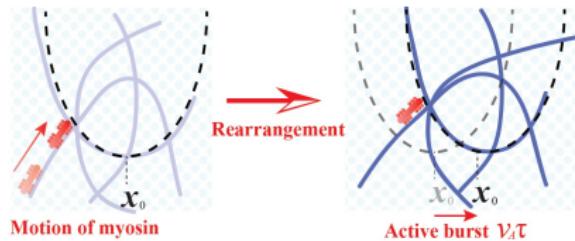


Tracer dynamics

$$\gamma \frac{d\mathbf{r}}{dt} = -k(\mathbf{r} - \mathbf{r}_0) + \xi$$

Phenomenological model

Active motion of local minimum

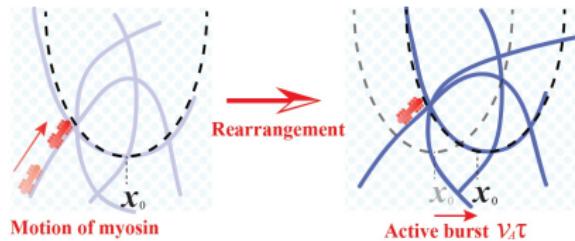


Tracer dynamics

$$\gamma \frac{d\mathbf{r}}{dt} = -k(\mathbf{r} - \mathbf{r}_0) + \boldsymbol{\xi}, \quad \gamma \frac{d\mathbf{r}_0}{dt} = \mathbf{F}_M$$

Phenomenological model

Active motion of local minimum

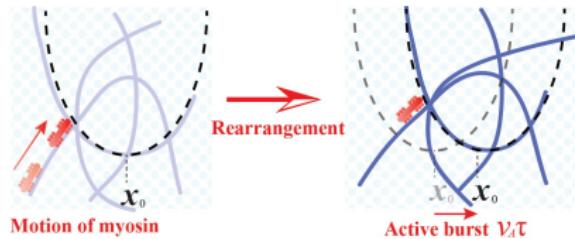


Tracer dynamics

$$\gamma * \frac{d\mathbf{r}}{dt} = -k(\mathbf{r} - \mathbf{r}_0) + \boldsymbol{\xi}, \quad \gamma * \frac{d\mathbf{r}_0}{dt} = \mathbf{F}_M$$

Phenomenological model

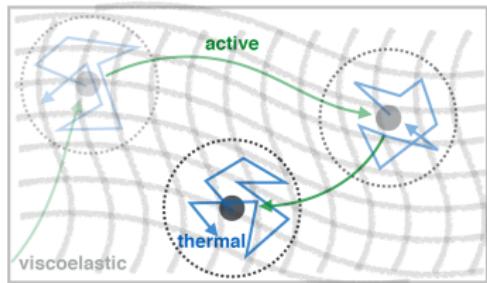
Active motion of local minimum



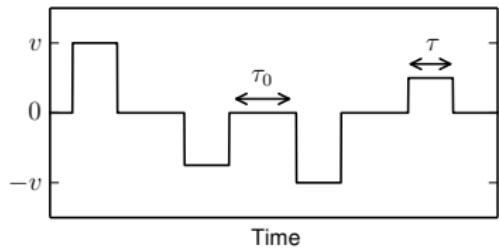
Tracer dynamics

$$\gamma * \frac{d\mathbf{r}}{dt} = -k\mathbf{r} + \underbrace{\mathbf{F}_A}_{k\mathbf{r}_0} + \boldsymbol{\xi}, \quad \gamma * \frac{d\mathbf{r}_0}{dt} = \mathbf{F}_M$$

