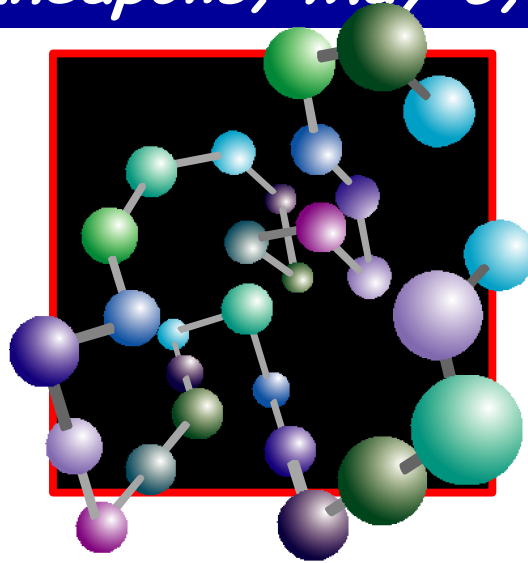


Two talks in one

Physics Inspired by Biology
Minneapolis, May 6, 2007



- Y.Rabin (Bar Ilan)
- E.Kussel (NYU)
- S.Leibler (Rockefeller)

- Solitary knots, with Y. Rabin

- Polymer-Population Mapping
and localization in the space of phenotypes, with E.Kussel
and S.Leibler

Knot Localization

PHYSICAL REVIEW E 75, 041105 (2007)

Size of knots in ring polymers

B. Marcone,¹ E. Orlandini,^{2,3} A. L. Stella,^{2,3} and F. Zonta¹

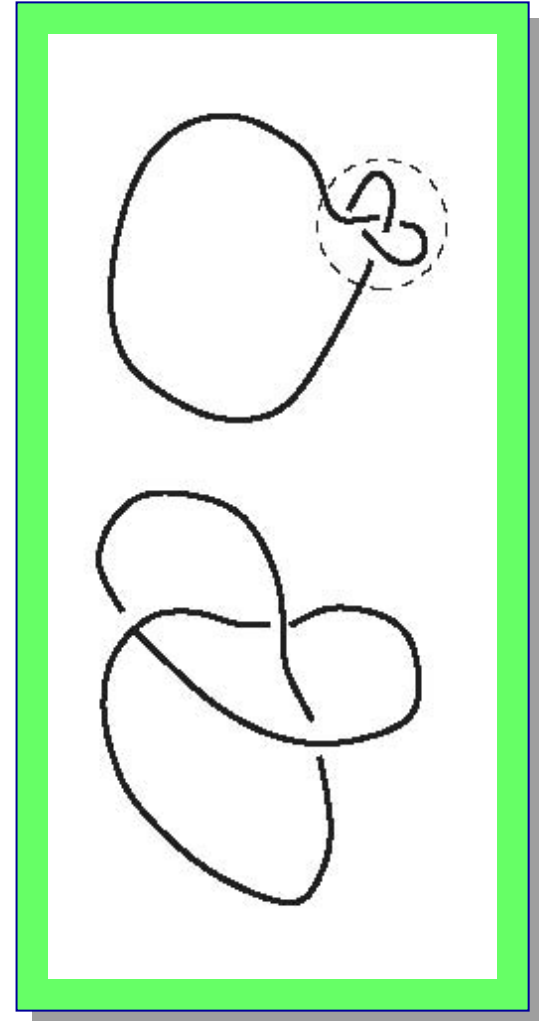
¹Dipartimento di Fisica, Università di Padova, I-35131 Padova, Italy

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(Received 6 December 2006; published 11 April 2007)

We give two different, statistically consistent definitions of the length l of a prime knot tied into a polymer ring. In the good solvent regime the polymer is modeled by a self avoiding polygon of N steps on cubic lattice and l is the number of steps over which the knot “spreads” in a given configuration. An analysis of extensive Monte Carlo data in equilibrium shows that the probability distribution of l as a function of N obeys a scaling of the form $p(l, N) \sim l^{-c} f(l/N^D)$, with $c \approx 1.25$ and $D \approx 1$. Both D and c could be independent of knot type. As a consequence, the knot is weakly localized, i.e., $\langle l \rangle \sim N^t$, with $t = 2 - c \approx 0.75$. For a ring with fixed knot type, weak localization implies the existence of a peculiar characteristic length $l^* \sim N^{\nu}$. In the scaling $\sim N^{\nu}$ ($\nu \approx 0.58$) of the radius of gyration of the whole ring, this length determines a leading power law correction which is much stronger than that found in the case of unrestricted topology. The existence of this correction is confirmed by an analysis of extensive Monte Carlo data for the radius of gyration. The collapsed regime is studied by introducing in the model sufficiently strong attractive interactions for nearest neighbor sites visited by the self-avoiding polygon. In this regime knot length determinations can be based on the entropic competition between two knotted loops separated by a slip link. These measurements enable us to conclude that each knot is delocalized ($t \approx 1$).



Kardar et al, Orlandini et al, Metzler et al ...

