CLAIMS

1. A method for detecting an analyte molecule present in a sample, the method comprising:

(a) providing a supramolecular structure comprising:

i. a core structure comprising a plurality of core molecules,

ii. a capture molecule linked to the core structure at a first location, and

iii. a detector molecule linked to the core structure at a second location, wherein the supramolecular structure is in an unstable state, such that the detector molecule is configured to be unbound from the core structure through cleavage of a link therebetween at the second location;

(b) contacting the sample with the supramolecular structure, such that the supramolecular structure shifts from the unstable state to a stable state wherein the detector molecule and the capture molecule are linked together through binding to the analyte molecule, thereby forming a link between the detector molecule and capture molecule;

(c) providing a trigger to cleave the link between the detector molecule and the core structure at the second location, wherein the detector molecule remains linked to the core structure through the link with the capture molecule; and

(d) detecting the analyte molecule based on a signal provided by the supramolecular structure that shifted to the stable state.

2. A method for detecting one or more analyte molecules present in a sample, the method comprising:

(a) providing a plurality of supramolecular structures, each comprising:

i. a core structure comprising a plurality of core molecules,

ii. a capture molecule linked to the core structure at a first location, and

iii. a detector molecule linked to the core structure at a second location, wherein the supramolecular structure is in an unstable state, such that the detector molecule is configured to be unbound from the core structure through cleavage of a link therebetween at the second location;

(b) contacting the sample with the plurality of supramolecular structures, such that at least one supramolecular structure shifts from the unstable state to a stable state wherein the corresponding detector molecule and capture molecule are linked together through binding to an analyte molecule of the one or more analyte molecules, thereby forming a link between the corresponding detector molecule and capture molecule;

(c) providing a trigger to cleave the link between each detector molecule and corresponding core structure at the second location of the plurality of supramolecular

structures, wherein the detector molecule for the at least one supramolecular structure that shifted to a stable state remains linked to the corresponding core structure through the link with the corresponding capture molecule; and

(d) detecting a respective analyte molecule of the one or more analyte molecules based on a signal provided by a respective supramolecular structure of the at least one supramolecular structure that shifted to the stable state.

3. The method of claim 2, further comprising isolating the plurality of supramolecular structures from any detector molecules unbound from any supramolecular structures that did not shift to a stable state.

4. The method of claim 1 or 2, further comprising quantifying the concentration of the analyte molecule in the sample.

5. The method of claim 1 or 2, further comprising identifying the detected analyte molecule.

6. The method of claim 1 or 2, further comprising detecting the analyte molecule based on the signal when the analyte molecule is present in the sample at a count of a single molecule or higher.

7. The method of claim 1 or 2, wherein the sample comprises a complex biological sample and the method provides for single-molecule sensitivity thereby increasing a dynamic range and quantitative capture of a range of molecular concentrations within the complex biological sample.

8. The method of claim 1 or 2, wherein the one or more analyte molecules comprises a protein, a peptide, a peptide fragment, a lipid, a DNA, a RNA, an organic molecule, an inorganic molecule, complexes thereof, or any combinations thereof.

9. The method of claim 1 or 2, wherein each supramolecular structure is a nanostructure.

10. The method of claim 1 or 2, wherein each core structure is a nanostructure.

11. The method claim 1 or 2, wherein the plurality of core molecules for each core structure are arranged into a pre-defined shape and/or have a prescribed molecular weight.

12. The method claim of 11, wherein the pre-defined shape is configured to limit or prevent cross-reactivity with another supramolecular structure.

13. The method of claim 1 or 2, wherein the plurality of core molecules for each core structure comprises one or more nucleic acid strands, one or more branched nucleic acids, one or more peptides, one or more small molecules, or combinations thereof.

14. The method of claim 13, wherein each core structure independently comprises a scaffolded deoxyribonucleic acid (DNA) origami, a scaffolded ribonucleic acid (RNA) origami, a scaffolded hybrid DNA:RNA origami, a single-stranded DNA tile structure, a multi-stranded DNA tile structure, a single-stranded RNA origami, a multi-stranded RNA tile structure, hierarchically composed DNA or RNA origami with multiple scaffolds, a peptide structure, or combinations thereof.

15. The method of claim 1 or 2, wherein the trigger comprises a deconstructor molecule, a trigger signal, or combinations thereof.

16. The method of claim 15, wherein the deconstructor molecule comprises DNA, RNA, a peptide, a small organic molecule, or combinations thereof.

17. The method of claim 15, wherein the trigger signal comprises an optical signal, an electrical signal, or both.

18. The method of claim 17, wherein the trigger optical signal comprises a microwave signal, an ultraviolet illumination, a visible illumination, a near infrared illumination, or combinations thereof.

19. The method of claim 1 or 2, wherein the respective analyte molecule is 1) bound to the capture molecule of the respective supramolecular structure through a chemical bond and/or 2) bound to the detector molecule of the respective supramolecular structure through a chemical bond.

20. The method of claim 1 or 2, wherein the capture molecule and detector molecule for each supramolecular structure independently comprise a protein, a peptide, an antibody, an aptamer (RNA and DNA), a fluorophore, a darpin, a catalyst, a polymerization initiator, a polymer like PEG, or combinations thereof.

