

Constrained nonlinear optimization for solubility parameters of poly(lactic acid) and poly(glycolic acid)—validation and comparison

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Abstract

An optimization technique has been proposed to determine Hansen solubility parameters (HSP) and radius of interaction (R) of PLA and PGA; objective function to be minimized being radius of interaction (R), and the constraints being that the solvents should be within and nonsolvents outside the interaction sphere. The proposed method has been validated and found to be most reliable. The values of HSP (δ_d , δ_p , δ_h) and R for PLA have been obtained as ((18.50, 9.70, 6.00) and 10.50) (J/cc)^{0.5} at 25 °C; and those of PGA as ((17.70, 6.21, 12.50) and 1.92) (J/cc)^{0.5} at 80 °C. For formulating the nonlinear inequality constraints known HSP data for 20 solvents and seven nonsolvents have been used for PLA at 25 °C; similarly HSP data for three newly found solvents (phenol, *m*-cresol and 4-chlorophenol), and five nonsolvents have been used for PGA at 80 °C. Established methods have been used for comparison. **HSP and R have been directly compared using the 3D intrinsic viscosity and classical methods.** Indirectly the total solubility parameter δ has been compared with the values obtained from the intrinsic viscosity 1D approach and group contribution method using Fedors and van Krevelen correlations. The 1D approach has led to an empirical correlation for intrinsic viscosities of PLA and PGA.

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1. Introduction

Poly(lactic acid) and poly(glycolic acid) belong to the family of aliphatic polyesters commonly made from α -hydroxy acids. PLA is a thermoplastic, high-strength, high-modulus polymer used in sutures and dental, orthopedic, and drug delivery systems. It is easily processed on standard plastics equipment to yield molded parts, films or fibres [1]. It is one of the few polymers in which the stereo-chemical structure can easily be modified by polymerizing a controlled mixture of the L- or D-isomers to yield high-molecular weight amorphous or crystalline polymers that can be used for food contact and are generally recognized as safe (GRAS) [2]. The above technique is also used for improving PLA processability based on melting point depression by the random incorporation of small amounts of lactide enantiomers of opposite configuration into the

polymer (i.e. adding a small amount of D-lactide to the L-lactide to obtain PDLLA). Noticeably, the melting point depression is accompanied by a significant decrease in crystallinity and crystallization rates [3]. PLA has a degradation time of the order of 6 months to 2 years, which compares to 500–1000 years for conventional polystyrene and polyethylene [4]. PGA or Dexon is the simplest poly (α -hydroxy acid). It is the first synthetic polymer which is used to make biomedical and pharmaceutical devices. Dexon is used for surgical sutures, drug delivery systems, and scaffolds for use in cell culture, transplantation and organ regeneration. Both polymers exhibit good biocompatibility, biodegradability mainly by hydrolysis and very good processability. Both are bioresorbable and their degradation rates, physical, mechanical and other properties can be tailored by varying molecular weights or by employing their copolymers.

Hansen [5,6] three-component solubility parameter (HSP) and Hildebrand [7,8] or total solubility parameter have been useful in predicting the solubility of polymers in

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various solvents, plasticizers and their compatibility with other polymers and pigments and thus in designing coating formulations. **The use of solubility parameter is the only practical way of predicting polymer solubility.** Hence various methods have been devised to predict the solubility parameter of polymers. (Hansen [5,6]; Van Dyk et al. [9]; Tanaka [10]; Panayiotou [11]; Segarceanu and Leca [12]). **However, the limitation of this approach is that it will not predict the extent of polymer solubility.**

1 **The experimental 3D intrinsic viscosity method proposed by Segarceanu and Leca [12] uses the intrinsic viscosities of polymer in different solvents as ‘weights’ of dissolving capacities of these solvents for the polymer.** Equations, corresponding to a system of material points placed into a 3D space, are used to determine HSP and the radius of interaction sphere R . In 1D method, intrinsic viscosity values of the swelling coefficients can be arranged in the form of a Gaussian shaped curve [13] to give total solubility parameter.

2 **The theoretical classical and group contribution methods are also common.** The classical method [5,6,14] consists of testing the polymer solubility in different solvents and plotting these solvents in 3D space. The farthest distance between any two solvents is taken as diameter of the sphere and the midpoint gives the values of HSP. Group contribution or additive methods have a long tradition of successful use in predicting properties of both ordinary molecules and polymers. **Hildebrand or total solubility parameter is the square root of the cohesive energy density.** **Cohesive energy of the polymer can be determined using Fedors [15,16] and van Krevelen [17,18] group contribution correlations in terms of connectivity indices.** The formalism of connectivity indices is an embodiment of graph theory which is in turn a sub-discipline of the topology of the material. Connectivity indices or topological indices are intuitively appealing because each index can be calculated exactly from valence bond (Lewis) diagrams familiar to organic chemists, which depict molecular structure in terms of atoms, inner shell and valence shell hybridization, σ and π electrons, bonds and lone pairs. The indices can then be correlated with physical or chemical properties of interest [19,20].

The present work estimates the HSP, Hildebrand parameter and radius of interaction sphere R of the biopolymers using above mentioned experimental and theoretical methods. **Intrinsic viscosity data obtained for PLA and PGA in the considered solvents has been used to determine the HSP and R by Segarceanu and Leca method [12] and the total solubility parameters by the Gaussian curve fitting method [13].** Classical method [5,6,14] again predicts the HSP and R while the group contribution correlations [15–20] give the total parameter for PLA and PGA.

