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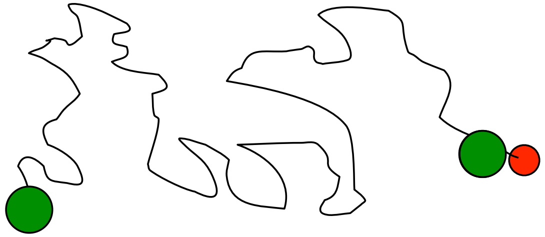
First-passage times and reaction kinetics in confined media

O. Bénichou, S. Condamin, Y. Klafter, B. Meyer, V. Tejedor, R. Voituriez

Laboratoire de Physique Théorique de la Matière Condensée,
Université Pierre et Marie Curie, Paris.

Models and Images for Porous Media Workshop

First-passage statistics : First definitions



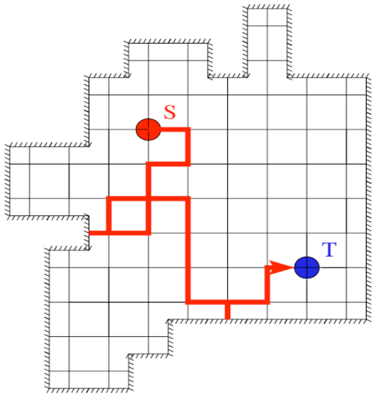
How long does it take a random walker to reach a target site ?

→ **First-passage time**

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

- Microscopic scale: diffusion limited reactions
- Macroscopic scale: search processes (animals looking for food ...)

$\langle \mathbf{T} \rangle$: mean first-passage time (MFPT) of a **symmetric** random walker

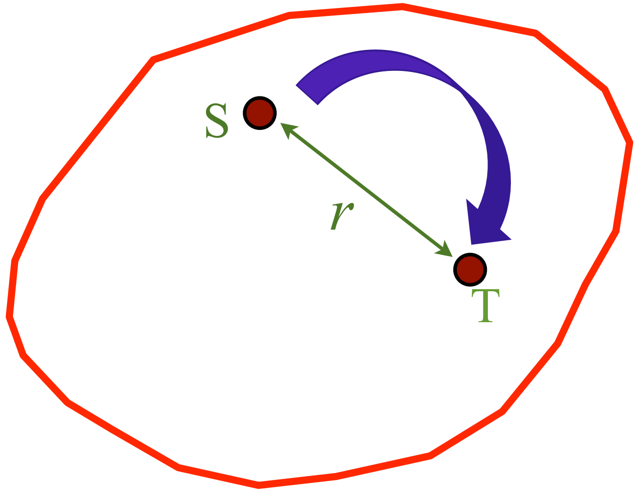


- In absence of confinement : $\langle \mathbf{T} \rangle = \infty$
- In presence of confinement : $\langle \mathbf{T} \rangle < \infty$

How does $\langle \mathbf{T} \rangle$ depend on the confinement and on the transport process?

Experimental context : Reactivity in confined media

Example : biomolecules (DNA-binding protein) reacting at a **specific location (specific gene)** in a cell



How $\langle \mathbf{T} \rangle$ depends on

1. the confining **volume *N*** ?

$\lim_{N\to\infty} \langle \mathbf{T} \rangle = \infty$, but how $\langle \mathbf{T} \rangle$ grows with *N* ?

2. the **distance *r*** between S and T ?

Is the **initial position** of the reactant an **important** parameter of the **kinetics** ?

3. the **transport** process ?

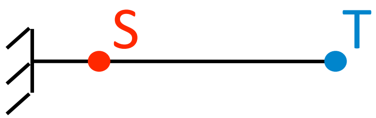
Effects of crowding, anomalous diffusion...

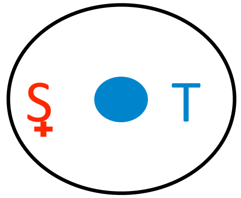
Theoretical context:

[highly non-exhaustive biblio…]

(quasi) 1D geometries

[Redner…]





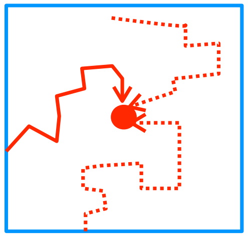
Main ingredient : backward equation.

$$\Delta_S \langle \mathbf{T} \rangle_S = -1 \quad \text{with} \quad \langle \mathbf{T} \rangle_{S=T} = 0; \;\; \partial_S \langle \mathbf{T} \rangle_{S \in \ bound.} = 0$$

follows from $\langle \mathbf{T} \rangle_S = 1 + \frac{1}{2} \left(\langle \mathbf{T} \rangle_{S-1} + \langle \mathbf{T} \rangle_{S+1} \right)$

