Modeling Methyl Methacrylate (MMA) Polymerization for Bone Cement Production

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Summary: Bone cements based on poly(methyl methacrylate) (PMMA) have been widely used in orthopedic surgeries for fixation of prostheses and filling of bone defects. Bone cements are produced through *in situ* and *in vivo* free radical bulk polymerizations, which are highly exothermic and are subject to strong gel and glass effects. As a consequence, high temperatures may be reached during application. Furthermore, residual monomer usually remains unreacted inside the body and may cause aseptic loosening and tissue damages.[1] In a companion work in this volume, it was shown that usual free-radical polymerization models might effectively describe the bone cement preparation[2] and therefore be used for quantitative analysis of the bone cement synthesis. In this work, a theoretical investigation based on a multicell reactor model is performed to study the bone cement production and allow for future optimization of the preparation procedure. It is shown that the degree of solubility of the pre-polymer powder in the liquid monomer is the most important variable during the bone cement preparation and that this variable should be manipulated for design and control of the operation in real applications.

Keywords: bone cement; heterogeneity; modeling; poly(methylmethacrylate); polymerization

Introduction

Bone cements based on poly(methyl methacrylate) (PMMA) have been widely used in orthopedic surgeries for fixation of prostheses and filling of bone defects.[1] Bone cements are produced through polymerization of methyl methacrylate (MMA) monomer initiated by benzoyl peroxide (BPO) and activated by a tertiary amine, frequently N,N-dimethyl-4-toluidine (DMPT). The polymerization is carried out in the presence of previously polymerized PMMA and radio-opacity is achieved through addition of an X-ray contrast, such as barium sulfate or zirconia. Initially, monomer, PMMA, contrast, initiator and activator are manually mixed during a short period of time (usually called the induction time). Then manual mixing is interrupted and the reaction medium stands still during the course of the polymerization (which takes approximately 20 minutes to be finished). Reaction temperatures increase spontaneously during the first 10 minutes of polymerization and decrease afterwards, due to heat exchange with the environment. After natural cooling, the obtained solid material is a complex heterogeneous composite of PMMA, X-ray contrast and residual monomer. Detailed description of bone cement constituents and preparation procedures are presented elsewhere.[3]

During the course of the bone cement preparation, the viscosity of the polymerization medium increases steadily and very fast until final solidification. This particular feature allows for *in situ* and *in vivo* bone

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cement polymerizations. Despite this advantage, *in situ* and *in vivo* bone cement applications can cause aseptic loosening and tissue damages if they are not controlled properly. These problems can be caused by the presence of high amounts of residual monomer in the final composite and by the high temperature values attained during the course of the polymerization, which is highly exothermic and undergoes strong gel and glass effects. In order to minimize the observed application problems, the purpose of this work is to investigate the reaction phenomena during bone cement production with the aid of a mathematical model.

It has been shown that a lumped free-radical polymerization model can be used effectively to describe the observed temperature profiles during the preparation of bone cements.[2] This model, however, assumed that temperature and concentrations are uniform inside the vessel where the bone cement is prepared. This is not necessarily true, given the high rates of reaction and the experimental observation that the degree of mixing of the recipe components influences the observed temperature profiles. Furthermore, it has been shown that heat transfer to the surroundings may be very important to explain the attainment of the high temperature peaks observed experimentally.[3]

Based on the previous discussion, the modeling approach proposed herein assumes that it is possible to describe the reaction medium as a combination of multiple interconnected well mixed tank reactors (multicell model), which are allowed to exchange heat (but not mass) with their immediate neighbors and the environment. This means that reaction conditions may be heterogeneous in the reaction *locus*, as it may be expected during actual preparation of the bone cement. Mass transfer effects are neglected because of the high viscosity of the reaction medium, as thoroughly discussed by Fontes *et al.*[4] As shown by these authors both theoretically and experimentally, mass transfer effects (caused both by natural convection and diffusion) can be neglected during reactive molding of fast reacting polymer mixtures, because of the significant temperature heterogeneity attained inside the vessels where test pieces are prepared.

