Passage through fluctuating geometrical bottlenecks. Subdiffusive
dynamics of the opening - exact solution

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Abstract

The usual Kramers theory of reaction rates in a condensed medium predict the rate to have an
$\eta^{-1}$ dependence, $\eta$ being the viscosity of the medium. However, experiments on ligand binding to
proteins performed long ago, showed the rate to have $\eta^{-\nu}$ dependence, with $\nu$ in the range 0.4 – 0.8.
Zwanzig (Journal of Chemical Physics 97, 3587 (1992)) suggested a model, in which the ligand has
to pass through a fluctuating opening to bind. Thus fluctuating gate model predicted the rate to
be proportional to $\eta^{-1/2}$. Experiments performed by Xie et. al. (Physical Review Letters 93, 1
(2004)) showed that the distance between two groups in a protein undergoes subdiffusion. Hence
in this paper, we suggest and solve a generalisation of the Zwanzig model, viz., passage through a
gate that undergoes subdiffusion. Our solution shows that the rate is proportional to $\eta^{-\nu}$ with $\nu$
in the range 0.5 – 1, and hence the model can explain the experimental observations.
I. INTRODUCTION

Simple, exactly solvable models of chemical reaction dynamics are very useful, as they give very valuable insights into the process. Among the very few such models is the one due to Zwanzig [1], for the passage of a ligand molecule through a fluctuating bottleneck. Many authors have suggested similar models for the removal of a steric constraint by fluctuations, for molecular rotation in liquids and glasses [2–6]. The model of Zwanzig is for the passage of a ligand to a binding site that is buried deep inside a cavity within a protein. It assumes that the rate of binding is proportional to the area of the opening, which undergoes time dependent fluctuations. The predictions of the model are, in general, in agreement with the experiments. The concentration of the ligand initially decays non-exponentially, but changes over to exponential at long times. Taking the time scale of decay of the fluctuations of the opening as proportional to the viscosity $\eta$ of the medium, the model predicts that the rate constant for long term decay is $\propto \eta^{-1/2}$. In comparison, the Kramers theory of activated processes leads to a rate proportional to $\eta^{-1}$. The experiments of Beece et al. [7] on the viscosity dependence of the rate, found an inverse fractional dependence of the form $\eta^{-\nu}$, in agreement with the Zwanzig theory. However, the value of $\nu$ was in the range $0.4 - 0.8$, prompting the study by Wang and Wolynes [8] of its extension to a non-Markovian model, in which the relaxation of the opening is a stretched exponential. They used the path integral technique to obtain exact solution in the long time limit. Their model lead to $\nu$ values that are strictly less than $1/2$. Over the years, there have been a few more investigations into this rather old problem [9–12]. Of particular interest is the paper by Bicout and Szabo [13] who obtained general result for the rate in the case where the opening undergoes non-Markovian fluctuations. Even though most of these papers were published long ago, we have not been able to find in the literature, a simple analytically solvable model that accounts for all the experimental results. It is the aim of this paper to provide such a simple model, based on very interesting experiments [14–17] that have become available, since these original investigations.

Most of the above investigations assume the radius of the opening to undergo diffusive motion in a harmonic potential. Thus it is an Ornstein-Uhlenbeck process, with an exponential correlation function. The major exception to this is the work of Wang and Wolynes [8], which models the correlation as a stretched exponential. In an elegant set of papers,
the group of Xie [14][17] investigated the dynamics of the distance between two units in a protein, that are not directly bonded. Using single molecule fluorescence as a probe of the distance $x$, they showed that $x$ undergoes subdiffusion, in which its mean square displacement is proportional to $(\text{time})^\beta$ with $\beta < 1$. Further, they also showed that the units may be modelled as being held together by a harmonic spring and that their motion is well described by the equation for subdiffusion (see Eq. (5)), given in Section I.

Interestingly, the problem of a “quadratic sink representing a gate whose dynamics is diffusive” is of interest in other areas of chemical physics. Thus, we have suggested a model for calculating the probability distribution of position of a particle that undergoes diffusion with stochastic diffusivity [18]. In this model, the probability distribution is the Fourier transform of the survival probability of a particle undergoing Brownian motion [19–23]. Another interesting study is the “Fluctuating Bottleneck model” for the passage of DNA through the $\alpha$-hemolysin pore by Bian et al. [24, 25], who found an approximate solution to the model, using the Wilhems-Fixman approach. It is of interest to note that our study provides an exact solution to this model, though we do not discuss our model in this context.