Averages over starting point

[Montroll…]

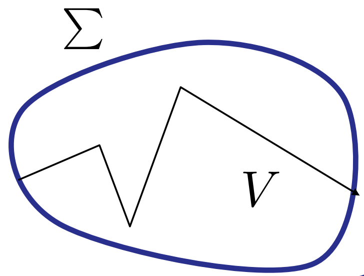


Mean *return* times

Blanco, Fournier (2003), Mazzolo (2004) :

Pearson walk of velocity *v*, and reorientation rate λ

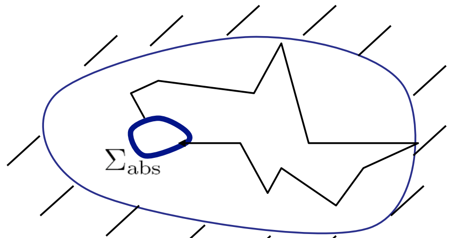
$$\langle t_1 \rangle_\Sigma = \frac{\eta_d}{v} \frac{V}{\Sigma}$$ ➡ Independent of λ !



Generalizations using Backward Chapman-Kolmogorov equation

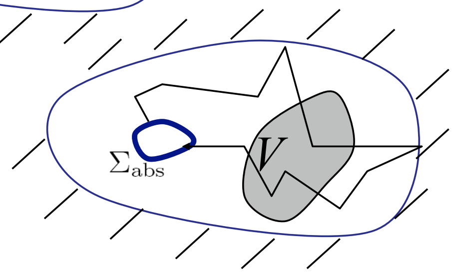
• General boundary conditions

$$\langle t_1 \rangle_{\Sigma_{\rm abs}} = \frac{\eta_d}{v} \frac{V}{\Sigma_{\rm abs}}$$



• Residence time in a subdomain *V'*

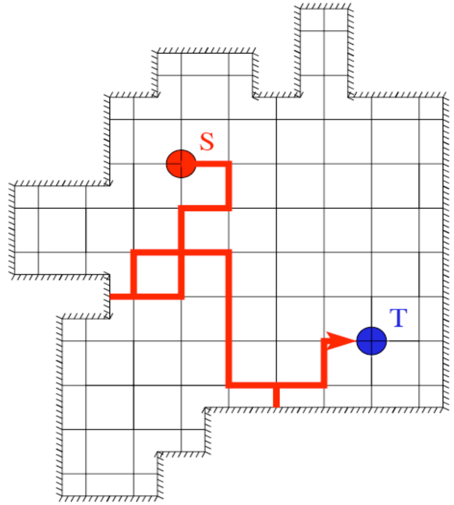
$$\langle \tau_1 \rangle_{\Sigma_{\rm abs}} = \frac{\eta_d}{v} \frac{V'}{\Sigma_{\rm abs}}$$



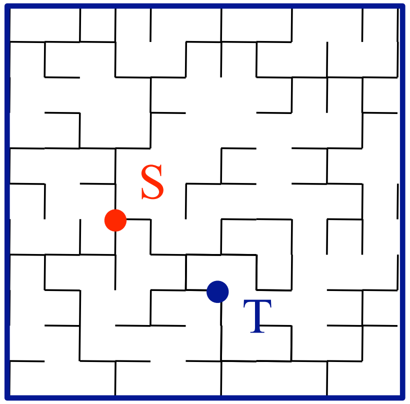
Discrete case : KAC formula (1947) $\langle \mathbf{T} \rangle_{return} = 1/P_{\rm stat} = N$

Outline

I MFPTs of **simple** random walks



II MFPTs in **complex** scale-invariant systems

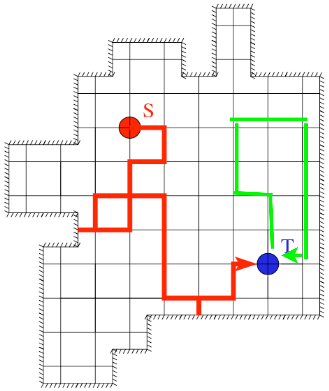


An exact formula for MFPTs

"Renewal equation" : relates

the propagator $W(\mathbf{r},t|\mathbf{r}')$

the first-passage time density $P(\mathbf{r},t|\mathbf{r}')$



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

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

$$\boxed{\langle \mathbf{T} \rangle = N(H(\mathbf{r}_T|\mathbf{r}_T) - H(\mathbf{r}_T|\mathbf{r}_S))}$$

