Statistical mechanics in the nanoscale: from physics to biology

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Giovanni Paladin conference, September 2013

Recent review: A. Alemany, M. Ribezzi and F.R. in *Nonequilibrium Statistical Physics of Small Systems: Fluctuation Relations and Beyond,* R.Klages, W.Just, C.Jarzynski (Eds.),Wiley-VCH 2012

Work also done in collaboration with A. Crisanti and M. Picco, E. Dieterich and U. Seifert

About nonequilibrium states

In equilibrium:

• No net energy & mass transfer between system and sources

• Boltzmann-Gibbs distribution

Out of equilibrium:

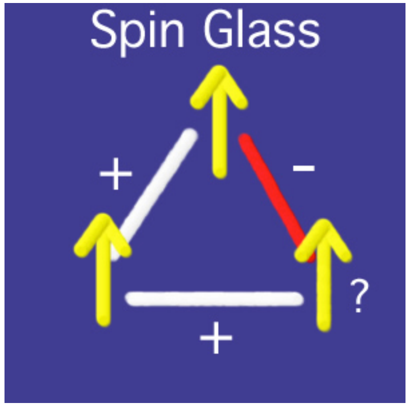
• Net energy & mass transfer

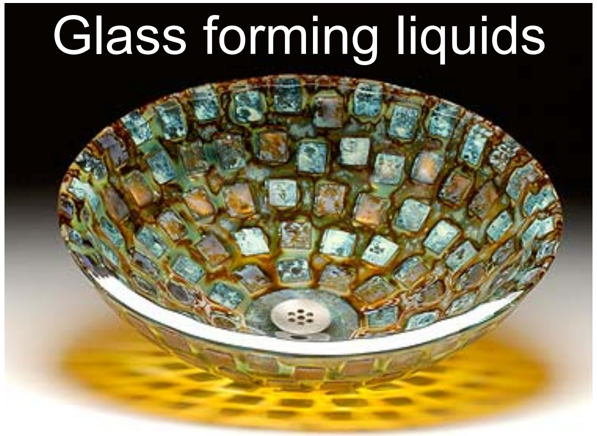
• Breakdown of maximum entropy principle

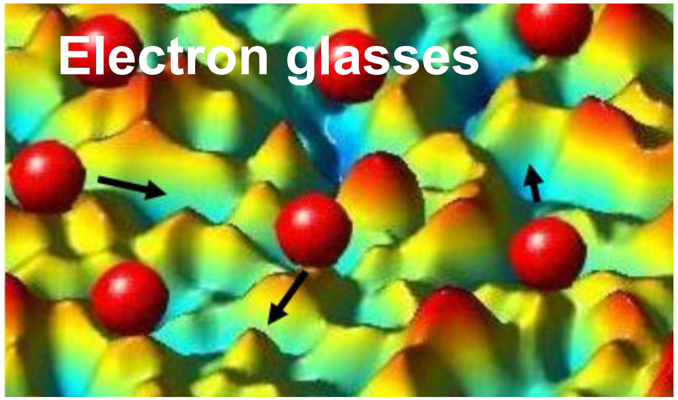
• Non-conservative or time-dependent forces

For a review, F. Ritort, Adv. Chem. Phys. **137** 31 (2008)

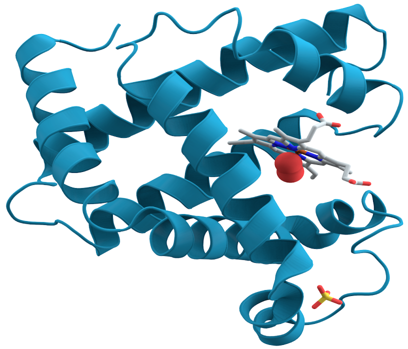
WEAKLY ERGODIC OR GLASSY SYSTEMS







Biomolecules



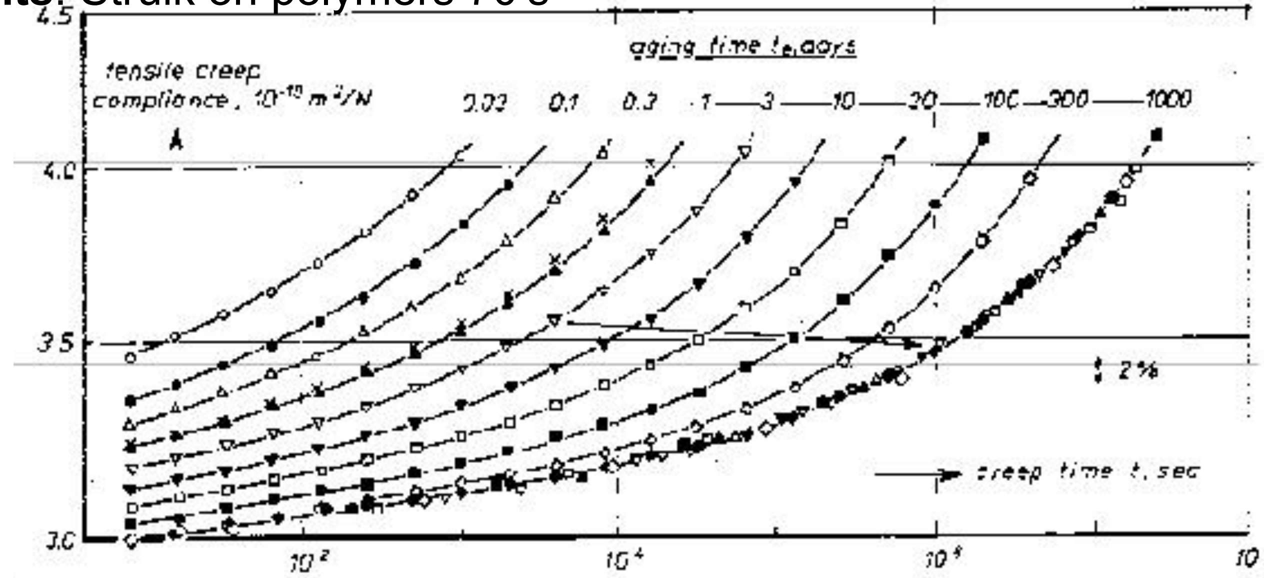
Slow dynamics or aging | FDT violations

Intermittent events | Kinetic heterogeneities

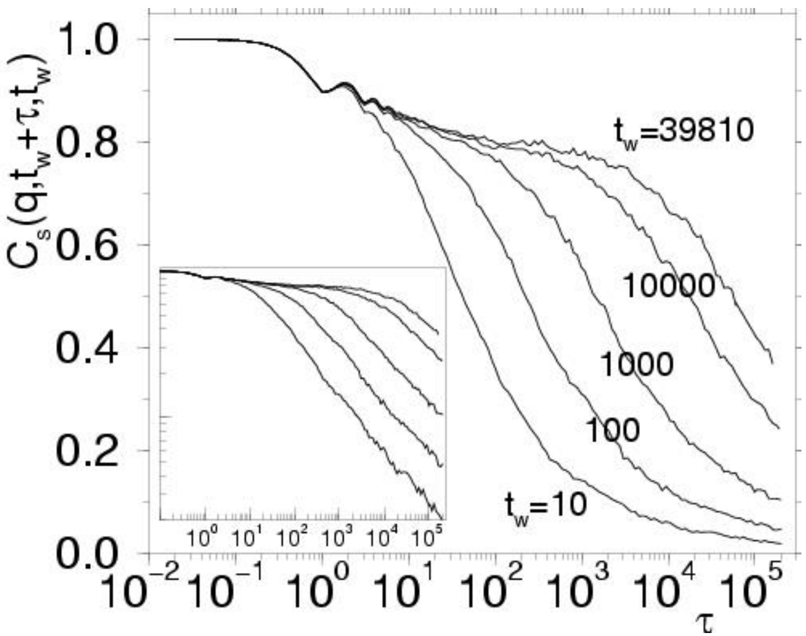
Non-equilibrium fluctuations due to **small** cooperatively rearranging regions (CRRs)

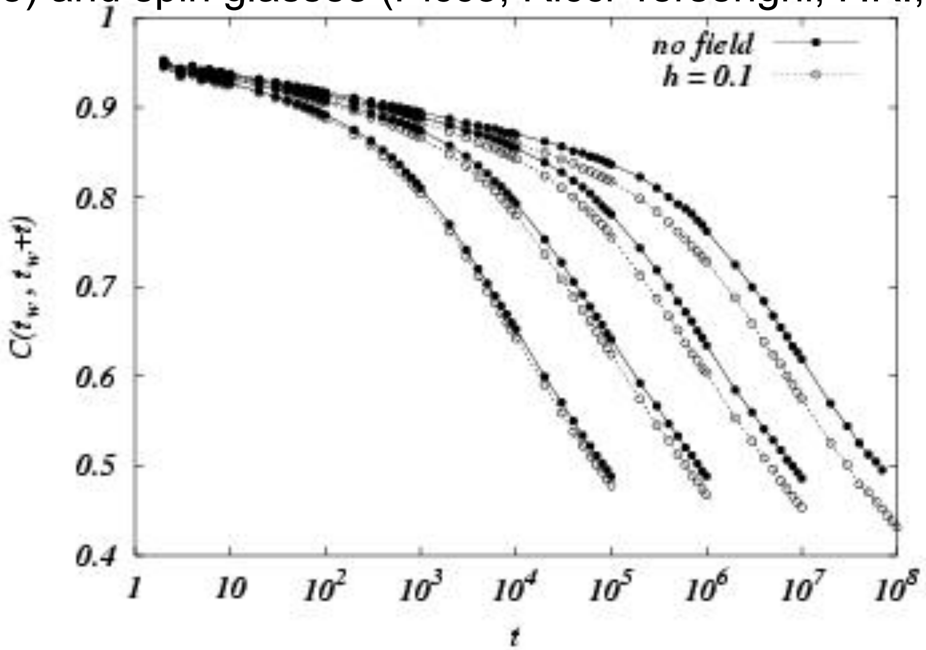
AGING

Experiments: Struik on polymers 70's



Simulations: Structural glasses (Kob, Barrat 98) and spin glasses (Picco, Ricci-Tersenghi, F.R.,2000)





FDT violations and effective temperatures

$$\boxed{k_B T_{eff}(\omega) = \frac{\pi\omega S(\omega)}{2\hat{\chi}''(\omega)}}$$

Power spectrum *(fluctuations)*

Susceptibility *(response)*

Two-times response Two-times correlation

$$T_{eff}(t_w) R(t, t_w) = \frac{\partial C(t, t_w)}{\partial t_w}$$

Cugliandolo and Kurchan, Phys. Rev. Lett. **71,** 173 (1993)

Q: Is there a thermodynamic nonequilibrium temperature?