21. The method of claim 1 or 2, wherein for each supramolecular structure:

(a) the capture molecule is linked to the core structure through a capture barcode, wherein the capture barcode comprises a first capture linker, a second capture linker, and a capture bridge disposed between the first and second capture linkers, wherein

the first capture linker is bound to a first core linker that is bound to the first location on the core structure, wherein the capture molecule and the second capture linker are linked together through binding to a third capture linker, and

(b) the detector molecule is linked to the core structure through a detector barcode, wherein the detector barcode comprises a first detector linker, a second detector linker, and a detector bridge disposed between the first and second detector linkers, wherein the first detector linker is bound to a second core linker that is bound to the second location on the core structure, wherein the detector molecule and the second detector linker are linked together through binding to a third detector linker.

22. The method of claim 21, wherein the capture bridge and detector bridge independently comprise a polymer core.

23. The method of claim 21, wherein the polymer core of the capture bridge and the polymer core of the detector bridge independently comprise a nucleic acid (DNA or RNA) of specific sequence or a polymer like PEG.

24. The method of claim 21, wherein the first core linker, second core linker, first capture linker, second capture linker, third capture linker, first detector linker, second detector linker, and third detector linker independently comprise a reactive molecule or DNA sequence domain.

25. The method of claim 24, wherein each reactive molecule independently comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.

26. The method of claim 21, wherein the linkage between the capture barcode and 1) the first core linker, and/or 2) the third capture linker comprises a chemical bond.

27. The method of claim 26, wherein the chemical bond comprises a covalent bond.

28. The method of claim 21, wherein the linkage between the detector barcode and 1) the second core linker, and/or 2) the third detector linker comprises a chemical bond.

29. The method of claim 28, wherein the chemical bond comprises a covalent bond.

30. The method of claim 21, wherein the trigger cleaves the linkage between 1) the first detector linker and the second core linker and/or 2) the first capture linker and the first core linker.

31. The method of claim 21, wherein the capture molecule is bound to the third capture linker through a chemical bond and/or the detector molecule is bound to the third detector linker through a chemical bond.

32. The method of claim 31, wherein the capture molecule is covalently bonded to the third capture linker and/or the detector molecule is covalently bonded to the third detector linker.

33. The method of claim 1 or 2, wherein each supramolecular structure in the unstable state comprises the respective capture molecule and detector molecule spaced apart at a pre-determined distance, so as to reduce or inhibit the occurrence of cross-reactions between capture and/or detector molecules of a first supramolecular structure and corresponding capture and/or detector molecules of a second supramolecular structure.

34. The method of claim 33, wherein the pre-determined distance is from about 3 nm to about 40 nm.

35. The method of claim 21, wherein each supramolecular structure further comprises an anchor molecule linked to the core structure.

36. The method of claim 35, wherein the anchor molecule is linked to the core structure via an anchor barcode, wherein the anchor barcode comprises a first anchor linker, a second anchor linker, and an anchor bridge disposed between the first and second anchor linkers, wherein the first anchor linker is bound to a third core linker that is bound to a third location on the core structure, wherein the anchor molecule is linked to the second anchor linker.

37. The method of claim 36, wherein the anchor molecule comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.

38. The method of claim 36, wherein the anchor bridge comprises a polymer core.

39. The method of claim 38, wherein the polymer core of the anchor bridge comprises a nucleic acid (DNA or RNA) of specific sequence or a polymer like PEG.

~~40. The method of claim 36, wherein the third core linker, first anchor linker, second anchor linker, and anchor molecule independently comprise an anchor reactive molecule or DNA sequence domain.~~

~~41. The method of claim 40, wherein each anchor reactive molecule independently comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.~~

~~42. The method of claim 36, wherein the anchor molecule is linked to the second anchor linker through a chemical bond.~~

~~43. The method of claim 42, wherein the anchor molecule is covalently bonded to the second anchor linker.~~

~~44. The method of claim 36, wherein the trigger further cleaves 1) the second anchor linker from the anchor molecule, 2) the first anchor linker from the third core linker, or combinations thereof.~~

~~45. The method of claim 36, wherein the first and second locations are situated on a first side of the core structure, and the third location is situated on a second side of the core structure.~~

~~46. The method of claim 21, wherein the signal comprises the detector barcode, the capture barcode, or combinations thereof, corresponding to a supramolecular structure that shifted to a stable state.~~

~~47. The method of claim 21, further comprising separating each detector barcode from a corresponding detector molecule for the at least one supramolecular structure that shifted to a stable state, such that the corresponding signal comprises the respective detector barcode for detection of the analyte molecule bound to the respective capture and detector molecules.~~

~~48. The method of claim 47, wherein each separated detector barcode provides a DNA signal corresponding to the analyte molecule bound to the respective detector molecule.~~

~~49. The method of claim 47, wherein the at least one separated detector barcodes are analyzed using genotyping, qPCR, sequencing, or combinations thereof.~~

50. The method of claim 47, wherein a plurality of analyte molecules in the sample are detected simultaneously through multiplexing via one or more supramolecular structures that shifted to a stable state.

51. The method of claim 21, wherein the capture and detector molecules for each supramolecular structure is configured for binding to one or more specific types of analyte molecules.

52. The method of claim 2, wherein each core structure of the plurality of supramolecular structures are identical to each other.

53. The method of claim 52, wherein each supramolecular structure comprises a prescribed shape, size, molecular weight, or combinations thereof, so as to reduce or eliminate cross-reactions between a plurality of supramolecular structures.

