Tracking nonequilibrium physics in living systems

Étienne Fodor, Paolo Visco, Frédéric van Wijland

Laboratoire Matière et Systèmes Complexes, Université Paris Diderot

Physics-Biology Interface Seminar
Université Paris Sud

Introduction

Biology-Physics collaboration

Biology

Maria Almonacid, Marie-Hélène Verlhac | Collège de France

Biophysics

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

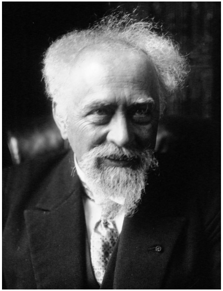
Ming Guo, David A. Weitz | University of Harvard

Physics

Nir S. Gov | Weizmann Institute of Science

Introduction

Jean Perrin



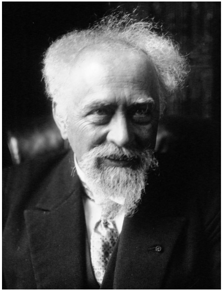
Paul Langevin

Tracer dynamics in thermal bath

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

Introduction

Jean Perrin



Paul Langevin

Tracer dynamics in thermal bath

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

Introduction

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

External perturbation $\mathbf{f}_\mathrm{P}$

$$0 = -\nabla V - \gamma \frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t} + \boldsymbol{\xi} + \mathbf{f}_\mathrm{P}$$

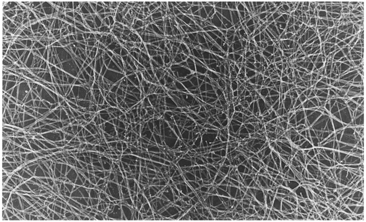
Response function $R(t)$

Fluctuation-dissipation theorem

$$R(t) = -\frac{1}{T}\frac{\mathrm{d}C}{\mathrm{d}t}$$

Introduction

Passive actin gel

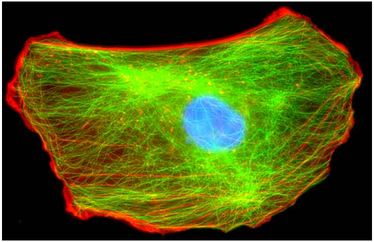


$$0 = -\nabla V - \int \mathrm{d}t' \gamma(t - t') \frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t'} + \boldsymbol{\xi}$$

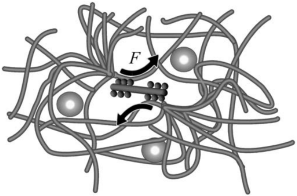
Fluctuation-dissipation theorem

$$R(t) = -\frac{1}{T}\frac{\mathrm{d}C}{\mathrm{d}t}$$

Introduction



Cytoskeletal network



Molecular motors

Deviation from equilibrium

$$R(t) \neq -\frac{1}{T}\frac{\mathrm{d}C}{\mathrm{d}t}$$

Outline

1. Microrheology techniques

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2. Phenomenological model

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2. Phenomenological model
3. Biological system

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2. Phenomenological model

3. Biological system

4. Comparison with experiments

Outline

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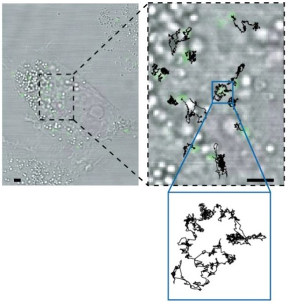
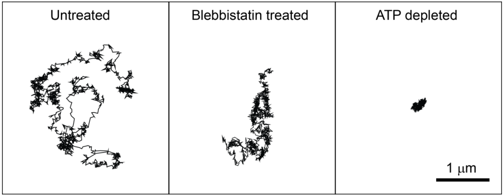
1. Microrheology techniques
2. Phenomenological model
3. Biological system
4. Comparison with experiments
5. Energy fluxes using stochastic thermodynamics

