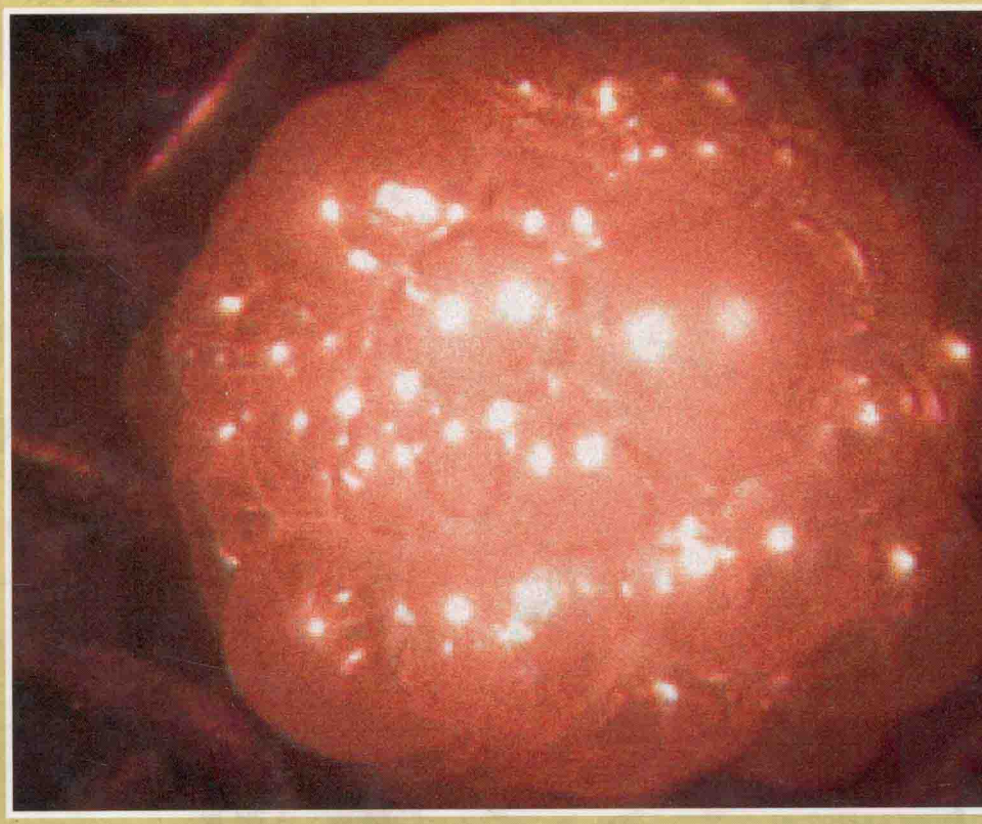
Robin A. Hutchinson (Ed.)

# Polymer Reaction Engineering VI



WILEY-VCH

Macromolecular Symposia Vol. 243

# Polymer Reaction Engineering VI

Selected Contributions
from the conference in
Halifax, Canada, May 21–26, 2006

Symposium Editor:
R. A. Hutchinson, Kingston (Canada)





WILEY-VCH

**Full text and further information: www.ms-journal.de**

**Editors** (all *Macromolecular* Journals):
Sandra Kalveram
Stefan Spiegel
Mara Staffilani
**Editorial Assistants:**
Sibylle Meyer
Carmen Teutsch
**Administration:**
Inge Dittmer
Petra Pinto
**Production:**
Katja Kornmacher
**Editorial Office:**
macro-symp@wiley-vch.de



**Macromolecular Symposia**
is published 14 times a year

**Annual subscription rates 2007**
Macromolecular Full Package
(All seven *Macromolecular Journals*; 101 issues in total):

| | | | |
|---|---|---|---|
| Europe | Euro | 8,445 | 9,290 |
| Switzerland | Sfr | 13,995 | 15,395 |
| All other areas | US$ | 11,145 | 12,260 |
| | | print only **or** electronic only | print **and** electronic |

Postage and handling charges included.
All Wiley-VCH prices are exclusive of VAT.
Prices are subject to change.
Individual subscriptions, single issues and back copies are available.
Please ask for details at: service@wiley-vch.de

