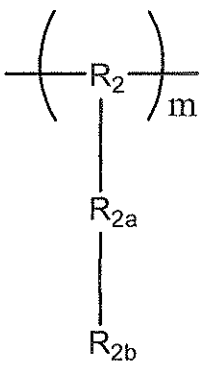
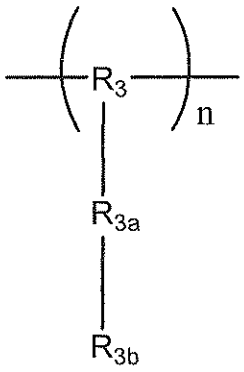
solve the problem completely due to residual microbes, which causes recurring infections. Several strategies have been devised to prevent biofilm formation. Some of these strategies employ antibiotics, silver ions or quaternized ammonium ions in a medical device. But these strategies also suffer from burst release, drug resistance and increase in biofilm formation. Another technique utilizes antifouling agents, such as zwitterions or hydrophilic poly(ethylene glycol). These methods may prevent the microbes from attaching to the surface for a certain period of time without killing the microbes, eventually leading to fouling. Therefore, there is an urgent need to develop novel methods and materials that possess robust antibacterial and antifouling properties in a sustained manner.

Summary

In the present disclosure, there is provided a copolymer comprising monomer units represented by formulas (I) and/or (II):



Formula (I)



Formula (II)

wherein the copolymer is terminated on one end by R_1 and on the other end by R_4;

R_1 comprises an antifouling moiety;

R_4 is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_2 and R_3 are independently optionally substituted hetero-C_{1-10}-alkyl, wherein one or more chain carbon atoms is optionally replaced by a heteroatom;

R_{2a} and R_{3a} are independently optionally substituted hetero-C_{1-10}-alkyl, wherein one or more chain carbon atoms is optionally replaced by a heteroatom;

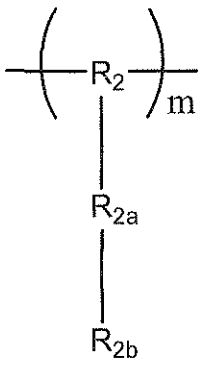
R_{2b} comprises an anchoring moiety;

R_{3b} comprises an antibacterial moiety;

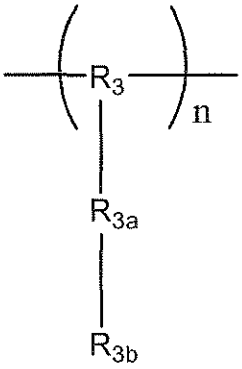
m is an integer in the range of 1 to 20; and

n is an integer in the range of 0 to 100.

In a first aspect of the present disclosure, there is provided a copolymer comprising monomer units represented by formulas (I) and (II):



Formula (I)



Formula (II)

wherein the copolymer is terminated on one end by R_1 and on the other end by R_4;

R_1 comprises an antifouling moiety;

R_4 is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_2 and R_3 are independently optionally substituted hetero-C_{1-10}-alkyl, wherein one or more chain carbon atoms is optionally replaced by a heteroatom;

R_{2a} and R_{3a} are independently optionally substituted hetero-C_{1-10}-alkyl, wherein one or more chain carbon atoms is optionally replaced by a heteroatom;

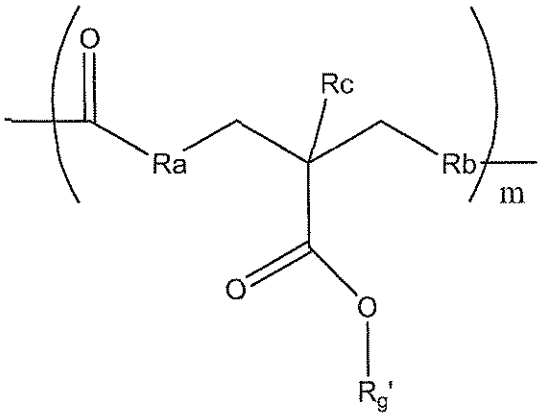
R_{2b} comprises an anchoring moiety;

R_{3b} comprises an antibacterial moiety;

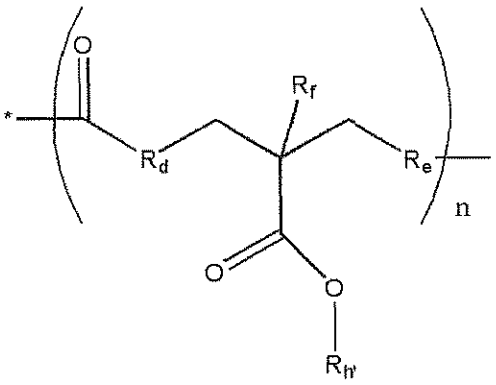
m is an integer in the range of 2 to 20; and

n is an integer in the range of 0 to 100.

