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Research paper

Numerical analysis of stochastic processes in the aggregation erythrocyte molecules : Application to deoxy-hemoglobin S

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Abstract

Previously, by analytical method, some authors have shown that the harmonic noise is more indicated in the aggregation of deoxy-hemoglobin S. The problem that still arises is the relationship between the energy spectra and the microscopic properties of dielectric substances. The numerical approach of the correlation function's Fourier transform of different random processes have permit to obtain the frequency distribution spectra of energy and the fluctuations of the amplitudes. The results have shown that (i) only a fine analysis of the curves can permit obtain sufficient precision on the noise indicated in the aggregation of deoxy-hemoglobin S, (ii) in the presence of harmonic noise, the frequency distribution of energy and fluctuations of the amplitudes are low compared to white and colored noise, (iii) method exploiting the frequency distribution of energy and the fluctuations of the amplitudes justify well that the harmonic noise is the best indicated in the aggregation of the deoxy-hemoglobin S.

Keywords: *Colored noise; Energy frequency distribution; Harmonic noise; White noise.*

1. Introduction

Over the past three decades, much research has investigated the flow properties of dispersions of a wide variety of systems found in nature and industry, especially, the suspension of colloidal particles such as deoxy-hemoglobin S. For example, the solution-to-gel transformation of sickle cell hemoglobin was firstly described by Hofrichter Ross and Easton in 1974 [2], then by Harris and Bensusan in 1980 [3]. [4] have shown that molecular aggregation combined with the orientation of aggregates is the basis of the phenomenon of erythrocyte sickling. Recently, attempts have been made to study the kinetics of this transformation by various techniques ([5], [6], [7], [8]). [1] have defined non-linear relaxation functions to describe the aggregation of deoxy-hemoglobin S. They have shown analytically that harmonic noise is the noise indicated in the aggregation of deoxy-hemoglobin S. However, the relationship between energy spectra and the microscopic properties of dielectric substances is little studied. In the present study, the numerical approach was adopted to investigate the best indicated random process in the aggregation of deoxy-hemoglobin S.

2. Material and Methods

The Fourier transform of the correlation function of the random process was used. This Fourier transform is generalized to the distributions to process the noisy signal.

2.1. Power spectral density of a random process

The power spectral density $\phi_\xi(\omega)$ determines the frequency distribution of the average energy of random process $\xi(t)$. It is defined by:

$$\phi_\xi(\omega) = \int_{-\infty}^{+\infty} R_\xi(t)\exp(-j\omega t)\,dt \tag{1}$$

The power spectral density $\phi_\xi(\omega)$ is defined as $]-\infty,+\infty[$ being the Fourier transforms of correlation function $R_\xi(t)$ of random process $\xi(t)$. The Langevin force $\xi(t)$ satisfies the following conditions:

$$\begin{cases} \langle\xi(t)\rangle = 0 \\ \langle\xi(t)\rangle\langle\xi(s)\rangle = R_\xi(s-t) \end{cases} \tag{2}$$

The Fourier transform is generalized to distributions for the purposes of signal processing. Beyond a function, the Dirac δ impulse is a distribution, that is to say a mathematical tool which generalizes the functions. In this paper, one considers the distribution $f_{T_0}(t)$ defined by ([9], [10], [11]):

$$f_{T_0}(t) = \frac{1}{T_0} rect\left(\frac{t}{T_0}\right) \tag{3}$$

It seems that, when T_0 tends towards 0 , the distribution $f_{T_0}(t)$ tends towards the Dirac impulse [9].