The effect of mixing on the polymerization reaction was analyzed by assuming that the initial conditions inside distinct cells may not be the uniform. Inefficient manual mixing effects were simulated by introducing random perturbations of the initial conditions in each of the reactor cells (while satisfying the overall mass balance). The results showed that local fluctuations of reaction temperature (due to heat transfer limitations) and of composition (due to poor micromixing of constituents) are not likely to exert significant influence on the course of the reaction

The role of the prepolymerized PMMA during the bone cement preparation was also investigated. It is known that the characteristics of the PMMA (particle size, molecular weight and relative amount) are of fundamental importance for the proper interpretation of the evolution of temperature profiles during the reaction.[5] It is assumed herein that the mentioned characteristics influence mainly the solubility of PMMA in the MMA monomer and that this affects the gel effect, which is the main cause for the fast increase of reaction rates in this system. The model results showed that the degree of solubility of the prepolymerized powder in the liquid monomer may exert significant influence on the course of the polymerization during the bone cement preparation. Therefore, this variable should be manipulated for design and control of the operation in real applications.

Mathematical Model

The mathematical model used to describe the bone cement production is based on the conventional free radical reaction scheme, as shown in Table 1, including some modifications due to the presence of the activator. Similar models have been proposed to describe the formation of acrylic

Table 1.
Polymerization mechanism.

Stage	Mechanism
Initiation	$I + A \xrightarrow{k_i} R_I + R_A$
	$I \xrightarrow{k_d} 2R_I$
	$R_I + M \xrightarrow{k_1} P_1$
	$R_A + M \xrightarrow{k_2} P_1$
Propagation	$P_i + M \xrightarrow{k_P} P_{i+1} \quad i \geq 1$
Termination	$P_i + P_j \xrightarrow{k_{td}} D_i + D_j \quad i,j \geq 2$
	$P_i + P_j \xrightarrow{k_{tc}} D_{i+j} \quad i,j \geq 2$

sheets and the reactive injection molding of test pieces.[4] In these cases, however, the reacting mixture was assumed to be homogeneous and the impact of mixing on the evolution of variable trajectories was neglected.

Tertiary aromatic amines, such as DMPT, have been used with BPO for many years for generation of free radicals at room temperatures in medical-related applications. The role of the amine is to react with BPO and form a chemical compound that is able to decompose through homolytic cleavage, forming free radicals at high rates at room temperature (Table 1).[10,11] Chain transfer reactions are neglected in the kinetic mechanism.

It is assumed here that the quasi-steady state hypothesis (QSSA) is valid for all living radicals, that reaction steps are irreversible and elementary, that rate constants are chain-length independent and that significant gel and glass effects are present. The independent reaction cell is modeled as well mixed batch reactor, which means that Equations (1–5) can be used to describe the mass balances inside a single reaction cell. Although Equation (5) is used to follow the modification of the cell volumes, overall volume effects are unimportant most of the times, because most bone cement formulations contain significant amounts of inert material. In spite of that, volume effects may exert significant effects on the system behavior because reaction takes place in the shrinking monomer phase. The presentation of the energy balance equations requires the definition of the reactor geometry, as discussed in the next section.

Initiator Balance

$$\frac{dI}{dt} = -k_i \frac{A}{V} \frac{I}{PM_A} - k_d I \tag{1}$$

Activator Balance

$$\frac{dA}{dt} = -k_i \frac{A}{V} \frac{I}{M_I} \tag{2}$$

Monomer Balance

$$\frac{dM}{dt} = -k_P \frac{P}{V} M - \left(\frac{2k_i AI}{M_A M_I} + \frac{2fk_d IV}{M_I}\right)\left(\frac{M_M}{V}\right) \tag{3}$$

Living Polymer Balance

$$\frac{dP}{dt} = -(k_{td} + k_{tc})\frac{P^2}{V} + \left(\frac{k_i AI}{M_A M_I} + \frac{2fk_d IV}{M_I}\right)\left(\frac{1}{V}\right) = 0 \tag{4}$$

Cell Volume

$$\frac{dV}{dt} = \left(\frac{1}{\rho_{MMA}} - \frac{1}{\rho_{PMMA}}\right)\frac{dM}{dt} - \left(\frac{M}{\rho_{MMA}^2}\right)\frac{d\rho_{MMA}}{dt} + \left(\frac{-M_0 + M - M_{PMMA_0}}{\rho_{PMMA}^2}\right)\frac{d\rho_{PMMA}}{dt} \tag{5}$$

In order to simulate the bone cement preparation, a reference recipe was proposed as described in Table 2. The recipe composition is in accordance with common

Table 2.
Bone cement base composition.

