Simulating cw-ESR Spectrum Using Discrete Markov Model of Single Brownian Trajectory

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Dynamic trajectories can be modeled with a Markov State Model (MSM). The reduction of continuous space coordinates to discretized coordinates can be done by statistical binning process. In addition to that, the transition probabilities can be determined by recording each event in the dynamic trajectory. This framework is put to a test by the electron spin resonance (ESR) spectroscopy of nitroxide spin label in X- and Q- bands. Calculated derivative spectra from MSM model with transition matrix obtained from a single Brownian trajectory by statistical binning process with the derivative spectra generated from the average of 100,000 Brownian trajectories, are compared and yield a very good agreement. It is suggested that this method can be implemented to calculate absorption spectra from molecular dynamics (MD) simulation data. One of its advantages is that due to its reduction of computational effort, the parametrization process will be quicker. Secondly, the transition matrix defined in this manner, records every possible type of jumps in the time evolution, so that it will take into account automatically the effective internal dynamics. Thirdly, one can calculate the ESR spectra from a single MD trajectory directly without extending it artificially in the time axis.

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I. INTRODUCTION

Spin labeling theory [1, 2] has many applications in understanding the dynamics of complex molecules in a liquid environment. The line shapes from the continuous wave electron spin resonance (cw-ESR) spectroscopy due to liquid environment had already been investigated by stochastic Kubo-Anderson approach [3, 4], approximation of relaxation times [5, 6], and spherical Stochastic Liouville Equation (SLE) [7] formalism.

The work by Robinson and co-workers [10] changed the perspective on looking to the problem by taking the rotational molecular trajectory as given. This has opened a new era, when the community started to infer possible interactions in the liquid environment that are effective on the cw-ESR spectrum by using molecular dynamics (MD) simulations following Steinhoff and Hubbell [11, 12]. This framework is based on calculating cw-ESR spectra of a spin label on a rotationally diffusing molecule from the motion of the three Euler angles (φ, θ, ψ) that represent the orientational dynamics, and can be modeled with isotropic and anisotropic rotational diffusion processes.

On the other hand, the diffusion of three Euler angles may depend on the internal dynamics and structural properties of the molecule and the spin label [13–15]. Thus, ESR spectroscopy is very helpful in understanding the features of intra- and inter-molecular phenomena, e.g. nitroxide spin label, freely diffusing in a liquid, which is a problem that has been discussed many times. The s-state Kubo-Anderson process, with Markovian jumps maintains a solution that takes relatively less computational effort than working on the continuous coordinate system. We show that a Brownian trajectory can be mapped to a MSM by using a statistically binning process of exhibited jumps from one microstate to another. Therefore, a comparison between, on the one hand, calculated derivative spectra from MSM model with transition matrix obtained from a single Brownian

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trajectory by statistical binning process and, on the other hand the derivative spectra generated from the average of 100,000 Brownian trajectories has been made and shows a very good agreement. In addition to that, extension to other coordinates, i.e., other rotation angles and hidden dynamics is noted. It is believed that this framework would fit into any given potential since it can record every possible jump in the resolution of the time step of the given Brownian trajectory, i.e., MD simulation trajectory. It also allows a faster parametrization process with less computational time by reducing the set of variables.

This article is organized as follows: The Kubo-Anderson process with s-state Markov model, generalization to s-state Kubo-Anderson process with discrete rotational diffusion, and continuous isotropic diffusion processes are overviewed in Secs. II, III, and IV respectively. In Sec. V, a reduction scheme from continuous coordinates to discrete coordinates by using statistical binning process is introduced, and put to a test for the nitroxide example. Finally, we note an extension scheme to other coordinates and discuss modeling different diffusion processes in Markov dynamics.

II. MARKOV STATE MODEL FOR DIFFUSION

For a Markov process, the master equation for microstate probability vector \( \langle p(t) \rangle \) is given as

\[
\frac{d \langle p(t) \rangle}{dt} = \langle p(t) \rangle K,
\]

where \( K \) is the transition rate matrix per unit time whose elements \( K_{ij} \) represents the transition rate from microstate \( i \) to \( j \), so that it is basically the diffusion operator. The time-dependent average magnetization is a function of these microstates, and it can be written as \( M(t) = \langle M(t) \rangle |p(t)\rangle \). Thus, the time evolution of probability-weighted magnetization vector is given as a Kubo-Anderson process.

\[
\frac{d \langle M(t) \rangle}{dt} = \langle M(t) \rangle (i\Omega + K),
\]

where \( \Omega \) is a diagonal matrix with the eigenfrequencies of the Hamiltonian. Here, \( \Omega \) is independent of time if the microstates are stationary. The decay rate of the average magnetization is given by the transition rate matrix. The cw-ESR signal is obtained from the Fourier transform of the time-dependent average magnetization. Taking the Fourier transform of both sides and multiplying by \( \omega \) in the resolution of the time step of the given Brownian trajectory, i.e., MD simulation trajectory; it also allows a faster parametrization process with less computational time by reducing the set of variables.