II. THE FLUCTUATING GATE MODEL

The process that we study is shown schematically in Fig. 1. In order to bind to the site that is inside the cavity, the ligand has to pass through a gate which is modelled as a circular opening of radius $r$. The survival probability of the ligand at the time $t$, $S(t)$ is assumed to obey the equation

$$\frac{dS(t)}{dt} = -K(r)S(t).$$

Zwanzig [1] takes the rate of passage of the ligand to be proportional to $\pi r^2$, the area of the circular gate so that

$$K(r) = kr^2.$$  

The radius of the pore undergoes thermal fluctuations, obeying the equation for overdamped motion

$$\zeta \frac{dr}{dt} = -m\omega_0^2 r + \sqrt{2\zeta k_B T} \xi(t),$$

where $m$ is the “mass” associated with the fluctuating co-ordinate, and $\frac{\zeta}{m\omega_0}$ is its time of relaxation. $\xi(t)$ is Gaussian white noise with mean zero with $\langle \xi(t)\xi(t') \rangle = \delta(t - t')$ and $T$
Figure 1. Schematic picture of gating

is the temperature. $\zeta$ is the friction coefficient and is directly proportional to the viscosity $\eta$ of the medium. (Note that our notation is different from that of Zwanzig. Zwanzig’s $\theta$ and $\lambda$ are related to our constants by $\lambda = m \omega_0^2 / \zeta$ and $\theta = k_B T / m \omega_0^2$). The quantity of interest is $\langle S(t) \rangle = \int_0^\infty dr \bar{S}(r, t)$, where the noise averaged concentration $\bar{S}(r, t)$ obeys the reaction-diffusion equation with a sink term that is quadratic in the co-ordinate $r$:

$$\frac{\partial \bar{S}}{\partial t} = -k r^2 \bar{S} + \frac{k_B T}{\zeta} \frac{\partial}{\partial r} \left( \frac{\partial \bar{S}}{\partial r} + \frac{m \omega_0^2}{k_B T} r \bar{S} \right). \quad (4)$$

Assuming that $\bar{S}$ has the equilibrium distribution at the initial time $t = 0$, the instant at which the sink term in Eq. (4) is switched on, this can be solved exactly. The solution leads to the following results: (1) The decay of $\langle S(t) \rangle$ is multi-exponential. (2) At short times, $\bar{S}(t) = 1 - k \frac{k_B T}{m \omega_0^2} t + O(t^2)$. (3) For long times, the decay is single exponential with a rate constant equal to $k_{eff} = \frac{1}{2} \left( \sqrt{4 \frac{k_B T}{\zeta} k + \left( \frac{m \omega_0^2}{\zeta} \right)^2} - \frac{m \omega_0^2}{\zeta} \right)$. For large $\frac{m \omega_0^2}{\zeta}$, one gets $k_{eff} \approx \left( k \frac{k_B T}{\zeta} \right)^{1/2}$. As $\zeta$ is proportional to $\eta$, we get $k_{eff} \propto \eta^{-1/2}$, in agreement with experimental observations of Beece et. al. of an $\eta^{-\nu}$ dependence with $\nu$ in the range $0.4 - 0.8$. The deviation of the predicted value of $\nu$ from the observed, shows that the model of Zwanzig can be considered only as a starting point. This prompted Wang and Wolynes (WW) to consider a model in which correlation $\langle r(t) r(t') \rangle$ has the form of a stretched
exponential given by $\theta \exp \left[ -(\lambda |t - t'|^\beta) \right]$, with $\beta \leq 1$. Note that $\beta = 1$ would be the case considered by Zwanzig [1], and $\beta < 1$ is a more general case of fluctuations, observed in biomolecules and glasses. In this more general case, Wang and Wolynes [8] found an approximate expression for the rate constant $k_{eff}$ which is proportional to $\eta^{-\beta/(1+\beta)}$. As $\beta \leq 1$, their model predicts $\nu \leq 1/2$. They conclude that the inclusion of direct coupling of the reaction coordinate with the viscous medium is required to have better agreement with experiment.

