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Effect of polymer molecular weight distribution on solute sequestration in two-phase partitioning bioreactors

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HIGHLIGHTS

- Solute PC was a predictable function of a polymer's number average molecular weight (M_n).
- PC was independent of molecular weight distribution (MWD) (e.g. unimodal, bimodal).
- Polymer complex modulus (G^*) was dependent on both M_n and MWD.
- Bimodal polymer formulations had higher PCs compared to unimodal materials at equivalent G^*.
- Mixtures of an organic solvent and high MW polymer exhibited further PC improvements.

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ABSTRACT

Polymeric solids are effective absorbents in two-phase partitioning bioreactors (TPPBs) when they provide adequate absorptive capacity for the target solute, as well as the physical properties required by solid–liquid TPPB operations. This study demonstrates the influence of molecular weight distribution (MWD) on solute uptake, as measured by solute partition coefficient (PC), and mechanical strength, as measured by the polymer's complex modulus (G^*). Experimental PC data for *n*-octanol absorption from aqueous solution by poly(dimethyl siloxane) (PDMS) demonstrate a decline in absorptive capacity with increasing number average molecular weight (M_n), in agreement with Flory–Huggins solution theory predictions. Importantly, MWD is shown to have no effect on solute uptake, with both unimodal and bimodal distributions generating the same PC at a given M_n. This is in contrast to G^*, whose MWD sensitivity is exploited to formulate bimodal mixtures of poly(isobutylene) (PIB) that provide high *n*-octanol PC values as well as satisfactory material strength. This bimodal MWD strategy to TPPB absorbent design is extended to miscible solutions of high MW PIB and cyclohexylbenzene, which are shown to generate superior *n*-octanol PC at a given G^*.

1. Introduction

Two-phase partitioning bioreactor (TPPB) technology is a proven means of improving bioreactor productivity by reducing substrate and/or product cytotoxicity. The first TPPB processes employed an organic solvent [1–5] or oligomeric liquid (e.g. silicone oil, poly(propylene glycol)) [6–11] as an immiscible second phase to selectively sequester inhibitory compounds from fermentation media. However, low molecular weight absorbents can suffer from biocompatibility and bioavailability issues, as well as operational challenges stemming from volatility, flammability, emulsification and foaming [1,12–17]. Viscoelastic polymers are a potential solution to these challenges [18–20], provided they possess the necessary absorptive capacity, and the physical integrity needed to survive within a bioreactor environment.

A principal polymer selection criterion is thermodynamic affinity for the target solute, as quantified by the partition coefficient (PC) between the polymer and an aqueous phase. The influence of chemical structure, crystallinity and phase transition temperatures on PC has been investigated in detail [21,22], as has the effect of these polymer characteristics on solute diffusivity and mass transfer rate [19,23–30]. The present work advances our understanding of the effect of polymer molecular weight distribution (MWD) on solute absorption. Our preliminary studies have shown that lowering the MW of poly(n-butyl acrylate) [21] and poly(propylene glycol) [9] has a positive effect on PC, presumably due to associated increases in the entropy of mixing [31]. These examples involved unimodal MWD's of linear polymer chains,

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leaving the potential advantages provided by other polymer architectures largely unexplored in the context of TPPB applications.

The central question addressed by this study is whether unimodal MWD polymers and bimodal MWD polymers differ appreciably in terms of solute uptake and material strength. We begin with PC measurements of *n*-octanol absorption by poly(dimethyl siloxane) (PDMS, silicone oil) samples of varying molecular weight and MWD. Both substances are well represented in the bioprocessing literature, with *n*-octanol forming the basis of tabulated $\log K_{o/w}$ data, and silicone oil finding frequent application in TPPB systems [6–8,10,11,32]. These data are discussed in the context of Flory–Huggins solution theory to provide a thermodynamic basis for observed MW effects.

The joint influence of MWD on solute uptake and material strength is examined using poly(isobutylene) (PIB), which provides the mechanical strength that is generally lacking in uncured PDMS materials. Measurements of *n*-octanol PC and complex modulus (G^*) reveal important differences between unimodal and bimodal MWD samples of linear PIB chains. Insights gained through these studies are used to formulate mixtures of high MW PIB with a high-boiling organic solvent, cyclohexylbenzene, which are designed to exploit the absorptive capacity of a low MW compound as well as the physical strength of a high MW polymer. The results are relevant to TPPB bioproduction/biodegradation processes and polymer-based product recovery processes that require solute affinity and mechanical rigidity, such as pervaporation, perstraction and vapor permeation.

2. Materials and methods

2.1. Materials and material preparation

All chemicals (purity ⩾98%) were purchased from either Sigma–Aldrich (Canada) or Fisher Scientific (Canada). All poly(dimethyl siloxane) (PDMS) samples (S-UM-1 to S-UM-5) were purchased from Scientific Polymer Products (Ontario, NY). PIB samples IB-UM-1 to IB-UM-4 were provided by TPC group (Houston, TX). PIB samples IB-UM-5 and IB-UM-6 were provided by Shandong Hongrui Petrochemical Co., Ltd (Jinan, China). Samples IB-UM-7 to IB-UM-9 were purchased from Scientific Polymer Products (Ontario, NY). Number average (M_n) and weight average (M_w) molecular weight data for each polymer are listed in Tables 1 and 2, experimentally determined as per Section 2.2.