Phenomenological model



Cage active motion



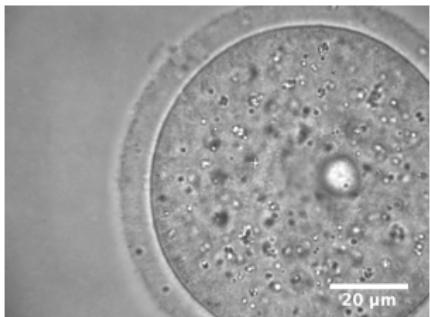
$$\langle F_M(t)F_M(0) \rangle \sim D_A \exp(-|t|/\tau)$$

$$D_A = \frac{(v\tau)^2}{3(\tau + \tau_0)}$$

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Biological system



Living mouse oocytes

Oocyte = Immature egg

Tracers = Vesicles

Motors = Myosin-V

É.F., W. W. Ahmed, M. Almonacid, M. Bussonnier, N. S. Gov,
M.-H. Verlhac, P. Visco, F. van Wijland, T. Betz, arXiv:1511.00921

W. W. Ahmed, É.F., M. Almonacid, M. Bussonnier, N. S. Gov,
M.-H. Verlhac, T. Betz, P. Visco, F. van Wijland, arXiv:1510.08299

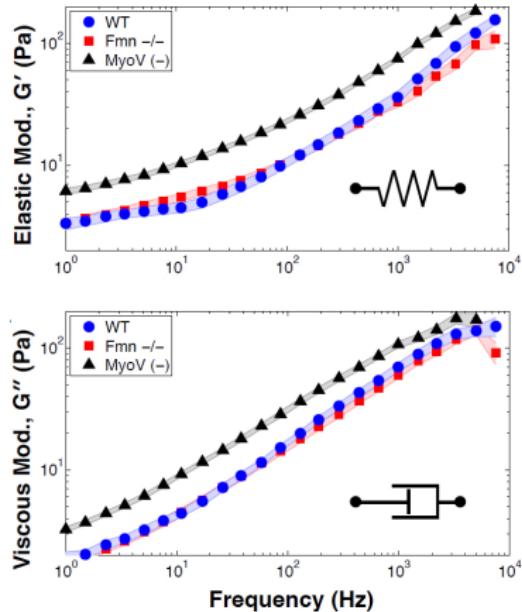
Biological system

$$R(\omega) \sim \frac{1}{G^*(\omega)}$$

Complex modulus
 $G^* = G' + iG''$

$$G^*(\omega) = G_0 [1 + (i\omega\tau_\alpha)^\alpha]$$

$$G_0 = 1.8 \text{ Pa}, \tau_\alpha = 0.1 \text{ s}, \alpha = 0.6$$



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Comparison with experiments

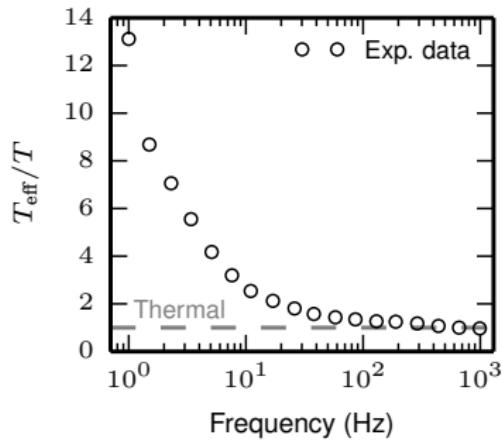
Deviation from equilibrium

$$R(t) \neq -\frac{1}{T} \frac{dC}{dt}$$

Effective temperature $T_{\text{eff}}(\omega) = \frac{\omega C(\omega)}{2R''(\omega)}$

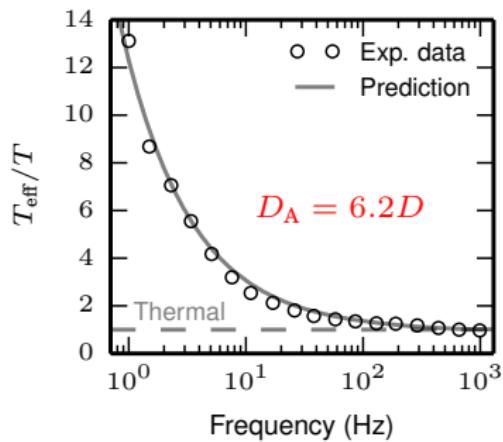
Comparison with experiments

Effective temperature $T_{\text{eff}}(\omega) = \frac{\omega C(\omega)}{2R''(\omega)}$



