



Review

Role and importance of solvents for the fractionation of lignocellulosic biomass

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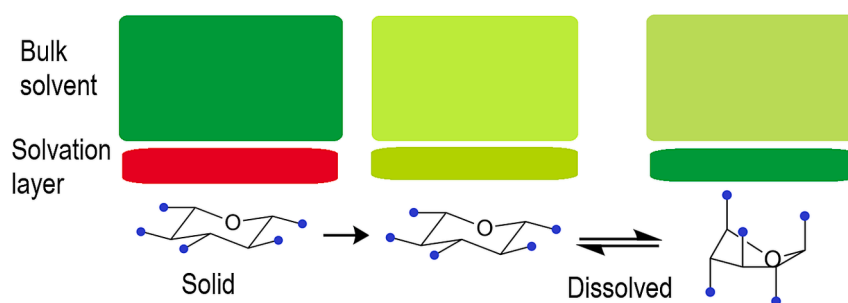
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HIGHLIGHTS

- Dissolution requires solute conformational flexibility.
- Polysaccharide dissolution are restricted because of inflexible sugar ring.
- Lignin dissolution is less hampered due to its dynamic aromatic nature.
- Solute dissolution can be modified similarly through temperature or solvent.
- Saturation is largely dictated by the potential energy minima of the bulk solvent.

GRAPHICAL ABSTRACT



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ABSTRACT

Lignocellulosic biomass is one of the most important renewable materials to replace carbon-based fossil resources. Solvent-based fractionation is a promising route for fractionation of biomass into its major components. Processing is governed by the employed solvent-systems properties. This review sheds light on the factors governing both dissolution and potential reactivities of the chemical structures present in lignocellulose, highlighting how proper understanding of the underlying mechanisms and interactions between solute and solvent help to choose proper systems for specific fractionation needs. Structural and chemical differences between the carbohydrate-based structural polymers and lignin require very different solvents capabilities in terms of causing and eventually stabilizing conformational changes and consequent activation of bonds to be cleaved by other active components in the. A consideration of potential depolymerization events during dissolution and energetic aspects of the dissolution process considering the contribution of polymer functionalities allow for a mapping of solvent suitability for biomass fractionation.

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1. Introduction

Within the pressing need of replacing fossil-based resources with renewable ones, lignocellulosic biomass plays a key role. Convenient strategies are necessary to tackle the compositional complexity of biomass to render it suitable for any downstream processing. Fractionation of woody biomass is one of the key approaches in this respect, with fractionation meaning especially the separation of the three main polymeric constituents, *i.e.*, cellulose, hemicelluloses, and lignin. This process is already done in remarkable efficiencies in well-established pulp and paper industries, *e.g.*, in form of the kraft process. While this process is optimized using an alkaline aqueous solvent system, modern biorefineries for the production of biofuels, bio-based platform chemicals, etc., might make use of mixed aqueous-organic solvent systems, pure organic solvents, ionic liquids (ILs), or deep eutectic solvents (DES). Modern biorefineries following either the ‘cellulose first’ or ‘lignin first’ school of thoughts do eventually struggle, however, in identifying the perfect solvent of choice between traditional and upcoming solvents, among which are presumably green ones like γ -valerolactone (GVL), such as to arrive at an overall sustainable and economically viable process, due to the immense impact of the choice of solvents on process performance and costs. Disregarding the costs connected to a specific solvent choice for this scientific review, but for rationalizing the ways the solvent can impact biomass fractionation at the mechanistic level, it is mandatory to have a correct picture regarding the molecular details of the components that comprise the largest part of biomasses to be fractionated, and subsequently their interaction with solvents. This largest part of lignocellulosic biomass is comprised of the name-giving biopolymers cellulose, hemicellulose, and lignin. While the first two are built of carbohydrates, lignin is made from hydroxyphenylpropanoids.

1.1. Cellulose

Compared to the other two structural plant polymers, cellulose represents a very regular structure, identical in terms of bonding motif and displayed functional groups, serving its fundamental function of contributing to mechanical stability. Polymer sizes between 300 and 1700 monomers were reported (Klemm et al., 2005). Rotational angles of ca. 180° are observed between monomers. Driven by the formation of thermodynamically favourable hydrogen-bonding patterns in sheet formation and electronic interactions, *i.e.*, hydrophobic and van der Waals interactions leading to aggregation of sheets, secondary structures such as cellulose I $_{\alpha}$ and cellulose I $_{\beta}$, which considerably differ in degree of crystallinity and stability. The spatial arrangement of the sheets overall can best be described as fibre-like, and the dimensions of these fibrils can exceed the simple size of the polymer chains (Nishiyama, 2009). The interplay between single cellulose chains generate the typical characteristics of cellulose, like extraordinary strength of fibres, insolubility under physiological conditions, resilience to chemical modification, and affinity to aromatic structures (Klemm et al., 2005).

1.2. Hemicelluloses

Hemicelluloses, located together with lignin between the cellulose fibrils in the cell walls (Pauly et al., 2013), comprise a wider variety of carbohydrate structures and bonding motifs with respect to cellulose. The main building blocks are *D*-glucose, *D*-mannose, *D*-galactose, *D*-xylose, *L*-arabinose, *L*-rhamnose and *L*-fucose as deoxyhexoses, as well as 4-*O*-methyl-*D*-glucuronic acid, *D*-galacturonic acid and *D*-glucuronic acid as carbohydrate derivatives (Khodayari et al., 2021; Silveira et al., 2013). In comparison to cellulose, hemicelluloses are much smaller polymers and are mechanically and chemically significantly less stable. Depending on their chemical structures and characteristics, different principal hemicelluloses are distinguished, such as xylans, glucomannans, galactans. Pectins and glucans, which are further divided in

xyloglucane, starch, callose and loricin represent other oligomeric and polymeric carbohydrates that, albeit formally not being part of the hemicelluloses, have to be considered in biomass fractionations. Xylans are xylose-based hemicelluloses isolated from soft- and hardwoods, characterised by a backbone consisting of β -*D*-xylopyranoses linked in 1→4-fashion, with wood-type-specific differences in the short side chains typical for xylans (Rennie and Scheller, 2014); softwood xylans display just less than 200, hardwood xylans just above 200 monomer units. Softwood xylans are more acidic and more regularly substituted with the acidity influencing 4-*O*-methyl-*D*-glucuronic acids than those isolated from hardwood. Herbaceous xylans show further structural variety. The side-chains present in the xylans prevent these from forming crystalline supramolecular structures. The structures that do form can be easily influenced by environmental conditions, since the hydrogen-bonding capabilities of the xylan-chains as such are poor. Xylan reactivity and stability is determined by the characteristic acetyl groups and by the linkage-type between the carbohydrate monomers: xylans are susceptible to acidic hydrolysis, and get degraded into their monomers at different rates depending on the substitution patterns. Glucomannans consist generally of linear chains of β -*D*-mannopyranosyl and β -*D*-glucopyranosyl monomers linked between positions 1 and 4 (Zhong et al., 2019). While the distribution of the two monomer types seems to be random, their ratios are always found to lie between 1/1 and 1/4. The mannosyl residues are irregularly acetylated, and in softwood (galacto)glucomannans, they additionally carry α -(1→6)-linked side groups of *D*-galactopyranosyl residues. As for xylans, the average degree of polymerisation differs between different plant species, with values of around 100 in softwoods and up to 70 in hardwoods, generally accompanied by a higher degree of polydispersity. Lacking important supermolecular structures, the linkages between the carbohydrate monomers in (galacto)glucomannans are generally acid-labile, with differences in the stability of β -*D*-mannosidic and β -*D*-glycosidic linkages, allowing for selective cleavages *via* pH-control of the solution. Galactans (Zhong et al., 2019) consist of a backbone of arabinogalactans carrying side chains consisting of β -*D*-galactopyranose chains of variable lengths, and of *L*-arabinose substituents that occur as pyrosinoses (ca. 67%) as well as furanoses (ca. 33%). Two main regimes of polymer sizes are generally found, and the arabinogalactans have been classified according to these differences in molecular weight in arabinogalactan A with mean average molecular weights (Mn) of around 11 kDa, and arabinogalactan B exhibiting typically a Mn of around 70 kDa.

