First-passage times of
Markovian and non Markovian random walks

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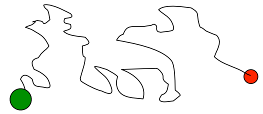
First-passage problems : First definitions



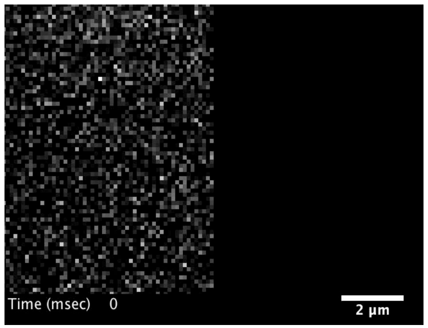
How long does it take a random walker to reach a target site ?

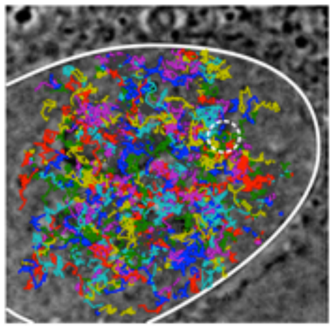
→ **First-passage time**

Many physical processes are controlled by **first-encounter** properties

Examples (i): diffusion limited reactions

Transcription kinetics: proteins searching for a specific target sequence on DNA



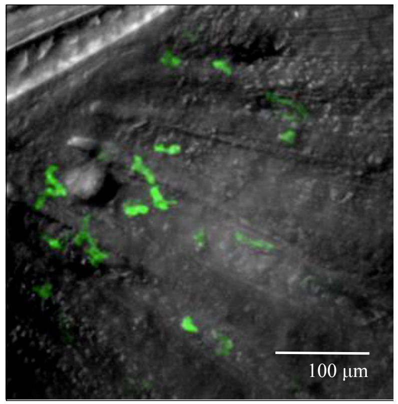


[with D. Normano, M. Dahan, Institut Curie]

- Unicity of a target gene among billions of b.p.
- Specific protein copy number can be < 10

Examples (ii): Immune cells

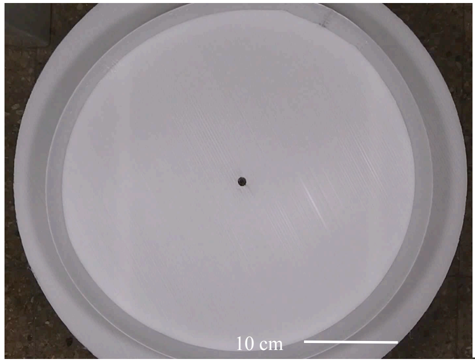
Immune cells searching for pathogens



[with M. Piel, AM Lennon, Institut Curie]

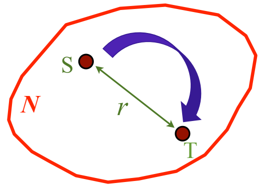
Examples (iii): ants

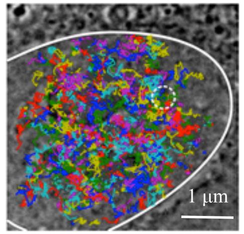
Ants searching for food



[data O. Feinerman, Weizmann Institute]

Efficiency of the search process? First-passage time statistics to a target



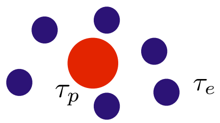


Main questions:

- How does the mean FPT depend on
  1. the confining **volume** N ?
  2. the **distance** r between S and T ?
  3. the **transport** process ? Effects of crowding, active/passive, anomalous transport

- Optimize ?