[Noh & Rieger (PRL 2004)]

where $H(\mathbf{r}|\mathbf{r}') = \int_0^\infty (W(\mathbf{r},t|\mathbf{r}') - 1/N)dt$ ➡ Exact, but **formal** expression of the MFPT

➡ **How to go further ???**

Large volume asymptotics

$$\lim_{N\to\infty}\langle\mathbf{T}\rangle/N = \lim_{N\to\infty}\left(H(\mathbf{r}_T|\mathbf{r}_T) - H(\mathbf{r}_T|\mathbf{r}_S)\right)$$

with $\lim_{N\to\infty} H(\mathbf{r}_T|\mathbf{r}')) = \int_0^\infty W_0(\mathbf{r},t|\mathbf{r}')dt$ = **infinite-space Green function**

$$\boxed{\langle\mathbf{T}\rangle \simeq N(G_0(0) - G_0(r))}$$

$\langle\mathbf{T}\rangle$ is **proportional to the confining volume *N***

(This is not a severe infinite-space approximation of the MFPT !)

Explicit dependence in the **source-target distance *r***

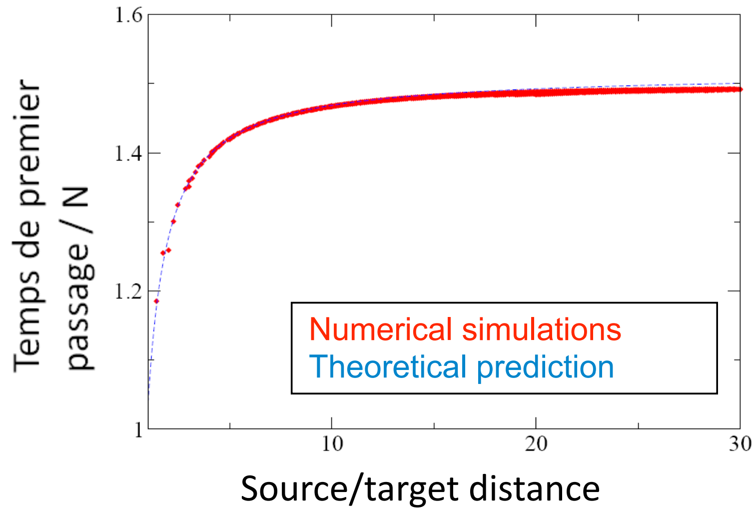
If d=3, $\langle\mathbf{T}\rangle \simeq N\left(G(0) - \dfrac{3}{2\pi r}\right)$ with $G(0) = 1.516386\ldots$

If d=2, $\langle\mathbf{T}\rangle \simeq N\left(\dfrac{3}{\pi}\ln 2 + \dfrac{2\gamma}{\pi} + \dfrac{2}{\pi}\ln r\right)$

3D Lattice Random Walks

[Condamin et al. PRL (2005)]

$$\langle \mathbf{T} \rangle \simeq N \left(G_0(0) - \frac{3}{2\pi r} \right)$$



Outline

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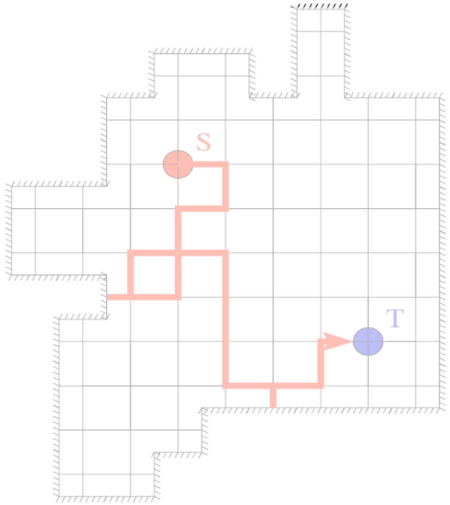
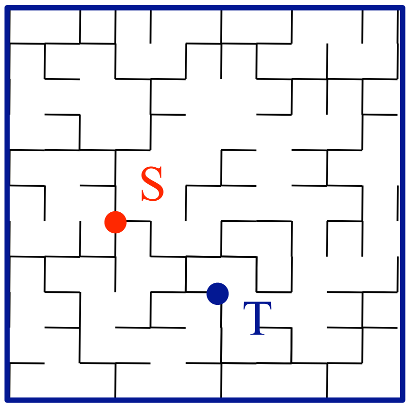
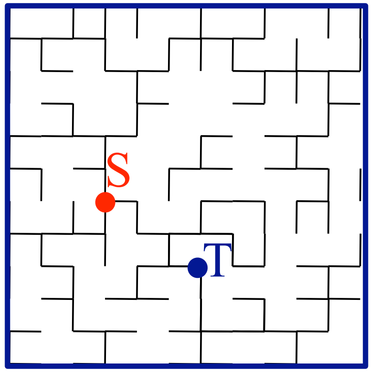


II MFPTs in **complex** scale-invariant systems



Other transport mechanisms ?



