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The physics of subcellular processes

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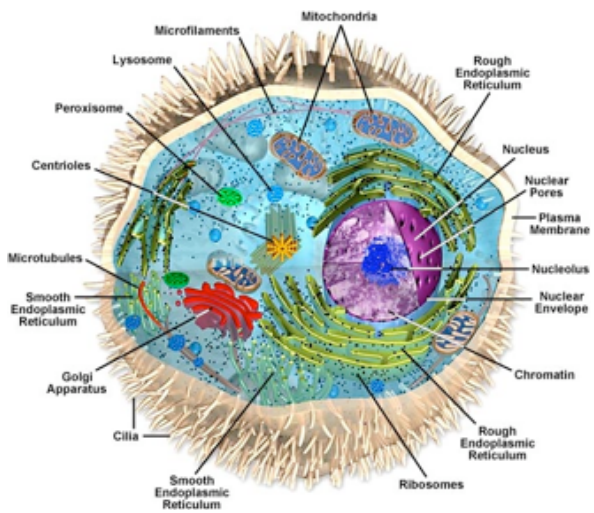


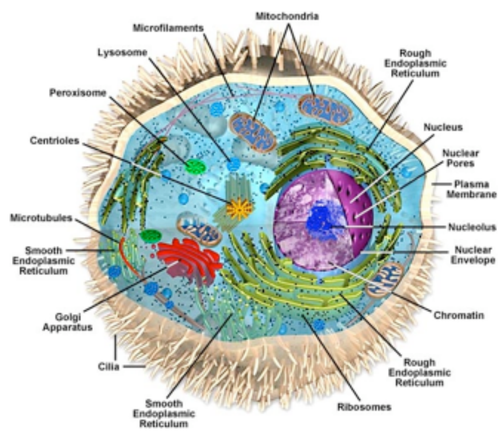
Department of Astronomy and Theoretical Physics

Galaxies,
Stars,
Planets(?)

10^{20} m → 10^{7} m

Humans,
Plants,
Cells

Computational
Biology and
Biological Physics



10^{-1} m→10^{-9} m

Elementary
Particles

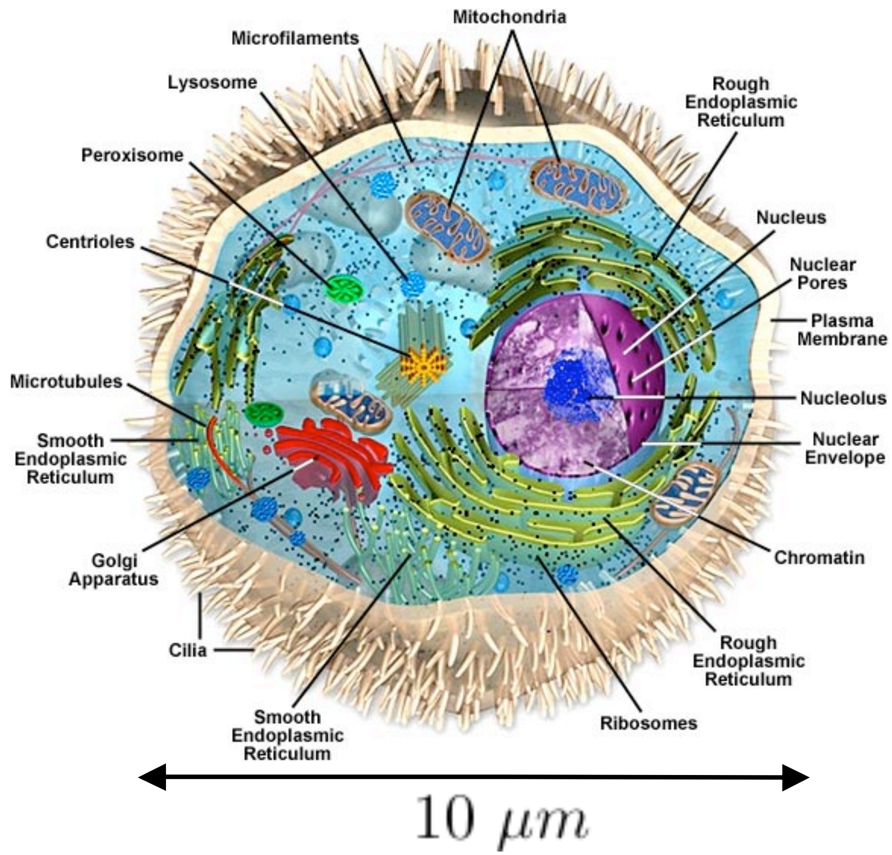
< 10^{-15} m

Cells - building block of all living beings

Blue whale 10^5 kg

Human beings 10^2 kg

Bacterium 10^{-15} kg



Subcellular physics, some characteristics:

- k_BT-physics (soft matter)
  Typical energies ~ k_BT
  (k_B=Boltzmanns konstant, T=temperatur)

- Low Reynolds numbers

$$\cancel{m\frac{d^2x}{dt^2}} = -\xi\frac{dx}{dt} + F + \eta(t)$$

Inertial term — Friktion — External force — Stochastic force

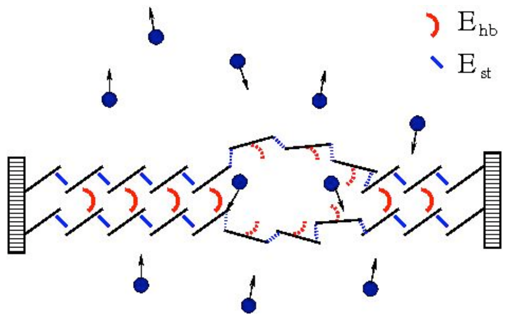
Navier-Stokes equations are linear

Aristoles's mechanics: no (net) motion unless there is a force..!

