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Deep eutectic solvents and applications in electrochemical sensing

Christopher M.A. Brett*

This review focusses on deep eutectic solvents (DES) and their applications in the construction of electrochemical sensing platforms. The preparation and properties of DES are first described, with a brief survey of their applications, focusing on recent advances concerning materials and coatings prepared in DES as solvent. Their importance in the preparation of electrochemical sensors is then addressed in more detail, particularly regarding electroactive conjugated polymer and redox polymer modified electrodes. Future perspectives in the electrochemical sensing and biosensing fields are discussed.

Address
Department of Chemistry, Faculty of Sciences and Technology, University of Coimbra, 3004-535 Coimbra, Portugal

*Corresponding author: Brett, Christopher M.A. (cbrett@ci.uc.pt)

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Introduction

Deep eutectic solvents (DES), introduced by Abbott *et al.* in 2001, [1], have shown themselves to be very interesting and useful alternatives to non-aqueous solvents and room temperature ionic liquids (IL), with applications in many fields. The increasing amount of interest has led to many reviews being published concerning the synthesis of DES, their properties and applications, recent examples being [2–4]. Less attention was given to the materials' aspects until the publication of a recent review, which discussed advances in the fields of polymer science, metal processing and nanotechnology [5•]. The field of DES is in rapid expansion as can be seen from the number of articles published, increasing from around 130 in 2013 to over 600 in 2017. This short review will briefly examine the different types of DES, their properties and fields of application. It will then address their use in the preparation of sensor platforms, and electrochemical sensing, which is an area that has, so far, been little exploited.

Types, preparation and properties of deep eutectic solvents

DES synthesis is a simple green method, in principle using non-toxic components, and not giving rise to any secondary products, unlike IL, which require organic synthetic procedures and whose toxicity has sometimes been called into question [6]. For a successful and widely-useable DES, the components should be safe, be low cost and be biodegradable, besides the low toxicity. Normally, they consist of just two components which interact strongly to form a eutectic mixture; DES refers to stoichiometric ratios that are close to the eutectic composition. Whereas the two components are solid at a temperature below 100°C, the mixture is liquid.

Deep eutectic solvents can be described by the general formula Cat^+-X^- zY with Cat^+ being ammonium, sulfonium, or phosphonium and X^- a Lewis base, normally a halide. The HBD, a Lewis or Brønsted acid, Y, forms a "complex" with X^-. DES are usually divided into four types: Type I (quaternary salt and metal halide), Type II (quaternary salt and hydrated metal halide), Type III (quaternary salt and hydrogen bond donor) and Type IV (metal halide and hydrogen bond donor), see Table 1 and Ref. [3•].

Most of the DES employed are Type III. Here, the formation of the eutectic is due to strong hydrogen bond interactions between a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD). One of the most prevalent Cat^+-X^- is choline chloride (ChCl) also known as Vitamin B4. Common examples of the Type III HBD are urea, ethylene glycol and glycerol, which give rise to DES with the common names of reline, ethaline and glyceline.

Thus, hydrogen bonding is an essential mechanism for the formation of these DES and influences their properties; this has been extensively discussed in the literature using data from computational studies [7]. The greater the hydrogen bonding network interaction, the greater the depression in melting point and the higher the viscosity of the mixture. Interestingly, and this is important for electrochemical applications, theoretical studies predict that the introduction of water at low mole fractions does not affect ionic diffusion since the water molecules are absorbed into the DES molecular matrix [8]. At higher mole fractions they have a pronounced effect, as would be expected.

Two special classes of DES have been recently gaining increasing attention and which can be expected to continue.

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Table 1

The main types of DES (adapted from ref [3•]) and identifying M and Z species (Lewis or Brønsted acids).