Example of a **percolation** cluster in **confinement**

⇒ MFPT to go from S to T ?

- **Renewal equation**

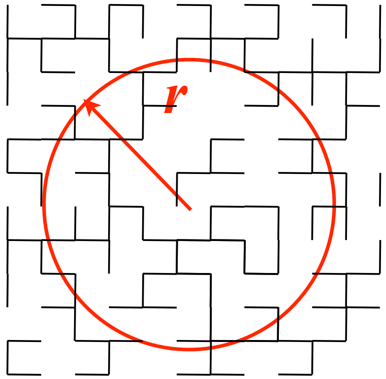
$$\langle \mathbf{T} \rangle = N(H(\mathbf{r}_T|\mathbf{r}_T) - H(\mathbf{r}_T|\mathbf{r}_S)) \quad \text{where} \quad H(\mathbf{r}|\mathbf{r}') = \int_0^\infty (W(\mathbf{r},t|\mathbf{r}') - 1/N)dt$$

- **Large volume asymptotics of the MFPT**

$$\lim_{N\to\infty} \frac{\langle \mathbf{T} \rangle}{N} = G(0) - G(r) \quad \text{where} \quad G(|\mathbf{r}-\mathbf{r}'|) \equiv \int_0^\infty W_\infty(\mathbf{r},t|\mathbf{r}')dt$$

to go further,
assumptions on the **infinite-space** propagator $W_\infty(\mathbf{r},t|\mathbf{r}')$ needed

Assumptions on the infinite-space problem



- 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

- time taken to a random walker to exit a circle of radius *r* : $T_r \propto r^{d_w}$

  where d_w is the **dimension of the walk**

- standard **scaling assumption of the infinite-space propagator** :

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

[ben-Avraham and Havlin, (2000)]

General scaling of the MFPT

[Condamin et al. Nature (2007)]

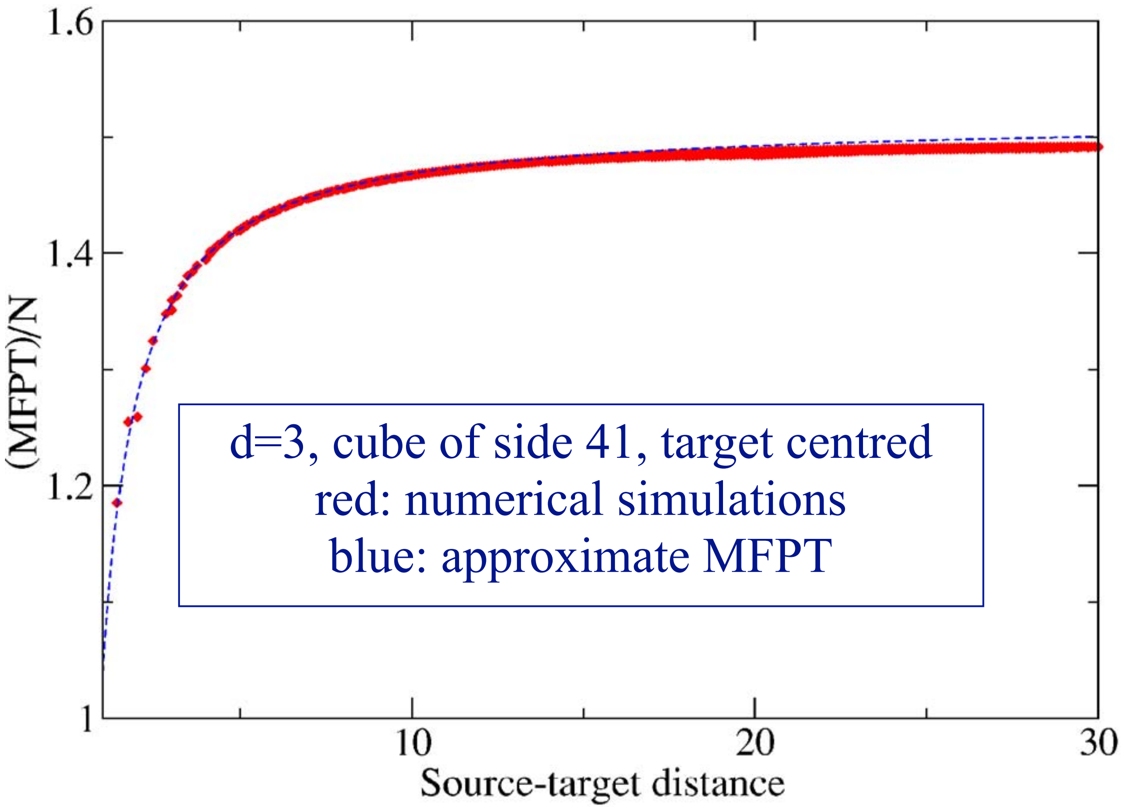
$$\langle \mathbf{T} \rangle \sim \begin{cases} N(A - Br^{d_w - d_f}) & \text{for } d_w < d_f \\ N(A + B\ln r) & \text{for } d_w = d_f \\ N(A + Br^{d_w - d_f}) & \text{for } d_w > d_f \end{cases}$$

