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Computer-Aided Design of Ionic Liquids for Hybrid Process Schemes

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Abstract

Hybrid process schemes that combine two (or more) units operating at their highest process efficiencies to perform one (or more) process tasks are considered as potentially innovative and sustainable processing options. Additionally, Ionic liquids (ILs), as well as certain organic chemicals, are good candidates for use as solvents in hybrid schemes that can replace energy-intensive processing steps. As successful design of solvent-based hybrid schemes depends on the specific properties of the solvent used, a computer-aided ionic liquid design (CAILD) toolbox was added to an existing tool for computer-aided molecular design for solvent selection-design. Promising IL solvent candidates were first identified through the formulation and solution of mixed-integer nonlinear programming (MINLP) problems for CAILD and were then further evaluated in the process simulation design stage, where the process variables were optimized by means of trade-off and sensitivity analysis. In order to understand and develop model-based hybrid reaction systems, a dynamic model that describes the behavior of the reaction system has been developed. Based on a wide range of collected experimental data, parameters of sub-models, used to calculate the temperature-dependent properties of ILs, are regressed for the purpose of process simulation. Consequently, a hybrid process design method combining CAILD and process design-simulation to identify the optimal IL and its corresponding hybrid process specifications has been proposed. The application of this design method has been illustrated through case studies including the separation of aqueous solutions using an IL-based hybrid distillation scheme and the bio-oxidation of alcohols using a hybrid reaction-separation scheme with continuous product removal.

Keywords: Hybrid process schemes, ionic liquids, CAILD, process intensification

Abbreviations

Groups for ionic liquids

CH ₃	methyl
CH ₂	methylene
dmN	dimethyl ammonium
1,3-dmIm (+)	1,3-dimethylimidazolium
1,2,3-tmIm (+)	1,2,3-trimethylimidazolium
1-mPy (+)	1-methylpyridinium
1,1-dmPyr (+)	1,1-dimethylpyrrolidinium
Am(1)111 (+)	Tetramethyl ammonium
1,1,1,1Ph (+)	Tetramethyl phosphonium
TDPh (+)	Trihexyl tetradecyl phosphonium
1,1-dmPip (+)	1,1-dimethylpiperidinium

[Tf ₂ N] ⁻	bis(trifluoromethanesulfonyl) amide
[BF ₄] ⁻	tetrafluoroborate
[PF ₆] ⁻	hexafluorophosphate
[Cl] ⁻	chloride
[Ac] ⁻	acetate
[MeSO ₄] ⁻	methyl sulfate
[EtSO ₄] ⁻	ethyl sulfate
[CF ₃ SO ₃] ⁻	trifluoromethanesulfonate
[Br] ⁻	bromide
[CF ₃ COO] ⁻	trifluoroacetate
[N(CN) ₂] ⁻	dicyanamide
[C(CN) ₃] ⁻	tricyanomethanide
[B(CN) ₄] ⁻	tetracyanoborate
[AlCl ₄] ⁻	tetrachloroaluminate
[InCl ₄] ⁻	tetrachloroindate
[DMP] ⁻	dimethylphosphate
[DEP] ⁻	diethyl phosphate
[FeCl ₄] ⁻	tetrachloroironate
[GaCl ₂] ⁻	tetrachlorogallate
[Pf ₂ N] ⁻	bis(perfluoroethylsulfonyl)imide
[SCN] ⁻	thiocyanate
[eFAP] ⁻	tris(pentafluoroethyl)trifluorophosphate

1. Introduction

Solvents and membranes have a wide range of applications in many chemical and related industries. Solvents can be used in a multipurpose role (e.g. reaction medium, extraction solvent) in different processing steps, such as chemical reaction and separation. For example, a reaction step usually carried out in one solvent and the separation step of product recovery requires another solvent or membrane (Papadakis et al., 2016). Therefore, it is advantageous to investigate hybrid schemes that allow solvent or membrane-based processing units operating at their highest efficiencies to perform one or more process tasks.

Separation operations to obtain pure products is found in almost all processing routes producing a chemical product, where, the processes involved, like distillation, account for 10–15% of the world's energy consumption. More energy efficient methods to purify chemicals could greatly reduce carbon dioxide emissions as well as energy cost (Sholl and Lively, 2016). As an important separation technique in chemical process industry, distillation is energy intensive and has the least thermal efficiency (Pellegrino et al., 2004). Nevertheless, nearly 80% of all vapor-liquid separations are performed by distillation. Its efficiency could significantly contribute to the overall energy consumption in chemical process industries and therefore intensified separation designs that allow energy efficient operation are attractive (Lutze et al., 2010; Babi et al., 2015). One such option is to use hybrid separation schemes, which combine one or more separation techniques operating at their highest energy efficiencies such that a target separation can be achieved at significantly lower energy consumption (Tula et al., 2017).

Bio-reactions, which involve the use of enzymes or living microorganisms for the production of chemical and biochemical substances, may often be carried out under mild conditions, they are highly specific, and involve high reaction rates, therefore, can act as possible alternatives for conventional synthesis routes. However, limitations of biocatalysts mostly related with product and/or substrate inhibition result in low productivity and highly diluted product, which leads in difficult downstream

separations (Woodley et al., 2008; Van Hecke et al., 2014; Woodley, 2017). In each case, the product needs to be removed as soon as it is formed in order to overcome these constraints and hence increase the product yields of the bio-catalytic process. Generally, recovery and purification stages in bioprocesses require numerous steps, associated with high chemicals and energy consumption, and usually represent 20–60% of the total cost, and even in some protein synthesis biological process this value may reach 90% (Martínez-Aragón et al., 2009). For these bioprocesses, hybrid schemes that involve the intensification of the reaction and separation processes are able to lower energy consumption, improve reaction performance as well as reduce the complexity.

Together with organic chemicals, ionic liquids (ILs) are being considered as solvents for use in hybrid schemes replacing energy intensive processes. IL-based separation processes are generally energy efficient because of their non-volatility and therefore low energy consuming solvent recovery operations (Seiler et al., 2004; Lei et al., 2014b). For the same reason, membrane-based separations are also promising alternatives for the energy intensive processes (Drioli et al., 2011). However, both IL-based and membrane-based separations are limited to low flux operations due to their operational and economic constraints (e.g. high viscosity or low flux rate, high cost). To overcome such limitations, hybrid schemes are promising innovative and sustainable processing options since processing units (e.g. reactor, column, membrane) are operating at their highest efficiencies in hybrid schemes. For example, reactive distillation (e.g. production of methyl acetate) integrates reaction and separation in a single operating unit resulting in reduced equipment sizes and lower operating cost. Distillation with membrane separation (e.g. n-butane from isobutane) is another example of combining unit operations to achieve lower energy consumption and improve quality of distillation cuts.

Although hybrid schemes have significant potential to contribute the development of the process industries, a main question is when such hybrid schemes can be applied, what characteristics the process problem should have, what the process specification should be and how much improvement can be expected. To find truly innovative and more sustainable solutions, Babi et al. (2015) proposed a computer-aided, multi-level, multi-scale method, where different hybrid schemes can be generated to test if any of them match the desired targets while also satisfying the process specifications. So far, hybrid schemes involving membrane-based separation with distillation (e.g. Figure 2) have been proposed for several separation processes, such as separation of azeotropic mixtures (Rautenbach and Albrecht, 1985; Goldblatt and Gooding, 1986), recovery of olefins (Davis et al., 1993; Moganti et al., 1994; Stephan et al., 1995; Pettersen et al., 1996; Caballero et al., 2009), and the separation of a mixture of alkanes (Tula et al., 2017). In contrast, studies regarding the hybrid process design using ILs as solvents are still scarce.

To achieve the full potential of the hybrid process schemes, the selection of optimal solvents or membranes is of great importance due to fact that different solvents or membranes are usually present with very distinct properties and separation performances, especially for ILs that combine diverse cations, anions and substituents (Holbrey and Seddon, 1999). Currently, ILs are usually selected based on experiments which can be time consuming and cost-intensive since many thousands of ILs may be considered as potential solvents. Therefore, in order to find suitable ILs for specific tasks confidently and rapidly, systematic solvent screening method like computer-aided ionic liquid design (CAILD) is attractive (Karunanithi and Mehrkesh, 2013). To date, studies on CAILD are mainly focusing on the separation of azeotropic mixtures (e.g. ethanol-water, acetone-methanol) and the CO₂ capture process, (Valencia-Marquez et al., 2011; Roughton et al., 2012; Karunanithi and Mehrkesh, 2013; Chong et al., 2015; Chong et al., 2016; Farahipour et al., 2016; Chen et al., 2019a). Most recently, CAILD method has been extended to the extractive desulfurization system (EDS) for fuel oils (Song et al., 2018).

Hybrid schemes have potential to contribute significantly to the sustainability of the process industry through the use of CAILD for the optimal design of ILs. This work presents a hybrid process design method combining CAILD with process design-simulation to identify the optimal IL and its corresponding hybrid process specifications. As proof of concept, results from two case studies, i.e. separation of aqueous solutions using hybrid distillation schemes and bio-oxidation of alcohols using hybrid reaction-separation schemes, are presented.

