

# Recent Developments in Solvent-Based Fluid Separations

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## Keywords

fluid separations, green solvents, ionic liquids, deep eutectic solvents, bio-based solvents, stimuli-responsive solvents

## Abstract

The most important developments in solvent-based fluid separations, separations involving at least one fluid phase, are reviewed. After a brief introduction and discussion on general solvent trends observed in all fields of application and discussion on general solvent trends observed in all fields of application, several specific fields are discussed. Important solvent trends include replacement of traditional molecular solvents by ionic liquids and deep eutectic solvents and, more recently, increasing discussion around bio-based solvents in some application fields. Furthermore, stimuli-responsive systems are discussed; the most significant developments in this field are seen for CO<sub>2</sub>-switchable and redox-responsive solvents. Discussed fields of application include hydrocarbons separations, carbon capture, biorefineries, and metals separations. For all but the hydrocarbons separations, newly reported electrochemically mediated separations seem to offer exciting new windows of opportunities.

## 1. INTRODUCTION

Fluid separations are key operations in many industrial processes, because fluid-phase conversions are predominant in virtually all chemistry-related industrial sectors. Considering the definition advocated by ProcessNet (1), “separations that involve at least one fluid phase,” to be probably the most clear and inclusive, we should include not only separations of homogeneous fluid phase mixtures but also those in which a fluid phase is used as solvent and applied to a mixture. This definition includes separations of mixtures as simple as homogeneous binary mixtures, as well as highly complex, nonhomogeneous mixtures, such as solids mixtures leached in mining applications and mixtures containing plant materials or cell cultures. We can thus distinguish two rudimentary categories of fluid separations: separations of homogeneous mixtures and of heterogeneous mixtures.

Approaches in these two fields differ markedly, because for homogeneous mixtures the standard approach has always been to first investigate whether distillation works and consider possible alternatives only when distillation is extremely inefficient, whereas for many heterogeneous mixtures, distillation is often obviously technically infeasible. The chemical industry’s strong preference for resolving homogeneous mixtures via distillation grew historically in a time frame in which energy was cheap and concerns about CO<sub>2</sub> footprint were nonexistent. Currently, awareness of the importance of reducing CO<sub>2</sub> footprint has led to a reorientation on existing separations and on opportunities to replace them with lower-CO<sub>2</sub>-footprint alternatives (2).

Among the alternatives for traditional distillation in which distillation is technically feasible, but not necessarily most efficient, the solvent-based fluid separations extractive distillation (ED) and liquid-liquid extraction (LLX) are most prominent. There are opportunities to reduce the chemical industry’s CO<sub>2</sub> footprint by replacing those distillations that are highly energy inefficient, for example, owing to unfavorable initial composition (3) or low relative volatility (3), with solvent-based fluid separations. Research on ED and LLX to separate hydrocarbon mixtures has been popular for many decades, and developments have also been reported recently, for instance, on the separation of aliphatics and aromatics (4). Therefore, we devote a section to this subject (see Section 3).

Next to limiting the CO<sub>2</sub> footprint via LLX and advanced distillation techniques, solvent-based fluid separations to advance CO<sub>2</sub> capture will likely have an even larger impact on our society, as reflected by continued attention from many scientists. Therefore, we also cover this topic here in Section 4. The third important field we discuss is that of bio-based chemicals and biorefineries, in which solvent-based approaches are essential to develop sustainable processes for recovery of bio-based molecules and materials from their complex feedstock mixtures. In Section 5, we include lignocellulose biorefineries, microalgae biorefineries, biological processes to digest wastewater, and a variety of other processes using microorganisms and cell cultures to produce bio-based chemicals.

We conclude with a discussion of metal separations in Section 6. Many metals are scarce elements, and even when not necessarily absolutely limited, the vast amount of metals used in consumer electronics generates large waste streams from which many valuable metals can be recycled. Furthermore, the electrification of society is driving up prices of lithium and other metals used for battery production, and efficient winning and recycling will become even more important in the future.

## 2. RECENT TRENDS IN SOLVENT DEVELOPMENTS

This review is structured according to the application areas of solvent-based fluid separations. Before discussing the latest trends in each of the abovementioned fields, we provide a concise

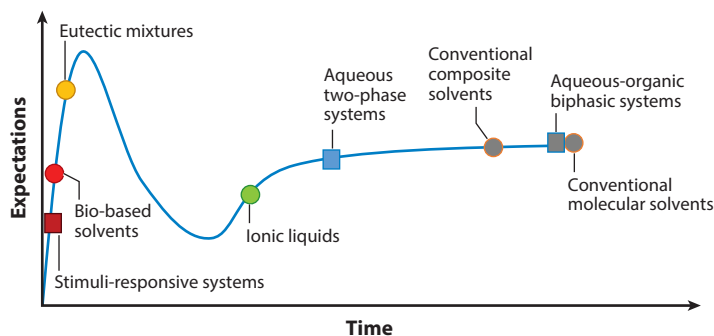
treatment of the general trends in solvent science and solvent use over the last decades to clarify more specific discussions in the subsections. Essentially, we distinguish six categories of solvents:

1. conventional molecular solvents,
2. ionic liquids (ILs),
3. deep eutectic solvents (DESs),
4. aqueous two-phase systems (ATPS),
5. bio-based solvents, and
6. stimuli-responsive solvents.

