



Multiscale mechanistic design of hydrophobic natural DES for PFAS extraction: from quantum chemistry to high-throughput screening

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ABSTRACT

Per- and polyfluoroalkyl substances (PFAS) are persistent, toxic pollutants that pose serious challenges for water remediation due to their resistance to degradation and the limitations of existing treatment technologies. In this study, we explore a nature-inspired strategy for PFAS extraction from water using hydrophobic natural deep eutectic solvents (HNADES), applying a multiscale *in silico* approach. Through quantum-chemical methods rooted in Density Functional Theory (DFT), COnductor-like Screening MOdel for Real Solvents (COSMO-RS) thermodynamic modeling and classical molecular dynamics (MD) simulations, we demonstrate that the selected HNADES exhibits strong affinity for three representative PFAS (PFOA, PFOS and HFPO-DA). This affinity arises from robust hydrogen bonding between PFAS acidic proton of the terminal functional group and the carbonyl group of decanoic acid, supported by favorable van der Waals interactions. The extraction process is further stabilized by internal hydrogen bonding within the HNADES, preserving its structural integrity. These molecular-level interactions translate into high PFAS solubilities and activity coefficients approaching zero, effectively enabling the disruption of PFAS hydration shells and facilitating their migration across the (HNADES)-(PFAS + water) interface into the organic phase. A strong correlation was observed between molecular descriptors and mixture behavior, laying the groundwork for predictive models of extraction efficiency. Building on these insights, we conducted an extended virtual screening of 1746 PFAS against 2589 HNADES combinations, identifying promising candidates for selective, scalable and environmentally friendly remediation technologies, with the most hydrophobic HNADES—primarily those containing linalool, verbenone and cineole—solubilizing the widest range of PFAS.

1. Introduction

PFAS are a large class of synthetic organofluorine compounds characterized by a hydrophobic and oleophobic perfluorinated carbon backbone and a terminal hydrophilic group, most commonly a carboxylic or sulfonic acid [1]. Due to their remarkable chemical and thermal stability, surfactant properties and dielectric characteristics [2], PFAS have been extensively employed in industrial and consumer products since the mid-20th century. Applications range from non-stick cookware, food packaging, waterproof textiles, stain-resistant upholstery, detergents and cosmetics; to paints, coatings, pesticides and fire-fighting foams [3,4]. The very property that makes PFAS so useful, the extraordinary thermodynamic stability of the carbon-fluorine bond—the strongest in organic chemistry—is equally responsible for their

environmental fate [5,6]. This structural robustness renders PFAS essentially inert to biological, chemical and photolytic degradation, enabling them to persist and accumulate across water, soil, sediment and biotic compartments globally. PFAS have now been detected ubiquitously in drinking water, wastewater and stormwater [7], and their capacity for biomagnification along food chains means that apex predators (including humans) carry the highest tissue burdens. The toxicological consequences of this persistence are severe. PFAS bioaccumulate preferentially in hepatic tissue and plasma proteins, resisting elimination and sustaining chronic internal exposure even after external contact ceases. Epidemiological and experimental evidence links PFAS exposure to a broad and serious spectrum of health outcomes: dyslipidemia, reproductive and developmental toxicity, immunotoxicity and profound disruption of the endocrine system, particularly of thyroid hormone

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Table 1

Electron densities (ρ) and bond distances associated with hydrogen bonds in the isolated HNADES.

Extractant molar ratio	ρ (a.u.) of BCP/bond distance (Å)		
	(Decanoic acid 1)	(Decanoic acid 2)	(Menthol 1)
	H...O(menthol 1)	H...O(decanoic acid 1)	H...O(menthol 2)
1:1	0.05165/1.65		
1:2	0.05607/1.61	0.04096/1.71	
2:1	0.06226/1.58		0.04023/1.76

homeostasis, with cascading effects on metabolism, neurological development and fertility [8,9]. Of particular concern is their carcinogenicity. Several long-chain PFAS compounds have been classified as possible or probable human carcinogens, with epidemiological studies consistently associating exposure with elevated risks of kidney and testicular cancers. Critically, short-chain PFAS developed as ostensibly safer replacements are increasingly recognized as raising comparable environmental persistence and toxicological concerns, undermining substitution as a viable long-term strategy [10]. Taken together, the combination of ubiquitous environmental distribution, resistance to remediation, progressive bioaccumulation and well-documented carcinogenic and endocrine-disrupting potential makes PFAS among the most consequential classes of emerging contaminants and underscores the urgent need for effective analytical and remediation strategies in environmental matrices.

In response, regulatory bodies have begun imposing strict limits on PFAS concentrations in water. The U.S. Environmental Protection Agency (EPA) recently introduced maximum contaminant levels of 4 ng/L for perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), and 10 ng/L for hexafluoropropylene oxide dimer acid (HFPO-DA or GenX) under the National Primary Drinking Water Regulation [11]. The European Commission, under Directive 2020/2184/EU [12], has adopted broader but more lenient thresholds for the total PFAS load. Moreover, PFOA and PFOS have been classified as Persistent Organic Pollutants (POPs) under the Stockholm Convention [13]. Although GenX was introduced as a safer replacement, its toxicity is now well documented [14]. Despite extensive research, the removal of PFAS from water remains a challenge. Conventional treatment technologies, such as coagulation, sedimentation and activated sludge systems, are largely ineffective [15]. Alternative strategies—including reverse osmosis, electrochemical oxidation and adsorption using activated carbon, ion-exchange resins, carbon nanotubes, metal-organic frameworks (MOFs) or covalent organic frameworks (COFs) [16]—have shown promise but suffer from major drawbacks, including low selectivity, high energy demands, long equilibrium times, material instability and secondary waste generation. Recent cost analyses indicate that PFAS treatment remains highly expensive, with typical costs around USD 1.50 per m³ and values reaching up to USD 2.71 per m³ depending on the technology, underscoring the substantial economic burden of large-scale implementation [17].

Among emerging strategies, liquid-liquid extraction has gained

traction due to its potential efficiency. However, conventional solvents often involve volatile, toxic and non-renewable compounds. In contrast, ionic liquids (ILs) and deep eutectic solvents (DESSs) have emerged as promising green alternatives [18]. ILs possess unique physicochemical properties, such as low volatility, high thermal stability and tunable polarity, but are often hindered by concerns over biodegradability, viscosity and synthesis complexity. HNADES, typically composed of a hydrogen bond acceptor compound (HBA) and a hydrogen bond donor compound (HBD), offer a more biodegradable, non-toxic and sustainable platform for extraction processes [19,20]. By carefully selecting naturally derived components such as sugars, amino acids, monoterpenes or fatty acids, their physicochemical properties—including viscosity (generally 10–200 mPa·s), polarity and microstructure—can be precisely tailored. This tunability, combined with their inherent hydrophobicity arising from hydrogen-bond network organization, results in minimized water solubility and enhanced selectivity for hydrophobic contaminants like PFAS [21]. Their successful application in other separation technologies—including CO₂ capture [22], bioactive compound recovery [23] and heavy metal removal [24]—further supports their relevance. In the specific case of PFAS, various preliminary studies have demonstrated their extractive capacity in aqueous media, positioning them as a promising alternative to conventional methods [25,26].

In this work, it is investigated an archetypical system composed of menthol (a cyclic monoterpene used as HBA) and decanoic acid (a saturated fatty acid used as HBD), selected for their natural origin, commercial availability and well-characterized behavior. The solid-liquid phase diagram for this binary system reveals melting points of 315.70 K for menthol and 304.95 K for decanoic acid, with an eutectic temperature ideally observed at approximately 283 K. The eutectic composition occurs near a molar fraction of 0.57 menthol to 0.43 decanoic acid, while computational predictions suggest a slightly shifted eutectic composition around 0.59 menthol and 0.41 decanoic acid with a eutectic temperature close to 272 K. To investigate the suitability of this system as an extraction medium, we consider three molar ratios (1:1, 1:2 and 2:1) of menthol and decanoic acid. While these compositions do not necessarily correspond to the eutectic point, they qualify as low-melting mixtures (LoMMs), a broader category defined by their depressed melting behavior. The extraction performance of these LoMMs is explored for three representative PFAS—PFOA, PFOS and

Table 3

Electron densities (ρ) and bond distances associated with hydrogen bonds between PFAS and HNADES in the clusters.

Analyte	ρ (a.u.) of BCP/bond distance (Å)		
	1:1 → (PFAS)H...O (decanoic acid 1)	1:2 → (PFAS)H...O (decanoic acid 2)	2:1 → (PFAS)H...O (decanoic acid 1)
PFOA	0.06302/1.54	0.06231/1.55	0.06217/1.56
PFOS	0.08653/1.43	0.07087/1.50	0.0796/1.46
HFPO-DA	0.06359/1.55	0.06593/1.53	0.0848/1.46

Table 2

Electron densities (ρ) and bond distances associated with hydrogen bonds in HNADES + PFAS clusters.

Extractant molar ratio	ρ (a.u.) of BCP/bond distance (Å)								
	(Decanoic acid 1)H...O(menthol 1)			(Decanoic acid 2)H...O(decenoic acid 1)			(decanoic acid 1)H...O(menthol 1)		
	PFOA	PFOS	HFPO-DA	PFOA	PFOS	HFPO-DA	PFOA	PFOS	HFPO-DA
1:1	0.05890/1.59	0.06249/1.57	0.06108/1.58						
1:2	0.05532/1.62	0.05748/1.60	0.05479/1.62	0.04949/1.64	0.04752/1.65	0.05039/1.64			
2:1	0.07168/1.52	0.07476/1.51	0.07563/1.50				0.04306/1.73	0.04255/1.73	0.04295/1.72

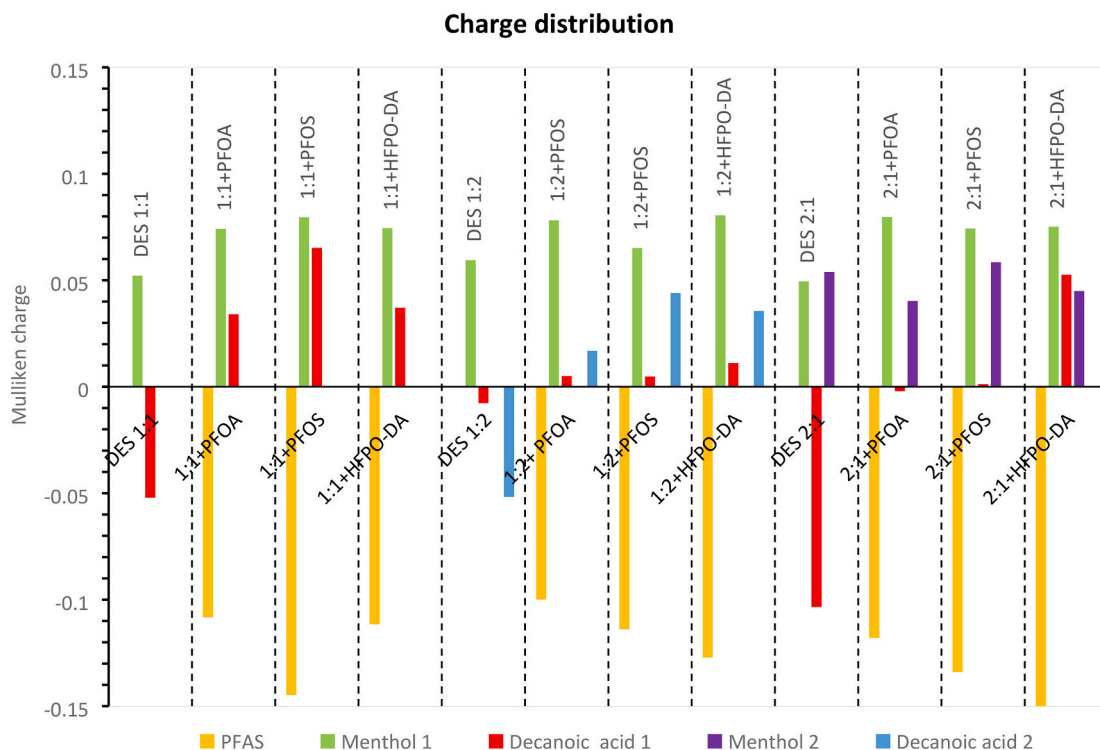


Fig. 1. Mulliken charge distribution for each molecule in the different HNADES + PFAS clusters. Charge transfer is predominantly observed between decanoic acid (molecule 1 in the 1:1 and 2:1 M ratios, and molecule 2 in the 1:2 ratio) and the PFAS compounds.