Figure 1: Framework of the computer-aided design of ionic liquids for hybrid process schemes

2. Hybrid process design

In this work, a hybrid process design method that combines CAILD and process design-simulation to identify the optimal IL and its corresponding hybrid process specifications has been proposed (see Figure 1). First, hybrid schemes that have the potential to satisfy the demands of lower energy consumption and/or improve the reaction performance (for biochemical processes) are generated. For the hybrid schemes involving reaction process, a dynamic-state simulation should be performed first to evaluate the reaction performance. The design step can go to the downstream separations if the desired performance is achieved, otherwise the hybrid schemes should be regenerated. Second, based on the IL design target(s) for separation system(s) in the generated hybrid schemes, CAILD including the constraints of IL structure, thermodynamic and physical properties is employed to the optimal design of ILs, where UNIFAC-IL model and physical property models are introduced as the property prediction models. Third, optimal IL candidates identified from the solution of the MINLP-based CAILD problems are further evaluated by means of steady-state simulation in ASPEN Plus, in which the information of thermodynamic model, physical and critical properties of ILs are provided. Among this information, sub-models of four temperature-dependent properties (i.e. C_{pL} , σ , η , λ) are regressed based on a large number of collected experimental data in this work. Finally, the final hybrid process

design can be identified if the desired results of the hybrid scheme are achieved, otherwise the design target(s) of IL for CAILD should be adjusted accordingly.

2.1. Generation of Hybrid Schemes

The generation of hybrid schemes is based on the method proposed by Babi et al. (2015). Based on the identified “hot-spots” of a process, design targets for its improvement that overcome the “hot-spots” are set. Two hybrid schemes, i.e. hybrid distillation with ionic liquid (see Figure 2b) and hybrid reaction-separation scheme (see Figure 3), are investigated and further demonstrated by case studies in this work. In the hybrid distillation scheme, a traditional energy intensive distillation operation is replaced by a combination of not are energy intensive distillation operation with an IL-based extraction distillation. The result is that the same separation is achieved at much lower cost, better environmental impact and reduced waste. In the hybrid reaction-separation scheme, a typical bioreactor operation is combined with solvent-based product recovery giving a higher product yield and avoiding catalyst (enzyme) inhibition.

Figure 2a: Hybrid distillation with membrane

Figure 2b: Hybrid distillation with ionic liquid

Figure 3: Hybrid bioreaction-separation scheme with continuous product removal

2.2. Computer-Aided Design of ILs

To achieve the full potential of the generated hybrid schemes using ILs as solvents, a systematic solvent screening method, CAILD, is considered for the optimal design of ILs in this work. In CAILD, various functional groups (cations, anions and substituents) are combined subject to the constraints of IL structure, thermodynamic and physical properties. The optimal IL candidates can be identified by maximizing or minimizing the objective function (i.e. design target) in CAILD. The CAILD can be summarized as the following MINLP problem

$$\max/\min_z f_{\text{obj}}(z)$$

$$\text{s. t. } \text{IL structural constraints}$$

thermodynamic property constraints

physical property constraints

where $f_{obj}(z)$ is the objective function and the vector z represents the molecular (IL) structure including the existence and the number of building blocks (cations, anions and substituents). For example, the objective function should be minimized when using Henry's constant as design target for the CO₂ capture process, while the objective function should be maximized when using relative volatility as design target for the distillation separation. The CAILD optimization problem has three main constraints: a) IL structural constraints that are introduced to ensure the feasibility (e.g. octet rule, bonding rule) and the complexity (e.g. numbers of substituents) of the IL molecule, the detailed description of these constraints is expressed by Eq.5-11; b) Thermodynamic property constraints that are considered to find more attractive ILs for industrial applications. For example, in a liquid-liquid extraction process, the solubility of the designed IL in raffinate (e.g. aqueous phase) should be constrained to avoid the solvent loss; c) Physical property constraints that are included to ensure the applicability of designed ILs in practical operations. For example, to avoid solidification, the melting point temperature of the designed IL must be at least 5 K less than the temperature at every point in the whole process, and the viscosity should be relatively low (e.g. less than 0.05 Pa.s) with the consideration of the process operation.

Objective function

In order to obtain an attractive separation performance of hybrid distillation with IL (see Figure 2b), a reasonable design target should be set for the CAILD optimization problem. As a measure comparing the vapor pressures of the components in a liquid mixture of chemicals, relative volatility can indicate the ease or difficulty of using distillation to separate the more volatile components from the less volatile components in a mixture. Since the components are to be easily separated from each other with high relative volatility, the maximization of the relative volatility between component (1) and component (2) in the ternary system containing IL is selected as the objective function. In the present work, two types of relative volatility: infinite dilution activity coefficients (γ^∞) based relative volatility ($\alpha_{1,2}^\infty$) and solvent-to-feed ratio (S/F) based relative volatility ($\alpha_{1,2}^{S/F}$) are considered. They are defined in Equations 2 and 3.

$$\alpha_{1,2}^\infty = \frac{\gamma_1^\infty P_1^{sat}}{\gamma_2^\infty P_2^{sat}} \quad 2$$

$$\alpha_{1,2}^{S/F} = \frac{\gamma_1^{S/F} P_1^{sat}}{\gamma_2^{S/F} P_2^{sat}} \quad 3$$

where P_1^{sat} and P_2^{sat} , respectively, represent the saturated pressure of component (1) and component (2). γ_1^∞ , γ_2^∞ are the infinite dilution activity coefficient of component (1) and component (2) while $\gamma_1^{S/F}$, $\gamma_2^{S/F}$ are the activity coefficient of component (1) and component (2) with certain S/F, respectively. In a ternary system containing IL, the IL interacts differently with the components of the mixture thereby causing their relative volatilities to change, and different ILs generally have different interaction with the components to be separated.

Together with relative volatility, the Hildebrand solubility parameter that can predict solvent-related properties is also considered as design target since compounds with similar solubility parameter are more likely to form a miscible solution (Barton et al., 2017). In this work, a group contribution (GC)-based model developed by Roughton et al. (2012) for predicting the Hildebrand solubility parameter of IL (δ_{IL}) is used, as given in Eq.4.

$$\delta_{IL} = \sum_{c=1}^{k_c} n_c \delta_c + \sum_{a=1}^{k_a} n_a \delta_a + \sum_{g=1}^{k_g} n_g \delta_g + b \quad 4$$

where parameters δ_c , δ_a and δ_g represent the group contributions from cations, anions and substituents for the Hildebrand solubility parameter while δ_c , δ_a and δ_g denote the number of cations, anions and substituents in the IL molecule, respectively. When using Hildebrand solubility parameter as design target in the CAILD optimization problem, the objective function is to minimize the difference between the solubility parameter of IL and the solubility parameter of the entrained component.

When choosing an IL as solvent for the product recovery (liquid-liquid extraction) in the proposed reaction-separation scheme (see Figure 3), its separation performance are generally described by solvent properties at infinite dilution such as distribution coefficient (D) and selectivity (S) (Kumar and Banerjee, 2009; Anantharaj and Banerjee, 2010; Gutiérrez et al., 2012; Karunanithi and Mehrkesh, 2013).

$$D = \frac{\gamma_{P,H_2O}^{\infty} M_{w,H_2O}}{\gamma_{P,IL}^{\infty} M_{w,IL}} \quad 5$$

$$S = \frac{\gamma_{R,IL}^{\infty}}{\gamma_{P,IL}^{\infty}} \quad 6$$

where γ_{P,H_2O}^{∞} is the infinite dilution activity coefficient of product P in the aqueous phase; γ_{P,H_2O}^{∞} , $\gamma_{R,IL}^{\infty}$ are the infinite dilution activity coefficients of product P and reactant R in the IL phase, respectively; in Eq.1, M_{w,H_2O} and $M_{w,IL}$ represent the molecular weights of water and IL, respectively. In this work, S and $\{D \times S\}$, respectively, are considered as the objective function in the CAILD optimization problem and both them should be maximized.

IL structural constraints

To ensure the feasibility and complexity of designed ILs, A detailed set of constraints proposed by (Karunanithi and Mehrkesh, 2013) is introduced, shown as in Eqs.7–13.

$$\sum_{i \in C} c_i = 1 \quad 7$$

$$\sum_{j \in A} a_j = 1 \quad 8$$

$$\sum_{l=1}^N x_l - \sum_{i \in C} c_i v_i = 0 \quad 9$$

$$\sum_{i \in C} (2 - v_i) c_i + \sum_{l=1}^N \sum_{k \in S} (2 - v_{kl}) x_l n_{kl} = 2 \quad 10$$

$$\sum_{k \in S} (2 - v_{kl}) x_l n_{kl} = 1 \quad 11$$

$$n_S^L \leq \sum_{l=1}^N \sum_{k \in S} x_l n_{kl} \leq n_S^U \quad 12$$

$$n_{Sl}^L \leq \sum_{k \in S} x_l n_{kl} \leq n_{Sl}^U \quad 13$$

where C , A , S are the sets of cations, anions and substituents, respectively; the cations are represented by the binary variable of c_i and the anions are represented by the binary variables of a_j . The vector x_l of binary variables represent the side chains l , while the vector n_{kl} of integer variables denotes the number of substituents of type k in the side chain l . Group valences of the cations and substituents, respectively, described by vectors of v_i and v_{sl} . As shown in Eqs.7 and 8, only one cation and one anion is available in each IL molecule. The octet rule that ensures the consistency between the number of side chains and the free valence of the cation is described by Eq.9. Meanwhile, Eqs.10 and 11 are utilized to ensure that any two adjacent groups are not linked by more than one covalent bond. As given in Eqs.12 and 13, minimum and maximum numbers of substituents n_S^L , n_{Sl}^L and n_S^U , n_{Sl}^U are, respectively, specified to the cation and each side chain l with the consideration of the size and complexity of designed IL candidates.

