Logarithmic Exchange Kinetics in Monodisperse Copolymeric Micelles

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Experimental measurements of the relaxation kinetics of copolymeric surfactant exchange for micellar systems unexpectedly show a peculiar logarithmic decay. Several authors use polydispersity as an explanation for this behavior. However, in coarse-grained simulations that preserve microscopic details of the surfactants, we find evidence of the same logarithmic behavior. Since we use a strictly monodisperse distribution of chain lengths such a relaxation process cannot be attributed to polydispersity, but has to be caused by an inherent physical process characteristic of this type of system. This is supported by the fact that the decay is specifically logarithmic and not a power law with an exponent inherited from the particular polydispersity distribution of the sample. We suggest that the degeneracy of the energy states of the hydrophobic block in the core, which is broken on leaving the micelle, can qualitatively explain the broad distribution of energy barriers, which gives rise to the observed nonexponential relaxation.

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Surfactant micelles are of special interest in a broad range of applications given their ability to spontaneously self-assemble when the surfactant concentration surpasses the so-called critical micelle concentration. The kinetics of chain exchange mechanisms have been found to be of paramount relevance in diverse industries, including drug transport and delivery systems in nanomedicine [1], foaming processes [2], and nanosurface design [3].

Research efforts have focused on the kinetic mechanisms relevant for micellar systems, either due to the change of micelle size and population (micelle fusion or fission), load exchange with the environment, or the dynamics of the surfactant exchange with the bulk solution. In particular, for block copolymer systems, the kinetics of exchange phenomena has been studied through diverse experimental techniques including temperature jump [4], ultrasonic relaxation [5], fluorescence cross-correlation spectroscopy 6]], and time-resolved small angle neutron scattering (TR-SANS) [7–12], which follows the traces of deuterated and hydrogenated copolymers when they redistribute in equilibrium micelles after mixing. The accepted theoretical framework for short surfactants [13,14] proposes a single relaxation mechanism for the exchange between the bulk solution and micellar aggregates. For longer molecules such as block copolymers Halperin and Alexander [15] followed the same assumption. From the definition of a time dependent relaxation function,

$$R(t) = \frac{f(t) - f(\infty)}{f(0) - f(\infty)}, \qquad (1)$$

where $f(t)$ is the fraction of labeled chains in the interior of the micelle at time t, these authors propose that $R(t) = \exp(-kt)$, where the exit rate constant k is only determined by the intermolecular interactions. Therefore, the energy barrier predicted for the escape rate depends on the length of the polymer, according to $k \sim \exp(-\Delta E/k_B T)$, where $\Delta E \sim N^\beta$ with N being the length of the hydrophobic block, and β takes a value between $2/3$ and 1, depending on the nature of the chain [9,16]. From this analysis a monodisperse sample should show a single exponential decay.

In contrast, more recent TR-SANS experiments for a series of block copolymer systems suggested the existence of a broad distribution of relaxation times [7,8] through a characteristic logarithmic dependence $R(t) \sim -\ln t$. Based on the aforementioned theoretical perspective, it has been argued that polydispersity is responsible for the observed behavior due to the assumed variation in the height of the energy barrier with polymer length [6,9,10,12,16].

However, we show that this nonexponential decay is present in monodisperse samples. Effectively, dynamic self-consistent field calculations with model triblock copolymers for a solution of identical copolymers suggest the existence of a broad distribution of escape rates. The molecular details of the model, chosen to mimic the experimental system, allows our simulation to reproduce the observed logarithmic decay over at least two time decades, similar to the one experimentally observed. Therefore, although polydispersity is expected to play a very important role, we can conclude that such a logarithmic decay must be due to an inherent mechanism of the polymer dynamics in a micelle, and not only as a result of any polydispersity in the experimental samples.

Theoretical analyses of the dynamics of micelles are scarce. Only a small number of simulation studies based on Monte Carlo (MC) simulations, molecular dynamics, dissipative particle dynamics, and Brownian dynamics have been used to study the kinetics of micellization and equilibrium exchange for oligomeric and polymeric systems [17–24]. Even fewer authors have addressed in detail the exchange mechanisms in dynamic equilibrium [18,20,21,23,24]. In these studies several issues impair an appropriate understanding of the physical process, for instance, the discretized space used in lattice simulations [20,21], a loss in accuracy for some coarse grained models [17], or the restriction of the study to short surfactants due to highly demanding computations [18].