Conventional molecular solvents that are derived mostly from fossil oil are the most mature class and include single-molecule as well as composite solvents, such as mixtures of extractants in diluents for LLX. The other classes of solvents are sometimes referred to as neoteric solvents (5).

Although the first IL was reported more than a century ago (6), they are still considered a neoteric class of solvents. After the big hype in the early 2000s and throughout the 2010s, a period of disillusionment followed in which the ILs were found to be too expensive and often not at all nontoxic. The field of ILs has begun to mature, in the sense that many applications have been developed toward commercialization (6), some of them at large scale, such as refinery alkylation by Chevron and Honeywell UOP (ISOALKY™) (7), which will be fully operational in 2020. In the Gartner hype cycle (8) (**Figure 1**), we classify ILs as solvents beyond the disillusion valley, which is defined as the period in which many initiatives are abandoned due to lack of success. We position ILs beyond this valley owing to commercial success stories like ISOALKY™. However, many new developments are still being published. It is now recognized by many that although ILs are not beneficial for all applications, they are for certain applications, and commercialization of IL-based processes is no longer merely a dream of scientists.

Eutectic mixtures, often referred to as deep eutectic solvents (DESs), form the third class we identify and are sometimes seen as possible cheaper replacements for ILs (9). Other claimed advantages of these mixtures include low solvent losses owing to low volatility, stability, lower viscosity, and their nonhazardous nature (10). DESs are certainly not always nontoxic (11, 12), and some DES combinations of hydrogen bond donors and acceptors can be more toxic than the individual



**Figure 1**

Gartner hype diagram with indicative positioning of types of solvents (*circles*) and solvent systems (*squares*). After the initial innovation trigger, the expectations reach a maximum in the inflated expectations peak, followed by a period of disillusion, climbing up the slope of enlightenment when commercial successes begin to emerge, and finally reaching a plateau at which commercial success has become normal.

compounds (12); they can also be more toxic than their IL equivalent (11). Nevertheless, better insights (13) and many developments are expected in the coming years concerning DESs (14). Research on this solvent class is still in the phase in which many publications appear on numerous topics (15–24); some fields of application might be a bit too optimistic; and first warnings are currently appearing, such as on the possibility of limited stability (25). A thorough evaluation is required for each of the studied topics, and the necessary period of disillusionment is probably still to come for DESs. But we expect that for certain application areas, DESs will find their way to commercialization.

ATPS form the next solvent class we discuss, and these systems are well-known for their benign nature, offering opportunities for delicate separations of vulnerable (bio)molecules, molecules not stable in, e.g., organic solvents and harsh conditions such as elevated temperature during distillation. ATPS are systems consisting of two aqueous-rich phases (26), typically formed by mixing two aqueous solutions of (*a*) two polymers, (*b*) a polymer and a salt, (*c*) a polymer and an IL, or (*d*) an inorganic salt and an IL. The incompatibility of the main constituents after water causes the phase split, allowing separations of, for example, cells, viruses, nucleic acids, proteins, and antibiotics (26) by partitioning over the two aqueous phases. Although elegant and very mild, ATPS processes are not so easy to design and operate. Because both phases are aqueous, typically the density difference and interfacial tension are low, which results in limited capacity to flow countercurrently through extraction columns and easy flooding of columns. Delicate operation is thus needed in countercurrent ATPS extractions but is certainly possible (27). Regeneration of the solvent phase is typically done via back-extraction, and to reverse the partitioning of molecules, often a swing in conditions is applied, such as a pH swing. Using  $\text{Na}_2\text{CO}_3$  and HCl for swinging the pH up and down was shown to be very effective (28). However, swinging the pH up and down with mineral bases and acids results in production of salts and water, and alternative swings, such as temperature (29) when the thermal stability of the product allows this, are desired to limit by-product formation. The recently shown electrochemical pH-swing (30) may also be a good solution for ATPS recoveries.

The next category of solvents in this review, bio-based solvents, includes more traditional examples, such as lactic acid, but also numerous examples that are still in the innovation trigger phase. This includes a range of solvents derived from lignocellulosic biomass, such as  $\gamma$ -valerolactone (31), 2-methyltetrahydrofuran (31, 32), dihydrolevoglucosenone (commercialized as Cyrene<sup>TM</sup>) (33), and derivatives thereof (34).

Dihydrolevoglucosenone is currently being explored as a replacement for *N*-methylpyrrolidone and *N,N*-dimethylformamide in a range of polymer and biomass applications (35–38), and also as an entrainer in ED (39). All of these remain in an opportunity-exploration stage. Given mankind's desire to eventually abandon the dependence on fossil oil, these bio-based solvents mark an important development. Another area that has received ample attention since Jessop et al.'s (40) seminal paper is that of  $\text{CO}_2$ -switchable solvents. Next to  $\text{CO}_2$ , other stimuli are applicable, such as redox (41, 42), and given the current societal shift toward electrification, including in the chemical industry, the electrochemically mediated amine regeneration (EMAR) process pioneered by Hatton and further elaborated more recently (41, 42) opens up a new field and appears to be one of the most important developments in fluid separations. Essentially, whether  $\text{CO}_2$ , electricity, or any other external stimulus is used, the stimulus offers an alternative to fossil fuel-powered solvent regeneration and as such is a very interesting field to further explore to reduce dependence on fossil oil and its coupled  $\text{CO}_2$  emissions. We conclude that this field is still in a nascent and exploratory stage. The following sections review solvent developments per application area.

