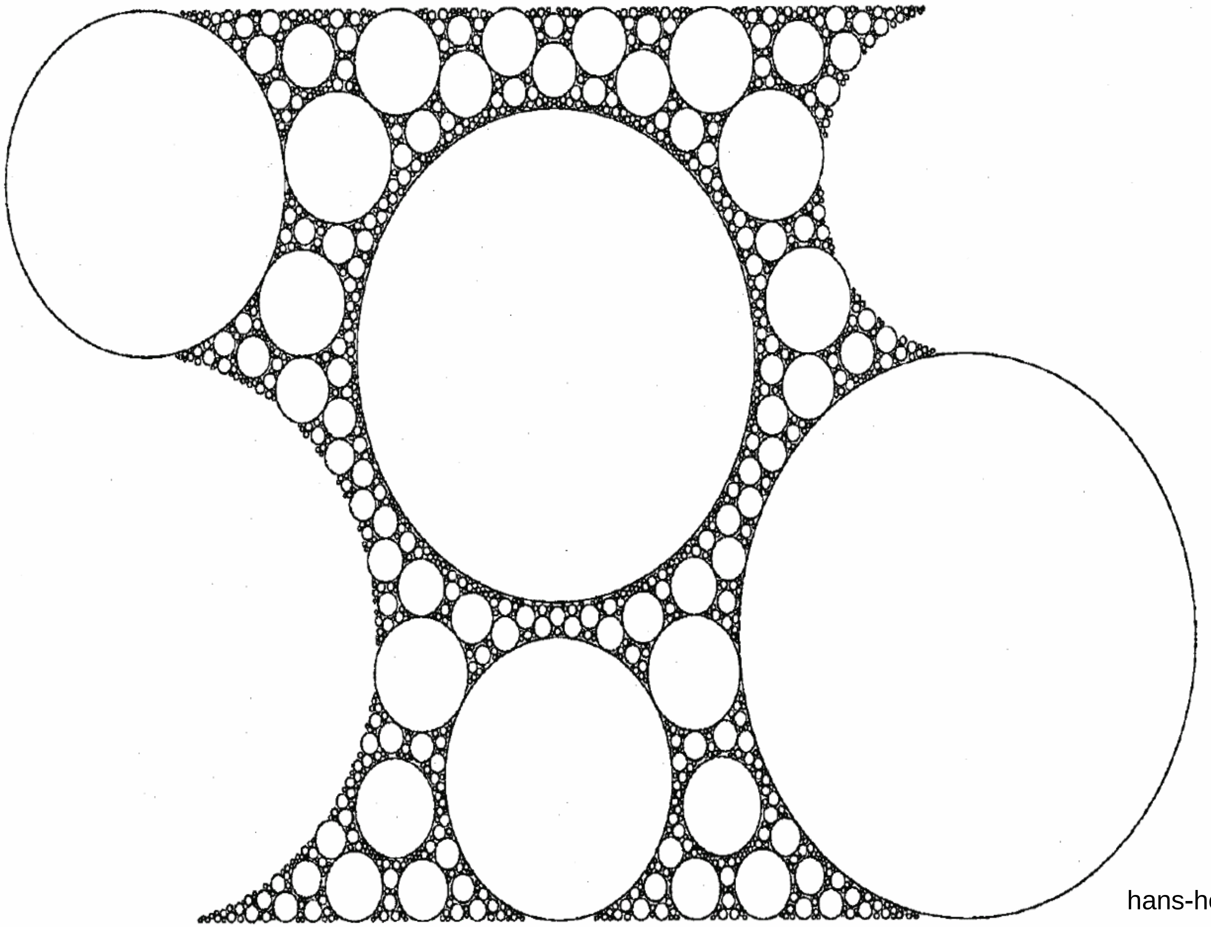
Jan Grzegorzewski

Freie Universität Berlin

Reaction-Diffusion Dynamics with Fractional Brownian Motion



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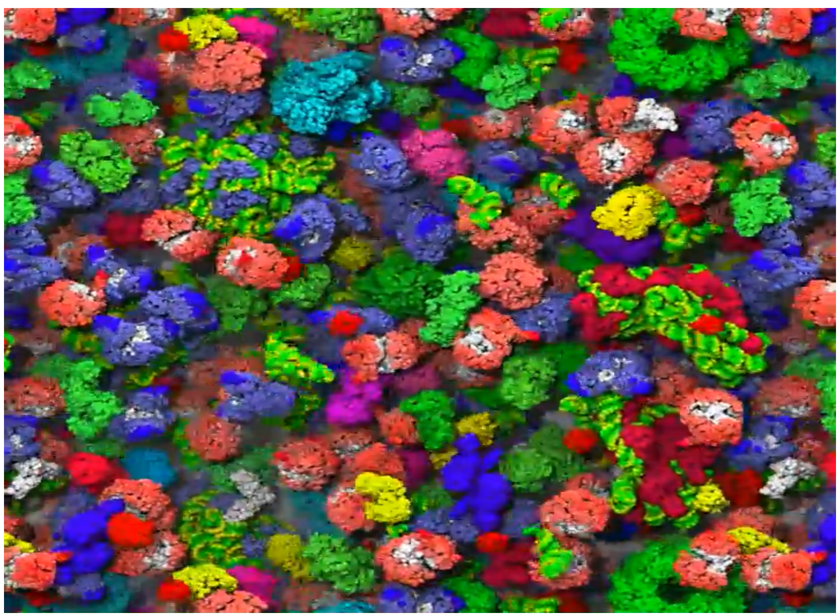
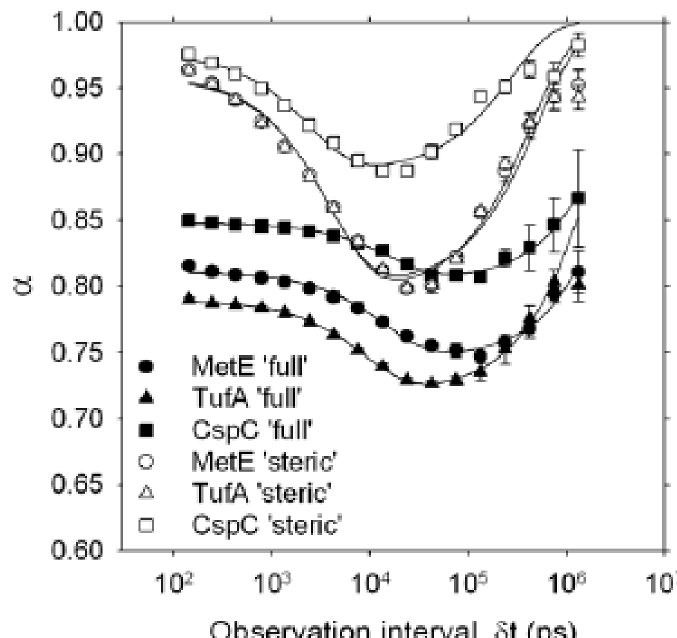
Motivation