54. The method of claim 52, wherein each supramolecular structure comprises a plurality of capture and detector molecules.

55. The method of claim 52 or 54, wherein each supramolecular structure comprises a prescribed stoichiometry of the capture and detector molecules so as to reduce or eliminate cross-reactions between the plurality of supramolecular structures.

56. The method of claim 2, wherein the unstable state for each supramolecular structure further comprises the capture and detector molecules spaced apart at a pre-determined distance so as to reduce or inhibit the occurrence of cross-reactions between capture and/or detector molecules of a first supramolecular structure and a second supramolecular structure.

57. The method of claim 56, wherein the pre-determined distance is from about 3 nm and about 40 nm.

58. The method of claim 56, wherein the mean distance between any two supramolecular structures is larger than the pre-determined distance between the capture and detector molecules of a respective supramolecular structure.

59. The method of claim 52, wherein the plurality of supramolecular structures are attached to one or more widgets, one or more solid supports, one or more polymer matrices, one or more solid substrate, one or more molecular condensates, or combinations thereof.

60. The method of claim 59, wherein the mean distance between any two supramolecular structures is larger than the pre-determined distance between the capture and detector molecules of a respective supramolecular structure.

61. The method of claim 59, wherein each polymer matrix of the one or more polymer matrices comprises a hydrogel bead.

62. The method of claim 61, wherein one or more supramolecular substrates are attached to a hydrogel bead.

63. The method of claim 62, wherein each supramolecular structure is co-polymerized with the hydrogel bead through a corresponding anchor molecule linked to the respective core structure of the corresponding supramolecular structure.

64. The method of claim 62, wherein the one or more supramolecular structures are embedded within the hydrogel bead.

65. The method of claim 62, wherein each hydrogel bead is contacted with a single cell in the sample for intracellular analyte molecule detection at a single cell resolution.

66. The method of claim 59, wherein each solid substrate of the one or more solid substrates comprises a microparticle.

67. The method of claim 66, wherein one or more supramolecular substrates are attached to a solid surface of the microparticle.

68. The method of claim 66, wherein the microparticle comprises a polystyrene particle, silica particle, magnetic particle, or paramagnetic particle.

69. The method of claim 66, wherein each solid substrate is contacted with a single cell in the sample for intracellular analyte molecule detection at a single cell resolution.

70. The method of claim 59, wherein each solid substrate of the one or more solid substrates comprises a planar substrate.

71. The method of claim 70, wherein a plurality of supramolecular structures are disposed on the planar substrate, wherein the planar substrate comprises a plurality of binding sites, wherein each binding site is configured to link with a corresponding supramolecular structure.

72. The method of claim 70, wherein the plurality of supramolecular structures are configured to detect the same analyte molecule.

73. The method of claim 70, further comprising providing a plurality of signaling elements configured to link with the detector molecules of the at least one supramolecular structure that shifted to the stable state.

74. The method of claim 73, wherein each signaling element comprises a fluorescent molecule or microbead, a fluorescent polymer, highly charged nanoparticles or polymer.

75. The method of claim 70, wherein at least one supramolecular structure of the plurality of supramolecular structures is configured to detect a different analyte molecule from the other supramolecular structures.

76. The method of claim 75, further comprising barcoding each supramolecular structure so as to identify the location of each supramolecular structure on the planar substrate.

77. The method of claim 76, further comprising providing a plurality of signaling elements configured to link with the detector molecules of the at least one supramolecular structure that shifted to the stable state.

78. The method of claim 77, wherein each signaling element comprises a fluorescent molecule or microbead, a fluorescent polymer, highly charged nanoparticles or polymer.

79. The method of claim 1 or 2, wherein the sample comprises a biological particle or a biomolecule.

80. The method of claim 1 or 2, wherein the sample comprises an aqueous solution comprising a protein, a peptide, a fragment of a peptide, a lipid, DNA, RNA, an organic molecule, a viral particle, an exosome, an organelle, or any complexes thereof.

81. The method of claim 1 or 2, wherein the sample comprises a tissue biopsy, blood, blood plasma, Urine, Saliva, Tear, Cerebrospinal fluid, extracellular fluid, cultures cells, culture media, discarded tissue, plant matter, a synthetic protein, a bacterial and/or viral sample or fungal tissue, or combinations thereof.

82. A substrate for detecting one or more analyte molecules in a sample, the substrate comprising a plurality of supramolecular structures, each supramolecular structure comprising:

(a) a core structure comprising a plurality of core molecules,

(b) a capture molecule linked to the supramolecular core at a first location, and

(c) a detector molecule linked to the supramolecular core at a second location, wherein the supramolecular structure is in an unstable state, such that the detector molecule is configured to be unbound from the core structure through cleavage of a link therebetween at the second location;

wherein each supramolecular structure is configured to shift from the unstable state to a stable state through interaction between the detector molecule, the capture molecule, and a respective analyte molecule of the one or more analyte molecules;
wherein, upon interaction with a trigger, a respective supramolecular structure that shifted to the stable state provides a signal for detecting the respective analyte molecule.

83. The substrate of claim 82, wherein upon interaction with the trigger, each detection molecule linked to a supramolecular structure in the unstable state becomes unbound from said supramolecular structure.