An optimization technique has been proposed to estimate the HSP and R for PLA and PGA, which takes into account both solvents and nonsolvents. The optimization method

minimizes the radius of the interaction sphere subject to the constraints that solvents lie within the sphere while nonsolvents lie outside the sphere. The problem is formulated as a single objective function with nonlinear inequality constraints corresponding to all solvents and non solvents. The optimized solution gives the HSP and R for PLA and PGA.

2. Estimation using available literature methods

2.1. Intrinsic viscosity 3D method

The intrinsic viscosity method [12] to calculate partial solubility parameters as well as the radius of the interaction sphere starts from the idea that the solvents which dissolve a polymer, form in the interior of its solubility range a system of material points, their ‘weights’ being given by the fractional intrinsic viscosities of the polymer in the considered solvents. The mass center coordinates of the material points system represent in fact Hansen solubility parameters of the polymer, and the radius of the interaction sphere, the distance from this center to the farthest point of material point system mentioned. It is obvious that mass center is closer to solvents with higher weights, the ones which dissolve it better, and away from those with smaller weights, the ones which are not good solvents of the polymer. The equations of the coordinates of the mass center are in Eq. (1).

$$\delta_{dp} = \frac{\sum(\delta_{di}[\eta]_i)}{\sum[\eta]_i}; \quad \delta_{pp} = \frac{\sum(\delta_{pi}[\eta]_i)}{\sum[\eta]_i};$$

$$\delta_{hp} = \frac{\sum(\delta_{hi}[\eta]_i)}{\sum[\eta]_i} \quad (1)$$

where $\sum[\eta]_i$ is the intrinsic viscosity of polymer in given solvent i . Once the mass centre coordinates of the sphere are determined, distance in three dimensional solubility space between a polymer and a solvent can be calculated from R_i given by Eq. (2), whose highest value is considered as the radius of interaction sphere, R .

$$R_i = \{[2(\delta_{dp} - \delta_{ds})]^2 + [\delta_{pp} - \delta_{ps}]^2 + [\delta_{hp} - \delta_{hs}]^2\}^{1/2} \quad (2)$$

where subscripts p and s refer to polymer and solvent, respectively. The intrinsic viscosity data [21] and HSP data [22] at 25 °C, for PLA in eight known solvents, is given in Table 1. Based on the experiments in our lab, three solvents namely phenol, *m*-cresol and 4-chlorophenol have been found to dissolve the PGA sample of low molecular weight at 80 °C. The experimental data of intrinsic viscosity of PGA at 80 °C in these solvents is given in Table 2. The data for two polymers is used in Eqs. (1) and (2) to find the HSP and R for PLA at 25 °C and for PGA at 80 °C. The results are reported in Tables 3 and 4, for PLA and PGA, respectively.

The values of δ_d , δ_p and δ_h for PGA solvents are

Table 1
Solubility parameters and intrinsic viscosities for PLA at 25 °C

Solvents	HSP (J/cc) ^{0.5} at 25 °C					[η] ^b
	δ _d ^a	δ _p ^a	δ _h ^a	δ _t		
Acetone	15.0	10.4	7	19.6	–	
Acetonitrile	15.3	18.0	6.1	24.4	0.051	
Benzene	18.4	0.0	2.0	18.5	0.062	
Chloroform	17.8	3.1	5.5	18.9	0.240	
<i>m</i> -Cresol	18	5.1	12.9	22.7	–	
Dimethyl formamide	17.4	13.7	11.3	24.9	0.075	
Dimethyl sulphoxide	18.4	16.4	10.0	26.6	0.010	
1-4 Dioxane	19.0	1.8	7.4	20.5	–	
1-3 Dioxolane	18.1	6.6	9.3	21.4	–	
Ethyl acetate	15.8	5.3	7.2	18.2	–	
Furan	17.8	1.8	5.3	18.7	–	
Hexafluoro isopropanol	17.2	4.5	14.7	23.1	–	
Isoamyl alcohol	15.8	5.2	13.3	21.3	–	
Methylene dichloride	18.2	6.3	6.1	20.2	0.240	
Methyl ethyl ketone	16.0	9.0	5.1	19.1	–	
<i>n</i> -Methyl pyrrolidone	18.0	12.3	7.2	23.0	–	
Pyridine	19.0	8.8	5.9	21.8	–	
Tetrahydrofuran	16.8	5.7	8.0	19.5	0.053	
Toluene	18.0	1.4	2.0	18.2	0.061	
Xylene	17.6	1.0	3.1	17.9	–	
Nonsolvents						
Isopropyl ether	13.7	3.9	2.3	14.4	–	
Cyclohexane	16.5	0.0	0.2	16.5	–	
Hexane	14.9	0.0	0.0	14.9	–	
Ethanol	15.8	8.8	19.4	26.5	–	
Methanol	15.1	12.3	22.3	29.6	–	
Water	15.5	16.0	42.3	47.8	–	
Diethyl ether	14.5	2.9	5.1	15.6	–	

^a Ref. [22].

^b Ref. [21].

estimated at 80 °C from the reported values at 25 °C using the correlations available for their variation with temperature [23] as given in Eq. (3).

$$\begin{aligned} d\delta_d/dT &= -1.25\alpha\delta_d; & d\delta_p/dT &= -\delta_p\alpha/2; \\ d\delta_h/dT &= -\delta_h(1.22 \times 10^{-3} + \alpha/2) \end{aligned} \quad (3)$$

where α (K⁻¹) is the volume expansion coefficient for the solvents estimated (for the range 25–125 °C) using ASPEN (version 10.0) [24] and is given in Table 2.