In the present disclosure, there is provided a method of synthesizing a copolymer comprising monomer units represented by formulas (IIIA) and/or (IIIB):



Formula (IIIA)



Formula (IIIb)

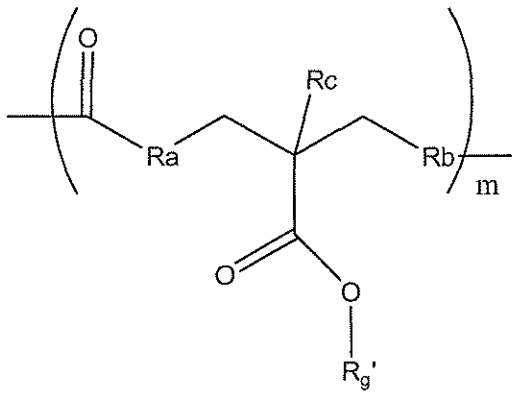
wherein the copolymer is terminated on one end by R_1 and on the other end by R_4;

R_1 is a polymer residue comprising an antifouling moiety;

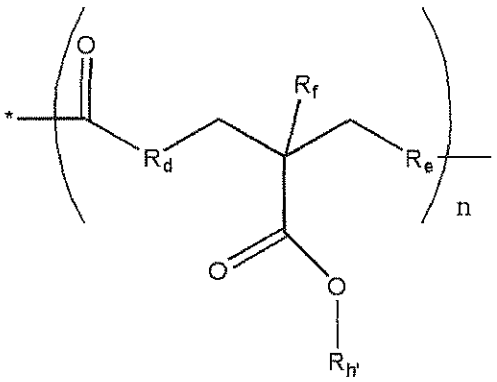
R_4 is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

thereby forming a copolymer comprising monomer units of Formula (IIIA) and/or (IIIB).

In a second aspect of the present disclosure, there is provided a method of synthesizing a copolymer comprising monomer units represented by formulas (IIIA) and (IIIB):



Formula (IIIA)



Formula (IIIb)

wherein the copolymer is terminated on one end by R_1 and on the other end by R_4;

R_1 is a polymer residue comprising an antifouling moiety;

R_4 is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_a, R_b, R_c, R_d, R_e and R_f are independently $C(R_5)_2$, O or $N(R_5)$;

R_5 is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_g' represents protected R_g, and R_h' represents aryl or heteroaryl substituted with at least one substituent capable of being quaternized,

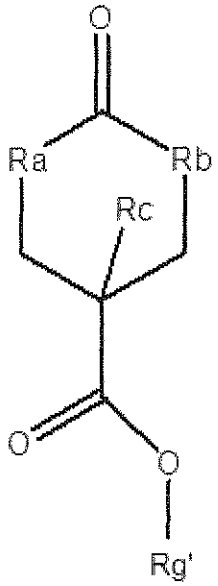
wherein R_g comprises an anchoring moiety;

m is an integer in the range of 2 to 20; and

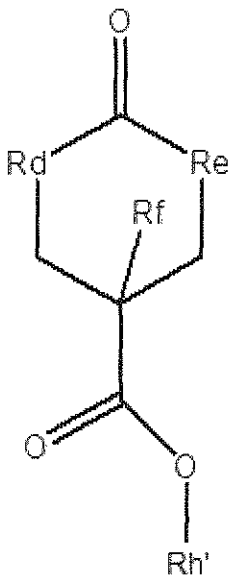
n is an integer in the range of 0 to 100,

the method comprising the step of:

(i) performing a ring-opening polymerization reaction in a reaction mixture comprising compounds of Formula (IC), H-R_1, and compounds of Formula (IIC):



Formula (IC)



Formula (IIC)

,

with the proviso that compounds of Formula (IIC) are present only when n≠0,

thereby forming a copolymer comprising monomer units of Formula (IIIA) and/or (IIIB).