84. The substrate of claim 82, wherein each core structure of the plurality of supramolecular structures is identical to each other.

85. The substrate of claim 84, wherein the mean distance between any two supramolecular structures is larger than the pre-determined distance between the capture and detector molecules of a respective supramolecular structure.

86. The substrate of claim 82, comprising a solid support, solid substrate, a polymer matrix, or a molecular condensate.

87. The substrate of claim 82, wherein the sample comprises a complex biological sample and the method provides for single-molecule sensitivity thereby increasing a dynamic range and quantitative capture of a range of molecular concentrations within the complex biological sample.

88. The substrate of claim 82, wherein the one or more analyte molecules comprises a protein, a peptide, a peptide fragment, a lipid, a DNA, a RNA, an organic molecule, an inorganic molecule, complexes thereof, or any combinations thereof.

89. The substrate of claim 82, wherein each supramolecular structure is a nanostructure.

90. The substrate of claim 82, wherein each core structure is a nanostructure.

91. The substrate of claim 82, wherein the plurality of core molecules for each core structure are arranged into a pre-defined shape and/or have a prescribed molecular weight.

92. The substrate of claim 91, wherein the pre-defined shape is configured to limit or prevent cross-reactivity with another supramolecular structure.

93. The substrate of claim 82, wherein the plurality of core molecules for each core structure comprises one or more nucleic acid strands, one or more branched nucleic acids, one or more peptides, one or more small molecules, or combinations thereof.

94. The substrate of claim 93, wherein each core structure independently comprises a scaffolded deoxyribonucleic acid (DNA) origami, a scaffolded ribonucleic acid (RNA) origami, a scaffolded hybrid DNA:RNA origami, a single-stranded DNA tile structure, a multi-stranded DNA tile structure, a single-stranded RNA origami, a multi-stranded RNA tile structure, hierarchically composed DNA or RNA origami with multiple scaffolds, a peptide structure, or combinations thereof.

95. The substrate of claim 82, wherein the trigger comprises a deconstructor molecule, a trigger signal, or combinations thereof.

96. The substrate of claim 95, wherein the deconstructor molecule comprises DNA, RNA, a peptide, a small organic molecule, or combinations thereof.

97. The substrate of claim 95, wherein the trigger signal comprises an optical signal, an electrical signal, or both.

98. The substrate of claim 97, wherein the trigger optical signal comprises a microwave signal, an ultraviolet illumination, a visible illumination, a near infrared illumination, or combinations thereof.

99. The substrate of claim 82, wherein the respective analyte molecule is 1) bound to the capture molecule through a chemical bond and/or 2) bound to the detector molecule through a chemical bond.

100. The substrate of claim 82, wherein the capture molecule and detector molecule for each supramolecular structure independently comprise a protein, a peptide, an antibody, an aptamer (RNA and DNA), a fluorophore, a darpin, a catalyst, a polymerization initiator, a polymer like PEG, or combinations thereof.

101. The substrate of claim 82, wherein for each supramolecular structure:

(a) the capture molecule is linked to the core structure through a capture barcode, wherein the capture barcode comprises a first capture linker, a second capture linker, and a capture bridge disposed between the first and second capture linkers, wherein the first capture linker is bound to a first core linker that is bound to the first location on the core structure, wherein the capture molecule and the second capture linker are linked together through binding to a third capture linker, and

(b) the detector molecule is linked to the core structure through a detector barcode, wherein the detector barcode comprises a first detector linker, a second detector linker, and a detector bridge disposed between the first and second detector linkers, wherein the first detector linker is bound to a second core linker that is bound to the second location on the core structure, wherein the detector molecule and the second detector linker are linked together through binding to a third detector linker.

102. The substrate of claim 101, wherein the capture bridge and detector bridge independently comprise a polymer core.

103. The substrate of claim 101, wherein the polymer core of the capture bridge and the polymer core of the detector bridge independently comprise a nucleic acid (DNA or RNA) of specific sequence or a polymer like PEG.

104. The substrate of claim 101, wherein the first core linker, second core linker, first capture linker, second capture linker, third capture linker, first detector linker, second detector linker, and third detector linker independently comprise a reactive molecule or DNA sequence domain.

105. The substrate of claim 104, wherein each reactive molecule independently comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.

106. The substrate of claim 101, wherein the linkage between the capture barcode and 1) the first core linker, and/or 2) the third capture linker comprises a chemical bond.

107. The substrate of claim 106, wherein the chemical bond comprises a covalent bond.

108. The substrate of claim 101, wherein the linkage between the detector barcode and 1) the second core linker, and/or 2) the third detector linker comprises a chemical bond.