Component	Mass (g)
BPO	0.35
DMPT	0.40
Barium sulfate	4.00
MMA	10.00
PMMA	16.00

Table 3.
Parameters and correlations.

Parameters	Units
$k_d(T) = 3.816 \cdot 10^{12} \exp(-27\,343.69/RT)$	s^{-1}
$k_P(T) = 7.000 \cdot 10^{9} \exp(-6\,300.00/RT) \cdot g_P(T)$	$cm^3/mol\ s$
$k_i(T) = k_P \cdot 10^{-7}$	$cm^3/mol\ s$
$k_{td}(T) = 1.760 \cdot 10^{12} \exp(-2\,800,00/RT) \cdot g_t(T)$	$cm^3/mol\ s$
$k_{tc}(T) = 1.360 \cdot 10^{8} \exp(-2\,840,00/RT)$	$cm^3/mol\ s$
$\Delta H_R = -137.70$	cal/g
$\rho_{MMA}(T) = 0.9654 - 0.00109 \cdot (T - 273.15) - 9,7 \cdot 10^{-7} \cdot (T - 273.15)^2$	g/cm^3
$\rho_{PMMA}(T) = \frac{\rho_{MMA}(T)}{0.754 - 9 \cdot 10^{-4} \cdot (T - 343.15)}$	g/cm^3
$\rho_{INERT} = 4.49$	g/cm^3
$c_{P_{MMA}} = 0.490$	cal/g K
$c_{P_{PMMA}} = 0.339 + 9.55 \cdot 10^{-4} \cdot (T - 298.15)$	cal/g K
$c_{P_{INERT}} = 0.6$	cal/g K

commercial formulations, as described elsewhere.[3]

The parameters and correlations required for simulation, including the correlations that describe the gel and the glass effects, were obtained from the literature.[3,4,6,7] Estimation of kinetic parameters was not performed. The model was solved with the aid of a standard Adams-Moulton integration procedure, with error control at each integration step. The relative precision used for simulations were always better that 1×10^{-8}.

Multicell Model

The proposed model was used to simulate the bone cement production in a cubic reactor (length of 5 cm) that simulates a human bone cavity or a mold for a test piece preparation. The reactor was divided into finite elements (cells), as shown in Figure 1. The reactor geometry was kept fixed, although it must be noticed that modification of the reactor geometry may be performed easily with the proposed discretization procedure. The main objective here is to analyze how heterogeneous reaction conditions may be during the bone preparation and how these differences can affect the course of the polymerization. Simulation of more complex and real reactor geometries is beyond the scope of this manuscript.

As described previously, the cells are assumed to exchange heat (but not mass) with their immediate neighbors. Although

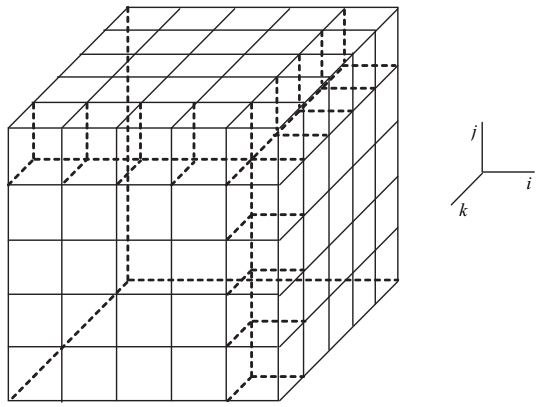

Figure 1.
Multicell model.

mass transfer effects are neglected, local concentrations are allowed to vary because of the different temperature histories experienced by each independent reactor cell or because of heterogeneous mixing of ingredients.