Thanks to the advances in single molecule experiments, we now have results on the fluctuations of the distance between two sub-units in a protein. Yang et. al. [14] showed that the distance $x$ between the Flavin mononucleotide (FMN) and the Flavin adenine dinucleotide (FAD) in the protein flavin reductase, isolated from Escheria coli, undergoes subdiffusive motion. Its dynamics is well described by the equation for a subdiffusive Brownian oscillator (SBO),

$$\zeta \int_{-\infty}^{t} dt' K_\alpha(t - t') \dot{x}(t') = -m \omega_0^2 x(t) + \sqrt{2k_B T} \xi^\alpha(t). \quad (5)$$

In the above, $\xi^\alpha(t)$ is fractional Gaussian noise (fGn) having the correlation function

$$\langle \xi^\alpha(t) \xi^\alpha(s) \rangle = K_\alpha(t - s), \quad (6)$$

where

$$K_\alpha(t - s) = (\alpha + 1)\alpha |t - s|^{\alpha-1} + 2(\alpha + 1)|t - s|^\alpha \delta(t - s),$$

with $0 \leq \alpha < 1$. $\alpha = 0$ corresponds to the usual Gaussian white noise. Note that Kou and Xie [15] use the parameter $H$ instead of our $\alpha$ and the two are related by $H = (\alpha + 1)/2$.

The use of such an equation is also justified using Rouse model by Dua and Adhikari [27]. These studies suggest strongly that a very simple model for the passage through a gate is to assume that the dynamics of the gate is subdiffusive. We discuss this model in the next Section.

### III. SUBDIFFUSIVE GATING

#### A. The Model

The instantaneous state of the opening may be described by the position vector $\mathbf{r} = x\hat{i} + y\hat{j}$, of a point on its circumference, with the origin of the co-ordinates located at its
center. The area of the opening is \( \pi r^2 = \pi r^2 = \pi (x^2 + y^2) \) (we use the notation \( r = |r| \)). We take \( r \) to obey the subdiffusion equation

\[
\zeta \int_{-\infty}^{t} dt' K_\alpha(t - t') \frac{dr(t')}{dt'} = -m\omega_0^2 r(t) + \sqrt{2k_B T} \xi^\alpha(t).
\]

For more details on this equation and its application to single molecule experiments, we refer the reader to the nice article by Kou [28, 29]. One can easily calculate the correlation function,

\[
C_\alpha(t, t') = \langle x(t)x(t') \rangle = \langle y(t)y(t') \rangle = \frac{k_B T}{m\omega_0^2} E_{1-\alpha}
\(-(|t - t'|/\tau)^{1-\alpha}\)  
\tag{7}
\]

with

\[
\tau = \left( \frac{\zeta \Gamma(\alpha + 2)}{m\omega_0^2} \right)^{1/(1-\alpha)}
\tag{8}
\]

and \( E_a(z) \) is the Mittag-Leffler function, defined by \( E_a(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(ak+1)} \). Also, \( \langle x(t)y(t') \rangle = 0 \). It is to be noted that the processes \( x(t) \) and \( y(t) \) are stationary. Hence we have \( C_\alpha(t, t') = C_\alpha(t - t') \). In the following we will also need the Fourier cosine transform of \( C_\alpha(t) \), defined by

\[
\tilde{C}_\alpha(\omega) = \int_0^{\infty} dt \cos(t\omega) C_\alpha(t) = \int_0^{\infty} dt \cos(t\omega) \frac{k_B T}{m\omega_0^2} E_{1-\alpha} \(-(|t - t'|/\tau)^{1-\alpha}\)  
\tag{9}
\]

\[
= \frac{k_B T}{m\omega_0^2} \left( \frac{\omega}{\tau} \right) \cos \left( \frac{\omega \tau}{2} \right) \left( \frac{\omega \tau}{2} \right)^{-\alpha} \cos \left( \frac{\pi \alpha}{2} \right) \left( \frac{\omega \tau}{2} \right)^{1-\alpha}.  
\tag{10}
\]

See the nice review by Kou [28] for the derivation of the correlation function.

