

REVIEW

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# Synthesis and application of non-bioaccumulable fluorinated surfactants: a review

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## Abstract

Due to negative effects of conventional fluorinated surfactants with long perfluorocarbon chain ( $C_xF_{2x+1}$ ,  $x \geq 7$ ) like perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), these conventional long perfluorocarbon chain surfactants have been restricted in many industrial applications. Nowadays, their potential non-bioaccumulable alternatives have been developed to meet the requirements of environmental sustainable development. In this paper, the recent advances of potential non-bioaccumulable fluorinated surfactants with different fluorocarbon chain structures, including the short perfluorocarbon chain, the branched fluorocarbon chain, and the fluorocarbon chain with weak points, are reviewed from the aspects of synthesis processes, properties, and structure-activity relationships. And their applications in emulsion polymerization of fluorinated olefins, handling membrane proteins, and leather manufacture also are summarized. Furthermore, the challenges embedded in the current non-bioaccumulable fluorinated surfactants are also highlighted and discussed with the hope to provide a valuable reference for the prosperous development of fluorinated surfactants.

**Keywords:** Non-bioaccumulable fluorinated surfactants, Synthesis, Structure-activity relationship, Application

## 1 Introduction

Fluorinated surfactants, acting as special surfactants, are composed of the hydrophilic polar head group and the oleophobic and hydrophobic fluorocarbon tail chain, where at least one hydrogen is replaced by fluorine in their hydrophobic tail. In general, compared with conventional hydrocarbon surfactants, fluorinated surfactants display some unique properties due to characteristics of the fluorine element. For instance, owing to the extremely strong electronegativity of fluorine, both the strong fluorine-carbon bond and the “shielding” effect of fluorine atoms on carbon-carbon bonds provide the outstanding thermal and chemical stability for fluorinated surfactants [1–3]; and the lower polarizability of fluorine compared to hydrogen results

in weaker attractive intermolecular forces, endowing fluorocarbon chains to hydrophobic-oleophobic properties as well as fluorinated surfactants to higher surface activity [4, 5]. Particularly in the aspect of surface activity, fluorinated surfactants can effectively reduce the surface tension of their aqueous solutions at a very low concentration, with the minimum surface tension of around 15–20 mN/m [6]. Hence, since fluorinated surfactants were unexpectedly discovered in the 1950s [7], their application potentials and developments have attracted extensive attentions. Various types of fluorinated surfactants now are widely used in many fields including cosmetic [8], textile, leather [9, 10], coating [11], fire-fighting foam [12–14], solar cell [15], and biomedicine [16] etc., which represents a multibillion dollar industry [7].

The most commonly manufactured and used fluorinated surfactants are these long perfluorocarbon chain ( $C_xF_{2x+1}$ ,  $x \geq 7$ ) surfactants, such as perfluorooctanoic

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acid (PFOA), perfluorooctane sulfonate (PFOS) and their derivatives. Nevertheless, many studies have revealed that these long perfluorocarbon chain surfactants are persistent in the natural condition, toxic and bioaccumulative in the organism [17–20] because of the very stable C-F bond which is not easy to be degraded under enzymatic or metabolic decomposition [21]. For example, the half-life of PFOA in humans is 3.26 years [22], and these long perfluorocarbon chain surfactants have been detected in the human blood all over the world [23]. As a consequence, long perfluorocarbon chain surfactants are been listed as persistent organic pollutants (POPs) under Stockholm Convention in 2009 and are subsequently restricted in production and utilization in many fields [19].

For above reasons, researchers and commercial companies have developed potential non-bioaccumulable alternatives of long perfluorocarbon chain surfactants to meet the requirements of environmental sustainable development. For example, since 2003, 3M Company has produced a series of shorter-chain homologue replacements based on C4 chemistry, such as perfluorobutane sulfonic acid [24]. In this review, according to the difference of the fluorocarbon chain structure, three kinds of fluorinated surfactants (as seen in Fig. 1) which are considered to be potentially non-bioaccumulable [25–27], including 1) surfactants with the short perfluorocarbon chain ( $C_xF_{2x+1}$ ,  $x \leq 6$ ), 2) surfactants with the weak points on the fluorocarbon chain, 3) surfactants with the branched fluorocarbon chain, are mainly focused. Their synthetic processes and properties, such as surface activity, wettability, and pH and salt resistance, are briefly described, and some structure-activity relationships are analyzed. Additionally, their applications in emulsion polymerization of fluorinated olefins, handling membrane proteins, and leather manufacture are summarized, and the future development direction is prospected.

## 2 Synthesis of non-bioaccumulable fluorinated surfactants

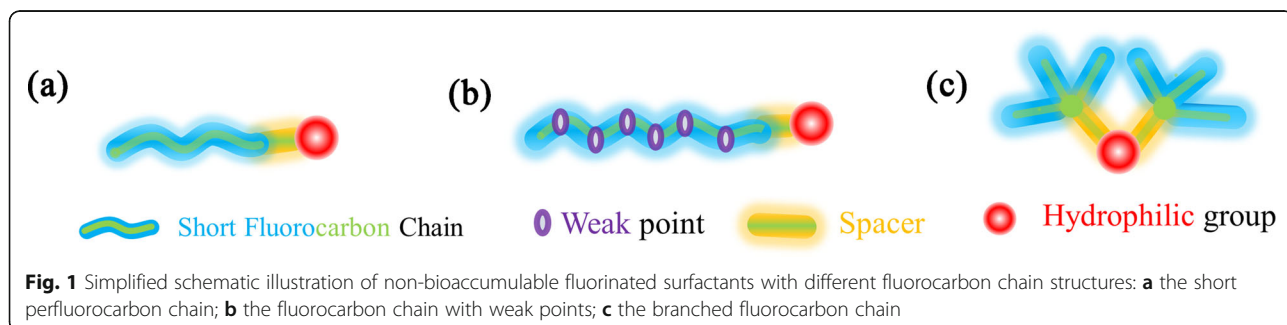
Prior to specific description, in order to facilitate readers to understand the research progress of non-bioaccumulable fluorinated surfactants, we provide

surface activity parameters, including the critical micelle concentration (CMC) and the surface tension at CMC ( $\gamma_{CMC}$ ) of some representative perfluorooctyl surfactants in Table 1, such as PFOA, sodium perfluorooctanoate (NaPFO), ammonium perfluorooctanoate (APFO), ammonium perfluorooctane sulphonate (APFOS) and potassium perfluorooctane sulphonate (KPFOS). Moreover, serum elimination half-lives of some fluorinated surfactants are shown in Table 2.

### 2.1 Surfactants with short perfluorocarbon chain

Among the non-bioaccumulable alternatives of long perfluorocarbon chain surfactants, the short perfluorocarbon chain surfactants (here, the length of short perfluorocarbon chain is less than or equal to C6) are focused by a large number of researches and reports. These short perfluorocarbon chain surfactants present potential non-bioaccumulation [40, 41]. For example, compared with PFOA (about 3.26 years), the half-life of perfluorobutane sulfonic acid is only 24 and 46 days in male and female human, respectively [22, 24].

However, with perfluorocarbon chain shortening, the surface activity of the short perfluorocarbon chain surfactants also decreases. Generally, the hydrocarbon moieties are introduced into these surfactant molecules to further increase the hydrophobicity and improve the surface activity. Lehaine et al. [42] synthesized a perfluorinated hexyl cationic fluorinated surfactants based on isourea, in which the condensation of a diisopropylcarbodiimide and a fluoroalkyl alcohol was used to obtain a fluorinated diisopropylisourea intermediate and then the intermediate reacted with the hydrohalogenated acid (HX, X=Cl or Br) to yield a salt  $\{[(CH_3)_2CHNH]_2COCH_2CH_2(CF_2)_5CF_3\}[X]$ , C8IF-X, X=Cl or Br) with surface activity. Since the perfluorinated hexyl and the hydrocarbon moiety can together improve hydrophobicity of surfactants, the prepared surfactants showed higher surface activity. And the  $\gamma_{CMC}$  of C8IF-Cl and C8IF-Br were 19.2 and 20.7 mN/m at 25 °C, respectively. Moreover, since the hydration between the bigger size counter ion with water was weaker, decreasing the electrostatic repulsion between surfactant molecules [43], the



**Table 1** CMC and  $\gamma_{CMC}$  of some perfluorooctyl surfactants

Surfactants	CMC (mmol/L)	$\gamma_{CMC}$ (mN/m)	References
PFOA	12.3	19.51	[28]
NaPFO	36	24.6	[29]
APFO	8.75	37.7	[30]
APFOS	5.5	27.8	[31]
KPFOS	8	34.5	[31]

CMC of C8IF-Br (0.211 mmol/L) was smaller than that of C8IF-Cl (1.421 mmol/L).

