



Historical Perspective

Customizing polyelectrolytes through hydrophobic grafting

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ABSTRACT

This up-to-date review describes the design, fabrication approaches, properties and applications that have been employed in the field of hydrophobically decorated polyelectrolytes (HD-PEs), used as functionalized building blocks for speciality materials with tuneable features. These include, in particular, synthetic strategies for modification/hydrophobization of polyelectrolytes, self-organization of HD-PEs in aqueous systems, adsorption phenomena and applications in the field of surface chemistry. Rationally engineered HD-PEs can be achieved via either step-growth copolymerization of different reactive end groups of monomers, followed by appropriate post-synthesis treatment or as a result of decoration of a given polymer backbone with hydrophobic side groups. The influence of HD-PEs' chemical structure on their self-assembling and interfacial properties is dependent on the overall hydrophobicity, i.e. length, number and type of side chains stretched out to charged segment, number, type and strength of ionizable groups. We also conclude that the linking entity structure (ester, secondary amide, etc.) between the hydrophobic side chain and the charged polyelectrolyte backbone in the tailor-made HD-PEs plays a crucial role in self-aggregation behaviour in water and at interfaces. The examples of the unique ability of HD-PEs to adsorb at hydrophilic and hydrophobic interfaces is discussed considering the effect of the self-aggregation on the interfacial properties.

1. Introduction

Polyelectrolyte-based materials, due to their unique properties, constitute valuable speciality products in different emerging applications, including surface engineering design [1,2], fabrication and functionalization of drug delivery systems [3–6], gene delivery and bioimaging [7–9], as well as soft nanotechnology and self-assembly approaches [10,11]. In general, amphiphilic polymers may self-assemble in water into a variety of structures, such as spheres or micelle-like core-shell aggregates, lamellae, cylinders as well as gyroids [12,13]. In the case of uncharged polymers, their aggregates' morphologies are controlled mainly by thermodynamic factors, i.e., interfacial tension and chain stretching energies [11,14]. The amphiphilic polyelectrolytes (APEs) self-assemble differently from their neutral counterparts, mainly because of additional effects resulting from long-range electrostatic interactions and the counterions distribution [5,11,15]. Additionally, the presence of hydrophobic groups (covalently attached to the polyelectrolyte backbone) contributes to hydrophobic

interactions during the APEs self-assembly process due to their incompatibility with the aqueous solvent. They may reduce the chain expansion resulting from the repulsive electrostatic forces between ionic groups [16–18]. One of the essential features of APEs is the possibility to fine-tune their properties, in particular related to their self-aggregation behaviour, by changing the number and the length of the hydrophobic alkyl or aryl fragments [19], the type of bonds/linkers between the charged backbone and the hydrophobic groups [20] and also a pK value of the macromolecule. Thus, APEs extend the conventional group of amphiphilic compounds, within which ionic surfactants or block copolymers belong, opening new opportunities to use them in numerous fields, from biomedical applications to engineered coating materials. Moreover, they seem promising materials that may mimic bio-macromolecules' behaviour.

Hydrophobically decorated polyelectrolytes (HD-PEs) belong to the most interesting tailor-made APEs. They represent a group of chemically modified polyelectrolytes, which structure is decorated by the selected hydrophobic units containing water-insoluble groups as long alkyl

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chains (typically, from *n*-dodecyl- to *n*-octadecyl) forming a linear-like functional PE architecture with shorter or longer side moieties [19–21]. (see Fig. 1) HD-PEs comprise water-soluble polymers that may associate in aqueous solutions, providing compact conformations similar to those of surfactant or soap micelles, so they are often referred to as “polysoaps” [22]. HD-PEs bearing a small percentage of hydrophobic side chains may form in aqueous media a variety of extended intra- and intermolecular structures with a tuneable rheologic behaviour [23,24]. They comprise a new class of industrially important speciality polymeric products of unusual micro- and macroscopic properties resulting from the hydrophobic association [25,26]. The hydrophobic side chains can be incorporated into the polymer molecule through various copolymerization procedures [27,28] or chemical grafting approaches [9,19]. They are described in detail in paragraphs 2.1 and 2.2. Briefly, the above-mentioned APEs can be classified as the following: (i) amphiphilic polyelectrolytes having in their structure ionizable groups, separated by hydrophobic units such as hexamethylene moiety forming alternate hydrophilic/hydrophobic linear sequences (i.e., diblock copolymers with hydrophilic and hydrophobic blocks being a special case) [29] and (ii) hydrophobically modified polyelectrolytes composed of polyelectrolyte (PE) backbone decorated with hydrophobic side groups (e.g., shorter or longer alkyl chains, aromatic rings, etc.) [16]. The second group comprises the actual hydrophobically decorated polyelectrolytes and constitutes the main point of interest of the present review.

This review aims to guide the design and fabrication of future new HD-PEs with various functionalized building blocks, active at the interfaces, for specialty products with tunable hydrophobicity, determining their performance at interfaces [4,30–32]. The issues discussed here concern diverse aspects of HD-PEs such as (i) synthesis utilizing a broad spectrum of approaches (step-by-step reactions and grafting hydrophobic groups to polyelectrolyte chain), (ii) self-assembling properties, methods of their investigation and also (iii) surface and interface

phenomena connected with adsorption of such amphiphilic compounds. The main aim of the present review is to indicate the most challenging aspects of their synthesis, self-assembly and adsorption toward engineered vesicles and coatings. The review collects detailed information about crucial issues affecting APEs’ self-assembling. Thus, it may inspire the design and fabrication of novel HD-PEs with fine-tuned properties desirable in numerous fields.

2. Design and fabrication of customized polyelectrolytes

Amphiphilic polyelectrolytes (APEs) as custom-designed structures may be prepared by two general approaches relying on: (i) step-growth reactions, giving rise to HD-PEs with an assumed regular or random sequence of hydrophobic and hydrophilic units [33], or (ii) reactions between reactive groups located on the polymer backbone that may utilize the presence of an appropriate linking group between the fragments of extreme hydrophobicity – preferably a chemodegradable moiety like ester, secondary or tertiary amide, acetal, carbamate or urea (see Table 1) [20]. The rationally designed HD-PEs have to meet appropriate synthetic, physicochemical and biological criteria to enable efficaciously assumed performance outcomes such as exemplary pH-sensitive functional nanosized thin films or nanocarriers designated for controlled and sustained release.

2.1. Step-by-step reactions involving hydrophobic and hydrophilic monomers

Step-by-step reactions lead to the formation of polyelectrolytes consisting of hydrophobic and ionizable units/building blocks. In some instances, the obtained polyelectrolytes need the proper post-synthesis treatment (mostly hydrolysis), yielding copolymers containing various alkyl chains [34]. The step-growth polymerization methodologies allow the preparation of amphiphilic copolymers with suitable hydrophobic/

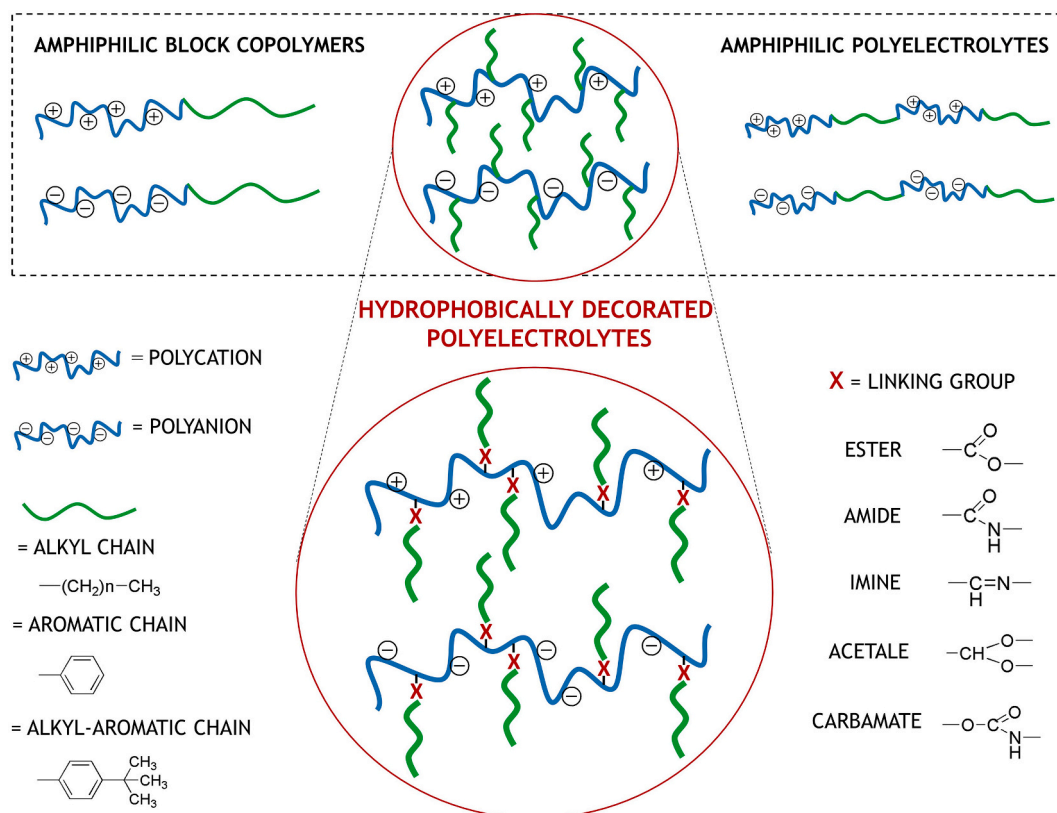


Fig. 1. Schematic definition of hydrophobically decorated polyelectrolytes (HD-PEs).