Finally, we note an extension scheme to other coordinates and discuss modeling different diffusion processes in Markov dynamics.

III. ISOTROPIC ROTATIONAL DIFFUSION IN DISCRETE FORM

MSM model can be used for describing the rotational diffusion process for molecules by using a discretized form of diffusion equation. The Hamiltonian that we consider here is the case where we have stationary eigenkets, i.e., we neglect the \( I_+ \) and \( I_- \) terms,

\[
\frac{H(t)}{\gamma_c} = \frac{1}{g_e}B_0 g_{zz}^{lab}(t)S_z + S_z A_{zz}^{lab}(t) I_z.
\]

The components \( g_{zz}^{lab} \) and \( A_{zz}^{lab} \) are found by a transformation using Euler angles \( (\phi, \theta, \psi) \) on the diagonal matrix consisting of their xx, yy, and zz components in the molecular frame. For the cases in which their plane components x and y are equal to each other, i.e., \( A_{xx} = A_{yy} \) and \( g_{xx} = g_{yy} \), the only relevant diffusion coordinate is the angle \( \theta \). Their transformation is given as

\[
g_{zz}^{lab} = \cos^2(\theta(t)) g_{zz}^{mol} + \sin^2(\theta(t)) g_{xx}^{mol} - \text{tr}(g)/3,
\]

\[
A_{zz}^{lab} = \cos^2(\theta(t)) A_{zz}^{mol} + \sin^2(\theta(t)) A_{xx}^{mol}.
\]

In the MSM model of rotational diffusion, \( \theta \) is discretized according to the number of states \( s \) in the form \( \theta_k = (k - \frac{1}{2}) \Delta \theta \), where \( k=1,2,...,s \) and \( \Delta \theta = \pi/s \). Following the arrangement of microstates, the purpose is to find the transition rate matrix \( K \) for the discretized \( \theta \) coordinate. The calculation of the transition rate matrix from the discretized form of the rotational diffusion equation by using finite difference method is given in detail in Ref. The model applies the same procedure with reflective boundary conditions, and use transition rate matrix \( K \) to solve Eq. (3), which takes much less time than taking average over various diffusion trajectories. The magnetization is a summation over different orientations of the nuclear spin \( m = -1, 0, 1 \), i.e., \( M_{+m}(t) = \sum_m M_{+m}(t)/3 \), where the magnetization components have their distinct time evolution \( M_{+m}(t) = \langle M_{+m}(t) | p(t) \rangle \), and therefore it
is convenient to solve their contribution on the absorption spectra $I(\omega)$ separately and add them together. As said before, the matrix $\Omega$ is the eigenfrequency matrix, whose components are in this case

$$\frac{\hbar \nu^m}{\gamma_e} = \frac{1}{g_e} B_0 g_{zz}^{lab} + m A_{zz}^{lab}. \quad (8)$$

Finally, for isotropic rotational diffusion, we have $\langle v_{eq.} \rangle = \langle \sin(\theta) \rangle$ in Eq.(3).

IV. ISOTROPIC ROTATIONAL DIFFUSION IN CONTINUOUS FORM

Another approach to this problem suggests generating Gaussian or uniform diffusion trajectories using the relevant diffusion constant and implying equilibrium conditions [11]. Accordingly, the rotation angle $\theta$ is continuous, i.e., we can reach any angle between 0 and $\pi$, but the time-axis is discretized.

The diffusion equation using the Euler angles is solved by the Itô process [36, 37]. The equation of motion for angle $\theta$ is given as

$$\Delta \theta_n = \sigma \Delta X_n + \frac{\sigma^2}{2 \tan \theta_n}, \quad (9)$$

where $n$ is the time step, $\Delta X_n$ is the Brownian with mean zero, and $\sigma = \sqrt{2D\Delta t}$. The second term in Eq.(9) is due to the potential maintaining the path being in spherical coordinates. When this process is carried out by using a finite $\Delta t$, it makes strong jumps near the boundaries $\theta = 0$ and $\theta = \pi$, which would cause a random noise. In order to get rid of this problem, it is convenient to take $\Delta t$ as small as possible, but this takes more computational time. Alternatively, this problem is solved by using quaternion based Monte-Carlo approach [23, 35].

The absorption spectrum is calculated through the Fourier transform of the average magnetization, i.e.,

$$I(\omega) = \sum_m \int_0^T \langle M_+^m(t) | p(t) \rangle e^{-i\omega t} dt, \quad (10)$$

where again the normalization factor for intensity is ignored. The contribution of each trajectory to the magnetization is done by introducing their initial configuration from the equilibrium distribution, i.e., $p_{eq.}(\theta) = \sin(\theta)$.