Mean-square-displasment (MSD) for normal diffusion: $\delta r^2(t) = 2dDt$

MSD for anomalous diffusion: $\delta r^2(t) \propto t^\alpha$





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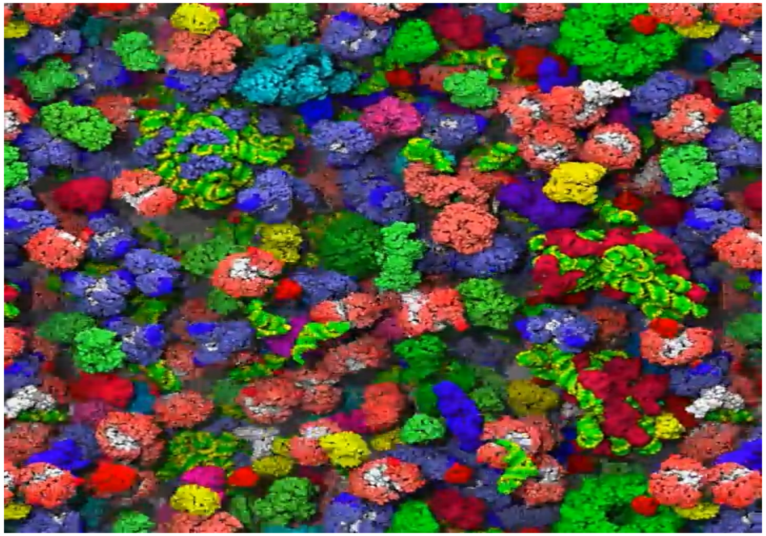

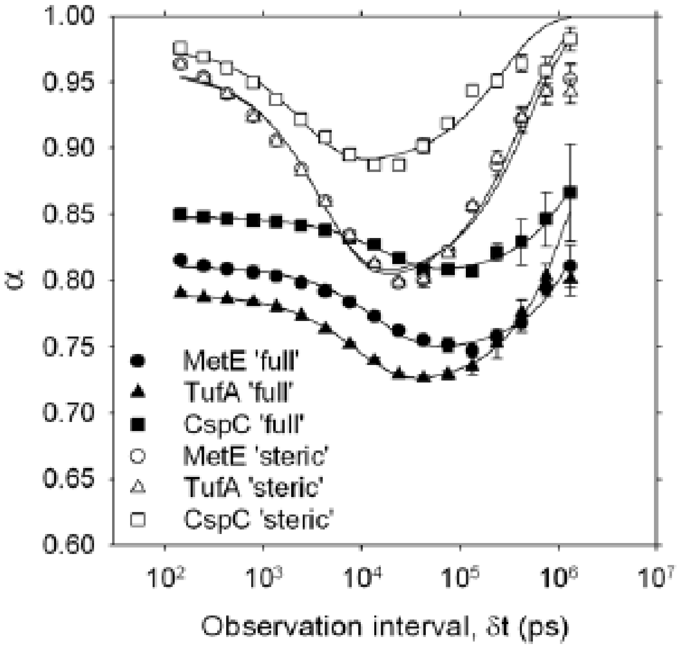

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Outline

1. Enzymatic Kinetics with Normal Diffusion

2. Fractional Brownian Motion

3. Anomalous Reaction Kinetics

Erban-Chapman Bi-molecular Reaction

Bi-molecular mechanism: $\mathrm{S} + \mathrm{E} \xrightarrow{k_+} \mathrm{ES}$

Reaction-diffusion equation: $$\frac{\partial \rho_t(r)}{\partial t} = \underbrace{-\left(\frac{\partial}{\partial_r} + \frac{2}{r}\right) j_t(r)}_{\text{diffusion}} \underbrace{- \frac{\mathrm{H}(\sigma)\lambda_+\rho_t(r)}{D}}_{\text{reaction}}$$

$\rho_t(r)$ - the distribution of substrates with distance r away from the enzyme.

$\mathrm{H}(\sigma)$ - the Heaviside step function, $j_t(r) = -D\frac{\partial \rho_t(r)}{\partial_r}$ - the flux ,

$D = D_{\mathrm{S}} + D_{\mathrm{E}}$ - the sum of diffusion constants of substrates and enzymes

σ - reaction distance

Erban-Chapman Bi-molecular Reaction

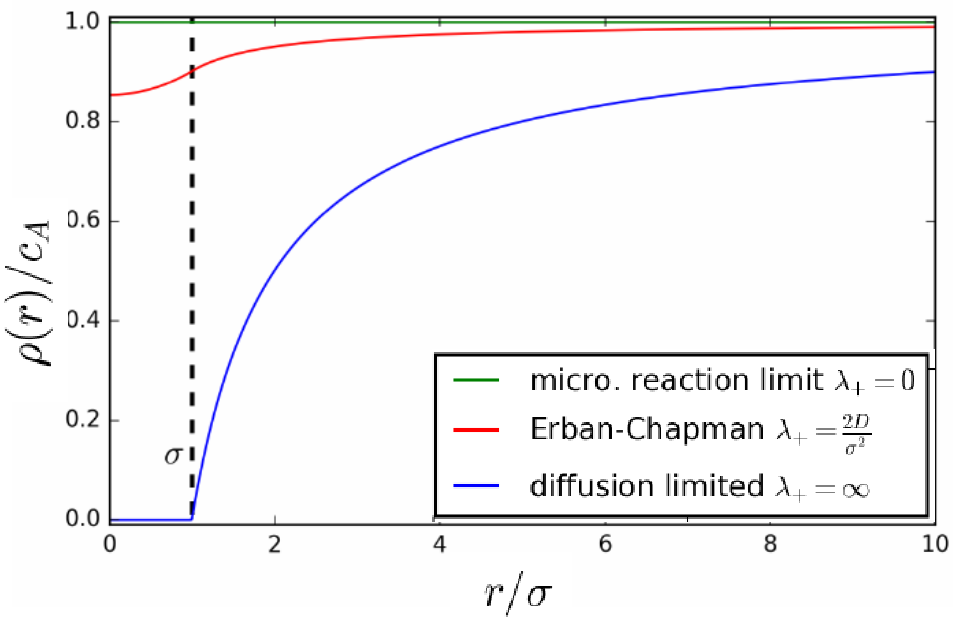
The stationary distribution $\rho^s(r)$ for a single enzyme and constant concentration of substrates at infinity: $\rho_t(r \to \infty) = c_{\mathrm{S}}$

Solution for reaction kinetics:

$$\mathrm{S} + \mathrm{E} \xrightarrow{k_+} \mathrm{ES}$$

$$\frac{dc_{\mathrm{ES}}}{dt} = -\int_{\partial V} j^s(\sigma) da \qquad \boxed{\kappa = \sqrt{\lambda_+/D}}$$

$$= c_{\mathrm{S}}\, c_{\mathrm{E}}\, \underbrace{4\pi D\sigma \left(1 - \frac{1}{\sigma\kappa} \tanh \sigma\kappa\right)}_{= k_+}$$



reaction limited by diffusion:	$k_+ = 4\pi D\sigma$

reactions limited by microscopic reaction rate:	$k_+ = \dfrac{4\pi\sigma^3\lambda_+}{3}$