Table 1
Summary of synthetic approaches for hydrophobically functionalized polyelectrolytes.

STEP-GROWTH REACTIONS OF HYDROPHOBIC AND HYDROPHILIC MONOMERS					
No.	Hydrophobic unit	Hydrophilic unit	Type of reaction	Process conditions	Ref.
1	NIEA	Acrylic acid, Acrylamide, MMIB	Co-polymerization	Dissolution of monomers in deionized water (55°C, water bath); addition of initiator (NH ₄) ₂ S ₂ O ₈ :NaHSO ₃ (molar ratio 1:1) under nitrogen flow; purification with ethanol; drying in a vacuum oven	[25]
2	tBAAm	HEAAm	Copolymerization	Dissolution of monomers in methanol; addition of initiator V-70 under nitrogen conditions (RT, 24 h); immersing the product in methanol; purification in water	[28]
3	Butyl acrylate	Acrylic acid, methyl methacrylate	Co-polymerization	The mixture of monomers was added to solution of ethylene glycol monobutyl ether and AIBN in isopropyl alcohol (80°C, 2–3 h, nitrogen inlet); cooling to 50°C; vacuum distillation	[35]
FUNCTIONALISATION OF POLYELECTROLYTES BY HYDROPHOBIC GRAFTING					
	Polyelectrolyte	Modifying agent	Type of reaction	Process conditions	
4	PDADMAC	<i>n</i> -hexyl/ <i>n</i> -octyl/ <i>n</i> -decyl/ <i>n</i> -dodecyl chloride	Quaternization	Selective demethylation of the PDADMAC using ethanolamine (165°C, 4 h). Requaternization of tertiary amine with <i>n</i> -alkylchlorides (DMF, 60°C, 120 h)	[37]
5	P4VP	Methyl iodide, ethyl/propyl bromide	Quaternization	Dissolution of P4VP in dimethyl sulfoxide; addition of methyl iodide or ethyl/propyl bromide (4 h, RT or 24 h, 40°C); precipitation in ethanol or THF; filtration; dissolving in NaCl; dialysis against NaCl and deionized water; lyophilisation	[39]
6	PIBMI	BuP, cybuP, prP, cyprP	Quaternization	Addition of BuP/cybuP/prP/cyprP to PIBMI in dry DMF/dry CHCl ₃ (75°C, 96 h); precipitation with diethyl ether; filtration; washing with diethyl ether; drying under vacuum (40°C, 6 h)	[38]
7	Sodium alginate (SA)	Cholesterol (AR)	Steglich esterification	Protonation of SA in FA/DMF (volume ratio 10/9) (stirring 55°C, 30 min); esterification in chloroform (40°C, 24 h, DMAP, DCC); precipitation in ethanol; centrifugation; neutralization using Na ₂ CO ₃ and NaHCO ₃ ; dialysis against distilled water; lyophilization	[30]
8	Poly(acrylic acid) (PAA)	Dodecanol, Hexadecanol	Steglich esterification	Dissolution of PAA in distilled water; addition of EDAC, DMSO, DMAP, dodecanol or hexadecanol (stirring, 50°C, 48 h); filtration; dialysis in distilled water; freeze-drying	[19]
9	PSS/MA	Dodecylamine, Hexadecylamine	Amidation	Preparation of PSS/MA solution in distilled water; addition of EDAC and NHS; dissolution of dodecylamine or hexadecylamine in hydrochloric acid; addition of catalyst-DMAP (stirring, 40°C/60°C, 48 h); filtration; dialysis in distilled water; freeze-drying	[20]
10	Chitosan (CS)	Deoxycholic acid (DCA)	Amidation	Addition of DCA in ethanol to CS acetic acid solution; addition of EDC (RT, 24 h); pouring the solution into ethanol/ammonia water solution; centrifugation; washing with water/methanol/ethanol; freeze-drying	[4]
11	PAH	Hexanal	Schiff Base reduction	Addition of NaOH to PAH; acidification; addition of hexanal (stirring, 25 h, 27°C); addition of NaBH ₄ (18 h, 26°C); dialysis against water and HCl; lyophilization	[47]
12	PAH	Benzaldehyde (BA)	Schiff Base reaction	Stirring the mixture of PAH and potassium hydroxide at RT in methanol; filtration; dialysis against methanol; addition of benzaldehyde; stirring (1200 rpm, 30 min, RT); evaporation	[45]
13	PMOX	Dodecyl bromide	Alkylation	First step: Hydrolysis of PMOX using HCl (18 h, 40°C). Second step (alkylation): addition of potassium carbonate and 1-bromododecane; stirring (60 h, 80°C); filtration; evaporation; washing with hexane; precipitation; dialysis using acidified water, sodium chloride and water; freeze-drying	[49]
14	PEI	(2-oxo-1,3-dioxolan-4-yl)methylalkylcarbamates: alkyl = C8, C10, C12, C14, C18	Alkylation	Mixing of PEI and modifying agent in DMF (60°C, 20 h, 3 days); purification by addition of Et ₂ O and decantation; drying in vacuum (RT); precipitation into Et ₂ O/pentane and decantation; drying in vacuum (RT)	[50]
15	Chitosan	Octanoyl, myristoyl, palmitoyl chlorides	Acylation	Stirring of chitosan and aqueous acetic acid (RT, 24 h); addition of NaOH and acid chloride (stirring, RT, 5 h); precipitation with acetone; filtration; washing with methanol (60°C); drying (60°C, 1 week)	[51]

NIEA: N-(2-(2-ethyl-4,5-dihydro-1H-imidazol-1-yl)ethyl)methacrylamide; MMIB: 4-methacryloyl-1-methylpiperazin-1-ium-4-methylbenzenesulfonate; tBAAm: N-tert-butylacrylamide; HEAAm: N-(2-Hydroxyethyl) acrylamide; V-70: 2,2'-azobis(4-methoxy-2,4-dimethyl); RT: room temperature; AIBN: Azo-bisisobutyronitrile; DMAc: *N,N*-dimethylacetamide; DMAP: 4-dimethyl aminopyridine; PDADMAC: Poly(dimethyl diallylammonium chloride); P4VP: Poly(4-vinylpyridine); PIBMI: Poly(isobutylene-*alt*-N-(*N,N'*-dimethylamino propyl)-maleimide); BuP: N-(butyl)-1-bromoethanamide; cybuP: N-(cyclobutyl)-1-bromoethanamide; prP: N-(propyl)-1-bromoethanamide; cyprP: N-(cyclopropyl)-1-bromoethanamide; DCC: dicyclohexylcarbodiimide; EDAC: N-Ethyl-N-(3-dimethylaminopropyl)carbodiimide hydrochloride; PSS/MA: Poly(4-styrenesulfonic-*co*-maleic acid) sodium salt; EDC: 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride; NHS: N-hydroxysuccinimide; PAH: Poly(allylamine hydrochloride); PMOX: polymethyloxazoline; PEI: polyethyleneimine; C8: (2-oxo-1,3-dioxolan-4-yl)methylheptylcarbamate; C10: (2-oxo-1,3-dioxolan-4-yl)methyldecylcarbamate; C12: (2-oxo-1,3-dioxolan-4-yl)methyl dodecylcarbamate; C14: (2-oxo-1,3-dioxolan-4-yl)methyltetradecylcarbamate; C18: (2-oxo-1,3-dioxolan-4-yl)methylhexadecylcarbamate.

hydrophilic balance (HLB parameter) that can be manipulated in a controlled manner through the alteration of the molecular parameters of building blocks [29]. This way, amphiphilic polymers with predetermined structures and preferred properties are synthesized.

Numerous APEs with unique properties have been widely studied in the last few decades. One of the most typical syntheses of amphiphilic copolymers is radical copolymerization which allows the formation of

modified polyelectrolytes with different types of hydrophobic and ionizable units, compositions and degrees of polymerization. For example, novel APEs were designed utilizing the hydrophobic associating polymers – poly(acrylamide) *co*-polymerized ionic liquid [25]. The research revealed that the synthesized acrylamide-based copolymer exhibited high solubility in aqueous systems, viscoelasticity and thermostability. Another example of copolymerization was reported by

Wang and co-workers. The study aimed to investigate the amphiphilic acrylic acid copolymer used to prepare waterborne resins [35]. Mechanical characterization and water solubility study revealed their usefulness in humidity-sensitive coatings. A series of amphiphilic random copolymers were prepared by polymerization of 2-(acrylamido)-2-methylpropanesulfonic acid with 2-(acrylamido)-octane sulfonic acid, 2-(acrylamido)-dodecane sulfonic acid and 2-(acrylamido)-hexadecane sulfonic acid [27]. The synthesized copolymers comprised the same number of hydrophobic/hydrophilic units as side alkyl chains but various chain lengths. The design of amphiphilic copolymers enabled establishing the dependence between the length of the side chain and the polymer intermolecular association properties in the solution.

The preparation of a copolymer of acrylamide and acrylate derivatives, including *N-tert*-butylacrylamide and *tert*-butyl acrylate, to obtain thermoresponsive hydrogels is an exemplary synthesis of APEs [28]. In this study, free radical copolymerization resulted in the synthesis of linear copolymers with various combinations of hydrophilic and hydrophobic units with random and block sequences. The polymerization was performed in methanol and initiated by 2,2'-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70) at ambient temperature (for details, see example 2 in Table 1). The obtained copolymers had a different fraction of hydrophobic segments varying from 10% to 60%. The reported results show that the design of the structure and the proper balance of hydrophobicity and hydrophilicity in the polymer chain determine the functional features of those novel materials. In particular, they determine the swelling behaviour and thermoresponsiveness of copolymer hydrogels.