Table 4

Mulliken charge distribution for each molecule in the different HNADES + PFAS clusters.

	Mulliken charge PFAS	Mulliken charge menthol 1	Mulliken charge decanoic acid 1	Mulliken charge menthol 2	Mulliken charge decanoic acid 2
DES 1:1		0.05215	-0.05210		
DES 1:1 + PFOA	-0.10826	0.07418	0.03407		
DES 1:1 + PFOS	-0.14480	0.07958	0.06524		
DES 1:1 + HFPO-DA	-0.11156	0.07447	0.03710		
DES 1:2		0.05946	-0.00771		-0.05174
DES 1:2 + PFOA	-0.09995	0.07813	0.00502		0.01682
DES 1:2 + PFOS	-0.11393	0.06508	0.00482		0.04400
DES 1:2 + HFPO-DA	-0.12720	0.08049	0.01117		0.03559
DES 2:1		0.04951	-0.10342	0.05389	
DES 2:1 + PFOA	-0.11792	0.07970	-0.00208	0.04028	
DES 2:1 + PFOS	-0.13401	0.07433	0.00120	0.05848	
DES 2:1 + HFPO-DA	-0.17275	0.07516	0.05261	0.04498	

HFPO-DA—each embodying a key structural subclass. A multiscale computational approach is adopted to elucidate the phase-transfer mechanisms and physicochemical interactions underpinning the extraction process. This includes quantum-chemical calculations based on DFT to optimize molecular clusters and analyze short-range intermolecular interactions via the Quantum Theory of Atoms in Molecules (QTAIM) and Non-Covalent Interaction (NCI) analysis. The solubility and thermodynamic compatibility of the PFAS in the solvent systems are predicted using COSMO-RS, while classical MD simulations provide insight into mass transfer kinetics across the HNADES-water interface. To extend beyond this archetypal system, machine learning techniques are employed to enhance prediction accuracy and accelerate the screening of solvent-PFAS interactions.

The present study was therefore conceived as a computationally driven molecular screening and mechanistic investigation framework aimed at identifying promising HNADES candidates for PFAS extraction prior to experimental implementation. Rather than relying on a single predictive methodology, the proposed approach combines

complementary levels of molecular description through DFT calculations, COSMO-RS thermodynamic modeling and classical MD simulations. The convergence of these independent methodologies toward consistent trends in PFAS affinity, interfacial behavior and intermolecular interaction patterns provides a coherent physicochemical basis for the proposed extraction mechanisms and for the rational prioritization of candidate HNADES systems for subsequent experimental validation.

2. Computational methods

2.1. Density functional theory calculations

To model the key intermolecular hydrogen bonding involved in PFAS extraction, minimal molecular clusters were created using Avogadro [27]. These clusters were designed to bring potential hydrogen-bond donors and acceptors into close spatial proximity. For each of the three HBA:HBD molar ratios (1:1, 1:2 and 2:1), nine initial cluster configurations were generated. From the most stable geometry

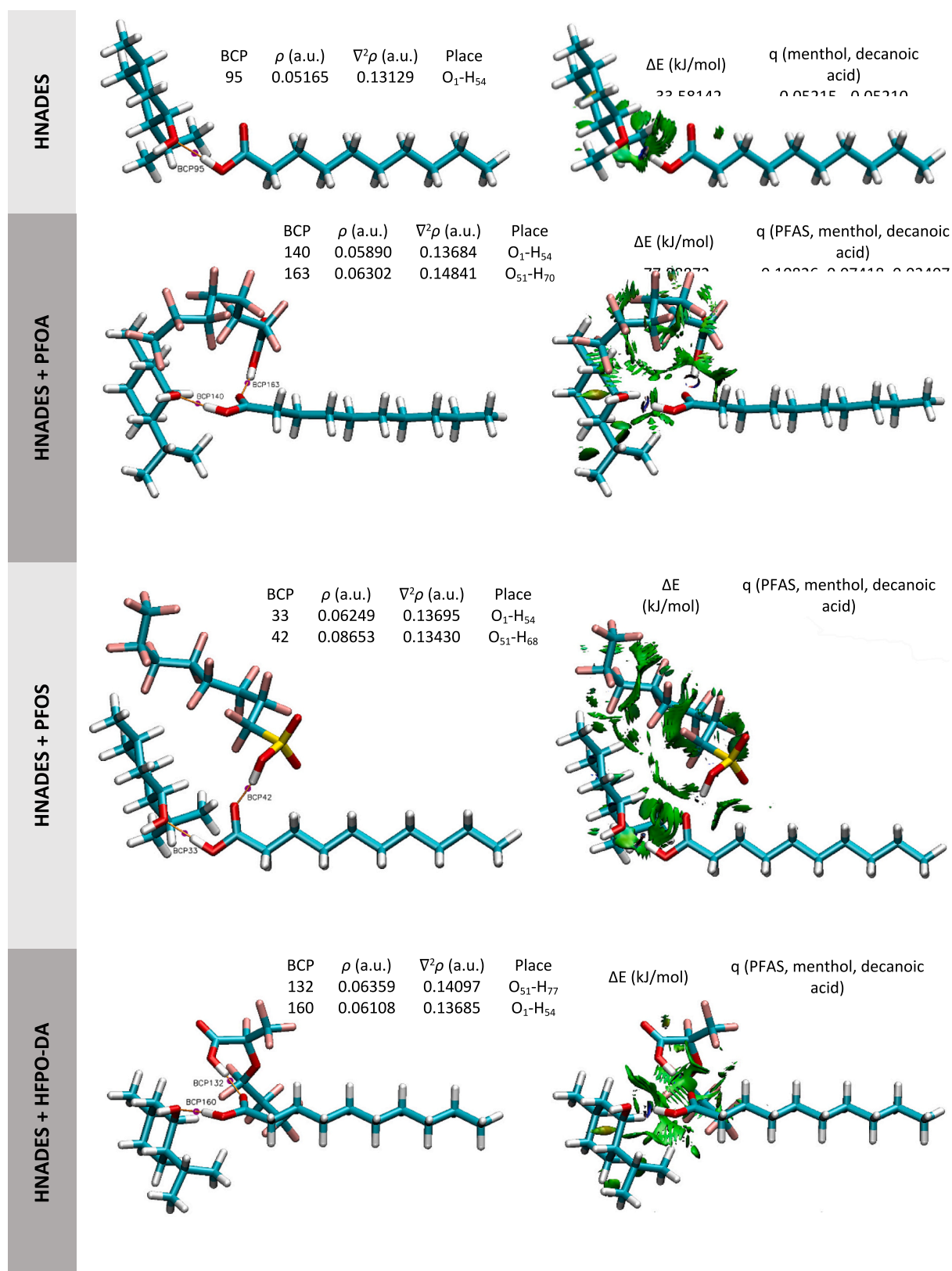
EXTRACTANT MOLAR RATIO 1:1

Fig. 2. Structural representations and associated analyses of optimized 1:1 menthol-decanoic acid clusters, isolated and with PFAS.

identified at each ratio, additional structures were built by adding one PFAS molecule (PFOA, PFOS or HFPO-DA) to the HNADES cluster. For

each PFAS-solvent system, six different configurations were optimized. Geometry optimizations were performed using TurbomoleX [28] with

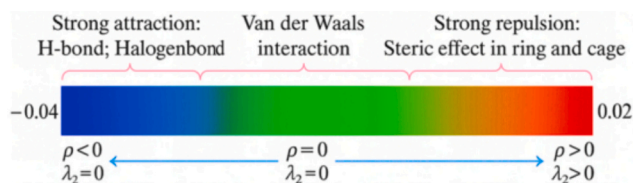


Fig. 2. (continued).

Table 5

Melting temperatures (T_m), boiling points (T_b) and enthalpies of fusion (ΔH_m) for the pure compounds.

	Menthol	Decanoic acid	PFOA	PFOS	HFPO-DA
T_m (K)	315.7	305.0	327.3	363.0	358.8
T_b (K)	489.6	530.0	465.0	522.0	469.7
ΔH_m (kJ/mol)	12.89	28.00	26.90	24.99	19.48

the B3LYP exchange-correlation functional [29–31], Grimme's D4 dispersion correction [32] and the def-TZVP basis set [33]. This choice is justified by the noncovalent interactions in PFAS-HNADES complexes, including dispersion, hydrophobic and CH- π contacts, which require long-range correlation effects that are inadequately described by standard hybrid functionals. Indeed, previous studies on similar systems demonstrate that dispersion-corrected functionals (D3/D4) are essential for obtaining reliable interaction energies. The calculations began with an initial estimate of the electron density, which was iteratively refined until self-consistent convergence was reached. Convergence thresholds were set as $\Delta E < 10^{-6}$ a.u., RMS density $< 10^{-7}$ a.u. and maximum gradient $< 10^{-4}$ a.u./Bohr, with SCF iterations converging below 10^{-7} – 10^{-8} a.u. using fine integration grids. Interaction energies (ΔE) were calculated as the difference between the total electronic energy of the optimized complex and the sum of the electronic energies of the isolated monomers, all at the same level of theory.