Type	Formula	Terms
I	$Cat^+X^-\ zMCl_x^-$	M: Zn, Sn, Fe, Al, Ga, In
II	$Cat^+X^-\ zMCl_x.yH_2O$	M: Cr, Co, Cu, Ni, Fe
III	$Cat^+X^-\ zRZ$	Z: $CONH_2$, COOH, OH
IV	$MCl_x + RZ = MCl_{x-1}{}^+.RZ + MCl_{x+1}$	M: Al, Zn; Z: $CONH_2$, OH

These are the natural deep eutectic solvents (NADES) and the therapeutic deep eutectic solvents (THEDES). NADES, the first report of which was in 2011 [9] are mixtures containing combinations of metabolites that occur in large amounts in cells, with a crucial role in cryoprotection, drought resistance, germination and dehydration. They have been regarded as the third liquid phase in living organisms, the solubility of many natural products being greater in NADES than in water. It was shown that there is hydrogen bonding between the constituents in mixtures of ChCl with a variety of natural products such as organic acids, alcohols, sugars or aminoacids and the future role of NADES in the food, cosmetic and pharmaceutical industries has been pointed out. NADES have been successfully applied in extraction and separation processes for example [10], and their importance in analytical chemistry has been assessed [11].

THEDES are bioactive eutectic systems composed of an active pharmaceutical ingredient as one of the DES constituents [12]. The interest is due to their potential use as improved pharmaceutical formulations, to increase drug solubility and permeability and thence provide more efficient drug delivery. It has been established that the dominant interactions are of a hydrogen bond nature.

The principle of preparation of DES is simple and is done in one of two ways: (1) the lower melting point component is first heated until it melts, and then the higher melting point compound is added to form the eutectic mixture; (2) when both constituents have high melting points, the two components are mixed and melted together. Many DES have been prepared; more details and many examples are given in [5•].

Besides the advantages of DES referred to above of high solubility, low toxicity and biodegradability they also exhibit low volatility, non-flammability, low vapour pressure, chemical and thermal stability [13]. As solvents, they are chemically tuneable, and their properties can be tailored to have different physicochemical properties, according to the applications envisaged. Extensive data on physicochemical properties such as phase behavior, density, viscosity, conductivity, surface tension, ionicity, electrochemical behavior, toxicity and environmental impact of numerous DES is available in the literature, for example [3,6,13,14].

Most research has been done in polymer, metal processing and nanomaterials science. In the following section, there is a short description of materials prepared with the use of DES in these three areas. All of these can have implications for the preparation of sensor platforms.

Applications of DES

DES have been used in polymer science as solvents, functional additives and monomers; further details can be found in [5•]. As solvents, the HBA has nearly always been ChCl, for example as reported in [15]. Reline (ChCl-urea) has even been suggested as solvent for redox flow batteries using the Fe(III)/Fe(II) couple [16]. DES have also been used in the electrochemical synthesis and deposition of conducting and redox polymers – this will be returned to later in the context of modified electrodes for sensors. Besides acting as solvents, DES can function as templates and/or ligand suppliers, and in extraction, separation and purification technologies. DES have been suggested as an eco-friendly choice in the preparation of molecularly imprinted polymers (MIPs), since these solvents can improve the affinity and selectivity of MIPs to a target molecule [17].

Electrodeposited coatings can exhibit a variety of different characteristics and functionalities; however, not all metal/substrate combinations are possible by electrodeposition in aqueous media. DES, like non-aqueous solvents, can extend the range of coating/substrate combinations, through an extended potential window and greater inertness [18]. This has included coatings for corrosion protection of less-noble metals, as well as in sensor technology, in combination with nanomaterials such as polymers and carbon materials. In this context, the temperature-viscosity dependence of DES has been investigated, due to its practical and industrial relevance in the electrodeposition of metals and alloys. Further details and examples may be found in [5•].

DES have been used as reaction media for nanomaterial synthesis and electrodeposition, and as dispersion medium for nanoparticles. Carbon nanomaterials have been the most popular, followed by metal oxide and gold nanoparticles, inorganic (bio)nanomaterials and metal (bio)organic framework materials. The use of DES in nanotechnology up until 2015 is described in [4].