Enzymatic Reactions

Michaelis-Menten mechanism: $\mathrm{S} + \mathrm{E} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \mathrm{ES} \xrightarrow{k_c} \mathrm{P} + \mathrm{E}$

$$\boxed{\begin{aligned}
\frac{dc_S(t)}{dt} &= k_- c_{ES}(t) - k_+ c_E(t) c_S(t),\\
\frac{dc_{ES}(t)}{dt} &= -k_c c_{ES}(t) - k_- c_{ES}(t) + k_+ c_E(t) c_S(t),\\
\frac{dc_P(t)}{dt} &= k_c c_{ES}(t),\\
\frac{dc_E(t)}{dt} &= k_c c_{ES}(t) + k_- c_{ES}(t) - k_- c_E(t) c_S(t),
\end{aligned}}$$

A closed solution with the quasi-steady state approximation ($dc_{ES}/dt = 0$) for $c_S(t)$:

$$\boxed{\begin{aligned}
c_S(t) &= K_M \mathrm{W}_0 \left(\frac{c_{S_0}}{K_M} \exp\left[\frac{-v_{max} t + c_{S_0}}{K_M} \right] \right),\\
c_{ES}(t) &= \frac{c_{E_0} c_S(t)}{K_M + c_S(t)} \{1 - \exp\left(-\left[K_M + c_S(t) k_+\right]\right)\},\\
c_E(t) &= c_{E_0} - c_{ES}(t),\\
c_P(t) &= c_{S_0} - c_S(t) + c_{ES}(t),
\end{aligned}}$$

with $K_M = \dfrac{k_- + k_c}{k_+}$, $v_{max} = k_c c_{E_0}$ and $W(z)$ the Lambert W function with $z = W(z) e^{W(z)}, z \in \mathbb{C}$.

Simulation Model

Two Reactions:

$$\mathrm{S} + \mathrm{E} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \mathrm{ES} \quad , \quad \mathrm{P} + \mathrm{E} \xleftarrow{k_c} \mathrm{ES}$$ with microscopic rates: $\overbrace{\boxed{\lambda_+ , \lambda_- , \lambda_c}}^{\text{parameters}}$

Units of length : σ ; Units of time: $\Gamma = \sigma^2/6D$

Length of simulation box with periodic boundary conditions: $L = 8\sigma$

Initial concentration of reactants: $c_{S_0} = 5/128\sigma^3$, $c_{E_0} = 1/512\sigma^3$, c_{P_0} =0 , c_{ES_0}=0

Enzyme position: center of simulations box   substrates positions : uniformly distributed

Diffusion constant for substrate: $D = 1\sigma^2/\Gamma$

Time step: $\Delta t = 0.05/6\Gamma$

Length of trajectory: $M = 2^{14}$

constants

Number of simulations per scenario: N > 2000

Observables

Number of substrates, enzymes, product, reactions forward:

$$N_S(t)\,,\ N_E(t),\ N_P(t)\,,\ N_{react}(t)$$

Radial distribution function of substrates around enzymes:

$$g_{S,E}(|\boldsymbol{r}|;t) = \frac{1}{N_S(t)N_E(t)} V \sum_{ij} \langle \delta(\boldsymbol{R}_{Si}(t) - \boldsymbol{R}_{Ej}(t) - \boldsymbol{r}) \rangle$$

$$g_{S,E}(r;t) = \frac{V\,dN_S(t)}{N_S(t)N_E(t)4\pi r^2 dr}$$

Macroscopic reaction rate forward:

$$k_+^{count}(t) = \frac{d\langle N_{react}(t)\rangle}{dt}\frac{1}{Vc_S(t)c_E(t)} = \frac{1}{Vc_S(t)c_E(t)}\lim_{\tau\to 0}\frac{\Delta N_{react}}{\tau}$$

One-Way Reaction

$$\mathrm{S} + \mathrm{E} \xrightarrow{k_+} \mathrm{ES} \xrightarrow{k_c} \mathrm{P} + \mathrm{E}$$

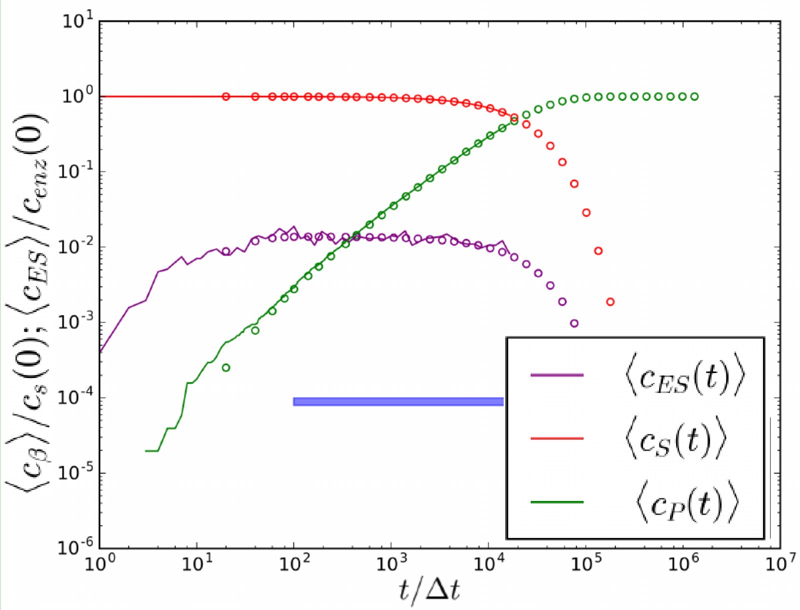
Scenarios:

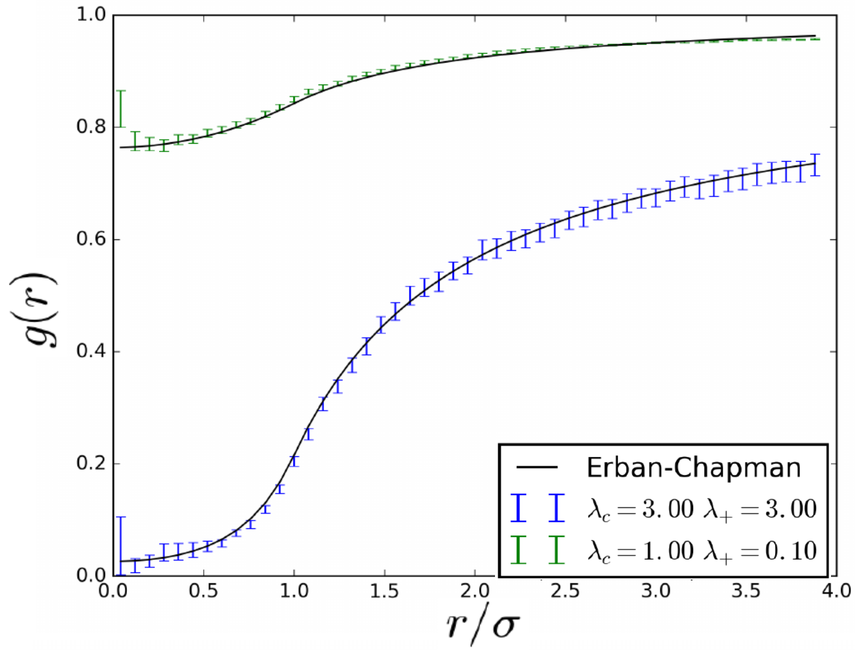
One-way "diffusion-limited" reaction:

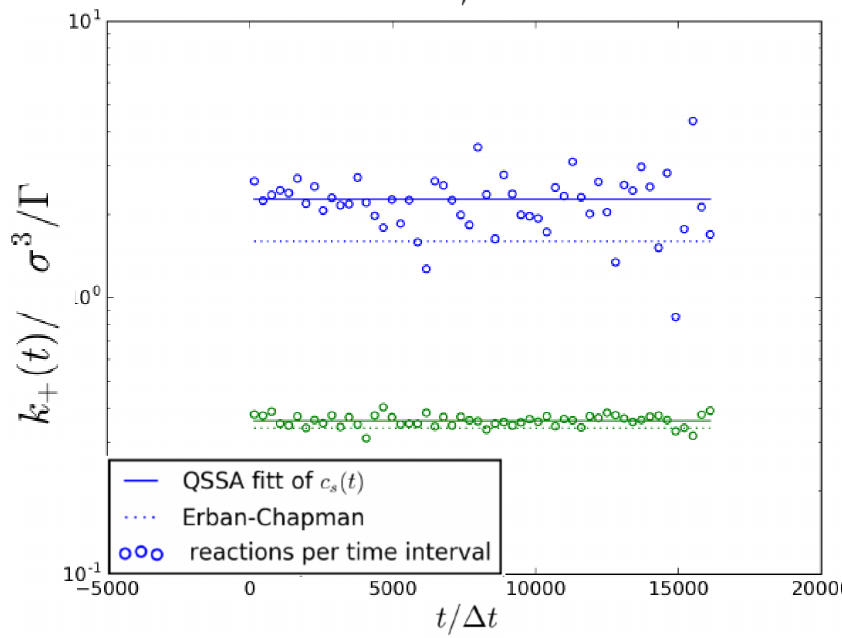
$$\lambda_+ = 3.0/\Gamma,\ \lambda_- = 0,\ \lambda_c = 3.0/\Gamma$$

One-way "Erban-Chapman" reaction:

$$\lambda_+ = 0.1/\Gamma,\ \lambda_- = 0,\ \lambda_c = 1.0/\Gamma$$



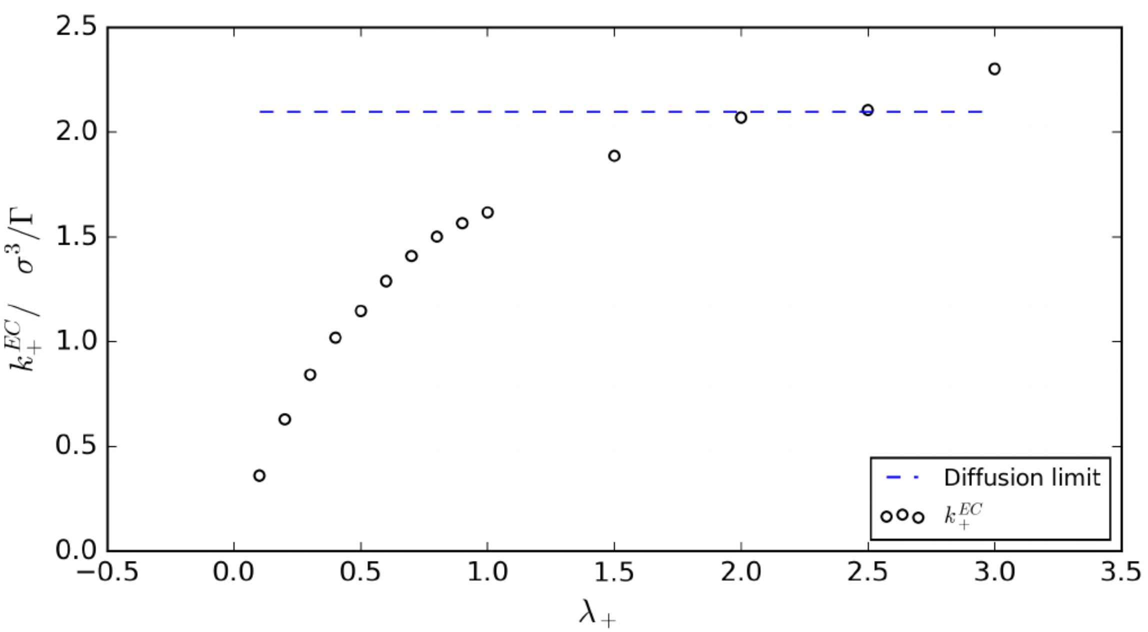




One-Way Reaction

$$\mathrm{S} + \mathrm{E} \xrightarrow{k_+} \mathrm{ES} \xrightarrow{k_c} \mathrm{P} + \mathrm{E}$$

Influence of diffusion on reaction rate: $0.1/\Gamma \leq \lambda_+ \leq 3.0/\Gamma,\ \lambda_c = 1.0/\Gamma, \quad \lambda_- = 0.$



Michaelis-Menten Mechanism

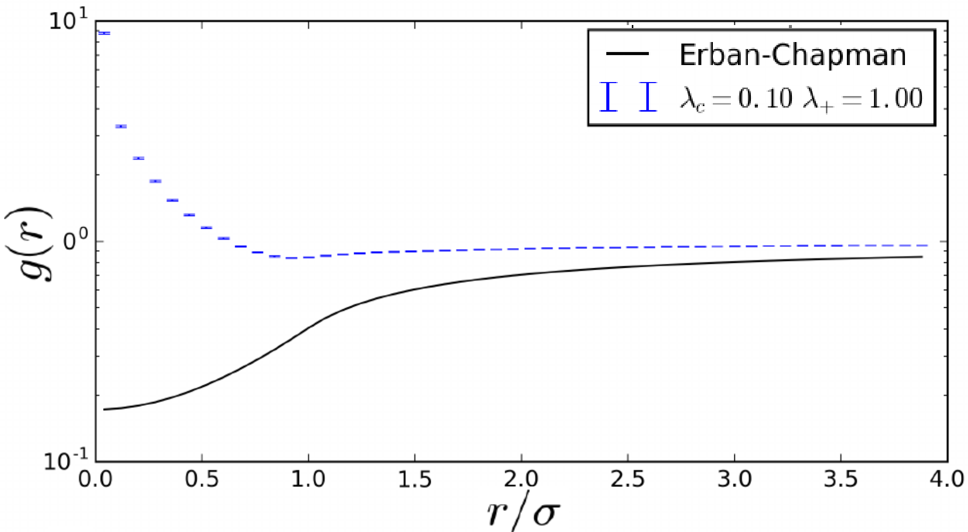
Scenarios: $\mathrm{S} + \mathrm{E} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \mathrm{ES} \xrightarrow{k_c} \mathrm{P} + \mathrm{E}$