To gain further insight into the nature of the intermolecular interactions, topological analysis based on the Quantum Theory of Atoms in Molecules (QTAIM) [34] was applied to the lowest-energy geometries using Multiwfn [35]. This analysis identified bond critical points (BCPs) and ring critical points (RCPs), where the gradient of the electron density vanishes. Strong hydrogen bonds were defined by a BCP electron density (ρ) between 0.002 and 0.0035 a.u., a Laplacian ($\nabla^2\rho$) in the

range of 0.024–0.139 a.u. [36], bond distances of 1.2–2.0 Å and donor-acceptor angles between 130° and 180° [37]. Additionally, Non-Covalent Interaction (NCI) analysis was carried out using the Reduced Density Gradient (RDG) method [38]. In the resulting isosurface maps, interactions were colour-coded: hydrogen bonds appeared in blue ($\rho > 0$, $\nabla^2\rho < 0$), van der Waals interactions in green ($\rho \approx 0$, $\nabla^2\rho \approx 0$), and repulsive interactions in red ($\rho > 0$, $\nabla^2\rho > 0$). All molecular visualizations were generated using Visual Molecular Dynamics (VMD) [39].

2.2. COSMO thermodynamic properties predictions

The molecular structures of all species were initially generated from their SMILES (Simplified Molecular Input Line Entry System) representations and subsequently optimized using Density Functional Theory (DFT) with TurbomoleX. Geometry optimizations and surface charge density calculations were performed using the BP86 exchange-correlation functional [29] in combination with the def-TZVP basis set, which offers a good balance between accuracy and computational efficiency, while ensuring compatibility with the original COSMO-RS [40] parametrization. The resulting .cosmo files, which contain essential information on the molecular surface polarization charge densities, were processed with the COSMOconf software [41]. This step systematically explores the conformational space of each compound (menthol, decanoic acid, PFOA, PFOS and HFPO-DA), generating multiple conformers and selecting the lowest-energy structure for use in subsequent calculations. COSMOtherm [42] was then used to calculate the infinite dilution activity coefficients (γ_∞) and solubility of the PFAS analytes in the menthol-decanoic acid binary mixtures at the three molar ratios. These calculations were performed as a function of temperature and rely on thermodynamic data for the pure components, including melting points, boiling points and enthalpies of fusion. This information was incorporated via reliable databases. In cases where experimental

Table 6

Infinite dilution activity coefficients ($\ln(\gamma_\infty)$) and solubility of PFOA, PFOS and HFPO-DA in the three extractant mixtures at 298 K.

Extractant molar ratio	$\ln(\gamma_\infty)$ at 298 K			Solubility ($g_{\text{solute}}/g_{\text{disolución}}$) at 298 K		
	PFOA	PFOS	HFPO-DA	PFOA	PFOS	HFPO-DA
1:1	-1.57	-1.83	-2.28	Fully soluble	0.78	Fully soluble
1:2	-0.97	-1.18	-1.68			
2:1	-2.24	-2.52	-2.94			

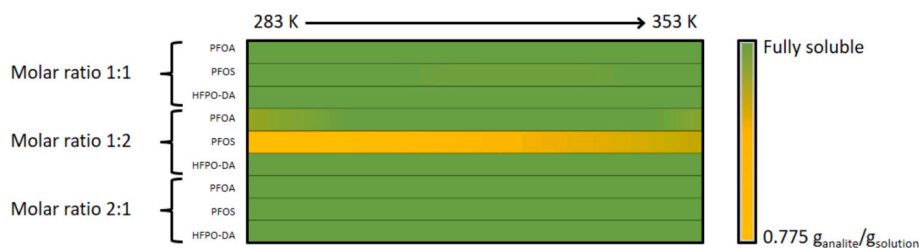


Fig. 3. Heat map of the solubilities of PFOA, PFOS and HFPO-DA in the three extractant mixtures within the 283–353 K temperature range.

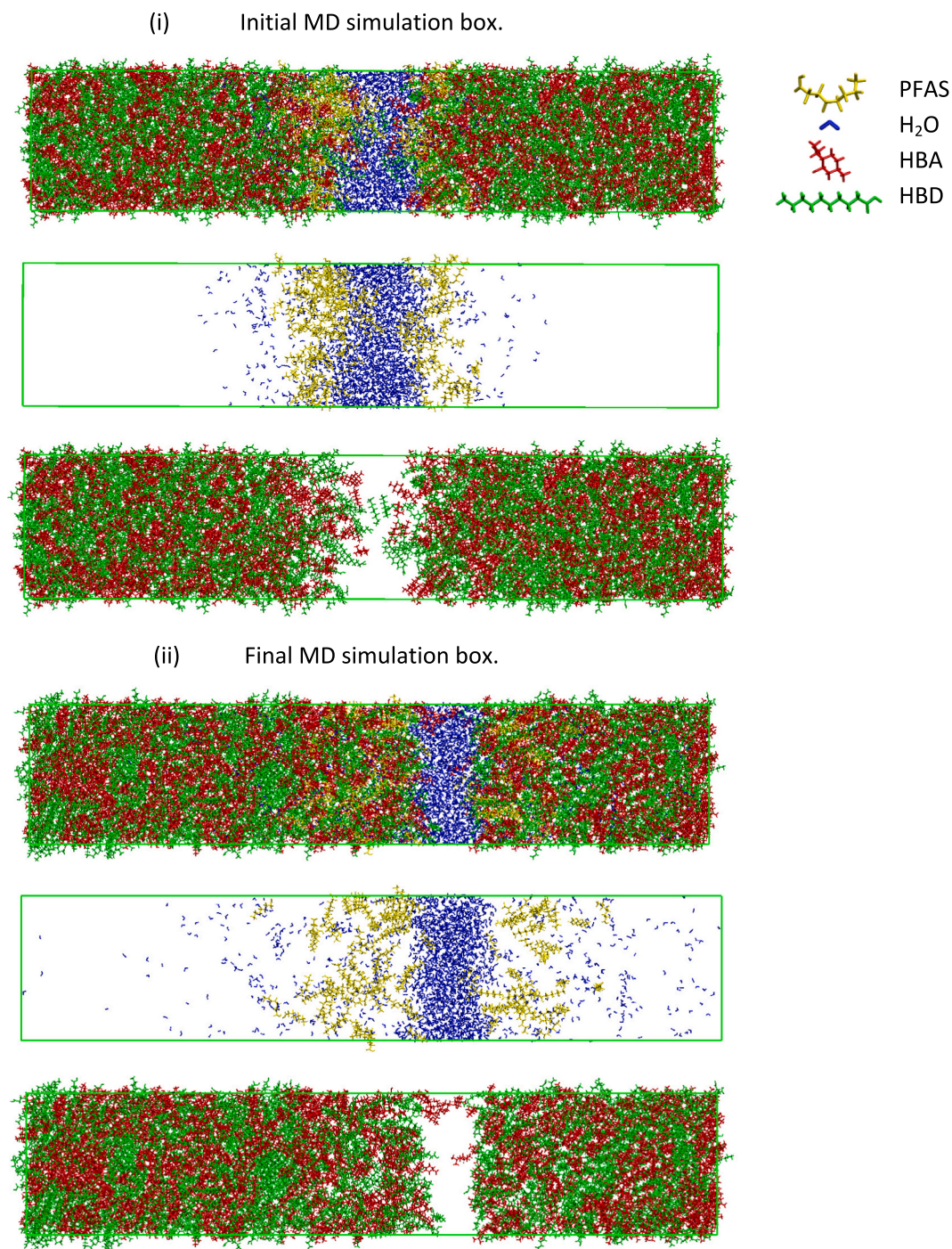


Fig. 4. Initial and final MD simulation boxes for a system containing 5% PFOA (yellow) in water (blue), using menthol (red) and decanoic acid (green) as extractants. A two-step extraction process is observed: formation of an interface followed by diffusion of PFOA into the HNADES phase. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

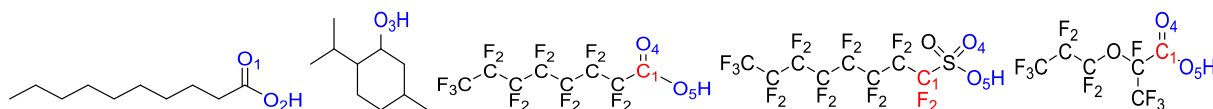


Fig. 5. Molecular structures and numbering of the most relevant interaction sites (atoms) for the components studied in this work (from left to right: decanoic acid, menthol, PFOA, PFOS, and HFPO-DA).

thermophysical properties were unavailable, missing values were estimated using the Joback group contribution method [43], which infers properties as additive functions of the molecule's functional groups.

2.3. Classical molecular dynamics simulations

MD simulations were employed to investigate the phase-transfer

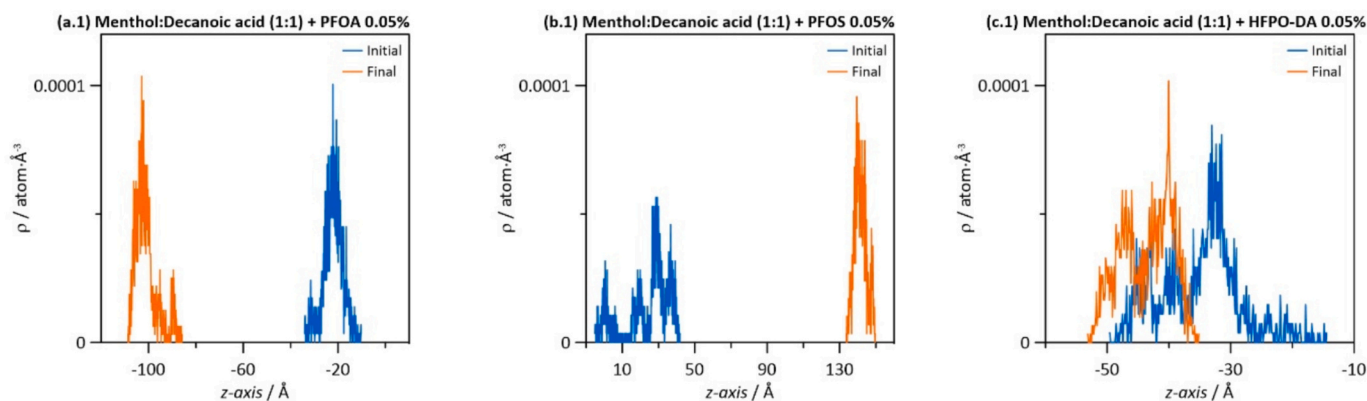


Fig. 6. Behavior of 0.05%, 0.1%, 1%, 2.5% and 5% PFAS in water at the interface with HNADES at 298 K and 1 bar, reporting the normalized density profiles (ρ) along the direction perpendicular to the interface for the C_1 atoms of the PFAS molecules. The blue curves represent the average behavior during the first nanosecond, while the orange curves, which are laterally broader, correspond to the final distribution. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