### B. Survival probability

On solving Eq. (1) using Eq. (2), we get the survival probability of the ligand after a time \( t \) to be

\[
\langle C_\alpha(t) \rangle = \left\langle \exp \left( -k \int_0^{t} ds r^2(s) \right) \right\rangle,
\tag{11}
\]

where the average \( \langle ... \rangle \) is over all possible realizations of \( r(s) \). We now introduce \( \eta(t) = \eta_x(t)\dot{i} + \eta_y(t)\dot{j} \), where \( \eta_i(t) \) with \( i = x, y \) are both Gaussian white noises, having mean zero and correlation \( \langle \eta_i(t)\eta_j(t') \rangle = \delta_{ij}\delta(t - t') \). Then it is possible to rewrite Eq. (11) as

\[
\langle C_\alpha(t) \rangle = \int D\eta(s) \left\langle \exp \left( -\int_0^{t} ds \eta^2(s) + 2i\sqrt{k} \int_0^{t} ds r(s).\eta(s) \right) \right\rangle,
\]
where the functional integral $\int D\eta(s)$ is over all possible realizations of $\eta(s)$. As $r(s)$ is a Gaussian stochastic process with mean zero, the average over it is easily performed to get

$$
\langle S(t) \rangle = \int D\eta(s) \exp \left( -\int_0^t ds\eta^2(s) - 2k \int_0^t ds' \int_0^t ds\eta(s).\langle r(s) r(s') \rangle \eta(s') \right)
$$

$$
= \int D\eta(s) \exp \left( -\int_0^t ds\eta^2(s) - 2k \int_0^t ds' \int_0^t ds\eta(s)\eta(s')C_\alpha(s-s') \right)
$$

$$
= A \left( \text{det} [\delta(s-s') + 2kC_\alpha(s-s')] \right)^{-1} \quad \text{with} \quad s, s' \in (0, t).
$$

(12)

In the above, $\delta(s-s') + 2kC_\alpha(s-s')$ is a functional matrix whose indices are continuous. $A$ is a constant, equal to $\text{det} [\delta(s-s')]$, which is divergent. Note that the value of $\langle S(t) \rangle$ is the ratio of two divergent quantities and is always finite, as it should be (see below). We use the identity $\text{det} B = \exp (\text{Tr} \ln B)$, where $\text{Tr}$ stands for the trace of the matrix, valid for any Hermitian matrix $B$, to write

$$
\langle S(t) \rangle = A \exp \left( -t \text{Tr} \ln [\delta(s-s') + 2kC_\alpha(s-s')] \right).
$$

Expanding the logarithm, and using the condition $\langle S(t) \rangle |_{k=0} = 1$, we get

$$
\langle S(t) \rangle = \exp \left( \sum_{n=1}^{\infty} (-1)^n (2k)^n \frac{n}{n} \text{Tr} C_\alpha^n \right),
$$

(13)

where $C_\alpha$ is the matrix with continuous indices $s, s'$, defined by $C_{\alpha,s,s'} = C_\alpha(s-s')$. Equation (13) is our final expression, and we can now analyse it to get the detailed behavior of the survival probability.

C. Short time behavior

For small times, i.e., $t \ll \tau$, we can approximate $C_\alpha(s-s')$ by $C_\alpha(0)$. Doing this in each term in Eq. (13), noting from Eq. (11) that $C_\alpha(0) = \frac{k_B T}{m\omega_0^2}$, and summing the resultant series gives

$$
\langle S(t) \rangle = \left( 1 + 2k \frac{k_B T}{m\omega_0^2} t \right)^{-1} \approx 1 - 2k \frac{k_B T}{m\omega_0^2} t + O(t^2),
$$

exactly as in the case of the Zwanzig model. Thus subdiffusion of the gate does not make any difference to the short term behavior of the survival probability.
D. An exact expression for numerical evaluation of $\langle S(t) \rangle$

