Understanding and Exploiting T_g Reduction for Surface and Bulk Modification of Polymers with CO_2

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Abstract

In addition to the well-known reduction of bulk T_g by CO_2, we have investigated the existence of a reduced T_g for the surface layer of a polymer, and evaluated the effects of CO_2 on this transition and the corresponding layer thickness. The ability to control the depth of the rubbery layer of a polymer affords even greater control over the impregnation process. We will present our current understanding of the fundamental basis for this behavior and a theoretical analysis centered on a description of the entropy density of the surface layer. Subsequently this phenomenon will be the framework for discussing several derivative applications including: modification of biomedical implants for controlled release of therapeutics, bulk extrusion of thermally labile drug compounds with pharmaceutical polymers, and bonding of polymer devices with nanoscale features.

Introduction

Environmental and toxicity concerns have been motivating tremendous efforts to develop CO_2-assisted polymer processing operations. The resulting products range from foam board insulation and high-impact polymer blends to surface-modified biomedical implants and biological micro-electromechanical system (bio-MEMs) devices [1]. These applications take advantage of the ability of CO_2 to penetrate into the space between polymer chains and alter the chain mobility and free volume characteristics of the matrix. Particularly, as a benign volatile solvent, CO_2 is a completely unregulated, non-contaminating processing aid that offers great potential for applications in biomedical field, such as surface modification, bulk impregnation and nanostructure assembling.

When CO_2 was applied to enhance the bonding between polymer layers, we discovered that the bonding conditions (temperature or gas pressure), are well below those where glass transition occurs to the bulk phase [2]. This experimental observation excitingly drove us to examine closer the dynamic behavior associated with polymer surface region. Consequently, an Atomic Force Microscopy (AFM) based technique capable of handling CO_2-involved measurements was developed to identify the typical parameter of polymer dynamics, namely surface glass transition point. A new theoretical model is subsequently proposed to reveal the reason behind this phenomenon. In addition to a brief description of experimental and modeling results, the impact of CO_2 technology on surface-related biomedical applications is also discussed in this paper.

Surface T_g Measurement

The polymeric materials under investigation include poly lactic-co-glycolic acid, PLGA (Alkermes Medisorb® 5050 DL High IV) and monodisperse polystyrene PS (Polymer Source Inc.). The principle of the measurement technique is to use gold nanoparticles as probes detecting the physical state of surface region. Providing polymer thin film with highly smooth surface (roughness:1~2nm), the gold nanoparticles deposited on it will either remain on the surface or embed, solely dependent on the thermal and/or CO_2 treatment conditions. As a result, the comparison between real particle size and detected particle height using Atomic Force Microscopy (AFM) provides an indication tells whether the surface region is rubbery or glassy.

Figure 1 shows results of particle height corresponding to various temperatures and CO_2 pressures for PLGA and PS, from which the surface T_g is evaluated. Any height measurement less than the particle size of 20.2 ± 1.6 nm is taken to mean that the surface is rubbery and the particle has embedded. For instance, at vacuum condition, the surface T_g of pure PLGA and PS should be between 15~25°C, and 60~70°C, respectively.
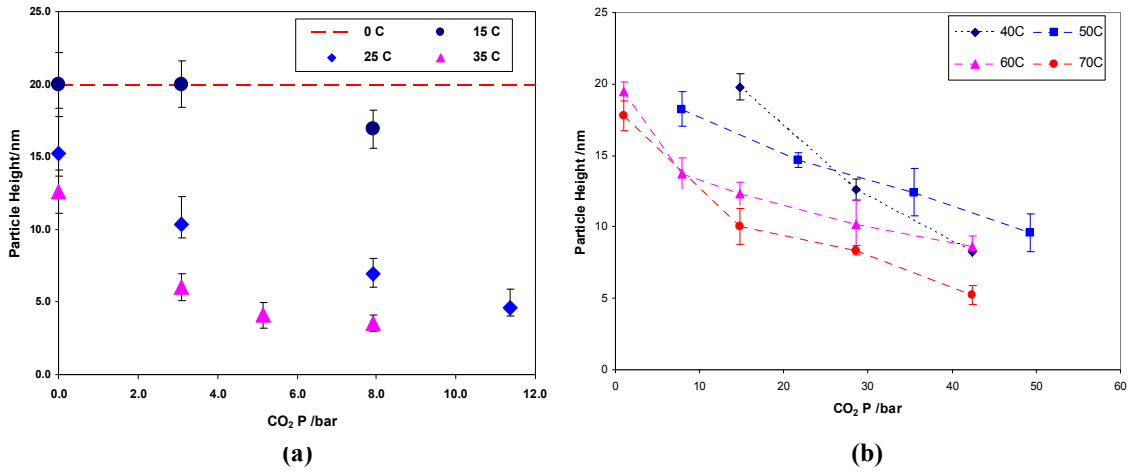
Figure 1 Effects of CO$_2$ on particle height for (a) PLGA (b) PS