behavior and interfacial dynamics of PFAS in HNADES-water systems. It is important to note that the PFAS species considered in the present study correspond to their neutral acid forms. Although PFOA, PFOS and related PFAS are predominantly present as anions under environmentally relevant aqueous conditions due to their low pKa values [9,10], which strongly influence properties such as logP/logD, hydration free energy, electrostatic interactions and diffusion behavior, the neutral-state approximation was adopted here to establish a consistent molecular-level framework for evaluating intrinsic PFAS-HNADES interactions. Future work will explicitly incorporate ionized PFAS species, counterions and pH-dependent speciation effects to assess their influence on extraction thermodynamics and interfacial transport behavior. The Merck Molecular Force Field (MMFF) was used for all components, with parameters generated using SwissParam [44], except for atomic charges, which were obtained from Mulliken population analysis based on DFT-optimized geometries at the B3LYP-D4/def-TZVP level of theory, as implemented in TurbomoleX. MMFF was selected because it was specifically parametrized to describe a broad range of organic functional groups relevant to the present systems, including carboxylic acids, fluorinated aliphatic chains and cyclic/alicyclic terpene-like structures. Therefore, the main molecular families investigated in this work — PFAS fluoroalkyl chains, decanoic acid and menthol — fall within the documented applicability domain of the force field. In addition, previous studies have successfully employed MMFF in molecular dynamics simulations of deep eutectic solvent systems. Notably, Mainberger et al. [45] reported a comparative evaluation of MMFF and GAFF for DES simulations, concluding that both force fields provide satisfactory structural and thermodynamic descriptions of these complex fluids. Simulations were performed in periodic cubic boxes. Each system consisted of a central aqueous phase containing 2000 water molecules and varying amounts of PFAS at molar concentrations of 0.05–5%, surrounded by a solvent region composed of 500 menthol and 500 decanoic acid molecules in a 1:1 M ratio. Box dimensions ranged with composition from $42 \times 42 \times 42 \text{ Å}^3$ to $54 \times 54 \times 250 \text{ Å}^3$. All MD simulations followed a three-step protocol. Systems were first constructed and packed using Packmol [46], followed by a 1 ns NVT equilibration at 298 K. This was succeeded by a 10 ns NPT equilibration at 298 K and 1 bar and a subsequent 40 ns production run under the same conditions for data collection and analysis. Temperature and pressure were controlled using Nosé-Hoover thermostats and barostats [47] with coupling constants of 30 ps and 1000 ps, respectively. Long-range electrostatic interactions were handled using the Ewald summation method [48] with a 15 Å cutoff, and Lennard-Jones cross-interactions were calculated using Lorentz-Berthelot mixing rules. The Tuckerman-Berne multiple time-

step algorithm [49] was applied with 1 fs (long) and 0.1 fs (short) time steps. Simulations were run using MDynaMix v.5.2 [50]. Visualization, trajectory postprocessing and analysis were carried out using VMD.

2.4. All-vs-all analysis in other PFASs and HNADES

The objective of this section is to perform an *in-silico* design and large-scale computational screening aimed at identifying optimal HNADES. To broaden the scope beyond the representative extraction of PFOA, PFOS and HFPO-DA using menthol-decanoic acid mixtures, an extensive analysis encompassing 1746 PFAS and 2589 HNADES is conducted (Table S1). From the broad class of PFAS, as defined according to a wide structural definition (consistent with OECD-type criteria), a pool of potentially tens of thousands of compounds was considered, including those listed in the ECHA database (21,566 potential PFAS). From this pool, we selected a subset of 2000 PFAS for the computational screening, prioritizing structures with lower molecular weight, which also correspond to the most commonly occurring representatives. After geometry optimization, 1746 structures were retained, excluding those with incompatible elements, radical character or redundancy. The 2589 HNADES were formed from binary combinations of 76 HBA and HBD candidates selected for low volatility, suitable molar ratios, moderate boiling points within the range of 180 °C to 470 °C and melting points below 25 °C [51]. The COSMO-based workflow was scaled and automated with Scilab and Python to compute activity coefficients and solubility for each PFAS-HNADES pair, omitting conformational sampling to reduce computational cost. Molecular descriptors, covering electronic, topological and spatial properties, were calculated with Materials Studio [52] and predictive models were developed in MATLAB. Four models were constructed: one for infinite dilution activity coefficients and three for solubility (mole fraction, weight fraction and molar solubility). Machine learning models were trained on 75% of the data with cross-validation and tested on the remaining 25%.

3. Results and discussion

3.1. Characterization of short-range interactions

Starting from nine carefully designed initial configurations aimed at optimizing the orientation between the acid and alcohol functional groups, the minimum energy geometry (i.e., the structure with the most negative energy value) was identified for three systems: (i) one menthol molecule and one decanoic acid molecule, (ii) one menthol molecule

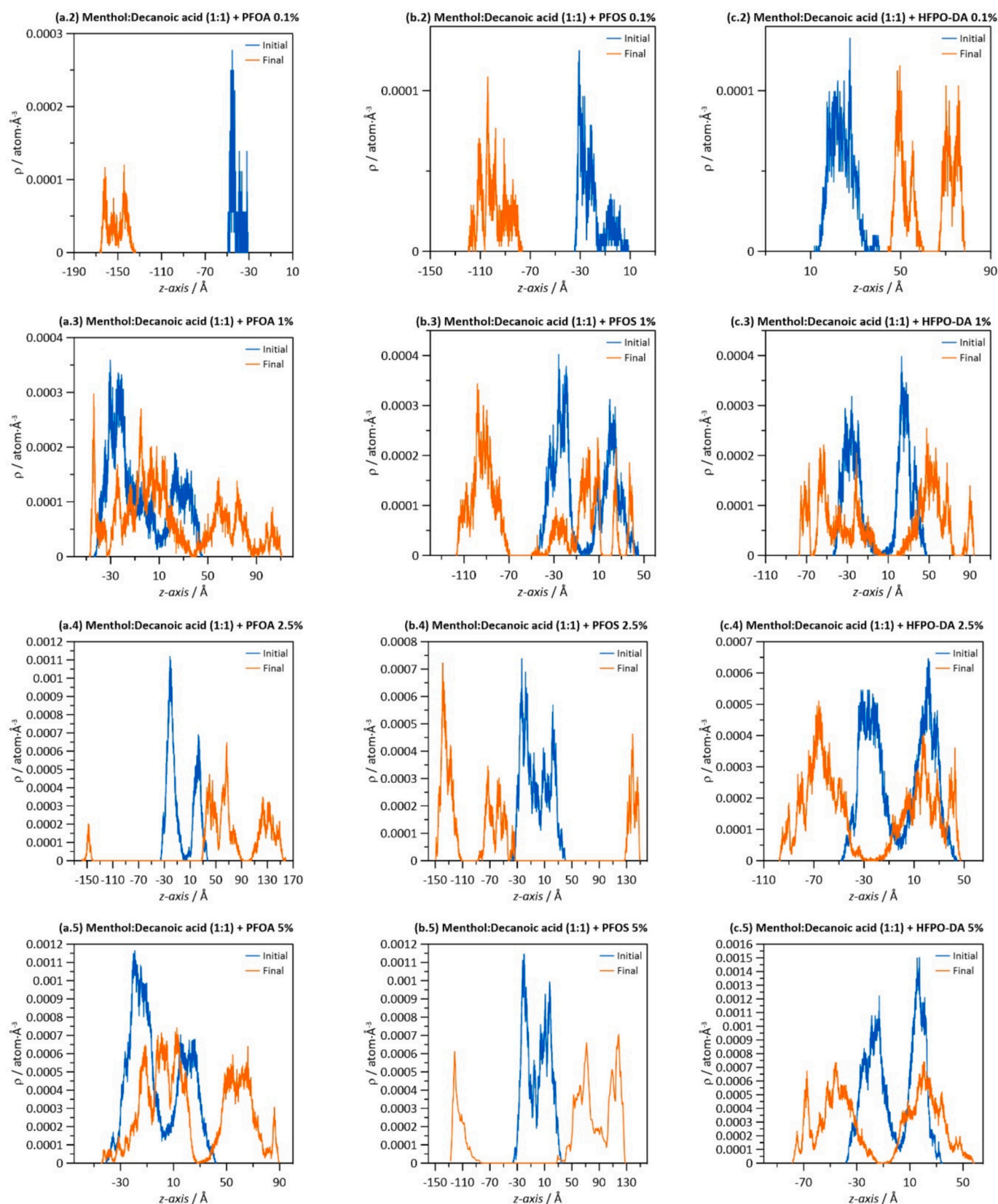


Fig. 6. (continued).

and two decanoic acid molecules and (iii) two menthol molecules and one decanoic acid molecule. Based on these thermodynamically most stable structures, six additional configurations were constructed by

incorporating an extra molecule of each analyte, which were subsequently optimized following the previously established methodological criteria.

