Origin of $1/f$ noise transition in hydration dynamics on a lipid membrane surface

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Water molecules on lipid membrane surfaces are known to contribute to membrane stability by connecting lipid molecules and acting as a water bridge. Although the number of water molecules near the membrane fluctuates dynamically, the hydration dynamics has been veiled. Here we investigate residence statistics of water molecules on the surface of a lipid membrane using all-atom molecular dynamics simulations. We show that hydration dynamics on the lipid membrane exhibit $1/f^\beta$ noise with two different power-law exponents, $\beta_i < 1$ and $\beta_h > 1$. By constructing a dichotomous process for the hydration dynamics, we find that the process can be regarded as a non-Markov renewal process. The result implies that the origin of the $1/f$ noise transition in hydration dynamics on the membrane surface is a combination of a power-law distribution with cutoff of interoccurrence times of switching events and a long-term correlation between the interoccurrence times.

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In numerous natural systems, the power spectra $S(f)$ exhibit enigmatic $1/f$ noise:

$$S(f) \sim \frac{A}{f^\beta} \ (0 < \beta < 2). \quad (1)$$

at low frequencies. In biological systems, $1/f$ noise has been reported for protein conformational dynamics [1–3], DNA sequences [4], biorecognition [5], and ionic currents [6–9], implying that long-range correlated dynamics underlie biological processes. Moreover, $1/f$ noise is involved in the regulation of permeation of water molecules in an aquaporin [3].

There are many mathematical models that generate $1/f$ noise including stochastic models [10–13] and intermittent dynamical systems [14–17]. The power-law residence time distribution is one of the most thoroughly studied origins for $1/f$ noise [12, 14–17]. In dichotomous processes, the power spectrum shows $1/f$ noise when the distribution of residence times of each state follows a power-law distribution with divergent second moment. For blinking quantum dots, which show a $1/f$ spectrum, residence times for “on” (bright) and “off” (dark) states have been experimentally shown to have a power-law distribution with a divergent mean [18, 19]. In stochastic models, this divergent mean residence time violates the law of large numbers which causes the breakdown of ergodicity, non-stationarity, and aging [20–23]. Conversely, the divergent mean residence time implies an infinite invariant measure in dynamical systems [24] and that the time-averaged observables are intrinsically random [24, 25].

In our previous work, we found that the residence times of water molecules on the lipid membrane surfaces followed power-law distributions [26, 27]. Therefore, it is physically reasonable to expect that the hydration dynamics on membrane surfaces also obey $1/f$ noise. Although little is known about the hydration dynamics, it is important to understand the dynamics of resident water molecules because these water molecules may play important roles in the overall dynamics of the membrane, and will affect membrane stability and biological reactions. In fact, such water molecules stabilize the assembled lipid structures [26, 28]; this water retardation increases the efficiency of biological reactions [27, 29, 30]. Water molecules enter and exit the hydration layer, and the number of water molecules near the lipid head group fluctuates.

In this letter, we perform a molecular dynamics (MD) simulation on water molecules plus a palmitoyl-oleoyl-phosphocholine (POPC) membrane at 310 K to investigate the hydration dynamics on the lipid surface [the details of the MD simulation are shown in [31]]. We find that fluctuations in the number of water molecules on the lipid surface show $1/f^\beta$ noise with two power-law exponents, i.e., $\beta_i < 1$ at low frequencies and $\beta_h > 1$ at high frequencies, and that the residence time distributions for “on” and “off” states follow power-law distributions with exponential cutoffs. Moreover, we construct a dichotomous process from the trajectory of the number of water molecules on a lipid molecule to clarify the origin of the two power-law exponents in the power spectrum. By analyzing the constructed dichotomous process, we find that there is a long-term correlation in residence times, which causes two different power-law exponents in the power spectrum.

Fluctuations of water molecules on the lipid head group.—We recorded the number of water molecules for which the oxygens were within interatomic distances of 0.35 nm from all atoms in lipid head groups [Fig. 1A]. The number fluctuates around an average of about 14. The number fluctuates around an average of about 14. Figure 1B shows the ensemble-averaged power spectral density (PSD) obtained from the average of the power spectra for the number of water molecules at 128 lipid molecules. The power spectrum exhibits two regimes with distinctive $1/f$ behavior. For frequencies above a transition frequency $f_t$, we have $S(f) \propto f^{-\beta_h}$ with $\beta_h =$.
1.35, while below this frequency we have \( S(f) \propto f^{-\beta_l} \) with \( \beta_l = 0.8 \); furthermore, the PSD shows a plateau at low frequencies. This crossover phenomenon is essential because \( S(f) \propto f^{-\beta} \) with \( \beta \geq 1 \) implies non-integrability and non-stationarity. We have confirmed that \( 1/f \) fluctuations of the number of water molecules are observed in boxes and spheres near the membrane surfaces but not in bulk water. A similar transition of the power-law exponent of the PSD has also been observed for the interchange dynamics of “on” and “off” states for quantum dot blinking \cite{32}. This behavior was described theoretically using an alternating renewal process, where the residence time distributions of “on” and “off” states are given by a power-law with an exponential cutoff \( \psi_{on}(\tau) \propto \tau^{-1-\alpha} e^{-\tau/\tau_c} \) and a power-law \( \psi_{off}(\tau) \propto \tau^{-1-\alpha} \) where \( \alpha < 1 \), respectively \cite{32}. The transition frequency \( f_t \) is related to the exponential cutoff in the quantum dot blinking experiment. In this case, the PSD exhibits aging, non-stationarity, and weak ergodicity breaking because the “off” time does not have a finite mean.