2.2. Intrinsic viscosity 1D method

Intrinsic viscosity data obtained for PLA and PGA (Tables 1 and 2) in the considered solvents has been used to determine the ID, i.e. the total solubility parameter of PLA and PGA, δ_t . The [η] values of the swelling coefficients are arranged in the form of a Gaussian shaped curve [13]:

$$[\eta] = [\eta]_{\max} \exp[-A(\delta_{ts} - \delta_t)^{-2}] \quad (4)$$

where δ_{ts} and δ_t are the total solubility parameters of the solvent and polymer, respectively. The maximum value, [η]_{max} is attributed to the solvent with the highest solvency power, and is expected when $\delta_{ts} = \delta_t$. This maximum

appears due to maximum coil extension or hydrodynamic volume after solvation by the most effective solvent. However, no well founded justification has yet been given for using the Gaussian curve.

On fitting the Gaussian curve to the intrinsic viscosity data, the empirical correlations obtained for the intrinsic viscosity of low molecular weight samples of PLA and PGA in various solvents are as follows:

$$\text{For PLA : } [\eta] = 0.24 \exp[-2.09(\delta_{ts} - \delta_t)^2]$$

$$\text{For PGA : } [\eta] = 0.3327 \exp[-0.243(\delta_{ts} - \delta_t)^2]$$

The values for δ_t are obtained in Tables 3 and 4, for PLA and PGA.

2.3. Classical 3D geometric method

To estimate the solubility parameter of PLA and PGA, their solubility in various solvents was tested. A small amount of the polymer was placed in the solvent of interest, and was stirred for 48 h, at 25 °C for PLA and, at 80 °C for PGA. If it gave a clear solution, the polymer was assumed to be soluble in the solvent else it was assumed to be insoluble. 20 solvents and seven nonsolvents thus tested are listed in

Table 2
Solubility parameters and intrinsic viscosities for PGA at 80 °C

Solvents	HSP (J/cc) ^{0.5} at 25 °C			α (Used in Eq. (3))	HSP (J/cc) ^{0.5} at 80 °C				
	δ_d	δ_p	δ_h		δ_d^a	δ_p^a	δ_h^a	δ_t	$[\eta]^b$
Phenol	18.0	5.9	14.9	0.000872	16.9	5.8	13.6	22.5	0.3327
<i>m</i> -Cresol	18.0	5.1	12.9	0.000788	17.1	5.0	11.8	21.3	0.2645
4-Chlorophenol ^c	19.5	7.6	14.4	0.000875	18.4	7.4	13.1	23.8	0.1984
Nonsolvents									
Water	15.5	16	42.3	0.000699	14.8	15.7	38.8	44.4	–
Hexane	14.9	0	0	0.001632	13.3	0	0	13.3	–
Acetone	15.5	10.4	7.0	0.001763	13.7	9.9	6.2	18.0	–
Benzene	18.4	0	0	0.001296	16.8	0	0	16.8	–
Chloroform	17.8	3.1	5.7	0.001446	16.1	2.9	5.1	17.2	–

^a Ref. [22].

^b This work.

^c See Appendix B.

Table 3
Solubility parameters for PLA at 25 °C

Method	δ_d (J/cc) ^{0.5}	δ_p (J/cc) ^{0.5}	δ_h (J/cc) ^{0.5}	δ_t (J/cc) ^{0.5}	R (J/cc) ^{0.5}
Intrinsic 3D viscosity method	17.61	5.30	5.80	19.28	13.53
Intrinsic 1D viscosity method	–	–	–	19.16	–
Classical 3D geometric method	16.85	9.00	4.05	19.53	9.74
Fedors group contribution	–	–	–	21.42	–
Van Krevelen group contribution	–	–	–	17.64	–
Optimization method	18.50	9.70	6.00	21.73	10.50

Table 4
Solubility parameters for PGA

Method	Temperature (°C)	δ_d (J/cc) ^{0.5}	δ_p (J/cc) ^{0.5}	δ_h (J/cc) ^{0.5}	δ_t (J/cc) ^{0.5}	R (J/cc) ^{0.5}
Intrinsic 3D viscosity method	80	17.34	5.92	12.88	22.39	2.57
Intrinsic 1D viscosity method	80	–	–	–	22.31	–
Classical 3D geometric method	80	17.72	6.21	12.46	22.53	1.92
Fedors group contribution	25	–	–	–	23.82	–
Van Krevelen group contribution	25	–	–	–	19.24	–
Optimization method	80	17.70	6.21	12.50	22.54	1.92

Table 1, for PLA; three solvents and five nonsolvents thus tested are listed in Table 2, for PGA.

The distance between all the possible pairs of solvents is calculated. For PLA, from 20 solvents listed in Table 1, this gives ${}^{20}C_2$, i.e. 190 possible combinations. The benzene and acetonitrile pair is the farthest apart. It is thus taken as the opposite ends of the diameter of the sphere of influence. The mid-point of this diameter is the center of the sphere giving the value of HSP for PGA, and the diameter corresponds to $2R$. The distance of any solvent from the center is R_i as shown in Fig. 1 and those values are reported in Tables 5 and 6 for PLA and PGA, respectively. For PGA, from the three solvents listed in Table 2, this gives 3C_2 , i.e. three possible combinations. The *m*-cresol and 4-chlorophenol pair is the farthest apart. The value of HSP and R are then obtained as for PLA. Using the above procedure, the results obtained for PLA and PGA, are reported in Tables 3 and 4, respectively.