Microrheology techniques





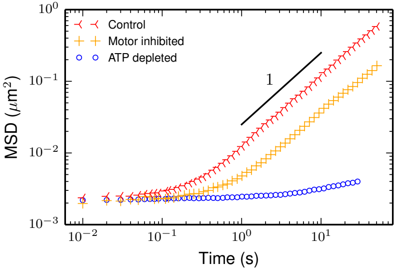
Living A7 cells

Tracers = Micro-size silica beads

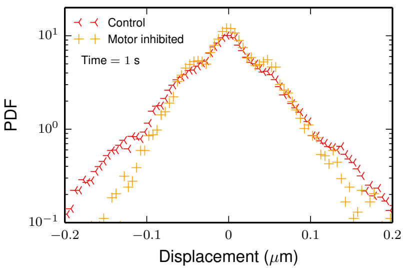
M. Guo, A. Ehrlicher, M. Jensen, M. Renz, J. Moore, R. Goldman,
J. Lippincott-Schwartz, F. MacKintosh, D. A. Weitz, Cell **158**, 822 (2014)

Microrheology techniques

Mean square displacement

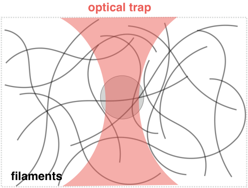


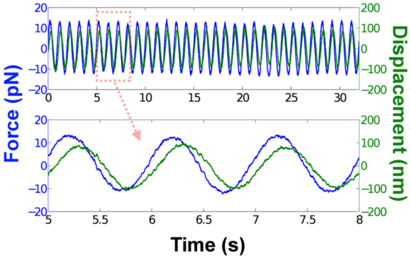
Distribution of displacement



É.F., M. Guo, N. S. Gov, P. Visco, D. A. Weitz,

F. van Wijland, EPL **110**, 48005 (2015)





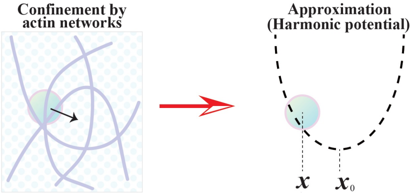
$$\langle \mathbf{r}(t) \rangle = \int \mathrm{d}t' \underbrace{R(t-t')}_{\text{Response}} \mathbf{f}_{\mathrm{P}}(t')$$

Outline

Phenomenological model

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

Phenomenological model

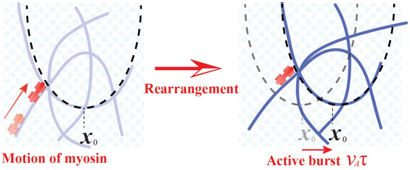


Tracer dynamics

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

Phenomenological model

Active motion of local minimum

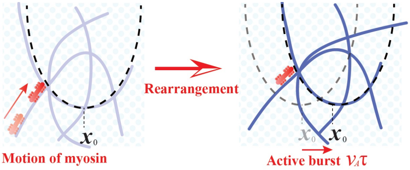


Tracer dynamics

$$\gamma\frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t} = -k(\mathbf{r}-\mathbf{r}_0)+\boldsymbol{\xi}, \quad \gamma\frac{\mathrm{d}\mathbf{r}_0}{\mathrm{d}t} = \mathbf{F}_{\mathrm{M}}$$

Phenomenological model

Active motion of local minimum

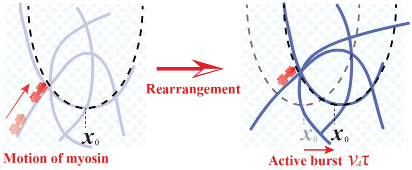


Tracer dynamics

$$\gamma * \frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t} = -k(\mathbf{r} - \mathbf{r}_0) + \boldsymbol{\xi}, \quad \gamma * \frac{\mathrm{d}\mathbf{r}_0}{\mathrm{d}t} = \mathbf{F}_{\mathrm{M}}$$

Phenomenological model

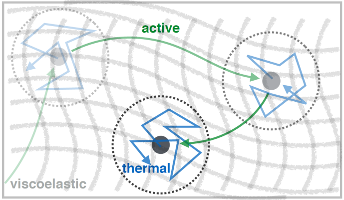
Active motion of local minimum

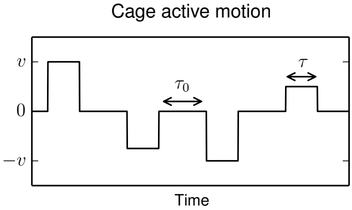


Tracer dynamics

$$\gamma * \frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t} = -k\mathbf{r} + \underbrace{\mathbf{F}_{\mathrm{A}}}_{k\mathbf{r}_0} + \boldsymbol{\xi}, \quad \gamma * \frac{\mathrm{d}\mathbf{r}_0}{\mathrm{d}t} = \mathbf{F}_{\mathrm{M}}$$