An exact expression, which may be used for numerical evaluation of the survival probability can be obtained by discretisation of the time interval $(0, t)$ into $N$ discrete intervals each of duration $\Delta t$, so that $N\Delta t = t$. Denoting $t_j = (j - 1)\Delta t$, with $j = 1, 2, 3, \ldots N$, and approximating the matrix $C_{\alpha;s,s'}$ by the finite dimensional matrix $C_{\alpha;N}$ with matrix elements $(C_{\alpha;N})_{ij} = C_{\alpha}(t_i - t_j)\Delta t$ in each term in the sum in the exponent of Eq. (13) gives

$$\langle S(t) \rangle = \lim_{N \to \infty, \Delta t \to 0, N\Delta t = t} (\det[I + 2kC_{\alpha;N}])^{-1},$$

where $I$ is the $N \times N$ identity matrix. The value of $N$ can be chosen sufficiently large to get the survival probability to any desired accuracy.

E. Survival probability in the long time limit

One can easily get an approximation for $\langle S(t) \rangle$ in the long time limit. First we note that the matrix $I + C_{\alpha;N}$ would be the Hamiltonian matrix for a chain of $N$ atoms, in a tight binding model, having one orbital on each, with all the diagonal elements equal to $1 + C_{\alpha}(0)\Delta t$ and the $ij$th offdiagonal element equal to $C_{\alpha}(\Delta t(i-j))$. We also note that $C_{\alpha}(t)$ is a decaying function of $t$, decreasing like $t^{\alpha-1}$ for large values of $t$, for $\alpha \neq 0$ (if $\alpha = 0$, then it decays exponentially). In either case, for large values of $t$ one expects that modifying the Hamiltonian matrix by imposing periodic boundary conditions on the chain of atoms will not cause a significant change to its eigenvalues. Once the condition is imposed, the eigenvalues of the matrix $C_{\alpha;N}$ are given by

$$\epsilon_j = 1 + 2k\Delta t \sum_{n=-N/2+1}^{N/2} C_{\alpha}(n\Delta t) \exp\left(i\frac{2\pi nj}{N}\right) \text{ for } j = 0, \pm 1, \pm 2, \ldots \quad (14)$$

In the limit $\Delta t \to 0$, and $N \to \infty$, with $N\Delta t = t$, noting that the correlation function $C_{\alpha}(s)$ is an even function of $s$, the sum in Eq. (14) becomes

$$\epsilon_j = 1 + 2k \int_{-t/2}^{t/2} ds C_{\alpha}(s) \cos\left(\frac{2\pi js}{t}\right).$$

Using the fact that $C_{\alpha}(s)$ is an even function, we get

$$\epsilon_j \approx 1 + 4k \int_0^{t/2} ds \cos\left(\frac{2\pi js}{t}\right) C_{\alpha}(s).$$
For large times, the upper limit of integration can be replaced with infinity, and then
\[ \epsilon_j \approx 1 + 4k C_\alpha(\frac{2\pi j}{T}) \] for \( j \neq 0 \).

The case where \( j = 0 \) needs special attention, and is evaluated below:

\[ \epsilon_0 = 1 + 4k \frac{k_B T}{m \omega_0^2} \int_0^{t/2} ds E_{1-\alpha}(-s/\tau)^{1-\alpha}. \] (15)

For \( t \to \infty \), the major contribution to the integral comes from large values of \( s \) at which one may use the asymptotic expression \( E_{1-\alpha}(-s/\tau)^{1-\alpha} \approx \frac{(s/\tau)^{\alpha-1}}{\Gamma(\alpha)} + O((s/\tau)^{2\alpha-2}) \). This gives

\[ \epsilon_0 \approx 1 + 4k \frac{k_B T \tau}{m \omega_0^2 \Gamma(\alpha + 1)} \left( \frac{t}{2\tau} \right)^\alpha \approx 2k \frac{k_B T \tau}{m \omega_0^2 \Gamma(\alpha + 1)} \left( \frac{t}{2\tau} \right)^\alpha. \] (16)