2.4. Group contribution method

The Hildebrand solubility parameter is given by the squareroot of the cohesive energy density (cohesive energy per unit molar volume of the polymer)

$$\delta = (\text{CED})^{1/2} = (E_{\text{coh}}/V)^{1/2} \quad (5)$$

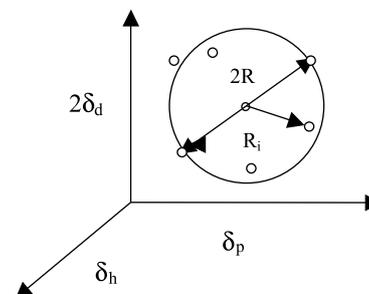


Fig. 1. Classical method for Hansen Solubility Parameters.

Table 5
RED values from classical and optimization methods for PLA

Solvents	R_i (classical)	RED (classical)	R_i (optimization)	RED (optimization)
Acetone	4.29	0.44	6.09	0.58
Acetonitrile	9.74	1.00	10.50	1.00
Benzene	9.74	1.00	10.50	1.00
Chloroform	6.43	0.66	6.72	0.64
<i>m</i> -Cresol	8.86	0.91	6.62	0.63
Dimethyl formamide	8.67	0.89	7.04	0.67
Dimethyl sulphoxide	9.93	1.02	7.88	0.75
1-4 Dioxane	9.06	0.93	8.09	0.77
1-3 Dioxolane	6.33	0.65	4.62	0.44
Ethyl acetate	5.26	0.54	7.04	0.67
Furan	7.60	0.78	8.09	0.77
Hexafluoro isopropanol	11.60	1.19	10.50	1.00
Isoamyl alcohol	1.36	0.14	10.19	0.97
Methylene dichloride	4.38	0.45	3.47	0.33
Methyl ethyl ketone	4.29	0.44	5.04	0.48
<i>n</i> -Methyl pyrrolidone	5.06	0.52	3.05	0.29
Pyridine	4.68	0.48	1.37	0.13
Tetrahydrofuran	2.05	0.21	5.57	0.53
Toluene	8.18	0.84	9.24	0.88
Xylene	8.18	0.84	9.35	0.89
Nonsolvents				
Isopropyl ether	8.28	0.85	11.76	1.12
Cyclohexane	9.84	1.01	11.97	1.14
Hexane	10.62	1.09	13.44	1.28
Ethanol	15.49	1.59	14.49	1.38
Methanol	18.80	1.93	17.96	1.71
Water	38.96	4.00	37.49	3.57
Diethyl ether	7.79	0.80	10.50	1.00

Cohesive energy has been estimated from the correlations based on the group contributions proposed by Fedors and by van Krevelen. These correlations are in terms of the zeroth-order or atomic (${}^0\chi$ and ${}^0\chi^v$) connectivity indices and first-order or bond (${}^1\chi$ and ${}^1\chi^v$) connectivity indices, for the repeat unit of the polymers, which are estimated from the hydrogen suppressed graph of the repeat unit [19,20]. The indices ${}^0\chi$ and ${}^0\chi^v$ are defined in terms of summations over vertices of the hydrogen suppressed graph while ${}^1\chi$ and ${}^1\chi^v$ are defined in terms of summations over edges of the hydrogen suppressed graph (see Appendix A for details).

The cohesive energy has been estimated, using the

Fedors [15,16] and van Krevelen [17,18] correlations from the repeat unit of PLA and PGA (Fig. 2). Molar volume V has been estimated from the correlation based on the group contributions proposed by van Krevelen [25] given in Eq. (11).

2.4.1. Correlation for Fedors-type cohesive energy

$$E_{\text{coh}} (\text{J/mol}) = 9882.5({}^1\chi) + 358.7(6N_{\text{atomic}} + 5N_{\text{group}}) \quad (6)$$

where dimensionless constants N_{group} and N_{atomic} are defined by Eqs. (7) and (8), respectively.

Table 6
RED values from classical and optimization methods for PGA

Solvents	R_i (classical)	RED (classical)	R_i (optimization)	RED (optimization)
Phenol	1.96	1.02	1.91	0.99
<i>m</i> -Cresol	1.92	1.00	1.92	1.00
4-Chlorophenol	1.92	1.00	1.92	1.00
Nonsolvents				
Water	28.69	14.94	28.60	14.89
Hexane	35.69	18.59	35.70	18.59
Acetone	10.80	5.63	10.78	5.62
Benzene	14.06	7.32	14.08	7.33
Chloroform	8.66	4.51	8.66	4.51

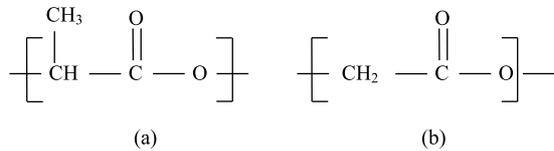


Fig. 2. Repeat units of PLA (a) and PGA (b).