Phenomenological model



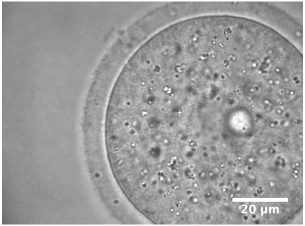


$$\langle F_{\mathrm{M}}(t) F_{\mathrm{M}}(0) \rangle \sim D_{\mathrm{A}} \exp\left(-|t|/\tau\right)$$

$$D_{\mathrm{A}} = \frac{(v\tau)^2}{3(\tau+\tau_0)}$$

Outline

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`

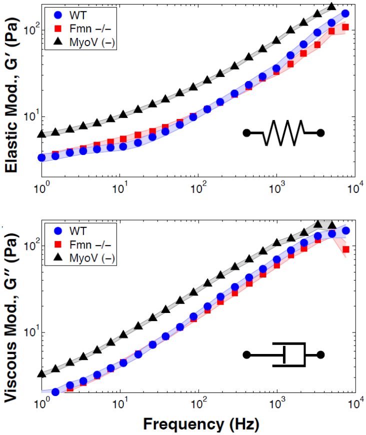
Biological system

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

Complex modulus
$G^* = G' + \mathrm{i}G''$

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

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



Outline

Comparison with experiments

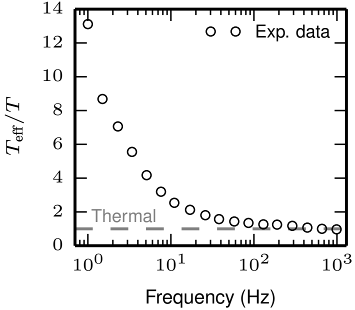
Deviation from equilibrium

$$R(t) \neq -\frac{1}{T}\frac{\mathrm{d}C}{\mathrm{d}t}$$

Effective temperature $\quad T_{\mathrm{eff}}(\omega) = \dfrac{\omega C(\omega)}{2R''(\omega)}$

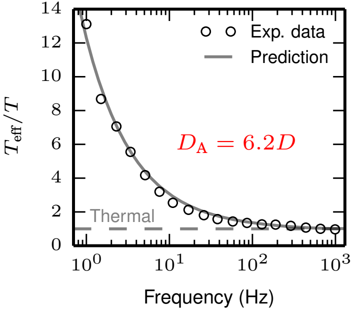
Comparison with experiments

Effective temperature $\quad \color{red}{T_{\text{eff}}(\omega)} = \dfrac{\omega C(\omega)}{2R''(\omega)}$



Comparison with experiments

Effective temperature $\quad T_{\mathrm{eff}}(\omega) = \dfrac{\omega C(\omega)}{2R''(\omega)}$



Comparison with experiments

Spectrum of stochastic forces

$$S_{\mathrm{cell}}(\omega) = \mathcal{F}\left\langle \left[\xi + \mathbf{F}_{\mathrm{A}}\right](t)\left[\xi + \mathbf{F}_{\mathrm{A}}\right](0)\right\rangle$$

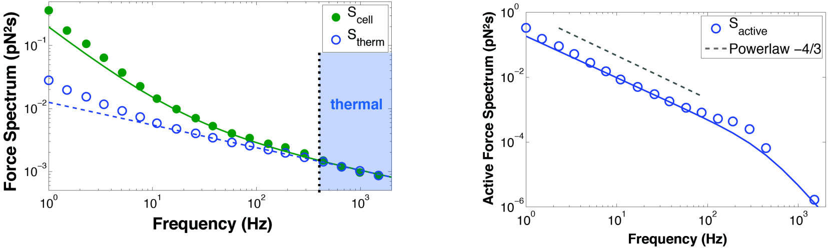
Combining response and fluctuations

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

Active and thermal contributions

$$S_{\mathrm{cell}}(\omega) = \underbrace{S_{\mathrm{th}}(\omega)}_{\mathrm{FDT}} + S_{\mathrm{A}}(\omega)$$

Comparison with experiments



Correlation time $\tau = 0.3\,\mathrm{ms}$

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

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)

