DETECTABLE ARRAYS, SYSTEMS FOR DIAGNOSIS, AND METHODS OF MAKING AND USING THE SAME

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application No. 61/881,754, filed September 24, 2013, which is incorporated by reference herein in its entirety.

BACKGROUND

[0002] Detectable arrays can bind or immobilize an analyte on a solid support for detecting the presence, absence, or concentration of the analyte. Typically, detectable arrays are limited to selectively binding a single analyte or a single type of analyte. For example, a detectable array may contain a plurality of DNA sequence probes for binding to DNA having sequences complementary to the sequences of the probes. In another example, arrays can include a plurality of potential ligand receptors for selectively binding to a ligand of interest.

[0003] The application of such prior-art arrays is limited. For example, because environmental samples may contain multiple analytes of interest, more than one array may be needed to bind and detect the presence of analytes. Further, while known arrays are specific for one analyte or one type of analyte, disease states of subjects may be characterized by the presence or absence of more than one analyte. Thus, there is a need for a detectable array that can both bind and detect multiple analytes, as well as methods of diagnosing using such detectable arrays.

SUMMARY ~~OF INVENTION~~

[0003a] In an aspect of the present disclosure, there is provided a label-free method of detecting an unlabeled analyte on a detectable array,

said detectable array comprising:

a substrate with a plurality of surfaces for binding one or more analytes, each surface independently comprising:

one or more substrate coatings on the surface for fixing one or more macromolecules to the surface of the substrate, said one or more substrate coatings comprising at least one silane or at least one siloxane; and

one or more macromolecules affixed to at least a portion of the one or more substrate coatings, the one or more macromolecules being arranged in a pattern on the substrate coating and comprising a plurality of binding sites for binding a plurality of analytes;

wherein each macromolecule has been affixed to the substrate coating by polymerizing a functional group on the silane or siloxane into the macromolecule backbone;

wherein each macromolecule comprises a polymer of monomers selected from a group consisting of acrylamide; 2-carboxyethyl acrylate; acrylic acid; N-[tris(hydroxymethyl)methy] acrylamide; hydroxypropyl acrylates; 4-hydroxybutyl acrylate; N-hydroxyethyl acrylamide; N,N-dimethylacrylamide; N-(1,1-dimethyl-3-oxobutyl) acrylamide; N-iso-propylacrylamide; (meth)acrylates; 2-cyanoethyl acrylate; ethylene glycol phenyl ether acrylate; N-tert-octylacrylamide; 1-(acryloyloxy)-3-(methacryloyloxy)-2-propanol; bis-acrylamide; trimethylolpropane triacrylate, and combinations thereof; and

wherein the identity, pattern, or both identity and pattern of the one or more macromolecules on the one or more substrate coatings of each of the plurality of surfaces is not identical to the identity, pattern, or both identity and pattern of the one or more macromolecules on any other substrate coating of any other of the plurality of surfaces;

said label-free method comprising:

contacting the unlabeled analyte with the detectable array to affix at least a portion of the analyte to the detectable array; and

heating the detectable array with the unlabeled analyte affixed thereto to cause a color change of at least one of the analyte and the detectable array, wherein the heating induces a non-enzymatic browning reaction, and wherein the heating comprises heating at a temperature of about 120°C to about 300°C for about 1 minute to about 5 minutes; and

assessing the color of each of the plurality of surfaces of the substrate by colorimetric analytical technique.

[0004] In one ~~embodiment~~example, a detectable array can comprise a substrate with a plurality of surface for binding one or more analytes, each surface independently comprising one or more substrate coatings for fixing one or more macromolecules to the surface of the substrate and one or more macromolecules affixed to at least a portion of the one or more substrate coatings, the one or more macromolecules being arranged in a pattern on the substrate coating and comprising a plurality of unbiased binding sites for binding a plurality of analytes, wherein the identity, pattern, or both identity and pattern of the one or more macromolecules on the one or more substrate coatings on each of the plurality of surfaces is not identical to the identity, pattern, or both identity and pattern of the one or more macromolecules on any other substrate coating of any other of the plurality of surfaces and

wherein the presence or absence of one or more analytes bound to each of the plurality of surfaces is detectable by a plurality of detection methods