In the present disclosure, there is provided a method of attaching a copolymer as defined above to a substrate, comprising attaching the anchoring moiety of said copolymer to an anchoring segment on said substrate.

In a third aspect of the present disclosure, there is provided a method of attaching a copolymer as defined above to a substrate, comprising attaching the anchoring moiety

of said copolymer to an anchoring segment on said substrate; optionally wherein the anchoring segment comprises one or more thiol groups; more optionally wherein the copolymer is attached to the substrate via a Michael addition.

In a fourth aspect of the present disclosure, there is provided an article comprising a substrate and a coating comprising the copolymer as defined above.

In a fifth aspect of the present disclosure, there is provided a use of a copolymer as defined above for imparting an antibacterial and/or antifouling surface to an article.

Definitions

The following words and terms used herein shall have the meaning indicated:

As used herein, the term "alkyl" includes within its meaning monovalent ("alkyl") and divalent ("alkylene") straight chain or branched chain saturated aliphatic groups having from 1 to 12 carbon atoms, eg, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 carbon atoms. For example, the term alkyl includes, but is not limited to, methyl, ethyl, 1-propyl, isopropyl, 1-butyl, 2-butyl, isobutyl, tert-butyl, amyl, 1,2-dimethylpropyl, 1,1-dimethylpropyl, pentyl, isopentyl, hexyl, 4-methylpentyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 1,2,2-trimethylpropyl, 1,1,2-trimethylpropyl, 2-ethylpentyl, 3-ethylpentyl, heptyl, 1-methylhexyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 4,4-dimethylpentyl, 1,2-dimethylpentyl, 1,3-dimethylpentyl, 1,4-dimethylpentyl, 1,2,3-trimethylbutyl, 1,1,2-trimethylbutyl, 1,1,3-trimethylbutyl, 5-methylheptyl, 1-methylheptyl, octyl, nonyl, decyl, undecyl, dodecyl and the like. Alkyl groups may be optionally substituted.

As used herein, the term "alkenyl" refers to divalent straight chain or branched chain unsaturated aliphatic groups containing at least one carbon-carbon double bond and having from 2 to 12 carbon atoms, eg, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 carbon atoms. For example, the term alkenyl includes, but is not limited to, ethenyl, propenyl, butenyl,

2. The copolymer according to claim 1, wherein R_1 is a polymer residue comprising an antifouling moiety, optionally the antifouling moiety comprises an alkoxyalkylene.

3. The copolymer according to claim 2, wherein said copolymer is a diblock copolymer, wherein one block consists of R_1, and the other block consists of repeating units of Formula (I); or

wherein said copolymer is a diblock copolymer, wherein one block consists of R_1, and the other block consists of randomly arranged monomer units of Formulas (I) and (II); or

wherein said copolymer is a triblock copolymer, wherein one block consists of R_1, the second block consists of Formula (I), and the third block consists of Formula (II); or

wherein said copolymer is a triblock copolymer, wherein one block consists of R_1, the second block consists of Formula (II), and the third block consists of Formula (I).

4. The copolymer according to any one of claims 1 to 3, wherein R_1 is a polymer residue selected from the group consisting of poly(oxyalkylene), methoxypoly(oxyalkylene), and poly(alkoxy acrylate); or

R_1 is a polymer residue selected from the group consisting of poly(ethylene glycol) (PEG), methoxypoly(ethylene glycol) (mPEG), poly(methoxyethyl methacrylate) and poly(ethoxyethyl methacrylate).

5. The copolymer according to any one of claims 1 to 4, wherein R_1 is a polymer residue with a molecular weight in the range of 2,000 to 20,000,

about 2,400 or
about 10,000.

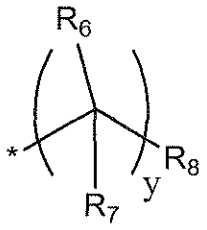
6. The copolymer according to any one of claims 1 to 5, wherein the anchoring moiety comprises an α-β-unsaturated carbonyl group; or

the anchoring moiety is selected from the group consisting of maleic acid, maleamic acid and maleimide groups; and wherein the antibacterial moiety comprises a cation; or

the antibacterial moiety comprises a quaternary ammonium.

