BRUSH POLYMER MACROMOLECULE STRUCTURES AND METHODS FOR DETECTING BIOMOLECULES

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 63/517,515, filed August 3, 2023, which is incorporated herein by reference in its entirety.

BACKGROUND

[0002] Analysis and separation of biomolecules typically requires laborious methods and relies of the fine tuning of analytical parameters. Often, the methods require inducing polymerization, which may not be feasible for all proteins or ligands, and is irreversible. There is a need for improved systems for separation and subsequent analysis of biomolecules. The present disclosure provides macromolecule structures, and compositions, methods, and systems thereof to address this need.

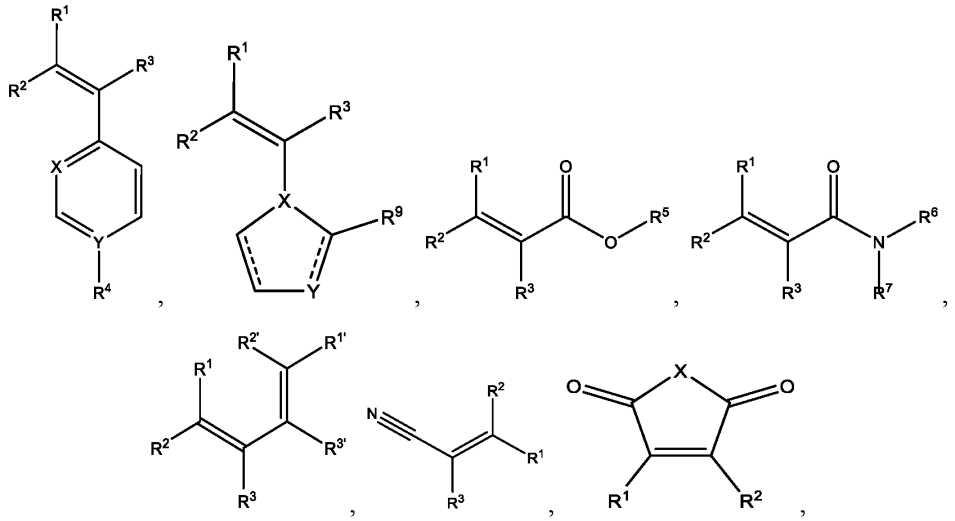
SUMMARY

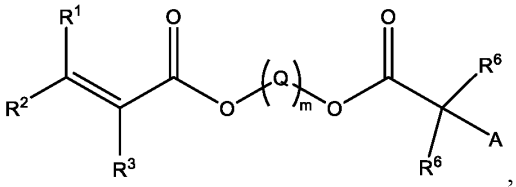
[0003] Provided herein are macromolecule structures comprising:

(I) a surface;

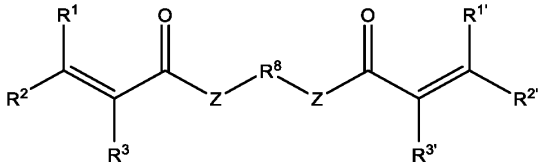
(II) a tethering moiety coupled to the surface; and

(III) a macromolecule chain, wherein a first end of the macromolecule chain is covalently attached to the tethering moiety, and wherein the macromolecule chain comprises two or more distinct recurring units derived from a monomer represented by a structure selected from the group consisting of:





, and

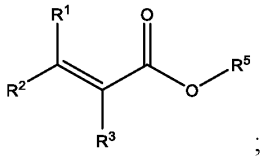


wherein each of X and Y is independently -C-, -O-, or -N-;

each Z is independently -O- or -NH;

Q is $-CH_2-$ or ethylene glycol;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by the structure:



;

m is an integer selected from 1-20;

=== is a single or double bond;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or -C_1-C_6 alkyl;

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, sulfonate, carboxylate, C_1-C_4 alkylene, amine, quaternary ammonium cation, or C_1-C_6 alkyl optionally substituted with halogen;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further optionally substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered

heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further optionally substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne;

R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide;

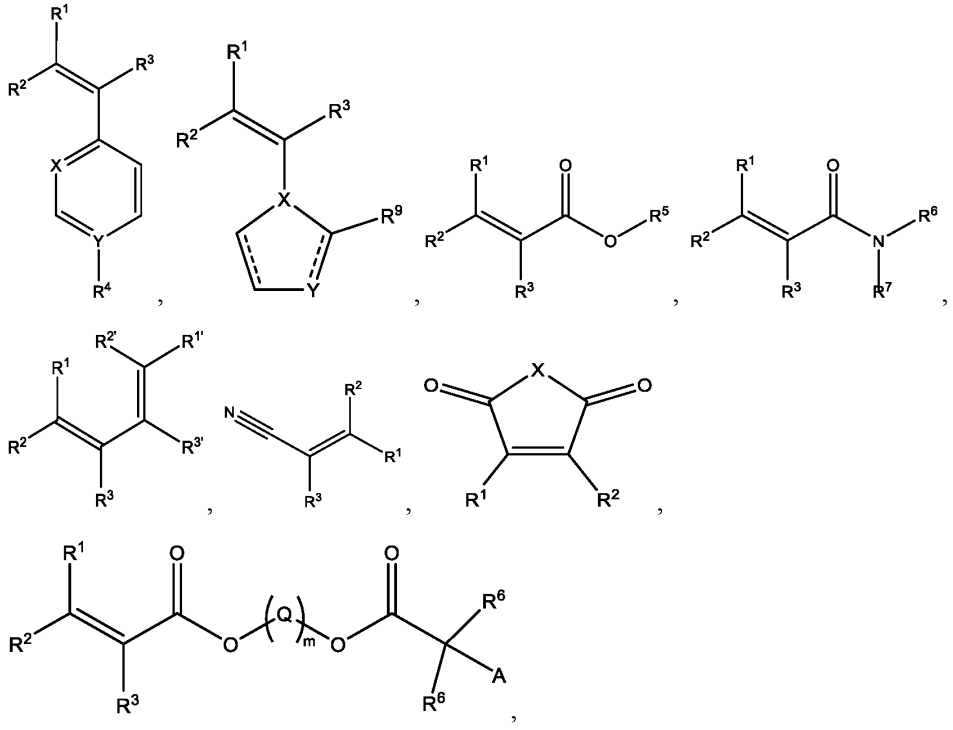
R^9 is hydrogen or oxo; and n^1 is an integer selected from 1-100. Further provided herein are macromolecule structures wherein R^3 is methyl. Further provided herein are macromolecule structures wherein R^5 is C_1-C_{n1} ethylene glycol.

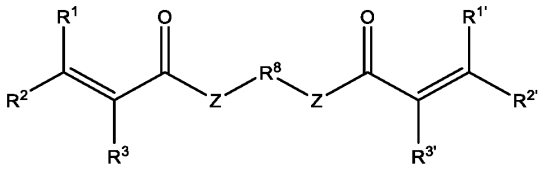
[0004] Provided herein are macromolecule structures comprising:

(I) a surface;

(II) a tethering moiety coupled to the surface; and

(III) a macromolecule chain, wherein a first end of the macromolecule chain is covalently attached to the tethering moiety, and wherein the macromolecule chain comprises a recurring unit derived from a monomer represented by a structure selected from the group consisting of:



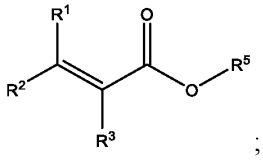
and 

wherein each of X and Y is independently -C-, -O-, or -N-;

each Z is independently -O- or -NH;

Q is $-CH_2-$ or ethylene glycol;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by the structure:

 ;

m is 1-6;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or C_1-C_6 alkyl

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, C_1-C_6 alkyl optionally substituted with halogen, C_1-C_4 alkylene, C_1-C_6 alkyl, sulfonate, amine, quaternary ammonium cation, or carboxylate;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or linear C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further

optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne; and

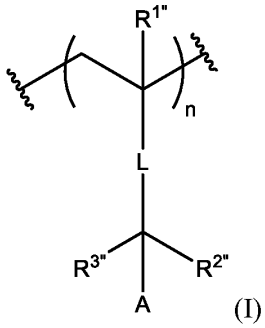
R^8 is C_1-C_6 alkyl, or symmetric or asymmetric disulfide;

R^9 is hydrogen or oxo;

n^1 is an integer selected from 1-100; and

provided that when R^3 is CH_3, R^4 is CH_3, or when R^5 is C_1-C_8 alkyl substituted with hydroxyl, C_1-C_8 is further substituted.

[0005] Provided herein are macromolecule structures comprising: (I) a surface and (II) a macromolecule chain coupled to the surface, wherein the macromolecule chain comprises a recurring unit of Formula (I):

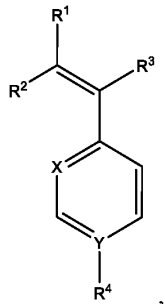


(I)

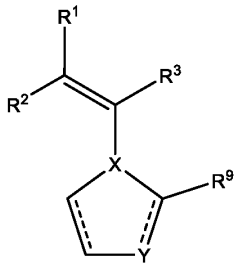
wherein each of $R^{1"}$, $R^{2"}$, and $R^{3"}$ is independently hydrogen or C_1-C_6 alkyl;

L is a linker moiety;

A is a polymeric side chain comprising a recurring unit derived from a monomer



represented by a structure selected from the group consisting of:



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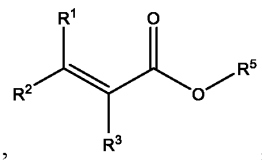

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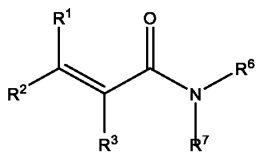

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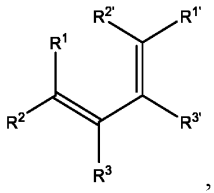

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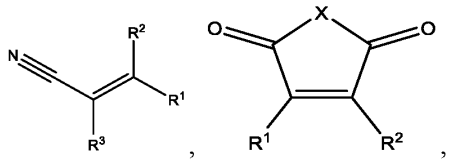
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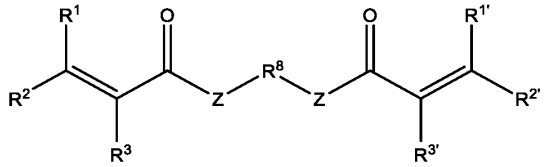


wherein each of X and Y is independently -C-, -O-, or -N-;

Z is -O- or -NH;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or C_1-C_6 alkyl;

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, sulfonate, carboxylate, C_1-C_4 alkylene, amine, quaternary ammonium cation, or C_1-C_6 alkyl optionally substituted with halogen;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or linear C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, substituted benzene, C_1-C_6 alkyl substituted with hydroxyl, optionally substituted C_1-C_8 alkyl sulfonate;

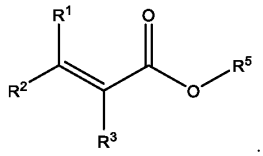
R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide;

R^9 is hydrogen or oxo;

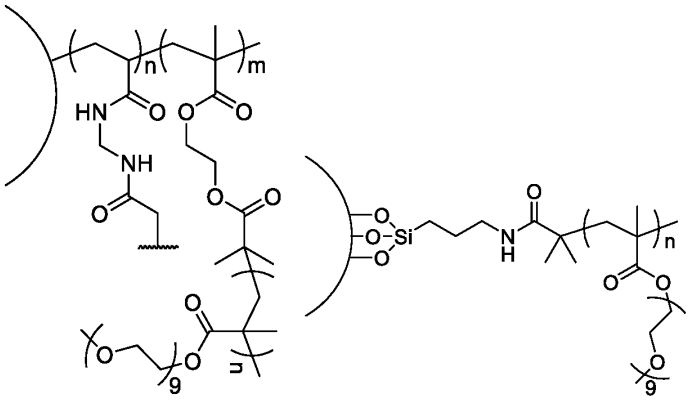
n^1 is an integer selected from 1-100; and

n is an integer selected from 1-10,000.

Further provided herein are macromolecule structures wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure:



. Further provided herein are macromolecule structures wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by a structure of **Table 1**. Further provided herein are macromolecule structures wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by a structure of **Table 2**. Further provided herein are macromolecule structures wherein the macromolecule structure has a structure represented by:



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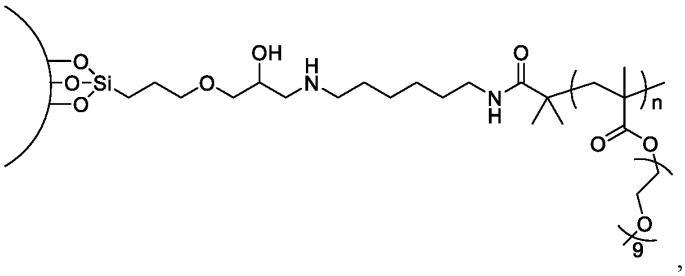

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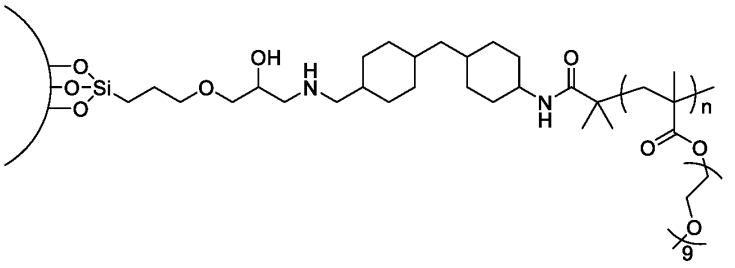

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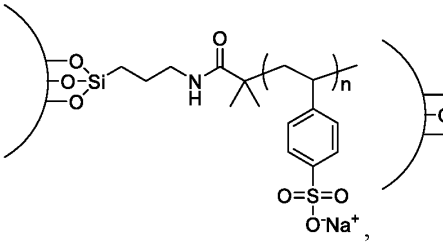

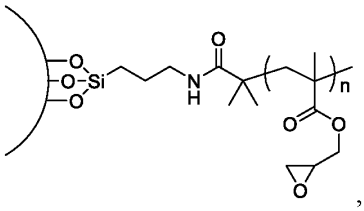

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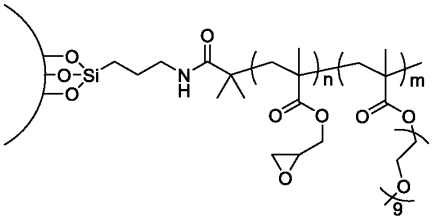
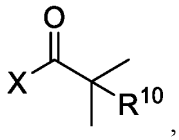


[0006] Provided herein are methods of making a macromolecule structure described herein, the method comprising: providing a surface; coupling a polymer initiator to the surface to form an initiator surface; and contacting the initiator surface with a monomer described herein to form the macromolecule structure. Further provided herein are methods wherein the surface comprises a particle. Further provided herein are methods wherein the particle comprises a diameter of about 100 nm to about 500 nm.

[0007] Provided herein are methods of making a macromolecule structure provided herein, the method comprising: providing a surface; coupling a vinyl group to the surface to form a vinyl-functionalized surface; contacting the vinyl-functionalized surface with a cross-linking monomer and a monomer selected from hydroxyalkyl methacrylate, aminoalkyl methacrylate, alkynyl methacrylate, glycidylalkyl methacrylate, hydroxyalkyl acrylate, aminoalkyl acrylate, alkynyl acrylate or glycidylalkyl acrylate to form a cross-linked polymer coupled to the surface; coupling a polymer initiator to the cross-linked polymer to form an initiator surface; contacting the initiator surface with a monomer described herein to form the macromolecule structure. Further provided herein are methods wherein the polymer initiator is represented by the structure: 

, wherein: X is a halogen; R^{10} is an initiator group.

[0008] Provided herein are compositions comprising a macromolecule structure described herein and a biomolecule adsorbed to the macromolecule structure. Further provided herein are compositions wherein at least 100 different biomolecules are adsorbed to the macromolecule structure.

[0009] Provided herein are methods of identifying proteins in a sample, the method comprising: incubating one or more macromolecule structures described herein with a biological sample

comprising biomolecules to form a biomolecule corona; isolating at least a portion of the biomolecules in the biomolecule corona; and assaying the biomolecule corona. Further provided herein are methods wherein the assaying is capable of identifying from 1 to 20,000 protein groups.

[0010] Provided herein are kits for identifying molecules in a biological sample, the kit comprising one or more macromolecule structures provided herein.

[0011] Provided herein are systems for identifying biomolecules in a biological sample, the system comprising: a macromolecule structure provided herein; a suspension solution; a biological sample comprising a concentration of proteins; and an automated system comprising a network of units with differentiated functions for isolating biomolecules adsorbed to the macromolecular structure, and wherein the automated system is programmed to perform a series of steps.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] The novel features of the disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the disclosure are utilized, and the accompanying drawings (also "Figure" and "FIG." herein), of which:

[0013] **FIG. 1** shows an exemplary synthetic scheme for preparation of a macromolecule structure herein by contacting a monomer with an initiator surface.

[0014] **FIG. 2** shows an exemplary synthetic scheme for preparation of a macromolecule structure herein by contacting a vinyl-functionalized surface with a cross-linking monomer and a second monomer.

[0015] **FIG. 3A** shows scanning electron micrographs of macromolecule structures described herein. **FIG. 3B** shows transmission electron micrographs of macromolecule structures described herein.

[0016] **FIG. 4** shows a synthetic scheme for the preparation of Compound 1.

[0017] **FIG. 5** shows a synthetic scheme for the preparation of Compound 2.

[0018] **FIG. 6** shows a synthetic scheme for the preparation of Compound 3.

[0019] **FIG. 7** shows a synthetic scheme for the preparation of block co-polymers.

[0020] **FIG. 8** shows a synthetic scheme for the preparation of macromolecule chains comprising varying monomers.

DETAILED DESCRIPTION

Certain Definitions

[0021] As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an agent" includes a plurality of such agents, and reference to "the cell" includes reference to one or more cells (or to a plurality of cells) and equivalents thereof known to those skilled in the art, and so forth. When ranges are used herein for physical properties, such as molecular weight, or chemical properties, such as chemical formulae, all combinations and subcombinations of ranges and specific embodiments therein are intended to be included. The term "about" when referring to a number or a numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and thus the number or numerical range may vary between 1% and 15% of the stated number or numerical range. The term "comprising" (and related terms such as "comprise" or "comprises" or "having" or "including") is not intended to exclude that in other certain embodiments, for example, an embodiment of any composition of matter, composition, method, or process, or the like, described herein, may "consist of" or "consist essentially of" the described features.

[0022] "Amino" refers to the $-NH_2$ radical.

[0023] "Cyano" refers to the -CN radical.

[0024] "Nitro" refers to the $-NO_2$ radical.

[0025] "Oxo" refers to the =O radical.

[0026] "Hydroxyl" refers to the -OH radical.

[0027] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this disclosure belongs. All patents and publications referred to herein are incorporated by reference.

[0028] "Alkyl" refers to an optionally substituted straight-chain, or optionally substituted branched-chain saturated hydrocarbon mono-radical, and preferably having from one to fifteen carbon atoms (*i.e.*, C_1-C_{15} alkyl). In certain embodiments, an alkyl comprises one to thirteen carbon atoms (*i.e.*, C_1-C_{13} alkyl). In certain embodiments, an alkyl comprises one to eight carbon atoms (*i.e.*, C_1-C_8 alkyl). In other embodiments, an alkyl comprises one to five carbon atoms (*i.e.*, C_1-C_5 alkyl). In other embodiments, an alkyl comprises one to four carbon atoms (*i.e.*, C_1-C_4 alkyl). In other embodiments, an alkyl comprises one to three carbon atoms (*i.e.*, C_1-C_3 alkyl). In other embodiments, an alkyl comprises one to two carbon atoms (*i.e.*, C_1-C_2 alkyl). Whenever it appears herein, a numerical range such as "C_1-C_3 alkyl" means that the alkyl group consists of 1 carbon atom, 2 carbon atoms, or 3 carbon atoms. In other embodiments, an alkyl comprises one carbon atom (*i.e.*, C_1 alkyl). In other embodiments, an alkyl comprises five to fifteen carbon atoms

(*i.e.*, C_5-C_{15} alkyl). In other embodiments, an alkyl comprises five to eight carbon atoms (*i.e.*, C_5-C_8 alkyl). In other embodiments, an alkyl comprises two to five carbon atoms (*i.e.*, C_2-C_5 alkyl). In other embodiments, an alkyl comprises three to five carbon atoms (*i.e.*, C_3-C_5 alkyl). In certain embodiments, the alkyl group is selected from methyl, ethyl, 1-propyl (*n*-propyl), 1-methylethyl (*iso*-propyl), 1-butyl (*n*-butyl), 1-methylpropyl (*sec*-butyl), 2-methylpropyl (*iso*-butyl), 1,1-dimethylethyl (*tert*-butyl), 1-pentyl (*n*-pentyl). In other embodiments, examples include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, 2-methyl-1-propyl, 2-methyl-2-propyl, 2-methyl-1-butyl, 3-methyl-1-butyl, 2-methyl-3-butyl, 2,2-dimethyl-1-propyl, 2-methyl-1-pentyl, 3-methyl-1-pentyl, 4-methyl-1-pentyl, 2-methyl-2-pentyl, 3-methyl-2-pentyl, 4-methyl-2-pentyl, 2,2-dimethyl-1-butyl, 3,3-dimethyl-1-butyl, 2-ethyl-1-butyl, n-butyl, isobutyl, sec-butyl, t-butyl, n-pentyl, isopentyl, neopentyl, tert-amyl, and hexyl, and longer alkyl groups, such as heptyl, octyl, and the like. The alkyl is attached to the rest of the molecule by a single bond. Unless stated otherwise specifically in the specification, an alkyl group is optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, sulfone, mercapto, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, the alkyl is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, $-NO_2$, or -C≡CH. In some embodiments, the alkyl is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the alkyl is optionally substituted with halogen such as F. In some embodiments, the alkyl is unsubstituted.

[0029] As used herein, C_1-C_x (or C_{1-x}) includes C_1-C_2, C_1-C_3... C_1-C_x. By way of example only, a group designated as "C_1-C_4" indicates that there are one to four carbon atoms in the moiety, i.e. groups containing 1 carbon atom, 2 carbon atoms, 3 carbon atoms or 4 carbon atoms. Thus, by way of example only, "C_1-C_4 alkyl" indicates that there are one to four carbon atoms in the alkyl group, *i.e.*, the alkyl group is selected from among methyl, ethyl, propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *sec*-butyl, and *t*-butyl. Also, by way of example, C_0-C_2 alkylene includes a direct bond, -CH_2-, and -CH_2CH_2- linkages.

[0030] "Alkoxy" refers to a radical bonded through an oxygen atom of the formula –O-alkyl, where alkyl is an alkyl chain as defined above. Unless stated otherwise specifically in the specification, an alkoxy group can be optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, an alkoxy is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, an alkoxy is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the alkoxy is optionally substituted with halogen. In some embodiments, the alkoxy is unsubstituted.

[0031] "Alkenyl" refers to an optionally substituted straight or branched hydrocarbon chain radical group containing at least one carbon-carbon double bond, and preferably having from two to twelve carbon atoms (*i.e.,* C_2-C_{12} alkenyl). In certain embodiments, an alkenyl comprises two to eight carbon atoms (*i.e.*, C_2-C_8 alkenyl). In certain embodiments, an alkenyl comprises four to eight carbon atoms (*i.e.*, C_4-C_6 alkenyl). In other embodiments, an alkenyl comprises six to eight carbon atoms (*i.e.*, C_6-C_8 alkenyl). In certain embodiments, an alkenyl comprises at least one double bond at the end of a carbon chain. In other embodiments, an alkenyl comprises at least one double bond in the middle of a carbon chain. The group can be in either the *cis* or *trans* configuration about the double bond(s), and should be understood to include both isomers. Examples include, but are not limited to, ethenyl (-CH=CH_2), 1-propenyl (-CH_2CH=CH_2), isopropenyl [-C(CH_3)=CH_2], butenyl, 1,3-butadienyl, and the like. Whenever it appears herein, a numerical range such as "C_2-C_6 alkenyl" means that the alkenyl group can consist of 2 carbon atoms, 3 carbon atoms, 4 carbon atoms, 5 carbon atoms, or 6 carbon atoms. Unless stated otherwise specifically in the specification, an alkenyl group is optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, an alkenyl is optionally substituted with oxo, halogen, -CN, -CF_3, -OH, -OMe, -NH_2, or -NO_2. In some embodiments, an alkenyl is optionally substituted with oxo, halogen, -CN, -CF_3, -OH, or -OMe. In some embodiments, the alkenyl is optionally substituted with halogen. The alkenyl is attached to the rest of the molecule by a single bond, for example, ethenyl (*i.e.*, vinyl), prop-1-enyl (*i.e.*, allyl), but-1-enyl, pent-1-enyl, penta-1,4-dienyl, and the like. Unless stated otherwise specifically in the specification, an alkenyl group is optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, an alkenyl is optionally substituted with oxo, halogen, -CN, -CF_3, -OH, -OMe, -NH_2, or -NO_2. In some embodiments, an alkenyl is optionally substituted with oxo, halogen, -CN, -CF_3, -OH, or -OMe. In some embodiments, the alkenyl is optionally substituted with halogen. In some embodiments, the alkenyl is unsubstituted.

[0032] "Alkynyl" refers to an optionally substituted straight or branched hydrocarbon chain radical group containing at least one carbon-carbon triple bond, and preferably having from two to twelve carbon atoms (*i.e.*, C_2-C_{12} alkynyl). In certain embodiments, an alkynyl comprises two to eight carbon atoms (*i.e.*, C_2-C_8 alkynyl). In other embodiments, an alkynyl comprises two to six carbon atoms (*i.e.*, C_2-C_6 alkynyl). In other embodiments, an alkynyl comprises two to four carbon atoms (*i.e.*, C_2-C_4 alkynyl). Whenever it appears herein, a numerical range such as "C_2-C_6 alkynyl" means that the alkynyl group can consist of 2 carbon atoms, 3 carbon atoms, 4 carbon atoms, 5 carbon atoms, or 6 carbon atoms. The alkynyl is attached to the rest of the molecule by

a single bond, for example, ethynyl, propynyl, butynyl, pentynyl, hexynyl, 2-propynyl, 2-butynyl, 1,3-butadiynyl, and the like. Unless stated otherwise specifically in the specification, an alkynyl group is optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, an alkynyl is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, an alkynyl is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the alkynyl is optionally substituted with halogen. In some embodiments, the alkynyl is unsubstituted.

[0033] "Alkylene" or "alkylene chain" refers to an optionally substituted straight or branched divalent hydrocarbon chain linking the rest of the molecule to a radical group containing no unsaturation, and preferably having from one to twelve carbon atoms, for example, methylene, ethylene, propylene, *n*-butylene, and the like. The alkylene chain is attached to the rest of the molecule through a single bond and to the radical group through a single bond. The points of attachment of the alkylene chain to the rest of the molecule and to the radical group can be through any two carbons within the chain. In certain embodiments, an alkylene comprises one to ten carbon atoms (*i.e.,* C_1-C_8 alkylene). In certain embodiments, an alkylene comprises one to eight carbon atoms (*i.e.*, C_1-C_8 alkylene). In other embodiments, an alkylene comprises one to five carbon atoms (*i.e.*, C_1-C_5 alkylene). In other embodiments, an alkylene comprises one to four carbon atoms (*i.e.*, C_1-C_4 alkylene). In other embodiments, an alkylene comprises one to three carbon atoms (*i.e.*, C_1-C_3 alkylene). In other embodiments, an alkylene comprises one to two carbon atoms (*i.e.*, C_1-C_2 alkylene). In other embodiments, an alkylene comprises one carbon atom (*i.e.*, C_1 alkylene). In other embodiments, an alkylene comprises five to eight carbon atoms (*i.e.*, C_5-C_8 alkylene). In other embodiments, an alkylene comprises two to five carbon atoms (*i.e.*, C_2-C_5 alkylene). In other embodiments, an alkylene comprises three to five carbon atoms (*i.e.*, C_3-C_5 alkylene). Unless stated otherwise specifically in the specification, an alkylene group can be optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, an alkylene is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, an alkylene is optionally substituted with oxo, halogen, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the alkylene is optionally substituted with halogen. In some embodiments, the alkylene is $-CH_2-$, $-CH_2CH_2-$, or $-CH_2CH_2CH_2-$. In some embodiments, the alkylene is $-CH_2-$. In some embodiments, the alkylene is $-CH_2CH_2-$. In some embodiments, the alkylene is $-CH_2CH_2CH_2-$. In some embodiments, the alkylene is unsubstituted.

[0034] "Aryl" refers to a radical derived from a hydrocarbon ring system comprising at least one aromatic ring. In some embodiments, an aryl comprises hydrogens and 5 to 30 carbon atoms.

The aryl radical can be a monocyclic, bicyclic, tricyclic, or tetracyclic ring system, which can include fused (when fused with a cycloalkyl or heterocycloalkyl ring, the aryl is bonded through an aromatic ring atom) or bridged ring systems. In some embodiments, the aryl is a 6- to 10-membered aryl. In some embodiments, the aryl is a 6-membered aryl. Aryl radicals include, but are not limited to, aryl radicals derived from the hydrocarbon ring systems of anthrylene, naphthylene, phenanthrylene, anthracene, azulene, benzene, chrysene, fluoranthene, fluorene, indane, indene, naphthalene, phenalene, phenanthrene, pleiadene, pyrene, and triphenylene. In some embodiments, the aryl is phenyl. Unless stated otherwise specifically in the specification, an aryl can be optionally substituted, for example, with halogen, amino, alkylamino, aminoalkyl, nitrile, nitro, hydroxyl, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, $-S(O)_2NH-C_1-C_6$alkyl, and the like. In some embodiments, an aryl is optionally substituted with halogen, methyl, ethyl, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, $-NO_2$, $-S(O)_2NH_2$, $-S(O)_2NHCH_3$, $-S(O)_2NHCH_2CH_3$, $-S(O)_2NHCH(CH_3)_2$, $-S(O)_2N(CH_3)_2$, or $-S(O)_2NHC(CH_3)_3$. In some embodiments, an aryl is optionally substituted with halogen, methyl, ethyl, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the aryl is optionally substituted with halogen. In some embodiments, the aryl is substituted with alkyl, alkenyl, alkynyl, haloalkyl, or heteroalkyl, wherein each alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl is independently unsubstituted, or substituted with halogen, methyl, ethyl, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, the aryl is unsubstituted.