Shin et al. [44] designed and synthesized a kind of environmentally benign anionic hemi-fluorinated surfactants with different short perfluorocarbon chains. In detail, alkyl iodides with different fluorocarbon chain length reacted with the phenylvinylsulfonate to form phenylsulfonates using a Zn/CuI mediated Michal-type addition reaction in imidazolium ionic liquids. Then, their potassium salts  $(CF_3(CF_2)_n(CH_2)_4SO_3K, n=0, 1, 2$  or 3) were obtained successfully by hydrolyzing phenylsulfonates with KOH in ethanol/water. To avoid the byproduct (phenol), the synthesis method was optimized by replacing the phenylvinylsulfonate with the ethyl vinylsulfonate to achieve same proposed products. Compounds  $n=0$  and 1 containing shorter perfluorocarbon chains cannot effectively decreased surface tension of their aqueous solution ( $\gamma_{CMC}$  of about 50 mN/m). While with the increase of fluorocarbon chain length, compounds  $n=2$  and 3 showed higher surface activity, whose  $\gamma_{CMC}$  were 21.8 and 17.7 mN/m, respectively, at their

CMCs of 5561 and 4681 mg/L, respectively. It was worth noting that although compounds  $n=2$  and 3 had stronger ability to reduce surface tension, their CMCs were approximately 10–100 times higher than that of most reported non-bioaccumulable fluorinated surfactants [45, 46], suggesting that higher costs are needed to achieve the desired effect.

In order to further improve the hydrophobicity of short perfluorocarbon chain surfactants, researchers also attempt to introduce two hydrophobic chains into a surfactant molecule. One of the schemes is to design a surfactant bearing a short perfluorocarbon chain and a hydrocarbon chain, namely the hydro-fluorocarbon hybrid surfactant. Kang et al. [47] synthesized a series of hybrid sulfonate fluorinated surfactants  $(F(CF_2)_2CH_2OCH_2CH(SO_3Na)CH_2O(CH_2)_xH, F_2H_x, x=2, 4, 6$  or 8) using glycidyl ethers with different alkyl chain length, pentafluoropropanol (the shortest fluorocarbon chain) and chlorosulfonic acid as raw materials. The results showed that with the increase of alkyl chain length, surface activity of synthesized surfactants increased.  $F_2H_8$  had the highest surface activity in  $F_2H_x$  when alkyl chain length of 8, and the  $\gamma_{CMC}$  was 31.9 mN/m at CMC of 0.1 mmol/L. Yang et al. [48] reported a pyridine-based hydro-fluorocarbon hybrid surfactants  $([CF_3(CF_2)_5CH(OH)pyC_nH_{2n+1}][Br], n=8, 10, 12, 14$  or 16) with longer alkyl chains. With the increase of alkyl chain length ( $n$  from 8 to 16), CMC decreased gradually from  $16.4 \times 10^{-3}$  to  $1.3 \times 10^{-3}$  mmol/L but  $\gamma_{CMC}$  increased gradually from 16.27 to 20.76 mN/m, indicating that a suitable alkyl chain is important for these hydro-fluorocarbon hybrid surfactants to obtain a better surface activity.

**Table 2** Serum elimination half-lives of some fluorinated surfactants (KPFOS, PFOA, perfluoroheptanoic acid (PFHA), perfluorohexanoic acid (PFHxA), potassium perfluorobutylsulfonate (KPFBS), ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy) propanoate acid (GenX) and ammonium 4,8-dioxo-3H-perfluorononanoate (ADONA)) in female (F) and male (M) rats, monkeys and humans

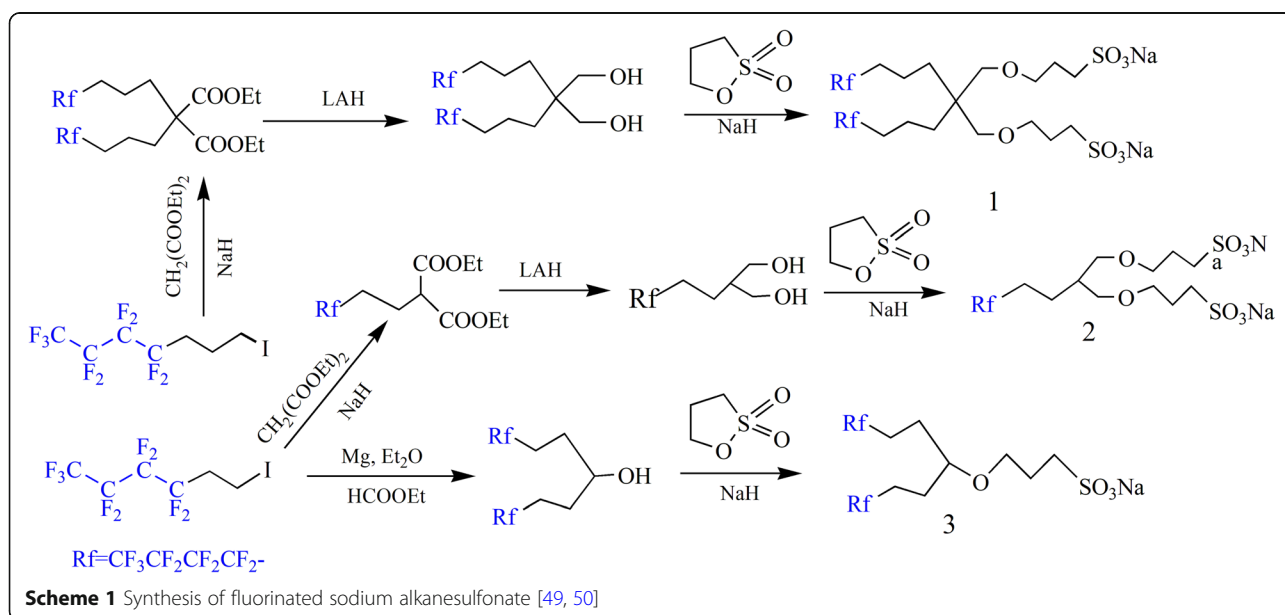
Surfactants	Sex	Serum elimination half-lives		
		Rats	Monkeys	Humans
KPFOS ( $C_8F_{17}SO_3K$ )	F	7.99±4.94 d [32]	110±15 d [32]	5.9 years [22]
	M	38 d [32]	131 ±7 d [32]	5.4 years [22]
PFOA ( $C_7F_{15}COOH$ )	F	1.9±0.7 h [33]	32.6 ±6.5 d [34]	3.3 years [22]
	M	5.63±1.2 d [33]	20.9 ±10.2 d [34]	3.8 years [22]
PFHA ( $C_6F_{13}COOH$ )	F	1.2 h [33]	–	70 d [35]
	M	2.4 h [33]	–	–
PFHxA ( $C_5F_{11}COOH$ )	F	0.4 h [36]	2.4±1.7 h [36]	–
	M	1 h [36]	5.3±2.5 h [36]	32 d [37]
KPFBS ( $C_4F_9SO_3K$ )	F	4.51±2.22 h [38]	95.2±27.1 h [38]	45.7 d [38]
	M	3.96±0.21 h [38]	83.2±41.9 h [38]	24.1 d [38]
GenX ( $C_3F_7OCF(CF_3)COONH_4$ )	F	< 12 h [24]	–	–
	M	< 12 h [24]	–	–
ADONA ( $CF_3OC_3F_6O COONH_4$ )	M	44 h [39]	–	23.3±10.6 d [39]

Besides the hydro-fluorocarbon hybrid surfactant, another option is to introduce two short perfluorocarbon chains into a surfactant molecule to increase its hydrophobicity. For example, Shin's group [49, 50] synthesized two di-perfluorobutyl substituted sodium alkanesulfonate derivatives, and compared their surface activity with mono-perfluorobutyl derivatives (Scheme 1). The results showed that the compound 3 exhibited the highest surface activity with  $\gamma_{CMC}$  of 22.2 mN/m at CMC of 3.2 mmol/L, which might be ascribed to the more appropriate structure of compound 3 bearing one hydrophilic sulfonates head and two hydrophobic perfluorobutyl tails. Consequently, in practice, the hydrophile-lipophile balance should be thoroughly considered when designing the structure of surfactants [51]. Moreover, these compounds could be moderately degraded at biodegradable points, such as ether links, hydrocarbon moieties, and were retained below 60% level at 28 days in biodegradability test.

