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Dynamics of encapsulation and controlled release systems based on water-in-water emulsions: Liposomes and polymersomes

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ABSTRACT

The deformation relaxation behavior of two types of vesicles, liposomes and polymersomes, was investigated using a general nonequilibrium thermodynamics theory based on the interfacial transport phenomena (ITP) formalism. Liposomes and polymersomes are limiting cases of this theory with respect to rheological behavior of the interfaces. They represent respectively viscous, and viscoelastic surface behavior. We have determined the longest relaxation time for a small perturbation of the interfaces for both these limiting cases. Parameter maps were calculated which can be used to determine when surface tension, bending rigidity, spontaneous curvature, interfacial permeability, or surface rheology dominate the response of the vesicles. In these systems up to nine different scaling regimes were identified for the relaxation time of a deformation with droplet size, with scaling exponent *n* ranging from 0 to 4.

1. Introduction

Liposomes and polymersomes are vesicles formed by self-assembly of respectively lipids, and amphiphilic block-copolymers [1–3]. They are examples of water-in-water emulsions, i.e. dispersions of an aqueous phase in another aqueous phase. They have high potential as controlled release or encapsulation systems in, for example, food, pharmaceutical applications, or cosmetic products.

The dynamic behavior of these types of water-in-water emulsions is highly complex. Several models have been proposed to describe this behavior [4], but none of these models cover the full spectrum of variables that influence the dynamic behavior. In particular the coupling between deformation of the vesicles and the transfer of mass to and from the interior phase are not adequately accounted for. Recent studies have shown that in water-in-water emulsions these processes are strongly coupled, and that mass transfer has a significant effect on stress–deformation behavior, and vise versa, that the stress–deformation behavior can affect mass transfer [5–11].

Recently a general theory was developed for the dynamic behavior of droplets in water-in-water emulsions, that accounts for the coupling between deformation and mass transfer [4]. The theory is a nonequilibrium thermodynamics theory based on the interfacial transport phenomena (ITP) formalism [12]. It describes the thermal fluctuations of the interfaces of spherical droplets (or vesicles), without an imposed external flow field and without external force fields. Starting with the principles of conservation of mass and momentum for multiphase systems with excess parameters (surface mass density, surface momentum, etc.) associated with the interfaces, differential balances are derived for the bulk phases and interfaces of these systems [4]. With an appropriate choice for the constitutive equation of the mass flux vectors a coupling is introduced between the deformation of the interfaces, and mass transfer across these interfaces [4]. We will briefly review the essential elements of this theory in the next paragraphs.

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The velocity and pressure fluctuations in the bulk phases are calculated from the linearized equations of continuity and differential momentum balances:

$$\frac{\partial \delta\rho^{(i)}}{\partial t} + \bar{\rho}^{(i)} \operatorname{div} \mathbf{v}^{(i)} = 0 \tag{1}$$

$$\nabla P^{(i)} = \nu^{(i)} \nabla (\operatorname{div} \mathbf{v}) + 2\eta^{(i)} \operatorname{div} \mathbf{D}^{(i)} + \mathbf{f}^{h(i)} \tag{2}$$

where $\delta\rho^{(i)}$ are the fluctuations of the total mass density, $\bar{\rho}^{(i)}$ is the equilibrium total mass density, $\nu^{(i)} = \eta_b^{(i)} - \frac{2}{3}\eta^{(i)}$, $\eta_b^{(i)}$ is the bulk viscosity, $\eta^{(i)}$ is the shear viscosity, $\mathbf{D}^{(i)}$ is the rate of deformation tensor and $\mathbf{f}^{h(i)}$ is the force resulting from thermal fluctuations. In arriving at (2) Newtonian behavior was assumed for both bulk phases.

The fluctuations of the position of the interface are calculated from the jump mass balances and the jump momentum balance [4]:

$$\frac{\partial R(\theta, \varphi, t)}{\partial t} - \lambda_p \left(P^{(1)} - P^{(2)} + \frac{2\gamma}{R_0} \right) - \left(\bar{z}^{(1)}_{(A)} v^{(1)}_r - \bar{z}^{(2)}_{(A)} v^{(2)}_r \right) = 0 \tag{3}$$

$$(\operatorname{div}_s \boldsymbol{\sigma}^s)_r + \left(\gamma_0 - kC_0R_0^{-1}\right) \nabla_s^2 R(\theta, \varphi, t) - \frac{1}{2} k \nabla_s^2 \nabla_s^2 R(\theta, \varphi, t) + P^{(1)} - P^{(2)} + \sigma_{rr}^{(2)} - \sigma_{rr}^{(1)} = 0 \tag{4}$$

