

WHAT IS CLAIMED IS:

1. A composition for capturing target polynucleotides at a surface of a substrate, the composition comprising:
 - a plurality of capture primers coupled to the surface of the substrate, each capture primer comprising modified nucleic acids; and
 - a plurality of orthogonal capture primers coupled to the surface of the substrate, each orthogonal capture primer comprising modified nucleic acids.
2. The composition of claim 1, wherein the modified nucleic acids of the capture primers comprise locked nucleic acid (LNA), peptide nucleic acid (PNA), or super T.
3. The composition of claim 1 or claim 2, wherein the capture primers further comprise deoxyribonucleic acid (DNA).
4. The composition of claim 3, wherein the modified nucleic acids and the DNA are distributed between a 5' end and a 3' end of the capture primers.
5. The composition of claim 3, wherein the modified nucleic acids are disposed at a 5' end of the capture primers and the DNA is disposed at a 3' end of the capture primers.
6. The composition of any one of claims 1 to 5, wherein the modified nucleic acids of the orthogonal capture primers comprise locked nucleic acid (LNA), peptide nucleic acid (PNA), or super T.
7. The composition of claim 6, wherein the orthogonal capture primers further comprise deoxyribonucleic acid (DNA).
8. The composition of claim 7, wherein the modified nucleic acids and the DNA are distributed between a 5' end and a 3' end of the capture primers.
9. The composition of claim 7, wherein the modified nucleic acids are disposed at a 5' end of the orthogonal capture primers and the DNA is disposed at a 3' end of the orthogonal capture primers.

10. The composition of any one of claims 1 to 9, further comprising:
first target polynucleotides each comprising a first adapter that is complementary to the capture primers, and a second adapter that is complementary to the orthogonal capture primers; and
second target polynucleotides that are complementary to respective ones of the first target polynucleotides.
11. The composition of claim 10, wherein the first adapters of some of the first target polynucleotides are hybridized to respective ones of the capture primers to form first duplexes, and wherein the second adapters of some of the first target polynucleotides are hybridized to respective ones of the orthogonal capture primers to form second duplexes.
12. The composition of claim 11, wherein the first and second duplexes each have a melting temperature (T_m) that is greater than a T_m of third duplexes that would be formed by hybridization of the second target polynucleotides to the respective ones of the first target polynucleotides to which the second target polynucleotides are complementary.
13. The composition of claim 11 or claim 12, wherein the first and second duplexes each have a melting temperature (T_m) that is between about 80°C and about 110°C.
14. The composition of any one of claims 11 to 13, wherein the first and second duplexes each have a melting temperature (T_m) that is between about 85°C and about 105°C.
15. The composition of any one of claims 11 to 14, wherein the first and second duplexes each have a melting temperature (T_m) that is between about 90°C and about 100°C.
16. The composition of any one of claims 11 to 15, wherein substantially none of the second target polynucleotides are hybridized in solution to any of the first target polynucleotides.
17. The composition of any one of claims 11 to 16, further comprising about 1% to about 1000% formamide (%v/v).

18. The composition of any one of claims 11 to 17, further comprising about 5% to about 80% formamide (%v/v).
19. The composition of any one of claims 11 to 18, further comprising about 100 to about 800 mM Na⁺.
20. The composition of any one of claims 11 to 19, further comprising about 200 to about 800 mM Na⁺.
21. The composition of any one of claims 1 to 20, wherein the capture primers are modified P5 capture primers, and wherein the orthogonal capture primers are modified P7 capture primers.
22. The composition of any one of claims 1 to 21, wherein each of the capture primers includes between about five and about twenty of the modified nucleic acids, and wherein each of the orthogonal capture primers includes between about five and about twenty of the modified nucleic acids.
23. The composition of any one of claims 1 to 22, wherein each of the capture primers includes at least about nine of the modified nucleic acids, and wherein each of the orthogonal capture primers includes at least about nine of the modified nucleic acids.
24. The composition of any one of claims 1 to 23, wherein each of the capture primers includes at least about twelve of the modified nucleic acids, and wherein each of the orthogonal capture primers includes at least about twelve of the modified nucleic acids.
25. The composition of any one of claims 1 to 24, wherein each of the capture primers includes at least about fifteen of the modified nucleic acids, and wherein each of the orthogonal capture primers includes at least about fifteen of the modified nucleic acids.