**Orders** may be placed through your bookseller or directly at the publishers:
WILEY-VCH Verlag GmbH & Co. KGaA,
P.O. Box 10 11 61, 69451 Weinheim, Germany,
Tel. +49 (0) 62 01/6 06-400,
Fax +49 (0) 62 01/60 61 84,
E-mail: service@wiley-vch.de

**Copyright Permission:**
Fax: +49 (0) 62 01/6 06-332,
E-mail: rights@wiley-vch.de

**For USA and Canada:** Macromolecular Symposia (ISSN 1022-1360) is published with 14 volumes per year by WILEY-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69451 Weinheim, Germany. Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Ave., Elmont, NY 11003, USA. Application to mail at Periodicals Postage rate is pending at Jamaica, NY 11431, USA. POSTMASTER please send address changes to: Macromolecular Symposia, c/o Wiley-VCH, 111 River Street, Hoboken, NJ 07030, USA.

Printed on acid-free paper.
Typesetting: Thomson Press (India) Ltd., India
Printing: Strauss Offsetdruck, Mörlenbach
Binding: Litges & Dopf, Heppenheim

Macromolecular Symposia | 243

# Polymer Reaction Engineering VI

Selected Contributions
from the conference in
Halifax, Canada, May 21–26, 2006

Symposium Editor:
R. A. Hutchinson, Kingston (Canada)

Ronald D. Sanderson, Harald Pasch (Eds.)

**Polymers in Novel Applications**

Vol. 225
ISBN 3-527-31328-1

Seung Soon Im, Young Ha Kim,
Jin-San Yoon, In-Joo Chin (Eds.)

**Bio-Based Polymers: Recent Progress**

Vol. 224
ISBN 3-527-31327-3

Thomas Heinze, Klaus Fischer (Eds.)

**Cellulose and Cellulose Derivatives**

Vol. 223
ISBN 3-527-31326-5

Yves Grohens (Ed.)

**Polymer–Solvent Complexes and Intercalates V**

Vol. 222
ISBN 3-527-31325-7

Dganit Danino, Daniel Harries,
Steven P. Wrenn (Eds.)

**Talking about Biocolloids**

Vol. 219
ISBN 3-527-31322-2

Engineering Conferences International, in technical co-sponsorship with the American Institute of Chemical Engineers, sponsored the sixth conference in this continuing series of triennial conferences, the major North American conference on emerging technologies and scientific advancements in the area of polymer reaction engineering. "PRE VI", held in Halifax, Canada from May 21–26, 2006, was chaired by Robin Hutchinson (Queen's University, Canada), Michael Muhle (ExxonMobil Chemical Co., USA) and Alex Penlidis (University of Waterloo, Canada). PRE VI continued the mandate of the PRE conference series to bring together the leading researchers from academia and industry to discuss a broad range of practical, theoretical and new topics in the area. Over 40% of the 119 attendees were from industry, continuing the strong academia-industry interactions in the area of PRE. Just over half of the attendees were from US and Canada, with the remaining 47% of participants coming from 19 other countries. The financial support from sponsoring companies – BASF, CiT GmbH, Degussa, ExxonMobil, LG Chemical Ltd, SABIC, Sumitomo Chemicals, and Woodbridge Foam Corp. – was an essential component in assembling the strong technical program.

As in previous editions of the conference, the majority of the presentations were invited lectures, organized into sessions on Polymerization Fundamentals, Mathematical Modeling Techniques, Process Measurement and Control, New Polymerization Systems, and Industrial Applications. There were more posters at the conference than ever before, with a total of 79 divided between the two poster sessions. Key topics included reaction engineered nanocomposites and nanoparticles, production of polymers with controlled architectures, online monitoring of polymerization systems, measurement and modeling of polyolefin particle growth and reactor hydrodynamics, and polymerization process intensification via novel reactor design. The contributions submitted for this special issue of Macromolecular Symposia provide a cross-section of the conference topics, reflecting the developing trend of applying PRE principles and skills not only to improvement of polymerization processes, but also to the design and development of new materials.

All agree that the meeting was a resounding success, and look forward to PRE VII in 2009, to be chaired by Alex Penlidis (U. of Waterloo, Canada) and cochaired by John Richards (DuPont, USA) and Marc Dubé (U. of Ottawa, Canada).