Mean-field methods are interesting alternatives for copolymer systems given their proficiency when predicting and comparing results with available experimental data. In this work we employ the so-called single-chain mean-field (SCMF) theory, which has been shown to efficiently predict equilibrium properties for short and copolymeric surfactant systems [25,26]. The SCMF theory describes a single chain subject to the influence of its intramolecular and intermolecular interactions, the latter obtained self-consistently. The intramolecular interactions are determined explicitly while the intermolecular interactions with the solvent and other polymer chains are calculated in terms of the mean molecular fields of both the solvent and average chain density. The input to the theory comes from the set of chain conformations $\{\alpha\}$, and the outputs are the probability density function $P[\alpha]$ and the solvent concentration profile that minimize the free energy functional [25–27]. The SCMF theory allows for the use of nonoverlapping chains with the intramolecular steric repulsions explicitly taken into account. This situation differs from other self-consistent field methods [28] in which chains with no explicit separation between inter- and intrachain interactions (Gaussian chains) are used to represent surfactant conformations, leading to a less accurate estimation of the free energy. To address the surfactant kinetic exchange, we have developed a dynamic version of the SCMF technique to monitor the entry (exit) of surfactant chains into (from) a micellar aggregate, in order to evaluate $R(t)$ as reported in TR-SANS experiments. We chose the nonionic triblock copolymer $HO(CH_2CH_2O)_{10}(CH(CH_3)\times CH_2O)_{23}(CH_2CH_2O)_{10}H$, also known by the trade name Pluronic L44 ($EO_{10}PO_{23}EO_{10}$), which belongs to the same family used by Zana *et al.* [29].

The coarse-grained model is taken from a previous work [26] where a model for Pluronic surfactants was successfully developed to predict the critical micelle concentrations via the equilibrium SCMF. Both hydrophilic EO and hydrophobic PO units are modeled as hard spheres of size σ, and individual chains are taken as nonoverlapping beads separated by σ. The rigidity of the chain is included by rigid Kuhn segments of four and five beads for the PO and EO segments, respectively. In the case that the length of a block and the Kuhn segment length are noncommensurable, we consider the residual beads as one rigid segment of shorter length. Individual chain intramolecular and intermolecular interactions are modeled through short-range square-well potentials for each bead in spherical volumes with inner and outer radii of σ and 1.62σ. Only three crossinteractions are considered through Flory-Huggins parameters, namely, EO-PO, EO-solvent, and PO-solvent with corresponding values of 0.006, 0.5, and 2.1. To build the dynamic SCMF we consider that the set of sampling chains $\{\alpha\}$ evolves in time through a Metropolis algorithm used in MC simulations of polymer systems [30], which respects the nonoverlapping nature of the polymer chains. Hence, one accepts or rejects trial moves between t_{cyc} and $t_{\mathrm{cyc}}+1$ cycles with individual probabilities

$$p(\alpha_{t_{\mathrm{cyc}}\to t_{\mathrm{cyc}}+1}) = \min\left(1, \exp\left(-\Delta H[\alpha]/k_B T\right)\right), \qquad (2)$$

where $\Delta H[\alpha] = H[\alpha_{t_{\mathrm{cyc}}+1}] - H[\alpha_{t_{\mathrm{cyc}}}]$ is the energy difference for a modified α configuration in the mean field, which is obtained from an average over the ensemble of configurations $\{\alpha\}_{t_{\mathrm{cyc}}}$ at cycle t_{cyc}. This procedure proposes the use of an individual trial move for each sampling chain in every cycle in an independent way due to the mean-field nature of the free energy. Parallelization is thus a straightforward exercise. Ultimately, one obtains the evolution of the fields derived from the ensemble of chain configurations. Implicitly, we assume that the incompressible solvent instantaneously responds to the polymer density variations, with the configurational changes of the polymers being the longest characteristic time of the process, which is perfectly resolved within our procedure. This assumption is similar in spirit to the one proposed by Müller and Smith [31] for polymer blends, but it differs from alternative SCMF methods [32,33] where the temporal behavior is obtained from the solution of a set of diffusion equations, and consequently the conformational chain dynamics is lost.