An example that is relevant for pointing the way towards the development of new nanomaterial-modified electrodes as electrochemical sensor platforms is the electrochemical synthesis of nanoporous gold decorated with manganese oxide nanowires [19]. The use of DES as

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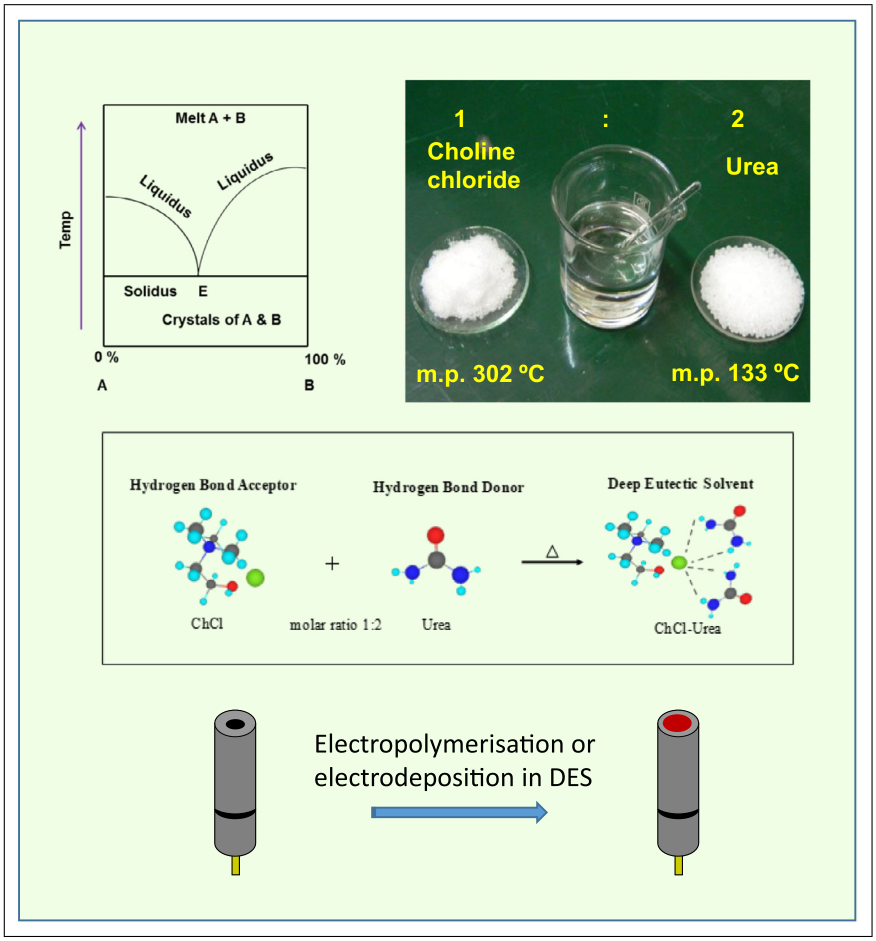
Figure 1



The principle behind Type III eutectic solvents, illustrated with reline (choline chloride and urea), and their use in altering the structure and morphology of modifier films on electrodes by electropolymerization or electrodeposition.

nanomaterial functionalization agents has focused on the functionalization of carbon nanotubes, partly to increase their dispersability; an application has been that of forming new adsorbents for the removal of heavy metal contaminants in waters, e.g. [20].

Modified electrodes and electrochemical sensing

DES have been used in analytical procedures, but the detection methods employed up until now have been essentially chromatographic or spectroscopic, see [21].

Interest has been shown in modifying electrode surfaces in DES as part of preparation methods for electrochemical sensors and biosensors with different properties, Figure 1. In a similar way as occurs in IL [22], the rationale is that the different surface morphologies, compared to aqueous solution, will condition access by the analyte to the sensor platform in a different way and the new surface structure may confer different, hopefully enhanced, sensing properties. Various techniques, including the electrochemical quartz crystal microbalance, have been used to follow the process of polymer film growth.

Conducting polymer films have been formed in DES. Early examples were polypyrrole in ethaline [23] and polyaniline in a 1:2 ChCl/1,2-ethanediol mixture [24]. In the latter case, examination of the morphology and optical properties of the polyaniline films by SEM and UV-vis spectroscopy, evidenced a nanoparticulate morphology and excellent conductivity.