[0035] "Aralkyl" refers to a radical of the formula $-R^c$-aryl where R^c is an alkylene chain as defined above, for example, methylene, ethylene, and the like.

[0036] "Aralkenyl" refers to a radical of the formula $-R^d$-aryl where R^d is an alkenylene chain as defined above. "Aralkynyl" refers to a radical of the formula $-R^e$-aryl, where R^e is an alkynylene chain as defined above.

[0037] "Carbocycle" refers to a saturated, unsaturated or aromatic rings in which each atom of the ring is carbon. Carbocycle can include 3- to 10-membered monocyclic rings and 6- to 12-membered bicyclic rings (such as spiro, fused, or bridged rings). Each ring of a bicyclic carbocycle can be selected from saturated, unsaturated, and aromatic rings. An aromatic ring, e.g., phenyl, can be fused to a saturated or unsaturated ring, e.g., cyclohexane, cyclopentane, or cyclohexene. Any combination of saturated, unsaturated and aromatic bicyclic rings, as valence permits, are included in the definition of carbocyclic. In an exemplary embodiment, an aromatic ring, e.g., phenyl, can be fused to a saturated or unsaturated ring, e.g., cyclohexane, cyclopentane, or cyclohexene. A bicyclic carbocycle includes any combination of saturated, unsaturated and aromatic bicyclic rings, as valence permits. A bicyclic carbocycle includes any combination of ring sizes such as 4-5 fused ring systems, 5-5 fused ring systems, 5-6 fused ring systems, 6-6 fused

ring systems, 5-7 fused ring systems, 6-5 fused ring systems, 6-7 fused ring systems, 5-8 fused ring systems, and 6-8 fused ring systems. Exemplary carbocycles include cyclopentyl, cyclohexyl, cyclohexenyl, adamantyl, phenyl, indanyl, and naphthyl. The term "unsaturated carbocycle" refers to carbocycles with at least one degree of unsaturation and excluding aromatic carbocycles. Examples of unsaturated carbocycles include cyclohexadiene, cyclohexene, and cyclopentene. The term "saturated cycloalkyl" as used herein refers to a saturated carbocycle. Exemplary carbocycles include cyclopropyl, cyclopentyl, cyclohexyl, cyclohexenyl, adamantyl, phenyl, indanyl, norbornyl, and naphthyl. Carbocycles can be optionally substituted by one or more substituents such as those substituents described herein.

[0038] "Cycloalkyl" refers to a stable, partially or fully saturated, monocyclic or polycyclic carbocyclic ring, which can include fused (when fused with an aryl or a heteroaryl ring, the cycloalkyl is bonded through a non-aromatic ring atom), bridged, or spiro ring systems. Representative cycloalkyls include, but are not limited to, cycloalkyls having from three to fifteen carbon atoms (C_3-C_{15} cycloalkyl), from three to ten carbon atoms (C_3-C_{10} cycloalkyl), from three to eight carbon atoms (C_3-C_8 cycloalkyl), from three to six carbon atoms (C_3-C_6 cycloalkyl), from three to five carbon atoms (C_3-C_5 cycloalkyl), or three to four carbon atoms (C_3-C_4 cycloalkyl). In some embodiments, the cycloalkyl is a 3- to 6-membered cycloalkyl. In some embodiments, the cycloalkyl is a 5- to 6-membered cycloalkyl. Monocyclic cycloalkyls include, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Polycyclic cycloalkyls or carbocycles include, for example, adamantyl, norbornyl, decalinyl, bicyclo[3.3.0]octane, bicyclo[4.3.0]nonane, cis-decalin, trans-decalin, bicyclo[2.1.1]hexane, bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, bicyclo[3.2.2]nonane, and bicyclo[3.3.2]decane, and 7,7-dimethyl-bicyclo[2.2.1]heptanyl. Partially saturated cycloalkyls include, for example, cyclopentenyl, cyclohexenyl, cycloheptenyl, and cyclooctenyl. Unless stated otherwise specifically in the specification, a cycloalkyl is optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, a cycloalkyl is optionally substituted with oxo, halogen, methyl, ethyl, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, a cycloalkyl is optionally substituted with oxo, halogen, methyl, ethyl, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the cycloalkyl is optionally substituted with halogen. In some embodiments, the cycloalkyl is unsubstituted.

[0039] "Cycloalkylalkyl" refers to a radical of the formula $-R^c$-cycloalkyl where R^c is an alkylene chain as described above.

[0040] "Cycloalkylalkoxy" refers to a radical bonded through an oxygen atom of the formula $-O-R^c$-cycloalkyl where R^c is an alkylene chain as described above.

[0041] "Halo" or "halogen" refers to halogen substituents such as bromo, chloro, fluoro and iodo substituents.

[0042] As used herein, the term "haloalkyl" or "haloalkane" refers to an alkyl radical, as defined above, that is substituted by one or more halogen radicals, for example, trifluoromethyl, dichloromethyl, bromomethyl, 2,2,2-trifluoroethyl, 1-fluoromethyl-2-fluoroethyl, and the like. In some embodiments, the alkyl part of the fluoroalkyl radical is optionally further substituted. Examples of halogen substituted alkanes ("haloalkanes") include halomethane (e.g., chloromethane, bromomethane, fluoromethane, iodomethane), di-and trihalomethane (e.g., trichloromethane, tribromomethane, trifluoromethane, triiodomethane), 1-haloethane, 2-haloethane, 1,2-dihaloethane, 1-halopropane, 2-halopropane, 3-halopropane, 1,2-dihalopropane, 1,3-dihalopropane, 2,3-dihalopropane, 1,2,3-trihalopropane, and any other suitable combinations of alkanes (or substituted alkanes) and halogens (e.g., Cl, Br, F, I, etc.). When an alkyl group is substituted with more than one halogen radicals, each halogen can be independently selected e.g., 1-chloro,2-fluoroethane.

[0043] "Fluoroalkyl" refers to an alkyl radical, as defined above, that is substituted by one or more fluoro radicals, for example, trifluoromethyl, difluoromethyl, fluoromethyl, 2,2,2-trifluoroethyl, 1-fluoromethyl-2-fluoroethyl, and the like.

[0044] "Hydroxyalkyl" refers to an alkyl radical, as defined above, that is substituted by one or more hydroxyls. In some embodiments, the alkyl is substituted with one hydroxyl. In some embodiments, the alkyl is substituted with one, two, or three hydroxyls. Hydroxyalkyl include, for example, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, or hydroxypentyl. In some embodiments, the hydroxyalkyl is hydroxymethyl.

[0045] "Aminoalkyl" refers to an alkyl radical, as defined above, that is substituted by one or more amines. In some embodiments, the alkyl is substituted with one amine. In some embodiments, the alkyl is substituted with one, two, or three amines. Aminoalkyl include, for example, aminomethyl, aminoethyl, aminopropyl, aminobutyl, or aminopentyl. In some embodiments, the aminoalkyl is aminomethyl.

[0046] "Disulfide" refers to two sulfur atoms bonded to each other, where each sulfur comprises an optionally substituted alkyl chain. In some embodiments a disulfide may be R-S-S-R'. In some embodiments, R and R' may be identical. In some embodiments, R and R' are different. Each R and R' may be independently selected from C_1-C_{12} alkyl. In certain embodiments, R or R' may be substituted with an amine, sulfone, or carboxylic acid.

[0047] The term "heteroalkyl" refers to an alkyl group in which one or more skeletal atoms of the alkyl are selected from an atom other than carbon, e.g., oxygen, nitrogen (e.g., -NH-, -N(alkyl)-), sulfur, or combinations thereof. A heteroalkyl is attached to the rest of the molecule at a carbon

atom of the heteroalkyl. In one aspect, a heteroalkyl is a C_1-C_6 heteroalkyl wherein the heteroalkyl is comprised of 1 to 6 carbon atoms and one or more atoms other than carbon, e.g., oxygen, nitrogen (e.g. -NH-, -N(alkyl)-), sulfur, or combinations thereof wherein the heteroalkyl is attached to the rest of the molecule at a carbon atom of the heteroalkyl. Examples of such heteroalkyl are, for example, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, $-CH_2CH_2OCH_2CH_2OCH_3$, or $-CH(CH_3)OCH_3$. Unless stated otherwise specifically in the specification, a heteroalkyl is optionally substituted for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, a heteroalkyl is optionally substituted with oxo, halogen, methyl, ethyl, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, a heteroalkyl is optionally substituted with oxo, halogen, methyl, ethyl, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the heteroalkyl is optionally substituted with halogen. In some embodiments, the heteroalkyl is unsubstituted.

[0048] "Heterocycloalkyl" refers to a stable 3- to 24-membered partially or fully saturated ring radical comprising 2 to 23 carbon atoms and at least one ring heteroatoms. In some embodiments, a heterocycloalkyl contains from one to 8 heteroatoms selected from the group consisting of nitrogen, oxygen, phosphorous, and sulfur. Unless stated otherwise specifically in the specification, the heterocycloalkyl radical can be a monocyclic, bicyclic, tricyclic, or tetracyclic ring system, which can include fused (when fused with an aryl or a heteroaryl ring, the heterocycloalkyl is bonded through a non-aromatic ring atom) or bridged ring systems; and the nitrogen, carbon, or sulfur atoms in the heterocycloalkyl radical can be optionally oxidized; the nitrogen atom can be optionally quaternized.

[0049] Representative heterocycloalkyls include, but are not limited to, heterocycloalkyls having from two to fifteen carbon atoms (C_2-C_{15} heterocycloalkyl), from two to ten carbon atoms (C_2-C_{10} heterocycloalkyl), from two to eight carbon atoms (C_2-C_8 heterocycloalkyl), from two to six carbon atoms (C_2-C_6 heterocycloalkyl), from two to five carbon atoms (C_2-C_5 heterocycloalkyl), or two to four carbon atoms (C_2-C_4 heterocycloalkyl). In some embodiments, the heterocycloalkyl is a 3- to 6-membered heterocycloalkyl. In some embodiments, the heterocycloalkyl is a 5- to 6-membered heterocycloalkyl. Examples of such heterocycloalkyl radicals include, but are not limited to, aziridinyl, azetidinyl, dioxolanyl, thienyl[1,3]dithianyl, decahydroisoquinolyl, imidazolinyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, octahydroindolyl, octahydroisoindolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, oxazolidinyl, piperidinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, pyrazolidinyl, quinuclidinyl, thiazolidinyl, tetrahydrofuryl, trithianyl, tetrahydropyranyl, thiomorpholinyl, thiamorpholinyl, 1-oxo-thiomorpholinyl, 1,1-dioxo-thiomorpholinyl, 1,3-dihydroisobenzofuran-1-yl, 3-oxo-1,3-dihydroisobenzofuran-1-yl, methyl-2-oxo-1,3-dioxol-4-yl,

and 2-oxo-1,3-dioxol-4-yl. The term heterocycloalkyl also includes all ring forms of the carbohydrates, including but not limited to, the monosaccharides, the disaccharides, and the oligosaccharides. It is understood that when referring to the number of carbon atoms in a heterocycloalkyl, the number of carbon atoms in the heterocycloalkyl is not the same as the total number of atoms (including the heteroatoms) that make up the heterocycloalkyl (i.e. skeletal atoms of the heterocycloalkyl ring). Unless stated otherwise specifically in the specification, a heterocycloalkyl is optionally substituted, for example, with oxo, halogen, amino, nitrile, nitro, hydroxyl, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, a heterocycloalkyl is optionally substituted with oxo, halogen, methyl, ethyl, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, a heterocycloalkyl is optionally substituted with oxo, halogen, methyl, ethyl, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the heterocycloalkyl is optionally substituted with halogen. In some embodiments, the heterocycloalkyl is unsubstituted.

[0050] "Heterocycle" or "heterocyclyl" refers to a saturated, unsaturated or aromatic ring comprising one or more ring heteroatoms. Exemplary heteroatoms include N, O, Si, P, B, and S atoms. Heterocycles include e.g., 3- to 10-membered monocyclic rings and 6- to 12-membered bicyclic rings (such as spiro, fused, or bridged rings). Unless stated otherwise specifically in the specification, the heterocyclyl radical is a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which optionally includes fused, bridged, or spirocyclic ring systems. The heteroatoms in the heterocyclyl radical are optionally oxidized. One or more nitrogen atoms, if present, are optionally quaternized. The heterocyclyl radical can be partially or fully saturated. The heterocyclyl is attached to the rest of the molecule through any atom of the ring(s). Examples of such heterocyclyl radicals include, but are not limited to, dioxolanyl, thienyl[1,3]dithianyl, decahydroisoquinolyl, imidazolinyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, octahydroindolyl, octahydroisoindolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, oxazolidinyl, piperidinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, pyrazolidinyl, quinuclidinyl, thiazolidinyl, tetrahydrofuryl, trithianyl, tetrahydropyranyl, thiomorpholinyl, thiamorpholinyl, 1-oxo-thiomorpholinyl, and 1,1-dioxo-thiomorpholinyl. Unless stated otherwise specifically in the specification, the term "heterocyclyl" is meant to include heterocyclyl radicals as defined above that are optionally substituted by one or more substituents. For example, a heterocyclyl can be optionally substituted by one or more substituents selected from alkyl, alkenyl, alkynyl, halo, fluoroalkyl, oxo, thioxo, cyano, nitro, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted carbocyclyl, optionally substituted carbocyclylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally

substituted heteroaryl, optionally substituted heteroarylalkyl, -R^b-OR^a, -R^b-OC(O)-R^a, -R^b-OC(O)-OR^a, -R^b-OC(O)-$N(R^a)_2$, -R^b-$N(R^a)_2$, -R^b-C(O)R^a, -R^b-C(O)OR^a, -R^b-C(O)$N(R^a)_2$, -R^b-CN, -R^b-O-R^e-C(O)$N(R^a)_2$, -R^b-$N(R^a)$C(O)OR^a, -R^b-$N(R^a)$C(O)R^a, -R^b-$N(R^a)S(O)_tR^a$ (where t is 1 or 2), -R^b-$S(O)_tR^a$ (where t is 1 or 2), -R^b-$S(O)_tOR^a$ (where t is 1 or 2) and -R^b-$S(O)_tN(R^a)_2$ (where t is 1 or 2), where each R^a is independently hydrogen, alkyl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), fluoroalkyl, cycloalkyl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), cycloalkylalkyl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), aryl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), aralkyl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), heterocyclyl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), heterocyclylalkyl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), heteroaryl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), or heteroarylalkyl (optionally substituted with halogen, hydroxy, methoxy, or trifluoromethyl), each R^b is independently a direct bond or a straight or branched alkylene or alkenylene chain, and R^e is a straight or branched alkylene or alkenylene chain, and where each of the above substituents is unsubstituted unless otherwise indicated.

[0051] "Heteroaryl" or "aromatic heterocycle" refers to a ring system radical comprising carbon atom(s) and one or more ring heteroatoms (e.g., selected from the group consisting of nitrogen, oxygen, phosphorous, silicon, and sulfur), and at least one aromatic ring. In some embodiments, a heteroaryl is a 5- to 14-membered ring system radical comprising one to thirteen carbon atoms, one to six heteroatoms selected from the group consisting of nitrogen, oxygen, phosphorous, and sulfur. The heteroaryl radical can be a monocyclic, bicyclic, tricyclic, or tetracyclic ring system, which can include fused (when fused with a cycloalkyl or heterocycloalkyl ring, the heteroaryl is bonded through an aromatic ring atom) or bridged ring systems; and the nitrogen, carbon, or sulfur atoms in the heteroaryl radical can be optionally oxidized; the nitrogen atom can be optionally quaternized. In some embodiments, the heteroaryl is a 5- to 10-membered heteroaryl. In some embodiments, the heteroaryl is a 5- to 6-membered heteroaryl. Examples include, but are not limited to, azepinyl, acridinyl, benzimidazolyl, benzothiazolyl, benzindolyl, benzodioxolyl, benzofuranyl, benzooxazolyl, benzothiazolyl, benzothiadiazolyl, benzo[b][1,4]dioxepinyl, 1,4-benzodioxanyl, benzonaphthofuranyl, benzoxazolyl, benzodioxolyl, benzodioxinyl, benzopyranyl, benzopyranonyl, benzofuranyl, benzofuranonyl, benzothienyl (benzothiophenyl), benzotriazolyl, benzo[4,6]imidazo[1,2-a]pyridinyl, carbazolyl, cinnolinyl, dibenzofuranyl, dibenzothiophenyl, furanyl, furanonyl, isothiazolyl, imidazolyl, indazolyl, indolyl, indazolyl, isoindolyl, indolinyl, isoindolinyl, isoquinolyl, indolizinyl, isoxazolyl, naphthyridinyl, oxadiazolyl, 2-oxoazepinyl, oxazolyl, oxiranyl, 1-oxidopyridinyl, 1-oxidopyrimidinyl, 1-

oxidopyrazinyl, 1-oxidopyridazinyl, 1-phenyl-1H-pyrrolyl, phenazinyl, phenothiazinyl, phenoxazinyl, phthalazinyl, pteridinyl, purinyl, pyrrolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinazolinyl, quinoxalinyl, quinolinyl, quinuclidinyl, isoquinolinyl, tetrahydroquinolinyl, thiazolyl, thiadiazolyl, triazolyl, tetrazolyl, triazinyl, and thiophenyl (i.e., thienyl). Unless stated otherwise specifically in the specification, a heteroaryl is optionally substituted, for example, with halogen, amino, nitrile, nitro, hydroxyl, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, and the like. In some embodiments, a heteroaryl is optionally substituted with halogen, methyl, ethyl, -CN, $-CF_3$, -OH, -OMe, $-NH_2$, or $-NO_2$. In some embodiments, a heteroaryl is optionally substituted with halogen, methyl, ethyl, -CN, $-CF_3$, -OH, or -OMe. In some embodiments, the heteroaryl is optionally substituted with halogen. In some embodiments, the heteroaryl is unsubstituted.

[0052] The term "substituted" refers to moieties having substituents replacing a hydrogen on one or more carbons or substitutable heteroatoms, e.g., NH, of the structure. It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, *i.e.*, a compound which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc. In certain embodiments, substituted refers to moieties having substituents replacing two hydrogen atoms on the same carbon atom, such as substituting the two hydrogen atoms on a single carbon with an oxo, imino or thioxo group. As used herein, the term "substituted" is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and non-aromatic substituents of organic compounds. The permissible substituents can be one or more and the same or different for appropriate organic compounds. For purposes of this disclosure, the heteroatoms such as nitrogen can have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valences of the heteroatoms.

[0053] In some embodiments, substituents can include any substituents described herein, for example: halogen, hydroxy, oxo (=O), thioxo (=S), cyano (-CN), nitro ($-NO_2$), imino (=N-H), oximo (=N-OH), hydrazine (=N-NH_2), $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2), and $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2); and alkyl, alkenyl, alkynyl, aryl, aralkyl, aralkenyl, aralkynyl, cycloalkyl, cycloalkylalkyl, and heterocycle, any of which can be optionally

substituted by alkyl, alkenyl, alkynyl, halogen, haloalkyl, haloalkenyl, haloalkynyl, oxo (=O), thioxo (=S), cyano (-CN), nitro ($-NO_2$), imino (=N-H), oximo (=N-OH), hydrazine ($=N-NH_2$), SF^5, $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2) and $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2); wherein each R^a is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, and heterocycle, wherein each R^a, valence permitting, can be optionally substituted with alkyl, alkenyl, alkynyl, halogen, haloalkyl, haloalkenyl, haloalkynyl, oxo (=O), thioxo (=S), cyano (-CN), nitro ($-NO_2$), imino (=N-H), oximo (=N-OH), hydrazine ($=N-NH_2$), $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2) and $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2); and wherein each R^b is independently selected from a direct bond or a straight or branched alkylene, alkenylene, or alkynylene chain, and each R^c is a straight or branched alkylene, alkenylene or alkynylene chain.

[0054] The term "optional" or "optionally" means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. For example, "optionally substituted alkyl" means either "alkyl" or "substituted alkyl" as defined above. Further, an optionally substituted group can be un-substituted (e.g., $-CH_2CH_3$), fully substituted (e.g., $-CF_2CF_3$), mono-substituted (e.g., $-CH_2CH_2F$) or substituted at a level anywhere in-between fully substituted and mono-substituted (e.g., $-CH_2CHF_2$, $-CH_2CF_3$, $-CF_2CH_3$, $-CFHCHF_2$, etc.).

[0055] The term "biomolecule" refers to biological components that may be involved in corona formation, including, but not limited to, for example, proteins, polypeptides, polysaccharides, a sugar, a lipid, a lipoprotein, a metabolite, an oligonucleotide, metabolome or combination thereof. It is contemplated that the biomolecule coronas of distinct particles may contain some of the same biomolecules, may contain distinct biomolecules with regard to the other sensor elements, and/or may differ in level or quantity, type or conformation of the biomolecule that binds to each sensor element. In one embodiment, the biomolecule is selected from the group of proteins, nucleic acids, lipids, and metabolomes.

[0056] Ranges provided herein are understood to be shorthand for all of the values within the range. For example, a range of 1 to 50 is understood to include any number, combination of numbers, or sub-range from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41,

42, 43, 44, 45, 46, 47, 48, 49, or 50, as well as all intervening decimal values between the aforementioned integers such as, for example, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, and 1.9. With respect to sub-ranges, "nested sub-ranges" that extend from either end point of the range are specifically contemplated. For example, a nested sub-range of an exemplary range of 1 to 50 can comprise 1 to 10, 1 to 20, 1 to 30, and 1 to 40 in one direction, or 50 to 40, 50 to 30, 50 to 20, and 50 to 10 in the other direction.

[0057] The compounds and structures provided herein may be stereoisomeric. In some cases, a compound or structure of the disclosure may form a stereoisomer. In some cases, the stereoisomer may be a diastereomer (e.g., a cis/trans isomer, E/Z isomer, conformer, or rotamer). In some cases, the stereoisomer may be an enantiomer (R,S enantiomers or +/- enantiomers). In some cases, the compound or structure of the disclosure may be enantiopure (e.g., 100% pure). In some cases, the compound or structure may form a racemic mixture of enantiomers (e.g., 50% pure). In some cases, a compound or structure of the disclosure may stabilize as a stereoisomer, where the compound or structure of the disclosure comprises at least about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 96%, about 97%, about 98%, about 98.5%, about 99%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, about 99.9%, or more of a mixture of the compound or structure and the corresponding stereoisomer.

Macromolecule Structures

[0058] Provided herein are macromolecule structures comprising a surface, a tethering moiety coupled to the surface, and a macromolecule chain. In some embodiments, the macromolecule structures provided herein comprise a surface and a macromolecule chain. In some embodiments, the macromolecule structure provided herein comprises a surface. In some embodiments, the macromolecule structure provided herein comprises a tethering moiety (e.g., coupled to the surface). In some embodiments, the macromolecule structure provided herein comprises a macromolecule chain. In embodiments, a first end of the macromolecule chain is covalently attached to the tethering moiety. In some embodiments, a second end of the macromolecule chain is not coupled to the surface. In some embodiments, the macromolecule chain comprises one or more (e.g., distinct) recurring units derived from a monomer.

[0059] In some embodiments, provided herein is a macromolecule structure comprising a surface, a tethering moiety coupled to the surface, and a macromolecule chain. In some embodiments, the macromolecule structure comprises a surface. In some embodiments, the macromolecule structure comprises a tethering moiety (e.g., coupled to the surface). In some embodiments, the macromolecule structure comprises a macromolecule chain. In some

embodiments, the macromolecule chain comprises two or more distinct recurring units derived from different monomer. In some embodiments, the macromolecule chain comprises at least two (e.g., at least three, at least four, at least five) distinct recurring units derived from different monomers. In some embodiments, the macromolecule chain comprises at most ten (e.g., at most nine, at most eight, at most six, at most four, at most three) distinct recurring units derived from different monomers. In some embodiments, the macromolecule chain comprises two distinct recurring units derived from different monomers. In some embodiments, the macromolecule chain comprises three distinct recurring units derived from different monomers. In some embodiments, the macromolecule chain comprises four distinct recurring units derived from different monomers. In some embodiments, the macromolecule chain comprises five distinct recurring units derived from different monomers.

[0060] In some embodiments, provided herein is a macromolecule structure comprising a surface, a tethering moiety coupled to the surface, and a macromolecule chain. In some embodiments, the macromolecule structure comprises a surface. In some embodiments, the macromolecule structure comprises a tethering moiety (e.g., coupled to the surface). In some embodiments, the macromolecule structure comprises a macromolecule chain. In some embodiments, the macromolecule chain comprise a recurring unit derived from a monomer. In some embodiments, the macromolecule chain is comprised of a single monomeric recurring unit.

[0061] In some instances, the tethering and recurring units used to functionalize the surface affect the physicochemical properties of the surface such as size, surface charge, hydrophobicity, hydrophilicity, surface functionality, surface topography, surface curvature, porosity, shape, and any combination thereof. The changes in physicochemical properties may affect the binding properties of the macromolecule structures to other compounds, such as biomolecules (e.g., proteins), leading to increased effectiveness or decreased effectiveness in binding.

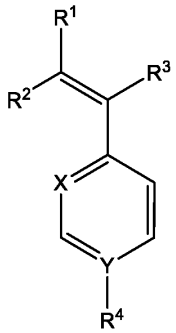
[0062] In some embodiments, the macromolecule structures provided herein comprise cross-linked polymers (e.g., crosslinked macromolecule chains). For example, the relative amount of crosslinking monomer relative to total monomer in the polymers by weight or number can be at least 0.1%, at least 0.5%, at least 1%, or at least 2%. In some embodiments, the macromolecule structures provided herein comprise substantially uncross-linked polymers (e.g., uncross linked macromolecule chains). For example, the relative amount of crosslinking monomer relative to total monomer in the polymers by weight or number can be less than 0.1%, less than 0.05%, less than 0.01%, or about 0%. In some embodiments, the macromolecule structures provided herein comprise polymer brushes (e.g., PEG brushes). For example, the polymer brushes may comprise sidechains with at least 5, at least 10, at least 15, or at least 20 recurring units derived from one or more monomers.

[0063] In some embodiments, is a macromolecule structure comprising Formula (A):

A-T-C

[0064] In some embodiments, A is a surface, such as a surface provided elsewhere herein. In some embodiments, T is a tethering moiety, such as a tethering moiety provided elsewhere herein. In some embodiments, C is a macromolecule chain, such as a macromolecule chain provided elsewhere herein. In some embodiments, C comprises a plurality of recurring units derived from monomers. In some embodiments, the plurality of recurring units comprise a single monomer. In other embodiments, the plurality of recurring units comprise two or more different monomers. In some embodiments, the monomers have a controlled distribution throughout the macromolecule chain. In some embodiments, the monomers have a random distribution throughout the macromolecule chain.

[0065] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[0066] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[0067] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

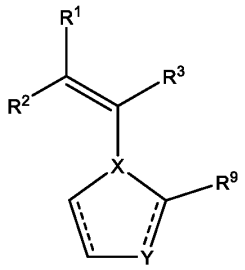
[0068] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[0069] In some embodiments, R^4 is hydrogen, sulfonate, carboxylate, C_1-C_4 alkylene, amine (e.g., quaternary ammonium cation), or C_1-C_6 alkyl optionally substituted with halogen. In some embodiments, R^4 is hydrogen. In some embodiments, R^4 is absent. In some embodiments, R^4 is sulfonate. In some embodiments, R^4 is an amine. In some embodiments, R^4 is a quaternary ammonium cation. In some embodiments, R^4 is carboxylate. In some embodiments, R^4 is C_1-C_4 alkylene. In some embodiments, R^4 is C_1-C_6 alkyl optionally substituted with halogen (e.g., haloalkyl).

[0070] In some embodiments, X is -C- or -N-. In some embodiments, X is -C-. In some embodiments, X is -N-.

[0071] In some embodiments, Y is -C- or -N-. In some embodiments, Y is -C-. In some embodiments, Y is -N-.

[0072] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[0073] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[0074] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[0075] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

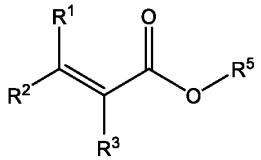
[0076] In some embodiments, R^9 is hydrogen or oxo. In some embodiments, R^9 is hydrogen. In some embodiments, R^9 is oxo.

[0077] In some embodiments, X is -C- or -N-. In some embodiments, X is -C-. In some embodiments, X is -N-.

[0078] In some embodiments, Y is -C-, -N-, or -O-. In some embodiments, Y is -C-. In some embodiments, Y is -O-. In some embodiments, Y is -N-.

[0079] In some embodiments, ≡ is a single bond or a double bond. In some embodiments, ≡ is a single bond. In some embodiments, ≡ is a double bond. In some embodiments, one of ≡ is a single bond and one of ≡ is a double bond. In some embodiments, both ≡ are single bonds. In some embodiments, both ≡ are double bonds.

[0080] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[0081] In some embodiments, a recurring unit is derived from an acrylate monomer. In some embodiments, a recurring unit is derived from a methacrylate monomer.

[0082] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[0083] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[0084] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is 3-, 5-, or 6-membered heterocycle optionally substituted with one or more methyl. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[0085] In some embodiments, R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne. In some embodiments, R^5 is C_1-C_{12} alkylamine.

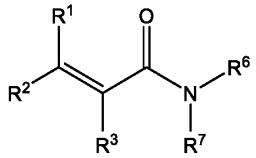
[0086] In some embodiments, R^5 is hydrogen. In some embodiments, R^5 is C_1-C_6 alkyl. In some embodiments, R^5 is C_1-C_4 alkylyne. In some embodiments, R^5 is C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol. In some embodiments, R^5 is C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, carbamate ester, asymmetrical disulfide, 3-,5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol. In some embodiments, R^5 is C_1-C_8 alkylamine. In some embodiments, R^5 is C_1-C_8 alkylamine substituted with amine. In some embodiments, R^5 is C_1-C_8 alkylamine substituted with hydroxyl and amine. In some embodiments, R^5 is C_1-C_8 alkylamine substituted with sulfonate. In some embodiments, R^5 is C_1-C_8 alkylamine substituted with aryl. In some embodiments, R^5 is C_1-C_8 alkoxy. In some embodiments, R^5 is C_1-C_8 alkoxy substituted with one or more oxo or halogen. In some embodiments, R^5 is C_1-C_8 alkoxy substituted with one or more oxo. In some embodiments, R^5 is

C_1-C_8 alkoxy substituted with one or more halogen. In some embodiments, the alkylamine comprises a quaternary ammonium cation.

