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# Optimal aqueous biphasic systems design for the recovery of ionic liquids

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## Abstract

Ionic liquid-based aqueous biphasic systems (IL-ABS) have attracted much attention in both academia and industries due to their superior performance in many applications. In order to better utilize these novel biphasic liquid-liquid systems for recovering hydrophilic ILs from their dilute aqueous solutions, a machine learning (ML)-based ABS design method is proposed for such a purpose in this work. In this method, a ML-based model, i.e., artificial neural network (ANN)-group contribution (GC) model, is employed to predict the phase equilibrium behaviours of IL-ABS. Based on the integration with computer-aided design technique, the optimal IL-ABS is determined by formulating and solving an optimization-based mixed-integer non-linear programming problem, where the structure of IL-ABS is denoted as the input vector in the ANN-GC model. As a proof of the concept, results of the recovery of 1-butyl-3-methylimidazolium chloride ([C<sub>4</sub>mIm][Cl]) and n-butylpyridinium trifluoromethanesulfonate ([C<sub>4</sub>Py][TfO]) from aqueous solutions are presented. The ABS [C<sub>4</sub>mIm][Cl]-H<sub>2</sub>O-(NH<sub>4</sub>)<sub>2</sub>SO<sub>3</sub> (identified in this work) gives an IL recovery efficiency of 95.0 wt% and a salting-out agent input of 2.36 kg/kg IL recovery, and for the ABS [C<sub>4</sub>mIm][Cl]-H<sub>2</sub>O-K<sub>2</sub>CO<sub>3</sub> (reported in the literature) they are 81.7 and 5.25, respectively. For the second case, our proposed ABS [C<sub>4</sub>Py][TfO]-H<sub>2</sub>O-KH<sub>2</sub>PO<sub>4</sub> gives an IL recovery efficiency of 95.6 wt% and a salting-out agent input of 1.81 kg/kg IL recovery, and for the reported ABS [C<sub>4</sub>Py][TfO]-H<sub>2</sub>O-(NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> they are 80.6 and 3.16, respectively.

**Keywords:** Ionic liquid recovery, ionic liquid aqueous solutions, ABS, Machine learning, ANN-GC model

## 1. Introduction

Ionic liquids (ILs) as innovative fluids have received wide attention in both academia and industries due to their unique properties such as negligible vapor pressure, non-flammability, wide electrochemical windows, excellent catalytic activities. They also exhibit good solubility and selectivity for a wide range of organic and inorganic chemicals.<sup>1</sup> In addition, ILs are recognized as “designer solvents”<sup>1</sup> since their properties can be tailored by tuning the molecular structure, which allows us to design ILs with desired properties for specific tasks. Great efforts have been made to facilitate their applications in separations<sup>2</sup> (e.g. carbon capture,<sup>3,4</sup> shale gas purification,<sup>5</sup> extractive desulfurization<sup>6,7</sup>), catalytic processes<sup>8</sup> (e.g. CO<sub>2</sub> conversion,<sup>9</sup> biomass conversion<sup>10</sup>), energy application,<sup>11</sup> etc. However, currently there are little industrial processes employing ILs mostly because their relatively high costs in comparison with conventional solvents and our limited understanding of their environmental impacts. For example, large volumes of dilute aqueous IL solutions will be produced during the dissolution and regeneration of cellulose when using ILs as solvents.<sup>12,13</sup> The disposal of these aqueous IL solutions will directly cause the loss of these high value solvents and this may even result in severe environment issues due to the toxicity and degradation of

the disposed ILs. Both economic and environmental concerns of using ILs can be offset to some extent if they are efficiently recycled.<sup>14</sup>

To date, various technologies including distillation,<sup>15</sup> extraction,<sup>16</sup> adsorption,<sup>17</sup> membrane separation,<sup>17</sup> aqueous two-phase extraction,<sup>18</sup> crystallization,<sup>19</sup> electrodialysis<sup>20</sup> and external force field separation<sup>21</sup> have been proposed for the recovery/recycling of ILs after their application. Each separation technology described above has its own advantages and shortcomings. For example, adsorption is considered to be a robust and non-destructive way to recover ILs, but the desorption of the adsorbed ILs is still a challenging problem.<sup>22</sup> Currently, distillation and extraction are two of the most widely studied separation approaches for the recovery/recycling of ILs. Due to the fact that most ILs have very low volatility, distillation is usually used for the recovery of ILs from volatile substances, while extraction is preferred in the case of separating ILs from non-volatile or thermally sensitive components.<sup>23</sup> When recovering ILs from dilute aqueous solutions, however, distillation method has an extremely low thermal efficiency since large volumes of water need to be evaporated, while extraction approach demands a large amount of solvent for achieving a high recovery yield. On the other hand, aqueous two-phase extraction, which is based on the formation of the aqueous biphasic systems (ABS), provides an alternative pathway for recovering ILs from dilute aqueous solutions. This is due to the fact that it allows the ILs to be efficiently concentrated or recovered in the IL-rich phase with the addition of a small amount of salting-out agent.<sup>23</sup> Although further purification process such as distillation is generally still required after aqueous two-phase extraction, significant energy savings can be obtained when compared to the recovery process only using distillation unit.

ABS refer to two aqueous-rich phases which are ternary systems composed of water and two solutes and ABS with water-miscible ILs (IL-ABS) were firstly proposed by Gutowski and co-workers<sup>18</sup> in 2003. These novel biphasic systems have proven to be rapid, low toxicity and scalable technologies for (i) the recovery/recycling of ILs from aqueous solutions, (ii) the separation and purification of bioproducts, and (iii) carrying out metathesis reactions in the formation of ILs<sup>24</sup>. For most aqueous IL solutions, the ABS could be formed through the addition of salting-out agents or introducing CO<sub>2</sub> or changing temperature. Inorganic salts such as NaH<sub>2</sub>PO<sub>4</sub>, K<sub>3</sub>PO<sub>4</sub> and (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> are the most commonly studied salting-out agents for the preparation of IL-ABS, while a certain number of more benign species including organic salts, amino acids, carbohydrates and polymers are also being introduced as alternatives to high-charge-density inorganic salts to induce phase split<sup>1</sup>. By far, IL-ABS have been widely used for the recovery of different bioactive compounds ranging from small organic compounds (e.g. phenolic acids, alkaloids, amino acids, lipids) to more complex molecules including nucleic acids, proteins, enzymes and antibodies.<sup>1</sup> Besides these, the application of IL-ABS in the recovery of ILs is also studied by different researchers. Deng et al.<sup>25</sup> used three potassium salts (K<sub>3</sub>PO<sub>4</sub>, K<sub>2</sub>HPO<sub>4</sub>, K<sub>2</sub>CO<sub>3</sub>) to recover 1-allyl-3-methylimidazolium chloride ([Amim][Cl]) from aqueous media and they found that the recovery efficiency increased in the order of K<sub>3</sub>PO<sub>4</sub> < K<sub>2</sub>HPO<sub>4</sub> < K<sub>2</sub>CO<sub>3</sub>. Similar results were obtained in Hofmeister's work and the highest efficiency (96.80%) was achieved with 46.48 wt% of K<sub>2</sub>HPO<sub>4</sub>. Li et al.<sup>26</sup> employed different sodium salts (Na<sub>3</sub>PO<sub>4</sub>, Na<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>SO<sub>4</sub>, NaH<sub>2</sub>PO<sub>4</sub>, NaCl) for recovering [C<sub>4</sub>mim][BF<sub>4</sub>] from aqueous solutions and 98.77% of the IL can be recovered when using 16.94 wt% of Na<sub>2</sub>CO<sub>3</sub>. Neves et al.<sup>27</sup> reported the recovery of imidazolium-, pyridinium-, and phosphonium-based ILs by using aluminium salts (Al<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>, AlK(SO<sub>4</sub>)<sub>12</sub>H<sub>2</sub>O) as salting-out agents and at least 96.0 wt% of the ILs were recovered from aqueous solutions. Shill et al. applied an aqueous concentrated phosphate solution to form a three-phase system for precipitating cellulosic components as well as recovering the pretreatment solvent, 1-ethyl-3-methylimidazolium acetate ([Emim][Ac]). Cláudio et al.<sup>28</sup> proposed a two-step ABS approach to recover gallic acid: 1<sup>st</sup> step, the biomolecule was concentrated into the IL-rich phase in an IL-ABS with sodium salt Na<sub>2</sub>SO<sub>4</sub>. 2<sup>nd</sup> step, the imidazolium-based ILs was recycled through the formation of a new IL-ABS with the addition of another sodium salt Na<sub>2</sub>CO<sub>3</sub>.