More recently, research concerned examination of the morphology and properties of PEDOT films with a view to their use in electrochemical sensors [25,26]. Comparison was made between polymer films formed in eutectic mixtures composed of ChCl and ethylene glycol, glycine or urea on glassy carbon electrode supports and those formed in aqueous solution. An example of morphological differences can be seen in Figure 2. Both reline and etha-

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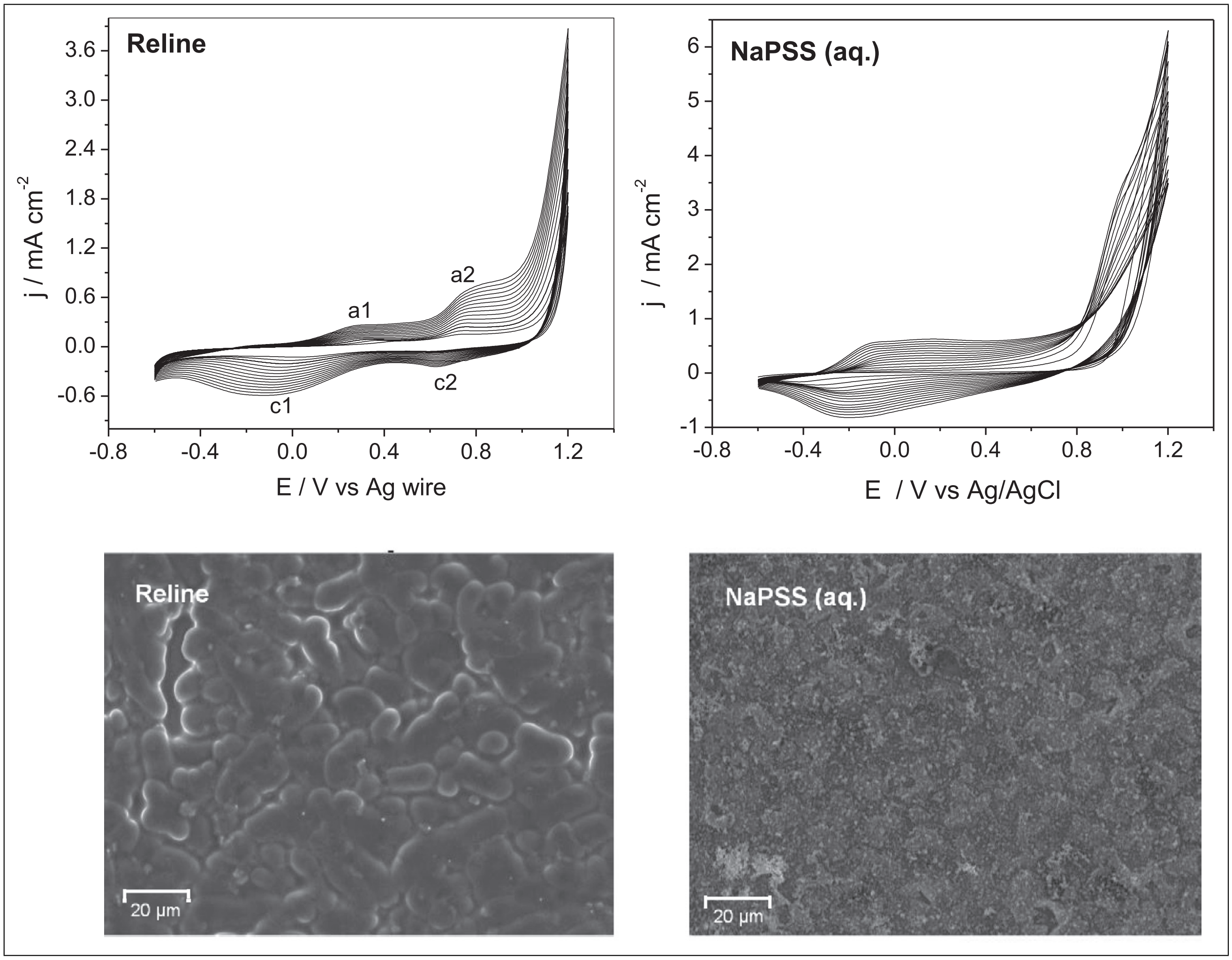
Figure 2