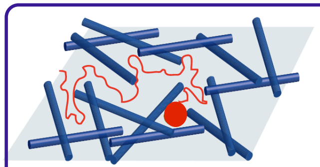
Diffusion in complex environments : Markov vs. non Markov



If $\tau_e \ll \tau_p$

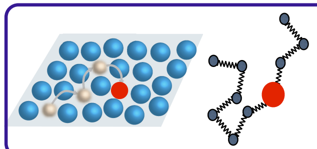
Markov process, no memory

ex. Brownian motion



If $\tau_e \gg \tau_p$

Brownian motion in a frozen disordered medium.
Markov process, no memory
ex. rw. on percolation cluster



If $\tau_e \sim \tau_p$

N particles system is Markovian,
but single particle non Markovian, memory
ex. monomer of a rouse chain

Note that different from anomalous vs normal diffusion

Theoretical context: Markov (almost) only

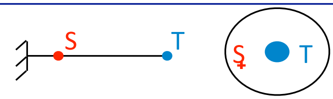
[highly non-exhaustive biblio…]

Infinite space

Persistence exponents (Markov and non Markov) [Majumdar, Bray...]

(quasi) 1D geometries

[see S. Redner's book]



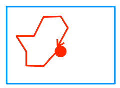
Singular perturbation of the Laplacian

(Brownian motion 2D and 3D) [Ward and Keller, Holcman and Schuss]

Mean return times

[Kac,Hilfer, Blumen…]

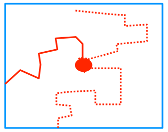
$$\langle \mathbf{T} \rangle_{return} = 1/P_{\text{stat}} = N$$



MFPT averaged over starting point

No information on the target : average over starting point (GMFPT)

For general scale invariant (d_w, d_f) random walks with $\langle \Delta r^2 \rangle \propto t^{2/d_w}$:



$$\langle \bar{\mathbf{T}} \rangle \sim \begin{cases} N & \text{if } d_w < d_f \text{ non compact (transient)} \\ N \ln(N) & \text{if } d_w = d_f \quad , \\ N^{d_w/d_f} & \text{if } d_w > d_f \text{ compact (recurrent)} \end{cases}$$

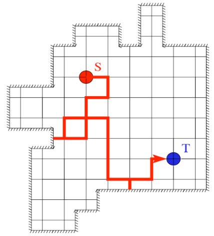
Markov: [Montroll 1965 (Euclidean lattices), ben Avraham 2005 (fractals)...]

➡ **Optimal strategy:**
less compact do better = minimize overlap

Effet of initial position ?

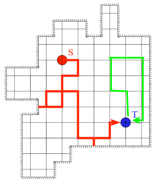
Outline

I/ Reminder :
First-passage time statistics in complex media
(Markovian scale-invariant processes)



Main ingredients

(i) **Markov process : "Renewal equation"** relates
the propagator $P(\mathbf{r}, t|\mathbf{r}')$
the first-passage time density $F(\mathbf{r}, t|\mathbf{r}')$



$$P(\mathbf{r}_T, t|\mathbf{r}_S) = \int_0^t F(\mathbf{r}_T, t'|\mathbf{r}_S)\, P(\mathbf{r}_T, t - t'|\mathbf{r}_T) dt'$$

first visit of T at *t'* — **return** at T in *t-t'*

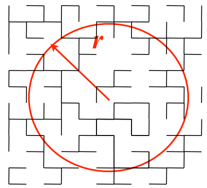
Exact expression: $\langle \mathbf{T} \rangle = N(H(\mathbf{r}_T|\mathbf{r}_T) - H(\mathbf{r}_T|\mathbf{r}_S))$ [Noh & Rieger (2004)]

where $H(\mathbf{r}|\mathbf{r}') = \int_0^\infty (P(\mathbf{r}, t|\mathbf{r}') - 1/N) dt$ is the pseudo-green function

(ii) **large volume asymptotics :** $\langle \mathbf{T} \rangle \simeq N(G_0(0) - G_0(r))$

where $G_0(r) = \int_0^\infty P_0(r, t) dt$ is the infinite-space Green function

(iii) Scale invariance



- number of sites enclosed in a circle of radius *r* : $M_r \propto r^{d_f}$
  where d_f is the **fractal dimension** of the medium
- mean square displacement $\langle \Delta r^2 \rangle \propto t^{2/d_w}$
  where d_w is the **dimension of the walk**
- standard **scaling assumption of the infinite-space propagator** :