*Robin A. Hutchinson*

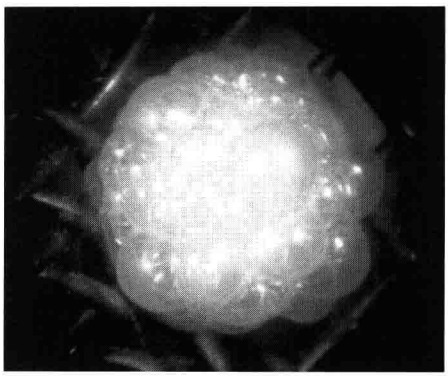
# Macromolecular Symposia

**Articles published on the web will appear several weeks before the print edition. They are available through:**

WILEY InterScience®

www.interscience.wiley.com

**Cover:** PRE VI, held in Halifax, Canada in May 2006, is the 6th in a continuing series of conferences on emerging technologies and scientific advancements in the area of polymer reaction engineering. Key topics discussed included reaction engineered nanocomposites and nanoparticles, production of polymers with controlled architectures, online monitoring of polymerization systems, measurement and modeling of polyolefin particle growth and reactor hydrodynamics, and polymerization process intensification via novel reactor design. The selected contributions in this issue reflect the developing trend of applying reaction engineering principles and skills not only to improvement of polymerization processes, but also to the design and development of new materials. The picture on the cover is an image of an expanding polystyrene particle, taken from the contribution of Salejova and Kosek.



## Polymer Reaction Engineering VI

Halifax, Canada, May 21–26, 2006

DOI: 10.1002/masy.200651101


# Theoretical and Experimental Investigation of the Production of PMMA-Based Bone Cement

*Jorge G. F. Santos Jr.,*[1] *Luciana S. Peixoto,*[1] *Márcio Nele,*[2] *Príamo A. Melo,*[1] *José Carlos Pinto**[1]

**Summary:** Poly(methyl methacrylate) (PMMA)-based polymers have been extensively used for manufacturing of artificial bone cements for treatment of osteoporosis. A typical bone cement recipe contains methyl methacrylate, which polymerizes *in situ* during cement application. An inherent problem of this reaction is the high amount of heat released during the cement preparation, which may lead to irreparable damage of living tissues. Optimization of PMMA-based bone cement (PMMABC) recipes is thus an important step towards safe and reliable clinical usage of these materials. A theoretical and experimental investigation is performed here to unveil the influence of some preparation variables on the production of PMMABC and to allow for future optimization of the PMMABC recipe. It is shown that the degree of mixing of the components of the recipe plays a fundamental role on the development of the temperature profile. For this reason, the PMMABC obtained with the *in-situ* blending of PMMA and barium sulfate during the suspension polymerization leads to much better homogeneity of the final test pieces and improved control of the temperature profile.

**Keywords:** biomaterials; bone cement; mixing; PMMA; suspension polymerization

## Introduction

Polymers constitute an important class of materials intended for biomedical applications, being largely used in medicine, biotechnology, and in the cosmetics and food industries.[1] When compared to other materials, such as metals and ceramics, polymers present a unique advantage, which lies in the fact that polymers may be synthesized to attend specific required characteristics for a certain application.[2] Among the polymeric materials normally used in biomedical applications, poly(methyl methacrylate) (PMMA)-based resins have played a prominent role due to their optical and physical properties, excellent biocompatibility and easiness of manipulation. Applications include blood pump devices and reservoirs, membranes for blood dialyzers, implantable ocular lenses, contact lenses, and bone and denture materials.[3]

PMMA gained fame in orthopedics due to the Judet brothers, who pioneered the production of PMMA prosthesis for bone reparation.[3] In 1958, John Charnley made the first significant use of PMMA for the support of medullar portions of total hip replacement, although there is a long history of applications in general surgery, which dates back into the 1940's.[4]

PMMA-based bone cement (PMMABC) is prepared during the application through the free radical bulk polymerization of MMA monomer, initiated by the decomposition of benzoyl peroxide (BPO) and activated by N,N dimethyl-p-toluidine (DMPT).[5] The recipe also contains a

[1] Programa de Engenharia Química/COPPE, Universidade Federal do Rio de Janeiro, Cidade Universitária, CP:68502, Rio de Janeiro, 21945-970 RJ, Brasil
E-mail: pinto@peq.coppe.ufrj.br
[2] Departamento de Engenharia Química / Escola de Química, Universidade Federal do Rio de Janeiro, Cidade Universitária, Rio de Janeiro, 21949-900 RJ, Brasil

prescribed amount of barium sulfate ($BaSO_4$), which is used to render the cement X-ray opaque, and PMMA particles, which are used to increase the viscosity of reaction medium and to accelerate the polymerization reaction due to gel effect.