1.3. Lignin

As polyphenol, and hence as a polymer displaying aromatic moieties, lignin is structurally distinct from the other main plant polymers, cellulose and hemicellulose (Ralph et al., 2019). Lignification occurs *via* free radical polymerization which produces irregularly inter-linked polymers from up to three different methoxylated monolignols. The proportions of the three main monolignols *p*-coumaryl alcohol (H), coniferyl alcohol (G) and sinapyl alcohol (S) vary according to botanical origin (Freudenberg and Neish, 1968). Typical classification recognizes three main types of lignins, G in softwood, GS in hardwood, and HGS in herbaceous species, based on the monolignols indicated above (Freudenberg and Neish, 1968). The oligomers and polymers resulting from lignification consist of carbon-carbon and ether linkages both in linear and cyclic arrangements. The most abundant bond type is the non-cyclic β -O-4' linkage that comprises approximately half of all bonds in native lignin, with higher relative abundance in hardwood lignins (Chakar and Ragauskas, 2004). Compared to thermochemically more resistant β - β' , 5-5', and 4-O-5' interunit bonding motifs the importance of α -ethers and β -ethers is obvious, since these thermochemically labile linkages determine reactivity of lignin in pretreatments and fractionation protocols. The association of lignin with other cell wall components is an issue that requires further elucidation. It is generally accepted, albeit still not fully proven, that lignin besides being physically associated with other

components, is covalently linked to certain plant cell walls polysaccharides, forming so-called lignin-carbohydrate complexes (LCCs). Linkages exist in form of benzyl ethers (BE), phenyl glycosides (PG), and γ -esters (GE) linkages, and were found in soft- and hardwoods, as well as in herbaceous material.

1.4. Emerging treatments using novel solvents and solvent systems

Solvent systems hold a promising potential in terms of biomass fractionation through selective extraction for effective downstream upgrading. Aqueous systems, both basic and acidic in nature, have long been known for dissolving lignocellulosic biomass, at rather harsh conditions (Aresta et al., 2021). In quest for solvents and solvent systems that work at less harsh conditions, several new approaches emerged in the more recent past: Some ionic liquids (ILs) such as 1-benzyl-3-methylimidazolium chloride (Xu et al., 2010) have been found to selectively dissolve cellulose and hemicellulose; protic ionic liquids were shown to bring preferentially lignin in solution (Haykir, 2022). Others were found to dissolve all structural polymers simultaneously (Roy and Chundawat, 2022). Both protic and non-protic ILs are generally suitable for increasing the amorphous character of cellulose, rendering it more accessible for downstream enzymatic biofuel production (Elgharabawy et al., 2016). The unique solvent properties of ILs and IL-containing solvent systems enable efficient delignification, with pretreatments becoming feasible at process temperatures of 80 to 170 °C (Ma et al., 2016; Sathitsuksanoh et al., 2014). ILs are not necessarily chemical inert: ILs were found to cause depolymerisation of lignin tackling especially the β -ether linkages (Brandt et al., 2013) causing internal condensation (Torr et al., 2012). Most obviously, ILs can thus be chosen to confer to the pretreatment a more acidic or alkaline note in terms of solvent-induced system reactivity. To overcome common drawbacks connected to ILs, deep eutectic solvents (DESs) (Florindo et al., 2019) are explored as strongly polar alternative to standard systems targeting the lignin removal (Loow et al., 2017). Yet, DESs-based systems were found less efficient with respect to ILs-based systems, especially when it comes to biofuel-relevant saccharification yields (Wahlström et al., 2016): acid-catalyzed cleavage of β -aryl ether linkages has been observed at elevated temperatures in the presence of DESs; Yet extensive side-chain fragmentation is not reported (Alvarez-Vasco et al., 2016). Most interestingly, the use of DESs holds the potential to arrive at a biorefinery that uses its very own products to achieve fractionation of biomass (Socha et al., 2014). Lignocellulose pretreatment in aqueous tetrahydrofuran (THF) effectively dissolves lignin and restricts its condensation in the solid fraction (Smith et al., 2016). Similar results are obtained using 2-methyltetrahydrofuran (2-MTHF); in contrast to the THF system, 2-MTHF can be recovered from the process due to its immiscibility with water. Fractionation of lignocellulose has been reported using aqueous GVL, representing a greener and more sustainable alternative to the above discussed THF-systems (Pateromichelakis et al., 2022). GVL was found to dissolve lignin and to promote hydrolysis of polysaccharides by reducing the activation energy of glycosidic bond cleavage during pretreatment (Mellmer et al., 2014). The β -ethers in lignin represent also for this system the most vulnerable point, but cleavage rate is only moderate (Zhou et al., 2016).

2. Solubility through stabilizing charge fluctuation within the solute

2.1. Stokes shift and solubility

Before entering into a discussion regarding the dissolution behaviour of the most relevant herbaceous and woody biomass polymers in certain solvents, the general mechanisms that bring organic molecules into solution and stabilize them in the dissolved state shall be discussed. One way of obtaining insights is the observation Stokes shifts of a given compound in various solvents. A Stokes shift is simply defined as the

difference in absorbed and emitted wavelengths as a specific light source is employed to bring a molecule in an excited electronic state while it is in solution. The observed shift depends on the electronic structure of the compound absorbing and re-emitting the light (Brennan et al., 2017). In case the system allows for excitations, and/or energetic management of the energetically demanding excited state throughout the entire molecule, a larger Stokes shift is observed (Ren et al., 2018), which is related to the physical molecular movement of the solute (Qin et al., 2020). The electronic state of any solute is largely dependent on the solvent it interacts with; for example, the solvent can stabilize movement of charge from aromatic structures into adjacent parts of the molecule through resonance (Orozco-Gonzalez et al., 2013). Consequently, different solvents will stabilize different electronic states for a certain compound, and obviously, different electronic states will have differing optimized geometries. Related to solubility, it has been found that, e.g., dissolving daidzein in acetonitrile as compared to water, reduces the energetic difference between various electronic states (Orozco-Gonzalez et al., 2013); in acetonitrile, daidzein is more likely to interchange among charged states and different geometries. Correspondingly, the solubility of daidzein is double in acetonitrile as compared to water over a broad temperature range (Fan et al., 2015). It is important to note from the latter work, that, due to the closely matching energy-levels of the electronic arrangements, any re-emitting of light disappears due to the ease and manifold possibilities of internal conversion of the absorbed energy. Nevertheless, there are some contradictory results on Stokes shifts and its translation into solubility. For example, prodan has an abnormally large Stokes shift in water despite being scarcely water-soluble (Bunker et al., 1993). Addition of alcohols have been found to promote prodan solubility in water (Rottenberg, 1992), even though prodan has lower Stokes shifts in pure alcohols (Baral et al., 2020). This leads to a work presented by Baral and co-workers which emphasizes the importance of the inherent resistance of polar solvents to actually re-arrange around the solute in order to stabilize new electric states, with such arrangements also causing increments in Stokes shift as energy is lost because of this solvent re-structuring (Baral et al., 2020). While a more polar solvent will take longer, and spend more of the absorbed energy to re-arrange, solvents with lower polarity are faster, but might on the other hand be poorer in stabilizing the new electronic states due to their low polarizability, as is the case of alkanes around the discussed dye molecules. The inherent polarity of water, in combination with the extensive hydrogen bonding, causes re-arrangement of water molecules to be slow, and increases the resistance for the solute to easily fluctuate between electronic states, causing the favouring of one geometric arrangement. The same trends observed for prodan are observed for curcumin, whose Stokes shifts have been measured in 13 different solvents (Patra and Barakat, 2011). In this case, water (Kurien et al., 2007) and alkanes (Cui et al., 2021) represent the outliers due to either their internal resistance to re-arrange, or because of their low polarity and polarization. Instead, the solvents in-between, such as dimethyl sulphoxide (DMSO), THF, and acetonitrile display lower Stokes shifts for curcumin while solubility increases (Cui et al., 2021; Patra and Barakat, 2011). This further illustrates that as long as the solvent molecules are capable of polarization and in this way able to accommodate charge re-distribution in the solute, they solvate towards dissolution, while simultaneously not generating a resistance too high to re-orient upon charge movement in the solute, facilitating solubility.