2.2. Correlation functions of different random processes

2.2.1. White noise correlation function

In a previous work [1], this function is defined by:

$$R_{\xi}(s-t) = 2D\,\delta(s-t) \tag{4}$$

D is the diffusion coefficient of white noise and δ Dirac momentum. For white noise, the Fokker-Planck equation of the probability density P of the pair $(x_1(t), x_2(t))$ of the linear oscillator is written in the form [12]:

$$\frac{\partial P}{\partial t} + \frac{\partial}{\partial x_1}\left(a_{x_1} P\right) + \frac{\partial}{\partial x_2}\left(a_{x_2} P\right) - \frac{1}{2}\left\{\frac{\partial^2}{\partial x_1^2}\left(b_{x_1 x_1} P\right) + 2\frac{\partial^2}{\partial x_1 \partial x_2}\left(b_{x_1 x_2} P\right) + \frac{\partial^2}{\partial x_2^2}\left(b_{x_2 x_2} P\right)\right\} = 0 \tag{5}$$

$x_1(t)$ and $x_2(t)$ are respectively the displacement and the velocity of particles of unit masses. By determining the coefficients a_{x_1} , a_{x_2} , $b_{x_1 x_1}$, $b_{x_1 x_2}$ and $b_{x_2 x_2}$, one obtain the non-stationary Fokker-Planck equation in the form the equation (6):

$$\frac{\partial P}{\partial t} = -x_1 \frac{\partial P}{\partial x_2} + \frac{\partial}{\partial x_1}\left\{\left(C_0\, x_1 + \omega_0^2 x_2\right) P\right\} + \frac{D}{2}\frac{\partial^2 P}{\partial x_1^2} \tag{6}$$

The stationary Fokker-Planck equation of the invariant measure $M(x_1 , x_2)$ of the linear oscillator is defined by the equation (7):

$$\frac{D}{2}\frac{\partial^2 M(x_1 , x_2)}{\partial x_1^2} - x_1 \frac{\partial M(x_1 , x_2)}{\partial x_2} + \frac{\partial}{\partial x_1}\left\{\left(C_0\, x_1 + \omega_0^2 x_2\right) M(x_1 , x_2)\right\} = 0 \tag{7}$$

The solution of the partial differential equation (7) is given by the equation (8):

$$M(x_1 , x_2) = C.\exp\left(\frac{-C_0}{D} x_1^2\right)\exp\left(\frac{-C_0\,\omega_0^2}{D} x_2^2\right) \tag{8}$$

The normalization constant C is such that from

$$\int_{-\infty}^{+\infty}\int_{-\infty}^{+\infty} M(x_1 , x_2)\, dx_1\, dx_2 = 1 \tag{9}$$

One obtains the relation (10):

$$C.\int_{-\infty}^{+\infty} \exp\left(\frac{-C_0}{D} x_1^2\right) dx_1 \int_{-\infty}^{+\infty} \exp\left(\frac{-C_0\,\omega_0^2}{D} x_2^2\right) dx_2 = 1 \tag{10}$$

Let us put the constant C_1 in the form:

$$C_1 = \int_{-\infty}^{+\infty} \exp\left(\frac{-C_0}{D} x_1^2\right) dx_1 \tag{11}$$

And

$$C_2 = \int_{-\infty}^{+\infty} \exp\left(\frac{-C_0\,\omega_0^2}{D} x_2^2\right) dx_2 \tag{12}$$

So one have:

$$C = \frac{C_0\,\omega_0}{D\pi} \tag{13}$$

Thus the exact analytical solution [12] of the invariant measure $M(x_1 , x_2)$ of the linear oscillator is given by the relation (14):

$$M(x_1 , x_2) = \frac{C_0\,\omega_0}{D\pi}\exp\left(\frac{-C_0}{D} x_1^2\right)\exp\left(\frac{-C_0\,\omega_0^2}{D} x_2^2\right) \tag{14}$$

Fig.1 and Fig.2 present respectively the Fokker-Planck probability densities for the linear oscillator over ($k = 1$; $C = 0{,}01$; $D = 0{,}032$) and ($k = 1$; $C = 0{,}01$; $D = 10$).

By fixing the stiffness constant $k = 1$ and the damping coefficient of the linear oscillator $C = 0{,}01$, the probability density curve remains

Gaussian when the noise coefficient Gaussian takes the maximum value $D = 0{,}032$ (Fig.1). For this coefficient, the distribution of the probability density of the linear oscillator is very strong. When the Gaussian noise coefficient is high ($D = 10$), the probability density is very low (order of 10^4). The dynamic system is chaotic (Fig.2).