[0005] In another ~~embodiment~~example, the one or more substrate coatings comprises at least one silane or at least one siloxane, for example, acrylosiloxanes, particularly one or more of 3-methacryloxypropyl trimethoxy silane, 3-acryloxypropyl trimethoxy silane, N-(3-acryloxy-2-hydroxypropyl-3-aminopropyltriethoxysilane, and 3-methacryloxy propyldimethylchlorosilane. In yet another ~~embodiment~~example, the one or more macromolecules comprises one or more of polymers, surfactants, nanospheres, nanotubes, dendrimers, microspheres, and polymerized microspheres, for example, one or more of (meth)acrylamides, (meth)acrylates, glycerol, and N,N'(alkylene)bisacrylamide. In still another ~~embodiment~~example, the one or more macromolecules comprise at least one copolymer. In another ~~embodiment~~example, the one or more macromolecules comprise one or more monomers, or two or more monomers, selected from the group consisting of 2-carboxyethyl acrylate, acrylic acid, acrylamide, histamine acrylate, N-[tris(hydroxymethyl)methyl]acrylamide, hydroxypropyl acrylates, 4-hydroybutyl acrylate, N-hydroxyethyl acrylamide, N,N,-dimethylacrylamide, N-(1,1-diemthyl-3-oxobutyl)acrylamide, N-isopropylacrylamide, ethylene glycol phenyl ether acrylate, N,N'-methylenebisacrylamide, 1,1,3,3,3-Hexafluoroisopropyl acrylate, and N-*tert*-octylacrylamide. In a further ~~embodiment~~example, the one or more macromolecules comprise one or more cross-linkers, such as at least one of bis-acrylamide, trimethylolpropane triacrylate, bisphenol A-bis(2-hydrxypropyl)acrylate, and 1-(acryloyloxy)-3-(methacryloyloxy)-3-methacryloyloxy)-2-propanol. In a further ~~embodiment~~example, the one or more macromolecules comprise a plurality of chemically distinct macromolecules, wherein each chemically distinct macromolecule is affixed to a different surface of the plurality of surfaces of the array. In additional ~~embodiment~~examples, the one or macromolecules comprise at least 2, at least 12, at least 72, at least 96, or at least 288 chemically distinct macromolecules.

[0006] In another ~~embodiment~~example, the plurality of detection methods includes one or more of Maillard reaction, caramelizing reaction with one or more amine reactive dyes, reaction with one or more thiol reactive dyes, reaction with one or more cellular dyes, reaction with one or more solvatochromic dyes, reaction with one or more acid indicators, reaction with one or more base indicators, reaction with one or more labeled antibodies, luminescence, surface texture analysis, photo-scanning, microscopy, photo-scanning with reflectance or transmittance illumination, photography with reflectance or transmittance illumination, mass spectrometry and spectroscopy.

[0007] In an additional ~~embodiment~~example, the substrate is glass.

[0008] In an additional ~~embodiment~~example, the substrate comprises one or more of glass, plastic, metal, composites, acrylics, or biologically active substrates, *e.g.*, wood.

[0009] In another additional ~~embodiment~~example, one or more analytes are bound to the one or more macromolecules. In a further additional ~~embodiment~~example, the detectable array further comprises one or more small molecules, proteins, peptides, nucleotides, nucleosides, bacteria, viruses, fungi cells, animal cells, or yeast cells bound to the one or more macromolecules.