The comparison of the derivative spectra calculated from Brownian trajectories and MSM model is given in Fig. 1, to point out once more the equivalence of two methods. The magnetic tensor parameters are given as

$$\langle g_{xx}, g_{yy}, g_{zz} \rangle^{mol} = (2.00210, 0.00210, 2.00775) \; G, \quad (11)$$

$$\langle A_{xx}, A_{yy}, A_{zz} \rangle^{mol} = (6.62, 6.62, 33.09) \; G. \quad (12)$$

For the discrete jump model, the convergence is reached with just $s = 36, 18, 12$ states for $D = 10^6, 10^8, 10^{10}$.
rad/s respectively. Thus, a lot of computational effort has been eliminated and minimized.

V. REDUCTION FROM CONTINUOUS SPACE TO DISCRETE COORDINATES

Reduction to finite number of microstates from the continuous model is done first by creating the discretized angle axis with the angle set $\theta = \theta_1, \theta_2, ..., \theta_s$, and then using binning procedure for the angle such that if angle $\theta(t)$ is between $\theta_k - \Delta\theta/2$ and $\theta_k + \Delta\theta/2$, it is set as $\theta(t) = \theta_k$ (Fig. 2). Accordingly, all the angles can be defined in such manner, and then we should be able to determine the transition probabilities between microstates.

![Diagram](image)

FIG. 2: Simple reduction scheme from continuous to discrete coordinates for a Brownian trajectory for the $s=4$ MSM model. If a point in the trajectory falls into one of these gridlines, it takes the value of that bin. Calculation of the transition matrix is done using the discretized coordinates determined by this scheme.

The solution to Eq. (1) is simply:

$$\langle p(t) \rangle = \langle p(0) \rangle |U(t)$$  \hspace{1cm} (13)

or

$$\langle p(t + \Delta t) \rangle = \langle p(t) \rangle |U(\Delta t)|$$  \hspace{1cm} (14)

where $U(t) = e^{Kt}$ is the propagator for the microstate probability vector, or simply the transition probability matrix. In order to create the transition matrix from a Brownian diffusion trajectory, we should first be able to calculate the propagator matrix, take its matrix logarithm, divide by $\Delta t$. Our interest is in Eq. (14) and since we allow at most a single jump within a time step $\Delta t$ and only one component of $\langle p(t) \rangle$ is equal to 1 in a random trajectory, we may define $\langle p(t) \rangle = \langle i \rangle$ and $\langle p(t + \Delta t) \rangle = \langle j \rangle$, where $\langle i \rangle$ and $\langle j \rangle$ are chosen among the orthonormal eigenbasis of microstates. Multiplying both sides by ket $\langle j \rangle$ gives the matrix elements of $U(\Delta t)$.

![Diagram](image)

FIG. 3: Derivative spectra generated from 100,000 Brownian trajectories (blue line) with time step $\Delta t=0.005$ ns, $\Delta t=0.025$ ns, $\Delta t=0.5$ ns and calculated from MSM model (red line) with transition matrix obtained from a single Brownian trajectory with 40,000 time steps having $s=12, 18, 36$ states from bottom to top are compared. The two results are indistinguishable on the scale of this figure. Lorentzian broadening with $T_2=0.8$ G is used. The magnetic tensor parameters are given in Eqs. (11,12).
1 = \langle i | U(\Delta t) | j \rangle. \quad (15)

Single jump at a time means that there is a contribution to a single component \((i,j)\) of the matrix \(U(t)\) at each time step. Therefore, we should cover a long trajectory, and then take an average. The total probability of transitions from a state should be conserved, hence we should normalize the rows of the transition probability matrix \(U(t)\).

The resolution of the transition probability matrix will be determined by the number of timesteps we take into account, and typically a minimum of 10,000 time steps is needed in order to have a reliable transition matrix. In this study, up to 40,000 time steps from single Brownian trajectories are taken into account, which is especially needed when approaching the rigid limit, i.e., for \(D = 10^6\) rad/s in Fig. 3.

Finally, the equilibrium probability density vector can be determined from both transition matrix or occupancy rates. In this study we use the latter. Now we have all entries for Eq.(3) and Eq.(4) and can solve for the absorption spectrum. Alternatively, one can always calculate the average magnetization in time domain with the given ingredients. The comparison between the derivative spectra generated from 100,000 Brownian trajectories and from MSM model with transition matrix obtained from a single Brownian trajectory with 40,000 time steps is given in Fig. 3.