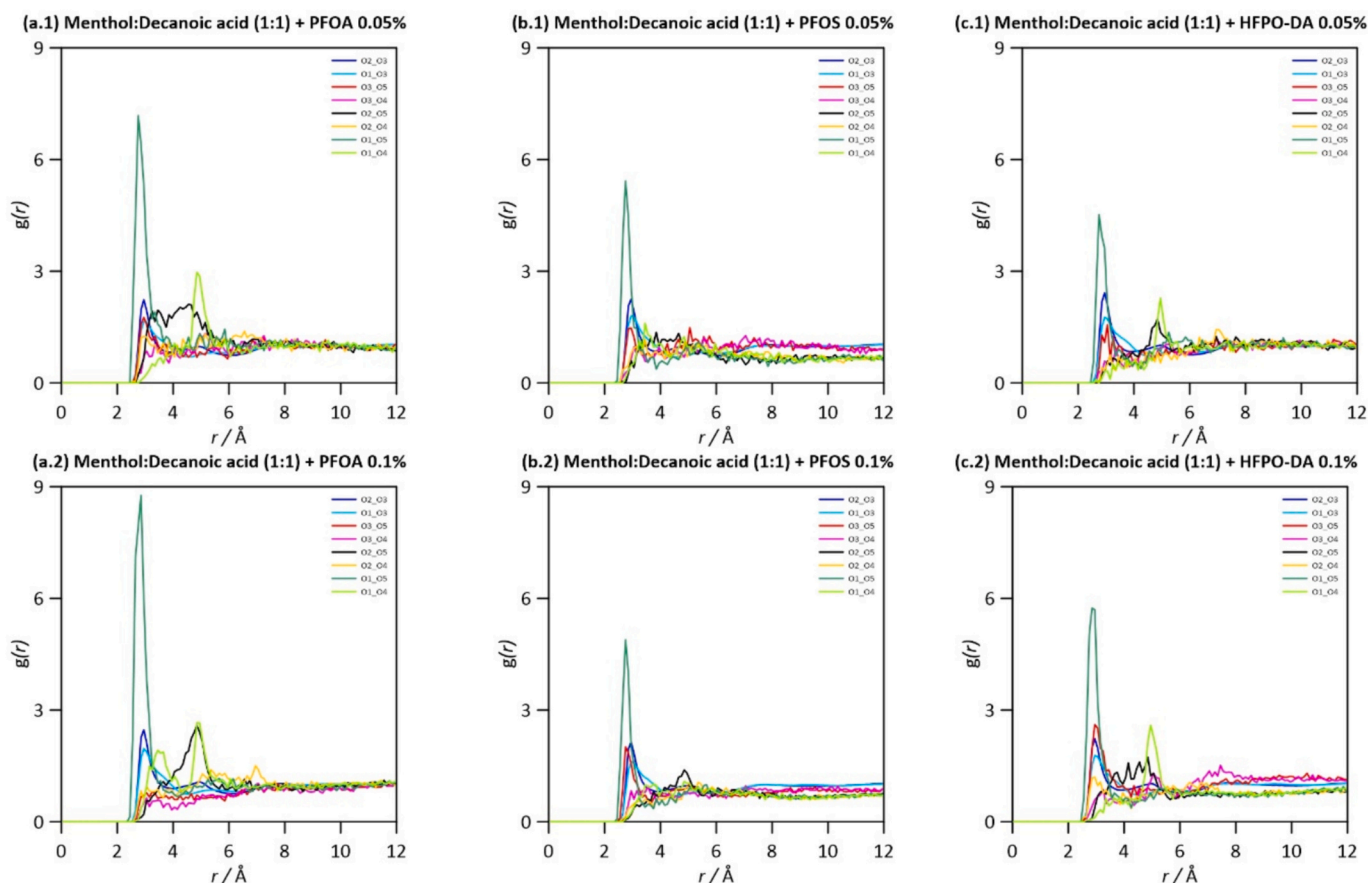


Fig. 7. Radial distribution functions (RDFs), $g(r)$, for the atomic pairs O_3-O_4 (pink, minor relevance), O_3-O_5 (red, PFAS–menthol interaction), O_1-O_4 (light green, minor relevance), O_2-O_4 (orange, minor relevance), O_1-O_5 (dark green, PFAS–decanoic acid interaction), O_2-O_5 (black, minor relevance), O_1-O_3 (light blue, menthol–decanoic acid interaction), and O_2-O_3 (dark blue, menthol–decanoic acid interaction) at the different interfaces. Labels according to Fig. 7. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

The interaction energies (ΔE) for the HNADES are -34 kJ/mol for the 1:1 ratio, -68 kJ/mol for 1:2 and -47 kJ/mol for 2:1. Upon formation of complete clusters with PFAS, the interaction energies become even more favorable, reaching values as low as -125 kJ/mol. Among the PFAS studied, no significant differences were observed in the favorability of interactions, as the variations are too small to draw definitive conclusions. Nevertheless, highly favorable interactions are consistently present across all cases. This behavior correlates with factors such as fluorination degree, charge distribution and the ability to form directional contacts, including hydrogen bonds and fluorine-hydrogen interactions. To support the interpretation of these interaction mechanisms, σ -profiles and σ -moments were analyzed. Based on these refined structural and energetic descriptors—together with Mulliken charges, bond distances, critical points and characterization of interaction types—the following results were derived.

When the extractant molar ratio is 1:1, a strong hydrogen bond is observed between the hydrogen of the carboxyl group of decanoic acid and the oxygen of the hydroxyl group of menthol, corroborated by the high electron density (ρ) and short bond distance reported in Table 1. In the 1:2 ratio, this interaction is supplemented by a second hydrogen bond established between the carboxylic hydrogen of the second decanoic acid molecule and the carbonyl oxygen of the first. In the 2:1 HNADES, besides the acid-menthol interaction, an additional hydrogen bond is detected between the hydroxyl group of the first menthol and the oxygen of the second. Van der Waals interactions are also identified in all systems.

The original HNADES interactions are strengthened upon

incorporation of PFAS molecules, as inferred from the comparison of ρ values at BCPs and bond distances of the isolated extractant (Table 1) with those corresponding to the complete clusters (Table 2). This increase in hydrogen bond strength suggests structural synergies favoring stabilization of the configurations associated with analyte uptake.

In all HNADES + PFAS clusters, a particularly strong hydrogen bond is identified between the hydrogen of the PFAS functional groups and the carbonyl oxygen of the decanoic acid molecule not involved in intrinsic HNADES interactions (corresponding to the single molecule present in 1:1 and 2:1 ratios, and the second molecule in 1:2; see Table 3). Additionally, extensive regions stabilized by van der Waals forces, predominantly $F\cdots H$ and $F\cdots O$ are detected. Although fluorine-hydrogen ($F\cdots H$) interactions are intrinsically weak, their directional nature contributes to the orientation and additional stabilization of the PFAS-HNADES clusters.

Complementary evidence is provided by Fig. 1 and Table 4, showing that this affinity is mediated by partial charge transfers. PFAS act as electron density acceptors from the HNADES, mainly from the decanoic acid involved in the hydrogen bond (PFAS)H $\cdots$ O(decanoic acid).

The data presented thus far, along with the location of the most relevant bond critical points and the corresponding NCI analysis maps (with hydrogen bonds in blue and van der Waals interactions in green), are collectively displayed in Figs. 2 (1:1 M ratio), S.1 (1:2), and S.2 (2,1).

3.1. Thermodynamic evaluation: activity coefficients and solubilities

Based on the charge densities of the most stable conformers and their

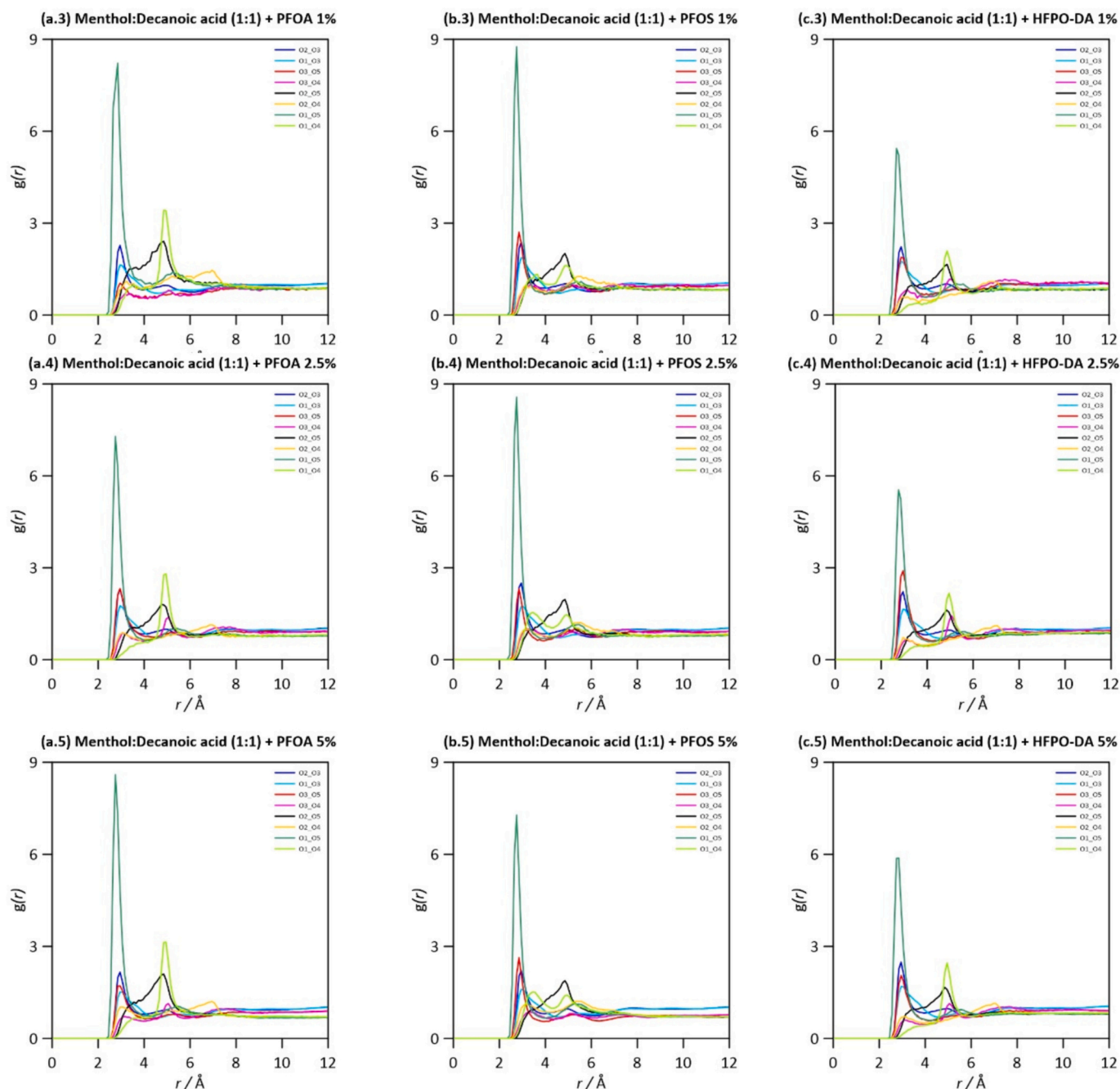


Fig. 7. (continued).

thermodynamic properties (Table 5), infinite dilution activity coefficients and solubilities of PFOA, PFOS, and HFPO-DA in menthol-decanoic acid mixtures were calculated at 298 K using COSMO-RS (Table 6). All $\ln(\gamma_\infty)$ values are negative, indicating strong solute-solvent interactions, in line with previously identified hydrogen bonding patterns from DFT and QTAIM analyses.

The 2:1 HNADES composition exhibits the most negative $\ln(\gamma_\infty)$ values, suggesting the highest extraction potential, whereas the 1:2 system appears less efficient. Among the analytes, HFPO-DA shows the highest affinity and solubility across all systems, followed by PFOS and PFOA. Notably, PFOA and HFPO-DA exhibit complete solubility in all tested mixtures, while PFOS displays a solubility decrease specifically in the 1:2 formulation. It should be emphasized that the term “fully soluble” in the present COSMO-RS analysis refers exclusively to the predicted thermodynamic solubility of PFAS within the HNADES phase at

infinite dilution conditions and does not imply macroscopic miscibility between the HNADES and aqueous phases. In the context of liquid-liquid extraction, PFAS compounds are treated as trace solutes partitioning between two immiscible bulk solvents. Therefore, the predicted high PFAS solubility within the HNADES phase is consistent with a strong extraction affinity rather than with the formation of a single homogeneous phase. The biphasic character of the menthol acid HNADES/water system remains governed by the intrinsic immiscibility of the two bulk liquids, which is preserved throughout the MD simulations by the persistence of a well-defined liquid-liquid interface. Consequently, the COSMO-RS results should be interpreted as indicators of favorable PFAS partitioning into the HNADES phase rather than as evidence of bulk solvent miscibility.