The bone cement preparation reaction begins by mixing the recipe components in a vessel. The system viscosity and the reaction rate increase quickly due to the gel effect, which is greatly enhanced by the presence of the PMMA particles. When a suitable viscosity (or degree of polymerization) is reached, the mixture is delivered to the patient. An inherent problem of this reaction is the high amount of heat released during the bone cement preparation, which may cause the reaction temperature to increase above 100 °C, possibly leading to irreparable damage of living tissues.[6]

PMMABC has been extensively studied in the past and there are many reports in the open literature about the influence of some preparation variables on the evolution of reaction variables (temperature and conversion) and on the final properties of the produced PMMABC.[5–13] Some of the analyzed preparation variables were the operation room temperature, the type and characteristics of the used pre-polymer, the monomer to powder ratio, the type and amount of radiopaque agent, and the amount of BPO and DMPT used. In spite of that, fundamental knowledge about how variables affect the bone cement preparation is not available yet, as much of the developed work is based on empirical cause-effect analysis of experimental observations.

Meyer *et al.*[7] verified that the maximum temperature reached during bone cement preparation can be minimized by reducing the operating room temperature. This indicates how important heat transfer effects may be during the bone cement preparation in a real application environment. Haas *et al.*[8] showed that, by using minimum amount of MMA monomer and maximum amount of PMMA particles, the polymerization rate and heat released during the reaction can be minimized. This can be easily explained in terms of the reduction of the MMA concentrations. It was also reported that the final compressive strengths of bone cements prepared with MMA(liquid)/PMMA(powder) mixtures varying from 0.33 to 0.66 mL/g were essentially the same. Nevertheless, Bellkok *et al.*[9] showed that the increase of the monomer-to-powder ratio may significantly reduce the ultimate compressive strength, the yield stress and the compressive modulus of the final cement.

Pascual *et al.*[6] found out that it is possible to improve the characteristics of PMMABC and control the observed reaction temperature peak through manipulation of the particle size distribution of PMMA. Liu *et al.*[10] showed that PMMA powders of different average particle sizes and average molecular weights produce PMMABCs with different mechanical properties. These results indicate that the final bone cement performance may depend on the initial bone cement formulation and on the properties of the PMMA powder. It was also shown that the molecular weight of PMMA may be reduced during sterilization due to scission of PMMA chains.[11] Besides, other variables, such as porosity, may also affect the mechanical performance of PMMABC.[12] In fact, Ries *et al.*[12] showed that there is an inverse relationship between fracture toughness and pore size.

Mechanical toughness of bone cement is strongly affected by the content of residual monomer (which acts as a plastifying agent[5]), the bone porosity[6] and the molecular weight of the polymer obtained.[14] The final content of residual monomer is partially due to the glass effect, which prevents total monomer conversion.[15] The formation of pores is a consequence of the fast evaporation of the monomer during the polymerization reaction and of the air entrapped during the mixing of the solid and liquid components of the recipe.[6] Barros[16] showed that the amount of pores in the PMMABC depends on the preparation technique, as also discussed by Lewis.[17]

Vazquez *et al.*[5] studied the influence of BPO and $BaSO_4$ on the bone cement preparation. BPO plays an important role in the reaction kinetics. They observed the increase of the temperature peak and the decrease of setting time when the BPO concentration was increased. This can be explained by the increase of free radical concentration in the reaction medium. Vazquez *et al.*[5] also observed that the tensile modulus of the bone cement progressively decreases with the increase of the concentration of $BaSO_4$ in the reaction medium. This indicates that the amount of X-ray contrast in the final cement material should be minimized. On the other hand, Kurtz *et al.*[13] verified that the addition of $BaSO_4$ does not necessarily compromise the static and fatigue properties of PMMABC used for the treatment of vertebral compression fractures.