To confirm whether the aging effect appears in the hydration dynamics on the lipid surface, we calculate the ensemble-averaged PSDs for different measurement times [Fig. 1C]. The magnitudes of the PSDs do not depend on the measurement time \( t \), i.e. there is no aging. It follows that the power-law distribution with an exponential cutoff considered in \cite{32} cannot explain hydration dynamics on lipid membranes.

**Dichotomous process.**—To consider the origin of \( 1/f \) noise, we constructed a dichotomous, i.e. two state, process from the time series of the number of water molecules; the “on” \( (N' = 1) \) or “off” \( (N' = -1) \) states are when the number of water molecules on each lipid molecule is above or below, respectively, the average number \cite{32}. This behavior was described theoretically using an alternating renewal process, where the residence time distributions of “on” and “off” states are given by a power-law with an exponential cutoff \( \psi_{on}(\tau) \propto \tau^{-1-\alpha} e^{-\tau/\tau_c} \) and a power-law \( \psi_{off}(\tau) \propto \tau^{-1-\alpha} \) where \( \alpha < 1 \), respectively \cite{32}. The transition frequency \( f_t \) is related to the exponential cutoff in the quantum dot blinking experiment. In this case, the PSD exhibits aging, non-stationarity, and weak ergodicity breaking because the “off” time does not have a finite mean.

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frequencies comes from the exponential cutoffs in the power law distributions.

Origin of the transit 1/f noise.—One important question remains unclear: What is the origin of the transition in the 1/f noise? In other words, does power law intermittency or long-term memory (as expected for a non-Markov process) contribute to the transition in the 1/f noise? To address this question, we calculated the ensemble-averaged PSD for a shuffled time series of dichotomous processes, where residence times for “on” and “off” states were shuffled among themselves randomly. The ensemble-averaged PSD of the shuffled time series is different from that of the original time series of the dichotomous process [Fig. 3]. The transition in the 1/f noise disappears, although the power spectrum shows 1/f noise at high frequencies even after shuffling. The power-law exponent of $S(f) \propto f^{-\beta}$ at high frequencies is about 0.8, and the PSD converges to a finite value at low frequencies. This suggests that the transition in the 1/f noise originates from the non-Markovian nature of the hydration dynamics. Following our observations, we performed a numerical simulation in which time series of “on” and “off” states were generated with random waiting times drawn from a power-law distribution with an exponential cutoff, where $\alpha = 1.2$, on: $\tau_c = 60$, off: $\tau_c = 1000$. In Markovian dichotomous processes, the power-law exponent $\beta$ in the PSD is given by the power-law exponent in the residence time distribution, i.e., $\beta = 2 - \alpha$ as $\alpha < 2$ [15]. The power-law exponent $\beta$ observed here in the PSD is consistent with this relationship.

To clarify the correlation of residence times, we considered three types of time series of residence times: $\{\tau^1, \tau^2, \ldots, \tau^n\}$, $\{\tau^1, \tau^2, \ldots, \tau^n\}$, and $\{\tau^1, \tau^2, \ldots, \tau^n\}$. Figure 4A shows correlations between “on” and “off” residence times. There are positive correlations of residence times between the previous “on” state and the current “on” state or the previous “off” state and the current “off” state, and negative correlations of residence times between an “on” state residence time and the next “off” state time or an “off” state residence time and the next
“on” state time. Moreover, the ensemble-averaged PSDs of the three types of time series of residence times exhibit $1/f$ noise [Fig. 4B]. This result means that the residence times have a long-term correlation.

What is a biological significance of $1/f$ noise in hydration dynamics on lipid membrane surfaces? The roles played by the water molecules near the membrane depend upon their structure and dynamics. The $1/f$ noise attributed to a non-Markov renewal process can contribute to the stability of the hydration layer, which is important for membrane stability and physiological processes.

In conclusion, we have used all-atom molecular dynamics simulations to show that the number of water molecules on the lipid molecules exhibits $1/f$ noise. The power law exponents are different below and above the transition frequency $f_t$. There is a transition from $\beta_l < 1$ at low frequencies to $\beta_h > 1$ at high frequencies, although the power spectrum does not break ergodicity. Moreover, we provide evidence that the transition in the $1/f$ noise and ergodicity are caused by non-Markov power-law intermittency with exponential cutoff. These results are relevant to a broad range of systems displaying $1/f$ fluctuations.

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