### 3. SOLVENTS FOR SEPARATIONS OF HYDROCARBON MIXTURES

Separation of unsaturated hydrocarbons from saturated hydrocarbons is an important industrial application area for fluid separations and can be divided into the fields of olefin/paraffin and aromatics/aliphatics separations. For olefin/paraffin separations, significant effort has been expended over the past decade to find solutions to replace highly energy intensive (cryogenic) distillations, and silver-containing ILs have been identified as a potential solvent class, selectively binding olefins (43). Replacing cryogenic distillations with extraction-based processes using silver-containing ILs is an example that shows there are windows of opportunity to replace existing distillation processes with more energy-effective extractions. ILs are often applied in a membrane-supported process (44, 45), as has been reported for silver-containing ILs (43). To limit the inventory of expensive silver even further, hybrid operations with distillation have also been considered (46).

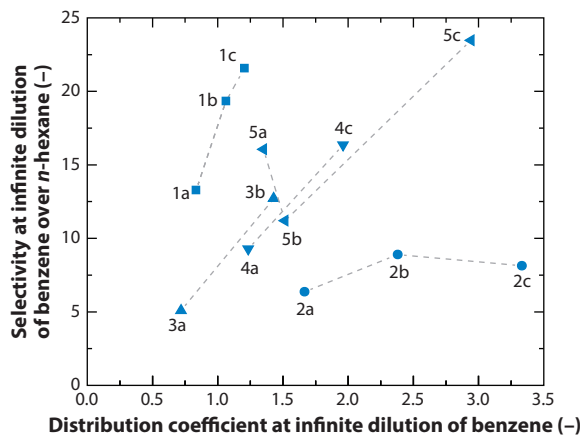
Researchers have turned their attention to a variety of possible solvent-based fluid separations for aromatics/aliphatics separations, which are very important to limit the aromatic content in petroleum fuels and impossible to achieve via distillation owing to overlapping boiling ranges. Where industrially polar nonprotic solvents such as sulfolane (3) are used in LLX and ED processes, recent academic interest has been focused mainly on IL-based processes (47–49), as well as DESs (50). Importantly, in using ILs in LLX for aromatics/aliphatics separations (51), raffinate aromatic contents remain too high to meet legislative requirements (52). For that reason, ED has been suggested, with the benefit that a single unit operation can reach the necessary composition, and additionally, recovery can be accomplished via stripping or flash distillation (47). However, distillation to obtain highly pure ILs is problematic in some situations owing to the negligible vapor pressure (53). For that reason, distillable ILs (54), e.g., from the class of CO<sub>2</sub>-switchable solvents, have also been considered (55). Other recent developments include the use of mixed (56), zwitterionic (57), and di- and tricationic (58, 59) ILs.

To fairly evaluate the potential of novel solvents, process simulations for the novel solvent processes (60, 61) should be compared with those using traditional solvents (62). To judge the value of new solvents, and their reported selectivities and capacities, understanding the necessary selectivity is key (3). Because hydrocarbon sources are composed of a certain hydrocarbon range, such as pyrolysis oil (C<sub>5</sub>–C<sub>9</sub> hydrocarbons) (63) and naphtha (C<sub>4</sub>–C<sub>10</sub> hydrocarbons) (64), future work should aim to identify solvents that can induce sufficient selectivity to reverse the boiling point order between the most volatile aromatic compound (benzene) and the least volatile aliphatic compound (e.g., *n*-decane) (3). The di- and tricationic ILs in particular show remarkable behavior, as transitioning from monocations via dicationic to tricationic improves both selectivity and capacity (65, 66) (see **Figure 2**), whereas these two process performance parameters typically must be traded off against each other (3).

### 4. CARBON CAPTURE

Carbon capture policies are the subject of ongoing debate. Some scientists argue it is better not to invest in carbon capture but rather to focus on preventing emissions, whereas others continue work on carbon capture with an aim toward negative-emission technology (67) that eventually would allow reductions in atmospheric CO<sub>2</sub> levels. Considering that we remain very far from CO<sub>2</sub> neutrality, aiming at negative-emission technology seems necessary to approach a climatologically acceptable atmospheric CO<sub>2</sub> level by the end of the century.