L.F.Cugliandolo, J.Kurchan and L. Peliti, Phys. Rev. E, **55,** 3898 (1998)

For "numerical evidence", see A. Crisanti and F. Ritort, J. Phys. A (Math. Gen.) **36,** R181 (2003)

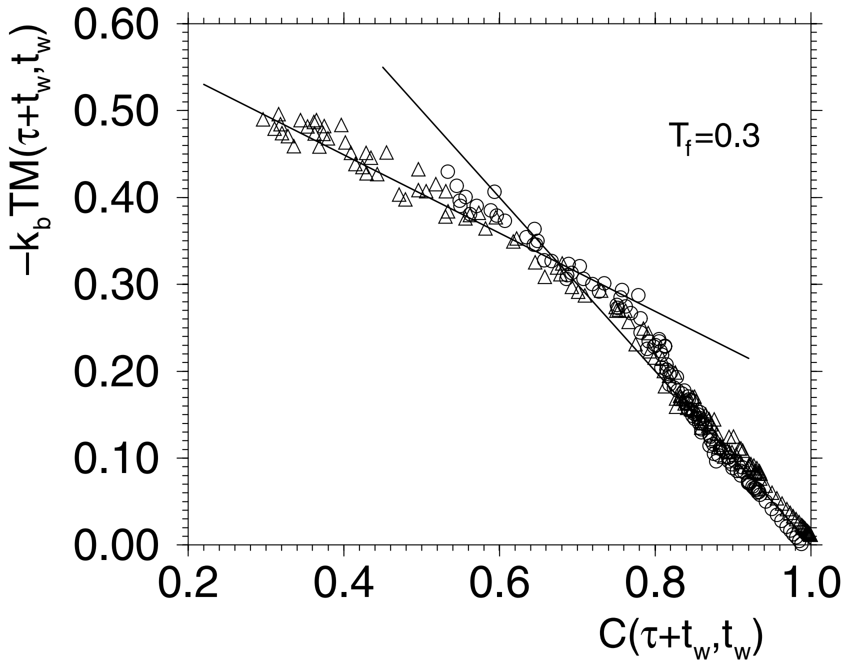
Fluctuation-dissipation plots (FD plots)

$$\boxed{\frac{1}{T_{eff}(t_w)} = \left.\frac{\partial \chi(t,t_w)}{\partial C(t,t_w)}\right|_{t_w \text{ fixed}}}$$

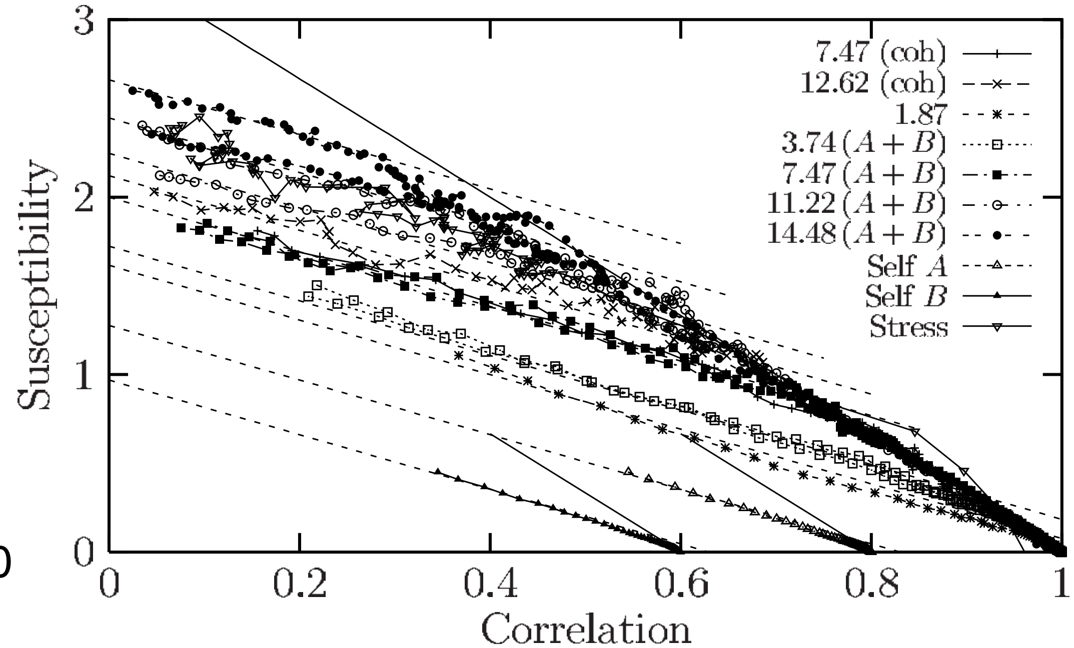
L.F. Cugliandolo and J. Kurchan, J. Phys. A (Math. Gen.) **27**, 5749 (1993)

For "numerical evidence", see A. Crisanti and F. Ritort, J. Phys. A (Math. Gen.) **36,** R181 (2003)

AGING Lennard-Jones systems **STEADY-STATES**



J. L. Barrat and W. Kob, 1999

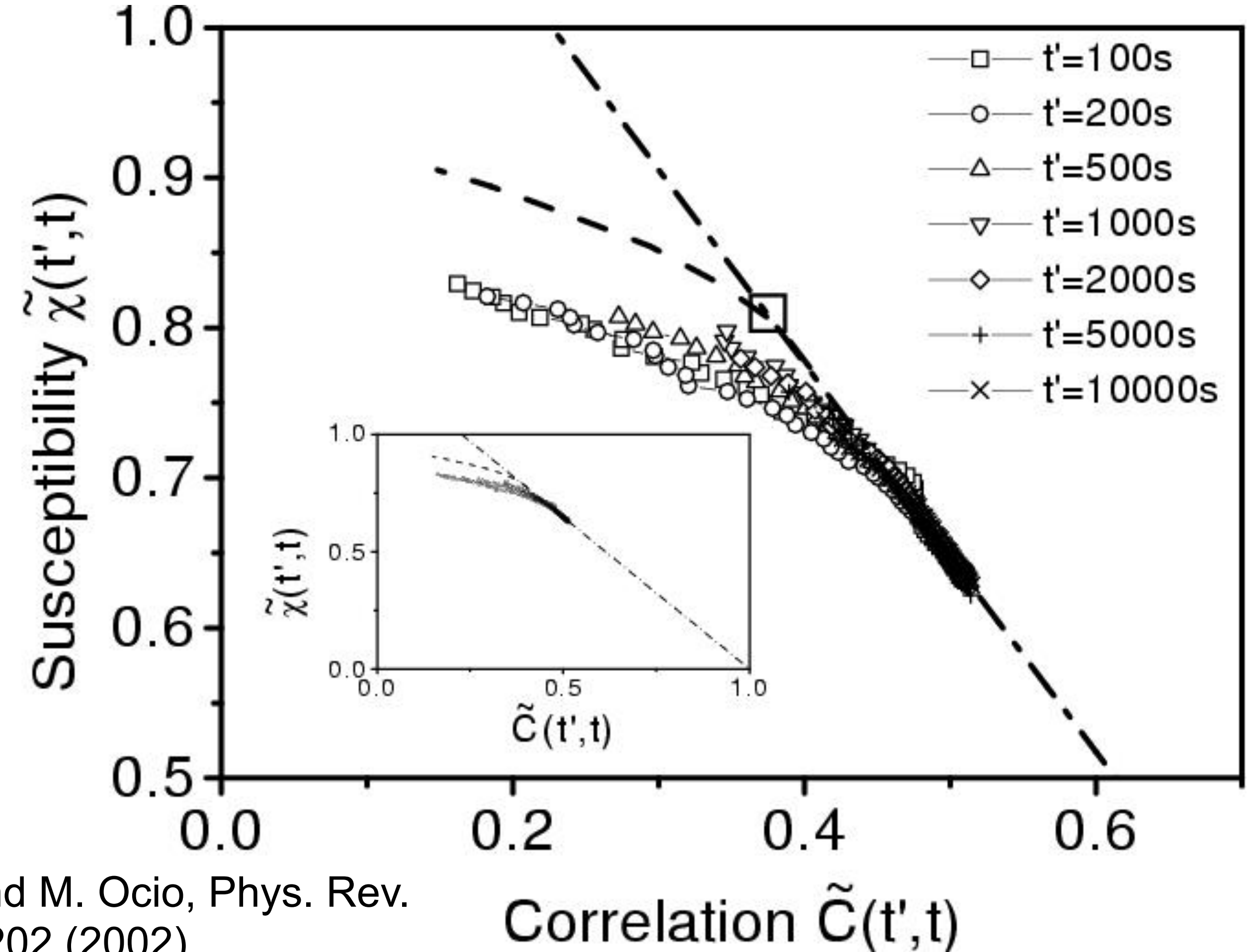


L. Berthier and J. L. Barrat, 2002

Fluctuation-dissipation plots

$$\boxed{\frac{1}{T_{eff}(t_w)} = \left.\frac{\partial \chi(t,t_w)}{\partial C(t,t_w)}\right|_{t_w \text{ fixed}}}$$

L.F. Cugliandolo and J. Kurchan,
J. Phys. A (Math. Gen.) **27**, 5749 (1993)