Electropolymerisation of EDOT in Reline and in 0.1 M sodium poly(styrene sulfonate) (NaPSS) with corresponding scanning electron microscopy images of the films formed. Adapted from [25].

line showed encouraging electrocatalytic and morphological properties, and demonstrated advantageous sensing characteristics compared to those of PEDOT-modified GCE prepared in aqueous solutions. They were successfully applied as sensors, in aqueous buffer solution, for mixtures of ascorbate, dopamine and uric acid as biomarkers. Detailed studies included the effect of varying the amount added of a second HBD, perchloric acid, and the influence of increasing temperature (decreasing the viscosity). Whereas the former has a significant effect, the latter was found to have less influence on the polymer film characteristics. It does demonstrate that experimental conditions need to be optimized for each case.

Other polymers of interest in electrochemical sensor and biossensor architectures are electroactive redox polymers. Many of these have been formed from phenazine and triaryl-methane monomers in aqueous solution, and used as modifiers together with nanomaterials such as carbon nanotubes or graphene, and have been shown to be excellent mediators in a number of sensor and biosensor architectures [27]. As for conducting conjugated polymers, the electrocatalytic effects and current enhancement in sensing if the films are formed in DES could be greater than those formed in aqueous media owing to the altered polymer film nanostructure and morphology. Such effects had already been noted with poly(neutral red) films formed in IL [22]. Poly(methylene blue) was deposited by electropolymerization in ethaline eutectic mixtures on glassy carbon electrodes and comparison was made with films formed in aqueous media [28]. It was seen that the influence of the rate of potential change on the potentiodynamic growth of the polymer film was an important factor for film growth, structure and morphology, owing to the

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viscous nature of the DES. Thus, an optimum scan rate was found, above which the diffusion of monomer from the bulk DES becomes a rate-limiting factor. In addition, the PMB films obtained in DES exhibited better sensing performance for ascorbate and acetaminophen in aqueous solution, compared to those prepared in aqueous media [29•].

Other electrochemical sensor applications in the literature involve carbon nanotube modified electrodes. Quercetin [30] and cadmium ions [31] were determined with enhanced sensitivity in reline DES. Finally, and as another type of application, an amperometric sensor has been developed for atmospheric oxygen using a thin film of ethaline DES directly on a membrane-free oxygen probe [32].

Conclusions and perspectives

As can be seen from the above, DES constitute an interesting tool in the preparation of new nanostructured materials on electrode substrates, some of which cannot be prepared in aqueous media. The DES medium also has an influence on the structure and morphology of such films, and thence electrocatalytic properties and active surface area. Owing to their non-toxic nature and generally extreme ease of preparation, DES will have a future ensured not only by their physicochemical properties but also by their economic viability, important in the context of sustainable development. The replacement of conventional solvents and IL by DES is definitely predicted to become an increasingly common practice. This short review has highlighted advantages, relevance and potentialities of DES in the context of creation of electrochemical sensor platforms and electrochemical sensing. DES is a field that has been in rapid expansion in the last decade, but this expansion has so far only been touched upon in the context of sensor construction. More research is needed in order to understand how to exploit DES in the most appropriate way. Much remains to be investigated and exploited with the ultimate goal of contribution towards increasing the efficiency and stability of electrochemical sensors and biosensors.

Conflict of interest

The author declares no conflict of interest.

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References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • Paper of special interest
- •• Paper of outstanding interest.

