CLAIMS

1. A method of aptamer detection, comprising:

contacting analytes of a sample with a plurality of aptamers under conditions that permit analyte-aptamer complexes to form, wherein different aptamers of the plurality of aptamers have specific affinity for respective different analytes of the analytes; and

detecting the analytes by detecting aptamers of the analyte-aptamer complexes, wherein detecting an individual aptamer of the plurality of aptamers comprises:

contacting the individual aptamer with a mixture of first probes that have specific affinity for the individaul aptamer such that a first complementary region of a first probe of the mixture hybridizes to individual aptamer, wherein the first complementary region of each first probe of the mixture can hybridize to a first region of the individual aptamer, wherein only a subset of the first probes in the mixture are coupled to an affinity tag, and wherein the first probe is in the subset comprising the affinity tag;

contacting the individual aptamer with a second probe to hybridize a second complementary region of the second probe to a second region of the individual aptamer to form a molecular complex comprising the individual aptamer, the first probe, and the second probe, and wherein the second probe comprises a nonhybridizing region extending from the complementary region, the nonhybridizing region comprising an identification sequence uniquely identifying for the individual aptamer, wherein the first complementary region and the second complementary region uniquely hybridize to the individual aptamer;

capturing the molecular complexvia binding of the affinity tag of the first probe to an affinity tag binder; and

detecting the identification sequence of the second probe of the molecular complex.

2. The method of claim 1, wherein the first region and the second region are spaced apart by at least one nucleotide.

3. The method of claim 1 or claim 2, wherein the affinity tag is biotin and the affinity tag capture molecule is avidin or streptavidin.

4. The method of any one of claims 1-3, wherein detecting the identification sequence of the second probe comprises contacting the second probe with primers to generate an amplification product.

5. The method of claim 4, wherein the primers comprise a first primer that binds to a first primer binding region of the nonhybridizing region and a second primer that binds to a complement of a second primer binding region of the nonhybridizing region, wherein the first primer binding region and the second primer binding region flank the identification sequence, optionally wherein the first primer comprises a first sequencing primer and the second primer comprises a second sequencing primer such that the amplification product comprises the first sequencing primer and the second sequencing primer.

6. The method of claim 4, wherein detecting the identification sequence of the second probe comprises sequencing the amplification product.

7. The method of any one of claims 1-6, further comprising generating a notification related to the individual aptamer based on detecting the identification sequence.

8. The method of any one of claism 1-7, further comprising separating the second probe from the first probe and the individual aptamer before detecting the identification sequence.

9. The method of any one of claism 1-8, further comprising ligating an oligonucleotide to an end of the second probe in the molecualr complex using a ligase and extending the ligated oligonucleotide before detecting the identification sequence or

hybridizing a first oligonucleotide and a second oligonucleotide to the second probe in the molecular complex and extending the first oligonucleotide using the second probe as a template to ligate the first oligonucleotide to the second oligonucleotide via extension ligation.

10. The method of claim 9, further comprising separating the ligated first oligonucleotide and second oligonucleotide from the second probe using a second affinity tag coupled to the second oligonucleotide.

11. The method of claim 10, further comprising hybridizing a third oligonucleotide to the ligated first oligonucleotide and second oligonucleotide and extending the ligated first oligonucleotide and second oligonucleotide and the hybridized third oligonucleotide to generate first and second complementary strands comprising 5' and 3' adapters for sequencing.

12. The method of any one of claism 1-11, further comprising cleaving at least a portion of the nonhybridizing region comprising the identification sequence from the second probe before detecting the identification sequence.

13. The method of claim 12, further comprising ligating a cleaved portion of the second probe to an end of an adapter after the cleaving.

14. The method of any one of claism 1-13, further comprising removing uncaptured probes before detecting the identification sequence.

15. The method of claim 14, wherein the uncaptured probes comprise probes in the mixture not in the subset, wherein the probes not in the subset are not coupled to the affinity tag.