[0010] In a further ~~embodiment~~example a system for diagnosing a disease, disorder or condition can comprise an input element for receiving one or more images of a first detectable array or a representation thereof, wherein the first detectable array is any of the aforementioned first detectable arrays, a database comprising one or more images of a plurality of second detectable arrays or representations thereof, wherein the second detectable array is any of the aforementioned first detectable arrays, and a comparison element for comparing the one or more images of the first detectable array or a representation thereof with the one or more images of a plurality of second detectable arrays or representations thereof. In a yet further ~~embodiment~~example, each of the images of the plurality of second detectable arrays or representations thereof are associated with a subject, an in-vitro sample, or an environmental sample having a known disease, disorder, or condition. In a still further ~~embodiment~~example, the first detectable array or representation thereof is associated with a subject, in-vitro sample, or condition having an unknown disease, disorder, or condition state. In a yet further ~~embodiment~~example, the comparison element of the system is capable of predicting a disease state of a subject, an in-vitro sample, or an environmental sample having an unknown disease state. In another further ~~embodiment~~example, the one or more images of the first detectable array or representation thereof are false color images. In still another further ~~embodiment~~example, the one or more images of the first detectable array or representation thereof represent one or more of fluorescence, phosphorescence, texture, roughness, color, ultraviolet absorption, infrared absorption, or lack of one or more of the foregoing, of the plurality of surfaces of the substrate.

[0011] In an ~~embodiment~~example, a method of determining disease, disorder, or condition state in a subject, in-vitro sample, or environmental sample comprises contacting a first detectable array, such as any of the arrays disclosed herein, with one or more analytes associated with the subject, in-vitro sample, or environmental sample. In another ~~embodiment~~example, the contacting step comprises contacting the first detectable array with one or more body samples of the subject. In a further ~~embodiment~~example, the contacting step includes contacting at least one of

blood, serum, plasma, urine, stool, saliva, bile, spinal fluid, interstitial fluid, gastric juice, tears, solvent, and milk of the subject, in-vitro sample, or environmental sample. In yet another ~~embodiment~~example, the contacting step comprises contacting the first detectable array with one or more of plasma and urine of the subject.

[0012] In a still further ~~embodiment~~example, the method further comprises obtaining the one or more analytes associated with the subject. In another further ~~embodiment~~example, the method further comprises detecting the one or more analytes associated with the subject, in-vitro sample, or environmental sample. In yet another ~~embodiment~~example, the method further comprises making one or more images of the detectable array or one or more representations thereof.

[0013] In yet another further ~~embodiment~~example, the method comprises one or more of heating the detectable array, causing a Maillard reaction of at least one of the one or more analytes, caramelizing at least one of the one or more analytes, reacting at least of the one or more analytes with one or more amine reactive dyes, reacting at least one of the one or more analytes with one or more thiol reactive dyes, reacting at least of the one or more analytes with one or more solvatochromic dyes, reacting at least one of the one or more analytes with one or more cellular dyes, reacting at least one of the one or more analytes with one or more labeled antibodies, reacting at least of the one or more analytes with one or more acid indicators, reacting at least of the one or more analytes with one or more base indicators, detecting the luminescence or lack thereof of the detectable array, surface texture analysis, photo-scanning, microscopy, photo-scanning with reflectance or transmittance illumination, photography with reflectance or transmittance illumination, mass spectrometry and spectroscopy.

[0014] In an ~~embodiment~~example, a method of making a detectable array, such as any of the detectable arrays described herein, comprises independently contacting the plurality of surfaces with at least one substrate coating to form a plurality of independently coated surfaces, and independently affixing at least one macromolecule or one or more precursors thereof to each of the independently coated surfaces. In a further ~~embodiment~~example, the method further comprises polymerizing at least one of the one or more precursors thereof on at least one of the independently coated surfaces. In another ~~embodiment~~example, the method includes initiating polymerization of at least one of the at least one precursors by applying one or more of light, heat, or a chemical initiator to the one or more precursors. In another ~~embodiment~~example, the method comprises initiating polymerization of at least one of the one or more precursors by applying one or more of electromagnetic radiation (*e.g.*, microwaves, ultraviolet light, visible light, heat), sound or a chemical initiator to the one or more precursors.