~~109. The substrate of claim 108, wherein the chemical bond comprises a covalent bond.~~

~~110. The substrate of claim 101, wherein the trigger cleaves the linkage between 1) the first detector linker and the second core linker and/or 2) the first capture linker and the first core linker.~~

~~111. The substrate of claim 101, wherein the capture molecule is bound to the third capture linker through a chemical bond and/or the detector molecule is bound to the third detector linker through a chemical bond.~~

~~112. The substrate of claim 111, wherein the capture molecule is covalently bonded to the third capture linker and/or the detector molecule is covalently bonded to the third detector linker.~~

~~113. The substrate of claim 82, wherein each supramolecular structure in the unstable state comprises the respective capture molecule and detector molecule spaced apart at a pre-determined distance, so as to reduce or inhibit the occurrence of cross-reactions between capture and/or detector molecules of a first supramolecular structure and corresponding capture and/or detector molecules of a second supramolecular structure.~~

~~114. The substrate of claim 113, wherein the pre-determined distance is from about 3 nm to about 40 nm.~~

~~115. The substrate of claim 101, wherein each supramolecular structure further comprises an anchor molecule linked to the core structure.~~

~~116. The substrate of claim 115, wherein the anchor molecule is linked to the core structure via an anchor barcode, wherein the anchor barcode comprises a first anchor linker, a second anchor linker, and an anchor bridge disposed between the first and second anchor linkers, wherein the first anchor linker is bound to a third core linker that is bound to a third location on the core structure, wherein the anchor molecule is linked to the second anchor linker.~~

~~117. The substrate of claim 116, wherein the anchor molecule comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.~~

~~118. The substrate of claim 116, wherein the anchor bridge comprises a polymer core.~~

~~119. The substrate of claim 118, wherein the polymer core of the anchor bridge comprises a nucleic acid (DNA or RNA) of specific sequence or a polymer like PEG.~~

~~120. The substrate of claim 116, wherein the third core linker, first anchor linker, second anchor linker, and anchor molecule independently comprise an anchor reactive molecule or DNA sequence domain.~~

~~121. The substrate of claim 120, wherein each anchor reactive molecule independently comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.~~

~~122. The substrate of claim 116, wherein the anchor molecule is linked to the second anchor linker through a chemical bond.~~

~~123. The substrate of claim 122, wherein the anchor molecule is covalently bonded to the second anchor linker.~~

~~124. The substrate of claim 116, wherein the trigger further cleaves 1) the second anchor linker from the anchor molecule, 2) the first anchor linker from the third core linker, or combinations thereof.~~

~~125. The substrate of claim 116, wherein the first and second locations are situated on a first side of the core structure, and the third location is situated on a second side of the core structure.~~

~~126. The substrate of claim 101, wherein the signal comprises the detector barcode, the capture barcode, or combinations thereof, corresponding to a supramolecular structure that shifted to a stable state.~~

~~127. The substrate of claim 101, wherein each detector barcode from a corresponding detector molecule for the at least one supramolecular structure that shifted to a stable state is configured to be separated from said corresponding detector molecule, such that the corresponding signal comprises the respective detector barcode for detection of the analyte molecule bound to said corresponding detector molecule.~~

~~128. The substrate of claim 127, wherein each separated detector barcode provides a DNA signal corresponding to the analyte molecule bound to the respective detector molecule.~~

~~129. The substrate of claim 127, wherein the at least one separated detector barcode is configured to be analyzed using genotyping, qPCR, sequencing, or combinations thereof.~~

~~130. The substrate of claim 127, wherein one or more supramolecular structures are configured for multiplexing the sample, wherein a plurality of analyte molecules in the sample are detected simultaneously.~~

~~131. The substrate of claim 101, wherein the capture and detector molecules for each supramolecular structure is configured for binding to one or more specific types of analyte molecules.~~

~~132. The substrate of claim 82, wherein each core structure of the plurality of supramolecular structures are identical to each other.~~

~~133. The substrate of claim 132, wherein each supramolecular structure comprises a prescribed shape, size, molecular weight, or combinations thereof, so as to reduce or eliminate cross-reactions between a plurality of supramolecular structures.~~

~~134. The substrate of claim 132, wherein each supramolecular structure comprises a plurality of capture and detector molecules.~~

~~135. The substrate of claim 132 or 134, wherein each supramolecular structure comprises a prescribed stoichiometry of the capture and detector molecules so as to reduce or eliminate cross-reactions between the plurality of supramolecular structures.~~

~~136. The substrate of claim 82, wherein the unstable state for each supramolecular structure further comprises the capture and detector molecules spaced apart at a pre-determined distance so as to reduce or inhibit the occurrence of cross-reactions between capture and/or detector molecules of a first supramolecular structure and a second supramolecular structure.~~

~~137. The substrate of claim 136, wherein the pre-determined distance is from about 3 nm and about 40 nm.~~

~~138. The substrate of claim 136, wherein the mean distance between any two supramolecular structures is larger than the pre-determined distance between the capture and detector molecules of a respective supramolecular structure.~~

~~139. The substrate of claim 82, wherein each substrate comprises a widget, a solid support, a polymer matrix, a solid substrate, or a molecular condensate.~~

~~140. The substrate of claim 139, wherein the mean distance between any two supramolecular structures is larger than the pre-determined distance between the capture and detector molecules of a respective supramolecular structure.~~

~~141. The substrate of claim 139, wherein the polymer matrix comprises a hydrogel bead.~~

~~142. The substrate of claim 141, wherein one or more supramolecular substrates are attached to the hydrogel bead.~~

~~143. The substrate of claim 141, wherein each supramolecular structure is co-polymerized with the hydrogel bead through a corresponding anchor molecule linked to the respective core structure of the corresponding supramolecular structure.~~

~~144. The substrate of claim 141, wherein the one or more supramolecular structures are embedded within the hydrogel bead.~~

~~145. The substrate of claim 141, wherein each hydrogel bead is configured to be contacted with a single cell in the sample for intracellular analyte molecule detection at a single cell resolution.~~