7. The copolymer according to any one of claims 1 to 6, wherein Formula (I) is of Formula (IA) and Formula (II) is of Formula (IIA):

8. The copolymer of claim 7, wherein R_g is of formula (i):



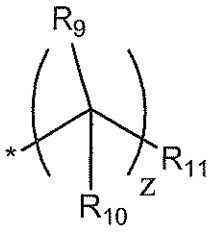
Formula (i)

wherein * is the point of attachment;

R_6 and R_7 are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_8 is an anchoring moiety comprising a α-β-unsaturated carbonyl group; and

y is an integer in the range of 1 to 5; or



Formula (ii)

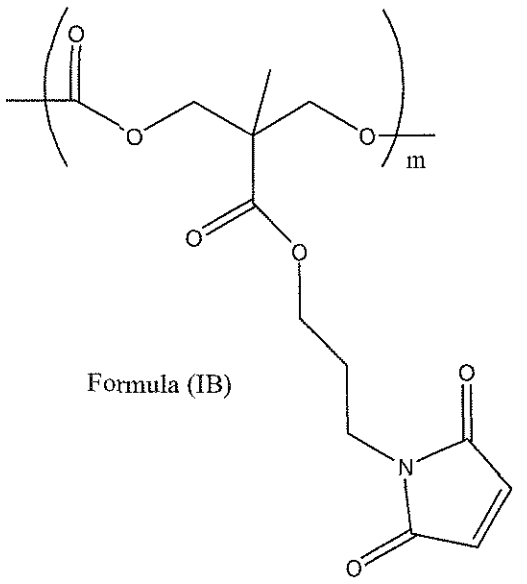
wherein R_h is of formula (ii): wherein R_9 and R_{10} are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_{11} is an aryl or heteroaryl substituted with at least one cation; and

Z is an integer in the range of 1 to 5.

9. The copolymer of claim 8, wherein R_8 is selected from the group consisting of maleic acid, maleamic acid and maleimide; and
R_{11} is selected from the group consisting of aryl or heteroaryl substituted with at least one quaternary ammonium cation.

10. The copolymer of any one of claims 1 to 9, wherein Formula (I) is of Formula (IB):

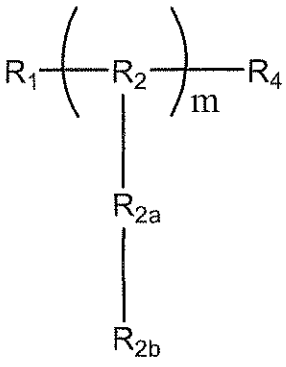


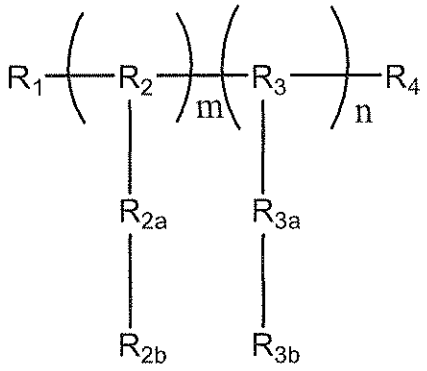
Formula (IB)

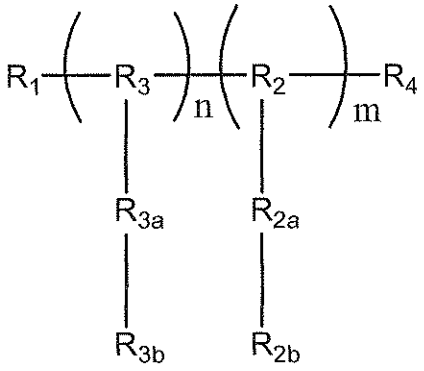
;

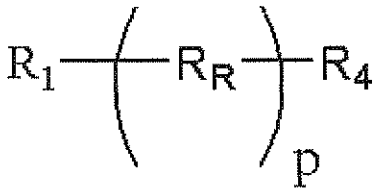
wherein m is as defined in claim 1; and
wherein Formula (II) is selected from the group consisting of:

11. The copolymer according to any one of claims 1 to 10, selected from the group consisting of:

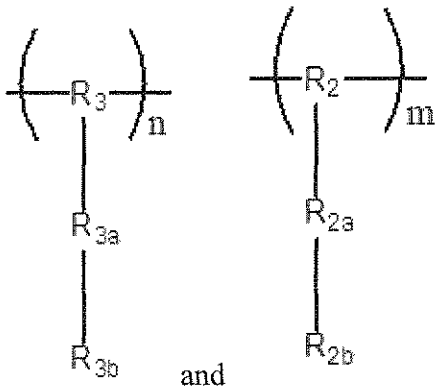
(i) 

(ii) 

(iii) 

(iv) ,

wherein R_R is a block consisting of randomly arranged monomer units of



and .