Comparison with experiments

Effective temperature $T_{\text{eff}}(\omega) = \frac{\omega C(\omega)}{2R''(\omega)}$



Comparison with experiments

Spectrum of stochastic forces

$$S_{\text{cell}}(\omega) = \mathcal{F} \langle [\xi + \mathbf{F}_A](t) [\xi + \mathbf{F}_A](0) \rangle$$

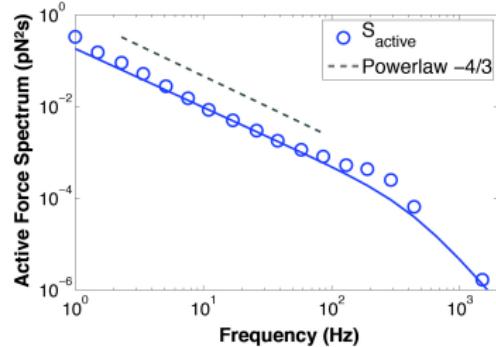
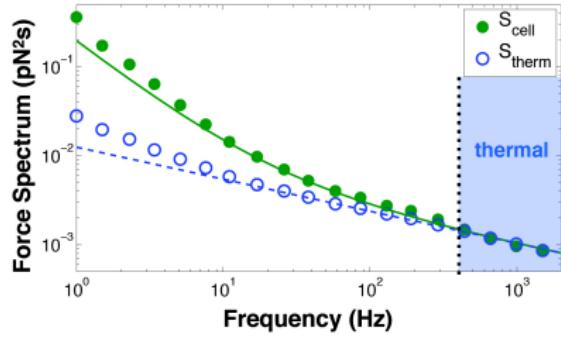
Combining response and fluctuations

$$S_{\text{cell}}(\omega) = \frac{C(\omega)}{|R(\omega)|^2}$$

Active and thermal contributions

$$S_{\text{cell}}(\omega) = \underbrace{S_{\text{th}}(\omega)}_{\text{FDT}} + S_A(\omega)$$

Comparison with experiments



Correlation time $\tau = 0.3 \text{ ms}$

Power stroke time of myosin-V $\sim 0.5 \text{ ms}$

G. Cappello, P. Pierobon, C. Symonds, L. Busoni, J. Christof, M. Gebhardt, M. Rief, J. Prost, Proc. Natl. Acad. Sci. U.S.A. **104**, 15328 (2007)

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Energy fluxes

Transfer of energy

Motors → Tracers → Thermostat

Stochastic thermodynamics

$$J = \langle \text{velocity} \times \text{force} \rangle$$

Energy fluxes

Power of thermal forces

$$J_{\text{diss}} = \langle \text{tracer velocity} \times \text{thermal forces} \rangle$$

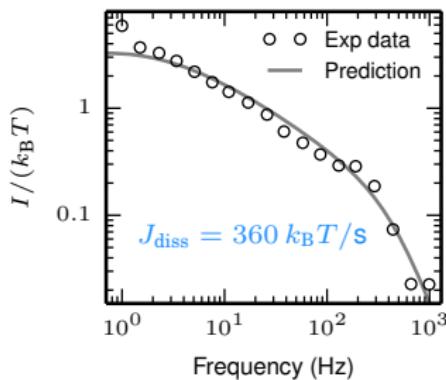
$$J_{\text{diss}} = \left\langle \frac{d\mathbf{r}}{dt} \left(\gamma * \frac{d\mathbf{r}}{dt} - \boldsymbol{\xi} \right) \right\rangle$$

