

WHAT IS CLAIMED IS:

1. A method of selecting an aptamer from a plurality of aptamer candidates, the method comprising:
coupling a target within each well of a plurality of wells that is disposed within a
5 substrate;
contacting each of the wells with a fluid comprising a plurality of aptamer candidates;
within at least one of the wells, coupling to the target any aptamer candidate that is
selective for the target;
removing any aptamer candidates that are not coupled to the target; and
10 sequencing, within the wells, any aptamer candidates that remain after the removing to
identify any aptamers that are selective for the target.
2. The method of claim 1, wherein coupling the target within each well of the plurality of
wells comprises:
15 coupling a first moiety within each of the wells;
coupling a plurality of second moieties to respective ones of the target; and
coupling the second moiety to the first moiety within each of the wells.
3. The method of claim 2, wherein the first moiety comprises streptavidin and the second
20 moiety comprises biotin.
4. The method of claim 2 or claim 3, wherein the first moiety is coupled within each of
the wells by a capture primer.
- 25 5. The method of claim 4, comprising detaching the first moiety from the capture primer
before performing the sequencing.
6. The method of any one of claims 1 to 5, wherein the substrate comprises detection
circuitry used to sequence the aptamer candidates that remain after the removing.
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7. The method of any one of claims 1 to 6, wherein the plurality of wells comprise flow
cells through which the fluid is flowed in parallel.

8. The method of any one of claims 1 to 7, wherein any aptamer candidate that is selective for the target has a tertiary structure that changes when becoming coupled to the target.
9. The method of any one of claims 1 to 8, further comprising generating amplicons of
5 any aptamer candidate that is selective for the target.
10. The method of claim 9, wherein generating amplicons of any aptamer candidate that is selective for the target comprises:
decoupling that aptamer candidate from the target; and
10 using polymerase chain reaction (PCR) to generate the amplicons using that aptamer candidate.
11. The method of claim 10, wherein the PCR is performed in an amplification chamber that is distinct from the wells.
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12. The method of any one of claims 9 to 11, further comprising:
contacting each of the wells with a fluid comprising the amplicons;
within each of the wells, coupling to the target any amplicon that is selective for the target; and
20 removing any amplicons are not coupled to the target.
13. The method of claim 12, wherein any aptamer candidates that are sequenced comprise any amplicons that remain after removing any amplicons that are not coupled to the target.
- 25 14. The method of claim 12 or claim 13, further comprising generating additional amplicons of any amplicon that is selective for the target.
15. The method of any one of claims 1 to 14, wherein sequencing any aptamer candidates comprises:
30 coupling, to capture primers disposed within the wells, any aptamer candidates that remain after the removing;
performing amplification within the wells to generate amplicons coupled to the capture primers; and
sequencing the amplicons coupled to the capture primers.

16. The method of claim 15, wherein the target is coupled within the wells via respective ones of the capture primers.

5 17. The method of claim 16, wherein the capture primers couple a first moiety within the wells, and a second moiety is coupled to the first moiety and to the target within the wells.

18. The method of claim 15, wherein the capture primers are coupled to the well separately from the target.

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19. The method of any one of claims 15 to 18, wherein each of the aptamer candidates comprises first and second adapters that are complementary to respective capture primers.

20. The method of claim 19, wherein each of the aptamer candidates further comprises a first spacer disposed between the first adapter and a region that is a candidate to be selective for the target, and a second spacer disposed between the second adapter and the region that is a candidate to be selective for the target.

21. The method of any one of claims 1 to 20, wherein each of the aptamer candidates comprises an oligonucleotide.

22. A system for selecting an aptamer from a plurality of aptamer candidates, the system comprising:

25 a substrate comprising a plurality of wells;
a target coupled within each of the wells;
a fluid comprising a plurality of aptamer candidates and contacting each of the wells, wherein any aptamer candidate that is selective for the target becomes coupled to the target; and

30 detection circuitry to sequence any aptamer candidates within the wells to identify any aptamers that are selective for the target.

23. The system of claim 22, wherein:

a first moiety is coupled within each of the wells;
a plurality of second moieties are coupled to respective ones of the target; and

the second moiety is coupled to the first moiety within each of the wells to couple the target within each of the wells.

24. The system of claim 23, wherein the first moiety comprises streptavidin and the second moiety comprises biotin.

25. The system of claim 23 or claim 24, wherein the first moiety is coupled within each of the wells by a capture primer.

26. The system of claim 25, wherein the first moiety is detachable from the capture primer.

27. The system of any one of claims 22 to 26, wherein the plurality of wells are disposed on the detection circuitry.

28. The system of any one of claims 22 to 27, wherein the plurality of wells comprise flow cells through which the fluid is flowed in parallel.

29. The system of any one of claims 22 to 28, wherein any aptamer candidate that is selective for the target has a tertiary structure that changes when becoming coupled to the target.

30. The system of any one of claims 22 to 29, wherein amplicons are generated of any aptamer candidate that is selective for the target.

31. The system of claim 30, wherein the amplicons of any aptamer candidate that is selective for the target are generated using steps comprising:

decoupling that aptamer candidate from the target; and

using polymerase chain reaction (PCR) to generate the amplicons using that aptamer candidate.

32. The system of claim 31, comprising an amplification chamber that is distinct from the wells to perform the PCR.

33. The system of any one of claims 30 to 32, further comprising:

a fluid comprising the amplicons and contacting each of the wells, wherein any amplicon that is selective for the target becomes coupled to the target.

34. The system of claim 33, wherein any aptamer candidates that are sequenced comprise
5 any amplicons that remain after removing any amplicons that are not coupled to the target.

35. The system of claim 34, further comprising additional amplicons of any amplicon that is selective for the target.

10 36. The system of any one of claims 22 to 35, further comprising:
capture primers disposed within the wells and coupled to any aptamer candidates that remain after the removing; and
amplicons of the aptamer candidates that are coupled to the capture primers,
wherein the detection circuitry is to sequence the amplicons coupled to the capture
15 primers.

37. The system of claim 36, wherein the target is coupled within the wells via respective ones of the capture primers.

20 38. The system of claim 37, wherein the capture primers couple a first moiety within the wells, and a second moiety is coupled to the first moiety and to the target within the wells.

39. The system of claim 36, wherein the capture primers are coupled to the well separately from the target.

25 40. The system of claim 36, wherein each of the aptamer candidates comprises first and second adapters that are complementary to respective capture primers.

41. The system of claim 40, wherein each of the aptamer candidates further comprises a
30 first spacer disposed between the first adapter and a region that is a candidate to be selective for the target, and a second spacer disposed between the second adapter and the region that is a candidate to be selective for the target.

42. The system of any one of claims 22 to 41, wherein each of the aptamer candidates comprises an oligonucleotide.