Most recently, various types of solvents have been evaluated for solvent-based carbon capture (68–70), including different types of ILs (71, 72), blends of ILs (73), and eutectic mixtures (74–76), as well as applications of amine blends (10, 68, 77) and dispersions of activated carbon (78) and



**Figure 2**

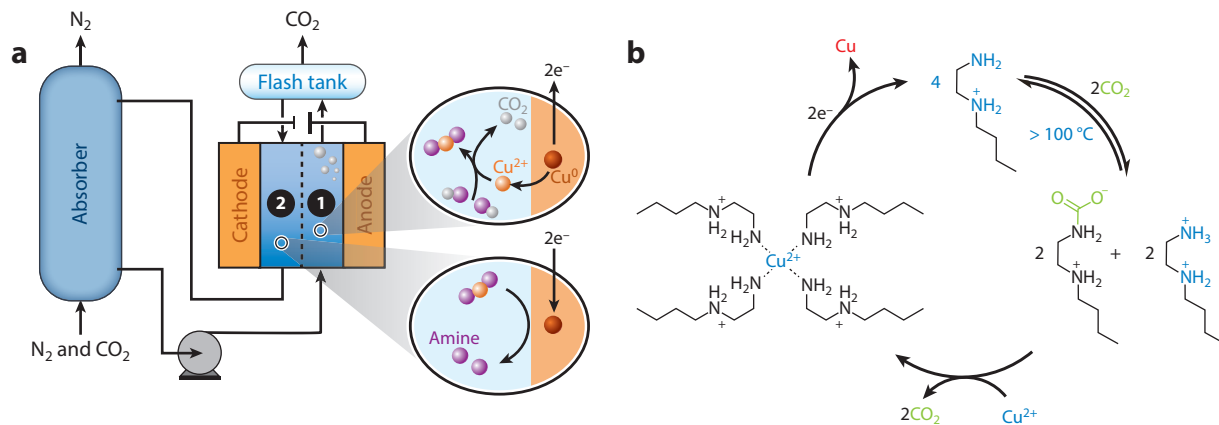
Distribution coefficient of benzene and the selectivity of benzene over *n*-hexane at infinite dilution in five series of mono-, di-, and tricationic ionic liquids (ILs) at  $T/K = 323$  (65, 66). Series 1: mono-, di-, and tri-imidazolium bis(trifluoromethylsulfonyl)imide ILs  $\{[\text{CH}_2\text{OC}_3\text{H}_7(\text{MIM})][\text{NTf}_2], [(\text{MIM})\text{CH}_2\text{OC}_3\text{H}_6\text{OCH}_2(\text{MIM})][\text{NTf}_2]_2, \text{ and } [(\text{MIM})\text{CH}_3\text{OCH}(\text{MIMCH}_2\text{OCH}_2)_2][\text{NTf}_2]_3\}$ . Series 2: mono-, di-, and tri-imidazolium bis(trifluoromethylsulfonyl)imide ILs  $\{[\text{CH}_2\text{OC}_3\text{H}_7(\text{OMIM})][\text{NTf}_2], [(\text{OMIM})\text{CH}_2\text{OC}_3\text{H}_6\text{OCH}_2(\text{OMIM})][\text{NTf}_2]_2, \text{ and } [(\text{OMIM})\text{CH}_2\text{OCH}(\text{OMIMCH}_2\text{OCH}_2)_2][\text{NTf}_2]_3\}$ . Series 3: mono- and di-imidazolium dicyanamide ILs  $\{[\text{CH}_2\text{OC}_3\text{H}_7(\text{OMIM})][\text{DCA}] \text{ and } [(\text{OMIM})\text{CH}_2\text{OC}_3\text{H}_6\text{OCH}_2(\text{OMIM})][\text{DCA}]_2\}$ . Series 4: mono- and tri-imidazolium bis(trifluoromethylsulfonyl)imide ILs  $\{[\text{CH}_2\text{OC}_3\text{H}_7(\text{CH}_2\text{BenzIM})][\text{NTf}_2] \text{ and } [(\text{CH}_2\text{BenzIM})\text{CH}_2\text{OCH}(\text{CH}_2\text{BenzIMCH}_2\text{OCH}_2)_2][\text{NTf}_2]_3\}$ . Series 5: mono-, di-, and tri-pyridinium bis(trifluoromethylsulfonyl)imide ILs  $\{[\text{N}(\text{CH}_3)_2\text{PyCH}_2\text{OC}_3\text{H}_6\text{OCH}_2\text{PyN}(\text{CH}_3)_2][\text{NTf}_2], [\text{N}(\text{CH}_3)_2\text{PyCH}_2\text{OC}_3\text{H}_6\text{OCH}_2\text{N}(\text{CH}_3)_2\text{Py}][\text{NTf}_2]_2, \text{ and } [(\text{N}(\text{CH}_3)_2\text{PyCH}_3\text{OCH}(\text{N}(\text{CH}_3)_2\text{PyCH}_2\text{OCH}_2)_3]\}$ .

other solid sorbents (79). The main factors governing limitations for industrial application include the viscosity (80), the heat capacity (74), and certainly the heat required for solvent regeneration (41). Key to solvent development is our understanding of intermolecular interactions, hydrogen bond formation, and water incorporation, as well as the effect of temperature on capture, e.g., as studied for deep eutectic mixtures (81, 82).