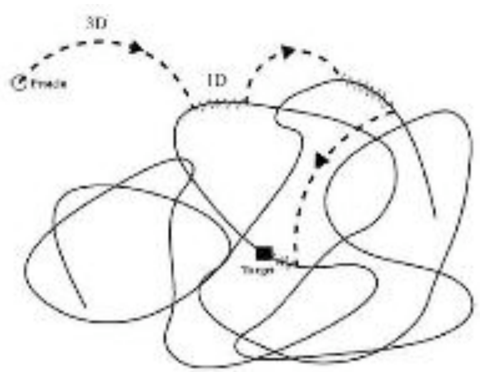
- Heterogeneity is important

Some projects…

- Biopolymer transport through nanopores in biomembranes
- DNA melting maps



- DNA breathing dynamics
- Biomembranes in electric fields
- Diffusion of proteins on DNA



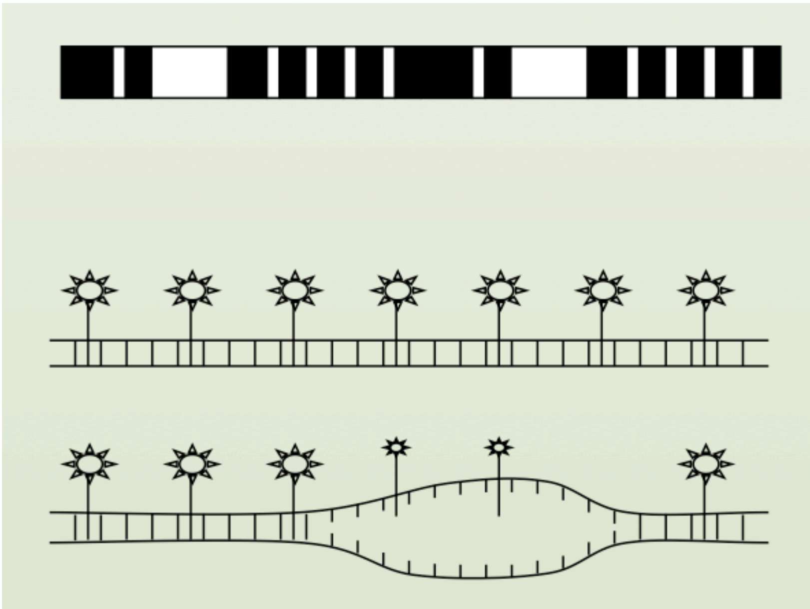
- Using localized surface plasmons for sensing biomolecules
- Electromagnetic response of dipole-dipole coupled systems - photosynthesis

Part I:

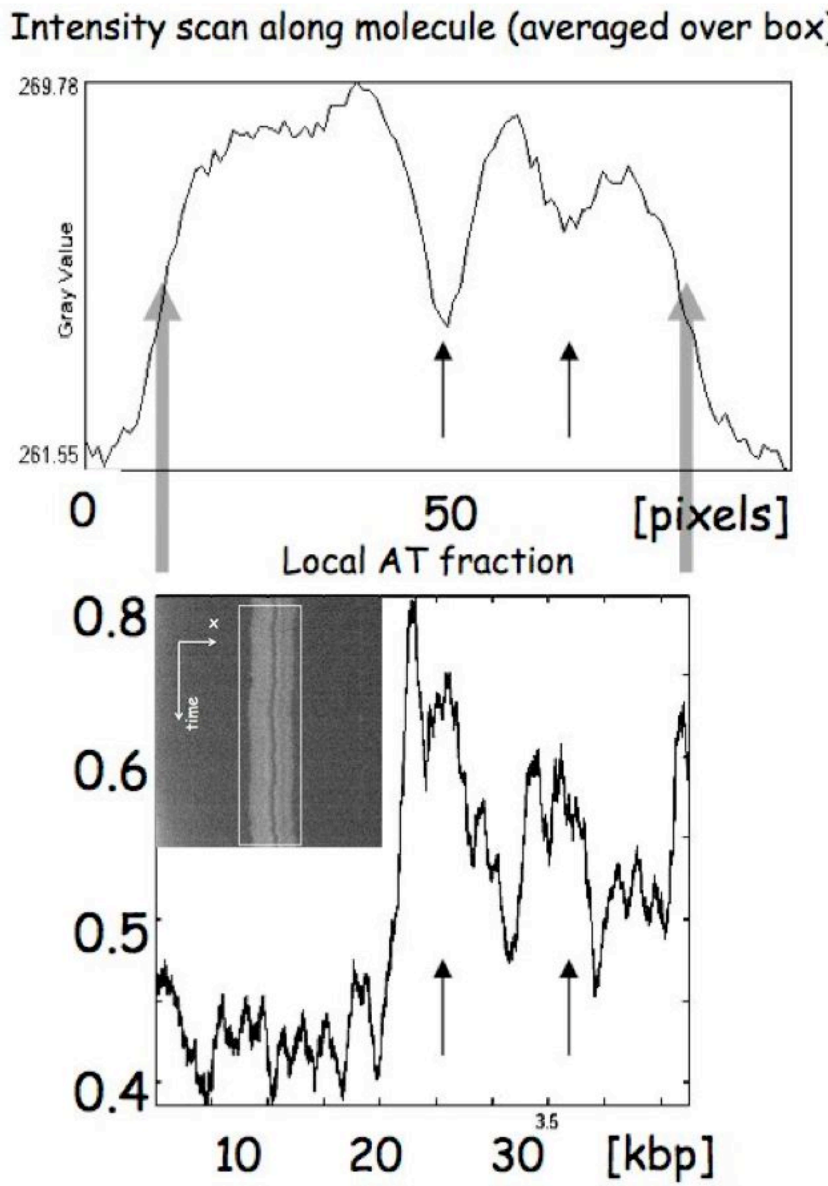
DNA melting maps

Ultra-fast discrimination of genomes

Experiments

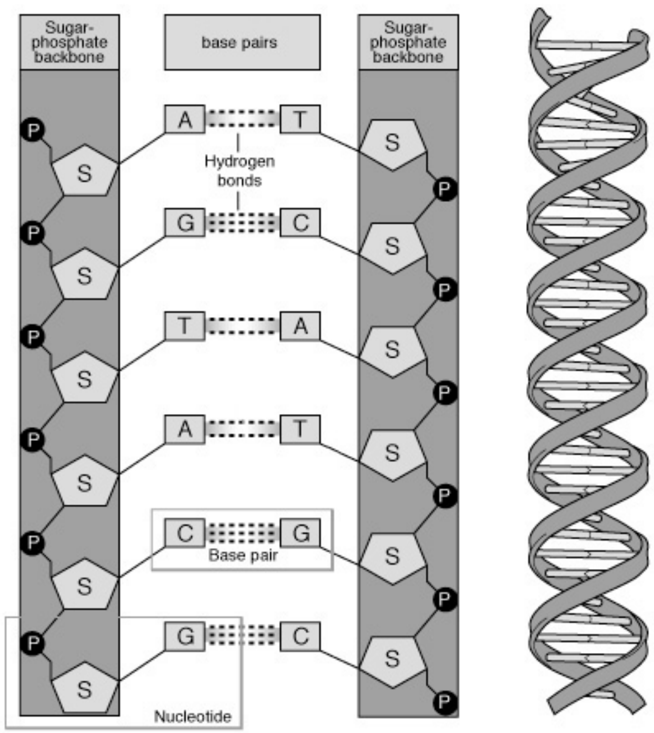


Jonas Tegenfeldt's labs,
Lund University &
Göteborg University



Double-stranded DNA

$d \simeq 2\ nm$



Available for any basepairs, NaCl conc. and temperature [has entropic contributions]

Stability of DNA:

$u_{st}=\exp(\beta E_{st})$ (10 param.)

$u_{hb}=\exp(\beta E_{hb})$ (2 param.)

$c \approx 1.76$ - loop exponent

$\xi \approx 10^{-3}$ - ring factor

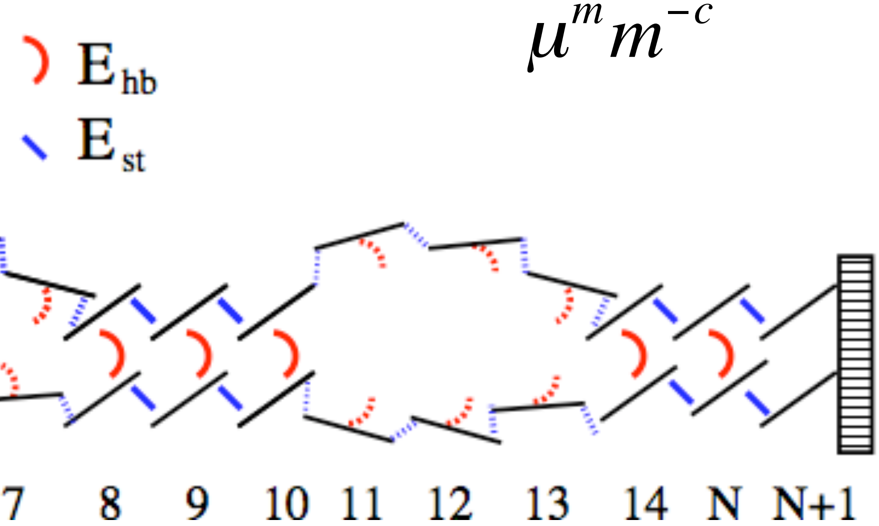
NOTE: u_{st} only recently measured! [Krueger et al, Biophys. J. 90, 3091 (2006)]