Wang et al. [52] reported the synthesis of a fluorinated Gemini sulfoacid surfactants with two perfluorohexyl chains ( $2C_6^F C_3$ -Sul). Firstly, 3-perfluorohexyl-1,2-epoxypropane reacted with hexamethylenediamine to produce the intermediate with two secondary amino groups, and then the intermediate reacted with 1,3-propanesultone to obtain  $2C_6^F C_3$ -Sul. Generally, the hydrophobicity of Gemini surfactants is stronger than that of monomeric surfactants in hydrocarbon surfactants, so Gemini surfactants are easier to form micelles in the aqueous solution and pack densely at the air-water interface than monomeric surfactants, presenting lower CMCs and surface tensions [43]. Here, this situation also is applicable for  $2C_6^F C_3$ -Sul, which showed a higher surface activity

with  $\gamma_{CMC}$  of 20.27 mN/m at CMC of 0.082 mmol/L. In this case, the decrease of electrostatic repulsion among polar head groups was also conducive to the close packing of surfactant molecules at the air-water interface [53]. With addition of NaCl, the electric double layer was compressed to decrease electrostatic repulsion among polar head groups of  $2C_6^F C_3$ -Sul, resulting in further decreasing CMC and  $\gamma_{CMC}$  (0.052 mmol and 17.17 mN/m, 50 mmol/mL NaCl). Furthermore, Wang's group [54] also investigated the effects of pH and inorganic salts on the surface activity of sodium salt of  $2C_6^F C_3$ -Sul. The results showed that the surface activity increased in alkali pH range and in inorganic salts solutions. Compared with NaCl,  $CaCl_2$  was more effective for the formation of micelles because the divalent  $Ca^{2+}$  bound more closely with the surfactant. The above results suggest that the surface activity of fluorinated surfactants can be improved in alkali pH range or adding inorganic salts, which might be an important way to save costs. Of course, it depends on the conditions of use.

Quagliotto et al. [55] also reported a series of Gemini fluorinated pyridinium surfactants with two perfluorohexyl chains ( $[C_6F_{13}CH_2CH_2py-(CH_2)_n-pyCH_2CH_2C_6F_{13}][Cl]_2$ ,  $n=3, 4, 8$  or  $12$ , FGPn), and investigated the effects of spacer length on the surface activity of FGPn. With the increase of spacer length, the  $\gamma_{CMC}$  of FGPn increased from 27.7 (FGP3) to 30.9 mN/m (FGP12), but the change trend of CMC was atypical, which was due to the fact that fluorinated chains are not compatible with the hydrocarbon spacer to prevent the spacer from folding towards the fluorinated chain and further to prevent perfluorocarbon chains from packing closely at the air-water interface [56]. This result is similar to that of some





conventional hydrocarbon surfactants [57, 58], indicating that a suitable spacer is meaningful to obtain a better surface activity effect in the design of surfactants. Furthermore, owing to the electrostatic interaction between the multiple cationic charges of FGPn and the negative charges of DNA phosphate groups, FGPn also were applied in the investigation of gene delivery [9, 59].

Shen et al. [60] also synthesized a series of special molecular structure nonionic short fluorocarbon chain surfactants ( $F_mEG_nF_m$ ) by connecting two short fluorocarbon chains ( $C_xF_{2x+1}$ ,  $x=6, 4$  or  $2$ ) to the ends of polyethylene glycol (PEG,  $M_n=600$  or  $800$  g/mol) with two isophorone diisocyanate units acted as spacers. Compared with other some non-bioaccumulable fluorinated surfactants [40, 41, 45, 61], the synthesis process of  $F_mEG_nF_m$  was simpler to some extent due to a facile two-step coupling one-pot method, and no organic solvent was used.  $F_{13}EG_{13}F_{13}$ , which contains two longer hydrophobic chains ( $CF_3(CF_2)_5-$ ) and a shorter PEG chain ( $M_n=600$  g/mol), showed the highest surface activity in the synthesized surfactants, whose  $\gamma_{CMC}$  was 17.8 mN/m with a low CMC of 0.17 mmol/L. Based on the special molecular structure,  $F_{13}EG_{13}F_{13}$  with two fluorocarbon chains can occupied more area than PFOA with a single fluorocarbon chain at the air-water interface (as seen in Fig. 2), resulting in a CMC of about 100 times lower. Apart from a high surface activity,  $F_{13}EG_{13}F_{13}$  showed excellent emulsifying ability and wettability, and simultaneously presented desirable salt and pH tolerance because the nonionic hydrophilic PEG chain is not easy to be affected by electrolytes. Furthermore, the cell cytotoxicity tests proved that  $F_{13}EG_{13}F_{13}$  has no significant cytotoxicity. Hence,  $F_{13}EG_{13}F_{13}$  can be used as a potential and promising alternative to PFOA.

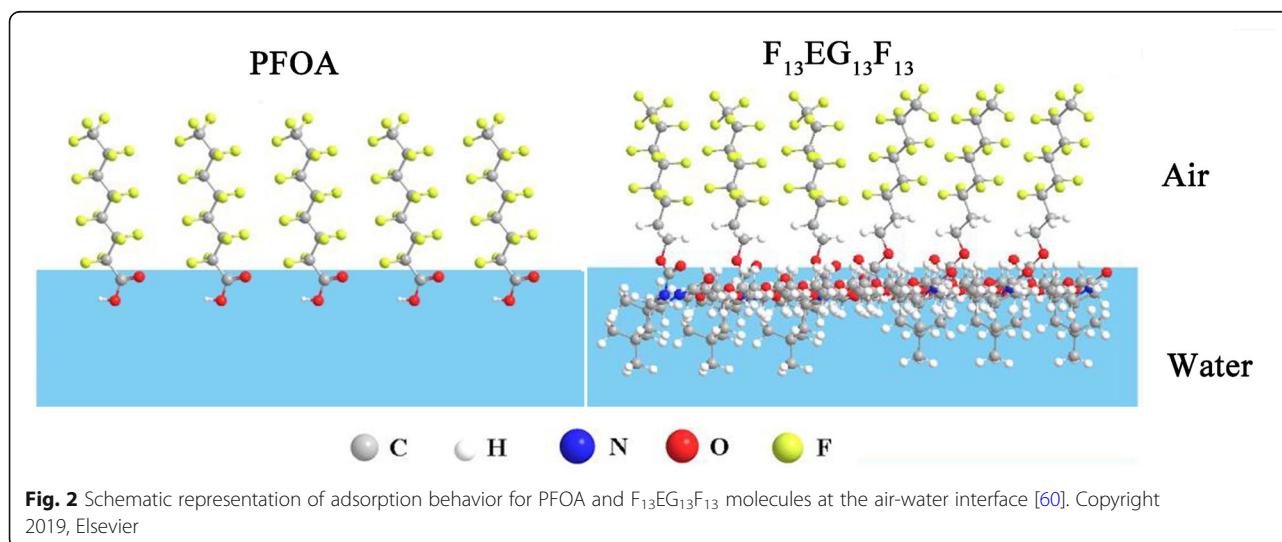
In fact, the structure design of non-bioaccumulable perfluorocarbon chain surfactants is considered not only

from the perspective of hydrophobic fluorocarbon chains, but also from the perspective of hydrophilic groups. For example, the easily available and eco-friendly multiplehydroxyl natural products, including glucose, maltose, and inositol, have introduced into non-ionic fluorinated surfactants to act as the hydrophilic moiety. The following is a brief introduction of some cases.

Bongartz et al. [62] synthesized a new fluorinated inositol-based surfactant containing two ethylene oxide units (as a spacer) and a  $CF_3(CF_2)_5-$ , whose  $\gamma_{CMC}$  was 17.4 mN/m at CMC of 0.39 mmol/L. Boussambe et al. [63] reported fluorinated diglucose surfactants ( $F_nH_2$ -DigluM) with a short fluorocarbon chain ( $C_nF_{2n+1}$ ,  $n=4$  or  $6$ ). As the increase of perfluorocarbon chain length from 4 to 6, CMCs of  $F_nH_2$ -DigluM sharply decreased from 14.4 to 0.72 mmol/L, while the ability to reduce surface tension did not increase and the  $\gamma_{CMC}$  of  $F_4H_2$ -DigluM was smallest (27.8 mN/m) in  $F_nH_2$ -DigluM, revealing once again that an appropriate hydrophobic chain length is very important to obtain a desired surface activity effect. Presently, this sort of fluorinated surfactants containing multiplehydroxyl natural product groups are mainly used in handling membrane proteins (see 3.2 section for details). Moreover, it is should be noted that the water solubility of the some surfactants bearing only one natural product hydrophilic unit is poor [64, 65]. The introduction of oxyethene fragments ( $-OCH_2CH_2-$ ) or the multiple natural product hydrophilic units into the hydrophilic moiety can improve the water solubility of the entire surfactant molecule.