2.2. Functionalization of polyelectrolytes by grafting with hydrophobic side groups

The functionalization of reactive polyelectrolytes grafted with hydrophobic side moieties leads to modified polyelectrolytes with a random distribution of hydrophobic groups along the polymer backbone [36]. It results in new functionalized polyelectrolytes with various lengths and hydrophobicity. The synthesis relies on easy derivatization of chemically reactive groups located along the polyelectrolyte backbone that form functional links as ester or amide. The reactions introduce the desired functionalities to native polyelectrolytes, opening possibilities for the chemical tailoring of polymer structure that can be controlled by polyelectrolyte design. Furthermore, the discussed strategy allows exploring the effect of the degree of functionalization on the self-assembly behaviour, hydrophobicity and applicable properties of HD-PEs. For example, the linking moiety with the required function allows the synthesis of stimuli-responsive HD-PEs used as building materials for intelligent drug delivery systems [16].

Recently, various approaches toward hydrophobic modification of polyelectrolytes have been widely investigated as quaternization, esterification, amidation, alkylation, Schiff base reduction or acylation. Each type of functionalization reaction varies in degree of complexity and the number of steps. Quaternization enables the preparation of hydrophobically modified polyelectrolytes bearing quaternary ammonium moieties of different alkyl chain lengths. An example of hydrophobic modification of poly(dimethyl diallylammonium chloride) by quaternization reaction has been reported by Rios and co-workers (for details, see example 4 in Table 1) [37]. A highly hydrophilic polyelectrolyte was modified with *n*-alkyl chlorides, resulting in HD-PEs with different lengths of side alkyl chains. The studied water-soluble amphipathic polyelectrolytes revealed high surface activity and enabled the formation of hydrophobic microdomains, which could stabilize the polyelectrolyte in an aqueous solution.

On the other hand, post-functionalization was performed by a three-step process, including quaternization with alkyl amide bromides [38]. Maleic anhydride based polymers were obtained with various hydrophobic side chains to investigate the influence of alkyl chain structure on

amphiphilicity. The advantage of the modified polyelectrolytes was the presence of biodegradable amide groups linking the side chains that provided degradation of polymers and release of bioactive moieties for biofilm disruption. In other work, poly(4-vinylpyridine) was quaternized with short alkyl substituents to obtain polyelectrolytes with varying side chain lengths [39]. This simple modification allowed determining the effect of hydrophobicity on the polyelectrolyte complexation and rheological behaviour.

Steglich esterification and amidation, based on the mechanism of carbodiimide chemistry, comprise very important approaches for polyelectrolytes' decoration with different chemical moieties. This strategy uses traditionally *N,N'*-dicyclohexylcarbodiimide (DCC) as a coupling agent and *N*-(dimethylamino)pyridine (DMAP) as a catalyst to activate an acid leading to the formation of ester or amide [40,41]. The reaction should be performed in water-free conditions in an organic solvent, so its usage for polyelectrolytes functionalization is limited. On the other hand, it is possible to perform Steglich esterification or amidation in aqueous conditions using water-soluble coupling agents (e.g. *N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) and *N*-hydroxysulfosuccinimide or its sodium salt) [42]. The advantage of this strategy is the synthesis in mild reaction conditions of various ester or amide derivatives of compounds with sensitive functional groups. For that reason, Steglich esterification and amidation are widely used for a simple and easy hydrophobic functionalization of polyelectrolytes. An effective modification of polyelectrolytes such as poly(acrylic acid) and poly(4-styrenesulfonic-*co*-maleic acid) was performed utilizing such carbodiimide coupling reactions (for details, see examples 8 and 9 in Table 1) [19,20]. Labile linkages in polyelectrolyte structure enabled the preparation of pH-sensitive polymers. They were obtained with a high yield reaching up to 75%, utilizing *N*-ethyl-*N'*-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) as a coupling agent. The synthesized HD-PEs were modified with alkyl chains of different lengths (C_{12} or C_{16}) and various degrees of substitution (15% or 40%) to study the effect of chemical structure on the aggregation properties. They exhibited high aqueous solubility, viscosity improvement and self-assembly behaviour in aqueous solution (formation of intramolecular pseudo-micellar structures). Similar properties of hydrophobically functionalized poly(acrylic acid) were studied by Aricov and co-workers, who prepared polyacrylic acids with randomly grafted decyl and dodecyl chains [24]. Successful preparation of hydrophobically modified poly(acrylic acid) was performed by the esterification of anionic polyelectrolyte with hydrophobic tetrahydrogeraniol derivative to obtain an emulsifier for the formation of nanoemulsions [43]. This study investigated the relationship between the substitution degree of hydrophobic groups and their self-assembly properties in solution toward nanoemulsion formation.

Among various hydrophilic polyelectrolytes, naturally occurring polysaccharides are frequently modified through available functional groups [44]. Due to the abundance of carboxyl and hydroxyl groups, sodium alginate can be easily functionalized, forming hydrophobic derivatives as building blocks for drug delivery systems. For example, Zhao and co-workers synthesized cholesteryl-grafted sodium alginate with various molecular weights by esterification [30]. The self-aggregation behaviour of prepared amphiphilic macromolecules enabled the fabrication of nanocarriers and efficient encapsulation of pesticides. In addition, the release rate of an active agent could be manipulated by changing the molecular weight of the modified polyelectrolytes. Another example of hydrophobic modification using the amidation reaction was the synthesis of deoxycholic acid-grafted chitosan [4]. The hydrophobic substituent was covalently attached to the main backbone of chitosan with varied substitution degrees. The functionalized polyelectrolyte was used to form drug-loaded nanoparticles with release controlled by the hydrophobization degree of chitosan.

Schiff base reactions were also applied to obtain hydrophobically modified polyelectrolytes. There are several reports on using this type of reaction to functionalise poly(allylamine hydrochloride) as a water-soluble polyelectrolyte with primary amino groups. For instance,

benzaldehyde was used to introduce hydrophobic groups to poly(allylamine hydrochloride) by Schiff reaction under alkaline conditions [45]. The increase in hydrophobicity led to the formation of self-aggregated structures exhibiting interfacial activity and the ability to form nanoparticles and stable foam systems. The existence of an imine bond between hydrophilic polyelectrolyte and benzaldehyde group enabled the preparation of pH-responsive polymers. More recently, amphiphilic polyelectrolytes were obtained by substitution of poly(allylamine hydrochloride) with hexyl chains using Schiff base reduction method with sodium borohydride followed by methylation (for details, see example 11 in Table 1) [46] or modification with appropriate strength ionic groups [47]. The synthesized polymers self-assembled into pseudomicellar structures and were able to form polyelectrolyte multilayers with different physicochemical features.

A commonly reported approach for preparing HD-PEs is the alkylation comprising a simple methodology for hydrophobic functionalization of polyelectrolytes with *n*-alkyl chains [48]. A series of amphiphilic macromolecules was synthesized by a two-step modification of polymethyloxazoline, including partial hydrolysis and alkylation [49]. The polymers were alkylated using bromododecane, forming side-modified derivatives with the desired hydrophobicity. The presence of long alkyl chains in the polymer structure led to the formation of aggregates and improved the antimicrobial activity of the studied macromolecules. Another example of the preparation of alkylated polyelectrolytes is the substitution of polyethyleneimine with alkyl chains of various lengths (C₈–C₁₆) [50]. The obtained HD-PEs were found to form intramolecular micelles. In addition, the amphiphilic polymers exhibited high surface activity and antibacterial properties depending on the length of hydrophobic chains.

Polyelectrolytes can also be hydrophobically modified using an acylation process. For example, the introduction of alkyl segments onto the chitosan backbone has been performed by Lopes's group using acyl chlorides with a different number of carbon atoms [51]. They investigated the effect of alkyl chain length on the rheological behaviour of modified polysaccharides. It should be noticed that alkylation (especially with alkyl halides comprising long chains, from octyl to hexadecyl) may be combined with quaternization of appropriate tertiary amine groups.

All the mentioned investigations concern various synthetic approaches and functionalization methods for synthesizing HD-PEs. However, plenty of essential reaction parameters affect the preparation of modified polyelectrolytes with desired physicochemical properties. These parameters include the type and distribution of polyelectrolyte charge, amount and type of hydrophobic substituents, the molecular weight of polymer, temperature, pH and type of solvent. It is possible to find the optimal ones by optimizing reaction conditions using novel computing optimal designs (design of experiment, DoE) [52].

To summarise this subchapter, post-functionalization of polyelectrolytes through chemical grafting with hydrophobic moieties offers a wide diversity of reactions. However, there are no general rules for identifying the best modification strategy; thus, it has to be chosen according to the desired outcome. Choosing of appropriate synthetic strategy as well as optimization of the reaction conditions constitute crucial steps toward the desired HD-PEs self-aggregation and interfacial adsorption performance.