The Poland-Scheraga model

Ising model with temperature-dependent magnetic field and a "long-range" term

No of configurations for a random walk that returns to the origin=

$$\mu^m m^{-c}$$



Statistical weight for configuration above: $[E_{hb} = k_B T \ln \mu + \varepsilon_0]$

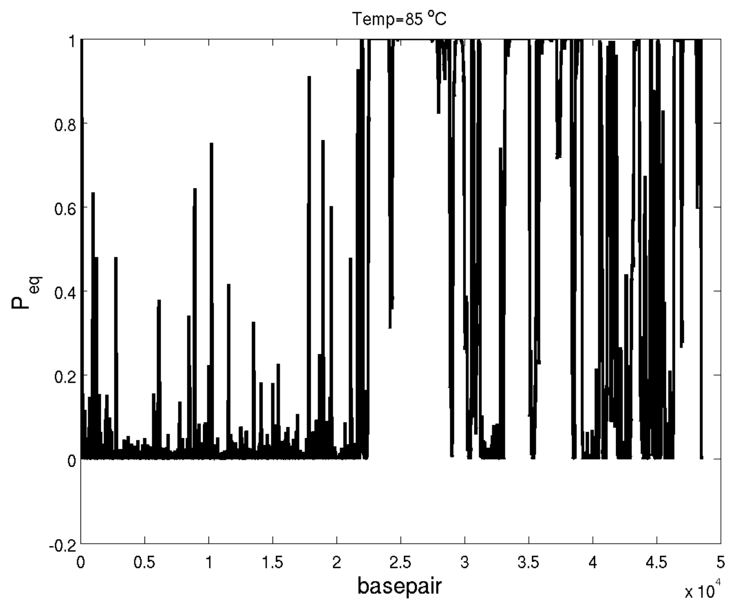
$$Z_{weight} = \xi \exp[\beta E_{st}(4,5)]\exp[\beta E_{hb}(5)]\exp[\beta E_{st}(5,6)]\exp[\beta E_{hb}(6)]$$ ⇐ First bubble

$$\exp[\beta E_{st}(6,7)]\exp[\beta E_{hb}(7)]\exp[\beta E_{st}(7,8)](8-4+1)^{-c}$$

$$\times[............................]$$ ⇐ Second bubble

Poland algorithm: partition function etc, can be obtained recursively (scales as N^2)