Let us tie a knot on a long dsDNA

VOLUME 91, NUMBER 26

PHYSICAL REVIEW LETTERS

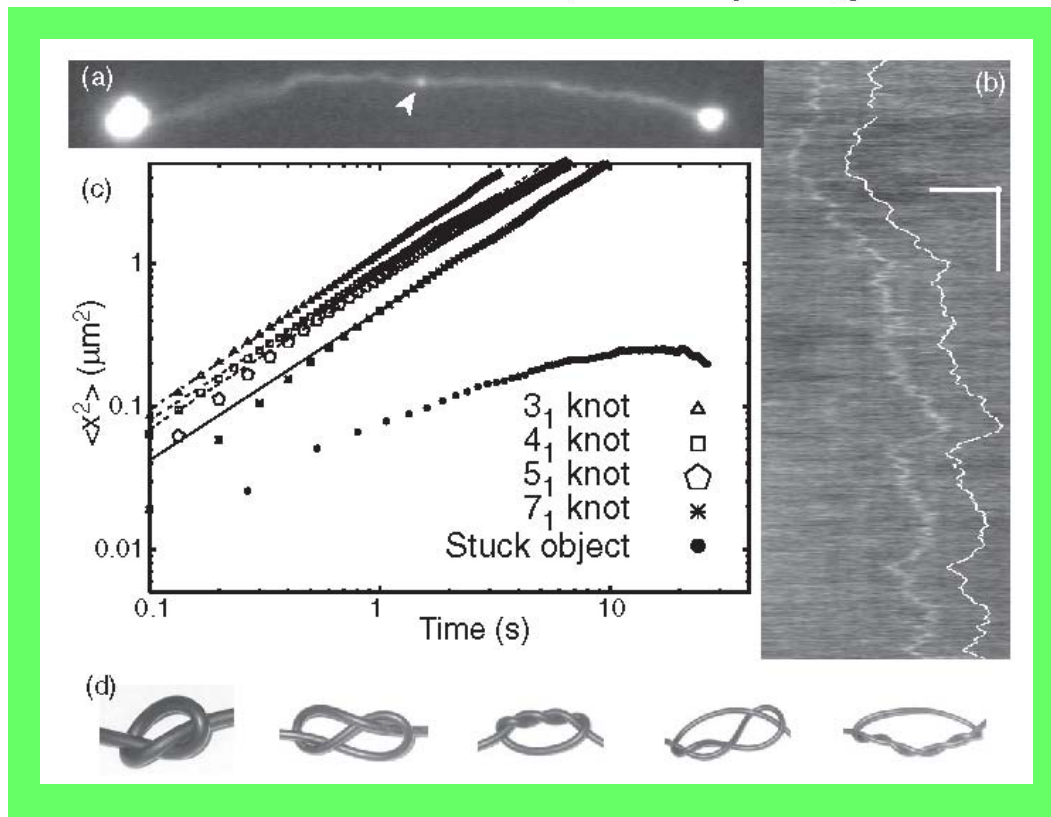
week ending
31 DECEMBER 2003

Behavior of Complex Knots in Single DNA Molecules

Xiaoyan R. Bao, Heun Jin Lee, and Stephen R. Quake

Department of Applied Physics, California Institute of Technology, Pasadena, California 91125, USA

(Received 1 August 2003; published 31 December 2003)

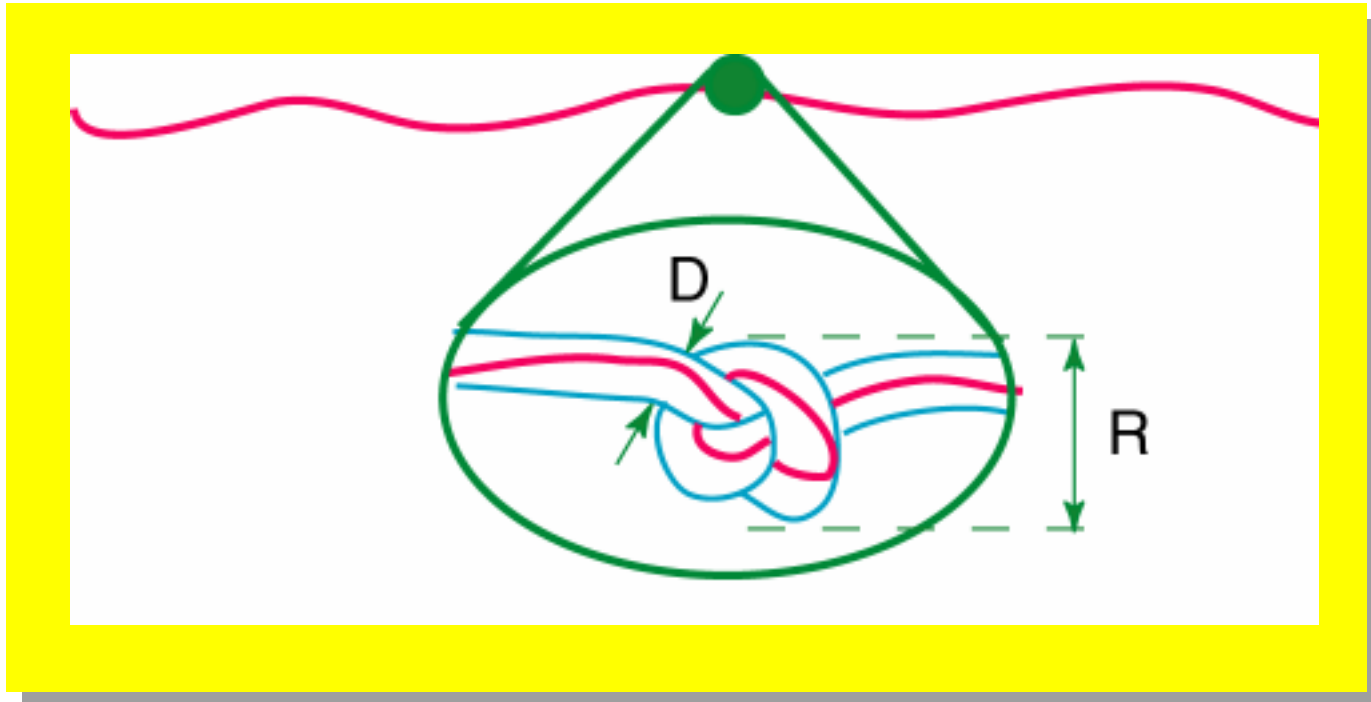


The knots were produced on purpose, by artfully manipulating optical tweezers.

It was believed that the knots remain tight because DNA is stretched.