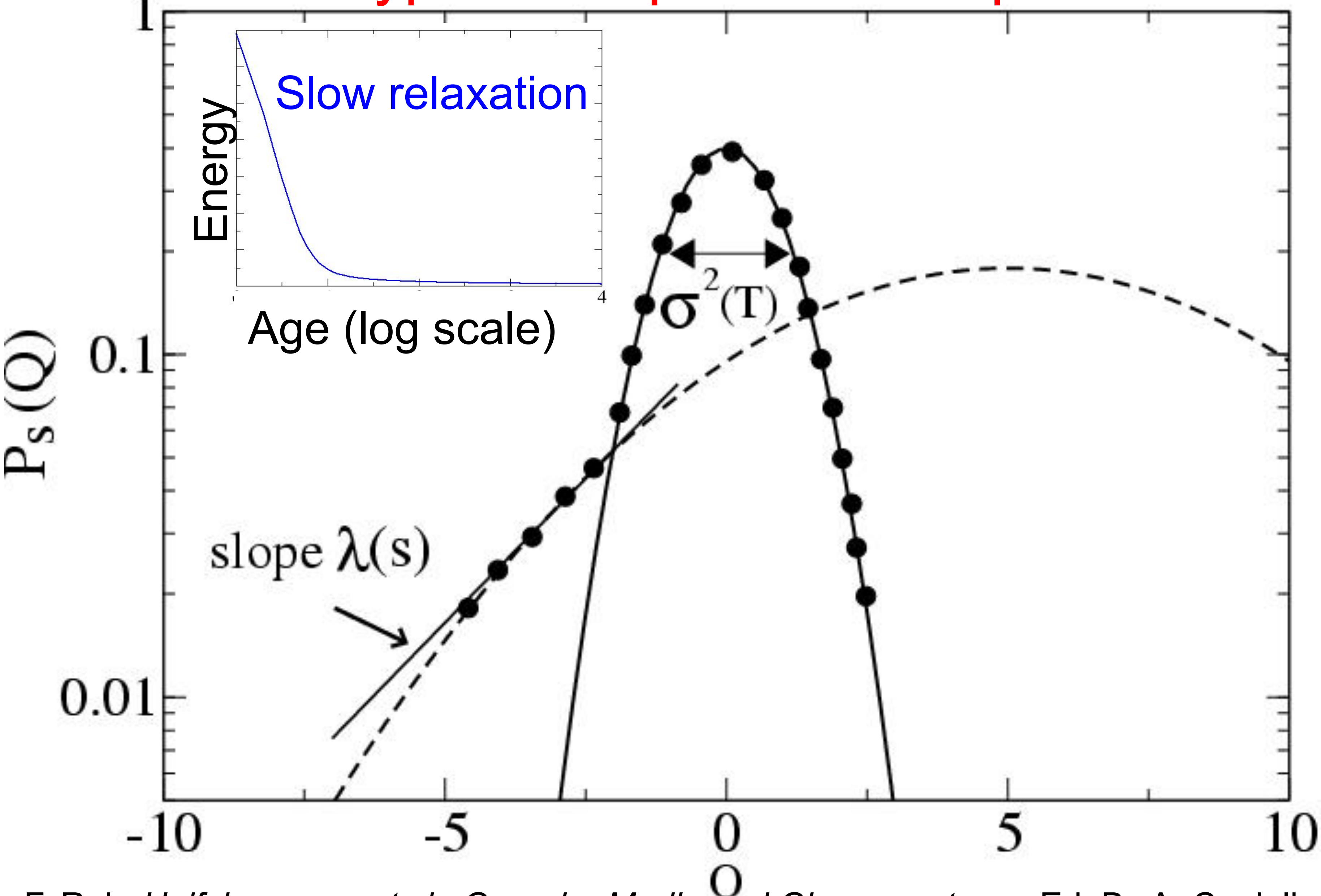


D. Herisson and M. Ocio, Phys. Rev. Lett., **88,** 257202 (2002)

Main idea: glassy systems exchange energy with the environment in a process dominated by rare and intermittent events (e.g. relaxation of internal stress) and large deviations respect to the average behavior.

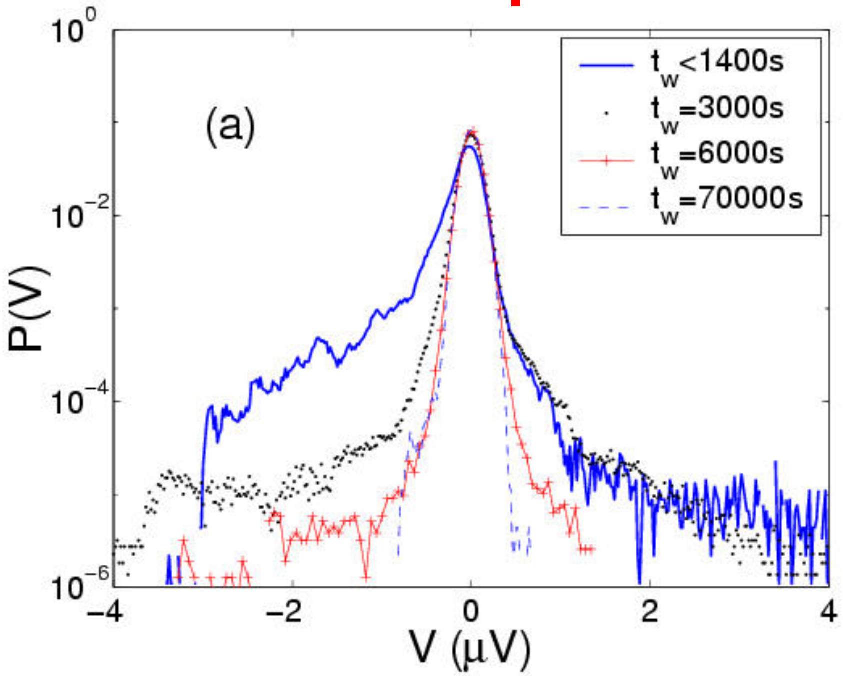
Strategy: The understanding of glassy behavior can be approached from the perspective of nonequilibrium thermodynamics of small systems (also called stochastic thermodynamics) and fluctuation theorems.

Typical shape of a heat pdf

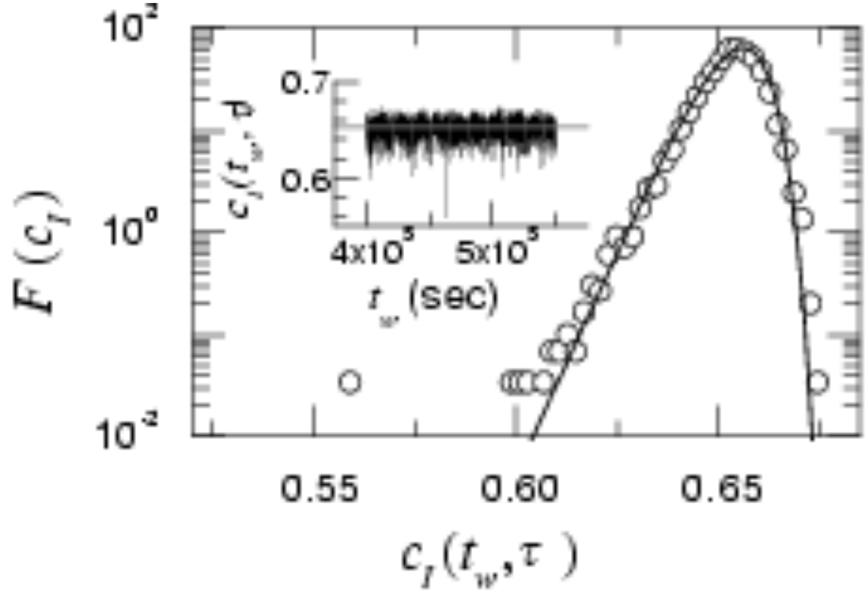


F. R. in *Unifying concepts in Granular Media and Glassy systems,* Ed. By A. Coniglio, A. Fierro and H. Hermann, Springer Verlag, Berlin 2004, page 129

Experimental evidence



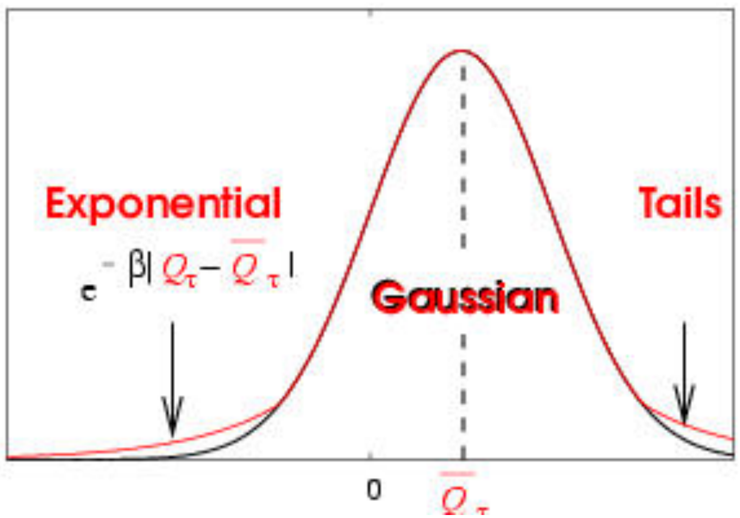
Noise measurements in glasses (laponite and polycarbonate)S.Ciliberto group in Lyon (France)



Confocal microscopy in colloids:L.Cipelletti (Montpellier) and E.Weeks (USA) groups

Also in steady states (theory)

Heat distribution for a particle confined in a quadratic potential and dragged through a solvent (E.D.G. *Cohen and R. Van Zon, 2003*)