Additionally, PFAS solubility was evaluated across a temperature range of 283–353 K. As shown in the heatmap (Fig. 3), solubility remains

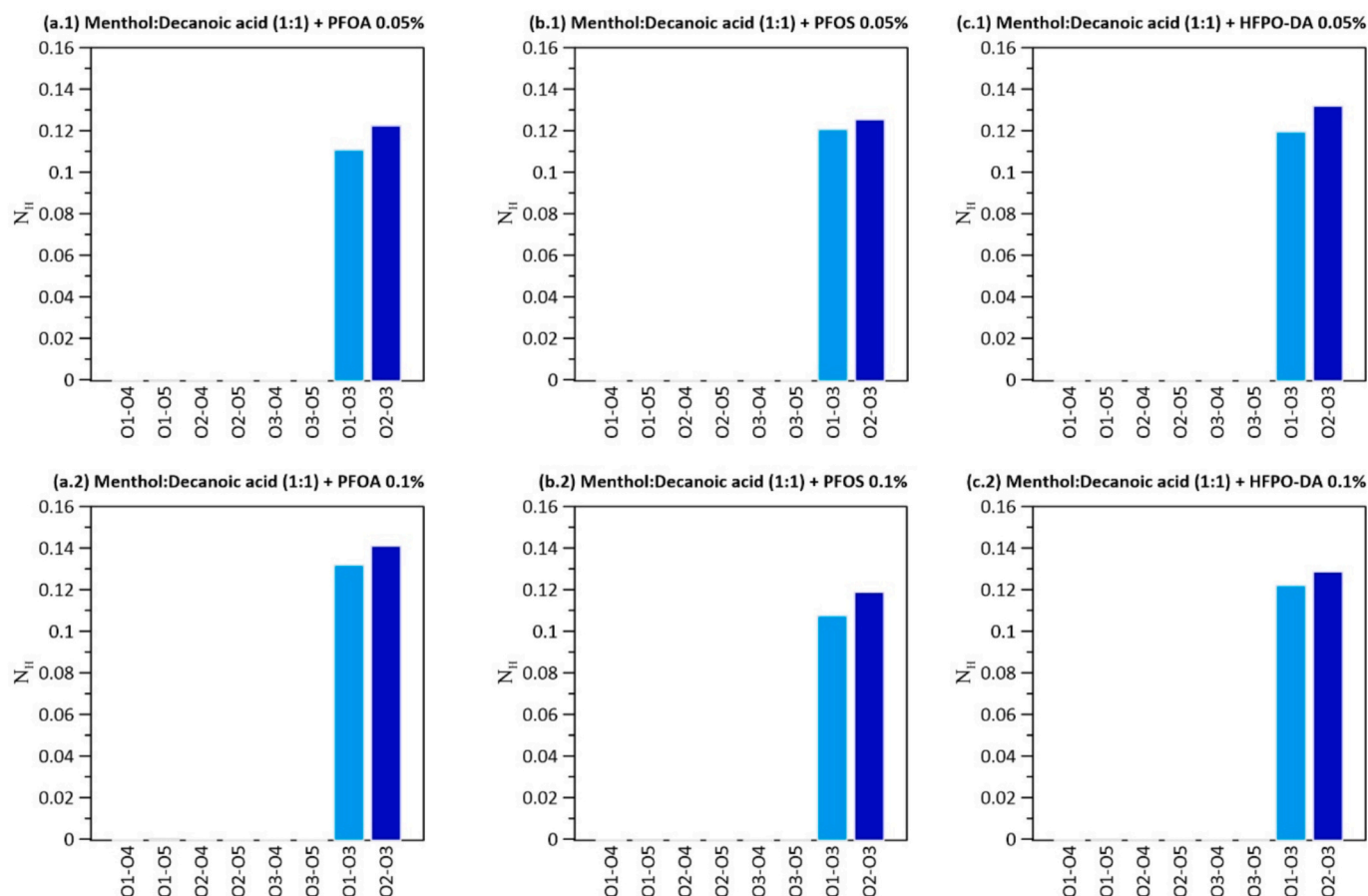


Fig. 8. Average number of hydrogen bonds (N_H) per HBA molecule for the atomic pairs O₃-O₄ (pink, minor relevance), O₃-O₅ (red, PFAS-menthol interaction), O₁-O₄ (light green, no relevance), O₂-O₄ (orange, minor relevance), O₁-O₅ (dark green, PFAS-decanoic acid interaction), O₂-O₅ (black, minor relevance), O₁-O₃ (light blue, menthol-decanoic acid interaction), and O₂-O₃ (dark blue, menthol-decanoic acid interaction) at the different interfaces. Labels according to Fig. 7. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

high throughout this interval, which is advantageous for extraction processes.

3.2. Interphase dynamics of PFOA, PFOS and HFPO-DA capture by menthol: Decanoic acid HNADES

The results obtained from MD simulations provide a detailed microstructural characterization of the collective behavior of the species present in the fluid medium. This information is essential for gaining an in-depth understanding of the diffusion mechanisms at the (HNADES)-(PFAS + water) interfaces, overcoming the spatial scale limitations inherent to DFT-based modeling approaches. The simulations were carried out at a constant temperature of 298 K and a pressure of 1 bar.

The fringe regions of the simulation boxes consist exclusively of HNADES, initially without the presence of PFAS, which are uniformly distributed within the central aqueous phase. As the simulations progress, the systems evolve from this two-phase arrangement toward the formation of a heterogeneous interfacial region: PFAS molecules gradually migrate from the aqueous phase toward the interface, where they establish interactions with the HNADES components (menthol and decanoic acid), thereby weakening their hydrogen-bonding interactions and solvation with water. Subsequently, the PFAS adsorbed at the interface diffuse into the hydrophobic core of the extractant.

The snapshots shown in Fig. 4 correspond to the system configurations containing 5% PFOA (as an example) after 1 ns (initial configuration) and final configuration of production simulation. It should be

noted that this concentration is very high compared to environmentally relevant levels and is considered only for modeling purposes. In view (i), a preferential accumulation of PFAS can be observed at the interfacial region between the HNADES and the aqueous phase. In view (ii), their progressive immersion into the organic phase becomes evident, indicating a spontaneous transfer process toward the core of the extractant. Despite the hydrophobic nature of the HNADES, a small fraction of water molecules is observed to channel into its interior, highlighting the advisability of subjecting the extractant to a drying process after use to prevent residual accumulation. On the other hand, the confined aqueous regions remain free of organic solvent, thereby minimizing the risk of cross-contamination, even considering the low toxicity of the HNADES.

For the subsequent analysis, it is necessary to identify certain key atoms according to the nomenclature shown in Fig. 5. The progressive migration of PFAS is confirmed by the normalized density (ρ) profiles shown in Fig. 6, which represent the average spatial distribution of the C₁ atoms of these molecules along the direction perpendicular to the interface (z-axis) of the simulation boxes. A depletion of these centers is observed in the central aqueous region (blue curves with a double-valley shape, reflecting the average behavior during the first nanosecond) and their systematic displacement toward the peripheral zones occupied by the extractant (orange curves corresponding to the final distribution).

All PFAS studied exhibit similarly rapid adsorption and diffusion behavior, with no single compound demonstrating markedly faster migration. The arrival at the interface is extremely fast, occurring within less than 0.5 ns. Although PFOS shows slightly faster kinetics, the

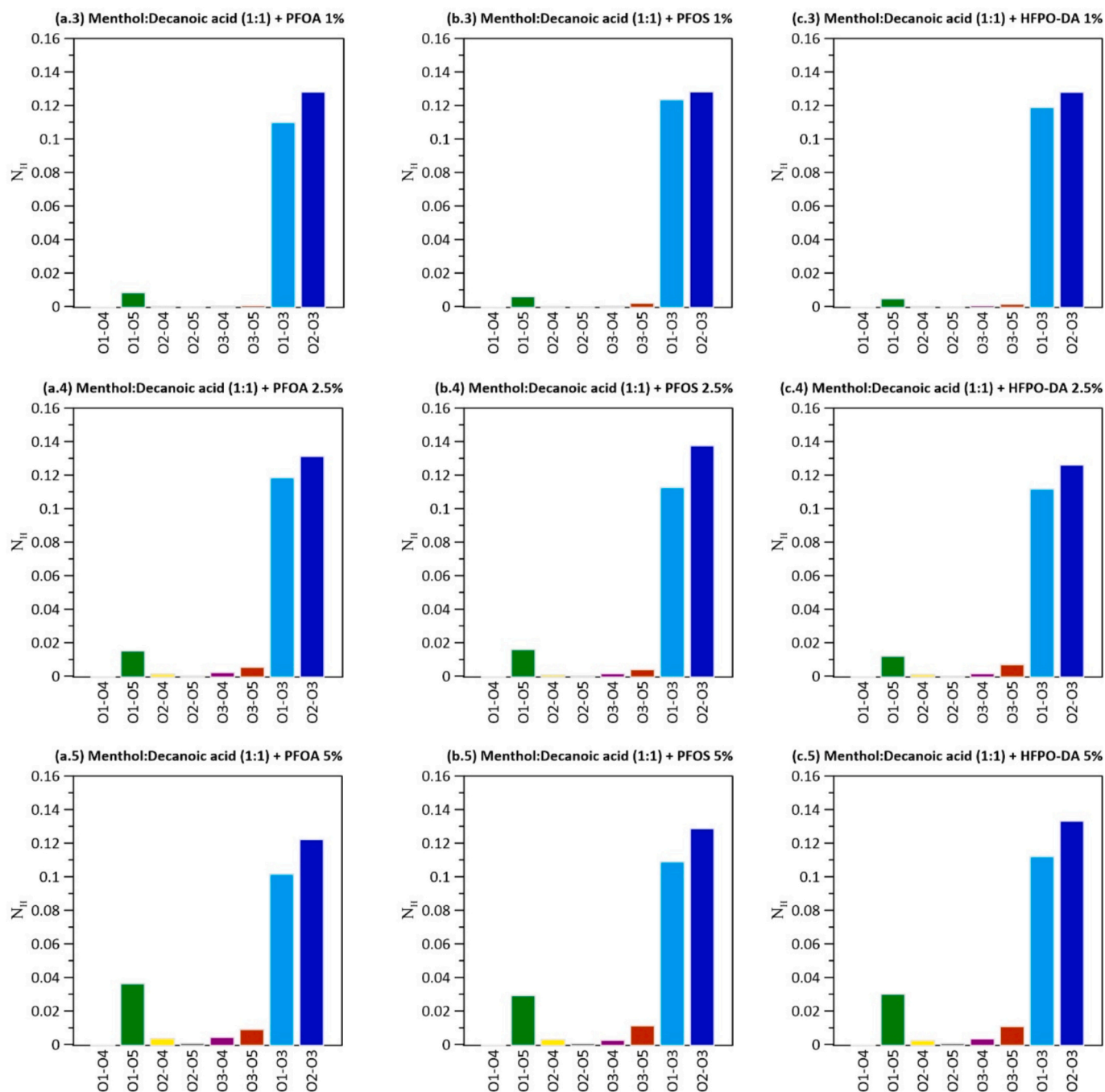


Fig. 8. (continued).

differences among PFAS are minimal and do not indicate significantly distinct migration mechanisms.

