Modeling of interfacial polymerization to nanocapsule formation

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Introduction

This work provides a better understanding for the effective control of the nanocapsules wall thickness. Polyamides based nanocapsules were prepared by the interfacial polymerization combined with spontaneous emulsification. A clear guideline of how a variety of factors, such as monomer concentration, diffusion, interfacial reaction, and water swelling influence the capsule formation is very important to the effective control of capsule wall structure and release performance. Different models for capsules have been developed in the literature [for instance see Enkelmann and Wegner (1972, 1975), Pearson and Williams (1985), Mikos and Kiparissides (1991), Janssen and Te Nijenhuis (1992a, 1992b), Janssen, Boersma and te Nijenhuis (1993), Ji et al. (2000, 2001a, 2001b)] but none of these models represents all the phenomena occurring in a satisfying way.

In this goal, the macroscopic plane models of the interfacial polycondensation between the diethylenetriamine and the sebacoyle chloride were studied experimentally. Firstly, the plane model is developed to examine the kinetic of the reaction and to perform the estimation of parameters thanks to the experiment measurements. Secondly, a spherical model is deduced from the first one. Conclusions are given on the properties of the wall of the capsule.

Experimental

An organic phase composed of a water miscible solvent (acetone), lipophilic monomer (sebacoyl chloride, A), oil and a lipophilic surfactant (Span® 85), is injected in an aqueous phase containing hydrophilic monomer triamine (diethylenetriamine) (B) and the hydrophilic emulsifying agent (Tween® 20). The water miscible solvent should diffuse to the aqueous phase, the oil precipitates as droplets, and the two monomers react at the interface, forming insoluble polymeric membrane around the nano emulsion leading to nanocapsules (see Bouchemal et al. (2004)).

Model development

The monomer B, present in the aqueous phase, diffuses towards the organic phase and reacts with monomer A at the interface of the polymer and the organic phase by forming polymer and the chloride acid (H): A + B = Polymer + H with the reaction rate $\mathrm{rs} = \mathrm{KC_A C_B}$. The polymer wall thickness results also on the swelling due to water sorption: Polymer + Eau = [polymer-water]

H, which diffuses through the membrane, reacts in the aqueous phase and in the polymer with the monomer B: H + B = B-protonic with the reaction rate $rv = kkC_B C_H$ and respectively $rv = kkC_{BP} C_{HP}$

The following assumptions for the spherical domain are made:

- Modeling is done on a population of identical particles of fixed diameter R_{em} = 200 nm.
- The radial coordinate $r=0$ at the center of the capsule. The internal radius $R(t)$ expands to the center of the capsule. $(R_{em}-R(t))$ results only from the reaction of polycondensation.
- The external radius $R'(t)$ expands outside of the capsule. $(R'(t)-R_{em})$ results only from swelling of polymer.

<u>Mass balance of B and H in the aqueous phase:</u>

$$-\overline{C_B}\frac{dR'(t)}{dt}+\frac{(R_i^3-R'^3(t))}{3R'^2(t)}\frac{d\overline{C_B}}{dt}=k_B(\overline{C_{BP}}-\overline{C_B})+kkC_{B0}\overline{C_B}\,\overline{C_H} \tag{1}$$

$$-\overline{C_H}\frac{dR'(t)}{dt}+\frac{(R_i^3-R'^3(t))}{3R'^2(t)}\frac{d\overline{C_H}}{dt}=k_H(\frac{\overline{C_H}}{X}-\overline{C_{HP}})+kkC_{B0}\overline{C_B}\,\overline{C_H} \tag{2}$$

<u>Mass balance of A in the polymer phase:</u>

$$\frac{R(t)}{3}\frac{d\overline{C_A}}{dt}+\overline{C_A}\frac{dR(t)}{dt}=K\overline{C_{A(R(t))}}\,\overline{C_{B(R(t))}}C_{B0} \tag{3}$$

<u>Mass balance of the polymer:</u>

$$\frac{dR(t)}{dt}=-\frac{M_p}{\rho_{app}}KC_{A0}C_{B0}\overline{C_{A(R(t))}}\,\overline{C_{B(R(t))}} \tag{4}$$

<u>Mass balance of the swelling:</u>

The variable $X(t)=\frac{V_e}{V_T}=\frac{R'^3(t)-R_{em}^3}{R'^3(t)-R^3(t)}$ represents the porosity of the polymer.

$$\frac{dR'(t)}{dt}=V_g\left(X_{eq}-\frac{R'^3(t)-R_{em}^3}{R'^3(t)-R^3(t)}\right) \tag{5}$$

<u>Mass balance of B in the polymer:</u>

We introduce the following coordinate transformation: $\varphi=\frac{r-R(t)}{R'(t)-R(t)}$ which introduces a new term related to convection (Alsoy S., Duda J.L, 2002), induced by the moving boundaries R(t) and R'(t):

$$(R'(t)-R(t))\frac{\partial\overline{C_{BP}}}{\partial t}+\frac{\partial\overline{C_B}}{\partial\varphi}\left[\frac{-dR(t)}{dt}-\varphi\frac{d(R'(t)-R(t))}{dt}\right]=$$
$$D_{BP}\frac{1}{\varphi(R'(t)-R(t))+R(t)}\left[\frac{2\partial\overline{C_{BP}}}{\partial\varphi}+\frac{\varphi(R'(t)-R(t))+R(t)}{R'(t)-R(t)}\frac{C_{B0}\partial^2\overline{C_{BP}}}{\partial\varphi^2}\right] \tag{6}$$