Outline

Energy fluxes

Transfer of energy

Motors $\rightarrow$ Tracers $\rightarrow$ Thermostat

Stochastic thermodynamics

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

Energy fluxes

Power of thermal forces

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

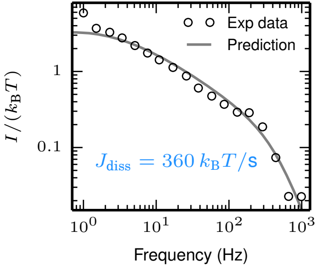
$$J_{\text{diss}} = \left\langle \frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t} \left(\gamma * \frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t} - \boldsymbol{\xi} \right) \right\rangle$$

Energy transfer from tracer to thermostat

Energy fluxes

Deviation from equilibrium

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



Energy fluxes

Other energy transfers

1. From the motors to the cage

$$J_{\mathrm{cage}} = \left\langle \frac{\mathrm{d}\mathbf{r}_0}{\mathrm{d}t} \mathbf{F}_{\mathrm{M}} \right\rangle$$

2. From the cage to the tracer

$$J_{\mathrm{tracer}} = \left\langle \frac{\mathrm{d}\mathbf{r}}{\mathrm{d}t} \mathbf{F}_{\mathrm{A}} \right\rangle$$

Energy fluxes

Other energy transfers

1. From the motors to the cage

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

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

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

2. From the cage to the tracer

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

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

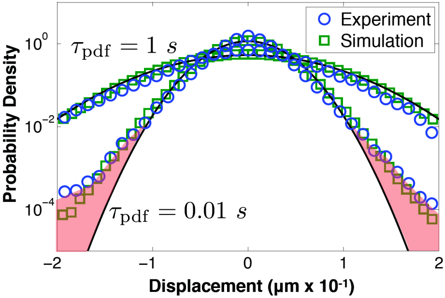
- M. Almonacid, M.-H. Verlhac | Collège de France
- W. W. Ahmed, M. Bussonnier, T. Betz | Curie Institute
- M. Guo, D. A. Weitz | University of Harvard
- N. S. Gov | Weizmann Institute of Science

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)

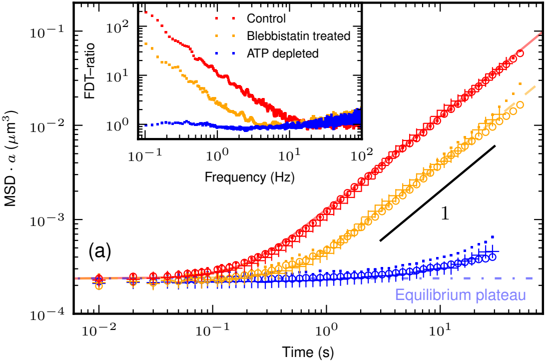
Comparison with experiments

Distribution of displacement



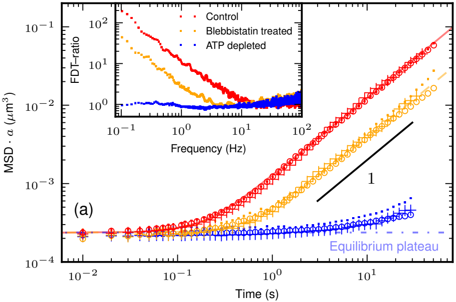
Comparison with experiments

Living A7 cells



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

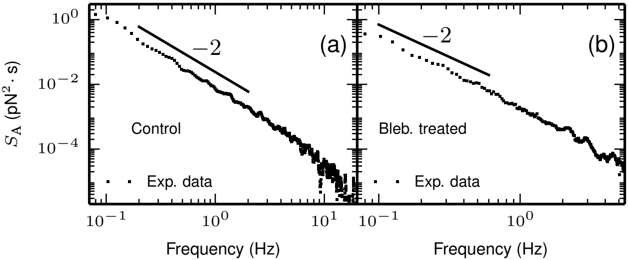
Comparison with experiments



	Control	Blebb.
$D_{\mathrm{A}}/D_{\mathrm{T}}$	2.8×10^{-3}	9×10^{-4}
τ (s)	0.16	0.39

Comparison with experiments

$$\underbrace{S_{\text{cell}} = S_{\text{th}}}_{\text{ATP depleted}} + \cancel{S_A}$$



Comparison with experiments

$$\underbrace{S_{\text{cell}} = S_{\text{th}}}_{\text{ATP depleted}} + \cancel{S_A}$$