doi: 10.31674/book.2025ccbsse006

Dynamics of Micelle-Vesicle Interconversion: Mechanisms and Modulation

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Abstract

The self-assembly of surfactant molecules in an aqueous medium not only produces micelles with polar head groups outside and nonpolar groups inside the core but can also assume the form of vesicles with closed bilayers. The vesicular and micellar structures of the fatty acid molecules can interconvert between themselves as Micelle ⇄ Vesicle in a rhythmic fashion when they are coupled to a pH-oscillator. Based on a two-state model where the two states correspond to two different forms of the self-assembled system, this micelle-vesicle transition has been explored. The theoretical analysis of the numerical simulation of pH-oscillation induced hopping between the two states shows how the phase of chemical oscillation can be used to estimate directly the rate of transition between the two unmodulated states of the self-assembly.

Keywords: *Micelles; pH Oscillators; Surfactants; Vesicles*

Introduction

Surfactants are compounds that lower the surface tension of a liquid, allowing easier spreading and lowering of the interfacial tension between two liquids or between a liquid and a solid (Menger, 1979). Surfactant molecules having two moieties with antagonistic properties, a polar hydrophilic moiety and a nonpolar hudrophobic moiety self-assemble and form micelles beyond the critical micellization concentration (CMC) (Leng, Egelhaaf & Cates, 2003). Some surfactants self-assemble into closed bilayers to form vesicles (or liposomes when formed from phospholipids). There is evidence that at very low concentrations, surfactants start forming micelles that may turn into vesicles at higher concentrations (Ghosh *et al*., 2013). The transition between the micellar and vesicular structures of surfactant molecules has been a major area of research in the last several years. Andelman, Kozlov and Helfrich (1994) have presented a model of phase transition between micelles and vesicles. Their model predicted a first-order transition between micelles and vesicles depending on the relative concentration of the two components. The phase transition boundaries were calculated as a function of the specific areas of the two components, their spontaneous curvatures and elastic moduli. Structural transitions between different forms of surfactant assembly are important in connection with drug targeting, which may be carried out using liposomes (vesicles) of phospholipid mixed with single-chain surfactants. Lagzi *et al*. (2010) have shown that the rhythmic interconversion of nanoscopic oleic acid (OA) vesicles and micelles can be controlled by a pH oscillator when coupled to a system of self-assembly of OA molecules. Their experiment reveals that the dynamic interconversion of micellar and vesicular structures of OA molecules critically depends upon the pH of the methylene glycol-sulphite-gluconolactone (MGSG) oscillator system.

As the two forms of molecular self-assembly are the distinct thermodynamic equilibrium states characterised by definite free energies, it is worthwhile to understand the rate of transition between the two different states when they are unmodulated. The focus of the present paper is to construct a two-state model of interconversion of the two forms. In what follows, a two-state model has been considered corresponding to a double well potential, and based on a rate equation approach, examine the modulation of the activation barrier for the interconversion. The numerical simulation of the differential equations for the coupled dynamics of the pH oscillator (MGSG)-two-state (micelle-vesicle) system is carried out to estimate the rate from the phase of oscillation of micelle (or vesicle) concentration.

Micelle-Vesicle Transition and a Two-State Model

The methylene glycol-sulphite reaction is a hydroxide ion clock reaction in batch, and this reaction displays complex behaviour in a flow reaction. Kovacs *et al*. (2007) have demonstrated a coupling mechanism of this reaction with hydrolysis of gluconolactone to create an organic-based pH oscillator. In this oscillator model the pH oscillates between 7 and 10. The detailed reaction scheme for the various species is given in Table 1. The dynamics of the stock solutions for different molecular and ionic components are governed by the kinetic equations which are discussed in detail. Furthermore, the dynamics of the reactions in the flow reactor are followed according to the scheme, which also includes all the rate constants as referred to. The flow rate k_0 is used as a control parameter for the dynamics.

Following Lagzi *et al*. (2010) let us now couple the above-mentioned MGSG system to the self-assembly of OA molecules. The pH oscillation within the reactor has a time period of approximately 85 sec for the fixed flow rate $k_0 = 5.4\text{x}10^{-3}$ sec^{-1}. When the oscillator is in the low pH range (e.g., pH=7-8.3), OA molecules form membrane vesicles (bilayer structures), burying the hydrophobic chain and presenting inner and outer hydrophilic surfaces with interspersed protonated and deprotonated carboxylic groups. When the oscillator is in the high pH range, e.g., around 9.4, the OAs become deprotonated and form unilamellar micelles presenting COO^- head groups. In other words, they interconvert between themselves following the kinectics micelle ⇄ vesicle.