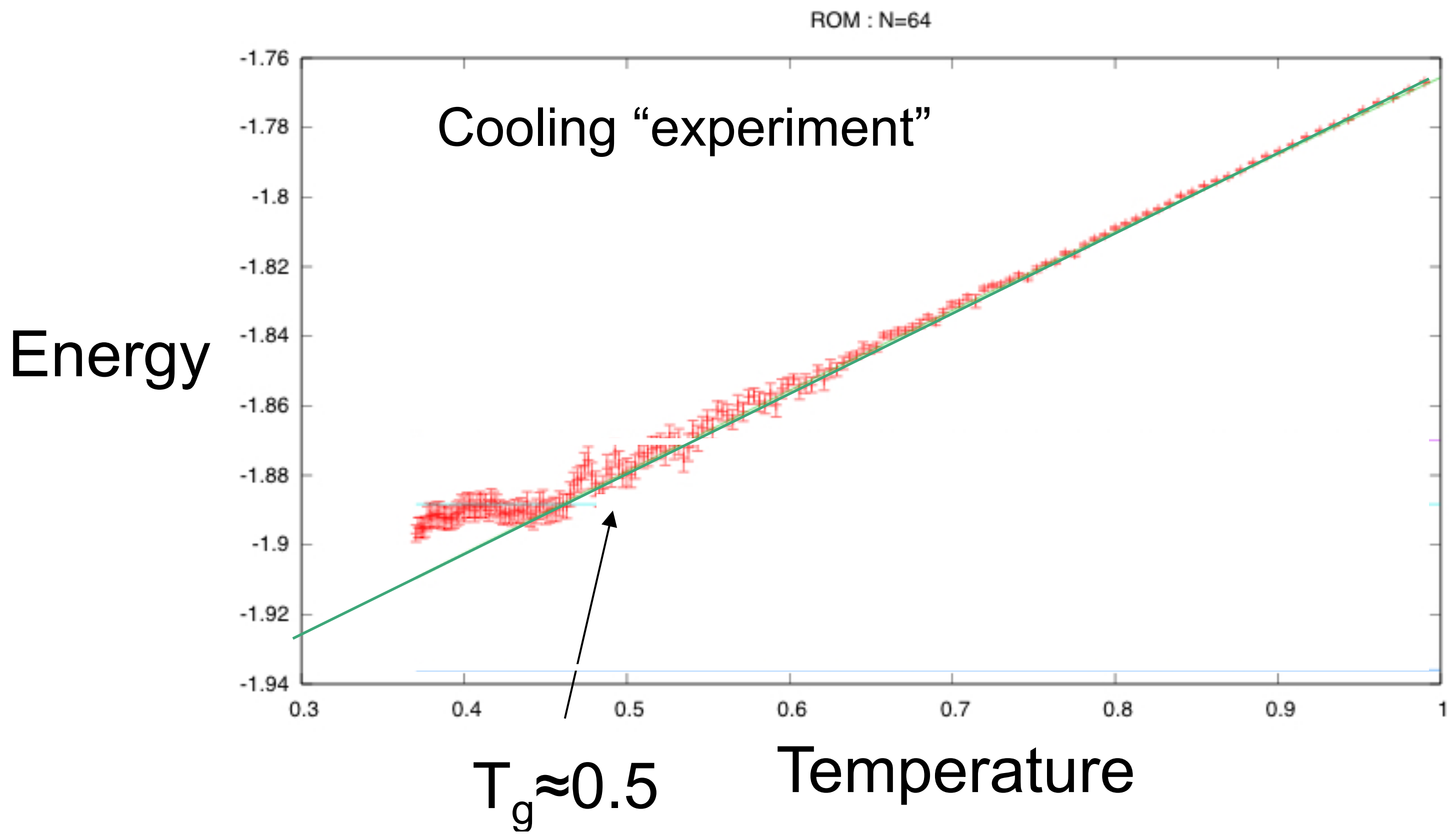


Glass transition in the random orthogonal model

A random matrix (Ising spin glass) model:

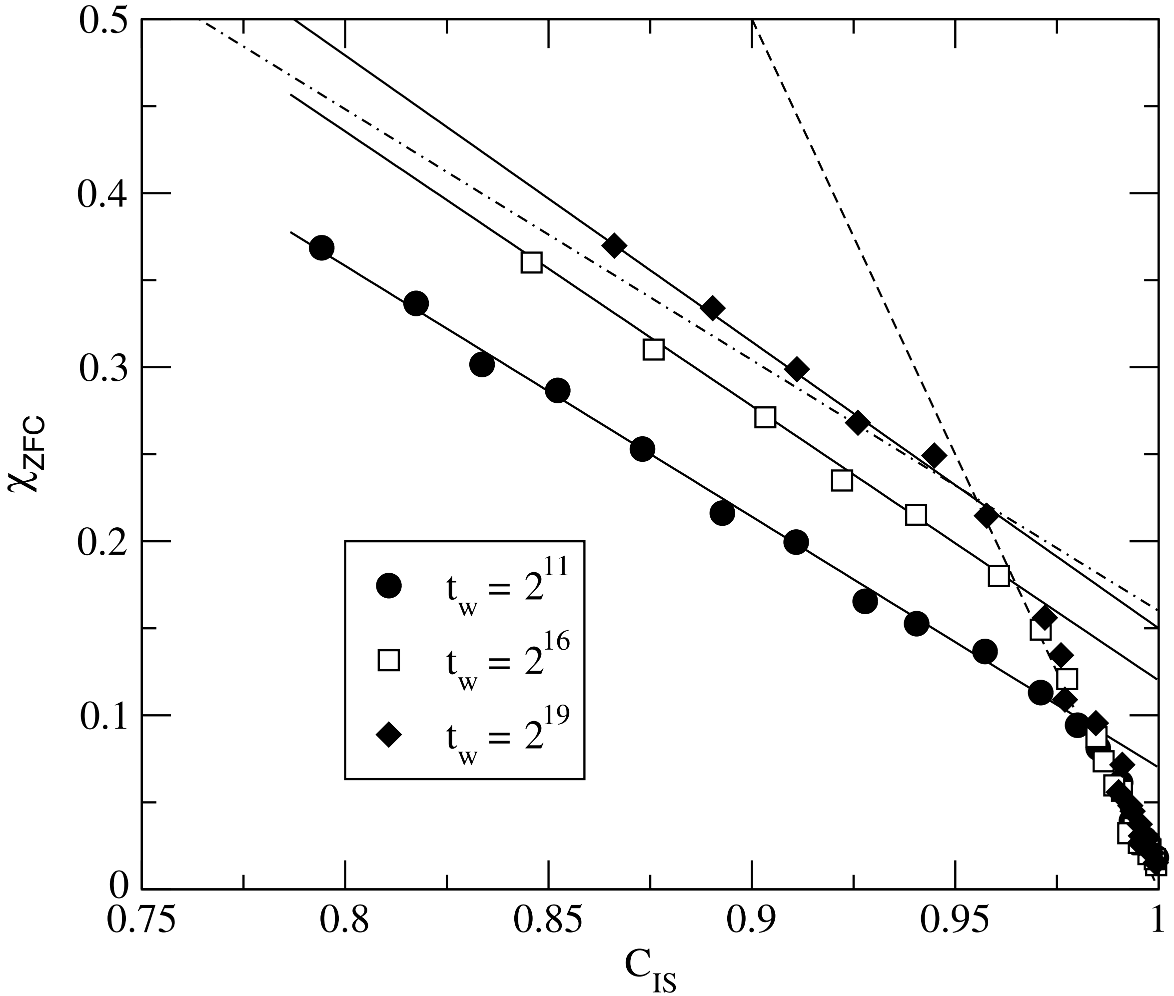
E. Marinari, G. Parisi, F. R. J. Phys. A **27,** 7647 (1994)

$$E = -\sum_{i<j}^{N} J_{ij}\sigma_i\sigma_j \qquad J^2 = 1 \qquad \sigma = \pm 1$$



FD plots in the random orthogonal model (ROM)

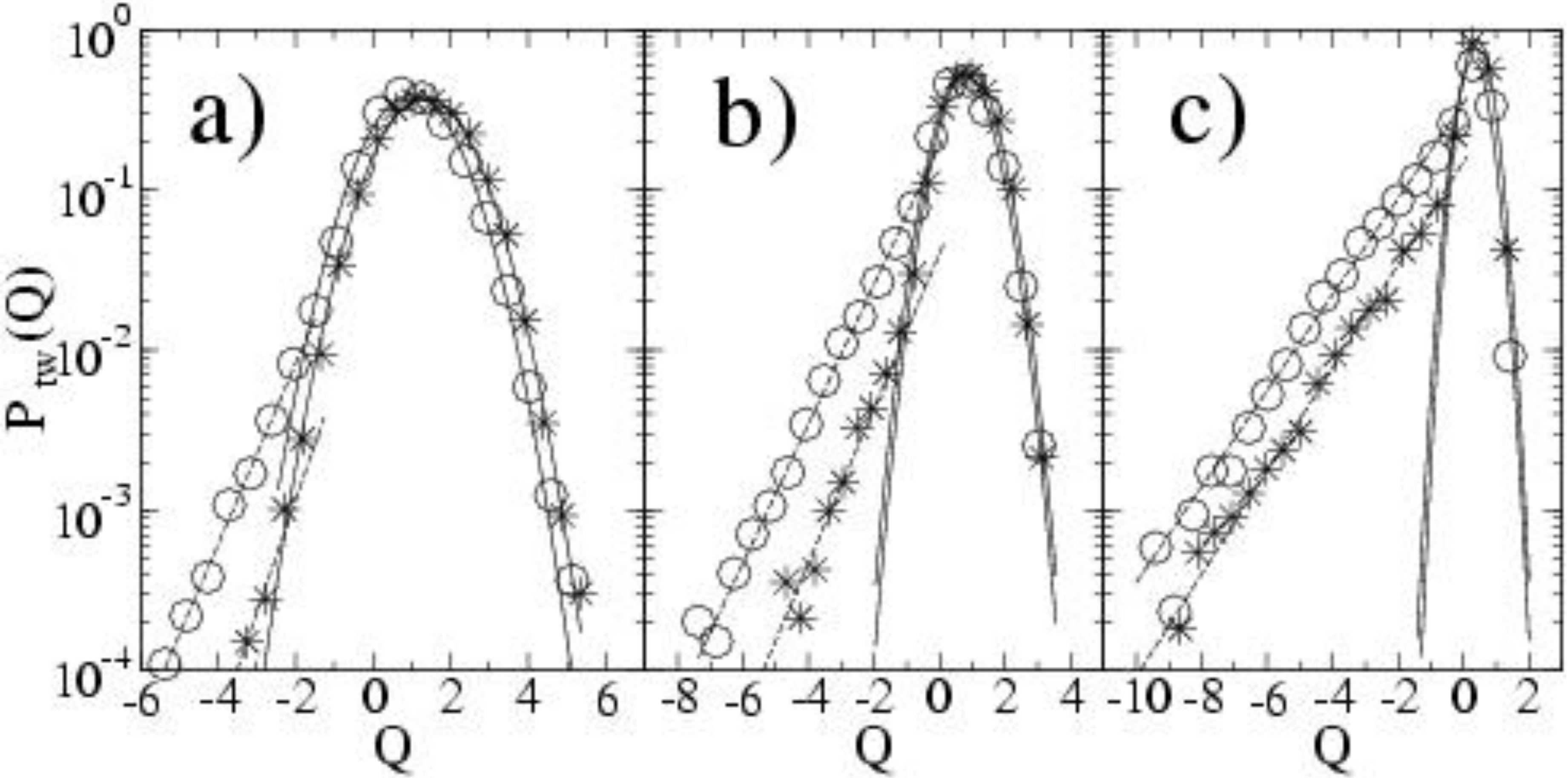
Parameters: N=64, $T_i = 3$, $T = 0.2$



A. Crisanti and F. R, Europhys. Lett. **66,** 253 (2004)

Heat pdfs in the random orthogonal model (ROM)

Parameters: N=64, $T_i = 3$, $T = 0.3, 0.2, 0.1$, $t_w = 2^{10}, 2^{15}$



A. Crisanti and F. R, Europhys. Lett. **66,** 253 (2004)

Can we experimentally test these ideas?

Use small systems as models where nonequilibrium fluctuations and large deviations are experimentally measurable

A NEW APPROACH TO UNDERSTAND THE EMERGENCE OF EFFECTIVE TEMPERATURES

Work done in collaboration with E. Dieterich and U. Seifert, Stuttgart

Question: Can we think of a nonequilibrium model that mimics the effect of the random thermal (Brownian) forces?