2.2. Solubility of lignocellulosic material

The discussion till now has focused on the quantification of solubility on the basis of Stokes shifts employing solutes that carry conjugated domains, i.e., structural motifs that are different from those present in the majority of structures in lignocellulosic biomass, the polysaccharides. More similarity exists with respect to the lignin component in biomass, but it must be noted that lignin does not represent a chromophore, and that resonance is present only within the aromatic rings.

Throughout the following paragraphs, both lignocellulosic polymers and their monomers will be discussed regarding conformational flexibility and their corresponding solubility and/or reactivity. It is important to emphasize that while conformer flexibility originating from the solute-solvent interplay appear crucial upon moving from the insoluble collapsed to liquid state, number and nature of possible conformers are largely different for monomers and polymers. While certain parallels can be drawn between aromatic dye molecules and simple lignin motifs, the sugar monomers change between different anomeric configurations due to their reducing end. Obviously, this is to a much lesser degree possible in lignocellulosic polycarbohydrates, where conformational variations occur mainly due to rotational freedom. If first considering the monomers comprising many of the polysaccharides found in lignocellulosic biomass, *i.e.*, glucose, mannose and galactose, it has been found that when the applied solvent allows for a more even distribution of α/β -conformers (Matsuo and Gekko, 2004) solubility increases (Alves et al., 2007; Gong et al., 2012; Gould, 1940). In other words, high solubility results if the solvent allows for an easy interchange between the sugar conformers. This alteration in anomeric configuration has recently been reviewed and considered to be, in polar solvents, a balancing act between solute-solvent hydrogen bonding and hyperconjugation through intramolecular delocalization, during which a lone pair reversibly occupies an empty σ^* orbital allowing additional stabilizing effects in specific conformations for conformational switches; different solvents display different abilities to achieve this (Alabugin et al., 2021). While the contribution of intra-molecular hyperconjugation affect the distribution of conformers in monomers, this exact contribution in polymers, where the anomeric hydroxyl is locked into the glycosidic linkage, is different, but not necessarily gone as the glycosidic linkage still has lone pairs but require different geometric arrangement of the ring for interaction with a σ^* orbital (de Chavez et al., 2021), causing an eventual change in configuration of the anomeric center in connection with hydrolytic depolymerization and eventual repolymerisation. It is important to specify in this context that the term hyperconjugation is used both when discussing intramolecular anomeric effects and when looking at intermolecular hydrogen bond formation, *e.g.*, proper/improper hydrogen bonding, where it appears alongside a rehybridization of the proton donor. Throughout this review, hyperconjugation will be used in the latter context unless else is specified.

Always with respect to the conformers of solutes, work performed by Jarin and Pfaendtner (2014) set out to investigate how different solvents change the free energy associated with various conformations of cyclic carbohydrates. Interestingly, a well performing cellulose solvent, in this case the IL [Bmim][Cl], energetically favored a 2S_0 skew ring conformation equally to the 4C_1 chair observed in the insoluble, crystalline cellulose state. Obviously, in order to minimize free energy, repulsive forces need to be minimized and functional groups need to be able, through interaction with the solvent, to change interactions allowing for additional rotational conformations. Thus, to advocate biopolymer dissolution the solute/solvent system should preferably be designed such that the entropic contribution from the solute is realized and can dominate the total free energy reduction of the system. Similar results are observed in form of additional rotational conformations adopted by cellulose moieties as they enter the dissolved state (Mostofian et al., 2014). Molecular dynamics have also been applied to display the difference between cellulose in liquid and solid state, which involve moving from the traditional 4C_1 chair to a ring-flipping between several boat-like conformers as well as greater rotational freedom for the hydroxymethyl sidechain in glucose (Tongye et al., 2009). While some of the reported results are by a large extent based on molecular dynamics and simulations, experimental work performed using nuclear magnetic resonance (NMR) techniques supports this idea. Significant up- or down-field shifts of certain atoms or groups of atoms, *i.e.*, motifs, within the polymer are eventually observed. As will be further explored in the following sections, cellulose solubility in caustic systems is highly dependent on concentration. Interesting work in this regard was

performed by Isogai (1997), who employed ${}^{13}C$ NMR analyses of cellulose in solution state to elucidate that up to NaOH concentrations of 12% (m/m), carbons not participating in any glycosidic linkages experienced a de-shielding effect upon dissolution. At higher concentrations of NaOH, the charge distribution between the carbon atoms in the glucose moiety segregates to a larger extent, with some of them, *i.e.*, C2, C3, C5, C6, experiencing large de-shielding, while C1 and C4 experience large shielding, suggesting the existence of a drastically preferred ring conformation. The down-field shifts for the carbon atoms linked to glucose hydroxyls indicate that they experience secondary effects of the re-hybridization from hydroxyl groups of the sugar ring engaging in bonding with the solvent (Alabugin et al., 2003). Similar results were found by Gustavsson et al. (2014) when studying cellulose dissolution in alkaline solutions by employing a polarization transfer solid-state NMR protocol on solid and dissolved cellulose material. It is important to mention that the shifts observed in NMR are time averages of different electronic configurations, nevertheless, they give an idea of charge distributions within the most relevant structures. Interestingly, solubility essentially relies on the nature of the most favorable electronic configuration within the polymer on the basis of the chemistry of its immediate surroundings. An example is the application of microwaves to promote cellulose dissolution in ILs (Sánchez et al., 2020): Heating adds kinetic energy to the molecules, and molecular rotation on the one hand and polarization in the solvent surrounding the solute on the other hand consequently increase and more flexibly change (Muley et al., 2021); 'brute-force' is thus essentially supportive establishing a certain electronic structure around the otherwise insoluble polymer on the one hand, and to force the solute to change/adopt its electrical and chemical arrangement due to the shifting environment on the other hand. Whether this effect originates from absorption of electromagnetic radiation predominantly by the solvent or by the solute, or a combination, will likely depend on the specific system; however, in either case the final consequence, *i.e.*, dissolution, is the same. To illustrate the efficiency of these types of systems, in combination with solvents which are efficient due to reasons which will be discussed further in the following sections, biomass has been fractionated in seconds (Chen and Wan, 2018).

