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A diffusion process in a medium with a thin layer seen as semi-permeable barrier

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Abstract

We construct a Brownian motion in a medium with a semi-permeable barrier. For this, we paste in a suitable way two elastic Brownian motions. This process is the limit of a diffusion process moving in a media with a thin layer of low diffusivity. A simulation algorithm is then given. The mean residence time in cells surrounded by such semi-permeable barriers is computed. Provided as a benchmark test, this problem is a simplified form of a real-life problem coming from brain imaging techniques. We also refine the ways to compute the exponential decaying rate from the distribution function of some random variables estimated through Monte Carlo techniques.

Keywords: elastic Brownian motion, thin layer problem, estimation of the mean-residence time, Monte Carlo methods, homogenization.

1 Introduction

Understanding the dynamic of a diffusive process in a medium with interfaces is of great importance both for modelling and simulations. An interface could be a permeable or a semi-permeable barrier, which arise as a limit for a sharp changes in the properties of the underlying materials. In geophysics, sudden changes of the diffusivity of the material give rise to such effect, just to cite one among the many possible domains of applications (See references in [11]).

A rather similar problem related to a media with a “thin layer” seen after some change of scale as a semi-permeable barrier. By a thin layer, we mean a layer of small width and a low diffusivity that the particle has difficulties to pass through. The membrane surrounding living cells is an example of such layer. Understanding the diffusive behavior of particles is of great importance for performing *diffusion Magnetic Resonance Imaging*, a brain imaging technique in which the mean square displacement of particles of water is recorded [6].

First, we give a brief presentation of some results found in [9], where a one-dimensional stochastic process describes the behavior of the particles close to such an interface. Therefore, we show it is the limit of the thin layer problem using a mixture of analytic and probabilistic arguments, so that the interpretation is very natural. This process is constructed by pasting a positively and a negatively reflected elastic Brownian motion. On the PDE side, this condition

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at interface is characterized by a continuous flow, while the solution itself is discontinuous with a jump proportional to the flow. This interface condition does not fall in the classical problem of pasting two one-dimensional diffusions on a single diffusion on \mathbb{R} , which was solved by W. Feller and others [7]. Actually, this diffusion is best seen as a kind of switching process.

In a second time, we present some Monte Carlo simulations for computing the mean residence time in an array of cells arranged periodically. Being related to the rate of convergence toward the steady state, this macroscopic parameter is of first importance for setting up simplified models relying on effective coefficients (See *e.g.* [3, 13]). This test is a benchmark, as the result could be compared to the eigenvalue of some Sturm-Liouville problem. The result shows that the method is effective unless the strength of the membrane is too strong. This means that from a Monte Carlo methodology, we have to use techniques related to rare events simulations instead. A full account of the simulations are given in [8].

In Appendix A, we also present an improved version of estimation technique to estimate a first eigenvalue of the underlying elliptic equation from Monte Carlo simulations, completing the work [10].

2 The Snapping Out Brownian motion

In this article, we derive a probabilistic representation for a diffusion in a media with a semi-permeable barrier seen as the limit of a thin layer problem.

In a one-dimensional media, this stochastic process cannot be a diffusion on the whole line¹, but a diffusion on the graph $\mathbb{G} = (-\infty, 0-) \cup (0+, +\infty)$ with two vertices and no common edge. Any function f on \mathbb{R} is naturally identified with a function of \mathbb{G} by setting $f(0+) = f(0-) = f(0)$. However, \mathbb{G} is not a metric graph, and the distance between $0+$ and $0-$ are at “infinite distance”.