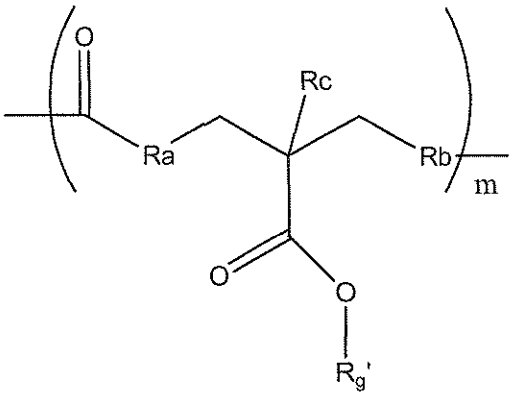
wherein R_1, R_2, R_3, R_4, R_{2a}, R_{2b}, R_{3a}, R_{3b}, m and n are as defined in any one of claims 1 to 10; and

p is an integer in the range of 1 to 50.

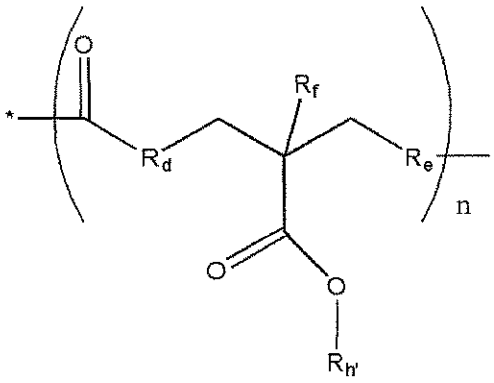
12. The copolymer of any one of claims 1 to 11, wherein m is in the range of 2 to 7; and

wherein n is in the range of 70 to 95.

13. A method of synthesizing a copolymer comprising monomer units represented by formulas (IIIA) and (IIIB):



Formula (IIIA)



Formula (IIIb)

wherein the copolymer is terminated on one end by R_1 and on the other end by R_4;

R_1 is a polymer residue comprising an antifouling moiety;

R_4 is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_a, R_b, R_c, R_d, R_e and R_f are independently $C(R_5)_2$, O or $N(R_5)$;

R_5 is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocycle, or optionally substituted heterocarbocycle;

R_g' represents protected R_g, and R_h' represents aryl or heteroaryl substituted with at least one substituent capable of being quaternized,

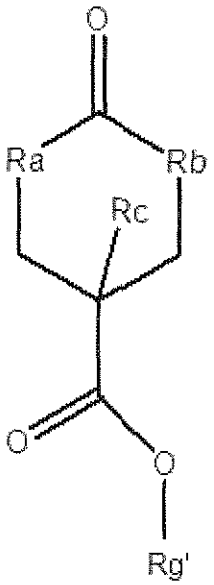
wherein R_g comprises an anchoring moiety;

m is an integer in the range of 2 to 20; and

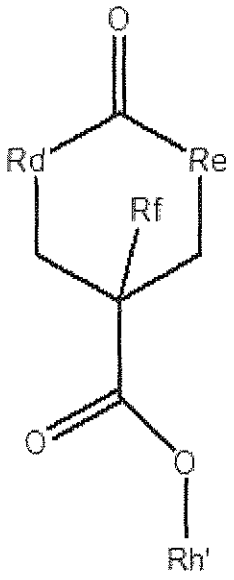
n is an integer in the range of 0 to 100,

the method comprising the step of:

(i) performing a ring-opening polymerization reaction in a reaction mixture comprising compounds of Formula (IC), H-R_1, and compounds of Formula (IIC):



Formula (IC)