Boundary conditions:

at $\varphi = 1$ $$-D_{BP}\frac{1}{R'(t)-R(t)}\frac{\partial\overline{C_{B(R(t),t)}}}{\partial\varphi}\bigg|_{\varphi=1} = k_B\left(\frac{\overline{C_{BP}}}{X}\bigg|_{\varphi=1} - \overline{C_B}\right) + \frac{dR'(t)}{dt}\overline{C_{BP(\varphi=1)}} \quad (7)$$

at $\varphi = 0$ $$-\frac{dR(t)}{dt}\overline{C_{BP(\varphi=0)}} - D_{BP}\frac{1}{R'(t)-R(t)}\frac{\partial\overline{C_{BP}}}{\partial\varphi}\bigg|_{\varphi=0} = KC_{A0}\overline{C_{A(\varphi=0)}}\frac{\overline{C_{BP}}}{X}\bigg|_{\varphi=0} \quad (8)$$

Mass balance of H in the polymer (*HP*):

$$(R'_{(t)}-R_{(t)})\frac{\partial\overline{C_{HP}}}{\partial t}+\frac{\partial\overline{C_{HP}}}{\partial\varphi}\left[\frac{-dR_{(t)}}{dt}-\varphi\frac{d(R'_{(t)}-R_{(t)})}{dt}\right]= D_{HP}\frac{1}{\varphi(R'_{(t)}-R_{(t)})+R_{(t)}}\left[\frac{2\partial\overline{C_{HP}}}{\partial\varphi}+\frac{\varphi(R'_{(t)}-R_{(t)})+R_{(t)}}{R'_{(t)}-R_{(t)}}\frac{C_{B0}\partial^2\overline{C_{HP}}}{\partial\varphi^2}\right] \quad (9)$$

Boundary conditions:

at $\varphi = 1$ $$-D_{HP}\frac{1}{R'(t)-R(t)}\frac{\partial\overline{C_{HP(R(t),t)}}}{\partial\varphi}\bigg|_{\varphi=1} = k_B\left(\frac{\overline{C_{HP}}}{X}\bigg|_{\varphi=1} - \overline{C_H}\right) + \frac{dR'(t)}{dt}\overline{C_{HP(\varphi=1)}} \quad (10)$$

at $\varphi = 0$ $$-\frac{dR(t)}{dt}\overline{C_{HP(\varphi=0)}} - D_{HP}\frac{1}{R'(t)-R(t)}\frac{\partial\overline{C_{HP}}}{\partial\varphi}\bigg|_{\varphi=0} = KC_{A0}\overline{C_{A(\varphi=0)}}\frac{\overline{C_{HP}}}{X}\bigg|_{\varphi=0} \quad (11)$$

Simulation and discussion

The equations are spatially approximated by using an orthogonal collocation method Villadsen (1978) and are solved by Petzold-Gear method (routine DASPG in the IMSL library (Visual Numerics)). An improvement is necessary since we have to use an interpolation routine to update the values of the state variables at the collocation points. Because of the moving boundary problem, when the time is running, the collocation points do not represent the same spatial position. This routine INTPR is given in Villadsen (1978).

The experimental data used to estimate model parameters are obtained in plane geometry at macro scale. The plane geometry model is based on the same hypothesis than the previous model. The estimation procedure based on the time domain fitting of these macro-parameters gives completely different results, depending on the state variable change is performed or not. The optimization is performed by a Levenberg-Marquard procedure (subroutine DBCLSF of the IMSL library) and the criterion $J(\theta)$ to minimise with respect θ is the sum of the square difference between the experimental results and the simulated ones under the physical constraint that macroparameters are non negative: $J(\theta) = min_{\theta\geq 0}(\sum(y_{meas}(t) - y_{mod}(t))^2$.

The precision of each macro-parameter θ_j is calculated as following: $\hat{\theta}_j - s_{N-k}\sqrt{H_{jj}\sigma^2} < \theta_j < \hat{\theta}_j + s_{N-k}\sqrt{H_{jj}\sigma^2}$ where $\hat{\theta}_j$ is the estimate of θ_j, H_{jj} is the j^{th} diagonal element of the Hessian matrix H, s_{N-k} is the Student variable and σ^2 is the variance (to see Couenne et al., 2005). The Student variable is chosen to have a confident interval of 95%.