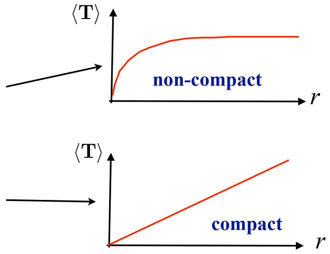
$$P_0(\mathbf{r}, t|\mathbf{r}') \sim t^{-d_f/d_w} \Pi \left(\frac{|\mathbf{r} - \mathbf{r}'|}{t^{1/d_w}} \right)$$

[ben-Avraham and Havlin, (2000)]

General scaling of the MFPT

[Condamin et al Nature (2007)]

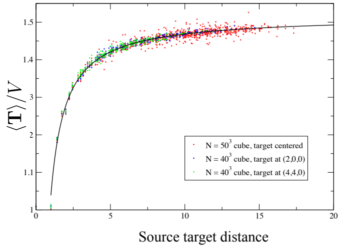
$$\langle T \rangle \sim \begin{cases} N(A - B r^{d_w - d_f}) & \text{for } d_w < d_f \\ N(A + B \ln r) & \text{for } d_w = d_f \\ N(A + B r^{d_w - d_f}) & \text{for } d_w > d_f \end{cases}$$



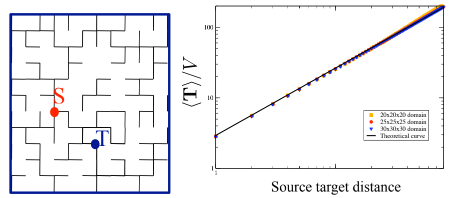
- A and B depend **only** on the infinite-space scaling
- **Linear dependence on the volume N**
- **non-compact** exploration ($d_w < d_f$) : memory of the initial position **lost**
- **compact** exploration ($d_w \geq d_f$): the **initial** position **always matters**

Numerics

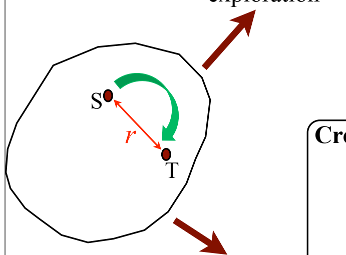
Non compact:
ex: Brownian diffusion in 3D



Compact:
ex: Diffusion on percolation cluster



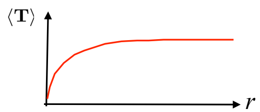
Reaction kinetics in complex media ?



Non-compact exploration

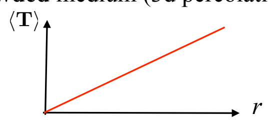
Compact exploration

Dilute medium (3d regular diffusion)



Initial position doesn't matter
1 time scale : first-order kinetics

Crowded medium (3d percolation cluster)

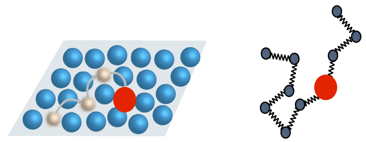


Initial position is a key parameter:
many time scales
⇨ **"Geometry controlled kinetics"**
[Nature Chemistry 2010]

Is intracellular transport in the nucleus compact or non compact ?

Outline

II/ General (Gaussian) non Markovian processes

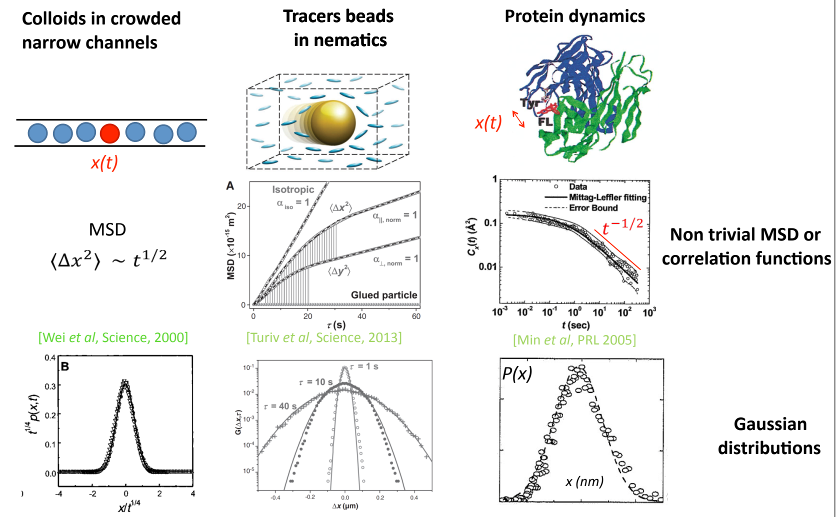


H: Gaussian process $x(t)$ with stationary increments: fully defined by

$$\psi(\tau) = \langle [x(t+\tau) - x(t)]^2 \rangle$$

here assumed given (obtained typically from single particle tracking)