$$\begin{aligned}
 N_{\text{group}} = & 12N_{\text{hydroxyl}} + 12N_{\text{amide}} \\
 & + 2N_{\text{(nonamide -(NH)- unit)}} - N_{\text{(alkylether -O-)}} \\
 & - N_{\text{(C=C)}} + 4N_{\text{[nonamide -(C=O)- next to nitrogen]}} \\
 & + 2N_{\text{[other -(C=O)]}} \\
 & + 7N_{\text{[-(C=O)- in carboxylic acid, ketone or aldehyde]}} \\
 & + 4N_{\text{(nitrogen atoms in six-membered aromatic rings)}} \quad (7)
 \end{aligned}$$

$$\begin{aligned}
 N_{\text{atomic}} = & 4N_{\text{(-S-)}} + 12N_{\text{sulfone}} - N_{\text{F}} + 3N_{\text{Cl}} + 5N_{\text{Br}} \\
 & + 7N_{\text{cyanide}} \quad (8)
 \end{aligned}$$

2.4.2. Correlation for van Krevelen-type cohesive energy

$$E_{\text{coh}} = 10570.9(^0\chi^v - ^0\chi) + 9072.8(2^1\chi - ^1\chi^v) + 1018.2N_{\text{VKH}} \quad (9)$$

where dimensionless constant N_{VKH} is defined by Eq. (10).

$$\begin{aligned}
 N_{\text{VKH}} = & N_{\text{Si}} + 3N_{\text{(-S-)}} + 36N_{\text{sulfone}} + 4N_{\text{Cl}} + 2N_{\text{Br}} \\
 & + 12N_{\text{cyanide}} + 8N_{\text{ketone}} \\
 & + 16N_{\text{[nonamide -(C=O)- next to nitrogen]}} \\
 & + 33N_{\text{(alcohol or phenol type -OH units)}} + 4N_{\text{cyc}} \\
 & + 19N_{\text{anhydride}} \\
 & + 2N_{\text{[nitrogen with } \delta=2 \text{ but not adjacent to C=O and not in a six} \\
 & \quad \text{membered aromatic ring]}^+} \\
 & 7N_{\text{(Nitrogen in six membered aromatic ring)}} + 20N_{\text{(carboxylic acid)}} \\
 & + \sum (4 - N_{\text{row}})_{\text{(substituents with } \delta=1 \text{ attached to aromatic} \\
 & \quad \text{rings in backbone)}} \quad (10)
 \end{aligned}$$

Here δ in the hydrogen suppressed graph is the number of edges emanating from a vertex.

N_{row} is the row of the periodic table in which the atom represented by the vertex with $\delta = 1$ is located.

2.4.3. Molar volume estimation from correlation by van Krevelen

$$\begin{aligned}
 V(\text{cc/mol}) = & 3.642770(^0\chi) + 9.798697(^0\chi) - 8.542819(^1\chi^v) \\
 & + 21.693912(^1\chi^v) + 0.978655(N_{\text{MV}}) \quad (11)
 \end{aligned}$$

where dimensionless constant N_{MV} is defined by Eq (12).

$$\begin{aligned}
 N_{\text{MV}} = & 24N_{\text{Si}} - 18N_{\text{(-S-)}} - 5N_{\text{sulfone}} - 7N_{\text{Cl}} \\
 & - 16N_{\text{Br}} + 2N_{\text{(backbone ester)}} + 3N_{\text{ether}} \\
 & + 5N_{\text{carbonate}} + 5N_{\text{(C=C)}} - 11N_{\text{cyc}} \\
 & - 7N_{\text{(fused-1)}} \quad (12)
 \end{aligned}$$

Last term to be used only when $N_{\text{fused}} \geq 2$ where N_{fused} is any ring structure containing atleast one aromatic ring which shares at least one edge with another ring, and all of the other rings with which it shares an edge.

The values of the connectivity indices (see Appendix A for calculations), cohesive energy and molar volume, along with the involved dimensionless constants, are given in Table 7. The results of Hildebrand solubility parameter for PLA and PGA at 25 °C, from Eq. (5), are reported in Tables 3 and 4, respectively.

3. Proposed optimization approach

The intrinsic viscosity and classical methods use only solvents for determining HSP and R . Several anomalies are possible due to this approach such as a nonsolvent lying inside the solubility sphere or as solvent lying outside the sphere. The proposed method takes into account both solvents and nonsolvents. The solubility parameter data set, for solvents and nonsolvents of PLA and PGA, is given in Tables 1 and 2, respectively. Here the swelling agents are considered as nonsolvents so as to get minimum value of R within which the solvents will dissolve the polymer completely. The fitting of the sphere to these data sets has been considered as an optimization problem. The problem has been defined as:

Find a sphere of minimum radius with the constraints that the solvents should lie within the sphere and the nonsolvents outside the sphere.

Mathematically,
Objective function:

$$\begin{aligned}
 \text{Minimize } R(\delta_{\text{dp}}, \delta_{\text{pp}}, \delta_{\text{hp}}, R) = & f[(\delta_{\text{di}}, \delta_{\text{pi}}, \delta_{\text{hi}}) \text{ for all } i \\
 = & 1, 2, \dots, N_{\text{S}}; (\delta_{\text{dj}}, \delta_{\text{pj}}, \delta_{\text{hj}}) \text{ for all } j = 1, 2, \dots, N_{\text{NS}}]
 \end{aligned}$$

where f is an implicit function of the HSP parameters of all solvents and nonsolvents subject to the nonlinear inequality