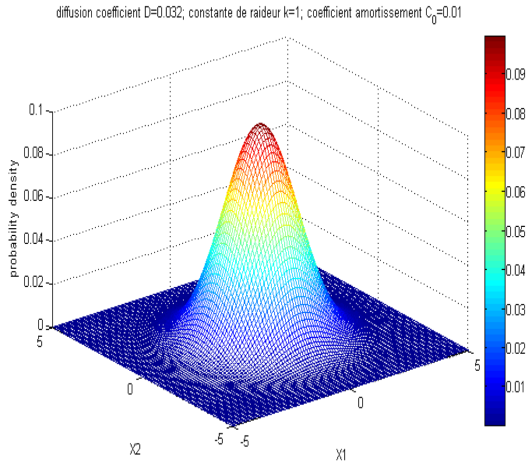

Fig. 1: Fokker-Planck probability densities for the linear oscillator with parameters $k = 1$; $C = 0.01$ and $D = 0{,}032$

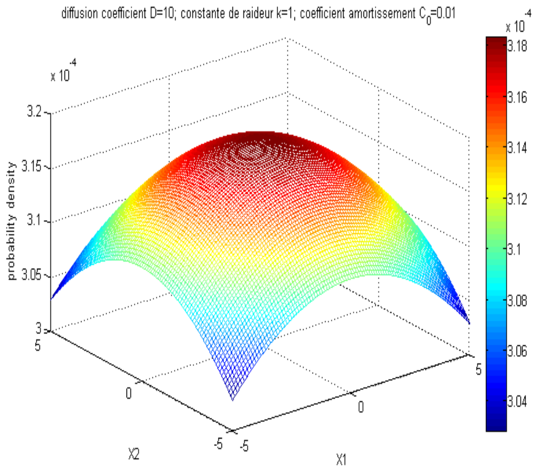

Fig. 2: Fokker-Planck probability densities for the linear oscillator with parameters $k = 1$; $C = 0.01$ and $D = 10$

2.2.2. Color noise correlation function

Colored noise has a different correlation function from the Dirac δ function [1]. It is defined by (15):

$$R_{\xi}(s-t) = \frac{D}{2\tau}\exp\left(-\frac{(s-t)}{\tau}\right) \tag{15}$$

When the noise considered in the modeling of random phenomena in physics and astronomy has a different covariance from the Dirac function δ , then the noise considered is not white but colored. The process C_t of colored noise is the Ornstein-Uhlenbeck process which is defined by the stochastic differential equation [13]:

$$dC_t = -\mu C_t + \sigma B_t \, dt \tag{16}$$

with μ and σ are real constants and B_t a Brownian motion of dimension 1. The process C_t satisfies the following properties:

$$\begin{cases} \langle \xi(t) \rangle = 0 \\ \langle \xi(t) \rangle \langle \xi(s) \rangle = \dfrac{\sigma^2}{2\mu}\left(\exp\left[-\mu(s-t)\right] + \exp\left[-\mu(s+t)\right] \right) \\ with \quad s \geq t \end{cases} \tag{17}$$

For long enough times, one have:

$$\langle \xi(t) \rangle \langle \xi(s) \rangle = \frac{\sigma^2}{2\mu}\left(\exp\left[-\mu(s-t)\right] \right) \tag{18}$$

Then, by setting the color with a single constant such that for a certain limit value γ_0 of γ one have:

$$\frac{\sigma^2(\gamma)}{2\mu(\gamma)}\left(\exp\left[-\mu(s-t)\right] \right) \rightarrow \delta(s-t) \tag{19}$$

By setting $\mu = \sigma = \gamma$, one obtains the equation (20):

$$\begin{cases} \dfrac{\gamma}{2}\left(\exp\left[-\gamma(s-t)\right] \right) \rightarrow \delta(s-t) \\ when \quad \gamma \rightarrow +\infty \end{cases} \tag{20}$$

Thus the color of the noise becomes white when the parameter γ becomes infinite. In an equivalent manner by setting $\tau = 1/\gamma$ with τ the correlation time, the colored noise becomes white when its correlation time tends to be zero. Thus the correlation function of colored noise is such that [13]:

$$\frac{D}{2\tau}\exp\left(-\frac{(s-t)}{\tau}\right) \to D\,\delta(s-t) \quad (21)$$