The sampling chains are initially homogeneously distributed in the simulation box with periodic boundary conditions. The sum over the actual chain conformations in the so-called configurational set at a given instant of time permits the calculation of average properties, including the self-consistent fields. Each chain in the configurational set is moved at every cycle according to the aforementioned scheme, to simulate the dynamic evolution of the physical system. Simulations were performed in the canonical ensemble with 145 physical chains. In Fig. 1 a schematic diagram of a cross section of a micelle is given. In addition, three characteristic chain conformations during the exit process are highlighted. The temperature was $T = 37\,^{\circ}\mathrm{C}$ and the box size was fixed to $(70\sigma)^3$ with $\mathcal{N} = 182$ sampling chains in the configurational set. To estimate the finite size effects we ran simulations with different box sizes. The physical time per MC cycle, t_{cyc}, is related to the time scale in diffusion experiments, t, through the relation $t = t_{\mathrm{cyc}} D_{\mathrm{cyc}} l^2 / D\sigma^2$, where D_{cyc} and D are the diffusion coefficients obtained by the dynamic SCMF simulation in a dilute solution without micelles and the experimental one, respectively, while l is the physical dimension of σ, chosen to be 0.2 nm. The diffusion coefficient of an L44 chain can be estimated from the Stokes-Einstein relation $D = k_B T/(6\pi\eta R_h)$, where $\eta = 6.91 \times 10^{-4}$ kg/ms is the viscosity

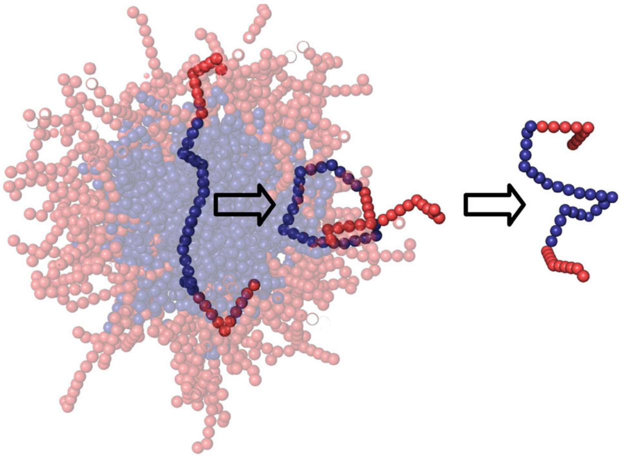

FIG. 1. Cross-section view of a micelle with an aggregation number of 145 for Pluronic L44, $EO_{10}PO_{23}EO_{10}$. The highlighted conformations correspond to three characteristic stages of a surfactant during the exit process. The red and blue beads represent hydrophilic EO and hydrophobic PO groups, respectively.

of water at 37 °C, and $R_h = 43\sigma/2 = 4.3$ nm is the hydrodynamic radius corresponding to the Rouse model for an L44 surfactant in this solvent. With this, the diffusion coefficients estimated from the simulation and the one from the Stokes-Einstein relation are $D_{\rm cyc} \approx 1.3 \times 10^{-3}\ \sigma^2/\text{cycle}$ and $D = 7.6 \times 10^{-11}\ \text{m}^2/\text{s}$, respectively, and hence, $t \approx 7.0 \times 10^{-13} t_{\rm cyc}$ s/cycle.

Once the system reaches thermodynamic equilibrium, we set $t = 0$ s and all the chains in $\{\alpha\}$ found in the interior of the aggregate are labeled. The exchange and reorganization of the chains with time is then monitored and represented through the autocorrelation function $R(t)$ defined in Eq. (1). Our relaxation function is comparable to the one used in the TR-SANS experiments [7–12]. In Fig. 2 a series of relaxation functions calculated from the dynamic SCMF simulations and Eq. (1) are presented for different simulation box sizes. As can be observed, the SCMF simulations are able to span several decades in time, presenting three well-defined regimes. First, we observe an initial regime that extends over one decade and is related to a fast reorganization of surfactants close to the inner core interface after the labeling. This trend has experimentally been observed for diblock poly(ethylene- *alt*-propylene)-poly(ethylene oxide) (PEP-PEO) [10] and poly(styrene)-poly[oligo(ethylene glycol) methyl ether methacrylate] (PS-POEGMA) [6] systems. Second, the central regime continues over more than two decades. This behavior corresponds to a gradual exit of the labeled chains. According to Fig. 2, the straight line behavior in this regime indicates that $R(t) \sim -\ln t$, which is similar to the experimentally reported behavior for different polymeric systems, as in the case of PEP-PEO [7,8,10], PS-PEP [9], PS-PEP-PS and PEP-PS-PEP [12], and PS-POEGMA [6]. In our system, this behavior must be the signature of the contribution of many relaxation times in the exit process, and cannot be caused by polydispersity because our chains are identical. This explanation was initially suggested by Lund and co-workers [7,8], although later the hypothesis that the polydispersity was the primary cause prevailed [9,16]. Therefore, our simulations unequivocally show that the logarithmic behavior is intrinsic in the nature of the system, which makes the theoretical perspective of the physics behind the system much richer.