2.1 An heuristic for the thin layer problem

For some parameters $\kappa > 0$ and $\epsilon > 0$, let us consider the one-dimensional, continuous Feller process X^ϵ with state-space \mathbb{R} with speed measure $M(x) = x$ and scale function S_ϵ with derivative

$$S'_\epsilon(x) = s_\epsilon(x) = \begin{cases} 1 & \text{if } x \notin [-\epsilon, \epsilon], \\ 1/\kappa\epsilon & \text{if } x \in [-\epsilon, \epsilon]. \end{cases}$$

Away from $[-\epsilon, \epsilon]$, the process X behaves like the Brownian motion. Using the Feller theory (See *e.g.* [2, Chap. 16]), its infinitesimal generator is $A^{X^\epsilon} = \frac{1}{2}D_M D_S = \frac{1}{2} \frac{d}{dx} \left(s_\epsilon^{-1} \frac{d}{dx} \right)$.

For a one-to-one function $\phi : \mathbb{R} \rightarrow \mathbb{R}$, set $\phi_* f = f \circ \phi^{-1}$ for any continuous function. Let us define Φ_ϵ by

$$\Phi'_\epsilon(x) = \phi_\epsilon(x) = \sqrt{s_\epsilon(x)} = \begin{cases} 1 & \text{if } x \notin [-\epsilon, \epsilon], \\ 1/\sqrt{\kappa\epsilon} & \text{if } x \in (-\epsilon, \epsilon). \end{cases}$$

The infinitesimal generator of $Y^\epsilon = \Phi_\epsilon(X^\epsilon)$ is $A^{Y^\epsilon} = \frac{1}{2}D_{(\Phi_\epsilon)_*M} D_{(\Phi_\epsilon)_*S}$ so that for a function f in the domain $\text{Dom}(A^{Y^\epsilon})$,

$$A^{Y^\epsilon} f(x) = \frac{\phi_\epsilon(x)}{2} \frac{d}{dx} \left(\frac{1}{\phi_\epsilon(x)} \frac{df(x)}{dx} \right) \text{ for } x \neq x_\epsilon \text{ with } x_\epsilon = \frac{\sqrt{\epsilon}}{\sqrt{\kappa}}.$$

Since $(\Phi_\epsilon)_*S$ is the scale function of Y^ϵ ,

$$\mathbb{P}_{x_\epsilon}[\tau_0 < \tau_{2x_\epsilon}] = \frac{x_\epsilon}{x_\epsilon(1 + 1/\sqrt{\kappa\epsilon})} = \frac{\sqrt{\kappa\epsilon}}{1 + \sqrt{\kappa\epsilon}} \sim_{\epsilon \rightarrow 0} \sqrt{\kappa\epsilon}. \quad (1)$$

¹This contradicts the possible conditions for knotting two diffusions together, see *e.g.* [7].

The excursions above and below x_ϵ of Y^ϵ are the same as the ones of the Brownian motion. Using the excursions' theory, the starting time of an excursion of Y^ϵ away from x_ϵ has an height higher than x_ϵ at the smallest time t at which $L_t^{x_\epsilon}(Y^\epsilon) \geq \xi$ with $\xi \sim \exp(1/x_\epsilon)$. Combining both results, the first hitting time τ_0^ϵ of 0 satisfies the relationship

$$L_{\tau_0^\epsilon}^{x_\epsilon}(Y^\epsilon) \geq \zeta_\epsilon \text{ with } \zeta_\epsilon \sim \exp\left(\frac{1 + \sqrt{\kappa\epsilon}}{\sqrt{\kappa\epsilon}} \times \frac{\sqrt{\epsilon}}{\sqrt{\kappa}}\right).$$

The parameter of the exponential random variable ζ_ϵ converges to $1/\kappa$ as $\epsilon \rightarrow 0$. This means that the process X^ϵ hits 0 shortly after then time t at which $L_t^{x_\epsilon}(X^\epsilon) \geq \zeta_\epsilon$ where the mean of ζ_ϵ is roughly κ , whatever ϵ .

With the Markov property, once at 0, Y^ϵ will reach $\pm x_\epsilon$ with probability $1/2$. Once at $\pm x_\epsilon$, we could start again the same construction.