Estimated parameters	(Value ± precision)
X_{eq}	(0.671 ± 0.024)
kk	(3.140 ±0.048) 10^{-9}
K	(1.099 ± 0.048) 10^{-8} $m^4.s^{-1}.mol^{-1}$
Vg	(7.830 ± 0.098) 10^{-10}
D_{BP}	(3.270 ± 0.095) 10^{-10} $m^3.mol^{-1}$
ρ_e/ρ_{app}	(0.950 ± 0.172)
M_p/ρ_{app}	(9.500 ± 0.165) 10^{-4} $m^3.mol$

According to the correlations quoted in Lieto (1998), the transfer mass coefficients are calculated: k_B = 0.774 10^{-2} $m.s^{-1}$, k_H =1.99 10^{-2} $m.s^{-1}$ and k_A=1.7 $10^{-2}m.s^{-1}$. The following initial conditions are chosen: C_{A0}=25 mol m^3, C_{B0}=125,4 mol/ m^3, C_{BP0}=0, the external radius $R'(0)$=200(1+10^{-6}) nm , the internal one $R(0)$=200(1-10^{-5}) nm .

These initial values correspond to experimental conditions under which the measurement of wall thickness is done with the transmission electron microscopy (TEM) Topcon® EM002B, 200kV. The result of this measurement is about 2nm and the precision is rough: it gives the order of magnitude.

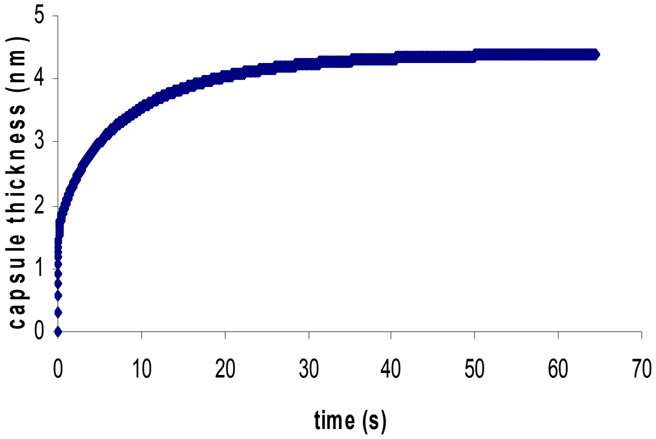

Figure 1: Thickness of the wall of the capsule versus time

The kinetics of the reaction of polycondensation is very fast. The reaction stops after the overall consumption of sebacoyle chloride (0.2 seconds). After this time, the thickness increase is only due to the swelling. The time corresponding to the swelling is very important with respect to the reaction time (48.2s). The final thickness of the capsule is estimated to 4.4 nm. This result is in the same order of magnitude than the measurement and considering the precision of the measurement, it appears to be satisfying. The membrane appears to be very porous, the porosity being equal to 0.67. D_{BP} is in the same order than the one computed by the correlation given in Lieto (1998) concerning of the molecular liquid-liquid diffusion (1998) D_{BP} =7.74 10^{-10} $m^3.mol^{-1}$. We conclude that the polymeric membrane does not offer resistance to the active principle but protects the latter.

Nomenclature

A	sebacoyle chloride	TDC	terephthaloyl dichloride
B	diethylenetriamine	H	chloride acid

Notations

$\overline{C_A}$	concentration of monomer A in the organic phase	(mol.m^{-3})
C_{A0}	initial concentration of monomer A in the organic phase	(mol.m^{-3})
$\overline{C_B}$	concentration of monomer B in the aqueous phase	(mol.m^{-3})
C_{B0}	initial concentration of monomer B in the aqueous phase	(mol.m^{-3})
$\overline{C_{BP}}$	concentration of monomer B in the polymer	(mol.m^{-3})
C_{BP0}	initial concentration of monomer B in the polymer	(mol.m^{-3})
$\overline{C_H}$	concentration of H at the at the interface of the reaction	(mol.m^{-3})
$\overline{C_{HP}}$	concentration of H in the polymer film	(mol.m^{3})
D_{BP}	diffusion coefficient of monomer B in the polymer film	(m^2.s^{-1})
D_{HP}	diffusion coefficient of H in the polymer film	(m^2.s^{-1})
$J(\theta)$	criteria to minimize	
K	rate constant	(m^4.s^{-1}.mol^{-1})
k	parameter number	(-)
kk	rate constant	(m^3.s^{-1}.mol^{-1})
k_B	mass transfer coefficient of Bin the water	(m.s^{-1})
k_H	mass transfer coefficient of H in the water	(m.s^{-1})
M_p	molecular weight of the polymer	(Kg.mol^{-1})
N	Experimental data number	(-)
r	radial coordinate	(m)
R_{em}	initial external radius of the sphere	(m)
Ri	fixed radius	(m)
$R_{(t)}$	internal radius of the sphere.	(m)
$R'_{(t)}$	external radius of the spheres	(m)
$S_{R'(t)}, S_{R(t)}$	external surface of the sphere of radius respectively R',R	(m^2)
t	time	(s)
V_e	water volume in the polymer	(m^3)
V_T	total volume of polymer and water	(m^3)
V_g	swelling rate of the polymer	(m.s^{-1})
X	porosity	
X_{eq}	porosity at equilibrium porosity	
y:	output	(-)
ρ_{app}	apparent mass density of the polymer	(Kg.m^{-3})
ρ_e	mass density of the water	(Kg.m^{-3})

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