A key tool for the structural analysis of the trajectories obtained from the MD simulations is the radial distribution function (RDF). Fig. 7 shows that the atomic pair O₁-O₅ (dark green) reaches the maximum $g(r)$ value at a very short distance. This highlights the strong interaction between the carbonyl oxygen of decanoic acid and the hydroxyl oxygen present in PFAS molecules, attributable to the formation of hydrogen bonds of the type (PFAS)H...O(decanoic acid), consistent with the most stable configuration predicted by previous DFT calculations. At slightly longer separations, although with lower intensity, the O₃-O₅ pair (red) is observed, suggesting a secondary participation of menthol in the interaction with the analytes. Pairs involving carbonyl or sulfonyl oxygens of the PFAS exhibit significantly lower $g(r)$ values and/or peaks shifted

toward longer distances, indicating a marginal contribution to the extraction mechanisms. Finally, short-distance peaks are detected for the O₁-O₃ (light blue) and O₂-O₃ (dark blue) pairs, resulting from the inherent structural proximity between the HNADES components.

Fig. 8 presents, through bar charts, the total average number of hydrogen bonds per HBA molecule for the most relevant atomic pairs at the different interfaces, generally confirming the interaction patterns previously described. For this analysis, a broad criterion was adopted for defining a hydrogen bond, considering as such any interaction with an O...H distance ≤ 3.5 Å. The most frequent hydrogen bonds, due to their higher relative concentration, occur between the HNADES components (O₁-O₃ and O₂-O₃, in blue), with a slight predominance of those formed between the hydroxyl groups of both compounds. In decreasing order of frequency, these are followed by the O₁-O₅ (PFAS-decanoic acid, dark

Table 7

Intermolecular interaction energies (sum of Lennard-Jones and electrostatic contributions), for the reported molecular pairs: PFAS-water, PFAS-menthol, PFAS-decanoic acid, menthol-decanoic acid, menthol-water and decanoic acid-water in the different systems (0.05%, 0.1%, 1%, 2.5%, and 5% PFAS in water + HNADES). More favorable interactions are associated with more negative interaction energy values.

	E_{int} (kJ/mol) PFAS-water	E_{int} (kJ/mol) PFAS-menthol	E_{int} (kJ/mol) PFAS-decanoic acid	E_{int} (kJ/mol) menthol-decanoic acid	E_{int} (kJ/mol) menthol-water	E_{int} (kJ/mol) decanoic acid-water
0.05% PFOA	-37.71	-45.57	-86.59	-52.09	-6.87	-13.44
0.1% PFOA	-33.56	-40.32	-84.49	-50.25	-5.79	-13.13
1% PFOA	-27.09	-52.13	-96.14	-49.64	-6.31	-13.89
2.5% PFOA	-23.21	-54.41	-72.14	-46.96	-5.57	-11.42
5% PFOA	-25.20	-35.40	-66.52	-44.77	-4.84	-10.06
0.05% PFOS	-57.91	-54.36	-41.85	-49.98	-6.89	-13.32
0.1% PFOS	-44.20	-96.92	-43.59	-50.67	-5.77	-13.48
1% PFOS	-29.96	-65.03	-71.11	-51.24	-5.38	-12.04
2.5% PFOS	-27.50	-49.31	-70.30	-48.22	-5.50	-9.82
5% PFOS	-29.11	-45.75	-65.27	-47.53	-5.40	-11.63
0.05% HFPO-DA	-46.75	-40.07	-33.05	-50.08	-6.38	-13.65
0.1% HFPO-DA	-25.10	-89.00	-70.13	-52.92	-6.33	-12.63
1% HFPO-DA	-18.76	-53.65	-58.91	-49.65	-6.04	-11.78
2.5% HFPO-DA	-19.87	-46.80	-64.42	-48.75	-5.63	-10.59
5% HFPO-DA	-20.70	-45.24	-59.23	-49.38	-4.78	-10.64

Table 8

Center of mass self-diffusion coefficients, D , of PFAS within the HNADES phase (HNADES) and across the HNADES-water interface (interface) calculated from MD simulations for the systems configurations containing 2.5 and 5% PFAS.

		$10^{-10} D/\text{m}^2 \cdot \text{s}^{-1}$	
		PFAS (HNADES)	PFAS (interface)
DES 1:1 + PFOA	2.5% PFOA in water	4.381	6.962
	5% PFOA in water	5.338	8.194
DES 1:1 + PFOS	2.5% PFOS in water	1.099	2.486
	5% PFOS in water	1.386	2.834
DES 1:1 + HFPO-DA	2.5% HFPO-DA in water	8.767	10.645
	5% HFPO-DA in water	10.328	12.602

green) and O₃-O₅ (PFAS-menthol, red) interactions. Other interactions, such as O₃-O₄, O₂-O₄, O₂-O₅, and O₁-O₅, display significantly lower frequencies, suggesting a secondary role in the molecular stabilization mechanisms.

Radial distribution functions together with hydrogen-bond population analyses indicate that the intrinsic menthol-decanoic acid hydrogen-bond network remains structurally preserved during PFAS extraction, in agreement with previous molecular-level studies of DES

supramolecular organization and hydrogen-bond dynamics [53]. The persistent short-range peaks and high hydrogen-bond populations associated with the O₁-O₃ and O₂-O₃ interactions confirm that PFAS uptake does not disrupt the HNADES supramolecular organization, but rather introduces additional PFAS-decanoic acid interactions superimposed onto the pre-existing solvent network.

To further probe the nature of PFAS-HNADES interactions at the molecular level, we performed a systematic analysis of F...O=C contacts throughout the MD trajectories, motivated by the well documented capacity of fluorine atoms in perfluorinated compounds to act as halogen bond donors toward electron rich acceptors. Although fluorine is generally considered a weak halogen bond donor due to its high electronegativity, the pronounced positive σ hole potential on fluorine atoms in strongly electron withdrawing environments — such as those found in perfluoroalkyl sulfonate and carboxylate moieties — renders F...O=C interactions geometrically and energetically plausible [54]. Contacts were identified by applying geometric criteria consistent with those established in the halogen bonding literature: F...O distances ≤ 3.5 Å and C-F...O angles $\geq 150^\circ$. This analysis revealed a non-negligible frequency of such contacts in the PFAS-HNADES complexes, with PFOS exhibiting a higher occurrence relative to PFOA, consistent with its greater fluorine content and the broader charge delocalization associated with its sulfonate headgroup. These confirm that halogen bonding

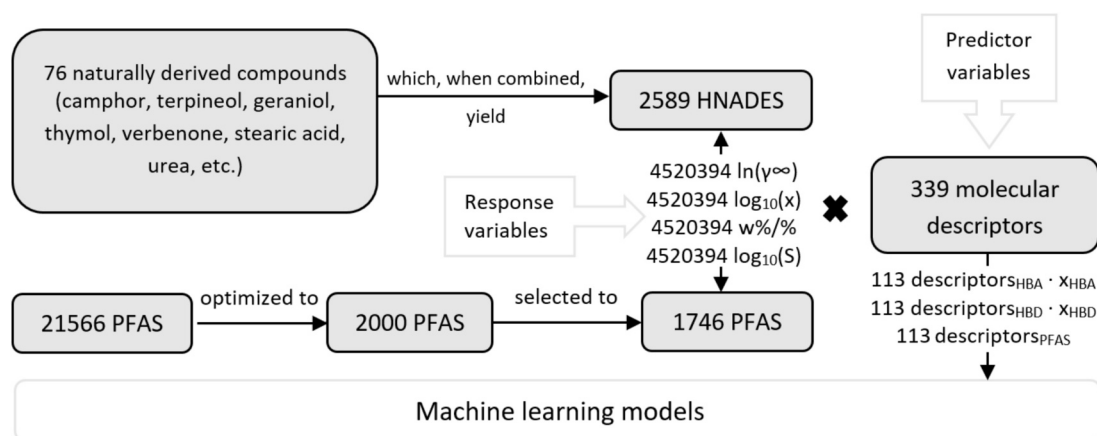


Fig. 9. Diagram of the input variables and the size of the dataset used in the modeling through machine learning of mixture descriptors based on molecular descriptors.

Table 9

Coefficients of determination (R^2), mean squared errors (MSE), root mean squared errors (RMSE) and mean absolute errors (MAE) obtained during the validation and test phases of the predictive models.

Response	R^2		MSE		RMSE		MAE	
	Validation	Test	Validation	Test	Validation	Test	Validation	Test
$\ln(\gamma^\infty)$ at 298 K	0.98	0.98	0.0719	0.0680	0.2682	0.2608	0.1565	0.1527
$\log_{10}(x)$ at 298 K	0.98	0.98	0.0109	0.0099	0.1046	0.0995	0.0582	0.0553
w%/ % at 298 K	0.95	0.95	0.0013	0.0012	0.0361	0.0340	0.0137	0.0128
$\log_{10}(S)$ at 298 K	0.98	0.98	0.0104	0.0091	0.1017	0.0953	0.0570	0.0538