~~146. The substrate of claim 139, wherein the solid substrate comprises a microparticle.~~

~~147. The substrate of claim 146, wherein one or more supramolecular substrates are attached to a solid surface of the microparticle.~~

~~148. The substrate of claim 146, wherein the microparticle comprises a polystyrene particle, silica particle, magnetic particle, or paramagnetic particle.~~

~~149. The substrate of claim 146, wherein each solid substrate is configured to be contacted with a single cell in the sample for intracellular analyte molecule detection at a single cell resolution.~~

~~150. The substrate of claim 139, wherein the solid substrate comprises a planar substrate.~~

~~151. The substrate of claim 150, wherein a plurality of supramolecular structures are disposed on the planar substrate, wherein the planar substrate comprises a plurality of binding sites, wherein each binding site is configured to link with a corresponding supramolecular structure.~~

~~152. The substrate of claim 150, wherein the plurality of supramolecular structures are configured to detect the same analyte molecule.~~

153. The substrate of claim 150, wherein a plurality of signaling elements are configured to link with the detector molecules of the at least one supramolecular structure that shifted to the stable state.

154. The substrate of claim 153, wherein each signaling element comprises a fluorescent molecule or microbead, a fluorescent polymer, highly charged nanoparticles or polymer.

155. The substrate of claim 150, wherein at least one supramolecular structure of the plurality of supramolecular structures is configured to detect a different analyte molecule from the other supramolecular structures.

156. The substrate of claim 82, wherein the sample comprises a biological particle or a biomolecule.

157. The substrate of claim 82, wherein the sample comprises an aqueous solution comprising a protein, a peptide, a fragment of a peptide, a lipid, DNA, RNA, an organic molecule, a viral particle, an exosome, an organelle, or any complexes thereof.

158. The substrate of claim 82, wherein the sample comprises a tissue biopsy, blood, blood plasma, Urine, Saliva, Tear, Cerebrospinal fluid, extracellular fluid, cultures cells, culture media, discarded tissue, plant matter, a synthetic protein, a bacterial and/or viral sample or fungal tissue, or combinations thereof.

159. A supramolecular structure for detecting an analyte molecule in a sample, the supramolecular structure comprising:

(a) a core structure comprising a plurality of core molecules,

(b) a capture molecule linked to the supramolecular core at a first location, and

(c) a detector molecule linked to the supramolecular core at a second location, wherein the supramolecular structure is in an unstable state, such that the detector molecule is configured to be unbound from the core structure through cleavage of a link therebetween at the second location;

wherein the supramolecular structure is configured to shift from the unstable state to a stable state through interaction between the detector molecule, the capture molecule, and an analyte molecule;

wherein, upon interaction with a trigger, the supramolecular structure that shifted to the stable state provides a signal for detecting the analyte molecule.

~~160. The supramolecular structure of claim 159, wherein the sample comprises a complex biological sample and the method provides for single-molecule sensitivity thereby increasing a dynamic range and quantitative capture of a range of molecular concentrations within the complex biological sample.~~

~~161. The supramolecular structure of claim 159, wherein the analyte molecule comprises a protein, a peptide, a peptide fragment, a lipid, a DNA, a RNA, an organic molecule, an inorganic molecule, complexes thereof, or any combinations thereof.~~

~~162. The supramolecular structure of claim 159, wherein the supramolecular structure is a nanostructure.~~

~~163. The supramolecular structure of claim 159, wherein the core structure is a nanostructure.~~

~~164. The supramolecular structure of claim 159, wherein the plurality of core molecules for the core structure are arranged into a pre-defined shape and/or have a prescribed molecular weight.~~

~~165. The supramolecular structure of claim 164, wherein the pre-defined shape is configured to limit or prevent cross-reactivity with another supramolecular structure.~~

~~166. The supramolecular structure of claim 159, wherein the plurality of core molecules for each core structure comprises one or more nucleic acid strands, one or more branched nucleic acids, one or more peptides, one or more small molecules, or combinations thereof.~~

~~167. The supramolecular structure of claim 166, wherein the core structure independently comprises a scaffolded deoxyribonucleic acid (DNA) origami, a scaffolded ribonucleic acid (RNA) origami, a scaffolded hybrid DNA:RNA origami, a single-stranded DNA tile structure, a multi-stranded DNA tile structure, a single-stranded RNA origami, a multi-stranded RNA tile structure, hierarchically composed DNA or RNA origami with multiple scaffolds, a peptide structure, or combinations thereof.~~

~~168. The supramolecular structure of claim 159, wherein the trigger comprises a deconstructor molecule, a trigger signal, or combinations thereof.~~

~~169. The supramolecular structure of claim 168, wherein the deconstructor molecule comprises DNA, RNA, a peptide, a small organic molecule, or combinations thereof.~~

~~170. The supramolecular structure of claim 168, wherein the trigger signal comprises an optical signal, an electrical signal, or both.~~

171. The supramolecular structure of claim 170, wherein the trigger optical signal comprises a microwave signal, an ultraviolet illumination, a visible illumination, a near infrared illumination, or combinations thereof.

172. The supramolecular structure of claim 159, wherein the analyte molecule is 1) bound to the capture molecule through a chemical bond and/or 2) bound to the detector molecule through a chemical bond.