3. Constructing hydration shells stabilizing solute charge mitigation and re-orientation

3.1. Carbohydrate-based structures

As discussed in the previous section, it is key to surround a polymeric solute with components which can stabilize the various structural conformations of the solute in order to facilitate its entering into a dissolved state as prerequisite for an efficient fractionation. Considering cellulose, the interaction of an anionic solvent component with the cellulose hydroxyl groups is considered crucial, especially when the cationic and anionic components of ILs are compared (Xu et al., 2010). It is hard, however, to visualize a system in which the anion solely drives dissolution of a polymer such as cellulose. As reported by Li et al. (2018), while the anion makes a 'first-contact' with the cellulose hydroxyls, forming hydrogen bonds, certain carbon atoms in the cation experience increasingly higher chemical NMR shifts as cellulose solubility increases. From the cited work, both the hydrogen bond accepting nature of the anion, and the capability of the cation to be polarized are the factors influencing cellulose solubility. The exact nature of the cation polarization could originate from direct interaction between the lone pairs of the chloride anion and the aromatic ring current of the cation, which should induce higher NMR carbon shifts in the cationic ring (Alabugin et al., 2003). The cited work also reports on the ability of oxygen lone-pairs to undergo similar interactions with sp^2 C-H groups. This, likely as secondary effect, could indicate a dual mechanism of interaction for the cation, *i.e.*, as partner for the anion, but for the sugar hydroxyls if needed. Yet, the interaction occurring in the bulk and on the

surface of a solute are not necessarily the same. Obviously, if any glucose ring in cellulose was to undergo rotational conformational change, it would be convenient if there existed a polarizable cation in the immediate vicinity which could shield any repulsive forces between H-bonded anions due to spatial adjustments. The importance of polarization during conformational change of the sugar rings has been illustrated in molecular simulations which employ polarizable force-fields as compared to fixed charged ones (Kan et al., 2017). These considerations regarding polarizability of the solvent and interplay with the solute can be transferred to emerging IL- and DES-based fractionation approaches. Systems different from ILs that dissolve cellulose are alkaline solutions, acknowledging the significant differences in dissolution capacity between LiOH, NaOH, and KOH (Xiong et al., 2013). Common to all system is apparently the pH, and the inherent reactivity of the hydroxyl anion that triggers numerous reactions with the two principal components of lignocellulosic biomass, i.e., the polycarbohydrates and the lignin. While sugars undergo peeling, and subsequently also stopping reactions, that break down hemicelluloses and cause reduction of polymer sizes in case of cellulose, lignin is largely structurally altered. As consequence, solubility in the various systems is commonly partly achieved also on the basis of a reduction in molecular size, and a change of structural features. Observable differences must be explained, in front of this common background, as suggested by Xiong et al. (2013), in the dissolution capacity that lies in whether or not the hydrated cations can generate stable complexes with cellulose or not. For example, the hydrated potassium ion is not able to form a stable cellulose complex, hampering dissolution. Following the logic applied in the discussion of IL-based systems, the basic hydroxyl ion in alkaline systems strongly interacts with the relatively acidic sugar hydroxyls, and the hydrated metal ions contribute to the stabilization of various conformers of the solute. Interesting in this regard is that the hydration complexes of lithium cations, associated with high cellulose solubility, can be of either a tetrahedral ($\text{Li}[\text{H}_2\text{O}]_4^+$) or octahedral configuration ($\text{Li}[\text{H}_2\text{O}]_6^+$), while sodium and potassium cations, that are restricted to octahedral ($\text{Na}[\text{H}_2\text{O}]_6^+$) and squared antiprism ($\text{K}[\text{H}_2\text{O}]_8^+$) geometries, respectively, appear less efficient (Persson, 2010). This hints at the fact that cation hydration, and thus cation size, plays another key role in alternations of polymer conformation. The two latter ions form relatively large hydrated complexes, similar in size to that of the hydrated bivalent zinc cation (Persson, 2010), which in form of a chloride salt in aqueous systems is able to dissolve cellulose (Losey, 2018). The size of the hydrated ion also reflects the effective charge distribution, and how it allows the hydration layer to respond to its surroundings. The water shell around the cations is also important with respect to the fact that Xiong et al. (2013) mention that the amount of water determines the type of interactions occurring between the polymer surface and the components in the solvent, which again is influenced by the type of cation. Work performed by Losey (2018) on hydrated zinc chlorides investigated the extraordinary cellulose dissolution capacity at a molar ratio water/ ZnCl_2 close to 3:1. Importantly, it was found that at this ratio the solvent species were comprised of two components, one strong hydrogen bond donor ($\text{Zn}(\text{OH})_2$), existing in equilibrium with a strong acceptor (ZnCl_4). Seeing this in light of what was mentioned for the ILs, the resemblance in solvent components and their properties hint at the fact that their mechanistic function on cellulose dissolution could be similar. It can be speculated that also the caustic systems, such as aqueous sodium hydroxide, might dissolve cellulose through similar actions apart from their chemistries. It is worth emphasizing that the majority of cellulose-dissolving systems are obtained by having dissociated salts in the main solvent component, thus species with both Lewis acidity and basicity. Summarizing, for cellulose dissolution it appears important to (1) initiate strong 'first-contact' between the polymer and the solvent anions, and (2) to further stabilize rotational conformational changes and the movement of the first hydration layer through a polarizable cation or a hydrated cation with some flexibility in hydration structure. Potential scenarios are presented in the Supplementary Materials. It has

been found that for both bamboo hemicelluloses (Hu et al., 2020) and eucalyptus cellulose (Sun et al., 2013), [Bmim][Ac] performs well for dissolving both polymers which further suggests that the polysaccharides are governed by similar driving forces upon dissolution. This is further supported by the fact that hemicelluloses are also soluble in specific alkaline solutions (Wen et al., 2011; Xu et al., 2007), as discussed above for cellulose (Kamida et al., 1984). However, as emphasized previously, this is highly dependent on the ratio of the alkali species to water (Kamida et al., 1984; Wen et al., 2011), with a small window of around 10% (m/m) alkali which appears to be especially suitable.

3.2. Polyphenolic structures

As mentioned by Hart et al. (2015) the application of ILs containing anions with low hydrogen bond acceptance are usually found to be poor solvents for cellulose, meanwhile, this is not the case for lignin. The effect on cellulose is likely related to the need for tight interaction between the anionic IL component with the sugar hydroxyls to efficiently establish a linkage between the solvent environment and the polymer. The discussion regarding the dissolution of lignin is more complex, due to the irregular alkyl aryl ether structure of lignin (*vide supra*), comprising differently polar elements in the form of methoxy groups, ether linkages, and hydroxy groups. The geometry of the polymer as function of the varying structural features and the interaction with the hemicelluloses would additionally explain why the combination of anion/cation is not necessarily the same when considering dissolution of lignin in ILs (Hart et al., 2015), exemplified with the ability of 1-benzyl-3-methylimidazolium chloride to dissolve cellulose, but not lignin (Mäki-Arvela et al., 2010). In case of cellulose, upon dissolution in ILs the rather flat cation is usually found hovering above/below the flat C-H side of cellulose, while the anions bound to the hydroxyls are covering the edges of the cyclic carbohydrates (Li et al., 2018). Looking into computational results considering the solvation layer of specific lignin moieties (β -O-4', 5-5', 4-O-5') with ILs, a similar solvent structuring seems likely, with the anion being found to concentrate in the first hydration layer and around the aromatic moieties. The cation is found to cover a larger, broader area in the second solvent layer, suggesting that the roles are similar as for polysaccharides in ILs (Hart et al., 2015). This further emphasizes that the geometrical fit needs to be taken into account when designing systems to be employed for the dissolution of a certain polymer. Such a retrofitting of the solute's immediate environment into towards a stabilizing nature with respect to shifts in the electronic configuration is further emphasized when looking into NMR results evaluating the solid and liquid state lignin. Specific aromatic and side-chain carbons experience strong and distinct resonances upon dissolution, indicative that these carbons and the domains which they exist in, to a larger extent are perturbed when dissolved (Maciel et al., 1981). These specific structures are the ones already indicated to have closest interaction with the anions when considering the work of Hart et al. (2015), suggesting that upon dissolution, these motifs are liberated from secondary inter/intra-molecular bonds, and freer to interact dynamically with the solvent upon dissolution. This is interesting considering shift-changes of relevant lignin moieties in model compounds upon dissolution. For example, structures similar to β - β' , when dissolved in CDCl_3 , display side-chain carbons which in general experience higher shifts upon dissolution, indicating that some electron density is 'redirected' through the aliphatic domain (Hawkes et al., 1993), potentially through bonding between lone electron pairs in the solvent, to empty anti-bonding orbitals (σ^*) in the side-chain (Alabugin et al., 2021). Previously, chloride electron donors have been shown to delocalize lone electron pairs to C-H (σ^*) donors (Alabugin et al., 2003). While hydrogen bonding in general involves both hyperconjugation and rehybridization, and while the longevity of the hyperconjugation phase is determined by both the strength of the Lewis base, and the ability of the donor to rehybridize, the fact that carbon atoms in the aliphatic part