Energy transfer from tracer to thermostat

Energy fluxes

Deviation from equilibrium

$$J_{\text{diss}} = \int \frac{d\omega}{2\pi} \underbrace{\frac{2[T_{\text{eff}}(\omega) - T]}{1 + [G'(\omega)/G''(\omega)]^2}}_{I(\omega)}$$



Other energy transfers

- ① From the motors to the cage

$$J_{\text{cage}} = \left\langle \frac{d\mathbf{r}_0}{dt} \mathbf{F}_M \right\rangle$$

- ② From the cage to the tracer

$$J_{\text{tracer}} = \left\langle \frac{d\mathbf{r}}{dt} \mathbf{F}_A \right\rangle$$

Energy fluxes

Other energy transfers

- ➊ From the motors to the cage

$$J_{\text{cage}} = 2 \times 10^5 k_{\text{B}} T / \text{s}$$

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

K. Fujita, M. Iwaki, A. H. Iwane, L. Marcucci, T. Yanagida, Nat. Com. 3, 956 (2012)

- ➋ From the cage to the tracer

$$J_{\text{tracer}} = J_{\text{diss}} = 360 k_{\text{B}} T / \text{s}$$

Energy fluxes

Transduction of power by the cage
from the motors to the tracer

$$\rho = \frac{J_{\text{tracer}}}{J_{\text{cage}}} \sim 10^{-3}$$

Conclusion

Caging model | Tracer in living cells

Short time Thermal, equilibrium

Large time Active, out-of-equilibrium

What have we learned about the system?

- ① Amplitude of active fluctuations
- ② Typical active time scales
- ③ Energy fluxes

Conclusion

Collaborators

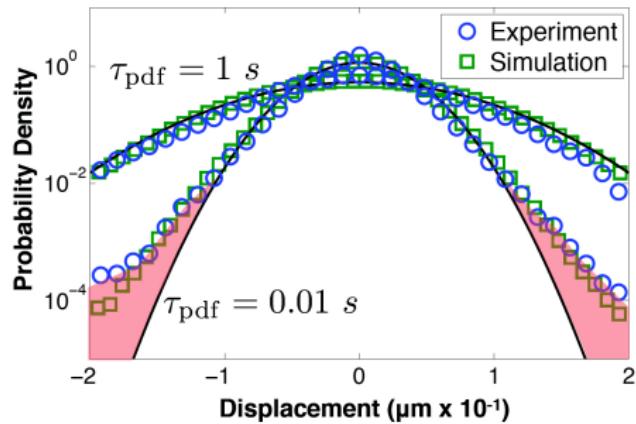
- M. Almonacid, M.-H. Verlhac | Collège de France
- W. W. Ahmed, M. Bussonnier, T. Betz | Curie Institute
- M. Guo, D. A. Weitz | University of Harvard
- N. S. Gov | Weizmann Institute of Science