This multicell approach allows for evaluation of reaction conditions as functions of the spatial positions if the cells are enumerated properly. In a reactor containing NC cells, the individual cells are assigned a number C according with the spatial coordinates (i, j, k) as:

$$C = (i-1)\cdot(NC)^{2/3} + (j-1)\cdot(NC)^{1/3} + k \quad (5)$$

Each cubic cell has 6 neighbors. The cell neighbors can be other reactor cells or the environment. In the first case, heat is exchanged through conduction; in the second case, heat is exchanged through convection. As reaction conditions may be very different in each cell, proper identification of cell neighbors is very important.

Heat transfer rates between adjacent cells were assumed to be proportional to the contact area and inversely proportional to the distance between their centers. Heat transfer rates between a reactor cell and the environment were assumed to be proportional to the contact area and the overall heat transfer coefficient. The resulting energy balance equation for a single cell becomes

$$\frac{dT_C}{dt} = \begin{bmatrix} \left[\Delta H_R\left(-\frac{k_P PM}{V}\right) - n_{conv}\alpha UA(T - T_{amb})\right. \\ -p_1\left(\frac{k_{cond}hw}{l}\right)(T_C - T_{C_1}) - p_2\left(\frac{k_{cond}hw}{l}\right)(T_C - T_{C_2}) \\ -p_3\left(\frac{k_{cond}hw}{l}\right)(T_C - T_{C_3}) - p_4\left(\frac{k_{cond}hw}{l}\right)(T_C - T_{C_4}) \\ \left.-p_5\left(\frac{k_{cond}hw}{l}\right)(T_C - T_{C_5}) - p_6\left(\frac{k_{cond}hw}{l}\right)(T_C - T_{C_6})\right]\left(\frac{1}{\rho c_P V}\right) \end{bmatrix} \quad (6)$$

n_{conv} represents the number of cell faces that are in contact with the environment. Variables $p_1, p_2 \ldots p_6$ are boolean variables that indicate whether the cell faces are in contact with distinct neighboring cells. These variables are set to zero when the corresponding face exchanges heat with the environment and are set to 1 otherwise. k_{cond} is the thermal conduction coefficient of the bone cement mixture, assumed to be constant and equal to $4.06 \cdot 10^{-4}$ cal/cm.s.K.[8] The overall heat transfer coefficient to the environment ($n_{conv}\,\alpha UA$, where n_{conv} is the total number of cell faces exposed to the environment) was assumed to be constant and equal to 0.017cal/K.s.[2] Although heat transfer coefficients may depend on the reaction conditions (and particularly on the reaction temperature), this effect was neglected here, based on the arguments thoroughly discussed by Fontes *et al.*[4]

Analysis of Temperature Homogeneity

Simulations were initially performed for different number of cells, assuming that the initial conditions in all cells were uniform and equal to the values presented in Table 2. The initial reaction temperature was set to 25 °C in all cases. This analysis was used to evaluate the convergence of the numerical procedures and the importance of local temperature effects during preparation of the bone cements. The obtained results are presented in Figure 2 in terms of the average monomer conversion and average reaction temperature profiles.

The analysis of Figure 2 shows clearly that both monomer conversion and reactor temperature increase as the number of cells increases. Besides, these variables level off for a sufficiently large number of cells (above 1331), indicating that numerical convergence is attained.

The number of cells needed for simulation can be related to the degree of uniformity in the reactor and should not be regarded as a simple numerical parameter. Uniformity is largely influenced by

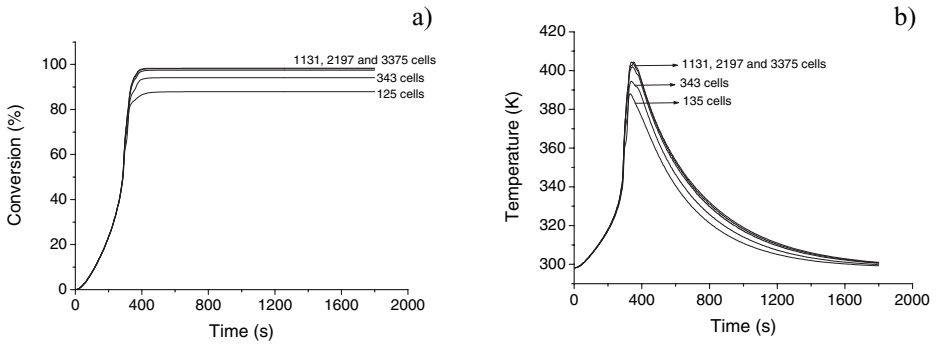

Figure 2.
(a) Average monomer conversion; (b) and average reaction temperature as function of time.