It is clear that, in order to obtain a PMMABC with appropriate characteristics, it is necessary to understand and control the process variables that affect final properties of the bone cement, including porosity, content of residual monomer, temperature profile during the reaction and molecular weight and particle size of PMMA. For this reason, the literature reports a number of mathematical modeling investigations, which have been carried out to allow for improved understanding of the bone cement preparation. The evolution of the temperature profile during the reaction normally is the investigated process variable, as it can be monitored in-line in the real application environment.[18–20] However, available modeling studies are based on modeling approaches that do not emphasize the importance of heat transfer and of the gel effect to explain the evolution of reaction variables.

An experimental and theoretical study is carried out in this work to provide better understanding of the bone cement preparation. This may be regarded as a first step towards the development of a methodology for PMMABC preparation that will allow for proper control of temperature profiles during the polymerization reaction in the real application environment. Experiments were performed at different operation conditions in order to evaluate the role of monomer and BPO purification, PMMA particle sizes and the mixing technique of the recipe components on the evolution of the reaction temperature. A mathematical model based on a typical free-radical polymerization mechanism is proposed to simulate the evolution of reaction temperatures during the bone cement preparation. It is shown that the proposed model is able to describe available experimental data very well and that heat transfer to surroundings and initial PMMA content of the recipe play fundamental roles on the evolution of reaction temperatures.

## Experimental

### Materials

MMA (Rhodia) was distilled at low pressures. BPO purchased from Fluka (97% pure on a dry basis) was used as received or purified. Purification was performed by dissolution of BPO powder in chloroform at room temperature, followed by re-crystallization in cold ethanol. BPO particles were then filtered and dried at room temperature under vacuum. DMPT (Aldrich) and $BaSO_4$ (Isofar) were used without further purifications.

Three PMMAs were used for the bone cement preparation, as described in Table 1. PMMA 1 (Aldrich) was obtained

***Table 1.***
PMMA characterization.

| PMMA | Diameter (μm) | Mw $\times 10^{-3}$ (Dalton) | Mn $\times 10^{-3}$ (Dalton) | Polydispersity |
|---|---|---|---|---|
| PMMA 1 | 75–300 | 1736 | 1389 | 1.25 |
| PMMA 2 | 5–10 | 301 | 148 | 2.03 |
| PMMA 3 | 35–50 | 602 | 330 | 1.83 |

commercially, whereas PMMA 2 and PMMA 3 were synthesized through free-radical suspension polymerization, using poly (vinyl alcohol) - PVA (Vetec) - as suspension agent and BPO as initiator.

### Casting Mold

Cylindrical test pieces for analysis of mechanical performance were molded in accordance with the ASTM D 695 – 85 (25.4mm tall and 12.7 mm diameter). Figure 1 shows the mold and some of the obtained test pieces.

### PMMA Particles

Two suspension polymerization runs were performed to produce PMMA particles for preparation of bone cements. PMMA 2 consists of pure poly(methyl methacrylate). PMMA 3 is an *in situ* blend of poly(methyl methacrylate) and $BaSO_4$, added to the reactor vessel as a suspension in the MMA monomer. Reactions were carried out in a glass stirred heated reactor. Firstly, an aqueous solution of PVA was delivered to the reactor. After temperature stabilization, a solution of BPO in MMA monomer (which may contain the suspended $BaSO_4$ particles) was added into the reactor. Figure 2 shows a typical MEV microscopy of a final PMMA 3 particle. Figure 2 shows some of the much smaller $BaSO_4$ particles placed on the final particle surface.

### Bone Cement

PMMABC were produced through free-radical bulk polymerization using an initiator (BPO)-activator (DMPT) system. The reactions were carried out in small 50-mL glass vessels. Solid and liquid components were weighed separately. Solid materials were mixed manually before addition of liquid components. Afterwards, the solid and liquid mixtures were mixed manually in the glass vessels. Mixing was conducted as normally performed in real surgery rooms. A thermocouple was placed in the center of the reaction medium in order to monitor the temperature profile during the reaction.

### Test Pieces

Test pieces were prepared following the same methodology used for bone cement preparation. However, after homogenization of the reaction medium, the mixture was carefully shed into the mold in order to avoid air bubble formation. Figure 1b shows the mold and some of the obtained test pieces. The toughness compression tests were carried out using a universal test machine INSTRON, model 4204. The used cell was able to support up to 5000 N of strength.

