SUMMARY

[0004] The present disclosure generally relates to systems, structures and methods for detection and quantification of analyte molecules in a sample.

[0005] Provided herein, in some examples, is a method for detecting an analyte molecule present in a sample, the method comprising: a) providing a solid support; b) patterning the solid support to form a plurality of binding sites on the solid support; and c) associating a single supramolecular structure with a binding site from among the plurality of binding sites on the solid support, wherein the supramolecular structure comprises: 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.

[0006] Provided herein, in some examples, is a method for detecting an analyte molecule using a substrate, the method comprising: providing the substrate, the substrate comprising a plurality of binding sites, wherein an individual binding site of the plurality of binding sites is associated with a supramolecular structure of a plurality of supramolecular structures, the supramolecular structure comprising: a core structure comprising a plurality of core molecules a capture molecule linked to the core structure at a first location, and 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; 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 and wherein each supramolecular structure in the unstable state comprises the respective capture molecule and detector molecule spaced apart at a pre-determined distance; 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 such that the analyte molecule is associated with the individual binding site; and detecting the analyte molecule based on a signal provided by the supramolecular structure

that shifted to the stable state. In other example, the supramolecular structure does not include an integral detector molecule, and the detection is mediated through a separate step.

[0007] Provided herein, in one aspect, is a method for forming a substrate for detection of an analyte molecule in a sample. The method includes the steps of providing a base layer; providing a binding layer on the base layer; depositing a top layer on the binding layer; patterning the top layer to expose portions of the binding layer, the exposed portions corresponding to a plurality of binding sites on the binding layer; and providing a supramolecular structure associated with each binding site of the plurality of binding sites, the supramolecular structure comprising: a core structure comprising a plurality of core molecules a capture molecule linked to the core structure at a first location, and 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 and such that the respective capture molecule and detector molecule spaced apart are at a pre-determined distance in the unstable state and wherein, in a stable state, 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, wherein the detector molecule remains linked to the core structure through the link with the capture molecule and such that the analyte molecule is associated with the individual binding site.

[0008] In some examples, any method disclosed herein further comprising quantifying the concentration of the analyte molecule in the sample. In some examples, any method disclosed herein further comprising identifying the detected analyte molecule. In some examples, any method disclosed herein 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. In some examples, the solid support is coupled to or associated with a detection system that generates a signal based on a detectable change indicative of the presence of or formation of a stable state, as a result of analyte capture or binding by the supramolecular structure, at an individual binding site.

[0009] In some examples, for any method disclosed herein, 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. In some examples, for any method disclosed herein, 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. In some examples, for any method disclosed herein, each supramolecular structure is a nanostructure.

[00010] In some examples, for any method disclosed herein, each core structure is a nanostructure. In some examples, for any method disclosed herein, the plurality of core molecules for each core structure are arranged into a pre-defined shape and/or have a prescribed molecular weight. In some examples, the pre-defined shape is configured to limit or prevent cross-reactivity with another supramolecular structure. In some examples, for any method disclosed herein, 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. In some examples, for any method disclosed herein, 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.

[00011] In some examples, for any method disclosed herein, the trigger comprises a deconstructor molecule, a trigger signal, or combinations thereof. In some examples, the deconstructor molecule comprises DNA, RNA, a peptide, a small organic molecule, or combinations thereof. In some examples, the trigger signal comprises an optical signal, an electrical signal, or both. In some examples, the trigger optical signal comprises a microwave signal, an ultraviolet illumination, a visible illumination, a near infrared illumination, or combinations thereof.

[00012] In some examples, for any method disclosed herein, 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. In some examples, for any method disclosed herein, 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. In some examples, for any method disclosed herein, 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. In some examples, the capture bridge and detector bridge independently comprise a polymer core. In some examples, 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. In some examples, 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. In some examples, 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. In some examples, the linkage between the capture barcode and 1) the first core linker, and/or 2) the third capture linker comprises a chemical bond. In some examples, the chemical bond comprises a covalent bond. In some examples, the linkage between the detector barcode and 1) the second core linker, and/or 2) the third detector linker comprises a chemical bond. In some examples, the chemical bond comprises a covalent bond. In some examples, 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. In some examples, for any method disclosed herein, 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. In some examples, the capture molecule is covalently bonded to the third capture linker and/or the detector molecule is covalently bonded to the third detector linker.

[00013] In some examples, for any method disclosed herein, 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. In some examples, for any method disclosed herein, the pre-determined distance is from about 3 nm to about 40 nm.

