A THEORETICAL MODEL OF A THERMAL-SENSITIVE GEL PARTICLE WITH CORE-SHELL STRUCTURE

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Summary Gel particles which are sensitive to temperature play an important role in drug delivery systems. This work studies a hybrid gel particle where a thermal-sensitive poly(N-isopropylacrylamide) gel is coated by a shell of phospholipid bilayer. By treating the phospholipid shell as a layer of elastomer, we propose a theoretical model for this hybrid gel particle. Our model shows that in such a core-shell structure, the coating elastic shell can significantly affect the thermal-responsive behavior of the poly(N-isopropylacrylamide) gel core.

INTRODUCTION

Poly(N-isopropylacrylamide) (PNIPAM) gels have drawn increasing attentions due to their thermal-responsive behaviors. For example, a PNIPAM gel in an aqueous solution exhibits a dramatic volume transition in response to temperature changes [1]. In order to gain a fast response rate, PNIPAM gels are typically fabricated into micro- or nano-particles. PNIPAM-based microgels with the thermal-response time of several milliseconds have been reported[2]. Thus, owing to their small size and fast response, PNIPAM microgels have enormous potential for making on-demand drug delivery systems [3-6]. However, the biocompatibility of PNIPAM microgels has raised a lot of controversy, limiting their use as drug carriers. In view of this, some researchers coated a membrane of biocompatible material onto the outer surface of PNIPAM microgels, resulting in hybrid gel particles with core-shell structure [7-9].

THEORETICAL MODEL FOR THE THERMAL-SENSITIVE GEL PARTICLE

This work studies a hybrid gel particle where a spherical core of PNIPAM gel is coated by a shell of phospholipid bilayer [10-13]. The structure is obtained by polymerizing a solution of PNIPAM inside a phospholipid giant unilamellar vesicle. The phospholipid membrane, which is compliant and permeable to water, separates the PNIPAM core from the external pure water. This hybrid gel particle is prepared at a constant room temperature T_0, which is much lower than the volume transition temperature T_{tr} of the PNIPAM gel, as shown in Fig. 1a.

At the instant when the particle has been prepared, the phospholipid membrane is a shell of thickness δ; meanwhile, the core gel is a sphere with radius A and swells by an isotropic stretch λ_0 relative to its dry network. We assume that the outer surface of the core gel is fully bounded with the inner surface of the membrane. We assume that the outer surface of the core gel is fully bounded with the inner surface of the membrane. The membrane is assumed to have no physical or chemical interaction with the solvent and to be un-sensitive to temperature. When the temperature rises, the hybrid gel particle shrinks remarkably first, and then keeps its volume constant at temperatures above the volume transition temperature of PNIPAM gels, as shown in Fig. 1b. The process is reversible. When the temperature is cooled back to room temperature again, the hybrid gel particle re-swells and recovers its initial shape. Interestingly, it is observed that during the volume transition, the phospholipid membrane is compliant and is strongly bonded to the PNIPAM core [12,13]. Compared to a stand-alone PNIPAM microgel, the presence of this phospholipid membrane in the hybrid gel particle should affect the thermal-responsive behavior of the PNIPAM core.

In order to investigate the effects of the phospholipid membrane on the PNIPAM core, we propose a theoretical model for such a core-shell gel particle. In this model, we treat the phospholipid membrane as a layer of elastomer, which is characterized by the classical neo-Hookean model. For the PNIPAM core, we adopt a free-energy function which has two contributions. The first contribution comes from the stretching of the PNIPAM gel. The second contribution is the free energy arising from the mixing of PNIPAM gel with water molecules. In particular, this mixing free energy contains a dimensionless parameter χ, called mixing enthalpy, which depends both on temperature and the volume fraction of solvent in the PNIPAM gel.

The deformation of the hybrid particle is taken to retain spherical symmetry, so that the deformation in the PNIPAM core is homogeneous. Denote the homogenous stretch (relative to the dry state) in the core by λ_h, then the degree of swelling of the core gel is defined as λ_h^3. We also introduce a ratio, $\mu=\mu^m/\mu^c$, to describe the stiffness of the membrane, where μ^m and μ^c ae respectively the shear moduli of the membrane and the core gel. Figure 2 plots the variation of the degree of swelling λ_h^3 with the temperature T at several values of the relative elastic modulus μ. As expected, the PNIPAM core shrinks substantially as the temperature rises during the volume transition (i.e., $T<T_{tr}$), but keeps its volume unchanged when the volume transition is complete (i.e., $T>T_{tr}$). This trend is in good consistency with experiment data [12]. The figure shows that the stiffer the membrane is, the less sensitive the structure to temperature. That is, a stiff membrane may suppress the thermal-responsive behavior of the hybrid gel particle. On the hand, this

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trend also implies that the thermal-responsive behavior of the hybrid gel particle can be easily changed by coating an elastic membrane with appropriate shear modulus.

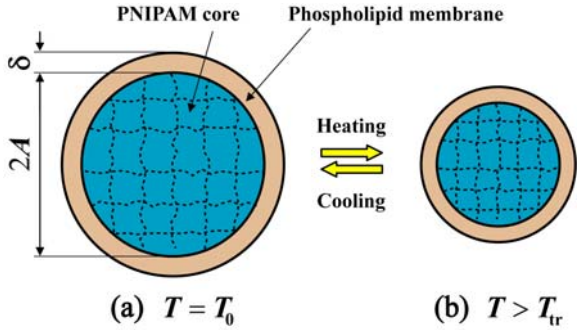

Fig. 1 A hybrid gel particle

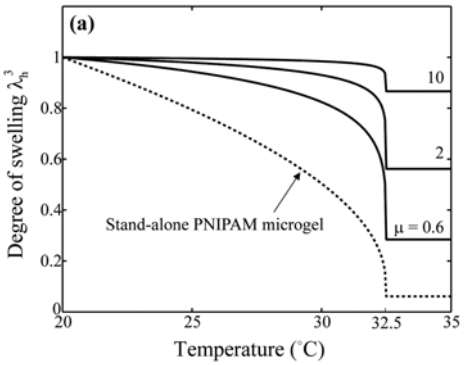

Fig .2 Degree of swelling λ_h^3 versus temperature

CONCLUSIONS

In this work, we have developed a theoretical model to account for the thermal-responsive swelling process in a hybrid gel particle of core-shell structure. Our result shows that the swelling behavior of the hybrid gel particle can be altered by changing the mechanical properties of the coating membrane, which may provide an efficient way to design new hybrid gel particles with appropriate thermal-responsive behavior.

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