[0087] In some embodiments, R^5 is C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine. In some embodiments, R^5 is C_1-C_3 alkyl substituted with pyrene. In some embodiments, R^5 is C_1-C_3 alkyl substituted with 2 or more 5-6 membered rings further optionally substituted, such as with 2 or more fused 6 membered rings further optionally substituted. In some embodiments, R^5 is C_1-C_3 alkyl substituted with optionally substituted benzyl. In some embodiments, R^5 is C_1-C_3 alkyl substituted with trimethoxysilane. In some embodiments, R^5 is C_1-C_3 alkyl substituted with phosphorocholine.

[0088] In some embodiments, R^5 is hydrogen, C_1-C_6 alkyl, or C_1-C_3 alkyl substituted with pyrene or 2 or more fused 5-6 membered rings optionally further substituted. In some embodiments, R^5 is hydrogen, C_1-C_6 alkyl, or C_1-C_3 alkyl substituted with pyrene or 2 or more fused 5-6 membered rings optionally further substituted and the macromolecule chain comprises two or more distinct recurring units.

[0089] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[0090] In some embodiments, a recurring unit is derived from an acrylamide monomer.

[0091] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[0092] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[0093] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is 3-, 5-, or 6-membered heterocycle optionally substituted with one or more methyl. In some embodiments, R^3 is 3,4-dimethyl-1*H*-pyrrole-2,5-dione. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

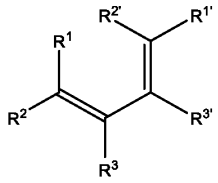
[0094] In some embodiments, R^6 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^6 is hydrogen. In some embodiments, R^6 is C_1-C_6 alkyl.

[0095] In some embodiments, R^7 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne.

[0096] In some embodiments, R^7 is hydrogen. In some embodiments, R^7 is C_1-C_6 alkyl. In some embodiments, R^7 is C_1-C_4 alkylyne. In some embodiments, R^7 is C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol. In some embodiments, R^7 is C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, carbamate ester, asymmetrical disulfide, 3-,5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol. In some embodiments, R^7 is C_1-C_8 alkylamine. In some embodiments, R^7 is C_1-C_8 alkylamine substituted with amine. In some embodiments, R^7 is C_1-C_8 alkylamine substituted with sulfonate. In some embodiments, R^7 is C_1-C_8 alkoxy. In some embodiments, R^7 is C_1-C_8 alkoxy substituted with one or more oxo or halogen. In some embodiments, R^7 is C_1-C_8 alkoxy substituted with one or more oxo. In some embodiments, R^7 is C_1-C_8 alkoxy substituted with one or more halogen. In some embodiments, R^7 is C_1-C_6 alkyl optionally substituted with hydroxyl, substituted benzene, or hydrogen.

[0097] In some embodiments, R^7 is C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine. In some embodiments, R^7 is C_1-C_3 alkyl substituted with pyrene. In some embodiments, R^7 is C_1-C_3 alkyl substituted with 2 or more 5-6 membered rings further optionally substituted, such as with 2 or more fused 6 membered rings further optionally substituted. In some embodiments, R^7 is C_1-C_3 alkyl substituted with optionally substituted benzyl. In some embodiments, R^7 is C_1-C_3 alkyl substituted with trimethoxysilane. In some embodiments, R^7 is C_1-C_3 alkyl substituted with phosphorocholine.

[0098] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[0099] In some embodiments, a recurring unit derived from a monomer can be a diene, such as a cis diene. In some embodiments, the diene may act as a cross-linking monomer.

[00100] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[00101] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

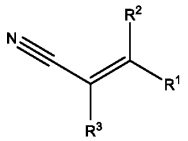
[00102] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[00103] In some embodiments, $R^{1'}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{1'}$ is hydrogen. In some embodiments, $R^{1'}$ is C_1-C_6 alkyl.

[00104] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{2'}$ is hydrogen. In some embodiments, $R^{2'}$ is C_1-C_6 alkyl.

[00105] In some embodiments, $R^{3'}$ is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is hydrogen. In some embodiments, $R^{3'}$ is C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is methyl.

[00106] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[00107] In some embodiments, a recurring unit is derived from an acrylonitrile monomer.

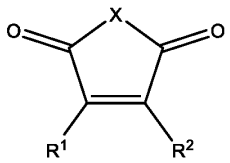
[00108] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[00109] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[00110] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[00111] In some embodiments, R^1 is hydrogen, R^2 is hydrogen, and R^3 is hydrogen.

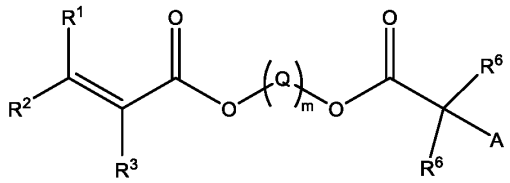
[00112] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[00113] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[00114] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[00115] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[00116] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[00117] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

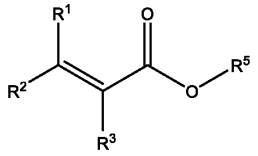
[00118] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[00119] In some embodiments, R^6 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^6 is hydrogen. In some embodiments, R^6 is C_1-C_6 alkyl. In some embodiments, R^6 is methyl.

[00120] In some embodiments, Q is $-CH_2-$ or ethylene glycol. In some embodiments, Q is $-CH_2-$. In some embodiments, Q is ethylene glycol.

[00121] In some embodiments, m is 1-20. In some embodiments, m is 1-10. In some embodiments, m is 1-5. In some embodiments, m is 5-10. In some embodiments, m is 10-20. In some embodiments, m is 2. In some embodiments, m is 1. In some embodiments, m is 3, 4, 5, 6, 7, 8, 9, or 10.

[00122] In some embodiments, A is a polymeric side chain comprising a recurring unit derived from a monomer represented by the structure:



[00123] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[00124] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

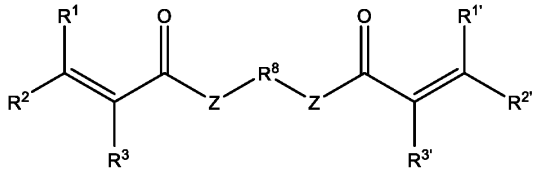
[00125] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[00126] In some embodiments, R^1 is hydrogen, R^2 is hydrogen, and R^3 is hydrogen.

[00127] In some embodiments, R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further optionally substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne. In certain embodiments, R^5 is polyethylene glycol. In some embodiments, R^5 is polyethylene glycol with a chain length of 9.

[00128] In some embodiments, R^1 is hydrogen, R^2 is hydrogen, R^3 is methyl, Q is -CH_2-, R^6 is methyl, and R^5 is polyethylene glycol.

[00129] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by the structure:



[00130] In some embodiments, a recurring unit is derived from a dimethacrylate monomer. In some embodiments, the dimethacrylate monomer is a cross-linking monomer.

[00131] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl.

[00132] In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[00133] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[00134] In some embodiments, $R^{1'}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{1'}$ is hydrogen. In some embodiments, $R^{1'}$ is C_1-C_6 alkyl.

[00135] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{2'}$ is hydrogen. In some embodiments, $R^{2'}$ is C_1-C_6 alkyl.

[00136] In some embodiments, $R^{3'}$ is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is hydrogen. In some embodiments, $R^{3'}$ is C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is methyl.

[00137] In some embodiments, Z is -O- or -NH. In some embodiments, Z is -O-. In some embodiments, Z is -NH.

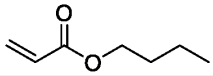
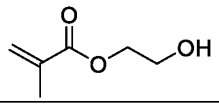
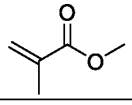
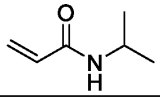
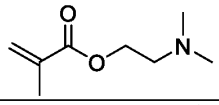
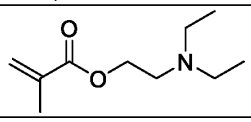
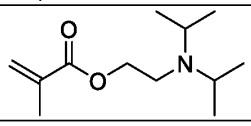
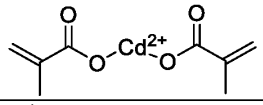
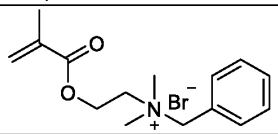
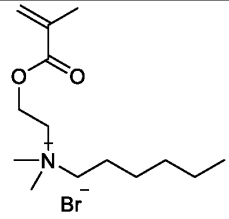
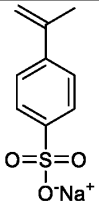
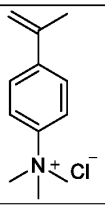
[00138] In some embodiments, R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide. In some embodiments, R^8 is C_1-C_6 alkyl. In some embodiments, R^8 is a divalent metal. In some embodiments, R^8 is cadmium(II). In some embodiments, R^8 is symmetric or asymmetric disulfide. In some embodiments, R^8 is a symmetric disulfide. In some embodiments, R^8 is symmetrical disulfide (e.g., CH_2CH_2S-SCH_2CH_2) or a divalent metal.

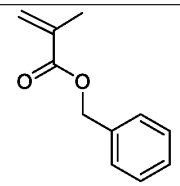
[00139] In any of the macromolecule structures provided herein, n^1 is an integer selected from 1-100. In some embodiments, n^1 is an integer selected from 1-20. In some embodiments, n^1 is an integer selected from 1-10. In some embodiments, n^1 is an integer selected from 1-5. In some embodiments, n^1 is an integer selected from 5-10. In some embodiments, n^1 is an integer selected from 10-20. In some embodiments, n^1 is 9. In some embodiments, n^1 is an integer selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

[00140] In some embodiments, any of the macromolecule chains provided herein may be terminated by a terminating group. The terminating group may be a halogen, epoxide, or olefin (e.g., alkylene). In some embodiments, the terminating group is a halogen. In some embodiments, the terminating group is a bromine. In some embodiments, the terminating group is an iodine. In some embodiments, the terminating group is a chloride. In some embodiments, the terminating group is an epoxide. In some embodiments, the terminating group is an olefin.

[00141] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by a structure of **Table 1**. In some embodiments, macromolecule chains comprise two or more distinct recurring units derived from a monomer represented by a structure of **Table 1**.

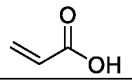
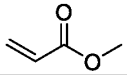
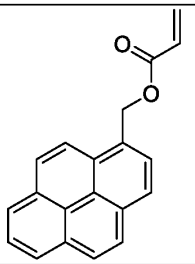
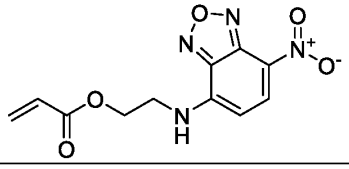
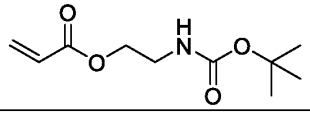
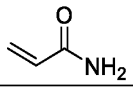
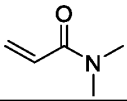
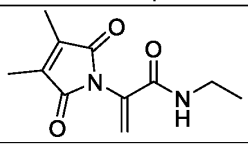
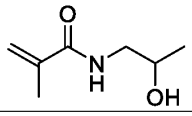
Table 1

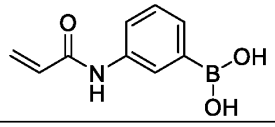
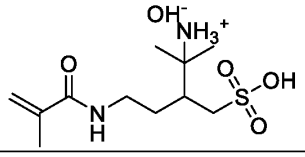
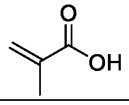
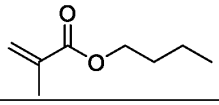
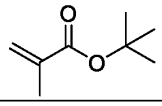
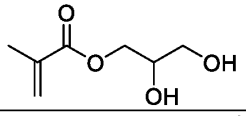
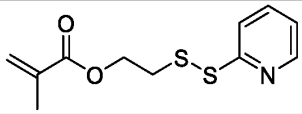
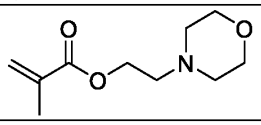
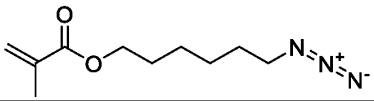
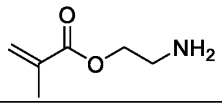
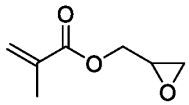
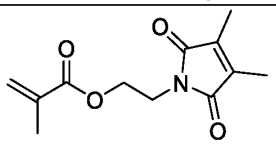
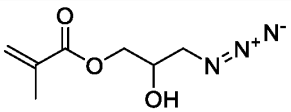
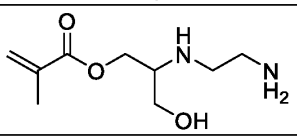
Recurring Unit No.	Structure
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

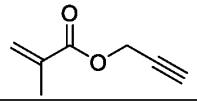
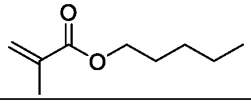
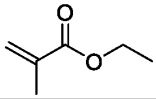
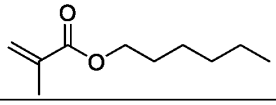
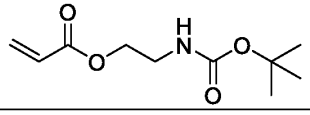
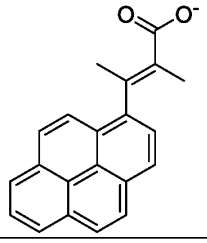
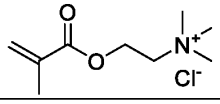
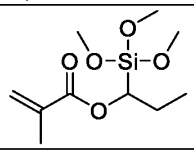
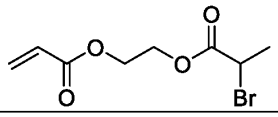
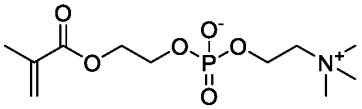
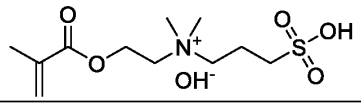
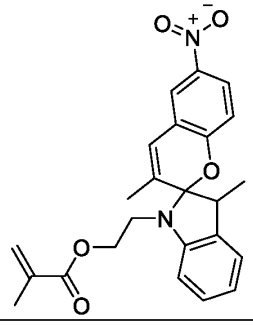
13	

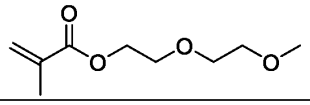
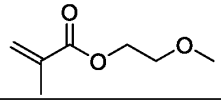
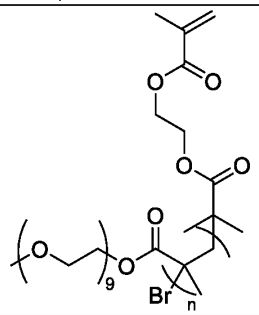
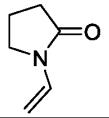
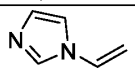
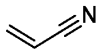
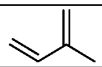
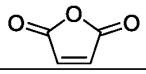
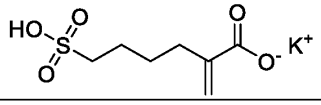
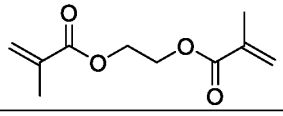
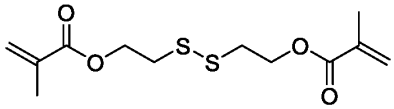
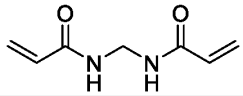
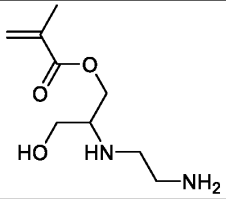
[00142] In some embodiments, the macromolecule chains provided herein comprise a recurring unit derived from a monomer represented by a structure of **Table 2**. In some embodiments, the macromolecule chain comprises a recurring unit (e.g., one or more) derived from a monomer represented by a structure of **Table 2**.

Table 2

Recurring Unit No.	Structure
14	
15	
16	
17	
18	
19	
20	
21	
22	

23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	

37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	

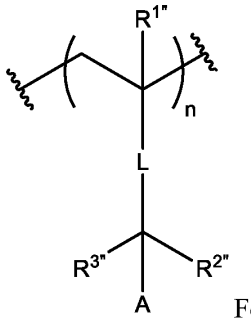
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	
61	

[00143] In some embodiments, the recurring units provided herein are randomly distributed throughout the macromolecule chain. In some embodiments, the recurring units provided herein have a controlled distribution throughout the macromolecule chain. In some embodiments, the

macromolecule chain is a homopolymer. In some embodiments, the macromolecule chain is a block copolymer. In some embodiments, the macromolecule chain is a random copolymer. The skilled artisan, guided by the disclosure herein, would understand how to provide polymers with randomly or controlled distributions of recurring units.

[00144] When multiple distinct recurring units are present in a macromolecule chain, the multiple recurring units may be present in equal or differing ratios. The ratio of distinct recurring units may be controlled according to methods known to one skilled in the art, including modifying the stoichiometry of monomers added.

[00145] Provided herein, in some embodiments, is a macromolecule structure comprising (I) a surface and (II) a macromolecule chain coupled to the surface. In some embodiments, the macromolecule chain comprises a recurring unit of Formula (I):



Formula (I).

[00146] In some embodiments, $R^{1"}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{1"}$ is hydrogen. In some embodiments, $R^{1"}$ is C_1-C_6 alkyl. In some embodiments, $R^{1"}$ is methyl.

[00147] In some embodiments, $R^{2"}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{2"}$ is C_1-C_6 alkyl. In some embodiments, $R^{2"}$ is methyl.

[00148] In some embodiments, $R^{3"}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{3"}$ is hydrogen. In some embodiments, $R^{3"}$ is C_1-C_6 alkyl. In some embodiments, $R^{3"}$ is methyl.

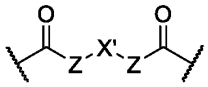
[00149] In some embodiments, $R^{1"}$, $R^{2"}$, and $R^{3"}$ are C_1-C_6 alkyl (e.g., methyl).

[00150] In some embodiments, n is an integer from 1 to 10,000. In some embodiments, n is an integer from 1 to 200. In some embodiments n is an integer of no more than 25,000 (e.g., no more than 20,000, no more than 15,000, no more than 10,000, no more than 5,000, no more than 2,500, no more than 1,000, no more than 500, no more than 100, no more than 50). In some embodiments, n is an integer from 1 to 5,000. In some embodiments, n is an integer from 1 to 2,500. In some embodiments, n is an integer from 1 to 1,000. In some embodiments, n is an integer of no more than 200. In some embodiments, n is an integer from 1 to 100. In some embodiments, n is an integer from 1 to 50.

[00151] In some embodiments, A is a polymeric side chain comprising any of the recurring units provided elsewhere herein. In some embodiments, A is a poly(alkylene oxide) methacrylate or

poly(alkylene oxide) acrylate. In some embodiments, A is poly(ethylene glycol) methacrylate or poly(ethylene glycol) acrylate. In some embodiments, A is a poly(alkylene oxide) methacrylamide or poly(alkylene oxide) acrylamide. In some embodiments, A is poly(ethylene glycol) methacrylamide or poly(ethylene glycol) acrylamide.

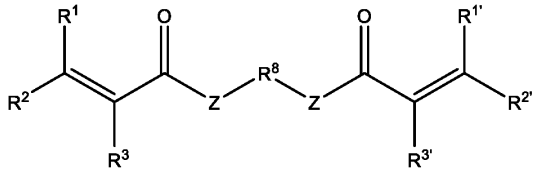
[00152] In some embodiments, L is a linker moiety. In some embodiments, the linker moiety is represented by the structure:



[00153] In some embodiments, each Z is independently -O- or -N-. In some embodiments, Z is -O-. In some embodiments, Z is -N-.

[00154] In some embodiments, X' is C_1-C_6 alkyl. In some embodiments, X' is methyl. In some embodiments, X' is ethyl. In some embodiments, X' is propyl.

[00155] In some embodiments, the macromolecule structure further comprises a cross-linking moiety. In some embodiments, the cross-linking moiety comprises a structure represented by:



[00156] In some embodiments, the cross-linking moiety is a derived from a dimethacrylate monomer, such as a dimethacrylate monomer as described elsewhere herein. In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[00157] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[00158] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[00159] In some embodiments, $R^{1'}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{1'}$ is hydrogen. In some embodiments, $R^{1'}$ is C_1-C_6 alkyl.

[00160] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{2'}$ is hydrogen. In some embodiments, $R^{2'}$ is C_1-C_6 alkyl.

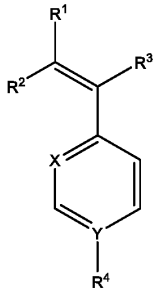
[00161] In some embodiments, $R^{3'}$ is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is hydrogen. In some embodiments, $R^{3'}$ is C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is methyl.

[00162] In some embodiments, Z is -O- or -NH. In some embodiments, Z is -O-. In some embodiments, Z is -NH.

[00163] In some embodiments, R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide. In some embodiments, R^8 is C_1-C_6 alkyl. In some embodiments, R^8 is a divalent metal. In some embodiments, R^8 is cadmium(II). In some embodiments, R^8 is symmetric or asymmetric disulfide. In some embodiments, R^8 is a symmetric disulfide.

[00164] In some embodiments, the cross-linking moiety is ethyleneglycol dimethacrylate (EGDMA). In some embodiments, the cross-linking moiety is ethyleneglycol dimethylacrylamide. In some embodiments, the cross-linking moiety is ethyleneglycol diacrylate. In some embodiments, the cross-linking moiety is ethyleneglycol diacrylamide.

[00165] In some embodiments, the cross-linking moiety comprises a structure represented by:



[00166] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

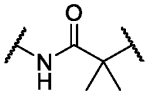
[00167] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[00168] In some embodiments, R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

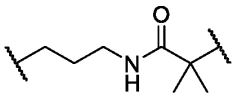
[00169] In some embodiments, R^4 is C_1-C_4 alkylene. In some embodiments, the cross-linking moiety is divinylbenzene.

[00170] In some embodiments, the macromolecule structures provided herein comprise a tethering moiety which couples the surface to the macromolecule chain. In some embodiments, the tethering moiety is C_1-C_{20} heteroalkyl optionally substituted with one or more C_1-C_6 alkyl, oxo, halo, or hydroxyl.

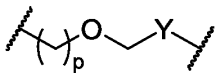
[00171] In some embodiments, the tethering moiety comprises the structure:



[00172] In some embodiments, the tethering moiety comprises the structure:

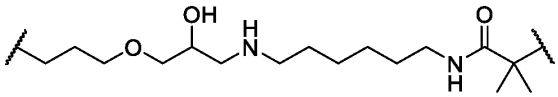


[00173] In some embodiments, the tethering moiety is C_1-C_{12} alkoxy optionally substituted with one or more C_1-C_{20} heteroalkyl, each of the C_1-C_{12} alkoxy and C_1-C_{20} heteroalkyl optionally substituted with one or more C_1-C_6 alkyl, oxo, halo, or hydroxyl. In some embodiments, the tethering moiety is represented by the structure:

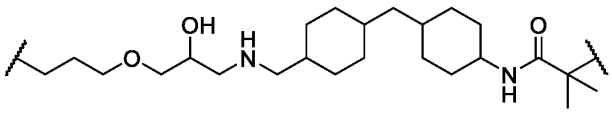


[00174] In some embodiments, Y is C_1-C_{20} heteroalkyl. In some embodiments, Y is C_1-C_{20} heteroalkyl optionally substituted with one or more C_1-C_6 alkyl, oxo, halo, or hydroxyl.

[00175] In some embodiments, p is an integer from 1 to 12. In some embodiments, p is an integer from 1 to 6. In some embodiments, p is an integer from 1 to 3. In some embodiments, p is 3. In some embodiments, the tethering moiety is represented by the structure:



[00176] In some embodiments, the tethering moiety is represented by the structure:

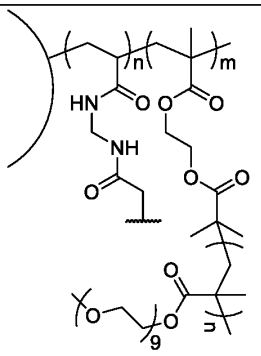
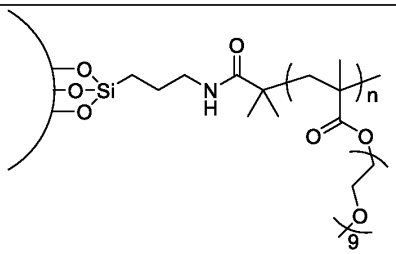
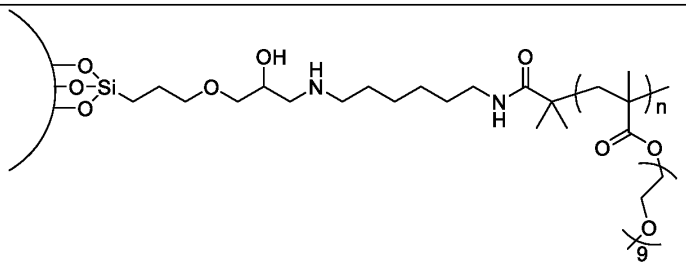
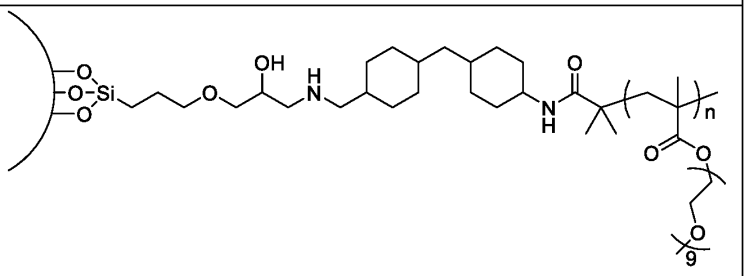
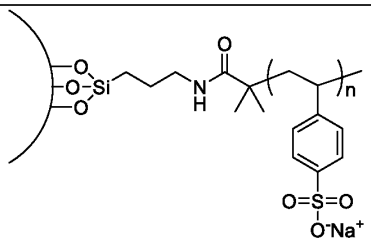


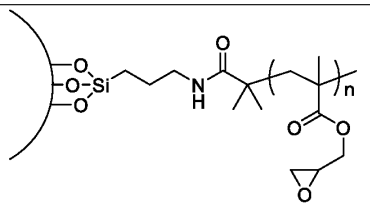
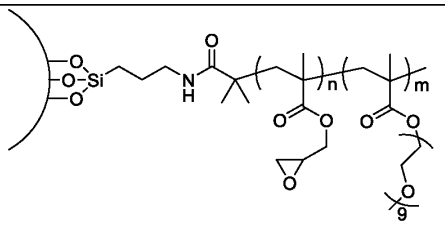
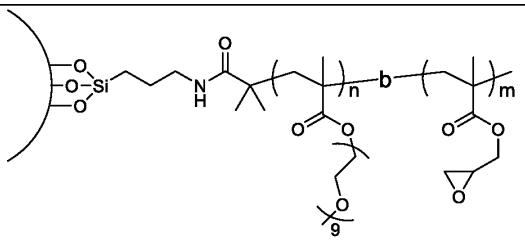
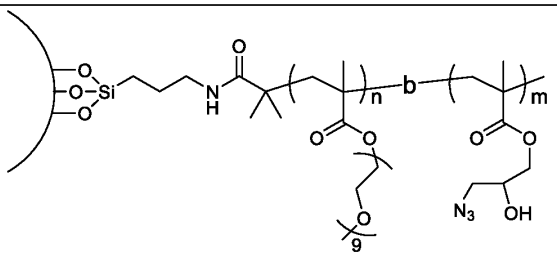
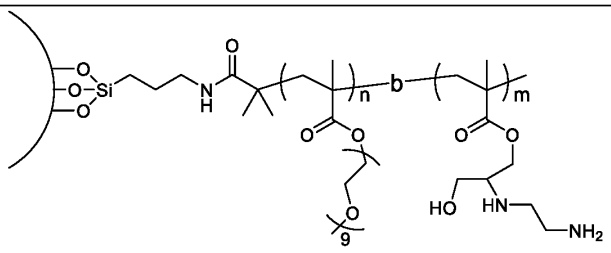
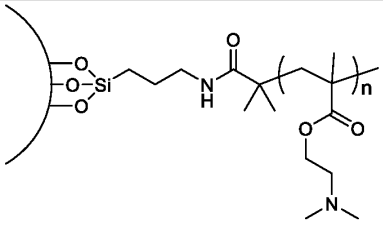
[00177] In any of the macromolecule structures provided herein, R^5 or R^7 may comprise polyethylene glycol. In some embodiments, polyethylene glycol may have a chain length of about 1 to about 50. In some embodiments, the polyethylene glycol may have a chain length of no more than 100. In some embodiments, the polyethylene glycol may have a chain length of at least 5. In some embodiments, the polyethylene glycol may have a chain length of about 5 to about 100 or about 5 to about 50. In some embodiments, the polyethylene glycol may have a chain length of about 9.

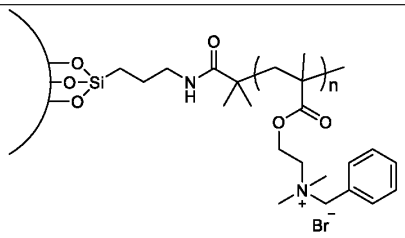
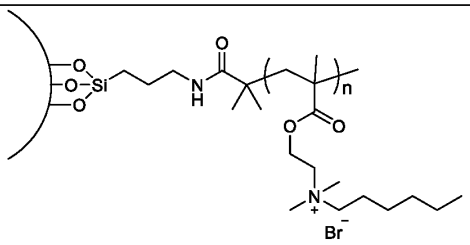
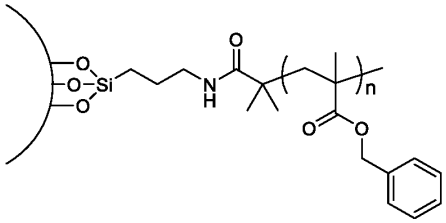
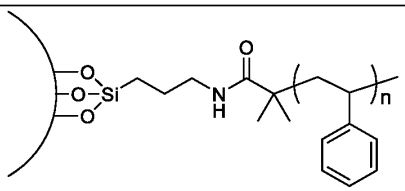
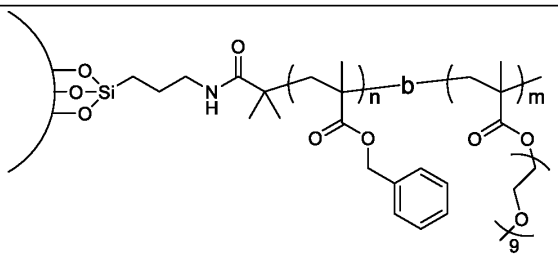
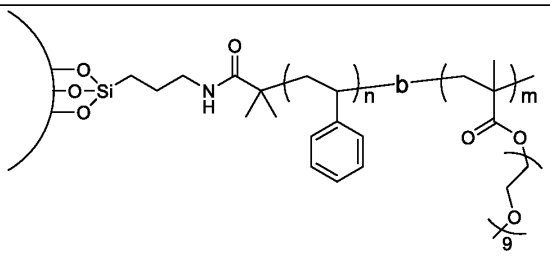
[00178] In some embodiments, the polyethylene glycol provided herein is an oligoethylene glycol. In some embodiments, the polyethylene glycol is a diethylene glycol. In some embodiments, the polyethylene glycol is a triethylene glycol. In some embodiments, the polyethylene glycol is a tetraethylene glycol.

