CLAIMS

1. A method for detecting different analytes, the method comprising: mixing different analytes with sensing probes, wherein at least some of the sensing probes are specific to respective ones of the analytes; respectively capturing the analytes by the sensing probes that are specific to those analytes; respectively coupling fluorophores to sensing probes that captured respective analytes; mixing the sensing probes with beads, wherein the beads are specific to respective ones of the sensing probes, and wherein the beads include different codes identifying the analytes to which those sensing probes are specific; respectively coupling the sensing probes to beads that are specific to those sensing probes; identifying the beads that are coupled to the sensing probes that captured analytes using at least fluorescence from the fluorophores coupled to those sensing probes; and identifying the analytes that are captured by the sensing probes coupled to the identified beads using at least the codes of those beads.

2. The method of claim 1, wherein each of the beads includes a first oligonucleotide having a sequence specific to one of the sensing probes, and wherein each of the sensing probes comprises a second oligonucleotide having a sequence that is complementary to the first oligonucleotide.

3. The method of claim 1 or claim 2, wherein the different codes comprise oligonucleotides having different sequences than one another.

4. The method of any one of claims 1 to 3, wherein at least one of the analytes comprises a nucleotide analyte.

5. The method of claim 4, wherein the sensing probe comprises an oligonucleotide sequence specific to hybridize to the nucleotide analyte, optionally a) wherein the nucleotide analyte comprises a DNA analyte, or b) wherein the nucleotide analyte comprises an RNA analyte.

6. The method of any one of claims 1 to 4, wherein at least one of the analytes comprises a non-nucleotide analyte, optionally a) wherein the non-nucleotide analyte comprises a protein, b) wherein the non-nucleotide analyte comprises a metabolite,

c) wherein the sensing probe comprises an antibody selective to the non-nucleotide analyte, or d) wherein the sensing probe comprises an aptamer selective to the non-nucleotide analyte.

7. The method of any one of claims 1 to 6, wherein the different analytes comprise a plurality of nucleotide analytes and a plurality of non-nucleotide analytes, further comprising at least one of:

(i) wherein the fluorophores are coupled to the sensing probes after the analytes are captured by the sensing probes,
(ii) wherein the fluorophores are coupled to the sensing probes before the sensing probes are coupled to the beads,
(iii) wherein the fluorophores are coupled to the sensing probes after the sensing probes are coupled to the beads,
(iv) wherein providing the fluorophores comprises coupling multiple fluorophores to the analytes, optionally wherein coupling multiple fluorophores to the analytes comprises using a hybridization chain reaction (HCR).

8. A system for detecting a plurality of different analytes, the system comprising: sensing probes that are specific to respective ones of the different analytes; beads that are specific to respective ones of the sensing probes and that include different codes respectively identifying the analytes to which those sensing probes are specific; fluorophores to respectively couple to sensing probes that capture analytes; and detection circuitry to identify beads that are coupled to the sensing probes that capture analytes, and to identify the analytes that are captured by the sensing probes coupled to those beads using at least the codes of those beads.

9. The system of claim 8, further comprising at least one of
a) wherein each of the beads includes a first oligonucleotide having a sequence specific to one of the sensing probes, and wherein each of the sensing probes comprises a second oligonucleotide having a sequence that is complementary to the first oligonucleotide,
b) wherein the different codes comprise oligonucleotides having different sequences than one another,

c) wherein at least one of the analytes comprises a nucleotide analyte, optionally wherein the sensing probe comprises an oligonucleotide sequence specific to hybridize to the nucleotide analyte, optionally

i) wherein the nucleotide analyte comprises a DNA analyte, or

ii) wherein the nucleotide analyte comprises an RNA analyte.

10. The system of any one of claims 8 or 9, wherein at least one of the analytes comprises a non-nucleotide analyte, optionally

i) wherein the non-nucleotide analyte comprises a protein,

ii) wherein the non-nucleotide analyte comprises a metabolite,

iii) wherein the sensing probe comprises an antibody selective to the non-nucleotide analyte,

iv) wherein the sensing probe comprises an aptamer selective to the non-nucleotide analyte,

v) wherein the different analytes comprise a plurality of nucleotide analytes and a plurality of non-nucleotide analytes,

vi) wherein the fluorophores are coupled to the sensing probes after the analytes are captured by the sensing probes,

vii) wherein the fluorophores are coupled to the sensing probes before the sensing probes are coupled to the beads,

viii) wherein the fluorophores are coupled to the sensing probes after the sensing probes are coupled to the beads, or

ix) wherein multiple fluorophores are coupled to the analytes, optionally wherein the multiple fluorophores are coupled to the analytes using a hybridization chain reaction (HCR).