- A and B depend **only** on the infinite-space scaling function Π
- **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**

3D Lattice Random Walks

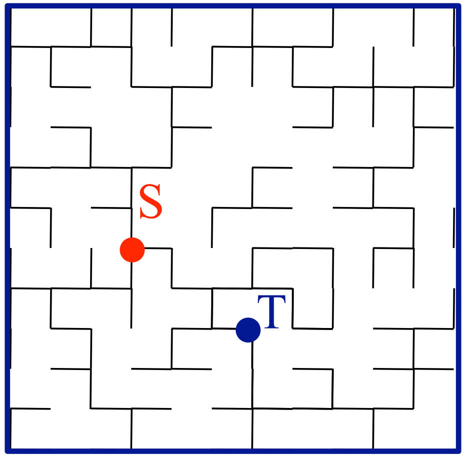
$$2 = d_w < d_f = 3$$

Non compact exploration



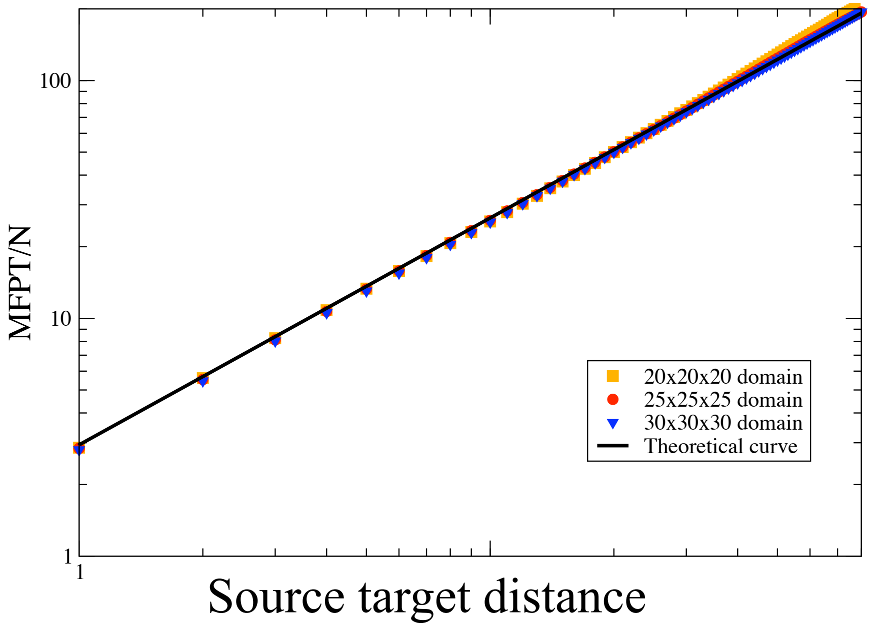
Critical percolation clusters

[Condamin et al, PNAS (2008)]