1. Abbott AP, Capper G, Davies DL, Munro HL, Rasheed RK, Tambyrajah V: **Preparation of novel, moisture-stable, Lewis-acidic ionic liquids containing quaternary ammonium salts with functional side chains**. *Chem Commun* 2001:2010–2011.
2. Wagle DV, Zhao H, Baker GA: **Deep eutectic solvents: sustainable media for nanoscale and functional materials**. *Acc Chem Res* 2014, **47**:2299–2308.
3. • Smith EL, Abbott AP, Ryder KS: **Deep eutectic solvents (DESs) and their applications**. *Chem Rev* 2014, **114**:11060–11082.
This review gives an excellent description of the different types of DES, their synthesis and physicochemical properties, as well as the range of applications in which they have been used up to 2014.
4. Abo-Hamad A, Hayyan M, AlSaadi MA, Hashim MA: **Potential applications of deep eutectic solvents in nanotechnology**. *Chem Eng J* 2015, **273**:551–567.
5. • Tomé LIN, Baião V, da Silva W, Brett CMA: **Deep eutectic solvents for the production and application of new materials**. *Appl Mater Today* 2018, **10**:30–50.
This review gives an up-to-date survey of materials applications of DES.
6. Kudłak B, Owczarek K, Namieśnik J: **Selected issues related to the toxicity of ionic liquids and deep eutectic solvents—a review**. *Environ Sci Pollut Res* 2015, **22**:11975–11992.
7. Perkins SL, Painter P, Colina CM: **Experimental and computational studies of choline chloride-based deep eutectic solvents**. *J Chem Eng Data* 2014, **59**:3652–3662.
8. Zhekenov T, Toksanbayev N, Kazakbayeva Z, Shah D, Mjalli FS: **Formation of type III deep eutectic solvents and effect of water on their intermolecular interactions**. *Fluid Phase Equilib* 2017, **441**:43–48.
9. Choi YH, van Spronsen J, Dai Y, Verberne M, Hollmann F, Arends IWCE, Witkamp G-J, Verpoorte R: **Are natural deep eutectic solvents the missing link in understanding cellular metabolism and physiology?** *J Am Soc Plants Biol.* 2011, **156**:1701–1705.
10. Li N, Wang Y, Xu K, Huang Y, Wen Q, Ding X: **Development of green betaine based deep eutectic solvent aqueous two-phase system for the extraction of protein**. *Talanta* 2016, **152**:23–32.
11. Espino M, Fernández MA, Gomez FJV, Silva MF: **Natural designer solvents for greening analytical chemistry**. *Trends Anal Chem* 2016, **76**:126–136.
12. Duarte ARC, Ferreira ASD, Barreiros S, Cabrita E, Reis RL, Paiva A: **A comparison between pure active pharmaceutical ingredients and therapeutic deep eutectic solvents: solubility and permeability studies**. *Eur J Pharm Biopharm* 2017, **114**:296–304.
13. Zhang Q, Vigier KO, Royer S, Jérome F: **Deep eutectic solvents: synthesis, properties and applications**. *Chem Soc Rev* 2012, **41**:7108–7146.
14. Mbous YP, Hayyana M, Hayyan A, Wong WF, Hashim MA, Looi CY: **Applications of deep eutectic solvents in biotechnology and bioengineering—promises and challenges**. *Biotechnol Adv* 2017, **35**:105–134.
15. Mota-Morales JD, Sánchez-Leija RJ, Carranza A, Pojman JA, del Monte F, Luna-Bárcenas G: **Free-radical polymerizations of and in deep eutectic solvents: green synthesis of functional materials**. *Prog Polym Sci* 2018, **78**:139–153.
16. Xu Q, Zhao TS, Wei L, Zhang C, Zhou XL: **Electrochemical characteristics and transport properties of Fe(II)/Fe(III) redox couple in a non-aqueous reline deep eutectic solvent**. *Electrochim Acta* 2015, **154**:462–467.
17. Ansaria S, Karimi M: **Recent configurations and progressive uses of magnetic molecularly imprinted polymers for drug analysis**. *Talanta* 2017, **167**:470–485.
18. Bernasconi R, Panzeri G, Accogli A, Liberale F, Nobili L, Magagnin L: **Electrodeposition from deep eutectic solvents**: *Progress and Development in Ionic Liquids*. Edited by Handy S: Intech; 2017:235–261.
19. Bozzini B, Busson B, Humbert C, Mele C, Tadjeddine A: **Electrochemical fabrication of nanoporous gold decorated with manganese oxide nanowires from eutectic urea/choline**

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chloride ionic liquid. Part III Electrodeposition of Au–Mn: a study based on in situ sum-frequency generation and Raman spectroscopies. *Electrochim Acta* 2016, **218**:208–215.