Besides inorganic salts, carbohydrates were also introduced as salting-out agents to induce phase separation for the recovery of ILs from aqueous solutions. Wu et al.<sup>29</sup> applied sucrose to recover three well-known hydrophilic ILs ([C<sub>4</sub>mim][BF<sub>4</sub>], [Amim][Br], and [Amim][Cl]) and the recovery efficiencies were 74%, 65% and 63%, respectively. They subsequently tried to use four types of saccharides (sucrose, glucose, xylose and fructose) to recover [C<sub>4</sub>mim][BF<sub>4</sub>], but the highest recovery was only 74%.<sup>30</sup> Although the carbohydrate-based IL-ABS are more environmentally friendly in comparison with their inorganic salt counterparts, their extraction efficiency still needs to be enhanced.<sup>23</sup> In addition, introducing CO<sub>2</sub> into aqueous IL solutions also leads to the formation of ABS, which provides a green alternative pathway to recover ILs.<sup>31-33</sup> However, this method generally requires high-cost equipment and technical skills.<sup>22</sup> As reported,<sup>34,35</sup> changing temperature is a very simple way to induce phase separation for aqueous IL solutions, but this method only limits to a certain specific class of ILs. In this work, we are mainly focusing on the IL-ABS with salting-out agents including inorganic salts, organic salts, carbohydrates and amino acids.

The formation and stability of IL-ABS is not only dependent on the structures of ILs such as cation types, lengths of alkyl chain and the anions, they are also highly associated with the type of salting-out agents.<sup>36</sup> ABS with different ILs and salting-out agents at different temperature generally present different phase behaviors, it is challenging to find optimal ABS for the recovery of various ILs. Due to the number of potential IL-ABS being so large, it would be time consuming and expensive to use the trial-and-error approach to search for the optimal ABS. On the other hand, the optimal design of compounds/systems through manipulating properties at the molecular level is often the key to considerable scientific advances and improved process systems performance.<sup>37</sup> To do this, it is important to have a good thermodynamic model to describe and predict liquid-liquid equilibrium conditions. However, currently such a thermodynamic model is not available for IL-ABS due to the high complexity of these systems. Fortunately, a machine learning-based nonlinear model developed in our most recent work<sup>38</sup> is capable of describing the phase equilibrium behaviors of IL-ABS. This ANN-GC model combines the artificial neural network (ANN) algorithm and the group contribution method. Based on this nonlinear ANN-GC model, the optimal IL-based ABS can be rapidly and reliably identified by formulating and solving an optimization-based mixed-integer non-linear programming (MINLP) problem, where the structures and concentrations of the IL and the salting-out agent as well as the system's temperature are denoted as input vector in the ANN-GC model. As a proof of the concept, results of the recovery of 1-butyl-3-methylimidazolium chloride ([C<sub>4</sub>mIm][Cl]) and n-butylpyridinium trifluoromethanesulfonate ([C<sub>4</sub>Py][TfO]) from aqueous solutions are presented.

## 2. Optimal design of IL-ABS

### 2.1. Descriptor of IL-ABS

Similar to the design of many other compounds/systems, a mathematical descriptor that can provide quantitative information of IL-ABS is also required for its optimal design through manipulating properties at the molecular level. Since both IL and salting-out agent have influence on the phase behavior of IL-ABS, their structural information should be included in the descriptor. As reported, ILs with different cations or anions generally exhibit different capabilities to produce IL-ABS. Likewise, salts with different cations or anions also present different salting-out strength in the formation of ABS.<sup>39</sup> For this reason, group contribution (GC) methods are employed to describe the structure of ILs and salting-out agents in the present work. The introduction of GC methods would largely improve the design space of ILs and salting-out agents, which means that we have more opportunities to find suitable IL-ABS with desired properties. In addition, GC methods can also be easily integrated in the computer-aided design technique<sup>40</sup> and such an integration has been widely used in the solvent and process design including absorbent design,<sup>41</sup> extractant design,<sup>42</sup> azeotropic separation process design,<sup>43</sup> and Diels–Alder reaction process design.<sup>44</sup>



such as ANN and SVM have been employed to build complex nonlinear GC or QSPR models for different properties<sup>49</sup> such as gas solubility,<sup>50-54</sup> surface tension,<sup>55</sup> viscosity,<sup>56</sup> toxicity,<sup>57,58</sup> melting point,<sup>59,60</sup> and the acid dissociation constants of organic compounds.<sup>61</sup> Besides these, some of ML-based models have been integrated into the computer-aided design method for addressing some optimal design problems such as CO<sub>2</sub> capture<sup>62,63</sup> and cosmetic formulation.<sup>64</sup> In addition, these ML-based design problems generally present less complex than those conventional thermodynamic model-based design problems.<sup>4,7</sup>

Most recently, ML-based modelling studies of IL-ABS were carried out in our group and a three-layer artificial neural network (ANN)-group contribution (GC) model was successfully developed to predict the phase equilibria conditions of IL-ABS.<sup>38</sup> This ANN-GC model gives a mean absolute error (MAE) between the experimental and model-calculated mass fraction of salting-out agent of 0.0175 and a coefficient of determination (R<sup>2</sup>) of 0.9316 for the 13,789 training data points, and for the 3,660 test data points they are 0.0177 and 0.9195, respectively. Together with the system's temperature and the mass fraction of IL, 34 IL functional groups and 37 salting-out agent functional groups are used as inputs (size of 73 x 1) in this ANN-GC model. The 34 IL functional groups are decomposed from 56 different ILs and these groups contain 6 cation cores, 23 anions, and 5 substituents. While the 37 salting-out agent functional groups are decomposed from 56 different salting-out agents and these groups include 23 salt cations, 17 salt anions, 6 carbohydrates, and 3 amino acids. All numbered elements in this input vector are provided in Table 1. The input layer reads the structure information of IL-ABS and then the hidden layer transfers and delivers this input information to the output layer where the phase composition of IL-ABS is quantified, as shown in Figure 3. The optimized model parameters ( $W_1$ ,  $b_1$ ,  $W_2$ ,  $b_2$ ) are given in Table A1 (see Appendix). The detailed information of all experimental data used for training and testing this ANN-GC model can be found in Supporting Information of our previous work.<sup>38</sup>