Examples of non Markovian Gaussian processes



Gaussian process with non linear MSD is non Markovian (Doob's theorem)

Main ingredients (i)

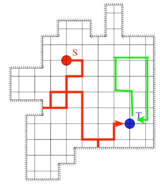
(i) **Generalized Renewal equation** relates

the 1 point pdf $P(x,t)$

the first-passage time density $F(\tau)$

$$p(\mathrm{T},t) = \int_0^t d\tau F(\tau) p(\mathrm{T},t|\mathrm{FPT}=\tau)$$

first visit of T at τ — **return** at T in *t*-τ



Exact expression: $\dfrac{\langle \mathbf{T} \rangle}{V} = \displaystyle\int_0^\infty dt [q_\pi(t) - p(\mathrm{T},t)]$

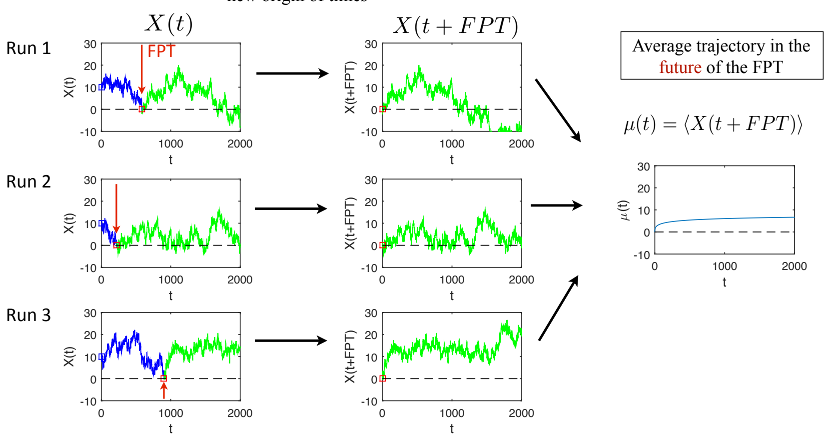
with the conditional 1 point pdf q_π of the process in the future of the FPT

$$q_\pi(t) = \int_0^\infty d\tau p(T,t+\tau|\mathrm{FPT}=\tau)F(\tau)$$

Process in the future of the FPT

Take the FPT as the new origin of times

Trajectories in the future of the FPT



Average trajectory in the future of the FPT

$\mu(t) = \langle X(t+FPT) \rangle$

Observation: PDFs of X(t+FPT) are almost indistinguishable from Gaussian histograms

Main ingredients (ii)+(iii)

(ii) **Large volume asymptotics**

(iii) **Gaussian approximation of** q_π

$$\langle \mathbf{T} \rangle = V \int_0^\infty dt \, \frac{e^{-\mu(t)^2/2\psi(t)} - e^{-x_0^2/2\psi(t)}}{[2\pi\psi(t)]^{1/2}}.$$

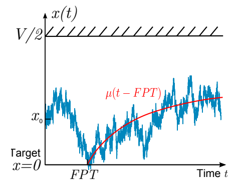
where $\mu(t)$ is the mean trajectory in the future of the FPT, defined by

$$\int_0^\infty \frac{dt}{\sqrt{\psi(t)}} \left\{ [\mu(t+\tau) - \mu(t)K(t,\tau)] \, e^{-\mu(t)^2/2\psi(t)} - x_0[1-K(t,\tau)]e^{-x_0^2/2\psi(t)} \right\} = 0,$$

$$K(t,\tau) = [\psi(t+\tau) + \psi(t) - \psi(\tau)]/[2\psi(t)]$$

Can be solved (at least numerically) + exact asymptotics for simple $\psi(t)$

-mean future trajectory matters
-defined by MSD function only
-Markov approx. $\mu(t) = 0$ overestimates MFPT