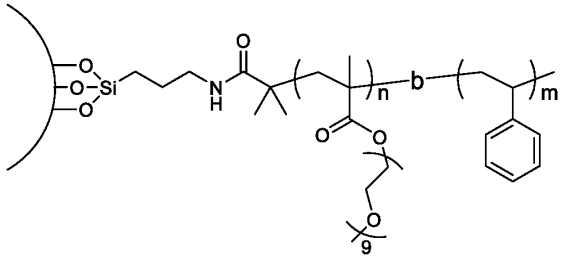
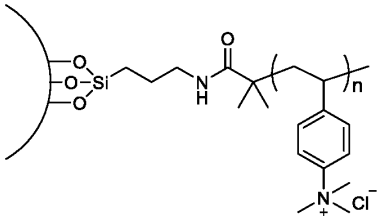
[00179] In some embodiments, the macromolecule structures provided herein may have a structure represented in **Table 3**.

Table 3

Macromolecule Structure	Structure
1	
2	
3	
4	
5	

6	
7	
8	
9	
10	
11	

12	
13	
14	
15	
16	
17	

18	
19	

[00180] In some embodiments, in **Table 3**, in any of the structures, "b" denotes a block-copolymer structure. In some embodiments, the block copolymer structures depicted in **Table 3** may alternatively be a random copolymer.

[00181] In any of the macromolecule structures provided herein, the macromolecule chains comprise from 1 to 1,000 recurring units. In some embodiments, the macromolecule chains comprise at least 1, at least 10, at least 50, at least 100, at least 250, at least 500, at least 750, or at least 1,000 recurring units. In some embodiments, the macromolecule chain comprises at most 2,500 recurring units. In some embodiments ,the macromolecule chains comprise at most 1,000 recurring units. In some embodiments, the macromolecule chains comprise at most 750 recurring units. In some embodiments, the macromolecule chains comprise at most 500 recurring units. In some embodiments, the macromolecule chains comprise at most 250 recurring units. In some embodiments, the macromolecule chains comprise at most 100 recurring units. In some embodiments, the macromolecule chains comprise about 1 to about 100 recurring units. In some embodiments, the macromolecule chains comprise about 1 to about 250 recurring units. In some embodiments, the macromolecule chains comprise about 1 to about 500 recurring units. In some embodiments, the macromolecule chains comprise about 1 to about 1,000 recurring units. In some embodiments, the macromolecule chains comprise about 100 to about 1,000 recurring units. In some embodiments, the macromolecule chains comprise about 1 to about 10 recurring units.

[00182] In any one of the macromolecule structures provided herein, the macromolecule chains comprise a molecular weight of about 0.1 kDa to about 500 kDa. In some embodiments, the macromolecule chains comprise a molecular weight of at least 0.1 kDa, at least 1 kDa, at least 5 kDa, at least 10 kDa, at least 20 kDa, at least 25 kDa, at least 50 kDa, at least 100 kDa, at least 250 kDa, or at least 500 kDa. In some embodiments, the macromolecule chains comprise a

molecular weight of no more than 1000 kDa, no more than 500 kDa, no more than 750 kDa, no more than 500 kDa, no more than 250 kDa, no more than 100 kDa, no more than 75 kDa, no more than 50 kDa, no more than 40 kDa, no more than 30 kDa, no more than 25 kDa, no more than 20 kDa, no more than 15 kDa, or no more than 10 kDa. In some embodiments, the macromolecule chain comprises a molecular weight of about 0.1 to about 500 kDa, about 0.1 to about 250 kDa, about 0.1 kDa to about 100 kDa, about 0.1 kDa to about 70 kDa, 0.5 kDa to about 10 kDa, 0.5 kDa to about 15 kDa, or about 1 kDa toa bout 25 kDa. In some embodiments, the macromolecule chain comprises a molecular weight of about 0.1 kDa to about 100 kDa. In some embodiments, the macromolecule chain comprises a molecular weight of about 0.1 kDa to about 50 kDa.

[00183] In some embodiments, the macromolecular chain comprises a block co-polymer. In some embodiments, the block co-polymer comprises a first block derived from a first monomer and a second block derived from a second monomer, wherein the first block is adjacent to the tethering moiety, and wherein the first monomer is more hydrophobic than the second monomer. In some embodiments, the block co-polymer comprises a first block derived from a first monomer and a second block derived from a second monomer, wherein the first block is adjacent to the tethering moiety, and wherein the first monomer is less hydrophobic than the second monomer. In some embodiments, the hydrophobicity of the first monomer and the second monomer can be determined by the estimated partition coefficient using XLOGP3. In some embodiments, an absolute difference between the estimated partition coefficients of the first monomer and the second monomer is at least 0.3, at least 0.5, at least 0.8, at least 1, at least 1.5, or at least 2. In some embodiments, an absolute difference between the estimated partition coefficients of the first monomer and the second monomer is no more than 3, no more than 2.5, no more than 2, no more than 1, or no more than 0.8.

[00184] In some embodiments, a surface is a particle. In some embodiments, a particle is a nanoparticle or a microparticle. In some embodiments, the particle is a nanoparticle. In some embodiments, the particle is a microparticle. In some instances, the particles provided herein have a diameter of at least 10 nm, at least 100 nm, at least 200 nm, at least 300 nm, at least 400 nm, at least 500 nm, at least 600 nm, at least 700 nm, at least 800 nm, or at least 900 nm. In some embodiments, the particles provided herein have a diameter of no more than 5000 nm, no more than 4000 nm, no more than 3000 nm, no more than 2000 nm, no more than 1000 nm, no more than 750 nm, or no more than 500 nm. In some embodiments, the particles provided herein have a diameter of from 10 nm to 50 nm, from 50 nm to 100 nm, from 100 nm to 150 nm, from 150 nm to 200 nm, from 200 nm to 250 nm, from 250 nm to 300 nm, from 300 nm to 350 nm, from 350 nm to 400 nm, from 400 nm to 450 nm, from 450 nm to 500 nm, from 500 nm to 550 nm, from 550 nm to 600 nm, from 600 nm to 650 nm, from 650 nm to 700 nm, from 700 nm to 750 nm,

from 750 nm to 800 nm, from 800 nm to 850 nm, from 850 nm to 900 nm, from 100 nm to 300 nm, from 150 nm to 350 nm, from 200 nm to 400 nm, from 250 nm to 450 nm, from 300 nm to 500 nm, from 350 nm to 550 nm, from 400 nm to 600 nm, from 450 nm to 650 nm, from 500 nm to 700 nm, from 550 nm to 750 nm, from 600 nm to 800 nm, from 650 nm to 850 nm, from 700 nm to 900 nm, or from 10 nm to 900 nm. The particle size (e.g., diameter) can be measured by dynamic light scattering (DLS) as an indirect measure of size. The DLS measurement can be an 'intensity-weighted' average, which means the size distribution that the mean is calculated from can be weighted by the sixth power of radius. This can be referred to herein as 'z-average' or 'intensity-mean'. Particle size can also be measured by electron microscopy (e.g., SEM, TEM).

[00185] In certain examples, the particles provided herein may comprise a diameter of about 100 nm to about 500 nm. In some embodiments, the particles comprise a diameter of about 100 nm to about 300 nm. In some embodiments, the particles comprise a diameter of about 100 nm to about 200 nm. In some embodiments, the particles comprise a diameter of about 150 nm to about 250 nm.

[00186] Additionally, particles can have a homogenous size distribution or a heterogeneous size distribution. Polydispersity index (PDI), which can be measured by techniques such as dynamic light scattering, is a measure of the size distribution. A low PDI indicates a more homogeneous size distribution and a higher PDI indicates a more heterogeneous size distribution. For example, particles disclosed herein can have a PDI of less than 0.5, less than 0.4, less than 0.3, less than 0.2, less than 0.15, or less than 0.1. In particular embodiments, the particles disclosed herein have a PDI of less than 0.1. In some embodiments, the particles disclosed herein have a PDI of more than 0.5, more than 1, or more than 2.

[00187] Particles provided herein can have a range of different surface charges. Particles can be negatively charged, positively charged, or neutral in charge. In some embodiments, particles have a surface charge of -150 mV to -100 mV, -100 mV to -90 mV, -90 mV to -80 mV, -80 mV to -70 mV, -70 mV to -60 mV, -60 mV to -50 mV, -50 mV to -40 mV, -40 mV to -30 mV, -30 mV to -20 mV, -20 mV to -10 mV, -10 mV to 0 mV, 0 mV to 10 mV, 10 mV to 20 mV, 20 mV to 30 mV, 30 mV to 40 mV, 40 mV to 50 mV, 50 mV to 60 mV, 60 mV to 70 mV, 70 mV to 80 mV, 80 mV to 90 mV, 90 mV to 100 mV, 100 mV to 110 mV, 110 mV to 120 mV, 120 mV to 130 mV, 130 mV to 140 mV, or 140 mV to 150 mV. In some embodiments, the particles have a surface charge of about 0 to -100 mV. In some embodiments, the particles have a surface charge of about 0 to 100 mV. The charge may, in some embodiments, be determined by measuring Zeta potential at neutral pH using an appropriate buffer.

[00188] Various particle morphologies are consistent with the particle types of the present disclosure. For example, particles may be spherical, colloidal, square shaped, rods, wires, cones, pyramids, or oblong.

[00189] In some embodiments, the surface (e.g., particle) comprises any suitable material according to one skilled in the art. In some embodiments, the particle is magnetic, such as any magnetic material suitable according to one skilled in the art. In some embodiments, the particle comprises a metal material. In some embodiments, the metal material comprises any one of or any combination of gold, silver, copper, nickel, cobalt, palladium, platinum, iridium, osmium, rhodium, ruthenium, rhenium, vanadium, chromium, manganese, niobium, molybdenum, tungsten, tantalum, iron and cadmium. In some embodiments, the particle comprises iron oxide. In some embodiments, the particle is a superparamagnetic iron oxide particle. In some embodiments, the particle has a core-shell structure. In some embodiments, the particle has an iron oxide core. In some embodiments, the particle comprises a silica shell. In some embodiments, the particle comprises an iron oxide core with a silica shell. In some instances, the silica shell can be functionalized with the tethering moieties or macromolecule chains provided elsewhere herein. In some embodiments, the particle comprises iron oxide crystals. In some embodiments, the particle comprises polystyrene. In some embodiments, the particle comprises iron oxide crystals embedded in a polystyrene core.

[00190] In some embodiments, the macromolecule structures provided herein comprise at least 5% w/w of a recurring unit provided herein. In some embodiments, the macromolecule structure comprises at least 10% w/w, at least 15% w/w, at least 20% w/w, at least 25% w/w, at least 30% w/w, at least 35% w/w, at least 40% w/w, at least 45% w/w, at least 50% w/w, at least 60% w/w, at least 75% w/w, at least 90% w/w, at least 95% w/w, at least 99% w/w, or about 100% w/w of a recurring unit provided herein. In some embodiments, the macromolecule structure comprises at most 95% w/w, at most 90% w/w, at most 85% w/w, at most 75% w/w, at most 70% w/w, at most 65% w/w, at most 60% w/w, at most 55% w/w, at most 50% w/w, at most 45% w/w, at most 40% w/w, at most 35% w/w, or at most 30% w/w of a recurring unit provided herein. In some embodiments, the macromolecule structure comprises about 5% to about 95% w/w of a recurring unit provided herein. In some embodiments, the macromolecule structure comprises about 5% to about 75% w/w of a recurring unit provided herein. In some embodiments, the macromolecule structure comprises about 10% to about 50% w/w of a recurring unit provided herein. In certain embodiments, the macromolecule structure comprises at least 10% w/w of the recurring unit. In certain embodiments, the macromolecule structure comprises at most 50% w/w of the recurring unit. The weight percentage of the recurring unit in the macromolecule structure may be determined by thermogravimetric analysis (TGA).

[00191] In some embodiments, the surfaces provided herein comprise the tethering units (e.g., and macromolecule chains) at any appropriate density according to one skilled in the art. In some embodiments, the surfaces comprise the tethering units (e.g., and macromolecule chains) at a density of at least 1 per 500 nm^2. In some embodiments, the surfaces comprise the tethering units (e.g., and macromolecule chains) at a density of at least 1 per 50 nm^2. In some embodiments, the surfaces comprise the tethering units (e.g., and macromolecule chains) at a density of at least 1 per 5 nm^2. In some embodiments, the surfaces comprise the tethering units (e.g., and macromolecule chains) at a density of at least 1 per 1 nm^2. In some embodiments, the surface comprises the tethering moiety (e.g., and macromolecule chain) at a density of about 1 per 50 nm^2 to about 1 per 5 nm^2.

Methods of Preparation

[00192] Provided herein are methods of making any of the macromolecule structures provided herein. In some embodiments, provided herein are methods of preparing macromolecule structures comprising a surface, a tethering moiety, and a macromolecule structure. Also provided herein are methods of preparing macromolecule structures comprising a surface and a macromolecule chain of Formula (I).

[00193] In some embodiments, the methods provided herein comprise surface-initiated polymerization.

[00194] In some embodiments, the macromolecule structure provided herein further comprise a terminating group. In some embodiments, the terminating group is a halogen, epoxide, or alkylene (e.g., olefin). In some embodiments, the terminating group is a halogen. In some embodiments, the terminating group is a bromine, chlorine, or iodine. In some embodiments, the terminating group is a bromine. In some embodiments, the terminating group takes part in surface initiated polymerization.

[00195] In some embodiments, provided herein is a method of making a macromolecule structure, such as any macromolecule structure provided elsewhere herein. In some embodiments, the method comprises providing a surface. In some embodiments, the method further comprises coupling a polymer initiator to the surface to form an initiator surface. In some embodiments, the method further comprises contacting the initiator surface with a monomer, such as a monomer provided elsewhere herein, to form the macromolecule structure.

[00196] In some instances, an exemplary synthetic scheme as described by the methods provided herein is provided in **FIG. 1**.

[00197] In some instances, the methods provided herein can also provide block co-polymers, such as by contacting a second recurring unit with an initiator surface provided by the first recurring unit. An exemplary synthetic scheme detailing this is shown in **FIG. 7**.

[00198] In some instances, the methods provided herein comprise contacting the initiator surface with more than one (differing) monomer, such as to form a heteropolymer. The monomers may be organized in a controlled distribution or a random distribution. An exemplary synthetic scheme detailing this is shown in **FIG. 8**.

[00199] In some embodiments, the method comprises providing a surface. The surface may comprise any surface (e.g., or particle) as described elsewhere herein. In some embodiments, the surfaces comprise a particle. In some embodiments, the particles are nanoparticles. In some embodiments, the particles are microparticles. In some embodiments, the surfaces comprise silicon dioxide. In some embodiments, the surface is functionalized with an amine, such as by functionalization with (3-aminopropyl)triethoxysilane (APTES). In some embodiments, the surface is functionalized with an epoxide using (3-glycidyloxypropyl)triethoxysilane followed by reaction with diaminohexane (**FIG. 6**) The skilled artisan would understand that a variety of silane coupling agents could be used to functionalize the surface, and if appropriate further modified, to achieve a variety of chain lengths and functionalities. Non-limiting examples of silane coupling agents include 3-Aminopropyltriethoxysilane (APTES), 3-Mercaptopropyltrimethoxysilane, 3-Glycidoxypropyltrimethoxysilane (GPTMS), (3-Triethoxysilylpropyl)diethylenetriamine (DETAS), N-(2-Aminoethyl)-3-aminopropyltrimethoxysilane, 3-Isocyanatopropyltriethoxysilane, 3-Chloropropyltrimethoxysilane, 3-Bromopropyltrimethoxysilane, 3-Iodopropyltrimethoxysilane, 3-[2-(2-Aminoethylamino)ethylamino]propyl-dimethoxymethylsilane, 3-[2-(2-Aminoethylamino)ethylaminopropyl]trimethoxysilane, Propargyltriethoxysilane, 3-Glycidyloxypropylheptamethyltrisiloxane, 3-(2-(2-Propynyloxy)ethoxy)propyltriethoxysilane, and the like.

[00200] In some embodiments, the functionalization of the (e.g., silicon dioxide) surface is described in Example 1, such as where the silicon dioxide surface is functionalized with APTES via amide coupling of a polymer initiator followed by polymerization.

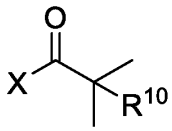
[00201] In some embodiments, the method further comprises coupling the polymer initiator to the surface to form an initiator surface. In some embodiments, coupling is completed using an organic solvent, such an organic solvent provided elsewhere herein. In some embodiments, the surfaces (e.g., particles) are contact with, or dispersed in, the organic solvent before coupling. In some embodiments, the organic solvent comprises dimethylformamide. In some embodiments, the organic solvent comprises tetrahydrofuran. In some embodiments, the organic solvent comprises N,N-dimethylacetamide.

[00202] In some embodiments, coupling further comprises the addition of a base. In some embodiments, the base comprises a weak base. In some embodiments, the base is an amine. In some embodiments, the base is an alkylamine. In some embodiments, the base is triethylamine.

[00203] In some embodiments, coupling is completed at below room temperature. In some embodiments, coupling is completed at a temperature of below 30°C. In some embodiments, coupling is completed at a temperature of no more than 30°C, no more than 25°C, no more than 20°C, no more than 15°C, no more than 10°C, no more than 5°C, or no more than 0°C. In some embodiments, coupling is completed at above the freezing point of the solvent. In some embodiments, coupling is completed at a temperature of about 0°C to about 30°C. In some embodiments, coupling is completed at a temperature of about 0°C to about 15°C. In some embodiments, coupling comprises a temperature of about -5°C to about 5°C. In some embodiments, coupling is completed at a temperature of about 0°C. In some embodiments, coupling is completed in an ice bath. In some instances, decreased temperatures are maintained upon addition of the base and upon addition of the polymer initiator.

[00204] In some embodiments, a polymer initiator is a C_1-C_8 haloalkyl substituted with oxo.

[00205] In some embodiments, the polymer initiator is represented by the structure:



[00206] In some embodiments, X is a halogen. In some embodiments, X is bromine. In some embodiments, X is chlorine.

[00207] In some embodiments, R^{10} is an initiator group. In some embodiments, the initiator group is a halogen. In some embodiments, the initiator group is bromine.

[00208] In some embodiments, the polymer initiator is 2-bromoisobutyryl bromide.

[00209] In some embodiments, the coupling step takes place for any suitable period of time according to one skilled in the art, such to obtain a suitable yield of product. In some embodiments, the coupling step takes place for at least 0.5 hr, 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 12 hr, or 16 hr. In some embodiments, the coupling step takes place for at most 36 hr, 24 hr, 20 hr, 18 hr, or 16 hr. In some embodiments, the coupling step takes place for about 0.5 hr to about 36 hr or for about 12 hr to about 20 hr. In some embodiments, the coupling step takes place for about 16 hrs, such as at 0°C.

[00210] In some embodiments, the coupling step is completed under inert conditions. In some embodiments, the coupling step is completed under N_2.

[00211] In some embodiments, the coupling step further comprises a washing step, such as after the reaction. In some embodiments, washing comprises washing with one or more organic or

aqueous solvents. In some embodiments, washing comprises washing with organic and aqueous solvents, separately.

[00212] In some embodiments, non-limiting examples of organic solvents provided herein include ethanol, methanol, isopropanol, butanol, dimethylsulfoxide, dimethylformamide, hexane, pentane, benzene, acetonitrile, acetone, carbon tetrachloride, chloroform, N,N-dimethylacetamide, cyclohexane, diethylene glycol, diethyl ether, ethyl acetate, and tetrahydrofuran. In some embodiments, the organic solvent is tetrahydrofuran. In some embodiments, the organic solvent is dimethylformamide. In some embodiments, the organic solvent is N,N-dimethylacetamide. In some embodiments, the organic solvents provided herein comprise a combination of organic solvents. In some embodiments, the organic solvents provided herein comprise an mixture of organic solvents and water.

[00213] In some embodiments, an example of the coupling step is described in Example 2.

[00214] In some embodiments, the methods comprise contacting the initiator surface with a monomer to form the macromolecule structure. In some instances, the monomer comprises any of the monomers provided elsewhere herein.

[00215] In some embodiments, contacting is completed under inert conditions. In some embodiments, contacting is completed under N_2.

[00216] In some embodiments, the methods comprise separately dissolving the monomer in a solvent before adding to the dispersion of the surface. In some embodiments, the solvent comprises an organic solvent, such as dimethylformamide.

[00217] In some embodiments, the contacting comprises sonication. In some embodiments, the solution is sonicated for at least 1 minute, at least 5 minutes, at least 10 minutes, or at least 15 minutes. In some embodiments, the solution is sonicated for 15 minutes.

[00218] In some embodiments, contacting further comprises adding a reducing agent. In some embodiments, the reducing agent is L-ascorbic acid. In some embodiments, the reducing agent is added after the monomer is added to the solution. In some embodiments, the reducing agent is adding at a specific rate, such as by a syringe pump. In some embodiments, the reducing agent is added at a range of about 0.05 mL/min. In some embodiments, the reducing agent is added at a rate of about 0.01 mL/min to about 0.5 mL/min.

[00219] In some embodiments, contacting comprises any suitable temperature according to one skilled in the art. In some embodiments, contacting comprises a temperature of at least 25°C. In some embodiments, contacting comprises a temperature of at least 30°C, 40°C, 50°C, 60°C, or 70°C. In some embodiments, the contacting comprises a temperature of at or below the boiling point of the solvent but above room temperature. In some embodiments, contacting comprises a

temperature of about 25°C to about 75°C. In some embodiments, contacting comprises a temperature of about 35°C.

[00220] In some embodiments, contacting is completed in an organic solvent, such as an organic solvent described elsewhere herein. In some embodiments, the organic solvent is dimethylformamide (DMF), ethanol, methanol, i-propanol, dimethylsulfoxide (DMSO), or combinations or aqueous mixtures thereof. In some embodiments, the contacting is completed in water. In some embodiments, the contacting is completed in dimethylformamide (DMF).

[00221] Provided herein in some embodiments, is a method of making a macromolecule structure. In some embodiments, the method comprises providing a surface. In some embodiments, the method comprises coupling a vinyl group to the surface to form a vinyl-functionalized surface. In some embodiments, the method comprises contacting the vinyl-functionalized surface with a cross-linking monomer and a monomer selected from hydroxyalkyl methacrylate, aminoalkyl methacrylate, alkynyl methacrylate, glycidylalkyl methacrylate, hydroxyalkyl acrylate, aminoalkyl acrylate, alkynyl acrylate or glycidylalkyl acrylate to form a cross-linked polymer coupled to the surface. In some embodiments, the method further comprises coupling a polymer initiator to the cross-linked polymer to form an initiator surface. In some embodiments, the method comprises contacting the initiator surface with a monomer, such as a monomer provided elsewhere herein, to form the macromolecule structure.

[00222] In some instances, an exemplary synthetic scheme as described by the methods provided herein is provided in **FIG. 2.** A vinyl-functionalized surface is subject to a polymerization reaction in the present of a diacrylamide cross-linking agent and hydroxyalkyl methacrylate monomer. A polymer initiator is coupled to the hydroxyalkyl sidechain of the cross-linked polymer. A second polymerization is performed to incorporate ethyleneglycol methacrylate monomers.

[00223] In some embodiments, the method comprises providing a surface, such as a surface provided elsewhere herein. In some embodiments, the surface is washed with a solvent, such as an organic solvent before the subsequent steps. In some embodiments, the surface comprises silicon dioxide.

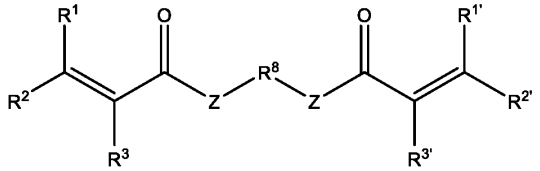
[00224] In some embodiments, the method comprises coupling a vinyl group to the surface to form a vinyl-functionalized surface. In some embodiments, coupling comprises dispersing the surfaces in a solvent. In some embodiments, the solvent is an organic solvent. In some embodiments, the solvent is dimethylformamide. In some embodiments, dispersion is completed with sonication. In some embodiments, the coupling of a vinyl group is completed under inert conditions. In some embodiments, the coupling of a vinyl group is completed under N_2. In some embodiments, the coupling of a vinyl group is completed at elevated temperatures. In some embodiments, the coupling of a vinyl group comprises temperatures of at least 80°C. In some

embodiments, the coupling of a vinyl group comprises temperatures of at least 90°C, 100°C, 110°C, or 120°C. In some embodiments, the coupling of a vinyl group comprises heating to at most 150°C, at most 140°C, at most 130°C, or at most 120°C. In some embodiments, the coupling of a vinyl group comprises heating at a temperature of about 120°C. In some embodiments, the coupling further comprises a wash step, such as a wash with an organic solvent (e.g., DMF).

[00225] In some embodiments, the method further comprises contacting the vinyl-functionalized surface with a cross-linking monomer and a monomer selected from hydroxyalkyl methacrylate, aminoalkyl methacrylate, alkynyl methacrylate, glycidylalkyl methacrylate, hydroxyalkyl acrylate, aminoalkyl acrylate, alkynyl acrylate or glycidylalkyl acrylate to form a cross-linked polymer coupled to the surface. In some embodiments, the monomer is hydroxyalkyl methacrylate. In some embodiments, the monomer is aminoalkyl methacrylate. In some embodiments, the monomer is alkynyl methacrylate. In some embodiments, the monomer is glycidylalkyl methacrylate. In some embodiments, the monomer is hydroxyalkyl acrylate. In some embodiments, the monomer is aminoalkyl acrylate. In some embodiments, the monomer is alkynyl acrylate. In some embodiments, the monomer is glycidylalkyl acrylate. In some embodiments, contacting comprises contacting as described elsewhere herein. In some embodiments, the vinyl functionalized surface comprises a vinyl acrylate.

[00226] In some embodiments, the cross-linking monomer is a diene. In some embodiments, the crosslinking monomer is ethyleneglycol dimethacrylate (EGDMA). In some embodiments, the crosslinking monomer is divinylbenzene.

[00227] In some embodiments, the cross-linking monomer comprises a structure represented by:



[00228] In some embodiments, R^1 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is C_1-C_6 alkyl.

[00229] In some embodiments, R^2 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is C_1-C_6 alkyl.

[00230] In some embodiments, R^3 is hydrogen or C_1-C_6 alkyl. In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is C_1-C_6 alkyl. In some embodiments, R^3 is methyl.

[00231] In some embodiments, $R^{1'}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{1'}$ is hydrogen. In some embodiments, $R^{1'}$ is C_1-C_6 alkyl.

[00232] In some embodiments, $R^{2'}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{2'}$ is hydrogen. In some embodiments, $R^{2'}$ is C_1-C_6 alkyl.

[00233] In some embodiments, $R^{3'}$ is hydrogen or C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is hydrogen. In some embodiments, $R^{3'}$ is C_1-C_6 alkyl. In some embodiments, $R^{3'}$ is methyl.

[00234] In some embodiments, the method further comprises coupling a polymer initiator to the cross-linked polymer to form an initiator surface. In some embodiments, the coupling is described elsewhere herein. In some embodiments, the polymer initiator is a polymer initiator as described elsewhere herein.

[00235] In some embodiments, the methods provided herein comprise polymerization. In some embodiments, the methods provided herein comprise surface initiated polymerization. In some embodiments, contacting the initiator surface comprises polymerization. In some embodiments, polymerization comprises free-radical polymerization. In other embodiments, polymerization comprises "Living"/controlled free-radical polymerization.

[00236] The methods provided herein may, in some embodiments, provide any one of the macromolecule structures of **Table 3**.

Compositions

[00237] In some embodiments, provided herein are compositions comprising any one of the macromolecule structures provided herein. In some embodiments, provided herein are compositions comprising a macromolecule structure, such as a macromolecule structure provided elsewhere herein (e.g., comprising a surface, a tethering moiety, and a macromolecule chain), and a biomolecule. In some embodiments, the biomolecule is adsorbed to the macromolecule structure. In some embodiments, provided herein is a composition comprising one or more macromolecule structures, such as macromolecule structures provided elsewhere herein (e.g., comprising a surface, a tethering moiety, and a macromolecule chain), and a biomolecule adsorbed to the macromolecule structure.

[00238] In some embodiments, the biomolecule adsorbed to the macromolecule structure form a biomolecule corona on the macromolecule structure.

[00239] In some embodiments, the compositions provided herein further comprise a biological sample contacted with the macromolecule structure. In some embodiments, a biological sample comprises a plurality of proteins. In some embodiments, a biological sample comprises plasma, serum, urine, cerebrospinal fluid, synovial fluid, tears, saliva, whole blood, milk, nipple aspirate, ductal lavage, vaginal fluid, nasal fluid, ear fluid, gastric fluid, pancreatic fluid, trabecular fluid, lung lavage, sweat, crevicular fluid, semen, prostatic fluid, sputum, fecal matter, bronchial lavage, fluid from swabbings, bronchial aspirants, fluidized solids, fine needle aspiration samples, tissue homogenates, lymphatic fluid. cell culture samples, or any combination thereof. In some embodiments, a biological sample comprises plasma, serum, or blood. In some embodiments, a biological sample comprises blood. In some embodiments, a biological sample comprises plasma.

In some embodiments, a biological sample comprises serum. In some embodiments, the biological sample is a biofluid. In some embodiments, the biological sample is a cell-free sample.