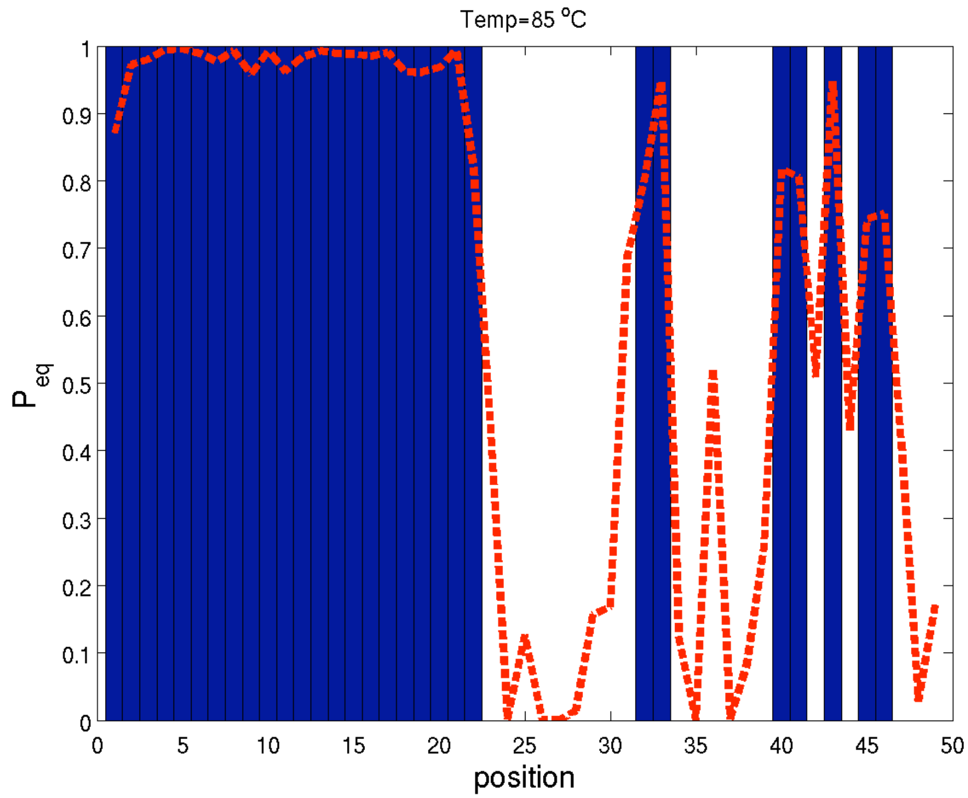
Case study: λ-phage DNA

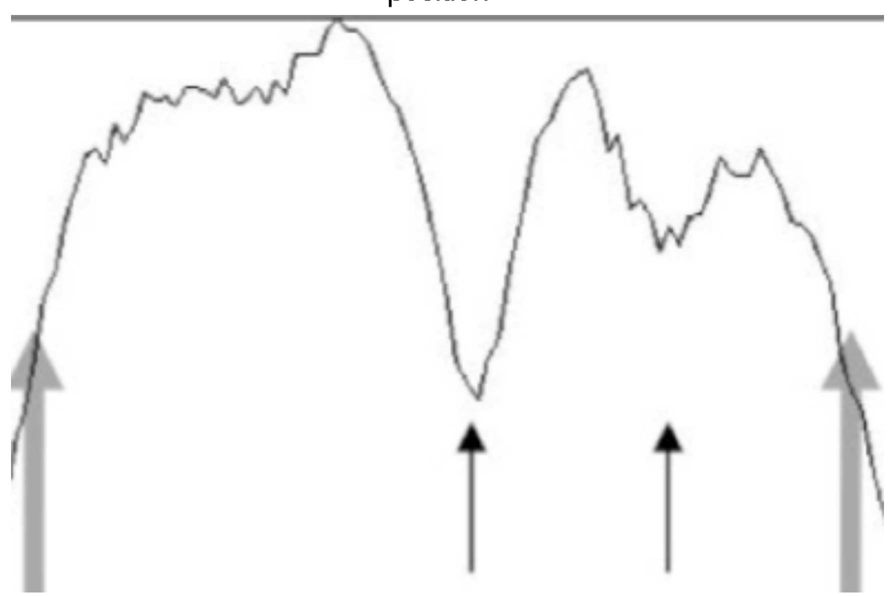


T=85 °C

100 mM NaCl

≈50000 basepairs





Collaborators:

Jonas Tegenfeldt
(Lund and Göteborg Uni.)

Bosse Söderberg
(Lund University)

Fredrik Persson
(Göteborg University)

Bernhard Mehlig
(Göteborg University)

Michaela Schad
(Starts her Phd
May 2010)

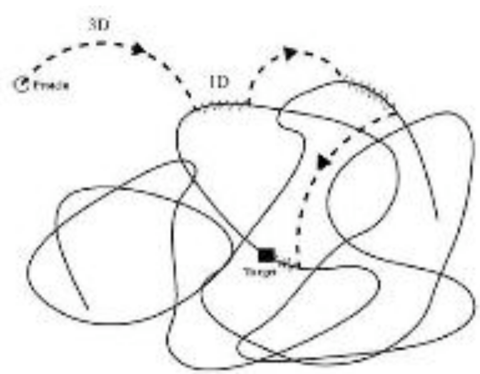
Lykke Pedersen
(MSc student,
Roskilde University)

Previous collaborator (DNA breathing dynamics):
Ralf Metzler (Technical Uni. Munich), Suman Banik (Bose Institute, Kolkata)
Oleg Krichevsky (Ben-Gurion Uni., Israel), Jonas Pedersen (DTU, Denmark),
Tomas Novotny (Charles University, Prague), Mikael Sonne Hansen (DTU).

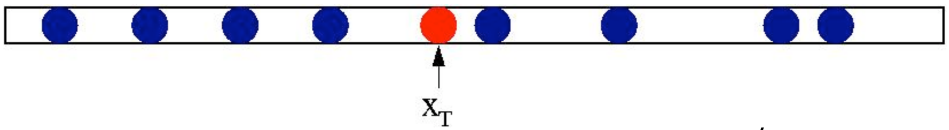
Part II:

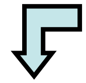
Diffusion of proteins along DNA

Single-file diffusion



Single-file diffusion, basic result



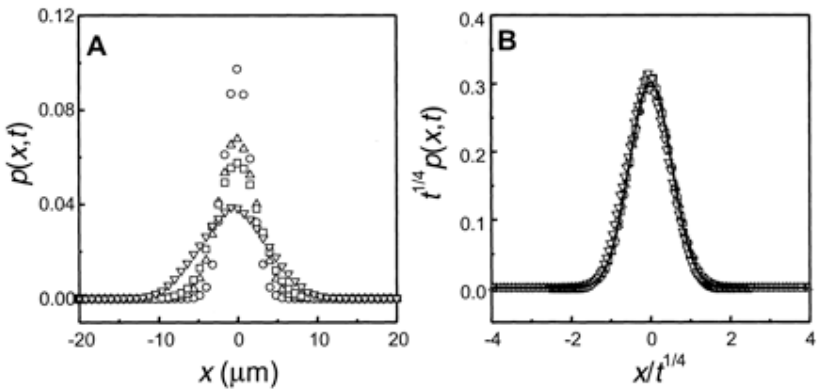


anomalous diffusion

Infinite system (fix concentration): $\left\langle (x_T - x_{T,0})^2 \right\rangle \propto t^{1/2}$

Probability density function (PDF) is Gaussian (T.E. Harris 1965)

First experiments: [Q.C. Wei, C. Bechinger, P. Leiderer, Science 297, 625 (2000)]:



$$\left\langle (x_T - x_{T,0})^2 \right\rangle = \frac{1}{\rho}\left(\frac{4Dt}{\pi}\right)^{1/2} \propto t^{1/2}$$