Thermodynamic property constraints

To find ILs with attractive process performance, some thermodynamic property constraints are necessary. For the ILs used in hybrid distillation, constraint of relative volatility that ensures the possibility of the separation process should be considered. On the other hand, when IL is selected as the solvent for liquid-liquid extraction in a dilute aqueous solution, the constraints of distribution coefficient, selectivity and solvent loss (Sl) should be introduced to the CAILD problem. In this work, Sl is described as the following equation

$$Sl = \frac{1}{\gamma_{IL,H_2O}^{\infty}} \quad 14$$

where $\gamma_{IL,H_2O}^{\infty}$ represents the infinite dilution activity coefficient of solvent (IL) in the aqueous phase.

To predict the thermodynamic behavior of the IL containing system, different types of methods have been introduced and extended. They can be summarized as conductor-like screening model (COSMO)-based priori thermodynamic methods including COSMO-RS (Klamt, 1995; Klamt et al., 1998; Klamt and Eckert, 2000; Eike et al., 2004; Lei et al., 2007; Gutiérrez et al., 2012) and COSMO-SAC (Lin and Sandler, 2002; Lin et al., 2004; Lee and Lin, 2015), equations of state like GCLF and PC-SAFT (Lei et al., 2012b; Dai et al., 2013; Paduszynski et al., 2015) and activity coefficient based methods such as UNIQUAC, NRTL and UNIFAC (Simoni et al., 2008; Santiago et al., 2009; Lei et al., 2010a; Santiago et al., 2010b; Lei et al., 2012a; Lei et al., 2014a; Roughton et al., 2012; Hector and Gmehling, 2014).

In this work, UNIFAC is considered as the thermodynamic method because of its reliable predictions and easy integration with the use of CAILD. Proper decomposition of ILs is required for the application of UNIFAC method, here the decomposition approach where the IL is divided into cation, anion, and substituents separately is employed since it can improve the design space and the flexibility of the CAILD optimization problem (Song et al., 2018).

Physical property constraints

Properties of ILs (ILs), especially the melting point and the viscosity, are important for the optimal design of ILs. For example, to avoid solidification of the solvent, the melting point temperature (T_m) of the designed IL must be at least 5 K less than the temperature at every point in the whole process (T_p) while the viscosity (η) has significant impact on the process operation. Therefore, constraints ensure the applicability of the designed ILs are added to these two properties (see Eq.15 and 16).

$$T_p - T_m < 5 \text{ (K)} \quad 15$$

$$\eta < 0.05 \text{ (Pa.s)} \quad 16$$

Several types of methods such as quantum chemistry-based method (Trohalaki et al., 2005; Sun et al., 2006; Palomar et al., 2007; Torrecilla et al., 2009), empirical correlations (Diedenhofen et al., 2007; Jacquemin et al., 2006; Guerrero et al., 2012; Fröba et al., 2010), GC-based methods (Paduszynski and Domanska, 2011; Gardas and Coutinho, 2009; Chen et al., 2019b) and corresponding states principle-based equations (Valderrama and Zarricueta, 2009; Mousazadeh and Faramarzi, 2011) have been developed for the physical property predictions of ILs. Among them, GC-based methods are preferred since it can be easily integrated with the use of CAILD. For this reason, two GC-based estimation methods developed in our previous work (Chen et al., 2019b) are used to calculate T_m and η of ILs.

2.3. Process Design-Simulation

Hybrid distillation with ionic liquid

As shown in Figure 2b, two separation techniques (a conventional distillation and an IL-based distillation) are combined in the proposed hybrid scheme involving IL-based distillation. Both

distillations have their regions of efficient operations. For conventional distillation, this should have significant energy savings and for IL-based distillation it reduces the amount of IL and also improves the column operation (e.g. low viscosity). So replacing the part of the separation where conventional distillation has very low driving force (or requires most of the energy) with a IL-based distillation that has higher separation efficiency in this region will ensure both the separation techniques are operating at their high efficiency regions. The hybrid scheme has better energy efficient and economical performance than any of the separation techniques on their own.

To evaluate the process performance of the hybrid distillation scheme using IL identified from the solution of the CAILD problems, detailed process simulations are performed in Aspen Plus. To date, ILs are still not included to the component database in Aspen Plus and therefore they should be defined as pseudo-components. For the purpose of these definition, properties of ILs such as molecular weights, densities and critical properties need to be specified. Likewise, information of the thermodynamic method for the IL containing system is also required.

Critical properties of ILs can be calculated using the fragment contribution-corresponding states method developed by Huang et al. (2013), as following equations

$$T_b = 198.2 + \sum_{i=1}^k n_i \Delta T_{b,i} \quad 17$$

$$T_c = \frac{T_b}{0.5703 + 1.0121 \sum_{i=1}^k n_i \Delta T_{c,i} - (\sum_{i=1}^k n_i \Delta T_{c,i})^2} \quad 18$$

$$P_c = \frac{M}{(0.34 + \sum_{i=1}^k n_i \Delta P_{c,i})^2} \quad 19$$

$$V_c = 28.8946 + 14.75246 \sum_{i=1}^k n_i \Delta V_{c,i} + \frac{6.03853}{\sum_{i=1}^k n_i \Delta V_{c,i}} \quad 20$$

$$\omega = \frac{T_b T_c}{(T_c - T_b)(0.7 T_c)} \log\left(\frac{P_c}{P_b}\right) - \frac{T_c}{(T_c - T_b)} \log\left(\frac{P_c}{P_b}\right) + \log\left(\frac{P_c}{P_b}\right) - 1 \quad 21$$

In Eqs.17–20, n_i denotes the number of fragment i that appears in the IL molecules; $\Delta T_{b,i}$, $\Delta T_{c,i}$, $\Delta P_{c,i}$, and $\Delta V_{c,i}$ represent the fragment increments of fragment i for the normal boiling temperature (T_b), critical temperature (T_c), critical pressure (P_c), critical volume (V_c), respectively; M is the molar mass in g.mol⁻¹. In Eq.21, ω is the acentric factor and P_b is the atmospheric pressure in bar.

To calculate the temperature-dependent properties such as heat capacity, surface tension, viscosity and thermal conductivity, prediction sub-models of these properties in Aspen Plus (Eqs.22-25) are extracted and further regressed based on a wide range of published experimental data (see Appendix and Supplementary material).

$$C_{pL} = C_{1pL} + C_{2pL}T + C_{3pL}T^2 + C_{4pL}T^3 + C_{5pL}/T^2 \quad 22$$

$$\sigma = C_{1\sigma} + C_{2\sigma}T + \dots + C_{10\sigma}T^9 \quad 23$$

$$\ln \eta = C_{1\eta} + C_{2\eta}/T + C_{3\eta} \ln T + C_{4\eta}T^2 + C_{5\eta}/T^2 \quad 24$$

$$\lambda = C_{1\lambda} + C_{2\lambda}T + C_{3\lambda}T^2 + C_{4\lambda}T^3 + C_{5\lambda}T^4 \quad 25$$

where, T is the absolute temperature in K; heat capacity C_{pL} (J.mol⁻¹.K⁻¹), surface tension σ (N.m⁻¹), viscosity η (Pa.s) and thermal conductivity λ (W.m⁻¹.K⁻¹) can be calculated from their corresponding modeling parameters C_{mpL} , $C_{m\sigma}$, $C_{m\eta}$ and $C_{m\lambda}$ ($m = 1, 2, 3 \dots$), respectively.

As in the design stage of CAILD, UNIFAC is also selected as the thermodynamic method in Aspen Plus for process simulation. In this work, group volume parameters (R_k), surface area parameters (Q_k) as well as interaction parameters (α_{mn} , α_{nm}) of UNIFAC-IL model are taken from the published works by Wittig et al. (2003) and Roughton et al. (2012). In their work, parameters R_k , Q_k were

calculated based on the rules of Bondi (Bondi, 1964) and parameters α_{mn} , α_{nm} were regressed on the basis of experimental data containing activity coefficients of different solutes at infinite dilution in various ILs. These parameters were validated by comparing experimental and calculated ternary VLE data of various binary aqueous mixtures (ethanol–water, 1-propanol–water and 2-propanol–water) with different ILs (Roughton et al., 2012).