Theoretical Model

While experiments have shown enhanced dynamics and modified Tg in polymer thin films for over a decade [3], theoretical approaches to describing the behavior have lagged [4,5]. The most recent descriptions of this behavior rely on regions of cooperative segmental motion arising from a liquid-like surface layer of temperature dependent thickness and hence the idea of thin films or surface regions displaying a "distribution of Tg's." [6,7] We propose an entropy-based approach to characterize this liquid-like surface layer in an inhomogeneous system.

Briefly, we use gradient theory [8] to provide the underlying thermodynamics of an inhomogeneous system and apply the Sanchez-Lacombe EOS [9] to arrive at quantitative values of entropy density in the system. The Gibbs-DiMarzio criterion (zero configurational entropy at Tg) is used to identify the position in the system where the Tg occurs for a particular system temperature.[10] During this process, we assumed that the SLEOS is still valid for liquid-like gradient region at low temperatures, and also the chemical potential from EOS for fluid is valid for glassy polymer when calculated with real glassy density.The equilibrium density profiles and corresponding entropy density profiles for PS are shown in Figure 2. The length scale may not be quantitatively accurate in these calculations since the gradient theory parameters were fit to describe the interfacial tension in the PS-CO$_2$ system. Further, the unrealistic negative entropy density values probably result from the inability of the EOS to describe the glassy state. The temperature dependence and relative length scales are precise. Note that 100.5^{o}C is the normal bulk T_g for PS.

The interface between rubbery and glassy states within surface region is revealed clearly as entropy density reaches zero. The positive value of entropy density at low temperatures strongly suggests a persistent liquid-like surface region. Since even at very low temperatures, the liquid-like layer still exists, it might not be appropriate to assign a

single surface T_g value for a given polymer in theoretical analysis. In this sense, an apparent surface T_g might appear and serve better for describing experiment results and practical applications. We believe these initial results of lower surface T_g confirm that part of the gradient region is the primary source of chain mobility for the whole system at low temperatures. However, due to the nature of polymer chains, the dynamics of regions underneath surface would be definitely influenced by this enhanced mobility through cooperative segmental motion. By following the behavior of mobility propagation, the relationship between T_g and system thickness might be eventually clarified.
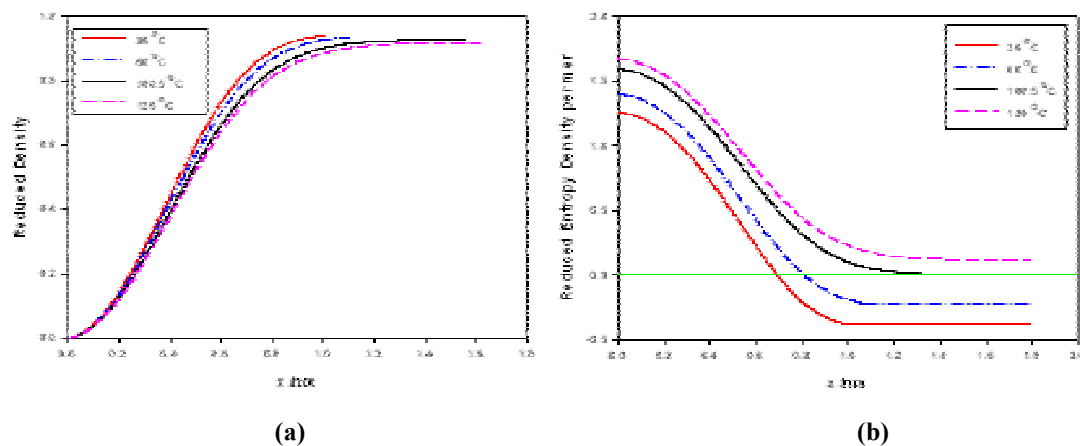