[00240] In some embodiments, multiple biomolecules may be adsorbed to a macromolecule structure provided herein. In some embodiments, multiple different biomolecules may be adsorbed to a macromolecule structure provided herein. In some embodiments, at least 5, at least 10, at least 20, at least 40, at least 60, at least 80, at least 100, at least 200, at least 400, at least 600, at least 800, at least 1000, or at least 2000 (e.g., different) biomolecules are adsorbed to a macromolecule structure provided herein. In some embodiments, at most 5000, at most 4000, at most 3000, at most 2000, at most 1000, at most 800, at most 600, at most 400, at most 200, at most 100, at most 60, or at most 20 (e.g., different) biomolecules are adsorbed to a macromolecule structure provided herein. In some embodiments, about 5 to about 5000, about 10 to about 2000, about 100 to about 2000, or about 100 to about 1000 (e.g., different) biomolecules are adsorbed to a macromolecule structure provided herein. In some embodiments, at least 100 (e.g., different) biomolecules are adsorbed to a macromolecule structure provided herein.

[00241] In some embodiments, a biomolecule is a protein, polypeptide, polysaccharide, a sugar, a lipid, a lipoprotein, a metabolite, an oligonucleotide, or metabolome. In some embodiments, a biomolecule is a protein. In some embodiments, a biomolecule is a polypeptide. In some embodiments, a biomolecule is a polysaccharide. In some embodiments, a biomolecule is a sugar. In some embodiments, a biomolecule is a lipid. In some embodiments, a biomolecule is a lipoprotein. In some embodiments, a biomolecule is a metabolite. In some embodiments, a biomolecule is an oligonucleotide. In some embodiments, a biomolecule is a metabolome.

[00242] In some embodiments, provided herein are compositions comprising a macromolecule structure, such as a macromolecule structure provided herein (e.g., comprising a surface, a tethering moiety, and a macromolecule chain), and a protein. In some embodiments, provided herein are compositions comprising one or more macromolecule structure, such as a macromolecule structure provided herein, and a protein.

[00243] In some embodiments, multiple proteins may be adsorbed to a macromolecule structure provided herein. In some embodiments, multiple different proteins may be adsorbed to a macromolecule structure provided herein. In some embodiments, at least 5, at least 10, at least 20, at least 40, at least 60, at least 80, at least 100, at least 200, at least 400, at least 600, at least 800, at least 1000, or at least 2000 (e.g., different) proteins are adsorbed to a macromolecule structure provided herein. In some embodiments, at most 5000, at most 4000, at most 3000, at most 2000, at most 1000, at most 800, at most 600, at most 400, at most 200, at most 100, at most 60, or at most 20 (e.g., different) proteins are adsorbed to a macromolecule structure provided herein. In some embodiments, about 5 to about 5000, about 10 to about 2000, about 100 to about 2000, or

about 100 to about 1000 (e.g., different) proteins are adsorbed to a macromolecule structure provided herein. In some embodiments, at least 100 (e.g., different) proteins are adsorbed to a macromolecule structure provided herein.

Methods of Protein Identification

[00244] Provided herein is a method of identifying proteins in a sample with the macromolecule structures provided elsewhere herein (e.g., comprising a surface, a tethering moiety, and a macromolecule chain). In some embodiments, the method comprises incubating one or more macromolecule structures with a biological sample comprising biomolecules. In some embodiments, incubating results one or macromolecule structures with a biological sample comprising biomolecules results in the formation of a biomolecule corona. In some embodiments, the method comprises isolating at least a portion of the biomolecules in the biomolecule corona. In some embodiments, the method comprises assaying the biomolecule corona. In some embodiments, the biomolecule is a biomolecule as described elsewhere herein. In some embodiments, a biomolecule is a protein.

[00245] In some embodiments, assaying the biomolecule corona may be capable of identifying from 1 to 50,000 protein groups or proteins. In some embodiments, 1 to 20,000 protein groups or proteins may be identified. In some embodiments, at least 100 protein groups may be identified. In some embodiments, at least 300 protein groups may be identified. In some embodiments, at least 500 protein groups may be identified. . In some embodiments, at least 1,000 protein groups may be identified. In some embodiments, 1,000 to 10,000 protein groups or proteins may be identified. In some embodiments, 1,000 to 5,000 protein groups or proteins may be identified. In some embodiments, 1,800 to 5,000 protein groups or proteins may be identified. In some embodiments, 1,200 to 2,200 protein groups or proteins may be identified. In some embodiments, a protein group or proteins may comprise a peptide sequence having a minimum length of 2 amino acid residues. In some embodiments, a protein group may comprise a peptide sequence having a minimum length of 2 amino acid residues. In some embodiments, a protein group may comprise a peptide sequence having a minimum length of 5 amino acid residues. In some embodiments, a protein group may comprise a peptide sequence having a minimum length of 7 amino acid residues. In some embodiments, a protein group may comprise a peptide sequence having a minimum length of 8 amino acid residues. In some embodiments, a protein group may comprise a peptide sequence having a minimum length of 9 amino acid residues. In some embodiments, a protein group may comprise a peptide sequence having a minimum length of 10 amino acid residues. In some embodiments, the method may further comprise lysing the proteins of the distinct biomolecule corona. In some embodiments, the method may further comprise digesting

the proteins of the distinct biomolecule corona. In some embodiments, the digested proteins may be purified.

[00246] In some embodiments, the method further comprises repeating the methods described herein, wherein, when repeated, the incubating, isolating, and assaying yields a percent quantile normalized coefficient (QNCV) of variation of 30% or less, as determined by comparing a peptide mass spectrometry feature from at least three full-assay replicates for each surface in the one or more surfaces. In some embodiments, when repeated, the incubating, isolating, and assaying yields a percent quantile normalized coefficient (QNCV) of variation of 25% or less, as determined by comparing a peptide mass spectrometry feature from at least three full-assay replicates for each surface in the one or more surfaces. In some embodiments, when repeated, the incubating, isolating, and assaying yields a percent quantile normalized coefficient (QNCV) of variation of 20% or less, as determined by comparing a peptide mass spectrometry feature from at least three full-assay replicates for each surface in the one or more surfaces. In some embodiments, the assaying is capable of identifying proteins over a dynamic range of at least 6, at least 7, at least 8, at least 9, or at least 10. In some embodiments, the assaying is capable of identifying proteins over a dynamic range of no more than 12, no more than 11, no more than 10, no more than 9, no more than 8, or no more than 7.

[00247] In some embodiments, the method may further comprise washing one or more surfaces at least one time after isolating the one or more surfaces from an unbound protein. In some embodiments, the method may further comprise washing one or more surfaces at least two times after isolating the one or more surfaces from an unbound protein. In some embodiments, the method may further comprise washing one or more surfaces at least three times after isolating the one or more surfaces from an unbound protein. The isolation may be performed, for example, using magnetic isolation or centrifugation.

[00248] In some embodiments, the method may further comprise desorbing the proteins of the biomolecule corona. In some embodiments, the method may further comprise denaturing the proteins of the biomolecule corona.

[00249] In some embodiments, the methods herein further comprise preparing analytes (e.g., proteins) from a biomolecule corona for analysis. In some embodiments, preparation for analysis comprises digesting the biomolecule corona, a subset of biomolecules within the protein corona, or biomolecules desorbed from the biomolecule corona to form a digested sample. Preparing analytes from the biomolecule corona for analysis may also comprise chemically modifying a biomolecule from the biomolecule corona, such as methylating or reducing the biomolecule. In some embodiments, preparing analytes from the biomolecule corona for analysis may comprise denaturing the analytes (e.g., proteins).

[00250] In some embodiments, the assaying comprises using mass spectrometry to identify proteins in the sample. In some embodiments, the assaying comprises using tandem mass spectrometry. In some embodiments, the assaying comprises using liquid chromatography tandem mass spectrometry. The assaying may comprise, in some embodiments, ELISA, Edman Degradation, immunoaffinity techniques, single-molecule protein sequencing, and the like.

[00251] In some embodiments, the assaying is performed in about 2 to about 4 hours. In some embodiments, the method is performed in about 1 to about 20 hours. In some embodiments, the method is performed in about 2 to about 10 hours. In some embodiments, the method is performed in about 4 to about 6 hours. In some embodiments, the isolating takes no more than about 30 minutes, no more than about 15 minutes, no more than about 10 minutes, no more than about 5 minutes, or no more than about 2 minutes.

[00252] In some embodiments, a plurality of spatially isolated samples are processed according to the method. In some embodiments, the plurality of samples comprises at least 10 spatially isolated samples, at least 50 spatially isolated samples, at least 100 spatially isolated samples, at least 150 spatially isolated samples, at least 200 spatially isolated samples, at least 250 spatially isolated samples, or at least 300 spatially isolated samples. In further embodiments, the plurality of samples comprises at least 96 samples.

[00253] In some embodiments, the one or more macromolecule structure comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure share at least one physicochemical property and differ by at least one physicochemical property, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different. Both macromolecule structures may have polymeric properties, but can exhibit different macromolecule structure, such as charges measured by zeta potential analysis. In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure share at least two physicochemical properties and differ by at least two physicochemical properties, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different. In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure share at least one physicochemical property and differ by at least two physicochemical properties, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different.

[00254] In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure share at least two physicochemical properties and differ by at least one physicochemical property, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different. In further embodiments, the physicochemical property comprises size, charge, core material, shell material, porosity, or macromolecule structure hydrophobicity. In further embodiments, size is diameter or radius, as measured by dynamic light scattering, SEM, TEM, or any combination thereof.

[00255] In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure comprise a surface charge of from 0 mV and -50 mV, wherein the first distinct macromolecule structure, the second distinct macromolecule structure, or both have a diameter of less than 400 nm. In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure comprise a diameter of 100 to 400 nm, wherein the first distinct macromolecule structure has a positive surface change, and wherein the second distinct macromolecule structure has a negative surface charge.

[00256] In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure are nanoparticles, wherein the first distinct macromolecule structure has a surface charge less than -20 mV and the second distinct macromolecule structure has a surface charge greater than 20 mV. In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure are microparticles, wherein the first distinct macromolecule structure has a negative surface charge, and wherein the second distinct macromolecule structure has a positive surface charge. In some embodiments, the one or more macromolecule structures comprises a subset of negatively charged nanoparticles, wherein each macromolecule structure of the subset differ by at least one surface chemical group. In some embodiments, the one or more macromolecule structures comprises a first distinct macromolecule structure, a second distinct macromolecule structure, and a third distinct macromolecule structure, wherein the first distinct macromolecule structure, the second distinct macromolecule structure, and the third distinct macromolecule structure comprise iron oxide

cores, and are less than about 500 nm in diameter, and wherein the first distinct macromolecule structure comprises a negative charge of less -40 mV, the second distinct macromolecule structure comprises a positive charge of more than 20 mV, and the third distinct macromolecule structure comprises a negative charge of -20 mV to -40 mV.

[00257] In some embodiments, at least one of the one or more distinct macromolecule structures comprises a carboxylated polymer, an aminated polymer, a zwitterionic polymer, or any combination thereof. In some embodiments, at least one of the one or more distinct macromolecule structures comprises a carboxylated polymer. In some embodiments, at least one of the one or more distinct macromolecule structures comprises an aminated polymer. In some embodiments, at least one of the one or more distinct macromolecule structures comprises a zwitterionic polymer.

[00258] In some embodiments, the one or more macromolecule structures comprise at least 2 distinct macromolecule structures. In some embodiments, the one or more macromolecule structures comprise at least 3 distinct macromolecule structures, at least 4 distinct macromolecule structures, at least 5 distinct macromolecule structures, at least 6 distinct macromolecule structures, at least 7 distinct macromolecule structures, at least 8 distinct macromolecule structures, at least 9 distinct macromolecule structures, at least 10 distinct macromolecule structures, at least 11 distinct macromolecule structures, at least 12 distinct macromolecule structures, at least 13 distinct macromolecule structures, at least 14 distinct macromolecule structures, at least 15 distinct macromolecule structures, at least 20 distinct macromolecule structures, at least 25 macromolecule structures, or at least 30 distinct macromolecule structures. In some embodiments, the one or more macromolecule structures comprise at most 50, at most 45, at most 40, at most 35, at most 30, at most 25, or at most 20 distinct macromolecule structures. In some embodiments, the one or more macromolecule structures comprise about 2 to about 30 distinct macromolecule structures. In some embodiments, the one or more macromolecule structures comprise at least 10 distinct macromolecule structures.

Analysis and Automated Systems

[00259] Provided herein, in some embodiments, is a system for identifying biomolecule in a biological sample, wherein the system may comprise (i) one or more macromolecule structures provided elsewhere herein; (ii) a biological sample comprising biomolecules; and (iii) an automated system comprising a network of units with differentiated functions for isolating biomolecules adsorbed to the macromolecular structure, and wherein the automated system is programmed to perform a series of steps.

[00260] In some embodiments, the macromolecule immobilized to a macromolecule structure provided elsewhere herein, the suspension solution, and the biological sample comprising a

concentration of protein may be incubated at a temperature of about 4 degrees Celsius (°C) to about 90 °C. In some embodiments, one or more components of the composition may be incubated at a temperature of about 20°C to about 90°C. In some embodiments, one or more components of the composition may be incubated at a temperature of about 20°C to about 50°C. In some embodiments, one or more components of the composition may be incubated at a temperature of about 4°C to about 40°C. In some embodiments, one or more components of the composition may be incubated at a temperature of about 25°C to about 40°C.

[00261] In some embodiments, the suspension solution may comprise Tris, EDTA, and CHAPS buffer. For example, the suspension solution may be Tris, EDTA in 150 millimolar (mM) KCl and 0.05% CHAPS buffer. In another example, the suspension solution may be 10mM Tris HCl pH 7.4, 1 mM EDTA.

[00262] In some embodiments, the present disclosure provides an automated system comprising a network of units as described in U.S. Patent No.11,428,688, which is incorporated herein by reference in its entirety. In some embodiments, the network of units may comprise differentiated functions in distinguishing states of a complex biological sample using a plurality of macromolecule structures having surfaces with different physicochemical properties wherein: a first unit comprises a multichannel fluid transfer instrument for transferring fluids between units within the system; a second unit comprises a support for storing a plurality of biological samples; a third unit comprises a support for a sensor array plate possessing partitions that comprise the macromolecular structure for a binding interaction with a population of analytes from the biological sample; a fourth unit comprises supports for storing a plurality of reagents; a fifth unit comprises supports for storing a reagent to be disposed of; a sixth unit comprises supports for storing consumables used by the multichannel fluid transfer instrument; and wherein the system is programed to perform a series of steps comprising: contacting the complex biological sample with a specified partition of the sensor array; incubating the complex biological sample with the plurality of macromolecule structures contained within the partition of the sensor array plate; removing components from a partition except the plurality of macromolecule structures and a population of analytes interacting with a macromolecule structure; and optionally preparing the population of analytes for analysis, such as mass spectrometry.

[00263] In some embodiments, the first unit comprises a degree of mobility that enables access to all other units within the system. In some embodiments, the first unit comprises a capacity to perform pipetting functions.

[00264] In some embodiments, the support of the second and/or third unit comprises support for a single plate, a 6 well plate, a 12 well plate, a 96 well plate, or a rack of microtubes. In some embodiments, the second and/or unit comprises a thermal unit capable of modulating the

temperature of said support and a sample. In some embodiments, the second and/or third unit comprises a rotational unit capable of physically agitating and/or mixing a sample.

[00265] In some embodiments, the plurality of macromolecule structures having surfaces with different physicochemical properties for binding a population of analytes within the biological sample are immobilized to a macromolecule structure within a partition of the sensory array. In some embodiments, the plurality of particles comprises a plurality of magnetic nanoparticles with different physicochemical properties for binding a population of analytes within the complex biological sample. In some embodiments, the system comprises a step wherein the sensor array plate is transferred to an additional seventh unit that comprises a magnetized support and a thermal unit capable of modulating the temperature of said support and a sample and incubated for an additional amount of time.

[00266] In some embodiments, the fourth unit comprises a set of reagents for: generating the sensor array plate; washing an unbound sample; and/or preparing a sample for mass spectrometry. In some embodiments, contacting the biological sample with a specified partition of the sensor array comprises pipetting a specified volume of the biological sample into the specific partition of the sensor array.

[00267] In some embodiments, contacting the biological sample with a specified partition of the sensor array comprises pipetting a volume of at least 10 microliters, at least 20 microliters at least 50 microliters, at least 100 microliters, at least 250 microliters, at least 500 microliters, or at least 1000 microliters of the biological sample into the specific partition of the sensor array. In some embodiments, contacting the biological sample with a specified partition of the sensor array comprises pipetting a volume of no more than 1000 microliters, no more than 500 microliters, nor more than 250 microliters, no more than 150 microliters, no more than 100 microliters, no more than 75 microliters, no more than 50 microliters, or no more than 30 microliters.

[00268] In some embodiments, the biological sample may be diluted with water or buffer. In some embodiments, the biological sample may be diluted at least 2-fold, at least 3-fold, at least 4-fold, or at least 5-fold. In some embodiments, the biological sample may be diluted no more than 20-fold, no more than 10-fold, no more than 8-fold, or no more than 5-fold. In some embodiments, biological sample is diluted with water or buffer from about 2-fold to about 5-fold.

[00269] In some embodiments, incubating the biological sample with the plurality of macromolecule structures contained within the partition of the sensor array plate comprises an incubation time of at least about 10 seconds, at least about 15 seconds, at least about 20 seconds, at least about 25 seconds, at least about 30 seconds, at least about 40 seconds, at least about 50 seconds, at least about 60 seconds, at least about 90 seconds, at least about 2 minutes, at least about 3 minutes, at least about 4 minutes, at least about 5 minutes, at least about 6 minutes, at least

about 7 minutes, at least about 8 minutes, at least about 9 minutes, at least about 10 minutes, at least about 15 minutes, at least about 20 minutes, at least about 25 minutes, at least about 30 minutes, at least about 45 minutes, at least about 50 minutes, at least about 60 minutes, at least about 90 minutes, at least about 2 hours, at least about 3 hours, at least about 4 hours, at least about 5 hours, at least about 6 hours, at least about 7 hours, at least about 8 hours, at least about 9 hours, at least about 10 hours, at least about 12 hours, at least about 14 hours, at least about 15 hours, at least about 16 hours, at least about 17 hours, at least about 18 hours, at least about 19 hours, at least about 20 hours, or at least about 24 hours. In some embodiments, incubating the biological sample with the plurality of macromolecule structures contained within the partition of the sensor array plate comprises an incubation time of no more than 24 hours, no more than 12 hours, no more than 6 hours, no more than 3 hours, no more than 2 hours, no more than 90 minutes, no more than 75 minutes, no more than 60 minutes, no more than 45 minutes, or no more than 30 minutes. In some embodiments, incubating the biological sample with the plurality of macromolecule structures contained within the partition of the sensor array plate comprises an incubation time of 30 minutes and 3 hours.

[00270] In some embodiments, incubating the biological sample with the plurality of macromolecule structures contained within the partition of the substrate comprises an incubation temperature between about 4° C to about 40° C. Incubating the biological sample with the plurality of macromolecule structures contained within the partition of the substrate may comprise an incubation temperature between about 4° C to about 37° C. Incubating the biological sample with the plurality of macromolecule structures contained within the partition of the substrate may comprise an incubation temperature between about 20° C to about 50° C. Incubating the biological sample with the plurality of macromolecule structures contained within the partition of the substrate may comprise an incubation temperature between about 4° C to about 100° C.

[00271] In some embodiments, the second unit can facilitate a transfer of the sample for mass spectrometry to a mass spectrometry unit.

[00272] In some embodiments, the present disclosure provides an automated apparatus to identify proteins in a biological sample, the automated apparatus comprising: a sample preparation unit; a substrate comprising a plurality of channels; a plurality of pipettes; a plurality of solutions, a plurality of macromolecule structures as described herein. In some embodiments, the automated apparatus is configured to form a protein corona and digest the protein corona.

[00273] In some embodiments, the automated apparatus further comprises a magnetic source. In some embodiments, the automated apparatus is configured for BCA, gel, or trypsin digestion of the protein corona.

[00274] In some embodiments, the automated apparatus is enclosed. In some embodiments, the automated apparatus is sterilized before use. In some embodiments, the automated apparatus is configured to a mass spectrometer. In some embodiments, the automated apparatus is temperature controlled.

[00275] The proteomic data of the sample can be identified, measured, and quantified using a number of different analytical techniques. For example, proteomic data can be analyzed using SDS-PAGE or any gel-based separation technique. Peptides and proteins can also be identified, measured, and quantified using an immunoassay, such as ELISA. Alternatively, proteomic data can be identified, measured, and quantified using mass spectrometry, high performance liquid chromatography, LC-MS/MS, Edman Degradation, immunoaffinity techniques, and methods disclosed in EP3548652, WO2019083856, WO2019133892, each of which is incorporated herein by reference in its entirety, and other protein separation techniques

[00276] In some embodiments, the present disclosure provides an automated apparatus for generating a subset of biomolecules from a biological sample, comprising: a substrate comprising a plurality of partitions, a first unit comprising the biological sample, and a loading unit that is movable across the substrate and is capable of transferring a volume (e.g., a volume of buffer) between different units of the apparatus. In some cases, the substrate is a multi-well plate.

[00277] The plurality of partitions may comprise a plurality of sensor elements. The plurality of sensor elements may comprise surfaces. The plurality of sensor elements may be macromolecule structures (e.g., particles) as disclosed herein. For example, the sensor elements may include a first distinct nanoparticle and a second distinct nanoparticle.

[00278] A partition from among the plurality of partitions may comprise 1 to 100 types of sensor elements (e.g., distinct macromolecule structures). A partition from among the plurality of partitions may comprise 2 to 50 types of sensor elements. A partition from among the plurality of partitions may comprise 2 to 20 types of sensor elements. A partition from among the plurality of partitions may comprise 2 to 5 types of sensor elements. A partition from among the plurality of partitions may comprise 3 to 8 types of sensor elements. A partition from among the plurality of partitions may comprise 4 to 10 types of sensor elements. A partition from among the plurality of partitions may comprise 5 to 12 types of sensor elements. A partition from among the plurality of partitions may comprise 6 to 15 types of sensor elements. A partition from among the plurality of partitions may comprise 8 to 20 types of sensor elements. A partition from among the plurality of partitions may comprise 2 types of sensor elements. A partition from among the plurality of partitions may comprise 3 types of sensor elements. A partition from among the plurality of partitions may comprise 4 types of sensor elements. A partition from among the plurality of partitions may comprise one sensor element.

[00279] Two or more partitions from among the plurality of partitions may comprise different quantities of sensor elements. Two or more partitions from among the plurality of partitions may comprise different types of sensor elements. A partition amongst a plurality of partitions may comprise a combination of types and/or quantities of sensor element(s) that differs from other partitions in the plurality. A subset of partitions in a plurality of partitions may each contain a combination of distinct sensor elements that is distinct from other partitions in the plurality.

[00280] Sensor elements may be stored in dry form inside of or within the partitions. Dry sensor elements may be reconstituted or rehydrated prior to use. Sensor elements may also be stored within solutions. For example, a substrate partition may comprise a solution comprising a high concentration of macromolecule structures.

[00281] Partitions from among the plurality of partitions comprise different concentrations or amounts (e.g., by mass/molar amount per unit volume of sample) of sensor elements. A partition from among the plurality of partitions may comprise from 1 pM to 100 nM of sensor elements. A partition from among the plurality of partitions comprise may from 1 pM to 500 pM of sensor elements. A partition from among the plurality of partitions may comprise from 10 pM to 1 nM of sensor elements. A partition from among the plurality of partitions may comprise from 100 pM to 10 nM of sensor elements. A partition from among the plurality of partitions may comprise from 500 pM to 100 nM of sensor elements. A partition from among the plurality of partitions may comprise from 50 μg/ml to 300 μg/ml of sensor elements. A partition from among the plurality of partitions may comprise from 100 μg/ml to 500 μg/ml of sensor elements. A partition from among the plurality of partitions may comprise from 250 μg/ml to 750 μg/ml of sensor elements. A partition from among the plurality of partitions may comprise from 400 μg/ml to 1 mg/ml of sensor elements. A partition from among the plurality of partitions may comprise from 600 μg/ml to 1.5 mg/ml of sensor elements. A partition from among the plurality of partitions may comprise from 800 μg/ml to 2 mg/ml of sensor elements. A partition from among the plurality of partitions may comprise from 1 mg/ml to 3 mg/ml of sensor elements. A partition from among the plurality of partitions may comprise from 2 mg/ml to 5 mg/ml of sensor elements. A partition from among the plurality of partitions may comprise more than 5 mg/ml of sensor elements.

[00282] The loading unit may be configured to move between and transfer volumes (e.g., a volume of a solution or a powder) between any units, compartments, or partitions within the apparatus. The loading unit may be configured to move precise volumes (e.g., within 0.1%, 0.01%, 0.001% of the specified volume). The loading unit may be configured to collect a volume from the substrate or a compartment or partition within the substrate, and dispense the volume back into the substrate or compartment or partition within the substrate, or to dispense the volume or a portion of the volume into a different unit, compartment, or partition. The loading unit may be

configured to move multiple volumes simultaneously, such as 2 to 400 separate volumes. The loading unit may comprise a plurality of pipette tips.

[00283] The loading unit may be configured to move a volume of a liquid. The volume may be about 0.1 μl, 0.2 μl, 0.3 μl, 0.4 μl, 0.5 μl, 0.6 μl, 0.7 μl, 0.8 μl, 0.9 μl, 1 μl, 2 μl, 3 μl, 4 μl, 5 μl, 6 μl, 7 μl, 8 μl, 9 μl, 10 μl, 12 μl, 15 μl, 20 μl, 25 μl, 30 μl, 40 μl, 50 μl, 60 μl, 70 μl, 80 μl, 90 μl, 100 μl, 120 μl, 150 μl, 180 μl, 200 μl, 250 μl, 300 μl, 400 μl, 500 μl, 600 μl, 800 μl, 1 ml, or more than 1 ml. The liquid may be a biological sample or a solution.

[00284] In some cases, the solution comprises a wash solution, a resuspension solution, a denaturing solution, a buffer, a reagent (e.g., a reducing reagent), or any combination thereof. In some cases, the solution comprises a biological sample.

[00285] In part owing to these functionalities, the loading unit can be capable of partitioning a sample. In some embodiments, this comprises dividing a sample into a number of partitions. A sample can be divided into at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 20, 25, 30, 40, 50, 60, 70, 80, 90, 100, 120, 150, 180, 200, 250, 300, 350, 400, 500, or more partitions. A sample can be divided into 96, 192, or 384 partitions. The automated apparatus can comprise multiple substrates comprising partitions. The automated apparatus may comprise 1, 2, 3, 4, 5, or more substrates comprising partitions. In some cases, the loading unit loads different volumes of the biological sample into different partitions. In some cases, the loading unit loads identical volumes into two or more partitions. The volume of biological sample loaded into a partition may be about 0.1 μl, 0.2 μl, 0.3 μl, 0.4 μl, 0.5 μl, 0.6 μl, 0.7 μl, 0.8 μl, 0.9 μl, 1 μl, 2 μl, 3 μl, 4 μl, 5 μl, 6 μl, 7 μl, 8 μl, 9 μl, 10 μl, 12 μl, 15 μl, 20 μl, 25 μl, 30 μl, 40 μl, 50 μl, 60 μl, 70 μl, 80 μl, 90 μl, 100 μl, 120 μl, 150 μl, 180 μl, 200 μl, 250 μl, 300 μl, 400 μl, 500 μl, 600 μl, 800 μl, 1 ml, or more than 1 ml. The volume of biological sample loaded into a partition may be about 10 μl to 400 μl. The volume of biological sample loaded into a partition may be about 5 μl to 150 μl. The volume of biological sample loaded into a partition may be about 35 μl to 80 μl. In some cases, the loading unit may partition two or more biological samples. For example, a sample storage unit may comprise two biological samples that the system partitions into one well plate. In some embodiments, the loading unit can facilitate a transfer of the sample for mass spectrometry to a mass spectrometry unit.

[00286] The system may be configured to perform a dilution on a sample or a sample partition. A sample or sample partition may be diluted with buffer, water (e.g., purified water), a non-aqueous solvent, or any combination thereof. The diluent may be stored in the automated apparatus prior to dispensation into a substrate partition. The automated apparatus may store a plurality of diluents differing in pH, salinity, osmolarity, viscosity, dielectric constant, or any combination thereof. The diluents may be used to adjust the chemical properties of a sample or

sample partition. The automated apparatus may dilute a sample or sample partition by 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 8-fold, 10-fold, 15-fold, 20-fold, 30-fold, 40-fold, 50-fold, 75-fold, 100-fold, 150-fold, 200-fold, 300-fold, 400-fold, 500-fold or greater. In some embodiments, the automated apparatus may dilute a sample or sample partition by about 2-fold to about 5-fold. The automated apparatus may perform different dilutions on two samples or sample partitions. The system may perform different dilutions on each partition from among a plurality of partitions. For example, the system may perform different dilutions on each of the 96 sample partitions in a 96 well plate. In some cases, the different dilutions comprise different degrees of dilution (e.g., 2-fold vs. 4-fold). In some cases, the different dilutions comprise dilution with different solutions (e.g., different buffers). In some cases, two sample partitions may be made to differ in one or more chemical properties, such as pH, salinity, or viscosity.

[00287] In some cases, the system may modify the chemical composition of a sample or sample partition. The system may modify or adjust the pH, salinity, osmolarity, dielectric constant, viscosity, buffer types, salt types, sugar types, detergent types, or any combination thereof for a sample or sample partition. Such modification or adjustments may comprise mixing a reagent from the fourth unit with a sample or sample partition. The system may differently modify the chemical composition of two samples or sample partitions.

[00288] A system or automated apparatus of the present disclosure may also comprise an incubation element. The incubation element may contact, support, or hold another component of the automated apparatus (e.g., the substrate or a unit). The incubation unit may contact, support, or hold multiple components of the automated apparatus. The incubation element may contact the substrate to facilitate heat transfer between the incubation element and the substrate. The incubation unit may be configured to control the temperature of the one or more components of the automated apparatus, such as by heating or cooling. The incubation element may be capable of cooling a component of the apparatus to from 20 °C to 1 °C. The incubation element may be capable of heating a component of the apparatus to from 25 °C to 100 °C. The incubation element may be capable of setting the temperature a component of the apparatus to from 4 °C to 37 °C. The incubation element may be configured to heat or cool different portions of a component of the automated apparatus to different temperatures. For example, the incubation element may hold a first partition in the substrate at 30 °C and a second partition in the substrate at 35 °C. The incubation element may control the temperature of a sample or partition. The incubation element may comprise a temperature sensor (e.g., a thermocouple) for detecting the temperature within a partition or container. The incubation element may calibrate its heating or cooling to the readout from the temperature sensor.