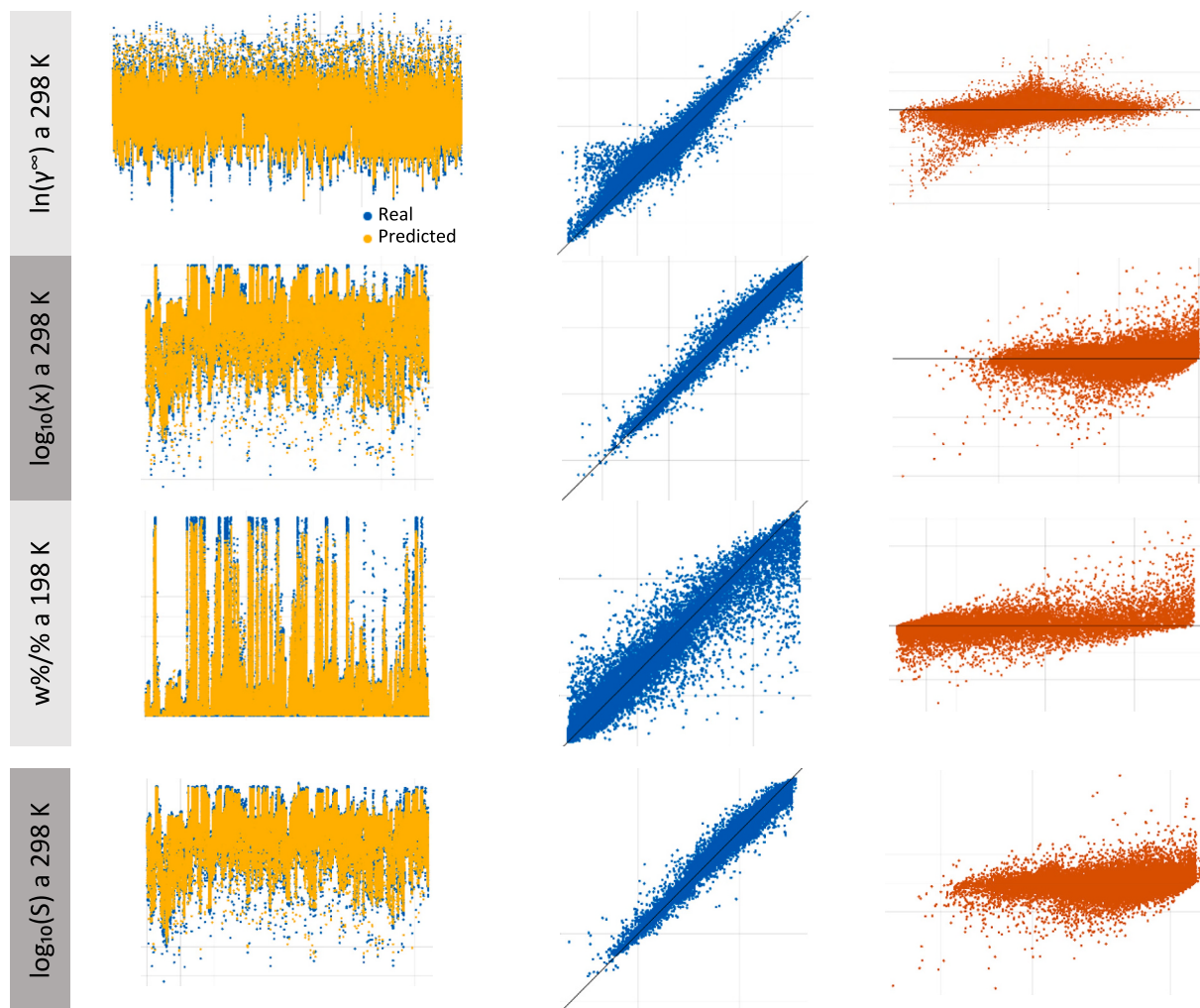


Fig. 10. From left to right: comparison between actual values (blue) and model-predicted values (yellow); scatter plot showing the correlation between predicted and actual values in the test set; and residual plot as a function of the predicted values for the same set. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

provides a supplementary stabilizing contribution to the overall PFAS-HNADES binding. These findings enrich the mechanistic picture by identifying an additional non covalent interaction mode that may influence the selectivity and affinity of HNADES toward fluorinated contaminants.

The following Table 7 presents the intermolecular interaction energies, calculated as the sum of the Lennard-Jones and electrostatic contributions. A progressive decrease is observed in the PFAS-water interaction, concomitant with an increase in the PFAS-menthol and, more markedly, PFAS-decanoic acid interactions. The latter behavior highlights the predominant role of decanoic acid in the formation of hydrogen bonds with the analytes, in agreement with the previous DFT results. The menthol-decanoic acid interaction remains practically

constant over time, ensuring the structural integrity of the HNADES. In contrast, the menthol-water and decanoic acid-water interactions are minimal, reinforcing the hydrophobic character of the extraction medium.

Finally, the translational mobility of PFAS during the extraction process was further quantified through the calculation of center-of-mass self-diffusion coefficients (D) from the MD trajectories (Table 8), determined from the slope of the Mean Square Displacements (MSD) (Fig. S3) using Einstein's equation. The diffusion coefficients were evaluated both within the HNADES phase and in the interfacial region between HNADES and water for systems containing 2.5 and 5% PFAS. In all cases, PFAS exhibit higher diffusivities at the interface than within the bulk HNADES phase, reflecting the lower local packing constraints

Table 10

Best-performing HNADES compositions (HBA/HBD ratios) and number of PFAS completely solubilized.

HBA	x _{HBA}	HBD	x _{HBD}	No. of PFAS completely solubilized
Urea	0.010	Verbenone	0.990	295
Cineole	0.999	Urea	0.001	292
Tetracaine	0.134	Verbenone	0.866	288
Cineole	0.937	Tetracaine	0.063	286
Cineole	0.821	Hinokitiol	0.179	275
Cineole	0.811	Germacrol	0.189	274
Cineole	0.154	Linalool	0.846	270
Linalool	0.877	Verbenone	0.123	270
Alantolactone	0.002	Linalool	0.998	267
Citronellal	0.002	Linalool	0.998	267

and enhanced molecular mobility at the heterogeneous boundary. The systematically lower diffusivities inside the HNADES phase compared to the interfacial region indicate that mass transport is partially limited by the highly structured hydrogen-bond network of the solvent. Nevertheless, the obtained diffusion coefficients remain within the characteristic range of moderately viscous supramolecular liquids, supporting sufficiently rapid PFAS migration toward the extractant phase. Likewise, HFPO-DA displays the highest diffusion coefficients both at the interface and within the bulk HNADES phase for 2.5 and 5% concentrations, followed by PFOA, whereas PFOS consistently exhibits the lowest mobility. This trend can be rationalized in terms of the molecular size and structural complexity of the PFAS molecules. HFPO-DA possesses a shorter and more branched perfluorinated backbone, resulting in a lower effective molecular volume and weaker steric hindrance during translational motion through both the interfacial region and the HNADES network. In contrast, PFOS, which contains a longer perfluorinated chain together with a bulkier sulfonic acid headgroup, experiences stronger intermolecular interactions and greater frictional resistance within the structured solvent environment, thereby reducing its diffusivity. PFOA shows intermediate behavior, consistent with its molecular dimensions and lower steric demand relative to PFOS but higher than HFPO-DA. Overall, these results suggest that, although interfacial adsorption occurs on sub-nanosecond timescales, the subsequent diffusion through the HNADES bulk may constitute the rate-limiting step governing the global extraction kinetics.

3.3. Large-scale screening of PFASs-HNADES combinations

The methodological framework, as said before, is structured around four predictive models: one aimed at estimating activity coefficients (as the dependent variable), and three focused on predicting the solubility of PFAS in HNADES. These solubilities are expressed as the decimal logarithm of the mole fraction ($\log_{10}(x)$), mass fraction ($w\%/%$) and volumetric solubility in logarithmic scale ($\log_{10}(S)$, mol/L).

A total of 339 variables are employed as predictors, corresponding to 113 molecular descriptors computed with models QSPR (Forcite, Dmol3) for each of the three species in the HBA + HBD + PFAS combinations (Fig. 9). For HBA and HBD, descriptor values are weighted according to the specific molar composition of each HNADES system. The descriptors encompass electronic properties (energies, orbitals, multipole moments, etc.), topological indices (connectivity, shape, etc.) and geometrical features (surface areas, volumes, moments of inertia, etc.).

The data output generated by COSMOtherm reaches the order of millions of data entries. To derive meaningful conclusions from this high-dimensional dataset, machine learning algorithms were applied. However, due to current limitations in computational resources and storage capacity, the modeling process (excluding activity coefficient estimation) was restricted to 10% of the total dataset, corresponding to 315,237 entries.

The resulting models belong to the Bagged Trees family, which does not yield explicit functional forms or easily interpretable equations. Instead, final predictions are obtained by averaging the outputs of multiple independently trained decision trees, each generated via bootstrap aggregation (random sampling with replacement). The Bagged Trees method was selected due to its robustness against overfitting, high predictive accuracy and ability to handle complex nonlinear relationships in the data. Alternative algorithms were tested but consistently demonstrated inferior performance in cross-validation. The predictive performance of the selected models is considered satisfactory, as evidenced by the results presented in Table 9 and Fig. 10.

Beyond the models, it was possible to identify specific correlations between the HNADES that solubilize a greater number of PFAS and the PFAS that dissolve in a greater number of HNADES. Focusing first on the HNADES (Table 10), the top 49 formulations are capable of completely solubilizing more than 250 PFAS. Among their constituents, the most frequently recurring compounds are linalool (appearing 30 times among the top formulations), verbenone (12 occurrences) and cineole (9 occurrences). As expected, these compounds share an extremely hydrophobic character. In contrast, HNADES formulated with polyols, aldehydes or acids tend to exhibit poorer extraction performance.

Regarding the PFAS, among the 1746 compounds analyzed, 386 are completely soluble in at least one of the HNADES evaluated. Among the most readily extractable PFAS—those that dissolve completely in more than 2000 HNADES—the majority correspond to linear sulfonic acids, followed by alcohols and polyols. In contrast, the PFAS with the poorest solubility are those with higher molecular mass—less relevant due to their lower prevalence—which typically contain additional heteroatoms such as chlorine or silicon and exhibit more complex branched structures and rings.

4. Conclusions

This study presents the first systematic multiscale assessment of the extraction of three industrially relevant PFAS (PFOA, PFOS and HFPO-DA) using menthol-based HNADES, combined with the first large-scale PFAS-DES screening reported to date. By integrating quantum-chemical calculations, classical molecular dynamics simulations and machine-learning approaches, the investigation provides detailed molecular-level insight into the underlying extraction mechanisms. Within the portion of the study examining the archetype menthol-decanoic acid HNADES, the results reveal that PFAS uptake is primarily driven by strong hydrogen bonding between the carboxylic groups of decanoic acid and the hydroxyl moieties of PFAS, supported by significant van der Waals interactions. Menthol contributes to maintaining the structural integrity of the eutectic solvent via an internal hydrogen-bonding network. These interactions remain consistent across a range of PFAS concentrations, leading to enhanced solubility and activity coefficients approaching zero, which in turn facilitate a stepwise mechanism that disrupts the native solvation shell of PFAS in water. Initially dispersed in the bulk aqueous medium, PFAS molecules migrate toward the liquid-liquid interface. Upon interfacial adsorption, they progressively diffuse into the interior of the HNADES phase.

The second part of the study, dedicated to the machine-learning design framework, identifies strong correlations between experimentally derived mixture descriptors (solubilities and activity coefficients) and molecular descriptors, laying the groundwork for the development of predictive models. Across the full dataset, preliminary results demonstrate high predictive performance and robustness. Future work will focus on experimental validation and process optimization. A central composite design is currently being employed to determine the optimal extraction conditions for PFOA, considering variables such as contact time, temperature, and solvent-to-water ratio. Concurrently, a comprehensive toxicological evaluation is planned, targeting interactions with human proteins and model membranes.

An important limitation of the present computational framework is

the use of neutral PFAS species as representative extraction-active states. Although environmentally relevant aqueous PFAS are predominantly present as anions, the present study was designed to investigate the intrinsic molecular affinity between PFAS and the hydrophobic HNADES phase under transfer-compatible conditions. Future work should explicitly incorporate charged PFAS species, counterions, interfacial protonation equilibria and pH-dependent partitioning phenomena to establish a more comprehensive description of PFAS extraction under realistic environmental conditions.

CRedit authorship contribution statement

Alba Pérez-Cortés: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Sergio de-la-Huerta-Sainz:** Writing – review & editing, Visualization, Validation, Investigation, Formal analysis, Data curation. **Sara Santamaría-Herrera:** Visualization, Investigation, Formal analysis, Data curation. **Santiago Aparicio:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Alberto Gutiérrez:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rechem.2026.103473>.

Data availability

Data will be made available on request.

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