11. A method for identifying target nucleic acids, comprising:

(a) hybridizing a plurality of probes to a plurality of nucleic acids comprising the target nucleic acids, wherein each probe comprises a 3' end capable of hybridizing to a target nucleic acid and a 5' end capable of hybridizing to a capture probe;

(b) extending the hybridized probes with a blocked nucleotide;

(c) removing the plurality of nucleic acids and non-extended probes from the extended probes; and

(d) hybridizing the extended probes to a plurality of capture probes immobilized on a surface.

12. The method of claim 11, wherein (a) - (c) are performed in solution,
optionally further comprising repeating (a) and (b),
optionally wherein the blocked nucleotide comprises a detectable label, optionally wherein the label comprises a fluorophore,
optionally wherein (b) comprises polymerase extension,
optionally wherein (b) comprises ligase extension,
optionally wherein (c) comprises enzymatic degradation,
optionally wherein (c) comprises contacting the plurality of nucleic acids and the non-extended probes with a 3' to 5' exonuclease and,
optionally wherein the 3' to 5' exonuclease is selected from the group consisting of Exonuclease I, Thermolabile Exonuclease I, Exonuclease T, Exonuclease III, and Klenow I fragment, optionally wherein the probes each comprise a 5' end resistant to enzymatic degradation,
optionally wherein the 5' end resistant to enzymatic degradation comprises a phosphorothioate bond, optionally wherein (c) comprises contacting the plurality of nucleic acids with a 5' to 3' exonuclease, optionally wherein the 5' to 3' exonuclease is selected from the group consisting of RecJf, T7 Exonuclease, truncated Exonuclease VIII, Lambda Exonuclease, T5 Exonuclease, Exonuclease VII, Exonuclease V, and Nuclease BAL-31,
optionally wherein a plurality of beads comprise the surface, optionally wherein the surface comprises a planar surface,
optionally wherein a flow cell comprises the surface,
optionally wherein (d) further comprises amplifying a signal from the hybridized extended probes,
optionally wherein (d) further comprises identifying the location of the hybridized extended probes on the surface,
optionally wherein the capture probes are different from each other, optionally wherein the plurality of capture probes comprise a decoded array of capture probes,

optionally further comprising decoding the location of the capture probes on the surface,

optionally wherein the plurality of capture probes each comprise a primer binding site and a decode polynucleotide, optionally wherein decoding comprises: hybridizing a sequencing primer to the primer binding site, extending the hybridized primer, and identifying the decode polynucleotide,

optionally wherein the plurality of nucleic acids comprises genomic DNA, optionally wherein the target nucleic acids comprise a single nucleotide polymorphism (SNP).

13. A system for identifying target nucleic acids, comprising: an extension solution comprising: a plurality of nucleic acids comprising the target nucleic acids, a plurality of probes, wherein each probe comprises a 3' end capable of hybridizing to a target nucleic acid and a 5' end capable of hybridizing to a capture probe, a plurality of blocked nucleotides, an extension enzyme; a degradation solution comprising a 3' to 5' exonuclease; an array of capture probes immobilized on a surface; and a detector to identify the location of an extended probe hybridized to a capture probe on the surface.

14. The system of claim 13, wherein a flow cell comprise the array of capture probes immobilized on a surface.

15. A system for identifying target nucleic acids, comprising: a flow cell comprising a surface, an inlet for adding solutions to the surface, and an outlet for removing solutions from the surface, wherein an array of capture probes is immobilized on the surface; an extension solution in contact with the inlet, the extension solution comprising: a plurality of nucleic acids comprising the target nucleic acids, a plurality of probes, wherein each probe comprises a 3' end capable of hybridizing to a target nucleic acid and a 5' end capable of hybridizing to a capture probe, a plurality of blocked nucleotides, an extension enzyme; a degradation solution comprising a 3' to 5' exonuclease; and a detector to identify the location of an extended probe hybridized to a capture probe on the surface.