[00289] The incubation element may be configured to physically agitate a component of the automated apparatus. The agitation may be in the form of shaking or spinning, vibrating, rocking, sonicating, or any combination thereof. The incubation element may be capable of providing multiple agitation intensities and/or frequencies. For example, the incubation element may comprise multiple settings for shaking at different frequencies and amplitudes. The incubation element may also be capable of stirring and or mixing a volume (e.g., a portion of the biological sample).

[00290] The automated apparatus may comprise a unit comprising a resuspension solution. The loading unit may be capable of transferring a volume of the resuspension solution to a partition from among the plurality of partitions of the substrate. In some cases, this results in the dilution of a sample present within the partition and can further result in the desorption of a plurality of biomolecules from a biomolecule corona disposed on a sensor element within the partition. The quantity of biomolecules desorbed from a biomolecule corona can depend on the volume of the resuspension solution added to the partition, the temperature of the partition, the composition of the resuspension solution (e.g., the salinity, osmolarity, viscosity, dielectric constant, or pH), the volume of the biological sample within the partition, and the sensor element type and the composition of biomolecules in the biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of less than 5% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 10% to 20% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 20% to 30% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 30% to 40% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 40% to 50% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 50% to 60% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 60% to 70% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 70% to 80% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of 80% to 90% of the biomolecules from a biomolecule corona. The transfer of a volume of the resuspension solution into a partition may result in the desorption of more than 90% of the biomolecules from a biomolecule corona.

[00291] In some cases, multiple rounds of desorption are performed. In each round, the supernatant comprising the desorbed biomolecules may be collected, analyzed, or discarded. The types and abundances of biomolecules in the supernatant may differ between desorption rounds. The automated apparatus may perform one or more desorption and discard cycles (i.e., washes), followed by one or more desorption cycles comprising sample collection and/or analysis.

[00292] The resuspension solution may be tailored to optimize enrichment of particular biomarkers. The resuspension solution may comprise a buffer, such as Tris-EDTA (TE), CHAPS, PBS, citrate, HEPES, MES, CHES, or another bio buffer. The resuspension solution may comprise Tris EDTA (TE) 150mM KCl 0.05% CHAPS buffer. The resuspension solution may comprise 10 mM TrisHCl pH 7.4, 1 mM EDTA. The resuspension solution may also contain or be highly purified water (e.g., distilled or deionized water). Biomolecule desorption may be augmented by heating or agitation by an incubation element. The supernatant may be transferred to a new partition following desorption. A resuspension solution may be used to dilute a sample.

[00293] The automated apparatus may comprise a unit comprising a denaturing solution. The denaturing solution may comprise a protease. The denaturing solution may comprise a chemical capable of performing peptide cleavage (e.g., cyanogen bromide, formic acid, or hydroxylamine, 2-nitro-5-thiocyanatobenzoic acid). The denaturing solution may comprise a chemical denaturant such as guanidine, urea, sodium deoxycholate, acetonitrile, trichloroacetic acid, acetic acid, sulfosalicylic acid, sodium bicarbonate, ethanol, perchlorate, dodecyl sulfate, or any combination thereof. The denaturing solution may comprise a reductant, such as 2-mercaptoethanol, dithiothreitol, or tris(2-carboxyethyl)phosphine. The protease may be trypsin. The denaturing solution may be added to a partition following desorption. The denaturing solution may be added to a partition comprising biomolecule coronas.

[00294] The automated apparatus may comprise a magnet or array of magnets. The automated apparatus may be capable of moving the substrate onto and off of the magnet or array of magnets. The array of magnets may be structured so that a plurality of magnets from the array of magnets can rest directly underneath a plurality of partitions from the substrate. The magnet may be capable of immobilizing magnetic sensor elements (e.g., magnetic particles such as coated or uncoated super paramagnetic iron oxide nanoparticles) within a partition on the substrate. For example, the magnet may prevent magnetic nanoparticles from being removed from a partition during a wash step. The magnet may also create a pellet from a collection of magnetic particles. The magnet may create a particle pellet in less than 10 minutes. The magnet may create a particle pellet in less than 5 minutes. The particle pellet may comprise a particle with a biomolecule corona.

[00295] The automated apparatus may comprise a purification unit. The purification unit may comprise a plurality of partitions comprising an adsorbent or resin. The purification unit may

comprise a solid-phase extraction array or plate. The solid-phase extraction array or plate may comprise a polar stationary phase material. The solid-phase extraction array or plate may comprise a non-polar stationary phase material. The solid-phase extraction array or plate may comprise a C18 stationary phase material (e.g., octadecyl group silica gel). The automated apparatus may comprises a unit with a conditioning solution for the purification unit (e.g., a conditioning solution for a solid-phase extraction material). The automated apparatus may comprise a unit with an elution solution for removing biomolecules from the purification unit.

[00296] In some embodiments, a supernatant is removed from the sensor array plate. In some instances, the automated apparatus may perform a series of wash steps. A wash step may remove biomolecules that are not bound to the sensor elements within the partition. A wash step may desorb a subset of biomolecules bound to sensor elements within a partition. For example, a wash step may result in the desorption and removal of a subset of soft corona analytes, while leaving the majority of hard corona analytes bound to the sensor element.

[00297] In some embodiments, the present disclosure provides an automated apparatus to identify proteins in a biological sample, the automated apparatus comprising: a sample preparation unit; a substrate comprising a plurality of channels; a plurality of pipettes; a plurality of solutions, a plurality of macromolecule structures, such as macromolecules provided elsewhere herein, and wherein the automated apparatus is configured to form a protein corona and digest the protein corona.

[00298] In some embodiments, the automated apparatus further comprises a magnetic source. In some embodiments, the automated apparatus is configured for BCA, gel, or trypsin digestion of the protein corona.

[00299] In some embodiments, the automated apparatus is enclosed. In some embodiments, the automated apparatus is sterilized before use. In some embodiments, the automated apparatus is configured to a mass spectrometry. In some embodiments, the automated apparatus is temperature controlled.

Kits

[00300] In one aspect, described herein is a kit for identifying biomolecules in a biological sample, wherein the kit may comprise one or more macromolecule structures as described elsewhere herein. The kit may be used, in some embodiments, to perform the method of identifying proteins in a sample as provided herein. The kit may be used, in some embodiments, may be configured to perform methods using the automated apparatus as provided herein.

[00301] A kit of the present disclosure may comprise one or more macromolecule structures (e.g., particles) to interrogate a sample. The kit may be pre-packaged in discrete aliquots. In another example, the kit can comprise one or more different macromolecule structures (e.g., particles with

different surface chemistries) that can be used to interrogate a sample. The plurality of different macromolecule structures can be pre-packaged where each macromolecule structure of the plurality is packaged separately. Alternately, the plurality of macromolecule structures can be packaged together to contain a combination of macromolecule structures in a single package. In some embodiments, the kit comprises two or more packages containing different macromolecule structure (e.g., particles), wherein at least one of the packages contains two or more different macromolecule structures (e.g., particles). The macromolecule structures (e.g., particles) may, in some embodiments, be freeze dried and stored in sealed containers.

[00302] In some embodiments, the kit further comprises a denaturing agent. In some embodiments, the denaturing agent comprises at least one of: sodium dodecyl sulfate, acetic acid, trichloroacetic acid, sulfosalicylic acid, sodium bicarbonate, ethanol, formaldehyde, glutaraldehyde, urea, guanidium chloride, lithium perchlorate, 2-mercaptoethanol, dithiothreitol, tris(2-carboxyethyl)phosphine (TCEP), or any combination thereof.

[00303] In some embodiments, the kit further comprises a reducing agent. In some embodiments, the reducing agent comprises TCEP, dithiothreitol, beta-mercaptoethanol, glutathione, cysteine, or any combination thereof.

[00304] In some embodiments, the kit further comprises an alkylating agent. In some embodiments, the alkylating agent comprises iodoacetamide, iodoacetic acid, acrylamide, chloroacetamide, or any combination thereof.

[00305] In some embodiments, the kit further comprises a digestion agent. In some embodiments, the digestion agent comprises trypsin, lysin, serine protease, or any combination thereof.

[00306] In some embodiments, the kit further comprises an elution buffer. In some embodiments, the elution buffer comprises triethylammonium bicarbonate, tris(hydroxymethyl)aminomethane, citrate, Tris, phosphate, ethylenediaminetetraacetic acid, or any combination thereof.

[00307] In some embodiments, the kit further comprises a washing agent. In some embodiments, the washing agent is water or a buffer.

[00308] In some embodiments, the kit further comprises a solid support for solid phase extraction. In some embodiments, the kit comprises a polar stationary phase material. In some embodiments, the kit comprises a non-polar stationary phase material. In some embodiments, the kit comprises a C18 stationary phase material (e.g., octadecyl group silica gel). In some embodiments, the kit comprises conditioning solution for the solid phase extraction material.

[00309] In some embodiments, the kit further comprises a multi-well plate. In some embodiments, the multi-well plate is a 4 well plate. In some embodiments, the multi-well plate is a In some embodiments, the multi-well plate is a 12 well plate. In some embodiments, the multi-well plate is a 24 well plate. In some embodiments, the multi-well plate is a 48 well plate. In some

embodiments, the multi-well plate is a 96 well plate. In some embodiments, the multi-well plate is a 384 well plate. In some embodiments, the multi-well plate is a 1536 well plate.

[00310] In some embodiments, the kit further comprises a diluent. In some embodiments, the diluent is an organic solvent. In some embodiments, the diluent is water. In some embodiments, the diluent is a buffer. In some embodiments, the diluent is an organic solvent, water, a buffer, or any combination thereof.

[00311] In some embodiments, the kit further comprises an organic solvent. In some embodiments, the kit further comprises a cysteine blocking reagent. In some embodiments, the cysteine blocking reagent comprises methyl methanethiosulfonate, iodoacetamide, N-ethylmaleimide, methylsulfonyl benzothiazole, or any combination thereof.

Numbered Embodiments

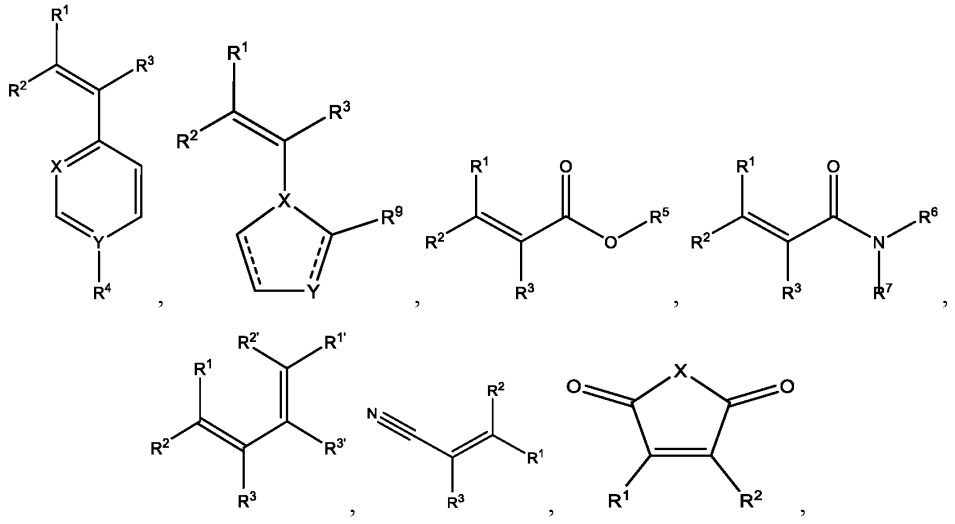
[00312] Provided herein are numbered embodiments 1-271.

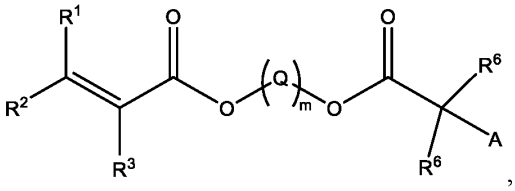
Embodiment 1. A macromolecule structure comprising:

(I) a surface;

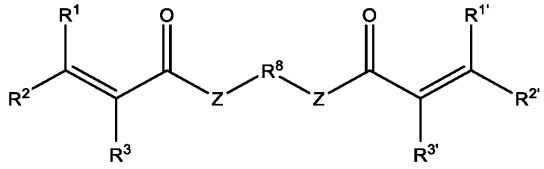
(II) a tethering moiety coupled to the surface; and

(III) a macromolecule chain, wherein a first end of the macromolecule chain is covalently attached to the tethering moiety, and wherein the macromolecule chain comprises two or more distinct recurring units derived from a monomer represented by a structure selected from the group consisting of:





, and

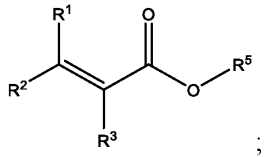


wherein each of X and Y is independently -C-, -O-, or -N-;

each Z is independently -O- or -NH;

Q is $-CH_2-$ or ethylene glycol;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by the structure:



;

m is an integer selected from 1-20;

═is a single or double bond;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or $-C_1$-C_6 alkyl;

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, sulfonate, carboxylate, C_1-C_4 alkylene, amine, quaternary ammonium cation, or C_1-C_6 alkyl optionally substituted with halogen;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further optionally substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, $-C_1$-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally

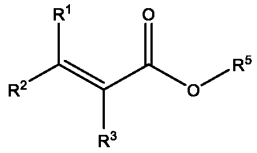
substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further optionally substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne;

R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide;

R^9 is hydrogen or oxo; and

n^1 is an integer selected from 1-100.

Embodiment 2. The macromolecule structure of embodiment 1, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure:



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Embodiment 3. The macromolecule structure of embodiment 1 or 2, wherein R^1 is hydrogen.

Embodiment 4. The macromolecule structure of any one of embodiments 1-3, wherein R^2 is hydrogen.

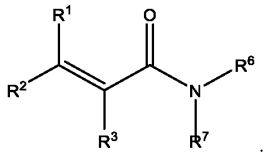
Embodiment 5. The macromolecule structure of any one of embodiments 1-4, wherein R^3 is hydrogen.

Embodiment 6. The macromolecule structure of any one of embodiments 1-5, wherein R^5 is hydrogen, C_1-C_6 alkyl, or C_1-C_3 alkyl substituted with pyrene or 2 or more fused 5-6 membered rings optionally further substituted.

Embodiment 7. The macromolecule structure of any one of embodiments 1-4, wherein R^3 is methyl.

Embodiment 8. The macromolecule structure of embodiment 7, wherein R^5 is C_1-C_{n1} ethylene glycol.

Embodiment 9. The macromolecule structure of any one of embodiments 1-8, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure :



.

Embodiment 10. The macromolecule structure of embodiment 9, wherein R^1 is hydrogen.

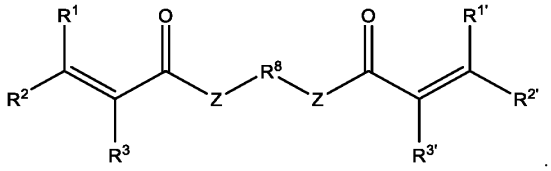
Embodiment 11. The macromolecule structure of embodiment 9 or 10, wherein R^2 is hydrogen.

Embodiment 12. The macromolecule structure of any one of embodiments 9-11, wherein R^3 is H.

Embodiment 13. The macromolecule structure of any one of embodiments 9-11, wherein R^3 is 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl.

Embodiment 14. The macromolecule structure of any one of embodiments 9-13, wherein R^6 is H.

Embodiment 15. The macromolecule structure of any one of embodiments 9-14, wherein R^7 is C_1-C_6 alkyl optionally substituted with hydroxyl, substituted benzene, or hydrogen.

Embodiment 16. The macromolecule structure of any one of embodiments 1-15, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

.

Embodiment 17. The macromolecule structure of embodiment 16, wherein R^1 is hydrogen.

Embodiment 18. The macromolecule structure of embodiment 16 or 17, wherein R^2 is hydrogen.

Embodiment 19. The macromolecule structure of any one of embodiments 16-18, wherein $R^{1'}$ is hydrogen.

Embodiment 20. The macromolecule structure of any one of embodiments 16-19, wherein $R^{2'}$ is hydrogen.

Embodiment 21. The macromolecule structure of any one of embodiments 16-20, wherein R^3 is methyl.

Embodiment 22. The macromolecule structure of any one of embodiments 16-21, wherein $R^{3'}$ is methyl.

Embodiment 23. The macromolecule structure of any one of embodiments 16-22, wherein each Z is O.

Embodiment 24. The macromolecule structure of any one of embodiments 16-23, wherein R^8 is C_1-C_6 alkyl.

Embodiment 25. The macromolecule structure of any one of embodiments 16-23, wherein R^8 is symmetrical disulfide (e.g., CH_2CH_2S-SCH_2CH_2) or a divalent metal.

Embodiment 26. The macromolecule structure of any one of embodiments 16-20, wherein R^3 is hydrogen.

Embodiment 27. The macromolecule structure of any one of embodiments 16-20, wherein $R^{3'}$ is hydrogen.

Embodiment 28. The macromolecule structure of any one of embodiments 26 or 27, wherein each Z is -N-.

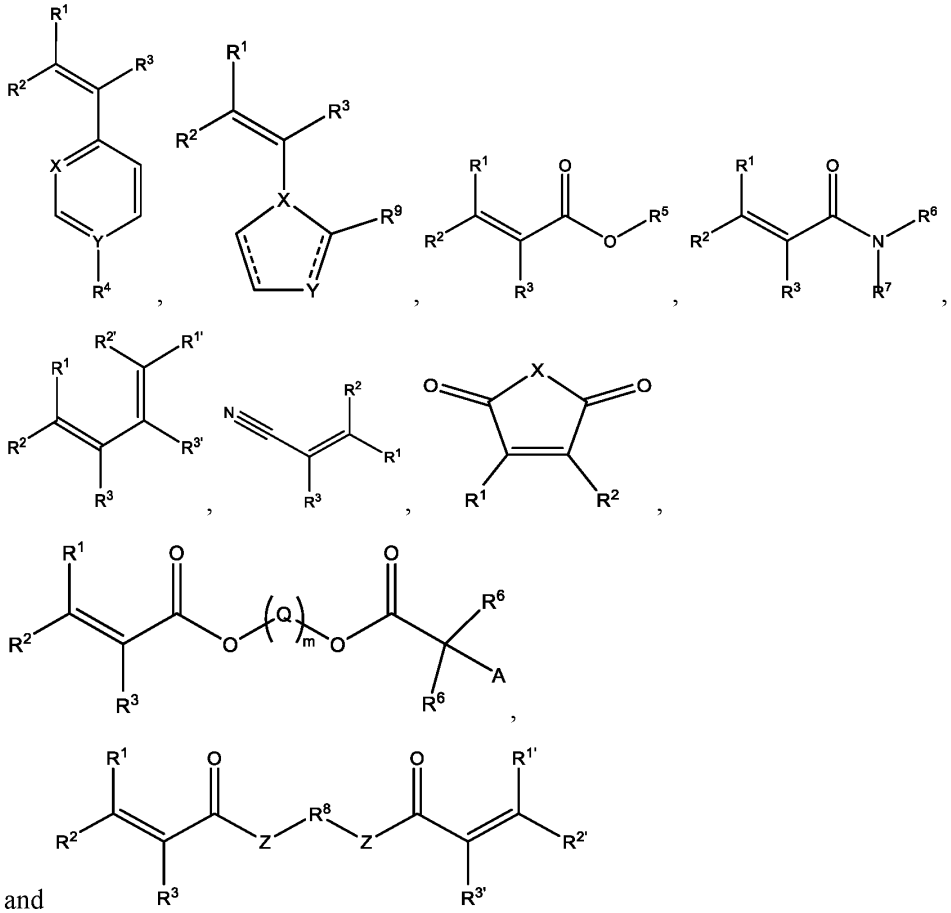
Embodiment 29. The macromolecule structure of any one of embodiments 26-28, wherein R^8 is C_1-C_6 alkyl.

Embodiment 30. A macromolecule structure comprising:

(I) a surface;

(II) a tethering moiety coupled to the surface; and

(III) a macromolecule chain, wherein a first end of the macromolecule chain is covalently attached to the tethering moiety, and wherein the macromolecule chain comprises a recurring unit derived from a monomer represented by a structure selected from the group consisting of:



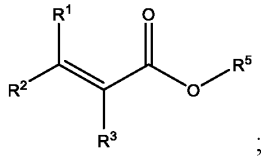
and

wherein each of X and Y is independently -C-, -O-, or -N-;

each Z is independently -O- or -NH;

Q is $-CH_2-$ or ethylene glycol;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by the structure:



;

m is 1-6;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or C_1-C_6 alkyl

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, C_1-C_6 alkyl optionally substituted with halogen, C_1-C_4 alkylene, C_1-C_6 alkyl, sulfonate, amine, quaternary ammonium cation, or carboxylate;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or linear C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne; and

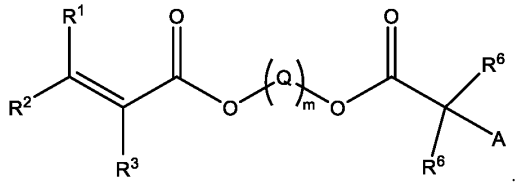
R^8 is C_1-C_6 alkyl, or symmetric or asymmetric disulfide;

R^9 is hydrogen or oxo;

n^1 is an integer selected from 1-100; and

provided that when R^3 is CH_3, R^4 is CH_3, or when R^5 is C_1-C_8 alkyl substituted with hydroxyl, C_1-C_8 is further substituted.

Embodiment 31. The macromolecule structure of any one of embodiments 1-30, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure:



Embodiment 32. The macromolecule structure of embodiment 31, wherein Q is $-CH_2-$.

Embodiment 33. The macromolecule structure of embodiment 31 or 32, wherein R^1 is hydrogen.

Embodiment 34. The macromolecule structure of any one of embodiments 31-33, wherein R^2 is hydrogen.

Embodiment 35. The macromolecule structure of any one of embodiments 31-34, wherein R^3 is methyl.

Embodiment 36. The macromolecule structure of any one of embodiments 31-35, wherein m is 2.

Embodiment 37. The macromolecule structure of any one of embodiments 31-36, wherein R^6 is C_1-C_6 alkyl.

Embodiment 38. The macromolecule structure of embodiment 31, wherein Q is ethylene glycol.

Embodiment 39. The macromolecule structure of embodiment 38, wherein R^1 is hydrogen.

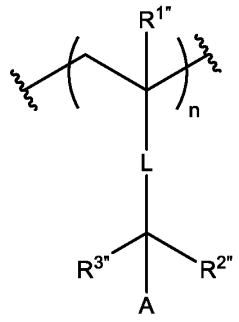
Embodiment 40. The macromolecule structure of embodiment 38 or 39, wherein R^2 is hydrogen.

Embodiment 41. The macromolecule structure of any one of embodiments 38-40, wherein R^6 is C_1-C_6 alkyl.

Embodiment 42. The macromolecule structure of any one of embodiments 38-41, wherein R^5 is C_1-C_{n1} ethylene glycol.

Embodiment 43. A macromolecule structure comprising:

(I) a surface and (II) a macromolecule chain coupled to the surface, wherein the macromolecule chain comprises a recurring unit of Formula (I):

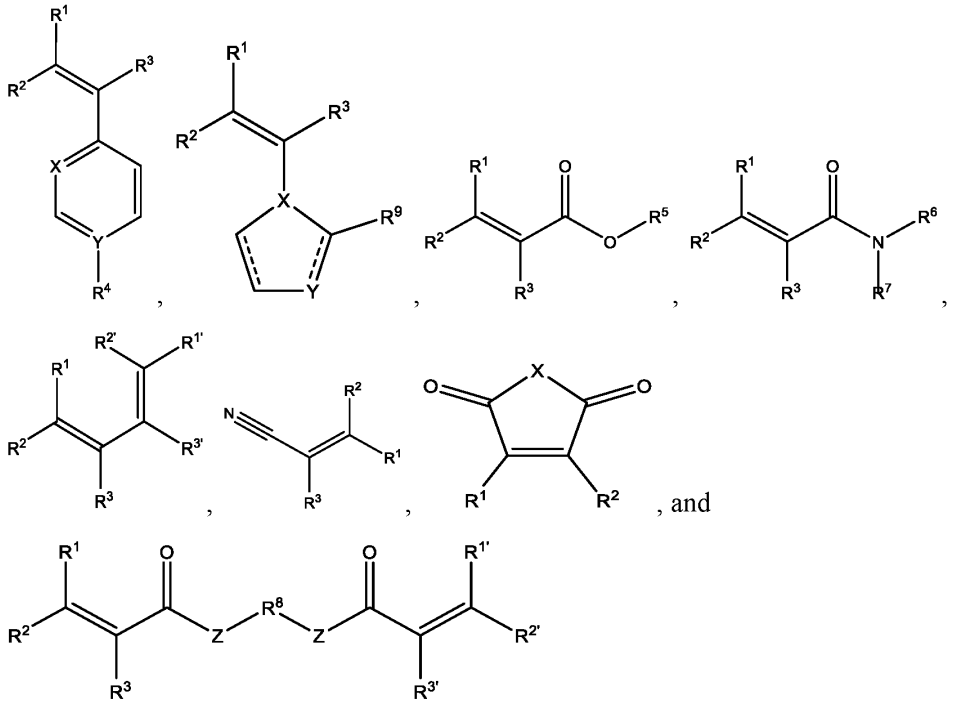


(I)

wherein each of $R^{1"}$, $R^{2"}$, and $R^{3"}$ is independently hydrogen or C_1-C_6 alkyl;

L is a linker moiety;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by a structure selected from the group consisting of:



wherein each of X and Y is independently -C-, -O-, or -N-;

Z is -O- or -NH;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or C_1-C_6 alkyl;

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, sulfonate, carboxylate, C_1-C_4 alkylene, amine, quaternary ammonium cation, or C_1-C_6 alkyl optionally substituted with halogen;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally

substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or linear C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, substituted benzene, C_1-C_6 alkyl substituted with hydroxyl, optionally substituted C_1-C_8 alkyl sulfonate;

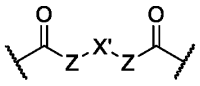
R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide;

R^9 is hydrogen or oxo;

n^1 is an integer selected from 1-100; and

n is an integer selected from 1-10,000.

Embodiment 44. The macromolecule structure of embodiment 43, wherein the linker moiety is represented by the structure:



wherein:

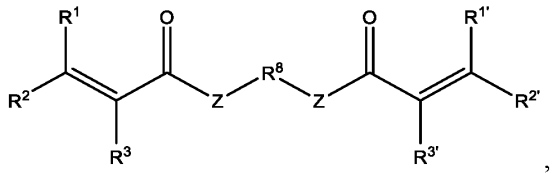
each Z is independently O or N; and

X' is C_1-C_6 alkyl.

Embodiment 45. The macromolecule structure of embodiment 43 or 44, wherein the macromolecule further comprises a tethering moiety.

Embodiment 46. The macromolecule structure of any one of embodiments 43-45, wherein the macromolecule structure further comprises a cross-linking moiety.

Embodiment 47. The macromolecule structure of embodiment 46, wherein the cross-linking moiety comprises a structure represented by



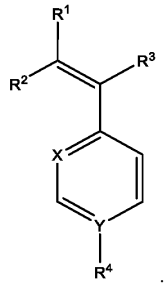
,

wherein:

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or C_1-C_6 alkyl;

Z is -O- or -NH; and

R^8 is -C_1-C_6 alkyl, divalent metal, symmetric or asymmetric disulfide.

Embodiment 48. The macromolecule structure of any one of embodiments 1-47, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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Embodiment 49. The macromolecule structure of embodiment 48, wherein R^1 is H.

Embodiment 50. The macromolecule structure of embodiment 48 or 49, wherein R^2 is H.

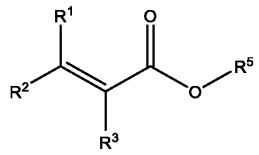
Embodiment 51. The macromolecule structure of any one of embodiments 48-50, wherein R^3 is H.

Embodiment 52. The macromolecule structure of any one of embodiments 48-51, wherein R^4 is C_1-C_6 alkyl optionally substituted with halogen, absent, hydrogen, carboxylate, or sulfonate.

Embodiment 53. The macromolecule structure of any one of embodiments 48-51, wherein R^4 is C_1-C_4 alkylene.

Embodiment 54. The macromolecule structure of any one of embodiments 48-53, wherein X is -C- or -N-.

Embodiment 55. The macromolecule structure of any one of embodiments 48-54, wherein Y is -C- or -N-.

Embodiment 56. The macromolecule structure of any one of embodiments 1-55, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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Embodiment 57. The macromolecule structure of embodiment 56, wherein R^1 is H.

Embodiment 58. The macromolecule structure of embodiment 56 or 57, wherein R^2 is H.

Embodiment 59. The macromolecule structure of any one of embodiments 56-58, wherein R^3 is H.

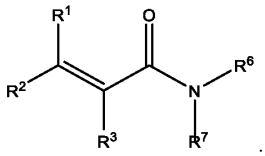
Embodiment 60. The macromolecule structure of any one of embodiments 56-59, wherein R^5 is C_1 alkyl, C_1-C_3 alkyl substituted with pyrene, -C_1-C_3 alkyl comprising 2 or more fused 5-6 membered rings optionally further substituted, or H.

Embodiment 61. The macromolecule structure of any one of embodiments 56-58, wherein R^3 is methyl.

Embodiment 62. The macromolecule structure of embodiment 61, wherein R^5 is H, C_2-C_6 alkyl, C_1-C_6 alkyl substituted with one or more hydroxyl, amine, azide, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne.

Embodiment 63. The macromolecule structure of embodiment 61, wherein R^5 is C_1-C_{n1} ethylene glycol.

Embodiment 64. The macromolecule structure of embodiment 61, wherein when R^5 is C_1-C_6 alkyl substituted with hydroxyl, C_1-C_6 alkyl is substituted with at least one further hydroxyl or azide.

Embodiment 65. The macromolecule structure of any one of embodiments 1-64, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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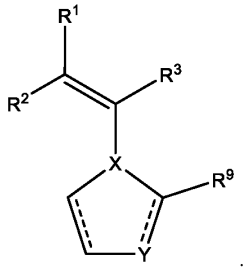
Embodiment 66. The macromolecule structure of embodiment 65, wherein R^1 is H.

Embodiment 67. The macromolecule structure of embodiment 65 or 66, wherein R^2 is H.

Embodiment 68. The macromolecule structure of any one of embodiments 65-67, wherein R^3 is H or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl.