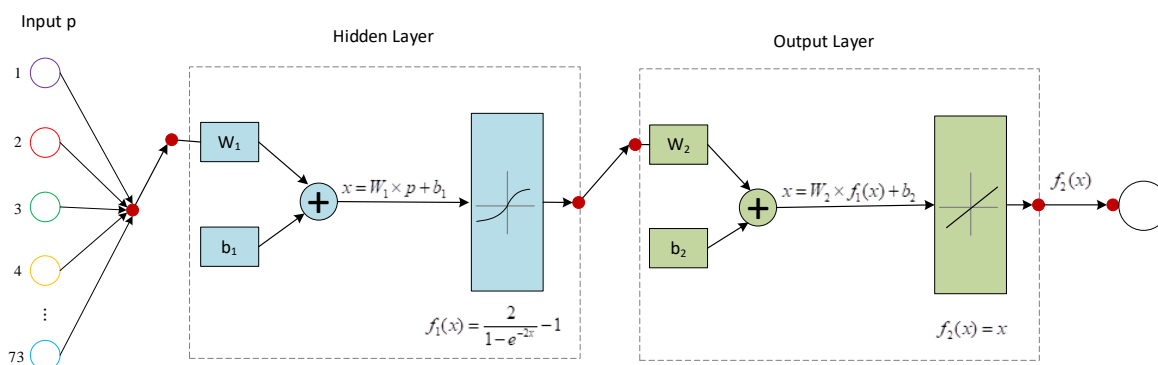


Figure 3. Structure of the three-layer ANN-GC model for ionic liquid-based aqueous biphasic systems.

Table 1. Elements of input vector for the ANN-GC model describing IL-ABS.

No.	Elements	No.	Elements
1	System's temperature T (K)		<i>Salting-out agents</i>
2	Mass fraction of ILs (wt%)		<i>Names</i>
	<i>ILs</i>		<i>Abbreviations</i>
	<i>Names</i>		<b>Salt anions, carbohydrates, amino acids</b>
	<i>Abbreviations</i>	37	2-hydroxypropane-1,2,3-tricarboxylate
	<b>Substituents</b>	38	dihydrogen phosphate
3	methyl	39	hydrogen phosphate
4	methylene	40	phosphate
			TO <sub>7</sub>
			H <sub>2</sub> PO <sub>4</sub>
			HPO <sub>4</sub>
			PO <sub>4</sub>

5	hydroxy	-OH	41	sulfate	SO <sub>4</sub>
6	vinyl	-CH=CH <sub>2</sub> -	42	carbonate	CO <sub>3</sub>
7	hydrogen	-H	43	ethanoate	CH <sub>3</sub> COO
	<b>Cations</b>		44	propanoate	C <sub>2</sub> H <sub>5</sub> COO
8	imidazolium	[Im]	45	sulfite	SO <sub>3</sub>
9	pyridinium	[Py]	46	tungstate	WO <sub>4</sub>
10	pyrrolidinium	[Pyr]	47	methanoate	HCOO
11	ammonium	[N]	48	meso-tartrate	meso-tartrate
12	phosphonium	[P]	49	succinate	succinate
13	N-(bis(dimethylamino)methylene)ethanaminium	[Nbis]	50	D-glucose	D-glucose
	<b>Anions</b>		51	D-maltose	D-maltose
14	4-sulfonatoxy-2,2,6,6-tetramethylpiperidine-1-yloxy	[STP]	52	D-sucrose	D-sucrose
15	tetrafluoroborate	[BF <sub>4</sub> ]	53	D-fructose	D-fructose
16	bromide	[Br]	54	D-sorbitol	D-sorbitol
17	chloride	[Cl]	55	L-serine	L-serine
18	trifluoromethanesulfonate	[TfO]	56	L-tartrate	L-tartrate
19	nitrate	[NO <sub>3</sub> ]	57	2-aminoacetic acid	2a-acid
20	dimethylphosphate	[DMP]	58	xylitol	xylitol
21	dicyanamide	[DCA]	59	nitric acid	N-acid
22	methyl sulfate	[MeSO <sub>4</sub> ]	60	(2R,3R)-2,3-dihydroxysuccinate	DDS
23	methanesulfonate	[MeSO <sub>3</sub> ]	61	(2R,3R)-2,3-dihydroxybutanedioate	DDB
24	tosylate	[Tos]	62	(2R,3S,4R,5R)-2,3,4,5,6-pentahydroxyhexanoate	PHH
25	bis((trifluoromethyl)sulfonyl)imide	[Tf <sub>2</sub> N]		<b>Salt cations</b>	
26	trifluoroacetate	[TFA]	63	sodium	Na
27	hexanesulfonate	[C <sub>6</sub> SO <sub>3</sub> ]	64	potassium	K
28	hexyl sulfate	[C <sub>6</sub> SO <sub>4</sub> ]	65	ammonium	NH <sub>4</sub>
29	octyl sulfate	[C <sub>8</sub> SO <sub>4</sub> ]	66	hydrogen	H
30	butanoate	[C <sub>3</sub> COO]	67	caesium	Cs
31	penanoate	[C <sub>4</sub> COO]	68	magnesium	Mg
32	hexanoate	[C <sub>5</sub> COO]	69	nickel	Ni
33	hepanoate	[C <sub>6</sub> COO]	70	lithium	Li
34	L-alaninate	L-alaninate	71	copper	Cu
35	L-serinate	L-serinate	72	manganese	Mn
36	glycinate	glycinate	73	zinc	Zn

### 2.3. Mathematical formulation of IL-ABS design problem

When tailoring an ABS for the recovery of ILs from aqueous solutions, the IL should be as much as possible to be concentrated in the IL-rich aqueous phase, while the salting-out agent and water should be at the other phase. As we know, the closer to the axis origin a binodal curve is, the greater is the ability of a salting-out agent to phase split, the tie-line length ( $TLL$ ) and slope of the tie-lines ( $S_{TL}$ ) are able to verify trends in the partition coefficients or recovery efficiencies of ABS.<sup>36</sup>

$$TLL = \sqrt{(x_S^T - x_S^B)^2 + (x_{IL}^T - x_{IL}^B)^2}$$

$$S_{TL} = \frac{x_{IL}^T - x_{IL}^B}{x_S^T - x_S^B} \quad 2$$

where the supercrits  $T$  and  $B$  designate the top phase (IL-rich phase) and the bottom phase (salt-rich phase), respectively, while the subscripts  $S$  and  $IL$  denote the equilibrium compositions of the salting-out agent and of the IL.