3. General features of HD-PEs

Research in colloid chemistry and polymer sciences have recently provided many examples of unique properties of modified polyelectrolytes. Recalling, polyelectrolyte backbone may be decorated with hydrophobic units by chemical modification using linear [46,47,53] and aromatic [17,39,45,52] carbohydrate groups linking to the hydrophilic polymer backbone by appropriate chemical links to obtain hydrophobically decorated polyelectrolytes (HD-PEs). The behaviour of such amphiphilic macromolecules in solution is highly dependent on the type

of solvent. We can group solvents into two main classes, i.e., nonselective and selective ones. The first one can simultaneously solvate both fragments of APEs with similar effectiveness. An example of such a solvent is acetone for amphiphilic polycations [54]. The selective solvent can solvate only particular groups within the amphiphilic macromolecule leaving the remaining fragments hardly solubilized. In such a case, self-aggregation phenomena may appear. Water is the most important selective solvent for numerous polymers [22,55,56]. Thus, the macromolecules may self-organize in an aqueous solution to form structures with microdomains of opposite nature, i.e. hydrophilic and hydrophobic, that are separated from each other. Depending on the chemical structure of HD-PEs, the solvated aggregates can take a variety of shapes, which are a consequence of the balance between two main forces i.e. long range electrostatic repulsion (Coulomb) of charged groups as well as van der Waals attraction and hydrophobic interactions of nonpolar groups within amphiphilic polyelectrolyte [36].

3.1. Self-assembly of HD-PEs in water

The solubility of HD-PEs in water depends on a number of factors as the charge density of the polyelectrolyte backbone (pH-dependent in case of weak polyelectrolytes), the density of grafting of hydrophobic moieties and their hydrophobicity (e.g. length of the hydrocarbon chain, salt concentration and the type of counterions). In general, the amphiphilic association tend to minimize the contact between water molecules and nonpolar groups while the charged moieties become hydrated. Thus, two main forces that act in the opposite way, i.e., electrostatic repulsion and hydrophobic attraction, have to be balanced within the macromolecules of HD-PEs. The equilibration of these two interactions (minimization of the free energy) can lead to the spontaneous formation of self-assembled structures in an aqueous solution [29,36]. Such inter- and intramolecular assemblies of HD-PEs may be additionally stabilized by the formation of hydrogen bonds or restricted due to steric forces of overlapping interfaces [29]. Recalling the opposite nature of charged and hydrophobic moieties within HD-PE, it seems evident that some fragments will be hydrated, in contrast to non-charged, hydrophobic units repelled by the external, i.e. hydrophilic, environment [57]. Thus, the transition between the stretched out and aggregated forms is the crucial step in the self-organizing of hydrophobically decorated polyelectrolytes in aqueous systems, as illustrated in Fig. 2.

At low salt conditions, separated HD-PEs are in the stretched, rod-like conformations due to repulsive electrostatic interaction between charged segments. Depending on their length and the charge density of the polyelectrolyte backbone, the hydrophobic units are either exposed to the aqueous environment or partially folded on the backbone. Upon addition of salt or decrease of polyelectrolyte charge and depending on the chain flexibility, the HD-PE chain locally folds and the hydrophobic nanodomains (pseudomicelles) are formed [36]. The macromolecule assumes a "pearl-necklace" conformation. The theory of that conformation was first suggested by Dobrynin et al. [55] and was confirmed by both experimental (e.g. dynamic light scattering [58], small-angle neutron scattering [54], nuclear magnetic resonance [59], conductometry [60]) and theoretical approaches [56,57]. It explains a good water solubility of hydrophobically modified macromolecules even for a high density of the hydrophobic grafting. HD-PEs are generally water-soluble and form transparent suspensions. That is characteristic for both weak electrolyte derivatives (e.g. containing only carboxylate groups) [19] as well as strong ones (e.g. quaternized poly(2-vinyl pyridine)) in poor-solvent conditions like water mixed with non-electrolyte compounds (e.g. ethylene glycol) due to lower degree of charged group ionization [60]. These findings were confirmed by both NMR and molecular modelling [20], whereas the conductivity measurements showed a good agreement with the polyelectrolyte scaling theory [60]. For less flexible PE chains and short hydrophobic units, the macromolecules assume coil-like conformations [57]. In the high salt conditions, the electrostatic repulsion between charged units is screened and the

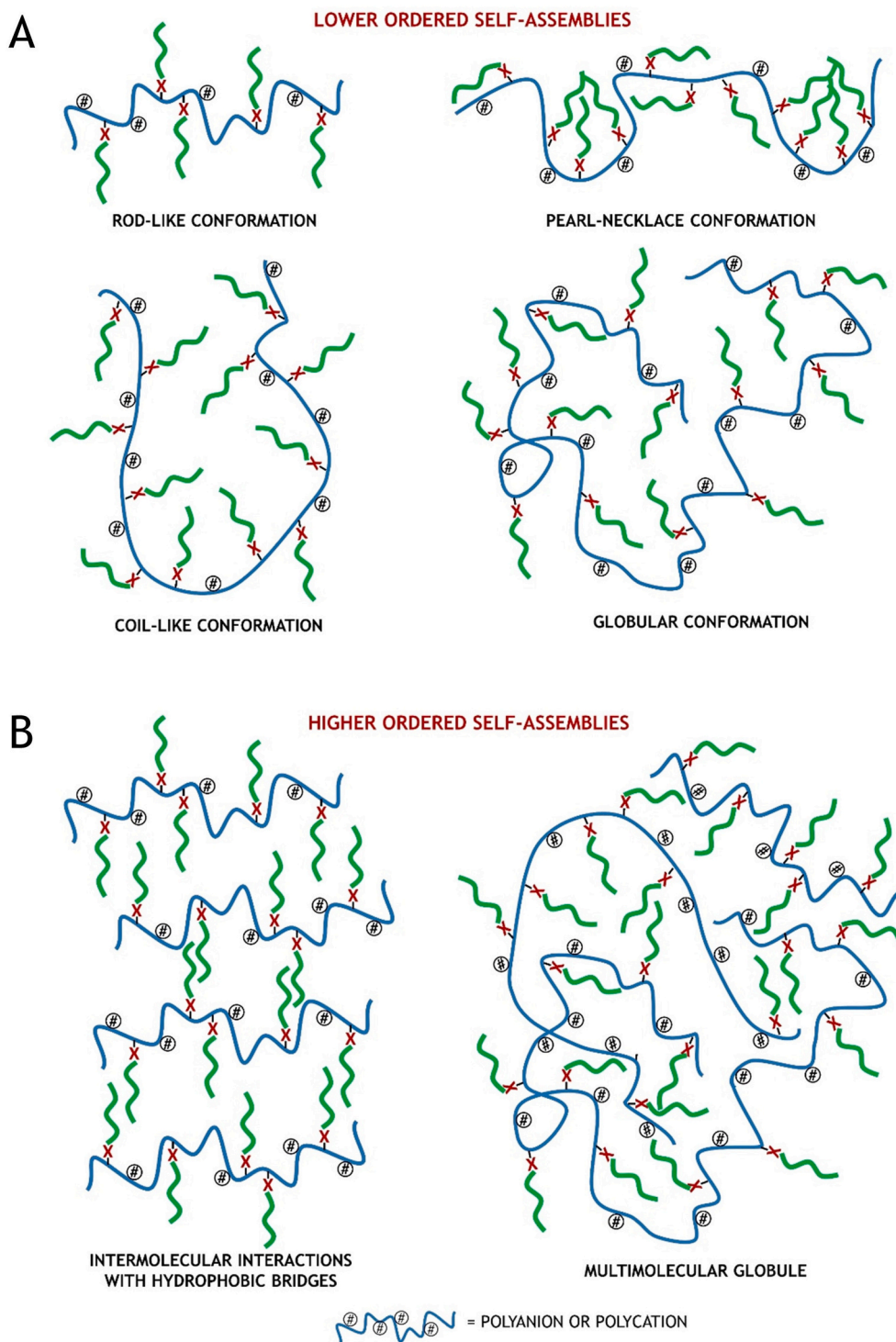


Fig. 2. Graphical representation of self-assemble aggregates of HD-PEs due to intra- (A) and intermolecular (B) interactions.

macromolecule assumes a globular conformation in which the “pearl-necklace” fragments can be preserved.

Although the “pearl-necklace” conformation originates from analysis of the single macromolecule behaviour, it may be extended into intermolecular aggregation, in which hydrophobic domains or bridges are formed by more than one HD-PE chain (Fig. 2B) [57,60]. Those aggregates are relatively sensitive to changes in the solution in contrast to more stable local micelles [19,20]. Consequently, the concentration is also a decisive factor that influences the aggregation behaviour of HD-PEs in aqueous solutions [61,62]. Increasing HD-PEs concentration

leads to a higher probability of the hydrophobic domain overlap and favouring the aggregation of HD-PE. The cross-linking by physical interactions leads to the formation of large intermolecular aggregates or gel-like structures [63]. On the other hand, in concentrated solutions, there is a high probability of disruption of larger aggregates due to their larger space demand [13].

The behaviour of particular HD-PE in an aqueous solution may be tuned by appropriate external stimuli such as ionic strength or pH changes that affect the screening of the electrostatic interactions or charge of the weak polyelectrolyte backbone [64,65]. The acidic

environment enhances the tendency to self-aggregate hydrophobically decorated weak polyanions, while the same effect is observed for the hydrophobized weak polycations in the basic solution.

The self-assembly of HD-PEs depends not only on the salt concentration but also on the type of inorganic ions in the aqueous solution [66]. That can be attributed to a different affinity to PE counterion to the charged polymer backbone. Counterions with higher affinity (more hydrophobic) are more effective in charge neutralization and screening electrostatic repulsion between polyelectrolyte segments. Differences in the counterions hydration can be the alternative cause of ion specificity, more hydrated ions leaving less space for hydrocarbon chains, thus, more extended aggregates [67].