$$d_w > d_f$$

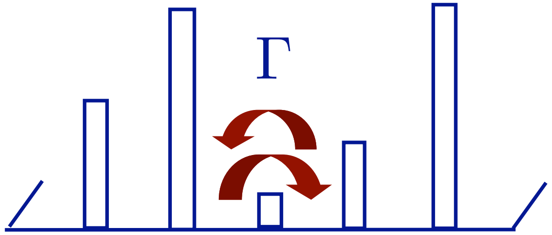
Compact exploration



$$\langle \mathbf{T} \rangle / N \sim A + B r^{d_w - d_f}$$

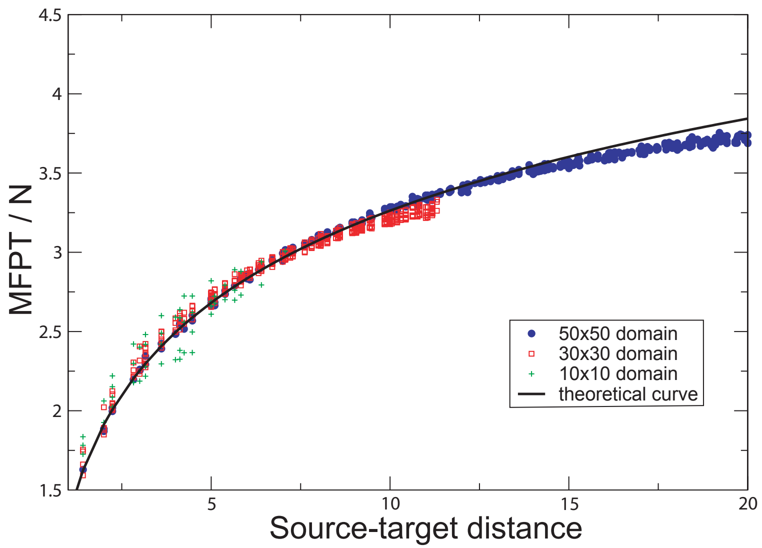
- data for different sizes collapse
- good agreement with the theoretical curve

2D Random barrier model



inhomogeneous transition rates Γ (quenched disorder)

- power law distribution of transition rates: $\rho(\Gamma) = (\alpha/\Gamma)(\Gamma/\Gamma_0)^\alpha$
- regular diffusion ($d_w = 2$) in dimension 2 ($d_f = 2$) with D_{eff} given by the effective medium approximation



$$\langle \mathbf{T} \rangle / N \sim \left(A + \frac{1}{2\pi D_{\text{eff}}} \ln r \right)$$

More about A and B:

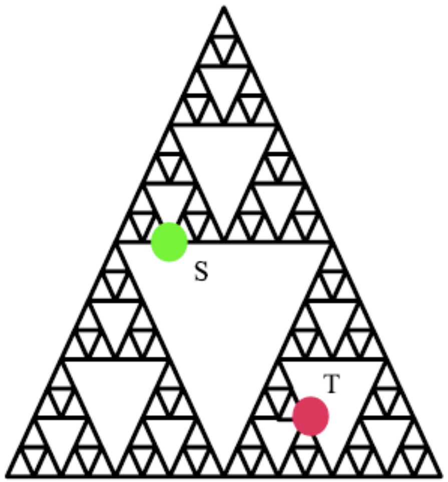
"Zero" constant formula (compact case)

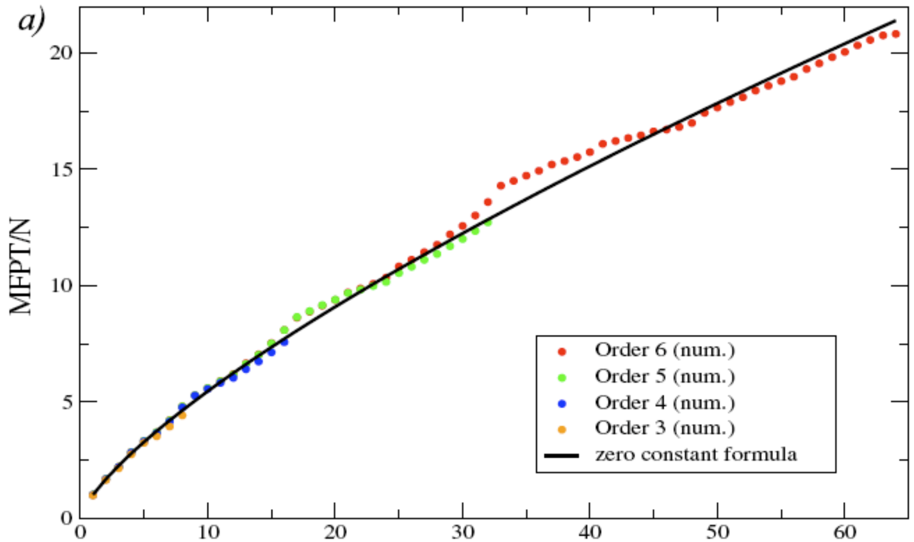
[Benichou et al. prl (2008)]

$$\langle \mathbf{T} \rangle / N \sim A + B r^{d_w - d_f} \quad \text{for } d_w > d_f$$