Table 7
Connectivity indices, cohesive energy and molar volume of PLA and PGA

Connectivity indices and constants appearing in Eqs. (6)–(12)	PLA	PGA	
Zeroth-order and first-order connectivity indices	${}^0\chi$	3.8618	2.9964
	${}^0\chi^v$	2.8938	2.0236
	${}^1\chi$	2.3045	1.89385
	${}^1\chi^v$	1.50998	1.05048
Cohesive energy (E_{coh}) from Fedors correlation	N_{group}	2	2
	N_{atomic}	0	0
	E_{coh} (J/mol)	26,361.22	22,303.47
Cohesive energy (E_{coh}) from van Krevelen correlation	N_{VKH}	0	0
	E_{coh} (J/mol)	17,884.16	14,552
	N_{MV}	2	2
Molar Volume (V) from van Krevelen correlation	V (cc/mol)	57.45	39.3

constraints for N_S solvents

$$R_i - R \leq 0 \quad \text{for solvents; } i = 1, 2, \dots, N_S \quad (13)$$

R_i being the distance between the solvent and the center of the sphere (δ_{dp} , δ_{pp} , δ_{hp}) and similarly subject to the nonlinear inequality constraints for N_{NS} nonsolvents

$$R - R_j \leq 0 \quad \text{for non-solvents; } j = 1, 2, \dots, N_{\text{NS}} \quad (14)$$

R_j being the distance between the nonsolvent and the center of the interaction sphere.

Both R_i and R_j are given by Eq. (2) and $N_S = 20$ and $N_{\text{NS}} = 7$ for PLA and $N_S = 3$ and $N_{\text{NS}} = 5$ for PGA.

This problem has been solved using *fmincon* function of optimization tool box of MATLAB (version 6.5) [29]. This function uses nonlinear programming to minimize the multivariable objective function within the given constraints.

For the function $f(x)$, the problem can be stated in general as follows:

Min $f(x)$ subject to

$$c(x) \leq 0; \quad \text{ceq}(x) = 0; \quad A \cdot x \leq b;$$

$$\text{Aeq} \cdot x = \text{beq}; \quad \text{lb} \leq x \leq \text{ub}$$

where x , b , beq , lb and ub are vectors. A and Aeq are matrices, $c(x)$ and $\text{ceq}(x)$ are functions that return vectors,

and $f(x)$ is a function that returns a scalar. $c(x)$, $\text{ceq}(x)$ are nonlinear functions.

The syntax for *fmincon* function is specified as follows;

$$x = \text{fmincon}(\text{fun}, x0, A, b, \text{Aeq}, \text{beq}, \text{lb}, \text{ub}, \text{nonlcon}, \text{options}) \quad (15)$$

For this problem, $x = [\delta_{\text{dp}} \delta_{\text{pp}} \delta_{\text{hp}} R]$ *fun* is the objective function taken as R . We have only nonlinear inequality constraints $c(x)$, corresponding to solvents (Eq. (13)) and nonsolvents (Eq. (14)) which are incorporated in function *nonlcon*. The other constraints are absent so the values of A , b , Aeq , beq , lb and ub are all set to [] as per *fmincon* syntax. The $x0$ is the starting vector corresponding to the initial guess taken as [10 10 10 10]. The function options specifies the default optimization parameters.

The optimized results $[\delta_{\text{dp}} \delta_{\text{pp}} \delta_{\text{hp}} R]$ obtained for PLA and PGA are reported in Tables 3 and 4, respectively.

4. Validation of the proposed method

We consider the polyesterimide resin example mentioned in Ref. [12] where solubility parameter data for six solvents and five nonsolvents has been given. The authors [12] considered both the dissolving (solvents 1–6 in Table 8) and swelling solvents (solvents 7–11 in Table 8) in their

Table 8
Solubility parameter and intrinsic viscosity data for polyesterimide Ref. [12]

Solvents	δ_d	δ_p	δ_h	$[\eta]$
<i>N</i> -Methylpyrrolidone	18.0	12.3	7.2	0.1014
Dimethyl Formamide	16.8	13.3	14.3	0.0990
Dimethyl Sulphoxide	18.4	16.4	10.2	0.0190
γ -Butyrolactone	19.1	16.6	6.6	0.0700
Morpholine	18.9	4.9	9.2	0.1045
Cyclohexane	17.8	8.4	5.1	0.0750
Nonsolvents				
Acetone	15.6	11.7	4.1	–
Methyldiethylene glycol	16.2	7.8	12.7	–
Cellosolve	16.0	9.2	16.4	–
Diacetonolcohol	15.6	8.2	10.9	–
Cellosolve acetate	15.8	4.7	10.4	–

Table 9
The HSP and R values for the polyesterimide resin

Method	δ_d (J/cc) ^{0.5}	δ_p (J/cc) ^{0.5}	δ_h (J/cc) ^{0.5}	δ_t (J/cc) ^{0.5}	R (J/cc) ^{0.5}
Intrinsic 3D viscosity method ^a	18.00	11.10	8.80	22.91	8.60
Modified intrinsic 3D viscosity method ^b	18.00	11.10	8.80	22.91	6.45
Classical 3D geometric method ^a	17.40	12.30	8.60	22.98	4.10
Optimization method ^c	18.48	11.13	9.45	23.55	6.29

^a Ref. [12].

^b This work in which the swelling solvents were taken as nonsolvents.

^c This work.

computation of HSP and R from intrinsic viscosity method. We repeated the method for only dissolving solvents and considered swelling solvents as nonsolvents (as we do in the proposed optimization method) which gave a value of R closer to classical value. This we call as the improved intrinsic viscosity 3D method. Then using the same solubility parameter data for solvents and nonsolvents we estimated value of HSP and R from our proposed method which gave quite a close match. Thus the optimization method has been proved to be reliable with the example of polyesterimide resin also. The solubility parameter data for solvents and nonsolvents and intrinsic viscosity data for polyesterimide is given in Table 8. The results from the source and this work are summarized in Table 9.