2.2 Letting an Elastic Brownian motion rebirth

The *elastic Brownian motion* is a positively or negatively reflected Brownian motion B which is killed once its local time $L_t^0(B)$ at 0 is greater than an independent exponential random variable ξ of parameter κ (See e.g. [5]). Its resolvent is for $f \in \mathcal{C}_b(\mathbb{G}, \mathbb{R})$

$$R_\alpha f(x) = \mathbb{E}_x \left[\int_0^{+\infty} \exp(-\kappa L_t^0(B)) f(\text{sgn}(x)|B_t|) ds \right].$$

For any $f \in \mathcal{C}_b(\mathbb{G}, \mathbb{R})$, $R_\alpha f$ is solution to

$$\left(\alpha - \frac{1}{2}\Delta\right)R_\alpha f(x) = f(x), \quad x \neq 0 \text{ with } D_x R_\alpha f(0\pm) = \pm \kappa R_\alpha f(0\pm).$$

Here, we wrote a single equation on \mathbb{G} , but the sign of the elastic Brownian motion never changes. The last equation contains two uncoupled equations, one on \mathbb{R}_- and the other on \mathbb{R}_+ .

The heuristic of Section 2.1 suggests that the limit X of $(X^\epsilon)_{\epsilon>0}$ is a process living in \mathbb{G} and constructed by the following manner:

1. When starting from $x \in \mathbb{G}$, X behaves like a (positively or negatively) reflected elastic Brownian motion, which is killed when $L_t^{0\pm}(X) \geq \zeta$ with $\zeta \sim \exp(1/\kappa)$.
2. Once killed, it is rebirth at ± 0 with probability $1/2$, using the ‘‘piecing out’’ procedure from N. Ikeda, M. Nagasawa and S. Watanabe [4]. It then follow again the dynamic given in Step 1.

Theorem 1 ([9]). *There exists a strong Markov process X on \mathbb{G} with jumps only at $0\pm$ that follows the above dynamics. This process is called a snapping out Brownian motion (SNOB). When f is a bounded, continuous function,*

$$\mathbb{E}_x[f(X_t)] = \mathbb{E}_x \left[\frac{1 + e^{-\kappa L_t^0(B)}}{2} f(|B_t|) \right] + \mathbb{E}_x \left[\frac{1 - e^{-\kappa L_t^0(B)}}{2} f(-|B_t|) \right] \text{ for } x \geq 0, \quad (2)$$

where B is a Brownian motion and $L_t^0(B)$ its symmetric local time at 0.

Let us consider the resolvent operator for $\alpha > 0$,

$$G_\alpha f(x) = \mathbb{E}_x \left[\int_0^{+\infty} e^{-\alpha t} f(X_t) dt \right], \quad x \in \mathbb{G}.$$

The infinitesimal generator A of X is characterized by $(G_\alpha)_{\alpha>0}$. In particular, its domain is the image of the space of continuous and bounded functions by G_α .

Proposition 1 ([9]). For any $f \in \mathcal{C}_b(\mathbb{G}, \mathbb{R})$, $G_\alpha f$ is of class $\mathcal{C}_b^2(\mathbb{G}, \mathbb{R})$ and satisfies:

$$\alpha G_\alpha f(x) - \frac{1}{2} \Delta G_\alpha f(x) = f(x) \text{ for } x \neq 0, \quad (3)$$

$$D_x G_\alpha f(0+) = D_x G_\alpha f(0-) \quad (4)$$

$$\text{and } \kappa(G_\alpha f(0+) - G_\alpha f(0-)) = 2D_x G_\alpha f(0). \quad (5)$$

3 Convergence of the thin layer problem

Proposition 2. Let $(G_\alpha(\epsilon))_{\alpha>0}$ be the resolvent of $\frac{1}{2}D_x D_{S_\epsilon}$ and f be a bounded, continuous functions. We identify $G_\alpha(\epsilon)f$ with a function on \mathbb{G} . Then $G_\alpha(\epsilon)f$ converges locally uniformly to $G_\alpha f$ on \mathbb{G} for any $\alpha > 0$.