2.2.3. Harmonic noise correlation function

It is defined by [1]

$$R_{\xi}(s-t) = C^2\,\delta(s-t) \quad (22)$$

In the model of the fluctuation of the harmonic oscillator, the constant C^2 is written as

$$C^2 = \frac{4D\omega_0{}^4}{\kappa} \quad (23)$$

With:

$$\begin{cases} 4\,\omega_0{}^2 = \dfrac{\varepsilon_\infty}{\tau_A{}^2} \\ \kappa = \lambda_1 - \lambda_2 \end{cases} \quad (24)$$

Where $\varepsilon_\infty = 56$ is the permittivity in an optical field, τ_A is the harmonic noise correlation time, λ_1 and λ_2 are the clean values of the matrix A associated with the stochastic flux equation (26). The characteristic polynomial associated with A is such that $\det(\lambda\,Id - A) = 0$. In this work, by numerical calculation the characteristic time of aggregation is fixed at the value $\tau_A = 32$ sec*ondes*. By simple calculation one find:

$$\kappa = \sqrt{C_0{}^2 - 4\,\omega_0{}^2} \quad (25)$$

The modeling of the fluctuating oscillator is described by Cramer's stochastic differential equation which reads as the stochastic flux in the form of the equation (26):

$$\begin{cases} dx_1 = -\left(C_0\,x_1 - \omega_0{}^2 x_2\right)dt + \xi(t) \\ dx_2 = x_1\,dt \end{cases} \quad (26)$$

3. Main body

3.1. Curves of energy frequency distribution and amplitude fluctuation

Figs 3, 4, 5 present respectively the energy frequency distribution with white noise, colored noise and harmonic noise over (2-period, D = 0.1); (2-period, D = 10); (4-period, D = 20). Moreover, Figs 6, 7, 8 present respectively the energy frequency distribution with harmonic noise over (2-period, D = 0.1); (2-period, D = 10); (4-period, D = 20).

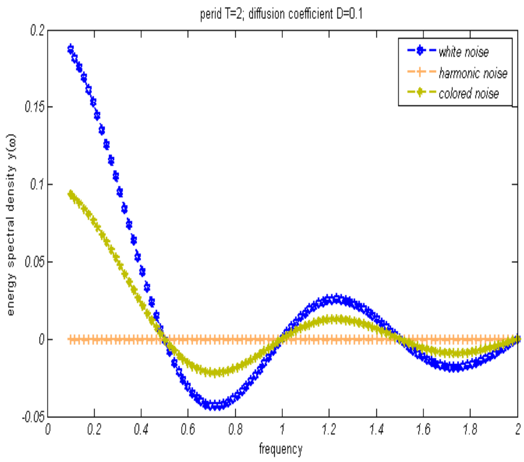

Fig. 3: energy frequency distribution with white noise, colored noise and harmonic noise over 2-period and D = 0.1

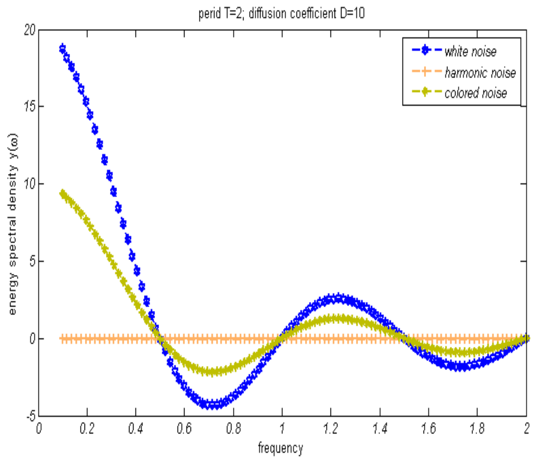

Fig. 4: energy frequency distribution with white noise, colored noise and harmonic noise over 2-period and D = 10.