Hypothesis: In principle, any external stochastic forcing applied to the system should be indistinguishable from a thermal-like Brownian force if the **characteristic timescale** of the stochastic force is shorter than the **intrinsic relaxation time** of the system

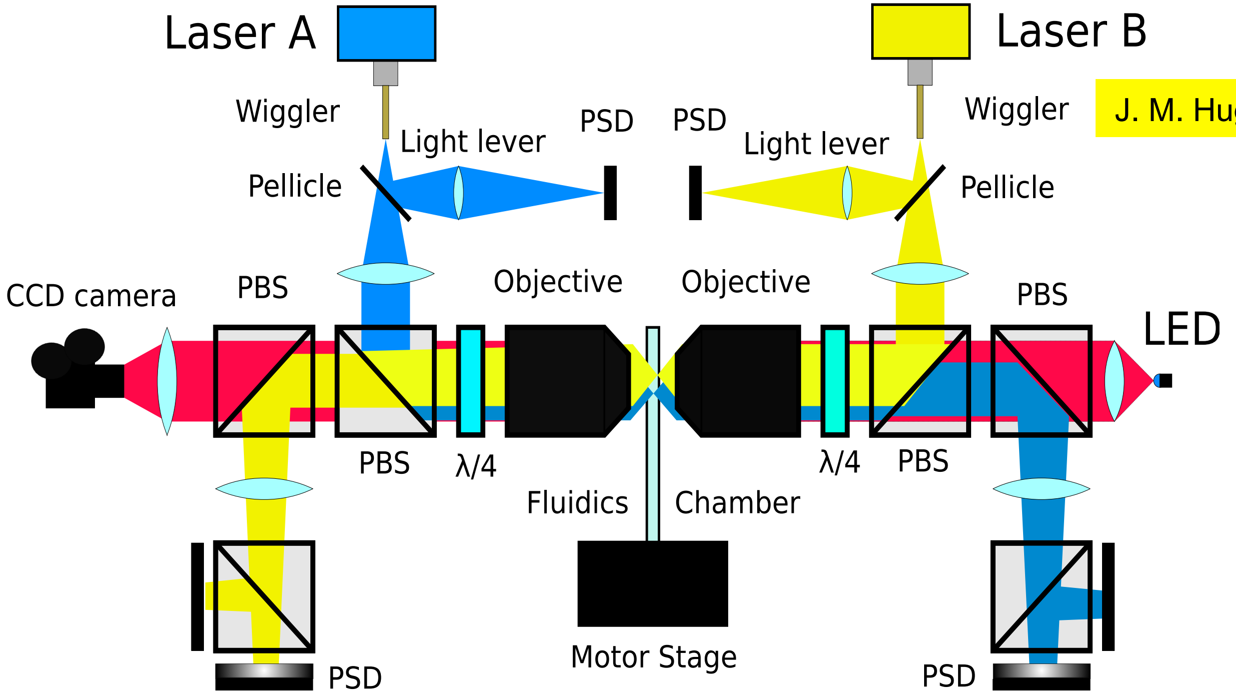
$$< f(0) f(t) >= A \exp(-t/\tau)$$

Strategy: Use **single molecules** with **stochastic driving** to generate **nonequilibrium steady states** with effective temperatures

Minitweezers: Experimental set-up

C. Bustamante and S. B. Smith et al., US Patent,**7**, 133, 132, B2 (2006)

J. M. Huguet et al., PNAS **107**: 15431-15436 (2010)



Small biosystems lab
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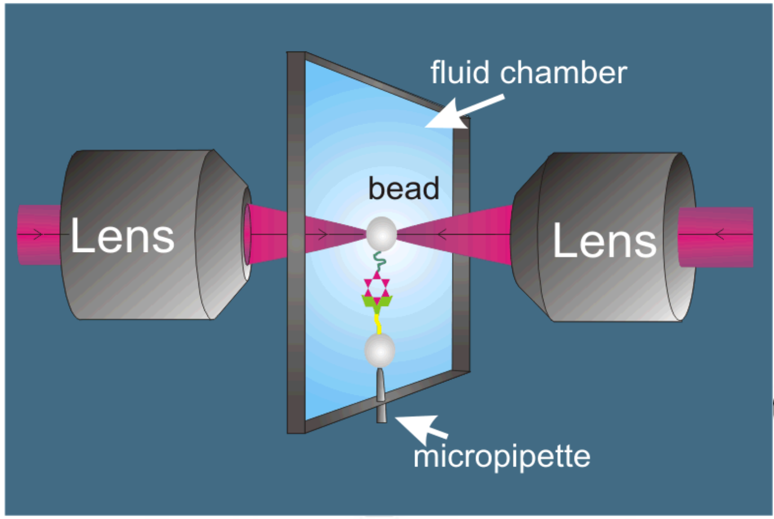
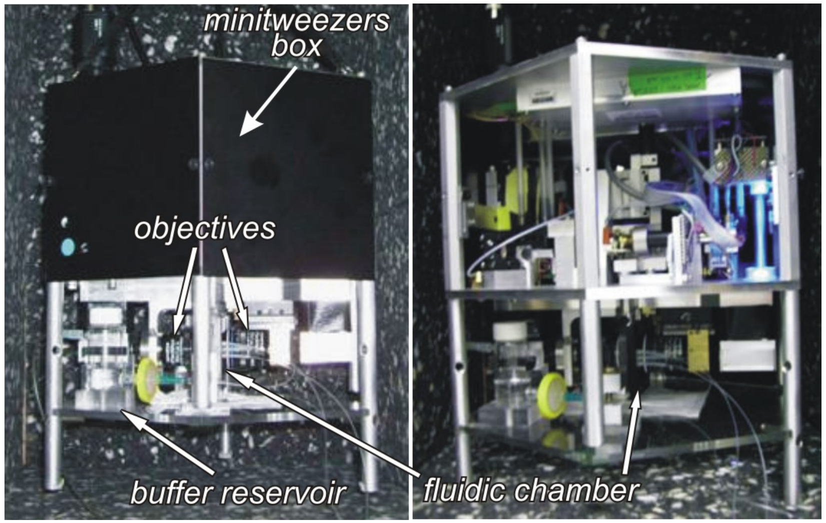
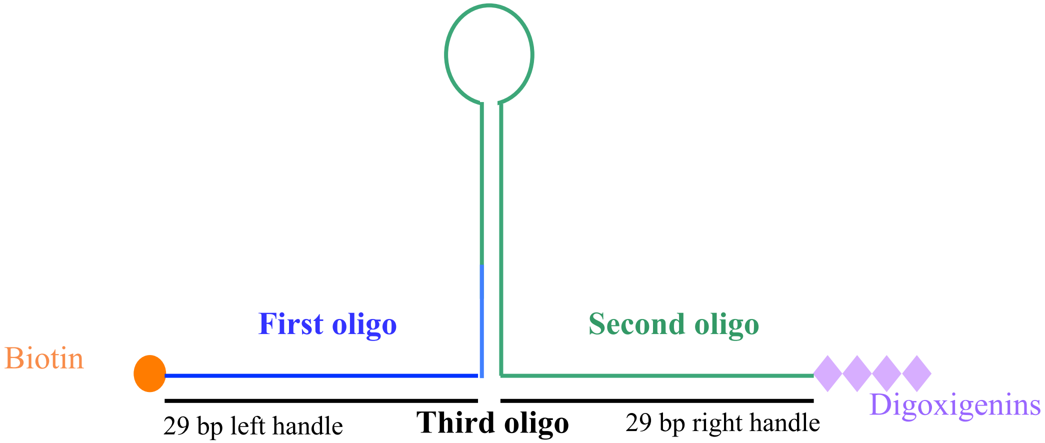
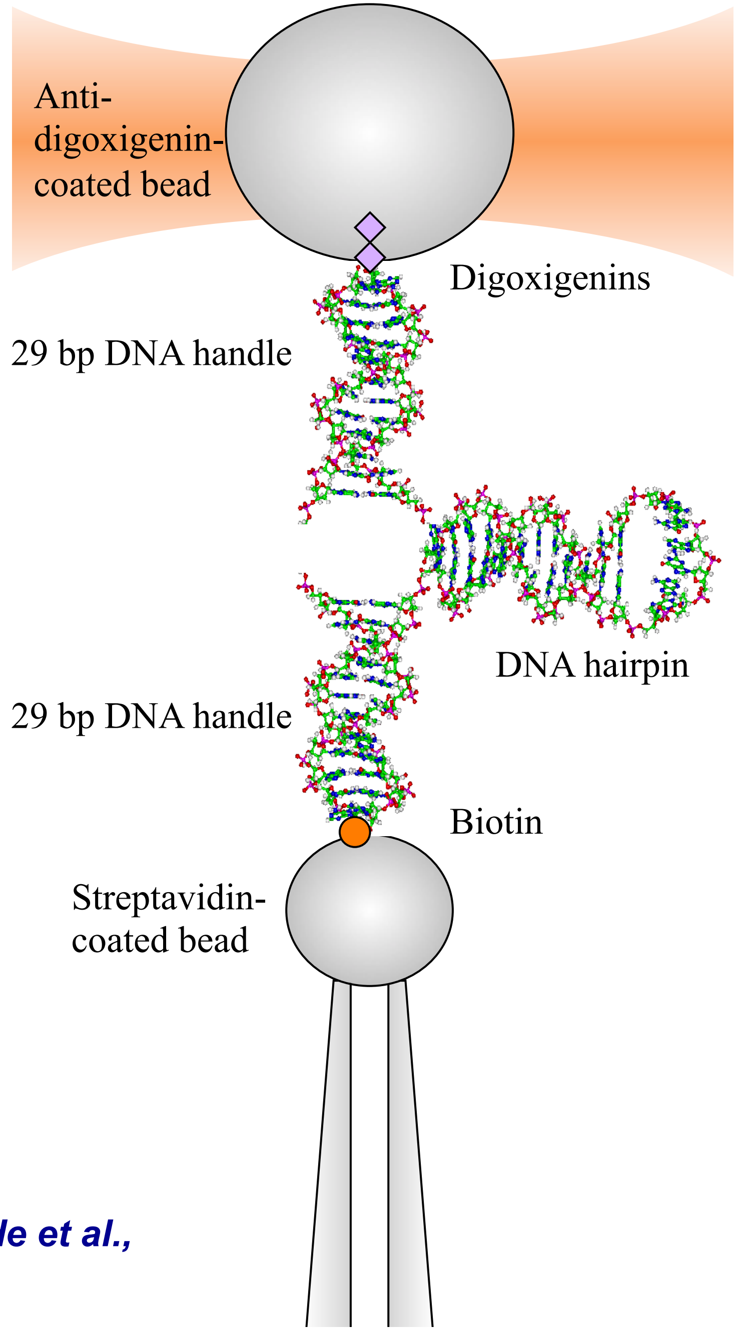