- Continuous space limit gives $\langle \mathbf{T} \rangle (r \to 0) = 0$ and therefore $A = 0$
- Kac formula gives $\langle \mathbf{T} \rangle (r = 1) = N$ and therefore $B = 1$

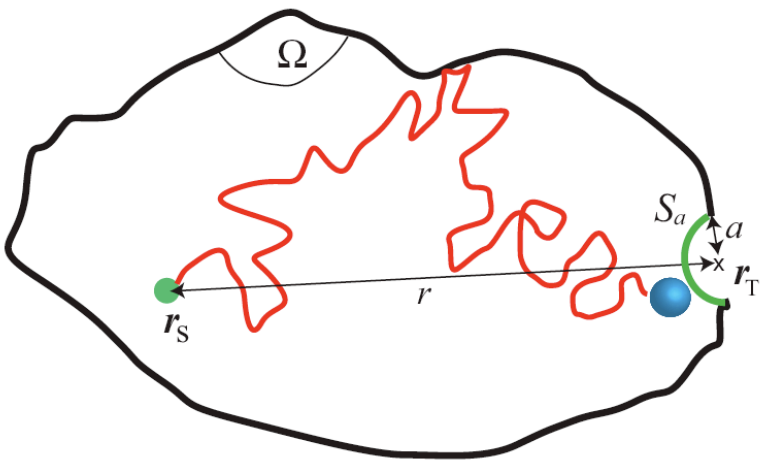
Then $\langle \mathbf{T} \rangle / N \sim r^{d_w - d_f}$





Extension (i) : narrow escape time

[PRL 2008]



Mean time to exit a bounded domain through a narrow aperture:

$$\lim_{V\to\infty} \langle \mathbf{T} \rangle / V = \begin{cases} \alpha(a^{d_w-d_f} - r^{d_w-d_f}) & \text{for } d_w < d_f \\ \alpha \ln(r/a) & \text{for } d_w = d_f \\ \alpha(r^{d_w-d_f} - a^{d_w-d_f}) & \text{for } d_w > d_f \end{cases}$$

Compact
exploration

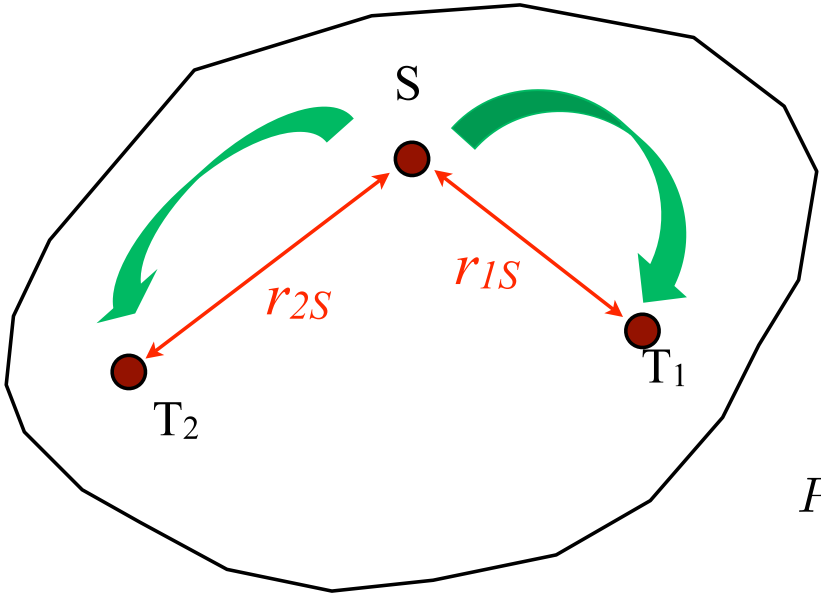
the starting point is important

Non-compact
exploration

weak dependence on the starting point

Extension (ii) : case of competitive reactions

[PNAS 2008]



Splitting probability P_1 **:**
probability to reach the target 1 before the target 2 ?

$$P_1 \sim \frac{A + B(r_{2S}^{d_w - d_f} + r_{12}^{d_w - d_f} - r_{1S}^{d_w - d_f})}{2(A + B r_{12}^{d_w - d_f})}$$