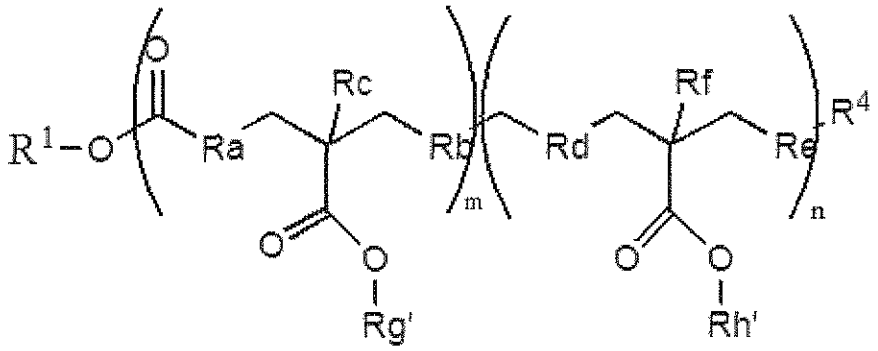
Formula (IIC)

,

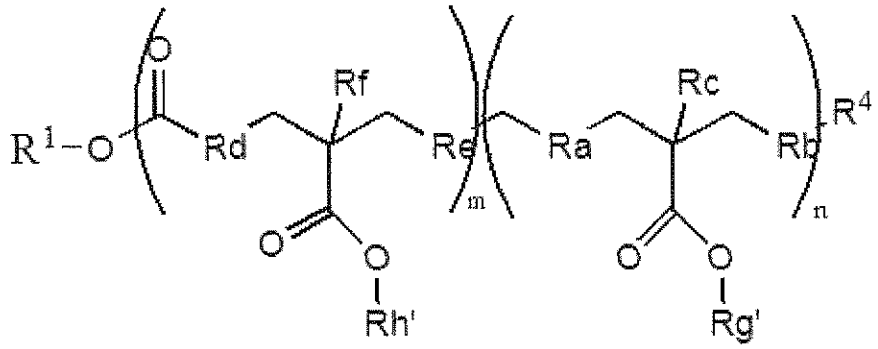
with the proviso that compounds of Formula (IIC) are present only when n≠0,

thereby forming a copolymer comprising monomer units of Formula (IIIA) and/or (IIIB).

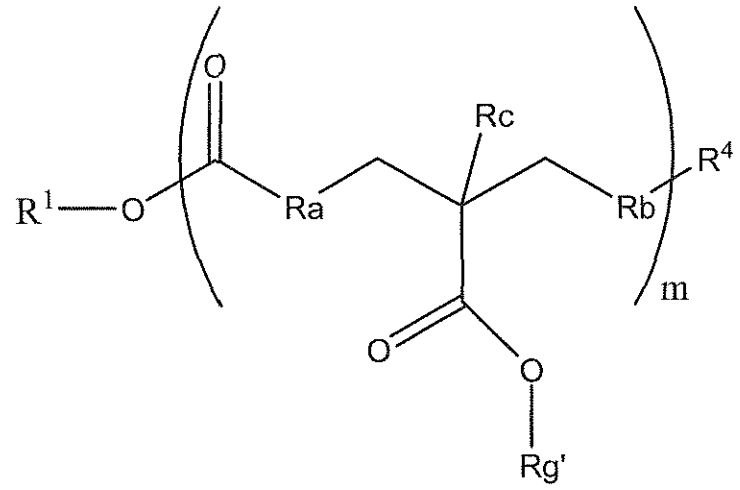
14. The method of claim 13, wherein the copolymer is selected from the group consisting of:



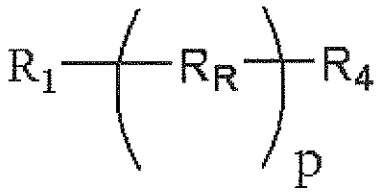
;



;