the bone cement preparation procedures. Simulations performed with a low number of cells can be related to conditions where the bone cement ingredients were mixed effectively, while simulations performed with a very high number of cells can be related to conditions were mixing of the ingredients was not uniform. Figure 2 shows that increasing the number of well mixed volumes can lead to an increase of up to 20 °C of the temperature peak, which may be undesired during real applications. However, smaller temperature peaks lead to incomplete monomer conversions, which may pose serious risks to the patient. Therefore, from a reaction point of view, it may be interesting to reduce the degree of uniformity during the preparation of the bone cement. The higher temperature values observed for smaller cells are related to the poor heat transfer of the organic material. This explains why monomer conversions are smaller when mixing is improved (number of cells is reduced). It is also important to notice that the calculated temperature peak values are similar to the ones reported in the literature, which provides independent experimental support to the proposed modeling scheme.[1,2]

In order to characterize the nonuniformity of the reactor temperature along the reaction course, the temperature average and variance were calculated as a function of time for the 1331 cells, as shown in Figure 3. It can be seen that temperature uniformity is affected by both reaction rate

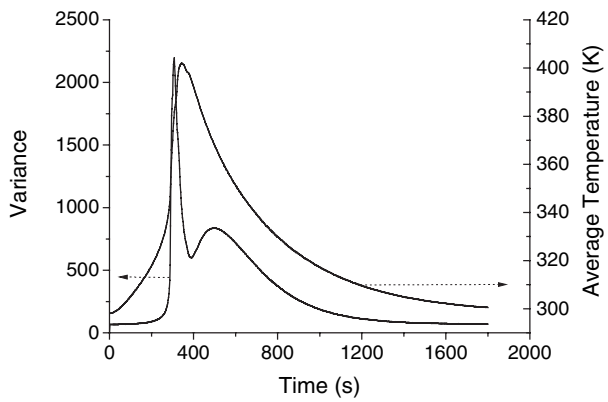

Figure 3.
Average temperature and temperature variance as a function of time.

and heat transfer to the surroundings, as the variance reaches its maximum at the point of maximum reaction temperature and rate and decreases as the reaction medium cools off due to heat transfer to the environment.

Figure 4 presents conversion and temperature spatial profiles when the temperature peak is attained. Results are presented for the reactor central plane. One should observe the extremely high monomer conversion values and maximum temperature differences of about 20–30 °C, indicating that significant temperature gradients are present within the reaction vessel. Sanchez *et al.*[9] observed similar temperature differences experimentally by comparing center and surface measurements during bone cement preparation in molds of similar dimensions. These results confirm qualitatively the simulations performed herein and lend confidence to the proposed modeling approach.

Analysis of Initial Mixture Heterogeneity

Bone cement heterogeneity induced by imperfect manual mixing of the recipe components is analyzed in this section. Simulations were performed with 1331 reaction cells, as discussed previously. Initial mixing effects were simulated by introducing random perturbations of the initial conditions in each cell, while keeping the overall mass balance consistent with the data presented in Table 2. Computation of initial compositions is performed as

$$M_C = \frac{M}{NC}(1 + A\ Random) \tag{7}$$

where M_C represents the mass in the analyzed cell, M is the overall mass value presented where M_C represents the mass in the analyzed cell, M is the overall mass value presented in Table 2, NC is the number of reaction cells, A is the amplitude of the perturbation and *Random* is a random number uniformly distributed in the interval [−1,1]. Compositions are then normalized to follow the recipe presented in Table 2. Results are summarized in Figure 5. Figure 5 indicates that initial mixing effects are not important when the number of reaction cells is large. Average monomer conversions and reaction temperatures are not sensitive to modification of the system composition, even when deviations of 20% of the reference recipe are allowed. As perturbations with amplitude of 20% are not expected to occur in real applications, it may be concluded that initial micromixing effects are