One-way "enzyme blocking" reaction:

$$\lambda_+ = 1/\Gamma, \ \boxed{\lambda_- = 0/\Gamma}, \lambda_c = 0.1/\Gamma.$$

$$k_+^{count} = (1.67 \pm 0.02)\sigma^3/\Gamma$$

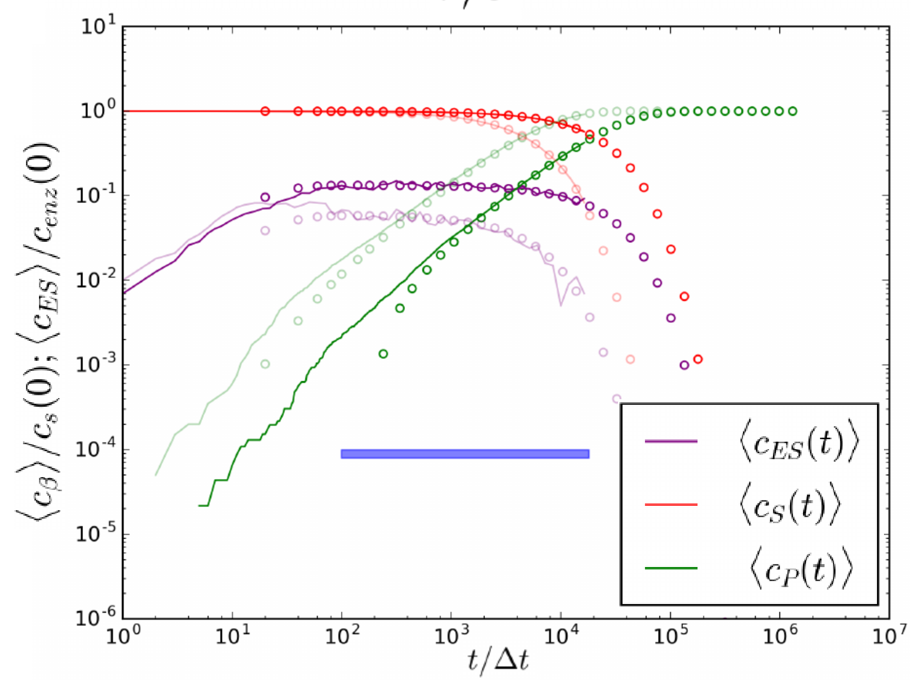
transparent



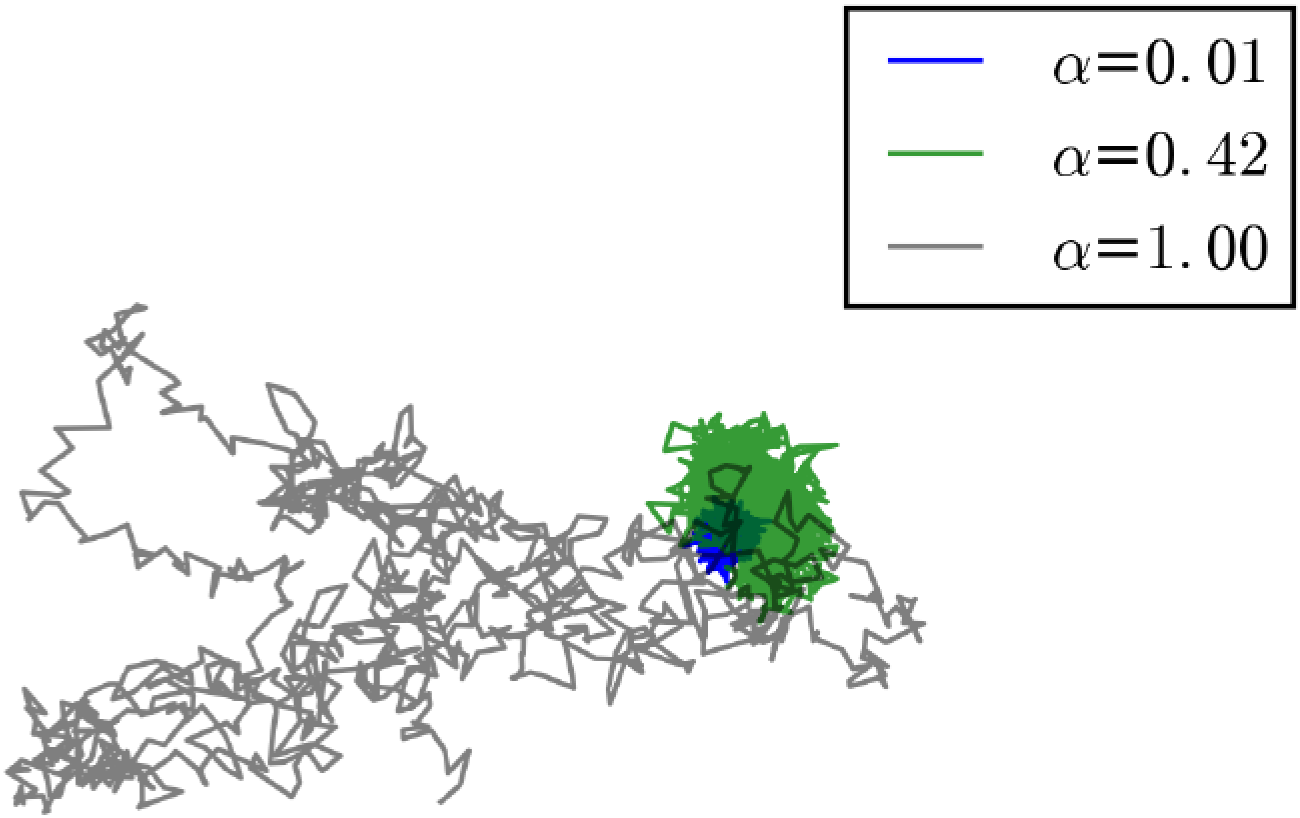
The "enzyme blocking" Michaelis-Menten:

$$\lambda_+ = 1/\Gamma, \ \boxed{\lambda_- = 1/\Gamma}, \lambda_c = 0.1/\Gamma.$$

$$k_+^{count} = (4.39 \pm 0.02)\sigma^3/\Gamma$$



2. Fractional Brownian Motion



Normal Diffusion

Central Limit Theorem:

$$Y = \frac{1}{\sqrt{N}} \sum_{j=1}^{N} X_j$$

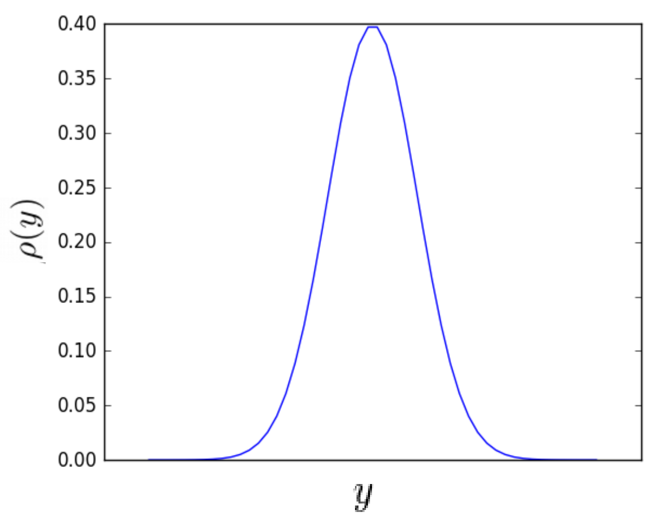
$$\rho(y)dy = \mathrm{P}(y < Y < y + dy)$$

Here, X_j independent and identically distributed (i.i.d.) random variable with $\langle X_j \rangle = 0$ and $\langle X_j^2 \rangle = \sigma^2$

Gaussian distribution:

$$\rho(y) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{y^2}{2\sigma^2}\right)$$

