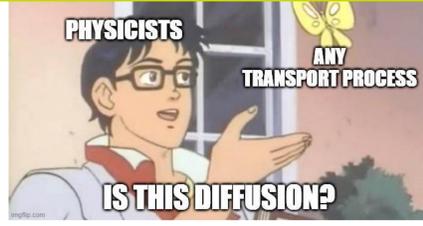
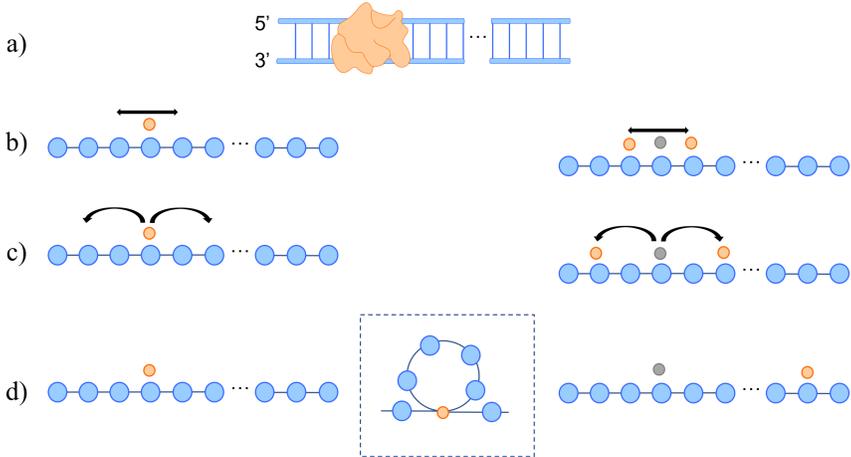


## Introduction

- Diffusion is ubiquitous in nature, but...
- Many real-world systems deviate from the predictions of the diffusion equation: **anomalous diffusion** [1].



- Example: diffusion of proteins along DNA chain [2]:
  - Subdiffusive motion: sliding (panel (b)) and hopping (panel (c)).
  - Superdiffusive motion: intersegmental transfer (panel (d))



- Need for a single equation that unifies subdiffusion and superdiffusion (in discrete space), and that takes into account the network structure.

## Definitions and setup

- Superdiffusion due to long range interactions: **d-path Laplacian graph operator**:

$$(L_d f)(v) = \sum_{w \in V: \text{dist}(v,w)=d} (f(v) - f(w))$$

- Long range interactions must decay as a power law: **Mellin-transformed d-path Laplacian** [3]:

$$\tilde{L}(s) = \sum_{d=1}^{\Delta} L_d d^{-s}$$

- Subdiffusion due to long waiting times: **Caputo time fractional derivative**:

$$D_t^\alpha f(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{f'(\tau)}{(t-\tau)^\alpha} d\tau$$

- Generalized diffusion equation (GDE)** [4]:

$$D_t^\alpha f(t) = -\tilde{L}(s) f(t)$$

- VS: standard diffusion equation:

$$\frac{\partial f(t)}{\partial t} = -L_1 f(t)$$

## Analytical predictions

- Solution of the GDE via Fourier-Laplace transforms [4].
- Determination of the diffusive regime by analyzing time scaling of two magnitudes:

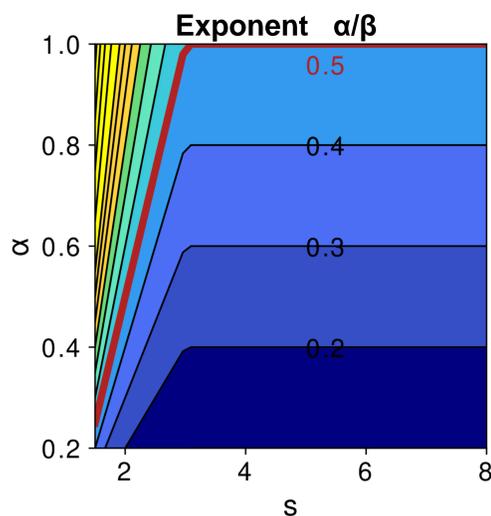
1) Height of the maximum of the pdf:  $f_{max}(t) \propto t^{-\frac{\alpha}{\beta}}$