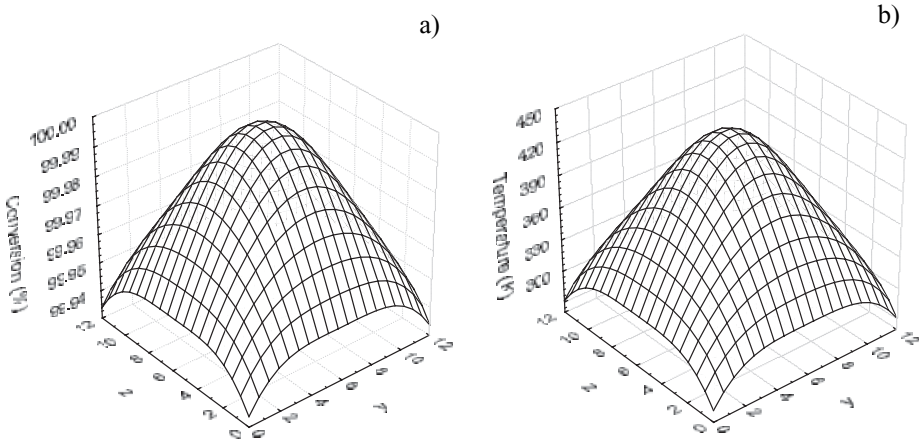

Figure 4.
(a) Monomer conversion and (b) reaction temperature spatial profiles at the central plane.

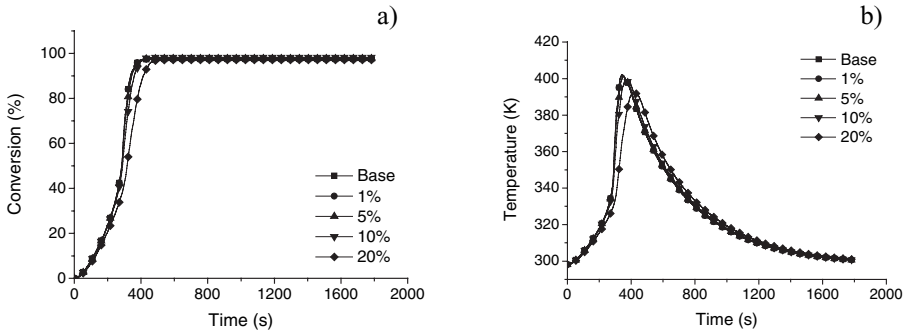

Figure 5.
Mixing effects on (a) average monomer conversion and (b) average reaction temperature. Simulations performed with 1331 cells for perturbations of different amplitudes.

seemingly unimportant during bone cement preparation.

In order to check whether worsening of the micromixing conditions might lead to significant modification of the reaction conditions, the number of reaction cells was reduced to 27. In this case, composition fluctuations would be observed along larger volumes of the reaction vessel. Obtained results are presented in Figure 6. It can be observed that the amplitude of the perturbations must be larger than 20% for significant modification of the reaction conditions to occur, which confirms that initial macromixing effects do not seem to exert significant influence on the course of the polymerization during bone cement preparation. Therefore, it is not expected that macromixing or micromixing effects strongly influence the bone cement polymerization reaction as it could be expected in recipe where the manual mixing of the components to form a heterogeneous viscous mixture is the first step.

Effect of the Solubility of the Pre-polymerized PMMA

A significant amount of pre-polymerized PMMA is added to bone cement recipes in order to increase the polymerization rate, taking advantage of the strong gel effect of the MMA polymerization. It is normally assumed that the PMMA dissolves completely in the liquid phase during prepara-

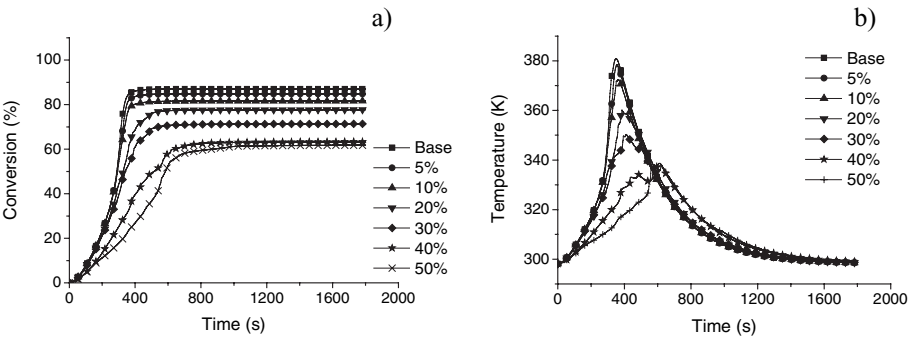

Figure 6.
Mixing effects on (a) average monomer conversion and (b) average reaction temperature. Simulations performed with 27 cells for perturbations of different amplitudes.