[00014] In some examples, for any method disclosed herein, each supramolecular structure further comprises an anchor molecule linked to the core structure. In some examples, 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. In some examples, 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. In some examples, the anchor bridge comprises a polymer core. In some examples, the polymer core of the anchor bridge comprises a nucleic acid (DNA or RNA) of specific sequence or a polymer like PEG. In some examples, the third core linker, first anchor linker, second anchor linker, and anchor molecule independently comprise an anchor reactive molecule or DNA sequence domain. In some examples, 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. In some examples, the anchor molecule is linked to the second anchor linker through a chemical bond. In some examples, the anchor molecule is covalently bonded to the second anchor linker. In some examples, 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. In some examples, 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.

[00015] In some examples, for any method disclosed herein, the signal comprises the detector barcode, the capture barcode, or combinations thereof, corresponding to a supramolecular structure

that shifted to a stable state. In some examples, any method disclosed herein, 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. In some examples, each separated detector barcode provides a DNA signal corresponding to the analyte molecule bound to the respective detector molecule. In some examples, the at least one separated detector barcodes are analyzed using genotyping, qPCR, sequencing, or combinations thereof. In some examples, 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. In some examples, for any method disclosed herein, the capture and detector molecules for each supramolecular structure is configured for binding to one or more specific types of analyte molecules.

[00016] In some examples, for any method comprising using a plurality of supramolecular structures disclosed herein, each core structure of the plurality of supramolecular structures are identical to each other. In some examples, 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. In some examples, each supramolecular structure comprises a plurality of capture and detector molecules. In some examples, 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.

[00017] In some examples, for any method comprising using a plurality of supramolecular structures disclosed herein, 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. In some examples, the pre-determined distance is from about 3 nm and about 40 nm. In some examples, 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. In some examples, 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. In some examples, the plurality of supramolecular structures are attached to one or more solid substrates. In some examples, each solid substrate of the one or more solid substrates comprises a planar substrate and/or comprises a planar substrate having a patterned or shaped surface having an array of binding sites. In some examples, a plurality of supramolecular structures are disposed on the substrate, wherein the substrate comprises a plurality of binding sites, wherein each binding site is associated with a corresponding supramolecular structure. In an example, an individual binding site of an array of binding sites of a substrate is associated with at most one supramolecular structure, e.g., only one supramolecular structure per binding site. In some examples, the plurality of supramolecular structures distributed on a substrate are configured to detect the same analyte molecule. In some examples, 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. In some examples, each signaling element comprises a fluorescent molecule or microbead, a fluorescent polymer, highly charged nanoparticles or polymer. In some examples, at least one supramolecular structure of the plurality of supramolecular structures on a substrate is configured to detect a different analyte molecule from at least one of the other supramolecular structures. In some examples, an individual supramolecular structure is barcoded with unique barcodes to distinguish each supramolecular structure on the substrate from one another so as to identify the location of each supramolecular structure on the substrate. In some examples a plurality of signaling elements link with the detector molecules of the at least one supramolecular structure that shifted to the stable state. In some examples, each signaling element comprises a fluorescent molecule or microbead, a fluorescent polymer, highly charged nanoparticles or polymer.

[00018] Provided herein is method for forming a substrate, the method comprising: providing a base layer; providing a binding layer on the base layer; depositing a top layer on the binding layer; patterning the top layer to expose portions of the binding layer, the exposed portions corresponding to a plurality of binding sites on the binding layer; and associating a molecule or structure at each binding site. In an example, the method includes providing a supramolecular structure associated with each binding site of the plurality of binding sites, the supramolecular structure comprising a core structure, the core structure comprising a plurality of core molecules. The core structure may be linked to one or more cargo molecules that have affinity for or that bind to an analyte. The present techniques may be generally used for organizing single molecules, e.g.,

one or more core structures of a supramolecular structure, and can thus find use in a variety of different areas. In an example, present techniques may be generally used for organizing a single quantum dot.

In some examples, for any method disclose herein, additional steps can be performed to regenerate a formed substrate after analyte detection is complete. Regeneration may include removing all or a portion of the supramolecular structure.

[00019] In some examples, an analyte or analyte molecule in a sample is detected. The analyte may comprises a biological particle or a biomolecule. In some examples, the analyte molecule comprises a chemical compound, a protein, a peptide, a fragment of a peptide, a lipid, a nucleic acid, DNA, RNA, an organic molecule, a viral particle, an exosome, an organelle, or any complexes thereof. In some examples, 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.