The solvent quality for the polyelectrolyte is another factor that influences the aggregation behaviour of HD-PEs and may be tuned by adding appropriate less polar liquids to water. The self-organization of HD-PEs is studied in an aqueous solution since water acts as a “better” solvent for ionic groups but “poorer” for non-charged ones. However, in numerous common organic solvents, even polar ones like methanol, polyelectrolytes are less dissociated than in water, consequently, they behave like weakly charged HD-PE. On the other hand, such mixtures as water with ethylene glycol are better solvents of the hydrophobic moieties. Thus, they provide an environment of tunable solvent quality [60]. If the HF-PE are hydrophobic with high hydrophobic moieties grafting density, they are soluble in organic solvents, forming quasi-reverse micelle systems with an inner polar core [37].

3.2. Methods for studying self-aggregation

Self-assembly of hydrophobically functionalized polyelectrolytes HD-PEs affects numerous micro- and macroscopic phenomena. Thus using adequate instrumental methods, it is possible to study the fine structure of created self-aggregates and their physicochemical properties in aqueous systems. The behaviour of HD-PEs can be investigated directly or indirectly by different experimental methods, but it also may

be predicted using molecular modelling.

The experimental methods may be divided into several groups. (see Fig. 3) The first one includes direct visualization methods (i.e. high-resolution microscopic techniques like atomic force microscopy (AFM) [46,68], scanning and transmittance electron microcopies (SEM and TEM, respectively) and, the most adequate for tested systems, cryo-TEM [46,69]. The second group of methods is based on the scattering of light (e.g. dynamic light scattering (DLS), static light scattering (SLS) and laser light scattering (LLS) [70]), X-rays (small-angle X-ray scattering (SAXS)) or neutron beams (small-angle neutron scattering (SANS)) [71]. The others are related to direct interactions with appropriate electromagnetic radiation (mainly high resolution nuclear magnetic resonance (HR NMR) [19,20]; macroscopic phenomena (mainly surface tension, rheological or viscoelastic behaviour [52]); titration (e.g. calorimetric [72] or potentiometric [73]) and finally probing with different molecules (e.g. exhibiting fluorescence, UV-Vis and spin responsivity) [46,67,74,75].

Microscopic methods are beneficial for direct studying the conformational behaviour of HD-PEs. However, such an approach has numerous drawbacks to overcome to get reliable results. First of all, the most common way in preparation of the sample for microscopic examination involves adsorption of the macromolecules or their aggregates on the surface, and in the case of electron microscopy techniques, followed by appropriate preparation of the sample, including drying and covering or saturation sample with appropriate contrast agent. Unfortunately, such sample modification significantly changes the conformation or even chemical structure of the examined HD-PE. The unique microscopic technique that eliminates such drawbacks is a direct measuring of the dynamic equilibrium of a soft sample (i.e. polymer or biological) in a liquid state using the AFM in non-contact, tapping mode or even using a modified AFM cantilever [68]. It should be noted that crucial parameters related to conformation like end-to-end distance (R), contour length (L) and persistence length (l_p) may be directly assessed from AFM images [68]. Although adsorption may significantly change

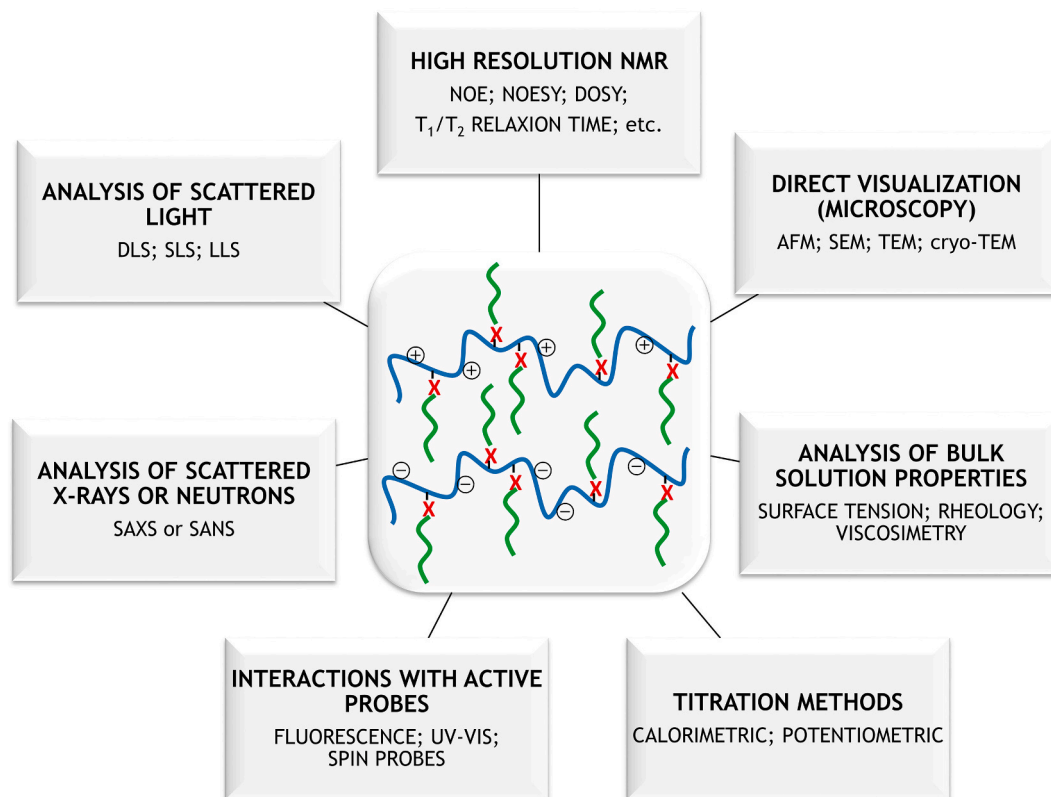


Fig. 3. Experimental research methods used for studying the behaviour of HD-PEs in an aqueous solution.

the conformation of the macromolecule in comparison to the equilibrium state in the solution, it is possible to adopt an appropriate correcting coefficient similarly as it was done for DNA. A unique opportunity for AFM analysis is a chemical modification of the tip. It allows analysis of the nature of interactions with moieties at the surface and may image the actual conformation of the macromolecules [76]. As it was mentioned before, the direct use of electron beam microscopy (TEM and SEM) for studying the conformational behaviour of HD-PEs is limited due to harsh conditions during samples preparation, including non-equilibrium adsorption, dehydration and metal sputtering, which may completely change the structure of the macromolecules' assemblies. Moreover, the measurements are performed in high vacuum conditions. The alternative seems to be cryo-TEM, where the morphology of the sample is conserved by fast freezing in amorphous ice. Therefore, it is possible to gain information about the HD-PE self-assemblies regularity and connections between particular substructures within the aggregate [46].

Methods based on the scattering phenomena allow determining different features of HD-PE structures in their dissolved or dispersed systems, enabling analysis of conformations of polymers and their aggregates in their native state. The main principle of the techniques constitutes the analysis of the scattered beam by the macromolecules in the solution or dispersion. They are helpful for any colloidal systems due to the possibility of conducting the not invasive measurements in the natural conditions of the analyzed sample. The data obtained from scattering methods include hydrodynamic diameter, its distribution, aggregate shape, and zeta potential. Nevertheless, some parameters such as refractive index within concentration increment range or absorptivity properties of the sample need to be determined prior to the analysis. Dynamic light scattering (DLS) is a versatile technique as it allows to determine the value of the hydrodynamic radius (R_h) of nano and sub-micron objects in a colloidal system and also study their higher-ordered structures in dilute solutions [77]. The determined intensity of an average size distribution allows analysis of all the peaks in the size spectrum and gain information not only about the main form of the HD-PE (the main peak that represents hydrodynamic diameter) but also about larger aggregates (the minor peaks attributed to the objects with the lower values of diffusion coefficient) [52]. Thus, the DLS investigation supported by a detailed statistical analysis of the collected data may help understand HD-PE aggregation behaviour, conformational changes of the aggregates, their disruption and formation of inter-chain associates. The mentioned behaviour of the aggregates was found to exhibit a high impact on the phenomena observed on the macroscale, like the rheological properties of HD-PE solutions [52]. Moreover, electrophoretic mobility assisted by DLS or SLS can be measured to gain information about single polymers or aggregates' zeta potential, which gives information about the electrostatic interaction. Similar physical phenomena are exploited by other scattering techniques like SAXS and SANS that utilize X-ray and neutron beams, respectively. Both methods are complementary and similar to each other and comprise one of the most complex approaches of HD-PEs structural analysis, allowing to gain crucial information about the whole secondary and tertiary structural elements of the self-assemblies. The SAXS and SANS examination provide the information not only about the mean aggregation number, i. e. the number of macromolecules involved in a single aggregate, but also related to the structure of the whole HD-PE assemblies in both local (like helical, rod-like, etc.) and general conformation of higher-ordered self-aggregates (like wormlike or "pearl-necklace") [78].

HR-NMR techniques constitute a powerful tool for analyzing subtle changes in colloidal systems. It has to be emphasized that these methodologies cause no changes in the sample, but some of them are time-consuming, thus the application of HR-NMR is limited to colloiddally and chemically stable samples. NMR techniques may involve through space interactions investigations via Overhauser effect (NOE), including two-dimensional approaches (2D NOESY), spin-lattice (T_1) and spin-spin (T_2) relaxometry, NMR diffusometry (DOSY) and also resonance

line broadening [19,20,74]. These methods are particularly useful for investigating very tiny structural elements of HD-PE, like local micelles, and may provide detailed information about their dimensions, internal structures and dynamics.