Hybrid reaction-separation scheme

Hybrid reaction-separation scheme is an intensified process operation where the conversion of the reactant(s) is completed in the reactor and the product recovery is performed externally with a separate loop where separation technique of liquid-liquid extraction is used, as presented in Figure 3. Bio-reactions are considered in this hybrid scheme, meaning that the medium of the reactor contains large amounts of water. In liquid-liquid extraction, the solvent should be able to extract the product (s) from the dilute water solution and separate it from the reactants. Meanwhile, the reactant (s) should remain dissolved in the aqueous phase and then recycled back to the reactor after decantation. After liquid-liquid extraction, the product (s) and the solvent are further separated in a flash evaporator, where the product s are recovered and the solvent is regenerated. In this case, a heavy solvent with very low volatility and water immiscibility is needed to achieve the separation target and therefore hydrophobic ILs are the potential solvent candidates. CAILD is selected as the solvent screening method and the feasibility of the product recovery with the identified ILs from solution of CAILD problem is evaluated by the liquid-liquid equilibrium (LLE) calculation of the studied IL containing system performed in Aspen Plus.

A dynamic-state simulation is required to evaluate the possibility of improving reaction performance by the continuous product removal from reactor (Figure 4). For this reason, a dynamic model that describes the behavior of the reaction system is developed for the dynamic-state simulation. The model aims to be applicable for any kind of reaction process catalyzed by enzymes with low substrate concentrations and low yields. Aerobic bio-reactions are also taken into consideration in this model and therefore the presence of the vapor phase is due to possible aeration requirements.

Figure 4: Schematic representation of the modelled reactor

In Figure 4, F_1 , F_2 , F_{AIR} and F_3 refer to the inlet and outlet molar flow rates of the liquid (F_1 , F_2) and the vapor phase (F_{AIR} , F_3) (kmol/h), respectively. F_1 , F_2 can be controlled by adjusting the value in the liquid outlet of the reactor. The dynamic model is expressed as following equations:

$$\frac{dn_i}{dt} = F_1 x_{1,i} - F_2 x_{2,i} + \gamma_i r - F_3 y_i \quad 26$$

$$F_3 y_i = F_{air} y_i - \vartheta_i^V F_{air} y_i + \vartheta_i^L n_i \quad 27$$

1	$x_{1,i} = \frac{f_{1,i}}{F_1}$	28
2	$x_{2,i} = \frac{n_i}{N}$	29
3	$y_i = \frac{f_{3,i}}{F_3}$	30
4	$F_1 = \sum_{i=1}^{NC} f_{1,i}$	31
5	$F_2 = C_v h$	32
6	$F_3 = \sum_{i=1}^{NC} f_{3,i}$	33
7	$N = \sum_{i=1}^{NC} n_i$	34
8	$\bar{\rho} = \sum_{i=1}^{NC} \rho_i n_i$	35
9	$h = \frac{N}{\bar{\rho} A}$	36
10	$V = hA$	37
11	$C_i = \frac{n_i}{V}$	38

12 where the total number of moles (N) in the reactor is equal to the sum of the moles of each components
13 i (n_i); the molar fraction of component i in the vapor phase (y_i) can be calculated by Eq.30, and the
14 molar fraction of component i in the liquid inlet ($x_{1,i}$) and outlet ($x_{2,i}$) of the reactor can be calculated
15 by Eq.28 and Eq.29, respectively. γ_i represents the stoichiometric coefficient of component i and C_v
16 describes the value coefficient; ϑ_i^V is the coefficient for the reacted gases while ϑ_i^L is the removal
17 coefficient of the moles of the liquid compounds. $f_{1,i}$, $f_{3,i}$ are the inlet molar flow rates of component
18 i in the inlet stream and the vapor outlet, respectively. Based on the ideal mixing rule (Eq.35), the
19 density of the liquid mixture ($\bar{\rho}$) can be calculated from the pure component density (ρ_i); the volume
20 of the liquid (V) is calculated as the product of the cross-sectional area (A) times the level of the liquid
21 (h). The concentrations of the enzyme (C_E) and the oxygen (C_O) are considered to be constant
22 throughout the reaction, while the concentrations of the substrate (C_S) and the product (C_P) change
23 with the time can be calculated by Eq.38.

24 The equations in this dynamic model are derived from the differential mass balance since the model
25 parameters such as the concentrations of substrate and product are changing over the time. Different
26 reaction systems have different reaction kinetic models and kinetic parameters. Generally, the kinetic
27 model and its corresponding kinetic parameters are developed and regressed from experimental work.
28 In this work, ICAS-MoT (Fedorova et al., 2015) is applied as the process simulator for dynamic-state.

29 Table 1 summarizes the overall information of the proposed design method for hybrid processes. In
30 the design stage of CAILD, besides the objective function and the constraints of the design problem,
31 thermodynamic method (UNIFAC) and group parameters (e.g. group sets, boundaries of group
32 number) are also included. The variables describing the IL structure are optimized by solving the
33 formulated MINLP problem for CAILD. Subsequently, the optimal IL identified from CAILD and
34 the information of its critical, physical and thermodynamic properties are used in the design stage of
35 process simulation. Meanwhile, process parameters such as feed information, operating conditions
36 are provided as well. The process variables (e.g. column configurations, solvent flowrate) are
37 optimized by means of trade-off and sensitivity analysis. On the other hand, when the IL is selected
38 as the solvent for the liquid-liquid extraction, the LLE calculation of the IL containing system is
39 performed aims to evaluate the possibility of the phase split. In the case of hybrid reaction-separation
40 scheme, a dynamic-state simulation is also needed to evaluate the possibility of improving reaction

performance (e.g. yield, reaction rate) by continuous product removal from reactor. As required, dynamic model describing the behavior of the reaction system, as well as kinetic parameters, reaction conditions etc., should be provided.

Table 1: Overall information of the proposed hybrid process design involving IL

CAILD (Stage 1)	
Objective function	e.g. $\max(\alpha_{1,2}^{\infty})$; $\max(\alpha_{1,2}^{S/F})$; $\min(\delta_{IL} - \delta_2)$; $\max(S)$; $\max(\{D \times S\})$ (Eqs.2-6)
IL structure constraints	Feasibility (Eqs.7-10), complexity (Eqs.12-13)
Thermodynamic property constraints	e.g. α (Eqs.1-2); S (Eq.5); D (Eq.6); Sl (Eq.14)
Physical property constraints	T_m , η (Eqs.15-16)
Thermodynamic method	UNIFAC
Fixed parameters	C , A , S , n_S^L , n_{Sl}^L , n_S^U , n_{Sl}^U
Optimization variables	c_i , a_j , x_l , v_i , v_{kl} , n_{kl}
Process design-simulation (Stage 2)	
Steady-state simulation	
Optimal IL (Identified from CAILD)	e.g. $[C_3mPy]^+ [BF_4]^-$; $[C_4mIm]^+ [Tf_2N]^-$
Critical properties	T_b , T_c , P_c , V_c , ω (Eqs.17-21)
Physical properties	C_{pL} , σ , η , λ (Eqs.22-25)
Thermodynamic properties	R_k , Q_k , α_{mn} , α_{nm} (UNIFAC-IL model)
Process parameters	Feed information (e.g. flowrate, composition), operating conditions (e.g. pressure, temperature)
Optimization variables	Number of stages, feed stage, reflux ratio, solvent flowrate
Dynamic-state simulation	
Dynamic model	Eqs.26-38
Fixed parameters	Kinetic parameters, reaction conditions
Performance indicator	Reaction rate, yield

3. Case studies

3.1. Separation process of aqueous solutions

Separation of aqueous solutions is widely encountered in process industries, such as in the separation process of the methanol-water mixture, where the energy requirement increases significantly with respect to the recovery of methanol from 0.98 to 0.998 (mole-based). Likewise, acetone separation from aqueous solution has a similar energy consumption distribution, as shown in Figure 5, where data points of both examples come from the process simulation in Aspen Plus. For both cases, “hot-spots” can be identified based on their energy consumption distribution. Considering the significant energy savings potential of using energy efficient process to replace the energy intensive separation task (i.e. remove “hot-spots”), sustainable hybrid distillation designs proposed in this work are promising alternatives for these separation processes.

In the process of methanol separation from aqueous solution, the process task can be defined as follows: a 1000 kmol.h⁻¹ liquid mixture consisting of 20 mol% methanol and 80 mol% water, to be separated by hybrid distillation with IL so that the methanol composition of distillate from extractive distillation column amounts to 99.8 mol%. For the case of acetone separation from aqueous solution, we consider a 1000 kmol.h⁻¹ liquid mixture consisting of 20 mol% acetone and 80 mol% water which is separated by hybrid distillation with IL for meeting the acetone purification of 99.8 mol%. In this work, IL-based extractive distillation is considered to perform the energy intensive separation task of the process for both cases. Fixed process parameters for the proposed hybrid process are given in Table 2.