With the use of an objective function combining  $TLL$  and  $S_{TL}$ , the optimal design of IL-ABS is formulated as a MINLP optimization problem mathematically described by Eq3. In IL-ABS, the specific IL is denoted by a vector  $H^{IL} = [H_1^{IL}, H_1^{IL} \dots H_{34}^{IL}]$ . The first 5 elements  $H_{1-5}^{IL}$  are integer variables describing the number of cation substituents, and the rest elements  $H_{6-34}^{IL}$  are binary variables denoting the existence of cations and anions. On the other hand, each generated salting-out agent is represented by a vector  $y = [y_1, y_2 \dots y_{37}]$ . The first 5 elements  $y_{1-26}$  are binary variables describing the existence of salt anions, carbohydrates, amino acids. The other elements  $y_{27-37}$  are integer variables denoting the number of salt cations. The best performance salting-out agent and its inputs can be determined for specific IL aqueous solutions (e.g., specific temperature  $T^{as}$ , IL structure  $H^{IL}$  and IL mass fraction in IL-water mixture  $G^{as}$ ) by maximizing  $f(z, y, T^{as}, H^{IL}, G^{as})$  that subjects to a series of design constraints.

$$\begin{aligned} \max_{z,y} TLL \cdot (-S_{TL})^r &= f(z, y, T^{as}, H^{IL}, G^{as}) \\ \text{s.t.} \quad &\text{salting-out agent structural constraints} \\ &\text{mass balance constraints} \\ &\text{phase equilibria constraints} \end{aligned} \quad 3$$

where vector  $z$  represents a continuous variable describing the ratio of added salting-out agent to the original IL-water mixture and  $r$  is an adjustable parameter describing the degree of influence from  $TLL$  and  $S_{TL}$ .

$$\sum_{i \in SA} y_i = 1 \quad 4$$

$$\sum_{i \in SC} y_i v_i - \sum_{i \in SA} y_i v_i = 0 \quad 5$$

$$x_{H_2O}^T + x_S^T + x_{IL}^T = 1 \quad 6$$

$$x_{H_2O}^B + x_S^B + x_{IL}^B = 1 \quad 7$$

$$x_{H_2O}^T \cdot M^T + x_{H_2O}^B \cdot M^B = x_{H_2O} \cdot M \quad 8$$

$$x_S^T \cdot M^T + x_S^B \cdot M^B = x_S \cdot M \quad 9$$

$$x_{IL}^T \cdot M^T + x_{IL}^B \cdot M^B = x_{IL} \cdot M \quad 10$$

$$x_S^T = W_2 \cdot \left( \frac{2}{1 + e^{-2(W_1 \cdot p + b_1)}} - 1 \right) + b_2 \quad 11$$



$$x_s^B = W_2 \cdot \left( \frac{2}{1 + e^{-2(W_1 \cdot p + b_1)}} - 1 \right) + b_2 \quad 12$$

$$p_i = T^{as} \quad i = 1 \quad 13$$

$$p_i = \frac{G^{as}}{1 + z} \quad i = 2 \quad 14$$

$$p_i = H_{i-2}^{IL} \quad i = 3, 4, \dots, 36 \quad 15$$

$$p_i = y_{i-36} \quad i = 37, 38, \dots, 73 \quad 16$$

The structural feasibility and valency rules on the salting-out agent molecules are expressed by Eqs.4 and 5, where  $SA = [y_1, y_2 \dots y_{26}]$  is the set of salt anions, carbohydrates, amino acids, and  $SC = [y_{27}, y_{28} \dots y_{37}]$  is the set of salt cations. Integer variables  $v_i$  denote the valency of carbohydrates, amino acids, salt anions and cations. In Eqs.6-7,  $x_{H_2O}^T$ ,  $x_S^T$ ,  $x_{IL}^T$  and  $x_{H_2O}^B$ ,  $x_S^B$ ,  $x_{IL}^B$  are the mass fractions of water, salting-out agent and IL at the top phase and the bottom phase, respectively. In Eqs.8-10,  $M^T$ ,  $M^B$  and  $M$ , respectively, represent the mass of the top phase, the bottom phase and the mixture. Eqs.6 -10 ensure the mass balance of each involved compounds in both top and bottom phases. Eqs.11 and 12 are utilized to describe the phase equilibrium conditions of IL-ABS.  $W_1$ ,  $W_2$ ,  $b_1$  and  $b_2$  in Eqs.11 and 12 are the ANN-GC model parameters and the input vector  $p = [p_1, p_2 \dots p_{73}]$  denotes the structure of IL-ABS including the system's temperature  $p_1$ , IL mass fraction  $p_2$ , IL structure  $p_{3-36}$  and salting-out agent structure  $p_{37-73}$ . These elements are, respectively, identified by Eqs.13-16.

### 3. Applications

1-butyl-3-methylimidazolium chloride ([C<sub>4</sub>mIm][Cl]) is a highly efficient direct solvent for the dissolution and regeneration of cellulose and large volumes of dilute IL aqueous solutions are produced during the precipitation of the regenerated cellulose.<sup>12,13</sup> Therefore, efficient recycling of [C<sub>4</sub>mIm][Cl] from these aqueous solutions is a critical step for the commercialization of this IL-based pretreatment technology. n-butylpyridinium trifluoromethanesulfonate ([C<sub>4</sub>Py][TfO]) is another well-known hydrophilic IL that has potential industrial applications and it's also important to recover them from aqueous solutions during these applications. In this section, the proposed ML-based ABS design method is used to search optimal IL-ABS for the recovery of [C<sub>4</sub>mIm][Cl] and [C<sub>4</sub>Py][TfO] from dilute aqueous solutions. For both cases, the formulated MINLP problems are solved by a deterministic global optimization solver, LINDOGLOBAL, in the modelling system GAMS 24.4.6 on an Intel(R) Xeon(R) E5-1620 3.70 GHz PC running Windows 10 system. This optimization solver calculates the feasible range (determined by an upper and lower bound) for every variable in each equation while all other variables are fixed to their level. For this reason, appropriate upper and lower bounds are specified to different variables. For example, the upper and lower bound of  $z$  are, respectively, set as 0 and 1. When using this global optimization solver, solutions must beat the incumbent by at least the relative optimality tolerance (1e-10) to become the new best solution.

### Results and discussions

In the case of aqueous solutions of [C<sub>4</sub>mIm][Cl], ammonium sulfite ((NH<sub>4</sub>)<sub>2</sub>SO<sub>3</sub>) presents the best ABS forming ability. For the same IL aqueous solutions, Zafarani-Moattar et al., (2010)<sup>48</sup> reported an [C<sub>4</sub>mIm][Cl]-based ABS through the addition of a potassium salt K<sub>2</sub>CO<sub>3</sub>. To compare the ABS

forming ability of  $(\text{NH}_4)_2\text{SO}_3$  and  $\text{K}_2\text{CO}_3$  in the  $[\text{C}_4\text{mIm}][\text{Cl}]$  involved aqueous solutions, a non-linear programming (NLP) problem that aims to optimize the mass fraction of  $\text{K}_2\text{CO}_3$  for IL-ABS ( $[\text{C}_4\text{mIm}][\text{Cl}]-\text{H}_2\text{O}-\text{K}_2\text{CO}_3$ ) is formulated and solved. Table 2 gives the optimization results of both MINLP and NLP problems for the ML-based ABS design targeting the recovery of  $[\text{C}_4\text{mIm}][\text{Cl}]$  from aqueous solutions. In this case, the salting-out agent,  $(\text{NH}_4)_2\text{SO}_3$ , determined in this work has better ABS forming ability than the reported salting-out agent  $\text{K}_2\text{CO}_3$ . For the recovery of 10 wt%  $[\text{C}_4\text{Py}][\text{TfO}]$  from aqueous solutions, the ABS of  $[\text{C}_4\text{mIm}][\text{Cl}]-\text{H}_2\text{O}-\text{K}_2\text{CO}_3$  gives an IL recovery efficiency of 95.0 wt% and a salting-out agent input of 2.36 kg/kg IL recovery, and for the ABS of  $[\text{C}_4\text{mIm}][\text{Cl}]-\text{H}_2\text{O}-\text{K}_2\text{CO}_3$  they are 81.7 and 5.25, respectively. As shown in Figure 4, the binodal curve of  $[\text{C}_4\text{mIm}][\text{Cl}]-\text{H}_2\text{O}-\text{K}_2\text{CO}_3$  is closer to the axis origin than that of  $[\text{C}_4\text{mIm}][\text{Cl}]-\text{H}_2\text{O}-\text{K}_2\text{CO}_3$ , indicating  $(\text{NH}_4)_2\text{SO}_3$  is easier to induce phase split in the aqueous solutions containing  $[\text{C}_4\text{mIm}][\text{Cl}]$ .