16. The system of any one of claims 13 to 15, wherein the blocked nucleotide comprises a detectable label,

optionally wherein the extension enzyme comprises a polymerase, optionally wherein the extension enzyme comprises a ligase, optionally wherein the 3' to 5' exonuclease is selected from the group consisting of Exonuclease I, Thermolabile Exonuclease I, Exonuclease T, Exonuclease III, and Klenow I fragment, optionally wherein the probes each comprise a 5' end resistant to enzymatic degradation, optionally wherein the 5' end resistant to enzymatic degradation comprises a phosphorothioate bond, optionally wherein the degradation solution further comprises a 5' to 3' exonuclease, optionally wherein the 5' to 3' exonuclease is selected from the group consisting of RecJf, T7 Exonuclease, truncated Exonuclease VIII, Lambda Exonuclease, T5 Exonuclease, Exonuclease VII, Exonuclease V, and Nuclease BAL-31, optionally wherein the surface comprises a plurality of beads, optionally wherein the capture probes are different from each other, optionally wherein the plurality of capture probes comprise a decoded array of capture probes, optionally wherein the plurality of capture probes each comprise a primer binding site and a decode polynucleotide, optionally wherein the plurality of nucleic acids comprises genomic DNA, optionally wherein the target nucleic acids comprise a single nucleotide polymorphism (SNP).

17. A method for detecting an element, the method comprising: coupling an element to a substrate; coupling a plurality of fluorophores to the element; and detecting the element using at least fluorescence from the plurality of fluorophores.

18. The method of claim 17, wherein the element comprises an analyte, optionally wherein the analyte is coupled to a sensing probe, optionally wherein the analyte is coupled to the substrate via the sensing probe, optionally wherein the plurality of fluorophores is coupled to the element via the sensing probe, optionally wherein the plurality of fluorophores is coupled to the element via the substrate, optionally wherein the plurality of fluorophores is coupled to the element before the element is coupled to the substrate, optionally wherein the plurality of fluorophores is coupled to the element after the element is coupled to the substrate, optionally wherein the substrate comprises a bead, optionally wherein the plurality of fluorophores is coupled to the element using rolling circle amplification, optionally wherein the rolling circle amplification generates an elongated, repeated sequence, and wherein the plurality of fluorophores is coupled to respective, repeated portions of that sequence,

optionally wherein the fluorophores are coupled to DNA intercalators, wherein the DNA intercalators couple to the elongated, repeated sequence, optionally wherein oligonucleotides comprising fluorophores and quenchers are hybridized to the repeated portions.

19. The method of claim 17, wherein the element is coupled to a trigger oligonucleotide to which a plurality of fluorescently labeled hairpins self-assemble, optionally wherein the element is coupled to a trigger oligonucleotide comprising a first trigger sequence A' and a second trigger sequence B', and wherein coupling the plurality of fluorophores to the element comprises contacting the trigger oligonucleotide with a plurality of first oligonucleotide hairpins and a plurality of second oligonucleotide hairpins, wherein each of the first oligonucleotide hairpins includes a first fluorophore, a single-stranded toehold sequence A complementary to first trigger sequence A', a first stem sequence B complementary to second trigger sequence B', a second stem sequence B' that is temporarily hybridized to first stem sequence B, and a single- stranded loop sequence C' disposed between the first stem sequence B and the second stem sequence B'; and wherein each of the second oligonucleotide hairpins comprises a second fluorophore, a single-stranded toehold sequence C complementary to single-stranded loop sequence C', a first stem sequence B complementary to second trigger sequence B', a second stem sequence B' that is temporarily hybridized to first stem sequence B, and a single-stranded loop sequence A' disposed between the first stem sequence B and the second stem sequence B', optionally wherein responsive to hybridization of the single- stranded toehold sequence A of one of the first oligonucleotide hairpins to first trigger sequence A' of the trigger oligonucleotide: the second stem sequence B' of that first oligonucleotide hairpin dehybridizes from the first stem sequence B of that first oligonucleotide hairpin; the single- stranded toehold sequence C of one of the second oligonucleotide hairpins hybridizes to the single-stranded loop sequence of that first oligonucleotide hairpin; and the second stem sequence B' of that second oligonucleotide hairpin dehybridizes from the first stem sequence B of that second oligonucleotide hairpin, optionally wherein responsive to hybridization of the single-stranded toehold sequence A of another one of the first oligonucleotide hairpins to single-stranded loop sequence A' of that second oligonucleotide hairpin: the second stem sequence B' of that first oligonucleotide hairpin dehybridizes from the first stem sequence B of that first oligonucleotide hairpin; the single- stranded toehold

sequence C of another one of the second oligonucleotide hairpins hybridizes to the single- stranded loop sequence of that first oligonucleotide hairpin; and the second stem sequence B' of that second oligonucleotide hairpin dehybridizes from the first stem sequence B of that second oligonucleotide hairpin.