of lignin dissolved in CDCl_3 experience down-field shifts indicates that these lignin-solvent interactions are dominated by hyperconjugation. On the other hand, in acetone/ D_2O mixtures, model structures similar to $\beta\text{-O-}4'$ experience significant changes in shifts, both up- and down-field, both in the aromatic and aliphatic domain upon dissolution. These results display that upon dissolution, and dependent on the applied solvent, electron density is re-directed from what is measured in the solid state (Maciel et al., 1981). The apparent higher flexibility in lignin and the generally more irregular structure render the establishment of tight intermolecular interactions as present in the case of ordered strands of cellulose much more difficult. In fact, quite simple solvent systems such as aqueous acetone mixtures have been found to readily dissolve certain lignin fractions (Domínguez-Robles et al., 2018; Wang et al., 2020). Investigations performed regarding the nature of aqueous ethanol solutions found that addition of water to ethanol enhances and broadens the polarity distribution within the solvent (Zhong and Patel, 2009). In the mentioned work, the ethanol hydroxyl is found to carry the potential of bonding more water molecules than its valence electrons should allow, causing as such electron density reduction in the aliphatic side chain. The ability of water to modify the ethanol polarity allows for a broad range of solvated structures, which together can work on solubilizing the respective biopolymer. Attractive interactions between positively polarized alkyl groups and an aromatic system has already been described (Nijamudheen et al., 2012), under the condition of fitting geometric orientations. Whether this interaction is purely electrostatic or whether there is any orbital overlap between a π -donor and a σ^* -acceptor, or a combination thereof, is open for debate, especially when considering that benzene, *i.e.*, a π -donor system, has been found to favor hyperconjugation in combination with a C-H (σ^* -) acceptor (Alabugin et al., 2003). It is important to keep in mind the properties of the accepting group as the balance of hyperconjugation/rehybridization will be determined by this. For example, central sp^3 carbons rehybridize quicker than sp^2 or sp carbons, thus reducing the actual time for intermolecular secondary bonding (Alabugin et al., 2003). Interestingly, illustrating a role of water as co-solvent, ILs have been found to benefit from addition of water upon lignin dissolution as it modulates the solvent interactions by liberating the ionic species from each other, allowing them to associate better with the polymer, thus aiding the dissolution process (Ge et al., 2022).

The interactions occurring at the solid/polymer-solution surface are a result of a broader picture including the state of the bulk solvent. For instance, the potential for a high water ‘coherency’ determines the driving force toward hydrophobic interaction and therefore precipitation of the components present in lignocellulosic material. An interesting notion is that, in aqueous ethanol, water percolation is no longer observed above a molar ratio of ethanol/water of approximately 3/10 (Zhong and Patel, 2009). At this ratio, an abrupt rise in lignin solubility is observed (Jääskeläinen et al., 2017). Another common solvent applied upon fractionation of lignocellulosic biomass is aqueous acetone, which displays altered dipole moments upon various water contents, attributed to the positive inductive effect of the methyl groups versus the carbonyl group upon water association with the carbonyl oxygen (Thompson, 1996). Interestingly, at molar ratios of acetone of 25–33% and above, corresponding to about 60% (v/v) acetone, specific acetone-water complexes with acetone/water ratios of 1/2 and 1/3, are formed. At higher water contents, isolated organosolv, kraft, and soda lignins experience steep decreases in solubility (Domínguez-Robles et al., 2018), indicating that specific bulk solvent states correlate with dissolution behavior. These acetone-water complexes, displaying particular distributions of electron density and polarizability, *i.e.*, acting as a soft acid in Pearson’s HSAB (hard and soft acids and bases) concept, ensure high lignin solubility. A potential scenario is illustrated and presented in Supplementary Materials.

Lignins are not completely comprised of aromatic units, as they also carry aliphatic moieties with different functionalities, and while electrostatic and hydrogen bond interactions have already been mentioned,

a type of dispersion interaction has been observed to occur between alkyl and aryl moieties where their close association has been found to display attraction by interchanging electron density via C-H (Danovich et al., 2013). While it seems reasonable to picture a similar situation for parts of the aliphatic lignin moieties with the organic part of the solvent, for such interactions to occur, it is likely necessary that the participating orbitals do not differ substantially in energy levels (Yadav et al., 2020). Hence, ethanol, for example, with a different polarization might be beneficial to match side-chain structures with various functionalities. The ability of the solvents to re-adjust for accommodating and stabilizing any polymer electronic and thus geometrical re-arrangement seems to be, at a first glance, less troublesome for solutes carrying aromatic and/or conjugated domains. None of the polysaccharides discussed herein are actually soluble in such simple systems. However, the mechanism laying behind the dissolution process seen for the polysaccharides (*vide supra*) also appears to hold for lignin, and for example, if the correct combination of Lewis acid/base is found, very high lignin solubilities can be achieved (Rashid et al., 2021).

4. Temperature and solvent – similar means for dissolution

4.1. Carbohydrate-based structures

While solute-solvent interactions can change upon changing solute conformers upon dissolution, the effect of temperature needs to be considered as well, since various temperatures confer various kinetic energies to both solvent molecules and solutes. With respect to the effect of temperature on the solubility of carbohydrate-structures in lignocellulosic biomass, it has been reported for α -lactose that the rate of α -lactose epimerization, by mutarotation, increases with temperature (Jawad et al., 2014), as does lactose solubility (Machado et al., 2000). This is in line with the fact that in solution different conformers represent different energy barriers to conformational changes (Stogiannidis et al., 2020). This barrier is gradually overcome by increasing temperature such that the interconversion between conformers, but also conformations accelerates as temperature and water mobility increases. The size of this barrier, in case of lactose represented by the α - β energy gap, depends on both type of solute and solvent (Alabugin et al., 2021). Importantly, moving from simple saccharides to polysaccharides, similar results are observed for cellulose regarding the effect of temperature and solvent, but instead of changing fundamental configurations, torsion angles (ω) of the side-chains and ring-flipping between several boat-like conformers are suggested, on the basis of molecular dynamics, upon hydration and temperature incrementation (Tongye et al., 2009). It is *de facto* the strong preference for polysaccharide monomers to take on low energy conformers such as the ${}^4\text{C}_1$ chair which locks them in a ‘low-mobility state’ (Peesapati et al., 2021).