Bimodal PDMS samples were prepared by adding varying quantities of S-UM-1 to S-UM-5 and agitated in an Innova 4400 incubator shaker at 30 °C and 180 rpm until the solution was homogeneous (one week). The solution was vortexed at least daily under high power to facilitate homogeneity. Bimodal PIB mixtures (IB-BM) were prepared by dissolving varying quantities of IB-UM-1 and IB-UM-9 as a ~15 wt% solution in hexanes in a sealed glass tube. The resultant polymer cement was agitated at 180 rpm in an Innova 4400 incubator shaker at 60 °C until the solution was homogenous (one week). The solution was vortexed at least daily under high power to facilitate homogeneity. Aliquots of the polymer mixtures were transferred to scintillation vials and allowed to dry at 60 °C for one week followed by atmospheric conditions for one additional week.

Table 1
M_n and M_w values for unimodal PDMS samples (S-UM) and bimodal mixtures of high MW PDMS mixed with oligomeric PDMS (S-BM). S-BM samples were made by combining S-UM-1 and S-UM-5.

Sample ID	Low MW component	Low MW fraction	M_n (g/mol)	M_w (g/mol)
S-UM-1	n/a[a]	0	100[b]	105[b]
S-UM-2	n/a[a]	0	1150	1,200
S-UM-3	n/a[a]	0	9220	15,500
S-UM-4	n/a[a]	0	21,600	48,400
S-UM-5	n/a[a]	0	69,700	135,300
S-BM-1	PDMS oligomer	0.95	105	6580
S-BM-2	PDMS oligomer	0.90	110	13,300
S-BM-3	PDMS oligomer	0.75	130	34,400
S-BM-4	PDMS oligomer	0.50	200	67,700
S-BM-5	PDMS oligomer	0.25	400	101,500
S-BM-6	PDMS oligomer	0.10	980	121,800
S-BM-7	PDMS oligomer	0.05	1880	128,300

[a] Unimodal sample.
[b] Nominal value from supplier.

Table 2
M_n and M_w values for unimodal PIB samples (IB-UM), bimodal mixtures of high MW PIB with oligomeric PIB (IB-BM) and bimodal mixtures of high MW PIB with CHB (IB-CHB). IB-BM samples were made by combining IB-UM-1 and IB-UM-9. IB-CHB samples made were made by combining IB-UM-9 with CHB.

Sample ID	Low MW component	Low MW fraction	M_n (g/mol)	M_w (g/mol)
IB-UM-1	n/a[a]	0	670	1100
IB-UM-2	n/a[a]	0	920	1790
IB-UM-3	n/a[a]	0	1470	3110
IB-UM-4	n/a[a]	0	2670	8490
IB-UM-5	n/a[a]	0	9490	51,400
IB-UM-6	n/a[a]	0	18,400	65,500
IB-UM-7	n/a[a]	0	21,200	119,800
IB-UM-8	n/a[a]	0	85,700	503,800
IB-UM-9	n/a[a]	0	320,000	4,912,000
IB-BM-1	PIB oligomer	0.75	890	1,229,000
IB-BM-2	PIB oligomer	0.50	1320	2,446,000
IB-BM-3	PIB oligomer	0.25	2640	3,677,000
IB-BM-4	PIB oligomer	0.10	6490	4,416,000
IB-BM-5	PIB oligomer	0.05	12,500	4,659,000
IB-BM-6	PIB oligomer	0.01	50,400	4,857,000
IB-CHB-1	Cyclohexylbenzene	0.25	640	3,684,000
IB-CHB-2	Cyclohexylbenzene	0.11	1520	4,396,000
IB-CHB-3	Cyclohexylbenzene	0.04	3860	4,710,000
IB-CHB-4	Cyclohexylbenzene	0.02	9160	4,828,000

[a] Unimodal sample.

Bimodal mixtures of high MW PIB and cyclohexylbenzene (IB-CHB) were prepared by adding varying quantities of cyclohexylbenzene (CHB) to IB-UM-9 and agitated in an Innova 4400 incubator shaker at 30 °C and 180 rpm until the solution was homogeneous (two weeks). The solution was vortexed at least daily under high power to facilitate homogeneity. The rational for selecting CHB is provided in considerable detail in Section 3.4. Low molecular weight component fractions (wt/wt) were calculated by determining the weight loss from a sample after drying in a 110 °C oven.

2.2. Molecular weight determination

PIB and PDMS samples with $M_n < 100{,}000$ g/mol were characterized by size exclusion chromatography (SEC) using a Waters 2960 separation module with Styragel packed columns HR 0.5, HR 1, HR 3, HR 4, and HR 5E (Waters Division Millipore) coupled with a refractive index (RI) detector operating at 35 °C. Tetrahydrofuran (THF) was used as eluent and the flow rate was set to 1.0 mL/min.

PIB samples with $M_n > 100{,}000$ g/mol were characterized by SEC using a Viscotek 270max separation module with an RI detector. A set of two porous PolyAnalytik columns with an exclusion limit molecular weight of 20×10^6 g/mol were used in series at 40 °C. Distilled THF was used as the eluent at a flow rate of 1.0 mL/min.

In both cases, the weight average molecular weight (M_w), number average molecular weight (M_n) and polydispersity index (PDI)