[0015] In another ~~embodiment~~example, a label-free method of detecting an unlabeled analyte comprises contacting the unlabeled analyte with a detectable array to affix at least a portion of the analyte to the detectable array and heating the detectable array with unlabeled analye affixed thereto to cause a color change of at least one of the analyte and the detectable array. In a further ~~embodiment~~example, the detectable array includes at least one array selected from the group consisting of an analytical microarray, a reverse-phase micro assay, a functional microarray, a cell-containing microarray, an expression microarray, and a high-throughput array. In a still further ~~embodiment~~example, the detectable array includes at least one array selected from the group consisting of an antibody array, and ELISA array, a peptide array, a protein array, a nucleotide array, a nucleoside array, an RNA array, a DNA array, a DNA-protein array, and a small molecule array. In a yet further ~~embodiment~~example, the unlabeled analyte is one or more of a body sample of a subject, an in-vitro sample, a environmental sample, and at least one component of one of the foregoing. In another further ~~embodiment~~example, the unlabeled analyte is at least one component of blood, serum, plasma, urine, stool, saliva, bile, spinal fluid, interstitial fluid, gastric juice, tears, solvent, and milk. In still another further ~~embodiment~~example, the heating induces a non-enzymatic browning reaction. In yet another further ~~embodiment~~example, the non-enzymatic browning reaction is at least one of a Maillard reaction and caramelization. In another ~~embodiment~~example, heating comprises heating at a sufficient temperature and for a sufficient time to induce one or more of caramelization and a Maillard reaction. In yet another ~~embodiment~~example, heating comprises heating at a temperature of about 120° C to about 300° C for about 1 minute to about 5 minutes.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] Figure 1 is a schematic drawing of a system for diagnosing a subject, in-vitro sample, or environmental sample.

[0017] Figure 2 is a detectable array with bound proteins.

[0018] Figure 3 is a detectable array with bound yeast cells.

[0019] Figure 4 is a detectable array with bound small molecules.

DETAILED DESCRIPTION

Definitions

[0020] Unless otherwise defined herein, all terms used in this Application are to be afforded their usual meaning in the art, as they would be understood by a person of ordinary skill at the time of the invention. It should be understood that throughout this application singular forms, such as “a,” “an,” and “the” are often used for convenience; however, singular forms

We claim:

1. A label-free method of detecting an unlabeled analyte on a detectable array,

said detectable array comprising:

a substrate with a plurality of surfaces for binding one or more analytes, each surface independently comprising:

one or more substrate coatings on the surface for fixing one or more macromolecules to the surface of the substrate, said one or more substrate coatings comprising at least one silane or at least one siloxane; and ~~; and~~

one or more macromolecules affixed to at least a portion of the one or more substrate coatings, the one or more macromolecules being arranged in a pattern on the substrate coating and comprising a plurality of ~~unbiased~~ binding sites for binding a plurality of analytes;

wherein each macromolecule has been affixed to the substrate coating by polymerizing a functional group on the silane or siloxane into the macromolecule backbone;

wherein each macromolecule comprises a polymer of monomers selected from a group consisting of acrylamide; 2-carboxyethyl acrylate; acrylic acid; N-[tris(hydroxymethyl)methy] acrylamide; hydroxypropyl acrylates; 4-hydroxybutyl acrylate; N-hydroxyethyl acrylamide; N,N-dimethylacrylamide; N-(1,1-dimethyl-3-oxobutyl) acrylamide; N-iso-propylacrylamide; (meth)acrylates; 2-cyanoethyl acrylate; ethylene glycol phenyl ether acrylate; N-tert-octylacrylamide; 1-(acryloyloxy)-3-(methacryloyloxy)-2-propanol; bis-acrylamide; trimethylolpropane triacrylate, and combinations thereof; and

wherein the identity, pattern, or both identity and pattern of the one or more macromolecules on the one or more substrate coatings of each of the plurality of surfaces is not identical to the identity, pattern, or both identity and pattern of the one or more macromolecules on any other substrate coating of any other of the plurality of surfaces; ~~and~~

said label-free method comprising:

contacting the unlabeled analyte with the detectable array to affix at least a portion of the analyte to the detectable array; and

heating the detectable array with the unlabeled analyte affixed thereto to cause a color change of at least one of the analyte and the detectable array, wherein the heating induces a non-enzymatic browning reaction, and wherein the heating comprises heating at a temperature of about 120°C to about 300°C for about 1 minute to about 5 minutes; and

assessing the color of each of the plurality of surfaces of the substrate by colorimetric analytical technique.