Figure 5: Energy consumption distribution in the separation process of aqueous solutions

Table 2: Fixed parameters and simulation results of the conventional distillation for the separation process of aqueous solution

Fixed parameters	Methanol-water	Acetone-water
Feed		
Flow rate	1000 kmol/h	1000 kmol/h
Mole-based composition	0.2 CH ₃ OH, 0.8 H ₂ O	0.2 (CH ₃) ₂ CO, 0.8 H ₂ O
Methanol purity	99.8 mol % CH ₃ OH	99.8 mol % (CH ₃) ₂ CO
Distillation Column		
Pressure at the top	1 bar	1 bar
Pressure at the bottom	1.2 bar	1.2 bar
Number of stages	20	33
Feed stage	13	31
Reflux ratio	1.95	2.95
Reboiler heat duty	5987 kW (99.8 mol% CH ₃ OH)	7022 kW (97 mol% (CH ₃) ₂ CO)

Table 3: Molecular building blocks for IL design in the case studies of aqueous separation

Type	Group	Subgroup	Type	Group	Subgroup
Substituents	CH ₃	CH ₃	Anions	[Tf ₂ N] ⁻	[Tf ₂ N] ⁻
		CH ₂		[BF ₄] ⁻	[BF ₄] ⁻
Cations	[Im] ⁺	[Im] ⁺		[PF ₆] ⁻	[PF ₆] ⁻
		[mIm] ⁺		[CF ₃ SO ₃] ⁻	[CF ₃ SO ₃] ⁻
	[Py] ⁺	[Py] ⁺		[CF ₃ COO] ^{-*}	[CF ₃ COO] ^{-*}
		[mPy] ⁺		[DMP] ⁻	[DMP] ⁻
				[SCN] ^{-*}	[SCN] ^{-*}

*NB: Groups only used in the case study of ethanol-water separation

As shown in Table 3, 2 widely studied 2 substituents, 2 cations and 7 anions were selected as building blocks for the IL design. Table 4 summaries the design information of the MINLP-based CAILD problem in these case studies. The formulated MINLP problem of both examples are solved using deterministic global optimization solvers (LINDOGLOBAL) in the modelling system GAMS.

Table 4: Design information of MINLP-based CAILD problem for the case studies of aqueous separation

Case	Number of continuous variables	Number of binary variables	Number of integer variables	Number of constraints		
				IL structure	Thermodynamic properties	Physical properties
Methanol-water	195	23	70	60	126	4
Acetone-water	195	21	70	60	126	4

By solving the MINLP-based CAILD optimization problem (see Equations 1-13) using γ^∞ based and S/F based relative volatility of methanol and water in the ternary system containing IL as objectives, 1-ethylpyridinium tetrafluoroborate ($[\text{C}_2\text{Py}]^+[\text{BF}_4]^-$) and 1-ethyl-3-methylpyridinium tetrafluoroborate ($[\text{C}_2\text{mPy}]^+[\text{BF}_4]^-$) are selected, respectively; meanwhile, 1-methylimidazolium tetrafluoroborate ($[\text{mIm}]^+[\text{BF}_4]^-$) is identified as entrainer while using the Hildebrand solubility parameter of ILs (δ_{IL}) as design target in the CAILD optimization problem. Similarly, for the separation process of acetone-water mixture, 3-methyl-1-propylpyridinium tetrafluoroborate ($[\text{C}_3\text{mPy}]^+[\text{BF}_4]^-$) and 1-methylpyridinium dimethylphosphate ($[\text{C}_1\text{Py}]^+[\text{DMP}]^-$) are identified, respectively, using γ^∞ based relative volatility (or δ_{IL}) and S/F based relative volatility as design targets. Table 5 provides the model statics from GAMS solution of the MINLP-based CAILD problem and the structures of the generated IL candidates are given by Figure 6.

Table 5: Model statistics from GAMS solution for the case studies of aqueous separation

Case	Number of continuous variables	Number of binary variables	Number of equations	Number of constraints	Objective function	Number of iterations	CPU time (s)
Methanol-water	195	23	191	190	$\alpha_{1,2}^\infty$	210	4
					$\alpha_{1,2}^{S/F}$	203475	24
Acetone-water	195	21	191	190	$\alpha_{1,2}^\infty$	43048	21
					$\alpha_{1,2}^{S/F}$	159953	16

As shown in Figure 2b, two distillation columns and a flash unit are included in the proposed hybrid distillation with IL. Column 1 is used as traditional separation unit while Column 2 is considered to perform the energy intensive task of the separation processes. Subsequently, the flash unit is employed for the entrainer (IL) regeneration. The simulation of this hybrid distillation process is performed in Aspen Plus (V8.6), where distillation columns (Column 1, Column 2) are modelled by the RadFrac block and flash unit is modelled by the flash evaporation. As compared, conventional process simulation is also performed for the same separation task.

In the design step of process simulation, key operating variables like the number of stages, feed location in Column 2 and the corresponding flow rates of IL are optimized by trade-off and sensitivity analysis. As demonstrated, sensitivity analysis on feed location in Column 2 with certain number of stages (N=12) for the use of $[\text{C}_3\text{mPy}]^+[\text{BF}_4]^-$ as entrainer at different flow rates is shown in Figure 7. Based on the trade-off analysis, the columns with optimal feed location at different IL flow rates, the

number of stages and flow rate yielding the minimum stages and energy requirements can be achieved (see Figure 8).

Figure 6. The structure of the designed ionic liquids for the hybrid distillation process:

(a) $[C_2Py]^+[BF_4]^-$, (b) $[C_2mPy]^+[BF_4]^-$, (c) $[mIm]^+[BF_4]^-$, (d) $[C_3mPy]^+[BF_4]^-$, (e) $C_1Py^+[DMP]^-$

Figure 7: Reboiler heat duty plotted against feed stage location for meeting the separation task of acetone-water mixture using various amounts of $[C_3mPy]^+[BF_4]^-$ as entrainer.

For the purposes of comparison, the conventional distillation process of both systems is also simulated and optimized. The simulation results of hybrid separation scheme for both systems are summarized in Tables 6 and 7. The results indicate that hybrid distillation with all IL identified using different selection criteria have significant energy savings in comparison to the conventional distillation process, where 5987 kW is required for meeting the methanol purification of 99.8 mol% while 7022 kW is required to obtain the acetone recovery of 97 mol% (see Table 6).

Figure 8: Reboiler heat duty plotted against the molar flow of $[\text{C}_3\text{mPy}]^+[\text{BF}_4]^-$ in the extraction distillation column with different number of column stages (N) for meeting the acetone purification requirement.

Table 6: Simulation results for hybrid distillation with IL for methanol-water system

Design target	$\alpha_{1,2}^\infty$	$\alpha_{1,2}^{S/F}$	δ_{IL}
IL	$[\text{C}_2\text{Py}]^+[\text{BF}_4]^-$	$[\text{C}_2\text{mPy}]^+[\text{BF}_4]^-$	$[\text{mIm}]^+[\text{BF}_4]^-$
Entrainer flow rate, kmol/h	11	8	12
Column 1			
Number of stages	16	16	16
Feed stage	11	11	11
Reflux ratio	1.43	1.43	1.43
Reboiler heat duty, kW	4991	4991	4991
Column 2			
Number of stages	6	6	5
Entrainer stage	2	2	2
Feed stage	4	4	4
Reflux ratio	0.119	0.095	0.091
Reboiler heat duty, kW	186	141	124
Flash drum			
Operating pressure (bar)	0.1	0.1	0.1
Heat duty, kW	67	65	76
Overall heat duty, kW	5244	5197	5191

For methanol-water system, all three IL candidates have similar energy requirement. Among them, $[\text{mIm}]^+[\text{BF}_4]^-$ requires the least column stages and $[\text{C}_2\text{mPy}]^+[\text{BF}_4]^-$ is found to be the best selection in terms of the solvent consumption. For the separation of acetone-water mixture, all three selected ILs provide significant energy savings. Although $[\text{mIm}]^+[\text{BF}_4]^-$ requires the least number of column stages while, $[\text{C}_2\text{mPy}]^+[\text{BF}_4]^-$ shows the most attractive separation performance with lowest energy input

and solvent consumption. Calculation results of both cases highlight the reliability and applicability of using $\alpha_{1,2}^{S/F}$ as design target to screen suitable ILs in the CAILD problem for separation processes of aqueous solution.

Although, only one main column is required for the conventional distillation process, hybrid scheme with IL can significantly reduce the energy consumption, especially for the acetone-water system where the purification would be very difficult after 96 mol% acetone. Additionally, the overall flow rate of ILs in the hybrid process is less than 20 kmol/h, which provides possibility of addressing the operational and economic constraints (e.g. high viscosity, high cost) in the use of ILs as solvents.