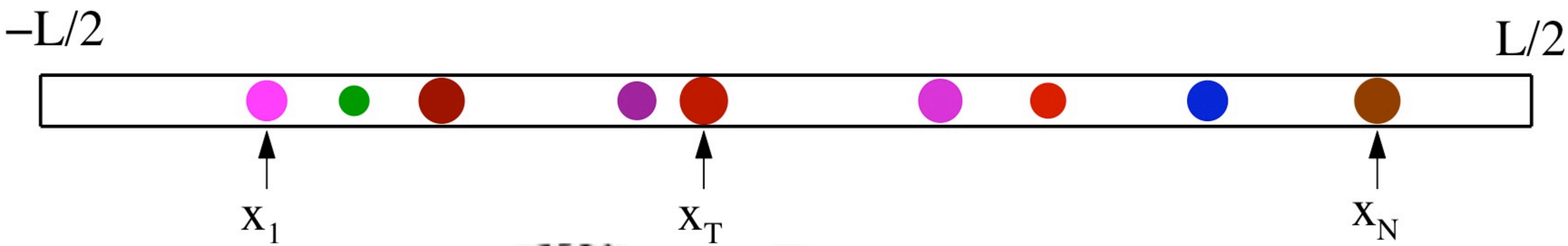
ρ = concentration

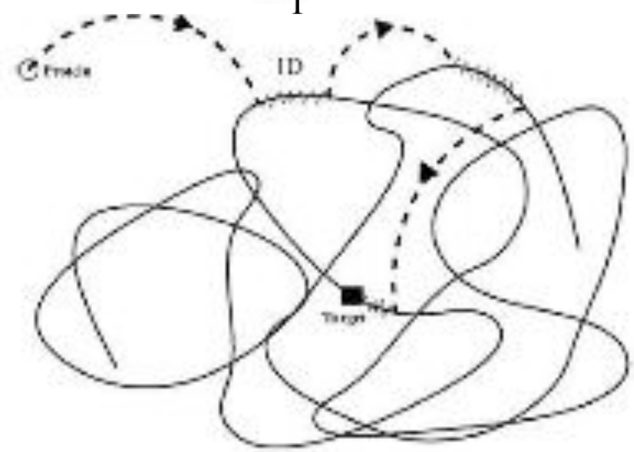
D=diffusion constant for each particle

[Compare to "ordinary" diffusion $\left\langle (x_T - x_{T,0})^2 \right\rangle = 2Dt$]

NOTE: results above for **identical** point-particles!

SFD with **different** diffusion constants





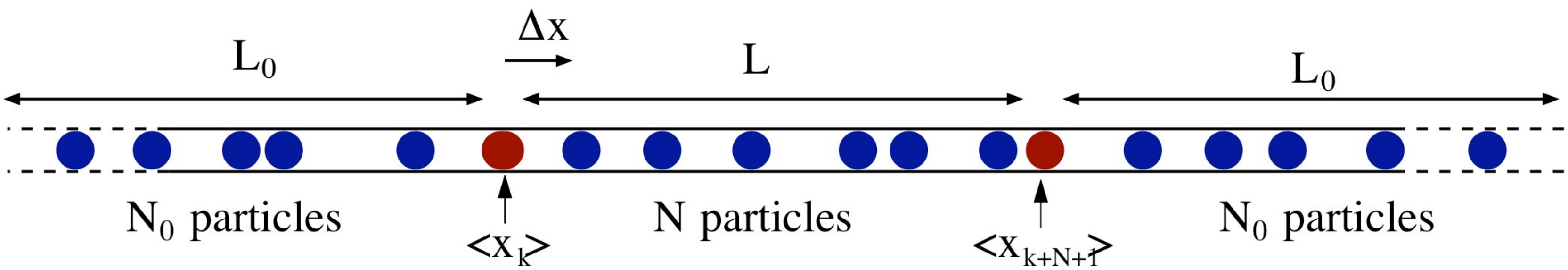
Protein diffusion on DNA

Draw friction constants ξ from a distribution $\rho(\xi)$

Harmonization + Effective medium approach

→ problem can solved analytically!

Harmonization



Entropic force: $$F = \underbrace{\frac{k_B T}{L}}_{K} \rho \Delta x$$

Effective spring constant between neighbours = NK, i.e.

$$\kappa = k_B T \rho^2$$

<u>Proposition</u>: For large distance (long times) the particles behave as (strongly damped) harmonically coupled beads in a heat bath

NOTE: our method can be generalized to any short-range interaction!

Simplified equations of motion

Force from left particle; Force from right particle; noise

$$\cancel{m\frac{d^2x_n}{dt^2}} + \xi_n \frac{dx_n}{dt} = \kappa(x_{n+1} - x_n - \cancel{\rho^{-1}}) - \kappa(x_n - x_{n-1} - \cancel{\rho^{-1}}) + \eta_n(t)$$

Eq. of motion for (1D) polymer!