4.2. Polyphenolic structures

Within the pre-treatment processes, a broad range of temperatures is employed for biomass fractionation in order to ease dissolution (Jones et al., 2016). Interestingly, through molecular dynamics studies it has been found that changes in temperature and hydration affect lignin motions in the same way (Vural et al., 2018). Essentially, lignin chain mobility can be enhanced by both temperature and level of hydration. While a tight interplay between the solvent and the solute is important, a too tightly bound aqueous hydration layer with an excessive number of hydrogen bonds at low temperatures has been found to be the main driving force for arriving at a collapsed lignin state (Petridis et al., 2011). The reason for this was found to be due to reduced entropy and slightly fewer hydrogen bonds formed by the water molecules existing in the restricted and dense lignin hydration layer. As temperature is increased, the reference bulk water state is comprised of a gradually ‘weaker bonded’ water, which upon temperature increase will generate a water reference state that allows the lignin to hydrate in the extended

conformation.

5. Altered charge distribution and its simultaneous effect on depolymerization events

The previously discussed mechanisms revolving around polymer dissolution are all the more interesting when the solubility aspects in biorefinery are extended to account also for eventually desired reactivities of the systems and the common attempts to aid biomass fractionation by (catalytic) degradation of at least one of the polymeric compounds. It is long known in chemistry that solvents play a crucial role in terms of system reactivity, being able to stabilize intermediates and thus determine and direct mechanistic pathways, and/or allow for faster reaction kinetics. Numerous examples have been studied in the last decades, and more recently for emerging alternative solvent systems (Varghese and Mushrif, 2019). An example is the study of cellulose dissolution in ILS (Hyvärinen et al., 2014): small amounts of moisture in the systems were enough to initiate cellulose hydrolysis. Similar findings are also reported elsewhere in both pure and binary systems containing IL (de Oliveira et al., 2015). The electronic structure in the solid-state crystalline cellulose has been reported to exhibit properties which in fact protect it from hydrolytic cleavage of the glycosidic bond (Loerbroks et al., 2013), where rotational conformational changes of the sugar rings, induced by specific solvents, represent one of the important steps during chain scission (Loerbroks et al., 2015a). While not being a lignocellulosic polymer, but useful to illustrate the point, chitin, through conformational changes and subsequent electron donation from non-bonding lone-pairs of the ring-oxygens into the antibonding σ^* orbital of the glycosidic oxygen, experiences enhanced glycosidic bond hydrolysis (de Chavez et al., 2021). Considering additionally the stabilization of unstable intermediates, the hydrolysis of cellulose and transition from the stable chair (4C_1) into a rotational transition-state conformer, being unfavorable in water, becomes significant in an ionic environment (Kunov-Kruse et al., 2013). As discussed in the first section when illustrating the relationship between solute charge fluidity and solubility, conformer flexibility allowing for charge dislocation and thus initiation/stabilization of the respective reaction intermediates is obviously important. This point is exemplary captured in the proceedings of glucan hydrolysis in certain glycosidases where the intermediate carbocation takes on a 1S_3 skew-boat conformation which is stabilized by lone electron pairs from organic acids in the active site (Rye and Withers, 2000). In a similar fashion, as illustrated through molecular dynamics on cellulose hydrolysis (Loerbroks et al., 2015b) solvent arrangement can determine which conformers are readily available in the energetic landscape experienced by the solvated solute, and thus eventual starting points for hydrolysis reactions. The potential of applying certain solvents to promote these reactions does not necessarily require solvents dissolving the polymer. Simple aqueous solutions containing NaCl were found to promote cellulose hydrolysis (Jiang et al., 2018), as has the use of inorganic salts in aqueous media when hydrolyzing xylan (Kang et al., 2013). Regarding the mode of action of aqueous NaCl solutions, it has been elucidated that the salt is predominantly affecting the ratio of overall solvent relaxation time to hydrogen bond lifetime, in a way which allows for more rapid hydrogen bond exchange (Luo et al., 2020), which intuitively should enhance proton diffusion. Purely inorganic chloride salts in aqueous solutions have been employed to facilitate cellobiose hydrolysis, and it was found that, in general, the salt constituted by a strongly hydrating cation, *i.e.*, kosmotropes (Mazzini and Craig, 2017), increases the reaction rate of cellobiose conversion (Yu et al., 2015). Similar results were found in early stages of xylan extraction from miscanthus when chloride salts were applied in pure water (Kang et al., 2013; Mazzini and Craig, 2017). When comparing the enhanced reaction kinetics in cellobiose depolymerisation observed for aqueous KCl as compared to aqueous NaCl (Yu et al., 2015), it is interesting to note that KCl enhances solvent structural relaxation times compared to NaCl (Luo et al., 2020), suggesting that a more adjustable

solvent landscape is favorable. With respect to divalent cations in inorganic chloride salts, *e.g.*, $MgCl_2$ and $CaCl_2$, it has been found that, albeit the differences being relatively small, calcium salts in general relax faster due to the larger ionic radius of calcium and more weakly bound water (Friesen et al., 2019). $CaCl_2$ does, however, present slower reaction kinetics when compared to $MgCl_2$ (Yu et al., 2015), at least at elevated temperatures. Work performed to directly compare the aqueous hydration structures of $CaCl_2$ to $MgCl_2$ found that the hydration shell around the Ca^{2+} cation often remains relatively intact even at increased temperatures as compared to the 'looser' Mg^{2+} shell (Bai et al., 2013). The comparisons NaCl against KCl, and $MgCl_2$ against $CaCl_2$ essentially point towards factors already indicated as important for dissolution, *i.e.*, a hydrated cation that can more easily re-structure its hydration layer to accommodate anion re-positioning for stabilizing the intermediate carbocation.

6. Specific solvent interactions with lignocellulosic constituents

6.1. Solute-solvent interactions in ionic liquids

As disclosed in the present review, the dissolution of polysaccharides in ILS essentially relies on the effect exerted by the anionic components and its ability to alternate its electron donation between the sugar-based hydroxyl groups and the cation in the surrounding solvation layer, this to accommodate for conformational changes. Apart from the already discussed chloride-containing ILS, acetate-containing ILS have also been found to dissolve cellulose (Tomimatsu et al., 2019), which is reasonable considering its small size, and the double lone-pair functionality allowing dynamics interaction with the solute and the surrounding solvent. For the cation, the importance of sp^2 groups in the IL cation was illustrated by Zhang et al. (2016), where apart from a cationic aromatic ring, a sidechain is beneficial for cellulose dissolution given that this side chain is relatively small and containing sp^2 hybridized carbons (Alabugin et al., 2003). In a similar fashion, ILS allow for lignin dissolution with the anionic components functioning as linkers between the solute and solvent, preferably linking conjugated sp^2 domains of the aromatic lignin regions and the IL cation. Importantly, it is likely the alternation in anion bonding, at any given time, to either the solute or the second hydration shell, which causes fluctuation in electron structure within the solute, consequential adaption of an optimal geometry by conformational changes, and thus ultimately an important entropic contribution to an overall reduced Gibbs energy, and thus dissolution. Another important factor, related to the one just discussed, is how many anions/cations are needed per glucose or lignin moiety for their dissolution. An ideal ratio far from the common IL anion/cation ratio of 1:1 could cause saturation to come early as the bulk solvent becomes unevenly electronically balanced and prohibit any efficient dissolution. In this sense, the geometrical fit of the solvent relative the solute becomes especially important.