173. The supramolecular structure of claim 159, wherein the capture molecule and detector molecule for each supramolecular structure independently comprise a protein, a peptide, an antibody, an aptamer (RNA and DNA), a fluorophore, a darpin, a catalyst, a polymerization initiator, a polymer like PEG, or combinations thereof.

174. The supramolecular structure of claim 159, wherein for each supramolecular structure:

(a) the capture molecule is linked to the core structure through a capture barcode, wherein the capture barcode comprises a first capture linker, a second capture linker, and a capture bridge disposed between the first and second capture linkers, wherein the first capture linker is bound to a first core linker that is bound to the first location on the core structure, wherein the capture molecule and the second capture linker are linked together through binding to a third capture linker, and

(b) the detector molecule is linked to the core structure through a detector barcode, wherein the detector barcode comprises a first detector linker, a second detector linker, and a detector bridge disposed between the first and second detector linkers, wherein the first detector linker is bound to a second core linker that is bound to the second location on the core structure, wherein the detector molecule and the second detector linker are linked together through binding to a third detector linker.

175. The supramolecular structure of claim 174, wherein the capture bridge and detector bridge independently comprise a polymer core.

176. The supramolecular structure of claim 174, wherein the polymer core of the capture bridge and the polymer core of the detector bridge independently comprise a nucleic acid (DNA or RNA) of specific sequence or a polymer like PEG.

177. The supramolecular structure of claim 174, wherein the first core linker, second core linker, first capture linker, second capture linker, third capture linker, first detector linker,

second detector linker, and third detector linker independently comprise a reactive molecule or DNA sequence domain.

178. The supramolecular structure of claim 177, wherein each reactive molecule independently comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.

179. The supramolecular structure of claim 174, wherein the linkage between the capture barcode and 1) the first core linker, and/or 2) the third capture linker comprises a chemical bond.

180. The supramolecular structure of claim 179, wherein the chemical bond comprises a covalent bond.

181. The supramolecular structure of claim 174, wherein the linkage between the detector barcode and 1) the second core linker, and/or 2) the third detector linker comprises a chemical bond.

182. The supramolecular structure of claim 181, wherein the chemical bond comprises a covalent bond.

183. The supramolecular structure of claim 174, wherein the trigger cleaves the linkage between 1) the first detector linker and the second core linker and/or 2) the first capture linker and the first core linker.

184. The supramolecular structure of claim 174, wherein the capture molecule is bound to the third capture linker through a chemical bond and/or the detector molecule is bound to the third detector linker through a chemical bond.

185. The supramolecular structure of claim 184, wherein the capture molecule is covalently bonded to the third capture linker and/or the detector molecule is covalently bonded to the third detector linker.

186. The supramolecular structure of claim 159, wherein the supramolecular structure in the unstable state comprises the respective capture molecule and detector molecule spaced apart at a pre-determined distance, so as to reduce or inhibit the occurrence of cross-reactions between capture and/or detector molecules of the supramolecular structure with corresponding capture and/or detector molecules of another supramolecular structure.

~~187. The supramolecular structure of claim 186, wherein the pre-determined distance is from about 3 nm to about 40 nm.~~

~~188. The supramolecular structure of claim 174, wherein the supramolecular structure further comprises an anchor molecule linked to the core structure.~~

~~189. The supramolecular structure of claim 188, wherein the anchor molecule is linked to the core structure via an anchor barcode, wherein the anchor barcode comprises a first anchor linker, a second anchor linker, and an anchor bridge disposed between the first and second anchor linkers, wherein the first anchor linker is bound to a third core linker that is bound to a third location on the core structure, wherein the anchor molecule is linked to the second anchor linker.~~

~~190. The supramolecular structure of claim 189, wherein the anchor molecule comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.~~

~~191. The supramolecular structure of claim 189, wherein the anchor bridge comprises a polymer core.~~

~~192. The supramolecular structure of claim 191, wherein the polymer core of the anchor bridge comprises a nucleic acid (DNA or RNA) of specific sequence or a polymer like PEG.~~

~~193. The supramolecular structure of claim 189, wherein the third core linker, first anchor linker, second anchor linker, and anchor molecule independently comprise an anchor reactive molecule or DNA sequence domain.~~

~~194. The supramolecular structure of claim 193, wherein each anchor reactive molecule independently comprises an amine, a thiol, a DBCO, a maleimide, biotin, an azide, an acrydite, a NHS-ester, a single stranded nucleic acid (RNA or DNA) of specific sequence, one or more polymers like PEG or polymerization initiators, or combinations thereof.~~

~~195. The supramolecular structure of claim 189, wherein the anchor molecule is linked to the second anchor linker through a chemical bond.~~

~~196. The supramolecular structure of claim 195, wherein the anchor molecule is covalently bonded to the second anchor linker.~~

197. The supramolecular structure of claim 189, wherein the trigger further cleaves 1) the second anchor linker from the anchor molecule, 2) the first anchor linker from the third core linker, or combinations thereof.

198. The supramolecular structure of claim 189, wherein the first and second locations are situated on a first side of the core structure, and the third location is situated on a second side of the core structure.

199. The supramolecular structure of claim 174, wherein the signal comprises the detector barcode, the capture barcode, or combinations thereof, corresponding to a supramolecular structure that shifted to a stable state.