~~wherein the presence or absence of one or more analytes bound to each of the plurality of surfaces is detectable by a plurality of detection methods.~~

2. The method ~~detectable array~~ of claim 1, wherein the non-enzymatic browning reaction is~~one or more substrate coatings comprise~~ at least one of a Maillard reaction and caramelization. ~~silane or at least one siloxane.~~

3. The method~~detectable array~~ of claim~~any of claims~~ 1 or 2, wherein the one or more substrate coatings comprise one or more acrylosiloxanes.

4. The method ~~detectable array~~ of any of claims 1-3, wherein the one or more substrate coatings comprise one or more of 3-methacryloxypropyl trimethoxy silane, 3-acryloxypropyl trimethoxy silane, N-(3-acryloxy-2-hydroxypropyl-3-aminopropyltriethoxysilane, and 3-methacryloxy-propyl dimethylchlorosilane.

~~5. The detectable array of any of claims 1-4, wherein the one or more macromolecules comprise one or more of polymers, surfactants, nanospheres, nanotubes, dendrimers, microspheres, and polymerized microspheres.~~

~~6. The detectable array of any of claims 1-5, wherein the one or more macromolecules comprise one or more of (meth)acrylamides, (meth)acrylates, glycerol, and N,N'(alkylene)bisacrylamide.~~

~~7. The detectable array of any of claims 1-6, wherein the one or more macromolecules comprise at least one copolymer.~~

~~8. The detectable array of any of claims 1-7, wherein the one or more macromolecules comprise one or more monomers selected from the group consisting of 2-carboxyethyl acrylate, acrylic acid, acrylamide, histamine acrylate, N-[tris(hydroxymethyl)methyl]acrylamide, hydroxypropyl acrylates, 4-hydroybutyl acrylate, N-hydroxyethyl acrylamide, N,N,-dimethylacrylamide, N-(1,1-diemthyl-3-oxobutyl)acrylamide, N-isopropylacrylamide, ethylene glycol phenyl ether acrylate, N,N'-methylenebisacrylamide, 1,1,3,3,3-Hexafluoroisopropyl acrylate, and N-*tert*-octylacrylamide.~~

~~9. The detectable array of any of claims 1-8, wherein the one or more macromolecules comprise two or more monomers selected from the group consisting of2-carboxyethyl acrylate, acrylic acid, acrylamide, histamine acrylate, N-[tris(hydroxymethyl)methyl]acrylamide, hydroxypropyl acrylates, 4-hydroybutyl acrylate, N-hydroxyethyl acrylamide, N,N,-dimethylacrylamide, N-(1,1-diemthyl-3-oxobutyl)acrylamide, N-isopropylacrylamide, ethylene glycol phenyl ether acrylate, N,N'-methylenebisacrylamide, ,1,1,3,3,3-Hexafluoroisopropyl acrylate, and N-*tert*-octylacrylamide.~~

~~10. The detectable array of any of claims 1-9, wherein the one or more macromolecules comprise at least one cross-linker.~~

~~11. The detectable array of any of claims 1-10, wherein the one or more macromolecules comprise at least one of bis-acrylamide, trimethylolpropane triacrylate, bisphenol A-bis(2-hydrxypropyl)acrylate, and 1-(acryloyloxy)-3-(methacryloyloxy)-3-methacryloyloxy)-2-propanol.~~

~~12. The detectable array of any of claims 1-11, wherein the one or more macromolecules comprise a plurality of chemically distinct macromolecules, and wherein each chemically distinct macromolecule is affixed to a different surface of the plurality of surfaces of the substrate.~~

~~13~~5. The ~~detectable array~~method of any of claims 1-~~12~~4, wherein the ~~one or more macromolecules~~ substrate comprises at least 2 chemically distinct macromolecules, and wherein each chemically distinct macromolecule is affixed to a different surface of the plurality of surfaces of the substrate, and wherein, optionally, the one or more macromolecules comprise~~.~~

~~14. The detectable array of any of claims 1-13, wherein the one or more macromolecules comprise~~ at least 12 chemically distinct macromolecules, ~~and wherein each chemically distinct macromolecule is affixed to a different surface of the plurality of surfaces of the substrate.~~