Table 2. Optimization results of the ML-based ABS design for the recovery of ILs from aqueous solutions .

Aqueous solutions	$[\text{C}_4\text{mIm}][\text{Cl}]$ (10 wt%)		$[\text{C}_4\text{Py}][\text{TfO}]$ (10 wt%)	
$TLL \cdot (-S_{TL})^r = f(z, y, T^{as}, H^{IL}, G^{as})$	$r = 1 (>0)$			
Optimization-based problem	MINLP	NLP	MINLP	NLP
	$(\text{NH}_4)_2\text{SO}_3$	$\text{K}_2\text{CO}_3$	$\text{KH}_2\text{PO}_4$	$(\text{NH}_4)_2\text{SO}_4$
Salting out-agent	(This work)	(Ref. <sup>48</sup> )	(This work)	(Ref. <sup>65</sup> )
$x_{IL}^T$	0.830	0.500	0.880	0.570
$x_S^T$	0.020	0.034	0.019	0.025
$x_{H_2O}^T$	0.150	0.466	0.101	0.405
$x_{IL}^B$	0.005	0.014	0.004	0.017
$x_S^B$	0.201	0.334	0.160	0.227
$x_{H_2O}^B$	0.795	0.651	0.836	0.756
$x_{IL}$	0.082	0.070	0.085	0.080
$x_S$	0.184	0.300	0.147	0.204
$x_{H_2O}$	0.735	0.630	0.768	0.717
$M^T$ (kg)	93.397	114.434	92.689	112.509
$M^B$ (kg)	906.603	885.566	907.311	887.491
$TLL$	0.845	0.571	0.887	0.589
$S_{TL}$	-4.565	-1.619	-6.215	-2.740
Recovery efficiency (wt%)	95.0	81.7	95.6	80.6
salting-out agent input (kg/kg IL recovery)	2.36	5.25	1.81	3.16

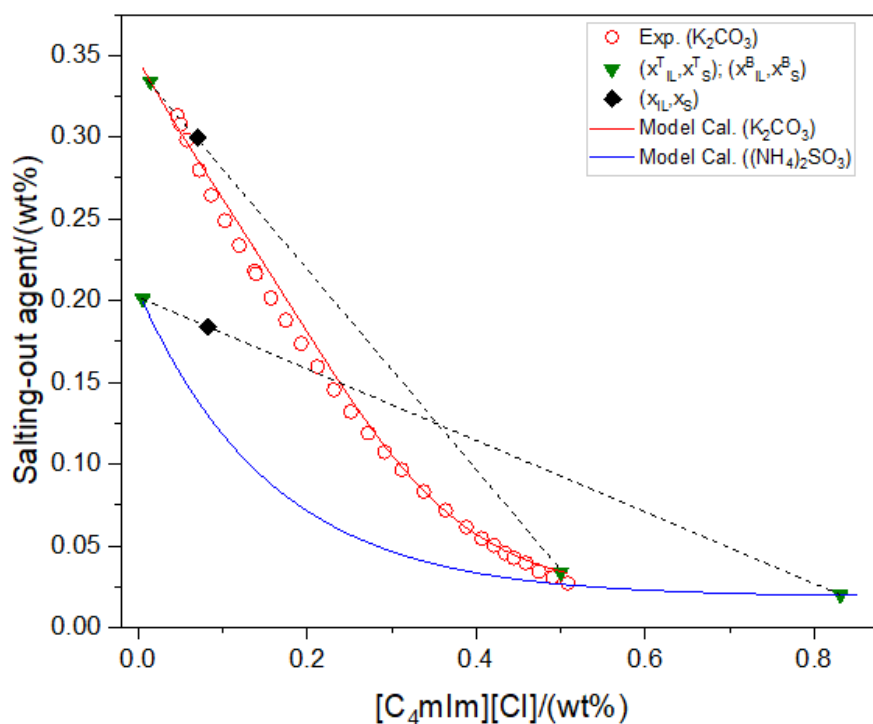


Figure 4. Comparisons 1) between the ternary phase diagrams of  $[\text{C}_4\text{mIm}][\text{Cl}]\text{-H}_2\text{O}\text{-(NH}_4)_2\text{SO}_3$  (model identified) and  $[\text{C}_4\text{mIm}][\text{Cl}]\text{-H}_2\text{O}\text{-K}_2\text{CO}_3$  (literature reported); 2) between the model-calculated and experimental data of  $[\text{C}_4\text{mIm}][\text{Cl}]\text{-H}_2\text{O}\text{-K}_2\text{CO}_3$ .

In the case of  $[\text{C}_4\text{Py}][\text{TfO}]$  involved aqueous solutions, potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ ) is found to be the best salting-out agent to produce ABS. Most recently, a  $[\text{C}_4\text{Py}][\text{TfO}]$ -based ABS was obtained by using ammonium sulfate ( $(\text{NH}_4)_2\text{SO}_4$ ) as the salting-out agent (Guo et al., 2020).<sup>65</sup> Similar to the first case, an NLP problem that aims to optimize the mass fraction of  $(\text{NH}_4)_2\text{SO}_4$  for IL-ABS ( $[\text{C}_4\text{Py}][\text{TfO}]\text{-H}_2\text{O}\text{-(NH}_4)_2\text{SO}_4$ ) is formulated and solved for comparing the phase inducing performance of  $\text{KH}_2\text{PO}_4$  and  $(\text{NH}_4)_2\text{SO}_4$  in the aqueous solutions of  $[\text{C}_4\text{Py}][\text{TfO}]$ . Likewise, the optimization results of the formulated design problems in this case are also provided in Table 2. The salting-out agent,  $\text{KH}_2\text{PO}_4$ , identified in this work also presents better phase inducing performance than the reported salting-out agent  $(\text{NH}_4)_2\text{SO}_4$ . For the aqueous solutions containing 10 wt%  $[\text{C}_4\text{Py}][\text{TfO}]$ , the ABS composed of  $[\text{C}_4\text{Py}][\text{TfO}]\text{-H}_2\text{O}\text{-KH}_2\text{PO}_4$  gives an IL recovery efficiency of 95.6 wt% and a salting-out agent input of 1.81 kg/kg IL recovery, and for the ABS composed of  $[\text{C}_4\text{Py}][\text{TfO}]\text{-H}_2\text{O}\text{-(NH}_4)_2\text{SO}_4$  they are 80.6 and 3.16, respectively. Figure 5 presents the ternary phase diagrams for ABS composed of  $[\text{C}_4\text{Py}][\text{TfO}]\text{-H}_2\text{O}\text{-(NH}_4)_2\text{SO}_4/\text{KH}_2\text{PO}_4$ . Clearly,  $\text{KH}_2\text{PO}_4$  has better ABS forming ability for the aqueous solutions containing  $[\text{C}_4\text{Py}][\text{TfO}]$  than that of  $(\text{NH}_4)_2\text{SO}_4$ .