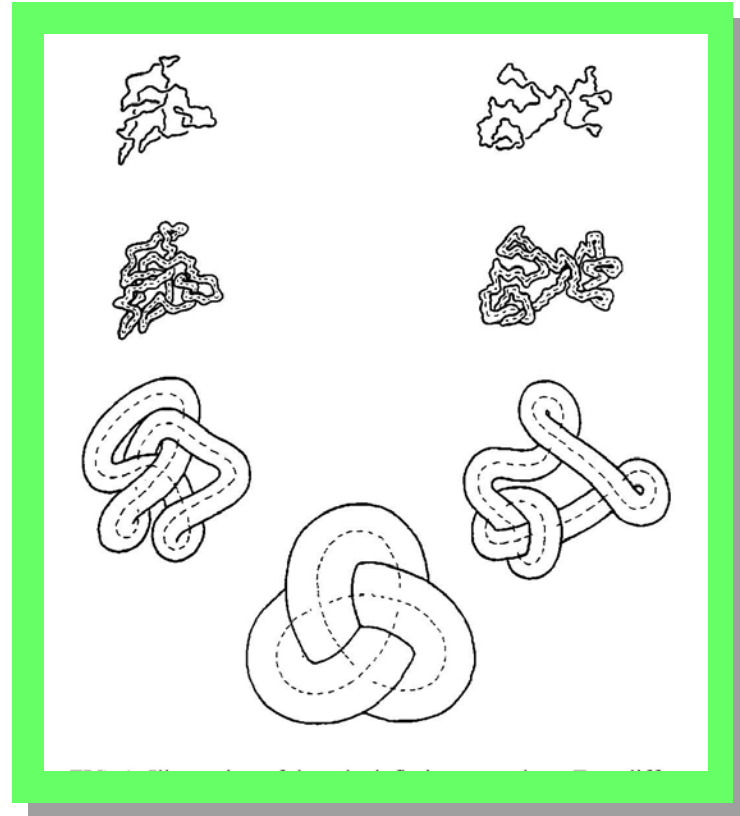
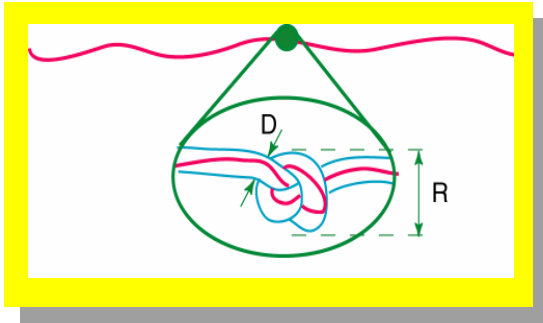
BUT...

But ... let us look at a knot:



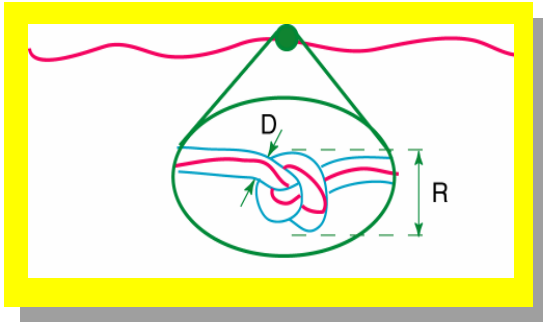
Knot self-consistently
confines polymer in an
effective tube

Optimal tube shape is a topological invariant:



A.Grosberg, Y.Rabin, 1994
A.Stasiak et al, 1996

Localized knot is (meta)stable :



$$pD \times D^2 \sim R^3$$

Knot compaction to size R costs bending energy and suppresses entropy of angular fluctuations:

$$\frac{F_{\text{bend}}}{T} \sim \frac{\ell \times pD}{R^2}$$

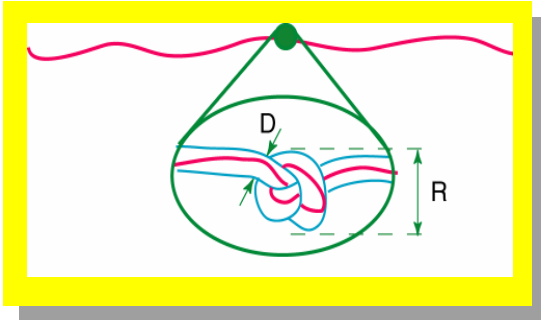
$$\frac{\Delta F}{T} \sim p^{1/3} \frac{\ell}{D} + p \left(\frac{D}{\ell} \right)^{1/3}$$

$$\frac{F_{\text{undul}}}{T} \sim \frac{pD}{\lambda} \sim \frac{pD}{(\ell D^2)^{1/3}}$$

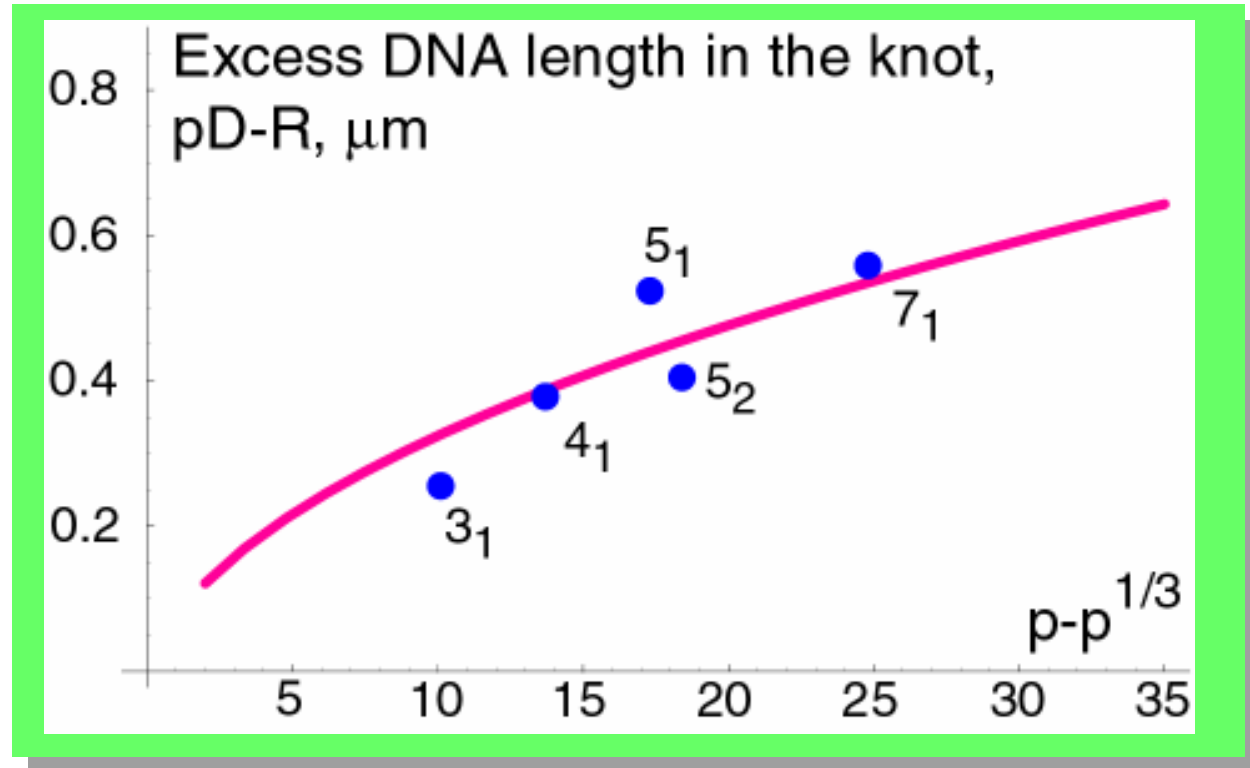
Each factor seems to favor expansion ... why is there optimal knot size????