26. A method for capturing and amplifying target polynucleotides at a surface of a substrate, the method comprising:
- contacting a composition with a fluid, wherein the composition comprises:
 - a plurality of capture primers coupled to the surface of the substrate, each capture primer comprising modified nucleic acids; and
 - a plurality of orthogonal capture primers coupled to the surface of the substrate, each orthogonal capture primer comprising modified nucleic acids; and
 - wherein the fluid comprises:
 - first target polynucleotides, each comprising a first adapter that is complementary to the capture primers and a second adapter that is complementary to the orthogonal capture primers; and
 - second target polynucleotides that are complementary to respective ones of the first target polynucleotides;
 - while inhibiting hybridization of the second target polynucleotides to the first target polynucleotides in the fluid:
 - hybridizing the first adapters of some of the first target polynucleotides to respective ones of the capture primers to form first duplexes;
 - hybridizing the second adapters of some of the first target polynucleotides to respective ones of the orthogonal capture primers to form second duplexes; and then
 - amplifying the first target polynucleotides, the amplifying comprising generating respective amplicons of the first target polynucleotides.
27. The method of claim 26, wherein the modified nucleic acids of the capture primers comprise locked nucleic acid (LNA), peptide nucleic acid (PNA), or super T.
28. The method of claim 26 or claim 27, wherein the capture primers further comprise deoxyribonucleic acid (DNA).
29. The method of claim 28, wherein the modified nucleic acids and the DNA are distributed between a 5' end and a 3' end of the capture primers.
30. The method of claim 28, wherein the modified nucleic acids are disposed at a 5' end of the capture primers and the DNA is disposed at a 3' end of the capture primers.

31. The method of any one of claims 26 to 30, wherein the modified nucleic acids of the orthogonal capture primers comprise locked nucleic acid (LNA), peptide nucleic acid (PNA), or super T.
32. The method of claim 31, wherein the orthogonal capture primers further comprise deoxyribonucleic acid (DNA).
33. The method of claim 32, wherein the modified nucleic acids and the DNA are distributed between a 5' end and a 3' end of the capture primers.
34. The method of claim 32, wherein the modified nucleic acids are disposed at a 5' end of the orthogonal capture primers and the DNA is disposed at a 3' end of the orthogonal capture primers.
35. The method of any one of claims 26 to 34, wherein the first and second duplexes each have a melting temperature (T_m) that is greater than a T_m of third duplexes that would be formed by hybridization of the second target polynucleotides to the respective ones of the first target polynucleotides to which the second target polynucleotides are complementary.
36. The method of any one of claims 26 to 35, wherein the first and second duplexes each have a melting temperature (T_m) that is between about 80°C and about 110°C.
37. The method of any one of claims 26 to 36, wherein the first and second duplexes each have a melting temperature (T_m) that is between about 85°C and about 105°C.
38. The method of any one of claims 26 to 37, wherein the first and second duplexes each have a melting temperature (T_m) that is between about 90°C and about 100°C.
39. The method of any one of claims 26 to 38, wherein substantially none of the second target polynucleotides are hybridized in solution to any of the first target polynucleotides.
40. The method of any one of claims 26 to 39, wherein the hybridizing is performed in about 1% to about 100% formamide (%v/v).

41. The method of any one of claims 26 to 40, wherein the hybridizing is performed in about 5% to about 80% formamide (%v/v).
42. The method of any one of claims 26 to 41, wherein the hybridizing is performed in about 100 to about 800 mM Na⁺.
43. The method of any one of claims 26 to 42, wherein the hybridizing is performed in about 200 to about 800 mM Na⁺.
44. The method of any one of claims 26 to 43, wherein the capture primers are modified P5 capture primers, and wherein the orthogonal capture primers are modified P7 capture primers.
45. The method of any one of claims 26 to 44, wherein each of the capture primers includes between about five and about twenty of the modified nucleic acids, and wherein each of the orthogonal capture primers includes between about five and about twenty of the modified nucleic acids.
46. The method of any one of claims 26 to 45, wherein each of the capture primers includes at least about nine of the modified nucleic acids, and wherein each of the orthogonal capture primers includes at least about nine of the modified nucleic acids.
47. The method of any one of claims 26 to 46, wherein each of the capture primers includes at least about twelve of the modified nucleic acids, and wherein each of the orthogonal capture primers includes at least about twelve of the modified nucleic acids.
48. The method of any one of claims 26 to 47, wherein each of the capture primers includes at least about fifteen of the modified nucleic acids, and wherein each of the orthogonal capture primers includes at least about fifteen of the modified nucleic acids.