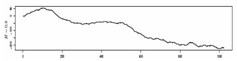
Results: Fractional Brownian motion

MSD $\langle [x(t) - x(t')]^2 \rangle = K(t-t')^{2H}$ $0 < H < 1$

Used in finance, biophysics…

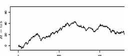
Limit of single file, Rouse, Edwards-Wilkinson

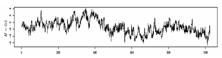
Model with **long-range correlated** increments :



Take the derivatives with respect to t and t' :

$$\langle \dot{x}(t)\dot{x}(t') \rangle = K2H(2H-1)\frac{1}{(t-t')^{2-2H}} \begin{cases} >0 \text{ if } H > \frac{1}{2} & \textbf{persistent superdiffusion} \\ =0 \text{ if } H = \frac{1}{2} & \textbf{regular diffusion} \\ <0 \text{ if } H < \frac{1}{2} & \textbf{anti-persistent subdiffusion} \end{cases}$$





Results: Fractional Brownian motion

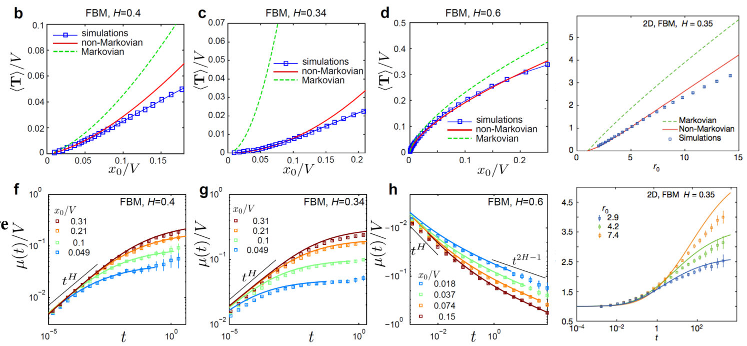
[Nature 2016]

$$\langle [x(t) - x(0)]^2 \rangle = K\, t^{2H}$$

1D, subdiffusive | 1D, superdiffusive | 2D, subdiffusive

MFPT

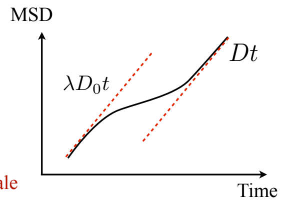
Mean future trajectory



Results: diffusion in viscoelastic fluids

[Nature 2016]

$$\langle [x(t) - x(0)]^2 \rangle \simeq D_0\left(1 - e^{-\lambda t}\right) + Dt$$

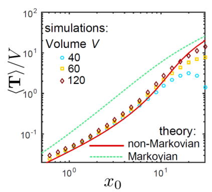


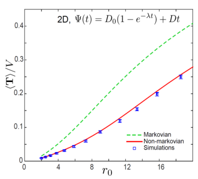
Simple model for
- Tracers in nematics [Turiv, 2013]
- diffusion in Maxwell fluids [Grimm et al, Soft Matt 2011]
- diffusion in polymer solutions [Ochab-Marcinek 2011]

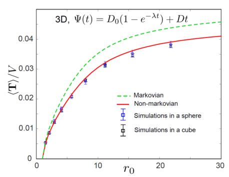
Diffusive at short times, diffusive at long times, single time scale

1D 2D 3D

MFPT

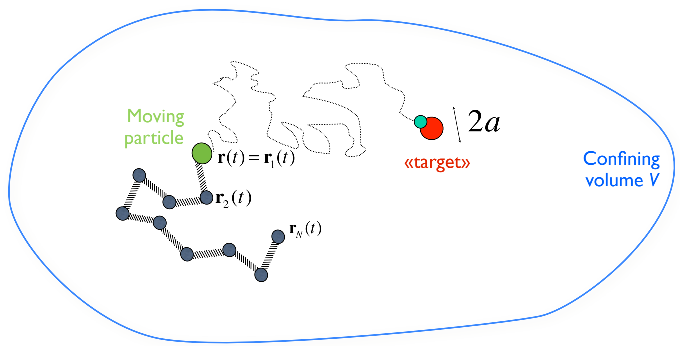






⇨ Even in the case of a MSD with only **1 relaxation time**, **memory** effects are **large**