## Mathematical Modeling

A mathematical model for the bone cement preparation is developed. The model takes into account mass and energy balances and is based on a classical kinetic mechanism for free radical polymerization of MMA.[21–23] The only significant difference is the fact that initiation may take place at

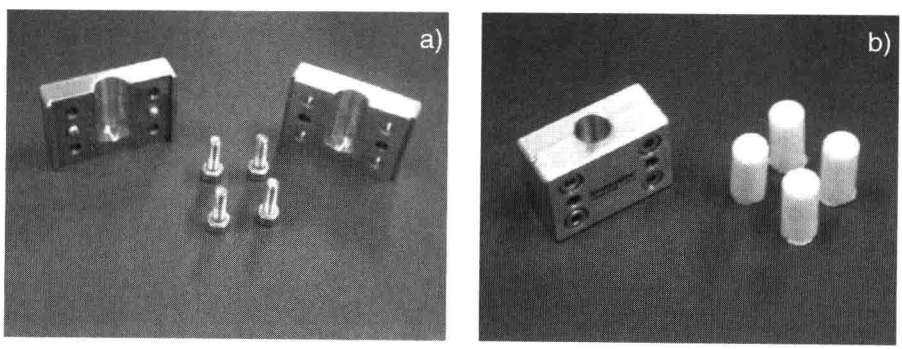



***Figure 1.***
Casting mold (a) opened and (b) closed and some test pieces obtained.

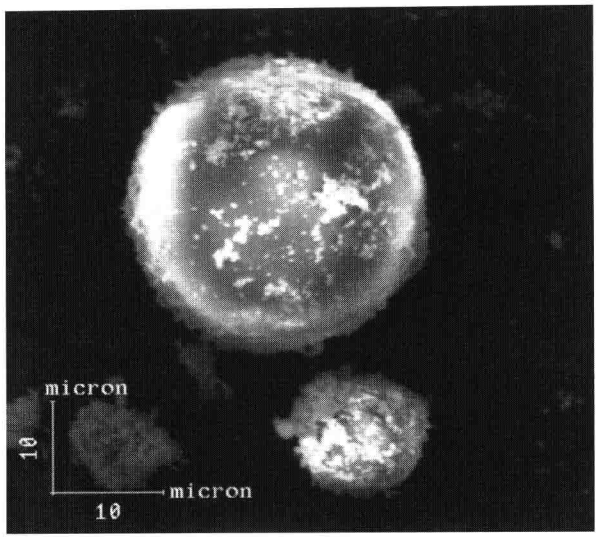



***Figure 2.***
MEV analysis of PMMA 3 particles.

low temperatures due to the presence of an initiation activator agent (DMPT).[24–26] As acknowledged by the literature,[24–26] the redox system activator/initiator mechanism is not well understood. Besides, it is uncertain whether the activator species are indeed consumed or not during the reaction. It should be pointed out, though, that the stoichiometric coefficients are not known precisely even when it is assumed that the activator species are consumed. From a practical point of view, though, the trajectories are not very sensitive to the activation step because initiation occurs mostly by thermal effects. The generation of radicals by the activator is only important when the temperature is very low (for reaction kick-off). This is because of the large temperature variations and the strong gel-effect of the MMA bulk polymerizations which control the dynamical evolution of reaction rates.

The reaction mechanism comprises the following steps:
Initiation:

$$At + I \xrightarrow{k_a(T)} At + 2R_0\cdot,$$

$$I \xrightarrow{k_d(T)} 2R_0\cdot,$$

$$R_0\cdot + M \xrightarrow{k_i(T)} P_1\cdot.$$

Propagation:

$$P_i\cdot + M \xrightarrow{k_p(T)} P_{i+1}\cdot, \quad i \geq 1$$

Termination:

$$P_i\cdot + P_j\cdot \xrightarrow{k_{tc0}(T)} \Lambda_{i+j}, \quad i,j \geq 2$$

$$P_i\cdot + P_j\cdot \xrightarrow{k_{td0}(T)} \Lambda_i + \Lambda_j. \quad i,j \geq 2$$