Table 7: Simulation results for hybrid distillation with IL for acetone-water system

Design target	$\alpha_{1,2}^{\infty}$	$\alpha_{1,2}^{S/F}$	δ_{IL}
IL	$[\text{C}_1\text{Py}]^+[\text{DMP}]^-$	$[\text{C}_3\text{mPy}]^+[\text{BF}_4]^-$	$[\text{mIm}]^+[\text{BF}_4]^-$
Entrainer flow rate, kmol/h	17	14	16
Column 1			
Number of stages	15	15	15
Feed stage	12	12	12
Reflux ratio	0.395	0.395	0.395
Reboiler heat duty, kW	3097	3097	3097
Column 2			
Number of stages	12	10	9
Entrainer stage	2	2	2
Feed stage	8	7	7
Reflux ratio	0.275	0.275	0.289
Reboiler heat duty, kW	241	233	230
Flash drum			
Operating pressure (bar)	0.1	0.1	0.1
Heat duty, kW	286	278	293
Overall heat duty, kW	3624	3608	3620

3.2. Bio-oxidation of alcohols

Aldehydes are important intermediates used in the manufacture of solvents, resins, plasticizers and pharmaceuticals because of their high chemical activity (<https://www.britannica.com/science/aldehyde>). Some sugars, hormones or vitamin derivatives are aldehydes (Smith and March, 2006). There are several methods for synthesizing aldehydes, and the method of alcohols dehydrogenation is widely used in industries (Colquhoun et al., 1991). In this work, we select the oxidation of alcohols as the synthesis method to produce aldehydes and the bio-catalyst (galactose oxidase) is used in these bio-reactions (see Table 8). Galactose oxidase is a copper-dependent enzyme that has shown promising results for the bio-catalysis of the oxidation of primary alcohols to the corresponding aldehydes (Whittaker, 2003). Although this synthesis method has many advantages such as low environmental impact and high reaction specification, the limitations of enzymes associated with product and substrate inhibition result in highly diluted product, which leads to difficulties in downstream separations. For this reason, the proposed hybrid reaction-separation scheme (see Figure 3) is considered as the solution for such limitations, and the application is illustrated through the bio-oxidation of benzyl alcohol to produce benzaldehyde.

Experimental work regarding the bio-catalytic oxidation of primary alcohols to aldehydes has been carried out by Toftgaard Pedersen et al. (2015). In their work, the oxidation of benzyl alcohol to

benzaldehyde using enzyme Galactose oxidase was in focus and a reaction kinetic model, as expressed by Eq.39, was developed.

$$\frac{dC_S}{dt} = -r = -\frac{k_{cat}C_EC_SC_O}{C_SC_O+K_{MO}C_S+K_{MS}C_O\left(1+\frac{C_P}{K_{IP}}\right)} \quad 39$$

Table 8: Information of the studied bio-oxidation of alcohols

Reaction scheme	$A + B \longrightarrow C + D$
Reaction class	Oxidation
Reactants	Primary alcohol, oxygen
Products	Aldehyde, water
Catalyst	Galactose oxidase
Reaction class form

where r is the reaction rate (mmol/l·min) and k_{cat} is the rate constant ($\mu\text{mol}/\text{min}\cdot\text{mg}$ CFE (cell-free extract)). C_O , C_S , C_P are the concentrations of oxygen, substrate and product, respectively (mmol/l); C_E is the enzyme concentration in mg/l; K_{MO} , K_{MS} , K_{IP} are Michaelis constants for oxygen, benzyl alcohol and benzaldehyde, respectively (mmol/l). Table 9 summarizes the reactor conditions and the kinetic parameters for this bio-reaction process.

Table 9: Reactor conditions and kinetic parameters for alcohols dehydrogenation using galactose oxidase as biocatalysts

Kinetic parameters			
Parameters	value	Parameters	value
k_{cat} (kmol/kg CFE)	0.066	C_E (kg/m ³)	0.0011
K_{MS} (kmol/m ³)	0.051	C_O (kg/m ³)	0.5
K_{IP} (kmol/m ³)	0.0017	C_S (kg/m ³)	0.265
Reactor conditions			
T (°C)	25	$C_{alcohol}$ (kmol/m ³)	0.05
P (atm)	1	Aeration (vvm*)	0.5

*vvm - volume of air (l) passing through a volume of medium (l) per unit time (min).

The performance of a reaction can be evaluated by the yield (Y), which is generally described as

$$Y = \frac{n_p - n_{0,p}}{n_{0,r}} \quad 40$$

where, $n_{0,p}$ and n_p are the initial moles of product and the moles of product formed, respectively, while $n_{0,r}$ is the moles of the limiting reactant (Liese et al., 2006).

Based on the developed dynamic model (Eqs.26-38), the molar composition in the reactor with respect to time is calculated using the reaction conditions and the kinetic parameters presented in Table 9. For comparison purposes, the simulation of the batch operation is also performed. Figure 9 illustrates the product yield and reaction rate between batch operation and continuous product removal (hybrid

reaction-separation scheme). Clearly the hybrid scheme involving continuous product removal has a better reaction and yield performance than the batch operation.

Figure 9: Comparison between batch operation and continuous product removal

In the downstream separation process, the solvent should be able to extract the product(s) from the aqueous phase and the reactant(s), and it should also be easily separated from the product(s). Since the separation technique of liquid-liquid extraction is considered, the separation feasibility of the selected solvent can be evaluated by the ternary plot for system of water + aldehyde + solvent.

Figure 10. Ternary plot for system of water + benzaldehyde + 5-nonanone

For bio-oxidation process of benzyl alcohol, an organic solvent, 5-nonanone (Figure 11(a)), is generated to separate benzaldehyde from water by using Pro-CAMD in ICAS (Gani et al., 1997) as organic solvent screening tool. Figure 10 presents the ternary plot for system of water + benzaldehyde + 5-nonanone. Although 5-nonanone is able to separate benzaldehyde from water, it is difficult to

separate benzaldehyde from benzyl alcohol + water due to the similarities between benzaldehyde and benzyl alcohol. Moreover, the recovery of benzaldehyde from n-octane is also difficult. On the other hand, experimental data in some published works (Heintz et al., 2006) shows that ILs might be the potential solvents to this separation task.

In this case, well-studied groups containing 2 cations, 2 anions and 2 substituents (see Table 10) were considered as molecular building blocks in CAILD. Table 11 summarizes the design information of the MINLP-based CAILD problem for this case study. The formulated MINLP problem is solved in the modelling system GAMS 24.4.6 on an Intel(R) Xeon(R) E5-1620 3.70 GHz PC running Windows 10 system, here we use a deterministic global optimization solver, LINDOGLOBAL.

Table 10: Molecular building blocks for IL design in the bio-oxidation of benzyl alcohol

Type	Group	Subgroup	Type	Group	Subgroup
Cations	[Im] ⁺	[Im] ⁺	Anions	[Tf ₂ N] ⁻	[Tf ₂ N] ⁻
		[mIm] ⁺		[BF ₄] ⁻	[BF ₄] ⁻
		[CH ₃ N] ⁺	Substituents	CH ₃	CH ₃
		[C ₂ H ₅ N] ⁺			CH ₂
		[C ₃ H ₇ N] ⁺			
		[C ₄ H ₉ N] ⁺			

Table 11: Design information of MINLP-based CAILD problem for the bio-oxidation of alcohols

Number of continuous variables	Number of binary variables	Number of integer variables	Number of constraints		
			IL structure	Thermodynamic properties	Physical properties
688	26	156	88	543	4

The same IL [C₄mIm]⁺[Tf₂N]⁻ is identified from the solution of the MINLP-based CAILD problem using different design targets (i.e. S and $\{D \times S\}$). Table 12 provides the model statics from GAMS solution for this MINLP problem. The structure of [C₄mIm]⁺[Tf₂N]⁻ is given by Figure 11(b) and the UNIFAC-IL calculated LLE for system of water + benzaldehyde + [C₄mIm]⁺[Tf₂N]⁻ is presented in Figure 12. This results can also be partly verified by the experimental work from Heintz et al. (2006), where the activity coefficients at infinite diution of of linear and branched C1-C6 alcohols and aldehydes in [C₆mIm]⁺[Tf₂N]⁻ shows its possibility to separate aldehydes from alcohols.

Table 12: Model statistics from GAMS solution for the bio-oxidation of alcohols

Number of continuous variables	Number of binary variables	Number of equations	Number of constraints	Objective function	Number of iterations	CPU time (s)
688	26	636	635	S	3000621	458
				$\{D \times S\}$	1854845	266

(a)

(b)

Figure 11. The structures of the selected organic and IL solvents: (a) 5-nonanone, (b) [C₄mIm]⁺[Tf₂N]⁻

Figure 12. Ternary plot for system of water + benzaldehyde + $[C_4mIm]^+[Tf_2N]^-$

4. Conclusions

This work presents a design method for hybrid process schemes that have the potential to satisfy the demands of lower energy consumption and reduced waste, as well as satisfying product specifications. The proposed IL-based hybrid schemes complement the ones using membranes (e.g. Figure 2a). Although both ILs and membranes have their regions of efficient operation, their potential for process improvements greatly depends on the studied system. In some cases, hybrid schemes involving ILs have guaranteed energy savings, but the ones using membranes have not, and vice versa. For some systems, if both ILs and membranes are available, the best scheme could be selected on the basis of an agreed set of performance criteria. For the purposes of process simulation, parameters of sub-models used to calculate four temperature-dependent properties of ILs were regressed based on a wide range of collected experimental data. By using this design method, optimal ILs are designed and further evaluated for case studies involving separation of aqueous solutions and bio-oxidation of alcohols. The identified ILs in both cases lead to process performance improvements and among the well-studied anions, $[BF_4]^-$ was found the most attractive for the extractive distillation of aqueous solutions.