Pressure of "vacuum"!!!!

Comparison with data:

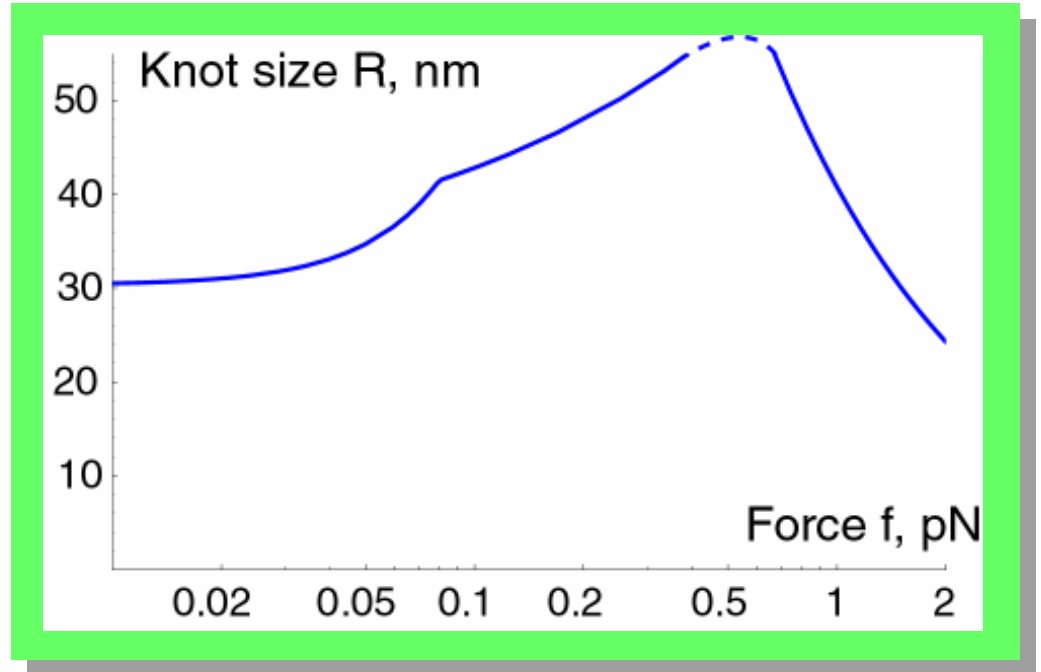
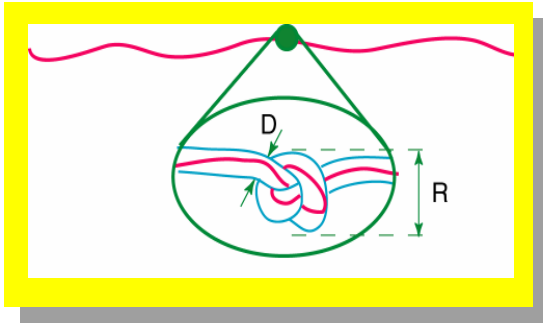


A.Grosberg, Y.Rabin, 2007



Compare at: K.Klenin et al, R.Metzler et al, E.Orlandini et al, M.Kardar et al:
knot in a loop is "localized" in the region $\sim N^{0.4}$

Prediction:



Knot is a material with negative Poisson ratio!

- Solitary knots, with Y. Rabin
- Polymer-Population Mapping and localization in the space of phenotypes, with E.Kussel and S.Leibler

Sensing or guessing?

Phenotypic Diversity, Population Growth, and Information in Fluctuating Environments

Edo Kussell* and Stanislas Leibler

Organisms in fluctuating environments must constantly adapt their behavior to survive. In clonal populations, this may be achieved through sensing followed by response or through the generation of diversity by stochastic phenotype switching. Here we show that stochastic switching can be favored over sensing when the environment changes infrequently. The optimal switching rates then mimic the statistics of environmental changes. We derive a relation between the long-term growth rate of the organism and the information available about its fluctuating environment.

Organisms adapt readily to regularly varying environments, for instance, by adjusting to the daily light cycles by using internal circadian clocks. Real problems arise when environmental fluctuations are irregular. Organisms can adapt to sudden changes in chemical composition, local temperature, or illumination by sensing the changes and responding appropriately, for example, by switching phenotype or

behavior. But there is a cost: each individual must maintain active sensory machinery.

Population diversity offers an alternate way to adapt to randomly fluctuating environments. Different subsets of the total population may be well-adapted to different types of environments. In genetically clonal populations, phenotypic diversity is generated by stochastic phenotype-switching mechanisms (1–9). Examples include flagellin phase variation in *Salmonella enterica* (6); microsatellite length variation (slipped-strand mispairing), controlling the expression of contingency genes in *Haemophilus influenzae* (2, 4); and swarming motility in *Bacillus subtilis* (8). The persistence

mechanism in *Escherichia coli*, by which cells switch spontaneously and reversibly to a phenotype exhibiting slower growth and reduced killing by antibiotics (9), allows cells to survive prolonged exposure to antibiotics (10). Many other switching mechanisms are known in diverse bacteria (2, 7), fungi (1, 3), and slime molds (1).