Although the switchable solvents Jessop et al. (83) classified into three categories—polarity, hydrophilicity, and water—appear interesting for  $\text{CO}_2$  capture, implementation can be challenging owing to environmental impact, solvent losses, equipment maintenance, precipitation, chemical stability, and oxidation product formation and the emissions from capture plants. Additional scale-up studies are required (84, 85).

Elegant approaches to circumvent the large penalty in fossil fuel use owing to the heat of regeneration include use of the amine solvent as a nitrogen source in microbial biorefinery (86) and direct conversion of  $\text{CO}_2$  to alkylcarbonates (87, 88), which, however, can never be applied on the total scale of carbon capture owing to a mismatch in available  $\text{CO}_2$  and market size for these solvents. Hatton and coworkers' (41, 42) EMAR process makes use of electrochemical solvent regeneration and certainly has potential (Figure 3). With the quickly rising availability of green electricity, regeneration can be accomplished very cleanly.

Along with amines, the Hatton group has also published on use of quinones and ferrocenes to electrochemically modify solvent properties (89, 90) and reviewed possible electrode materials (91). Next to carbon capture, other fields of application are also of interest. For example, redox-responsive materials were applied to induce potential-dependent, switchable ion selectivity



**Figure 3**

(a) The electrochemically mediated amine regeneration process and (b) the solvent chemistry cycle. Figure reproduced with permission from Reference 36; copyright 2020 American Chemical Society.

in aqueous media using titanium disulfide (92). This type of redox electrolyte-based system can be applied for electrochemical seawater desalination (93). The strongly tunable and specific characteristics of these materials can be applied in gels (94) and nanoparticles (95), allowing for applications in, e.g., sensors, actuators, and the biomedical field, in which redox stimuli result in changing material characteristics. The stimuli-responsive ion gels are generally based on ILs and DESs, although focusing only on DESs may be more promising given their potentially bio-based starting materials (96). Scale-up remains unresolved for all gel-based systems (96), which appears to be a next logical stage for further development of EMAR and similar processes.

## 5. SOLVENT SYSTEMS FOR BIOREFINERY APPLICATIONS

Biorefineries hold great potential for producing chemicals from green resources via efficient and environmentally friendly methods. To truly make biorefineries green, green solvents must also be applied in these systems, meaning they must be environmentally friendly and preferably biocompatible to allow for process integration (97). Biomass is often highly temperature sensitive, involatile, and often present in diluted streams, posing a challenge for the separation processes and solvents involved in the biorefinery. The trend from conventional molecular solvents to ILs, from DESs to natural DESs (NADESs), and combinations thereof is clear (98).

The combination of CO<sub>2</sub>-emission reduction and CO<sub>2</sub> capture is closely related to developments within the field of biorefineries. With the aim of improving sustainability in biorefineries, there is a focus on synergy between CO<sub>2</sub> use and biorefinery processes, e.g., through production of carbon-negative formate chemicals, but also through the products plants provide us with. Numerous products, such as sugar and coffee, but also paper and wood for construction purposes, have been obtained from biological sources for many years, whereas others, such as hemp, only recently have become legal and openly available on a large scale in several countries. Recent trends in biorefinery science focus on more complete refining of the bio-source. This includes, for example, valorizing lignin and other components from lignocellulose sources such as coffee beans, hemp plants, or hard- and softwood. To accomplish this, solvent-based fluid separations are invaluable. Below, we describe recent trends in solvent-based fluid separations in lignocellulose biorefineries (Section 5.1), as well as the strongly developing microbiological production

of chemicals (Section 5.2); there as well, solvent-based fluid separations are invaluable. Our discussion of microbiological production broths (Section 5.2) contains subsections on microalgae and other biomasses. In general, for biorefinery fluid separations that are applied directly to treat biomass, the operation modes should be selected carefully to be robust and able to deal with impurities, including solid particulates. Solid-liquid extractions are therefore typically applied not in countercurrent extraction columns but in cross-current mode using stirred vessels (99). For treatment of fermentation broths as well, there is a risk of emulsification owing to the presence of solid particulates and cells, and owing to the type of solvent, as some solvents exhibit emulsification behavior. One approach to prevent emulsification is by applying immobilized liquids, as is done in membrane-assisted extractions (100). Furthermore, one aspect of biorefinery feedstocks is that compositional variations may impact the performance of the process, and process design should take this into account.

### 5.1. Lignocellulose

Lignocellulosic biomass consists of three main polymers: cellulose, hemicellulose, and lignin. Three approaches can be distinguished among biorefineries based on lignocellulosic biomass: those that destroy all biopolymers (through pyrolysis), nurture the cellulose structure, and selectively break down cellulose and convert the sugars into value-added products. In pyrolysis-based processes, complex mixtures are obtained, and downstream fractionations are essential for valorization of as many components as possible, and not only using the caloric value of the pyrolytic bio-oils. Fractionation based on selective aromatics extraction from pyrolytic sugars by phosphonium ILs, after which the ILs could be regenerated, has shown promise (101). And direct extraction from pyrolysis oil has been applied using ILs for extraction of acetic acid, glycolaldehyde, and acetol (102).