Introduction of Mass Action Kinetics

In order to explore quantitatively this interconversion of the two forms, two rate equations have been introduced following mass action kinetics

$$\frac{dn_a}{dt} = -k_{mv}(H^+)n_a + k_{vm}(OH^-)n_b \qquad (1)$$

$$\frac{dn_b}{dt} = -k_{vm}(OH^-)n_b + k_{mv}(H^+)n_a \qquad (2)$$

where n_a and n_b are the concentrations of the micelle and vesicles, respectively, and k_{mv} and k_{vm} are the rate constants, which depend on the concentration of H^+ and OH as shown (Sen, Riaz & Ray, 2008; Sen, Riaz & Ray, 2009).

The rationale behind such a choice of form of coefficients of n_a and n_b is as follows: Since the vesicle-micelle transition is assisted by H^+ or OH^- concentrations (controlled by the MGSG oscillator through dehydration of methylene glycol along with catalytic production of OH^- and hydrolysis of gluconolactone by OH^-, the autocatalytic species.) the scheme micelle ⇄ vesicle interconversion clearly suggests that the rate constants of Eq. 1 and Eq. 2 should be the functions of $[H^+]$ and $[OH^-]$ as the activation barrier is expected to be modulated by pH. This modulation is adiabatic in the sense that the rate of transition between the two states in the absence of modulation of the barrier is much faster than the modulation of the activation barrier. It is therefore assumed that very weak dependence of rate constants on H+ and OH^- ion concentrations in the following form:

$$k_{mv}(H^+) \sim \exp\left(\frac{-E_0 + \alpha[H\text{-}^+]}{RT}\right)$$

$$\sim k_{oa} + \alpha[H^+]$$

and

$$k_{vm}(OH^-) \sim \exp\left(\frac{-E_0 + \beta[OH^-]}{RT}\right)$$

$$\sim k_{ob} + \beta[OH^-]$$

Here E_0 and T refer to the activation barrier for the micelle-vesicle transition and the temperature, respectively. In the present problem the parameters k_{oa}, k_{ob}, α and β are adjusted in relation to the entries in Table I of Kovac *et al*. (Scot) and are set as $k_{oa} = 10^{-4}\ sec^{-1}$, $k_{ob} = 10^{-4}\ sec^{-1}$, $\alpha = 107\ M^{-1}\ sec^{-1}$ and $\beta = 105\ M^{-1}\ sec^{-1}$. The coupled dynamics of the MGSG oscillation, as well as the components in the flow reactor according to the scheme and the rate equations for the micelle-vesicle transition, are followed by numerical integration performed using the package XPPAUT. The method of integration was CVODE with a time step of 0.01 sec and the tolerance set at 1×10^{-7}.The results are shown in Figs 2 and 3 for the set of parameter values as mentioned. In Figure 1(a) it has been displayed the variation of pH as a function of time for the fixed flow rate $k_0 = 5.4 \times 10^{-3}\ sec^{-1}$. It is found that after some induction period, pH settles down for sustained oscillation with a time period of ≈ 85 sec, which can be estimated from Figure 2(b). The steady oscillations of concentration of micelle (*na*) and vesicle (*nb*) are shown in Figs. 2(a) and 2(b), respectively, after the lapse of the initial period of induction.

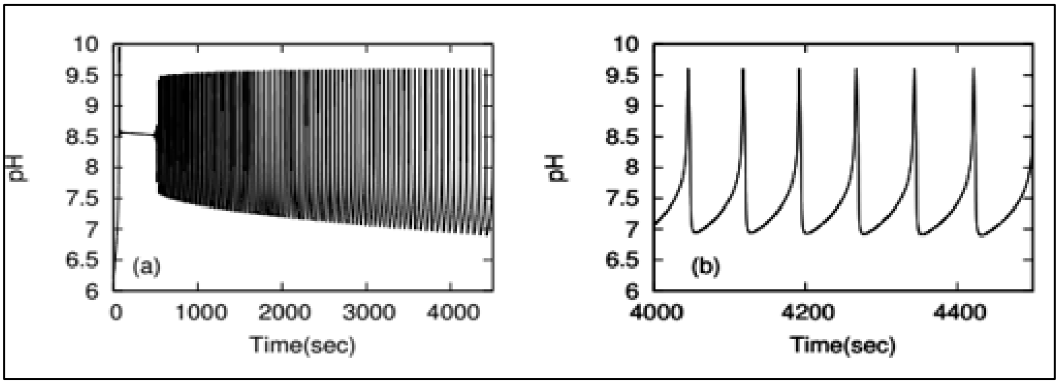

Figure 1: Oscillatory Variation of pH with Time (a) between t=0 to t=4500 sec, (b) between t=4000 sec to t=4500 sec for the Set of Parameter Values Mentioned in the Text and for the Flow Rate $k_0 = 5.4 \times 10^{-3}$