where $R(\theta, \varphi, t)$ is the parametrization of the interface, (r, θ, φ) are spherical coordinates, λ_p is the permeability of the interface, $P^{(i)}$ is the pressure in phase i, γ_0 is the surface tension of the flat interface, k is the bending rigidity of the interface, and C_0 is the spontaneous curvature. R_0 is the radius of the non-deformed vesicle, $\bar{z}^{(i)}_{(A)} = \bar{\rho}^{(i)}_{(A)}/\Delta\bar{\rho}_{(A)}$, $\Delta\bar{\rho}_{(A)} = \bar{\rho}^{(1)}_{(A)} - \bar{\rho}^{(2)}_{(A)}$, $\bar{\rho}^{(i)}_{(A)}$ is the equilibrium density of species A in phase i, and $v_r^{(i)}$ is the r-component of the mass-averaged velocity in phase i; $(\operatorname{div}_s \boldsymbol{\sigma}^s)_r$ denotes the r-component of the surface divergence of the surface extra stress tensor $\boldsymbol{\sigma}^s$, ∇_s^2 denotes the surface Laplacian, and $\sigma_{rr}^{(i)}$ is the rr-component of the extra stress tensor of phase i.

Eq. (3) describes the time rate of change of the position of the interface as a result of a diffusive mass flux across the interface, and a convective term, proportional the difference in the bulk velocities evaluated at the interface. In arriving at (3) it was assumed that the mass flux vectors of species A in the mixture, evaluated at the interface, are given by

$$(\mathbf{j}^{(1)}_{(A)} - \mathbf{j}^{(2)}_{(A)}) \cdot \boldsymbol{\xi} = \lambda_p \Delta\bar{\rho}_{(A)} \left(P^{(1)} - P^{(2)} - \Delta\bar{P} \right) \tag{5}$$

where $\mathbf{j}^{(i)}_{(A)}$ denotes the mass flux vector of A in phase i, $\boldsymbol{\xi}$ is the unit vector normal to the interface, and $\Delta\bar{P} = -2\gamma/R_0$ is the Laplace pressure of the non-deformed droplet. By assuming (5) the interface is basically modelled as a permeable membrane. The equation predicts zero mass transfer when the droplet is not deformed, and predicts an increasing mass transfer with increasing deformation. As a result of the second term in the jump mass balance (3) this equation is coupled to the jump momentum balance (4) through the Laplace pressure drop that appears in the latter expression. This coupling gives us the coupling between mass transfer and stress–deformation behavior observed for these systems.

The first term in the jump momentum balance (4) represents the interfacial viscous stresses. It is through this term that we will incorporate the effects of the surface rheological properties of the interface on the relaxation behavior. The second and third terms in (4) are the familiar surface tension and bending rigidity terms we also encounter in for example membranes [13,14]. The last term in (4) represents the viscous stresses exerted on the interface by the adjoining bulk phases.

The set of four differential equations (1) through (4) needs to be closed with a constitutive equation for the surface extra stress tensor. In this paper we will focus on the dynamic behavior of liposomes and polymersomes, and for the extra stress tensor of the interfaces we will assume either viscous, or linear viscoelastic surface behavior [12]. The assumption of viscous behavior will be valid for liposomes with bilayers composed of simple lipids. For liposomes with more complex lipids, multilayer liposomes, and polymersomes a linear viscoelastic model would be more appropriate. The particular form of these constitutive models will be discussed in the next section. In Sections 3 and 4 we will use the model described above to study the dynamic behavior of liposomes and polymersomes. We will limit ourselves to the calculation of the longest relaxation time for a small perturbation of the interfaces in these systems, and subsequently analyze the scaling behavior of this relaxation time with droplet radius R_0. In spite of the fact that the theory is valid only for small deformations, it provides a lot of insight into the complex behavior of these systems (up to nine scaling regimes are identified). It also suggests new experiments to characterize the interfacial properties in water-in-water emulsions.

2. Rheological behavior of the interfaces

The surface extra stress tensor of viscous interfaces can be described with the linear Boussinesq model [15]. According to this model

$$\boldsymbol{\sigma}^s = (\varepsilon_d - \varepsilon_s)(\operatorname{div}_s \mathbf{v}^s)\mathbf{P} + 2\varepsilon_s \mathbf{D}^s \tag{6}$$

where ε_d is the surface dilatational viscosity, ε_s is the surface shear viscosity, $\mathbf{P}$ is the surface projection tensor, and