(a)   (b)

Figure 3 Profiles across surface region for PS (a) Mass density (b) Entropy density

Extrusion Compounding of Pharmaceutical Formulations

The reduction of surface Tg is an extension of the commonly recognized reduction of bulk Tg by supercritical fluids. A quick demonstration of the relevance of this phenomena is demonstrate in the formulation of pharmaceutical compounds. Extrusion of polymer melts has developed into a pharmaceutical unit operation over the past decade to form amorphous solid dispersions of crystalline drug compounds [11-13]. The resultant advantage is better dissolution characteristics than the native drug. The disadvantage is that relatively few drug compounds can withstand the temperatures necessary to melt polymers. The reduction of Tg and hence the reduction of extrusion temperature by adding CO_2 may greatly extend this technique to a larger number of drug candidates. Table 1 below gives some sample results of temperature reduction in extrusion for three model pharmaceutical polymers that are currently used in formulations: Polyvinylpyrrolidone-vinyl acetate copolymer (Kollidon VA-64, BASF), Butyl methacrylate-2-(dimethylamino)ethyl methacrylate-methyl methacrylate (1:2:1) (Eudragit E100, Rohm Pharma), and Ethyl cellulose (ETHOCEL Standard 20 Premium, Dow Europe S.A.). Further results on formulations are available. [14]

Table 1. Minimum possible extrusion temperatures and corresponding injection pressure of CO_2 for processing pharmaceutical polymers.

Polymer	$T_{set, minimal}$ (K) without CO_2	$T_{set, minimal}$ (K) with CO_2	$P_{max, CO2}$ (MPa)
PVP-VA 64	423	393	5.5
Eudragit E100	403	388	4.5
EC 20 cps	413	348	12.5

Surface and Bulk Modified Biomedical Implants

Taking advantage of only the surface Tg reduction allows for surface modification of biomedical implants without altering the form or underlying mechanical properties that such implants provide. An example is the partitioning of paclitaxel into an FDA approved maxillofacial reconstructive plate made of polylactic acid (PLA, Synthes® Resorbable Fixation System, Paoli, PA). To retain the form of the implant, only subcritical pressures are required for the impregnation. Subcritically embedded paclitaxel imparts cytotoxic activity toward MCF-7 breast cancer adenocarcinoma cells. When paclitaxel is present within the PLA, its release *in vitro* induces significant levels of cell death within 5 days and produces a zone around the PLA in which no cells survived. Those cells remaining exhibit a 93% increase in apoptosis after 7 total days of culture relative to controls. In the absence of subcritically-embedded paclitaxel, adjacent breast cancer adenocarcinomal cells aggressively repopulate/coat the surface of the implant. Without a change in implant form, subcritical CO_2 can be used to 'piggyback' chemotherapeutic function into the FDA approved biomedical device in a manner that completely prevents this regrowth.

Assembly of Polymeric Micro- and Nanostructures

The final example that truly exploits the reduction in surface Tg only is the bonding or welding of polymer structures containing nanoscale features. The adhesive strength of poly(DL-lactide-co-glycolide) (PLGA) bonded to itself approached 1 MPa after 30 min at 35°C and 0.79 MPa CO_2 pressure. By taking advantage of a nanoscale rubbery layer via surface Tg reduction, polymers can be purposefully fabricated into structures containing microfeatures such as lattice-work tissue engineering scaffolds to tailor the 3-D environment to stimulate growth [15], or nanofeatures such as controlled pores and channels in fluidic devices. In another exciting approach, colloidal polystyrene crystals may be welded to form very uniform thin films. [16]

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