Taking into account of the fact that \( \epsilon_0 \) is non-degenerate, and all other eigenvalues are doubly degenerate, we get

\[ \langle S(t) \rangle = \left( \det[I + 4k C_\alpha N] \right)^{-1} = \frac{1}{\epsilon_0 \prod_{j=1}^{\infty} \epsilon_j^2}. \] (17)

which may be approximated as

\[ P \approx \exp \left[ - \sum_{j=-\infty}^{\infty} \ln \left( 1 + 4k C_\alpha \left( \frac{2\pi |j|}{T} \right) \right) \right] = \exp \left[ - \frac{t}{\pi \tau} \int_0^\infty d\omega \ln \left( 1 + 4k \frac{k_B T}{m \omega_0^2} \frac{\cos \left( \frac{\pi \omega}{\tau} \right) \omega^{-\alpha}}{1 + \omega^{2-2\alpha} + 2 \sin \left( \frac{\pi \omega}{\tau} \right) \omega^{1-\alpha}} \right) \right]. \] (18)

Notice that the integrand is divergent at \( \omega = 0 \), this being a result of the divergence of the \( j = 0 \) eigenvalue in the \( t \to \infty \) limit. This does not cause any particular problem, as the integral in Eq. (18) is well behaved.

It is convenient to introduce the dimensionless variables \( \bar{t} = t/t_0 \), where \( t_0 = \frac{m \omega_0^2}{k_B T} \) and \( \bar{\tau} = \frac{\tau}{t_0} \). Then, the survival probability \( S \) is a function of these two reduced variables alone. Plots of this function are shown in Figures 2 and 3. We have also compared the values of \( k_{eff} \) obtained by fitting the numerical results with \( k_{eff} \) calculated numerically using equation (18) in Tables I and II. It is to be noted that in general the agreement is good for small values of \( \alpha (\leq 1/2) \) but not so for higher values of \( \alpha \). See the result for \( \alpha = 3/4 \) in table II. This because for higher values of \( \alpha \) the Mittag-Leffler function \( E_{1-\alpha}(-(t/\tau)^{1-\alpha}) \sim \frac{(t/\tau)^{\alpha-1}}{\Gamma(\alpha)} \), which means that \( C_\alpha(t) \) decays very slowly with and hence our approximation of using periodic boundary condition becomes poor as the value of \( \alpha \) approaches unity.
F. The effective rate constant, $k_{eff}$

It is clear that the long term decay is exponential, being of the form $e^{-k_{eff}t}$. From Eq. (18), an approximation to $k_{eff}$ is

$$k_{eff} = \frac{1}{\pi \tau} \int_0^\infty d\omega \ln \left(1 + 4k\frac{k_B T}{m \omega_0^2} \frac{\cos \left(\frac{\alpha}{2}\right) \omega^{-\alpha}}{(1 + \omega^{2-2\alpha} + 2 \sin \left(\frac{\alpha}{2}\right) \omega^{1-\alpha})}\right),$$

(19)

which in terms of the dimension-less quantities $\bar{t}$, $\bar{\tau}$ and $\bar{k}_{eff} = k_{eff}t_0$ may be written as

$$\bar{k}_{eff} = \frac{1}{\bar{\tau}} \int_0^\infty d\omega \ln \left(1 + 4\bar{\tau} \frac{\cos \left(\frac{\alpha}{2}\right) \omega^{-\alpha}}{(1 + \omega^{2-2\alpha} + 2 \sin \left(\frac{\alpha}{2}\right) \omega^{1-\alpha})}\right).$$

(20)

For $\alpha = 0$, the integral can be evaluated, to get the result

$$\bar{k}_{eff} = \frac{1}{\bar{\tau}} \left(\sqrt{1 + 4\bar{\tau}} - 1\right),$$

(21)