20. AlOmar MK, Alsaadi MA, Hayyan M, Akib S, Hashim MA: **Functionalization of CNTs surface with phosphonium based deep eutectic solvents for arsenic removal from water**. *Appl Surf Sci* 2016, **389**:216–226.

21. Shishov A, Bulatov A, Locatelli M, Carradori S, Andruch V: **Application of deep eutectic solvents in analytical chemistry. A review**. *Microchem J* 2017, **135**:33–38.

22. Pauliukaite R, Doherty AP, Murnaghan KD, Brett CMA: **Application of some room temperature ionic liquids in the development of biosensors at carbon film electrodes**. *Electroanalysis* 2008, **20**:485–490.

23. Skopek MA, Mohamoud MA, Ryder KS, Hillman AR: **Nanogravimetric observation of unexpected ion exchange characteristics for polypyrrole film p-doping in a deep eutectic ionic liquid**. *Chem Commun* 2009:935.

24. Fernandes PMV, Campina JM, Pereira NM, Pereira CM, Silva F: **Biodegradable deep-eutectic mixtures as electrolytes for the electrochemical synthesis of conducting polymers**. *J Appl Electrochem* 2012, **42**:997–1003.

25. Prathish KP, Carvalho RC, Brett CMA: **Highly sensitive poly(3,4-ethylenedioxythiophene) modified electrodes by electropolymerisation in deep eutectic solvents**. *Electrochem Commun* 2014, **44**:8–11.

26. Prathish KP, Carvalho RC, Brett CMA: **Electrochemical characterisation of poly(3,4-ethylenedioxythiophene) film modified glassy carbon electrodes prepared in deep eutectic solvents for simultaneous sensing of biomarkers**. *Electrochim Acta* 2016, **187**:704–713.

27. Barsan MM, Ghica ME, Brett CMA: **Electrochemical sensors and biosensors based on redox polymer/carbon nanotube modified electrodes: a review**. *Anal Chim Acta* 2015, **881**:1–23.

28. Hosu O, Barsan M, Cristea C, Sandulescu R, Brett CMA: **Nanostructured electropolymerized poly(methylene blue) films from deep eutectic solvents. Optimization and characterization**. *Electrochim Acta* 2017, **232**:285–295.

29. Hosu O, Barsan MM, Cristea C, Sandulescu R, Brett CMA:
• **Nanocomposites based on carbon nanotubes and redox-active polymers synthesized in a deep eutectic solvent as a new electrochemical sensing platform**. *Microchim Acta* 2017, **184**:3919–3927.
This article demonstrates clearly how the growth of polymers can be monitored in DES and characterised with a view to film optimisation.

30. Zheng Y, Ye L, Yan L, Gao Y: **The electrochemical behavior and determination of quercetin in choline chloride/urea deep eutectic solvent electrolyte based on abrasively immobilized multi-wall carbon nanotubes modified electrode**. *Int J Electrochem Sci* 2014, **9**:238–248.

31. Gao J, Xiong H, Gao Y, Zhang J, Yang H, Ma X: **The electrochemical analysis of cadmium in choline chloride/urea deep eutectic solvent electrolyte at carbon nanotubes modified electrode**. *Int J Electrochem Sci* 2016, **11**:6306–6314.

32. Toniolo R, Dossi N, Svigelj R, Pigani L, Terzi F, Abollino O, Bontempelli G: **A deep eutectic solvent-based amperometric sensor for the detection of low oxygen contents in gaseous atmospheres**. *Electroanalysis* 2016, **28**:757–763.

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