Remark 1. The interface condition is deduced from a limiting argument. Using the above construction from the Elastic Brownian motion and playing with symmetries, one could also characterize the resolvent. Yet the proof we give could be generalized to a more general class of diffusions. Eqs. (3)-(5) characterize the infinitesimal generator of X as well as its domain.

3.1 Simulation

Formula (2) for the semi-group of the SNOB involves the Brownian motion and its local time. Actually, the couple $(L_t^0(B), |B_t|)$ is easily simulated by using the algorithm proposed by D. Lépingle in [12]. Using (2), it is easy to simulate the SNOB starting from 0_\pm . In addition, since the SNOB behaves like a Brownian motion until it reaches 0, a Brownian bridge technique [1, 11] and an explicit formula for the first exit time of the BM allows one to simulate exactly the SNOB until it reaches 0. A complete algorithm is given in [8, 9].

In presence of multiple interfaces, one could simulate the process locally around each interface as a SNOB, since the probability of crossing an interface “far enough” is exponentially small and could then be neglected (See the discussion in [11]).

4 A computational example: estimation of a mean residence time in cells

Diffusion magnetic resonance imaging (dMRI) is a brain imaging technique. Using a magnetization scheme, it records the mean square displacement of water molecules with a diffusive behavior. In the tissue, cells are surrounded by membranes which are commonly modelled as a thin layer. Reconstructing the brain activity is done by estimating the diffusion coefficient through an inverse problem, solved through a direct problem (See *e.g.* [6]).

We test our simulation scheme on a simple situation and is compared to the numerical, deterministic estimation of an eigenvalue problem.

The *mean residence time* in the cells is an important macroscopic parameter related to the rate of convergence toward equilibrium. It could serves as an input for simplified, homogenized models (See *e.g.* [3, 13]).

Our test case is the following: we consider a cell surrounded by two thin membranes in a periodic media. The diffusivity D_{intra} in the cell is the same as the diffusivity D_{extra} outside the cell. In the thin membrane, of width 2ϵ , the diffusivity is $D_{\text{memb}} = \mu\epsilon$.

The infinitesimal generator of X is $A = \frac{1}{2}\nabla(D\nabla\cdot)$ with $D(x) = D_{\text{intra}}$ or $D(x) = D_{\text{memb}}$ according to the position of x inside or outside the membrane. At each membrane at position y , the thin

layer approximation means that any solution to $Au = f$ with f continuous satisfies

$$\mu(u(y+) - u(y-)) = D_{\text{intra}} D_x u(y\pm).$$

The mean residence time θ is defined as the rate of convergence toward a constant value of $\mathbb{P}[X_t \in C]$, where $C = L_{\text{period}}\mathbb{Z} + [a, b]$ where $[a, b]$ is an interval of $[0, 1]$ with membranes at a and b . The period of the media is L_{period} and the cell size is $L_{\text{intra}} = b - a$.

Let \mathcal{A} be the infinitesimal generator of X . Two cases are considered:

- (a) the membrane has width 2ϵ and diffusivity $D_{\text{intra}} = 2\epsilon\mu$;
- (b) the membrane has width 0 and is a semi-permeable membrane of strength μ . As seen, this is the homogenized situation of (a) as $\epsilon \rightarrow 0$.

To perform the simulation, we simulate the process $Y_t = X_t/\sqrt{2D_{\text{intra}}}$. Thus, this process Y has diffusivity 1 outside and inside the cell. At each membrane, Y acts like a SNOB with parameter $\kappa = 2\sqrt{2}\mu/\sqrt{D_{\text{intra}}}$.