ILs have also been applied in different steps to recover value-added molecules from lignocellulose, including pretreatment of the lignocellulose (103) and fractionation of the biomass itself (21). With biocompatible and low-cost protic ILs, pretreatment, hydrolysis, and fermentation processes can be integrated and ethanol can be produced from lignocellulosic biomass (104). Scale-up for IL pretreatment of biomass conversion has also been applied successfully (105).

Along with protic ILs, renewable DESs, notable for their low cost and easy synthesis, can also be applied for biopolymer dissolution and processing in a closed-loop biorefinery (10, 106). Furthermore, phenolic aldehyde DESs can be derived from lignin sources and then applied for pretreatment in converting lignocellulosic biomass into fuel (106).

Aside from approaches aimed at valorizing sugars as fuel by fermenting their broken-down monomers, increasing attention has been devoted to processing biomass with ILs or DESs while keeping the sugar polymers intact; for example, recovery of chitin from shrimp cells was shown to be feasible using ILs (107). DESs based on choline chloride and several carboxylic acids were applied for wood and pulp delignification (21, 108), and the delignification reactions have been studied in detail (109). The halide ion's important role in DES systems was revealed (21, 109), explaining the higher rate of delignification than with acids without the halide salts present in the DESs. A recyclable para-toluene sulfonic acid hydrotrope was also used for delignification, which is of interest because it was operable in mild conditions (110). Alternatively, composite alkaline solvents (NaOH solutions in 1,4-butanediol) can be applied for delignification but require much higher temperature to be effective, as shown for extraction of lignin from corn stover (111). Interestingly, initially separating the corn stover into its different parts allowed obtainment of low-polydispersity lignins, while also reducing the energy demand (111). Because neither the lignin nor the DES is volatile, precipitation is often applied, but use of bio-based solvents in LLX to recover lignin has also been reported (32).



Next to extracting lignin with DESs, aqueous solutions of DESs were also shown to be able to solubilize xylans with a yield of up to 90% (20). And recently, microcrystalline cellulose was shown to be soluble in guanidine-based DESs (112). Thus, it appears that all three main biomass polymers (hemicellulose, cellulose, and lignin) can be dissolved to at least some extent using either ILs or DESs, and when desired, they can be precipitated as polymer or applied as a medium for depolymerization when the aim is to produce fuel.

Other applications of ILs and DESs in similar processes include extractions from herbs, such as complex organic acids (113). SUPRAS, or supramolecular solvents, are in essence very similar to DESs and have been reported for extraction of bioactives from coffee pulp (114). Furthermore, hydrophobic DESs were applied for 5-hydroxymethylfurfural (HMF) extraction in biorefinery processes (115). Similar to HMF, levulinic acid is a potential platform chemical that can be derived from lignocellulosic materials. Processes to obtain levulinic acid include a reactive section, which may be enhanced via in situ extraction with a volatile solvent (116), and carboxylic acid recovery, which can be accomplished selectively from the homogeneous catalyst via use of a composite solvent (117).

## 5.2. Microbiological Production

One of the major routes in bio-based chemical production is via microbiological production (118); a wide range of products can be made using cell cultures or microorganisms. The major difference between fluid separations from broths and lignocellulose is that microbiological productions yield aqueous, typically diluted broths from which the products must be recovered. When attempting to recover the products directly from the broth using a solvent, the solvent must be hydrophobic. For this reason, many of the recently investigated ILs and DESs are unsuitable. However, both hydrophobic ILs (119) and DESs (120) have been reported for extractions from dilute aqueous streams. For direct extraction from broths or cultures, we specify two situations. First, when the desired product is still inside cells, some method must be applied to allow the solvent to extract the product, such as cell disruption or use of a solvent that penetrates the cell walls. This situation also offers the opportunity to concentrate the biomass prior to product extraction. When biomass is dried prior to extraction, hydrophilic solvents may also be applied without loss through leaching to the raffinate. In the second situation, the product is excreted by the biomass and present in the broth, though often highly diluted. When using solvent-based fluid separation to recover highly diluted bio-based products, such as carboxylic acids, solvent hydrophobicity is important, as a second liquid phase should be formed next to the aqueous phase of the broth. Though significant attention has been paid recently to microalgae biorefineries, other types of microbiological biomass have also been applied for the production of, e.g., bio-polymers and other molecules, such as acids in fermentation broths (100, 119). Recovery from sources other than microalgae is described below.

**5.2.1. Microalgae.** Many types of microalgae have been studied, and a challenge for valorization of chemicals from microalgae is typically the presence of cell walls (121). Solvents for extraction of components such as lipids and proteins from algae must overcome this barrier (99), for which ILs are promising (122). CO<sub>2</sub>-switchable solvent systems also have been applied in the field of lipid extraction from algae (99); these solvent systems typically consist of amines that can enter and extract lipids from the microalgae cells. After extraction, the lipids can be recovered from the lipid-loaded amine phase via bubbling CO<sub>2</sub>. Alternatively, for the secondary amine ethylbutyl amine, phase splitting by cooling below the lower critical solution temperature was found to be energetically more interesting (123). Along with extracting hydrophobic lipids with the more hydrophobic