Notably, the structure of HD-PEs in the dissolved state influences the macroscopic parameters of the solution, especially the behaviour upon shear, related to the rheological properties. Thus, HD-PEs are commonly used as thickeners or viscosifiers. The rheological parameters are easily measurable by different techniques and give information about the conformation and internal structure of the HD-PE in the solution. Fitting the measured viscosity to the viscoelastic models provides information about the storage and the loss moduli related to the material's ability to store energy elastically and dissipate stress through heat, respectively. The obtained data may be helpful in the interpretation of the HD-PE systems as solid or liquid-like, providing information about the time needed to respond to the force change [79]. At low salt concentrations, the increased stretching of the polymer chains and interchain interaction leads to a viscosity increase [80], while at higher ionic strength, the electrostatic interactions are reduced, and more compact conformations are assumed due to hydrophobic interactions and the viscosity decreases. The detailed analysis of the rheological behaviour of HD-PEs solutions, supported by appropriate techniques like oscillatory frequency sweep measurements and DLS tests, allows indicating which particular changes within the microstructure of HD-PE aggregates are responsible for the effect observed in the macro scale [52].

The measurements of static and dynamic surface or interfacial tension (e.g. by drop or bubble shape analysis) provide information about the surface activity and adsorption kinetics, i.e., the rate of diffusion of HD-PE macromolecules from bulky solution to the interface and the conformational changes therein [79]. Other methods that are used for investigations of self-assembly properties of HD-PEs encompass titration procedures. The addition of appropriate titrant, e.g. electrolyte, pH or solvent, to the solution of HD-PE may induce measurable changes in different parameters like conductivity, electric potential, ion activity and heat of chemical or physical transitions. The most useful titration approaches are isothermal calorimetric titration and potentiometric titration [72,73]. The first method provides information about the enthalpy of mixing HD-PEs with appropriate low molecular weight electrolytes to give information about the electrostatic interactions. The energetical effects are dependent on the charge and hydrophobicity of the HD-PE and the type of the added salt. The second method is used to determine the pK_a value indicating the strength of ionizable groups within HD-PE and allows to predict the behaviour of HD-PE depending on the pH of the solution.

It is sometimes difficult to investigate subtle changes or specific parameters of HD-PEs solutions by conducting direct measurements. In such cases, the addition of highly sensitive chemical or physical probes, e.g. fluorescence, spin or UV-vis susceptible ones, may be helpful to overcome the obstacles to find the subtle structure of HD-PE assemblies. The chemical probe may be introduced into the HD-PE solution in the form of the species incorporated physically within its structure or chemically attached as the pendant group to macromolecule of hydrophobic polyelectrolyte. The first method may result in significant changes in HD-PE structure, especially when the used probe, e.g. hydrophobic pyrene with conjugated bonds and planar structure, may influence the conformation of the amphiphilic macromolecule [46,74]. The second may introduce some sterical barriers influencing the macromolecule structure.

Spin probes may provide information about the mobility, viscosity and polarity of the surrounding microenvironment. Thus, they are very useful for studying the behaviour of amphiphilic structures in solution. The use of spin probes for HD-PE investigations may be exemplified by the careful studies of enzyme-mediated radical polymerization of ionic liquids [75]. Finally, UV-vis probing may exploit the possibility of binding a particular probe, like methyl orange, to appropriate hydrophobic domains in nanoaggregates [67].

The results obtained by the abovementioned experimental methods can be supported by different theoretical methodologies based on molecular modelling encompassing the quantum chemical approach and/or molecular dynamic simulations. Nowadays, due to the fast development of computational possibilities, it becomes feasible to support the interpretation of experimental results, particularly for the single HD-PE chain conformation or their aggregates, the effect of charging of polyelectrolyte backbone, type of hydrophobic moieties and linking groups [19,20,81]. Therefore, the combination of experimental methods and theoretical investigations based on molecular simulation can provide a complete description of the HD-PEs systems in bulk and at interfaces.

3.3. Adsorption of hydrophobically decorated polyelectrolytes

As HD-PEs contain both hydrophilic and hydrophobic domains in their structure, their behaviour is similar to surfactants. Therefore, unlike unmodified polyelectrolytes, they can adsorb on either hydrophilic or hydrophobic surfaces (Fig. 4). The driving forces for the adsorption of hydrophilic (water-soluble) HD-PEs at hydrophilic surfaces are the electrostatic interactions between the charged polymer backbone and the surface, hydrogen bonds between donor and acceptor groups and the hydrophobic interactions of the hydrophobic chains in an aqueous solvent [82].

The adsorption of HD-PE at a solid hydrophilic surface with the opposite charge is mainly irreversible, driven by electrostatic interactions and the entropic effect of the release of counterions. Adsorption is accompanied by the re-conformation at the interface that depends on the electrolyte concentration in the HD-PE solution. At low salt conditions, they stretch upon adsorption, whereas at higher electrolyte concentrations, the coiled conformation is preserved [83]. Additionally, polymer aggregates can be formed at the surface due to screened repulsion between macromolecules. The adsorption kinetics is initially controlled by diffusion. Then, after the surface is overcharged by adsorbed polymer, the adsorption rate is reduced by the electrostatic barrier and surface blocking. Upon adsorption, the hydrophobic domains can be exposed to the aqueous phase, increasing surface hydrophobicity [84]. Like unmodified polyelectrolytes, the HD-PEs can also be incorporated in the polyelectrolyte multilayers [85,86]. During the formation of the consecutive layers, the polymers are de-coiled, but the “pearl-necklace” structure can be preserved due to the hydrophilicity of the multilayers [47,87]. Thus, hydrophobic species can be effectively introduced into the multilayer structure [86].

HD-PEs can effectively adsorb at hydrophobic surfaces. For example, it was demonstrated by Paris and Cohen-Stuart that hydrophobically modified pullulan with dodecyl chains could be adsorbed at polystyrene, and the adsorbed amount was dependent on the pH of the solution and the degree of hydrophobization [88]. At low pH, the polyelectrolyte was uncharged and adsorbed much more strongly than the parent pullulan. For charged polymer, at high pH, the adsorption was strongly dependent on the grafting ratio of dodecyl chains. Zue et al. demonstrated that a hydrophobically modified polyacrylamide with hexadecyl chains could adsorb at hydrophilic silica and hydrophobic asphaltene surfaces [89]. The adhesion force on silica was driven by electrostatic interaction and hydrogen bonding. It is stronger than on asphaltene, where it is

controlled by hydrophobic interactions and van der Waals interactions between long hydrocarbon chains and asphaltene.

Typically strong polyelectrolytes are not surface active, do not adsorb at the water/air or water/oil interface, and do not decrease the interfacial tension. The addition of ionic surfactants with the headgroup charge opposite to the charge of the polymer chain is required to obtain complexes that can lower surface/interfacial tension at relatively low concentrations [90]. Hydrophobic modification of polyelectrolyte is an alternative to obtain surface active components without the necessity of additional surfactants, which can be beneficial to the application where the presence of low molecular weight surface active species should be minimized.

Bulk and interfacial properties and microscopic foam films of solution of polyacrylic acids with randomly grafted decyl and dodecyl chains were studied by Aricov et al. in dependence on pH and sodium chloride concentration. They found that the highest surface activity was observed at pH 3–4 when the carboxylic groups were uncharged. For higher pH values addition of salt caused a decrease of the dynamic and equilibrium surface tension due to screening of the electrostatic interactions. Interestingly, higher surface activity was observed for polyelectrolyte grafted with decyl than dodecyl chains. A similar observation was made by Jarek et al., who investigated adsorption at air/water and water/decane interfaces of poly(4-styrene sulfonic-co-maleic acid) polyelectrolyte unmodified and hydrophobized by grafting alkyl side chains (C12 or C16) via amid linker with 15% and 40% grafting ratio [84]. They found that higher surface activity was observed at both interfaces for the HD-PE with C12 side chains (PSS/MA-g-C12NH₂) for the lower grafting ratio (cf. Fig. 5). Simultaneously surface activity for the copolymer with the same grafting ratio was higher for C12 than C16 side chain. The addition of electrolyte increased the surface activity of hydrophobized PSS/MA polyelectrolyte. That effect was much more pronounced at the decane/solution interface. Similar findings were obtained by Théodoly et al., who studied the adsorption at the air/water interface of hydrophobic polyelectrolyte polystyrene with various degrees of sulphonation [91]. They found that such polyelectrolyte’s surface activity first increased with the charged fraction, reached an optimum at 55%, and then decreased. They explained the presence of optimum adsorption with the degree of sulfonation by a conformational barrier effect, more hydrophobic chains assuming the compact shape of a charged colloid that prevented adsorption. Similarly, Barazza et al. studied the adsorption of hydrophobically modified polyelectrolytes, poly(maleic anhydride-co-vinyl-*n*-alkyl), with *n* = 8, 10, 12, 14, and 16 carbon atoms, at the air/water [92] and *n*-octane/water interface [93]. They found that the surface tension decrease with HD-PE concentration was inversely proportional to the length of the hydrocarbon chain and the adsorption effectiveness was higher at the aqueous solution/*n*-octane interface than at the aqueous solution/air interface. They concluded that the decrease of adsorption efficiency could be attributed to the formation of polymer micelles, which were more stable for long alkyl side chains. The free energy of adsorption could be split into contributions arising from two processes, the distribution of the polymer between the bulk of the solution and interface and the arrangement of the macromolecule at the interface.