2) Full Width at Half Maximum of pdf:  $\text{FWHM} \propto t^{\frac{\alpha}{\beta}}$

- Analytical predictions:

- Superdiffusion if  $\beta > 2\alpha$
- Subdiffusion if  $\beta < 2\alpha$
- Standard diffusion if  $\beta = 2\alpha$

with  $\beta = \begin{cases} s-1 & \text{if } 1 < s < 3, \\ 2 & \text{if } s > 3. \end{cases}$

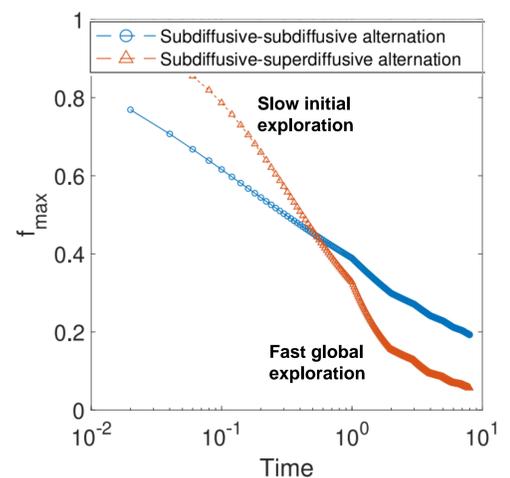
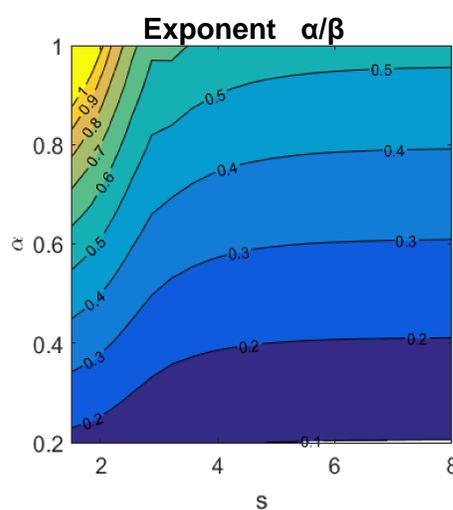


## Numerical simulations

- Numerical simulations confirm the emergence of subdiffusive and superdiffusive regimes [4].

- The GDE with time-dependent parameters accurately models the motion of transcription factors along DNA.

- The alternation of subdiffusive and superdiffusive regimes allows for a careful exploration of the DNA chain at initial times, while global exploration becomes faster for sufficiently large times.



## Conclusions

- The generalized diffusion equation (GDE) reproduces normal and anomalous (sub- and super) diffusive processes.
- Numerical simulations confirm analytical predictions.
- The motion of proteins along DNA can be captured by the GDE.
- An alternation of subdiffusion and superdiffusion allows for careful local explorations of a DNA chain with a fast global exploration.

## References

- [1] Metzler R, Klafter J. The random walk's guide to anomalous diffusion: a fractional dynamics approach. Phys Rep 20 0 0;339(1):1–77.
- [2] J. Gorman and E. C. Greene, Visualizing one-dimensional diffusion of proteins along DNA, Nature structural and molecular biology, vol. 15, no. 8, pp. 768–774, 2008.
- [3] E. Estrada, E. Hameed, N. Hatano, and M. Langer, Path Laplacian operators and superdiffusive processes on graphs. I. One-dimensional case,” Linear Algebra and its Applications, vol. 523, pp. 307–334, June 2017.
- [4] F. Diaz-Diaz and E. Estrada, “Time and space generalized diffusion equation on graph/networks,” Chaos, Solitons and Fractals, vol. 156, p. 111791, Mar. 2022.

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