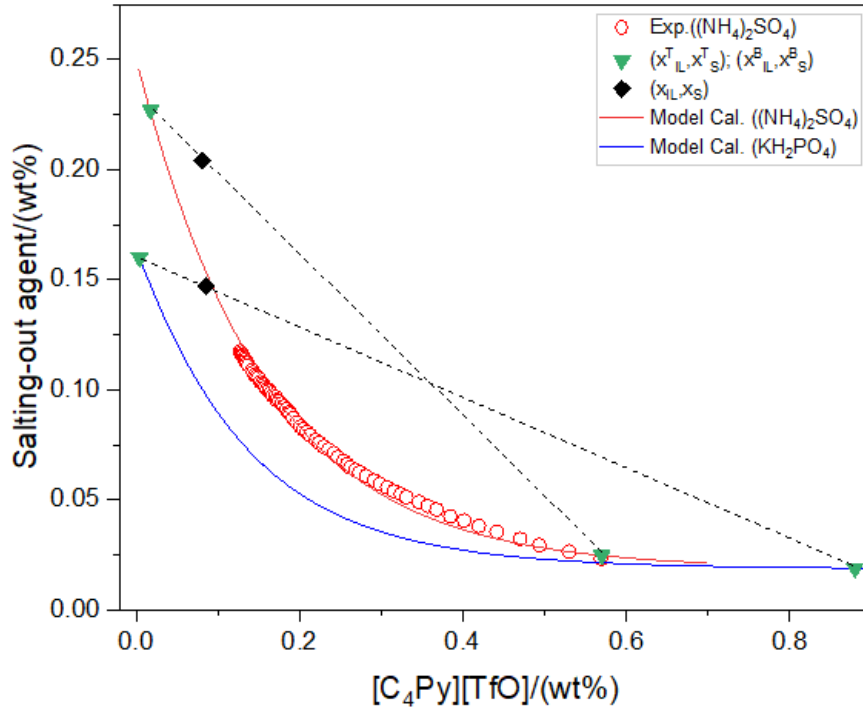


Figure 5. Comparisons 1) between the ternary phase diagrams of [C<sub>4</sub>Py][TfO]-H<sub>2</sub>O-KH<sub>2</sub>PO<sub>4</sub> (model identified) and [C<sub>4</sub>Py][TfO]-H<sub>2</sub>O-(NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (literature reported); 2) between the model-calculated and experimental data of [C<sub>4</sub>Py][TfO]-H<sub>2</sub>O-(NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>.

In this work, the MAE between the experimental and model-calculated mass fraction of IL in the ternary system of [C<sub>4</sub>mIm][Cl]-H<sub>2</sub>O-K<sub>2</sub>CO<sub>3</sub> and [C<sub>4</sub>Py][TfO]-H<sub>2</sub>O-(NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> are 0.0062 and 0.0027, respectively. This indicates that IL-ABS can be well described by the ANN-GC model. Besides this, the proposed ML-based ABS design method also indicate that this ANN-GC model can be easily integrated into the computer-aided design technique, which allows us to have more opportunities to find optimal IL-ABS for specific tasks in a time- and cost-effective way. Remarkably, the excellent recovery performance of both [C<sub>4</sub>mIm][Cl]-H<sub>2</sub>O-(NH<sub>4</sub>)<sub>2</sub>SO<sub>3</sub> and [C<sub>4</sub>Py][TfO]-H<sub>2</sub>O-KH<sub>2</sub>PO<sub>4</sub> obtained in this work highlight the applicability and effectiveness of the proposed ML-based ABS design method for addressing the recovery problem of ILs from dilute aqueous solutions. On the other hand, the optimization results are obtained by solving the MINLP model that considers structural constraints of the salting-out agent, mass balance and phase equilibria constraints, and an objective function. It's to be noted that the design constraints are non-convex, which may cause difficulties for solution convergence due to the existence of binary and integer decision variables.

Table 3. Comparisons between different optimal IL-ABS identified by using positive and negative values of  $r$  in the objective function: Exemplified for 10 wt% [C<sub>4</sub>Py][TfO] aqueous solution.

Aqueous solutions	[C <sub>4</sub> Py][TfO] (10 wt%)	
$TLL \cdot (-S_{TL})^r = f(z, y, T^{as}, H^{IL}, G^{as})$	$r > 0$	$r < 0$
Salting out-agent	KH <sub>2</sub> PO <sub>4</sub>	NH <sub>4</sub> HM-tartate
$x_{IL}^T$	0.880	0.700
$x_S^T$	0.019	0.021

$x_{H_2O}^T$	0.101	0.279
$x_{IL}^B$	0.004	0.0001
$x_S^B$	0.160	0.314
$x_{H_2O}^B$	0.836	0.686
$x_{IL}$	0.085	0.072
$x_S$	0.147	0.284
$x_{H_2O}$	0.768	0.644
$M^T$ (kg)	92.689	102.148
$M^B$ (kg)	907.311	897.852
$TLL$	0.887	0.759
$S_{TL}$	-6.215	-2.388
Recovery efficiency (wt%)	95.6	99.9
salting-out agent input (kg/kg IL recovery)	1.81	3.94

As aforementioned, both  $TLL$  and  $S_{TL}$  are useful for verifying trends in the partition coefficients of ABS and  $r$  represents the degree of their influences. For this reason, we investigate the impact of this parameter on the optimization results of the formulated MINLP problem. We find that  $KH_2PO_4$  is identified as the best salting-out agent with positive values of  $r$ , while another salting-out agent,  $NH_4HM$ -tartate, gives the maximum design target when the value of  $r$  is negative. The optimization results of these two IL-ABS are given in Table 3. Although the recovery efficiency of  $[C_4Py][TfO]-H_2O-NH_4HM$ -tartate is slightly higher than that of  $[C_4Py][TfO]-H_2O-KH_2PO_4$ , it requires much more salting-out agent input than that of  $[C_4Py][TfO]-H_2O-KH_2PO_4$ . As shown in Figure 6, the binodal curve of  $[C_4Py][TfO]-H_2O-KH_2PO_4$  is closer to the axis origin than that of  $[C_4Py][TfO]-H_2O-NH_4HM$ -tartate, indicating  $KH_2PO_4$  has higher ABS forming ability in the studied IL aqueous solutions, which means that the objective function with a positive value of  $r$  would give better suggestions for recovering ILs from aqueous solutions. This can be explained by that when IL-ABS (with a certain value of  $TLL$ ) have larger absolute values of  $S_{TL}$ , they require less salting-out agent inputs, and therefore maximizing the objective function (in Eq.3) with positive values of  $r$  will give better solutions. For the same IL aqueous solutions, different salting-out agents generally present different ABS formation abilities and the concentration of the IL aqueous solutions also has impacts on the ABS formation. As shown in Figure 7, the minimum amount of salting-out agent required to induce phase split decreases with the increase of the concentration of the IL aqueous solutions, which means that we need more salting-out agents to recover ILs from the dilute aqueous solutions. On the other hand, the recovery efficiency of the IL increases when we put more salting-out agents into the IL aqueous solutions, as shown in Figure 8. Therefore, the trade-off between the recovery efficiency of the IL and the input amount of the salting-out agent should be considered in the practical operations. This is the intention why both  $TLL$  and  $S_{TL}$  are included in the objective function when we are formulating the optimal IL-ABS design problem.