[00020] Provided herein, in some examples, is a substrate for detecting one or more analyte molecules in a sample, the substrate comprising a plurality of binding sites associated with a respective 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.

[00021] Provided herein, in another aspect, is a substrate for detecting one or more analyte molecules in a sample, the substrate comprising: a base layer; a binding layer on the base layer; a patterned top layer exposing portions of the binding layer, the exposed portions corresponding to a plurality of binding sites on the binding layer; and a supramolecular structure associated with each binding site of the plurality of binding sites. The supramolecular structure comprises a core

structure comprising a plurality of core molecules, a capture molecule linked to the supramolecular core at a first location, and 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 and 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.

[00022] In some examples, wherein upon interaction with the trigger, each detection molecule linked to a supramolecular structure in the unstable state becomes unbound from said supramolecular structure. In some examples, each core structure of the plurality of supramolecular structures is identical to each other. In some examples, 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. In some examples, the substrate comprises a solid support or a solid substrate.

[00023] In some examples, each core structure of the plurality of supramolecular structures are identical to each other. In some examples, 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. In some examples, each supramolecular structure comprises a plurality of capture and detector molecules. In some examples, 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. In some examples, 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. In some examples, the pre-determined distance is from about 3 nm and about 40 nm. In some examples, 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.

[00024] In some examples, each substrate comprises a widget, a solid support, a polymer matrix, a solid substrate, or a molecular condensate. In some examples, 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. In some examples, the solid substrate comprises a planar substrate. In some examples, a plurality of supramolecular structures are disposed on the substrate, wherein the substrate comprises a plurality of binding sites, wherein each binding site is configured to link with a corresponding supramolecular structure. In some examples, the plurality of supramolecular structures are configured to detect the same analyte molecule. In some examples, 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. In some examples, each signaling element comprises a fluorescent molecule or microbead, a fluorescent polymer, highly charged nanoparticles or polymer. In some examples, at least one supramolecular structure of the plurality of supramolecular structures is configured to detect a different analyte molecule from the other supramolecular structures.

[00025] In some examples, 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 and/or to align with a size and shape of a binding site in the substrate. In one example, the dimensions of the supramolecular structure in an x-y plane are selected to conform to or overlap a binding site size and shape. To encourage the association of only one supramolecular structure with one binding site, the binding site and the supramolecular structure may be sized and shaped such that two supramolecular structures would not fit on a single binding site. In an example, the supramolecular structure may be smaller than an individual binding site in at least one dimension when associated with the binding site. In some examples, the supramolecular structure comprises a plurality of capture and detector molecules. In some examples, 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.

BRIEF DESCRIPTION OF THE DRAWINGS

[00026] Specific embodiments of the disclosed devices, delivery systems, or methods will now be described with reference to the drawings. Nothing in this detailed description is intended to imply that any particular component, feature, or step is essential to the invention.

[00027] FIG. 1A depicts an exemplary supramolecular structure and the related subcomponents.

[00028] FIG. 1B depicts an exemplary supramolecular structure and the related subcomponents.

WHAT IS CLAIMED IS:

1. A method for forming a substrate for detection of an analyte molecule in a sample, the method comprising:

providing a base layer;

providing a binding layer on the base layer;

depositing a top layer on the binding layer;

patterning the top layer to expose portions of the binding layer, the exposed portions corresponding to a plurality of binding sites on the binding layer; and

providing a supramolecular structure associated with each binding site of the plurality of binding sites, the supramolecular structure comprising:

a core structure comprising a plurality of core molecules

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

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 and such that the respective capture molecule and detector molecule spaced apart are at a pre-determined distance in the unstable state and wherein, in a stable state, 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, wherein the detector molecule remains linked to the core structure through the link with the capture molecule and such that the analyte molecule is associated with the individual binding site.

2. The method of claim 1, comprising activating the patterned top layer and depositing a passivating layer on the activated top layer, wherein the passivating layer is not reactive with the exposed portions of the binding layer.

3. The method of claim 2, wherein activating the patterned top layer comprises plasma or chemical treatment.

4. The method of claim 2, wherein the passivating layer is a polymer layer reactive with reactive group on the top layer formed by the activating.

5. The method of claim 1, comprising activating exposed portions of the binding layer to form the plurality of binding sites.