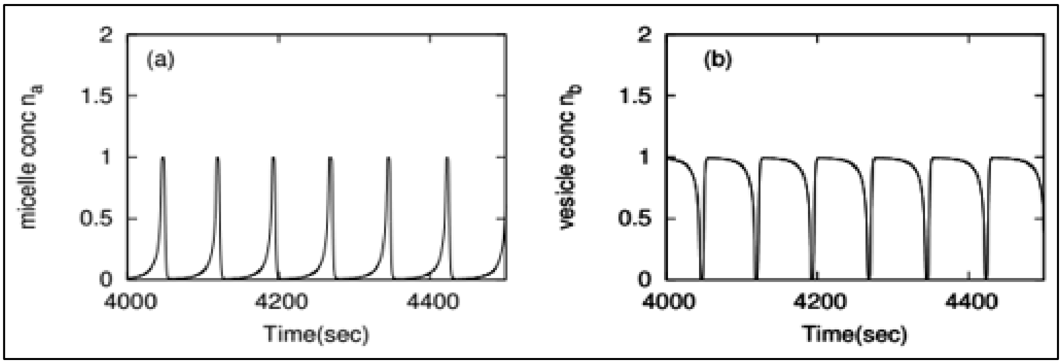

Figure 2: Variation of (a) Micelle Concentration n_a and (b) Vesicle Concentration n_b with Time for the Set of Parameter Values as Mentioned in the Text and for k_0=5.4 × 10^{-3} sec^{-1}

The dynamics of transition between the two states of molecular assembly are assisted by modulation of the pH oscillation of the MGSG oscillator. As the two states, i.e., the vesicle and micelle, are thermodynamically distinct, it is worthwhile exploring the unmodulated activation barrier and the associated Kramers rate. In the end, there has been a plan to make a theoretical analysis of the oscillation to estimate the rate of transition over the unmodulated activation barrier between the two states from the phase of the chemical oscillation.

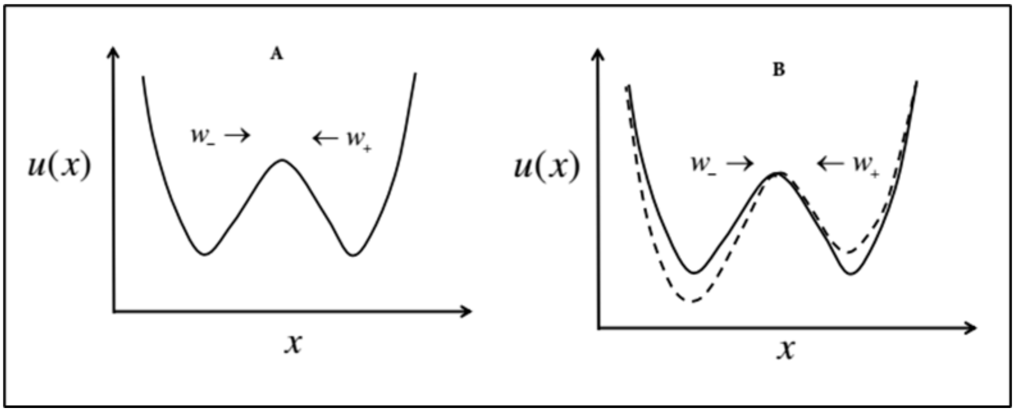

Figure 3: The Schematic Diagram of the Double Well in (a)Absence and (b)Presence of Periodic Modulation of the Barrier

Future Endeavours

There can represented in a schematic diagram a double well potential with two minima separated by a barrier. Micelles and vesicles are in each of the two wells of the double well. A natural simplification of this continuum model is a discrete two-state system. This two-state model has been used in widely different contexts, e.g., stochastic resonance, resonance activation, and dynamic hysteresis in polymer gel to name a few. Introducing transition probabilities for jumping from one well to another and then applying a probabilistic approach, the rate of transition can be calculated. This will be analysed in upcoming issues.

Conclusion

In this chapter a pH oscillator is considered an oscillator in conjunction with a pH-sensitive molecular assembly which can assume micellar and vesicular forms depending on the pH of the solution. The micelle and the vesicle are the two distinct stable thermodynamic states of the molecular assembly separated by an activation barrier. The oscillation of pH modulates the activation barrier, which leads to oscillatory population changes of the two species. It has been numerically simulated the dynamics of the pH oscillator (MGSG) coupled to the molecular self-assembly (oleic acid) to follow the oscillation of the two states. The oscillatory profile of the concentration of micelle/vesicle is planned to be analysed in light of the theoretical scheme for the two-state model in the next issues.

Acknowledgment: The author gratefully acknowledges Prof Debshankar Ray for his valuable support and encouragement throughout the course of this work.

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