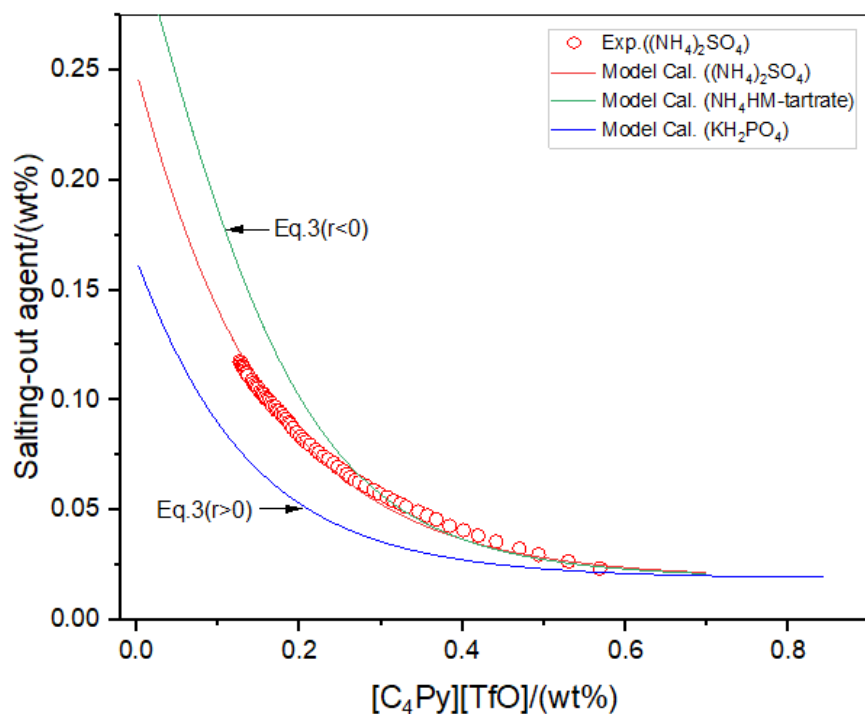


Figure 6. Comparisons between the ternary phase diagrams of  $[C_4Py][TfO]-H_2O-KH_2PO_4$  (identified with  $r > 0$  in Eq.3) and  $[C_4Py][TfO]-H_2O-NH_4HM-tartrate$  (identified with  $r < 0$  in Eq.3).

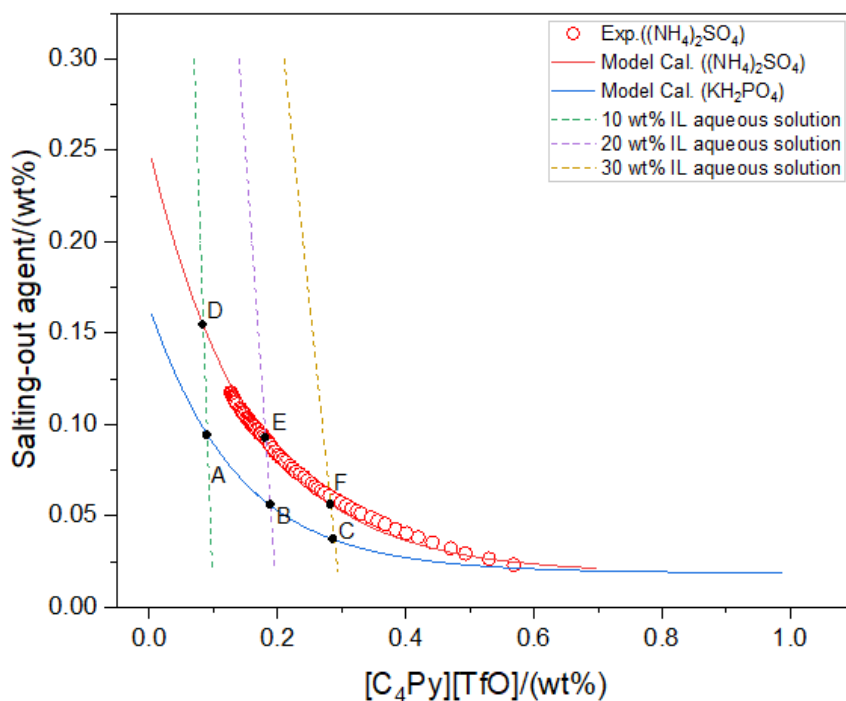


Figure 7. Comparisons between the minimum salting-out agent inputs for inducing phase separation in 10 wt%, 20 wt% and 30 wt%  $[C_4Py][TfO]$  aqueous solutions: Exemplified for  $[C_4Py][TfO]-H_2O-KH_2PO_4/(NH_4)_2SO_4$ .

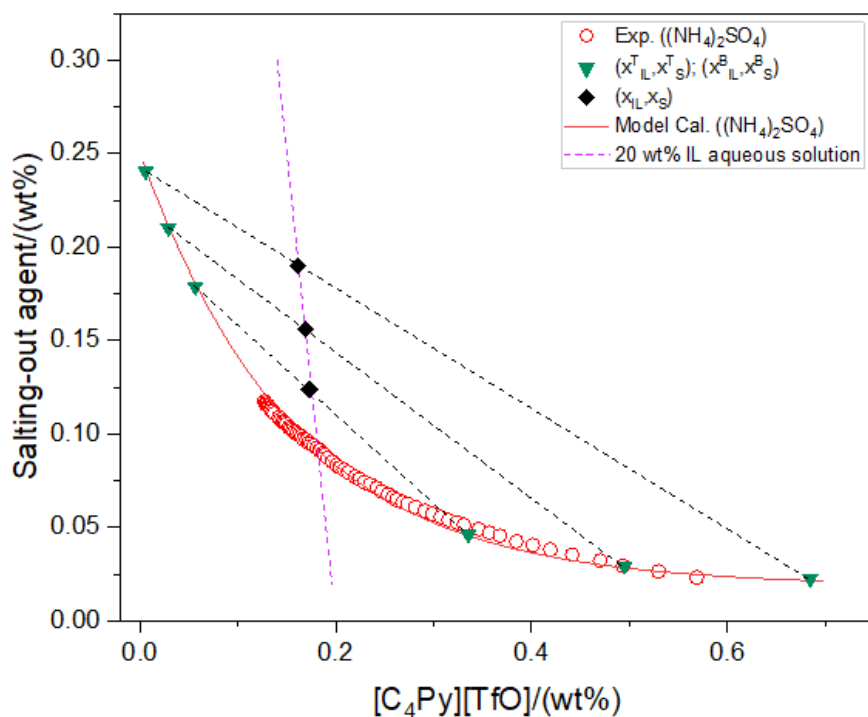


Figure 8. Comparisons between the phase compositions of  $[C_4Py][TfO]-H_2O-(NH_4)_2SO_4$  with different salting-out agent inputs: Exemplified for 20 wt%  $[C_4Py][TfO]$  aqueous solution.