200. The supramolecular structure of claim 174, wherein the detector barcode from a corresponding detector molecule for a supramolecular structure that shifted to a stable state is configured to be separated from said corresponding detector molecule, such that the corresponding signal comprises the respective detector barcode for detection of the analyte molecule bound to said corresponding detector molecule.

201. The supramolecular structure of claim 200, wherein the separated detector barcode provides a DNA signal corresponding to the analyte molecule bound to the respective detector molecule.

202. The supramolecular structure of claim 200, wherein the separated detector barcode is configured to be analyzed using genotyping, qPCR, sequencing, or combinations thereof.

203. The supramolecular structure of claim 174, wherein the capture and detector molecules for the supramolecular structure is configured for binding to one or more specific types of analyte molecules.

204. The supramolecular structure of claim 159, wherein the supramolecular structure comprises a prescribed shape, size, molecular weight, or combinations thereof, so as to reduce or eliminate cross-reactions with another supramolecular structure.

205. The supramolecular structure of claim 159, wherein the supramolecular structure comprises a plurality of capture and detector molecules.

206. The supramolecular structure of claim 204 or 205, wherein the supramolecular structure comprises a prescribed stoichiometry of the capture and detector molecules so as to reduce or eliminate cross-reactions with another supramolecular structure.

~~207. The supramolecular structure of claim 159, wherein the sample comprises a biological particle or a biomolecule.~~

~~208. The supramolecular structure of claim 159, wherein the sample comprises an aqueous solution comprising a protein, a peptide, a fragment of a peptide, a lipid, DNA, RNA, an organic molecule, a viral particle, an exosome, an organelle, or any complexes thereof.~~

~~209. The supramolecular structure of claim 159, wherein the sample comprises a tissue biopsy, blood, blood plasma, Urine, Saliva, Tear, Cerebrospinal fluid, extracellular fluid, cultures cells, culture media, discarded tissue, plant matter, a synthetic protein, a bacterial and/or viral sample or fungal tissue, or combinations thereof.~~

1. A supramolecular structure configured to capture and detect an analyte molecule, comprising:

a core structure including a plurality of molecules linked together;

a capture molecule configured to bind with the analyte molecule and linked to the core structure at a first location; and

a detector molecule spaced apart from the capture molecule at a pre-determined distance, configured to bind with the analyte molecule, and linked to the core structure at a second location by forming a linkage with a detector barcode which forms a linkage with the core structure;

wherein the capture molecule and the detector molecule are configured to be simultaneously linked to the analyte molecule;

wherein the detector molecule is configured to be separated from the core structure upon being subjected to a first trigger, thereby remaining linked to the core structure only when linked to the capture molecule through binding with the analyte molecule; and

wherein the detector molecule remains linked to the detector barcode after being subjected to the first trigger.

2. The supramolecular structure of claim 1, wherein the distance between the capture molecule and the detector molecule is between 1nm-60nm.

3. The supramolecular structure of claim 2, wherein the distance between the capture molecule and the detector molecule is between 3nm-40nm.

4. The supramolecular structure of claim 1, wherein the capture molecule is linked to the core structure through a capture barcode including DNA or RNA of a specific sequence.

5. The supramolecular structure of claim 1, wherein the first trigger includes one or more deconstructor molecules.

6. The supramolecular structure of claim 1, wherein the first trigger includes an electrical signal, a microwave signal, ultraviolet illumination, visible illumination or near infra-red illumination.

7. The supramolecular structure of claim 1, wherein the detector barcode includes DNA or RNA of a specific sequence.

8. The supramolecular structure of claim 1, wherein the detector barcode is configured to be cleaved from the detector molecule by a second trigger.

9. The supramolecular structure of claim 8, wherein the second trigger is a detector barcode release molecule.

10. A method for detecting analyte molecules in a sample, comprising:

providing a supramolecular structure including:

a core structure including a plurality of molecules linked together;

a plurality of capture molecules configured to bind with the analyte molecules and each linked to the core structure at respective first locations; and

a plurality of detector molecules each spaced apart from one of the capture molecules by a pre-determined distance, configured to bind with the analyte molecules, and each linked to the core structure by forming a linkage with detector barcodes which form linkages with the core structure at respective second locations ;

wherein each capture molecule and each detector molecule is configured to be simultaneously linked to a respective one of the analyte molecules;

contacting the sample with the supramolecular structure for a time sufficient to allow binding of the capture molecules and the detector molecules with the analyte molecules;

providing a first trigger to cleave the links between the detector molecules and the core structure, wherein the detector molecules remain linked to the detector barcodes after the links between the detector molecules and the core structure are cleaved;

after providing the first trigger, separating detector molecules unbound from the core structure from detector molecules bound to the core structure; and

identifying the analyte molecules by analyzing the detector barcodes of the detector molecules which bound to the core structure after providing the first trigger.

11. The method of claim 10, further comprising providing a second trigger to cleave the links between the detector barcodes and the detector molecules before analyzing the detector barcodes.

12. The method of claim 11, wherein the second trigger is a detector barcode release molecule.

13. The method of claim 11, wherein providing the second trigger is performed after separating detector molecules unbound from the core structure from detector molecules bound to the core structure.

14. The method of claim 11, wherein the second trigger comprises a nucleic acid.

15. The method of claim 14, wherein cleaving the links between the detector barcodes and the detector molecules is accomplished through nucleic acid strand displacement.