Physical picture: the Rouse chain



The evolution of $\mathbf{r}_1(t)$ depends on the whole configuration $\{\mathbf{r}_1(t), \mathbf{r}_2(t), \ldots, \mathbf{r}_N(t)\}$

⇨ $\mathbf{r}_1(t)$ is a non-Markovian variable

amenable to Markovian problem (but higher dimensional)

Non Markovian theory

[Nature Chemistry 2012]

$$\langle T \rangle = V \int_0^\infty dt \left[P\left(x_1 = 0, t \middle| \pi, 0\right) - P\left(x_1 = 0, t \middle| \text{ini}, 0\right) \right]$$

$\pi(\{x_i\})$ — Probability density of the configuration $\{x_i\}$ at the very instant of reaction

How can we calculate $\pi(\{x_i\})$?

- Wilemski-Fixman approx: replace π by the equilibrium distribution

$$\pi(\{x_i\}) = P_{\text{stat}}\left(\{x_i\} \middle| x_1 = 0\right)$$

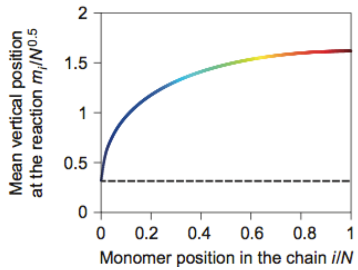
- Our approach: find the ***Gaussian*** distribution that is the closest from π

Solve closure equations for :

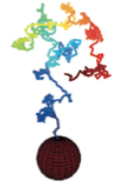
m_i average positions of monomers at first contact

Configurations at first contact

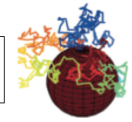
[Nature Chemistry 2012]



Conformations at first contact (non-Markovian theory)



Equilibrium conformations

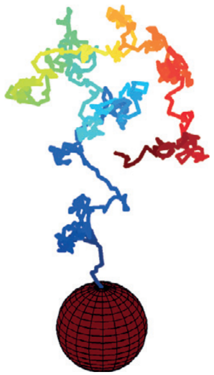


Elongated shape at first contact ➡ faster kinetics / Markovian theory

2 equivalent descriptions

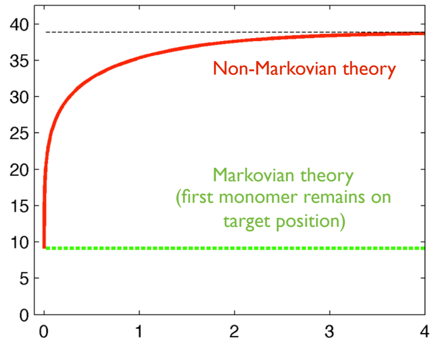
[Nature Chemistry 2012]

Positions of all the non-reactive monomers at first contact



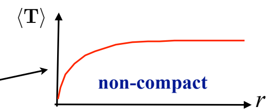
Average path after first contact

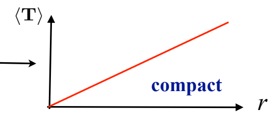
$\langle \mu(t_{\text{Futur}}) \rangle$



Finally : General scaling of the MFPT

$$\langle \mathbf{T} \rangle \sim \begin{cases} N(A - B r^{d_w - d_f}) & \text{for } d_w < d_f \\ N(A + B \ln r) & \text{for } d_w = d_f \\ N(A + B r^{d_w - d_f}) & \text{for } d_w > d_f \end{cases}$$





True for Markov and non Markov

Non trivial even if it looks trivial:
- the Markov approx. $\mu = 0$ can be very wrong (scaling wise)
- 2 or 3 length scales in the problem
- prefactor can depend a lot on non Markovian effects

Finally

- if no information on the target : less compact walks do better
- if the target is close : compact walks can yield short time scales

Thanks

O. Bénichou, T. Guerin, N. Levernier