which is the same as that obtained by Zwanzig [1] (Note that while Zwanzig considers one dimensional version of the problem, while our analysis is for a two dimensional opening, and hence Zwanzig’s rate is only half of ours). On taking $\tau \propto \zeta \propto \eta$, for large values of $\frac{k_B T}{m \omega_0^2}$ (i.e., $\bar{\tau} \gg 1$), we find $k_{eff} \propto \eta^{-1/2}$,which is the result of Zwanzig. We now consider the situation where the radius of the opening undergoes subdiffusion. For $\alpha > 0$, we have not been able to evaluate $k_{eff}$ analytically. Hence we calculate the integral in Eq. (19) numerically, and find its dependence on $\zeta$. We took $\bar{\tau}$ to be large and to vary from 1000 to 10,000. The value of $\bar{k}_{eff}$ was calculated for each $\bar{\tau}$, using Eq. (19) and MATHEMATICA. For each value of $\alpha$, plots of $\ln \bar{k}_{eff}$ against $\ln \bar{\tau}$ were then made, and were found to be linear with negative slope. This implies $\bar{k}_{eff} \propto (\bar{\tau})^{-\gamma}$. As $\bar{\tau} \propto \zeta^{1/(1-\alpha)}$ (see Eq. (8)), we get $\bar{\tau} \propto \eta^{-\nu}$, with $\nu = \gamma/(1 - \alpha)$. The results for $\gamma$ and $\nu$ are plotted in Fig. 4, for various values of $\alpha$. It is clear that the values range from 0.5 to greater than unity (it is greater than unity for values of $\alpha$ very close to 1). Remembering that $\zeta$ is proportional to the viscosity $\eta$, this is in better agreement with the experiments, than the simple diffusive model to Zwanzig [1], or the stretched exponential model of Wang and Wolynes [8].

IV. SUMMARY AND CONCLUSIONS

We have found exact solution to the problem of quadratic sink for Brownian oscillator that undergoes sub-diffusion. This is a problem of great interest in different areas of chemical
\[ \alpha = 0 \]
\[ \alpha = \frac{1}{4} \]
\[ \alpha = \frac{1}{2} \]
\[ \alpha = \frac{2}{3} \]
\[ \alpha = \frac{3}{4} \]

\[ \tau = 2 \]

**Figure 2.** Plots of survival probability as a function of time \( \bar{t} = t/t_0 \) for different values of \( \alpha \). \( \bar{\tau} = \tau/t_0 \) is taken to be 2. The plots show that the decay is exponential for long times. Slopes obtained by fitting the data are given in Table I.

| \( \alpha \) | \( \bar{k}_{eff} \) (fitted) | \( \bar{k}_{eff} \) (from Eq. (20)) |
|-------------|-----------------------------|-----------------------------------|
| 0           | 0.9997                      | 0.9999                            |
| \( \frac{1}{4} \) | 1.0821                     | 1.0824                            |
| \( \frac{1}{2} \) | 1.1404                     | 1.1398                            |
| \( \frac{2}{3} \) | 1.1544                     | 1.1398                            |
| \( \frac{3}{4} \) | 1.1491                     | 1.0968                            |

Table I. Values of \( k_{eff} \) for different values of \( \alpha \). All the results are for \( \bar{\tau} = 2 \).

physics [1, 8, 24] and for which only approximate solutions were known [24]. Our solution was used to analyse the problem ligand passage through a fluctuating bottle neck. It was found that the model predicts an effective rate constant proportional to \( \eta^{-\nu} \), \( \eta \) being the viscosity of the medium, with a \( \nu \geq 1/2 \). This is in better agreement with experiments (\( \nu \) in the range 0.4 to 0.8) than the previous models, which predict \( \nu \leq 1/2 \) [1, 8]. Hence sub-diffusion [15, 30] of the opening can explain the experimental observations [1, 7] on the viscosity dependence of ligand binding to a protein.
Figure 3. Plots of survival probability as a function of time $\bar{t} = t/t_0$ for different values of $\alpha$. $\bar{\tau} = \tau/t_0$ is taken to be 10. The plots show that the decay is exponential for long times.

| $\alpha$ | $\bar{k}_{eff}$ (fitted) | $\bar{k}_{eff}$ (from Eq. (20)) |
|----------|--------------------------|-------------------------------|
| 0        | 0.5402                   | 0.5403                        |
| $\frac{1}{4}$ | 0.6586                   | 0.6575                        |
| $\frac{1}{2}$ | 0.8052                   | 0.8000                        |
| $\frac{2}{3}$ | 0.9127                   | 0.8910                        |
| $\frac{3}{4}$ | 0.9634                   | 0.9038                        |

Table II. Values of $\bar{k}_{eff}$ for different values of $\alpha$. All the results are for $\bar{\tau} = 10$. It is to be noted that the agreement is good for smaller values of $\alpha$, but for $\alpha = 3/4$, the agreement is not so good.

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Figure 4. Plot of $\gamma$ and $\nu$ against $\alpha$.

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