References

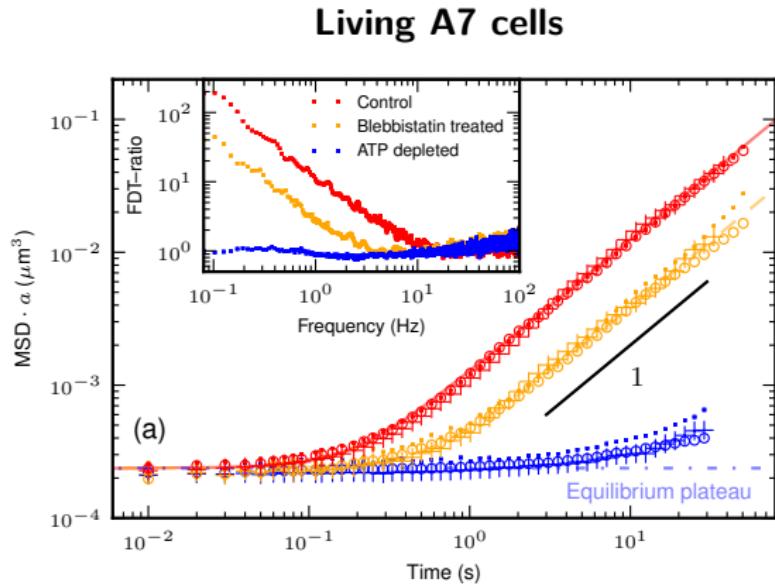
- É.F., W. W. Ahmed, M. Almonacid, M. Bussonnier, N. S. Gov, M.-H. Verlhac, P. Visco, F. van Wijland, T. Betz, arXiv:1511.00921
- W. W. Ahmed, É.F., M. Almonacid, M. Bussonnier, N. S. Gov, M.-H. Verlhac, T. Betz, P. Visco, F. van Wijland, arXiv:1510.08299
- É.F., M. Guo, N. S. Gov, P. Visco, D. A. Weitz, F. van Wijland, **EPL** **110**, 48005 (2015)

Comparison with experiments

Distribution of displacement

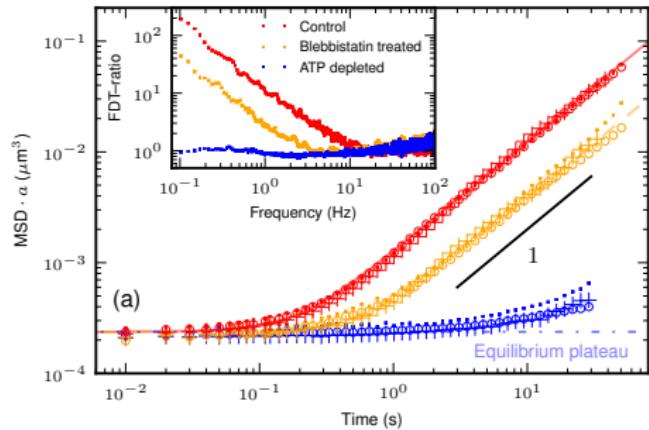


Comparison with experiments



$$T_{\text{eff}}(\omega) = \frac{\omega C(\omega)}{2R''(\omega)}, \quad \text{FDT-ratio} = \frac{T_{\text{eff}}(\omega)}{T}$$

Comparison with experiments

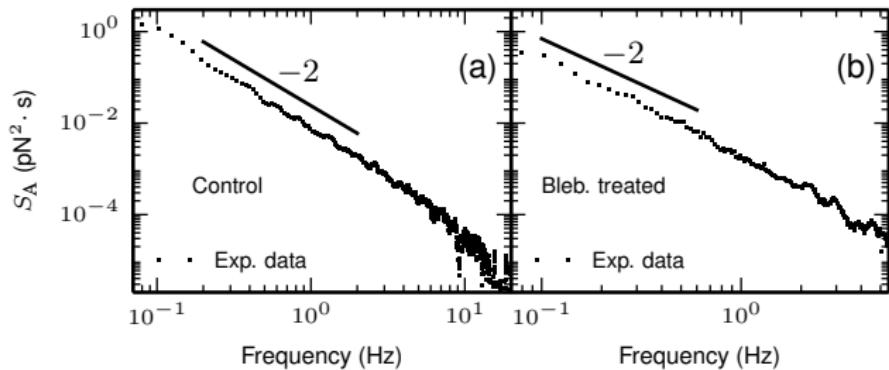


	Control	Blebb.
D_A/D_T	2.8×10^{-3}	9×10^{-4}
τ (s)	0.16	0.39

Comparison with experiments

$$S_{\text{cell}} = S_{\text{th}} + \cancel{S_A}$$

ATP depleted



Comparison with experiments

$$S_{\text{cell}} = S_{\text{th}} + \cancel{S_A}$$

ATP depleted