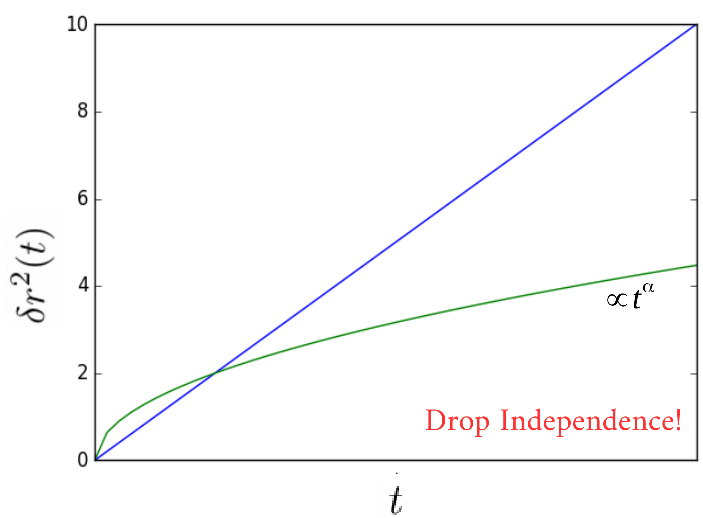
=> Wiener process



Normal diffusion:

$$\frac{\partial c(r,t)}{\partial t} = D \nabla^2 c(r,t)$$

$$\delta r^2(t) = \sigma^2 t = 2dDt$$



Assumption: i.i.d. random variables , $-J(r,t) = \nabla c(r,t)$ and continuity equation $\partial_t c(r,t) + \nabla c(r,t) = 0$

Fractional Brownian Motion and Fractional Gaussian Noise

Fractional Brownian motion is a stochastic process. It is fully specified by its mean : $\langle B_t \rangle = 0$

and covariance function: $\mathrm{Cov}[B_t^\alpha, B_s^\alpha] = \frac{\sigma^2}{2}[t^\alpha - 2(s-t)^\alpha + s^\alpha]$ for $t < s$

Power-law behavior of MSD: $\langle (B_t^\alpha - B_s^\alpha)^2 \rangle = (s-t)^\alpha \sigma^2$

Fractional Gaussian noise is a relate stationary stochastic process: $B_t^\alpha = \sum_{n=0}^{k} X_{tn}^\alpha$ with $t_n = t_0 + n\Delta t$

Its mean: $\langle X_t^\alpha \rangle = 0$

Its auto-covariace function: $\mathrm{Cov}[X_0^\alpha, X_n^\alpha] = \frac{\Delta t^\alpha \sigma^2}{2}[(n-1)^\alpha - 2n^\alpha + (n+1)^\alpha]$

Connection to the physical world: $\sigma^2 = 2dK_\alpha$

Here, $K_\alpha > 0$ is the generalized diffusion coefficient of physical dimension $\mathrm{cm}^2/\mathrm{sec}^\alpha$.

Davis-Harte Algorithm

1. Compute the auto-covariance function R_n^ξ of a periodic stochastic process ξ_n:

$$R_n^\xi = \begin{cases} K_\alpha \Delta t^\alpha \left[(n-1)^\alpha - 2n^\alpha + (n+1)^\alpha\right] & \text{for } 0 \leq n \leq M \\ R_{2M-n}^\xi & \text{for } M \leq n \leq 2M \end{cases} \tag{1.52}$$

2. Transform the auto-covariance function via FFT. The result is called the spectral density of the stochastic process ξ_n:

$$S_k^\xi = \mathrm{FFT}(R_n^\xi; k) \tag{1.53}$$

3. Calculate $\tilde{\xi}_k$ the Fourier transform of the stochastic process ξ_n:

$$\tilde{\xi}_k = \begin{cases} \sqrt{2S_k^\xi M}(\eta_k) & \text{for } k = 0 \\ \sqrt{S_k^\xi M}(\eta_k + i\eta_k) & \text{for } 0 \leq k \leq M \\ \sqrt{2S_k^\xi M}(\eta_k) & \text{for } k = M \\ \tilde{\xi}_{2M-k}^* & \text{for } M \leq k \leq 2M \end{cases} \tag{1.54}$$

{$*$} denotes the complex conjugate, η_k is a random Gaussian variable with zero mean and variance 1 [$\eta_k \sim \mathcal{N}(0,1)$].

4. Perform the inverse Fourier transform on $\tilde{\xi}_k$ and use the first half of the resulting stochastic process ξ_n:

$$\xi_n = \frac{1}{\sqrt{2M}} \mathrm{FFT}^{-1}(\tilde{\xi}_k; n) \qquad \text{for} \quad 0 \leq n \leq N \tag{1.55}$$

5. perform the cumulative sum on the increments:

$$B_n^\alpha = \sum_{j=0}^{n} \xi_j \qquad \text{for} \quad 0 \leq n \leq M \tag{1.56}$$

Idea: Artificial modification of the power spectrum of a Wiener process to obtain the power spectrum of fractional Brownian noise.

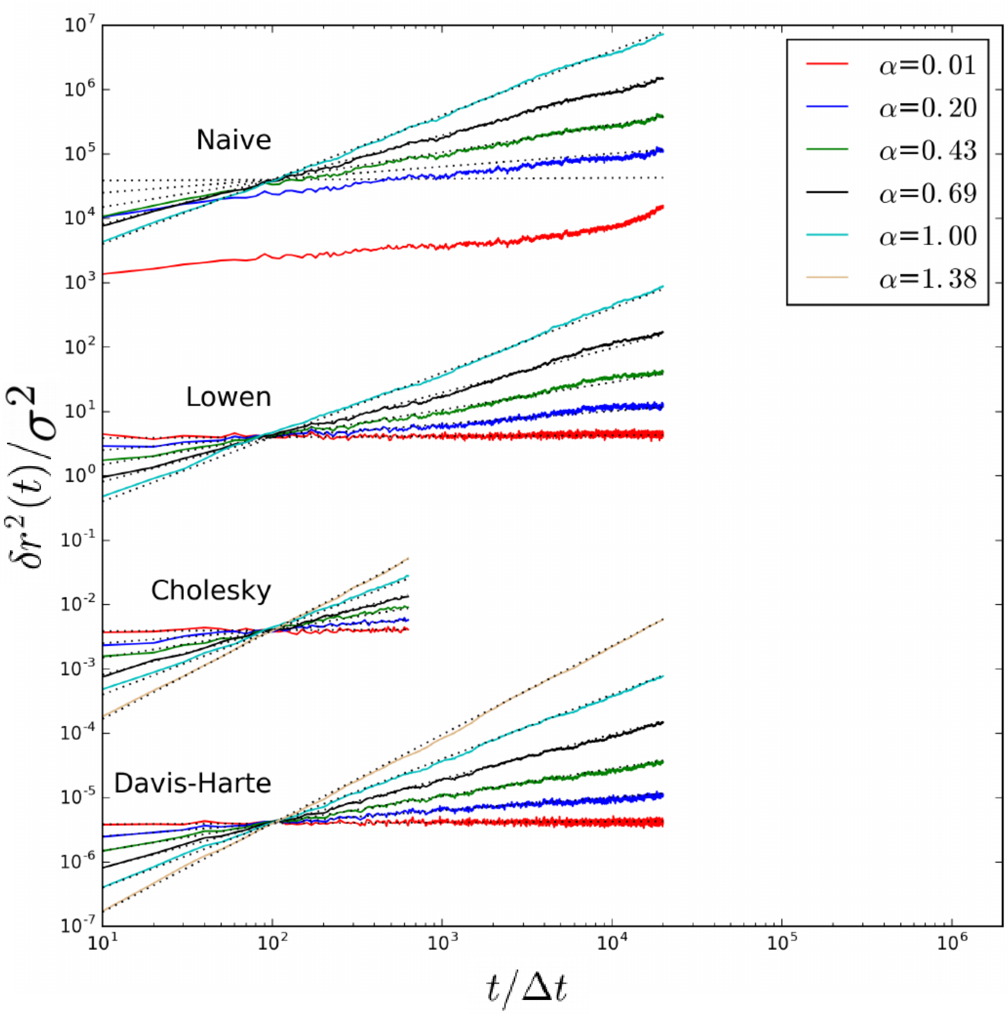
Wiener-Khinchin theorem:
A wide-sense-stationary random process has a spectral decomposition given by the power spectrum of that process.