form of the switchable solvents, the solvent can also be switched prior to extraction, allowing for extraction of more hydrophilic molecules as well. This combination of two extraction stages with the same solvent in two states is known as circular extraction (124). Switchable hydrophilicity NADES in a dilute amine solution may also be applied in biorefineries, where addition of water results in a modest range of hydrophilicity variation and addition of the dilute amine solution results in a more feasible range (125). Wang et al. (126) developed another method for concentrating both hydrophilic and lipophilic components based on temperature-responsive ILs. This method can be applied in extraction from medicinal plants and of natural products, because no volatile organic solvents are required, although recycling of the ILs remains a challenge (126). Desai et al. (127) applied single-step biorefining of both hydrophobic and hydrophilic molecules from complex mixtures using a microgel emulsion based on aqueous-phase IL droplets. In another extraction study on microalgae producing astaxanthin, use of sustainable almond oil instead of common organic solvents allowed efficient removal of the component without affecting algae activity (128). Similar processes hold potential for applications in the food and pharmaceutical industries, and recent developments in the field of food-grade extraction surfactants for ATPS (129) are seen as key developments for microalgae biorefineries, where some of the products can be applied in food.

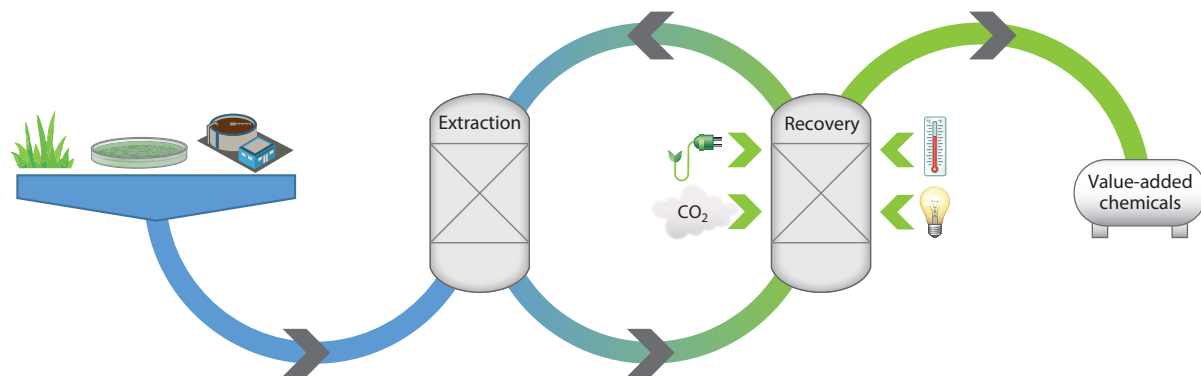
**5.2.2. Other microbiological biomass.** Solvent-based fluid separation methods have been devised for recovery of carboxylic acids such as volatile fatty acids (130), as well as lactic acid (100) and succinic acid (131). The acids have wide applications, for example, as food ingredients or as monomers to make biopolymers. Although alcohols are also commonly produced biologically, and must be recovered from their broth (132–134), the main application of alcohols is as biofuel. A range of other products are made and recovered from broths or cell cultures, including proteins (29, 135), amino acids (26), and monoclonal antibodies (27). Dynamic and reversible biphasic systems have received much attention for their potential in efficient mild separation processes and fast partitioning owing to their large interfacial area (135). Stimuli-induced phase separations have been shown in ATPS with ILs via variations in pH (136) or temperature (29), where the temperature sensitivity of ATPS can be enhanced by tuning the critical micelle concentration (137, 138).

Dynamic equilibria that offer opportunities for swings in conditions to enhance concentrations appear to be very important for the effectiveness of the downstream operation owing to the low concentrations in the broth, that make efficient [e.g., *in situ* (100, 139)] recovery of paramount importance and not straightforward (119). An important recent development in the field, allowing concentration swing in extraction of carboxylic acids, involves electrochemically swinging the pH (29).

Further studies on such innovative extraction processes should consider several aspects that are inherent to fermentation processes and complicate recovery. Dissolved salts negatively affect chemical recovery owing to the coextraction of anions, which may increase the pH of the aqueous solution and compete for solvent capacity when they are coextracted (130).

Direct biological production of polymers is an interesting field that arises next to the production of bio-based polymers through fermentative production of their monomers. Polyhydroxyalkanoates are a class of bio-based and biodegradable polymers; they can be produced from waste, and extraction from their broth is important to allow for their valorization. Limited research has been published in this field, but in one example, cell disruption was required prior to extraction of polyhydroxyalkanoate from the biomass in an ATPS (140). Alternatively, the biomass could be pyrolyzed to obtain 2-butenic acid (crotonic acid) as an unsaturated volatile fatty acid (141).

For biorefineries to become highly sustainable, product recovery through a solvent-based separation and stimulus-responsive concentration step appears very promising. This section has presented a variety of examples and suggested future research directions for innovative product



**Figure 4**

Value-added chemical obtained through biorefinery extraction and stimulus-responsive recovery.

recovery opportunities to broaden the scope of products and routes toward such green products (**Figure 4**).