This approach can easily be applied to the calculation of absorption spectra from a single MD trajectory, and resolution of time steps can be taken same as the relevant MD simulation. One would get the correct motional process including the potential change due to internal dynamics, since the transition matrix records every possible type of jump in the trajectory. Hence the slowly varying potential changes due to hidden variables will not be disregarded. In the next section, the extension to another rotation angle will be demonstrated and we will discuss the possibilities of having a continuous spatial diffusion entangled to a m-state Markov model.

VI. EXTENSION TO OTHER COORDINATES

The diffusion operator that we want to consider is in the form

\[
D = \frac{\partial^2}{\partial \phi^2} + \frac{\partial^2}{\partial \psi^2}. \quad (16)
\]

Let us define the transition rates for diffusion operator for angle \(\theta\) with \(s_1 \times s_1\) matrix \(K_\theta\) and for the operator \(D \partial^2/\partial \psi^2\) with \(s_2 \times s_2\) as \(K_\psi\) matrix, where \(s_1, s_2\) are the numbers of eigenstates for angles \(\theta\) and \(\psi\) respectively. Hence, the transition rate operator in Eq.(3) will be a \(s_1 s_2 \times s_1 s_2\) matrix

\[
K_{\theta \psi} = K_\theta \otimes I_{s_2} + M \otimes K_\psi. \quad (17)
\]

\(M\) is a \(s_1 \times s_1\) diagonal matrix with elements \(1/sin^2(\theta_k)\) remembering \(k = 1, 2, ..., s_1\). The transition matrix in this case is expanded in \(|\theta, \psi\rangle = |\theta\rangle_{s_1} |\psi\rangle_{s_2}\) space,

\[
|\theta, \psi, m\rangle = |\theta\rangle_{s_1} |\psi\rangle_{s_2} |m\rangle_3, \quad (18)
\]

where \(\theta, \psi, m\) are respectively \(s_1, s_2, 3\) dimensional vectors. At equilibrium, the state vector becomes \(|\sin \theta\rangle |1\rangle\). Thus, it is the general formalism for an electron spin that is coupled to a magnetic field and nuclear spin, on a rotating frame with Euler angles \((\theta, \psi)\). For simplicity, we eliminated the ket \(|m\rangle\), in Sec. III, by calculating a simple summation over \(m\) states. The equation for absorption spectra in Eq.(3) becomes

\[
I(\omega) = \langle 1 | \langle \sin \theta \rangle (i\omega - i\tilde{H} - K_{\theta \psi m})^{-1} |1\rangle_{s_1 \times s_2 \times 3}, \quad (19)
\]

where \(\tilde{H}\) is the Hamiltonian extended to \(\theta\) and \(\psi\) basis. We have concluded that the Hamiltonian in Eq. (19) is our relevant Liouvillian operator using the Hermiticity of both the Hamiltonian and the density matrix [38].

Having a process such as spatial diffusion of molecule under a potential that is an element of \(m\)-state potential space in which the potential is selected by a Markov process, may be helpful in understanding the effect of conformational changes in the spin dynamics [25]. For example, a diffusive process that has a \(m\)-fold selective potential for the angle \(\theta\) can be introduced, such as with \(m=A\) state for \(\theta \in [0, \pi/2]\) and \(m=B\) state \(\theta \in [\pi/2, \pi]\). This will help to get a quick feedback about the credibility of the model for the given MD simulation results by reducing the set of variables. If the simulations are done distinctly for two different types of potentials [21, 22], then the overall transition rate matrix can be created by their extension to the potential subspace, i.e., taking their kronecker product with potential change rate matrix, and summing them up. Alternatively, these two simulations can be defined in one transition probability matrix, by adding their records of jumps as if they are in the same trajectory, one being in the starting section, and the other in the second section, and their own lengths in time axis will be directly related to their equilibrium distribution and transition rates among these two types of potentials.

VII. CONCLUSION

We have simulated the cw-ESR spectrum of a spin-1/2 electron coupled to a magnetic field and spin-1 nucleus for X- and Q-bands by using both discrete isotropic rotational diffusion and continuous Brownian diffusion processes. In addition to that, calculated derivative spectra from the MSM model with transition matrix obtained from a single Brownian trajectory by statistical
binning process and the spectra generated from the average of 100,000 Brownian trajectories are compared and resulted in a very good agreement. It is suggested that this method can be implemented to calculate absorption spectra from MD simulation data. One of its advantages is that due to its reduction of computational effort, the parametrization process will be quicker. Secondly, the transition matrix defined in this reduction scheme is considered to record every possible type of jumps in the time evolution, so that it will take into account automatically the effective internal dynamics. Thirdly, one can calculate the ESR spectra from a MD trajectory without extending it artificially in the time axis. On the other hand, if there is a requirement of high precision in the extended coordinates, it will enlarge the transition matrix and therefore will take more computational time. It is hoped that, in the following studies, this framework will be helpful in extracting the statistics of motional information of a molecule under any kind of potential.

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