Experimental Dielectric Spectroscopic Investigation of Room Temperature Biodegradable Eutectic Solvents and Related Chemical Systems

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Abstract

The main focus of this Thesis is the study of interaction and relaxation dynamics of room temperature biodegradable eutectic solvents and other complex systems via experimental dielectric relaxation (DR) spectroscopy, time-resolved fluorescence (TRF) spectroscopy and other measurement methods, and molecular dynamics simulations. A significant part of the work in this thesis is dedicated to deep eutectic solvents (DES), which includes ionic DES, naturally abundant DES (NADES), therapeutic DES (THEDES) and low viscosity green solvent. The selection of DESs components have been inspired by certain industrial needs and aims to minimize the ecological footprint through suitable replacement of common organic solvents. The need to explore new solvents also arises from the solubility aspects of drugs and therapeutic administration. In this Thesis we have extensively explored the interaction and dynamics of these DESs via DR, TRF and complemented the findings, wherever possible, with results from molecular dynamics simulations.

A combined experimental and simulation study of DR in a naturally abundant DES composed of betaine, urea and water was carried out to explore the interaction and dynamics of the system by separating out the constituent contributions arising from the self and the cross interactions via molecular dynamics simulations. Simulation results suggested that the collective single molecule reorientational relaxation and the structural hydrogen bond fluctuation dynamics, not the hydrodynamic single molecular rotations, hold the key to understand the multiple relaxation timescales measured DR experiments.

We next studied ionic acetamide DESs containing NaSCN and KSCN salts where focus was on to explore and understand the impact of successive replacement of K^+ by Na^+ on the measured DR. Both experimental and simulated DR showed multi-Debye relaxations and a decrease in the static dielectric constant (ε_s) upon Na^+ substitution. Na^+-DES exhibited stronger viscosity decoupling, higher glass transition temperature (~220 K), and increased fragility compared to K^+-DES. Simulations suggested significant rupture of the acetamide-acetamide H-bond network structure in this DES and a linear decrease of the ε_s with the average number of H-bonds per acetamide molecule. Cation-dependent cross interactions had negligible impact on ε_s.

The poor water solubility of aspirin, a nonsteroidal anti-inflammatory drug, led to the engineering of a THEDES containing aspirin and menthol at 1:4 molar ratio which significantly enhanced the solubility of aspirin. Preliminary investigation of its structure and dynamics was carried out by combining TRF with computer simulations. TRF revealed a strong temporal heterogeneity in the medium and a significant decoupling between medium viscosity and solute dynamics. Computer simulations revealed extensive inter-molecular H-bond formation.

To counter the adverse effects of high viscosity on important chemical reactions, we have developed a low-viscosity, transparent, multi-component molten mixture using biocompatible sorbitol, urea, and water. The ε_s of this molten mixture is similar to that of water ($\varepsilon_s{\sim}80$) and makes it an excellent solvent, even though its dynamics are much slower than water. Frequency-dependent DR measurements within the range $0.2 \leq \nu/GHz \leq 50$ unveil multi-Debye relaxation steps in this medium, with the average relaxation time spanning from ~400 ps to 100 ps. Fluorescence emission studies using fluorescent dyes, namely coumarin 153 (C153) and coumarin 343 (C343), suggest the medium being spatially homogeneous, although the study of rotational dynamics indicates presence of weak temporal heterogeneity.

Apart from preparing designer solvents, this Thesis deals with capturing ultrafast solvation of glycerol and ethylene glycol (EG) using a streak camera providing a temporal resolution ~2 ps. We combined streak camera and time-correlated single photon counting (TCSPC) data which captured nearly 90% of the total solvation of EG and suggested that solute lifetime may play an important role in capturing sub-picosecond solvent response.

Addressing organ dysfunction stemming from hyaluronic acid (HA) aggregation in aqueous environments necessitates a thorough investigation of concentration-dependent HA aggregation. This is pivotal as the minimum concentration threshold for HA aggregation ($c_{\mathrm{HA}}^{\mathrm{Aggre}}$) governs structural transitions, leading to slower relaxation dynamics in bulk water. Analysis of various parameters in DR and conductivity measurements indicates approximately 0.5 - 0.66 wt% HA in water as the critical concentration for HA aggregation. DR measurements reveal the emergence of biphasic water dynamics with 'slow' and bulk-like relaxations having time constants around 0.3-4 ns and ~10 ps, respectively, as $c_{\mathrm{HA}}^{\mathrm{Aggre}}$ was approached. Differential scanning calorimetric measurements further supported the existence of two types of water.

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