The idea that randomization of phenotype can be advantageous in fluctuating environments is well established in the ecology and population genetics literature (where it is known as bet-hedging). This idea has found applications in diverse contexts (11), and it was previously analyzed in several theoretical and computational studies (12–18).

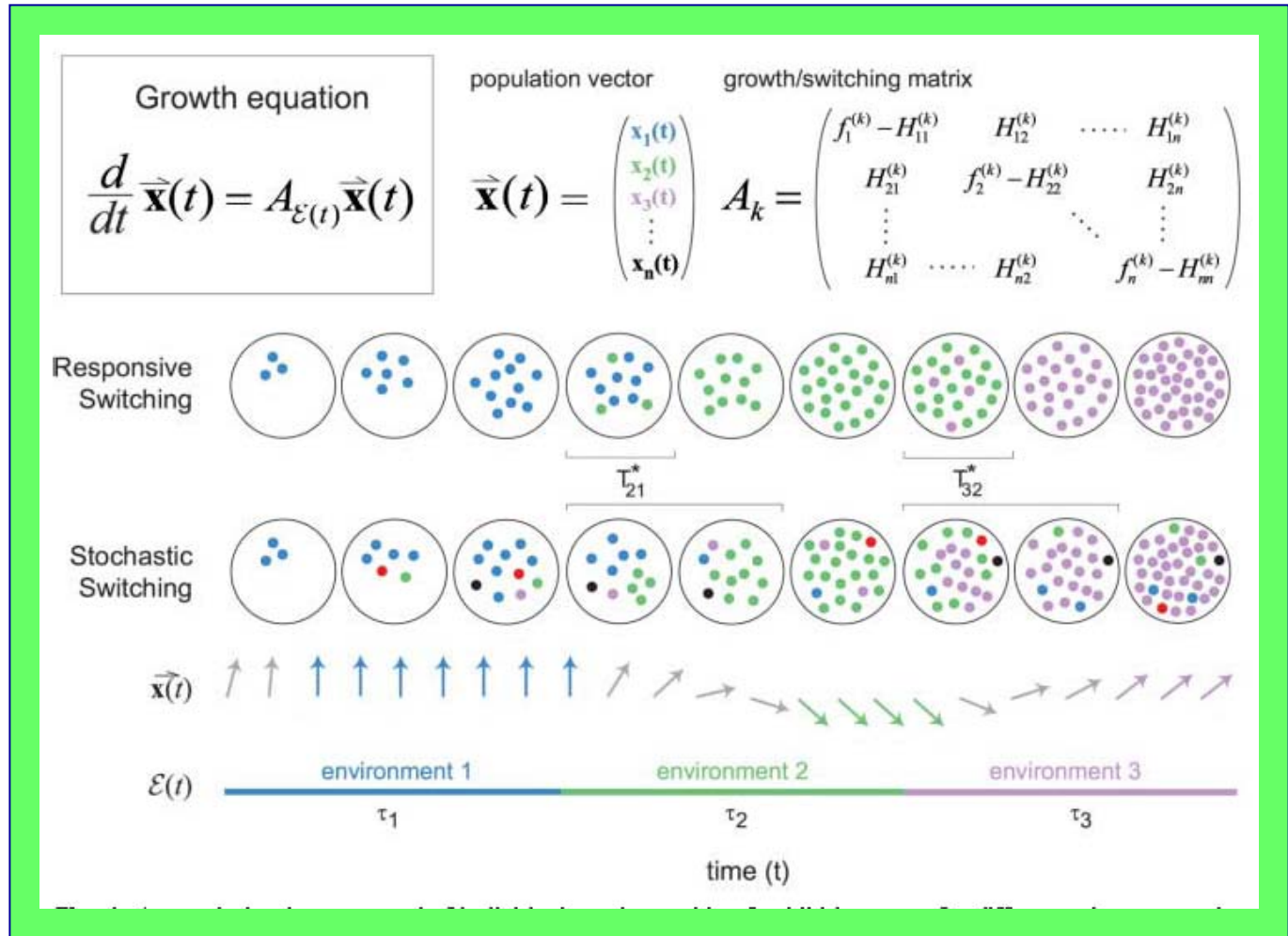
We consider two extreme types of phenotype switching: responsive switching (R), occurring as a direct response to an outside cue detected by a sensing mechanism, and spontaneous stochastic switching (S), occurring without any direct sensing of the environment. Within a theoretical model, we address several questions. First, under which circumstances should each mechanism be used? For instance, if the detection of a sudden unfavorable environmental change, or the subsequent response, would be too slow, then it could be advantageous to have a subpopulation ready in an appropriate phenotype, before the environmental change.

Second, what determines parameters such as the switching rates? Random environmental

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Population vector dynamics



“Similar equations have similar solutions” (Feynman)

- Populations:

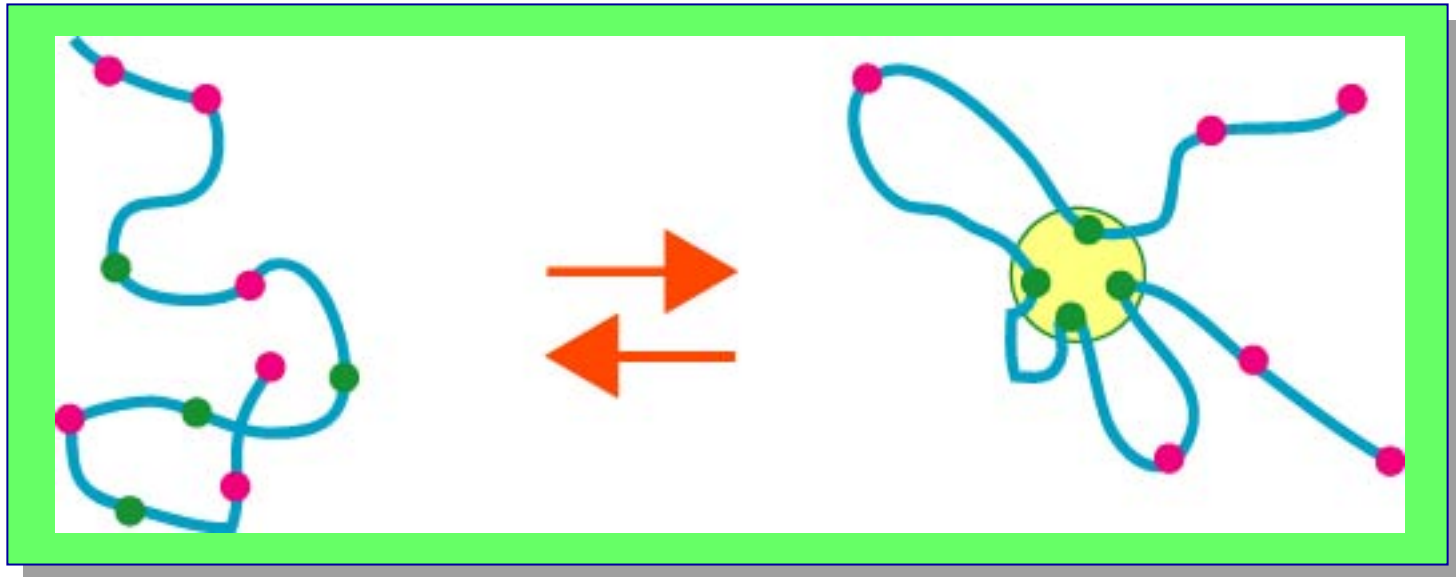
$$\frac{d}{dt}X_i(t) = f_i^\varepsilon X_i(t) + \sum_j h_{ij}X_j(t).$$

- Heteropolymers:

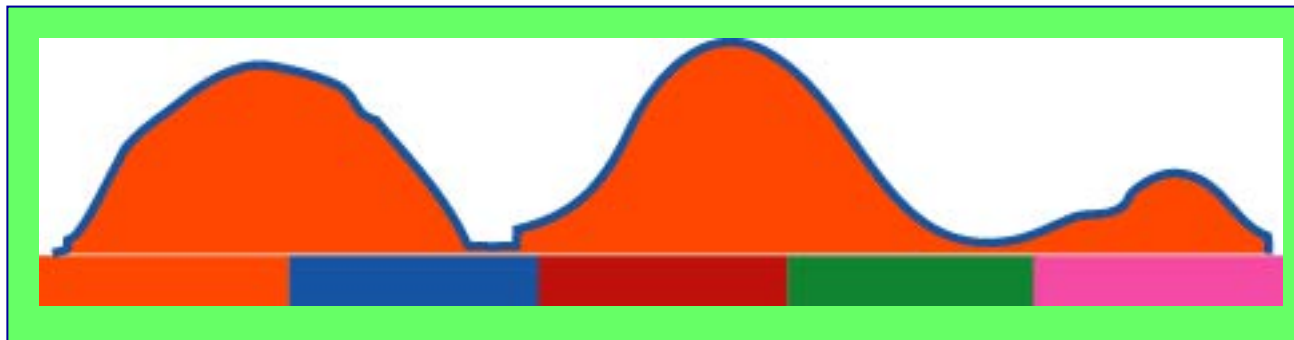
$$\frac{d}{dt}G_r(t) = -\frac{\phi_r^\alpha}{T}G_r(t) + a^2\nabla^2G_r(t).$$

Examples:

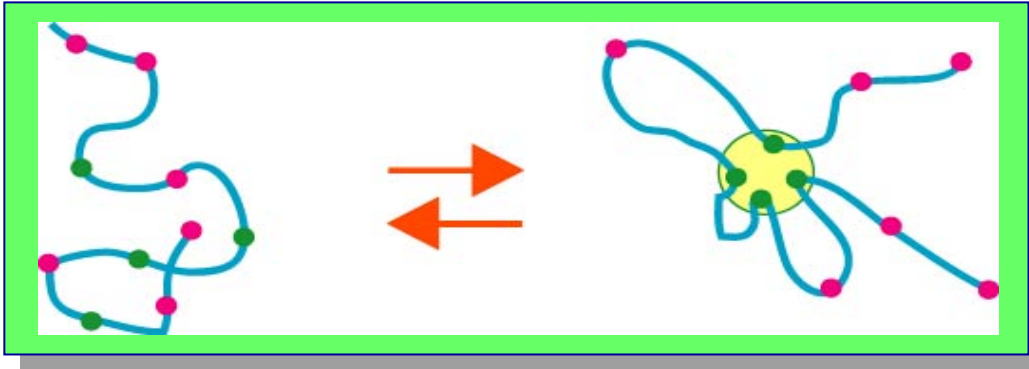
Polymer adsorption on a "point"



Equivalent problem: wetting of a disordered substrate:



Some known results:



$$e^{-\phi/T} = 1 + \beta \delta(x)$$

- For a homopolymer, adsorption at $\beta > \beta_c$ where $\beta_c = 0$ at $D < 2$ and $\beta_c > 0$ at $D > 2$.
- For a heteropolymer, the transition is at $\langle \beta \rangle = \beta_c$