## 2.2 Surfactants with weak points on fluorocarbon chain

The introduction of weak points into the fluorocarbon chain of surfactants, such as the methylene group and the ether bond, is deemed to facilitate fluorocarbon



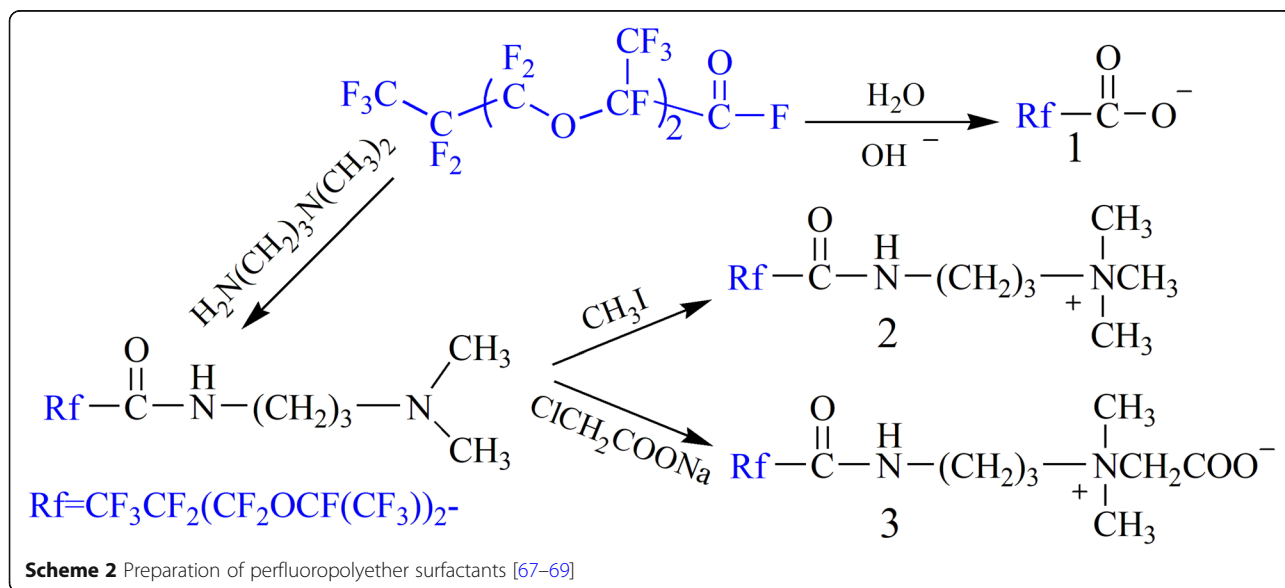
chain degradation and realize non-bioaccumulation [9]. There are two most common reaction routes to inset weak points into the fluorocarbon chain [66], including the anionic ring opening oligomerization of hexafluoropropylene oxide to form the perfluoropolyether chain and the radical telomerization of non-perfluoro olefins such as vinylidene fluoride ( $\text{CH}_2\text{CF}_2$ , VDF) and 3,3,3-trifluoropropene ( $\text{CF}_3\text{CHCH}_2$ , TFP) to inset methylene groups or methine groups into the fluorocarbon chain.

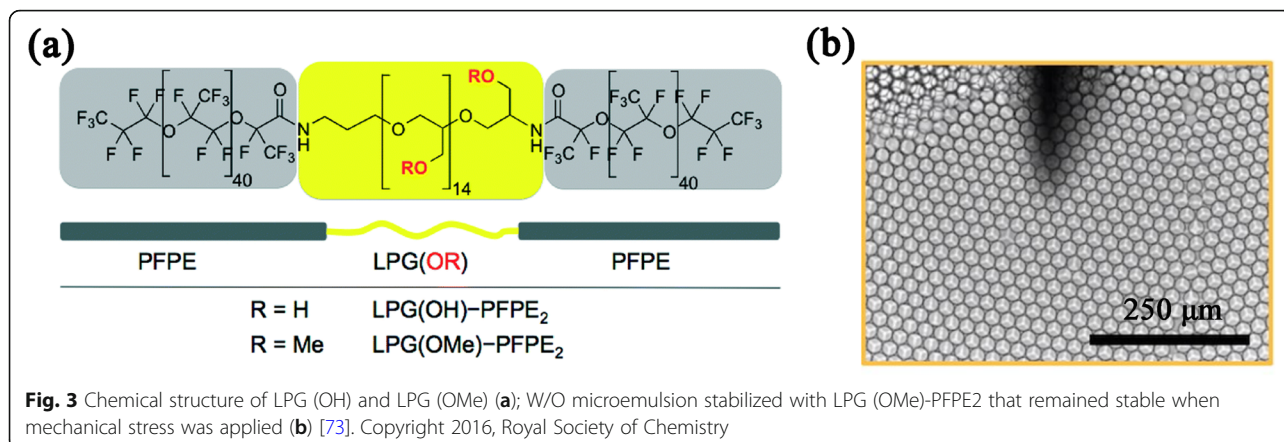
Perfluoropolyetheracyl halide or carboxylic acid compounds, which are derived from the anionic ring opening oligomerization of hexafluoropropylene oxide, are common commercial intermediates for the synthesis of perfluoropolyether surfactants. Wang's group [67–69] reported three perfluoropolyether surfactants with different hydrophilic head groups (Scheme 2). Due to the high fluorine content, these perfluoropolyether surfactants exhibited high surface activity, with  $\gamma_{\text{CMC}}$  of 16–17 mN/m. And their hydrophobic chain was formed by connecting shorter fluorocarbon units with multiple ether bonds which gave biodegradation and non-bioaccumulation to perfluoropolyether surfactants. At the same time, these surfactants also showed excellent wettability and could effectively reduce the contact angle on polytetrafluoroethylene (PTFE) and paraffin film, which are two typical low-energy hydrophobic surfaces.

In some special condition, surfactants with longer perfluoropolyether chains can better meet the application requirements. For example, compared with typically perfluorinated C8-based surfactants, surfactants with longer perfluoropolyether chains can achieve a sufficient long-term emulsion stability to water-in-fluorocarbon oil emulsions [70–72]. Wagner et al. [73] synthesized two triblock nonionic perfluoropolyether (40 repeating units)

surfactants with the linear polyglycerol (LPG (OR)) as the hydrophilic group (as seen in Fig. 3a). The synthesis process is as follows: firstly, the poly(perfluoropropylene glycol) (PFPE) carboxylic acid was converted to the acid chloride using dichlorosulfoxide; then, the acid chloride reacted with corresponding linear polyglycerol diamine to yield the target surfactants with hydroxyl groups (LPG (OH)-PFPE<sub>2</sub>) or methyl groups (LPG (OMe)-PFPE<sub>2</sub>). The interface tension between fluorinated oil (HFE7500, 3M) and water was 18 mN/m at CMC of 0.02 wt% LPG (OMe)-PFPE<sub>2</sub>, and the water-in-oil emulsion microdroplet composed of deionized water, HFE7500, and LPG (OMe)-PFPE<sub>2</sub> was very stable (as seen in Fig. 3b); LPG (OH)-PFPE<sub>2</sub> water-in-oil emulsion was unstable and the interface tension at CMC could not be measured accurately due to the uncontrolled aggregation of LPG (OH)-PFPE<sub>2</sub> induced by its stronger hydrogen bonding. Hence, compared with PEG fluorinated surfactants, the performances of linear polyglycerol fluorinated surfactants can be adjusted not only by the molecular weight, but also by the side-chain modification [72]. In addition, the in vitro translation (IVT) experiment carried out in LPG (OMe)-PFPE<sub>2</sub> water-in-oil emulsion droplets proved that the surfactant has excellent biocompatibility and can be used in biological analysis.