In our present work, the design problem of hybrid process was addressed by a two-stage based solution strategy, although more reliable global optimization results consist of optimal IL solvent and corresponding process specifications can be simultaneous obtained by using an integrated solvent and process design method, computational efficiency remains a limiting factor with a significant increase in the complexity and the design space of the global-based MINLP problem. Since the limited property information of IL containing systems, only well-studied IL groups were considered as building blocks. However, more attractive IL candidates may be generated once further IL groups are included where their property information is available. Additionally, verification by experiment will be necessary considering some designed IL(s) have never been studied or synthesized before. Future

work will expand the specific design method into a generalized one that covers a wide range of processes with “hot-spots”, and improve the CAILD toolbox consisting of databases, models, and solution strategies for hybrid schemes.

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Appendix. Property prediction modeling

In Eq.14, the impact of parameters C_{4pL} and C_{5pL} on the heat capacity of ILs is negligible and therefore their values are set to zero. Other modeling parameters C_{mpL} ($m = 1, 2, 3$) can be obtained from group contributions, as shown in Eq.A1.

$$C_{mpL} = \sum_{i=1}^k n_i c_{i,mpL} \quad A1$$

where k represents the total number of different groups in the IL molecule and n_i denotes the number of groups of type i . Group contribution $c_{i,m\eta}$ ($m = 1, 2, 3$) are regressed by fitting experimental data into Eq.14 to minimize the AARD(%), as expressed by Eq.A2.

Table A1: Regressed Group Contribution Parameters $c_{i,mpL}$ ($m = 1, 2, 3$) for Eq.A1 in the Temperature Range of 189.66-524.87K

	$c_{i,1pL}$ (J.mol ⁻¹ .K ⁻¹)	$c_{i,2pL}$ (J.mol ⁻¹ .K ⁻²)	$c_{i,3pL}$ (J.mol ⁻¹ .K ⁻³)
Substituents			
CH ₃	1095.40	-7.998	0.014
CH ₂	43.48	-0.106	2.31E-04
dmN	178.245	-0.864	0.002
Cations			
1,3-dmIm (+)	12.35	-1.784	4.12E-05
1-mPy (+)	-104.238	-0.739	-0.002
1,1-dmPyr (+)	0.00	-1.713	1.08E-04
Am(1)111 (+)	728.417	-5.938	0.006
TDPh (+)	-1641.998	13.508	-0.0230
1,1-dmPip (+)	37.277	-1.632	0.00
Anions			
[Tf ₂ N] ⁻	278.805	2.542	-5.09E-04
[BF ₄] ⁻	175.466	1.984	2.04E-04
[PF ₆] ⁻	15.59	3.145	-0.001
[Cl] ⁻	196.372	1.519	9.47E-04
[Ac] ⁻	244.629	1.505	0.001
[MeSO ₄] ⁻	-274.08	4.791	-0.004
[EtSO ₄] ⁻	315.9	1.566	9.44E-04
[CF ₃ SO ₃] ⁻	75.285	3.134	-0.002
[Br] ⁻	170.98	1.745	4.16E-04
[CF ₃ COO] ⁻	196.953	2.102	2.26E-05
[N(CN) ₂] ⁻	226.563	1.743	5.45E-04
[C(CN) ₃] ⁻	541.00	0.00	0.003
[DMP] ⁻	-3520.00	24.842	-0.035
[FeCl ₄] ⁻	36.00	3.39	-0.002

[SCN] ⁻	-398.00	4.956	-0.003
[eFAP] ⁻	2192.205	-9.673	0.02

$$O.F. = AARD(\%) = \frac{100 \times \sum_{i=1}^N |(\rho_{cal} - \rho_{exp}) / \rho_{exp}|_i}{N} \quad A2$$

$$RD(\%) = 100 \times (\rho_{cal} - \rho_{exp}) / \rho_{exp} \quad A3$$

In Eqs.A2 and A3, N represents the number of experimental data points while subscripts exp and cal denote experimental and calculated properties, respectively.

A number of 2022 data points for 67 ILs covering 6 cation cores, 16 anions and 3 substituents in a wide range of temperature, 189.66-524.87K are used. The AARD (%) of this estimation model for heat capacity is 0.7%. The obtained group contributions $c_{i,m\sigma}$ are provided in Table A1 and comparison between experimental and calculated heat capacity using this model are given in Figure A1.

Figure A1. Comparison between experimental and calculated heat capacity using estimation model, Eq.14

For the surface tension of ILs, the values of parameters $C_{m\sigma}$ ($m = 4, 5, \dots, 10$) in Eq.15 are given as zero because of their negligible influence. Remaining parameters $C_{m\sigma}$ ($m = 1, 2, 3$) can be calculated according to

$$C_{m\sigma} = \sum_{i=1}^k n_i c_{i,m\sigma} \quad A4$$

where k is the total number of different groups in the molecule while n_i denotes the number of groups of type i , and group contributions $c_{i,m\sigma}$ ($m = 1, 2, 3$) are obtained by the regression of experimental data into Eq.15 using Eq.A5 as the objective function.

$$O.F. = \frac{100 \times \sum_{i=1}^N |(\sigma_{cal} - \sigma_{exp}) / \sigma_{exp}|_i}{N}$$

A5

A number of 1577 data points for 110 ILs involving 6 cation cores, 20 anions and 2 substituents in the temperature range of 262.89-393 K are employed. The AARD (%) of this estimation model for surface tension is 3.4%. The regressed group contribution parameters $c_{i,m\sigma}$ are provided in Table A2 and comparison between experimental and calculated surface tension using this model is given in Figure A2.

Table A2: Regressed Group Contribution Parameters $c_{i,m\sigma}$ ($m = 1, 2, 3$) for Eq.A4 in the Temperature Range of 262.89-393 K

	$c_{i,1\sigma}$ (N.m ⁻¹)	$c_{i,2\sigma}$ (N.m ⁻¹ .K ⁻¹)	$c_{i,3\sigma}$ (N.m ⁻¹ .K ⁻²)
Substituents			
CH ₃	8.48E-04	2.18E-04	-2.07E-07
CH ₂	0.005	-4.23E-05	6.90E-08
Cations			
1,3-dmIm (+)	0.003	2.41E-04	-2.31E-07
1-mPy (+)	-4.43E-04	2.71E-04	-2.78E-07
1,1-dmPyr (+)	-2.10E-05	2.46E-04	-1.95E-07
Am(1)111 (+)	-4.90E-04	3.40E-04	-4.34E-07
TDPh (+)	-6.00E-04	1.89E-04	-1.82E-07
1,1-dmPip (+)	-7.47E-05	2.71E-04	-2.85E-07
Anions			
[Tf ₂ N] ⁻	-3.29E-04	1.89E-05	-2.56E-07
[BF ₄] ⁻	-4.71E-04	1.30E-04	-4.90E-07
[PF ₆] ⁻	3.11E-04	5.56E-05	-2.90E-07
[Cl] ⁻	8.60E-04	7.82E-05	-3.46E-07
[Ac] ⁻	3.30E-06	6.54E-05	-3.87E-07
[MeSO ₄] ⁻	-1.75E-04	1.62E-04	-5.96E-07
[EtSO ₄] ⁻	5.50E-05	1.21E-04	-4.90E-07
[CF ₃ SO ₃] ⁻	4.86E-04	2.33E-05	-2.56E-07
[Br] ⁻	-7.32E-05	8.57E-05	-3.89E-07
[CF ₃ COO] ⁻	-2.39E-04	3.79E-05	-3.09E-07
[N(CN) ₂] ⁻	-3.10E-04	1.16E-04	-3.91E-07
[C(CN) ₃] ⁻	0.001	1.36E-04	-4.97E-07
[AlCl ₄] ⁻	-3.51E-04	1.04E-04	-4.17E-07
[InCl ₄] ⁻	-2.93E-05	8.71E-05	-3.61E-07
[DMP] ⁻	-5.56E-05	1.70E-04	-6.51E-07
[FeCl ₄] ⁻	-1.09E-04	9.11E-05	-3.95E-07
[GaCl ₂] ⁻	-2.28E-05	1.07E-04	-4.24E-07
[Pf ₂ N] ⁻	0.00	0.00	-2.11E-07
[SCN] ⁻	-3.73E-04	1.77E-04	-6.30E-07
[eFAP] ⁻	0.002	9.57E-06	-2.52E-07

Figure A2. Comparison between experimental and calculated surface tension using estimation model, Eq.15

Parameters $C_{m\eta}$ ($m = 1, 2, 3, 4, 5$) of viscosity in Eq.16 are obtained through the following group contribution method:

$$C_{m\eta} = \sum_{i=1}^k n_i c_{i,m\eta} \quad A6$$

where k is the total number of different groups in the molecule and n_i denotes the number of groups of type i . Group contributions $c_{i,m\eta}$ ($m = 1, 2, 3, 4, 5$) are regressed by fitting experimental data into Eq.16 using Eq.A7 as the objective function.

$$O.F. = \frac{100 \times \sum_{i=1}^N |(\eta_{cal} - \eta_{exp}) / \eta_{exp}|_i}{N} \quad A7$$

A number of 1842 data points for 86 ILs containing 8 cation cores, 18 anions and 3 substituents in the temperature range of 268.15-413.85 K are collected. The AARD (%) of this estimation model for viscosity is 5.1%. The generated group contributions $c_{i,m\eta}$ are provided in Table A3 and comparison between experimental and calculated viscosity using this model are given in Figure A3.