The observed phenomena can be attributed to the presence of

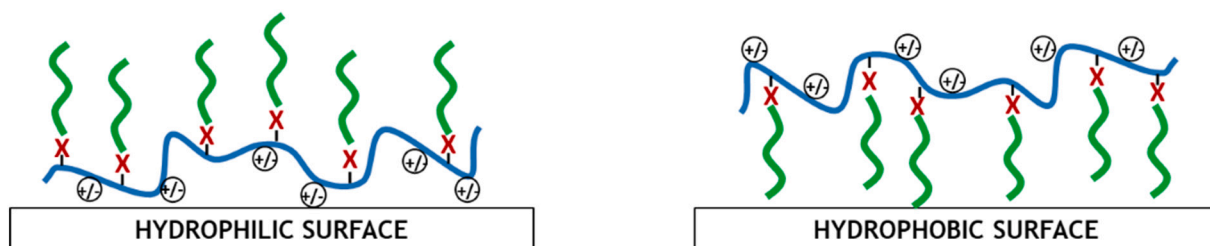


Fig. 4. Schematics of the HD-PE adsorption at a hydrophilic and hydrophobic surface.

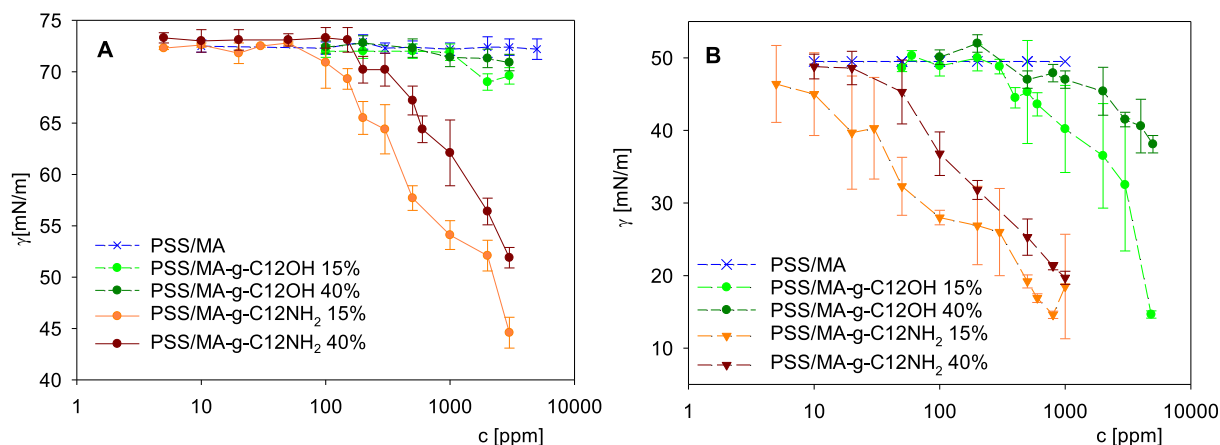


Fig. 5. The dependence of the surface tension at water/air (A) and interfacial tension at water/decane interfaces for poly(4-styrene sulfonic-co-maleic acid) with dodecyl side chains with 15% and 40% grafting density and ester and amid linkers.

hydrophobic nanodomains and the “pearl-necklace” conformation of the HD-PE. With increasing grafting density, the possibility of forming such domains increases, and they involve more hydrophobic chains. For the polymer to be adsorbed at the air/water or oil/water interface, it needs to unfold and the micelles re-conform with the alkyl chains exposed to the hydrophobic phase. The longer is the hydrophobic chain, the lower is the free energy gain of the transfer of hydrophobic moiety from the nanodomain to the interface. This gain is higher at the water/oil than water/air interface. The addition of salt makes the polyelectrolyte backbone more flexible with tighter domains due to screening of the repulsion between charged segments. Therefore, the effect of salt could be preferentially observed at the water/oil interface.

On the other hand, Rioz et al. investigated the surface activity of

cationic HD-PE, poly (*N,N*-dimethyl-*N,N*-diallyl ammonium) chloride hydrophobized by aliphatic chains with 6, 8, 10 and 12 carbon atoms with a high grafting ratio [37]. They showed that standard free energy increased linearly with the length of the chain, which evidenced that adsorption was driven by the hydrophobic effect. The discrepancy with respect to the abovementioned results could result from the stiffness of the polymer backbone and high grafting rating density that prevents the formation of nanodomains due to steric restrictions.

Synthesis of the polyallylamine hydrochloride-benzaldehyde with cleavable imine linker was proposed as pH-sensitive cationic HD-PE [92]. At pH 7.4, it exhibited a decrease in surface tension to 55 mN/m, whereas, at pH 2.5, the decrease was much lower. As in both conditions, the polyelectrolyte backbone was charged, the difference could

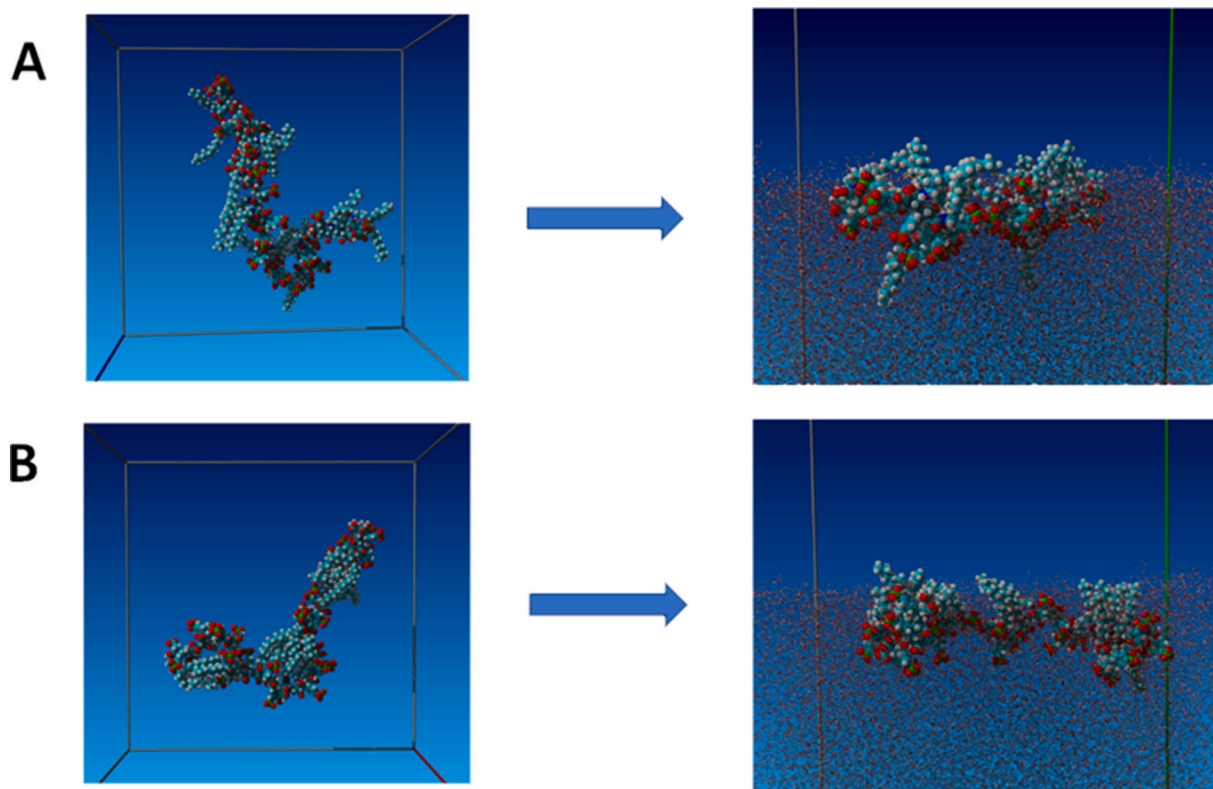


Fig. 6. The illustration of the effect of the linker on the adsorption of the HD-PE at the water/air interface based on the snapshots of the molecular dynamics simulations for poly(4-styrene sulfonic-co-maleic acid) with dodecyl side chains with 15% grafting density. A – amide linker, B – ester linker.

be attributed to the cleavage of the linker that produced unmodified non-surface active polycation.

Recently it was demonstrated by Warszynski et al. that the surface activity of HD-PE may depend on the type of linker between the polyelectrolyte backbone and hydrophobic side chains [94]. They studied adsorption at air/water and water/decane interfaces of poly(4-styrene sulfonic-co-maleic acid) with dodecyl side chains with 15% and 40% grafting density. The side chains were linked with the polyelectrolyte backbone with the ester (PSS/MA-g-C12OH) and amide (PSS/MA-g-C12NH₂) linkers. As shown in Fig. 5, the decrease of the surface and interfacial tension was much higher for the HD-PE with an amide linker. That was explained by forming more tight hydrophobic domains along the (PSS/MA) backbone by alkyl side chains connected with ester linkers. Due to intramolecular hydrogen bonds between amide groups of the linker and adjacent carboxylic groups [20], the conformations of alkyl chains are more restricted and more exposed to water. Therefore, the free energy gain is higher when they are transferred to the water/air interface. That hypothesis was supported by the results of the molecular dynamics simulations, as shown in Fig. 6.

The HD-PE with high hydrophobic moieties grafting density, soluble in organic solvents, can adsorb at the water/oil interface. Since in these solvents they behave as nonionic polymers with a minimal dissociation degree, they cannot interact electrostatically with the aqueous phase. The adsorption is driven by the enthalpy of hydration of the charged segments as the polyelectrolyte is adsorbed on the water/oil interface [82]. Babak and Boury investigated adsorption kinetics of commercial oil-soluble HD-PE, i.e. Eudragit (ammonio polymethylmethacrylate). They found three-step adsorption kinetics attributed to diffusion to the interface of the polymers in the form of reversed micelles, unfolding with the exposure of chargeable segments to water phase accompanied by dissociation, compression of the adsorbed layer depending on the electrolyte concentration in water [82]. Rioz et al. studied the interfacial properties of poly-2-(dimethylamino) ethyl methacrylate-N-alkyl quaternized with octyl, decyl, dodecyl and tetradecyl bromide dissolved in chloroform [95]. They found that the shorter polyelectrolyte aliphatic side chains were, the higher the interfacial activity was. That could be attributed to stronger van der Waals interactions of longer chains with a non-aqueous phase. The temperature dependence of the interfacial tension suggested that the adsorption was driven by entropy.