In the synthesis of fluorinated surfactants, the radical telomerization is an important method to control the extension of the fluorocarbon chain length. When using the non-perfluoro olefin as the telomeric monomer, the biodegradable and non-bioaccumulable fluorinated surfactant can be obtained. Boutevin et al. [74] prepared two anionic fluorinated surfactants with a carboxylate ( $\text{C}_n\text{F}_{2n+1}(\text{CH}_2\text{CF}_2)_2\text{CH}_2\text{COOH}$ ,  $n=2$  and 4, and





abbreviated as F-surf 2–2 and F-surf 4–2, respectively) using the radical telomerization of VDF with 1-iodoperfluoroalkane [75–77] (Scheme 3). In order to control the chain length of fluorotelomers and obtain suitable low molecular weight fluorotelomers, the experimental conditions (solvents, initiators and temperature) were also investigated in detail. The  $\gamma_{CMC}$  for F-surf 2–2, whose carbon chain length is same with that of PFOA, was 19.8 mN/m at 5 g/L (about 3.5 times of CMC). This method based on the radical telomerization of VDF provides weak sites in the hydrophobic chain, such as methylenes whose C-H bonds is weaker compared to C-F [78], and is valuable for the development of novel fluorinated surfactants with degradable ability.

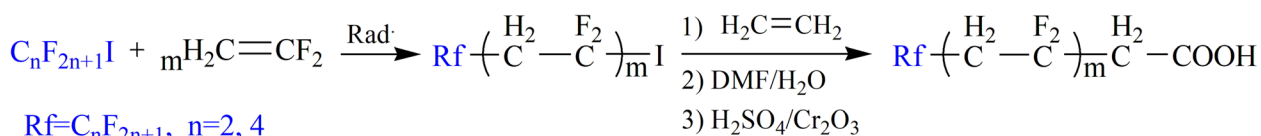
Yake et al. [79] reported two kind of fluorinated cationic surfactants with pyridinium sulfonates or ammonium hydrochlorides, whose fluoroalkyl chain was interrupted by the ether bond or methylene. Here, some representative examples are selected (as seen in Table 3). VDF and TFE (trafluoroethylene) units were inserted into the surfactant molecules to extend fluorocarbon chain length and improve the ability of reducing surface tension, and the ether bond or methylene in surfactants provided degradable sites. Compared with compound II-B, compound III-B with an isopropylidene group as a spacer had a lower efficiency to reduce the surface tension because the isopropylidene group could interrupt the tight packing of molecules on the air-water interface and disrupt

the hydrophilic-lipophilic balance of the surfactant [80]. Furthermore, both III-A and II-B showed an excellent foaming ability and stability in the simulative foam drilling fluid condition (2% KCl and 15% HCl aqueous solutions).

### 2.3 Surfactants with branched fluorocarbon chain

In the reported literatures [81–83], the branched fluorinated surfactants denote the surfactants containing multiple fluorinated side groups like CF<sub>3</sub>- and (CF<sub>3</sub>)<sub>2</sub>CF- on the fluorocarbon main chain. These branched fluorinated surfactants are based on hexafluoropropylene oligomer such as hexafluoropropylene dimer and hexafluoropropylene trimer, whose length of fluorinated main chains are shorter than or equal to C<sub>6</sub>.

Jiang's group [84–88] prepared several branched fluorinated surfactants bearing a branched CF<sub>3</sub>CF<sub>2</sub>CF<sub>2</sub>C(CF<sub>3</sub>)<sub>2</sub>- group using hexafluoropropylene dimer as a starting material (Scheme 4). The surface tension of the synthesized branched fluorinated surfactants can be effectively reduced to around 20 mN/m. It should be pointed out that the CMC of sample 1 with only a CF<sub>3</sub>CF<sub>2</sub>CF<sub>2</sub>C(CF<sub>3</sub>)<sub>2</sub>- group is relatively higher, indicating that a larger dosage is needed to obtain a better effect in practice. When a hydrophobic chain or a rigid spacer was introduced into the branched fluorinated surfactants based on sample 1, CMCs of the prepared surfactants sharply decreased. For example, the CMC of sample 1 was  $1.41 \times 10^{-2}$  mol/L,



**Scheme 3** The radical telomerization of VDF with C<sub>n</sub>F<sub>2n+1</sub>I to synthesize fluorinated surfactants [74]

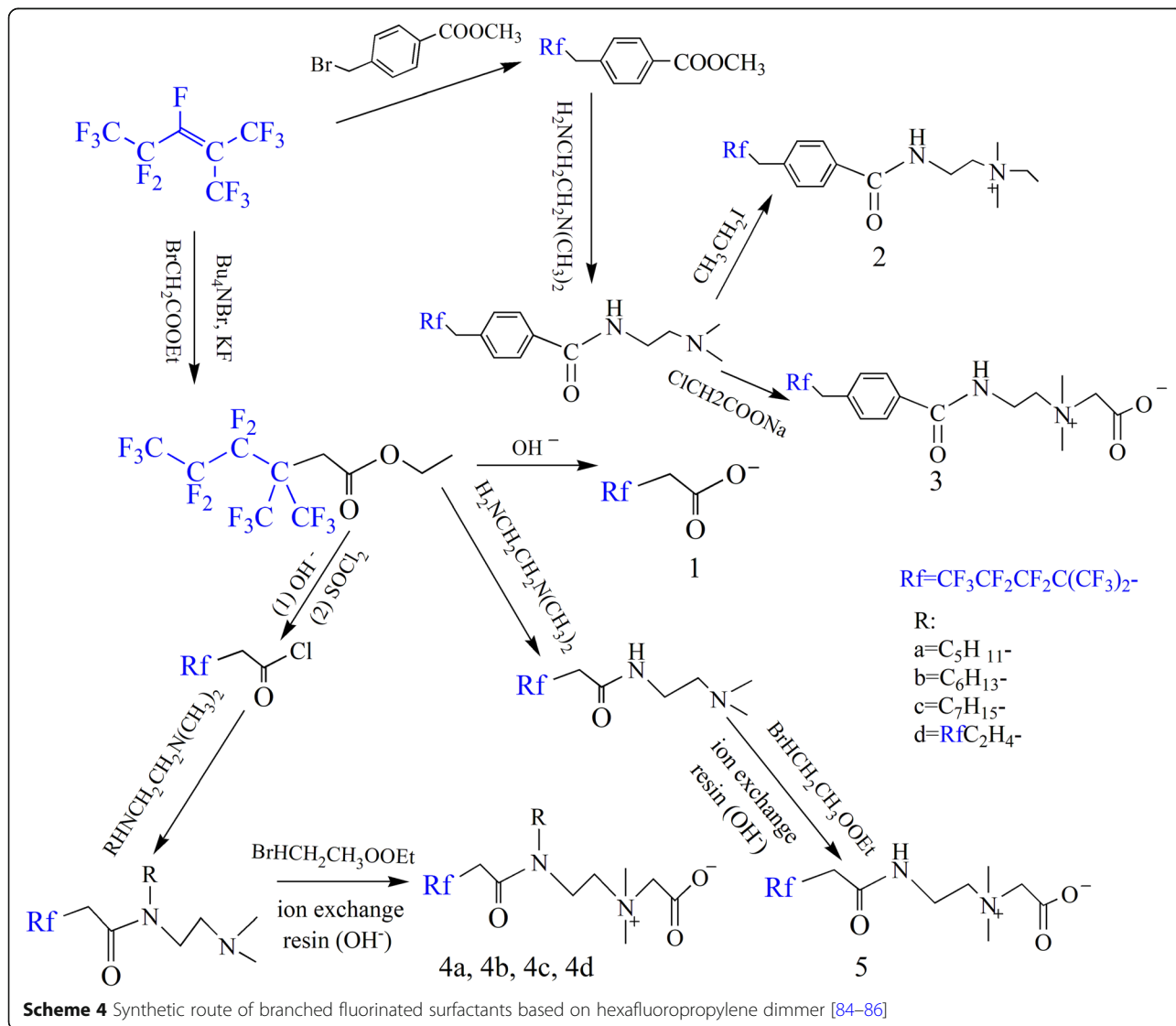
**Table 3** Surface tensions (mN/m) of fluorinated pyridinium and ammonium cationic surfactants in deionized water at 23 °C [79]