## 6. SOLVENT SYSTEMS FOR SEPARATIONS OF METALS

Hydrometallurgy, or the recovery of metals from ores through leaching and LLX, has been studied for many decades, and although the literature on it is extremely extensive, an apparent shift in focus has occurred recently. For many years, industrial solvent extraction of metals primarily involved composite solvents in which an extractant is applied, e.g., a chelating oxime that is diluted in a hydrocarbon diluent such as kerosene. Although many good scientific publications continue to propose modifications of extractant–diluent combinations for more-or-less-classical hydrometallurgical winning of metals from ores and separation of metals, e.g., developing tripodal polyamine extractants (142), there is a growing focus on metal recycling. Such important topics include recycling from spent fluid catalytic cracking catalyst (143), consumer electronics (144, 145), and batteries (146). As a result of the enormous growth in the lithium market owing to the replacement of many fossil-fueled vehicles with electric vehicles, the need for efficient lithium extraction is great, and an innovative approach was reported recently using a photoresponsive extractant (147). The extractant, a spiropyran, is a photochromic compound that can be switched between a closed spiropyran and an open merocyanine form using UV light. The merocyanine form can chelate with metal ions, and using a crown ether moiety, Li et al. (147) observed selective extraction of  $\text{Li}^+$ .

Unfortunately, many of these scientifically interesting and societally relevant innovations still make use of highly flammable volatile organic compounds. Ideally, such great advances in extractant chemistry would be coupled to more benign diluents; several papers that report ILs and DESs for metal extractions show this not only is possible (148, 149) but also offers great new windows of opportunity. One such opportunity is that, given the electrolyte nature of ILs, it is possible to apply electrowinning directly on the IL phase to obtain the metals in their metallic form (150) (in contrast to traditional hydrometallurgy, in which a back-extraction into an aqueous back-extract phase is necessary). Tan et al. (150) demonstrated electrowinning from IL for recycling of lead from spent lead–acid batteries. Because lead is, along with lithium, still an important metal for batteries, this is an important development toward sustainable battery life cycles.

A range of metals, including lead and lithium, have been extracted for battery recycling via use of DESs (17, 23). Karimi et al. (17) showed that choline chloride DESs can extract lead and cadmium from edible oils, whereas Zürner et al. (149) and Su et al. (22) used oxalic acid–based

**Table 1 Summary of most important developments per area of application**

Application area	Key development	References
Hydrocarbons separations	Dicationic and tricationic ILs show both higher capacity and higher selectivity at infinite dilution towards unsaturated hydrocarbons.	65, 66
Carbon capture	Electrochemically mediated solvent regeneration can facilitate the use of green electric energy instead of burning gas for thermal regeneration of the solvent for the carbon capture.	41, 42, 89, 90
Biorefineries	Electrochemically driven pH swing can significantly reduce the waste generated via pH swinging using acids and bases in traditional operations.	30
Metals separations	Extraction into an IL followed by electrowinning directly from the IL is safer and simpler than traditional extraction using a hydrocarbon diluent requiring back-extraction prior to electrowinning.	150

Abbreviation: IL, ionic liquid.

DESs to extract indium and tin from zinc flue dust and lead from mining soil, respectively. Of note, all of these applications are nonaqueous, and when DESs are applied in aqueous systems, miscibility of the DES with water should be considered, which limits the freedom to select DES constituents.

## 7. SUMMARY AND CONCLUSIONS

To distill general conclusions and future directions for the field of solvent-based fluid separations from all of the developments discussed in Sections 3–6, a comprehensive overview is useful, and therefore the developments with the highest potential to change the field are listed in **Table 1**. With the exception of aromatics/aliphatics separations, for all other areas we rate the separations involving electrochemical solvent regeneration and electrochemical pH swing among the most interesting developments. In comparison with developments in the use of IL and DES in various applications, these electrochemically assisted separation processes are still highly novel, and only a few papers have appeared. We expect that many more studies will be performed in these areas in the near future.

In different areas of application, use of bio-based solvents, including NADES but also sugar-derived furans, has shown promising results indicating that these natural solvents can replace fossil oil-based solvents. Similar to the field of stimuli-responsive separations (redox), NADES and other bio-based solvents are still early in the hype cycle, as displayed in **Figure 1**, whereas for ILs some application areas have reached maturity and processes have been commercialized. Based on the interesting development of using dicationic and tricationic ILs in the application area for aromatics/aliphatics separations, the interest in using such ILs may grow, and we expect that in the field of dicationic and tricationic ILs interesting developments are still possible. A possible hinderance might be that the synthesis of such complex ILs can be laborious and costly, and for implementation of a new technology, it helps when the solvent is not too expensive. The bio-based solvents, including NADESs, clearly have an advantage in this aspect, as they are generally much cheaper. For the identified electrochemically assisted separations, a great advantage is that several relatively inexpensive chemical systems (e.g., the amines and quinones from the Hatton group) seem to be applicable.

## DISCLOSURE STATEMENT

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## Errata

An online log of corrections to *Annual Review of Chemical and Biomolecular Engineering* articles may be found at <http://www.annualreviews.org/errata/chembioeng>