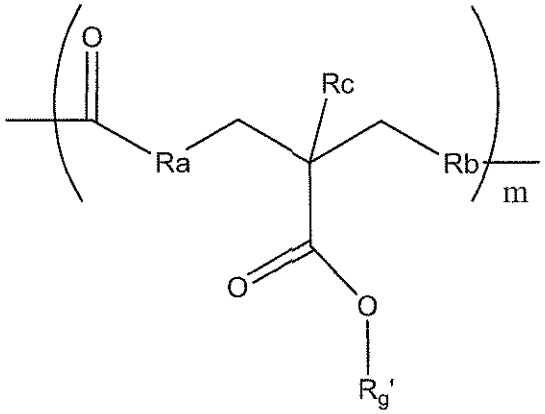
; and



,

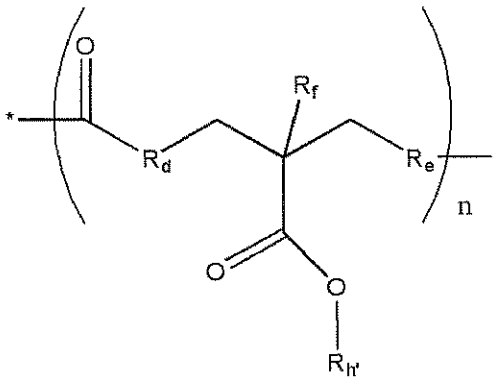
wherein Ra, Rb, Rc, Rd, Re, Rf, Rg', Rh', R_1, R_4, m and n are as defined in claim 13;

R_R is a block consisting of randomly arranged monomer units of



Formula (IIIA)

and



Formula (IIIb)

;

p is an integer in the range of 1 to 50; and

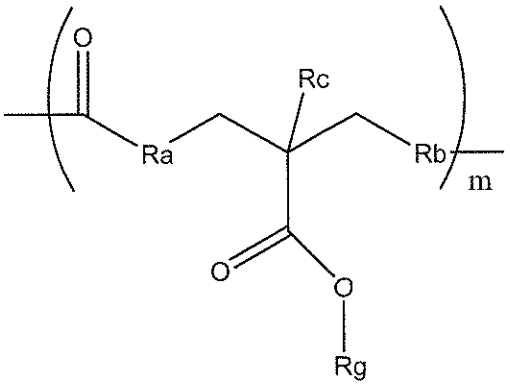
H-R_1 is selected from the group consisting of poly(ethylene glycol) (PEG), methoxypoly(ethylene glycol) (mPEG), poly(methoxyethyl methacrylate) and poly(ethoxyethyl methacrylate).

15. A method of claim 13 or 14, further comprising

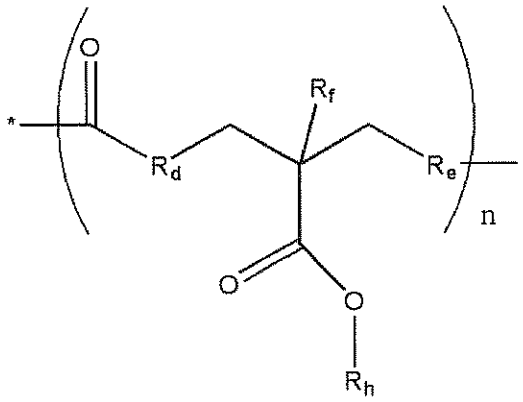
(ii) performing a deprotection reaction on the copolymer formed in claim 13, thereby exposing the R_g anchoring moiety(s); and

(iii) when $n \neq 0$, performing a quaternization reaction,

thereby forming a copolymer comprising monomer units represented by formulas (IA) and/or (IIA):



Formula (IA)



Formula (IIA)

wherein the copolymer is terminated on one end by R_1 and on the other end by R_4;

R_1, R_2, Ra, Rb, Rc, Rd, Re, Rf, Rg, m and n are as defined in claim 13; and

R_h comprises a cation.

16. The method according to any one of claims 13 to 15, wherein step (i) further comprises a ring opening polymerization catalyst; optionally

the ring-opening polymerization catalyst is selected from the group consisting of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), tin(II) 2-ethylhexanoate ($Sn(Oct)_2$) and tin(II) trifluoromethanesulfonate ($Sn(OTf)_2$).

17. The method according to claim 15 or 16, wherein the deprotection is carried out by dissolving the copolymer formed in step (i) in toluene; and

the quaternization reagent is selected from the group consisting of amine, dimethylbutylamine, dimethyloctylamine, dimethylbenzylamine, and trimethylamine.

18. A method of attaching a copolymer according to any one of claims 1 to 12 to a substrate, comprising attaching the anchoring moiety of said copolymer to an anchoring segment on said substrate; optionally

wherein the anchoring segment comprises one or more thiol groups; more optionally wherein the copolymer is attached to the substrate via a Michael addition.

19. An article comprising a substrate and a coating comprising the copolymer according to any one of claims 1 to 12.

20. Use of a copolymer according to any of claims 1 to 12 for imparting an antibacterial and/or antifouling surface to an article.