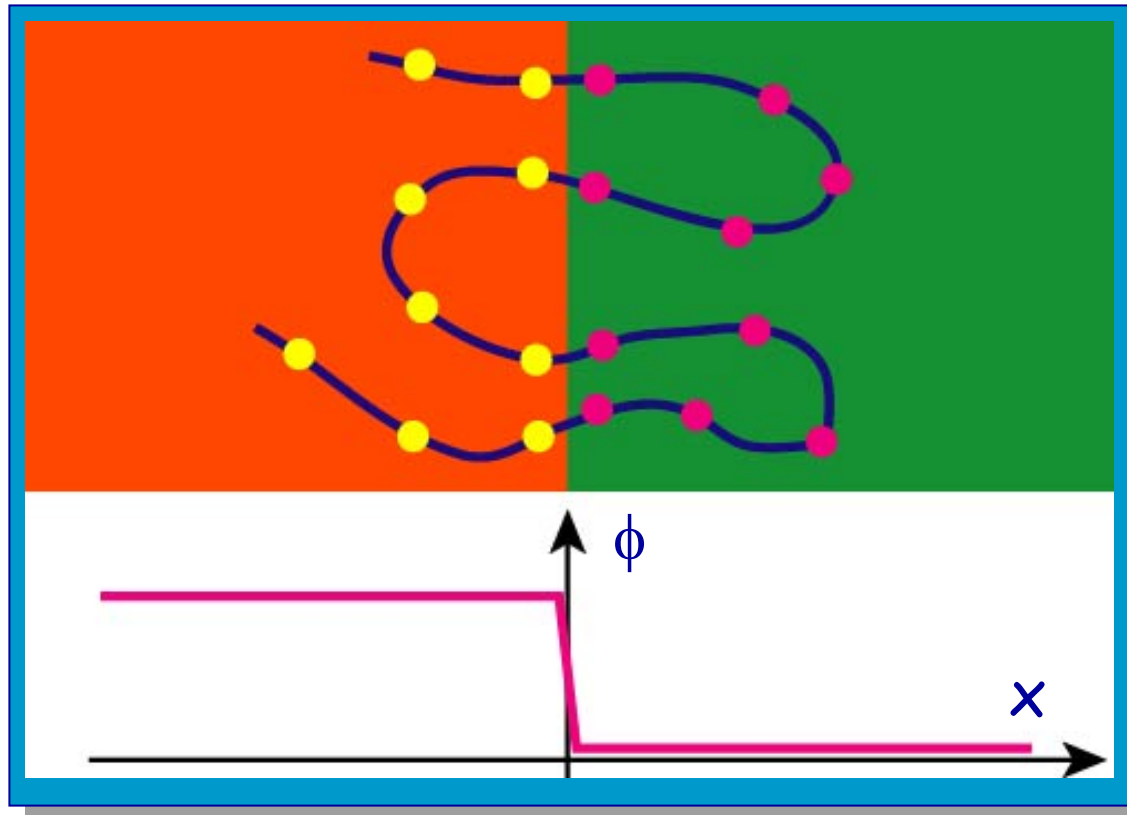
A.G., E. Shakhnovich, May 8, 1986;

H. Orland et al, July 11, 1986.

- Recently confirmed (that the simulation were right) **Cond-mat**, 2007

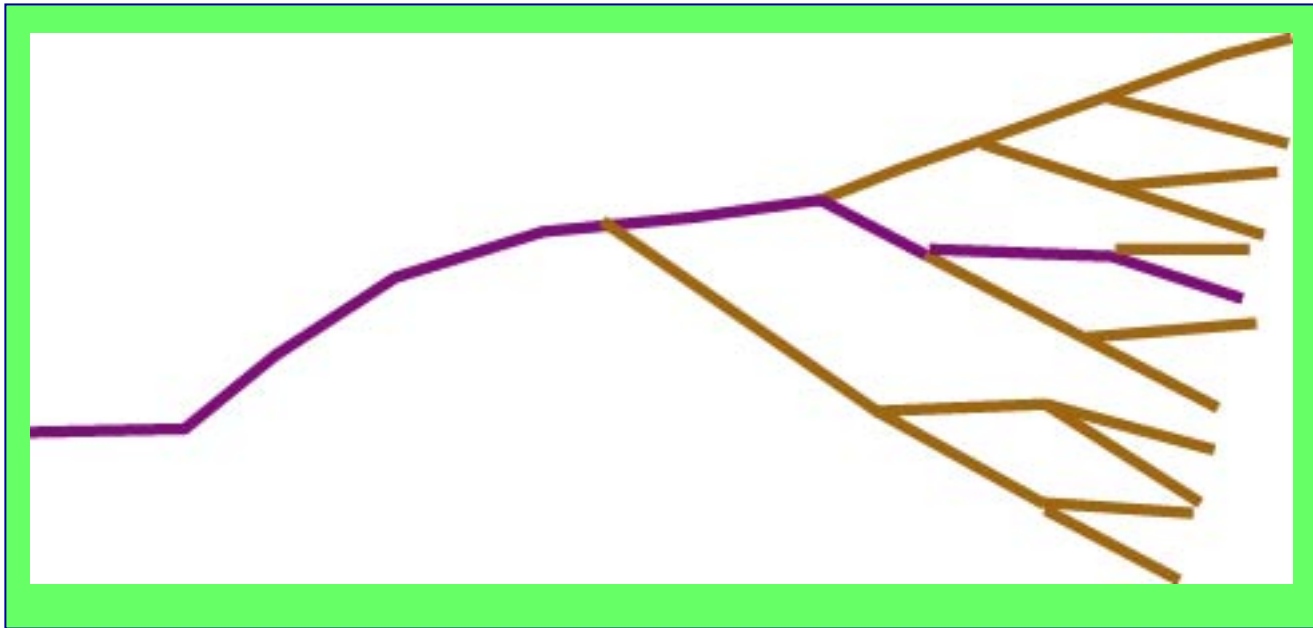
Examples:

Localization at the interface



No analog for homopolymer...

Conformation: one particular line in the tree



“Energy” is the property of an organism determined by its entire ancestral history.