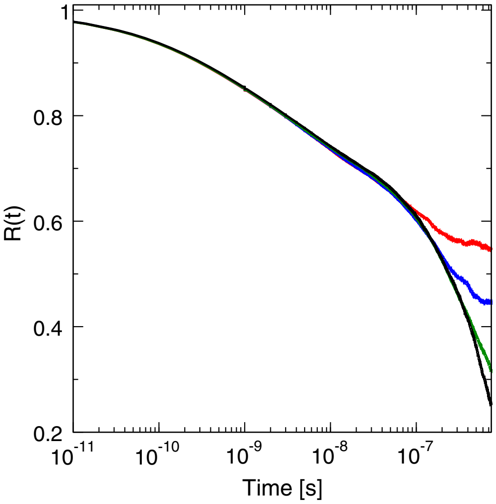

FIG. 2. Relaxation kinetics of the L44 micellar system predicted from dynamic SCMF simulations. The red, blue, green, and black lines refer to correlation functions obtained from simulation boxes with volumes $(25\ \text{nm})^3$, $(30\ \text{nm})^3$, $(35\ \text{nm})^3$, and $(40\ \text{nm})^3$, respectively, from top to bottom.

To shed some light on the physical nature of the process, let us assume that $n(x,t)$ is the number of tagged surfactants in the micelle at a given time t with a configurational dependent parameter x, not yet defined. We further consider that the surfactant escape rate is dependent on x and follows an exponential law $k(x) \sim k_0 \exp(-x/x_0)$, which is a reasonable assumption if one expects an Arrhenius form of the energy dependence of the escape rate. For constant x, the population at a given time is given by $n(x,t) = n(x,0)\times \exp(-k(x)t)$. Hence the autocorrelation function is expressed as

$$R(t) \sim \int dx n(x,0) e^{-k(x)t}. \tag{3}$$

In order to find the asymptotic behavior of this integral, we introduce the change of variable $dk/k = -dx/x_0$, which follows from the form of $k(x)$ assumed. If

$$R(t) \sim \int_{k_c}^{\infty} \frac{dk}{k} n(x(k),0) e^{-kt} \sim -\ln t, \tag{4}$$

then $n(x(k),0) \sim 1$ over a significant range of values of k, namely, x has a broad distribution. The physical cutoff k_c is introduced to avoid the $k \rightarrow 0$ divergence. Hence, the logarithmic regime is limited to time $t < 1/k_c$. If k follows an Arrhenius form, then Eq. (4) indicates that the population of surfactants in the micelle sees a very broad distribution of energy barriers, characterized by x. Moreover, x being a configurational property, one can further write

$$n(x(k), 0) = n_{\mathrm{eq}}(x) \sim e^{-E(x)/k_B T} g(x) \sim 1, \qquad (5)$$

where $g(x)$ is the density of states with a given x and $E(x)$ stands for the energy associated with x, according to the Boltzmann law. Notice that, since the system is in equilibrium, the initial distribution of tagged molecules with a given x should be the same as the equilibrium one. Therefore, the fact that $n_{\mathrm{eq}}(x) \sim 1$ indicates that the entropic contributions contained in $g(x)$ should compensate the energetic factor $\exp(-E(x)/k_B T)$.

The physically relevant question to be answered is then what type of physical property could be associated with this parameter x. We propose that x is proportional to the number of interchain contacts in the core of the micelle for the hydrophobic segment of a given surfactant. Let us distinguish between interchain and intrachain contacts between hydrophobic segments. As far as equilibrium considerations are concerned, the system does not distinguish between both in a core densely populated with hydrophobic segments. In this sense, the energy states are degenerated since many different conformations may have the same energy. However, if a given conformation is taken from the inner core and placed into the solvent, only the interchain contacts would be replaced by unfavorable hydrophobic segment-solvent contacts. As a consequence, the degeneracy of the states in the core is broken in the process of exiting, giving rise to a broad distribution of energy barriers. As a matter of fact, in the corona the dominant type of contacts are strongly repulsive hydrophobic segment-solvent contacts, since the solvent density in the corona is about 50%. Notice that this effect would be lost in a system of significantly shorter or more rigid chains, where the conformation space is reduced and, consequently, a much narrower spectrum of relaxation rates is then to be expected [11,34].