Surfactants	Concentration (wt%)	
	0.1	0.5
[C <sub>4</sub> F <sub>9</sub> CH <sub>2</sub> CF <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> py][p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> ] (I-A)	43.1	22.8
[C <sub>4</sub> F <sub>9</sub> (CH <sub>2</sub> CF <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> py][p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> ] (II-A)	30.5	19.5
[C <sub>6</sub> F <sub>13</sub> (CH <sub>2</sub> CF <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> py][p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> ] (III-A)	18.8	18.3
[C <sub>8</sub> F <sub>17</sub> CH <sub>2</sub> CH <sub>2</sub> py][p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> ] <sup>a</sup>	17.2	17.0
[C <sub>3</sub> F <sub>7</sub> O(CF <sub>2</sub> CF <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> NH <sub>3</sub> ][Cl] (I-B)	25.8	14.3
[C <sub>3</sub> F <sub>7</sub> O(CF <sub>2</sub> CF <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> NH <sub>3</sub> ][Cl] (II-B)	16.4	14.8
[C <sub>3</sub> F <sub>7</sub> O(CF <sub>2</sub> CF <sub>2</sub> ) <sub>3</sub> C(CH <sub>3</sub> ) <sub>2</sub> NH <sub>3</sub> ][Cl] (III-B)	54.7	28
[RfCH <sub>2</sub> CH <sub>2</sub> NH <sub>3</sub> ][Cl] <sup>b</sup>	23.7	20.9

<sup>a</sup> the reference of fluorinated pyridinium cationic surfactants<sup>b</sup> the reference of fluorinated ammonium cationic surfactants (where Rf is the mixture of C<sub>8</sub>F<sub>17</sub> and C<sub>10</sub>F<sub>21</sub> (molar ratio of 45:55))

while the CMCs of sample 4d with two branched CF<sub>3</sub>CF<sub>2</sub>CF<sub>2</sub>C(CF<sub>3</sub>)<sub>2</sub>- group and sample 3 containing a rigid benzene ring were  $1.74 \times 10^{-6}$  and  $1.04 \times 10^{-4}$  mol/L, respectively. Once again, the results proved that the introduction of an appropriate hydrophobic structure into the surfactant is beneficial to the formation of micelles and the decrease of CMC.

Wei et al. [89] synthesized a branched fluorinated surfactant (BFIS, as seen in Fig. 4a), which derived from hexafluoropropene trimer and 4-hydroxybenzyl alcohol, and compared its surface activity with a straight chain surfactant (SFIS, as seen in Fig. 4b). Owing to the existence of rigid benzene ring and imidazole ring spacers, CMCs of BFIS and SFIS were lower but not distinctly different, with 0.122 and 0.181 mmol/L, respectively. And the surface tension could be effectively reduced to 18.66 mN/m for BFIS and 18.48 mN/m for SFIS,





respectively, at 5 mmol/L. Since the packed adsorption layer of BFIS was denser than that of SFIS on the metal surface, BFIS showed better anticorrosion performance, indicating that the branched fluorinated surfactant can be used as a promising metal corrosion inhibitor. The adsorption behavior at the air-solid interface and metal corrosion inhibition mechanism of BFIS and SFIS is shown in Fig. 4c.

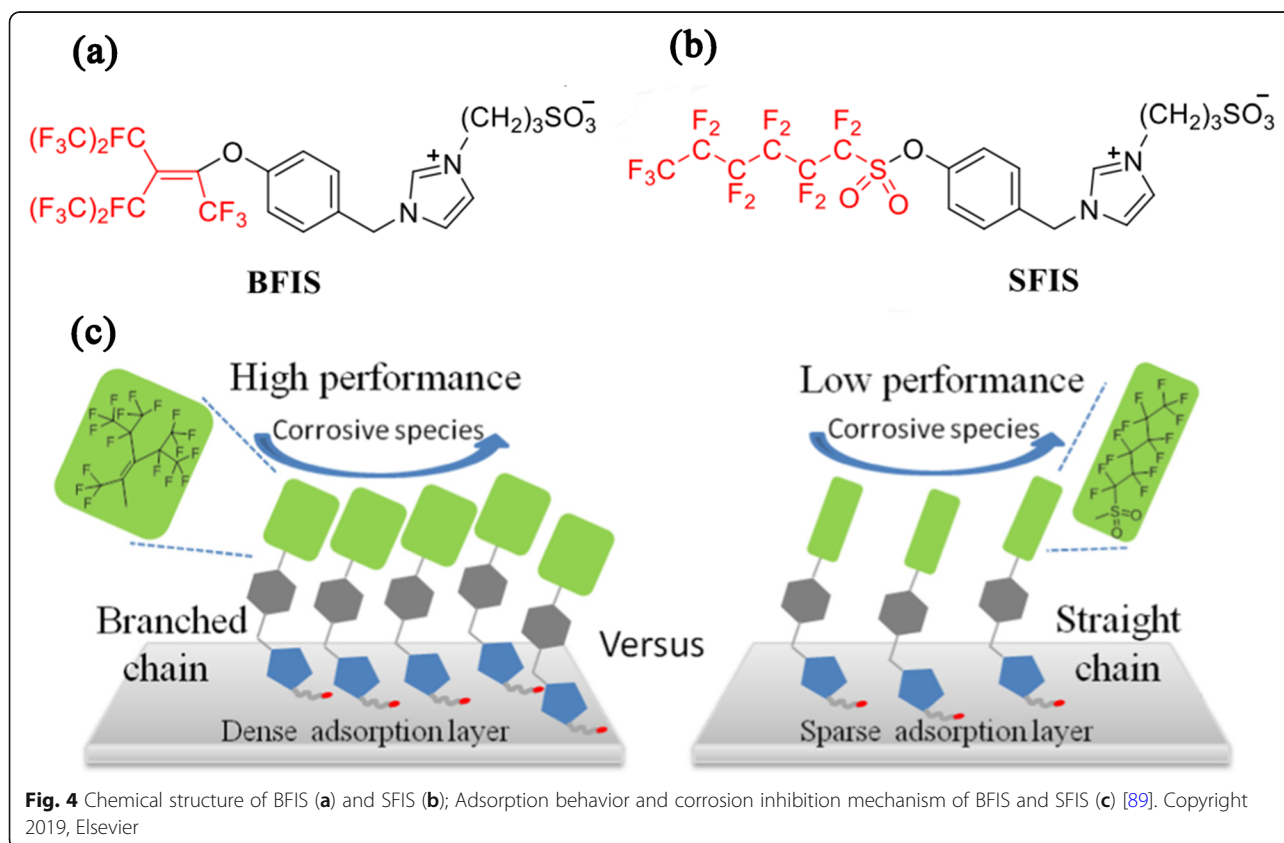
### 3 Application of non-bioaccumulable fluorinated surfactants