tion of the polymerizing mixture (as implicitly assumed in the previous simulations). However, as reaction occurs very fast, it is not clear whether there is sufficient time for complete dissolution of the PMMA in the MMA liquid. It is very probable that part of the PMMA remains in the solid phase during the polymerization and does not contribute to the gel effect. This may explain, for instance, why the average particle size of the PMMA powder seems to affect the course of the polymerization, as dissolution of large PMMA particles in the MMA monomer requires a longer time. Therefore, larger particles might lead to lower dissolved PMMA contents in the MMA monomer and consequently to lower reaction rates due to a reduced gel effect.

In order to investigate whether the degree of PMMA dissolution in the MMA liquid monomer can influence the course of the polymerization, simulations were performed for different degrees of PMMA solubility, assuming no swelling or reaction in the solid phase. In order to perform the simulations, the initial composition of the liquid phase was allowed to vary. Part of the PMMA was assumed to readily dissolve in the liquid phase and the remaining PMMA was assumed to be in the solid phase, as an inert material. Simulations were performed with 1331 reaction cells. Obtained results are summarized in Figure 7.

Figure 7 shows that the PMMA solubility is an extremely important factor during the bone cement preparation. The degree of PMMA solubility affects simultaneously the temperature peak value, the position of the temperature peak and the monomer conversion. Therefore, PMMA solubility can influence the reaction course and final properties of the bone cement very significantly. As the PMMA solubility decreases, the maximum temperature decreases, the overall monomer conversion decreases, the temperature profile becomes broader and the reaction rate decreases. Even more important, the PMMA solubility (or PMMA content of the liquid phase) can be used for design of the temperature profile and of the reaction time and simultaneously guarantee the attainment of high monomer conversions. This significant effect of dissolved PMMA is related to the increase of the reacting medium viscosity at the beginning of the reaction, leading to a faster and more pronounced gel effect along the reaction course.

According to the literature, PMMA particles with diameter smaller than 20 μm dissolve completely in the liquid phase during the reaction. However, bigger PMMA particles may be only partially soluble.[1,5] If one considers that particle size distributions produced in suspension polymerization reactors are relatively broad, one will conclude that significant amounts of the PMMA powder may remain in the solid phase as inert materials. Besides, it is also known that smaller molecular weights cause faster dissolution of polymer materials in solvents. Therefore,

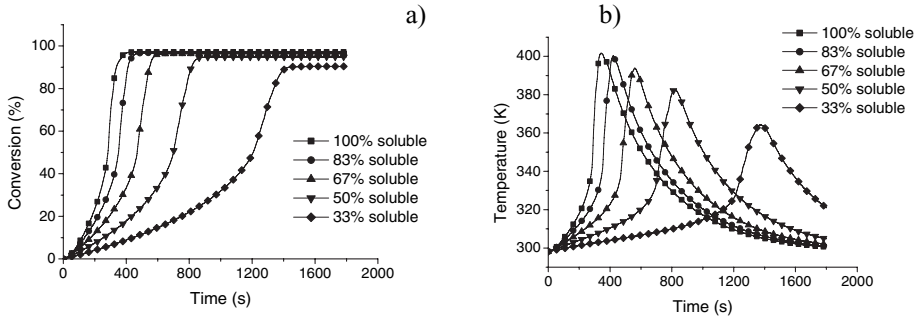

Figure 7.
Solubility effects on (a) average monomer conversion and (b) average reaction temperature.

the decrease of the average molecular weight of the PMMA powder may cause the relative increase of the PMMA solubility in the liquid phase.[5] In summary, Figure 7 explains why the average particle sizes and average molecular weights of the PMMA powder affect the reaction course during preparation of bone cements.