THE WORLD'S SHORTEST HANDLES



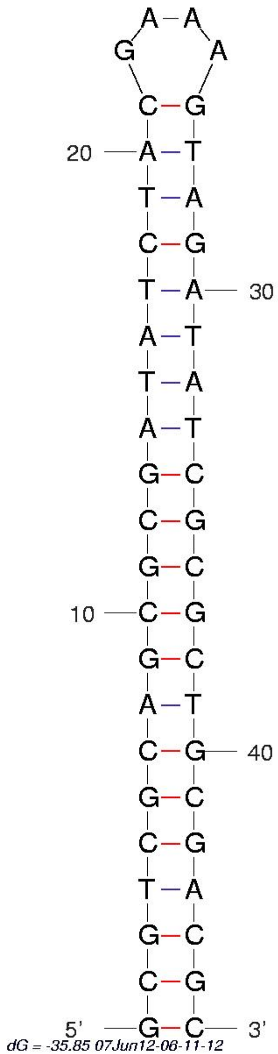


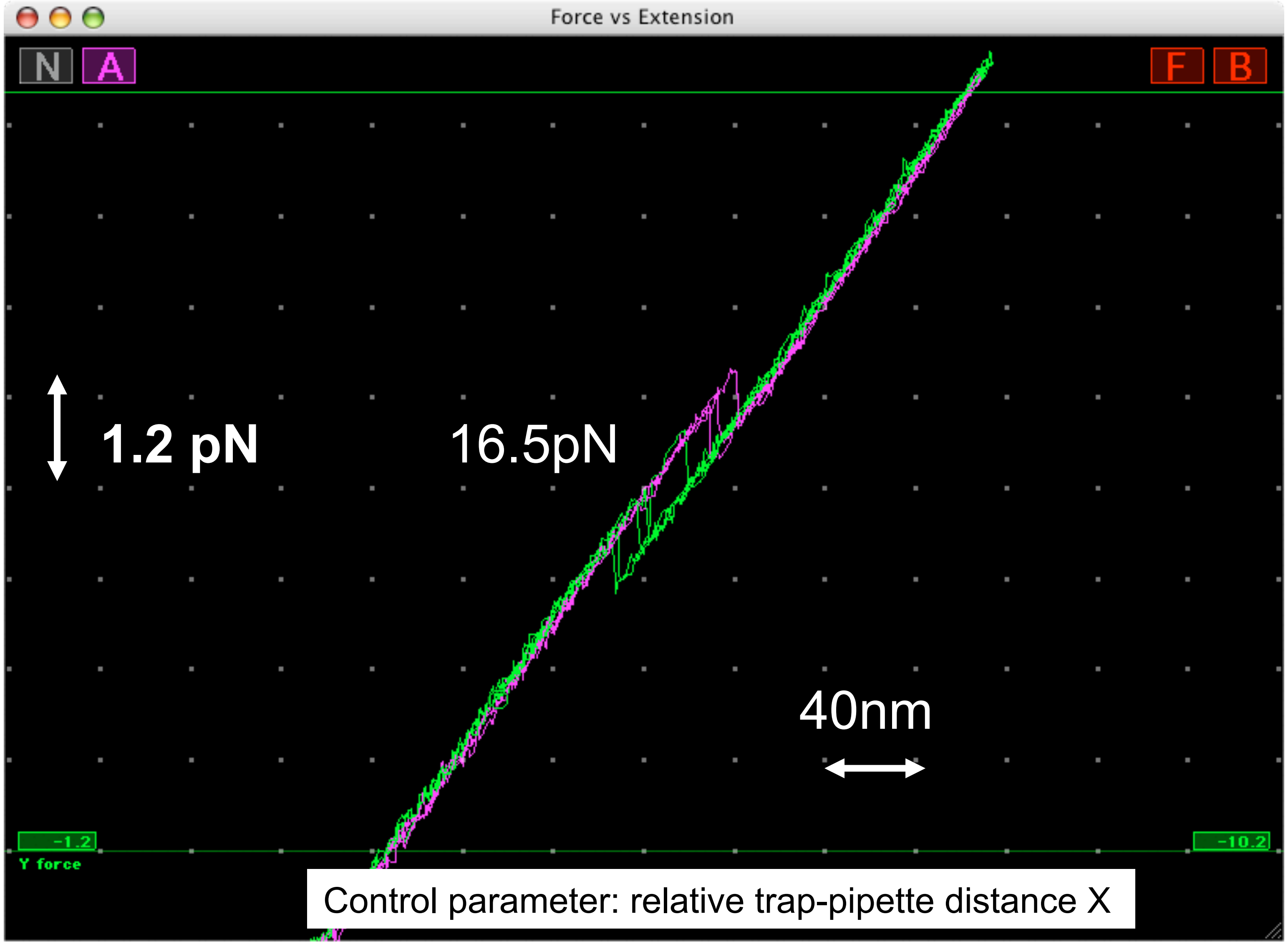
N. Forns et al., Biophys. J., **100,** 1765 (2011)

hairpin	
1st oligo	**AGTTAGTGGTGGAAACACAGTGCCAGCGC**G CGAGCCATAAT
2nd oligo	CTCATCTGGAAACAGATGAGATTATGGCTCGCA **GTTAGTGGTGGAAACACAGTGCCAGCGC**
3rd oligo	
GCGCTGGCACTGTGTTTCCACCACTAACT	

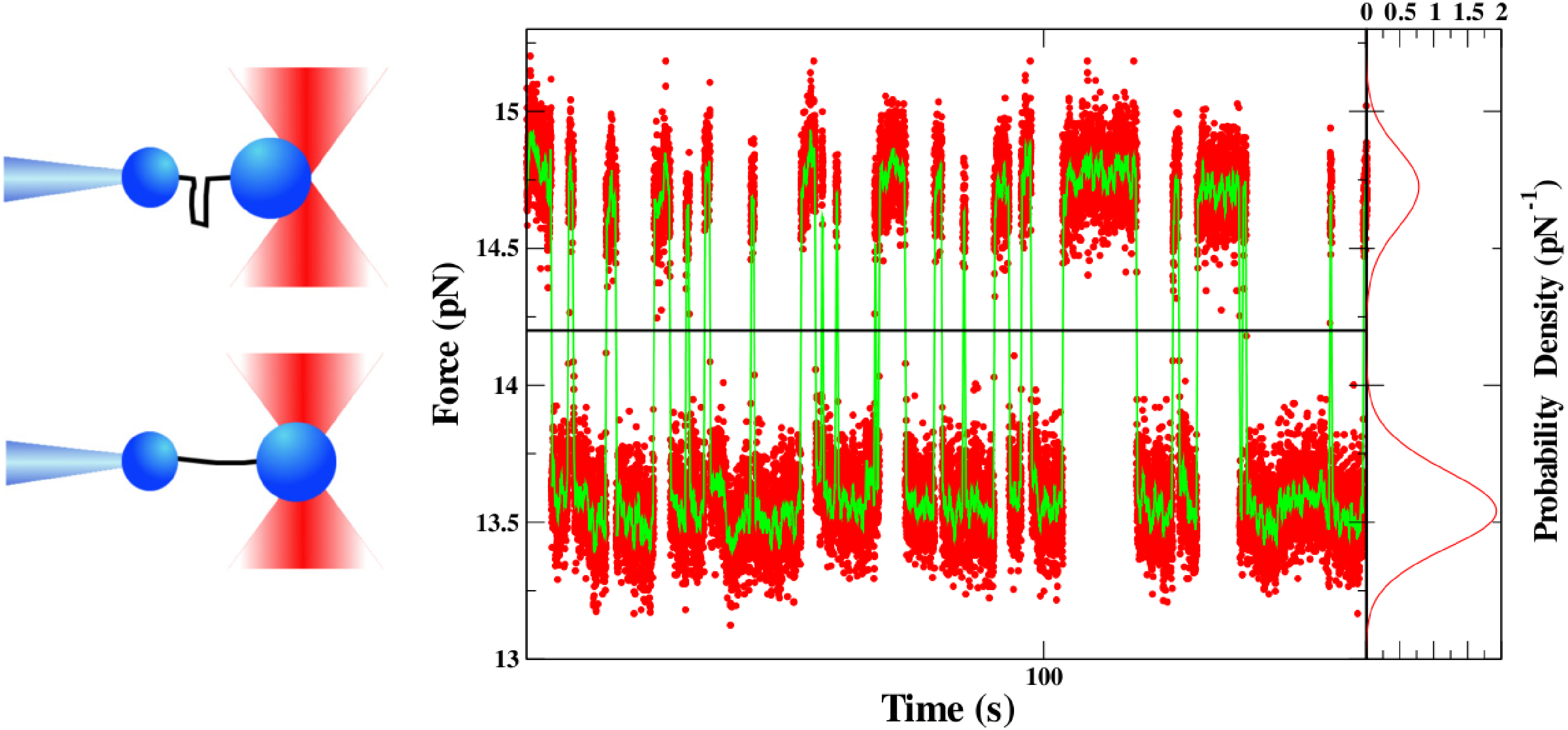
✓Experiments similar to those carried out by M. T. Woodside et al., Science 314, 1001 (2006); PNAS vol. 103, 6190-6195 (2006)