Embodiment 69. The macromolecule structure of any one of embodiments 65-68, wherein R^6 is H or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl.

Embodiment 70. The macromolecule structure of any one of embodiments 65-69, wherein R^7 is C_1-C_2 alkyl, -C_1-C_6 alkyl substituted with hydroxyl, substituted benzene, or hydrogen.

Embodiment 71. The macromolecule structure of any one of embodiments 1-70, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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Embodiment 72. The macromolecule structure of embodiment 71, wherein R^1 is hydrogen.

Embodiment 73. The macromolecule structure of embodiment 71 or 72, wherein R^2 is hydrogen.

Embodiment 74. The macromolecule structure of any one of embodiments 71-73, wherein R^3 is hydrogen.

Embodiment 75. The macromolecule structure of any one of embodiments 71-74, wherein == is a double bond.

Embodiment 76. The macromolecule structure of any one of embodiments 71-75, wherein X is -N-.

Embodiment 77. The macromolecule structure of any one of embodiments 71-76, wherein Y is -N-.

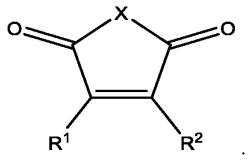
Embodiment 78. The macromolecule structure of any one of embodiments 71-77, wherein R^9 is hydrogen.

Embodiment 79. The macromolecule structure of any one of embodiments 71-74, wherein == is a single bond.

Embodiment 80. The macromolecule structure of embodiment x, wherein 79 is -N-.

Embodiment 81. The macromolecule structure of embodiment 79 or 80, wherein Y is -C-.

Embodiment 82. The macromolecule structure of any one of embodiments 79-81, wherein R^9 is oxo.

Embodiment 83. The macromolecule structure of any one of embodiments 1-82, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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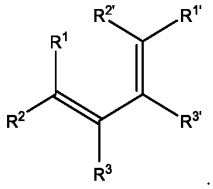
Embodiment 84. The macromolecule structure of embodiment 83, wherein X is -O-.

Embodiment 85. The macromolecule structure of embodiment 83 or 84, wherein R^1 is hydrogen.

Embodiment 86. The macromolecule structure of any one of embodiments 83-85, wherein R^2 is hydrogen.

Embodiment 87. The macromolecule structure of any one of embodiments 1-86, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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Embodiment 88. The macromolecule structure of embodiment 87, wherein R^1 is hydrogen.

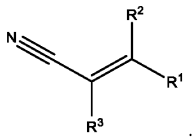
Embodiment 89. The macromolecule structure of embodiment 87 or 88, wherein R^2 is hydrogen.

Embodiment 90. The macromolecule structure of any one of embodiments 87-89, wherein R^3 is hydrogen.

Embodiment 91. The macromolecule structure of any one of embodiments 87-90, wherein $R^{3'}$ is methyl.

Embodiment 92. The macromolecule structure of any one of embodiments 87-91, wherein $R^{1'}$ is hydrogen.

Embodiment 93. The macromolecule structure of any one of embodiments 87-92, wherein $R^{2'}$ is hydrogen.

Embodiment 94. The macromolecule structure of any one of embodiments 1-93, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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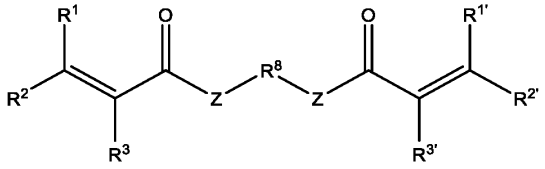
Embodiment 95. The macromolecule structure of embodiment 94, wherein R^1 is hydrogen.

Embodiment 96. The macromolecule structure of embodiment 94 or 95, wherein R^2 is hydrogen.

Embodiment 97. The macromolecule structure of any one of embodiments 94-96, wherein R^3 is hydrogen.

Embodiment 98. The macromolecule structure of any one of embodiments 1-97, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure: 

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Embodiment 99. The macromolecule structure of embodiment 98, wherein R^1 is hydrogen.

Embodiment 100. The macromolecule structure of embodiment 98 or 99, wherein R^2 is hydrogen.

Embodiment 101. The macromolecule structure of any one of embodiments 98-100, wherein $R^{1'}$ is hydrogen.

Embodiment 102. The macromolecule structure of any one of embodiments 98-101, wherein $R^{2'}$ is hydrogen.

Embodiment 103. The macromolecule structure of any one of embodiments 98-102, wherein R^3 is methyl.

Embodiment 104. The macromolecule structure of any one of embodiments 98-103, wherein $R^{3'}$ is methyl.

Embodiment 105. The macromolecule structure of any one of embodiments 98-104, wherein Z is O.

Embodiment 106. The macromolecule structure of any one of embodiments 98-105, wherein R^8 is C_1-C_6 alkyl.

Embodiment 107. The macromolecule structure of any one of embodiments 98-105, wherein R^8 is symmetrical disulfide (e.g., CH_2CH_2S-SCH_2CH_2).

Embodiment 108. The macromolecule structure of any one of embodiments 98-102, wherein R^3 is hydrogen.

Embodiment 109. The macromolecule structure of any one of embodiments 98-102, wherein $R^{3'}$ is hydrogen.

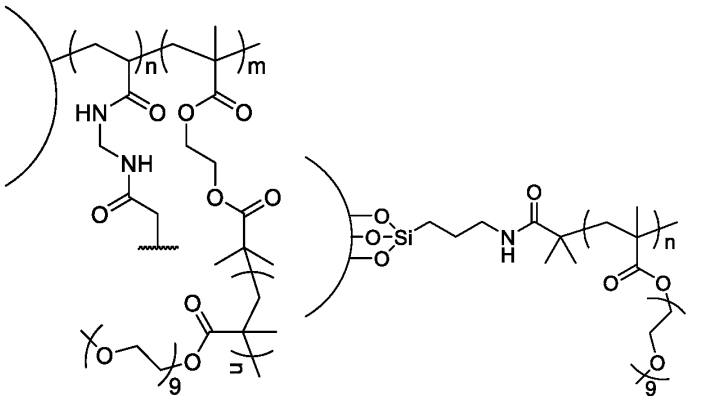
Embodiment 110. The macromolecule structure of any one of embodiments 108 or 109, wherein Z is -N-.

Embodiment 111. The macromolecule structure of any one of embodiments 108-110, wherein R^8 is C_1-C_6 alkyl.

Embodiment 112. The macromolecule structure of any one of embodiments 1-111, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by a structure of **Table 1**.

Embodiment 113. The macromolecule structure of any one of embodiments 1-112, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by a structure of **Table 2**.

Embodiment 114. The macromolecule structure of any one of embodiments 1-113, wherein the macromolecule structure has a structure represented by:



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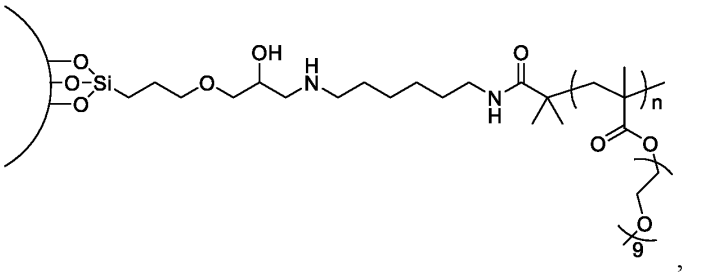

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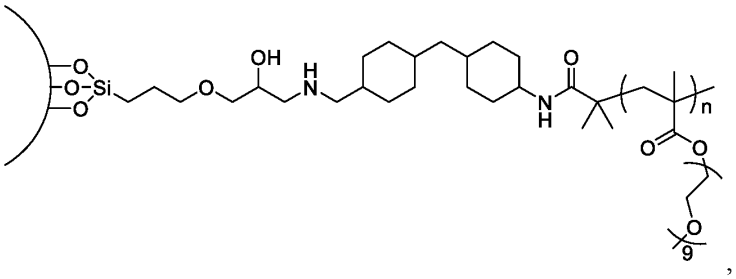

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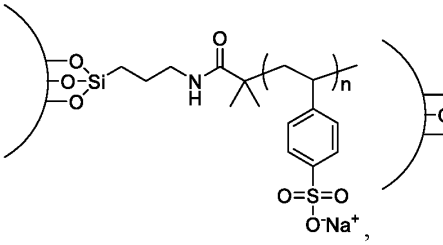

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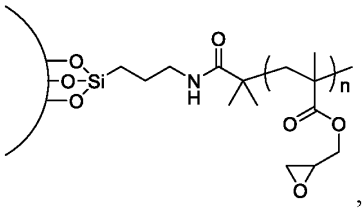
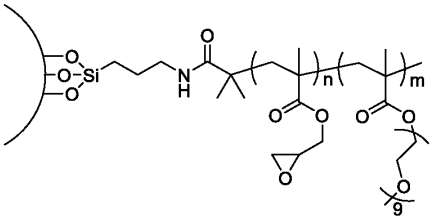


, or



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Embodiment 115. The macromolecule structure of any one of embodiments 1-114, wherein the surface comprises a particle.

Embodiment 116. The macromolecule structure of embodiment 115, wherein the particle is a nanoparticle.

Embodiment 117. The macromolecule structure of embodiment 115, wherein the particle is a microparticle.

Embodiment 118. The macromolecule structure of any one of embodiments 115-117, wherein the particle comprises a diameter of about 100 nm to about 500 nm.

Embodiment 119. The macromolecule structure of any one of embodiments 115-118, wherein the particle comprises a diameter of about 100 nm to about 300 nm.

Embodiment 120. The macromolecule structure of any one of embodiments 115-119, wherein the particle comprises a polydispersity index (PDI) of about 0.01 to about 1.

Embodiment 121. The macromolecule structure of any one of embodiments 115-120, wherein the particle comprises a PDI of less than about 0.1.

Embodiment 122. The macromolecule structure of any one of embodiments 115-121, wherein the particle comprises iron oxide.

Embodiment 123. The macromolecule structure of any one of embodiments 115-122, wherein the particle has an iron oxide core.

Embodiment 124. The macromolecule of any one of embodiments 115-123, wherein the particle is magnetic.

Embodiment 125. The macromolecule structure of any one of embodiments 115-124, wherein the particle is a superparamagnetic iron oxide particle.

Embodiment 126. The macromolecule structure of any one of embodiments 115-125, wherein the particle has a core shell structure.

Embodiment 127. The macromolecule structure of any one of embodiments 115-126, wherein the particle comprises an iron oxide core with a silica shell.

Embodiment 128. The macromolecule structure of any one of embodiments 115-126, wherein the particle comprises iron oxide crystals embedded in a polystyrene core.

Embodiment 129. The macromolecule structure of any one of embodiments 1-128, wherein the macromolecule structure comprises at least 10% w/w of the recurring unit.

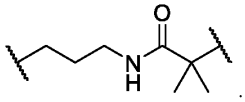
Embodiment 130. The macromolecule structure of any one of embodiments 1-129, wherein the macromolecule structure comprises at most 50% w/w of the recurring unit.

Embodiment 131. The macromolecule structure of any one of embodiments 1-130, wherein the tethering moiety is covalently coupled to the surface.

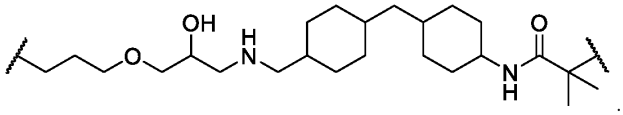
Embodiment 132. The macromolecule structure of any one of embodiments 1-131, wherein the tethering moiety is non-covalently coupled to the surface.

Embodiment 133. The macromolecule structure of any one of embodiments 1-132, wherein the tethering moiety is C_1-C_{20} heteroalkyl optionally substituted with one or more C_1-C_6 alkyl, oxo, halo, or hydroxyl.

Embodiment 134. The macromolecule structure of embodiment 133, wherein the tethering moiety is represented by the structure:

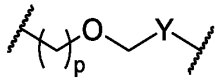


Embodiment 135. The macromolecule structure of any one of embodiments 1-132, wherein the tethering moiety is represented by the structure:



Embodiment 136. The macromolecule structure of any one of embodiments 1-132, wherein the tethering moiety is C_1-C_{12} alkoxy optionally substituted with one or more C_1-C_{20} heteroalkyl, each of the C_1-C_{12} alkoxy and C_1-C_{20} heteroalkyl optionally substituted with one or more C_1-C_6 alkyl, oxo, halo, or hydroxyl.

Embodiment 137. The macromolecule structure of embodiment 135, wherein the tethering moiety is represented by the structure:

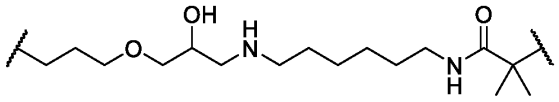


wherein:

Y is C_1-C_{20} heteroalkyl optionally substituted with one or more C_1-C_6 alkyl, oxo, halo, or hydroxyl; and

p is an integer from 1-12.

Embodiment 138. The macromolecule structure of embodiment 135 or 137, wherein the tethering moiety is represented by the structure:



Embodiment 139. The macromolecule structure of any one of embodiments 1-137, wherein the macromolecule chain is a homopolymer.

Embodiment 140. The macromolecule structure of any one of embodiments 1-137, wherein the macromolecule chain is a block copolymer.

Embodiment 141. The macromolecule structure of any one of embodiments 1-137, wherein the macromolecule chain is a random copolymer.

Embodiment 142. The macromolecule structure of any one of embodiments 1-137, wherein the macromolecule chain is not cross-linked.

Embodiment 143. The macromolecule structure of any one of embodiments 1-142, wherein the macromolecule chain comprises about 1 to about 100 recurring units.

Embodiment 144. The macromolecule structure of any one of embodiments 1-143, wherein the macromolecule chain comprises about 1 to about 50 recurring units.

Embodiment 145. The macromolecule structure of any one of embodiments 1-144, wherein the macromolecule chain comprises a molecular weight of about 0.5 kDa to about 25 kDa.

Embodiment 146. The macromolecule structure of any one of embodiments 1-145, wherein the macromolecule chain comprises a molecular weight of about 0.5 kDa to about 10 kDa.

Embodiment 147. The macromolecule structure of any one of embodiments 1-146, wherein a second end of the macromolecule chain is not coupled to the surface.

Embodiment 148. The macromolecule structure of any one of embodiments 1-147, wherein the surface comprises the tethering moiety at a density of at least 1 tethering moiety per 50 nm^2.

Embodiment 149. The macromolecule structure of any one of embodiments 1-148, wherein the surface comprises the tethering moiety at a density of about 1 tethering moiety per 50 nm^2 to about 1 tethering moiety per 5 nm^2.

Embodiment 150. A method of making a macromolecule structure of any one of embodiments 1-149, the method comprising:

(a) providing a surface;

(b) coupling a polymer initiator to the surface to form an initiator surface; and

(c) contacting the initiator surface with a monomer of any one of embodiments 1-113 to form the macromolecule structure.

Embodiment 151. The method of embodiment 150, wherein the surface comprises a particle.

Embodiment 152. The method of embodiment 150 or 151, wherein the particle is a nanoparticle or microparticle.

Embodiment 153. The method of any one of embodiments 150-152, wherein the particle comprises a diameter of about 100 nm to about 500 nm.

Embodiment 154. The method of any one of embodiments 150-153, wherein the particle comprises a diameter of about 100 nm to about 300 nm.

Embodiment 155. The method of any one of embodiments 150-154, wherein the particle comprises iron oxide.

Embodiment 156. The method of any one of embodiments 150-155, wherein the particle has an iron oxide core.

Embodiment 157. The method of any one of embodiments 150-156, wherein the particle is a superparamagnetic iron oxide (nano)particle.

Embodiment 158. The method of any one of embodiments 150-157, wherein the particle comprises silicon dioxide.

Embodiment 159. The method of any one of embodiments 150-158, wherein the particle has a core shell structure.

Embodiment 160. The method of any one of embodiments 150-159, wherein the particle comprises an iron oxide core with a silica shell.

Embodiment 161. The method of any one of embodiments 150-160, wherein the surface is functionalized with an alkoxy silane.

Embodiment 162. The method of any one of embodiments 150-161, wherein the surface is functionalized with aminopropyltetraethoxy silane (APTES).

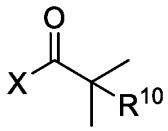
Embodiment 163. The method of any one of embodiments 150-162, wherein coupling comprises addition of a base.

Embodiment 164. The method of embodiment 163, wherein the base comprises triethylamine.

Embodiment 165. The method of embodiment 163 or 164, wherein the base is added at about 0°C.

Embodiment 166. The method of any one of embodiments 150-165, wherein coupling comprises providing the polymer initiator to the surface at about 0°C.

Embodiment 167. The method of any one of embodiments 150-166, wherein the polymer initiator is represented by the structure:



wherein:

X is a halogen;

R^{10} is an initiator group.

Embodiment 168. The method of embodiment 167, wherein the initiator group is a halogen.

Embodiment 169. The method of any one of embodiments 150-168, wherein contacting comprises a temperature of at least 25°C.

Embodiment 170. The method of any one of embodiments 150-169, wherein contacting comprises a temperature of about 25°C to about 75°C.

Embodiment 171. The method of any one of embodiments 150-170, wherein contacting comprises contacting the initiator surface with a mixture of the monomer and an organic solvent.

Embodiment 172. The method of embodiment 171, wherein the organic solvent is dimethylformamide.

Embodiment 173. A method of making a macromolecule structure of any of embodiments 1-149, the method comprising:

(a) providing a surface;

(b) coupling a vinyl group to the surface to form a vinyl-functionalized surface;

(c) contacting the vinyl-functionalized surface with a cross-linking monomer and a monomer selected from hydroxyalkyl methacrylate, aminoalkyl methacrylate, alkynyl methacrylate, glycidylalkyl methacrylate, hydroxyalkyl acrylate, aminoalkyl acrylate, alkynyl acrylate or glycidylalkyl acrylate to form a cross-linked polymer coupled to the surface;

(d) coupling a polymer initiator to the cross-linked polymer to form an initiator surface;

(e) contacting the initiator surface with a monomer of any one of embodiments 1-113 to form the macromolecule structure.

Embodiment 174. The method of embodiment 173, wherein the surface comprises a particle.

Embodiment 175. The method of embodiment 173 or 174, wherein the particle is a nanoparticle or microparticle.

Embodiment 176. The method of any one of embodiments 173-175, wherein the particle comprises a diameter of about 100 nm to about 500 nm.

Embodiment 177. The method of any one of embodiments 173-176, wherein the particle comprises a diameter of about 100 nm to about 300 nm.

Embodiment 178. The method of any one of embodiments 173-177, wherein the particle comprises iron oxide.

Embodiment 179. The method of any one of embodiments 173-178, wherein the particle has an iron oxide core.

Embodiment 180. The method of any one of embodiments 173-179, wherein the particle is magnetic.

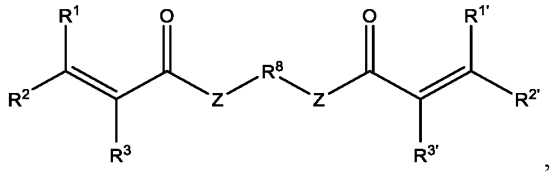
Embodiment 181. The method of any one of embodiments 173-180, wherein the particle is a superparamagnetic iron oxide (nano)particle.

Embodiment 182. The method of any one of embodiments 173-181, wherein the particle has a core shell structure.

Embodiment 183. The method of any one of embodiments 173-182, wherein the particle comprises an iron oxide core with a silica shell.

Embodiment 184. The method of any one of embodiments 173-183, wherein the vinyl-functionalized surface comprises a vinyl acrylate.

Embodiment 185. The method of any one of embodiments 173-184, wherein the cross-linking monomer comprises a structure represented by



,

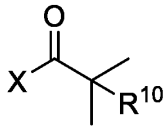
wherein:

each of R^1, R^2, R^3, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or -C_1-C_6 alkyl;

Z is -O- or -NH; and

R^8 is -C_1-C_6 alkyl, divalent metal, symmetric or asymmetric disulfide.

Embodiment 186. The method of any one of embodiments 173-185, wherein the polymer initiator is represented by the structure:



wherein:

X is a halogen;

R^{10} is an initiator group.

Embodiment 187. The method of embodiment 186, wherein the initiator group is selected from a halogen, an epoxide, or a double bond.

Embodiment 188. The method of any one of embodiments 173-187, wherein contacting comprises a temperature of at least 25°C.

Embodiment 189. The method of any one of embodiments 173-188, wherein contacting comprises a temperature of about 25°C to about 75°C.

Embodiment 190. The method of any one of embodiments 173-189, wherein contacting comprises contacting the initiator surface with a mixture of the monomer, cross-linking monomer, and an organic solvent.

Embodiment 191. The method of embodiment 190, wherein the organic solvent is dimethylformamide.

Embodiment 192. The method of any one of embodiments 173-191, wherein contacting comprises inert conditions.

Embodiment 193. The method of any one of embodiments 173-192, wherein coupling comprises inert conditions.

Embodiment 194. A composition comprising a macromolecule structure of any one of embodiments 1-149 and a biomolecule adsorbed to the macromolecule structure.

Embodiment 195. The composition of embodiment 194, wherein the biomolecule adsorbed to the macromolecule structure form a biomolecule corona on the macromolecule structure.

Embodiment 196. The composition of embodiment 194 or 195, wherein the composition comprises a biological sample contacted with the macromolecule structure.

Embodiment 197. The composition of embodiment 196, wherein the biological sample comprises plasma, serum, or blood.

Embodiment 198. The composition of embodiment 196 or 197, wherein the biological sample comprises a plurality of proteins.

Embodiment 199. The composition of any one of embodiments 194-198, wherein at least 100 different biomolecules are adsorbed to the macromolecule structure.

Embodiment 200. The composition of any one of embodiments 194-199, wherein about 100 to about 1000 different proteins are adsorbed to the macromolecule structure.

Embodiment 201. The composition of any one of embodiments 194-200, wherein the biomolecule comprises a protein.

Embodiment 202. A method of identifying proteins in a sample, the method comprising:
(a) incubating one or more macromolecule structures of any one of embodiments 1-113 with a biological sample comprising biomolecules to form a biomolecule corona;
(b) isolating at least a portion of the biomolecules in the biomolecule corona; and
(c) assaying the biomolecule corona.

Embodiment 203. The method of embodiment 202, wherein the assaying is capable of identifying from 1 to 20,000 protein groups.

Embodiment 204. The method of embodiment 202 or 203, wherein the assaying is capable of identifying from 1000 to 10,000 protein groups.

Embodiment 205. The method of any one of embodiments 202-204, wherein the assaying is capable of identifying from 1,000 to 5,000 protein groups.

Embodiment 206. The method of any one of embodiments 202-205, wherein the assaying is capable of identifying from 1,200 to 2,200 protein groups.

Embodiment 207. The method of any one of embodiments 202-206, wherein the protein group comprises a peptide sequence having a minimum length of 7 amino acid residues.

Embodiment 208. The method of any one of embodiments 202-207, wherein the assaying is capable of identifying from 1,000 to 10,000 proteins.

Embodiment 209. The method of any one of embodiments 202-208, wherein the assaying is capable of identifying from 1,800 to 5,000 proteins.

Embodiment 210. The method of any one of embodiments 202-209, wherein the sample comprises a plurality of samples.

Embodiment 211. The method of any one of embodiments 202-210, wherein the plurality of samples comprises at least two or more spatially isolated samples.

Embodiment 212. The method of any one of embodiments 211, wherein the incubating comprises contacting the at least two or more spatially isolated samples with the one or more macromolecule structures at the same time.

Embodiment 213. The method of embodiment 211 or 212, wherein isolating comprises magnetically isolating the one or more macromolecule structures from unbound protein in the at least two or more spatially isolated samples of the plurality of samples at the same time.

Embodiment 214. The method of any one of embodiments 211-213, wherein the assaying comprises assaying a plurality of distinct biomolecule coronas to identify proteins in the at least two or more spatially isolated samples at the same time.

Embodiment 215. The method of any one of embodiments 202-214, further comprising repeating the wherein, when repeated, the incubating, isolating, and assaying yields a percent quantile normalized coefficient (QNCV) of variation of 20% or less, as determined by comparing a peptide mass spectrometry feature from at least three full-assay replicates for each macromolecule structure in the one or more macromolecule structures.

Embodiment 216. The method of any one of embodiments 202-215, wherein, when repeated, the incubating, isolating, and assaying yields a percent quantile normalized coefficient (QNCV) of variation of 10% or less, as determined by comparing a peptide mass spectrometry feature from at least three full-assay replicates for each macromolecule structure in the one or more macromolecule structures.

Embodiment 217. The method of any one of embodiments 202-216, wherein the assaying is capable of identifying proteins over a dynamic range of at least 6, at least 7, at least 8, at least 9, or at least 10.

Embodiment 218. The method of any one of embodiments 202-217, further comprising washing the one or more macromolecule structures at least one time or at least two times after isolating the one or more macromolecule structures from the unbound protein.

Embodiment 219. The method of any one of embodiments 202-218, wherein after the assaying the method further comprises lysing the proteins in the plurality of distinct biomolecule coronas.

Embodiment 220. The method of any one of embodiments 202-219, further comprising digesting the proteins in the plurality of distinct biomolecule coronas to generate digested peptides.

Embodiment 221. The method of any one of embodiments 202-220, further comprising purifying the digested peptides.

Embodiment 222. The method of any one of embodiments 202-221, wherein the assaying comprises using mass spectrometry to identify proteins in the sample.

Embodiment 223. The method of any one of embodiments 202-222, wherein the assaying is performed in about 2 to about 4 hours.

Embodiment 224. The method of any one of embodiments 202-223, wherein the method is performed in about 1 to about 20 hours.

Embodiment 225. The method of any one of embodiments 202-224, wherein the method is performed in about 2 to about 10 hours.

Embodiment 226. The method of any one of embodiments 202-225, wherein the method is performed in about 4 to about 6 hours.

Embodiment 227. The method of any one of embodiments 202-226, wherein the isolating takes no more than about 30 minutes, no more than about 15 minutes, no more than about 10 minutes, no more than about 5 minutes, or no more than about 2 minutes.

Embodiment 228. The method of any one of embodiments 202-227, wherein the plurality of samples comprises at least 10 spatially isolated samples, at least 50 spatially isolated samples, at least 100 spatially isolated samples, at least 150 spatially isolated samples, at least 200 spatially isolated samples, at least 250 spatially isolated samples, or at least 300 spatially isolated samples.

Embodiment 229. The method of any one of embodiments 202-228, wherein the plurality of samples comprises at least 96 samples.

Embodiment 230. The method of any one of embodiments 202-229, wherein the one or more macromolecule structures comprises at least 2 distinct macromolecule structures, at least 3 distinct macromolecule structures, at least 4 distinct macromolecule structures, at least 5 distinct macromolecule structures, at least 6 distinct macromolecule structures, at least 7 distinct macromolecule structures, at least 8 distinct macromolecule structures, at least 9 distinct macromolecule structures, at least 10 distinct macromolecule structures, at least 11 distinct macromolecule structures, at least 12 distinct macromolecule structures, at least 13 distinct macromolecule structures, at least 14 distinct macromolecule structures, at least 15 distinct macromolecule structures, at least 20 distinct macromolecule structures, at least 25 macromolecule structures, or at least 30 distinct macromolecule structures.

Embodiment 231. The method of any one of embodiments 202-230, wherein the one or more macromolecule structures comprises at least 10 distinct macromolecule structures.

Embodiment 232. The method of any one of embodiments 211-231, wherein the at least two spatially isolated samples differ by at least one physicochemical property.

Embodiment 233. The method of any one of embodiments 202-232, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure share at least one physicochemical property and differ by at least one physicochemical property, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different.

Embodiment 234. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure share at least two physicochemical properties and differ by at least two physicochemical properties, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different.

Embodiment 235. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure share at least one physicochemical property and differ by at least two physicochemical properties, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different.

Embodiment 236. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the

second distinct macromolecule structure share at least two physicochemical properties and differ by at least one physicochemical property, such that the first distinct macromolecule structure and the second distinct macromolecule structure are different.

Embodiment 237. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure comprise a carboxylate material, wherein the first distinct particle is a microparticle, and wherein the second distinct macromolecule structure is a nanoparticle.

Embodiment 238. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure comprise a surface charge of from 0 mV and -50 mV, wherein the first distinct macromolecule structure has a diameter of less than 200 nm, and wherein the second distinct macromolecule structure has a diameter of greater than 200 nm.

Embodiment 239. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure comprise a diameter of 100 to 400 nm, wherein the first distinct macromolecule structure has a positive surface change, and wherein the second distinct macromolecule structure has a neutral surface charge.

Embodiment 240. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure are nanoparticles, wherein the first distinct macromolecule structure has a surface charge less than -20 mV and the second distinct macromolecule structure has a surface charge greater than -20 mV.

Embodiment 241. The method of any one of embodiments 202-233, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure and a second distinct macromolecule structure, wherein the first distinct macromolecule structure and the second distinct macromolecule structure are microparticles, wherein the first distinct macromolecule structure has a negative surface charge, and wherein the second distinct macromolecule structure has a positive surface charge.

Embodiment 242. The method of any one of embodiments 202-241, wherein the one or more macromolecule structures comprises a subset of negatively charged nanoparticles, wherein each particle of the subset differ by at least one surface chemical group.

Embodiment 243. The method of any one of embodiments 202-242, wherein the one or more macromolecule structures comprises a first distinct macromolecule structure, a second particle, and a third distinct macromolecule structure, wherein the first distinct macromolecule structure, the second distinct macromolecule structure, and the third distinct macromolecule structure comprise iron oxide cores, polymer shells, and are less than about 500 nm in diameter and wherein the first distinct macromolecule structure comprises a negative charge, the second distinct macromolecule structure comprises a positive charge, and the third distinct macromolecule structure comprises a neutral charge, wherein the diameter is a mean diameter as measured by dynamic light scattering.

Embodiment 244. The method of any one of embodiments 202-243, wherein at least one distinct macromolecule structure of the one or more macromolecule structures is a nanoparticle.

Embodiment 245. The method of any one of embodiments 202-244, wherein at least one distinct macromolecule structure of the one or more macromolecule structures is a microparticle.

Embodiment 246. The method of any one of embodiments 202-245, wherein at least one distinct macromolecule structure of the one or more macromolecule structures is a superparamagnetic iron oxide particle.

Embodiment 247. The method of any one of embodiments 202-246, wherein each particle of the one or more macromolecule structures comprise an iron oxide material.