It is assumed that the quasi-state steady hypothesis is valid for radicals, that termination takes place solely by disproportionation, that the activator promotes the degradation of the initiator, and that the reactivity of macroradical $P_i$ depends only on the last added monomer unit (terminal model). Therefore, the mass balances for monomer, initiator and activator and the energy balance are given by:

$$\frac{dM}{dt} = -k_p(T)[P\cdot]M, \tag{1}$$

$$\frac{dI}{dt} = -k_d(T)I - k_a(T)[At]I, \tag{2}$$

$$\frac{dAt}{dt} = 0, \tag{3}$$

$$\rho c_p V(1+\varepsilon)\frac{dT}{dt} = (-\Delta H)k_p(T)[P\cdot]M - \alpha UA(T - T_{amb}), \tag{4}$$

where $[P\cdot]$ represents the molar concentration of free radicals $P\cdot$, and is given by:

$$[P\cdot] = \left(\frac{f[I](2k_a(T)[At] + 2k_d(T))}{k_t(T)}\right)^{1/2}, \quad (5)$$

$\varepsilon$ represents the external thermal capacitance factor[27] and $\alpha UA$ represents the heat transfer coefficient between reactor and environment. The external thermal capacitance factor represents the ratio of the thermal capacitance of externals (e.g. tube walls, connections, valves, recycling pump, *etc.*) to that of the reaction mixture. The formulation for the external thermal capacitance presented assumes that the externals are in thermal equilibrium with the reactor contents.[27] All physical parameters and kinetic constants described in the model equations are shown in Table 2.

In order to take the gel-effect into account, the termination rate constant is assumed to depend on both the reaction temperature and the monomer conversion, as proposed by Ross and Laurence.[33] The termination constant is rewritten as follows:

$$k_t(T) = k_{t0}(T)g_t(T) \quad (6)$$

where $g_t(T)$, the gel-effect function, is given by

$$g_t = \begin{cases} 0.10575\exp(17.5\upsilon_f - 0.01715(T - 273.15)), & \upsilon_f > \upsilon_{ftc} \\ 2.3\cdot 10^{-6}\exp(75\upsilon_f), & \upsilon_f \le \upsilon_{ftc} \end{cases} \quad (7)$$

where $\upsilon_f$ is the total free volume and $\upsilon_{fc}$ is a critical free volume, given by:

$$\upsilon_f = \upsilon_{f_{MMA}}\nu_{MMA} + \upsilon_{f_{PMMA}}\nu_{PMMA}, \quad (8)$$

$$\upsilon_{ftc} = 0.1856 - 2.965 \cdot 10^{-4}(T - 273.15). \quad (9)$$

Free volumes of MMA and PMMA are given by:

$$\upsilon_{f_{MMA}} = 0.025 + 0.001(T - 167), \quad (10)$$

$$\upsilon_{f_{PMMA}} = 0.025 + 0.00048(T - 387). \quad (11)$$

## Results and Discussion

### Parameter Estimation

Equation (4) presents two thermal parameters, representing the heat transfer to the environment ($\alpha UA$) and the external thermal capacitance factor ($\varepsilon$). These parameters were estimated by fitting simulated temperature profiles to observed experimental profiles for experimental runs performed without reaction (without the initiator / activator system). In a typical heat transfer experiment, equal amounts of MMA (inhibited with 2 wt% of hydroquinone in order to avoid spontaneous thermal polymerization) and PMMA were

***Table 2.***
Parameters describing the MMA polymerization.

| Parameter | References |
|---|---|
| $k_p(T) = 7.0\cdot 10^9\exp(-6300/RT)$ cm³/mol s | [28] |
| $k_d(T) = 6.94\cdot 10^{13}\exp(-29220/RT)$ s$^{-1}$ | [29] |
| $kt(T) = 1.76\cdot 10^{12}\exp(-2800/RT)\cdot g_t(T)$ cm³/mol s | [28] |
| $\rho_{MMA}(T) = 0.9654 - 0.00109(T - 273.15) - 9.7\cdot 10^{-7}(T - 273.15)^2$ g/cm³ | [30] |
| $\rho_{PMMA}(T) = \frac{\rho_{MMA}(T)}{0.754 - 9\cdot 10^{-4}\cdot(T - 343.15)}$ g/cm³ | [30] |
| $\rho_{BaSO_4} = 4.50$ g/cm³ | [31] |
| $c_{p_{MMA}} = 0.490$ cal/g K | [30] |
| $c_{p_{PMMA}}(T) = 0.339 + 9.55\cdot 10^{-4}\cdot(T - 298.15)$ cal/g K | [30] |
| $c_{p_{BaSO_4}} = 0.104$ cal/g K | [31] |
| $\Delta H = 137.70$ cal/g | [32] |
| f = 0.6 | Mean value from various references in [28] |