6. The method of claim 5, wherein activating the exposed portions of the binding layer comprises plasma or chemical treatment.

7. The method of claim 1, wherein the top layer has a prescribed thickness, and wherein patterning the top layer forms a plurality of wells in which the respective plurality of binding sites are disposed, wherein walls of the wells are formed by material of the top layer.

8. The method of claim 7, wherein the wells are between 5 angstroms and 300nm in depth.

9. The method of claim 1, wherein depositing or growing a binding layer on the base layer further comprises:

protecting a portion of the binding layer with a sacrificial film;

etching or removing an unprotected portion of the binding layer to form a patterned surface in the binding later; and

removing the sacrificial film to expose the patterned surface in the binding layer, wherein the top layer is deposited on the patterned surface.

10. The method of claim 1, wherein the binding layer comprises silicon, silicon dioxide, silicon nitride, graphene, quarts, gold, silver, metal, platinum, palladium, PDMS, or a polymer film.

11. The method of claim 1, wherein the top layer comprises a metal oxide, graphene, HfO_2, or CO_2.

12. The method of claim 1, wherein the base layer comprises a planar support.

13. The method of claim 1, comprising coupling the substrate to a detection system that detects a shift of the supramolecular structure from the unstable state to the stable state at each binding site of the plurality of binding sites.

14. The method of claim 13, comprising forming, in the base layer, a plurality of light pipes coupled to each respective binding site of the plurality of binding sites, and wherein the detection system comprises a photodiode coupled to each light pipe of the plurality of light pipes.

15. The method of claim 13, comprising coupling each binding site of the plurality of binding sites to one or more electrical leads, and wherein the detection system comprises a field effect transistor.

16. The method of claim 1, wherein providing the supramolecular structure associated with each binding site of the plurality of binding sites comprises associating an individual core structure with an individual binding site of the plurality of binding sites and, subsequent to the associating, linking the capture molecule to the core structure at the first location and linking the detector molecule linked to the core structure at the second location.

17. The method of claim 1, comprising removing the supramolecular structure from each binding site to regenerate the substrate.

18. The method of claim 1, comprising removing only a portion of the supramolecular structure from each binding site to regenerate the substrate.

19. The method of claim 18, wherein providing the supramolecular structure associated with each binding site of the plurality of binding sites comprises associating an individual core structure with an individual binding site of the plurality of binding sites and, subsequent to the associating, linking the capture molecule to the core structure at the first location and linking the detector molecule linked to the core structure at the second location.

20. A substrate for detecting one or more analyte molecules in a sample, the substrate comprising:

a base layer;

a binding layer on the base layer;

a patterned top layer exposing portions of the binding layer, the exposed portions corresponding to a plurality of binding sites on the binding layer; and

a supramolecular structure associated with each binding site of the plurality of binding sites, the supramolecular structure comprising:

a core structure comprising a plurality of core molecules,
a capture molecule linked to the supramolecular core at a first location, and
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 and 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.

21. The substrate of claim 20, comprising a passivating layer disposed on the top layer and not on the binding layer.

22. The substrate of claim 21, wherein the passivating layer is a polymer layer reactive with reactive group on the top layer formed by the activating.

23. The substrate of claim 20, wherein the top layer has a prescribed thickness and forms a plurality of wells in which the respective plurality of binding sites are disposed, wherein walls of the wells are formed by material of the top layer.

24. The substrate of claim 23, wherein the wells are between 5 angstroms and 300nm in depth.

25. The substrate of claim 20, wherein the binding layer comprises silicon, silicon dioxide, silicon nitride, graphene, quarts, gold, silver, metal, platinum, palladium, PDMS, or a polymer film.

26. The substrate of claim 20, wherein the top layer comprises a metal oxide, graphene, HfO_2, or CO_2.

27. The substrate of claim 20, wherein the base layer comprises a silicon wafer.

28. The substrate of claim 20, wherein the substrate is coupled to a detection system that detects a shift of the supramolecular structure from the unstable state to the stable state at each binding site of the plurality of binding sites.

29. The substrate of claim 28, wherein the base layer comprises a plurality of light pipes coupled to each respective binding site of the plurality of binding sites, and wherein the detection system comprises a photodiode coupled to each light pipe of the plurality of light pipes.

30. The substrate of claim 28, wherein each binding site of the plurality of binding sites is coupled to one or more electrical leads, and wherein the detection system comprises a field effect transistor.

31. The substrate of claim 20, 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.