In both cases, let λ be the smallest positive eigenvalue of

$$\mathcal{A}\phi(x) = -\lambda\phi(x).$$

This eigenvalue has multiplicity one. Its associated eigenfunction ϕ is positive. From standard results on self-adjoint operators,

$$p(t, x, y) = \frac{1}{L_{\text{period}}} + \phi(x)\phi(y)\exp(-\lambda t) + o(\exp(-\lambda t))$$

where ϕ is normalized to that $\int_0^{L_{\text{period}}} \phi(x)^2 dx = 1$. Then for $K(x) = \phi(x) \int_0^{L_{\text{period}}} \phi(y) dy$,

$$p(t) = \mathbb{P}_x[X_t \in \text{cell}] = \frac{L_{\text{intra}}}{L_{\text{period}}} + K(x)\exp(-\lambda t) + o(\exp(-\lambda t)). \quad (6)$$

The mean residence time $1/\tau$ in the cell is then given approximatively by the formula [3, 8]

$$\frac{1}{\tau} \approx L_{\text{intra}}\lambda.$$

We use a realistic range of parameters described in Table 1. Performing N independent simulations to obtain empirical estimation $p_N(t_k)$ of $p(t_k)$ given by (6) at a given set of times $0 < t_1 < \dots < t_M \leq T$. A regression is used to estimate λ from the slope of $\{\log(p_N(t_k) - L_{\text{intra}}/L)\}_{k=1, \dots, M}$. In Section A, we give a procedure that filters out the effects of the other eigenvalues as well as the Monte Carlo error.

Being the first non-zero eigenvalue of \mathcal{A} , λ could also be computed deterministically as solution to a Sturm-Liouville problem. Numerically, it is easily checked that using (a) and (b) leads to pretty close eigenvalues (See [8]). The process is simulated only on case (b), which leads to faster computations, while the case (a) could be done using the algorithms given in [11], as the thinness of the layer forces to use a very small time step.

Numerical results are given in Section 1. Unless μ is too small, the Monte Carlo results are in good agreements with the deterministic approach. A small value of μ means that the strength of the membrane is high and particles have difficulties to pass through it. This problem is related to a rare events simulation problem.

A A procedure to estimate some exponential rate from Monte Carlo measurement

Let $p(t)$ be the probability of an event which decreases to 0 with the time t at some exponential rate λ . This is typical for first eigenvalues problems, such as (6) and the estimation of survival probability of a Brownian motion killed when it exits from a domain [10].

Name	Quantity	From	To
D_{intra}	cells' diffusivity	$2 \times 10^{-3} \frac{\mu\text{m}^2}{\mu\text{s}}$	$3 \times 10^{-3} \frac{\mu\text{m}^2}{\mu\text{s}}$
D_{extra}	diffusivity outside the cells		$= D_{\text{intra}}$
D_{memb}	membrane diffusivity		
2ϵ	membrane width		$0.01 \mu\text{m}$
$\mu = \frac{D_{\text{memb}}}{2\epsilon}$	membrane strength	$10^{-6} \frac{\mu\text{m}}{\mu\text{s}}$	$10^{-4} \frac{\mu\text{m}}{\mu\text{s}}$
L_{intra}	cell size	$5 \mu\text{m}$	$20 \mu\text{m}$
L_{extra}	outer cell size		$\approx L_{\text{intra}}/10$
L_{period}	media's period		$L_{\text{intra}} + L_{\text{extra}}$
T	max. observation time	$20000 \mu\text{s}$	$50000 \mu\text{s}$

Table 1: A realistic range of parameters.