Pulling experiments

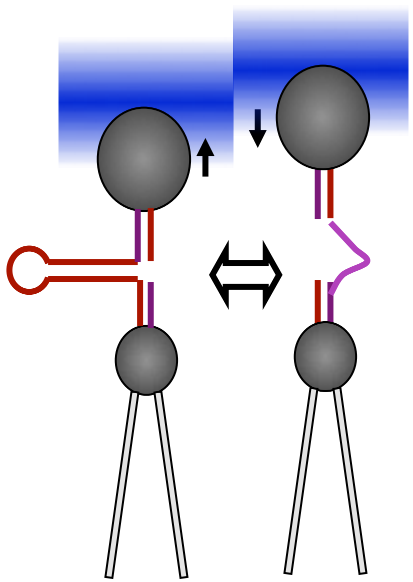


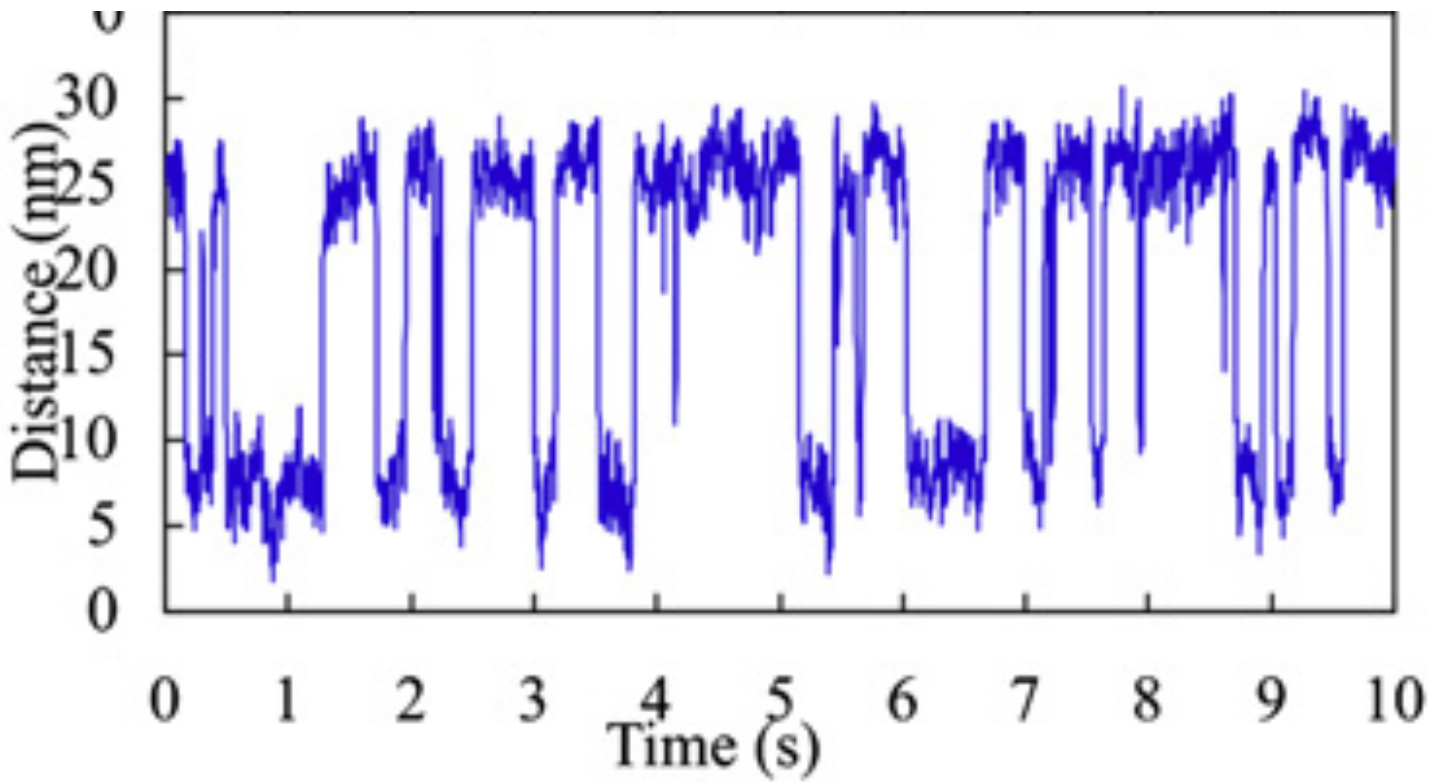


Hopping traces (passive mode)



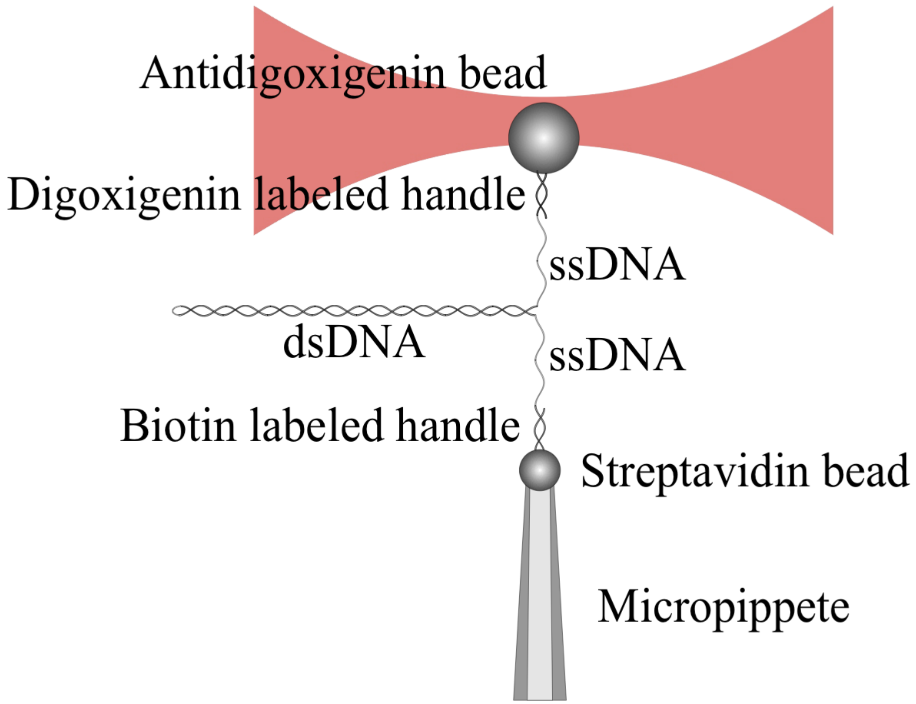
Hopping traces (force feedback)

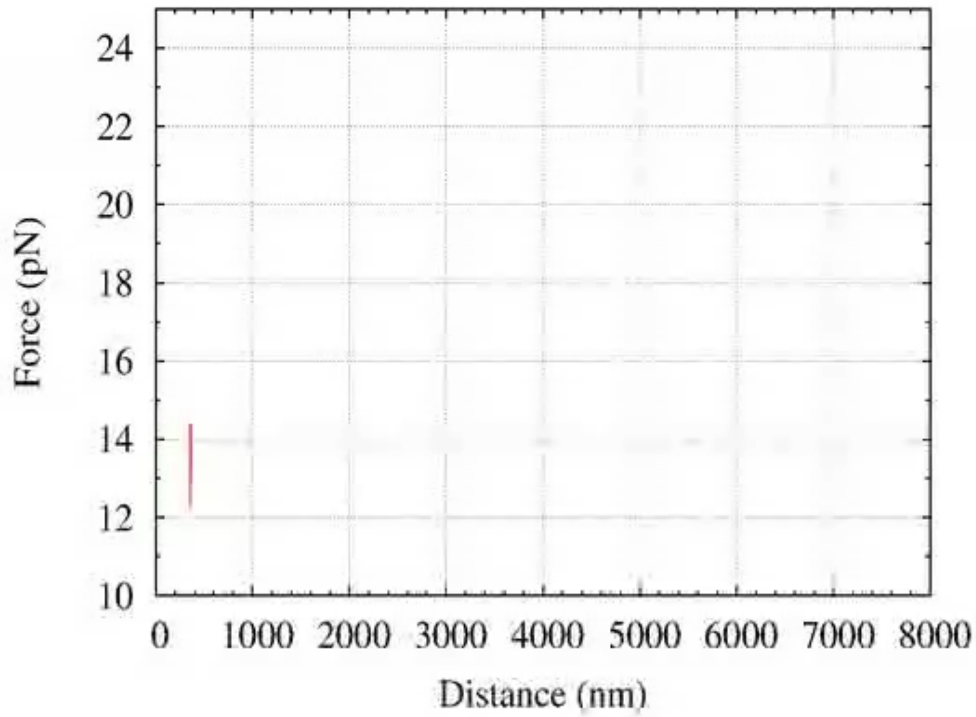




A DNA hairpin with many intermediates

Optical tweezers: B. Essevaz-Roulet, U. Bockelmann , F. Heslot F (1997) *Proc Natl Acad Sci* USA 94:11935-11940
AFM: M. Rief, H. Clausen-Schaumann, H.E. Gaub (1999) *Nat Struct Biol* 6:346-349
Magnetic tweezers: C. Danilowicz et al. (2003) *Proc Natl Acad Sci* USA 100:1694-1699