Summing up, the adsorption of HD-PE is a more complicated process than in the case of simple polyelectrolytes. It is mainly governed by electrostatic and hydrophobic interactions and affected by the charge and charge density at the polyelectrolyte backbone, its stiffness, type, length and grafting density of the hydrophobic side chains. The type of linking moiety between the backbone and the side chains and its responsiveness to the chemical stimuli (e.g. pH) can also influence the HD-PE adsorption properties.

4. Application potential of HD-PEs

HD-PEs containing both hydrophilic and hydrophobic functionalities, the latter distributed along the polymer chain, find many practical applications. They combine features of surfactants and polyelectrolytes with affinity to both polar and non-polar media. Moreover, they exhibit self-aggregation and self-organization properties, forming intra- and intermolecular hydrophobic domains. Their conformations in a solution and at interfaces and aggregation properties are dependent on a series of parameters such as electrolyte concentration, pH, temperature, quality of solvent, etc.

The incorporation of hydrophobic groups in a polyelectrolyte chain results in systems with unique rheological characteristics in an aqueous solution, which is an important aspect of cosmetic formulations [96]. Interaction of the side chains with oil and surfactant can enhance shear-thickening [97]. Depending on HD-PE concentration and the ionic strength of the solution, the hydrophobic moieties associate and build a three-dimensional network (gel) that induces a strong increase in

viscosity.

The ability to control viscosity at various shear rates renders these systems useful in applications that include enhanced oil recovery [98], drilling fluids, aircraft anti-icing fluids [99], coatings or cosmetics formulations [100,101] or environmental remediation [102]. The polyelectrolytes containing both ionized and hydrophobic segments demonstrate thickening ability and salt resistance and temperature endurance, making them favourable in oil recovery technology [103,104].

HD-PEs are efficient flocculants in modern dewatering technologies. Commonly used polymer flocculants hold great amounts of water due to their hydrophilic nature and form loosely packed flocs. Therefore, the polyelectrolyte modification from hydrophilic to partly hydrophobic can improve the flocculation process due to the presence of hydrophobic domains, which can remove the water entrapped in the sediment. For example, the synthesized multifunctional poly(N-isopropyl acrylamide/acrylic acid/N-tertbutylacrylamide) (p(NIPAM-AA-NTBA)) was used as a flocculant exhibiting thermo-sensitivity and hydrophobic association [105]. The hydrophobically modified polyelectrolytes showed dewaterability of sediments, lowered turbidity, and improved the initial settling rates. The balance between the hydrophobic and hydrophilic units, charge density adjustment, and physical properties of prepared HD-PEs enabled to obtain effective flocculant for enhanced dewatering systems.

Hydrophobically functionalized polyelectrolytes can be used as stabilizers of foams and emulsions [43,45] or dispersants for hydrophobic nanoparticles [106]. Various types of emulsions, including oil-in-water emulsions, water-in-oil emulsions, or nanoemulsions, can be produced utilizing HD-PEs [107]. They proved to be more efficient emulsion stabilizers than the conventional surfactants due to slower desorption kinetic at the droplet interphase. For example, hydrophobically modified poly(acrylic acid) grafted with bio-based tetrahydrogeraniol side chains was used as an emulsifier to form terpene-in-water transparent nanoemulsion [43]. The functionalization of polyelectrolyte with different degrees of substitution of hydrophobic side chains allows obtaining oil-in-water nanoemulsions with the required properties. Furthermore, HD-PEs are potential candidates for stabilizing hydrophobic particles in aqueous solutions. Their alkyl groups can anchor at the surface and the hydrophilic polymer backbone can form a protective electrostatic layer around the particle [108]. Due to their surface activity and aggregation properties, HD-PE can also be used to form Pickering foams or emulsions [45]. Hydrophobically modified polysaccharides and their self-assembled systems can be used to improve the nutritional value and properties of food products [109].

One of the most interesting applications of HD-PE is drug delivery. Due to the creation of self-organized structures with hydrophobic domains, they can be used for nanoprecipitation and nanoencapsulation of hydrophobic active compounds [4,30] or DNA [8]. Hydrophobic functionalization of cationic polyelectrolytes enhances gene delivery activity, explained by hydrophobic interactions resulting in the complex formation between hydrophobized polyelectrolytes and genes, and by the improved cellular uptake by the hydrophobic moieties [70].

The functionalized polyelectrolytes with varied hydrophobic moieties constitute the promising building blocks for multilayer films and coatings for nano- or microparticles. HD-PEs can be built into the polyelectrolyte multilayer structures to add new functionality [47]. Self-assembled films containing HD-PEs are thicker as hydrophobic moieties can sterically impede electrostatic effects. Moreover, they provide a polymeric coating for hydrophobic surfaces, as they reveal good wettability and adhesion properties [86]. Due to their adsorption properties, HD-PEs can easily modify the bio-active surface constructed by LbL self-assembly films for biomedical applications [110]. A promising approach is the fabrication of antibacterial HD-PEs and their application in bioactive coatings [38]. For instance, hydrophobically modified poly(acrylic acid) complexes with cationic surfactants formed the multilayer films exhibiting antimicrobial activity against *S. aureus* and *C. albicans* [86]. Thus, HD-PEs can be considered as an attractive

material to create thin films with antimicrobial efficiency, low cytotoxicity, and high stability, which can find application in self-cleaning, antibacterial, and antifungal coatings for biomedical devices. Besides numerous technological, medical or pharmaceutical applications, HD-PEs may be applied in catalytic systems.

The HD-PEs can also be utilized to anchor the polyelectrolyte multilayer coatings at the surface of nanoemulsion droplets [3,111,112] or form the external layer of microgel capsules with antibacterial properties. For instance, decorated poly(acrylic acid) with different hydrophobic chains and various degrees of substitution of quaternary ammonium groups was used as the outer antimicrobial layer of curcumin-loaded microparticles [113]. The modification of microcarriers' surfaces provided the development of microsystems with desirable physicochemical and biological properties, as well as improved therapeutic application. They can be utilized to form responsive (reversible) gels for cell encapsulation for 3-D cell culture, cellular therapy, tissue sealants and homeostatic materials, and tissue engineering [114].

The key issue for the biomedical or cosmetic application of the HD-PEs is their biocompatibility. That is defined as the ability of a material to perform its desired functions for medical therapy, induce an appropriate host response in a specific application and interact with living systems without having any risk of injury, toxicity, or rejection by the immune system and undesirable or inappropriate local or systemic effects (e.g., skin irritation by cosmetic products) [115]. The introduction of longer or shorter alkyl chains into the polymer backbone should not affect those features, as well as the compatibility with the payload or other building blocks of the carrier systems. For this purpose, the hydrophobic modification of polyelectrolytes can be tuned, mainly by selecting polymer structure, molecular weight, functional groups, and hydrocarbon units [116]. Among the available polymers, the natural polyelectrolytes, especially polysaccharides, can be applied in drug delivery systems due to their biodegradability, biocompatibility, non-toxicity, and bio-functional activity, high stability, and water solubility. Therefore, sodium alginate, hyaluronic acid [117], or chitosan [4,32,118] are frequently used for further functionalization. For example, the derivative of hyaluronic acid containing hydrophobic nanocavities and poly(L-lysine) or quaternized chitosan were used to form PE multilayer shells of paclitaxel-loaded microcapsules. The prepared microcarriers coated with HD-PEs were able to release the drug in a controlled manner and revealed effective paclitaxel activity [116]. The biodegradation of HD-PEs can be controlled by the labile linking group (i.e. ester or amide) between the polyelectrolyte backbone and hydrophobic chain [119]. The sensitive linkage allows for hydrolytic or enzymatic degradation of synthetic or natural polymers, limiting the risk of harmful effects during systemic circulation or environmental impact. However, even if the natively biocompatible and biodegradable PEs are used for hydrophobic modification, it does not mean that the resulting HD-PEs will maintain those properties (even if it is modified with natural substances) [109]. They should be confirmed for every investigated system in physiological conditions, thus, the necessity for long-term in vitro and in vivo testing is a major challenge.

5. Concluding remarks and future perspectives

The aspects related to the hydrophobic decoration of polyelectrolytes to obtain {HD-PE} are reviewed. Various synthetic approaches for their fine-tuned hydrophobization involving copolymerization and chemical grafting routes are presented. The approaches are described in the context of the development of hydrophobically decorated polyelectrolyte-based materials adjusted to the required functionalities, which originates from their ability to self-assemble in aqueous solutions. Customizing various polyelectrolytes through rational design and synthesis methods makes them suitable for many specific applications, ranging from technological to biomedical. The broad spectrum of polyelectrolytes available for modification, types of hydrophobic

moieties and linking groups allows forming materials with required properties and responsiveness to physical and/or chemical stimuli. Unlike typical polyelectrolytes, the hydrophobically decorated ones can adsorb at hydrophilic and hydrophobic interfaces, which opens the possibility for a broad spectrum of applications, e.g., functional surfaces, active multi-films as semi-permanent coatings, stabilized interfaces of biomedically oriented systems. Interpretation of the experimental results and their theoretical description is still a challenge due to many parameters controlling the properties of HD-PEs. The advanced experimental techniques should be combined with the methods of molecular simulations to predict their functional features.

Declaration of Competing Interest

None.

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