#### 4. Conclusion

In this work, a novel ABS design method that integrates the machine learning algorithm and the computer-aided design technique has been proposed for tailoring optimal IL-ABS for the recovery of hydrophilic ILs from dilute aqueous solutions. Compared with treating ILs and salting-out agents as whole molecular groups, the introduction of GC methods to describe the structure of ILs and salting-out agents in this work largely improves the design space of the IL-based ABS, allowing us to have more opportunities to find suitable ones for processing various IL aqueous solutions. Two case studies are performed to test this ML-based ABS design method by formulating and solving their optimization-based MINLP problems. In both cases, the salting-out agents, i.e.  $(NH_4)_2SO_3$  and  $KH_2PO_4$ , identified in this work have better ABS forming ability than their counterparts  $K_2CO_3$  and  $(NH_4)_2SO_4$  reported in the literature. For the recovery of 10 wt%  $[C_4Py][TfO]$  from aqueous solutions, the ABS composed of  $[C_4mIm][Cl]-H_2O-(NH_4)_2SO_3$  gives an IL recovery efficiency of 95.0 wt% and a salting-out agent input of 2.36 kg/kg IL recovery, and for the ABS of  $[C_4mIm][Cl]-H_2O-K_2CO_3$  they are 81.7 and 5.25, respectively. For the aqueous solutions containing 10 wt%  $[C_4Py][TfO]$ , the ABS composed of  $[C_4Py][TfO]-H_2O-KH_2PO_4$  gives an IL recovery efficiency of 95.6 wt% and a salting-out agent input of 1.81 kg/kg IL recovery, and for the ABS composed of  $[C_4Py][TfO]-H_2O-(NH_4)_2SO_4$  they are 80.6 and 3.16, respectively.

Besides the efforts of developing the ML-based ABS design method, we also investigate the impact of  $TLL$  and  $S_{TL}$  (represented by  $r$  in Eq.1) on the optimization results of the formulated MINLP problem. We find that the objective function with a positive value of  $r$  is capable to give better suggestions for processing aqueous solutions. On the other hand, the minimum amount of salting-out agent required to induce phase split decreases with the increase of the concentration of the IL aqueous solutions, which means that we need more salting-out agents to recover ILs from the dilute aqueous solutions. Meanwhile, the recovery efficiency of the IL increases when we put more salting-out agents into the IL aqueous solutions. Therefore, the trade-off between the recovery efficiency of the

IL and the input amount of the salting-out agent should be considered in the practical operations. All conclusions mentioned above could be a guidance in the design of ABS for the efficient recovery of ILs from aqueous solutions. Efficient recovery of ILs from dilute aqueous solutions is a critical step to make IL-based technologies cost-effective and environmentally friendly. This work will have a significant impact on the commercialization of IL-based technologies in various fields, especially in the pretreatment of lignocellulosic biomass, which would undoubtedly boost the development of biorefineries.

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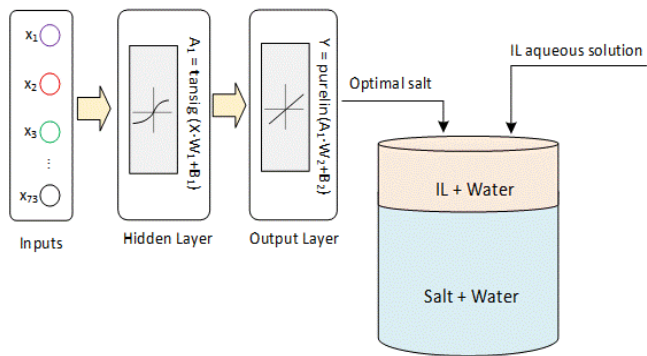
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1 **Appendix**

2 Table A1. Parameters of ANN-GC model used in the ML-based ABS design method.<sup>38</sup>

$W_1(2 \times 73)$	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<b>11</b>	<b>12</b>	<b>13</b>
	0.0001	5.6575	-1.3667	0.0224	-0.6323	0.1277	-1.4800	1.6234	4.0890	3.0856	0.1205	0.2192	-3.1026
	-0.0055	3.1681	0.4301	0.1264	0.4543	0.1085	0.3365	-0.3197	-0.6087	-1.2609	-0.3486	4.7024	0.6819
	<b>14</b>	<b>15</b>	<b>16</b>	<b>17</b>	<b>18</b>	<b>19</b>	<b>20</b>	<b>21</b>	<b>22</b>	<b>23</b>	<b>24</b>	<b>25</b>	<b>26</b>
	-3.5490	1.0996	-1.1118	-1.2802	1.5548	-1.3679	-1.8647	6.1633	-1.2190	-1.9697	-1.5906	-2.6060	4.2710
	0.0193	-1.7419	-1.6357	-1.7236	-1.7200	-1.6272	-1.8039	-1.8883	0.4090	-1.6206	4.7825	2.5562	-1.7843
	<b>27</b>	<b>28</b>	<b>29</b>	<b>30</b>	<b>31</b>	<b>32</b>	<b>33</b>	<b>34</b>	<b>35</b>	<b>36</b>	<b>37</b>	<b>38</b>	<b>39</b>
	-1.7989	0.9301	-0.6748	-1.6187	-1.5513	-1.8242	-1.9704	-1.5454	-2.2112	-1.4603	-4.5858	-3.8641	-3.9346
	-0.9271	-1.5487	-0.4356	-2.1302	-2.0893	-2.1357	-2.1305	-1.8095	-2.5117	-2.4586	-0.3888	0.0435	-0.0330
	<b>40</b>	<b>41</b>	<b>42</b>	<b>43</b>	<b>44</b>	<b>45</b>	<b>46</b>	<b>47</b>	<b>48</b>	<b>49</b>	<b>50</b>	<b>51</b>	<b>52</b>
	-2.8809	-3.4236	-2.5878	-1.3985	-4.9182	0.5896	-4.1142	3.4893	-4.4597	2.4642	1.3825	-1.7410	-2.3853
	-0.1949	-0.2995	0.0302	-0.5633	4.0932	-0.2475	-0.3261	-0.6555	-0.3947	-0.3836	-0.8963	-0.7105	-0.5921
	<b>53</b>	<b>54</b>	<b>55</b>	<b>56</b>	<b>57</b>	<b>58</b>	<b>59</b>	<b>60</b>	<b>61</b>	<b>62</b>	<b>63</b>	<b>64</b>	<b>65</b>
	1.0148	1.4678	-0.7193	-3.3751	-1.7788	1.1906	-2.3678	4.2627	-4.5446	-1.8589	1.2025	0.9972	0.6285
-0.8782	-0.5063	-0.4666	-0.4312	-0.1451	-0.9261	2.8176	-0.5004	-0.2367	-0.5444	0.0296	-0.0522	0.0301	
<b>66</b>	<b>67</b>	<b>68</b>	<b>69</b>	<b>70</b>	<b>71</b>	<b>72</b>	<b>73</b>						
0.4876	0.6675	0.9252	1.9610	0.8437	2.5048	1.1390	1.9111						
0.2541	-0.3353	3.2609	0.5571	2.1269	0.3549	0.8397	0.6391						
$b_1(2 \times 1)$													
6.0140													
2.7800													
$W_2(1 \times 2)$													
-0.1035    -0.9328													
$b_2(1 \times 1)$													
1.0550													



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