From our simulations one can extract information about the available volume for contacts of segments within the core with the surrounding medium, recalling that every chain conformation interacts with the mean field, characterized by the densities of hydrophilic, hydrophobic, and solvent units. Then, if $x = V$ is such an available volume, in jumping from the core to the corona, the energy barrier to be overcome is proportional to V times the energy jump involved in the change of the environment of the chain. The histogram of V from our simulations is very broad, with a standard deviation of about $36\sigma^3$, which corresponds to a standard deviation in the energy barrier of about $3.5 k_B T$, in our model, when the number of contacts and the energy differences are taken into account. The fact that this dispersion is larger than $1 k_B T$ demonstrates that the escape rates have to be exponentially distributed, as supposed.

To end our analysis of Fig. 2, the terminal regime is an exponential decay for the longest relaxation time with $t > 1/k_c$. The cutoff exit rate k_c is physically due to the finiteness of the chain. As can be observed in Fig. 2, as the size of the box increases, $R(t)$ deviates more markedly from the tendency of the central regime. Such a terminal regime has been subtly observed, but not sufficiently commented on, in experimental autocorrelation functions [9,12] devoted to stress the logarithmic behavior. However, the experimental analysis of Zana *et al.* [29] is completely devoted to the terminal regime. What we observe in our simulations agrees with the Alexander-Halperin predictions [15]. Moreover, without fitting parameters, the values of the exit rate constant found are quantitatively in agreement with the reported values of Ref. [29] (for Pluronic L64 we find $k_c = 5.4 \times 10^5\ \mathrm{s}^{-1}$, while experimentally $2.0 \times 10^5\ \mathrm{s}^{-1}$ is found), which is a strong proof of the physical consistency of our approach [35]. During the exit process in this long time regime we observe that the hydrophobic block effectively crumples without collapsing when crossing the core-corona interface, to slightly swell later when entering the bulk and reach its equilibrium conformation. This swelling is probably due to the access of less constrained conformations than inside the micelle (see Fig. 1). A complete analysis will be found elsewhere.

In our simulations, smaller boxes show a slower decay due to the reentrance of tagged surfactants through the periodic boundary conditions. We can hence conclude that our explicit dynamic SCMF simulations are able to model the exchange mechanism of a triblock copolymer surfactant into and out of a micelle. We observe that the surfactant exchange kinetics in the simulation is consistent with the available experimental data, in which an unexpected logarithmic behavior is found in the central regime, which spans over more than two decades of time. Previous analyses attribute such nonexponential behavior primarily to the effect of polydispersity of the polymeric surfactants in the experiments. However, the same behavior is obtained in our calculations of a strictly monodisperse system. Although polydispersity can cause nonexponential decays in the autocorrelation function $R(t)$, due to its strong impact on the escape rate, we are convinced that the logarithmic decay expresses a fundamental physical mechanism in micelles of long flexible surfactants. From our point of view, the strength of the latter statement lies in the fact that the decay is logarithmic in particular, and not simply nonexponential with a system-dependent power law, fixed by the type of polydispersity distribution. Although rather heuristic, we have qualitatively rationalized a physical explanation for such a logarithmic behavior. The main argument proposes that different conformations are equally likely when the hydrophobic segment is immersed into the micelle core but, at the same time, its escape rate is exponentially hampered by a conformation-dependent energy barrier. Implicit in our analysis is the assumption that the chain conformations do not significantly vary during exit, at least when crossing the core-corona interface. Probably, the diffusion process and the conformational changes have quite similar time scales. However, the opposite is clearly wrong since the assumption that the conformational relaxation is faster than the chain expulsion would yield a single exponential relaxation process involving an averaged conformation. Therefore, our analysis provides a significant new insight into the understanding of the dynamic processes in micellar systems.

Finally, we ought to point out the limitations of our study. First, the SCMF simulations employ an implicit solvent that involves parameters whose temperature dependence is unknown. However, since experiments have been carried out over a range of temperatures, the study of the explicit temperature dependence of the phenomenon could shed some light on the validity of our arguments, particularly due to the assumed Arrhenius form of the escape rate k, which carries a specific temperature dependence. Second, simulations with different types of chains involving, for instance, shorter chains, or with a higher degree of rigidity, would also bring some additional insight into the origin of the observed logarithmic decay. We have simulated a few other cases of longer flexible Pluronics, obtaining the same qualitative behavior, although the general study for a large variety of chain types lies beyond the scope of the present work. Lastly, effects due to the correlated behavior of several chains cannot be described within the framework of self-consistent field theories. Unfortunately, fully microscopic molecular dynamics simulations, which would take such correlations into account, are extremely costly, as can be seen by the limited number of works available.

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