Compact exploration

the **furthest** target is **almost never reached first**

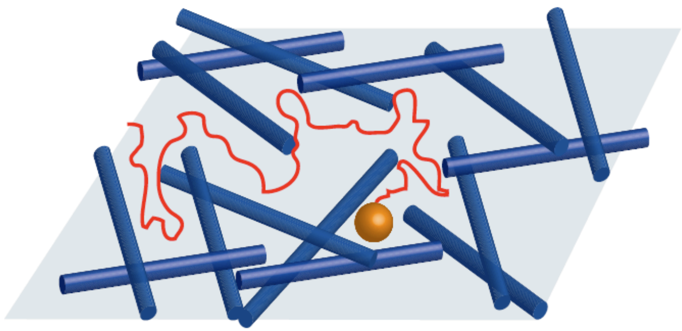
Non-compact exploration

the **furthest** target has a **finite probability to be reached first**

FPTs and subdiffusion

[PNAS 2008]

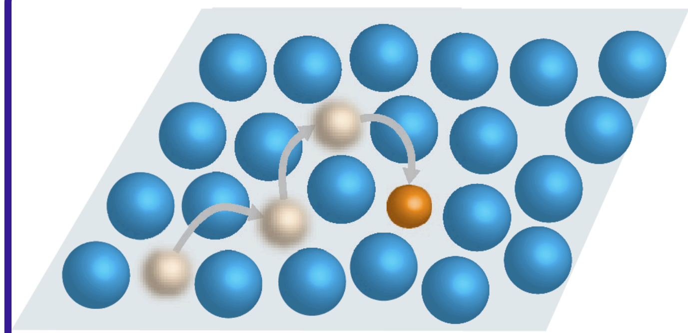
$\langle \Delta \mathbf{r}^2 \rangle \sim t^\beta$ with $\beta < 1$



"Fractal" static medium

$$\langle \mathbf{T} \rangle / N \sim r^{d_w - d_f}$$

where $d_w = 2/\beta$



"Dynamic" crowded medium

Continuous Time RW $\psi(t) \sim C/t^{1+\beta}$

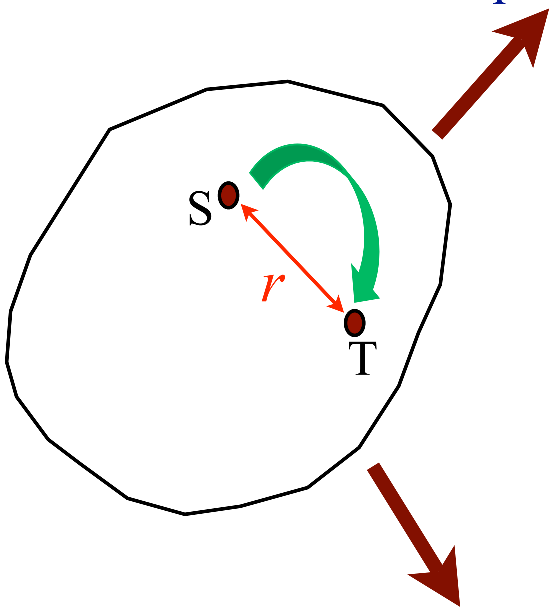
$$\text{Prob.}(\mathbf{T} = t) \sim C\langle n \rangle / t^{1+\beta}$$

where $\langle n \rangle \sim N(A - B/r) \quad (d = 3)$

Very different dependence on geometry

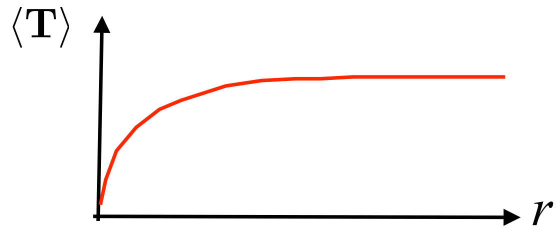
Concluding remarks: reactivity in confined media like cells?

Non-compact exploration



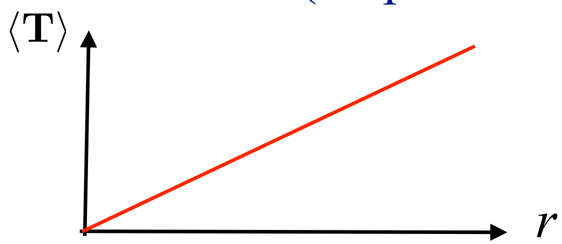
Compact exploration

Dilute medium (3d regular diffusion)



the initial position doesn't matter

Crowded medium (3d percolation cluster)



the initial position is a key parameter

⇨ **spatial organization is crucial**

Thanks

O. Benichou, M. Moreau, J. Klafter
S. Condamin, V. Tejedor, B. Meyer, C. Chevalier