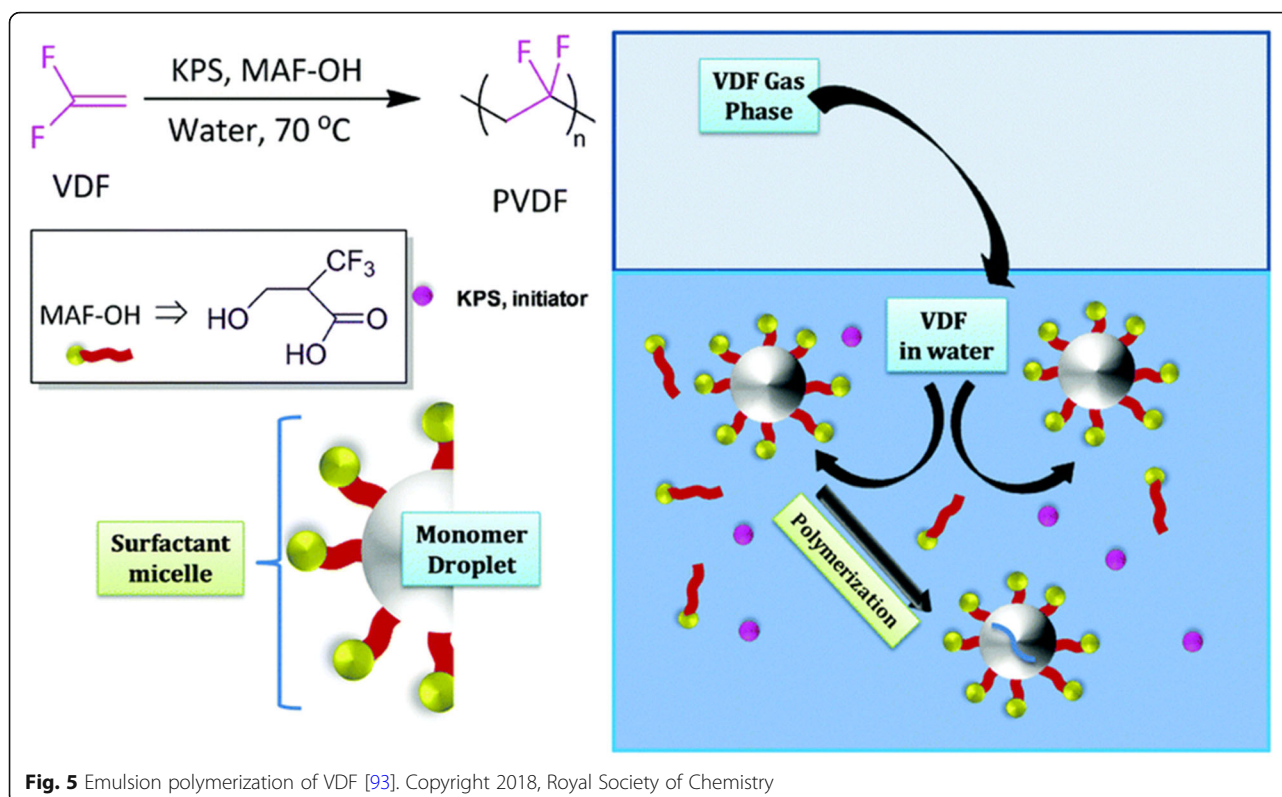
Because of their excellent performances, the fluorinated surfactants sometimes play an important and special role which cannot be replaced by common hydrocarbon surfactants in practical applications. The non-bioaccumulable fluorinated surfactants, serving as the alternatives of conventional fluorinated surfactants with long fluorocarbon chain, now have been used in emulsion polymerization of fluorinated olefins, membrane proteins treatment, leather manufacture and other fields, which meet not only environmental requirements but also requirements for use.

#### 3.1 Application in emulsion polymerization of fluorinated olefins

Since the miscibility between fluorinated monomers with conventional hydrocarbon surfactants is poor, fluorinated surfactants are usually selected as an emulsifier in the emulsion polymerization of fluoropolymers according to the principle of “like dissolves like” [90]. For example, APFO and NaPFO are acted as emulsifiers in the emulsion polymerization of PTFE, perfluorinated ethylene-propylene copolymer (FEP), and perfluoroalkoxy polymer (PFA) [24]; and APFO is used as an emulsifier in the emulsion polymerization of polyvinylidene fluoride (PVDF) [91, 92].

Now non-bioaccumulable fluorinated surfactants have been used as emulsifiers in the emulsion polymerization of fluorinated olefins. For instance, Banerjee et al. [93] prepared a PVDF emulsion using a degradable fluorinated surfactant 3-hydroxy-2-(trifluoromethyl) propanoic acid (MAF-OH) as an emulsifier (as seen in Fig. 5). Average particle diameter of the prepared PVDF latex particles decreased with the increase of MAF-OH concentration, about 100 nm at 2.0 wt% MAF-OH, and the prepared PVDF latex particles were perfectly spherical. Kang et al. [47] also prepared a PVDF emulsion using the synthesized non-bioaccumulable hybrid surfactant  $F_2H_8$  (see section 2.1) as an emulsifier. Compared with a

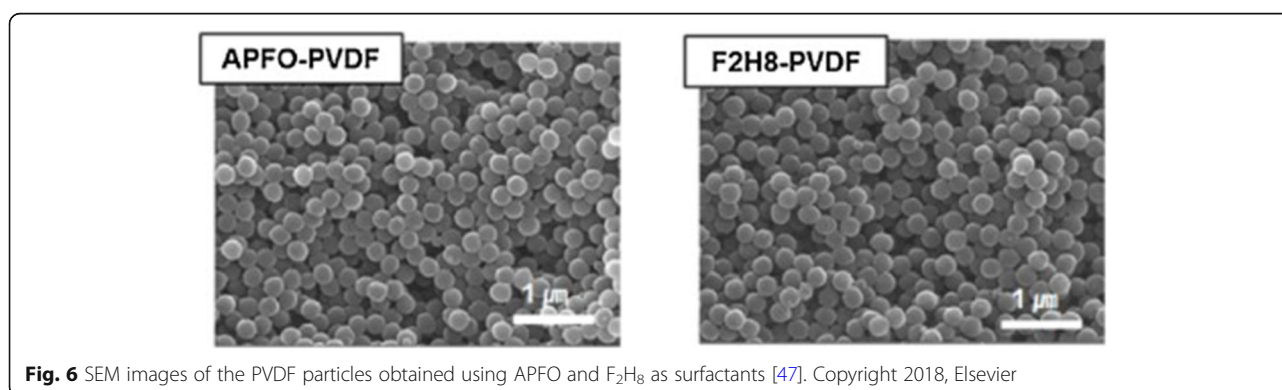




PVDF emulsion with APFO under same conditions, their effects (i.e.,  $F_2H_8$  and APFO) were almost the same, with the solid content of 22 and 23 wt% and average diameters of 257.4 and 242.7 nm, respectively. Scanning electron microscope (SEM) images of PVDF particles are shown in Fig. 6.

In order to avoid the disadvantages of desorption or migration of conventional fluorinated surfactants from the polymer, polymerizable fluorinated surfactants are also generated and applied. Zhao et al. [94] synthesized a polymerizable non-bioaccumulable fluorinated surfactant perfluoro (4-methyl-3,6-dioxaoct-7-ene) sodium sulfonate (PSVNa), which could reduce the surface tension of its aqueous solution to a minimum of 26 mN/m

at 4.0 wt%. Using PSVNa, PSVNa/sodium dodecyl sulfate (SDS) binary mixtures and PFOA as emulsifiers, the effects of different emulsifiers on latex particles of DFHM A/MMA copolymer were studied. The results showed that the gel content of emulsion with only PSVNa was lowest (0.6 wt%). Meanwhile, since PSVNa has a double bond, PSVNa can be covalently linked to the polymer chain during the emulsion polymerization, remaining the stability of the emulsion. Emulsions with PSVNa or PSVNa/SDS were very stable and could be stored for at least 3 years at the ambient temperature, far exceeding PFOA (a half year).



### 3.2 Application in handling membrane proteins

In the treatment of membrane proteins including extraction, purification and structural characterization, fluorinated surfactants are usually used as a solubilizer to solubilize biological membranes. Compared with hydrocarbon surfactants, the fluorocarbon chain of fluorinated surfactants is bulkier and more rigid, and the affinity between hydrogenated surfaces of membrane proteins and fluorinated surfactants is little, so they are less likely to intrude into the protein structure, avoiding inactivation of membrane proteins [95].

Since they are used for handling membrane proteins, fluorinated surfactants have achieved encouraging results in stability of membrane protein [96]. Presently, the most commonly used fluorinated surfactants for membrane protein studies are fluoroalkyl glycosides such as the maltoside and glucoside series because of their mildness [97–99]. And they are mostly fluorinated surfactants based on C4 or C6 fluorocarbon chain. For example, Durand's group [100] found that F6-Diglu, where "F6" denotes six fluorinated carbons of the hydrophobic tail and "Diglu" represents two glucose moieties, could self-assemble into small and homogeneous globular micelles (5–6 nm) which can stabilize membrane proteins. Subsequently, the research group reported several fluorinated surfactants based on F6-Diglu and their application in handling membrane proteins [101, 102], which could self-assembled into small aggregates in the aqueous solution, about 5–11 nm. In the stabilization experiments of the model membrane protein bacteriorhodopsin, fluorinated surfactants/membrane protein bacteriorhodopsin heterogeneous complexes could be stable for 3 months. In addition, this group [63] also extracted proteins from native *Escherichia coli* membranes using the synthesized fluorinated surfactants  $F_nH_2$ -DigluM ( $n=4$  or 6, see 2.1 section). The results showed that  $F_4H_2$ -DigluM could essentially complete the solubilization of membrane proteins after 15 h, and  $F_4H_2$ -DigluM presented a good membrane protein extracting efficiency, which was similar with DDM (*n*-dodecyl- $\beta$ -D-maltopyranoside, a commonly used detergent in membrane proteins extraction) at 1–2 mmol/L above the respective CMC, about 5%.