ξ_n=friction constant=k_BT/D_n

The noise is delta-correlated: $\langle \eta_n(t) \rangle = 0$

$$\langle \eta_n(t)\eta_m(t') \rangle = k_B T \xi_n \delta_{n,m} \delta(t - t')$$

For identical particles the solution (in double Fourier-space) is (continuum limit):

$$x_q(\omega) = \frac{\eta_q(\omega)}{\kappa q^2 - i\omega\xi}$$

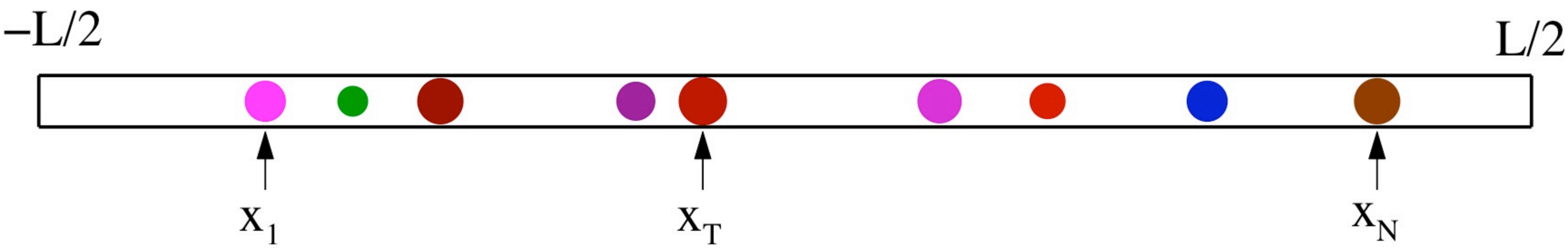
Going back to real time and space:

$$\langle [x_n(t) - x_n(0)]^2 \rangle = \frac{2k_BT}{\kappa} \int_{-\infty}^{\infty} \frac{dq}{2\pi} \frac{1}{q^2} (1 - e^{-(\kappa/\xi)q^2 t})$$

$$= (\frac{k_BT}{\kappa})^{1/2} (\frac{4Dt}{\pi})^{1/2} = \frac{1}{\rho} (\frac{4Dt}{\pi})^{1/2} \qquad (!!)$$

L. Lizana, T.A., A. Taloni, E. Barkai, and M.A. Lomholt (submitted), arXiv:0909.0881

Different particles, $\xi_1 \neq \xi_2 \neq \xi_3 \neq \ldots \neq \xi_N$



Draw friction constants ξ from a distribution ρ(ξ)

Harmonization + Effective medium approach

- we can identify two classes of systems

- "Nice" distribution with $\langle \xi \rangle = \int \xi \rho(\xi) d\xi < \infty$
- (Power-law) distribution with $\langle \xi \rangle = \int \xi \rho(\xi) d\xi = \infty$

[M. Lomholt,L. Lizana,T. Ambjörnsson,in preparation]

Different ξ - nice distributions, ⟨ξ⟩<∞

$$\left\langle (x_T - x_{T,0})^2 \right\rangle = \frac{1}{\rho}\left(\frac{4D_{eff}t}{\pi}\right)^{1/2} \propto t^{1/2}$$

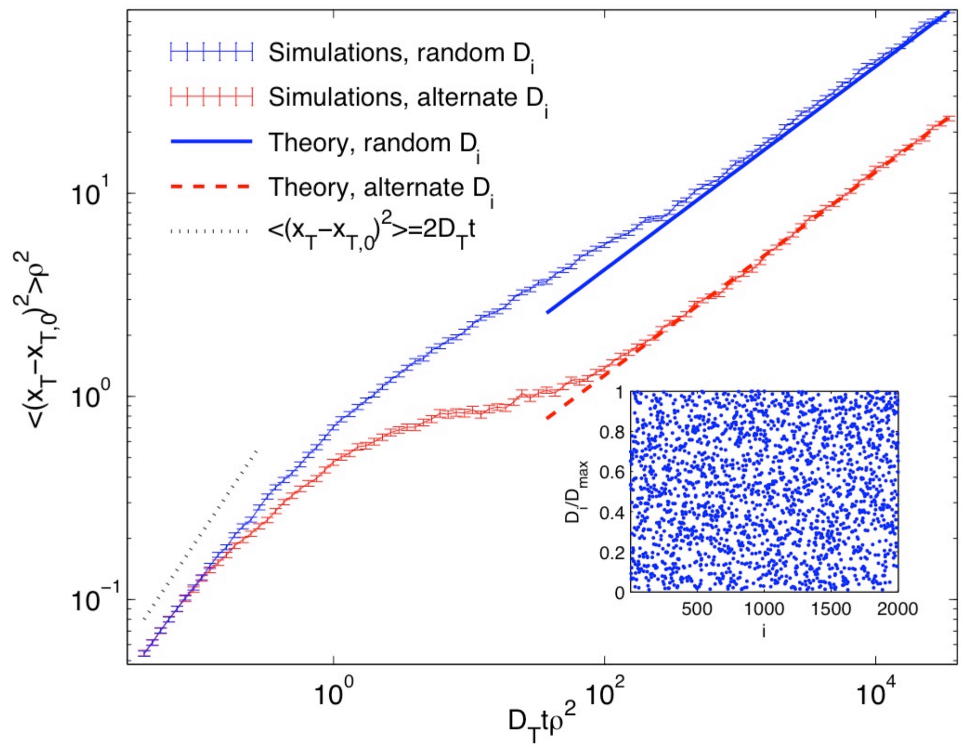
where

$$D_{eff} = \frac{k_B T}{\xi_{eff}}$$

$$\xi_{eff} = \int \xi p(\xi) d\xi$$

Average over friction constants

M. Jara and P. Gonçalves,
J. Stat. Phys. 132, 1135 (2008)
for lattice systems.



T.A, L. Lizana, M.A. Lomholt and R.J. Silbey,
J. Chem. Phys. 129, 185106 (2008).