20. The method of claim 17, wherein the element is coupled to an oligonucleotide primer, and wherein coupling the plurality of fluorophores to the element comprises: hybridizing an amplification template to the oligonucleotide primer; and extending the oligonucleotide primer, using at least the amplification template, with a plurality of fluorescently labeled nucleotides to generate an extended strand comprising the plurality of fluorophores, optionally wherein at least one of the fluorophores is different than at least one other of the fluorophores, optionally further comprising dehybridizing the amplification template and forming the extended strand into a hairpin structure, optionally wherein the element is coupled to an oligonucleotide primer, and wherein coupling the plurality of fluorophores to the element comprises: hybridizing an amplification template to the oligonucleotide primer; extending the oligonucleotide primer, using at least the amplification template, with a plurality of nucleotides that are respectively coupled to additional oligonucleotide primers; hybridizing additional amplification templates to the additional nucleotide primers; and extending the additional nucleotide primers, using at least the additional amplification templates, with a plurality of nucleotides that is either respectively coupled to fluorophores or is respectively coupled to further additional oligonucleotide primers, optionally further comprising hybridizing further additional amplification templates to the further nucleotide primers; and extending the additional nucleotide primers, using at least the additional amplification templates, with a plurality of nucleotides that are either respectively coupled to fluorophores or are respectively coupled to still further additional oligonucleotide primers, optionally wherein the element is coupled to a DNA origami comprising the plurality of fluorophores, optionally wherein the DNA origami comprises a combination of different fluorophores, optionally wherein the element is coupled to the DNA origami via copper(I)-catalyzed click reaction, strain-promoted azide-alkyne cycloaddition, hybridization of an oligonucleotide to a complementary oligonucleotide, biotin- strep tavidin interaction, NTA-His-Tag interaction, or Spytag-Spycatcher interaction.

21. The method of claim 17, wherein the element is coupled to an oligonucleotide, wherein the oligonucleotide comprises the plurality of fluorophores, optionally wherein the oligonucleotide comprises a hairpin, optionally wherein the oligonucleotide further comprises a radical scavenger, optionally wherein the element is directly coupled to a first oligonucleotide, and the first oligonucleotide is hybridized to a second oligonucleotide that comprises the plurality of fluorophores.

22. A method for detecting a nucleotide, the method comprising: adding the nucleotide to a first polynucleotide using at least a sequence of a second polynucleotide, wherein the added nucleotide includes a first moiety; coupling a label to the added nucleotide by reacting the first moiety with a second moiety of the label, wherein the label comprises a plurality of fluorophores; and detecting the added nucleotide using at least fluorescence from the plurality of fluorophores.

23. A method for detecting a nucleotide, the method comprising: adding the nucleotide to a first polynucleotide using at least a sequence of a second polynucleotide, wherein the added nucleotide is coupled to a label comprising a plurality of fluorophores; and detecting the added nucleotide using at least fluorescence from the plurality of fluorophores.

24. A method for detecting a nucleotide, the method comprising: adding the nucleotide to a first polynucleotide using at least a sequence of a second polynucleotide, wherein the added nucleotide includes a first moiety; coupling a label to the added nucleotide by reacting the first moiety with a second moiety of the label; coupling multiple fluorophores to the coupled label; and detecting the added nucleotide using at least fluorescence from the plurality of fluorophores.

25. A composition, comprising: a substrate; an oligonucleotide coupled to the substrate; a nucleotide coupled to the oligonucleotide; a moiety coupled to the nucleotide; a label coupled to the moiety, wherein the label comprises a plurality of fluorophores; and detection circuitry configured to detect the nucleotide using at least fluorescence from the plurality of fluorophores.