6.2. Solute-solvent interactions in protic solvents

For protic solvents, the enthalpic most interesting sites for interaction with the sugar structure of lignocellulosic polycarbohydrates are the various hydroxyl groups and the ether linkages, *i.e.*, the ring oxygen and the glycosidic linkage. For dissolution, the possibility for the solvent to re-structure upon either rotational or anomeric conformational change is important (*vide supra*). Meanwhile, as illustrated for monosaccharides in protic solvents increasingly 'bulky' alcohols and their growing inability to dissolve glucose and other cyclic carbohydrates (Montañés et al., 2007), the only real interaction occurring is likely proton exchange and hydrogen bonding between the hydroxyl groups, and hydrogen bonding in case of the ring-oxygen, essentially locking up the sugar ring as any re-structuring of the solvent becomes troublesome with their increased size. For water, as briefly outlined before regarding the solubility of simple sugars in water, the scenario is widely different,

as it displays both electron donor and acceptor properties and thus a greater reactive flexibility. An interesting illustration of the cause behind this can be found when comparing carbohydrates to their solubility in D₂O as compared to H₂O. More precisely, it has been found that di-, tri-, and cyclic saccharides experiencing low solubility in pure water (H₂O), experience larger solubility decreases in D₂O as compared to those readily dissolved in regular water (Cardoso et al., 2012). This was explained by the greater cohesive energy in D₂O, which should restrict any solvent re-structuring, and is also visible by the lower self-diffusion observed for D₂O as compared to H₂O (Mills, 1973). This can be seen as the foundation for the hydrophobic effect which plays a very important part in the dissolution of larger polysaccharides such as cellulose in water and contributes to its biologically important microfibril structure (Medronho et al., 2012). The same effect is observed for structurally rather unaltered lignins, such as milled wood lignins (MWL) (Crestini et al., 2011), in water, which are largely insoluble due to the same reason (Sameni et al., 2017). Interestingly, and just as for the polysaccharides, solubility of certain lignins in pure, protic solvents such as methanol and ethanol are low (Sameni et al., 2017), following nevertheless similar trends found for polysaccharides, seeing small alcohols generally perform better than the larger and more bulky ones. An example has been reported for kraft lignins (Melro et al., 2018). More interestingly to note from the last cited work is that polyols such as glycerol and ethylene glycol largely outperform the simplest alcohols like methanol and ethanol. Considering what was mentioned for the ionic liquids and the role of the anion to offer linking between the solute and the second hydration layer, a similar role could be taken by multi-functional solvents such as the polyols. Similarly, bifunctional solvents including ethanolamine and ethylene glycol has been found to promote coil extension of dextrans, as when to for example compared to water (Antoniu et al., 2010). For the simpler alcohols, after solvent-solute hydroxyl interaction, there are no obvious alternatives nor any low-enthalpy links to the aliphatic segment of the linked alcohol in the first hydration layer. An important difference regarding the solute-solvent interactions which are possible when comparing lignin and polysaccharides are those displayed by the aromatic domains, as these offer the possibility of donating π electrons upon interaction with for example C-H acceptors (Alabugin et al., 2003), and in the case for polyol hydroxyls, the proton should be more acidic all which would give an alternative to electronic interactions of aromatic moieties in lignin, commonly colloquially referred to as π - π aggregation or 'stacking' (Deng et al., 2011) while still maintaining bonding to the outer hydration layers with the second hydroxyl group. Similar scenarios should be possible due to lone pairs of the lignin methoxyl groups, which essentially could pay for the loss of aromatic stacking.

6.3. Solute-solvent interactions in aprotic and mixed solvents

For polysaccharides the path to dissolution in aprotic solvents and solvent systems appear potentially more troublesome as the more constrained sugar ring and its mobility needs to be carefully accommodated for. Despite not having the same possible conformers as the polysaccharides, looking into the exemplary solubility of relevant monosaccharides in aprotic solvents, the dissolution capacity for galactose, glucose, and mannose in acetone is reportedly low at room temperature (0.05–1.9 mM) (Arcos et al., 1998). Nevertheless, the aprotic solvents can be polar and strong electron donors and tend to force simple sugar ring conformers into a polar structure, strongly favoring, for example, an equatorial conformation as compared to the axial due to steric repulsions (Alabugin et al., 2021). As with the protic alcohols discussed in Section 6.2, this would largely generate a hydration layer where the aliphatic domain of the acetone molecule points outwards toward the second hydration layer. There are no obvious interactions readily available between this first layer to the second, rendering the initial hydration structure non-connected with the surrounding solvent locking it up.

Among the polar aprotic solvents, acetone is considered of low polarity, while solvents such as DMSO are of greater polarity. It has been found in the case for DMSO through molecular dynamics, that the lone pairs of its oxygen atom are capable of interacting strongly with the methyl groups of a second DMSO molecule (Strader and Feller, 2002), which should increase with the polarity of the molecule, and thereby, for DMSO gives a coherence between the sugar solute and the surrounding solvent, thus explaining the fairly high solubility of glucose in DMSO (Gajula et al., 2017). In addition, this polarity provides certain acidity to the methyl protons, allowing some interaction with the lone pair of the oxygen in the sugar ring thereby disturbing the intramolecular hyperconjugation not only by disturbing the anomeric hydroxyl through the DMSO lone pairs. This strong dipole moment of DMSO has been correlated with increased coil extension of dextrans, for example (Antoniu et al., 2010). Meanwhile, solubility of polymers such as cellulose in DMSO is still limited (Shigemasa et al., 1990). The strong secondary bonding capability of DMSO in cellulose systems has been illustrated (Voronova et al., 2006) through the high stability/low system energy achieved upon hydration of the cellulose surface. This strong hydration, and the incapability of DMSO to alternate the direction of the charge responsible for cellulose surface bonding, away from the polymer and towards the second hydration layer in an efficient manner essentially renders cellulose insoluble in this solvent. Considering lignin and its solubility in aprotic solvents, it is interesting to note that dissolution is especially poor for lignins with low S unit content (Sameni et al., 2017). Noteworthy, the lignin type is also the one with the highest potential interaction energy through lignin hydroxyl groups. The fraction shows significantly reduced solubility in acetone, tetrahydrofuran, and ethyl acetate. This is interesting considering that the aprotic solvents essentially act as hydrogen acceptors in terms of hydrogen bonding, suitable for interaction with lignin hydroxyls acting as hydrogen donors, and could hint towards a lower capability of sp²-type C-H in syringyl units to act as hydrogen donors as compared to sp²-type C-H in guaiacyl units, and that interactions with the aromatic rings are the dominating factor in dissolution of the polyphenolic polymer. The lignin used in the study was a softwood kraft lignin, for which chemical structures of acetone insoluble and acetone soluble fractions have been proposed (Crestini et al., 2017). Considering the chemical differences between the soluble and insoluble part, it is shown that the acetone soluble lignins are of lower molecular weights, but also to a greater extent cross-linked and/or condensed, as for example through 5-5' linkages and through a higher degree of aromatic substitution. Lignins of a more 'native' structure, i.e., exhibiting a low degree of condensation and high β -O-4' content are considerably more flexible (Besombes and Mazeau, 2004), and can in any pure solvent system experience a free-energy pay-off through various mechanisms: i) hydrophobic interactions, as function of the total hydrophobic area, displayed functional groups and/or molecular weight (Vermaas et al., 2019) if proper aromatic interactions can be achieved, and ii) interactions offered by the solvent. This chain flexibility is lost when condensed aliphatic and aromatic structures, e.g., β -5', β - β ', or 5-5', dominate in the lignin (Vermaas et al., 2019). By looking into the acetone soluble lignin fraction (Crestini et al., 2017), this illustrates a scenario where the interactions offered by the solvent can overcome those offered between the lignin molecules. Considering the interactions that the acetone molecule could offer to the lignin structures, traditional hydrogen bonding with aliphatic or aromatic hydroxyls are likely important. Hydrogen acceptor capacities towards to the sp² C-H groups have already been mentioned as important for cellulose dissolution in ionic liquids. However, as discussed earlier in the case of chloroform as solvent for lignin dissolution, also the σ^* orbitals of the sp³ C-H groups appear susceptible for this type of interaction. Oxygen-bound lone pairs are also present in the lignin in form of the aryl-alkyl ethers and the methoxy groups and could potentially offer lone-pairs to, for example, σ^* orbitals of the acetone C-H. This effect, as well as the one occurring between σ^* of C-H in acetone and a lignin-based π -donor (Nijamudheen et al., 2012), appear favoured in case of mixed solvent systems as with