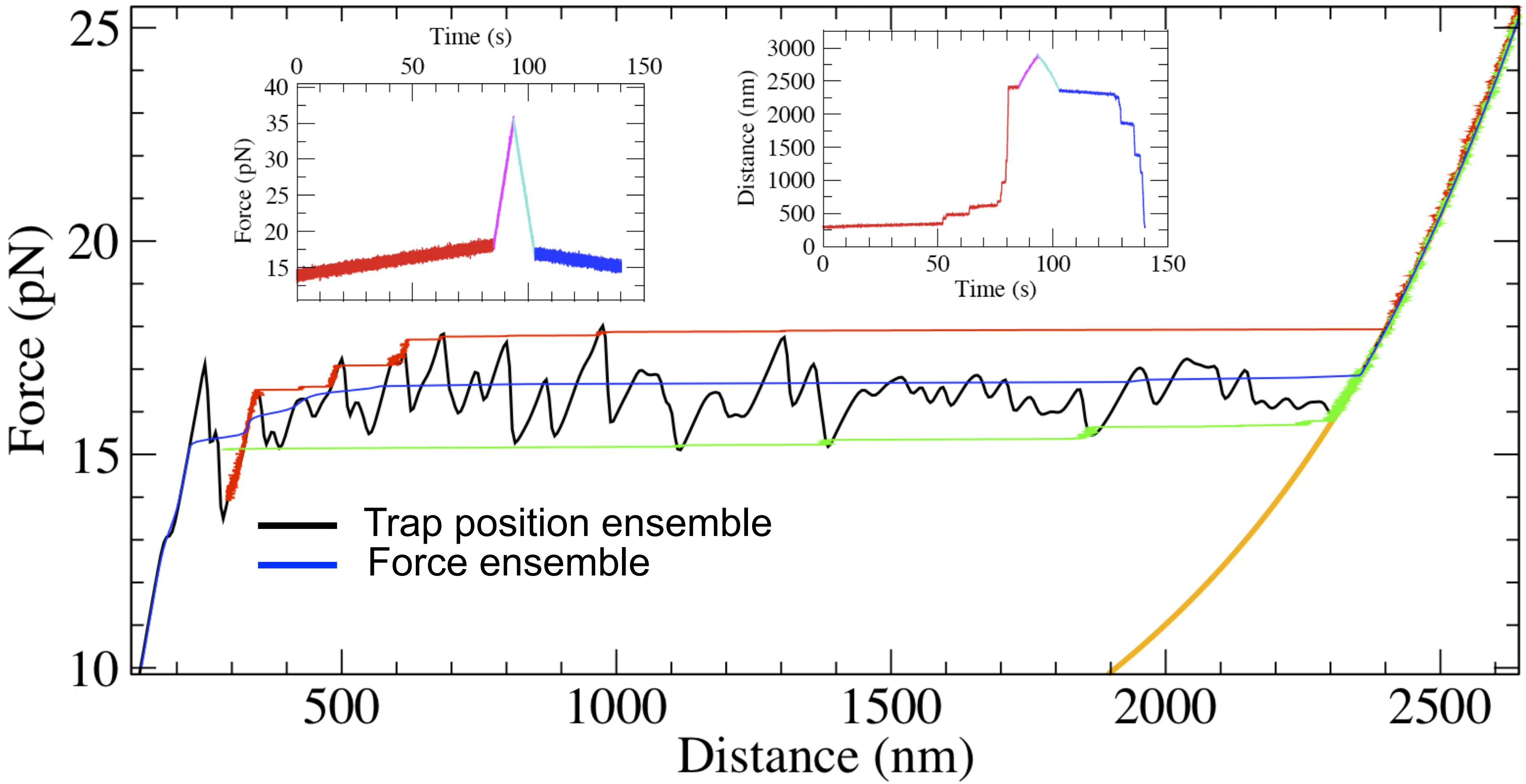




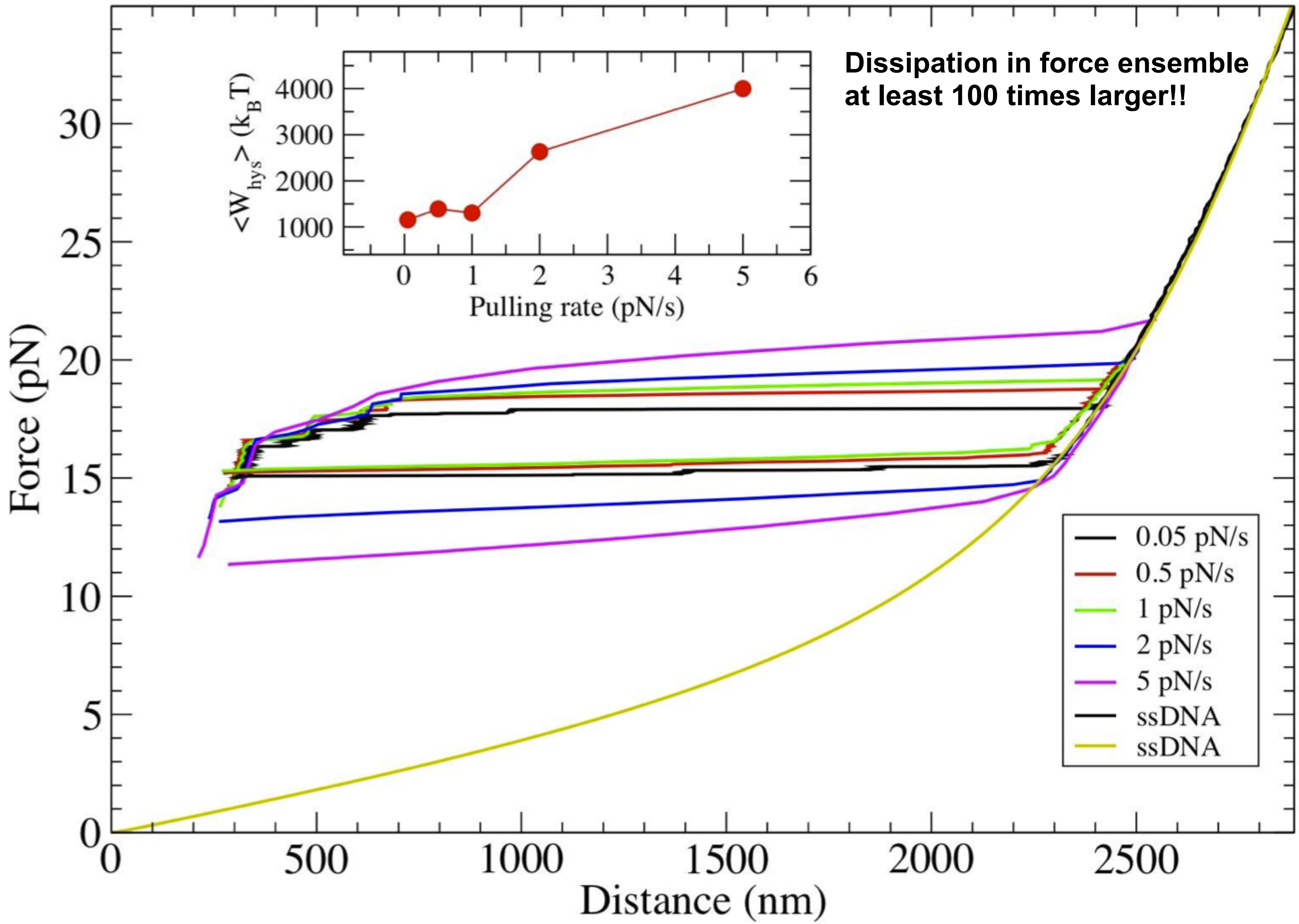
Short handles (29bp~10nm)

N. Forns et al., Biophys. J. **100** 1765-1774 (2011)

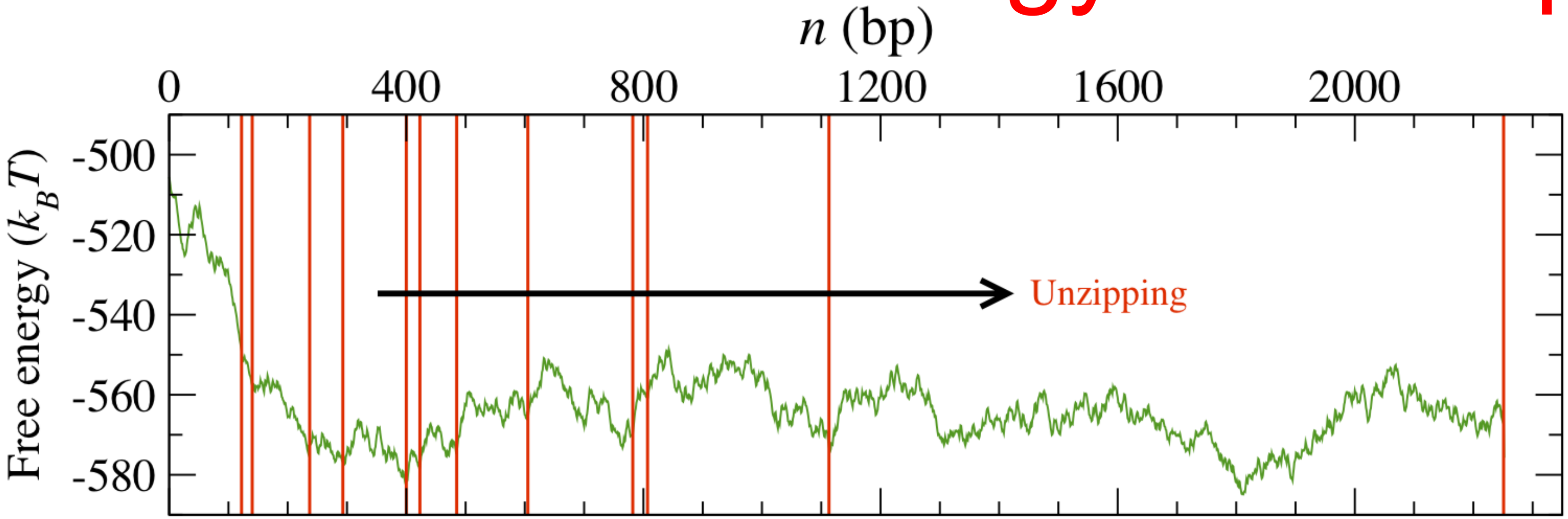
What happens with controlled force?



Extremely slow kinetics



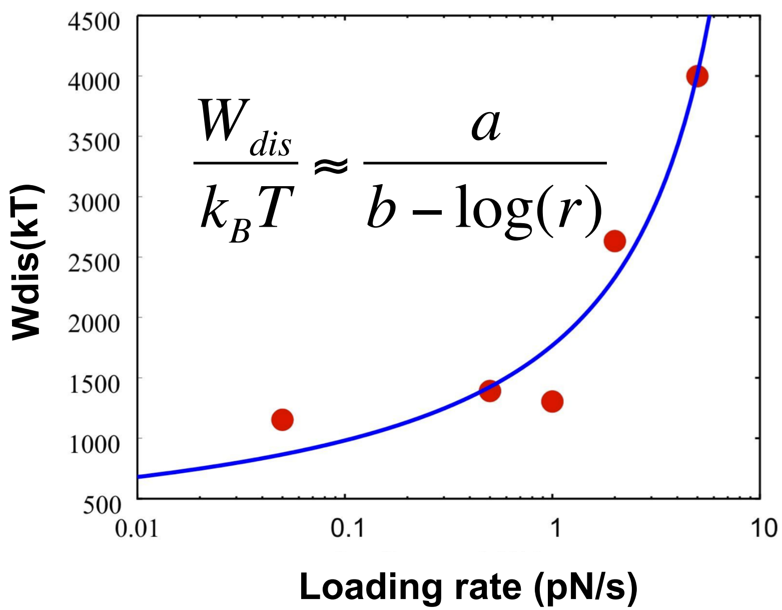
Disordered free energy landscape



Experimental realization of the Sinai model: $E(t)-E(\infty) \to a/\log(t)$

To dissipate a few per cent of these values (aprox. 20kT like in the trap ensemble) would require a loading rate of

10^{-100} pN/s !!!!



Take home messages….

- **In glassy systems** an **effective temperature** describes the relation between correlations and responses at **low frequencies**, probably due to **intermittent relaxational events** that are indistinguishable from **Brownian-like forces**.
- **Small systems** and **stochastic thermodynamics** are the ideal framework to theoretically understand and experimentally measure effective temperatures.
- **Noise experiments** much needed: **single molecules** are excellent candidate systems. The **high signal-to-noise ratios** of single molecule techniques have provided new tools for exploring the world of nonequilibrium phenomena

Members: **A. Alemany, J. Camunas, S. de Lorenzo, J. M. Huguet, M. Manosas, M. Ribezzi, M. Martí, S. Frutos**

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