5. Results and discussion

The value of R_i/R is termed as the relative energy difference (RED) [22]. The values of RED up to 1.0 indicate solvents for the polymer while higher values indicate nonsolvents. As seen from Table 5, dimethylsulfoxide and hexafluoroisopropanol are having RED greater than 1.0 from classical method although they are good solvents for PLA at 25 °C. Also, isopropylether and diethylether show RED less than 1.0 but they are nonsolvents for PLA. Similarly, as seen from Table 6, phenol has RED greater than 1.0 from classical method although it is a good solvent for PGA at 80 °C. These anomalies have been removed by the optimization method, which gives the RED less than or equal to 1.0 for all the solvents and greater than 1.00 for the nonsolvents, as seen in Tables 5 and 6. At 25 °C, Hexafluoroisopropanol is the only reported solvent for PGA [27,28]. The experimental, classical and optimization values for PGA have been estimated at 80 °C where phenol, *m*-cresol and 4-chlorophenol were used to dissolve the low molecular weight PGA sample. Group contribution correlations predict the values at 25 °C and give a rough estimate for the total solubility parameter value of PGA at 80 °C.

The summary of the values obtained for Hansen partial solubility parameters, Hildebrand or total solubility parameter and radius of the interaction sphere, of PLA and PGA, is presented in Tables 3 and 4, respectively. The value of δ for PGA obtained at 25 °C by group contribution of Fedors (23.82) matches well with the δ value of

hexafluoroisopropanol (23.07) which should be nearly equal to that of polymer as it is the only reported solvent at 25 °C. The values of δ of PGA at 80 °C are slightly lower than those at 25 °C, as expected for a reasonable value of α (used in Eq. (3)). The values obtained for PLA and PGA, are thus reasonably reliable and give a good estimate for the applications of these biopolymers at the considered temperatures. The value of R for PLA and PGA comes out to be relatively larger from the intrinsic viscosity method. This can be attributed to the contribution of intrinsic viscosities and to the method in itself [12].

6. Conclusions and future work

A comparative study has been presented for the common estimation methods of the solubility parameters. The values of HSP and R have been reported for PGA for the first time to the best of our knowledge. The results obtained by experimental, classical, group contribution and optimization methods are found to be consistent with close values of HSP for both PLA and PGA. The optimization method is superior to other methods because it considers the nonsolvent data also as a part of the procedure for obtaining the sphere of influence. This translates to obtaining a better fit of the data. It also ensures that there will be no anomalous points, or even if the anomalous points are there, the optimizer will try to minimize them. Hence we recommend the HSP and R values obtained from proposed optimization method to be considered most reliable. Apart from this, an empirical correlation for the intrinsic viscosity, has been proposed for low molecular weight samples of PLA and PGA.

The effect of molecular weight on solubility parameters is still to be investigated for these biopolymers. This will explore the possible wider range of their applications as compatible blends or copolymers. The parameters of the Mark–Houwink equation for PGA in the relevant solvents also need to be determined for a rigorous database of the polymer.

Appendix A. Calculation of zeroth-order and first-order connectivity indices for the polymer repeat unit

The graph theoretical treatment of molecular species, for the estimation of connectivity indices, starts by the

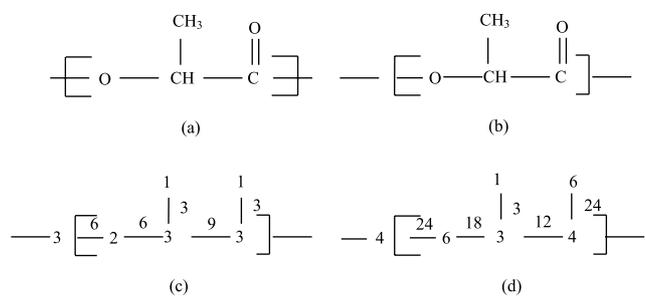


Fig. 3. Determination of Connectivity Indices for PLA.

construction of the hydrogen-suppressed graph of the molecule. The construction of the hydrogen suppressed graph for PLA and PGA (Figs. 3 and 4) is done by omitting the hydrogen atoms from the valence bond (Lewis) structure of the repeat unit of the polymer (Fig. 2). For polymers, this procedure utilizes the repeat unit. It takes chain continuation into account without considering truncation errors [19,20].

The value of two indices (δ and δ^v) which describe the electronic environment and the bonding configuration of each non-hydrogen atom in the molecule, are next assigned, and listed at the vertices of the hydrogen suppressed graph. The first atomic index, i.e. the simple connectivity index δ , equals the number of non-hydrogen atoms to which a given non-hydrogen atom is bonded. Equivalently, the δ of any vertex in the hydrogen-suppressed graph is the number of edges emanating from it. The second atomic index is the valence connectivity index δ^v , incorporating information on details of the electronic configuration of each non-hydrogen atom. Its value for the lowest oxidation states of the element will be generally assigned by Eq. (A1), where Z^v is the number of valence electrons of an atom, N_H is the number of hydrogen atoms bonded to it, and Z is its atomic number (i.e. Z equals Z^v plus the number of inner shell electrons).

$$\delta^v \equiv \frac{Z^v - N_H}{Z - Z^v - 1} \quad (\text{A1})$$

Bond indices β and β^v can be defined (Eq. (A2a)) for each bond not involving a hydrogen, as products of the atomic indices (δ and δ^v) at the two vertices (i and j) which define a given edge or bond. Zeroth-order (atomic) connectivity indices ${}^0\chi$ (simple index) and ${}^0\chi^v$ (valence

index) for the repeat unit are defined in terms of summation (Eq. (A2b)) over vertices of the hydrogen suppressed graph. First-order (bond) connectivity indices ${}^1\chi$ (simple index) and ${}^1\chi^v$ (valence index) for the repeat unit are defined in terms of summations (Eq. (A2c)) over the edges of the hydrogen suppressed graph [19,20].