Similarly, maltose-based non-bioaccumulable fluorinated surfactants were also applied in handling membrane proteins. For example, Polidori et al. [103] synthesized two new maltose-based fluorinated surfactants ( $F_2H_9\beta M$  and  $F_4H_5\beta M$ ) containing either a  $CF_3CF_2(CH_2)_9$ - or a  $CF_3(CF_2)_3(CH_2)_5$ - at the end of the hydrophobic chain. The  $\gamma_{CMC}$  values of  $F_2H_9\beta M$  and  $F_4H_5\beta M$  were 26 and 22 mN/m, respectively, and their CMC values were 1.14 and 2.16 mmol/L, respectively. In the stabilization test, the model membrane protein bacteriorhodopsin was stable over approximately a month

in  $F_2H_9\beta M$  but for more than a year in  $F_4H_5\beta M$ , and the effect of  $F_4H_5\beta M$  was almost the same as that of commercial fluorinated octyl maltoside ( $F_6H_2\beta M$ ) [104].

### 3.3 Application in leather manufacture

Owing to their excellent performances, fluorinated surfactants can be applied in leather manufacture to impart leather some special properties and further improve significantly the quality of leather. After the conventional perfluorooctyl surfactant products such as 3M Scotch-guard™ FC-805 (a typical finishing agent based on PFOA) [105] are banned, non-bioaccumulable fluorinated surfactants have been used in leather manufacture.

In the wet finishing process of leather manufacture, fluorinated surfactants acting as the auxiliary can promote permeation, absorption or diffusion of other leather chemicals in leather fiber to achieve a desired process effect and further improve the use value and economic value of leather. The U.S. patent [106] reported a kind of non-bioaccumulable perfluoropolyether surfactant, which can be used as the dye dispersant. And Sagisaka et al. [107] proved that the sulfonate fluorinated surfactants bearing double  $-(CF_2)_4F$  groups (with  $\gamma_{CMC}$  18 mN/m at 0.26 mmol/L) could quickly dissolve a hydrophilic dye methyl orange into water/supercritical  $CO_2$  microemulsions in just a few seconds. Of course, in the processing process, fluorinated surfactants also will be adsorbed or bound on the fiber surface of leather to make its surface tension lower than that of water, playing a role of water repellent for leather. Our group [108] used the synthesized nonionic short-chain fluorinated surfactants (Fm-Fm, m represents the length of fluorocarbon chain, see 2.1 section [60]) as fatliquoring auxiliaries in the fatliquoring process of chrome-tanned goat skin to investigate the effect of type and dosage of surfactants as well as fatliquoring temperature on fatliquoring properties. The results showed that at 40 °C, 1 wt% F4-F4 with two perfluorobutyl groups exhibited significant effect on improving softness and physical mechanical properties of the resultant leather. And compared with leather treated without fluorinated surfactants (contact angle of 82°), the maximum contact angle of the leather treated with F6-F6 was 110°, enhancing water-proofness of leather.

In the dry finishing process of leather manufacture, the fluorinated surfactants can be used as the water- and oil-repellent finishing agent of leather, whose fluorinated moieties provide a water and oil resistance and hydrophilic moieties (such as hydroxy groups, carboxyl groups and oxyethene fragments) realize the easy washing and decontamination of the resultant leather. At present, the most popular water- and oil-repellent leather finishing agents are the non-bioaccumulable fluorinated acrylates copolymer, and the Capstone™ LPA based on the short

C4 fluorocarbon chain (Chemours Company)([www.chempoint.com/products/chemours/capstone-fluorosurfactants/capstone-repellents-for-leather](http://www.chempoint.com/products/chemours/capstone-fluorosurfactants/capstone-repellents-for-leather)) is one of the most representative commercial products. These kinds of leather finishing agents are also reported on some patents [109, 110]. Due to the possible commercial interests, their detailed formulas are mostly unclear. And only few articles publicly report their details. For instance, Liu et al. [111] reported a non-bioaccumulable water-repellent leather finishing agent. Firstly, the macromolecule fluorinated surfactant was prepared (F-SAA) using 1H,1H,7H-dodecafluoroheptyl methacrylate ( $R_fAA$ ,  $R_f = \text{CHF}_2(\text{CF}_2)_5-$ ), acrylic acid (AA) and hydroxypropyl acrylate (HPAA) (molar ratio, 1:2:1) as monomers. Then, the  $R_fAA$ /SMA/HPAA emulsion (FSH) was successfully prepared by emulsifier-free polymerization with  $R_fAA$ , stearyl methacrylate (SMA), and HPAA (80 wt%:16.5 wt%:3.5 wt%) as monomers and F-SAA as an emulsifier. Average size (109.9 nm) and its distribution range (polydispersity index of 0.326) of the prepared FSH latex particles were smaller, which contributed FSH to permeate and spread in the leather fiber. The goat wet blue skin treated with FSH showed an excellent water-repellent effect due to the higher fluorine content of F-SAA, with the contact angle of 137.6°.

#### 4 Conclusion and outlook

So far, non-bioaccumulable fluorinated surfactants have made tremendous progress in its preparation and application. In this review, many listed non-bioaccumulable fluorinated surfactants with different fluorocarbon chain structures including the short perfluorocarbon chain, the fluorocarbon chain with weak points, and the branched fluorocarbon chain, present excellent performances, which is comparable to PFOA. And their performances can be further adjusted by the length of spacers, the type of counter ions and other factors. We summarize these structure-activity relationships with expect to provide meaningful references for the development of non-bioaccumulable fluorinated surfactants with a higher surface activity. At the same time, in some application fields listed in this article, non-bioaccumulable fluorinated surfactants also exhibit better practical application effects, which take into account environmental protection and usability.

Of course, the current challenges faced by non-bioaccumulable fluorinated surfactants have to be considered. On the one hand, the surfactants based on C6 fluorocarbon chain, which usually show a better surface activity than surfactants based on C4 fluorocarbon chain, are regarded as non-bioaccumulable according to current regulations [10], but the studies [38, 112] reveal that the bioaccumulation of surfactants with C4 fluorocarbon chain is lower and hardly considered. Meanwhile,

although fluorine-free surfactants (such as silicon-based surfactants) are also extensively concerned, their performances are not as good as those of fluorinated surfactants [113, 114]. Therefore, it is an urgent research topic to develop surfactants with shorter fluorocarbon chain and excellent performance. On the other hand, the preparation process of most reported non-bioaccumulable fluorinated surfactants is relatively complicated, which is not conducive to large-scale application. Therefore, simplifying the preparation process and reducing costs are also important directions for subsequent development of non-bioaccumulable fluorinated surfactants. In order to overcome these challenges, researchers still need to make continuous efforts to provide creative answers for the prosperous development of non-bioaccumulable fluorinated surfactants.

#### Abbreviations

PFOA: Perfluorooctanoic acid; VDF: Vinylidene fluoride; NaPFO: Sodium perfluorooctanoate;  $\gamma_{CMC}$ : Surface tension at CMC; APFO: Ammonium perfluorooctanoate; TFP: 3,3,3-trifluoropropene; CMC: Critical micelle concentration; TFE: Tetrafluoroethylene; PFOS: Perfluorooctane sulfonate; AA: Acrylic acid; APFOS: Ammonium perfluorooctane sulphonate; IVT: In vitro translation; KPFOs: Potassium perfluorooctane sulphonate; SDS: Sodium dodecyl sulfate; PFPE: Poly (perfluoropropylene glycol); SMA: Stearyl methacrylate; SEM: Scanning electron microscope; PEG: Polyethylene glycol; DFHMA: Dodecafluoroheptyl methacrylate; HPAA: Hydroxypropyl acrylate; DDM: n-dodecyl- $\beta$ -D-maltopyranoside; PFA: Perfluoroalkoxy polymer; FEP: Perfluorinated ethylene-propylene copolymer; MMA: Methyl methacrylate; POPs: Persistent organic pollutants; PVDF: Polyvinylidene fluoride;  $R_fAA$ : 1H,1H,7H-dodecafluoroheptyl methacrylate; PTFE: Polytetrafluoroethylene; MAF-OH: 3-hydroxy-2-(trifluoromethyl) propanoic acid; PSVNa: Perfluoro (4-methyl-3, 6-dioxaoct-7-ene) sodium sulfonate

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#### Authors' contributions

RZ: designing the outline, writing this review article; YJ: revising the language and logic; YS, PZ and YZ: collecting references, proposing opinions. The author(s) read and approved the final manuscript.

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#### Competing interests

The authors declare that they have no competing interests.

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