Density distribution etc

Heteropolymer thermodynamics

Population dynamics

Position along chain t

Time t

Spatial position r

Phenotype i

Monomer sequence $\alpha(t)$

Environment $\mathcal{E}(t)$

External field ϕ_r^α

Reproduction rates $f_i^\mathcal{E}$

Green's function $G_r(t)$

Population vector $X_i(t)$

Partition function $Z(t)$

Population size $N(t)$

Free energy \mathcal{F}

Lyapunov exponent Λ

Polymer conformation $r(t)$

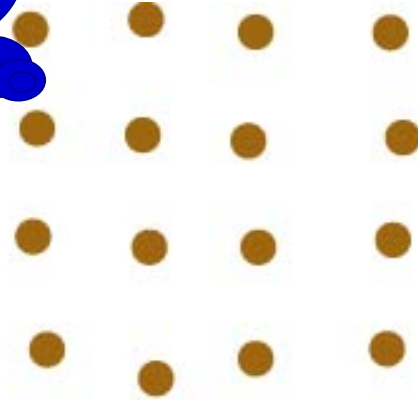
Organism history $\sigma(t)$

Monomer density n_r^α

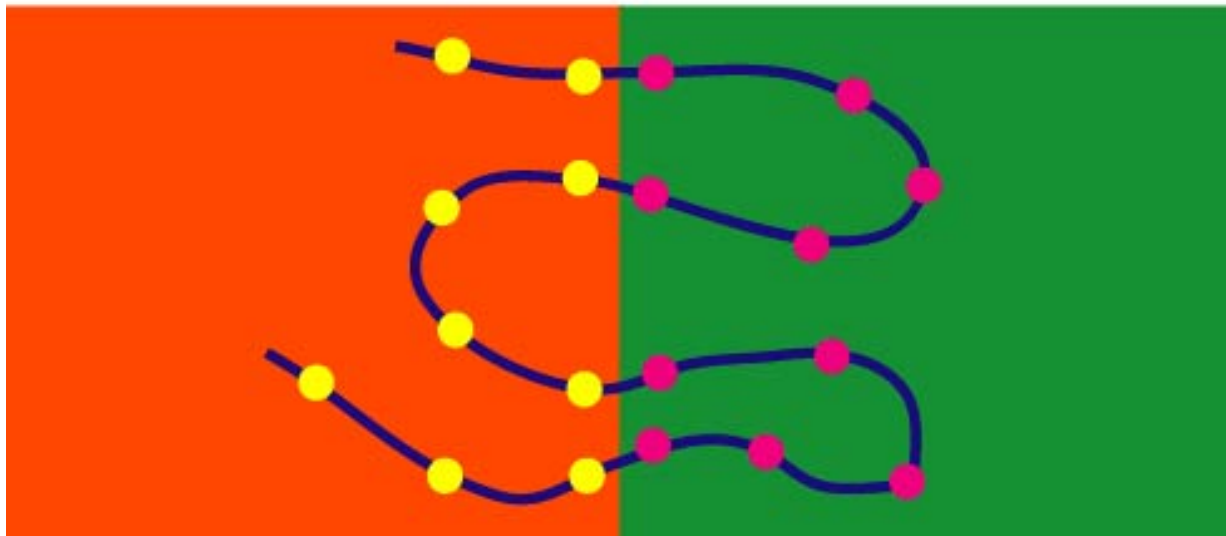
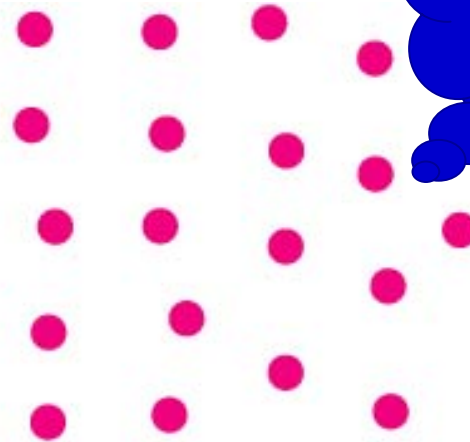
Ancestral distribution $\mu_i^\mathcal{E}$

Mapping to populations:

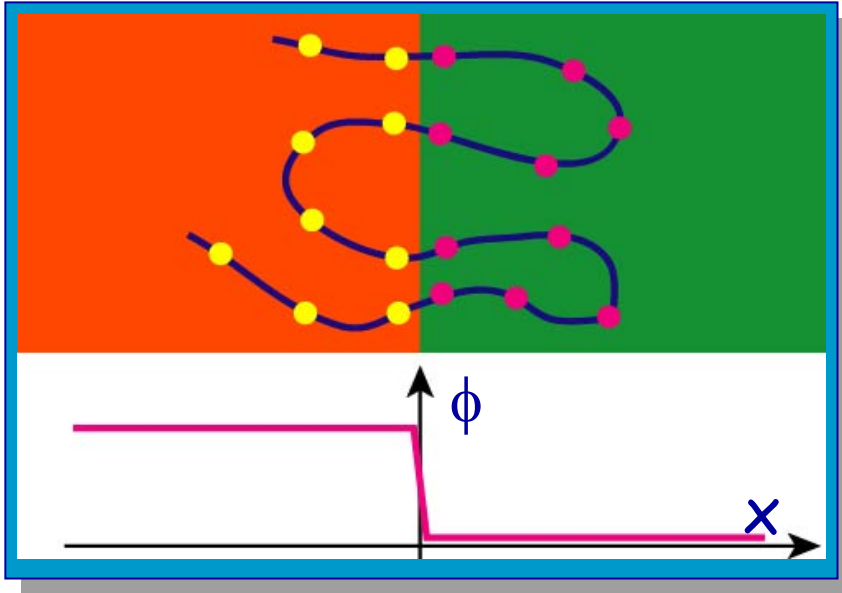
These phenotypes prefer environment O



These phenotypes prefer environment G



Conditions of localization:



- Energy preference should be sufficient to pay for entropy of localization to half space: $\varepsilon > kT \ln \tau$
- Overall width must be large enough to house a loop: $R > (a \tau)^{1/2}$

In population language: $M^2/h > \tau > 1/f$

M - total number of phenotypes; f - growth rate;
 h - switching rate; t - typical time of environmental change.

C_v

- C_v might be a good measure to decide if the population is sensing its environment;
- **If** we have a movie of the population over a long period of time, and **if** we have some kind of a label that tells us phenotype of each cell, and **if** we know fitness of each phenotype, and **if** we know the history of the environment - then we could calculate energy of every history and find C_v as energy variance.

C_V

- But ... what if we do not know phenotypes of the cells, and don't know fitnesses, and don't know environments ... then?
- $\langle E \rangle = \langle X \rangle$, where X is the number of cell divisions over a long time. That does not require anything but the movie...

C_V

- $\text{Var}(X) = \langle \text{Var}(X|E) \rangle + \text{Var}(\langle X|E \rangle)$
- $X|E$ is the number of cell divisions in the history with energy E \rightarrow Poisson distributed with mean E ;
- Therefore, $\text{Var}(E) = \text{Var}(X) - \langle X \rangle$