Different ξ - Power-law distributions, ⟨ξ⟩=∞

Take friction constants
from a power-law distributions:

$$\rho(\xi) \propto \xi^{-1-\alpha}, 0 < \alpha < 1$$

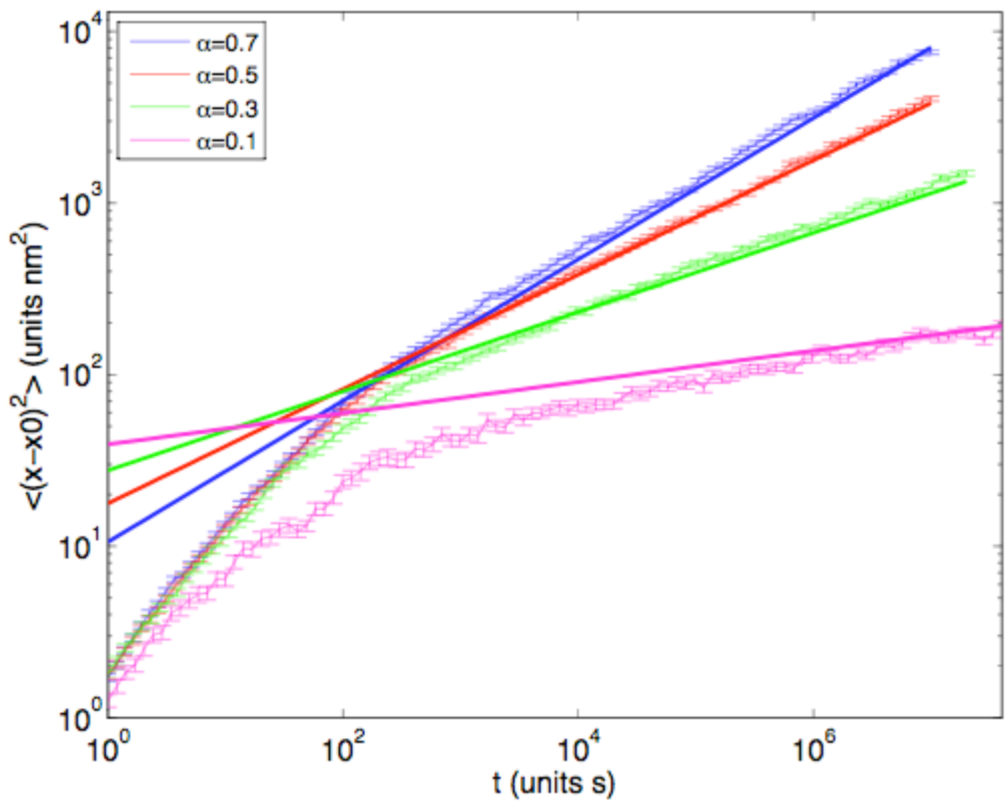
for large ξ. Then

$$\left\langle [x_T(t) - x_T(0)]^2 \right\rangle \propto t^{\delta}$$

where

$$\delta = \frac{\alpha}{1+\alpha} < \frac{1}{2}$$

ultra-slow dynamics!



Further results

	Nice distributions	Power-law distributions
▪ If harmonically time-varying force acts on the tagged particle there is a phase lag $[\delta = \alpha/(1+\alpha)]$	$\phi_0 = \frac{\pi}{4}$	$\phi_0 = \frac{\delta\pi}{2}$
▪ The density relaxations (dynamic structure factor) is:	$S(Q,t) = \exp[-D_c Q^2 t]$	$S(Q,t) \propto E_{2\delta}[-CQ^2 t^{2\delta}]$ (Mittag-Leffler function)

[M. Lomholt, L. Lizana, T. Ambjörnsson, in preparation]

Collaborators:

Michael Lomholt
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Robert Silbey
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Alessandro Taloni
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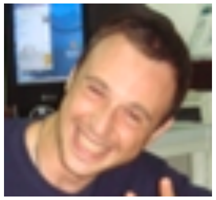

Lloyd Sanders
(Just started his PhD)

Karl Fogelmark
(MSc student working
on s similar topic)

Thanks: Milton Jara, Mehran Kardar, Igor Sokolov, Ed Di Marzio, Ralf Metzler, Knut&Alice Wallenberg Foundation

Summary

- Subcellular processes occur on length scales 1 nm-10μm: $k_B T$-physics, low Reynolds numbers and heterogeneity

- DNA melting maps: ultra fast DNA discrimination, disordered Ising model with long-range coupling

- Protein diffusion along DNA: Solvable many-body problem. Harmonization + effective medium → mean square displacement for a tagged particle $\sim t^{\delta}$ with $\delta \leq 1/2$ for the case of distributed diffusion constants.