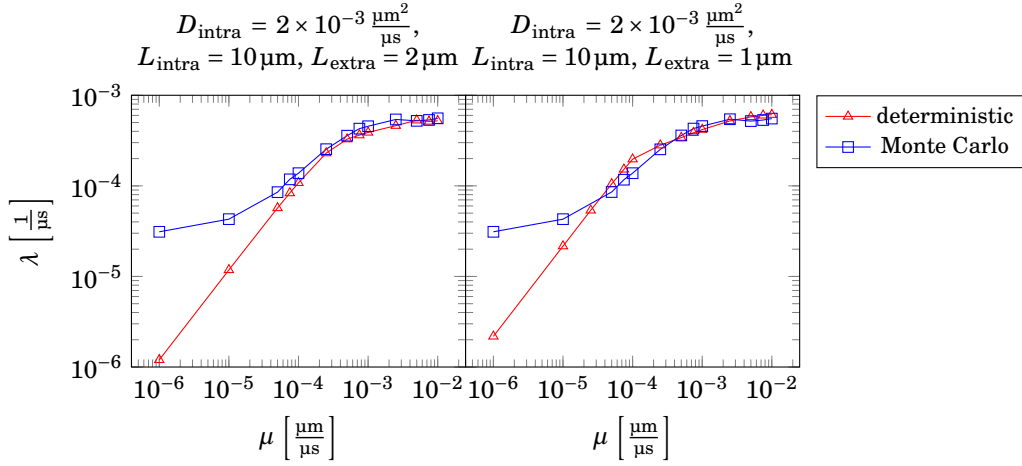


Figure 1: Estimation of λ by a deterministic method and a Monte Carlo one with $N = 100000$ particles.

More precisely, we state that

$$p(t) = p_\infty + c \exp(-\lambda t) + r(t) \text{ with } r(t) = o_{t \rightarrow \infty}(\lambda t), \quad (7)$$

where $p_\infty \geq 0$ is known, yet $c > 0$, $\lambda > 0$ and r are unknown. In particular, we ignore how fast $r(t)\exp(\lambda t)$ decreases to 0.

Our aim is then to estimate λ and c .

At different times $0 < t_1 < \dots < t_M$, this quantity $p(t_i)$ is estimated by $p_N(t_i)$ from a Monte Carlo estimation with N independent samples. A confidence interval allows one to assert that with a probability α for times t of observations hold:

$$|p(t) - p_N(t)| \leq c_\alpha \frac{\sqrt{p(t)(1-p(t))}}{\sqrt{N}} \text{ for } N \text{ large enough,} \quad (8)$$

with *e.g.*, $c_\alpha = 2.57$ for $\alpha = 99\%$.

Without the Monte Carlo error and the remainder term r , the problem of estimation of λ is pretty simple, as $\log(p(t) - p_\infty) = \log c - \lambda t$. One has then only to estimate the slope of $\log(p(t) - p_\infty)$, using for example a linear regression.

Our problem is then to filter out the times at which $r(t)$ (for small t) and the Monte Carlo error have small impact and $\log(p_N(t) - p_\infty)$ is close to be linear.

The Monte Carlo error has an impact when $c_\alpha \sqrt{p(t)(1-p(t))/\sqrt{N}}$ has the same order as $p(t) - p_\infty = c \exp(-\lambda t)$. Hence, it is useless to consider $p_N(t)$ at times t such that

$$c_\alpha \frac{\sqrt{p_N(t)(1-p_N(t))}}{\sqrt{N}} \geq \beta(p_N(t) - p_\infty) \text{ with say } \beta = \frac{1}{10}.$$

This criteria fixes a limit for the maximum sampling time t_M to consider. After this time, the estimations are no more relevant as being “flooded” by the Monte Carlo error.

Getting rid of $r(t)$ is more cumbersome, as this function is generally unknown. We should then rely on a graphical procedure to check whether or not $\log(p_N(t) - p_\infty)$ is straight on some large enough time interval.

In [10], we have proposed several criteria to test for the best time interval $[t_-, t_+]$ to consider on which λ is estimated through a linear regression using least squares: with

$$\text{SQ}(t_-, t_+; c, \lambda) = \sum_{\substack{i=1, \dots, M \\ t_- \leq t_i \leq t_+}} (\log c - \lambda t_i - \log(p_N(t_i) - p_\infty))^2,$$

we compute c_{est} and λ_{est} are the values which minimize $\text{SQ}(t_-, t_+; c, \lambda)$. We then set

$$\text{RSS}(t_-, t_+) = \text{SQ}(t_-, t_+; c_{\text{est}}, \lambda_{\text{est}}) = \min_{c, \lambda} \text{SQ}(t_-, t_+; c, \lambda). \quad (9)$$

In the report [8], we have proposed a new methodology in which t_- and t_+ are determined automatically using the Akaike Information Criteria (AIC) (See *e.g.* [14, Example 13.6, p. 179]). This approach is suitable as the number of values $p_N(t_i)$ to use varies with t_- and t_+ .