~~15. The detectable array of any of claims 1-14, wherein the one or more macromolecules comprise~~ at least 72 chemically distinct macromolecules, ~~and wherein each chemically distinct macromolecule is affixed to a different surface of the plurality of surfaces of the substrate.~~

~~16. The detectable array of any of claims 1-15, wherein the one or more macromolecules comprise~~ at least 96 chemically distinct macromolecules, or~~and wherein each chemically distinct macromolecule is affixed to a different surface of the plurality of surfaces of the substrate.~~

~~17. The detectable array of any of claims 1-16, wherein the one or more macromolecules comprise~~ at least 288 chemically distinct macromolecules~~, and wherein each chemically distinct macromolecule is affixed to a different surface of the plurality of surfaces of the substrate~~.

~~18. The detectable array of any of claims 1-17, wherein the plurality of detection methods include one or more of Maillard reaction, caramelizing, reaction with one or more amine reactive dyes, reaction with one or more thiol reactive dyes, reaction with one or more cellular dyes, reaction with one or more solvatochromic dyes, reaction with one or more acid indicators, reaction with one or more base indicators, reaction with one or more labeled antibodies, luminescence, surface texture analysis, photo-scanning, microscopy, photo-scanning with reflectance or transmittance illumination, photography with reflectance or transmittance illumination, mass spectrometry and spectroscopy.~~

~~19~~6. The ~~detectable array~~method of any of claims 1-~~18~~5, wherein the substrate comprises one or more of glass, plastic, metal, composites, acrylics, or biologically active substrates.

~~20. The detectable array of any of claims 1-19, further comprising one or more analytes bound to the one or more macromolecules.~~

~~21. The detectable array of any of claims 1-20, further comprising one or more small molecules, proteins, peptides, nucleotides, nucleosides, bacteria, viruses, fungi cells, animal cells, or yeast cells bound to the one or more macromolecules.~~

~~22. A system for diagnosing a disease, disorder, or condition comprising~~

~~an input element for receiving one or more images of a first detectable array or a representation thereof, wherein the first detectable array or representation thereof is a detectable array of any of claims 20-21 or a representation thereof;~~

~~a database comprising one or more images of a plurality of second detectable arrays or representations thereof, wherein the second detectable arrays or representations thereof are detectable arrays of any of claims 20-21 or representations thereof; and~~

~~a comparison element for comparing the one or more images of the first detectable array or representation thereof to the one or more images of the plurality of second detectable arrays or representations thereof.~~

~~23~~7. The ~~system~~ method of any of claims 1-6~~22~~, wherein ~~each of the plurality of second detectable arrays or representations thereof are associated with~~ the unlabeled analyte is selected from (i) a body sample of a subject, (ii) an in-vitro sample, (iii) an~~or~~ environmental sample, and (iv) a component of one of the foregoing ~~having a known disease, disorder, or condition state~~.

~~24. The system of any of claims 22-23, wherein the first detectable array or representation thereof is associated with a subject, in-vitro sample, or environmental sample having an unknown disease, disorder, or condition state.~~

~~25. The system of any of claims 22-24, wherein the comparison element is capable of predicting a disease state of a subject, an in-vitro sample, or an environmental sample having an unknown disease state.~~

~~26. The system of any of claims 22-25, wherein the one or more images of the first detectable array or representation thereof are false color images.~~

~~27. The system of any of claims 22-26, wherein the one or more images of the first detectable array or representation thereof represents one or more of fluorescence, phosphorescence, texture, roughness, color, ultraviolet absorption, infrared absorption, color, or lack of one or more of the foregoing, of the plurality of surfaces of the substrate.~~

~~28. A method of determining disease, disorder, or condition state in a subject, in-vitro sample, or environmental sample, comprising~~

~~contacting a first detectable array of any of claims 1-21 with one or more analytes associated with the subject, in-vitro sample, or environmental sample.~~

~~29. The method of claim 28, wherein contacting step comprises contacting the first detectable array with one or more body samples of the subject.~~

30. The method of any of claims 28-29, wherein the contacting step comprises contacting the first detectable array with at least one of blood, serum, plasma, urine, stool, saliva, bile, spinal fluid, interstitial fluid, gastric juice, tears, solvent, and milk of the subject, in-vitro sample, or environmental sample.