Conclusions

A multicell model was developed to describe the bone cement preparation in a cubic mold. According to the simulation results, significant temperature heterogeneity may occur during bone cement production when mixing of recipe ingredients is poor or when reaction temperatures are close to the peak value. According to the simulations, the initial micromixing of constituents does not exert much influence on the course of the polymerization.

The results also indicate that the solubility of the pre-polymerized PMMA in the initial bone cement mixture is the most important process variable, exerting a significant influence upon the evolution of the reaction temperature and monomer conversion. As the polymer solubility is related to the molecular weight and the particle size of the pre-polymerized PMMA, these properties should be carefully controlled to obtain bone cements with desirable characteristics.

Nomenclature

A– DMPT mass (g);
C– Cell number;
$c_{P_{INERT}}$– Specific heat capacity of $BaSO_4$ (cal/g K);
$c_{P_{MMA}}$– Specific heat capacity of MMA (cal/g K);
$c_{P_{PMMA}}$– Specific heat capacity of PMMA (cal/g K);
f– BPO efficiency (dimensionless);
I– BPO mass (g);
k_d– BPO decomposition rate constant (s^{-1});
k_i– BPO and DMPT reaction rate constant (cm^3/gmol s)
k_p– Propagation rate constant (cm^3/gmol s);
k_{tc}– Combination rate constant (cm^3/gmol s);
k_{td}– Disproportionation rate constant (cm^3/gmol s);
M– Monomer mass (g);
M_A– DMPT molecular weight (g/gmol);
M_I– BPO molecular weight (g/gmol);
M_M– MMA molecular weight (g/gmol);
NC– Total number of cells;
P– Number of moles of polymer formed during reaction (gmol);
T– Temperature (K);
t– Time (s);
T_{amb}– Ambient temperature (K);
V– Reactor volume (cm^3);

Greek Symbols

αUA– Heat transfer coefficient to environment (cal/K s);
ΔH_R– Reaction enthalpy (cal/g);
ρ– Specific mass of reaction mixture (g/cm^3).
ρ_{INERT}– Specific mass of $BaSO_4$;
ρ_{MMA}– Specific mass of MMA;
ρ_{PMMA}– Specific mass of PMMA.

Subscripts

C– reference cell;
C_1, C_2, C_3, C_4, C_5, C_6– Adjacent cells number.

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[1] B. Pascual, B. Vázquez, M. Gurruchaga, I. Goñi, M. P. Ginebra, F. J. Gil, J. A. Planell, B. Levenfeld, J. San Román, *Biomaterials*, **1998**, *17*, 509.
[2] J. G. F. Santos, L. S. Peixoto, M. Nele, P. A. Melo, J. C. Pinto, *Macromol. Symp.* **2006**, submitted.
[3] B. Vazquez, S. Deb, W. Bonfield, *J. Mater. Sci. - Mater. Med.*, **1997**, *8*, 455.
[4] C. E. Fontes, P. L. C. Lage, J. C. Pinto, *Polym. Eng. Sci.*, **2002**, *42*, 1370.

[5] C. Z. Liu, S. M. Green, N. D. Watkins, A. W. McCaskie, *J. Mater. Sci. Lett.*, **2003**, *22*, 1147.
[6] J. C. Pinto, W. H. Ray, *Chem. Eng. Sci.*, **1995**, *50*, 715.
[7] M. S. Matheson, E. E. Auer, E. B. Bevilacqua, E. J. Hart, *J. Amer. Chem. Soc.*, **1949**, *71*, 497.
[8] C. LI, S. Kotha, C. Huang, S. Schmid, J. Mason, D. Yakimicki, M. Hawkins, *Bioengineering Conference – ASME*, **2001**, *50*, 235.
[9] M. A. Sanchez, W. Sutton, W. Rizk, J. TompkinsII, J., "*Thermal curing and strength of PMMA bone cement*", HT2003-47067, ASME Heat Transfer Conference, Las Vegas, **2003**, p. 1.
[10] D. S. Achilias, I. D. Sideridou, *Macromolecules*, **2004**, *37*, 4265.
[11] B. Vazquez, B. Levenfeld, J. San roman, *Polym. Int.*, **1998**, *46*, 241.