Embodiment 248. The method of any one of embodiments 202-247, wherein at least one distinct macromolecule structure of the one or more macromolecule structures has an iron oxide core.

Embodiment 249. The method of any one of embodiments 202-248, wherein at least one distinct macromolecule structure of the one or more macromolecule structures has iron oxide crystals embedded in a polystyrene core.

Embodiment 250. The method of any one of embodiments 202-249, wherein each distinct macromolecule structure of the one or more macromolecule structures is a superparamagnetic iron oxide particle.

Embodiment 251. The method of any one of embodiments 202-250, wherein each distinct macromolecule structure of the one or more macromolecule structures comprises an iron oxide core.

Embodiment 252. The method of any one of embodiments 202-251, wherein each one distinct macromolecule structure of the one or more macromolecule structures has iron oxide crystals embedded in a polystyrene core.

Embodiment 253. The method of any one of embodiments 202-252, wherein at least one distinct macromolecule structure of one or more macromolecule structures comprises a carboxylated polymer, an aminated polymer, a zwitterionic polymer, or any combination thereof.

Embodiment 254. The method of any one of embodiments 202-253, wherein at least one macromolecule structure of the one or more macromolecule structures comprises an iron oxide core with a silica shell coating.

Embodiment 255. The method of any one of embodiments 202-254, wherein at least one distinct macromolecule structure of the one or more macromolecule structures comprises a negative surface charge.

Embodiment 256. The method of any one of embodiments 202-255, wherein at least one distinct macromolecule structure of the one or more macromolecule structures comprises a positive surface charge.

Embodiment 257. The method of any one of embodiments 202-256, wherein at least one distinct macromolecule structure of the one or more macromolecule structures comprises a neutral surface charge.

Embodiment 258. A kit for identifying molecules in a biological sample, the kit comprising one or more macromolecule structures of embodiments 1-113.

Embodiment 259. The kit of embodiment 258, wherein the kit further comprises a lysing agent.

Embodiment 260. The kit of embodiment 258 or 259, wherein the kit further comprises a digestion agent.

Embodiment 261. The kit of any one of embodiments 258-260, wherein the kit further comprises a washing agent.

Embodiment 262. The kit of any one of embodiments 258-261, wherein the kit further comprises an elution buffer.

Embodiment 263. The kit of any one of embodiments 258-262, wherein the kit further comprises a solid support for solid-phase extraction.

Embodiment 264. The kit of any one of embodiments 258-263, wherein the kit further comprises a multi-well plate.

Embodiment 265. The kit of any one of embodiments 258-264, wherein the kit further comprises a diluent.

Embodiment 266. A system for identifying biomolecules in a biological sample, the system comprising:

(a) a macromolecule structure of any one of embodiments 1-113;

(b) a suspension solution;

(c) a biological sample comprising a concentration of proteins; and

(d) an automated system comprising a network of units with differentiated functions for isolating biomolecules adsorbed to the macromolecular structure, and wherein the automated system is programmed to perform a series of steps.

Embodiment 267. The system of embodiment 266, wherein the network of units comprises:

(a) a first unit comprising a multichannel fluid transfer instrument for transferring fluids between units within the system;

(b) a second unit comprising a support for storing a plurality of biological samples;

(c) a third unit comprising a support for a sensor array plate possessing partitions that comprise the macromolecular structure for a binding interaction with a population of analytes from the biological sample;

(d) a fourth unit comprising supports for storing a plurality of reagents;

(e) a fifth unit comprising supports for storing a reagent to be disposed of; and

(f) a sixth unit comprising supports for storing consumables used by the multichannel fluid transfer instrument.

Embodiment 268. The system of embodiment 266 or 267, wherein the series of steps comprises:

(a) contacting the biological sample with a specified partition of the sensor array;

(b) incubating the biological sample with the macromolecular structure contained within the partition of the sensor array plate;

(c) removing a supernatant from the sensor array plate; and

(d) preparing biomolecules adsorbed to the macromolecular structure for mass spectrometry.

Embodiment 269. The system of any one of embodiments 266-268, wherein i.-iii. are incubated at a temperature of about 20 degrees Celsius to about 80 degrees Celsius.

Embodiment 270. The system of any one of embodiments 266-269, wherein the suspension solution comprises Tris EDTA 150 mM KCl, 0.05% CHAPS buffer.

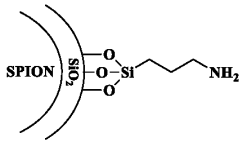
Embodiment 271. The system of any one of embodiments 266-270, wherein the suspension solution comprises 10 mM Tris HCl pH 7.4, 1 mM EDTA.

[00313] While preferred embodiments of the present disclosure have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in

the art without departing from the disclosure. It should be understood that various alternatives to the embodiments of the disclosure described herein may be employed in practicing the disclosure. It is intended that the following claims define the scope of the disclosure and that methods and structures within the scope of these claims and their equivalents be covered thereby.

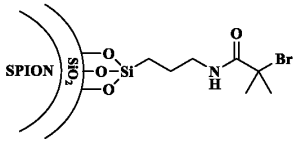
EXAMPLES

Example 1: Synthesis of SPION@SiO_2-APTES



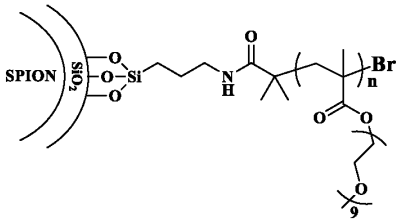
[00314] Silica coated super paramagnetic iron oxide nanoparticles (SPION@SiO_2) were suspended in DMF and sonicated for 15 minutes. The nanoparticle solution was purged with N_2 gas for 20 minutes and the particle solution was heated to 120°C for 4 hours. After cooling, the SPION@SiO_2 were washed with DMF 3 times, then isolated. The isolated particles were dispersed in N,N-dimethylacetamide (DMAc) (2 L). To the solution, 4.50 g of (3-aminopropyltriethoxysilane) (APTES) was added and the resulting solution was reacted at 120°C for 4 hours to obtain the SPION@SiO_2-APTES product.

Example 2: Synthesis of SPION@SiO_2-APTES-Br



[00315] SPION@SiO_2-APTES in DMF was washed two times with tetrahydrofuran (THF) then resuspended in THF (801 mL) with sonication for 15 minutes. In an ice bath (0°C), under N_2, triethylamine (10.40 g) was added. After addition of the triethylamine, 2-bromoisobutyryl bromide (2.509 g) was added dropwise at 0°C. The reaction was stirred overnight at room temperature (16 hours). The resulting material was washed 1 time with THF, 1 time with ethanol, 1 time with water, and then 1 time with THF. The final product was dried with N_2.

Example 3: Synthesis of Compound 2, SPION@SiO_2-SIP-POEGMA



[00316] Initiator particle SPION@SiO_2-APTES-Br (1.000 g), $CuBr_2$ (0.010 g), N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA) (0.240 g), monomer Oligo(ethylene glycol) Methyl Ether Methacrylate (OEGMA, MW500) (5.000 g) and 25 mL of dimethylformamide (DMF) were added in a 3-neck flask. The mixture was sonicated for 15 min and purged with N_2 for another 15 min. Separately, 0.500 g of L-ascorbic acid was dissolved in 10 mL of DMF and purged with N_2 for at least 15 minutes. The mixture containing the monomer and nanoparticle suspension was heated to 35°C under N_2 and the L-ascorbic acid solution was added via syringe pump at 0.05 mL/min. The reaction mixture was maintained at 35°C for 16 hours to obtain Compound 2.

Example 4: Characterization of Macromolecule Structures

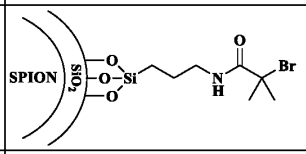
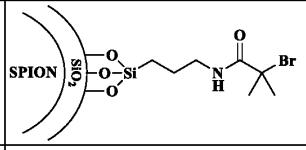
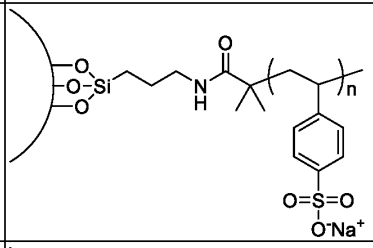
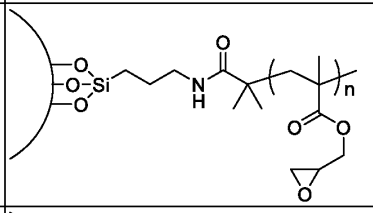
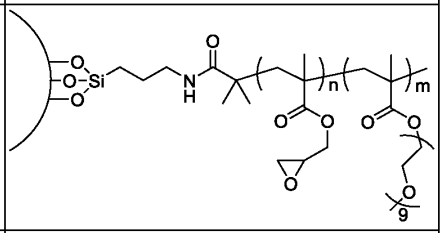
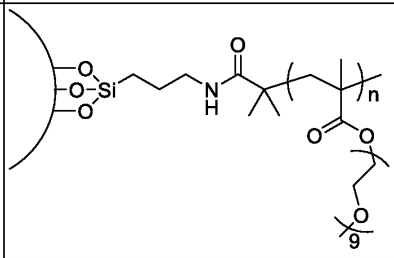
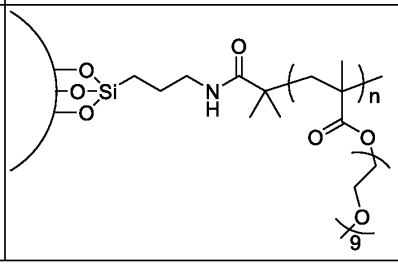
[00317] Compounds 1-3 were synthesized according to modified versions of the syntheses described in Examples 1-3 and the scheme depicted in **FIG. 1**. An exemplary synthetic scheme for Compound 1 is shown in **FIG. 4**. An exemplary synthetic scheme for Compound 2 is shown in **FIG. 5**. An exemplary synthetic scheme for Compound 3 is shown in **FIG. 6**. The particle size was characterized by DLS, surface charge by zeta potential, and macromolecule chain% by TGA (weight loss%). The particle sizes were compared to the particle sizes before functionalization with the macromolecule chains. The resulting data is found in **Table 4**.

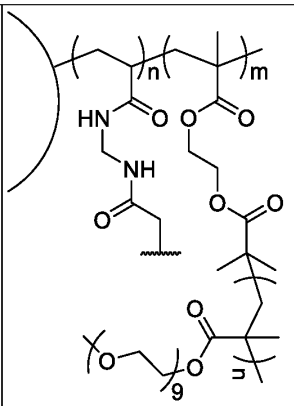
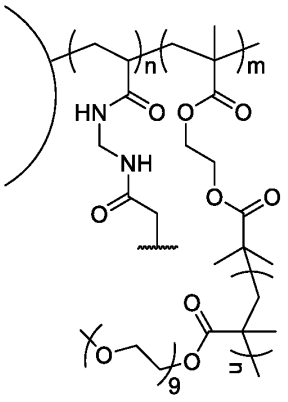
Table 4

Compound No.	Diameter (nm)	PDI	Zeta (mV)	Weight Loss (%)	SPION diameter (nm)	SPION@SiO_2 diameter (nm)
1	1082.7	0.096	2.2	40.1	195	251
1	531.1	0.057	0.4	31.7	195	251
2	459.4	0.054	1.1	15.9	195	251
2	447.8	0.141	3.0	12.7	195	251
2	633.6	0.183	0.4	11.3	248	297
2	477.7	0.158	0.4	15.0	232	276
2	575.3	0.155	-0.4	12.3	248	295
3	408.9	0.037	-0.2	12.6	195	251
3	556.3	0.143	-0.3	11.6	248	295

[00318] Compounds 5, 6, and 7 were also synthesized using the general procedures of Examples 1-3. Compound 1, 2, 5, 6, and 7 were analyzed by thermogravimetric analysis for the % organics. The results of which are in **Table 5**. The % organics in the particles ranged from 9.14% to 15.88%, increased from the % organics found on the initiator surface before further functionalization.

Table 5

Compound	Weight Loss %	Polymer Structure
Initiator Surface	7.99	
Initiator Surface	7.95	
5	9.14	
6	12.55	
7	13.27	
2	15.88	
2	12.6	

1	40.1	
1	31.7	

[00319] Scanning electron microscopy (SEM) images of compounds 2, 5, 6, and 7 are shown in **FIG. 3A**. Compound 5 has a size of 296 nm by SEM, Compound 6 has a size of 230 nm by SEM, Compound 2 has a size of 311 nm by SEM, and Compound 7 has a size of 302 nm by SEM. **FIG. 3B** shows transmission electron microscopy images of compound 2, highlighting the polymer brush formed on the surface of the particle.

CLAIMS

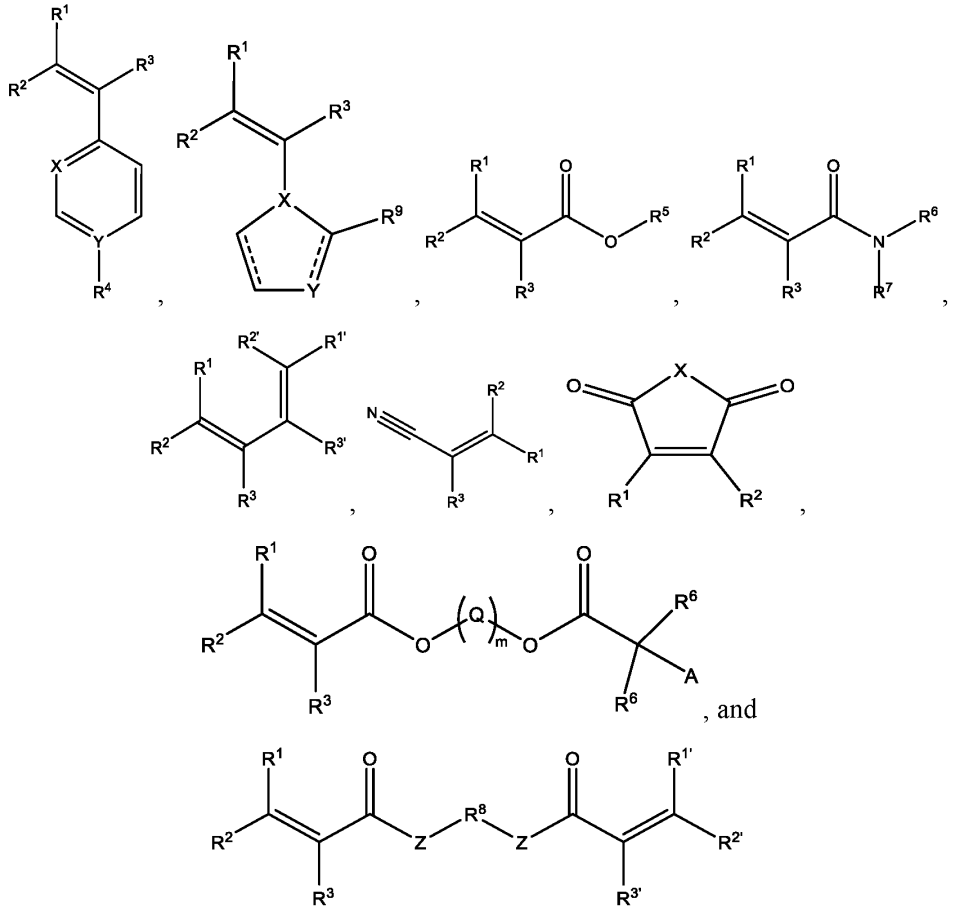
We claim:

1. A macromolecule structure comprising:

(I) a surface;

(II) a tethering moiety coupled to the surface; and

(III) a macromolecule chain, wherein a first end of the macromolecule chain is covalently attached to the tethering moiety, and wherein the macromolecule chain comprises two or more distinct recurring units derived from a monomer represented by a structure selected from the group consisting of:



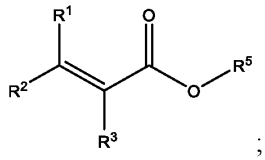
, and

wherein each of X and Y is independently -C-, -O-, or -N-;

each Z is independently -O- or -NH-;

Q is $-CH_2-$ or ethylene glycol;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by the structure:



;

m is an integer selected from 1-20;

=== is a single or double bond;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or -C_1-C_6 alkyl;

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, sulfonate, carboxylate, C_1-C_4 alkylene, amine, quaternary ammonium cation, or C_1-C_6 alkyl optionally substituted with halogen;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further optionally substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further optionally substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted, optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne;

R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide;

R^9 is hydrogen or oxo; and

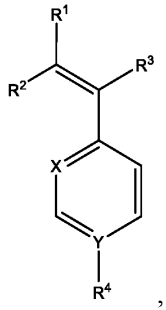
n^1 is an integer selected from 1-100.

2. The macromolecule structure of claim 1, wherein R^3 is methyl.
3. The macromolecule structure of claim 2, wherein R^5 is C_1-C_{n1} ethylene glycol.
4. A macromolecule structure comprising:

(I) a surface;

(II) a tethering moiety coupled to the surface; and

(III) a macromolecule chain, wherein a first end of the macromolecule chain is covalently attached to the tethering moiety, and wherein the macromolecule chain comprises a recurring unit derived from a monomer represented by a structure selected from the group consisting of: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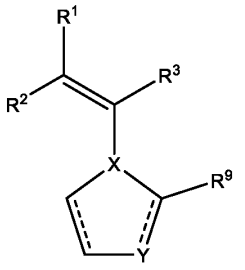
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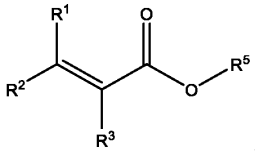
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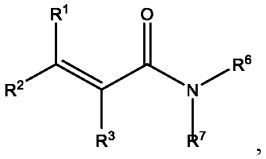
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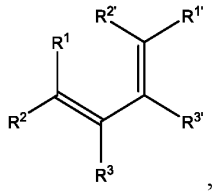
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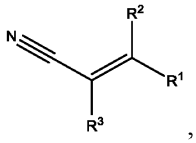
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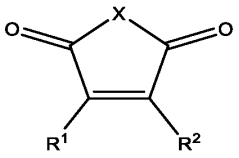
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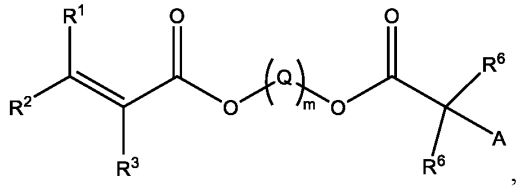
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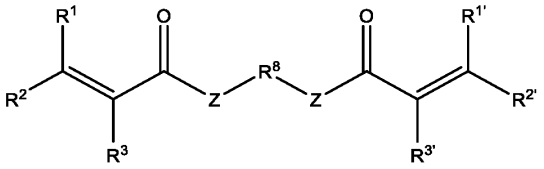
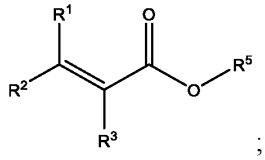

and

wherein each of X and Y is independently -C-, -O-, or -N-;

each Z is independently -O- or -NH;

Q is -CH_2- or ethylene glycol;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by the structure:


;

m is 1-6;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or C_1-C_6 alkyl

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, C_1-C_6 alkyl optionally substituted with halogen, C_1-C_4 alkylene, C_1-C_6 alkyl, sulfonate, amine, quaternary ammonium cation, or carboxylate;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or linear C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, or C_1-C_4 alkylyne; and

R^8 is C_1-C_6 alkyl, or symmetric or asymmetric disulfide;

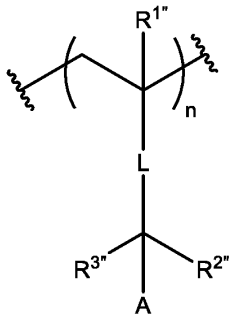
R^9 is hydrogen or oxo;

n^1 is an integer selected from 1-100; and

provided that when R^3 is CH_3, R^4 is CH_3, or when R^5 is C_1-C_8 alkyl substituted with hydroxyl, C_1-C_8 is further substituted.

5. A macromolecule structure comprising:

(I) a surface and (II) a macromolecule chain coupled to the surface, wherein the macromolecule chain comprises a recurring unit of Formula (I):

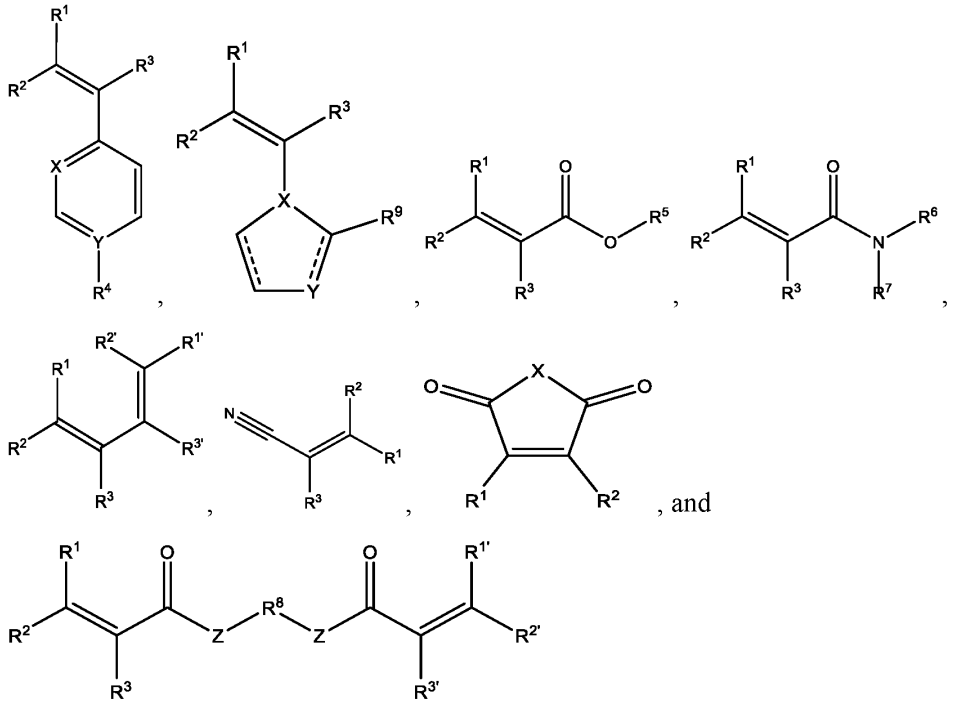


(I)

wherein each of $R^{1"}$, $R^{2"}$, and $R^{3"}$ is independently hydrogen or C_1-C_6 alkyl;

L is a linker moiety;

A is a polymeric side chain comprising a recurring unit derived from a monomer represented by a structure selected from the group consisting of:



wherein each of X and Y is independently -C-, -O-, or -N-;

Z is -O- or -NH;

each of R^1, R^2, $R^{1'}$, $R^{2'}$, and $R^{3'}$ is independently selected from hydrogen or C_1-C_6 alkyl;

R^3 is hydrogen, C_1-C_6 alkyl, or 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl;

R^4 is absent, hydrogen, sulfonate, carboxylate, C_1-C_4 alkylene, amine, quaternary ammonium cation, or C_1-C_6 alkyl optionally substituted with halogen;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_8 alkyl substituted with one or more hydroxyl, amine, azide, sulfonate, carbamate ester, asymmetrical disulfide, 3-, 5-, or 6-membered

heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, or C_1-C_{n1} ethylene glycol, C_1-C_8 alkylamine further substituted with amine, hydroxyl, aryl, or sulfonate, C_1-C_8 alkoxy optionally substituted with one or more oxo or halogen, -C_1-C_3 alkyl optionally substituted with one or more pyrene, 2 or more fused 5-6 membered rings further optionally substituted (e.g., with 2 or more fused 6 membered rings further optionally substituted), optionally substituted benzyl, trimethoxysilane, or phosphorocholine, C_1-C_{12} alkylamine, or C_1-C_4 alkylyne;

R^6 is hydrogen or linear C_1-C_6 alkyl,

R^7 is hydrogen, C_1-C_6 alkyl, 3-, 5-, or 6-membered heterocycle optionally substituted with one or more C_1-C_6 alkyl or oxo, substituted benzene, C_1-C_6 alkyl substituted with hydroxyl, optionally substituted C_1-C_8 alkyl sulfonate;

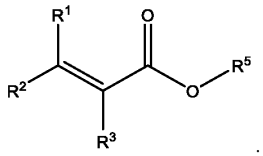
R^8 is C_1-C_6 alkyl, divalent metal, or symmetric or asymmetric disulfide;

R^9 is hydrogen or oxo;

n^1 is an integer selected from 1-100; and

n is an integer selected from 1-10,000.

6. The macromolecule structure of any one of claims 1-5, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by the structure:



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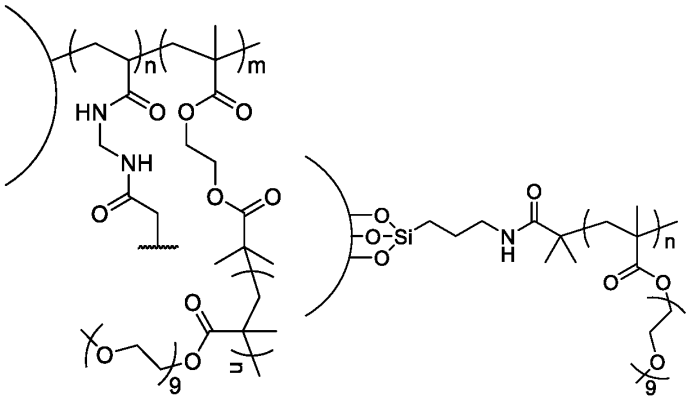
7. The macromolecule structure of any one of claims 1-6, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by a structure of **Table 1**.
8. The macromolecule structure of any one of claims 1-7, wherein the macromolecule chain comprises the recurring unit derived from a monomer represented by a structure of **Table 2**.
9. The macromolecule structure of any one of claims 1-8, wherein the macromolecule structure has a structure represented by:



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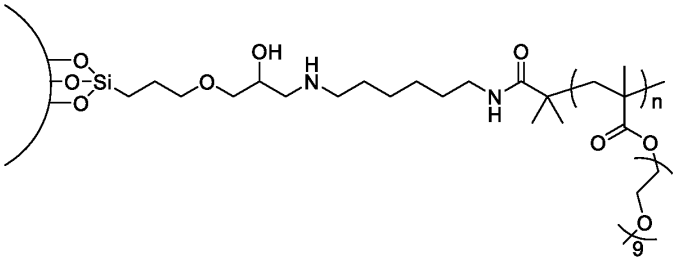

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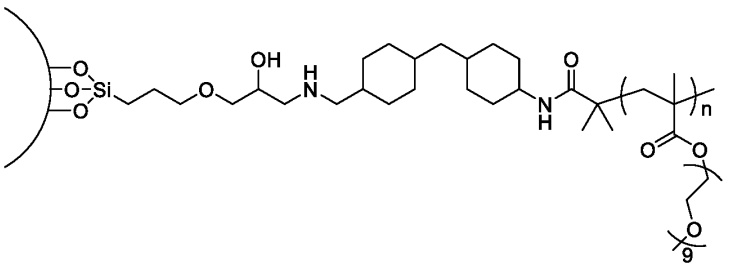

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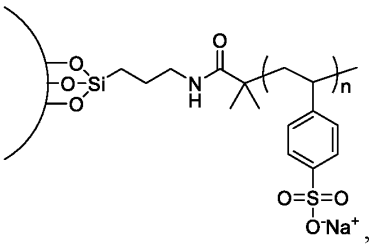

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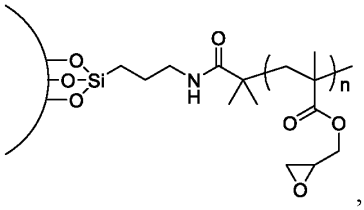
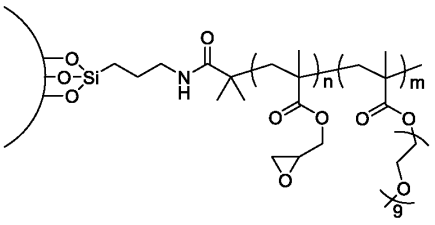


, or



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10. A method of making a macromolecule structure of any one of claims 1-9, the method comprising:

(a) providing a surface;

(b) coupling a polymer initiator to the surface to form an initiator surface; and

(c) contacting the initiator surface with a monomer of any one of claims 7-8 to form the macromolecule structure.

11. The method of claim 10, wherein the surface comprises a particle.

12. The method of claim 11, wherein the particle comprises a diameter of about 100 nm to about 500 nm.

13. A method of making a macromolecule structure of any of claims 1-9, the method comprising:

(a) providing a surface;

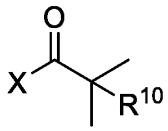
(b) coupling a vinyl group to the surface to form a vinyl-functionalized surface;

(c) contacting the vinyl-functionalized surface with a cross-linking monomer and a monomer selected from hydroxyalkyl methacrylate, aminoalkyl methacrylate, alkynyl methacrylate, glycidylalkyl methacrylate, hydroxyalkyl acrylate, aminoalkyl acrylate, alkynyl acrylate or glycidylalkyl acrylate to form a cross-linked polymer coupled to the surface;

(d) coupling a polymer initiator to the cross-linked polymer to form an initiator surface; and

(e) contacting the initiator surface with a monomer of any one of claims 7-8 to form the macromolecule structure.

14. The method of claim 13, wherein the polymer initiator is represented by the structure:



wherein:

X is a halogen; and

R^{10} is an initiator group.

15. A composition comprising a macromolecule structure of any one of claims 1-14 and a biomolecule adsorbed to the macromolecule structure.

16. The composition of claim 15, wherein at least 100 different biomolecules are adsorbed to the macromolecule structure.

17. A method of identifying proteins in a sample, the method comprising:

(a) incubating one or more macromolecule structures of any one of claims 1-9 with a biological sample comprising biomolecules to form a biomolecule corona;

(b) isolating at least a portion of the biomolecules in the biomolecule corona; and

(c) assaying the biomolecule corona.

18. The method of claim 17, wherein the assaying is capable of identifying from 1 to 20,000 protein groups.

19. A kit for identifying molecules in a biological sample, the kit comprising one or more macromolecule structures of any one of claims 1-9.

20. A system for identifying biomolecules in a biological sample, the system comprising:

(a) a macromolecule structure of any one of claims 1-9;

(b) a suspension solution;

(c) a biological sample comprising a concentration of proteins; and

(d) an automated system comprising a network of units with differentiated functions for isolating biomolecules adsorbed to the macromolecular structure, and wherein the automated system is programmed to perform a series of steps.