31. The method of any of claims 28-30, wherein the contacting step comprises contacting the first detectable array with one or more of plasma and urine of the subject.

32. The method of any of claims 28-31, further comprising obtaining the one or more analytes associated with the subject, in-vitro sample, or environmental sample.

33. The method of any of claims 28-32, further comprising detecting the one or more analytes associated with the subject, in-vitro sample, or environmental sample.

34. The method of any of claims 28-33, further comprising making one or more images of the detectable array or one or more representations thereof.

35. The method of any of claims 28-34, further comprising one or more of heating the detectable array, causing a Maillard reaction of at least one of the one or more analytes, caramelizing at least one of the one or more analytes, reacting at least of the one or more analytes with one or more amine reactive dyes, reacting at least one of the one or more analytes with one or more thiol reactive dyes, reacting at least of the one or more analytes with one or more solvatochromic dyes, reacting at least one of the one or more analytes with one or more cellular dyes, reacting at least one of the one or more analytes with one or more labeled antibodies, reacting at least of the one or more analytes with one or more acid indicators, reacting at least of the one or more analytes with one or more base indicators, detecting the luminescence or lack thereof of the detectable array, surface texture analysis, photo-scanning, microscopy, photo-scanning with reflectance or transmittance illumination, photography with reflectance or transmittance illumination, mass spectrometry and spectroscopy.

36. A method of making a detectable array of any of claims 1-21, comprising

independently coating the plurality of surface of the substrate with at least one substrate coating to form a plurality of independently coated surfaces, and

independently affixing at least one macromolecule or one or more precursors thereof to each of the independently coated surfaces.

37. The method of claim 36, further comprising polymerizing at least one of the one or more precursors on at least one of the independently coated surfaces.

38. The method of any of claims 36-37, further comprising initiating polymerization of at least one of the one or more precursors by applying to the one or more precursors, one or more of: electromagnetic radiation selected from the group consisting of microwaves, ultraviolert light, visible light and heat; sound; or a chemical initiator.

39. A label-free method of detecting an unlabeled analyte comprising

~~contacting the unlabeled analyte with a detectable array to affix at least a portion of the analyte to the detectable array; and~~

~~heating the detectable array with unlabeled analyte affixed thereto to cause a color change of at least one of the analyte and the detectable array.~~

~~40. The method of claim 39, wherein, the detectable array includes at least one array selected from the group consisting of an analytical microarray, a reverse-phase micro assay, a functional microarray, a cell-containing microarray, an expression microarray, and a high-throughput array.~~

~~41. The method of any of claims 39-40, wherein the detectable array includes at least one array selected from the group consisting of an antibody array, and ELISA array, a peptide array, a protein array, a nucleotide array, a nucleoside array, an RNA array, a DNA array, a DNA-protein array, and a small molecule array.~~

~~42. The method of any of claims 39-41, wherein the unlabeled analyte is one or more of a body sample of a subject, an in-vitro sample, a environmental sample, and at least one component of one of the foregoing.~~

~~43~~8. The method of any of claims ~~39~~1-~~42~~7, wherein the unlabeled analyte is at least one component of blood, serum, plasma, urine, stool, saliva, bile, spinal fluid, interstitial fluid, gastric juice, tears, solvent, and milk.

~~44~~9. The method of any of claims ~~39~~1-~~43~~8, wherein the unlabeled analyte comprises a protein or peptide~~heating induces a non-enzymatic browning reaction~~.

~~45. The method of claim 44, wherein the non-enzymatic browning reaction is at least one of a Maillard reaction and caramelization.~~

~~46. The method of any of claims 39-45, wherein heating comprises heating at a sufficient temperature and for a sufficient time to induce one or more of caramelization and a Maillard reaction.~~

~~47. The method of any of claims 39-46, wherein heating comprises heating at a temperature of about 120° C to about 300° C for about 1 minute to about 5 minutes.~~