Since there are two parameters (c and λ) to estimate, we use the customary simplified formula

$$\begin{aligned} \text{AIC}(t_-, t_+) &= n \log(\text{RSS}(t_-, t_+)) - n \log n + 4 \\ &\text{with } n = \#\{t_- \leq t_i \leq t_+; i = 1, \dots, M\}. \end{aligned}$$

We draw randomly some pairs (t_-, t_+) with $t_- < t_+$ and we select the one for which $\text{AIC}(t_-, t_+)$ is minimized.

This procedure, whose result in illustrated in Figure 2, appears to be effective and no longer relies on a graphical interpretation as in [10].

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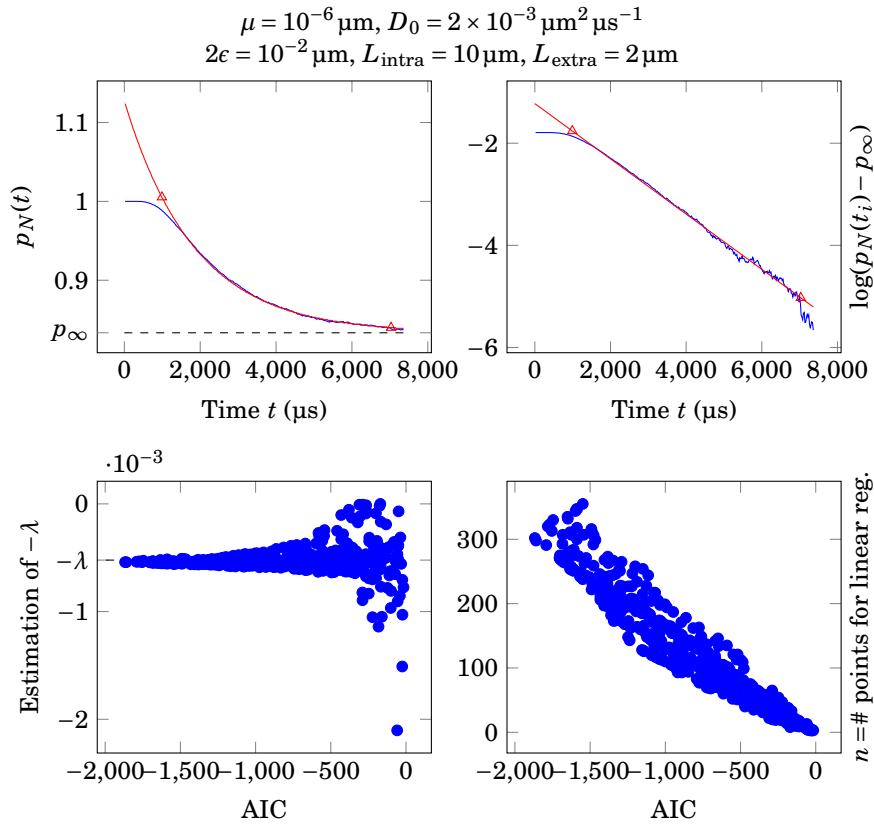


Figure 2: Estimation of λ using a least square procedure. The curve in red represents the estimated function $c \exp(-\lambda t)$ from the time interval $[t_-, t_+]$ delimited by the triangle. The two bottoms figures shows that the values which are close to the minimum of AIC provides pretty close estimated values of λ and use a lot of sample times. We have used $N = 100\,000$ paths and $t_{i+1} - t_i = 20 \mu\text{s}$.

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