Table A3: Regressed Group Contribution Parameters $c_{i,m\eta}$ ($m = 1, 2, 3, 4, 5$) for Eq.A6 in the Temperature Range of 268.15-413.85 K

	$C_{1\eta}$ (Pa.s)	$C_{2\eta}$ (Pa.s.K)	$C_{3\eta}$ (Pa.s.K ⁻¹)	$C_{4\eta}$ (Pa.s.K ⁻²)	$C_{5\eta}$ (Pa.s.K ²)
Substituents					
CH ₃	-0.754	-1.846	0.187	-2.25E-06	-0.005
CH ₂	1.957	2.09	-0.309	-6.06E-07	-0.013
dmN	0.026	-2.882	0.435	-2.26E-05	-0.018
Cations					
1,3-dmIm (+)	1.18	0.747	-0.077	1.16E-05	0.069
1,2,3-tmIm (+)	0.354	-3.198	0.495	-6.88E-06	-0.038

1-mPy (+)	1.409	-1.45	0.049	3.27E-06	-0.053
1,1-dmPyr(+)	0.496	-0.273	0.016	1.52E-05	0.005
Am(1)111 (+)	2.03	-0.628	-0.218	1.34E-05	-0.004
1,1,1,1Ph (+)	-0.23	0.333	0.549	-1.34E-05	0.003
TDPh (+)	0.833	-2.294	0.902	-2.40E-05	-0.014
1,1-dmPip (+)	4.616	-1.60	-0.195	-5.69E-06	-0.008
Anions					
[Tf ₂ N] ⁻	-0.88	-1.46	-0.05	-4.72E-05	-0.053
[BF ₄] ⁻	0.185	-2.07	0.221	-6.62E-05	-0.007
[PF ₆] ⁻	0.477	-2.76	0.498	-7.65E-05	-0.003
[Cl] ⁻	-1.58	-0.362	0.074	-2.67E-05	-0.007
[Ac] ⁻	-0.005	0.655	0.014	-5.78E-05	0.014
[MeSO ₄] ⁻	3.023	0.061	-0.398	-5.94E-05	0.007
[EtSO ₄] ⁻	-0.092	0.512	0.181	-6.01E-05	0.093
[CF ₃ SO ₃] ⁻	1.768	-0.049	-0.499	-4.46E-05	0.003
[Br] ⁻	-1.842	-4.655	0.278	-5.98E-05	-0.019
[CF ₃ COO] ⁻	0.249	-1.862	-0.134	-5.29E-05	-0.004
[N(CN) ₂] ⁻	-0.332	-1.45	-0.308	-4.28E-05	-0.039
[C(CN) ₃] ⁻	0.832	8.35	-0.528	-4.31E-05	0.041
[AlCl ₄] ⁻	-1.064	-11.153	-0.335	-3.46E-05	-0.07
[DMP] ⁻	0.342	1.668	0.329	-6.47E-05	0.042
[FeCl ₄] ⁻	2.203	0.883	-0.657	-4.42E-05	-0.007
[Pf ₂ N] ⁻	1.506	0.106	0.021	-6.81E-05	-0.005
[SCN] ⁻	5.079	-0.185	-1.27	-3.88E-05	0.001
[eFAP] ⁻	0.127	-0.592	-0.305	-4.00E-05	-0.008

Figure A3. Comparison between experimental and calculated viscosity using estimation model, Eq.16

As well as heat capacity, the values of parameters $C_{m\lambda}$ ($m = 4, 5$) for the thermal conductivity in Eq.17 are set to zero. A group contribution method (see Eq. A8) is used to calculate the remaining parameters $C_{m\lambda}$ ($m = 1, 2, 3$).

$$C_{m\lambda} = \sum_{i=1}^k n_i c_{i,m\lambda} \quad A8$$

where k is the total number of different groups in the molecule and n_i is the number of groups of type i . Group contributions $c_{i,m\lambda}$ ($m = 1, 2, 3$) are obtained by the regression of experimental data into Eq.17 using Eq.A9 as the objective function.

$$O.F. = \frac{100 \times \sum_{i=1}^N |(\lambda_{cal} - \eta_{exp}) / \lambda_{exp}|_i}{N} \quad A9$$

A number of based on a number of 381 data points for 64 ILs involving 6 cation cores, 16 anions and 3 substituents in the temperature range of 273.15-390 K are considered. The AARD (%) of this estimation model for viscosity is 2.6%. The regressed group contributions $c_{i,m\lambda}$ are provided in Table A4 and comparison between experimental and calculated viscosity using this model are given in Figure A4.

Table A4: Regressed Group Contribution Parameters $c_{i,m\lambda}$ ($m = 1, 2, 3$) for Eq.A8 in the Temperature Range of 273.15-390 K

	$c_{i,1\lambda}$ (W.m ⁻¹ .K ⁻¹)	$c_{i,2\lambda}$ (W.m ⁻¹ .K ⁻²)	$c_{i,3\lambda}$ (W.m ⁻¹ .K ⁻³)
Substituents			
CH ₃	-0.047	3.50E-04	-6.24E-07
CH ₂	-0.035	2.12E-04	-3.37E-07
dmN	-0.09	3.75E-04	-1.92E-07
Cations			
1,3-dmim (+)	0.195	-3.82E-04	3.78E-05
1-mpy (+)	0.347	-0.001	3.85E-05
1,1-dmpyr (+)	0.506	-0.002	4.10E-05
Am1,1,1,1 (+)	0.845	-0.004	4.38E-05
Ph1,1,1,1 (+)	0.627	-0.003	4.40E-06
TDph (+)	0.34	-0.001	3.92E-05
Anions			
[Tf ₂ N] ⁻	0.108	-6.74E-04	-3.61E-05
[BF ₄] ⁻	-0.171	0.001	-3.86E-05
[PF ₆] ⁻	0.149	-7.86E-04	-3.60E-05
[Cl] ⁻	-0.15	0.001	-3.92E-05
[Ac] ⁻	-0.122	0.002	-4.00E-05
[MeSO ₄] ⁻	0.119	-3.83E-04	-3.66E-05
[EtSO ₄] ⁻	0.763	-0.005	-3.01E-05
[CF ₃ SO ₃] ⁻	-0.02	5.87E-04	-3.80E-05
[CF ₃ COO] ⁻	-0.02	3.47E-04	-3.77E-05
[N(CN) ₂] ⁻	1.191	-0.007	-2.69E-05
[C(CN) ₃] ⁻	0.166	-5.67E-04	-3.65E-05
[B(CN) ₄] ⁻	0.017	3.96E-04	-3.81E-05
[DMP] ⁻	-0.172	-0.013	-1.30E-05
[DEP] ⁻	2.174	0.00	-1.84E-05
[SCN] ⁻	-0.02	5.87E-04	-3.80E-05
[eFAP] ⁻	-0.172	0.001	-3.89E-05

Figure A4. Comparison between experimental and calculated thermal conductivity using estimation model, Eq.17

A summary of property estimation of ILs using GC methods for these empirical equations extracted from Aspen plus is given in Table A5, where the number of regressed data points and the AARD% of each family of cation-based ILs as well as all families for the four properties are provided.

Table A5. Summary of Property Estimation of ILs using Sub-models Extracted from Aspen Plus

Properties	Cation-based	Data points	Average Absolute Relative Deviation (%)
Heat capacity (Eq.19)	Imidazolium-	1233	0.61
	Pyridinium-	442	0.81
	Pyrrolidinium-	102	1.25
	Alkyl ammonium-	31	0.2
	Phosphonium-	191	0.81
	Piperidinium-	23	0.09
	All families	2022	0.7
Surface tension (Eq.23)	Imidazolium-	940	3.63
	Pyridinium-	281	2.90
	Pyrrolidinium-	130	2.25
	Alkyl ammonium-	111	3.47
	Phosphonium-	94	5.66
	Piperidinium-	21	0.34
	All families	1577	3.4
Viscosity (Eq.26)	Imidazolium-	1028	5.87
	Pyridinium-	280	4.66
	Pyrrolidinium-	76	5.10
	Alkyl ammonium-	149	4.77
	Phosphonium-	253	2.85

Thermal conductivity (Eq.29)	Piperidinium-	56	4.12
	All families	1842	5.1
	Imidazolium-	309	2.94
	Pyridinium-	15	1.29
	Pyrrolidinium-	16	1.55
	Alkyl ammonium-	9	0.47
	Phosphonium-	32	0.82
	All families	381	2.4

Supplementary material

Tables summarizing the information of the experimental data collected in this work. These data are used to regress the corresponding parameters of sub-models for calculating temperature-dependent properties (heat capacity, surface tension, viscosity and thermal conductivity) required in the process simulation in Aspen Plus.

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