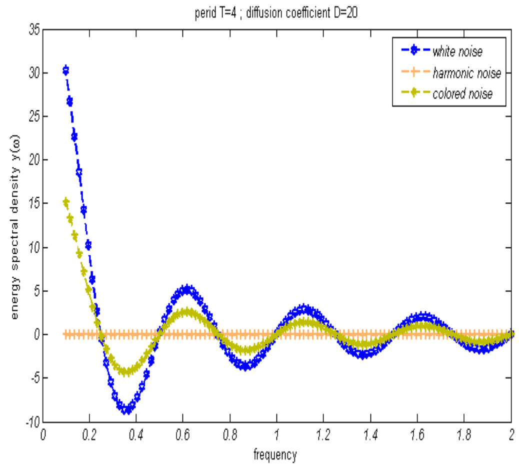

Fig. 5: energy frequency distribution with white noise, colored noise and harmonic noise over 4-period and D = 20.

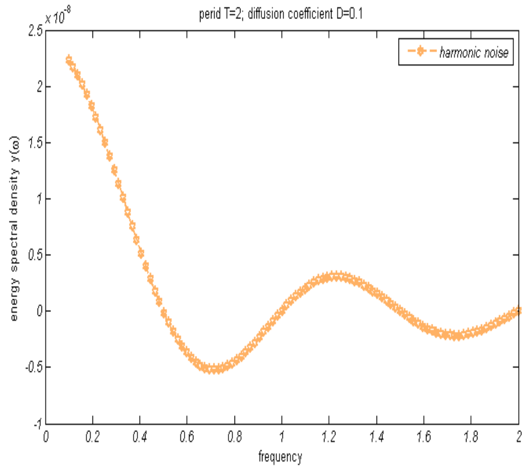

Fig. 6: energy frequency distribution with harmonic noise over 2-period and D = 0.1

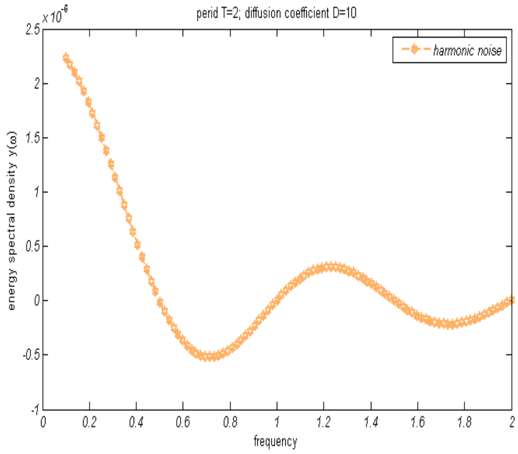

Fig. 7: energy frequency distribution with harmonic noise over 2-period and D = 10

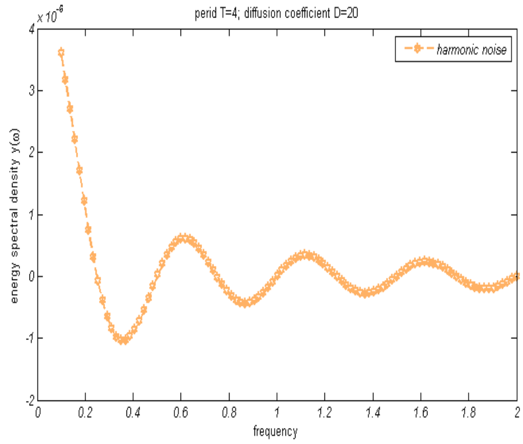

Fig. 8: energy frequency distribution with harmonic noise over 4-period and D = 20

Figs. 9, 10, 11, 12 respectively show the fluctuations of the amplitudes with the Fourier transform (FFT): (centered FFT); (shifted FFT); (inverse FFT); (centered inverse FFT).