Power spectrum density:

$$S(\omega) = \int_{-\infty}^{\infty} \mathrm{Cov}[X_t, X_0] \exp[-2\pi i \omega t] dt$$

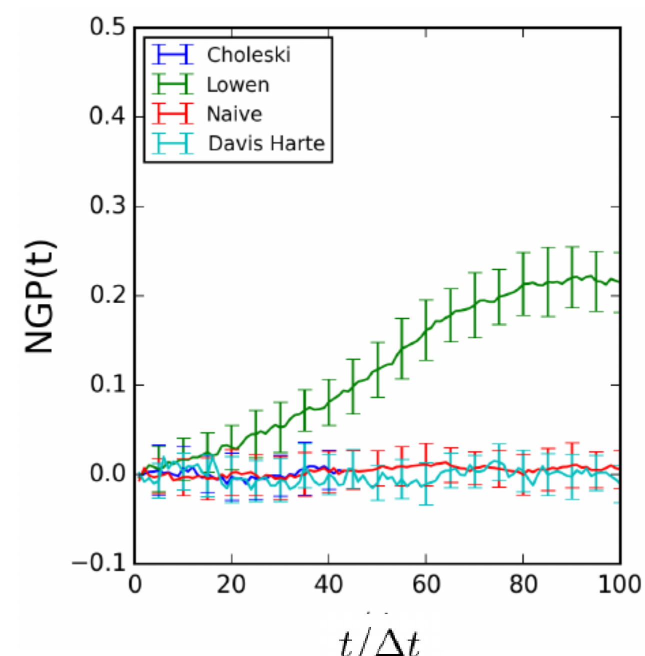
Algorithm Accuracy

Mean Square Displacement:



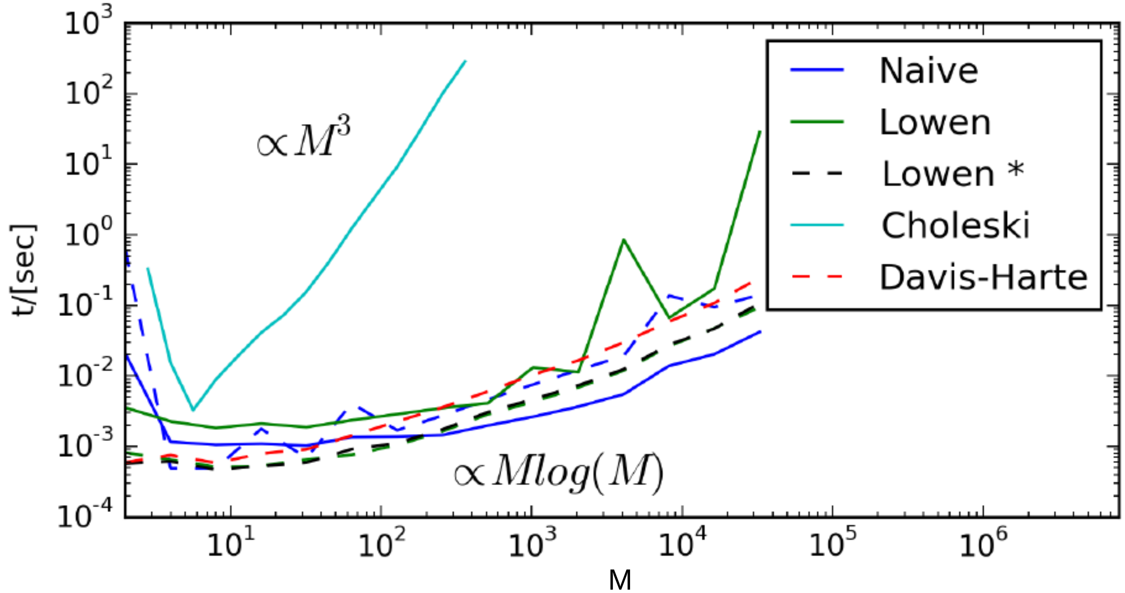
Non-Gaussian parameter:

$$\mathrm{NGP}(t) = \frac{d\delta r^4(t)}{(d+2)[\delta r^2(t)]} - 1$$



Algorithm Performance

Algorithmic scaling of computational time with the trajectory length:



Davis-Harte algorithm implemented in RevReaDDy

3. Anomalous Reaction Kinetics

Scenarios: $\mathrm{S} + \mathrm{E} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \mathrm{ES} \xrightarrow{k_c} \mathrm{P} + \mathrm{E}$

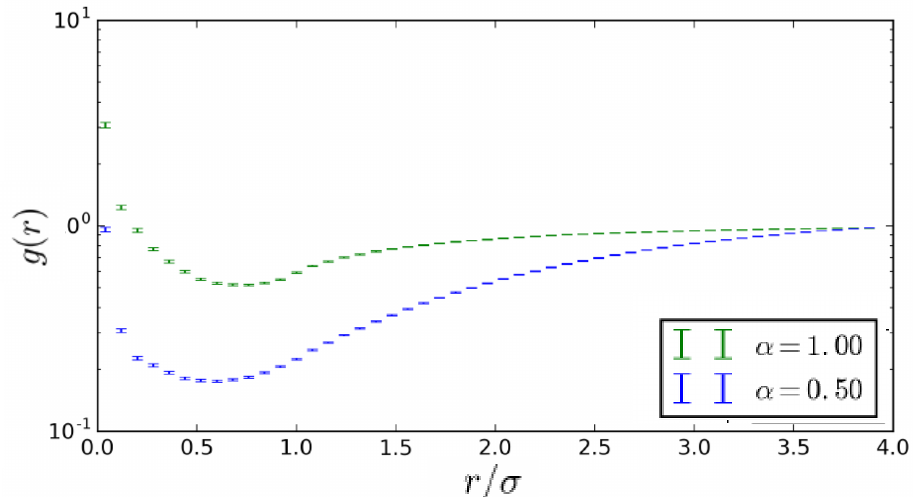
Michaelis-Menten with normal diffusion:

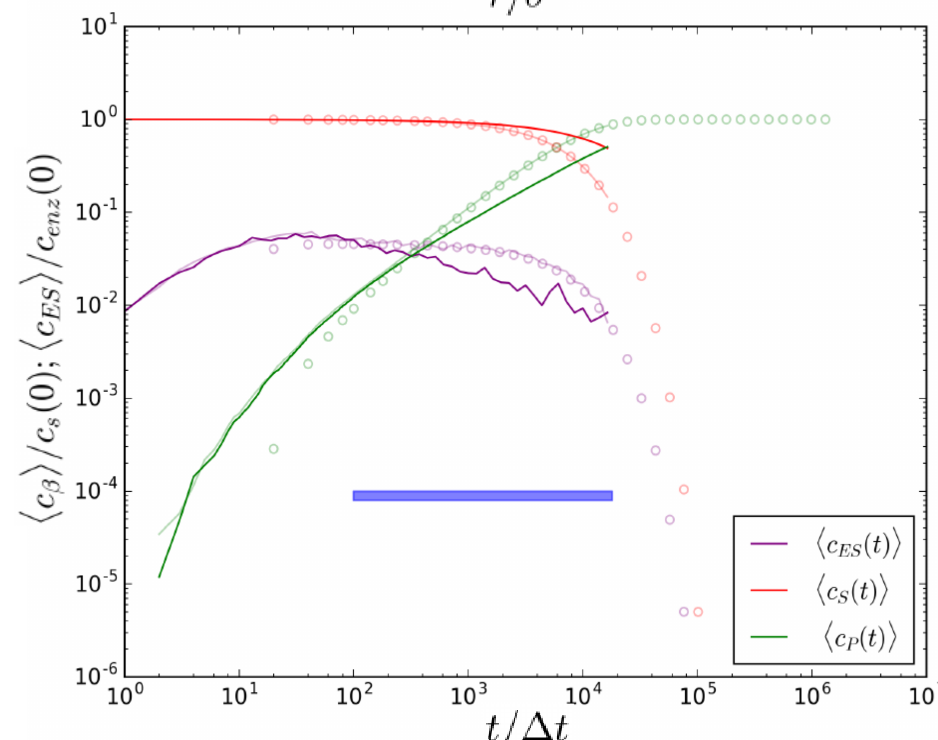
$\lambda_+ = 1/\Gamma, \quad \lambda_- = 1/\Gamma, \lambda_c = 0.1/\Gamma, \quad \boxed{\alpha = 1.0}$

transparent

Michaelis-Menten with fBm:

$\lambda_+ = 1 \quad , \quad \lambda_- = 1/\Gamma, \lambda_c = 0.1/\Gamma, \quad \boxed{\alpha = 0.5}$





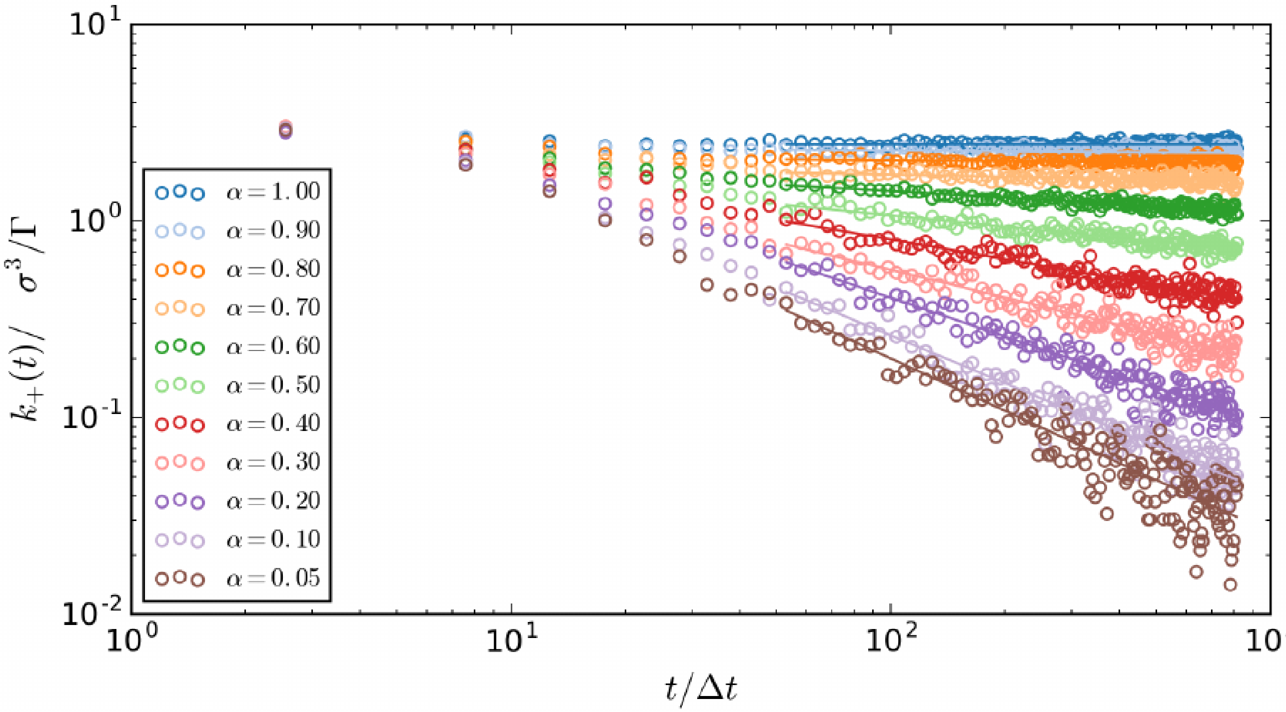
3. Fractional Reaction Kinetics

Time-dependent reaction rate: $k(t) = k_0 t^{-h}$ for $0 \leq h \leq 1$ and $t \geq 1,$

Here, h is fractional kinetics exponent.

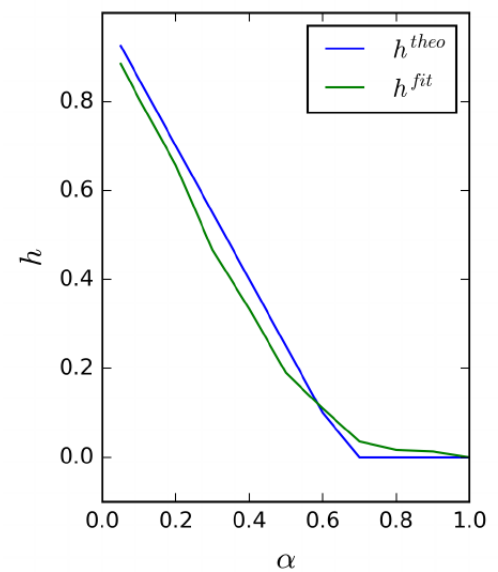
Michaelis-Menten with fBm:

$\lambda_+ = 1.0/\Gamma,\ \lambda_- = 1.0/\Gamma,\ \lambda_c = 1.0/\Gamma$ $\boxed{0.05 \leq \alpha \leq 1.0}$



Theory for percolation cluster

$$h = 1 - \frac{3\alpha}{2} \quad \text{for} \quad 0 < \alpha < 2/3$$
$$h = 0 \quad \text{for} \quad 2/3 < \alpha < 1$$



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