water/acetone. This was also found to promote lignin solubility on the basis of a putative water-driven polarization of acetone (Zhong and Patel, 2009). NMR data obtained for various lignin model compounds, investigating the change in chemical shifts for a β -O-4' dimer support this theory: A large down-field shift of C-2 which occurs at the same time as for the C-4' on the second ring (Hawkes et al., 1993). These carbons are either π electron donors or close to electron donors, with C-4' being adjacent the aryl-ether oxygen and ring C-5', and both experience down-field shifts in acetone/water as they should upon rehybridization of surrounding carbons interacting through a lone pair to C-H (Alabugin et al., 2003). This effect can be enhanced by the addition of water due to two reasons. (1) Water polarizes the acetone molecule by hydrating the carbonyl oxygen making the methyl hydrogens slightly more acidic and better acceptors upon interaction with lignin π donors (Alabugin et al., 2003), thus making both sides of the acetone molecule capable of interacting with the aromatic functionality of lignin: through polarized methylene groups with lignin π donors (Nijamudheen et al., 2012), and by the free carbonyl group potentially donating lone pairs to the sp^2 C-H. (2) In addition, exposing lignin to the employed solvent system is likely to shift the equilibrium state of the bulk solvent, due to differing affinities for the specific solvent structures, and by the tendency of the water structure to remain intact, and hence essentially 'phase-separating' and enhancing acetone-lignin interaction.

In terms of lignin solubility in DMSO, a situation different from that delineated for carbohydrates is encountered. The polyphenolic lignin structure is far more irregular, the functionalities more sporadic and less prone to too strong aggregation and solvent hydration, as illustrated with the increase in lignin solubility (Jääskeläinen et al., 2017) when water percolation is lost (Zhong and Patel, 2009). The structure of the bulk solvent and its effect on dissolution is further illustrated when comparing acidic systems with alkaline ones; the heat of hydration of the hydronium ion is almost three times that of the hydration of a hydroxyl ion in water (Zatsepina, 1972); the hydronium ion also experiences a far greater proton transfer relative to the isolated hyper-coordinated hydroxyl ion (Chen et al., 2018). These aspects lead to an overall increased solution coherency for acidic systems. These two systems would present cases where the enthalpic drive exerted by the bulk reference toward hydrophobic interactions among biopolymeric species go in opposing directions when compared to pure water. This is exploited for example when performing acid gradient precipitation of lignin (Santos et al., 2014), with lignin dissolution increasing upon increased alkalinity (Melro et al., 2020).

7. Importance of a holistic view where the solute and hydrated solute structures equilibrate each other

When bringing collapsed, solid polymers with specific functional groups to a solution system, emerges the possibility of re-distributing the solvent species, their coordination number and structure. While one type of solvent structures might exist prior to mixing the solvent with the polymer, this will change as for example the cellulose hydroxyls are introduced. As the driving forces for specific polymer-solvent interaction is the lowering of the Gibbs energy, the contribution from the polymer will be significant for the nature of the chemical equilibrium especially at higher polymer concentrations. This emphasizes the important aspect that it is essentially the state of the pure solvent, and the nature and structural and electronic flexibility of the polymer in question which dictates when this equilibrium is reached, meaning that there is no energetic reason for the bulk solvent to further re-adjust, as any additional increase/decrease in polymer entropy/enthalpy will not cause the Gibbs energy to decrease and one reaches saturation. This is illustrated, for example, by the modes the bulk-solvent structures, in this case a choline-chloride-glycerol-water system, rearrange as they are exposed to a solid surface, *i.e.*, Mica (Elbourne et al., 2021). It was found that the hydration structure of the solid interface was different from the bulk, and importantly, both continuously changed as the DES-to-water content was

altered. Obviously, the ratio of solid interface, or solute, to solvent would also change the interface hydration structure, which is relevant when evaluating solid/liquid ratios for systems set to process biomass. Any specific polymer will, in any solvent system, have an ideal solvent composition/structure in its hydration layer for liberation of the entropic potential and dissolution, meanwhile, this specific molecular construct of the solvent around the solute might be energetically expensive in terms of increased/decreased enthalpy/entropy of the bulk solvent, causing polymer dissolution to be a compromise between the state of the bulk and the hydrated polymer.

8. Future perspectives

Most of today's processes developed for treatment of lignocellulosic material employ substantially high temperatures in order to achieve proper biomass fractionation. This is essentially a necessity in order to operate at conditions where the polymers in the material experience structural and eventually even electronic mobility such as that the components undergo dissolution and depolymerization into smaller fragments. Often insufficiency of solvent systems is sought to be overcome by employing elevated temperatures. Obviously, the application of high temperatures does not only cause issues when considering economically viable processes due to high energy consumption, but give rise also to problems related to continuous processing when employing volatile organic solvents that necessitate high processing pressures. To contrast this, novel systems are investigated which achieve full dissolution of entire wood by fulfilling the innate requirements the components in lignocellulosic biomass pose for dissolution and depolymerisation at temperatures around 100 °C. This is achieved by considering the necessities required to actually cause polymer chain movement. From the discussions in the present work, a few interesting routes emerge. First, considering efficient dissolution of entire lignocellulosic biomass, the fact that all the constituents essentially can benefit from the fundamentals governing cellulose dissolution is interesting. As discussed, the presence of hydration structures which operate dynamically between solute and bulk solvent is key to allow for conformational fluctuations in the solute. In the first layer, anions such as chloride and acetate are proven to work. In the second layer, mostly cations with aromatic properties have found to work especially when considering ILs. DES-based systems have allowed to evaluate several other combinations, but the systems are often more complex in which the hydration layer forming around solutes such as cellulose are harder to predict. It would seem nevertheless feasible that binary systems based on the summarized findings herein, employing components specifically set to take their place in the second layer, and allowing an interaction similar to that of chloride or acetic acid, seem reasonable as starting points for the development of novel systems for biomass dissolution, *i.e.*, systems that allow for a certain anion to interact dynamically between the first and second solvent layers, employing solvent components with certain functionality, allowing hence for a dynamic solvation structure. Solvent composition, however, would have to be optimized, also in light of the amount and the specific type of biopolymers/biomass exposed to the solvent.

Naturally occurring and renewable aromatic solvent structures also dedicated to the second layer could be based on furans, although their thermal stability is likely to represent a challenge. Another promising route which could allow easy manipulation of the solvent-solute dynamics is the use of solid, inert surfaces with selected functionalities that cause solvent equilibrium shifts and thus changes in the modes of hydrating the relevant biopolymers. Finally, electromagnetic waves were shown to polarize the solvent in close proximity to the solute in question, forcing the solute to re-adjust its electronic structure to that of the moving solvent molecules surrounding it. Such an approach is interesting as it should reduce the longevity of secondary bonds in the bulk solvent thus reducing the energetic threshold for when the solute entropy increase is favorable. This seems a strategy which could hold

significant potential if adapted to a suitable scale.

9. Conclusion

This review highlights the fundamentals governing the solubility of the relevant constituents of lignocellulosic biomasses. The fundamental processes, most noteworthy, do not necessarily require a chemical alteration of the structures in terms of bond cleavages *per se*, but work on the basis of close interactions between solute and solvent and resulting conformational changes. The insights generated on the basis of the combined and holistic reviewing of the archival literature form the ground for new ideas and methods to develop, such as that competitive extraction of single polymeric products, *i.e.*, carbohydrates or lignins, can be achieved in the most efficient way.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.biortech.2022.128447>.

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