The construction of the hydrogen suppressed graph for PLA and PGA is shown in Figs. 3 and 4, respectively.

$$\beta_{ij} \equiv \delta_i \delta_j; \quad \beta_{ij}^v \equiv \delta_i^v \delta_j^v \quad (\text{A2a})$$

$${}^0\chi \equiv \sum_{[\text{vertices}]} (1/\delta); \quad {}^0\chi^v \equiv \sum_{[\text{vertices}]} \left(1/\sqrt{\delta^v} \right) \quad (\text{A2b})$$

$${}^1\chi \equiv \sum_{[\text{edges}]} \left(1/\sqrt{\beta} \right); \quad {}^1\chi^v \equiv \sum_{[\text{edges}]} \left(1/\sqrt{\beta^v} \right) \quad (\text{A2c})$$

Calculation of the zeroth-order and first-order connectivity indices for PGA using Eqs. (A2b) and (A2c) is shown as follows:

$${}^0\chi = \frac{1}{\sqrt{2}} + \frac{1}{\sqrt{3}} + \frac{1}{\sqrt{1}} + \frac{1}{\sqrt{2}} = 2.9964$$

$${}^1\chi = \frac{1}{\sqrt{4}} + \frac{1}{\sqrt{6}} + \frac{1}{\sqrt{3}} + \frac{1}{\sqrt{6}} = 1.893847$$

$${}^0\chi^v = \frac{1}{\sqrt{2}} + \frac{1}{\sqrt{4}} + \frac{1}{\sqrt{6}} + \frac{1}{\sqrt{6}} = 2.023603$$

$${}^1\chi^v = \frac{1}{\sqrt{12}} + \frac{1}{\sqrt{8}} + \frac{1}{\sqrt{24}} + \frac{1}{\sqrt{24}} = 1.050477$$

Following the same procedure for PLA, the zeroth-order and first-order connectivity indices for PLA using Eqs. (A2b) and (A2c) are as follows:

$${}^0\chi = 3.8618; \quad {}^0\chi^v = 2.8938$$

$${}^1\chi = 2.3045; \quad {}^1\chi^v = 1.50998$$

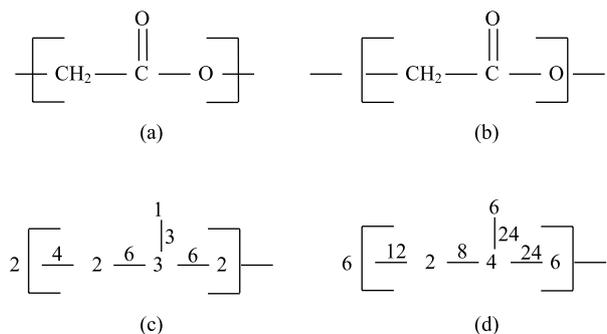


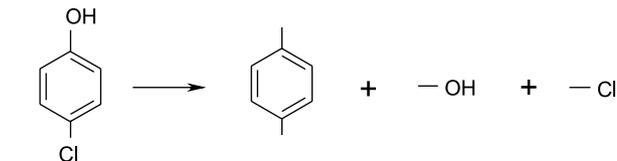
Fig. 4. Determination of Connectivity Indices for PGA.

Appendix B. Determination of HSP for 4-chlorophenol

The values of HSP for the solvent 4-chlorophenol have been obtained using the group contributions by van Krevelen and Hoftyzer [26]. They have reported the group contributions for F_d (dispersion component of molar attraction constant), F_p (polar component of molar attraction constant) and E_h (hydrogen bonding component of total cohesive energy). The values of F_d , F_p , E_h is given in Table B1 for three groups into which the structure of 4-chlorophenol is divided as shown below.

Table B1
Group contributions [26], towards F_d , F_p and E_h , of each constituent structural group of 4-chlorophenol

Name of the structural group	F_{di} (J/cc) ^{0.5}	F_{pi} (J/cc) ^{0.5}	E_{hi} (J/mol)
	1270	110	0
-OH	210	500	20,000
-Cl	450	550	400



Expressions for HSP in terms of F_{di} , F_{pi} , E_{hi} are given in Eq. (B1), where i stands for the individual group.

The values of $\sum F_{di}$, $\sum F_{pi}^2$, $\sum E_{hi}$ are found to be 1930, 564,600, 20,400.

Molar volume of 4-chlorophenol = 98.87 cc/mol.

$$\delta_d = \frac{\sum F_{di}}{V}; \quad \delta_p = \frac{\sqrt{\sum F_{pi}^2}}{V}; \quad \delta_h = \frac{\sqrt{\sum E_{hi}}}{V} \quad (\text{B1})$$

Using Eq. (B1), values of δ_d , δ_p and δ_h obtained are 19.52, 7.6 and 14.36 J/cc^{0.5}, respectively. These values are used in Table 2.

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