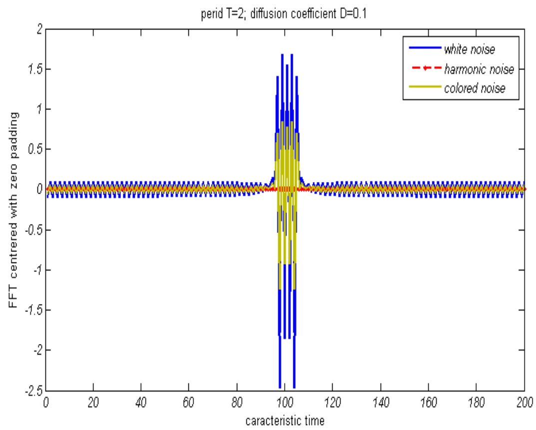

Fig. 11: FFT Inverse.

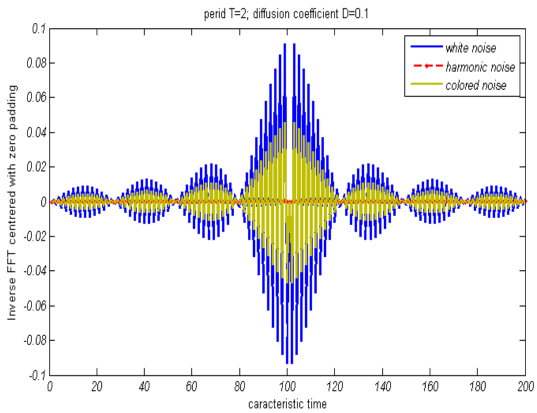

Fig. 12: FFT Inverse centered

3.2. Analysis and interpretation of curves

Figs. 3, 4, 5 illustrate spectral energy density in term of the frequency of deoxy-hemoglobin S solution. The discretization of the frequency made it possible to obtain the sinusoidal curves represented on 2-periods (Fig.3 and Fig.4) and on 4-periods (Fig.5). These curves define the distribution curves very well. They can therefore adjust the frequency distribution of energy during the deformation or aggregation of deoxy-hemoglobin S in the presence of the three types of noise. For the diffusion coefficients D = 0.1, D = 10 and D = 20, the energy dissipation with harmonic noise is zero compared to the energy distribution with white and colored noise (Fig.3, Fig.4 and Fig.5). One can claim to say that there is no energy dissipation from deoxy-hemoglobin S deformation or aggregation with harmonic noise. When the harmonic noise diffusion coefficient is equal to D = 0.1, we notice that the weak frequency distribution of energy is of the order of 10^8. This energy distribution is of the order of 10^7 for the coefficient D = 10 but it increases to the order of 10^6 for D = 20 (Fig.6, Fig.7 and Fig.8). Thus, the energy distribution with the harmonic noise increases when the diffusion increases. This result is an excellent finding of interpretation and for the choice of the noise most indicated in the aggregation of erythrocyte molecules. One has defined in the numerical code of our work, a function (y_f) is obtained by adding 100 points to the initial signal of the correlation function's Fourier Transform (FFT) of different noises. Fig.9 presents centered fluctuations of the real part of the function (y_f) whose amplitudes are well determined. Fig.10 shows a shifted display of fluctuations. This display made it possible to better appreciate the fluctuations whose phase oscillates rapidly with white and colored noises. By the Inverse Fourier Transform (IFFT), the fluctuations are almost zero with harmonic noise (Fig.11 and Fig.12). Thus, the amplitudes of the fluctuations are low with harmonic noise compared to white and colored noise whose amplitudes are large. Our results obtained by the numerical method justify that harmonic noise is the best indicated in the aggregation of deoxy-hemoglobin S. This finding is in agreement with those obtained by Massou et al. [1]. They have found similar results using analytical method.

4. Conclusion

By a numerical method, the energy distribution and the amplitude's fluctuations for different stochastic processes of the aggregation of deoxy-hemglobin S have been studied in this paper. The results confirmed that harmonic noise is the noise most indicated in the aggregation of deoxy-hemoglobin S. The aggregation kinetics of deoxy-hemoglobin S is best interpreted by the numerical approach. The results suggest that the models of energy frequency distribution and amplitude fluctuations developed in the present study are good models for interpreting the aggregation kinetics of deoxy-hemoglobin S in order to prevent the aggregation of erythrocytes, in people with sickle cell disease.

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